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## Original article

## Association Between Insomnia and Constipation: A Multicenter Three-year Cross-sectional Study Using Shift Workers' Health Check-up Data

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## ABSTRACT

**Background:** Although insomnia and constipation are highly prevalent worldwide, studies examining a possible association between them are lacking. We examined the relationship between insomnia and constipation in shift workers who have a high prevalence of insomnia and other diseases.

**Methods:** This study had a multicenter cross-sectional design and conducted using health examination data including self-reported questionnaires. In total, 12,879 and 4,650 shift workers were enrolled in Severance Hospital and Wonju Severance Hospital, respectively, during 2015–2017. Multivariate logistic regression models and subgroup analysis were performed in each center with the same protocol, using a common data model.

**Results:** The mean age of the total population was 44.35 (standard deviation = 8.75); the proportion of males was 56.9%. Female sex, being underweight and non-smoker were strongly associated with an increased risk of constipation symptom ( $p < 0.001$ ). Pooled odds ratios (ORs) were calculated using ORs of both centers with weights; there was a significant dose–response relationship (sub-threshold 1.76 [95% confidence interval [CI] 1.62–1.91]; moderate 2.28 [95% CI 2.01–2.60]; severe 4.15 [95% CI 3.18–5.41] in the final model,  $p$  for trend  $< 0.001$ ). Subgroup analysis performed by stratifying sex and pooled ORs showed a similar trend to that of the entire group.

**Conclusion:** We observed a strong correlation between insomnia and constipation in this population. Our findings may help in formulating guidelines and policies to improve quality of life in shift workers through the management of sleep quality and proper bowel function. This study is the first to report this relationship among people working in shifts.

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### Statement of significance

This study is the first to report the relationship between sleep disturbance and constipation among people working in shifts. Our findings suggest clinicians involved in prescribing medication for sleep to consider constipation as comorbidity status. Furthermore, the role of gastrointestinal dysfunction including constipation should be highlighted when considering the management and control of sleep quality. Finally, this study laid down the foundation for future prospective cohort studies that are needed to better understand the causal relationship between insomnia and constipation.

## 1. Introduction

Insomnia is one of the most common health problems worldwide and is linked to various diseases. The America Insomnia Survey estimated the prevalence of insomnia according to Diagnostic and Statistical Manual of Mental Disorders-fourth edition-text revision as 22.1% [1]. Using the same data, four cardinal night-time symptoms, namely, insomnia, difficulty in initiating sleep, difficulty in maintaining sleep, early morning awakening, and nonrestorative sleep, were proved to be related to several mental and physical conditions including high blood pressure, arthritis, headaches, depression, and digestive symptoms [2]. Furthermore, approximately 20% of people were reported to have insomnia symptoms in South Korea, which indicates that insomnia is highly prevalent [3,4].

There is a considerable relationship between shift work and sleep dysfunction due to irregular circadian rhythm. In general, when workers work outside of typical “nine-to-five” workday, it is called shift work. This usually includes assignments outside of traditional daytime hours, including fixed early morning, evening, and night work, in addition to roster work, and two or more shift rotations [5,6]. Several recent studies confirmed that shift work increases the odds of sleep disturbance and results in a higher probability of various diseases [7–9]. Particularly, many studies elucidated a correlation between sleep dysfunction and gastrointestinal disorders [10–13]. Even though it is evident that shift work and insomnia are related to gastrointestinal disorders such as gastroesophageal reflux disease (GERD) or inflammatory bowel disease (IBS), there is a lack of studies focusing on constipation, which is an important factor affecting quality of life. One study suggested that the constipation symptom in constipation-predominant IBS is improved by melatonin administration; however, it merely focused on IBS, not constipation [14].

The prevalence of functional constipation is 7.8%, which is approximately 5 times larger than that of opioid-induced constipation [15]. Despite this prevalence, constipation is often overlooked because it is not considered a significant factor leading to mortality. However, some studies suggest that constipation is associated with an increased risk of gastrointestinal cancers, cardiovascular diseases, and even death [16–18]. The American Gastroenterological Association’s Technical Review on Constipation identified the following risk factors: low socioeconomic status; low parental education rates; less physical activity; medication; depression; and stressful life events, among others [19].

To this end, there is a lack of reports evaluating the relationship between sleep dysfunction and constipation, although there might be a possible link between insomnia and constipation, which could

be interpreted by the sympathetic nerve system [20]. It is well known that shift work is associated with insomnia [21,22]; therefore, other health effects should also be explored. Hence, our study aimed to elucidate the relationship between sleep dysfunction and constipation in shift workers using a comprehensive analysis of our multicenter data.

## 2. Materials and methods

### 2.1. Data set

Common data models (CDMs) of Korea Workers Health Examination (KWHE) among nine hospitals in Korea were conducted and two hospitals (Severance and Severance Wonju) were included in this study. CDM is a tool to facilitate data standardization and sharing between heterogeneous local database systems [23]. KWHE-CDM harmonizes the multiple disparate databases into four domains: general measurement, common questionnaire, special questionnaire, and night questionnaire. The general terminology was standardized using Systematized Nomenclature of Medicine-Clinical Terms, Logical Observation Identifiers Names and Codes, and Nebraska Lexicon, and the questionnaires were standardized into KWHE-defined coding [23].

In the current study, we included participants from two hospitals based on the following criteria: age  $\geq 30$  years and shift worker who answered special night questionnaires in 2015, 2016, and 2017. Age criteria was established regarding previous studies [24,25]. Special night questionnaires in check-up are performed when the workers take up night works four times per month. The exclusion criteria were as follows: examinees who did not answer insomnia and constipation questionnaires; being engaged in shift work for less than 5 years; age below 30 years; and examinees who had missing essential data in each category of the questionnaire. Among a total of 142,157 examinees (76,119 in Seoul and 66,038 in Wonju), 42,690 answered night-shift worker health examination (25,137 in Seoul and 17,553 in Wonju), and 17,529 participants (12,879 in Seoul and 4,650 in Wonju) were finally enrolled in this study, after excluding workers who had missing data of variables including insomnia severity, presence of constipation symptom, BMI, exercise, smoking history, working hour, working interval, working year, or shift type.

The study protocol was in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of Severance Hospital (IRB: Y-2020-0011). The need for obtaining informed consent from the participants was waived due to the retrospective nature of this study.

### 2.2. Definition and evaluation of data

The primary outcome of the study was the presence of constipation symptom. Participants were asked to indicate any symptoms they had during the last 6 months, with subcategories of gastrointestinal problems including constipation. The response options were “severe,” “mild,” and “none.” The presence of constipation symptom was defined when the answer was “mild” or “severe” to the constipation subcategory in the special questionnaire of health check-up.

Insomnia was measured using the Insomnia Severity Index (ISI) questionnaire, which has been broadly used as a reliable scale of insomnia. ISI is a useful survey tool to quantify insomnia severity [26] and was also proved to be valid in Korea [27]. Each question of ISI is rated according to the 5-point Likert scale, yielding a total score ranging from 0 to 28. Based on the score, the participants were categorized into 4 groups, as follows: 0–7, absence of

insomnia; 8–14, sub-threshold insomnia; 15–21, moderate insomnia; and 22–28, severe insomnia [28].

Covariates used for adjusting confounders were body mass index (BMI), exercise, smoking history, and working profiles, such as working year, shift type, working hours, and working interval. The data of all these covariates were obtained from health check-up questionnaires and measurements. The obesity group was determined by the BMI and was defined as follows: underweight ( $<18.5$  kg/m<sup>2</sup>); normal (18.5–22.9 kg/m<sup>2</sup>); overweight (23–24.9 kg/m<sup>2</sup>); obese ( $\geq 25$  kg/m<sup>2</sup>). Workers who did high- or medium-intensity exercise more than twice a week on average were classified as the “exercise group,” while the others were classified as the “non-exercise group.” Smoking history was stratified into three groups: “non-smoker,” “ex-smoker,” and “current-smoker.” Shift type was divided into “three shifts” and “others,” which is not included in the three shifts group. In a previous study by the ILO, work for more than 15 years was classified as long-term work, so we divided the period of work into two groups in this study [29,30]. The three-shift system consists of day shift, evening shift, and night shift to provide coverage 24/7. The traditional form of three-shift work is an 8-hour shift schedule with shifts starting at 7 am (day), 3 pm (evening), and 11 pm (night) [31]. Based on the maximum allowable working hours in accordance with Article 50 and Article 51 of the Korean Labor Standards Act, long working hours per week was defined when a participant worked for more than 52 hours per week [32,33]. Working interval was defined as the interval between the end of the previous shift and the beginning of the next shift. Short working interval was defined when a worker returned to work within 11 hours after the end of their previous shift.

### 2.3. Statistical analysis

The difference between examinees with and without constipation was compared using the independent t-test and the chi-square test for continuous data and categorical data, respectively. Odds ratio (ORs) with 95% confidence intervals (CIs) of constipation were calculated using the multiple logistic regression model. Several covariates, including baseline characteristics, work-related factors, lifestyle, and related conditions, were included in multivariate logistic regression models. Each medical institution analyzed its own data with the same statistical methods. Pooled ORs and 95% CIs of constipation were calculated using the weight obtained through the standard error. The fixed-effect model was used when all results of *p*-value in heterogeneity tests were below 0.05. Sensitivity analyses were further performed as follows. First, subgroup analyses stratified by sex were performed in each center. Second, time-serial ORs and 95% CIs were estimated using stratification analysis for each year. Third, other various symptoms including headache and body mass were adjusted in the models to consider reporting bias of workers. All statistical tests were two-sided, and a *p*-value of less than 0.05 was considered statistically significant. All statistical analyses were performed using R, version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria).

### 3. Results

Table 1 summarizes the characteristics of shift-workers with and without a constipation symptom. The mean age of the total population was 44.35 (standard deviation = 8.75); the proportion of males was 56.9%. Factors such as female sex, smoking history, and being underweight and a non-smoker were strongly associated with an increased risk of constipation symptom ( $p < 0.001$ ). In terms of working profiles, working year, working hour, and working interval were all associated with the presence of constipation symptom. Most shift workers were in the three shifts group

**Table 1**  
Prevalence of constipation by characteristics of examinees

Variable	Normal	Constipation	<i>p</i> -value
<b>Insomnia</b>			$<0.001$
None	8625 (84.00%)	1643 (16.00%)	
Sub-threshold	4156 (74.39%)	1431 (25.61%)	
Moderate	984 (69.30%)	436 (30.70%)	
Severe	147 (57.87%)	107 (42.13%)	
<b>Age (<math>\geq 30</math>years)</b>			$<0.001$
Mean (SD)	44.65 (8.76)	43.20 (8.63)	
<b>Age group</b>			$<0.001$
30–39	4494 (76.07%)	1414 (23.93%)	
40–49	5273 (80.04%)	1315 (19.96%)	
50–59	3549 (81.81%)	789 (18.19%)	
$\geq 60$	596 (85.76%)	99 (14.24%)	
<b>Sex</b>			$<0.001$
Female	5267 (69.72%)	2287 (30.28%)	
Male	8645 (86.67%)	1330 (13.33%)	
<b>Smoking history</b>			$<0.001$
Non-smoker	7103 (75.24%)	2338 (24.76%)	
Ex-smoker	2978 (84.75%)	536 (15.25%)	
Current smoker	3831 (83.76%)	743 (16.24%)	
<b>BMI</b>			$<0.001$
Underweight	5019 (75.34%)	1643 (24.66%)	
Normal	547 (74.22%)	190 (25.78%)	
Overweight	3432 (81.27%)	791 (18.73%)	
Obese	4914 (83.19%)	993 (16.81%)	
<b>Exercise</b>			$<0.001$
Yes	5974 (83.38%)	1191 (16.62%)	
No	7938 (76.59%)	2426 (23.41%)	
<b>Working hour</b>			0.04
$<52$ hours	11,259 (79.06%)	2982 (20.94%)	
$\geq 52$ hours	2653 (80.69%)	635 (19.31%)	
<b>Working interval</b>			0.017
Long	11,449 (79.71%)	2914 (20.29%)	
Short	2463 (77.80%)	703 (22.20%)	
<b>Shift type</b>			0.067
Three shifts	10,899 (79.07%)	2885 (20.93%)	
Others	3013 (80.45%)	732 (19.55%)	
<b>Working year</b>			$<0.001$
$<15$ years	7327 (77.36%)	2144 (22.64%)	
$\geq 15$ years	6585 (81.72%)	1473 (18.28%)	

SD, standard deviation.

(78.6%), and the others were stratified into two shifts (14.4%), every other day (2.11%), fixed (1.22%), irregular (3.60%). Table 2 summarizes the characteristics of shift-workers according to insomnia. The mean age of non-insomnia group was older compared to other insomnia groups. (mean (SD) 44.96 (8.89),  $p < 0.001$ ) Workers with working 52 hours or more ( $p = 0.018$ ), three shifts, and short working interval ( $p < 0.001$ ) had a significantly higher prevalence of insomnia.

Fig. 1a shows the prevalence of constipation stratified by sex and age. Males have a similar prevalence of constipation regardless of age, and the prevalence of constipation tends to increase in female as their age decreases. Fig. 1b shows the association between insomnia and constipation stratified by sex. It shows that females have a higher prevalence of constipation than males, and constipation and insomnia are positively correlated to each other.

Table 3 shows the pooled ORs and 95% CIs for the constipation symptom in workers stratified by ISI scores using multivariate logistic regression models. Model 0 was for univariate logistic regression, and the pooled OR of constipation increased as insomnia worsened. Models 1, 2, and 3 were sequentially performed by adding covariates to adjust for possible confounding bias. Model 1 was compensated with baseline covariates (age and sex). Factors related to health effects and lifestyle (BMI, exercise, smoking history) were added as

**Table 2**  
Prevalence of insomnia by characteristics of examinees

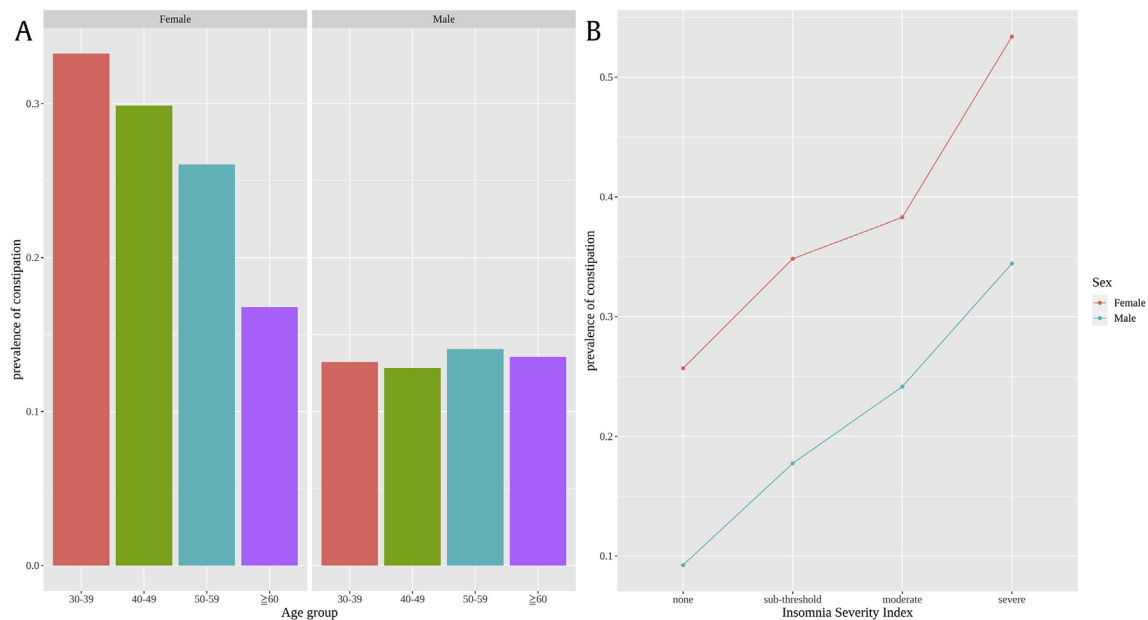
Variable	None	Mild	Moderate	Severe	p-value
<b>Constipation</b>					<0.001
No	8625 (62.00%)	4156 (29.87%)	984 (7.07%)	147 (1.06%)	
Yes	1643 (45.42%)	1431 (39.56%)	436 (12.05%)	107 (2.96%)	
<b>Age</b>					<0.001
Mean (SD)	44.96 (8.89)	43.63 (8.48)	42.87 (8.45)	43.76 (8.40)	
<b>Sex</b>					<0.001
Female	4221 (55.88%)	2572 (34.05%)	658 (8.71%)	103 (1.36%)	
Male	6047 (60.62%)	3015 (30.23%)	762 (7.64%)	151 (1.51%)	
<b>Age group</b>					<0.001
30–39	3226 (54.60%)	2011 (34.04%)	577 (9.77%)	94 (1.59%)	
40–49	3896 (59.14%)	2120 (32.18%)	491 (7.45%)	81 (1.23%)	
50–59	2624 (60.49%)	1308 (30.15%)	329 (7.58%)	77 (1.78%)	
≥60	522 (75.11%)	148 (21.29%)	23 (3.31%)	2 (0.29%)	
<b>Body Mass Index</b>					<0.001
18.5–22.9	3751 (56.30%)	2203 (33.07%)	607 (9.11%)	101 (1.52%)	
<18.5	380 (51.56%)	271 (36.77%)	74 (10.04%)	12 (1.63%)	
23–24.9	2533 (59.98%)	1307 (30.95%)	320 (7.58%)	63 (1.49%)	
≥25	3604 (61.01%)	1806 (30.57%)	419 (7.09%)	78 (1.32%)	
<b>Smoking history</b>					0.053
Non-smoker	5411 (57.30%)	3092 (32.75%)	805 (8.53%)	134 (1.42%)	
Ex-smoker	2119 (60.30%)	1077 (30.65%)	270 (7.68%)	48 (1.37%)	
Current-smoker	2738 (59.87%)	1418 (31.01%)	345 (7.54%)	72 (1.57%)	
<b>Working hours</b>					0.018
<52 hrs	8389 (58.91%)	4527 (31.79%)	1135 (7.97%)	190 (1.33%)	
≥52 hrs	1879 (57.15%)	1060 (32.24%)	285 (8.67%)	64 (1.95%)	
<b>Shift type</b>					<0.001
Three shifts	7891 (57.24%)	4502 (32.66%)	1183 (8.58%)	209 (1.52%)	
Others	2377 (63.49%)	1085 (28.98%)	237 (6.33%)	45 (1.20%)	
<b>Working interval</b>					<0.001
Long	8655 (60.26%)	4432 (30.86%)	1085 (7.55%)	191 (1.33%)	
Short	1613 (50.95%)	1155 (36.48%)	335 (10.58%)	63 (1.99%)	
<b>Working year</b>					0.163
<15 yrs	5574 (58.86%)	3023 (31.92%)	752 (7.94%)	121 (1.28%)	
≥15 yrs	4694 (58.25%)	2564 (31.82%)	668 (8.29%)	13 (1.65%)	

SD, standard deviation.

covariates for Model 2. In this model, among shift workers, the OR for constipation was 4.17 (95% CI 3.20–5.44) times higher in the group with severe insomnia than the group without insomnia. Working profiles (working year, shift type, working interval, working hour) were finally added to Model 3. There was no significant change in the

trend of the pooled ORs for constipation with insomnia during the process of adding covariates.

The final Model 3 in Seoul had significantly increased pooled ORs for constipation with insomnia (OR: sub-threshold 1.76 [95% CI 1.62–1.91]; moderate 2.28 [95% CI 2.01–2.60]; and severe 4.15 [95%



**Fig. 1.** a) Prevalence of constipation stratified by sex and age. (b) Association between insomnia and constipation stratified by sex.

**Table 3**  
Pooled ORs and 95% CIs for constipation with insomnia

	Model 0	Model 1	Model 2	Model 3
<b>Insomnia</b>				
None	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Sub-threshold	1.82 (1.68–1.97)	1.77 (1.63–1.92)	1.76 (1.62–1.91)	1.76 (1.62–1.91)
Moderate	2.35 (2.07–2.66)	2.31 (2.03–2.63)	2.29 (2.02–2.61)	2.28 (2.01–2.60)
Severe	3.84 (2.98–4.95)	4.18 (3.21–5.44)	4.17 (3.20–5.44)	4.15 (3.18–5.41)
<i>p</i> for trend	<0.001			
<b>Sex</b>				
Female		1.00 (reference)	1.00 (reference)	1.00 (reference)
Male		0.35 (0.33–0.38)	0.30 (0.27–0.34)	0.29 (0.26–0.33)
<b>Age</b>		0.99 (0.99–1.00)	1.00 (0.99–1.00)	1.00 (0.99–1.00)
<b>BMI</b>				
Underweight			0.82 (0.68–0.98)	0.82 (0.68–0.98)
Normal			1.00 (reference)	1.00 (reference)
Overweight			0.97 (0.87–1.07)	0.97 (0.88–1.08)
Obese			0.88 (0.80–0.97)	0.88 (0.80–0.97)
<b>Exercise</b>				
Yes			1.00 (reference)	1.00 (reference)
No			1.24 (1.14–1.34)	1.24 (1.14–1.34)
<b>Smoking history</b>				
Non-smoker			1.00 (reference)	1.00 (reference)
Ex-smoker			1.32 (1.15–1.50)	1.33 (1.16–1.52)
Current smoker			1.33 (1.18–1.51)	1.33 (1.17–1.51)
<b>Working hours</b>				
<52 hours				1.00 (reference)
≥52 hours				1.05 (0.93–1.18)
<b>Working interval</b>				
Long				1.00 (reference)
Short				1.07 (0.97–1.18)
<b>Working year</b>				
<15 years				1.00 (reference)
≥15 years				0.99 (0.90–1.10)
<b>Shift type</b>				
Three shifts				1.00 (reference)
Others				1.05 (0.93–1.19)

Data presented as OR (95% CI).

Model 0: crude model.

Model 1: adjusting for age and sex.

Model 2: Model 1 + adjusting for BMI, exercise, and smoking history.

Model 3: Model 1 + adjusting for working year, shift type, working interval, and working hours.

OR, odds ratio; CI, confidence interval.

**Table 4**  
Pooled ORs and 95% CIs for constipation with insomnia stratified by sex

	Model 0	Model 1	Model 2	Model 3
<b>Insomnia (male)</b>				
None	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Sub-threshold	2.20 (1.93–2.50)	2.18 (1.91–2.48)	2.15 (1.89–2.45)	2.13 (1.87–2.43)
Moderate	3.34 (2.76–4.04)	3.29 (2.72–3.98)	3.21 (2.65–3.88)	3.12 (2.57–3.79)
Severe	5.52 (3.89–7.81)	5.43 (3.83–7.69)	5.40 (3.81–7.67)	5.22 (3.66–7.42)
<b>Insomnia (female)</b>				
None	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Sub-threshold	1.55 (1.39–1.72)	1.51 (1.36–1.68)	1.52 (1.36–1.69)	1.52 (1.36–1.69)
Moderate	1.80 (1.51–2.13)	1.72 (1.44–2.04)	1.74 (1.46–2.07)	1.74 (1.46–2.07)
Severe	3.29 (2.22–4.89)	3.18 (2.14–4.72)	3.23 (2.17–4.81)	3.23 (2.17–4.81)

Data presented as OR (95% CI).

Model 0: crude model.

Model 1: adjusting for age and sex.

Model 2: Model 1 + adjusting for BMI, exercise, and smoking history.

Model 3: Model 1 + adjusting for working year, shift type, working interval, and working hours.

OR, odds ratio; CI, confidence interval.

CI 3.18–5.41] compared to the absence of insomnia, *p* for trend <0.001). The dose–response relationship between constipation and insomnia was observed from the trend of pooled ORs. All models showed a strong association between the prevalence of insomnia and constipation, and the respective analysis for each center also shows a significant relationship between constipation symptom and insomnia. The complete versions of multiple logistic regression models in each center are summarized in [Supplementary Tables S1 and S2](#).

As shown in [Fig. 1b](#), females have a much higher prevalence of constipation symptom than males, subgroup analyses were performed by stratifying into sex. Pooled ORs and 95% CIs for constipation with insomnia divided by sex are summarized in [Table 4](#). The dose–response relationship and the positive relationship between constipation symptom and insomnia shown in [Table 2](#) was still preserved, and males showed a higher correlation. Results of all subgroup analyses in both centers are summarized in [Supplementary Tables S3–S6](#).



The results of other sensitivity analyses were further shown in [Supplementary Tables S7-S8](#). In time-series analysis by each year, association between insomnia and constipation was still significant ([Table S7](#)). Moreover, after adjusting various other symptoms including feeling lumps, headache, dizziness, forgetfulness, numbness, and poor concentration, the association was in the same direction ([Table S8](#)).

#### 4. Discussion

Our current study of a total of 17,529 shift workers showed that insomnia is considerably associated with constipation. Further adjustment for working hours, working interval, working year, shift type, and baseline characteristics such as age, sex, diabetes history, BMI, exercise, and smoking history did not attenuate the relationship. Moreover, there was a dose-response relationship, implying that with increasing severity of insomnia, the odds of constipation symptoms increased.

Several studies demonstrated that shift workers tend to report insomnia and other mental health problems such as depression more than other workers [21,34,35]. Therefore, shift workers may be prone to increased risks of other medical conditions. Sleep disorders are associated with functional gastrointestinal disorders (FGID), and patients with FGID frequently experience dyspepsia, IBS, and constipation [36]. Although IBS is relatively frequently studied among FGID, there is a dearth of investigation particularly for constipation. For example, the odds of IBS are almost two times higher in insomnia patients and show a high correlation ( $r = 0.32$ ) with increase in insomnia scores [37,38]. Those studies suggest that a link between the autonomic nervous system and the neuro-hormonal system may explain this association [39]. Notably, the autonomic nervous and neuro-hormonal systems are also related to constipation [40]. Although there is a paucity of studies particularly focused on constipation, in the current study, we highlighted the relationship between insomnia and constipation symptoms in a large, multicenter sample of Korean shift workers.

Further, many studies have focused on drug-induced or disease-related constipation [41–43]. Nonetheless, addressing chronic functional constipation is also crucial for improving the quality of life and reducing the risk of constipation-related comorbidities such as type 2 diabetes mellitus (DM), IBS, and GERD [16,17,44]. This result emphasizes the importance of controlling and preventing constipation to avoid the risk of constipation-related diseases. Our study suggests that insomnia could be one of the risk factors for constipation, a finding that was previously unknown. This finding could be the basis for an in-depth approach to prevent constipation in shift workers.

The increased odds of constipation with insomnia could be postulated as the function of the sympathetic and parasympathetic nervous systems [20]. The connection between the brain and the gastrointestinal system works through mechanisms involving entero-endocrine signaling using a network of the central, autonomic, and enteric nervous systems [20,45]. Circadian rhythm and sleep regulation pathways could be effected by the brain-gut axis in terms of the sympathetic and parasympathetic systems. As it is known that constipation-predominant IBS is closely related to central sympathetic effects within the brain-gut axis [46], further studies are warranted to clarify the pathophysiological relationship between constipation and sleep disturbance.

Based on our stratified analyses and logistic regression models, we found that females were at higher odds of experiencing constipation than males. This result could be due to several reasons including hormonal factors and damage to the pelvic muscle nerves associated with childbirth and gynecological surgery [47]. This study proved a strong relationship between insomnia and

constipation symptom even after performing subgroup analysis, which strengthens the validity of the results. Pooled OR in males presented a higher OR than that in females, which indicated that male shift workers with insomnia should be considered as a high-risk group and be managed well. In terms of age, our study showed reverse association of constipation with old age. According to Sanne et al., the probability of constipation in males and females was lowest around an age of 55 years and curves were U-shape [48]. Since most participants of our study were younger than 55, it could be inferred that the prevalence of constipation might show reverse association with old age, which was equivalent with the result of this study.

Current smoking was highly correlated to constipation in both centers, which supported the hypothesis that smoking is associated with constipation [49]. This result was converse to the result that the simple chi-square analysis showed. This implies that sex as a factor is much stronger than smoking as the proportion of non-smokers in females (91.7%) is higher than that in males (25.2%). There are relatively few studies examining the relationship between smoking and constipation compared to other gastrointestinal disorders such as peptic ulcers, GERD, IBS, cancer, and FGIDs [50–52]. Because constipation is highly prevalent and related to serious diseases, further study of an association between smoking and constipation is warranted [16,18].

Interestingly, workers who did not exercise also showed a positive correlation with the presence of constipation in this study. Several studies demonstrated that physical activity is associated with decreasing prevalence of constipation and improvement in the defecation pattern and constipation-related quality of life, especially in females [53–55]. Among them, a randomized controlled trial included 20–40-year-old obese women with constipation who underwent interventions of physical activity and a low-calorie diet. The results showed that physical activity and weight reduction significantly improved Patient Assessment of Constipation Symptoms and Patient Assessment Quality of Life scores [54].

This study has several strengths. First, the number of examinees included in the study is large. A multicenter study was conducted by gathering data from approximately 12,879 and 4,650 people in Seoul and Wonju, respectively, and similar results were obtained by applying the same data structure and analysis protocol through distributed CDM. Pooled ORs also add strength to the relationship between insomnia and constipation. Moreover, this finding differs from that of previous studies in that the group included in the study is a special group (night and shift workers) of young age. Lastly, because sleep disorders have not been studied much as a correlation to functional constipation, this study may support the need for sufficient research between these two variables in the future.

This study also has several limitations. First, because this study was cross-sectional, the correlation between constipation and sleep can be seen, but the causal relationship cannot be proved. Therefore, further studies are needed to analyze causal relations through cohort analysis. Second, reliable diagnostic criteria such as the Rome criteria were not used for the outcome of this study. However, constipation is a symptom of a disease, and the questionnaire containing the patient's experience was considered as a patient-reported outcome. Third, although most variables that show differences between groups or may affect the dependent variable were used for analysis as covariates, other variables such as alcohol intake, sleep disorder history that were unknown or not measured properly may have acted as confounding factors. However, this study enrolled a sufficient number of participants to dilute possible errors related to past history or lifestyle. Finally, our data do not include self-reports of the use of medication, such as opioids, or comorbidities that causes constipation [19].

We observed a strong correlation between sleep disturbances and constipation symptom among people working in shifts. Regarding this study, health education including sleep hygiene, increase in water and fiber intake, and regular physical exercise [56] can be implemented in workplaces. In addition, primary care physicians can take advantage of the fact that occupational factors and sleep disturbances may be related to constipation. In conclusion, this could be an opportunity to propose policies or prepare guidelines to improve the quality of life, especially for shift workers, through the management of sleep quality and proper bowel movements.

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### Conflicts of interest

All authors have no conflicts of interest to declare.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.shaw.2022.01.001>.

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