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Association between exposure to heavy metals  
in atmospheric particulate matter and sleep quality

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# Association between exposure to heavy metals in atmospheric particulate matter and sleep quality

A Master Thesis

Submitted to the Department of Public Health  
and the Graduate School of Yonsei University  
in partial fulfillment of the  
requirements for the degree of  
Master of Public Health

Byung Kwon Kim

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This certifies that the master thesis of Byung Kwon Kim is approved.

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The Graduate School

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## ABSTRACT

### **Association between exposure to heavy metals in atmospheric particulate matter and sleep quality**

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(Directed by Professor Jaelim Cho)

**Background:** Recent studies have demonstrated that long-term exposure to particulate matter (PM) is associated with poor sleep quality. However, no studies have linked PM constituents, particularly heavy metals, to sleep quality. This study investigated the association between exposure to heavy metals in PM and sleep quality.

**Methods:** We obtained nationwide data from the Korean Community Health Survey conducted between August and October 2018 in adults aged 19 –80. Sleep quality was evaluated using Pittsburgh Sleep Quality Index (PSQI). PSQI was calculated using the data answered in self-

diagnosis questionnaire. Poor sleep quality was defined as PSQI  $\geq 5$ . One-year and three-month average concentrations of heavy metals (lead, manganese, cadmium, and aluminum) in PM with diameter  $\leq 10 \mu\text{m}$  were obtained from nationwide air quality monitoring data and linked to the survey data based on individual district-level residential addresses. Logistic regression analyses were performed after adjusting for age, sex, education level, marital status, smoking status, alcohol consumption, history of hypertension, history of diabetes, temperature and humidity.

**Results:** Of 32,050 participants, 17,082 (53.3%) reported poor sleep quality. Increases in log-transformed one-year average lead (odds ratio, 1.14; 95% confidence interval, 1.08–1.20), manganese (1.31; 1.25–1.37), cadmium (1.03; 1.00–1.05), and aluminum concentrations (1.17; 1.10–1.25) were associated with poor sleep quality. Increases in log-transformed three-month average manganese (odds ratio, 1.13; 95% confidence interval, 1.09–1.17) and aluminum concentrations (1.28; 1.21–1.35) were associated with poor sleep quality.

**Conclusion:** This study investigated the impact of exposure to air pollutants and the heavy metals contained in air pollutants on the sleep quality of adults at the community level. The results showed that PM<sub>10</sub>, PM<sub>2.5</sub>, and the heavy metals (Al<sub>10</sub>, Mn<sub>10</sub>, and Pb<sub>10</sub>) in PM<sub>10</sub> were strongly associated with poor sleep quality. These findings have significant value at the community level and can be useful for formulating public health policies.

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**Key words:** Heavy metal exposure; Sleep quality; Atmospheric particulate matter

# I. INTRODUCTION

## 1. Background

Over one-third of adults suffer from sleep problems such as insomnia (Ohayon 2002). Poor sleep quality is associated with adverse cardiometabolic outcomes such as hypertension and diabetes mellitus (Dzhambov and Dimitrova 2016), as well as neuropsychological outcomes including Parkinson's disease (Ranteallo et al. 2021) and depression (Hsu et al. 2021). Generally, factors related to sleep quality include demographics, socioeconomic status, and lifestyle behaviors, such as alcohol consumption and smoking (Cai et al. 2023; Chen et al. 2019; Lawrence et al. 2018; Lee et al. 2021b).

Ambient air pollution is a major environmental factor associated with various health problems including neurological diseases (Potter et al. 2021). Mounting evidence suggests that the inhalation of air pollutants may induce neurotoxicity via neuroinflammation and oxidative stress (Iqbal et al. 2020; Potter et al. 2021). Several studies have demonstrated that ambient air pollution is associated with poor sleep quality and sleep deprivation (Chen et al. 2019; Lawrence et al. 2018; Lee et al. 2021b). In a cohort study in rural Henan, China, higher concentrations of particulate matter (PM) with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) and nitrogen dioxide were associated with poor sleep quality (Chen et al. 2019). A cross-sectional study in northeast China showed that long-term exposure to PM<sub>2.5</sub> and nitrogen dioxide was associated with an increased risk of sleep disorders in children (Lawrence et al. 2018). A longitudinal study of adults in 141 communities in the Republic

of Korea reported that long-term exposure to PM<sub>2.5</sub> and nitrogen dioxide was associated with an increased prevalence of chronic sleep deprivation (Lee et al. 2021b).

PM is a mixture of pollutants including heavy metals. PM inhalation increases exposure to airborne heavy metals (Hamanaka and Mutlu 2018; Kim 2017; Liu et al. 2018). Given that exposure to heavy metals is known to exert neurotoxic effects via various mechanisms, including oxidative stress, mitochondrial dysfunction, and decreased neurogenesis (Ijomone et al. 2020; Pyatha et al. 2022), exposure to airborne heavy metals in PM may affect sleep health. To date, there is little evidence regarding the association between heavy metals and sleep health. A recent study demonstrated that serum lead and mercury levels are associated with sleep duration in women (Nguyen 2023). However, no studies have linked airborne heavy metals with sleep quality.

## **2. Objectives of the study**

This study aimed to evaluate the association between heavy metals in PM and sleep quality by linking data from a nationwide health survey and those from monitoring air pollution.

- (1) To evaluate the association between exposure to heavy metals among atmospheric particulate matter and sleep quality, we used the 2018 Community Health Survey provided by Korea Centers for Disease Control and Prevention and nationwide air quality monitoring data provided by the Ministry of Environment.

- (2) To evaluate the association between exposure to heavy metals and sleep quality, the Pittsburgh Sleep Quality Index (PSQI) was calculated using the 2018 community health survey data.
- (3) The average concentrations of  $PM_{10}$ ,  $PM_{2.5}$ ,  $Al_{10}$ ,  $Mn_{10}$ ,  $Pb_{10}$ , and  $Cd_{10}$  during a 1-year period (November 2017 to October 2018) and a 3-month period (August 2018 to October 2018) was collected.
- (4) Data linking the PSQI and the average concentration of  $PM_{10}$ ,  $PM_{2.5}$ ,  $Al_{10}$ ,  $Mn_{10}$ ,  $Pb_{10}$ , and  $Cd_{10}$  was constructed.
- (5) Multivariate logistic regression analysis was conducted to investigate the associations of the 3-month and 1-year average concentrations of  $PM_{10}$ ,  $PM_{2.5}$ ,  $Pb_{10}$ ,  $Mn_{10}$ ,  $Cd_{10}$ , and  $Al_{10}$  with poor sleep quality.

## II. LITERATURE REVIEW

### 1. Effects of heavy metals in particulate matter

Inhalation of airborne particulate matter can lead to exposure to heavy metals contained in particulate matter (Hamanaka et al., 2018; Liu et al., 2018; Kim et al., 2017). Chronic exposure to heavy metals in humans can also lead to neurological disorders by making the brain vulnerable to neurotoxic damage through mechanisms such as oxidative stress, DNA damage, mitochondrial dysfunction, decreased neurogenesis, and impaired energy metabolism (Iqbal et al., 2020; Pyatha et al., 2022). Numerous epidemiological studies have shown that both single and combined exposure to heavy metals such as iron, mercury, manganese, copper, lead, cadmium, and aluminum are associated with cognitive impairment and Parkinson's disease (Iqbal et al., 2020; Li et al., 2021; Payatha et al., 2022; Bakulski et al., 2020). In particular, although aluminum is a widely distributed element in the environment, it does not have important biological functions in the human body. Some studies have shown that even low levels of aluminum exposure can induce oxidative stress and have harmful effects on long-term memory (Skalny et al., 2022; Wang et al., 2018; Fernandes et al., 2020).

The association between heavy metal exposure and sleep quality found in this study may be explained by the neurotoxicity of heavy metals. Chronic exposure of humans to heavy metals renders the brain vulnerable to neurotoxic damage by mechanisms such as oxidative stress, DNA damage, mitochondrial dysfunction, decreased neurogenesis, and impaired

energy metabolism, leading to neurological disorders (Iqbal et al., 2020; Pyatha et al., 2022). Many epidemiological studies have shown that single and combined exposures to heavy metals such as iron, mercury, manganese, copper, lead, cadmium and aluminum are associated with cognitive decline and Parkinson's disease (Iqbal et al., 2020; Li et al., 2021; Payatha et al., 2022; Bakulski et al., 2020; Vellingiri et al., 2022). In particular, aluminum, despite being a widely distributed element in the Earth's crust, does not have a significant biological function in the human body, and some studies have observed oxidative stress even at low concentrations of aluminum and identified detrimental effects on long-term memory (Skalny et al., 2022; Wang et al., 2018; Fernandes et al., 2020). Although the biological mechanisms of the association between air pollutants such as fine particulate matter and sleep quality are unclear, previous studies have suggested several potential pathways (Li et al., 2022; Lin et al., 2022; Li et al., 2018; You et al., 2022; Lee et al., 2021; Bakulski et al., 2020). Exposure to heavy metals such as Pb, Mn, Cd, and Al in fine particulate matter, which are well-known neurotoxins, can affect the central nervous system, which in turn can affect sleep quality. Recent studies have shown that inhaled particulate matter and heavy metals are closely associated with brain damage, mainly cerebrovascular damage (stroke) and neurological damage (changes in cognitive function, dementia, mental disorders, etc.) (Li et al., 2022:). In addition, these air pollutants can cross the lung-gas-blood barrier and the gut-microbiota-brain axis to cause systemic oxidative stress and inflammation, or directly penetrate brain tissue through the olfactory nerve to damage cerebral blood vessels and cranial nerves (Li et al., 2022). In particular, since the present

study confirmed the effect of sleep on inhalation exposure to heavy metals, it can be considered as a neurotoxic effect due to the direct exposure route through the olfactory nerve. Among the heavy metals, we found that aluminum and manganese were highly associated with poor sleep quality. This may be explained by the fact that these heavy metals can enter the brain and damage cerebral blood vessels and cranial nerves, and the resulting neuroinflammation may cause harmful effects on sleep and wake cycles, as reported in previous studies (Zhang et al., 2019; Dzhambov et al., 2016). Table 1 summarizes the recent research results related to the exposure to heavy metals in particulate matter (PM) and health effects.



**Table 1. Exposure to heavy metals in particulate matter (PM) and health effects**

Paper title	contents	Reference
Particulate Matter and Associated Metals: A Link with Neurotoxicity and Mental Health	Toxic and neurotoxic metals such as Mn, Zn, Pb, Cu, Ni, and Ba can adsorb to the PM surface and potentially contribute to the neurotoxic effects associated with PM exposure	Potter et al. 2021
Astrocytes in heavy metal neurotoxicity and neurodegeneration	Excessive intake of heavy metals, such as As, Mn, Hg, Al, Pb, Ni, Bi, Cd, Cu, Zn and Fe, is neurotoxic and it promotes neurodegeneration.	Li et al., 2021
Role of heavy metals (Cu, As, Cd, Fe, Li) induced neurotoxicity	Increase or decrease in heavy metals involve in regulation of neuronal functions that have an impact on neurodegeneration process.	Vellingiri et al., 2022
Association between Heavy Metal Exposure and Parkinson's Disease: A Review of the Mechanisms Related to Oxidative Stress	This review focuses on the roles of Hg, Pb, Mn, Cu, and Fe in the development and progression of PD. Moreover, it explores the plausible roles of heavy metals in neurodegenerative mechanisms that facilitate the development of PD.	Pytha et al., 2022
Heavy Metals Exposure and Alzheimer's Disease and Related Dementias	Given the widespread and global exposure to lead, cadmium, and manganese, even small increases in the risks of Alzheimer's disease and related dementias would have a major population impact on the burden on disease.	Bakulski et al., 2020

## 2. Korean version of the Pittsburgh Sleep Quality Index (K-PSQI)

Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a self-administered questionnaire that assesses the quality of sleep for a month. It consists of 7 domains and 19 items with the global score between 0 and 21 (Buysse et al., 1989). Each sub-category is related on a scale of 0 to 3, and total score is 21 points. The higher PSQI score indicates poorer sleep quality. Sensitivity and specificity were found to be high when the total PSQI score exceeded the cut-off of 6 points. Therefore, 6 or more scores of PSQI were categorized into the good sleep group. The 7 domains of the PSQI are as follows: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, sleep medication use, and daytime dysfunction.

The Korean version of the Pittsburgh Sleep Quality Index (K-PSQI) was used to measure the Pittsburgh Sleep Quality Index. The PSQI-K was determined the reliability and validity (Sohn et al., 2012). Studies related to the Korean version of PSQI and other papers related to sleep quality are summarized in Table 2 (Clement-Carbonell et al., 2021; Chen et al., 2019; 2021; Hsu et al., 2021; Kim 2018; Kim et al., 2019; Park et al., 2015; Shin et al., 2020; Sohn et al., 2012; Zhang et al., 2019). In the study, we classified all participants into two groups according to the commonly used cut-off global score of 5 (Kim et al., 2019). A global score  $\geq 5$  was considered as poor sleep quality, while a global score  $< 5$  was considered as good sleep quality. Previous study reported that the cut-off had a sensitivity of 89.6% and specificity of 86.5% (Buysse et al., 1989).

**Table 2. Research of the Pittsburg Sleep Quality Index**

PSQI	Paper title	Poor sleep cut off	Reference
Korean	The reliability and validity of the Korean version of the Pittsburgh Sleep Quality Index	PSQI-K $\geq 8.5$	Sohn et al., 2012
	The reliability and validity testing of Korean version of the Pittsburgh Sleep Quality Index	PSQI-K $\geq 6$	Shin et al., 2020
	Factors associated with personal and social performance status in patients with bipolar disorder	PSQI-K $\geq 5$	Kim et al., 2019
	Quality of sleep and heart rate variability by physical activity in high school students	PSQI-K $\geq 8$	Park et al., 2015
	Factors related with quality on sleep of daytime workers	PSQI-K $\geq 6$	Kim et al., 2018
Others	The Pittsburg sleep quality Index: A new instrument for psychiatric practice and research	PSQI $> 5$	Buysse et al., 1989
	The association between PSQI score and hypertension in a Chinese rural population: the Henan Rural Cohort Study	PSQI $> 3, 6, 9$	Zhang et al., 2019
	Is long-term exposure to air pollution associated with poor sleep quality in rural China?	PSQI $> 5$	Chen et al., 2019
	Sleep Quality, Mental and Physical Health: A Differential Relationship	PSQI $> 7.03$	Clement-Carbonell et al., 2021
	Subjective sleep quality and association with depression syndrome, chronic diseases and health-related physical fitness in the middle-aged and elderly	PSQI $> 5$	Hsu et al., 2021

### 3. Association between sleep quality and particulate matter

Recently, research results on the association between air pollution and sleep quality have been reported (Chen et al, 2019; Lee et al, 2021; Zhang et al., 2019). According to the Henan Rural Cohort established during 2015–2017, long-term exposures to PM<sub>2.5</sub>, PM<sub>10</sub> and NO<sub>2</sub> were associated with poor sleep quality in rural China. Improvement of air quality may help to improve sleep quality in approximately 27,417 adults (Chen et al, 2019). According to another study, 59 754 children aged 2–17 years were randomly selected from 27 districts in seven northeastern Chinese cities during 2012–2013. Four years average concentrations of pollutants were calculated for PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, and CO from monitoring stations. This study found that 10 µg/m<sup>3</sup> increases in PM<sub>10</sub> and PM<sub>2.5</sub> were associated with 17% and 47% higher risks of poor sleep quality, respectively (Lawrence et al. 2018). In this study, the gender-specific differences for the effects of ambient air pollutants' exposures on sleep score were stronger in female than in male children. In addition, a longitudinal study of adults in 141 communities in the Republic of Korea reported that long-term exposure to PM<sub>2.5</sub> and nitrogen dioxide was associated with an increased prevalence of chronic sleep deprivation (Lee et al. 2021b). The associations between PM<sub>10</sub> and sleep outcomes were higher in females than males and in the older age groups (≥ 60-years) than in younger age groups (19–39 and 40–59 years). However, the association between NO<sub>2</sub> and sleep outcomes were higher in males than in females and in the younger age groups (19–39 years) than other age groups.

## **II. MATERIALS AND METHODS**

### **1. Study design**

The Community Health Survey (CHS) is a nationwide cross-sectional study conducted annually in 255 public health centers to produce comparable community health statistics for adults aged 19 and above (Korea Centers for Disease Control and Prevention, Ministry of Health and Welfare, <http://chs.cdc.go.kr>). The first (2010–2013), second (2014–2017), and third (2018–2021) phases of the CHS were conducted. This study used data from the 2018 survey (conducted between August and October 2018), which included questions related to sleep quality. The survey data included information on demographics, socioeconomic status, health behavior, disease history, and mental health status. This study was approved by the Institutional Review Board of Yonsei University Healthcare System (approval number:4-2023-0484).

### **2. Sleep quality assessment**

Sleep quality was evaluated using the Korean version of the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a commonly used tool for assessing sleep quality and consists of 19 items with a global score ranging from 0 to 21. A higher PSQI score indicates poorer sleep quality. Participants were classified into two groups based on the commonly used cutoff score of 5. A global score  $\geq 5$  was considered as poor sleep quality, while a global

score <5 was considered as good sleep quality. PSQI was calculated using the data answered in self-diagnosis questionnaire.

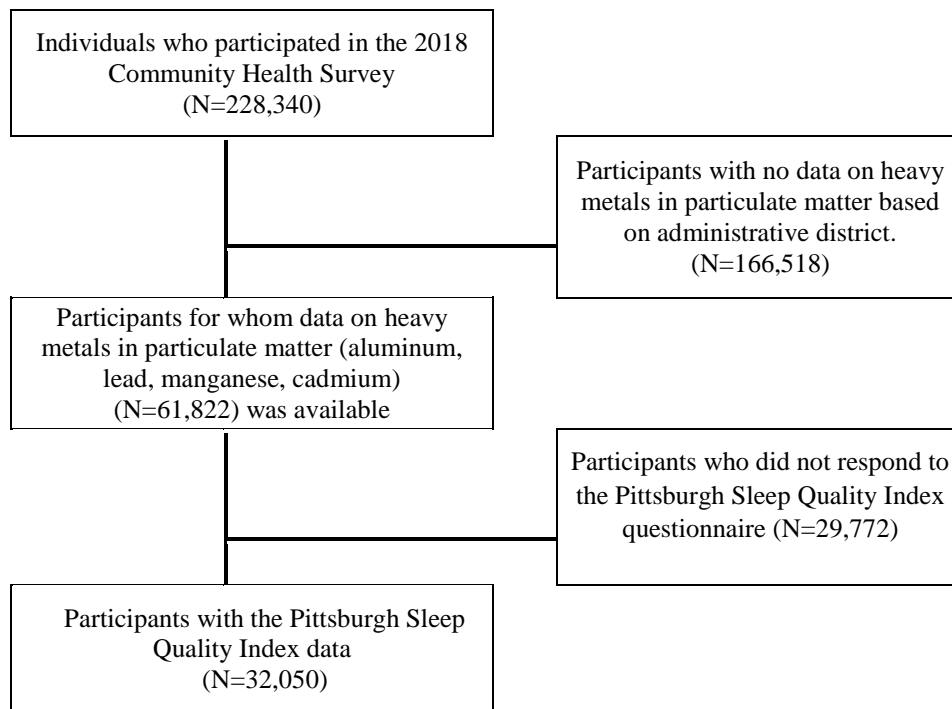
### **3. Exposure assessment**

Daily concentrations of airborne PM<sub>10</sub> (particulate matter with aerodynamic diameters  $\leq 10 \mu\text{m}$ ), PM<sub>2.5</sub>, and heavy metals in PM<sub>10</sub> (Al<sub>10</sub>: aluminum in PM<sub>10</sub>; Mn<sub>10</sub>: manganese in PM<sub>10</sub>; Pb<sub>10</sub>: lead in PM<sub>10</sub>; Cd<sub>10</sub>: cadmium in PM<sub>10</sub>) were obtained from nationwide air quality monitoring data provided by the Ministry of Environment. In 2018, there were 56 stations equipped to monitor air quality for heavy metals in PM<sub>10</sub>. We linked air quality data and CHS data based on administrative districts ('si-gun-gu'). There were multiple air quality monitoring stations in eight of the linked administrative districts, and the concentrations from multiple stations were averaged. Data on Al<sub>10</sub>, Mn<sub>10</sub>, Pb<sub>10</sub>, and Cd<sub>10</sub> were available for 44 of the 255 public health centers in the CHS data. This study used the average concentrations of PM<sub>10</sub>, PM<sub>2.5</sub>, Al<sub>10</sub>, Mn<sub>10</sub>, Pb<sub>10</sub>, and Cd<sub>10</sub> during a 1-year period (November 2017 to October 2018) and a 3-month period (August 2018 to October 2018).

### **4. Statistical analysis**

Of the total number of CHS participants in 2018 (N=228,340), 198,569 completed the PSQI (Figure 1). After excluding 166,518 participants due to lack of data on heavy metal exposure, 32,050 participants were included. The significance of the p-values was tested

using the independent *t*-test (for continuous variables) or the chi-square test (for categorical variables). Multivariate logistic regression analysis was conducted to investigate the associations of the 3-month and 1-year average concentrations of PM<sub>10</sub>, PM<sub>2.5</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, Cd<sub>10</sub>, and Al<sub>10</sub> with poor sleep quality. In this analysis, the concentrations of Pb<sub>10</sub>, Mn<sub>10</sub>, Cd<sub>10</sub>, and Al<sub>10</sub> were log-transformed because of their highly skewed distributions. We adjusted for age, sex, smoking status (nonsmoker, former smoker, or current smoker), alcohol consumption, history of hypertension, history of diabetes, educational level (middle school or below, high school, college, or no response), marital status (spouse, single, spousal death/divorce/separation, or no response), temperature and humidity. The strength of the association was expressed as the odds ratio (OR) per 10-unit increase in PM and log-transformed Pb<sub>10</sub>, Mn<sub>10</sub>, Cd<sub>10</sub>, and Al<sub>10</sub> with corresponding 95% confidence intervals (CI). Additionally, we performed the above logistic regression analyses after stratification by gender, geographical region (metropolitan and rural or urban areas), and PM<sub>10</sub> tertile.



**Figure 1. Flowchart of participant selection**



### III. RESULTS

#### 1. Characteristics of participants

The characteristics of the participants are summarized in Table 3. Of the 32,050 participants included in this study, 17,082 (53.3%) reported poor sleep quality. There was no significant difference in the mean age between participants with poor sleep quality and those with good sleep quality ( $p=0.775$ ). The proportion of women was significantly higher among participants with poor sleep quality (58.9%) than among those with good sleep quality (50.9%) ( $p<0.001$ ). PSQI was calculated using the data answered in self-diagnosis questionnaire. The participants with poor sleep quality were younger on average than those with good sleep quality. Non-smokers and former smokers had a higher proportion of poor sleep quality, while current smokers had no significant difference in sleep quality. Additionally, there was a slightly higher proportion of participants with poor sleep quality (44.6%) than those with good sleep quality (40.4%) in relation to alcohol consumption. However, for those with a history of hypertension or diabetes, the proportion of participants with poor sleep quality was 1.68 times and 1.78 times higher, respectively, than those with good sleep quality. With respect to marital status, the proportion of participants with poor sleep quality was 2.1 times higher among those who had experienced spouse death/divorce/separation than those who were currently married. Figure 2 shows the distribution of sleep quality for male and female, and Participants characteristic are shown in Figure 3.

**Table 3. Characteristics of study participants**

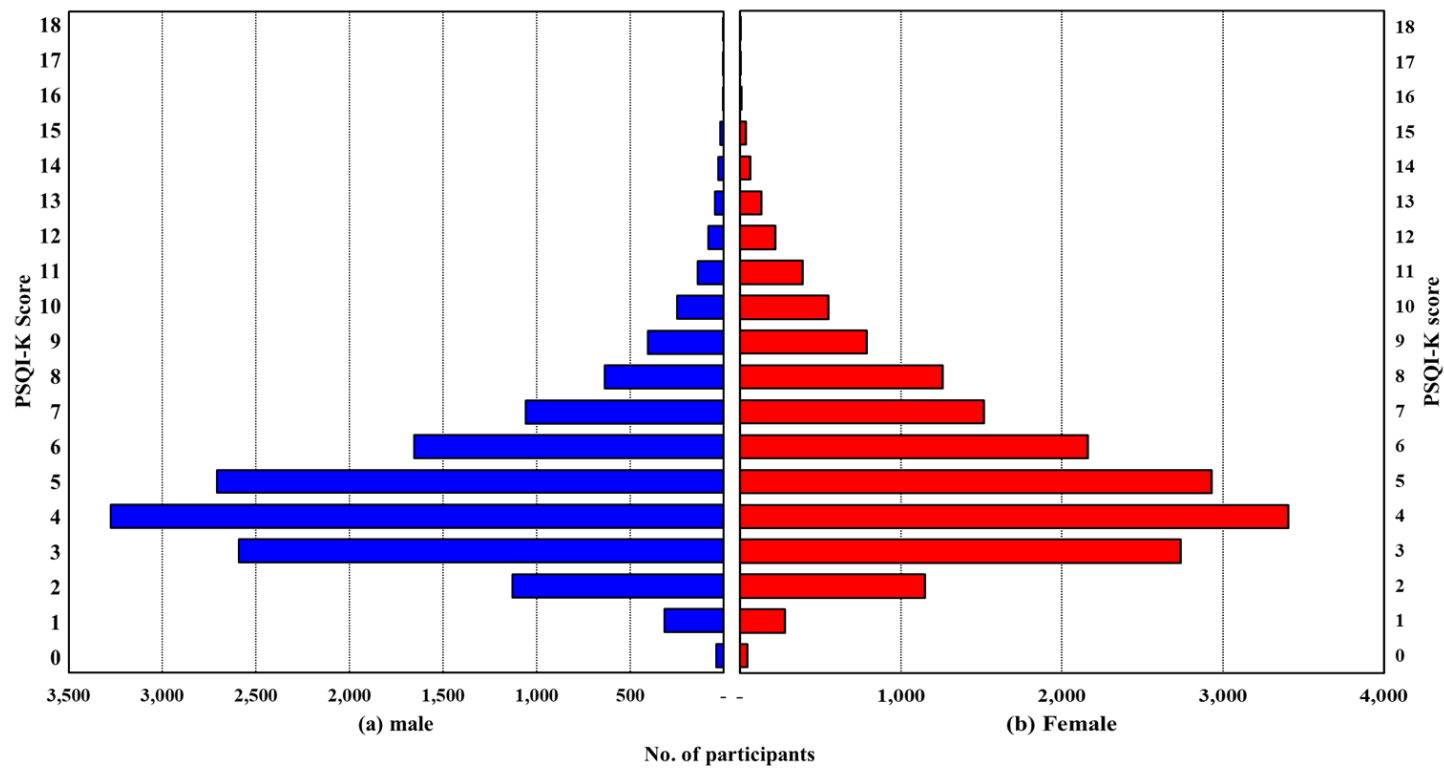
Variables	Total (N=32,050)	Participants with poor sleep quality (N=17,082)	Participants with good sleep quality (N=14,968)	p
Age (years), mean (SD)	53.3(16.7)	50.1(16.4)	56.0(16.4)	<0.001
Gender, N (%)				<0.001
Women	17,673(55.2)	10,059(58.9)	7,614(50.9)	
Men	14,377(44.8)	7,023(41.1)	7,354(49.1)	
Smoking, N (%)				<0.001
Never smoker	20,843(65.0)	11,210(65.6)	9,633(64.4)	
Former smoker	5,761(18.0)	3,126(18.3)	2,635(17.6)	
Current smoker	5,446(17.0)	2,746(16.1)	2,700(18.0)	
Alcohol drinking, N (%)	27,240(85.0)	14,278(83.6)	12,962(86.4)	<0.001
History of hypertension, N (%)	8,326(26.0)	5,231(30.6)	3,095(37.2)	<0.001
History of diabetes mellitus, N (%)	3,374(10.5)	2,142(12.5)	1,232(8.2)	<0.001
Education level, N (%)				<0.001
Middle school under	9,295(29)	6,187(36.2)	3,108(20.8)	
High school	9,720(30.33)	5,185(30.4)	4,535(30.3)	
University	13,000(40.56)	5,688(33.3)	7,312(48.8)	
No answer / Unknown	35(0.11)	22(0.13)	13(0.09)	
Marital status, N (%)				<0.001
Spouse	22,106(69.0)	11,546(67.6)	10,560(70.6)	
Single	4,708(14.7)	2,004(11.7)	2,704(18.1)	
Spouse death/divorce/Separation	5,170(16.1)	3,503(20.5)	1,667(11.1)	
No answer/Unknown	66(0.21)	29(0.2)	37(0.25)	

**Table 3. Characteristics of study participants (*continued*)**

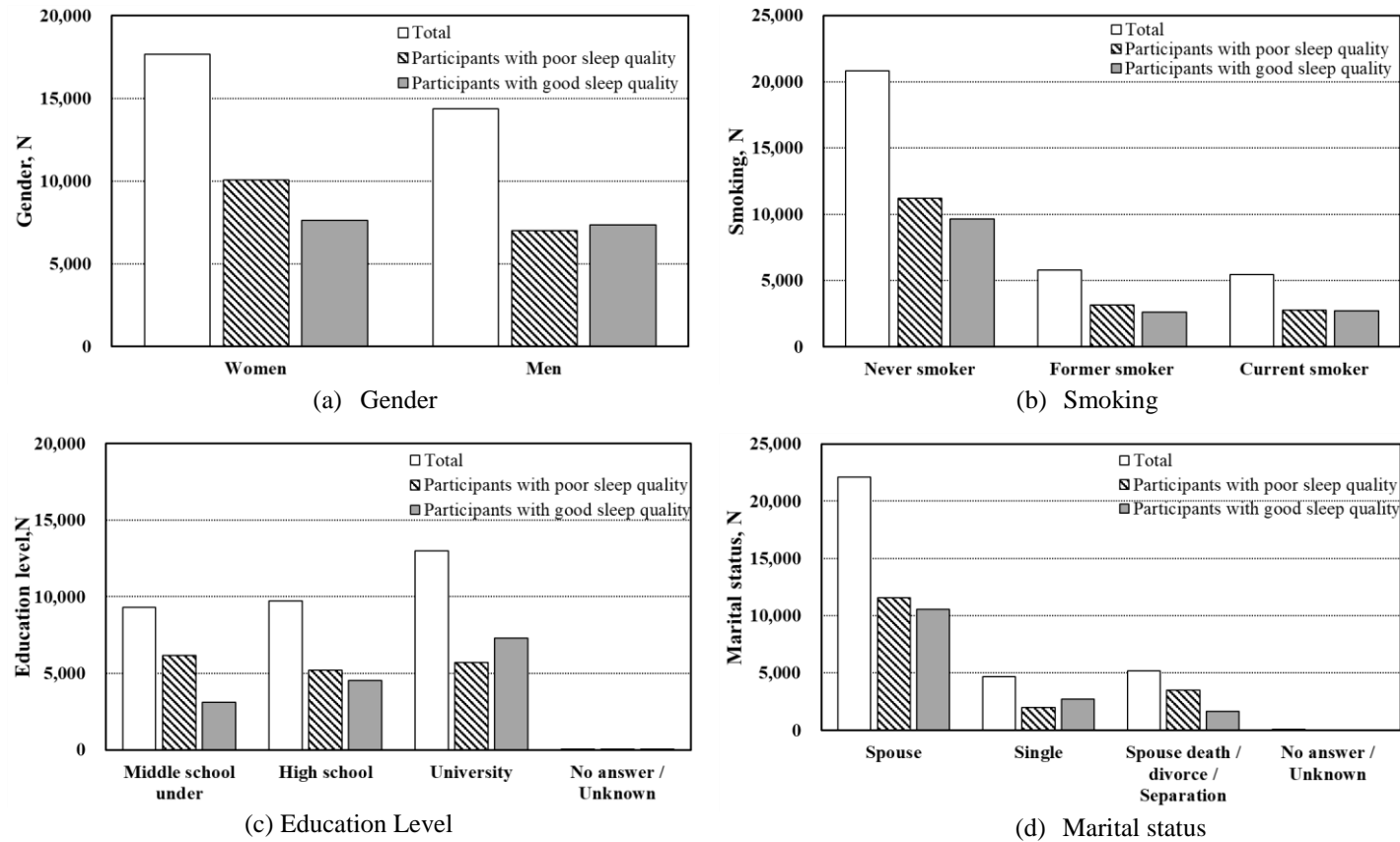
Variables	Total (N=32,050)	Participants with poor sleep quality (N=17,082)	Participants with good sleep quality (N=14,968)	p
Air pollutants ( $\mu\text{g}/\text{m}^3$ ), 3-month				
PM <sub>10</sub> , mean (SD)	27.0(3.79)	27.1(3.9)	26.8(3.7)	<0.001
PM <sub>2.5</sub> , mean (SD)	13.8(2.31)	13.9(2.3)	13.7(2.3)	0.372
Pb <sub>10</sub> , median (25%–75%)	1.20(1.0)	1.3(1.0)	1.2(1.05)	0.257
Mn <sub>10</sub> , median (25%–75%)	1.6(1.0)	1.6(1.17)	1.59(0.95)	<0.001
Cd <sub>10</sub> , median (25%–75%)	0.83(0.82)	0.83(0.82)	0.83(0.82)	<0.001
Al <sub>10</sub> , median (25%–75%)	1.49(0.99)	1.52(1.16)	1.49(0.82)	<0.001
Air pollutants ( $\mu\text{g}/\text{m}^3$ ), 1-year				
PM <sub>10</sub> , mean (SD)	41.5(4.16)	41.5(4.2)	41.4(4.1)	<0.001
PM <sub>2.5</sub> , mean (SD)	23.1(2.78)	23.2(2.9)	23.0(2.7)	<0.001
Pb <sub>10</sub> , median (25%–75%)	2.39(1.01)	2.39(1.01)	2.39(1.01)	0.399
Mn <sub>10</sub> , median (25%–75%)	2.54(0.99)	2.54(1.17)	2.54(1.05)	<0.001
Cd <sub>10</sub> , median (25%–75%)	2.67(1.27)	2.67(1.27)	2.75(1.27)	<0.001
Al <sub>10</sub> , median (25%–75%)	2.06(1.0)	2.06(1.0)	2.06(1.01)	0.001

SD: standard deviation.

Footnotes: Data are presented in mean  $\pm$  SD for continuous variables (age, air pollutants for 1-year and 3-month exposure periods), and sample size (percentages) for categorical variables (gender, smoking, alcohol consumption, history of hypertension, history of diabetes mellitus, education level, marital status). \*P-values for age, PM<sub>10</sub>, and PM<sub>2.5</sub>, were calculated using a *t*-test, while the other variables were obtained using a chi-square test.

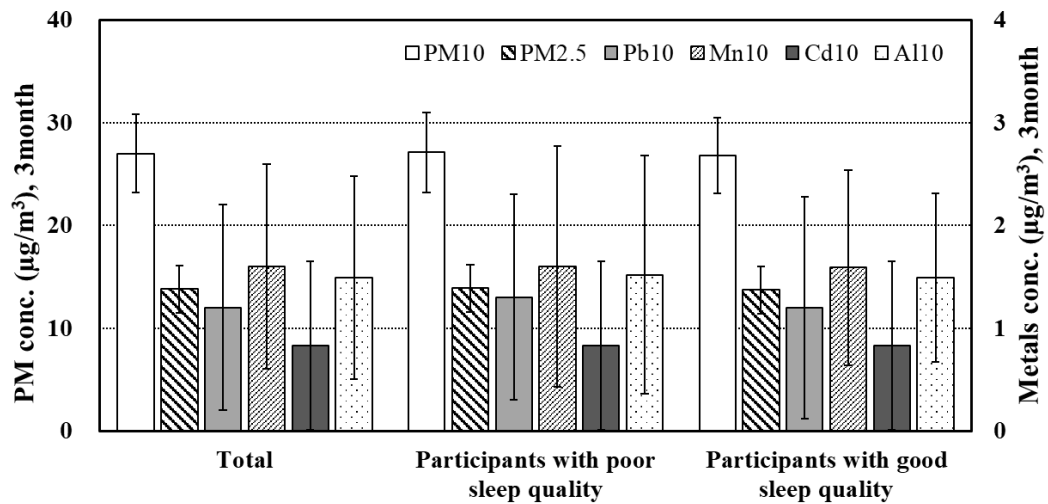


**Figure 2. Distribution of sleep quality for male and female by region**

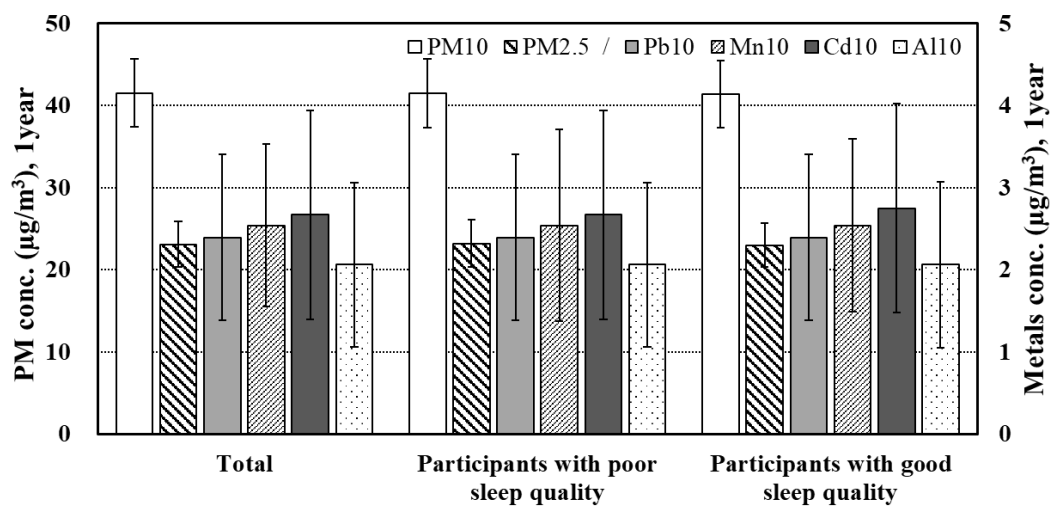


**Figure 3. Characteristics of participants**

The average concentrations and standard deviations of  $PM_{10}$  and  $PM_{2.5}$  over a period of three months were  $27.0 \pm 3.79 \mu\text{g}/\text{m}^3$  and  $13.8 \pm 2.31 \mu\text{g}/\text{m}^3$ , respectively. The annual averages for  $PM_{10}$  and  $PM_{2.5}$  were  $41.5 \pm 4.16 \mu\text{g}/\text{m}^3$  and  $23.1 \pm 2.78 \mu\text{g}/\text{m}^3$ , respectively. The 3-month and 1-year concentrations of  $PM_{10}$  were  $26.8 \pm 3.7 \mu\text{g}/\text{m}^3$  and  $41.4 \pm 4.1 \mu\text{g}/\text{m}^3$ , respectively, for participants with good sleep quality and  $27.1 \pm 3.9 \mu\text{g}/\text{m}^3$  and  $41.5 \pm 4.2 \mu\text{g}/\text{m}^3$ , respectively, for those with poor sleep quality. The distribution of metal concentrations in  $PM_{10}$  used the median value. The 3-month median (interquartile range) concentrations of  $Mn_{10}$ ,  $Al_{10}$ ,  $Pb_{10}$ , and  $Cd_{10}$  were  $1.60 (1.0) \mu\text{g}/\text{m}^3$ ,  $1.49 (1.0) \mu\text{g}/\text{m}^3$ ,  $1.20 (1.0) \mu\text{g}/\text{m}^3$ , and  $0.83 (0.8) \mu\text{g}/\text{m}^3$ , respectively. The 1-year median (interquartile range) concentrations of  $Mn_{10}$ ,  $Al_{10}$ ,  $Pb_{10}$ , and  $Cd_{10}$  were  $2.54 (1.0) \mu\text{g}/\text{m}^3$ ,  $2.06 (1.0) \mu\text{g}/\text{m}^3$ ,  $2.39 (1.0) \mu\text{g}/\text{m}^3$ , and  $2.67 (1.3) \mu\text{g}/\text{m}^3$ , respectively. The 1-year average concentrations of heavy metals in  $PM_{10}$  were Cd  $2.67 \pm 1.27 \mu\text{g}/\text{m}^3$ , Mn  $2.54 \pm 0.99 \mu\text{g}/\text{m}^3$ , Pb  $2.39 \pm 1.01 \mu\text{g}/\text{m}^3$ , and Al  $2.06 \pm 1.0 \mu\text{g}/\text{m}^3$ , with Cd, Mn, Pb, and Al in order of abundance. Air pollutants concentration by exposure period are shown in Figure 4.



(a) Exposed for 3-months



(b) Exposed for 1-year

**Figure 4. Air pollutants concentration by exposure period**

## 2. Association between heavy metals in PM and poor sleep quality

The associations between air pollutants, including  $PM_{10}$  and  $PM_{2.5}$ , and heavy metals in  $PM_{10}$  with poor sleep quality are summarized in Table 4 and Figure 5. The odds ratios (ORs) for 1-year exposure to  $PM_{10}$  and  $PM_{2.5}$  were 1.137 (95% confidence interval (CI) 1.075, 1.204) and 1.262 (95% CI 1.161, 1.372), respectively. The ORs for 3-month exposure were 1.255 (95% CI 1.179, 1.366) and 1.494 (95% CI 1.350, 1.654), respectively.

Increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.311; 95% CI, 1.252–1.373),  $Al_{10}$  (1.170; 1.098–1.248),  $Pb_{10}$  (1.139; 1.080–1.202), and  $Cd_{10}$  (1.027; 1.001–1.054) were significantly associated with an increased risk of poor sleep quality. Increases in the 3-month average concentrations of  $Mn_{10}$  (OR, 1.127; 95% CI, 1.086–1.169) and  $Al_{10}$  (OR, 1.277; 95% CI, 1.211–1.348) were significantly associated with an increased risk of poor sleep quality.  $Pb_{10}$  (OR, 1.039; 95% CI, 0.993–1.087) and  $Cd_{10}$  (OR, 0.991; 95% CI, 0.967–1.016) were not significantly associated with poor sleep quality.

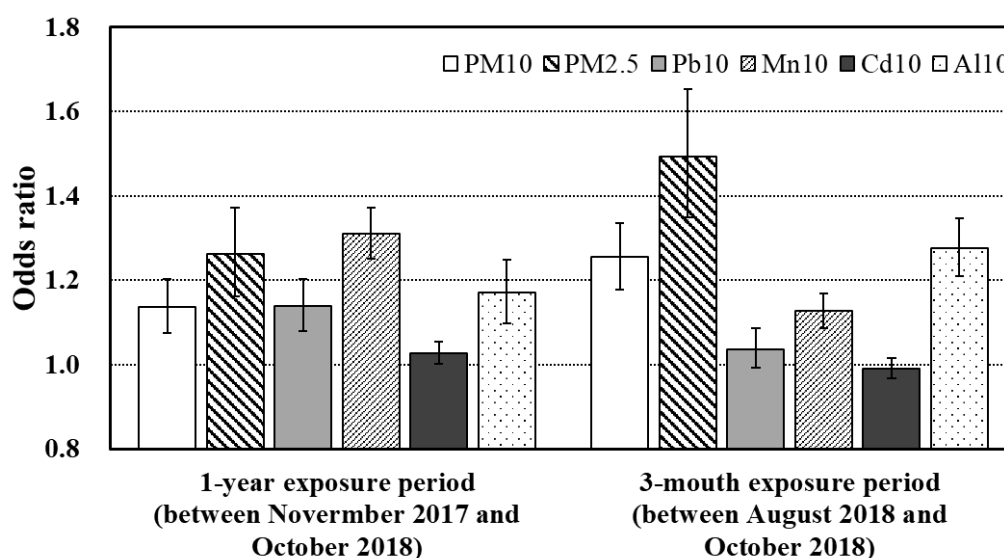
The associations between air pollutants and poor sleep quality, further adjusting for depression symptom score (PHQ-9) are summarized in Table 5. As a result of additional analysis of the depression PHQ-9 (cut off 10), the association with sleep quality in  $PM_{10}$  and  $PM_{2.5}$  for 1-year exposure period and  $Pb_{10}$  for 3 months exposure period was found to be different from previous research results.



**Table 4. Association between air pollutants (1-year and 3-month exposure periods) and poor sleep quality**

Air pollutants	1-year exposure period (between November 2017 and October 2018)	3-month exposure period (between August 2018 and October 2018)
	Odds ratio (95% CI)	Odds ratio (95% CI)
PM <sub>10</sub>	1.137 (1.075–1.204)	1.255 (1.179–1.336)
PM <sub>2.5</sub>	1.262 (1.161–1.372)	1.494 (1.350–1.654)
Pb <sub>10</sub>	1.139 (1.080–1.202)	1.039 (0.993–1.087)
Mn <sub>10</sub>	1.311 (1.252–1.373)	1.127 (1.086–1.169)
Cd <sub>10</sub>	1.027 (1.001–1.054)	0.991 (0.967–1.016)
Al <sub>10</sub>	1.170 (1.098–1.248)	1.277 (1.211–1.348)

PM<sub>10</sub>: particulate matter 10  $\mu$ m or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5  $\mu$ m or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log-transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.



**Figure 5. Odds ratio of poor sleep quality according to air pollution exposure period**

**Table 5. Association between air pollutants (1-year and 3-month exposure periods) and poor sleep quality, further adjusting for depression symptom score (PHQ-9)**

Air pollutants	1-year exposure period (between November 2017 and October 2018)	3-month exposure period (between August 2018 and October 2018)
	Odds ratio (95% CI)	Odds ratio (95% CI)
PM <sub>10</sub>	0.975 (0.920–1.034)	1.083 (1.016–1.156)
PM <sub>2.5</sub>	0.987 (0.904–1.076)	1.129 (1.016–1.255)
Pb <sub>10</sub>	1.110 (1.126–1.190)	1.052 (1.004–1.103)
Mn <sub>10</sub>	1.197 (1.141–1.255)	1.078 (1.038–1.120)
Cd <sub>10</sub>	1.042 (1.014–1.070)	1.022 (0.996–1.049)
Al <sub>10</sub>	1.098 (1.028–1.173)	1.164 (1.101–1.230)

PM<sub>10</sub>: particulate matter 10 µm or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5 µm or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log-transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.

### 3. Association between heavy metals in PM and poor sleep quality by gender

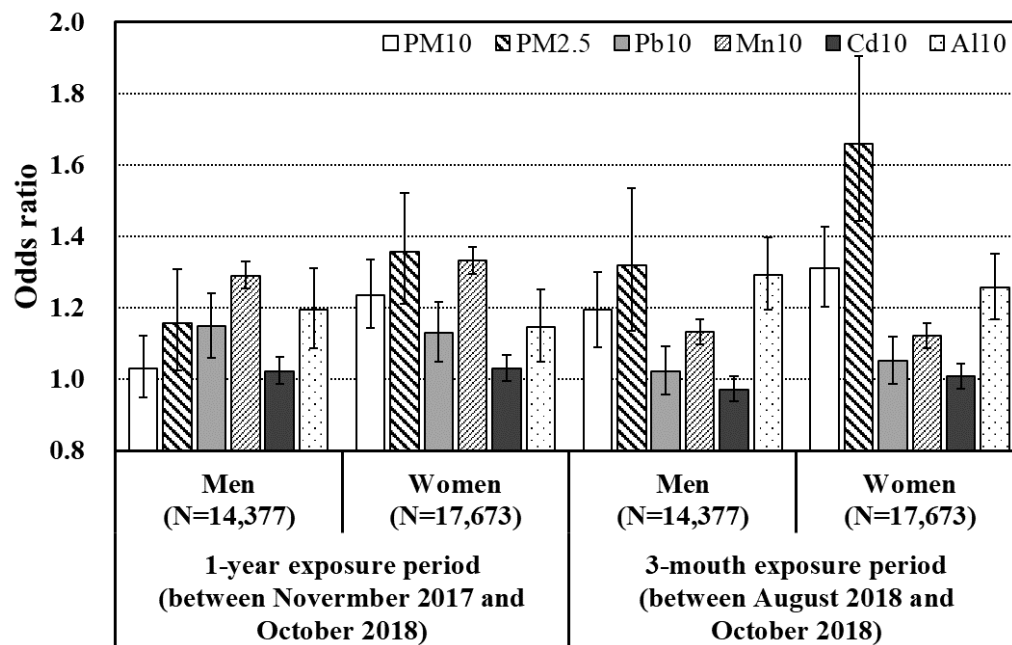
The association between air pollutants ( $PM_{10}$ ,  $PM_{2.5}$ , and heavy metals in  $PM_{10}$ ) and poor sleep quality by gender were summarized in Table 6 and Figure 6. Both 1-year and 3-month exposures showed higher odds ratios (ORs) for poor sleep quality in females compared to males. The ORs for females exposed to  $PM_{10}$  and  $PM_{2.5}$  for 1-year were 1.236 (95% CI 1.144-1.335) and 1.357 (95% CI 1.210-1.521), respectively, which were higher than those for males, 1.031 (95% CI 0.949-1.121) and 1.157 (95% CI 1.024-1.309), respectively. Specifically, for the 3-month exposure, the ORs for females exposed to  $PM_{10}$  and  $PM_{2.5}$  were 1.310 (95% CI 1.203-1.427) and 1.659 (95% CI 1.444-1.905), respectively, which were also higher than those for males, 1.195 (95% CI 1.090-1.309) and 1.320 (95% CI 1.136-1.534), respectively. This suggests that females exposed to  $PM_{10}$  and  $PM_{2.5}$  are more strongly associated with poor sleep quality than males.

Among men, increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.290; 95% CI, 1.206–1.380),  $Al_{10}$  (OR, 1.194; 95% CI, 1.088–1.310), and  $Pb_{10}$  (OR, 1.148; 95% CI, 1.061–1.241) were significantly associated with an increased risk of poor sleep quality. Among women, increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.332; 95% CI, 1.250–1.419),  $Al_{10}$  (OR, 1.146; 95% CI, 1.049–1.252), and  $Pb_{10}$  (OR, 1.130; 95% CI, 1.050–1.217) were significantly associated with an increased risk of poor sleep quality. No significant sex-based differences were observed in the association between airborne heavy metals and poor sleep quality.

**Table 6. Association between air pollutants (1-year and 3-month exposure periods) and poor sleep quality, stratified by gender**

Air pollutants	1-year exposure period (between November 2017 and October 2018)			3-month exposure period (between August 2018 and October 2018)		
	Men (N=14,377)	Women (N=17,673)	p for interaction	Men (N=14,377)	Women (N=17,673)	p for interaction
	Odds ratio (95% CI)			Odds ratio (95% CI)		
PM <sub>10</sub>	1.031 (0.949–1.121)	1.236 (1.144–1.335)	0.002	1.195 (1.090–1.309)	1.310 (1.203–1.427)	0.148
PM <sub>2.5</sub>	1.157 (1.024–1.309)	1.357 (1.210–1.521)	0.064	1.320 (1.136–1.534)	1.659 (1.444–1.905)	0.028
Pb <sub>10</sub>	1.148 (1.061–1.241)	1.130 (1.050–1.217)	0.78	1.023 (0.957–1.092)	1.052 (0.988–1.119)	0.544
Mn <sub>10</sub>	1.290 (1.206–1.380)	1.332 (1.250–1.419)	0.502	1.132 (1.072–1.194)	1.122 (1.068–1.179)	0.825
Cd <sub>10</sub>	1.023 (0.986–1.062)	1.030 (0.994–1.067)	0.801	0.972 (0.938–1.009)	1.008 (0.974–1.044)	0.156
Al <sub>10</sub>	1.194 (1.088–1.310)	1.146 (1.049–1.252)	0.533	1.292 (1.195–1.398)	1.257 (1.169–1.352)	0.616

PM<sub>10</sub>: particulate matter 10 µm or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5 µm or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log-transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.



**Figure 6. Odds ratio of poor sleep quality according to air pollution exposure period, stratified by gender**

#### 4. Association between heavy metals in PM and poor sleep quality by age

The association between air pollutants ( $PM_{10}$ ,  $PM_{2.5}$ , and heavy metals in  $PM_{10}$ ) and poor sleep quality by age were summarized in Table 7. In the exposure for 1-year and 3-months, the odds ratio (ORs) of poor sleep quality was higher in people under 65 years of age than in people over 65 years of age. The ORs for those under 65 years of age exposed to  $PM_{10}$  and  $PM_{2.5}$  for 1-year were 1.174 (95% CI 1.098–1.255) and 1.398 (95% CI 1.267–1.543), respectively. For the 3-month exposure, the ORs for those under 65 years of age exposed to  $PM_{10}$  and  $PM_{2.5}$  1.328 (95% CI 1.234–1.430) and 1.618 (95% CI 1.488–1.897), respectively. This suggests that age < 65 exposed to  $PM_{10}$  and  $PM_{2.5}$  are more strongly associated with poor sleep quality than age  $\geq$  65.

For age < 65, increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.351; 95% CI, 1.280–1.426),  $Al_{10}$  (OR, 1.209; 95% CI, 1.124–1.301), and  $Pb_{10}$  (OR, 1.158; 95% CI, 1.089–1.234) were significantly associated with an increased risk of poor sleep quality. For age < 65, increases in 3-months average concentrations of  $Al_{10}$  (OR, 1.343; 95% CI, 1.262–1.430),  $Mn_{10}$  (OR, 1.148; 95% CI, 1.100–1.198), and  $Pb_{10}$  (OR, 1.054; 95% CI, 1.001–1.1104) were significantly associated with an increased risk of poor sleep quality.

**Table 7. Association between air pollutants (1-year and 3-month exposure periods) and poor sleep quality, stratified by age**

Air pollutants	1-year exposure period (Between November 2017 and October 2018)			3-month exposure period (Between August 2018 and October 2018)		
	Age < 65 (N=23,253)	Age ≥ 65 (N=8,797)	p for interaction	Age < 65 (N=23,253)	Age ≥ 65 (N=8,797)	p for interaction
PM <sub>10</sub>	1.174 (1.098–1.255)	1.045 (0.940–1.162)	0.068	1.328 (1.234–1.430)	1.087 (0.966–1.222)	0.0045
PM <sub>2.5</sub>	1.398 (1.267–1.543)	0.956 (0.815–1.121)	0.0001	1.681 (1.488–1.897)	1.143 (0.946–1.381)	0.0008
Pb <sub>10</sub>	1.159 (1.089–1.234)	1.080 (0.971–1.200)	0.255	1.054 (1.001–1.110)	0.986 (0.898–1.082)	0.217
Mn <sub>10</sub>	1.351 (1.280–1.426)	1.208 (1.105–1.320)	0.035	1.148 (1.100–1.198)	1.070 (0.997–1.148)	0.093
Cd <sub>10</sub>	1.029 (0.999–1.061)	1.020 (0.972–1.071)	0.758	0.988 (0.960–1.017)	0.999 (0.950–1.050)	0.713
Al <sub>10</sub>	1.209 (1.124–1.301)	1.048 (0.919–1.195)	0.062	1.343 (1.262–1.430)	1.098 (0.989–1.217)	0.001

PM<sub>10</sub>: particulate matter 10 µm or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5 µm or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.

## **5. Association between heavy metals in PM and poor sleep quality by residential area**

The results of the stratified analysis of the association of air pollutants ( $PM_{10}$ ,  $PM_{2.5}$ ) and heavy metals in  $PM_{10}$  with poor sleep quality by residential areas are presented in Table 8 and Figure 7. The study analyzed the association between air pollutants ( $PM_{10}$ ,  $PM_{2.5}$ ) and heavy metals in  $PM_{10}$  with poor sleep quality based on the residential areas. The analysis included 20,364 people living in the metropolitan area and 11,687 people living in other parts of the country. The odds ratios (ORs) for both 1-year and 3-month exposure to air pollutants were higher for those living in rural areas, indicating a greater association with poor sleep quality. Residents in areas exposed to air pollutants for 3 months were associated with poorer sleep quality for  $PM_{10}$ ,  $PM_{2.5}$ , and heavy metals (Pb, Mn, and Al) in  $PM_{10}$ , but less so for  $Cd_{10}$ .

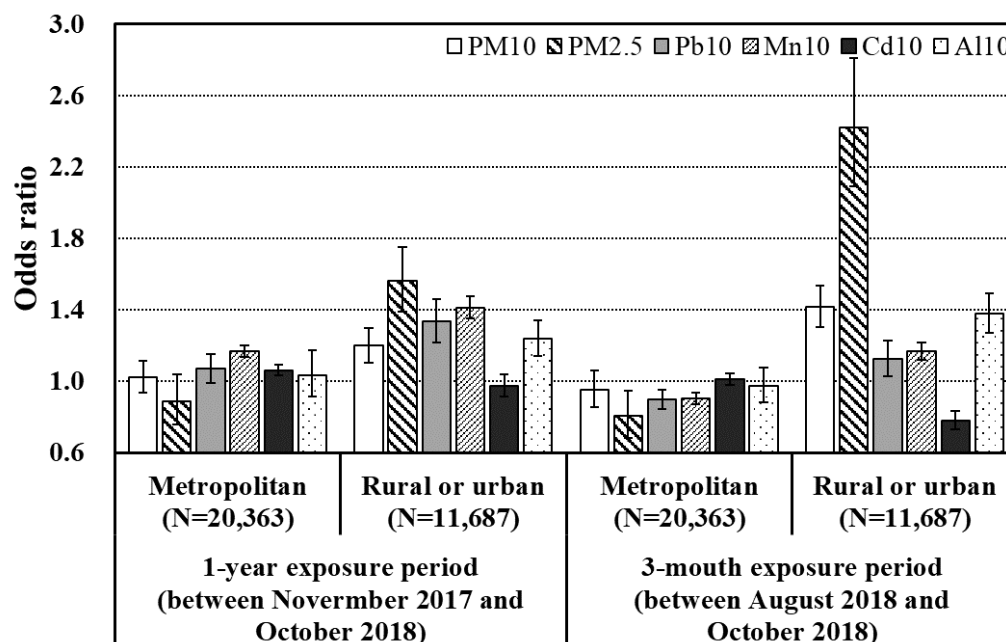
Among participants dwelling in metropolitan areas ( $N=20,363$ ), increases in the 1-year average concentrations of  $Mn_{10}$  (OR, 1.168; 95% CI, 1.087–1.254) and  $Cd_{10}$  (1.062; 1.031–1.093) were significantly associated with an increased risk of poor sleep quality (Table 8). Among participants dwelling in rural or urban areas ( $N=11,687$ ), increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.411; 95% CI, 1.318–1.511),  $Al_{10}$  (OR, 1.238; 95% CI, 1.142–1.343), and  $Pb_{10}$  (OR, 1.334; 95% CI, 1.217–1.461) were significantly associated with an increased risk of poor sleep quality. The risk of poor sleep quality associated with  $Pb_{10}$  ( $p < 0.001$ ),  $Mn_{10}$  ( $p < 0.001$ ), and  $Al_{10}$  ( $p < 0.001$ ) levels was higher in the rural and urban areas than in the metropolitan areas.



**Table 8. Association between air pollutants (1-year and 3-month exposure periods) and poor sleep quality, stratified by region**

Air pollutants	1-year exposure period (between November 2017 and October 2018)			3-month exposure period (between August 2018 and October 2018)		
	Metropolitan (N=20,363)	Rural or urban (N=11,687)	p for interaction	Metropolitan (N=20,363)	Rural or urban (N=11,687)	p for interaction
	Odds ratio (95% CI)			Odds ratio (95% CI)		
PM <sub>10</sub>	1.020 (0.934–1.114)	1.199 (1.106–1.300)	0.008	0.951 (0.853–1.059)	1.415 (1.302–1.537)	<0.001
PM <sub>2.5</sub>	0.887 (0.757–1.039)	1.561 (1.390–1.753)	<0.001	0.804 (0.683–0.947)	2.422 (2.089–2.807)	<0.001
Pb <sub>10</sub>	1.069 (0.991–1.153)	1.334 (1.217–1.461)	<0.001	0.897 (0.844–0.953)	1.124 (1.027–1.230)	<0.001
Mn <sub>10</sub>	1.168 (1.087–1.254)	1.411 (1.318–1.511)	<0.001	0.904 (0.843–0.970)	1.166 (1.111–1.223)	<0.001
Cd <sub>10</sub>	1.062 (1.031–1.093)	0.974 (0.914–1.038)	0.02	1.010 (0.979–1.042)	0.781 (0.733–0.831)	<0.001
Al <sub>10</sub>	1.034 (0.913–1.171)	1.238 (1.142–1.343)	0.02	0.973 (0.881–1.074)	1.376 (1.270–1.491)	<0.001

PM<sub>10</sub>: particulate matter 10 µm or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5 µm or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log-transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.

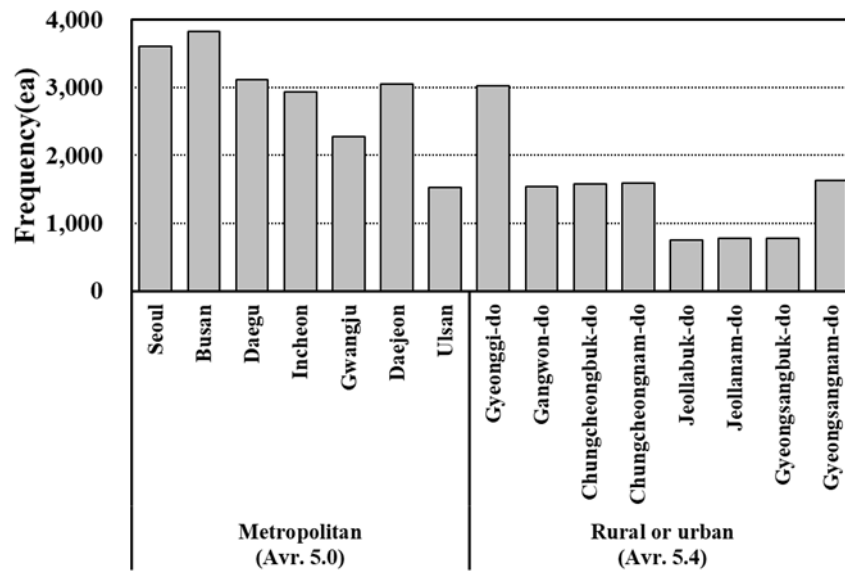


**Figure 7. Odds ratio of poor sleep quality according to air pollution exposure period, stratified by region**

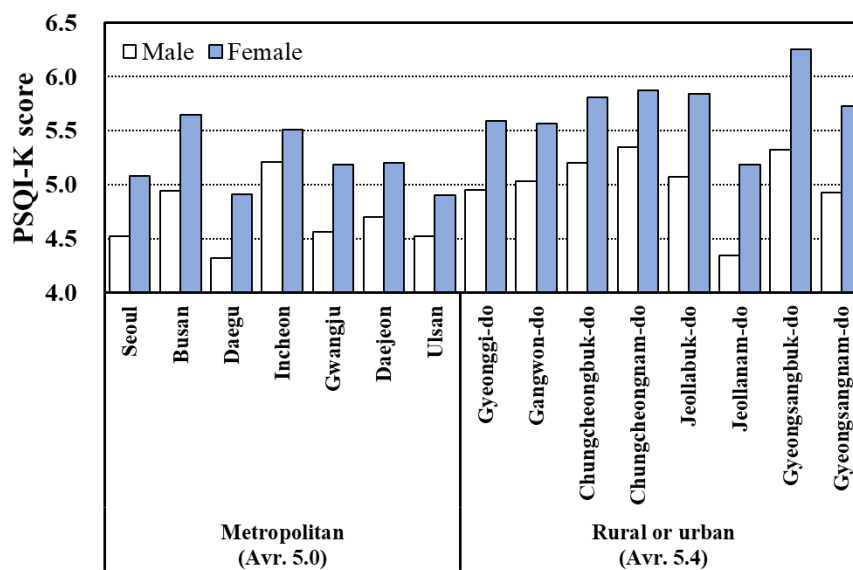
Table 9 summarizes the number of participants and average PSQI by administrative region. The average PSQI of all participants was 5.1, and the average sleep quality of metropolitan and rural or urban was 5.0 and 5.4, respectively. The average PSQI for metropolitan for male and female was 4.7 and 5.2, and for rural or urban it was 5.2 and 5.7. Compared to urban areas, the average PSQI of rural or urban was found to be slightly higher for both male and female. Additionally, the average PSQI of women in the region was the highest at 5.7. The distribution of sleep quality by administrative district is summarized in Figure 8.

**Table 9. Average PSQI of participants by administrative region**

Administrative District	Number of participants			Average of PSQI		
	Total	Male	Female	Total	Male	Female
Seoul	3,608	1,524	2,084	4.8	4.5	5.1
Busan	3,829	1,685	2,144	5.3	4.9	5.6
Daegu	3,122	1,401	1,721	4.6	4.3	4.9
Inchon	2,931	1,315	1,616	5.4	5.2	5.5
Gwangju	2,282	1,050	1,232	4.9	4.6	5.2
Daejon	3,058	1,374	1,684	5.0	4.7	5.2
Ulsan	1,533	738	795	4.7	4.5	4.9
Gyeonggi-do	3,029	1,399	1,630	5.3	5.0	5.6
Gangwon-do	1,539	706	833	5.3	5.0	5.6
Chungcheongbuk-do	1,576	711	865	5.5	5.2	5.8
Chungcheongnam-do	1,598	738	860	5.6	5.3	5.9
Jeollabuk-do	755	316	439	5.5	5.1	5.8
Jeollanam-do	780	353	427	4.8	4.3	5.2
Gyeongsangbuk-do	781	352	429	5.8	5.3	6.3
Gyeongsangnam-do	1,629	715	914	5.4	4.9	5.7
Metropolitan	20,363	9,087	11,276	5.0	4.7	5.2
Rural and urban (Do)	11,687	5,290	6,397	5.4	5.0	5.7
<b>Total</b>	<b>32,050</b>	<b>14,377</b>	<b>17,673</b>	<b>5.1</b>	<b>4.8</b>	<b>5.4</b>



(a) Participants



(b) Average PSQI

**Figure 8. Distribution of participants and PSQI in metropolitan and rural or urban**

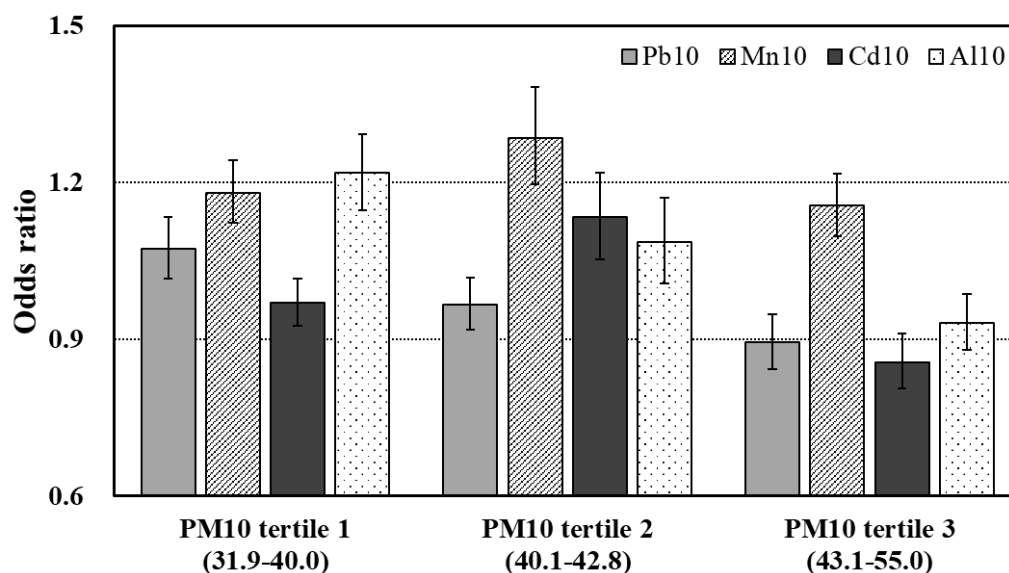
## **6. Association between heavy metals in PM and poor sleep quality by PM<sub>10</sub> level**

In individuals in the lowest tertile of PM<sub>10</sub> concentration, increases in the 1-year average concentrations of Pb<sub>10</sub> (OR, 1.073; 95% CI, 1.016–1.133), Mn<sub>10</sub> (OR, 1.180; 95% CI, 1.122–1.242), and Al<sub>10</sub> (OR, 1.218; 95% CI, 1.146–1.293) were associated with poor sleep quality (Table 10, Figure 9). In individuals in the tertile 2 of PM<sub>10</sub> concentration, increases in the 1-year average concentrations of Al<sub>10</sub> (OR, 1.086; 95% CI, 1.007–1.170), Cd<sub>10</sub> (OR, 1.133; 95% CI, 1.052–1.219), and Mn<sub>10</sub> (OR, 1.285; 95% CI, 1.196–1.382) were associated with poor sleep quality. In individuals in the highest tertile of PM<sub>10</sub> concentration, an increase in the 1-year average concentration of Mn<sub>10</sub> (OR, 1.155; 95% CI, 1.097–1.217) was associated with poor sleep quality.

**Table 10. Association between air pollutants (1-year exposure periods) and poor sleep quality, stratified by PM<sub>10</sub> tertile**

Air pollutants	PM <sub>10</sub> tertile 1 (31.9–40.0)	PM <sub>10</sub> tertile 2 (40.1–42.8)	PM <sub>10</sub> tertile 3 (43.1–55.0)
Pb <sub>10</sub>	1.073 (1.016–1.133)	0.966 (0.918–1.017)	0.894 (0.843–0.948)
Mn <sub>10</sub>	1.180 (1.122–1.242)	1.285 (1.196–1.382)	1.155 (1.097–1.217)
Cd <sub>10</sub>	0.969 (0.925–1.015)	1.133 (1.052–1.219)	0.856 (0.805–0.911)
Al <sub>10</sub>	1.218 (1.146–1.293)	1.086 (1.007–1.170)	0.931 (0.879–0.986)

PM<sub>10</sub>: particulate matter 10 µm or less in diameter; PM<sub>2.5</sub>: particulate matter 2.5 µm or less in diameter; Al: aluminum; Cd: cadmium; CI: confidence interval; Mn: Manganese; OR: odds ratio; Pb: Lead. Footnotes: Values are expressed as odds ratios and 95% confidence intervals (per 10 unit increase in PM<sub>10</sub> and PM<sub>2.5</sub>; log-transformed Al<sub>10</sub>, Pb<sub>10</sub>, Mn<sub>10</sub>, and Cd<sub>10</sub>), estimated from logistic regression models adjusted for age, sex, education level, marital status, smoking, alcohol consumption, history of hypertension, and history of diabetes mellitus.



**Figure 9. Odds ratio of poor sleep quality according to air pollution exposure period, stratified by PM<sub>10</sub> tertile**

## IV. DISCUSSION

### 1. Summary of findings

To our knowledge, this is the first study to investigate the association between airborne heavy metals and sleep quality. This study linked data from nationwide community health surveys and those from air quality monitoring for heavy metals in PM<sub>10</sub> (Al<sub>10</sub>, Mn<sub>10</sub>, Pb<sub>10</sub>, and Cd<sub>10</sub>). We found that 1-year average concentrations of Mn<sub>10</sub>, Al<sub>10</sub>, Pb<sub>10</sub>, and Cd<sub>10</sub> increased the risk of poor sleep. Among the heavy metals, Mn<sub>10</sub> exhibited the strongest association with poor sleep quality. Furthermore, the associations of Pb<sub>10</sub> and Mn<sub>10</sub> with poor sleep quality were greater in rural and urban areas than in metropolitan areas. In the lowest tertile of PM<sub>10</sub> concentration (40 µg/m<sup>3</sup> or below), increases in Pb<sub>10</sub>, Mn<sub>10</sub>, and Al<sub>10</sub> concentrations were significantly associated with poor sleep quality.

### 2. Discussion of study findings

Several studies have investigated the effect of PM exposure on sleep quality. A cohort study in rural China reported that long-term exposure to PM<sub>10</sub> and PM<sub>2.5</sub> was associated with an increased risk of poor sleep quality and higher global PSQI scores in approximately 27,000 adults (Chen et al. 2019). Another study conducted in northeastern China found that 10 µg/m<sup>3</sup> increases in PM<sub>10</sub> and PM<sub>2.5</sub> were associated with 17% and 47% higher risks of poor sleep quality, respectively, in 59,754 children (Lawrence et al. 2018). However, the

exact constituents of PM that contribute to the increased risk of poor sleep quality remain unclear. In addition to the associations between PM<sub>10</sub> and PM<sub>2.5</sub>, and poor sleep quality, the present study, including over 32,000 adults, showed that Mn<sub>10</sub>, Al<sub>10</sub>, Pb<sub>10</sub>, and Cd<sub>10</sub> concentrations were positively associated with the risk of poor sleep quality. This is the first study to suggest that inhalation of heavy metals in PM may adversely affect sleep quality.

### **3. Implications of the study**

The association between heavy metal exposure and sleep quality may be explained by heavy metal neurotoxicity. Numerous epidemiological studies have shown that exposure to heavy metals, including Mn, Pb, Cd, and Al, is associated with cerebrovascular damage and neurodegenerative diseases (Bakulski et al. 2020; Ijomone et al. 2020; Iqubal et al. 2020; Li et al. 2021; Li et al. 2022; Potter et al. 2021; Pyatha et al. 2022). Inhalation of heavy metals may upregulate oxidative stress and systemic inflammation, resulting in neuroinflammation (Lee et al. 2021a). Furthermore, ultrafine particles, including heavy metals (Potter et al. 2021) can directly enter the brain tissue through the olfactory nerve and induce neuroinflammation (Calderón-Garcidueñas et al. 2010; Li et al. 2018; Li et al. 2022; You et al. 2022). As we targeted heavy metals in PM, our findings underscore the neurotoxicity of inhalation exposure to heavy metals. Among heavy metals, we found that aluminum and manganese are highly associated with poor sleep quality. It is possible that



neuroinflammation induced by inhalation exposure to these heavy metals affects the sleep and wake cycles, as reported in previous studies (Dzhambov and Dimitrova 2016; Zhang et al. 2019).

#### **4. Limitation**

This study has several limitations. First, sleep-related variables were collected using self-reported questionnaires. Information on the exact date of the onset of sleep problems was not provided. Therefore, the factors needed to calculate the Pittsburgh Sleep Quality Index may have been underestimated or overestimated because sleep quality was assessed based on participants' memories. However, the PSQI is a widely used tool to assess sleep quality with a sensitivity and specificity of 90% and 87 %, respectively, at a cutoff value of 5 (Buysse et al. 1989). Second, we did not assess individual-level exposure to air pollution. The survey and air pollution data were linked based on administrative districts, but the resulting Berkson-type error was more likely to be a random error. Exposure assessments in this study indicate that participants are exposed to air pollution throughout the day, but it is nighttime behavior that contributes to poor sleep quality. This discrepancy in timing can lead to exposure misclassification. Additionally, individual changes in space cannot be reflected during the 1-year and 3-month exposure periods. Third, there is the possibility of unmeasured confounders. For example, although light and noise/vibration pollution may affect sleep quality, this study did not consider light pollution as a confounder. In our

stratified analysis, the association between heavy metal exposure and poor sleep quality was stronger in urban and rural areas than in metropolitan areas with high light pollution levels. Hence, residual confounding due to light pollution is likely to be null. In addition, there is a need to check the impact of additional confounding variables such as green space and living safety etc. (Halperin 2014; Hill et al. 2016; Johnson et al., 2018; Shin et al., 2020).

Nevertheless, this study has several key strengths that may offset the limitations mentioned above. This study covered a large, representative sample of adults living in urban communities in South Korea, with over 300,000 participants in 2018. This large-scale study investigated the impact of air pollution and heavy metals in PM10 on sleep quality by calculating the Pittsburgh Sleep Quality Index. Although there is a biological mechanism, few previous studies have investigated the association between heavy metals in air pollutants and sleep quality due to the cost and institutional limitations of measuring sleep quality and concentrations of heavy metals in air pollutants in a large number of participants. Therefore, although the results of this study have some limitations in terms of clinical interpretation, this study has sufficient value at the community level for the relationship between heavy metals in air pollutants and sleep quality. In addition, it will be very useful in establishing public health policies by investigating indicators in various regions that can cause confusion in assessing the impact of heavy metals among air pollutants on sleep quality.

## V. CONCLUSIONS

This study investigated the impact of exposure to air pollutants and the heavy metals contained in air pollutants on the sleep quality of adults at the community level. The results showed that  $PM_{10}$ ,  $PM_{2.5}$ , and the heavy metals ( $Al_{10}$ ,  $Mn_{10}$ , and  $Pb_{10}$ ) in  $PM_{10}$  were strongly associated with poor sleep quality. These findings have significant value at the community level and can be useful for formulating public health policies.

- (1) We found that 1-year average concentrations of  $Mn_{10}$ ,  $Al_{10}$ ,  $Pb_{10}$ , and  $Cd_{10}$  increased the risk of poor sleep. Among the heavy metals,  $Mn_{10}$  exhibited the strongest association with poor sleep quality. Furthermore, the associations of  $Pb_{10}$  and  $Mn_{10}$  with poor sleep quality were greater in rural and urban areas than in metropolitan areas. In the lowest tertile of  $PM_{10}$  concentration ( $40 \mu g/m^3$  or below), increases in  $Pb_{10}$ ,  $Mn_{10}$ , and  $Al_{10}$  concentrations were significantly associated with poor sleep quality.
- (2) In 1-year exposure of average concentrations, the odds ratio was in the order of  $Mn_{10}$  (OR, 1.311; 95% CI, 1.252–1.373),  $Al_{10}$  (1.170; 1.098–1.248),  $Pb_{10}$  (1.139; 1.080–1.202), and  $Cd_{10}$  (1.027; 1.001–1.054), with Mn having the greatest impact on poor sleep quality.
- (3) In the 3-month average concentrations, the odds ratio showed that  $Mn_{10}$  (OR, 1.127; 95% CI, 1.086–1.169) and  $Al_{10}$  (OR, 1.277; 95% CI, 1.211–1.348) were

significantly associated with an increased risk of poor sleep quality, but  $Pb_{10}$  (OR, 1.039; 95% CI, 0.993–1.087) and  $Cd_{10}$  (OR, 0.991; 95% CI, 0.967–1.016) were not significantly associated with poor sleep quality.

- (4) In 1-year exposure of average concentrations, the odds ratio of the  $Mn_{10}$  (OR, 1.332; 95% CI, 1.250–1.419) was higher in female, and the odds ratio of  $Pb_{10}$  (OR, 1.148; 95% CI, 1.061–1.241) and  $Al_{10}$  (OR, 1.194; 95% CI, 1.088–1.310) was higher in male. In the 3-month average concentrations, Al and Mn were found to be more associated with poor sleep quality in both male and female.
- (5) As a result of stratification analysis by residential area, the odds ratio was higher in rural and urban areas than metropolitan, showing that rural and urban areas were more closely related to poor sleep quality. Among participants dwelling in rural or urban areas (N=11,687), increases in 1-year average concentrations of  $Mn_{10}$  (OR, 1.411; 95% CI, 1.318–1.511),  $Al_{10}$  (OR, 1.238; 95% CI, 1.142–1.343), and  $Pb_{10}$  (OR, 1.334; 95% CI, 1.217–1.461) were significantly associated with an increased.
- (6) In individuals in the lowest tertile of  $PM_{10}$  concentration, increases in the 1-year average concentrations of  $Al_{10}$  (OR, 1.218; 95% CI, 1.146–1.293) showed the highest correlation with poor sleep quality. In individuals in the highest tertile of  $PM_{10}$  concentration, an increase in the 1-year average concentration of  $Mn_{10}$  (OR, 1.155; 95% CI, 1.097–1.217) was associated with poor sleep quality.

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## ABSTRACT (KOREAN)

### 대기 입자상 물질 중 중금속류 노출과 수면의 질과의 연관성 연구

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김 병 권

**연구배경:** 최근 대기오염물질에 장기간 노출이 나쁜 수면의 질과 연관성이 있는 것으로 나타났다. 인간이 흡입 노출을 통해 미세먼지 내 중금속에 지속하여 노출되면 중금속의 뇌신경 독성으로 인해 수면에 영향을 미칠 수 있다. 그러나, 미세먼지(PM)의 구성 성분인 중금속류의 흡입 노출 관점에서 뇌신경독성과의 연관성을 조사한 연구는 매우 제한적이며, 수면과의 연관성에 관한 연구도 찾아보기 어렵다. 따라서 본 연구에서는 한국의 지역사회건강조사 결과와 전국 대기측정망 자료(환경부 에어코리아)를 연계하여 대기오염 물질인 PM<sub>10</sub>, PM<sub>2.5</sub> 및 PM<sub>10</sub> 중의 중금속류(Al, Mn, Pb, Cd) 등 미세먼지의 오염 특성과 수면의 질과의 상관성을 평가하였다.

**연구방법:** 본 연구는 2018년 지역사회건강조사 참가자의 수면의 질을 PSQI로 평가하였으며, 글로벌 점수 5에 따라 PSQI  $\geq 5$ 는 나쁜 수면의 질로 평가하고 PSQI  $< 5$ 는 좋은 수면의 질로 간주하였다. PM<sub>10</sub> 중의 중금속류 노출

농도는 지역사회건강조사가 수행된 지역 보건소 255개소 중 44개의 보건소에 어코리아의 대기측정망과 연계되어 대기 중 중금속류 자료 확보할 수 있었다. 따라서 본 연구에서는 지역사회건강 조사가 수행된 3개월('18년 8월~10월) 및 1년('17년 11월~'18년 10월) 동안의 대기 중의 입자상 물질과 중금속류의 평균 농도를 활용하였다. 이 연구에서는 다변수 선형회귀분석 수행하였으며, 로지스틱 회귀분석을 통해 입자상 물질( $PM_{10}$ ,  $PM_{2.5}$ ) 및  $PM_{10}$  중 중금속류의 평균 농도와 나쁜 수면의 질과의 연관성을 조사하였다. 또한, 남성과 여성, 광역시와 그 외의 지역으로 성별 및 지역별로 구분하여 층화 분석을 수행하였다.

**연구결과:** 본 연구에 포함된 32,050명의 참가자 중 17,082명 (53.3%)가 나쁜 수면의 질을 나타내었고, 14,968명(46.7%)이 좋은 수면의 질을 나타내었다. 1년간의  $PM_{10}$  중 중금속류(log 변환)의 노출과 나쁜 수면의 질의 오즈비는 Pb 1.14 (95%CI 1.08-1.20), Mn 1.31 (95%CI 1.25-1.37), Cd 1.03 (95%CI 1.00-1.05) 및 Al 1.17 (95%CI 1.10-1.25)로 수면의 질과 연관성이 있는 것으로 나타났다. 또한, 3개월 동안 중금속류의 노출과 나쁜 수면의 질의 오즈비는 Mn 1.13 (95%CI 1.09-1.17) 및 Al 1.28 (95%CI 1.21-1.35)로 나쁜 수면의 질과 연관성이 있는 것으로 나타났다. 이 연구는 수면의 질과 대기오염물질 내 중금속과의 연관성을 조사한 첫 번째 연구이며,  $PM_{10}$  중의 중금속류(Pb, Mn, Cd 및 Al)가 나쁜 수면의 질과 연관성이 높은 것으로 나타났다.

**결론:** 이 연구는 대기오염물질 및 대기오염물질에 함유된 중금속류에 대한 노출이 성인의 수면의 질에 미치는 영향을 지역사회 수준에서 조사하였다. 그 결과 대기오염물질  $PM_{10}$ ,  $PM_{2.5}$  및  $PM_{10}$  중의 중금속류(Al, Mn, Pb)가 나쁜 수면의 질과 연관성이 높은 것으로 나타났다. 본 연구결과는 지역사회 수준에서 충분한 가치가 있으며 공중보건정책 수립에 유용하게 활용할 수 있을 것이다.

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**키워드:** 중금속류 노출, 수면의 질, 대기 입자상 물질