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Longitudinal Course of Depression Scores with and without Insomnia in Non-Depressed Individuals: A 6-Year Follow-Up Longitudinal Study in a Korean Cohort

Sooyeon Suh, PhD, CBSM[1,2]; Hyun Kim, MSc[1,3]; Hae-Chung Yang, PhD[1]; Eo Rin Cho, PhD[1]; Seung Ku Lee, PhD[1]; Chol Shin, MD, PhD, FCCP[1,3,4]

[1]Korea University Ansan Medical Center, Institute of Human Genomic Study, Ansan, Republic of Korea; [2]Stanford University, Department of Psychiatry; Palo Alto, CA; [3]Brain Korea 21 Program in Biomedical Sciences, Korea University School of Medicine, Anam, Republic of Korea; [4]Division of Pulmonary, Sleep and Critical Care Medicine, Department of Internal Medicine, Korea University Ansan Hospital, Ansan, Republic of Korea

Study Objective: This is a population-based longitudinal study that followed insomnia symptoms over a 6-year period in non-depressed individuals. The purpose of the study was to (1) investigate the longitudinal course of depression based on number of insomnia episodes; and (2) describe longitudinal associations between insomnia and depression, and insomnia and suicidal ideation.

Design: Population-based longitudinal study.

Setting: Community-based sample from the Korean Genome and Epidemiology Study (KoGES).

Participants: 1,282 non-depressed individuals (44% male, mean age 52.3 ± 7.14 years)

Measurements and Results: This study prospectively assessed insomnia, depression, and suicidal ideation with 4 time points. Individuals were classified into no insomnia (NI), single episode insomnia (SEI), and persistent insomnia (PI; ≥ insomnia at 2+ time points) groups based on number of times insomnia was indicated. Mixed effects modeling indicated that depression scores increased significantly faster in the PI group compared to the NI ($P < 0.001$) and SEI ($P = 0.02$) groups. Additionally, the PI group had significantly increased odds of depression as compared to NI or SEI (OR 2.44, $P = 0.001$) groups, with 18.7% meeting criteria for depression compared to the NI (5.3%) and SEI (11.6%) groups at end point. The PI group also had significantly increased odds of suicidal ideation as compared to NI or SEI (OR 1.86, $P = 0.002$) groups.

Conclusions: Persistent insomnia significantly increases the rate in which depression occurs over time in non-depressed individuals, which ultimately leads to higher risk for depression. Additionally, having persistent insomnia also increased the risk of suicidal ideation.

Keywords: Insomnia, depression, suicidal ideation, epidemiology, mental health

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INTRODUCTION

The prevalence of depression and suicide has been increasing worldwide.[1-6] It has been well-established from longitudinal epidemiology studies that insomnia is a risk factor for psychiatric disorders, especially depression. Research has indicated that people who have insomnia at baseline have a markedly increased risk for developing depression at future follow-up compared to individuals who do not have insomnia at baseline.[7-16] However, many of these studies are limited by the duration and frequency of follow-up, and there are few studies that have investigated whether single episode of insomnia compared to persistent insomnia predicts the longitudinal course of depression.

Recent longitudinal studies have ascertained insomnia as both a symptom and a disorder. Past studies have highlighted that insomnia disorder is a highly persistent condition, with persistence rates ranging from 44% to 46%, that is likely to partially remit and recur.[17-21,23,24] On the other hand, research has indicated that *insomnia symptoms* have higher remission rates.[19,22] A study by Morin and colleagues investigated 388 individuals with insomnia at baseline from a population-based study, following them over a course of 3 years.[19] Participants in their study were classified into insomnia disorder (having dissatisfaction with their sleep, insomnia symptoms ≥ 3 nights/week for ≥ 1 month and substantial distress over condition OR using prescribed sleep-promoting medication ≥ 3 nights/week), insomnia symptoms (having insomnia symptoms ≥ 3 nights/week without fulfilling all diagnostic criteria for insomnia syndrome), and good sleepers. Compared to individuals who had insomnia disorder, individuals with insomnia symptoms had higher rates of remission at 1-year follow-up (34.8% vs. 17%).

Several studies have reported that insomnia increases the risk of developing depression, although odds ratios have varied widely across studies (OR 1.60–6.86).[12,15,17,18,25-27] One reason for this wide range may be that there is significant variability in how insomnia and depression are defined and measured, making it difficult to compare across studies. Another concern is that the majority of studies investigating insomnia and depression used two time points to investigate the relationship between insomnia and depression, using follow-up intervals of one year up to 12 years.[7,10,11,13,15,16] In one of the first epidemiological studies investigating insomnia and depression, Ford and Kamerow found that the risk of developing a new major depressive episode was approximately 40 times greater in individuals who had complaints of insomnia at both baseline and follow-up.[7] That risk decreased significantly (odds ratio [OR] 1.6) for individuals who had insomnia only at the first visit but not at the second visit. These results are consistent with the study by Okajima et al.,[16] who found that having insomnia at both of two

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Address correspondence to: Chol Shin, MD, PhD, Division of Respiratory and Critical Care, Department of Internal Medicine, Ansan Hospital, Korea University, 516, Gojan-1-dong, Danwon-gu, Ansan-si, Gyeonggi-do, 425-707, Korea; Tel: 82-31-412-5603; Fax: 82-31-412-5604; E-mail: chol-shin@korea.ac.kr

time points was associated with the new appearance of depression (OR 7.0), but having remitted insomnia was not significantly associated with incident depression.

Other studies that have used more than one follow-up point show similar results. One study by Chang et al.[12] used a prospective longitudinal design to study the relationship between self-reported sleep disturbances and subsequent clinical depression in men who attended medical school over 34 years. Their findings suggested that insomnia was indicative of higher risk for subsequent clinical depression that persisted for at least 30 years. Another study by Buysse et al.[17] investigated the longitudinal associations between insomnia and depression with 6 time points over 20 years in individuals aged 20 to 40. They distinguished between 4 duration-based subtypes of insomnia (1-month insomnia associated with significant distress, 2- to 3-week insomnia, recurrent brief insomnia, and occasional brief insomnia). Approximately 35% of the individuals who indicated 1-month insomnia had the same diagnosis at a later interview, and 99% of those individuals had some type of insomnia in 99% of previous interviews and in 82% of subsequent interviews, demonstrating that 1-month insomnia was indeed a highly stable condition. Additionally, results from their study demonstrated that 17% to 50% of subjects with insomnia lasting 2 weeks or longer developed a major depressive episode at a subsequent time point, with insomnia free of depression consistently predicting insomnia comorbid with depression at subsequent time points (OR 3.2–7.1), but not depression without insomnia.

Recent developments in the associations between insomnia and depression have also lead to an interest in insomnia as a risk factor for suicide.[28-31] Several population-based studies have found difficulty maintaining sleep and poor sleep quality increased the risk of suicide in Japanese and US populations. Additionally, a recent study in a Norwegian population-based study found the frequency of sleeping problems increased the risk of suicide.[32]

Although there is considerable evidence suggesting that insomnia predicts subsequent depression, the longitudinal course of depression in individuals who have persistent insomnia symptoms compared to good sleepers is yet unknown. Additionally, while the study of Buysse et al.[17] demonstrates that 1-month insomnia is a highly stable condition, the influence of persistent 1-month insomnia on the risk of developing depression is yet unknown. To the best of our knowledge, no studies have yet investigated the longitudinal course of depression based on number of insomnia episodes in a population-based sample. Additionally, no studies have investigated the risk of depression or suicidal ideation in a non-depressed sample based on number of insomnia episodes in a population-based longitudinal study.

The current study is a population-based longitudinal study investigating insomnia symptoms and depression over a 6-year period. Insomnia symptoms have been shown to be present in approximately 17% of the Korean population, with 5% meeting criteria for insomnia disorder, comparable with Western countries.[33] In the current study, we hypothesized that non-depressed individuals who indicate insomnia at two or more time points would have a larger increase in depression symptoms over time during the 6-year period compared to those with no insomnia or those with a single episode of insomnia. Additionally, we also hypothesized that non-depressed individuals who endorse insomnia symptoms at multiple time points would have higher likelihood of becoming depressed at 6-year follow-up and higher risk of suicidal ideation compared to individuals who either had no insomnia or a single episode of insomnia symptoms.

MATERIALS AND METHODS

Study Design and Sample

Participants of the present study were part of a larger study, namely the Korean Genome and Epidemiology Study (KoGES), which is an ongoing, population-based cohort study that started in 2001 under the original title, Korean Health and Genome Study. Detailed information on the study design and aims of the KoGES has been previously reported.[34] The current study used a subset of individuals from the original cohort members recruited from Ansan, South Korea, starting in 2005 (Baseline). This time point was used because this was when the Beck Depression Inventory (BDI), the main outcome measure for the current study, was added to the study. All participants in the current study were followed with biennial examinations, with 4 data points spaced 2 years apart (Baseline, Time 1, Time 2, and Time 3).

The current study focuses on 1,639 participants who were present at baseline in 2005 (age range 43-73 years). Because the main topic of the present paper is about the longitudinal course of depression in non-depressed individuals, individuals who were classified as depressed (BDI $\geq$ 16) at baseline were excluded, which resulted in 1,301 individuals. One participant who was taking antidepressants but had BDI < 16 was also excluded. Four participants were identified as having a previous diagnosis of depression, but did not currently endorse depression. Although these 4 participants were not excluded from the study, separate analyses were conducted with and without these participants to verify that the results were not different. We further excluded participants with cerebrovascular disease (n = 12) and/or traumatic brain injury (n = 7), resulting in a total number of 1,282 participants (see Figure 1). An informed consent form was signed by each participant, and the study procedure was approved by the institutional review board of the Korea University Ansan Hospital.

Across 6 years of follow-up, 84% (n = 1,089) of the original sample continued to participate until Time 3. Specifically, 74.5% participated in all 4 time points (n = 955), an additional 16.9% (n = 217) in $\geq$ 3 time points, and 8.6% (n = 110) in $\geq$ 2 time points. Individuals who dropped out of the study during the 6-year follow-up (n = 193) differed significantly in age, sex, and employment status compared to the individuals who remained in the study. Dropouts were significantly older (P = 0.02), had higher employment rates (P = 0.03), and higher ratio of men (P = 0.001). There was no significant difference between marital status, smoking status, or heavy drinking.

Measures

Demographic Variables

All participants completed information at baseline about age, gender, marital status, employment status, general physical health, smoking status, and alcohol habits (heavy drinking). General

physical health was measured with a one-item question asking, "In general, how would you rate your current physical health?" on a 5-point Likert scale, ranging from "very unhealthy" to "very healthy." Demographic information can be found in Table 1.

Beck Depression Inventory

The BDI is a 21-item self-report inventory used to assess the severity of depressive symptoms. Participants are asked to indicate which statement best describes the way they have been feeling over the past week. Total scores on the BDI can range from 0 to 63, with higher scores reflecting greater levels of depressive symptoms. All BDI scores were calculated with and without the sleep item. The BDI has yielded adequate reliability estimates, and has been well validated as a measure of depressive symptomatology.[35]

Insomnia

All participants were asked 4 questions about insomnia based on their symptoms during the past month: (1) "Do you have difficulty initiating sleep?" (2) "Do you have difficulty maintaining sleep?" (3) "Do you experience early morning awakenings?" and (4) "Do you feel unrefreshed in the morning?" The participants were asked to rate each question on a 4-point Likert scale (1 = Never, 2 = 1-2 times/week, 3 = 3-4 times/week, and 4 = > 5 times/week). Individuals who experienced ≥ 1 of these 4 symptoms > 3-4 times/week (score > 3) were categorized as individuals with insomnia. Individuals who were taking sleep medication > 3 times/week were also assessed. There were 3, 10, 12, 17 participants who met this criterion for each time point, respectively. All participants taking sleep medication > 3 times/week met criteria for insomnia. Thus, no participants were classified as having insomnia on the basis of sleep medication alone.

Insomnia groups were formed based on how many times they met criteria for insomnia during baseline and follow-up. Preliminary analyses determined that individuals with insomnia at 2, 3, or 4 time points showed similar trajectories of depression that were not significantly different (P > 0.10), and thus those with insomnia at ≥ 2 time points were grouped together. Individuals were divided into 3 groups based on insomnia status: (a) "no insomnia (NI)": Participants who did not indicate insomnia symptoms during baseline or any time during the 3 follow-ups; (b) "single episode insomnia (SEI)": Individuals who indicated insomnia symptoms at 1 time point during baseline or follow-up; and (c) "persistent insomnia (PI)": Individuals who indicated presence of insomnia symptoms at ≥ 2 time points during baseline or follow-up.

Statistical Analysis

The primary objective of the study was to evaluate whether the longitudinal course of depression (excluding sleep item)

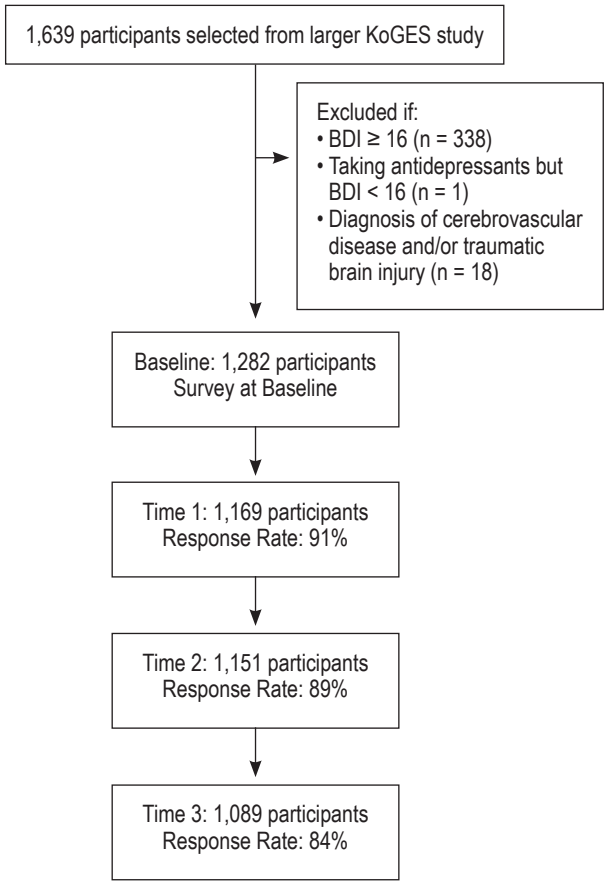

Figure 1—Participants flowchart.

Table 1—Demographic data at baseline and differences among insomnia groups

Characteristic	Total (N = 1,282)	NI (n = 705)	SEI (n = 273)	PI (n = 304)	P-value
Male, n (%)	564 (44)	339 (48.1)	118 (43.2)	107 (35.2)	0.001
Age, mean (SD)	52.3 (7.14)	52.01 (6.81)	52.60 (7.25)	52.76 (7.74)	0.24
Employed, n (%)	735 (57.3)	428 (60.7)	150 (54.9)	157 (51.6)	0.02
Married, n (%)	1,201 (93.7)	671 (95.2)	257 (94.5)	273 (89.8)	0.005
Education, n (%)					< 0.001
0-6 years	220 (17.2)	94 (13.3)	55 (20.1)	71 (23.4)	
6-12 years	773 (60.3)	428 (60.7)	159 (58.2)	186 (61.2)	
12+ years	289 (22.5)	183 (26)	59 (21.6)	47 (15.5)	
Currently smoking, n (%)	172 (13.4)	98 (13.9)	39 (14.3)	35 (11.5)	0.53
Heavy drinking (≥ 15 g/day), n (%)	190 (14.8)	97 (13.8)	45 (16.5)	48 (15.8)	0.48
Physical health, mean (SD)	3.24 (0.79)	3.38 (0.74)	3.18 (0.81)	2.99 (0.81)	< 0.001

NI, no insomnia group; SEI, single episode of insomnia group; PI, persistent insomnia group.

Table 2—Insomnia status at each follow-up according to insomnia status at baseline (n = 1,282)

	Time 1		Time 2		Time 3	
Baseline Status	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
No Insomnia (n = 985)	771/900 (85.7%)	129/900 (14.3%)	740/892 (83%)	152/892 (17%)	734/834 (88%)	100/834 (12%)
Insomnia (n = 297)	132/271 (48.7%)	139/371 (51.3%)	121/259 (46.7%)	138/259 (53.3%)	133/257 (51.8%)	124/257 (48.2%)

between the 3 insomnia groups were different from baseline to 6-year follow-up. Mixed-effects modeling[36] was used to estimate the baseline depression level (without sleep item) as well as the rate of change over time for the 3 insomnia groups using all available data from all 1,282 participants. Mixed-effects models are advantageous for analyzing longitudinal data because the procedure accounts for the correlations among repeated assessments within an individual. Additionally, no missing data imputation techniques were used, as the multilevel modeling approach is robust against the effects of missing data compared to other methods.[37] Both the fixed-effects (group average effects) and random-effects (within and between individual variability) were estimated. Determination of linear versus quadratic change was made by comparison of relative fit of models using a likelihood ratio test. The linear model was retained unless the fit of the quadratic model was significantly better than that of the linear model. Once the shape of unconditional growth curve of depression was determined, the effects of "Insomnia group" and "Insomnia group × Time" were added to the model. The effects of relevant covariates (age, sex, employment status, marital status, physical health, heavy drinking status, and smoking status) and their interaction with time were also tested. A backward elimination procedure was used in which nonsignificant covariates ($P > 0.10$) were removed from the model until a final solution was reached. Continuous variables were centered at the mean for easier interpretation. All statistical tests were two-sided.

Secondary analyses were conducted to investigate whether the groups differed in terms of depression incidence (BDI ≥ 16, including sleep item) at Time 3. Participants were classified as "depressed" or "non-depressed" based on their depression score at Time 3. Multivariate logistic regression analyses were conducted to estimate an odds ratio (OR) of depression between the 3 insomnia groups with 95% confidence interval (CI). Potential confounding variables included in the multivariate model were baseline depression, age, sex, employment status, education, smoking status, and heavy drinking.

A third analysis was conducted investigating suicidal ideation among groups at Time 3. Suicidal ideation was assessed using BDI item 9 (score range 0-3). Individuals who scored ≥ 1 on BDI item 9 were classified as having suicidal ideation. Multivariate logistic regression analyses were conducted to estimate an OR of suicidal ideation between the 3 insomnia groups with 95% CI. Potential confounding variables included in the multivariate model included baseline suicidal ideation, age, sex, employment status, education, smoking status, and heavy drinking.

RESULTS

Of the 1,282 participants who participated in the study, 705 participants (55%) did not report insomnia at any time point, 273 participants (21.3%) reported single episode insomnia, and 304 participants (23.7%) reported persistent insomnia (See Table 1). Among participants with persistent insomnia, 52% (n = 158) reported 2 insomnia episodes, 30.9% (n = 94) reported 3 insomnia episodes, and 17.1% (n = 52) reported 4 insomnia episodes. Further analysis of individuals in the PI group revealed that 51.7% (n = 157) had insomnia at consecutive time points (e.g., insomnia at time 1 and 2, time 1, 2, and 3, etc.); 18% (n = 55) had insomnia at distinct time points (e.g., insomnia at time 1 and 3, time 1 and 4, time 2 and 4, etc.); and 12.1% (n = 37) had insomnia at both consecutive and discrete time points (e.g., insomnia at time 1, 2 and 4, time 1, 3, and 4). Approximately 18% (n = 55) of the PI group could not be characterized due to missing data points. Thus, a majority of individuals in the PI group had insomnia at consecutive time points.

In our sample, 297 (23%) indicated they had insomnia at baseline. Among these participants, 48.2% continued to have insomnia at end point (See Table 2). A total of 3 participants reported taking hypnotic medication use for sleep, and an additional 3 participants reported taking other prescription medications with sedating effects, such as antidepressants and benzodiazepines, at baseline. The 3 insomnia groups were not significantly different for most demographic variables (Ps > 0.06) except sex, employment status, marital status, and physical health (Ps < 0.001). Individuals who were in the PI group had higher ratio of females, fewer married individuals, lower rates of unemployment, and worse physical health. Baseline mean scores for BDI (including the sleep item) were 5.00 (SD = 3.82) for the NI group, 6.20 (SD = 4.39) for the SEI group, and 7.42 (SD 4.28) for the PI group. Mean BDI scores and percentage of individuals classified as being depressed (BDI > 15) or having suicidal ideation (BDI Item 9 > 0) for each time point based on insomnia group can be found in Table 3.

Mixed Effects Model Results

Outcomes from the mixed effects models are presented in Table 4. Figure 2 shows the longitudinal course of depression by insomnia group estimated by the mixed effects model. The fit of the quadratic model was significantly better than that of the linear model. The final model included age, sex, education, marital status, smoking status, age × time, marital status × time, and education × time as controls. Baseline depression levels of both SEI and PI groups were significantly higher than that of the NI group (Ps < 0.008). A follow-up analysis indicated that the difference in depression between the SEI and PI groups was also significant (P = 0.001). With regard to the rate of change in depression, the level of depression was increased significantly faster in the PI group compared to the NI (P < 0.001) and the SEI (P = 0.02) groups. However, there was no significant dif-

Table 3—Mean BDI scores (with sleep item), depression and suicide prevalence at each time point divided by insomnia group

	Insomnia Group	Baseline	Time 1	Time 2	Time 3
BDI score, mean (SD)	NI	5.00 (3.82)	4.72 (4.47)	4.93 (4.78)	5.91 (5.29)
	SEI	6.20 (4.38)	5.79 (5.29)	6.18 (4.85)	8.12 (6.35)
	PI	7.42 (4.29)	8.22 (5.80)	8.55 (6.41)	10.38 (7.01)
Depression category,* N (%)	NI	–	24 (3.8)	28 (4.5)	31 (5.3)
	SEI	–	12 (4.9)	10 (4.3)	26 (11.6)
	PI	–	28 (9.7)	30 (10.9)	51 (18.7)
Prevalence of suicidal ideation,† N (%)	NI	47 (6.7)	34 (5.4)	46 (7.3)	73 (12.4)
	SEI	16 (5.9)	19 (7.8)	18 (7.6)	29 (12.8)
	PI	39 (12.8)	39 (13.5)	35 (12.5)	164 (15)

NI, no insomnia group; SEI, single episode of insomnia group; PI, persistent insomnia group. *Depression category: BDI ≥ 16. †Prevalence of suicidal ideation: BDI Item 9 > 0. Time 1 = 2-year follow-up; Time 2 = 4-year follow-up; Time 3 = 6-year follow-up.

Table 4—Fixed effects from mixed effects models estimating the longitudinal course of depression during 6 years based on insomnia group

Model / Variable	Estimate	SE	t	P-value
Step 1. Unconditional growth curve model				
Intercept	5.57	0.12	46.14	< 0.001
Time	-0.43	0.15	-2.78	0.005
Quadratic term	0.30	0.05	5.53	< 0.001
Step 2. Conditional growth curve model[a]				
Intercept	8.73	1.00	8.69	< 0.001
NI	Reference			
SEI	1.46	0.27	5.39	< 0.001
PI	0.63	0.27	2.28	0.02
Time	-1.85	0.46	-3.96	< 0.001
Quadratic term	0.30	0.05	5.61	< 0.001
NI × Time	Reference			
SEI × Time	0.15	0.12	1.27	0.20
PI × Time	0.48	0.11	4.07	< 0.001

[a]Adjusted for age, sex, education level, employment status, marital status, physical health, smoking status, heavy drinking (> 15 g/day), and time interactions with each covariate. BDI scores without the sleep item were used for the mixed effects model analysis. NI, no insomnia group; SEI, single episode of insomnia group; PI, persistent insomnia group.

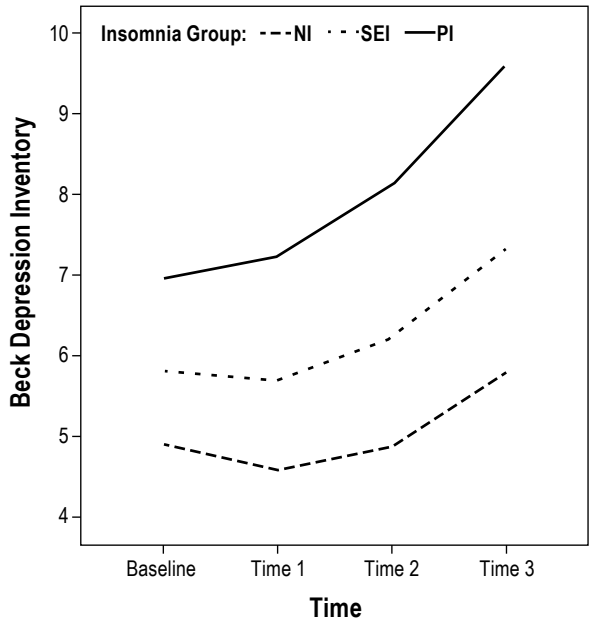

Figure 2—Longitudinal course of depression by insomnia group from mixed effects model. Depression scores using predicted depression scores (without sleep item) from mixed effects model. NI, no insomnia group; SEI, single episode of insomnia group; PI, persistent insomnia group.

ference in the rate of change between the SEI and the NI group (P = 0.20).

These results did not change when 4 participants who reported previous diagnosis of depression were excluded from the analysis.

Longitudinal Associations between Insomnia and Depression / Suicidal Ideation

At time 3, 5.3% (n = 31) participants who belonged to the NI group had developed depression (BDI ≥ 16) at Time 3, compared to 11.6% (n = 26) in the SEI group and 18.7% (n = 51) in the PI group.

The results of the multivariate logistic regression analysis showed that the PI group had an OR of 2.44 (95% CI 1.47–4.05; P = 0.001) of having depression compared to the NI group, even when controlling for covariates. There was a statistical trend for a significant OR of 1.63 (95% CI 0.92–2.90; P = 0.09) comparing SEI to the NI group.

Additionally, existence of suicidal ideation using BDI item 9 at Time 3 was compared between the 3 groups. The PI group had an OR of 1.86 (95% CI 1.25–2.75; P = 0.002) of having suicidal ideation compared to the NI group, even when controlling for covariates. There was no significant difference when comparing SEI group to the NI group for suicidal ideation (OR 0.97; 95% CI 0.61–1.56; P = 0.97). We conducted additional post hoc analyses by adding depression scores at end point as a covariate to investigate whether there was an insomnia-suicide relationship independent of insomnia and depression. When we did this, insomnia groups no longer emerged as a significant predictor in the logistic regression model. Results are presented in Table 5.

Table 5—Odds ratio of depression and suicidal ideation at Time 3 by insomnia group (n = 1,089)

	Insomnia Group	n	Crude OR (95% CI)	P-value	Multivariate OR (95% CI)	P -value
Depression at Time 3[a]	NI	586	1.0 (Reference)	–	1.0 (Reference)	–
	SEI	224	2.33 (1.35-4.03)	0.002	1.63 (0.92-2.90)	0.09
	PI	273	4.11 (2.56- 6.59)	< 0.001	2.44 (1.47-4.05)	0.001
Suicidal Ideation[b] (BDI Item 9)	NI	586	1.0 (Reference)	–	1.0 (Reference)	–
	SEI	224	1.03 (0.65-1.64)	0.87	0.97 (0.61- 1.56)	0.97
	PI	273	2.04 (1.40-2.97)	< 0.001	1.86 (1.25-2.75)	0.002

[a]Multivariate OR adjusted for baseline depression, age, sex, education level, employment status, marital status, physical health, smoking status, heavy drinking (≥ 15 g/day). [b]Multivariate OR adjusted for baseline suicidal ideation, age, sex, education level, employment status, marital status, physical health, smoking status, heavy drinking (≥ 15 g/day). NI, no insomnia group; SEI, single episode of insomnia group; PI, persistent insomnia group.

DISCUSSION

This was a population-based longitudinal study over a 6-year interval examining the longitudinal course of depression in non-depressed individuals. We compared groups of individuals based on number of times they indicated having insomnia symptoms over 6 years, depending on whether they had no insomnia, a single episode of insomnia, or persistent insomnia (insomnia at 2+ time points) using mixed effects modeling. In our sample, single episode insomnia had a prevalence of 21% in our sample, which is consistent with the prevalence of insomnia symptoms from other studies.[19,33,38] Our sample also had a high prevalence of individuals with persistent insomnia (24%), indicating that our sample also had a high percentage of individuals with chronic insomnia and remitting chronic insomnia cases. Additionally, insomnia was persistent across time points, ranging from 20% to 25%. The characterization of our sample is consistent with prevalence and incident rates that have been found in previous studies of 1-month insomnia.[19,21,39]

The main finding from our study indicated that the longitudinal course of depression for non-depressed individuals who had persistent insomnia increased significantly faster from those who had no insomnia or experienced only one episode of insomnia. However, depression in individuals who reported one episode of insomnia did not differ from those who had never experienced insomnia. Additionally, there were no significant differences in the longitudinal course of depression in individuals with persistent insomnia (insomnia at more than 2 time points), and they were equally at elevated risk for depression compared to those who did not have insomnia or indicated insomnia at only one time point. This indicates that having insomnia that persists for more than two years significantly increases the risk of depression, regardless of the number of episodes.

Additionally, persistent insomnia significantly increased the likelihood of meeting criteria for depression at end point (18.7%) compared to single episode insomnia (11.6%) or no insomnia (5.3%). Having persistent insomnia was a risk factor for the existence of depression (OR 2.44) at end point after controlling for covariates when comparing with individuals who had never experienced insomnia or had a single episode of insomnia during follow-up. Our odds ratio was also lower than that found by Okajima and colleagues,[16] who found there was increased risk of depression (OR = 7.0) for individuals who had persistent insomnia (indicated by insomnia at both baseline and follow-up), but not for those who had insomnia at baseline only. However, their study used two time points, and found increased risk of depression in individuals with more recent episodes of insomnia than those with insomnia only at baseline. Our study did not account for the timing in which the insomnia episode occurred over the six years, which may have contributed to the difference in our findings. Additionally, their study included individuals who were either currently depressed or had a history of depression. This is consistent with a recent meta-analysis by Baglioni and colleagues,[27] who found an overall twofold risk of non-depressed people with insomnia to develop depression, compared to individuals without insomnia, in a summary of studies using only two time points. Of particular interest, our study findings were not different compared to the studies included in the meta-analysis that used only two time points to assess insomnia.

This is also confirmed by the findings of Buysse et al.,[17] which showed that insomnia free of depression was strongly associated with insomnia comorbid with depression longitudinally at multiple time points. Our study confirms this relationship is stable across all age groups, as participants in our study were significantly older than those in their study. Prevalence rates from our study for 1-month insomnia were also similar to their study (20%). Additionally, our study adds to the literature by demonstrating that not only do insomnia symptoms increase the risk of insomnia, but considering the number of episodes/duration of insomnia symptoms is also important.

Having persistent insomnia was also a risk factor for suicidal ideation (OR 1.76) at end point after controlling for covariates when compared to no insomnia or insomnia at one time point in non-depressed individuals. While these results are consistent with recent research indicating sleeping problems increases the risk of suicide, previous studies investigating the relationship between sleep and suicidal ideation have been conducted mainly in psychiatric patients or including depressed individuals.[29,32,40,41] This is the first study showing persistent insomnia increases the risk of suicidal ideation in non-depressed individuals in a population-based sample.

Individuals who had persistent insomnia (insomnia at more than 2 time points) during the 6-year interval had higher depression scores at baseline than those with a single episode of insomnia or no insomnia. Additionally, individuals who had single episode insomnia also had higher baseline depression

scores than those who did not have insomnia. This is consistent with the previous study by Vgontzas,[21] who found that persistent insomnia was strongly associated with mental health problems at baseline compared to normal sleep at baseline, and to a lesser degree, fully remitted insomnia. This can also be explained by the high correlation between insomnia and depression in previous studies.[42,43] Individuals with either a single episode or persistent insomnia included individuals who endorsed insomnia at baseline compared to the no insomnia group. Thus, it is not surprising that those with persistent insomnia had higher baseline depression scores than those with a single episode of insomnia or no insomnia. This is the first study examining the longitudinal course of depression in non-depressed individuals based on number of times insomnia was indicated in a population-based sample. The results of our study suggest that persistent insomnia over a long-term period confer significant risk of depression in non-depressed individuals. Single episode insomnia was not significantly different from individuals who had never experienced insomnia. Due to recent research highlighting the persistent/recurring nature of the natural history of insomnia,[18-20] our study results highlight the importance of measuring insomnia at multiple time points and differentiating individuals who have persistent insomnia symptoms when assessing risk for depression, especially in non-depressed samples.

Our findings from this study suggests that clinicians who treat patients with insomnia complaints over a long period of time should be more attentive about their vulnerability towards developing depression and suicidal ideation in the future, even if the patients do not complain of depression at the time. Insomnia is a condition that is often not adequately addressed in clinical settings because of lack of providers or over-burdened clinicians. Thus, it will be important to train clinicians in diagnosing and treating insomnia in primary care settings. Additionally, making simple preventative methods or screening measures for depression readily available in primary care will be important. A recent report from the U.S. Preventative Services Task Force[43] recommended using a 2-item screening measure for depression and found it was as effective as more formal instruments. This especially has implications for early intervention for insomnia prior to developing into persistent insomnia, as it may be an opportunity for preventing future episodes or early intervention for depression.

Limitations

Several limitations should be noted in the present study. First, the presence of both insomnia and depression were both based on symptoms rather than disorder definitions. In our study, we did not differentiate those with insomnia disorder and insomnia symptoms, although the characterization of our sample reflects that there was a high prevalence for both. Past research with Korean samples investigating insomnia have shown that the prevalence is about 17% for insomnia symptoms, and 5% for insomnia disorder. While the prevalence of insomnia symptoms from other epidemiology studies was consistent with our study with single episode insomnia demonstrating a prevalence of 21%,[33] the prevalence rate for those with persistent insomnia was as high as 24%, indicating that our sample comprised both persistent insomniacs and incident and remitting chronic insomnia cases. In our study, diagnosis of insomnia was based on the frequency of sleep problems during the past month. While a comprehensive measure of insomnia based on DSM-IV criteria, inclusive of interference of daily functioning and how long the participant has experienced insomnia would have been ideal, many epidemiology studies use frequency measures as a measure of insomnia.[35] Nonetheless, although our sample measured participants with insomnia symptoms without full diagnostic information about insomnia, the findings still suggest that the presence of persistent insomnia symptoms can be a risk factor for depression, even considering higher rates of remission compared to insomnia disorder. These results suggest that having persistent insomnia disorder can be equally risky and opens the possibility that it confers an even greater risk compared to the findings from our study.

One interesting issue worth noting was the low rates of current hypnotic use in the current sample. Past studies investigating insomnia in South Korean samples have found that treatment rates for insomnia were significantly low (approximately 6.8% of insomnia patients).[44] However, the rates found in our study were lower than that found in previous studies. One possible reason may be that our study excluded individuals with elevated levels of depression at baseline. While there are no previous studies confirming this, it is possible that many individuals who seek treatment for insomnia also receive treatment for depression, thus excluding a significant number of individuals receiving insomnia treatment. Another explanation may be that information on medication use was collected using open-ended questions to the participants, and not through systematic examination of medical charts. Thus, there may have been an underreporting of sleep medication use by the participants.

Additionally, we used a cutoff score for the BDI to diagnose depression in this sample and did not use a structured interview based on DSM-IV criteria. While a more accurate diagnosis of depression could have been obtained through a structured interview, the BDI has high sensitivity and specificity for diagnosing individuals with depression.[33]

Third, we did not take into account the timing of the insomnia episodes over the six-year period. This may have weakened the relationship between insomnia and depression, as past studies have noted the increased likelihood of depression based on recent insomnia incidence.[7,16]

CONCLUSION

The current study indicates that two or episodes of insomnia symptoms in non-depressed individuals significantly increase the rate in which depression occurs over time, which ultimately leads to higher risk of depression. Having persistent insomnia also increased the risk of suicidal ideation. This has implications for the prevention of depression and suicide in non-depressed individuals with persistent insomnia. Additionally, considering the remitting and recurring nature of insomnia symptoms compared to insomnia disorder, it will be important to measure insomnia at more than one time point when investigating consequent risks.

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DISCLOSURE STATEMENT

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