

## Insomnia affects future development of depression in workers: a 6-year cohort study

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### ABSTRACT

The purpose of this study was to investigate the relationship between insomnia and future risk of developing depression. This was a 6-year cohort survey from 2011 to 2017. A questionnaire was conducted with male workers in a manufacturing industry. The questions included the Center for Epidemiologic Studies Depression Scale (CES-D) for evaluating depression and the Athens Insomnia Scale (AIS) for rating insomnia. Data from 1,332 daytime workers aged less than 60 years who had no depressive symptoms at baseline were analyzed. The risk of developing depression in the future was associated with insomnia at baseline, after adjusting for age (hazard ratio [HR] 1.64). Even after adjusting for the covariances of job type, living with family, sleeping time, and undergoing treatment or taking medication, insomnia was associated with the onset of future depression (HR 1.58). In addition, the HR increased as the total AIS score increased: total AIS score 1–3 points (HR 1.99; 95% CI 1.23–3.22), 4–5 points (HR 3.58; 95% CI 2.18–5.89), and 6 points and above (HR 4.24; 95% CI 2.49–7.21). The risk of developing depression in the future increased in correlation with greater severity of insomnia at baseline, suggesting that even slight insomnia can be a risk of future developing depression. It may be important to measure the level of insomnia using an indicator such as AIS, and to improve sleep quality in workers to prevent depression.

Keywords: depression, insomnia, CES-D, AIS, workers

#### Abbreviations:

CES-D: Center for Epidemiologic Studies Depression Scale

AIS: Athens Insomnia Scale

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### INTRODUCTION

Depression is often accompanied by insomnia. Recent studies have also found that persistent insomnia is associated with a high risk of future depression.<sup>1</sup> One study found that insomnia lasting more than 2 weeks is a risk factor for future depression,<sup>2</sup> and another study reported that elderly people aged 65 years and older who had insomnia had a three times greater risk for

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developing depression after 3 years.<sup>3</sup> A 3-year Japanese follow-up survey of community residents aged 65 years and older found that the risk of developing depression was about 1.6 times greater in those with sleep onset disturbance.<sup>4</sup> Other studies have also pointed out that insomnia is strongly linked to fatigue and depression.<sup>5-9</sup> In a previous study, we demonstrated that insomnia could be a risk factor for future depression in workers,<sup>10</sup> as well as an association between job stress and insomnia.<sup>11</sup> In addition, our 3-year cohort study showed an association between a higher severity of insomnia and a higher onset of developing depression in the future.<sup>12</sup> However, there are few cohort studies of over 5 years regarding insomnia and depression in Japanese workers. In order to obtain more reliable data on workers, the authors performed a long-term study of 6 years. In this study, we conducted a 6-year cohort study to confirm the relationship between the risk of developing depression and the severity of insomnia as well as insomnia itself.

Insomnia can be both a risk for and a consequence of depression.<sup>13</sup> Improving sleep quality might reduce the risk for future onset of depression, and could be a useful measure for the prevention of depression. Mental health is a major issue in the workplace and effective countermeasures are required. The aim of this study was to investigate the relationship between insomnia and future risk of developing depression in workers. It is important and useful to clarify the link between insomnia and the development of depression in workers, and then to consider the preventive measures in the workplace.

## METHODS

### *Subjects*

About 2,000 male workers employed at a manufacturing workplace were asked to complete a self-administered questionnaire survey at the same time as their annual health checkup between May and July. Only day workers were selected as study subjects because there were very few shift workers in this workplace. Questionnaires were distributed about 1 week before health checkups and collected with consent on the day of the checkup. This was a 6-year cohort survey conducted from 2011 to 2017. Questionnaires were distributed to 1,871 workers in 2011, 1,929 workers in 2012, 2,060 workers in 2013, 2,035 workers in 2014, 2,020 workers in 2015, 2,144 workers in 2016 and 2,067 workers in 2017. The numbers of respondents who provided consent were 1,608 in 2011 (collection rate 85.9%), 1,788 in 2012 (92.7%), 1,850 in 2013 (89.8%), 1,833 in 2014 (90.1%), 1,785 in 2015 (88.4%), 1,810 in 2016 (84.4%), and 1,819 in 2017 (88.0%). After excluding about 50 subjects with a history of, or currently being treated for, mental disorder and sleep apnea syndrome, then the study subjects were limited to day workers under 60 years old: 1,258 workers in 2011, 1,381 in 2012, 1,433 in 2013, 1,489 in 2014, 1,331 in 2015, 1,407 in 2016 and 1,408 in 2017. The Center for Epidemiologic Studies Depression Scale (CES-D)<sup>14</sup> was used to measure depression. A cutoff of 16 points can generally be used when evaluating depression with the CES-D. Therefore, subjects with a CES-D score of <16 points in the first survey (baseline) in each year were selected as the cohort in this study. As a result, the subjects at baseline selected in each year were 739 in 2011, 248 in 2013, 87 in 2014, 58 in 2015, and 200 in 2016. In total 1,332 workers (mean age 38.8±14.3 years) constituted the study cohort.

This study was approved by the Ethics Committee of Nagoya University Graduate School of Medicine (No.1120-2).

### *Basic attributes and lifestyle habits*

Workers completed a self-administered survey questionnaire that asked about age, work format (day work or shift work), living situation (living with family or alone), job type (clerical job,

technical, sales, and other), overtime work (mean number of hours per week, excluding holidays), commuting time, mean sleep duration (mean number of hours on work days), and medical treatment/medication status (undergoing treatment or taking medication). In addition, the health checkup interview sheet was used to investigate lifestyle habits such as whether and how often the worker exercised (response choices of Yes or No), smoking status (response choices of Yes, Past or No) and alcohol consumption (response choices of Daily, Sometimes or No). These same questions were asked each year.

### *CES-D*

The CES-D was developed by the United States National Institute of Mental Health as a scale for detecting depression in the general population. It is short and simple, consisting of 20 items, and has well-established reliability and validity. The Japanese version of the CES-D has high equivalence with the original, and its reliability and validity have also been confirmed.<sup>14</sup> Each question asks about the frequency of a symptom in the week before taking the test, and is rated on a 4-point scale of 0, 1, 2 or 3. The total score from all 20 questions is calculated, with higher scores considered to indicate greater severity of depression. The highest possible score is 60, the lowest is 0, and 16 is considered the cutoff point of depression: people with a total CES-D score of 16 points or more can be suspected of having depression. In this survey, workers with a total CES-D score of 16 points or more were defined as having depression and those with less than 16 points were defined as not having depression.

### *Sleep quality*

Sleep quality was investigated using the Athens Insomnia Scale (AIS),<sup>15,16</sup> a world-wide evaluation method of insomnia, which was proposed by the World Health Organization. The Japanese version of the AIS has been validated and has a Cronbach alpha of 0.78 to 0.88.<sup>17</sup> It has been used by some Japanese researchers to study the circumstances of insomnia.<sup>18-20</sup> Eight sleep factors are investigated in the AIS: time needed to fall asleep after going to bed (sleep induction), awakenings during sleep (nocturnal awakening), waking up earlier than desired and subsequently remaining awake (early morning awakening), sufficiency of total sleep duration (total sleep duration), satisfaction with overall sleep quality regardless of length of sleep (sleep quality), mood during the day, daily activities and daytime sleepiness. Each response is selected from a four-point scale of 0 (no problem), 1 (minor problem), 2 (considerable problem) and 3 (severe problem such as sleepless all night). Insomnia is evaluated from the total score of the eight AIS questions with a total of less than 4 points defined as no problem, 4-5 points warrants consultation with a doctor if possible (insomnia possible) and 6 or more points warrants consultation with a doctor (insomnia suspected). According to total AIS scores of the present subjects, the severity of insomnia was divided into four categories of 0 points, 1-3 points, 4-5 points, and 6 points or more for the analysis.

### *Analytical method*

Subjects without depression (CES-D score less than 16) at baseline were included in the analysis and those with depression (CES-D score of 16 or more) were excluded. Subjects with CES-D scores of 16 or more in the subsequent annual surveys were defined as having developed depression. Using the 1,332 subjects without depression (CES-D score less than 16), age-adjusted Cox regression analysis was applied to factors including basic attributes, lifestyle habits and insomnia status at baseline, and subsequent risk of developing depression. The analysis found that items with  $p < 0.05$  were living situation, sleep duration, medical treatment/medication status, and AIS items. The item of job type showed borderline significance ( $p=0.077$ ) with depression,

indicating that it could be a factor affecting mental health. Hence, job type was also added as a covariate in this study. The risk of developing depression based on insomnia severity (AIS score classification) was then investigated by Cox regression analysis after adjusting for age together with job type, living situation, sleep duration, and medical treatment/medication status. SPSS 25.0J was used for the analysis.

## RESULTS

### *Basic attributes and lifestyle habits*

Analysis of the 1,332 subjects without depression at baseline revealed that the mean age  $\pm$  standard deviation was  $38.8 \pm 14.3$  years, about 28% were smokers, and about 25% drank alcohol every day. About 18% of the subjects were undergoing medical treatment or taking medication for some kind of illness. About 74% of the subjects answered that they worked overtime, and the mean duration of overtime per week was 7 hours. Mean sleep duration was about 6 hours. The mean AIS score was  $2.7 \pm 2.1$  and the mean CES-D score was  $9.1 \pm 3.9$  (Table 1).

**Table 1** Basic attributes and lifestyle habits of 1,332 subjects without depression at baseline

Attribute	Value
Age, years <sup>1</sup>	38.8 $\pm$ 14.3
Lives with family <sup>2</sup>	829 (62.4)
One-way commute time, minutes <sup>1</sup>	35.8 $\pm$ 56.4
Smokes (Yes) <sup>2</sup>	375 (28.2)
Exercises ( $\geq 30$ minutes, $\geq 2$ times/week for more than 1 year) <sup>2</sup>	343 (25.8)
Daily alcohol consumption <sup>2</sup>	336 (25.2)
Works overtime <sup>2</sup>	986 (74.0)
Overtime work hours (h/week) <sup>1</sup>	6.9 $\pm$ 8.9
Average sleeping time <sup>1</sup>	6.4 $\pm$ 0.9
Undergoing treatment or taking medication <sup>2</sup>	244 (18.3)
Mean AIS <sup>3</sup> score <sup>1</sup>	2.7 $\pm$ 2.1
Mean CES-D <sup>4</sup> score <sup>1</sup>	9.1 $\pm$ 3.9

1: Mean (standard deviations).

2: Number of subjects (percentage).

3: AIS: Athens Insomnia Scale.

4: CES-D: Center for Epidemiologic Studies Depression Scale.

### *Lifestyle habits associated with future depression*

The 1,332 subjects with CES-D scores below 16 at baseline were followed up from 2011 to 2017 in this cohort study. The mean observation period was 2.9 years and 352 subjects (incidence rate 26.4%) developed depression (CES-D score 16 or more) during the 6-year follow-up period.

Age-adjusted Cox regression analysis was applied to the lifestyle habits shown in Table 1 to identify which habits were risk factors for future depression. The age-adjusted analysis (Table 2) identified a risk associated with AIS insomnia scale scores (score 0 (reference), hazard ratio

[HR] 1.64; 95% confidence interval [CI] 1.45–1.86,  $p < 0.001$ ), as well as a risk associated with undergoing medical treatment or taking medication (HR 2.22; 95% CI 1.63–3.03,  $p < 0.001$ ) and a risk related to living alone without family (HR 1.13; 95% CI 1.04–1.23,  $p < 0.05$ ). In addition, the risk was associated with a shorter sleeping duration (HR 0.88; 95% CI 0.77–1.00,  $p < 0.05$ ), and job type (HR 1.06; 95% CI 0.99–1.13,  $p < 0.1$ ). No significant differences were found in other lifestyle habits such as smoking, drinking and exercise.

After adjusting all covariates in Table 2 (living situation, sleep duration, medical treatment/medication status and job type) and age, the risk of insomnia for future depression was 1.58 times greater than the risk of no insomnia (score 0 (reference), HR 1.58; 95% CI 1.39–1.79,  $p < 0.001$ ) (Table 3). When examined in detail, the HR increased as the AIS total score increased: the risk was 1.99 times greater at 1–3 points (HR 1.99; 95% CI 1.23–3.22,  $p = 0.005$ ), 3.58 times greater at 4–5 points (HR 3.58; 95% CI 2.18–5.89,  $p < 0.001$ ), and 4.24 times greater at 6 points and above (HR 4.24; 95% CI 2.49–7.21,  $p < 0.001$ ).

**Table 2** Risk of developing depression associated with each baseline attribute and lifestyle habits, based on age-adjusted Cox regression analysis

Attribute (baseline)	Adjusted for age HR <sup>1</sup>	95% CI <sup>3</sup>	<i>p</i> value
Job type (clerical job, technical, sales, the others)	1.06	0.99–1.13	0.077
Living with family	1.13	1.04–1.23	0.005
One-way commute time	1.00	0.99–1.00	0.997
Smokes (No, Past, Yes)	0.98	0.87–1.12	0.781
Exercises ( $\geq 30$ minutes, $\geq 2$ times/week for more than 1 year) (No, Yes)	1.03	0.80–1.33	0.827
Alcohol consumption (No, Sometime, Daily)	0.93	0.80–1.08	0.327
Overtime work (h/week)	0.99	0.97–1.00	0.144
Sleeping time (h)	0.88	0.77–1.00	0.048
Undergoing treatment or taking medication	2.22	1.63–3.03	$< 0.001$
Total AIS <sup>2</sup> score (0, 1–3, 4–5, $\geq 6$ )	1.64 <sup>4</sup>	1.45–1.86	$< 0.001$

1: HR: hazard ratios.

2: AIS: Athens Insomnia Scale.

3: 95% CI: 95% confidence intervals.

4: Score 0 (reference).

**Table 3** Risk of developing depression by severity of insomnia, based on Cox regression analysis in 2011–2017

Attribute (baseline)	n (%)	Depression (CES-D <sup>4</sup> ≥16)		No depression (CES-D <sup>4</sup> <16)		Adjusted for age		Adjusted for factors in footnote <sup>1</sup>	
		n (%)	n (%)	n (%)	n (%)	HR <sup>2</sup>	95% CI <sup>5</sup>	p value	HR <sup>2</sup>
Total AIS <sup>3</sup> score (0, 1–3, 4–5, ≥6)	1332 (100)	320 (24.0)	1012 (76.0)	1.64 <sup>6</sup>	1.45–1.86	<0.001	1.58 <sup>6</sup>	1.39–1.79	<0.001
Total AIS <sup>3</sup> score (0)	199 (14.9)	19 (9.5)	180 (90.5)	1			1		
Total AIS <sup>3</sup> score (1–3)	710 (53.4)	144 (20.3)	566 (79.7)	2.14	1.32–3.45	0.002	1.99	1.23–3.22	0.005
Total AIS <sup>3</sup> score (4–5)	283 (21.2)	97 (34.3)	186 (65.7)	3.93	2.40–6.42	<0.001	3.58	2.18–5.89	<0.001
Total AIS <sup>3</sup> score (≥6)	140 (10.5)	60 (42.9)	80 (57.1)	4.97	2.97–8.33	<0.001	4.24	2.49–7.21	<0.001

1: Adjusted for factors in footnote (age, job type, living with family, sleeping time, and undergoing treatment or taking medication).

2: HR: hazard ratios.

3: AIS: Athens Insomnia Scale.

4: CES-D: Center for Epidemiologic Studies Depression Scale.

5: 95% CI: 95% confidence intervals, 6: Score 0 (reference).

## DISCUSSION

In this 6-year cohort study, we investigated the association between insomnia and future risk for developing depressive symptoms in male workers without depression. Insomnia was found to be a high-risk factor for future depression, as shown in Tables 2 and 3. Furthermore, the risk of developing depression increased with severity of insomnia. The risk for depression was about 3.6 times greater in workers with AIS scores of 4–5, and 4.2 times greater in those with AIS scores of 6 and above, even after adjusting for other relevant factors. In general, AIS scores of 4–5 are suggestive of insomnia and scores of 6 and above are strongly suggestive of insomnia. Our study showed that subjects with these AIS scores also had a considerably increased risk of future depression. These results suggest that the risk for future depression can be predicted by measuring the severity of insomnia, and that improving insomnia may contribute to the prevention of depression in the workplace.

Previous studies have similarly found a strong link between insomnia and depression,<sup>5-7</sup> and have shown that people with persistent insomnia are likely to go on to develop depression.<sup>4,21,22</sup> For example, a 3-year follow-up study of subjects aged 21–30 years found that the risk of developing depression was four times higher in subjects with insomnia than those without insomnia.<sup>21</sup> A 1-year longitudinal study in subjects aged 50 years and older had similar results, although in this case the correlation was found only in female and elderly subjects.<sup>22</sup> In Japan, a 3-year follow-up study of community residents aged 65 years and older had reported that those with insomnia had a 1.6 times greater risk of developing depression.<sup>4</sup> However, there are few studies on the relationship between insomnia and future depression in workers. We previously conducted a 2-year survey<sup>10</sup> and a 3-year survey<sup>11</sup> on workers, and these studies also indicated that insomnia can be a risk of developing depression in the workplace. After extending the survey period to 6 years, the results of this cohort study confirmed the association between insomnia and future depression onset, and also a positive correlation between severity of insomnia and future depression development. This survey also showed that even workers with mild insomnia (AIS score 1–3) are at risk for depression. Even workers with mild insomnia may require some degree of healthcare to prevent depression.

This study showed that insomnia was strongly related to future depression in workers. This indicates the importance of focusing on sleep as a key aspect for promoting mental health activities in the workplace. In this survey, we measured the state of insomnia using the AIS. The use of AIS may be a useful tool to examine the sleeping state. The severity of insomnia rated by the AIS scores was associated with the risk for future depression. It is hence considered that the objective assessment of insomnia is important to assess the risk for depression. Moreover, it is suggested that based on the assessment of insomnia, support measures to improve insomnia among workers may be effective in preventing depression in the workplace. Health activities such as health education and counseling for sleep might contribute to preventing depression. Further intervention studies will be needed on this matter.

This study had the following limitations. Firstly, the results were based entirely on surveys using self-administered questionnaires. Depression and insomnia were not diagnosed clinically. Secondly, this survey did not include a detailed investigation of job stress, although in previously published research we demonstrated a link between insomnia and job stress.<sup>11</sup> It is generally considered that job stress has a considerable effect on insomnia in workers, and other research has demonstrated a link between workload and insomnia,<sup>23</sup> an association between low control and increased sleep disturbance,<sup>23,24</sup> and greater interpersonal conflict and less social support among people with insomnia.<sup>5,25-27</sup> Further studies may be required to examine associations among insomnia, depression, and job stress. The third limitation was that this study only analyzed male

day workers in a manufacturing industry. Further investigation will be required with broader surveys encompassing other industries, shift workers, and female workers. Despite these limitations, this study showed that insomnia was a risk of developing future depression, and the risk increased with severity of insomnia. These findings will be helpful for promoting mental health activities in the workplace.

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### CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

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