

Sex Differences in Insomnia: A Meta-Analysis

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Study Objective: Most but not all epidemiologic evidence suggests a female predisposition of insomnia. We applied meta-analytic methods to investigate sex differences in the risk of insomnia among the published epidemiologic studies.

Design: Meta-analysis with Comprehensive Meta-Analysis (Englewood, NJ); 9 different analyses were performed to investigate the sex difference of insomnia among different conditions.

Setting: A comprehensive search of the medical literature databases was performed to identify epidemiologic studies of insomnia. A rolling snowball method was also used.

Participants: General population.

Interventions: N/A.

Result: Thirty-one related papers were found, but 2 studies only reported the subtype prevalence of insomnia. All other studies (1,265,015 participants, female/male: 718,828/546,187) were included in the overall analysis of insomnia. A risk ratio of 1.41 [95% confidence interval: 1.28-1.55] for female versus male was found. The female excess in the risk of insomnia in large and quality studies was much higher than that of small and nonquality studies. The trend of female predisposition was consistent and progressive across age, with more significance in the elderly. The use of various criteria and frequency and duration of insomnia did not influence the predisposition of female in the risk of developing insomnia. Although obvious female excess in the risk of insomnia exists among different regions, there was a relatively lower female excess in East Asia.

Conclusion: This meta-analysis confirmed a female predisposition of insomnia. Further studies will be needed to examine the roles of different factors in leading to the sex difference of insomnia.

Keywords: Meta-analysis, sex differences, insomnia

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INTRODUCTION

INSOMNIA IS THE MOST COMMON SLEEP COMPLAINT AND DISORDER WITH SIGNIFICANT MORBIDITIES.¹⁻³ A LARGE BODY OF EVIDENCE SUGGESTED THAT women complain more frequently of insomnia than do men.⁴⁻³⁹ A sex difference in the risk of insomnia might shed light on the etiology, pathogenesis, healthcare utilization, as well as the treatment and prognosis of the disorder. In order to investigate sex differences in the risk of insomnia, we applied meta-analytic methods to integrate results from the published literature of the epidemiologic studies.⁴⁻³⁴ Most of these studies were conducted across different settings, criteria, and samplings.⁴⁻³⁹ Although meta-analysis could not correct the original limitations of the published studies, it could help to establish whether sex differences found in previous studies were due to biases such as heterogeneity between the results from larger, higher-quality studies and those of smaller and lower-quality studies. In addition, further subgroup analysis will be conducted to examine whether the sex effect is universal or modified by other factors such as age and ethnicity.

METHODS

Literature Search

Using the terms insomnia, sleeplessness, quality of sleep, sleep complaint, sleep problem, sleep disturbance, or sleep disorder and epidemiology, prevalence, or survey, we performed a comprehensive search of MEDLINE (1966 through April 2004), PubMed (1980 through April 2004), EMBASE (1980 through April 2004), PsycINFO (1872 through April 2004), and CINAHL (1960 through April 2004) databases to identify epidemiologic studies of insomnia. Our search identified more than 4000 reports, all of which were checked for relevance by examining the titles, abstracts, and full-text papers. A rolling snowball method was also used, in which reference lists from identified articles were reviewed. Conference proceedings and unpublished data were excluded.⁴⁰ Qualified studies had to fulfill the following criteria: inclusion criteria were epidemiologic study of the general population, reporting of sex-specific prevalence figures; provision or use of a denominator in computing prevalence; a minimum study population of 500 people, and publication in English; exclusion criteria included studies only conducted in children and adolescents (aged < 15 years), studies on primary care or hospitalized patients, and studies mainly in people with depression, anxiety, schizophrenia, personality disorders, or substance abuse. Using these criteria, all relevant studies were screened. The investigators were not blinded to the source and authors of the reports. Finally, 36 studies⁴⁻³⁹ met all of the criteria. Altogether 5 identified studies³⁵⁻³⁹ were excluded for their overlapping data with a large-scale integrated report.²⁶ Among 31 remaining papers, 2 studies only revealed the prevalence of subtypes of insomnia: difficulty in initiating sleep, difficulty in maintaining sleep, early morning awakening, and nonrefreshing sleep.^{33,34}

Disclosure Statement

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Meta-Analysis Procedure

All meta-analyses were analyzed using Comprehensive Meta Analysis (CMA), a software package developed by Biostat (Englewood, NJ). In medical research, the estimation of both risk ratio (RR) and odds ratio (OR) has been widely used. However, if the outcome event occurred commonly, the OR would tend to overestimate RR. As a result, RR, not OR, was used in this research.⁴¹⁻⁴⁵

Identifying and properly accounting for heterogeneity between studies was a critical step in the meta-analysis process. Heterogeneity in epidemiology stems from differences in study design, disease definition, exposure assessment, and demographic variability in study populations.⁴⁶⁻⁴⁸ In this study, the Q statistics (provided by CMA) were used to test the homogeneity of the specific set of effect sizes and the significance of moderators. A significant Q statistic indicated heterogeneity of the individual study-effect sizes. Generally, researchers preferred to use fixed-effects models in homogeneity and random-effects models in heterogeneity.⁴⁶⁻⁴⁸ Q_w was tested to determine whether studies within an analysis could be considered to share a common population effect size; Q_b (a between-category homogeneity statistic) was tested to determine whether such groups differed significantly in their mean-effect sizes.⁴⁶ Because significant heterogeneity (various study design and definition of insomnia) existed across most of the recruited epidemiologic studies, a random-effects model was predominantly used in the meta-analysis. The weight of each study was calculated by the DerSimonian and Laird method (a method to compute weights for random effects).⁴⁹

Nine different analyses were carried out to investigate the sex difference in the risk of insomnia among different conditions.

Analysis 1

Except 2 studies that did not report the prevalence of general insomnia,^{33,34} all of the other 29 studies were included.⁴⁻³²

Analysis 2

To prevent studies with large samples from dominating the result,⁵⁰ large studies (≥ 5000 people)^{5,8-10,13,14,19-21,25} and small studies (< 5000 people)^{4,6,7,11,12,15-18,22-24,26-32} were analyzed separately.

Analysis 3

To investigate the genuine sex difference in the risk of insomnia, we paid more attention to quality studies.^{5,10,20,25} To be considered to be quality studies, they must have met the following criteria: (1) large study (≥ 5000 people), (2) semistructured or structured diagnostic interviews, and (3) based on stringent operational criteria such as Diagnostic and Statistical Manual of Mental Disorders (DSM)⁵¹⁻⁵³ or International Classification of Sleep Disorder-Diagnostic and Coding Manual (ICSD).⁵⁴

Analysis 4

Different studies have employed various questionnaires and criteria in defining insomnia. In order to investigate the frequency effect on the sex difference in the risk of insomnia, we divided 29 studies into 3 groups: any frequency (studies that did not define the frequency of insomnia well or included a wide range of different frequency and severity criteria),^{4,7,12-14,18,19,29-32} frequent or always

(those studies reporting the presence of frequent, often, or always insomnia or a criteria of insomnia ≥ 3 times per week),^{8,9,15-17,21-23,27} and severe (being based on stringent criteria such as the DSM-IV criteria with daytime consequences).^{5,6,10,11,20,24-26,28}

Analysis 5

While some studies reported the current prevalence (recent 1 week to 6 months), some studies measured the long-term prevalence of insomnia (recent 1 year and lifetime). Thus, 29 studies were divided into 2 groups: current insomnia studies^{4,8-13,15-22,24-31} and long-term insomnia studies.^{5-7,14,23,32}

Analysis 6

To explore possible time trend, studies that were conducted before 1990^{4,6,8-10,13-16,18,19,22,23,29,31} and after 1990^{5,7,11,12,17,20,21,24-28,30,32} were analyzed separately.

Analysis 7

Eight studies^{8,14,16,20,21,26,29,31} provided detailed reports of the sex-related prevalence rates of insomnia across different age categories. In addition, there were 4 studies of elderly populations (≥ 65 years),^{7,9,12,22} 1 study of a middle-aged population (31-64 years),¹³ and 1 study of young adults (15-30 years).⁶ The sex difference of insomnia among an elderly population,^{7-9,12,14,16,20-22,26,29,31} a middle-aged population,^{8,13,14,16,20,21,26,29,31} and young adults^{6,8,14,16,20,21,26,29,31} were analyzed accordingly.

Analysis 8

Studies in America,^{4-6,9,10,16,18,19,23,26,30} Europe,^{8,11,13-15,20,22,25,28,39,31} East Asia,^{7,17,21,24,32} and Australia^{12,27} were analyzed separately.

Analysis 9

Some studies explored subtypes of insomnia: difficulty in initiating sleep,^{4,21,24,25,28,33,34} difficulty in maintaining sleep,^{4,21,24,25,28,33,34} early morning awakening,^{4,21,24,25,28,33,34} and nonrefreshing sleep.^{21,24,25,28,34} These subtypes were analyzed separately.

RESULTS

According to our criteria, 31 studies were recruited in our meta-analysis. The characteristics of these individual studies⁴⁻³⁴ are reported in Table 1. The results of the meta-analysis are summarized in Table 2.

In analysis 1, 29 studies (1,265,015 participants, female/male: 718,828/546,187) were involved.⁴⁻³² A random-effects model was adopted in this meta-analysis, as there was significant heterogeneity among these studies ($Q_w=862.69$, $p < .01$). An overall RR of 1.41 (95% confidence interval [CI], 1.28-1.55) was yielded. A sex difference was not found in 3 individual studies^{13,17,27} (Table 1). The analysis 1 was also reported by the Forest plot (Figure 1). This plot showed the RR of each study with its associated 95% CI. An RR of 1 indicates no difference between women and men in the prevalence of insomnia.

Analysis 2 compared 10 large studies (sample size ≥ 5000)^{5,8-10,13,14,19-21,25} and 19 relatively smaller studies (sample size < 5000).^{4,6,7,11,12,15-18,22-24,26-32} Both of them showed a female preponderance in the risk of insomnia, but the sex difference in large

Table 1—Characteristics of Studies in the Meta-Analysis

Author (ref) Published year	Site	Sample size (Female/Male)	Instrument	Age (Years)	Insomnia duration (1/2*)	Insomnia frequency (1/2/3#)	Insomnia% (Female/Male)	Risk ratio (Female/Male, 95% CI)
Bixler et al (4) 1979	United States	1,006 (563/443)	Subjective response to questions about sleep complaints Several sleep questions	≥ 18	Current (1)	Any frequency (1)	34.8/28.8	1.22 (1.002-1.45)
Bixler et al (5) 2002	United States	16,583 (12,219/4,364)	Phase I: telephone interview Phase II: one-night PSG	20-100	Recent 1 year (2)	Severe (3)	9.0/5.9	1.53 (1.34-1.74)
Breslau et al (6) 1996	United States	1,007 (619/388)	Subjective response to questions about sleep complaints (NIMH) DSM-III-R	21-30	Lifetime (2)	Severe (3)	26.7/21.4	1.28 (1.01-1.61)
Chiu HF et al (7) 1999	Hong Kong	1,034 (530/504)	Subjective response to questions about sleep complaints Self-developed questionnaire	≥ 70	Recent 1 year (2)	Any frequency(1)	44.5/29.6	1.51 (1.28-1.78)
Cirignotta et al (8) 1985	Italy	5,713 (2,855/2,858)	Subjective response to questions about sleep complaints Self-developed questionnaire	3-99	Current (1)	Frequent (2)	16.4/9.6	1.71 (1.49-1.97)
Foley et al (9) 1995	United States	9,282 (5,682/3,600)	Subjective response to questions about sleep complaints Five common sleep complaints from the Established Populations for Epidemiologic Studies of the Elderly (EPESE)	≥ 65	Current Unspecified (1)	Frequent (2)	31.2/20.9	1.49 (1.39-1.61)
Ford and Kamerow (10) 1989	United States	7,954 (4,755/3,199)	Interview by trained lay interviewers DSM-III	19-65+	Recent 6 months (1)	Severe (3)	12.1/7.9	1.53 (1.33-1.76)
Hajak et al (11) 2001	Germany	1,913 (1,016/897)	Face-to-face interview An algorithm compatible with the principal criteria for severe insomnia defined in DSM-IV	≥ 18	Recent 1 month (1)	Severe (3)	5.0/3.0	1.67 (1.06-2.64)
Henderson et al (12) 1995	Australia	933 (466/467)	Subjective response to questions about sleep complaints Self-developed questionnaire	≥ 70	Recent 2 week (1)	Any frequency (Yes/no) (1)	18.0/12.6	1.43 (1.05-1.94)
Hublin et al (13) 1996	Finland	11,354 (6,136/5,218)	Subjective response to questions about sleep complaints Self-developed questionnaire Twin-cohort study	33-60	Current (1)	≥1/week (1)	18.4/18.1	1.04 (0.96-1.12)
Husby and Lingjaerde (14) 1990	Norway	12,432 (6,122/6,310)	Subjective response to questions about sleep complaints Self-developed questionnaire	20-54	Recent 1 year (2)	Any frequency (1)	41.7/29.9	1.41 (1.35-1.49)
Hyypä et al (15) 1997	Finland	1,405 (722/683)	Subjective response to questions about sleep complaints Self-developed questionnaire	28-75	Current Unspecified (1)	Often and always (2)	41.0/37.0	1.11 (1.01-1.21)
Karacan et al (16) 1976	United States	1,645 (845/800)	Subjective response to questions about sleep complaints Six individual items concerning sleep problem in a health survey	19-70+	Current (1)	Often or all the time (2)	15.4/10.9	1.42 (1.10-1.82)
Kim et al (17) 2000	Japan	3,030 (1,548/ 1,482)	Interviewed in their home with Self-developed questionnaire by well-trained interviewers	20-70	Recent 1 month (1)	Often and always (2)	20.5/22.3	0.92 (0.80-1.05)

Table 1—Continued

Author (ref) Published year	Site	Sample size (Female/Male)	Instrument	Age (Years)	Insomnia duration (1/2*)	Insomnia frequency (1/2/3#)	Insomnia% (Female/Male)	Risk ratio (Female/Male, 95% CI)
Klink and Quan (18) 1987	United States	2,187 (1,242/945)	Subjective response to questions about sleep complaints Self-developed questionnaire	49.1±19.7 (including 65+)	Current (1)	Any frequency (1)	42.1/32.1	1.31 (1.17-1.47)
Kripke et al (19) 2002	United States	1,116,936 (636,095/ 480,841)	Subjective response to questions about sleep complaints Health questionnaire	30-103	Current (1)	≥ 1/week (1)	16.6/8.5	1.95 (1.93-1.97)
Leger et al (20) 2000	France	12,778 (6,772/ 6,006)	Subjective response to questions about sleep complaints DSM-IV	18-65+	Recent 1 month (1)	Severe (3)	12.0/6.3	1.92 (1.71-2.16)
Li et al (21) 2002	Hong Kong	9,876 (5,237/ 4,539)	Telephone survey with a structured questionnaire by trained interviewers	18-65	Recent 1 month (1)	≥3/week (2)	14.0/9.3	1.51 (1.35-1.69)
Maggi et al (22) 1998	Italy	2,398 (1,531/867)	EPESE (Italian version)	≥ 65	Current (1)	Often and always (2)	54.0/36.0	1.50 (1.36-1.66)
Mellinger et al (23) 1985	United States	3,161 (1,827/1,334)	Two sleep symptoms checklist	18-79	Recent 1 year (2)	Frequent (2)	20.0/14.0	1.43 (1.21-1.68)
Ohayon and Hong (24) 2002	South Korea	3,719 (1,877/1,842)	Sleep-EVAL expert system	≥ 15	Current (1)	Severe (3)	19.1/14.8	1.29 (1.12-1.49)
Ohayon and Roth (25) 2001	Europe	24,600 (12,665/ 11,935)	DSM-IV and ICSD -90 Sleep-EVAL expert system	≥ 15	Current (1)	Severe (3)	13.5/8.5	1.59 (1.48-1.71)
Ohayon et al (26) 1997	Canada	1,722 (895/827)	DSM-IV and ICSD-90 Sleep-EVAL expert system	15-100	Current (1)	Severe (3)	24.2/18.9	1.27 (1.06-1.53)
Olson (27) 1996	Australia	535 (337/198)	A telephone survey	16-75+	Current (1)	Often and always (2)	24.9/17.3	1.44 (0.97-1.90)
Pallesen et al (28) 2001	Norway	2,001 (1,001/1,000)	Subjective response to questions about sleep complaints (DSM-IV)	18-99	Recent 1 month (1)	Severe (3)	14.7/8.5	1.73 (1.34-2.22)
Quera-Salva et al (29) 1991	France	1,003 (540/463)	Subjective response to questions about sleep complaints Expert interviewers of survey company	16-91	Current (1)	Any frequency (1)	53.0/41.9	1.27 (1.11-1.45)
Roberts et al (30) 1999	United States	2,380 (1,343/ 1,037)	Subjective response to questions about sleep complaints	50-102 (64.9±10.2)	Recent 2 weeks (1)	Any frequency (Yes/no) (1)	29.3/20.9	1.40 (1.21-1.62)
Weyerer and Dilling (31) 1991	Germany	1,539 (845/684)	Subjective response to questions about sleep complaints Interviewed by trained psychiatrists	15-70+	Recent 1 week (1)	Any frequency (From mild to severe) (1)	34.3/21.4	1.60 (1.38-1.89)
Yeo et al (32) 1996	Singapore	2,418 (1,209/ 1,209)	Subjective response to questions about sleep complaints Self-developed questionnaire	15-55	Recent 1 year (2)	Any frequency (Yes/no) (1)	17.5/12.9	1.36 (1.12-1.60)
Ganguli et al (33) 1996	United States	1,050 (601/449)	Subjective response to questions about sleep complaints	66-97 (74.4±5.5)	Current (1)	Usually (2)	No prevalence of overall insomnia	
Lindberg et al (34) 1997	Sweden	529 (271/258)	Self-developed questionnaire Phase I: postal questionnaire Phase II: structured interview and examination Self-developed questionnaire	20-45	Current (1)	≥3/week (2)	No prevalence of overall insomnia	

*1=Current, 2=lifetime

1=any frequency, 2=frequent/always, 3=severe (based on DSM or ICSD)

Table 2—Meta-Analysis of Sex Differences in the Risk For Insomnia

	Effect size	No of cases (Female/Male)	RR (Female/Male, 95% CI)	Q_w^s	Q_B^s
All studies	29	1,265,015 (718,828/546,187)	1.41 (1.28-1.55)	862.69***	
Sample size					97.35***
≥ 5000	10	1,230,989 (699,913/531,076)	1.54 (1.33-1.77)	503.39***	
< 5000	19	34,026 (18,915/15,111)	1.32 (1.23-1.42)	48.42***	
Quality studies					176.10***
Quality	4	61,916 (36,411/25,505)	1.64 (1.48-1.81)	9.59*	
Non-quality	25	1,203,099 (682,417/520,682)	1.38 (1.23-1.54)	832.73***	
Frequency of insomnia					91.18***
Any frequency	11	1,155,792 (656,425/499,367)	1.37 (1.15-1.64)	543.29***	
Frequent/always	9	36,945 (20,584/16,361)	1.56 (1.45-1.63)	27.37***	
Severe	9	72,278 (41,819/30,459)	1.40 (1.35-1.46)	58.69***	
Duration of insomnia					5.38
Current	23	1,228,380 (696,302/532,078)	1.41 (1.26-1.58)	701.90*	
Long-term	6	36,635 (22,526/14,109)	1.42* (1.37-1.48)	3.01	
Sample years					7.82
≤ 1990	15	1,181,592 (671,713/509,879)	1.39 (1.21-1.60)	646.11***	
> 1990	14	83,423 (47,115/36,308)	1.43 (1.29-1.59)	79.21***	
Age cutoff					107.62***
≥ 65 years	12	22,410 (12,447/9,963)	1.73 (1.65-1.83)	91.63***	
31-64 years	9	39,658 (21,734/17,924)	1.46 (1.29-1.63)	18.70***	
15-30 years	9	16,524 (8,506/8,018)	1.28 (1.13-1.43)	486.52***	
Regional sample					119.27***
America	11	1,166,312 (667,615/498,697)	1.45 (1.26-1.66)	188.73***	
Europe	11	78,528 (40,516/38,012)	1.45 (1.30-1.62)	119.27***	
East Asia	5	18,707 (10,401/8,306)	1.29 (1.07-1.56)	34.20**	
Australia	2	1,468 (803/665)	1.39* (1.10-1.74)	0.08	
Subtype					70.88***
DIS	7	41,896 (21,840/20,056)	1.50 (1.07-1.93)	27.28**	
DMS	7	41,896 (21,840/20,056)	1.62 (1.39-1.87)	14.24*	
EMA [#]	7	22,261 (11,768/10,493)	1.19 (1.07-1.32)	11.25*	
NRS	5	40,701 (21,175/19,526)	1.02 (0.74-1.31)	29.54**	

* $P \leq 0.05$ ** $P \leq 0.01$ *** $P \leq 0.001$

& Fixed effects model

In European study (reference 26), only England data were available.

^s Q_w : a statistic to determine whether studies within an analysis sharing a common population effect size^s Q_B : a statistic to determine between-category homogeneity statistic

studies was significantly higher than that of small studies (RR: 1.54/1.32; $Q_B = 97.35$, $p < .01$).

Analysis 3 concerned 4 high-quality studies with more rigorous methodology^{5,10,20,25} and 25 nonquality studies.^{4,6-9,11-19,21-24,26-32} Both of them showed a female preponderance in the risk of insomnia. The sex difference in quality studies was significantly higher than that of nonquality studies (RR: 1.64/1.32; $Q_B = 176.10$, $p < .01$).

Analysis 4 concerned about the impact of different frequency criteria on the sex difference of insomnia. Female excess in the risk of insomnia was demonstrated across different frequency studies, but the divergence among them was significant ($Q_B = 91.18$, $p < .01$). The highest female excess was seen in the frequent or always insomnia group (RR: 1.56), and the lowest female excess was reported in the any frequency group (RR: 1.37).

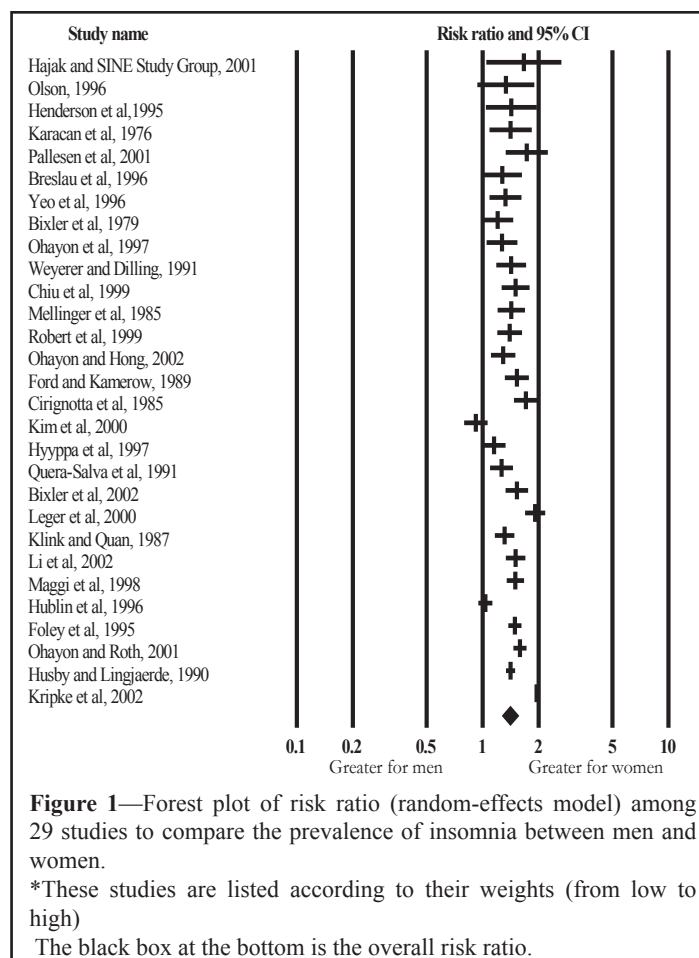
Analysis 5 compared 23 current insomnia studies^{4,8-13,15-22,24-31} and 6 long-term insomnia studies.^{5-7,14,23,32} The Q_w (3.01) of long-term studies indicated homogeneity, so the fixed-effects model was applied in this group. Both of them showed similar female preponderance in the risk of insomnia (RR: 1.41/1.42; $Q_B = 5.38$, $p = .08$).

Analysis 6 examined the results across different periods. Fif-

teen studies that were conducted before 1990^{4,6,8-10,13-16,18,19,22,23,29,31} and 14 studies after 1990^{5,7,11,12,17,20,21,24-28,30,32} showed similar female excess in the risk of insomnia (RR: 1.39/1.43; $Q_B = 7.82$, $p = .08$).

Analysis 7 compared the sex difference in the prevalence of insomnia among elderly (≥ 65 years), middle-age (31-64 years), and young adult subjects (15-30 years). All 3 groups showed a female preponderance in the risk of insomnia, but the overall RR progressively increased from 1.28 in young adults to 1.73 in elderly subjects.

In analysis 8, studies of different regions were explored. Twenty-nine studies were divided into 4 continents: 11 studies in America,^{4-6,9,10,16,18,19,23,26,30} 11 studies in Europe,^{8,11,13-15,20,22,25,28,39,31} 5 studies in East Asia,^{7,17,21,24,32} and 2 studies in Australia.^{12,27} The Q_w (0.08) of Australian studies indicated a homogeneity, so a fixed-effects model was applied in this group. Although female excess in the risk of insomnia was demonstrated in all regions, the divergence among them was significant ($Q_B = 119.27$, $p < .01$). The highest female excess was reported in European (RR: 1.45) and American (RR: 1.45) studies, followed by Australian (RR: 1.39) and Asian studies (RR: 1.29).

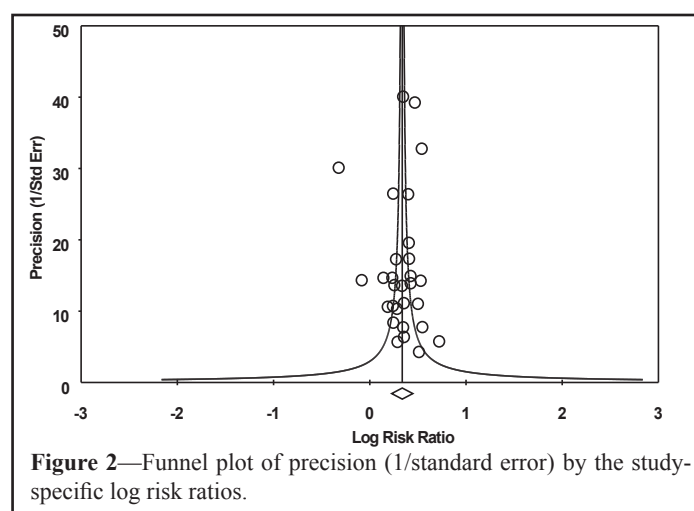


In analysis 9, the sex difference in the prevalence of subtypes of insomnia was studied. Except nonrestorative sleep (RR=1.02 [0.74-1.31]), all other subtypes of insomnia had a significant female preponderance. The female excess among these subtypes was different ($Q_B=70.88$, $p < .01$); it became progressively greater in the following sequence: early morning awakening (RR: 1.19), difficulty in initiating sleep (RR: 1.50), and difficulty in maintaining sleep (RR: 1.62).

Potential biases, such as publication bias and bias in location and selection of studies, have been recognized as a major problem in interpreting medical research, including meta-analysis.⁵⁵⁻⁵⁹ To evaluate such potential bias, a funnel plot (plot of effect estimates versus the inverse of their standard errors) was used to assess the validity of meta-analyses.⁶⁰⁻⁶² A formal investigation of the degree of asymmetry was performed using the Egger test.⁶² The funnel plot of precision (1/ standard error) by the study-specific log RR is shown in Figure 2. It has normal distribution without being skewed and suggested that potential biases did not significantly obscure our result (intercept: 0.27 (95% CI: -0.20 - 0.74), $p = .81$).

DISCUSSION

Our systematic review of published epidemiologic studies confirmed a female excess in the risk of insomnia. To the best of our knowledge, it was the first meta-analysis of sex differences in insomnia. Altogether, 29 studies were used in the analysis of general insomnia. Similar to the overall meta-analysis result, female excess for insomnia was shown in almost all individual stud-



ies, except 3.^{13,17,27} The Finnish study that did not report any sex difference in insomnia¹³ was a large study (N = 11,354), but it was undertaken in a twin-cohort population. On the other hand, female excess in the risk of insomnia was reported by another epidemiologic study in Finland at the same period of time.¹⁵ The Australian study²⁷ was only undertaken in a limited sample population (535 subjects) with a large range of RR (1.37, 95%CI: 0.97-1.90). Similarly, 2 other small studies (< 500 people) that were not included in our meta-analysis also did not demonstrate any sex difference in the risk of insomnia.^{63,64} The sex difference was, however, reported by a larger study of Australian elderly.¹² In contrast, the Japanese study that did not report a sex difference¹⁷ had a reasonable sample size (N = 3030) and used a stratified random sampling methodology. The authors postulated that their finding might be related to the unique sociodemographic and psychological characteristics of the Japanese society, for example, less marked variation in the economic status in the Japanese population than in Western countries.¹⁷ The possibility of cross-cultural differences in the sex risk of insomnia was further suggested by our meta-analysis. Although obvious female excess in the risk of insomnia existed among different regions, the female excess in East Asia was the lowest. Nevertheless, before accepting the finding, some limitations of the methodology of the studies in East Asia must be noted. Firstly, only 5 studies were included. Most of these studies, except the Hong Kong adult study,²¹ involved relatively smaller sample size (fewer than 5000 people). In this regard, a similar female excess in the risk of insomnia in both the Hong Kong adult and elderly population, relative to that of the American and European studies, was found.^{7,21} On the other hand, in addition to the Japanese study,¹⁷ a study in northern China with 1289 subjects, which was not included in the meta-analysis because it was published in Chinese, also did not report a sex difference in the risk of insomnia.⁶⁵ This study, however, was limited by the sampling methodology. Nonetheless, the presence of cross-cultural differences in the sex risk of insomnia warrants further investigation, especially on the effect of culture, sleeping habits, and sociodemographic variation upon insomnia.

The female excess in the meta-analysis of large and quality studies was much higher than that of small and nonquality studies. In addition, a female preponderance of insomnia was found among different criteria, frequencies, and duration of insomnia. As a result, it conveyed rigorous information to us that a genuine female predisposition in the risk of insomnia indeed exists.

No significant time trend was revealed in our study, but the

prevalence of insomnia in early studies (female: 28.2%, male: 20.2%) was much higher than that of recent studies (female: 12.8%, male: 9.7%). Because most of stringent operational diagnostic criteria of insomnia (DSM-IV and ICSD-90) were published after 1990, this finding suggests that the criteria of recent studies were more rigorous and the estimation of the prevalence rate was more reliable.

A major question was whether the female excess of insomnia was simply an epiphenomenon of sex difference in the underlying depressive and anxiety disorders or it represented genuine sex-specific changes in sleep physiology and primary insomnia. An insomnia complaint is a common symptom of psychiatric disorders, especially depression and anxiety.⁶⁶⁻⁷⁰ Nonetheless, the sex differences in insomnia could not be solely explained by the higher prevalence of anxiety and depression in females because the sex differences persist even after the underlying psychiatric disorders have been taken into account and a substantial proportion of patients with insomnia (especially in the community) might not have psychiatric diagnoses.^{10,34} Nevertheless, the current finding of putative risk factors leading to sex differences in depression might help to shed light on the etiology of insomnia. Genetic factors do not seem to contribute to the increased risk of women to depression by a direct mechanism,^{68,71} but genetic factors might indirectly increase female vulnerability to depression through temperamental features, such as low self-esteem.^{72,73} Furthermore, women with depression or anxiety are more likely to complain of somatic symptoms (e.g., sleep disturbances and pain) than are men.⁷⁴⁻⁷⁶ The sex difference in symptom endorsement might be related to the greater bodily vigilance and awareness among women, as well as socially sanctioned culture that encourages women to more readily express emotional distress and somatic symptoms.⁷⁷⁻⁷⁹ This may be partially supported by our subgroup meta-analysis that found that women still complained of more sleep disturbances despite having a similar degree of waking in the morning feeling refreshed, as compared with men.

Controversies exist on whether there are specific sex-related sleep changes. An actigraphy investigation showed that, irrespective of age, women exhibited better sleep quality, longer sleep duration, and shorter sleep latency than men.⁸⁰ Two other polysomnography research studies, however, expressed far fewer significant sex differences in sleep variables.^{81,82} Nevertheless, it has to be cautioned that it might be difficult, and even inappropriate, to compare epidemiologic studies using questionnaire data with the highly selected samples in polysomnography studies. On the other hand, studies have demonstrated that insomnia is common for women across different menstrual phases⁸³⁻⁹⁰ and suggested a higher susceptibility of insomnia in women. Our meta-analysis suggested a progressive trend of female excess across age, with elderly women having the highest risk of developing insomnia. In this regard, further investigations on the effects of menopause and hormonal changes as they relate to the development of insomnia may shed some light on the interaction of age and sex.⁹⁰

Several limitations existed in our study. Blind assessment was not applied in this review. It has been suggested that blind assessment produces significantly lower and more consistent scores than does open assessment.^{91,92} In addition, the criteria for defining high-quality studies and cutoff sample size of the studies were subjective and arbitrary, and the review only included studies published in English. Finally, most data of the included studies showed significant heterogeneity, and we had to use a random-effects model in most analyses. The random-effects model is less

likely to show a significant effect than is a fixed-effects model.^{48,49} Despite all of these potential limitations, the normal distribution of the funnel plot suggests that the results of our study were not obscured by these biases.

In summary, this meta-analysis confirmed a female predisposition toward insomnia. The trend of female predisposition was consistent and progressive across age and was not affected by the use of various criteria, frequencies and duration of insomnia. Our study also suggests the presence of cross-cultural differences in the sex-based risk of insomnia, with relatively lower female excess in East Asian countries, as compared with Western countries. Further studies will be needed to examine the role of different factors in leading to the sex difference in the prevalence of insomnia.

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