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Letter to the Editor

Insomnia and risk of cardiovascular disease: A meta-analysis of cohort studies

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Insomnia, the most prevalent sleep disorder, defined as a subjective feeling of having difficulty initiating or maintaining sleep or having a feeling of non-restorative sleep [1]. According to the definition, insomnia prevalence varies from 6% to an average of 33% in more than 50 epidemiological studies [2]. In addition, insomnia affects 10% to 30% of the general population in the United States [3], it has been estimated that the annual expenditure on insomnia is estimated at 92.5 to 107.5 billion [4], this creates a major public health burden. From the public health perspective, the issue of sleep problems is important.

During the last years, insomnia was of particular concern because it could increase the risk of depression [5], hypertension [6], and metabolic syndrome [7]. Meanwhile, a considerable number of cohort studies showed a significant association between insomnia and cardiovascular diseases (CVDs) [8–13]. Nevertheless, whether insomnia independently increases myocardial infarction (MI) risks, stroke risks, and coronary heart disease (CHD) risks specifically, or whether insomnia independently increases CVD mortality, results to date have been inconsistent. Meta-analysis might help to resolve this inconsistency. A recent published meta-analysis of 13 prospective studies showed that insomnia was associated with an increased risk of fatal and/or non-fatal from CVD (pooled relative risk = 1.45, 95% confidence interval: 1.29–1.62) [14]. However, that meta-analysis found insufficient evidence on the association between insomnia and risk of individual types of CVD, including MI, stroke, CHD, and cardiovascular mortality. Moreover, the data from studies included by previous meta-analysis were limited to December 2011. To our knowledge, some new cohort studies on the association between insomnia and risk of CVD have been published since than [8–13]. Therefore, we carried out a meta-analysis of cohort studies to quantitatively estimate whether insomnia independently increases the risk of CVD, using the most recent data.

This meta-analysis was performed and reported according to the standard criteria of the Meta-analyses of Observational Studies in Epidemiology (MOOSE) conference statement [15]. A systematic search of published articles (through 17 May 2014) was performed by using electronic databases including PubMed, Cochrane Library, and ISI Web of Science databases. We used the following keywords: insomnia, sleep*,

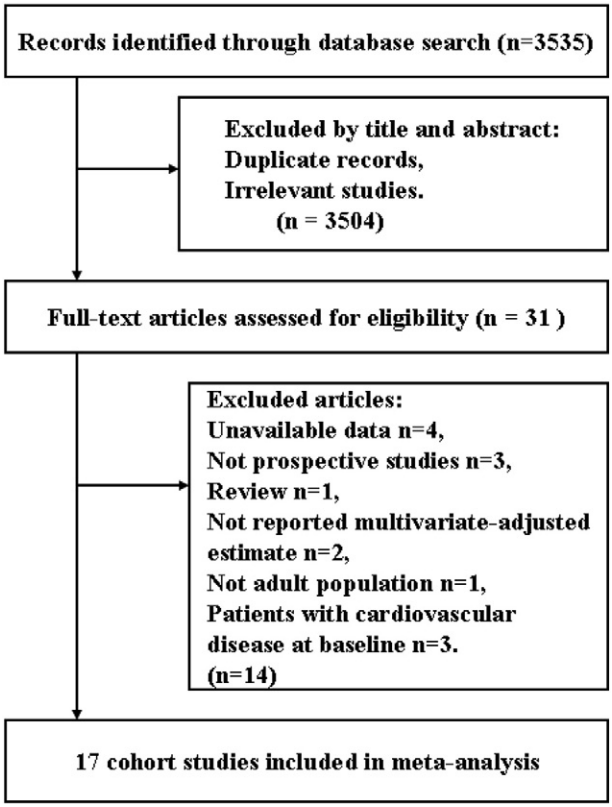

Fig. 1. Flow chart of study selection.

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Table 1
Characteristic of included cohort studies.

Author	Publication, (year)	Country	Cohort	Sex	Sample size (n)	Outcome(s)	Follow-up. (year)	Age, (year)	Outcome assessment	Insomnia assessment	Exposure categories	Adjusted variables
Eaker et al [17]	1992	USA	Framingham Study	F	749	MI, CVD mortality	20	45–64	Clinical manifestations and hospital records	TFA	Yes/No	Age, SBP, TC/HDL, diabetes, cigarettes, BMI
Schwartz et al [18]	1998	USA	Piedmont Health Survey	F M	2960	MI	3	65–101	ICD-9	TFA	Most of the time/Never	Age, sex, race, education, prescriptions, self-rated health, depression
Mallon et al [19]	2002	Sweden	County of Dalarna registry	F M	1870	CVD mortality	12	45–65	ICD-9	DIS	Yes/No	Age, not married, living alone, smoking habit, BMI > 28, HT, cardiac disease, respiratory disease, diabetes, joint pain, GID, depression, sleep duration, snoring, sleeping pill usage
Elwood et al [20]	2006	UK	Caerphilly cohort study	M	1874	CHD, Stroke	5	55–69	ICD-10	Insomnia	Frequent/None	Age, social class, smoking habit, alcohol consumption, BMI, neck circumference
Phillips et al [21]	2007	USA	ARIC study	F M	11,863	CHD	6.3	44–64	Hospital records and standardized diagnoses	TFA/sleep continuity disturbance/non-restorative sleep	Yes/No	Age, sex, race, education, BMI, depression, lung function, smoking habit, diabetes
Meisinger et al [22]	2007	Germany	MONICA/KORA	F M	6896	MI	10.1	45–75	ICD-9, ESC and ACC criteria	DIS/TFA	Yes/No	Age, survey, BMI, education, dyslipidemia, alcohol intake, parental history of MI, physical activity, smoking habit, HT, diabetes
Suzuki et al [23]	2009	Japan	Shizuoka study	F M	11,395	CVD mortality	5.3	65–85	ICD-10	DFA	Yes/No	Age, sex, BMI, smoking habit, alcohol, physical activity, socioeconomic status, mental health, HT, diabetes
Chien et al [24]	2010	China	Chin-Shan community study	F M	3430	CVD mortality	15.9	>35	Official death certificates and house-house visits	Frequency of insomnia	Nearly every day/No	Age, sex, BMI, smoking habit, alcohol, marital status, education, occupation, exercise, family history of CHD, HT, diabetes, lipids, glucose, uric acid
Chandola et al [25]	2010	UK	Whitehall II	F M	10,308	MI, CVD mortality	15	35–55	ICD-10	Restless, disturbed nights	More than usual/No	Age, sex, ethnicity, employment grade, car access, housing tenure, self-rated health status, cholesterol, HT, BMI, diabetes, smoking habit, alcohol, exercise, fruit and vegetable consumption
Hulvej Rod et al [26]	2011	France	GAZEL cohort study	M	12,524	CVD mortality	19	36–52	ICD-9, ICD-10	DFA	Yes/No	Age, socioeconomic status, marital status, smoking habit, alcohol, BMI, night work, HT, diabetes
Laugsand et al [27]	2011	Norway	Nord-Trondelag Health Study	F M	52,610	MI	11.4	≥65	ESC and ACC criteria	DIS	Almost every night/Never	Age, sex, education, marital status, shift work, SBP, cholesterol, diabetes, BMI, physical activity, smoking habit, depression, anxiety
Westerlund et al [8]	2013	Sweden	Nation March Cohort study	F M	41,192	CVD mortality	13.2	52.8	ICD-9, ICD-10	DFA	Mostly/always/ Never	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, HT
Sands-Lincoln et al [9]	2013	USA	Women's Health Initiative	F	86,329	CHD, CVD mortality	10.3	50–79	medical records, death certificates	WHIIRS	WHIIRS ≥ 9/<3	Age, race, education, income, smoking, BMI, physical activity, alcohol intake, depression, diabetes, high blood pressure, hyperlipidemia, comorbid conditions
Hulvej Rod et al [10]	2014	France	Whitehall II	F M	9098	CVD mortality	22	35–55	ICD-9, ICD-10	Restless, disturbed nights	More than usual/Not at all	Age, employments grade, ethnicity, marital status
Canivet et al [11]	2014	Sweden	Malmo Diet and Cancer study	F M	13,277	CVD mortality	13	45–64	ICD-9, ICD-10	DSM-IV	Yes/No	Age,socieconomic position, marital status, social participation, smoking status, low physical activity, obesity, HT, diabetes mellitus, neck, shoulder, lumbar pain
Li et al [12]	2014	USA	Health Professionals Follow-Up study	M	23,447	CVD mortality	6	68.6	ICD-8	DFA	Most of the time/Never	Age, ethnicity, smoking status, alcohol drinking, BMI, physical activity, alternate healthy eating index, marriage status, living status, regular use of aspirin,
Wu et al [13]	2014	China	NHIRD	F M	21,438	Stroke	4	52	ICD-9	ICD-9	Yes/No	Age, sex, comorbidities, socioeconomic status, geographic region

TFA: trouble falling asleep; DFA: difficulty initiating sleep; DIS: difficulty initiating sleep; ICD: International Classification of Diseases; CVD: cardiovascular disease; CHD: coronary heart disease; MI: myocardial infarction; F: female; M: male; and WHIIRS: The Women's Health Initiative Insomnia Rating Scale; NHIRD.
National Health Insurance Research Database; BMI: body mass index; SBP: systolic blood pressure; HT: hypertension; TC: total cholesterol; HDL: high density lipoprotein; GID: gastrointestinal disease. ESC: the European Society of Cardiology; and ACC: American College of Cardiology.