Prolonged Short-Term Exposure To A High Concentration of Ambient Fine Particulate Matter And Effect Modification On Daily Mortality

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Research

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Abstract

Background: Although the evidence for the effect of short-term mortality is very high, epidemiologic studies on the effect of prolonged continuous exposure to high concentrations are rare. This study aimed to investigate how the size of the mortality effect of PM$_{2.5}$ would be modified when a high concentration period persisted.

Methods: We used daily mortality counts (ICD-10, non-traumatic all-cause: A00-R99, respiratory: J00-J98, and cardiovascular: I00-I99), simulated levels of daily PM$_{2.5}$, measured daily mean temperature, and relative humidity data in seven metropolitan cities from 2006 to 2019. Generalized additive models (GAMs) with quasi-Poisson distribution in seven cities and random-effects meta-analyses to pool city-specific effects were used to examine the short-term effects of PM$_{2.5}$. To investigate effect modification by continuous exposure to prolonged high concentrations, we applied categorical consecutive day variables to the GAMs as effect modification terms of PM$_{2.5}$. Subgroup analyses were performed to examine the variation in effect modification according to the age group.

Results: The mortality risk according to increase of 10 µg/m$^3$ of PM$_{2.5}$ concentration was increased by 0.30% (95%CI, 0.13–0.49), 0.48% (95%CI, 0.09–1.05), and 0.23% (95%CI, -0.10–0.57) based on the model with 0-1 lag day, for all-cause, respiratory, and cardiovascular diseases, respectively. The risk for all-cause mortality per 10 µg/m$^3$ increase of PM$_{2.5}$ in the first and fourth consecutive days were significantly increased by 0.61% (95%CI, 0.17–1.06) and 0.34% (95%CI, 0.03–0.65). The effect modification was prominent in the 65 years old group.

Conclusions: We found a significantly increased risk of all-cause, respiratory, and cardiovascular mortality for daily PM$_{2.5}$ exposure when the day of high concentration began and the days lasted for more than 4 days with high concentration of ≥35 µg/m$^3$. The elderly showed a stronger effect of persistently high PM$_{2.5}$.

Introduction

It has been well-known that exposure to ambient fine particulate matter (PM$_{2.5}$) is designated a group 1 carcinogen by the International Agency for Research on Cancer (IARC), and the background level of PM$_{2.5}$ concentration in the Republic of Korea has been much higher than in other Western countries. According to the Korean Ministry of Environment, the average annual concentration of PM$_{2.5}$ in all regions of Korea in 2019 was 23 µg/m$^3$. In 2011, the Korean government established a new air quality guideline for PM$_{2.5}$, which was strengthened by a daily average of 50 µg/m$^3$ and an annual average of 25 µg/m$^3$ to 35 µg/m$^3$ and 15 µg/m$^3$, respectively in March 2018 [1]. As a result, a day exceeding the standard was frequently notified to the public. Moreover, if the hourly average concentration exceeds 75 or 150 µg/m$^3$ for more than 2 h, an advisory or alert is regionally issued, which increases public concerns on health effects.

The average duration of concentrations above 35 µg/m$^3$ in the first quarter of Korea was reported to increase from 16.2 h in 2015 to 26.5 h in 2018, and the average 1 h concentration also slightly increased from 95.4 µg/m$^3$ in 2015 to 102.0 µg/m$^3$ in 2018 [2]. Despite its heterogeneity across different cities worldwide, several time-series studies on the short-term mortality in association with exposure to ambient PM$_{2.5}$ have shown consistent pooled effect sizes [3–6], and evidence for causality has recently been reported [7, 8]. However, there are relatively few observational reports on the effects of continuous exposure to prolonged high concentrations [9, 10].

We aimed to investigate the short-term effect of ambient PM$_{2.5}$ exposure on daily mortality in Korean and assess the effect of continuous exposure to prolonged high-concentration PM$_{2.5}$ by testing whether the effect sizes were modified depending on the days of prolongation.

Methods

Study area and population

The study areas are Seoul, the capital city of the Republic of Korea, and the six metropolitan cities of Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan (seven major cities; See Figure S1, Additional File 1). The study population of these seven cities was approximately 22.6 million as of 2019, covered approximately 43.7% of the total population of the nation. The study was conducted from January 1, 2006, to December 31, 2019, for a total of 5,113 days. The institutional review board of the Dankook University, Republic of Korea, exempted this study from review because of using only de-identified secondary data (iRb no. DKU 2021-03-042).

Mortality data

We used the Cause of Death Statistics data from the MicroData Integrated Service (MDIS, https://mdis.kostat.go.kr/) of Statistics Korea for mortality data, an open-source data accessible to the public for research purposes. In anonymized form, cause of death (International Classification of Diseases, 10th Revision, ICD-10 code), date of death, area of death (city and province), sex, age, nationality, occupation, marital status, and educational level were individually provided.

We counted daily mortalities for non-accidental all-cause (ICD-10 codes, A00 to R99), respiratory disease (J00 to J98), and cardiovascular disease (I00 to I99) in seven major cities from January 1, 2006, to December 31, 2019.

PM$_{2.5}$ mass concentration data

Ambient PM$_{2.5}$ has been measured through the national air pollution monitoring network since 2015 in Korea. Therefore, we used simulated data considering weather conditions, anthropogenic and biogenic emissions, and chemical transport [11, 12] which was recently used in several epidemiological studies of
Korean air pollution [13, 14].

We used the Community Multiscale Air Quality (CMAQ, version 4.7.1) system with the AEROS aerosol module, chemical mechanism, and the Statewide Air Pollution Research Center 99 (SAPRC99). Weather simulations were performed using the Weather Research and Forecasting (WRF version 3.3.1) model using the National Center for Environmental Protection FNL (Final) data as the initial field. The Meteorology Interface Processor version 3.6 was used to prepare the CMAQ-ready meteorological input. The Clean Air Policy Support System 2010, which is the Korean national emissions inventory, was processed through the Sparse Matrix Operator Kernel Emission (SMOKE, version 3.1) to estimate anthropogenic emissions, and biogenic emissions were estimated using the Model of Emissions of Gases and Aerosols from Nature (MEGAN). We applied a 27-km modeling domain (covering Northeast Asia, including China, Japan, and Korea) and a 9-km horizontal resolution, and a 27-km modeling domain simulation value was applied to the boundary condition of the 9-km modeling domain. We calculated the daily average PM$_{2.5}$ concentration for each of the seven major cities from January 1, 2006, to December 31, 2019.

**Meteorological data**

We collected daily average temperature and relative humidity data (one measurement point per city) for seven major cities from January 1, 2006, to December 31, 2019, which are open-source data available at the National Climate Data Center of the Korea Meteorological Administration (https://data.kma.go.kr/).

**Statistical analysis**

We first evaluated the association between daily PM$_{2.5}$ concentration and daily non-accidental all-cause, respiratory disease, and cardiovascular disease mortality using time-series analyses as basic procedures. As a statistical model, a generalized additive model (GAM) with quasi-Poisson distribution was used, and the commonly applied model equation is as follows:

$$\log \left[ E \left( Y_{t,c} \right) \right] = \beta_0 + \beta_{PM_{2.5}} \times PM_{2.5, t, c} + s \left( temp_{lag90-1,c} \right) df = 6 + s \left( rh_{t,c} \right) df = 3 + s \left( time_t \right) df = 7 + \text{numberofyears} + \eta \times \text{factor}$$

Where $E \left( Y_{t,c} \right)$ is the expected death count on day $t$ in city $c$, $PM_{2.5, t, c}$ is the averaged 24-h mean PM$_{2.5}$ concentration ($\mu g/m^3$) on day $t$ applied lag $l$ (0 to 6 d, and 2-day to 7-day moving average), which means the average over the current and previous days and the current to sixth day before, respectively, in city $c$, $temp_{lag90-1,c}$ is the averaged 24-h mean temperature ($^\circ C$) on day $t$ and day $t-1$ (lag 0–1) in city $c$, $rh_{t,c}$ is mean relative humidity (%) on day $t$ in city $c$, $time_t$ is a continuous variable-processed of day $t$ to consider the time trend of death, and $dow_{t,c}$ is a categorical day-of-week and holiday variable of day $t$, which has four levels (weekday, Sunday and holiday, the day after Sunday and holiday, and Saturday) [14]. Where $s$ represents the smooth spline function, $df$ represents the degree of freedom applied to each function, and $\eta$ represents the coefficients of dummy variables of $dow_{t,c}$. For temperature, lag 0–1 was determined because the generalized cross validation (GCV) score was the lowest among the various lag applied models; $dfs$ for temperature, relative humidity, and time trend were determined based on the model methodology of the most recently reported and large-scale multicity time series study [3].

We pooled the coefficients ($\beta_{PM_{2.5}}$) paired for each lag structure from the above city-specific models using random-effects meta-analyses and estimated the mortality risk percentage change per increase of 10 $\mu g/m^3$ of PM$_{2.5}$ concentration using the following equation:

$$\text{Percentage change (\%)} = \left( e^{\text{Pooled}\beta} - 1 \right) \times 100$$

For the second step, when the averaged 24-h mean PM$_{2.5}$ concentration was $\geq$35 $\mu g/m^3$, it was defined as a high-concentration day. To investigate whether the effect size of PM$_{2.5}$ changed during prolonged exposure to high PM$_{2.5}$ concentration, we added the consecutive day variable and its effect modification term to PM$_{2.5}$ concentration in quasi-Poisson GAM as follows:

$$\log \left[ E \left( Y_{t,c} \right) \right] = \beta_0 + \beta_{PM_{2.5}} \times PM_{2.5, t, c} + s \left( \text{con\_day}_{t,c} \right) df = 6 + s \left( \text{time}_t \right) df = 3 + s \left( \text{dow}_t \right)$$

where $\text{con\_day}_{t,c}$ is a six-level categorical variable that specifies how many days the high concentration lasted on day $t$ applied lagged exposure ($l$) in city $c$ (no high concentration day, the first to fourth day, and the fifth or more day; an example of coding variable is shown in Figure S2, Additional File 1), and the rest are the same as the basic GAM above. Using these models, we estimated six PM$_{2.5}$ coefficients in the strata of consecutive days. We excluded the single effect of $\text{factor} \left( \text{con\_day}_{t,c} \right)$ in the models because we could not find a difference in model fitness depending on whether the independent effect was applied.

We pooled the PM$_{2.5}$ coefficients paired for each lag structure and level of consecutive day variables using random-effects meta-analyses and estimated the mortality risk percentage change per increase of 10 $\mu g/m^3$ of PM$_{2.5}$ concentration for each consecutive day variable level using the following equation:

$$\text{Percentage change (\%)} = \left( e^{\beta_{PM_{2.5}: \text{con\_day}, i}} - 1 \right) \times 100$$

where $\beta_{PM_{2.5}: \text{con\_day}, i}$ is a stratum-specific PM$_{2.5}$ coefficient, where $i$ represents the six-level of $\text{con\_day}$ variable.

Furthermore, to investigate the possible effect modification by age group, the above analyses were performed by two stratified age groups, 20–64 years old and $\geq$65 years old.

Page 3/11
All dataset set-ups and statistical analyses were performed using R software, version 3.6.3 (Foundation for Statistical Computing, Vienna, Austria). We also used the "mgcv" package for GAM modeling and the "metafor" package for random-effects meta-analyses in the R software. The statistical significance level for the two-tailed test was set at 0.05.

Results

Table 1 summarizes non-traumatic all-cause, respiratory, and cardiovascular mortality in seven major cities from 2006 to 2019. In the study area, the total numbers of non-traumatic all-cause, respiratory, and cardiovascular deaths were 1,314,829 (daily mean, 257.2), 120,094 (daily mean, 23.5), and 326,034 (daily mean, 63.8), respectively.

Table 1. All-cause (non-traumatic), respiratory, and cardiovascular mortality (N) in seven major cities in Republic of Korea from 2006 to 2019

The mean concentration of PM$_{2.5}$ throughout the study period ranged from 23.0 to 27.4 µg/m$^3$ by city, and over the past 14 years, a roughly declining trend has been observed. However, the annual average concentration of all seven cities was over 20 µg/m$^3$ in 2019, exceeding the annual governmental air quality guideline of 15 µg/m$^3$. In 2019, the average annual concentration in Seoul was 25.7 µg/m$^3$, the highest among the seven cities (See Table S1, Additional File 1).

For the day of high concentration defined by an average 24-h mean PM$_{2.5}$ concentration of 135 µg/m$^3$, the proportion of days of high concentration in seven cities during the study period ranged from 13.6% in Gwangju (693 out of 5,113 days) to 22.9% in Seoul (1,171 out of 5,113 days). From 2006 to 2019, the annual proportion of high-concentration days gradually decreased (See Table S2, Additional File 1).

A summary of consecutive days with prolonged high concentrations of PM$_{2.5}$ in seven cities is shown in Table 2. In the case of Seoul, 679 days (13.3%) lasted for more than two consecutive days of high concentration from 2006 to 2019. Furthermore, consecutive days lasting more than 5 days accounted for 0.8-2.7% by city. In all seven cities, although the number of days of high concentration had decreased until 2019, the episodes when the high concentration lasted a long time did not disappear, and there were still consecutive days lasting more than a week in Seoul, Incheon, Gwangju, and Daejeon in 2019 (Figure 1).

Table 2. Consecutive days and proportion with daily mean PM$_{2.5}$ concentration of 35 µg/m$^3$ or more in seven major cities in Republic of Korea for 5113 days, 2006 to 2019

Figure 1. Distributions of consecutive days with high concentration (35 µg/m$^3$ or more) of PM$_{2.5}$ in seven cities, Republic of Korea by year from 2006 to 2019. The x-axis represents the year, and the y-axis represents the number of days with high PM$_{2.5}$ concentration (reference: 35 µg/m$^3$) by year. It is expressed that the more the days of high concentration prolonged, the darker the blue color becomes.

From 2006 to 2019, the percentages of risk changes per an increase of 10 µg/m$^3$ of PM$_{2.5}$ concentration in non-traumatic all-cause, respiratory, and cardiovascular mortality in the lag 0-1 models were 0.30% (95%CI, 0.13–0.48), 0.48% (95%CI, -0.09-1.05), and 0.23% (95%CI, -0.10–0.57), respectively (Table 3). The effect estimates for each city and the pooled values derived from the various lag models are presented in Table S3, Additional File 1. The largest effects per 10 µg/m$^3$ of increase in non-traumatic all-cause, respiratory, and cardiovascular mortalities were 0.31% (95%CI, 0.16–0.46, lag 0 model), 0.61% (95%CI, -0.02–1.24, lag 0-2 model), and 0.37% (95%CI, 0.08–0.66, lag 0 model), respectively (See Table S3, Additional File 1).

Table 3. Pooled effects of daily ambient PM$_{2.5}$ exposure and their modification by consecutive days with high concentration on daily mortality in seven cities of Republic of Korea from 2006 to 2019

In the models that apply the effect modification of consecutive days with high concentration, the pooled effect estimates for each level of consecutive days are presented in Table 3. For non-traumatic all-cause mortality per increase of 10 µg/m$^3$ applied lag 0-1 exposure, we found 0.61% (95%CI, 0.17–1.06) on the first day and 0.34% (95%CI: 0.03–0.65) on the fourth day, which is higher than the effect size we found in the basic model. This pattern was similar for respiratory and cardiovascular mortality (Table 3). In particular, for respiratory mortality in lag 0-1 models, we found 0.86% (95%CI, 0.03–1.69) on the first day and 1.39 (95%CI, 0.42–2.37) on the fourth day (Table 3). The effect estimates for each city and the pooled values derived from the various lag models are presented in Table S3, Additional File 1. The largest percentages of risk changes per an increase of 10 µg/m$^3$ were 0.86% (95%CI, 0.13–0.48) and 0.61% (95%CI, -0.02–1.24) on the fourth day (Table 3). In 2019, the average annual concentration in Seoul was 25.7 µg/m$^3$, the highest among the seven cities (See Table S1, Additional File 1).
model, for cardiovascular mortality, no noticeable modification patterns were found other than 0.76% (95% CI, 0.10–1.62) on the first days in the lag 2 model (Figure 2; See Table S7, Additional File 1).

In the ≥65 years old group, for respiratory mortality in the lag 0-1 model, 1.05% (95% CI, 0.19–1.93) on the first consecutive day, and 1.38% (95% CI, 0.3–2.41) on the fourth day, which were consistent with the estimates found in the whole age group analyses (Figure 2; See Table S8, Additional File 1). The percentage change in risk of 1.87% (95% CI, 0.43–3.33) was noticeable on the fourth consecutive day in the lag 1 model (See Table S8, Additional File 1). For cardiovascular mortality, the highest effect sizes were observed in the lag 0-1 model, and we observed 0.74% (95% CI, 0.19–1.30) on the first consecutive day and 0.61% (95% CI, -0.04–1.27) on the fourth day, which was the pattern observed in the analyses of whole age group (Figure 2; See Table S8, Additional File 1).

Discussion

We found a short-term positive effect of PM$_{2.5}$ on mortality in this multi-city time-series design for seven major Korean cities from 2006 to 2019. Considering continuous exposure to prolonged high concentrations that exceeded the daily mean of 35 µg/m$^3$, the effects of PM$_{2.5}$ on daily all-cause, respiratory, and cardiovascular mortality were higher on the first and fourth consecutive days with high concentrations. In addition, the effect was mainly shown in the elderly population aged 65 years or more.

There are more reports of short-term effects of PM$_{2.5}$ on mortality compared to long-term effects in Korea; however, the effect sizes vary greatly depending on the spatiotemporal background of each study, the applied statistical model and exposure assessment [15]. Moreover, to date, only two multi-city designs have been published for the effect of particulate matter (PM$_{10}$) on mortality [3, 16]; to the best of our knowledge, no studies have reported the pooled effect of PM$_{2.5}$ through multi-city design in Korea.

Two studies reported the short-term effect of PM$_{2.5}$ on daily mortality for each city. Jung et al. [17] reported that the total daily mortality risk in individuals aged ≥60 years old increased by 0.36% per increase of 10 µg/m$^3$ from 2000 to 2012 in Seoul, Republic of Korea, using Poisson GAM applied lag 0 exposure; however, no estimates were presented for the entire population. Kim et al. [18] found that the risk of total daily mortality increased with an increase of 10 µg/m$^3$ with 0.34%, 1.18%, and 0.43% in Seoul, Busan, and Incheon, respectively, from 2006 to 2012 using quasi-Poisson GAM applied lag 0-1 exposure. We also found that total daily mortality increased by 0.44% (95% CI, 0.18–0.69%, per an increase of 10 µg/m$^3$) in the ≥65 years old group in Seoul, which is somewhat consistent with the result of Jung et al. [17] (See Table S6, Additional File 1). However, we found that the risk increases in Seoul, Busan, and Incheon were 0.24%, 0.25%, and 0.13%, respectively, in the lag 0-1 models (Table S3), which was not consistent with the results of Kim et al. [18]. This previous study used actual monitoring of PM$_{2.5}$; however, we used a simulated dataset. Furthermore, there is a difference in the statistical models that we did not consider barometric pressure to covariate and in the study period that we expanded to 2019. Finally, the number of reports of PM$_{2.5}$ problems in the mass media in Korea has increased rapidly since 2012 [19]; thus, we probably assumed that this was reflected in the increase in the rate of wearing health masks due to increased risk awareness [20].

Two studies have focused on the short-term effects of prolonged continuous exposure to high PM$_{2.5}$. The first study presented the excess risk of cardiovascular and respiratory mortality for continuous exposure to high concentrations in Beijing, China, from 2010 to 2012. Using GAM, the PM$_{2.5}$ concentration variable was not added, and instead, the categorical variable specified how long the high concentration lasted based on the daily mean 75, 85, 105, 115 µg/m$^3$ criteria applied to the models. Focusing on the susceptible group rather than the entire population, the main result was that on the ninth day of the consecutive high concentration duration of 105 µg/m$^3$ or more, a 53% increase in the risk of cardiovascular mortality was reported in outdoor workers [9].

The second study reported the short-term durational effect of prolonged exposure to high concentrations of PM$_{10}$ in 28 cities in China, Japan, and Korea. Using quasi-Poisson GAM, the effect of the change in PM$_{10}$ concentration and duration (the number of consecutive days with 75 µg/m$^3$ or more) was separated. In Korea, the estimated increases in risk for each additional consecutive day with high concentration were 0.48% for non-traumatic all-cause mortality, 0.48% for cardiovascular mortality, and 1.13% for respiratory mortality, and minimal effect modification by two age groups based on 65 [10].

Both studies suggested their own health effects, and the magnitude of the effects could be increased when high concentrations were continuously prolonged. However, the health effect of consecutive high concentration duration was also associated with exposure to PM$_{2.5}$. Therefore, we thought it was necessary to investigate whether the short-term mortality effect of PM$_{2.5}$ was modified to a greater size when the high concentration persisted and apply the effect modification term between PM$_{2.5}$ concentration and the high concentration consecutive day variable in our GAMs. To the best of our knowledge, this study is the first to report the effect modification of the short-term effect of PM$_{2.5}$ when a high concentration persists.

A new finding of this study was that the short-term effects of PM$_{2.5}$ on daily non-traumatic all-cause, respiratory, and cardiovascular mortality on the first and fourth consecutive days with high PM$_{2.5}$ concentrations were greater than the estimated effect for the entire period. From a short-term perspective, it was interesting to note that the risk did not increase linearly as the continuous exposure to high concentrations increased but increased from the first transition to the day with high concentration and at some point, i.e., the fourth day of consecutive duration.

As a result of age stratification, in the 20–64 years old group, we could not observe noticeable significant effect change due to the relatively low number of deaths in the group. If the high concentration lasts approximately 4 days, the respiratory effect may increase, future research with greater statistical power will be required. In the ≥65 years old group, the effect on the first consecutive day with high concentration was remarkable. The finding suggests that the health effect is greater when the level of exposure to high concentrations of PM$_{2.5}$ increases dramatically in a short period of time, and it can be thought that the population more susceptible to PM$_{2.5}$ was greatly affected on the first day of consecutive duration.
We found that a high concentration of PM$_{2.5}$, lasting $\geq$7 days, was still observed in 2019. However, there is still insufficient understanding of intermittent high concentrations of PM$_{2.5}$ episodes in Korea, and there is also a spatial difference in the contribution sources and components of PM$_{2.5}$ [2]. In general, when the influence of China is large, sulfate increases, and nitrate and organic particles are known to be generated locally. Recently, in most high-concentration consecutive duration episodes without yellow dust storms in the western, central, and southeastern parts of the Korean peninsula, the increase in sulfate, nitrate, and ammonium ion concentrations, rather than organic carbon, inorganic carbon, and heavy metals, was more pronounced than that of the PM$_{2.5}$ mass concentration [2, 21].

A study suggested null findings on the short-term mortality effects of sulfate, nitrate, and ammonia ions in Korea [22]. However, in other studies, the effects of sulfate, nitrate, and ammonia ions on cardiovascular mortality from 2008 to 2009 and emergency hospital visits for cardiovascular disease from 2010 to 2013 in Seoul were greater than those of PM$_{2.5}$ mass concentration [23, 24]. In a multi-city study of six cities in Korea from 2013 to 2015, the pooled effect size of nitrate and sulfate was not greater than that of the mass concentration of PM$_{2.5}$ [25]. With the findings reported in Korea, the evidence for these three water-soluble ions is still insufficient and inconsistent.

As a result of a meta-analysis of studies published before August 2018, the short-term risk increases of nitrates and sulfate for cardiovascular mortality were 0.58% and 0.33% (per interquartile range(IQR) increase), respectively, with statistical significance even after adjusting for the mass of PM$_{2.5}$. For hospitalization for respiratory disease, the short-term risk increase of nitrates was 0.68% (per IQR increase) with statistical significance [26]. We carefully speculate whether the effect of PM$_{2.5}$ on daily mortality increases with the high concentration consecutive duration was probably due to a variation in PM composition, especially the increase in nitrates and sulfates.

The exposure-response curve for the effect of cardiovascular mortality according to the duration and intensity of exposure to PM$_{2.5}$ has been reported to have a downward curve shape [27]. Pope et al. [27] examined the curve of the high concentration range by extrapolating from the results of smoking or specific circumstances of high PM$_{2.5}$ exposure. Meanwhile, a recently reported study from 2009 to 2012 in Beijing, China (annual average PM$_{2.5}$ of 84.9 µg/m$^3$) showed that the relative risks of total and cardiovascular mortality increased as the background concentration increased (50 µg/m$^3$ or more). Conversely, in the case of respiratory mortality, the relative risk decreased as the background concentration increased [28]. In this study, we estimated the relative risks for all-cause mortality across the 10 µg/m$^3$ intervals of background PM$_{2.5}$ concentration (See Figure S3, Additional File 1). We found higher risk estimates on the first and fourth consecutive days than those derived in the high PM$_{2.5}$ concentration intervals of more than 40 µg/m$^3$ (See Figure S3, Additional File 1); therefore, it could be possible to see that the effect modification we observed was not simply an effect of the background effect of high concentration.

This study had several limitations. There may be misclassifications in the exposure assessment. In other words, the local variation in PM$_{2.5}$ concentration in the same metropolitan area cannot be reflected. In addition, the specific cause of the regional and temporal variation in the effect of PM$_{2.5}$ cannot be explained in our study. Demographic characteristics such as age, sex, population density, traffic volume, and access to medical institutions are possible effect modifiers [29, 30]. Finally, the short-term effect of PM$_{2.5}$ on daily mortality increases and the variation in effect size within a short period of time with a high concentration consecutive duration cannot be explained by significant scientific evidence. Future studies are needed to investigate the effect in susceptible groups in detail and apply the components of PM$_{2.5}$ to the models with reflected effect modification by a high concentration consecutive duration, as we proposed in our study.

Despite several shortcomings, we also have several strengths. Focusing on the change in the effect size of PM$_{2.5}$, when the high concentration persists, which is problematic in East Asia, we found that the mortality effect of PM$_{2.5}$ may increase short-term even more during the period of high concentration. Moreover, among the time series for short-term mortality effect reported in Korea, this study has the longest period of 14 years, and is the first multi-city study for the short-term effect of PM$_{2.5}$ on mortality, including more than half of the entire Korean population.

**Conclusion**

We investigated the short-term effect of fine particulate matter on daily non-traumatic all-cause, respiratory, and cardiovascular mortality in seven major cities in Korea from 2006 to 2019 and found a greater effect on daily mortality when the high PM$_{2.5}$ concentration duration began during the day and lasted for about 4 days. The elderly may be more affected by persistently high PM$_{2.5}$. When the causes of high concentration episodes and their components are identified, our results could be used as scientific evidence for risk communication and policy-making to the public.

**Declarations**

**Ethics approval and consent to participate**

The institutional review board of the Dankook University, Republic of Korea, exempted this study from review because we used only de-identified secondary data (IRB no. DKU 2021-03-042).

**Consent for publication**

Not applicable

**Availability of data and materials**
The mortality and daily climate datasets analysed during the current study are available in the MicroData Integrated Service (MDIS, https://mdis.kostat.go.kr/) of Statistics Korea and the National Climate Data Center of the Korea Meteorological Administration (https://data.kma.go.kr/), which are accessible to the public for research purpose. But the simulated pollutant datasets implemented during the current study are not publicly available due to data ownership but are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Author's contributions**

H.L. was a major contributor in writing the manuscript. S.B., H-J. B., M.H. & H-J. K. conceptualized and supervised the study. J.C. & K-H. C. contributed to the implementation and validation of the methodology. S.K. generated and provided the simulated exposure assessment datasets. All authors read and approved the final manuscript.

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**References**


Tables

Table 1. All-cause (non-traumatic), respiratory, and cardiovascular mortality (N) in seven major cities in Republic of Korea from 2006 to 2019.

<table>
<thead>
<tr>
<th>City</th>
<th>Population in 2019</th>
<th>All-cause mortality (non-traumatic, N)</th>
<th>Respiratory mortality (N)</th>
<th>Cardiovascular mortality (N)</th>
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<td>Daily mean (SD)</td>
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</tr>
<tr>
<td>Incheon</td>
<td>2957026</td>
<td>160818</td>
<td>31.5 (7.0)</td>
<td>15425</td>
</tr>
<tr>
<td>Gwangju</td>
<td>1456468</td>
<td>84898</td>
<td>16.6 (4.6)</td>
<td>9342</td>
</tr>
<tr>
<td>Daejeon</td>
<td>1474870</td>
<td>81039</td>
<td>15.8 (4.4)</td>
<td>7798</td>
</tr>
<tr>
<td>Ulsan</td>
<td>1148019</td>
<td>57064</td>
<td>11.2 (3.6)</td>
<td>5350</td>
</tr>
<tr>
<td>Total</td>
<td>22617362</td>
<td>1314829</td>
<td>257.2 (31.5)</td>
<td>120094</td>
</tr>
</tbody>
</table>

SD: Standard deviation

Table 2. Consecutive days and proportion with daily mean PM$_{2.5}$ concentration of 35 μg/m$^3$ or more in seven major cities in Republic of Korea for 5113 days, 2006 to 2019
Table 3. Pooled effects of daily ambient PM$_{2.5}$ exposure and their modification by consecutive days with high concentration on daily mortality in seven cities of Republic of Korea from 2006 to 2019

<table>
<thead>
<tr>
<th>City</th>
<th>Prolonged high concentration of ≥35 μg/m$^3$ [number of days, (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No high day</td>
</tr>
<tr>
<td>Seoul</td>
<td>3942 (77.1)</td>
</tr>
<tr>
<td>Busan</td>
<td>4074 (79.7)</td>
</tr>
<tr>
<td>Daegu</td>
<td>4195 (82.0)</td>
</tr>
<tr>
<td>Incheon</td>
<td>4107 (80.3)</td>
</tr>
<tr>
<td>Gwangju</td>
<td>4421 (86.5)</td>
</tr>
<tr>
<td>Daejeon</td>
<td>4336 (84.8)</td>
</tr>
<tr>
<td>Ulsan</td>
<td>4290 (83.9)</td>
</tr>
</tbody>
</table>

The city specific estimated effects were from quasi-Poisson generalized additive models (GAMs) with two-day moving average (the average over the current and previous day, lag 0-1) of PM$_{2.5}$ concentration and then pooled with random-effect meta-analyses.

Figures
Figure 1

Distributions of consecutive days with high concentration (35 μg/m³ or more) of PM$_{2.5}$ in seven cities, Republic of Korea by year from 2006 to 2019. The x-axis represents the year, and the y-axis represents the number of days with high PM$_{2.5}$ concentration (reference: 35 μg/m³) by year. It is expressed that the more the days of high concentration prolonged, the darker the blue color becomes.
Figure 2

Non-traumatic all-cause, respiratory, and cardiovascular mortality risk percent changes per 10 μg/m³ increase of daily average PM$_{2.5}$ and their modification by consecutive days with high concentration (35 μg/m³ or more) in model applied lag 0-1 exposure. This graph shows the risk percent changes in total population (left column), the age between 20 and 65 group (middle column), and the age of 65 or more group (right column). The red square boxes are estimates of the effects over the whole study period in basic models without applying consecutive day variable. Others represents estimates of six coefficients in the strata of consecutive days (no high concentration day, the first to fourth day, and the fifth or more day) in the effect modification models. Vertical lines with point estimates denote 95% confidence intervals.

Supplementary Files

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