Effect of high PM2.5 concentrations on cardiovascular disease:

A South Korean cohort study

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Abstract

Background: Many studies have analyzed the relationship between average particulate matter less than 2.5µm in diameter (PM2.5) exposure and the human health, but few studies have focused on the effect of the frequency of PM2.5 concentration. The main purpose of this study is to analyze the relationship between the first occurrence of hospitalization for cardiovascular disease (CVD) and PM2.5 exposure, considering average PM2.5 concentration and the frequency of high PM2.5 concentration simultaneously.

Methods: We used large-scale cohort data from the National Health Insurance Service of Korea from 2002 to 2018, which includes a study population of 3,147,595. We estimated hazard ratios (HR) and 95% confidence intervals (CI) using the Cox proportional-hazards model with time-dependent covariates, including annual average PM2.5 and the annual hours of PM2.5 concentration exceeding 55.5 µg/m³ (FH55), considering the individual residential moving.

Results: We found that the risk was elevated by 6.7% (95% CI, 6.2-7.3) for all CVD, by 7.1% (95% CI, 5.9-8.4) for ischemic heart disease (IHD), and by 7.5% (95% CI, 6.0-9.1) for stroke per 1µg/m³ increase of average PM2.5. Interestingly, the 10-hour increase of FH55 decreased the risk of all CVD, IHD, and stroke by 7.0% (95% CI: 7.0–7.1), 7.3% (95% CI: 7.1–7.4), and 7.4% (95% CI: 7.2-7.6), respectively. This is due to people checking real-time or daily PM2.5 concentration information and voluntarily avoiding outdoor activities and exposure to high PM2.5 concentrations.

Conclusions: Based on the results, we conclude that accurate forecasts, information disclosure, and timely warning of high concentrations of PM2.5 at the national level have the potential to reduce the risk of CVD occurrence.
Keywords: particulate matter, cardiovascular disease, ischemic heart disease, stroke, Cox proportional hazards model
1. Introduction

Interest in particulate matter (PM) is growing as it is one of the most lethal threats to human health. PM penetrates deep into the body through the respiratory tract as the size decreases (Kim et al., 2015). Fine particles of 1–5µm in diameter can penetrate deep into the body and can spread to the blood vessels, thereby causing cardiovascular disease (CVD) (O’Donnell et al., 2011). There have been many studies analyzing the relationship between average PM less than 2.5µm in diameter (PM2.5) concentration and CVD mortality (Atkinson et al., 2014; Hoek et al., 2013; Laden et al., 2006; Li et al., 2018) and morbidity (Bai et al. 2019; Cesaroni et al., 2014; Kim et al., 2017; Liang et al., 2020; Yuan et al., 2019).

Because of the apparent evidence that PM has a negative effect on health, the Korean government has been trying to reduce the levels of PM that people are exposed to. Nevertheless, most Koreans believed that the PM concentration in 2018 was higher than that 10 years prior (Joo et al., 2018). However, the actual annual average PM less than 10µm in diameter (PM10) concentration in Korea declined from approximately 54µg/m³ in 2008 to approximately 41µg/m³ in 2018 (MOE, 2020). Similarly, the annual average PM2.5 concentration declined from approximately 26µg/m³ in 2015 to approximately 23µg/m³ in 2018. This discrepancy between the public perception of PM concentration and the actual trend of annual average PM2.5 concentration appears to be because of the increased frequency of exposure to high concentrations of PM in the short term. Figure 1 shows the trend of PM2.5 alerts¹ of some major regions in Korea from 2016 to 2019 (MOE, 2020). The total sum of days during which the alert is issued and then withdrawn has increased in 2016-2019. More details are shown in

¹ Currently, in Korea, the PM2.5 alert is issued when the hourly average PM2.5 concentration is above 75µg/m³ for over 2 hours and is withdrawn when it drops below 35µg/m³. Before July 1, 2018, these criteria were 90µg/m³ and 50µg/m³.
the Supplementary materials (Table S1). In addition, the annual hours when the average PM2.5 concentration exceeded 55.5µg/m³ in Seoul, Korea increased from 4.1% in 2016 to 6.5% in 2019 (IQAir, 2020).

Figure 1 PM2.5 alerts trends by region between 2016 and 2019 (Source: MOE, 2020)

Although the frequency of high PM2.5 concentration is increasing, to the best of our knowledge, there has been no study analyzing the relationship between PM2.5 exposure and CVD using the frequency of high PM2.5 concentration and average PM2.5 concentration simultaneously. Some studies using the sub-time PM concentration, that is, using PM information for a specific time as a variable instead of annual average PM concentration, found that the sub-time variable is significantly related to human health (Burgan et al., 2010; Delfino et al., 1998; Son and Bell, 2013). In contrast to these studies, in this study, we analyzed the relationship between the first occurrence of hospitalization for CVD and the frequency of high
PM2.5 concentration. For this, we used the Cox proportional-hazards model with time-varying variables using cohort data in Korea. To accurately analyze the effect of high PM2.5 concentration exposure, we used the annual hours of high PM2.5 concentration and average PM2.5 concentration in the model considering the individual residential region if the participant moved their residence. This study is organized as follows. We explain the data and models used in this study in Section 2. The estimation results are provided in Section 3. Finally, we discuss the implications, limitations, and further research topics in Section 4.

2. Materials and methods

2.1. Study population and health outcomes

We used cohort data provided by the National Health Insurance Service (NHIS) of Korea. All residents in Korea are obliged to partake in the NHIS; thus, NHIS cohort data covers the entire population living in Korea, including Koreans and foreigners. There are two types of cohort data provided by the NHIS: the NHIS-National Sample Cohort (NHIS-NSC) and NHIS-National Health Information Database (NHIS-NHID) (Lee et al., 2016; Sang et al., 2016). The NHIS-NSC are randomly selected data from approximately one million people of the total population in 2002–2015; thus, the data are reduced and refined for the convenience of the researcher. The NHIS-NHID contains data that can be extracted depending on specific patient characteristics according to the needs of the researcher. Therefore, it is useful for analyzing specific diseases during a specific period, although the data are raw and include missing values and errors. In this study, we used NHIS-NHID data because we targeted a specific disease, CVD, and a specific period, 2015–2018. We refined the raw data for analysis considering missing values and errors.
The cause of CVD in this study is defined according to the International Classification of Diseases 10th codes (ICD-10). We analyzed the first occurrence of hospitalization for all cases of CVD (ICD-10: I00–I99), ischemic heart disease (ICD-10: I20-I25), and stroke (ICD-10: I60–I64) in 2018. In the NHIS-NHID, the disease of the patient is recorded as the principal diagnosis and there are 1st to 4th additional diagnoses; the principal is the disease that mostly affects a patient's symptoms, and the latter ones are optionally recorded diseases. In this study, we analyzed the patients whose principal diagnosis and 1st additional diagnoses were recorded as CVD. Considering previous studies (Aigner et al. 2017; Ariesen et al. 2003; O’Donnell et al., 2010), we selected individual-level covariates such as age, sex, health insurance quartiles, body mass index (BMI) (kg/m²), total cholesterol (mg/dL), history of diabetes, smoking status (Non-smoker and Smoker), and alcohol intake (day/week). For this, we used the medical checkup data of the NHIS-NHID. In Korea, health insurance premiums are determined by household income; therefore, we considered health insurance quartiles as the subject’s economic level. For age, sex, and health insurance quartile, we used the 2018 data. For the other covariates, we used the most recent available data among the medical checkup data from the period 2015–2018 because the NHIS provides the medical checkup service biennially and since this medical checkup is not enforceable it is common for people to skip it.

For the analysis, we initially selected 5,502,448 people with a history of medical checkups in the period 2015–2018 among people without a history of CVD in the period 2002–2017. Next, we excluded 1,248,717 people (22.69%) due to a lack of residence address and pollution exposure. Then, we also excluded 1,106,136 people (20.1%) whose individual-level data is missing. Finally, we obtained 3,147,595 participants (57.2%) for analysis. The disease-

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*NHIS provides medical checkups to those over 20 years old, so this study includes subjects who are over 20 years old only.*
specific data selection process is shown in the Supplementary materials (Figure S1).

The Institutional Review Board of Yonsei University reviewed and approved this study (IRB no. 7001988-201907-HR-628-01E).

2.2. Air pollution and meteorological data

We used national hourly PM2.5 concentration data provided by the Korea Environment Corporation since 2015. The number of PM2.5 monitoring stations increased from 123 in 2015 to 325 in 2018. However, we only included monitoring stations, where more than 90% of the data were collected over a year, to exclude the cases in which data were collected in the second half of the year or were not reliably collected for various reasons. Finally, we selected the 232 monitoring stations, and the number of monitoring stations by region are shown in the Supplementary materials (Table S2). We averaged measurements from all selected monitoring stations in the same regions and used a single average value for each region. The frequency of high PM2.5 concentration (FH) was calculated by the annual hours when average PM2.5 concentration was above 55.5µg/m³ (hereafter, FH55) during individual exposure periods (from January 1, 2015 to the date of censoring by an individual). Regarding meteorological data, we considered temperature by region, which was obtained from the Korean National Meteorological Administration. If there were multiple weather stations in a region, all of the measurements from the weather stations in the same region were averaged into a single value.

The average PM2.5 concentration and meteorological data were averaged from the hourly measurements for each region during individual exposure periods. We also matched the PM2.5 exposure and meteorological data corresponding to the individual residential region if the participant moved their residence.
2.3. Statistical analyses

We used the extended Cox proportional-hazards model with time-dependent covariates, which was developed by Fisher and Lin (1999). The Cox model is a widely used survival analysis method for analyzing long-term health effects and air pollution (Cox, 1972). The main assumption of the standard Cox model is that it has a constant hazard ratio (HR) over time (Cox 1972). However, in this study, the exposure period varies by individual, i.e., the hazard rate changes according to the exposure period of the individual. To consider this characteristic, we used the extended Cox model, which is free of the constant HR over time. We created four periods for time-dependent variables, PM2.5 exposure, and temperature; period 1, period 2, and period 3 are for 2015, 2016, and 2017, respectively, and period 4 is from January 1, 2018 to the date of censoring (disease occurrence, death, or the end of the study).

The extended Cox model is expressed as follows,

\[ h_i(t) = h_0(t) \cdot \exp(\alpha \cdot X_i + \beta \cdot X_i(t)), \number{1} \]

where \( h_0(t) \) is the baseline hazard function; \( X_i \) is the vector of time-independent variables of the subject \( i \) such as sex, age, health insurance quartiles, BMI, total cholesterol, history of diabetes, smoking status, and alcohol intake; \( X_i(t) \) is the vector of time-dependent variables such as average PM2.5, FH55, and temperature; and \( \alpha \) and \( \beta \) are coefficients of time-independent and time-dependent variables to be estimated, respectively.

We used equation [1] according to the type of disease (all CVD, IHD, and stroke) and PM2.5 exposure (average PM2.5 and FH55). Moreover, we also performed subgroup analysis by sex (Male and Female), age (Younger, \( \leq 65 \) years old; Older, \( > 65 \) years old), health insurance quartiles (Covered by medical aid; Lower; Lower middle; Upper middle; Upper),
BMI (Underweight, < 18.5 kg/m²; Normal, 18.5 to 30 kg/m²; Obese, ≥ 30 kg/m²), total cholesterol (Normal, < 240 mg/dL; High, ≥ 240 mg/dL), history of diabetes (No and Yes), smoking status (Non-smoker, Smoker), and alcohol intake (Non-drinker, 0 day/week; Drinker, 1-7 day/week). All analyses were conducted using STATA (version 16; Stata Corporation, College Station, TX, USA).

3. Results

Table 1 shows the characteristics of the study population, which includes 47,160 cases, 9,442 cases, and 6,508 cases of all CVD, IHD, and stroke, respectively. In the entire cohort without CVD, the average age of the study population was 43.6 years, and 59.4% were men. The proportions of non-smokers and smokers were 57.1% and 42.9%, respectively. Especially, in the female group, the smoker group (6.4%) was very small compared to the non-smoker group (93.6%). On the other hand, in the male group, the proportion of the smoker group (67.8%) was higher than their counterparts (32.2%). For IHD and stroke, the proportions of the groups with male, older, high total cholesterol, and history of diabetes were relatively higher than those of other groups.

Table 1 Characteristics of the study populations (NHIS-NHID cohort data in Korea)

| Characteristic | Entire cohort without CVD (N = 3,100,435) | All CVD (I00–I99) (N = 47,160) | IHD (I20-I25) (N = 9,442) | Stroke (I60–I64) (N = 6,508) |
|---------------|-------------------------------------------|-------------------------------|--------------------------|-------------------------------|
| Sex [n (%)]   |                                           |                               |                          |                               |
| Male          | 1,840,390 (59.4)                          | 28,028 (59.4)                 | 7,262 (76.9)             | 4,449 (68.4)                 |
| Female        | 1,260,045 (40.6)                          | 19,132 (40.6)                 | 2,180 (23.1)             | 2,059 (31.6)                 |
| Age [n (%)]   |                                           |                               |                          |                               |
| Younger       | 2,973,869 (95.9)                          | 38,607 (81.9)                 | 7,533 (79.8)             | 4,541 (69.8)                 |
| Older         | 126,576 (4.1)                             | 8,553 (18.1)                  | 1,909 (20.2)             | 1,967 (30.2)                 |
| Average age of occurrence [years] | 43.6 (11.2) | 53.5 (12.5) | 55.7 (11.0) | 58.4 (12.5) |
|-----------------------------------|-------------|-------------|-------------|-------------|

| Health insurance quartiles [n (%)] |
|-----------------------------------|-------------|-------------|-------------|-------------|
| Covered by medial aid             | 11,155 (0.4) | 673 (1.4)   | 159 (1.7)   | 145 (2.2)   |
| Lower                             | 816,375 (26.3) | 13,035 (27.6) | 1,984 (21.0) | 1,592 (24.5) |
| Lower middle                      | 890,323 (28.7) | 11,550 (24.5) | 2,402 (25.4) | 1,787 (27.5) |
| Upper middle                      | 630,188 (20.3) | 10,390 (22.0) | 2,183 (23.1) | 1,403 (21.6) |
| Upper                             | 752,394 (24.3) | 11,512 (24.4) | 2,714 (28.7) | 1,581 (24.3) |

| Body mass index (BMI) [n (%)] |
|--------------------------------|-------------|-------------|-------------|-------------|
| Underweight                     | 111,420 (3.6) | 1,449 (3.1) | 170 (1.8)   | 201 (3.1)   |
| Normal                           | 2,822,470 (91.0) | 42,813 (90.8) | 8,770 (92.9) | 5,985 (92.0) |
| Obese                            | 166,545 (5.4) | 2,898 (6.1) | 502 (5.3)   | 322 (4.9)   |
| Average BMI [kg/m³]              | 23.9 (3.5)   | 24.3 (3.5)  | 24.6 (3.2)  | 24.1 (3.4)  |

| Total cholesterol [n (%)] |
|--------------------------|-------------|-------------|-------------|-------------|
| Normal                   | 2,725,395 (87.9) | 39,375 (83.5) | 7,484 (79.3) | 5,368 (82.5) |
| High                     | 375,040 (12.1) | 2,898 (6.1) | 1,958 (20.7) | 1,140 (17.5) |
| Average total cholesterol [mg/dL] | 197.7 (36.6) | 202.2 (42.4) | 207.5 (45.0) | 203.4 (51.5) |

| History of diabetes [n (%)] |
|-----------------------------|-------------|-------------|-------------|-------------|
| No                          | 3,041,707 (98.1) | 43,982 (93.3) | 8,627 (91.4) | 5,848 (89.9) |
| Yes                         | 58,728 (1.9)   | 3,178 (6.7) | 815 (8.6)   | 660 (10.1)   |

| Smoking status [n (%)] |
|------------------------|-------------|-------------|-------------|-------------|
| Non-smoker             | 1,771,706 (57.1) | 24,373 (51.7) | 3,564 (37.7) | 2,907 (44.7) |
| Male non-smoker        | 592,885 (32.2) | 6,765 (24.1) | 1,564 (21.5) | 1,044 (23.5) |
| Female non-smoker      | 1,178,821 (93.6) | 17,608 (92.0) | 2,000 (91.7) | 1,863 (90.5) |
| Smoker                 | 1,328,729 (42.9) | 22,787 (48.3) | 5,878 (62.3) | 3,601 (55.3) |
| Male smoker            | 1,247,505 (67.8) | 21,263 (75.9) | 5,698 (78.5) | 3,405 (76.5) |
| Female Smoker          | 81,224 (6.4)   | 1,524 (8.0)  | 180 (8.3)    | 196 (9.5)    |

| Alcohol intake [n (%)] |
|------------------------|-------------|-------------|-------------|-------------|
| Non-drinker            | 1,499,112 (48.4) | 24,490 (51.9) | 4,829 (51.1) | 3,363 (51.7) |
| Drinker                | 1,601,323 (51.6) | 22,670 (48.1) | 4,613 (48.9) | 3,145 (48.3) |
| Average alcohol intake [day/week] | 1.1 (1.3) | 1.1 (1.6) | 1.1 (1.6) | 1.3 (1.8) |

* Data is presented as mean (standard deviation)

Table 2 shows the average PM2.5 and FH55 during the individual exposure period.
The average annual PM2.5 concentration was 24.6 µg/m³ with a standard deviation (SD) of 1.8 µg/m³. The average FH55 exposures in the groups with the occurrence of disease were small compared to the entire cohort without CVD because the number of exposure days in period 4 is less.

Table 2 Average values for air pollutant and meteorological variables during individual exposure periods

| Exposure period | Entire cohort without CVD | All CVD (I00–I99) | IHD (I20-I25) | Stroke (I60–I64) |
|-----------------|---------------------------|-------------------|---------------|------------------|
|                 | PM2.5 (µg/m³)             |                   |               |                  |
| Period 1        | 24.5 ± 1.1                | 24.6 ± 1.1        | 24.6 ± 1.1    | 24.6 ± 1.2       |
| Period 2        | 26.0 ± 1.4                | 26.0 ± 1.4        | 26.0 ± 1.4    | 26.0 ± 1.4       |
| Period 3        | 24.9 ± 1.6                | 24.9 ± 1.6        | 25.0 ± 1.6    | 24.9 ± 1.6       |
| Period 4        | 23.1 ± 1.6                | 26.4 ± 4.4        | 26.5 ± 4.4    | 26.4 ± 4.4       |
| Average         | 24.6 ± 1.8                | 25.5 ± 2.6        | 25.5 ± 2.6    | 25.5 ± 2.6       |
|                 | FH55 (days)               |                   |               |                  |
| Period 1        | 366.2 ± 91.5              | 366.1 ± 92.2      | 366.6 ± 92.8  | 367.9 ± 94.3     |
| Period 2        | 303.7 ± 74.9              | 302.3 ± 76.8      | 303.7 ± 77.0  | 302.8 ± 74.5     |
| Period 3        | 392.9 ± 137.5             | 385.2 ± 142.4     | 386.9 ± 146.0 | 386.6 ± 144.4    |
| Period 4        | 431.0 ± 162.8             | 275.7 ± 155.3     | 274.9 ± 157.5 | 275.2 ± 152.5    |
| Average         | 373.4 ± 130.4             | 332.4 ± 129.2     | 333.0 ± 131.3 | 333.1 ± 129.3    |
|                 | Temperature (°C)          |                   |               |                  |
| Period 1        | 13.6 ± 1.0                | 13.6 ± 1.1        | 13.6 ± 1.1    | 13.6 ± 1.1       |
| Period 2        | 13.7 ± 1.1                | 13.7 ± 1.1        | 13.7 ± 1.1    | 13.7 ± 1.1       |
| Period 3        | 13.1 ± 1.3                | 13.2 ± 1.3        | 13.1 ± 1.3    | 13.2 ± 1.3       |
| Period 4        | 13.0 ± 1.2                | 8.2 ± 6.6         | 8.0 ± 6.7     | 8.2 ± 6.7        |
| Average         | 13.3 ± 1.2                | 12.2 ± 4.2        | 12.1 ± 4.2    | 12.2 ± 4.2       |

Table 3 shows the estimation results of the extended Cox model in terms of HR and 95% CI. The risks were elevated by 6.7% (95% CI: 6.2–7.2) for all CVD, 7.2% (95% CI: 6.0–8.4) for IHD, and 7.6% (95% CI: 6.1–9.1) for stroke per a 1µg/m³ increase of average PM2.5. These results were statistically significant at the 99% significance level.
Table 3 Hazard ratios and 95% CI for all CVD and stroke

| Variable                                      | Hazard ratios (95% confidence interval) |
|-----------------------------------------------|----------------------------------------|
|                                               | All CVD (I00–I99) | IHD (I20–I25) | Stroke (I60–I64) |
| Average PM2.5 (per 1µg/m³)                   | 1.067 (1.062, 1.073) | 1.071 (1.059, 1.084) | 1.075 (1.060, 1.091) |
| Sex (male vs. female)                        | 1.195 (1.165, 1.226) | 0.670 (0.629, 0.713) | 0.935 (0.871, 1.004) |
| Age (per 1 year)                              | 1.053 (1.052, 1.054) | 1.074 (1.072, 1.076) | 1.083 (1.081, 1.085) |
| Health insurance quartiles                    | 0.989 (0.981, 0.996) | 1.064 (1.046, 1.083) | 0.998 (0.978, 1.019) |
| BMI (per 1 kg/m²)                             | 1.030 (1.028, 1.033) | 1.053 (1.046, 1.059) | 1.029 (1.021, 1.037) |
| Total cholesterol (per 1 mg/dl)               | 1.000 (1.000, 1.000) | 1.002 (1.002, 1.002) | 1.002 (1.001, 1.002) |
| History of diabetes (no vs. yes)              | 1.519 (1.465, 1.576) | 1.617 (1.503, 1.739) | 1.779 (1.638, 1.933) |
| Smoking Status (No vs. yes)                   | 1.212 (1.182, 1.242) | 1.406 (1.332, 1.484) | 1.363 (1.277, 1.455) |
| Alcohol intake (per 1 day/week)               | 1.054 (1.047, 1.060) | 1.011 (0.997, 1.025) | 1.067 (1.051, 1.083) |
| Temperature (per 1 °C)                        | 0.517 (0.514, 0.520) | 0.470 (0.464, 0.476) | 0.466 (0.458, 0.473) |

* HR is the ratio of the hazard rate in the treatment group versus the control group; if the variable is continuous, HR is the change in the risk of disease occurrence probability when the variable is increased by one unit.

** For each dummy variable, we set the first and the latter in the square bracket as the control group (coded as 0) and the treatment group (coded as 1).

* Significant at 5% level. ** Significant at 1% level.

Furthermore, we analyzed the effects of FH55 instead of the average PM2.5 and Table 4 shows the estimated HR with 95% CI. The ten hours increase of FH55 reduced the risk of all CVD, IHD, and stroke by 7.0% (95% CI: 7.0–7.1), 7.3% (95% CI: 7.1–7.4), and 7.4% (95% CI: 7.2–7.6), respectively. These results were statistically significant at the 99% significance level.

Table 4 Hazard ratios and 95% CI for 10 hours increase in FH55

| Hazard ratios (95% confidence interval) |
|----------------------------------------|
| All CVD (I00–I99) | IHD (I20–I25) | Stroke (I60–I64) |
| 0.930 (0.929, 0.930) | 0.927 (0.926, 0.929) | 0.926 (0.924, 0.928) |

In addition, we conducted subgroup analysis by sex, age, health insurance quartiles, BMI, total cholesterol, history of diabetes, smoking status, and alcohol intake to identify those sensitive to average PM2.5 exposure. Figure 2 presented the HR and 95% CI for all CVD by
subgroups and those of IHD and stroke are shown in the Supplementary materials (Figure S2 and Figure S3). We found that the risk of the female smoker group was the highest. In addition, the estimated HR of the female, younger, and no diabetes history groups were higher than each comparative groups for all CVD occurrences. For IHD, the vulnerable groups were the same for all CVD. On the other hand, for stroke, the group of obesity, high total cholesterol, and history of diabetes had a higher risk.

Figure 2 Hazard ratios and 95% CIs for all CVD by subgroups

* Significant at 5% level. ** Significant at 1% level.
4. Discussion

In this study, we analyzed the effect of PM2.5 exposure on the first occurrence of hospitalization for CVD, considering the average PM2.5 exposure and frequency of high PM2.5 concentration using large-scale cohort data in Korea. From the analysis, we found that the first occurrence of all CVD, IHD, and stroke is related to the average PM2.5, and this is consistent with previous studies (Bai et al., 2019; (Hart et al., 2015); Kim et al., 2017; Kim et al., 2020; Liang et al., 2020; Miller et al., 2007; Qiu et al., 2017). For all CVD, the estimated HR of the female group was higher than that of the male group, which indicates that females are more vulnerable to annual PM2.5 exposure than males. This result is similar to previous studies (Bai et al., 2019; Kim et al., 2017; Kim et al., 2020; Liang et al., 2020), but some studies are showing the opposite result (Qiu et al., 2017); (Stafoggia et al., 2014). In terms of diabetes, the results are similar to (Hart et al., 2015), although they only included women in their analysis. They found that the risk of all CVD occurrence was higher in people without a history of diabetes and the risk of stroke occurrence was higher in people with a history of diabetes. In terms of smoking status, the HR of the smoker group was higher than the non-smoker group, especially the risk of female smoker group was highest. These results are consistent with (Qiu et al., 2017). They conducted the analysis classifying the smoking status into never, former, and current smoker and found that the risks of female former and current smoker groups were higher than that of male groups as well as female never smoker group. In contrast, some studies found that the HR of the non-smoker group was higher than that of the smoker group (Kim et al., 2017); (Liang et al., 2020); (Stafoggia et al., 2014), and regarding these results, Puett et al. (2008) argued that the health effects of smoking may dilute the health effects of air pollution.

The estimated risk in this study was higher than in previous studies analyzing other
countries. The reasons could be due to the following differences between this study and previous ones. First, the average PM2.5 concentration in this study was higher than in the studies in western countries. In previous studies, the mean PM2.5 concentration exposures were 9.6µg/m³ in Canada (Bai et al., 2019), 13.4µg/m³ (Hart et al., 2015), 13.5µg/m³ (Miller et al., 2007), and 17.8µg/m³ (Puett et al., 2011) in the United States, and 10µg/m³ (Cai et al., 2018), and less than 19µg/m³ (Cesaroni et al., 2014) in Europe except for Italy, whereas the mean PM2.5 concentration exposure in this study (Korea) was 24.6µg/m³. Second, the health endpoints and data coverage were different. In this study, we selected the first occurrence of hospitalization for all CVD, IHD, and stroke as the endpoint. For example, in a recent study conducted in Hong Kong, Qiu et al. (2017) selected the first occurrence of emergency hospital admissions as a health endpoint and used the health record data collected from public hospitals, excluding private hospitals. The NHIS-NHID data used in this study was more extensive data, including those from not only public hospitals but also private hospitals. Third, Korea is one of the most densely populated countries among the Organisation for Economic Cooperation and Development countries (OECD, 2020). In a recent study conducted in China, the cohort they used included 15 provinces, including Beijing (1,324 people/km²), which has a high population density, as well as Qinghai (8.2 people/km²), which is less densely populated (Huang et al., 2019; Liang et al., 2020; Ma et al., 2017). This study covered 13 of the 16 regions in Korea that have a very high population density at more than 200 people/km² (KOSTAT, 2020).

Next, we also analyzed the effect of annual hours when the average PM2.5 concentrations above 55.5 µg/m³, which has not been examined in previous studies. We found that FH55 decreases the risk of CVD occurrence. This finding was unexpected and could be attributed to people’s perception and adaptive behavior to PM. Cho and Kim (2019) surveyed 171 Korean people using a five-point Likert scale (1 point: very unlikely – 5 points: very likely)
regarding the perception of PM and response behavior in Seoul, Korea. Respondents gave 4.00 and 3.43 points for “Checking the PM concentration every day” and “Refraining from going out when the PM concentration is high,” respectively. Wells et al. (2012) analyzed 10,898 adults to determine if they tried to mitigate exposure when air pollution was severe using the data from the 2007–2010 National Health and Nutrition Examination Survey in the United States. They defined the susceptible groups as the elderly, people with respiratory disease, and people with CVD. They found that 14.2% of elderly people, 25.1% of people with respiratory disease, and 15.5% of people with CVD changed their behavior according to atmospheric PM levels. In particular, 65.9% of those who said they changed their behavior reported that they “spent less time outdoors.” Moreover, air quality alerts can help to change the behavior of people when air quality is very poor. Noonan (2014) surveyed to determine whether smog alerts could change people’s behavior in Atlanta, United States. He found that the issuance of smog alerts reduced park usage in the elderly and those exercising groups. Saberian et al. (2017) analyzed cycling use changes in Sydney due to air pollution. They analyzed the cycle movement count collected from electronic path-side devices installed at 31 points in the designated cycle paths from May 2008 to September 2013. They found a 14–35% reduction in cycle movement when air quality alerts were issued. Similarly, it appears that these perceptions and behaviors reduced the risk of disease occurrence despite the increased annual hours when the average PM2.5 concentration was above 55.5µg/m³. This means that people refrain from outdoor activities and reduce PM exposure voluntarily when it is predicted that PM is high, and this contributes to a decrease in HR even though FH55 is increased.

The meanings of this study are as follows. First, the results show a relationship between PM2.5 concentration and CVD occurrence. Average PM2.5 concentration exposure increased the risk of all CVD, IHD, and stroke, and most results were statistically significant. However, FH55 was statistically significant but decreased the risk of disease occurrence. We
interpret these results as people avoiding high PM exposure voluntarily by checking real-time PM2.5 concentration information and air quality alerts. Accurate forecasts, information disclosure, and timely warning of high PM2.5 concentrations at the national level have the potential to reduce the risk of CVD occurrence. Second, we used a large-scale cohort with 3,147,595 study participants. The NHIS is a universal coverage health insurance system that is mandatory for citizens in Korea. Most previous studies conducted in Korea used NHIS-NSC data, which includes one million randomly extracted people from the total population regardless of disease. However, this study used NHIS-NHID data, which includes all CVD patients in 2018 without a previous history of the disease. With this large amount of data, we were able to estimate the effect of PM2.5 exposure on CVD more precisely and derive more reliable and generalizable results. Third, we considered the residential moves of the study population during exposure periods.

Despite the strengths, this study has a few limitations that could be overcome by further research. First, there have been no previous studies that analyzed the frequency of high air pollution concentration; therefore, it is difficult to compare and generalize our results, which are based on people’s regional adaptive behaviors in Korea. The annual average PM2.5 concentration in Korea is decreasing gradually but is still higher than that in other countries. Likewise, the global annual average PM2.5 concentration is steadily decreasing (HEI, 2019; EEA, 2019). However, cities in some countries still experience high PM2.5 concentrations for many hours of the year (IQAir, 2020). In countries where PM2.5 measurement, prediction, and forecasting are not systematically performed, the frequency of high PM2.5 concentration may affect the occurrence of disease. Therefore, various follow-up studies are needed to investigate the relationship between the frequency of high PM2.5 concentrations and human health. Second, the PM2.5 concentration data in Korea is incomplete; 124 monitoring stations have collected nationwide PM2.5 concentration data since 2015, and the number increased to 324
stations in 2018 (MOE, 2020). This means that there are no data for some regions in 2015. Therefore, future studies that incorporate PM2.5 data for all regions are necessary. Third, we used PM2.5 concentrations in residential regions, not workplace regions. As is the case for many workers, the region where they spend their most time for working is different from the region where they reside. This study considered only the residential region.

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Competing interests

The authors declare that they have no competing interests.
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