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Air Pollution and Heat Waves

Long-term exposure to moderate fine particulate matter concentrations and cause-specific mortality in an ageing society

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Abstract

Background: Long-term exposure to particulate matter $<2.5\,\mu m$ in size ($PM_{2.5}$) is considered a risk factor for premature death. However, only a few studies have been conducted in areas with moderate $PM_{2.5}$ concentrations. Moreover, an ageing society may be more susceptible to environmental exposure and future burden of mortality due to $PM_{2.5}$.
Methods: This study estimates hazard ratios (HRs) for all-cause and cause-specific mortality from long-term exposure to moderate $PM_{2.5}$ concentrations in the elderly populations of seven cities in South Korea. We also projected nationwide elderly mortality caused by long-term exposure to $PM_{2.5}$, accounting for population ageing until 2045. Mortality in 1 720 230 elderly adults aged $\geq$65 years in 2008 was monitored across 2009–16 and linked to modelled $PM_{2.5}$ concentrations.
Results: A total of 421 100 deaths occurred in 2009–16, and the mean of annual $PM_{2.5}$ concentration ranged between 21.1 and 31.9 $\mu g/m^3$ in most regions. The overall HR for a 10 $\mu g/m^3$ increase in a 36-month $PM_{2.5}$ moving average was 1.024 (95% confidence intervals: 1.009, 1.039). We estimated that 11 833 all-cause nationwide elderly deaths were attributable to $PM_{2.5}$ exposure. Annual death tolls may increase to 17 948 by 2045. However, if $PM_{2.5}$ is reduced to 5 $\mu g/m^3$ by 2045, the tolls may show a lower increase to 3646.
Conclusions: Long-term exposure to moderately high levels of $PM_{2.5}$ was associated with increased mortality risk among the elderly. Thus, $PM_{2.5}$ reduction in response to the projected ageing-associated mortality in South Korea is critical.

Key words: Ageing society, burden of mortality, particulate matter, survival analyses

Key Messages

- Globally, particulate matter <2.5 μm in size ($PM_{2.5}$) caused ~2.2 million deaths in the elderly population in 2015. If the current $PM_{2.5}$ concentration level remains, and the elderly population increases in the future, the population may face more significant negative health impacts.
- We estimated that 11 833 all-cause nationwide elderly deaths were attributable to $PM_{2.5}$ exposure in 2015. Annual death tolls may increase to 17 948 by 2045. However, if $PM_{2.5}$ is reduced to 5 $\mu g/m^3$ by 2045, the tolls may decrease to 3646.
- The projection of mortality attributable to long-term exposure to $PM_{2.5}$ indicated the urgent need for emission control and reduction in $PM_{2.5}$ concentration levels in South Korea over the coming decades to safeguard the vulnerable ageing population.

Introduction

Long-term exposure to particulate matter <2.5 μm in size ($PM_{2.5}$) has been suggested as a risk factor for premature death due to ischaemic heart disease (IHD), stroke, chronic obstructive pulmonary disease (COPD), lung cancer and lower respiratory tract infections. Globally, $PM_{2.5}$ caused ~4.2 million premature deaths in all age groups and 2.2 million deaths in the elderly population in 2015.[1] If the current $PM_{2.5}$ concentration level is maintained and the elderly population increases in the future, the population may face more significant negative health impacts.

Several concentration–response (CR) functions integrating long-term $PM_{2.5}$ exposure and mortality have been used to estimate $PM_{2.5}$-associated deaths. Currently, integrated exposure–response (IER) functions developed based on cohort studies are widely used.[1] However, IER functions are limited due to their reliance on cohort studies from Western countries where $PM_{2.5}$ concentrations are relatively low compared with other regions. Recent cohort studies in Asia[2,3] have led to a reduction in CR function uncertainties at higher $PM_{2.5}$ concentration ranges. However, significant uncertainties still remain regarding the shape of the CR functions in mid-range exposure (20–40 $\mu g/m^3$). Estimating the health effects of $PM_{2.5}$ in South Korea may help to fill the knowledge gap regarding the long-term health effects of mid-range $PM_{2.5}$ exposure. Moreover, previous $PM_{2.5}$ health impact studies in South Korea have been conducted by applying the IER functions, or the previously reported linear CR functions.[4,5] However, no studies have calculated the burden of mortality due to $PM_{2.5}$ using locally estimated CR functions.

Elderly adults do not respond well to external environmental stresses and thus are most susceptible to the adverse effects of $PM_{2.5}$ exposure.[6] After exposure to air pollution, inflammatory and autonomic responses have been shown to be weak in elderly adults, due to a decline in physiological functions, resulting in increased comorbidity from diseases associated with air pollution.[7,8] Given that approximately half of Korean elderly adults have at least one chronic disease, such as hypertension, diabetes mellitus or dyslipidaemia,[9] the elderly may be more susceptible to the adverse health effects associated with air pollution.[10]

The Korean Statistical Information System (KOSIS) has estimated that the elderly population will triple by 2045 (i.e. ~17.2 million) compared with 2015 (i.e. ~6.6 million) in 16 regions of South Korea.[11] Therefore, an estimation of $PM_{2.5}$ health effects on elderly adults as well as the burden of mortality due to $PM_{2.5}$, not only accounting for the current elderly population but also the growth in the ageing population over the next few decades, may provide evidence to gauge the degree of required emission control and enable policymakers and stakeholders to develop preventive strategies regarding air pollution.

Therefore, health insurance claims data from South Korea were used herein to estimate hazard ratios (HRs) of long-term $PM_{2.5}$ exposure in all-cause and cause-specific elderly mortality from 2009 to 2016. Using the estimated HRs, we projected the nationwide elderly mortality attributable to long-term $PM_{2.5}$ exposure from 2020 to 2045.

Methods

Study population

This study was conducted in two stages: estimation of HRs and burden of mortality due to $PM_{2.5}$. Two study populations are described separately according to the research aims.

Study population for long-term $PM_{2.5}$ exposure HR estimation

The study population was comprised of residents from seven major cities in South Korea, aged ≥65 years in 2008, and registered as insurance policyholders or dependents in the National Health Information Database (NHID). The NHID covers >50 million (97%) Korean citizens; more detailed information on the NHID can be found in previous work.[12] Due to the limited data access to the NHID for external researchers, seven cities were included in this study: Seoul (25 districts), Busan (16 districts), Daegu (8 districts), Incheon (10 districts), Gwangju (5 districts), Daejeon (5 districts) and Ulsan (5 districts). Out of 1 874 159 elderly adults in the seven cities aged ≥65 years in 2008, 153 929 were excluded from this study due to missing covariate data (sex, age, or income- and wealth-based insurance premiums). Therefore, data from a total of 1 720 230 elderly individuals were included in our HR estimation analysis. Death certificates collected by Statistics Korea were linked to the eligible individuals, including the date and cause of death. Statistics Korea linked the data internally using a unique 13-digit personal identification number and provided the death data to the NHID with a decoded identification of individuals.

Cause-specific mortality was determined based on the 10th revision of the International Classification of Diseases (ICD-10) between 2009 and 2016. In addition to all-cause mortality, cardiovascular mortality (ICD-10, I00–I99), respiratory (ICD-10, J00–J99), cancer (C00-C99), IHD (I20–I25), stroke (I60–I69), haemorrhagic stroke (I60–I62), ischaemic stroke (I63–I66), COPD (J40–J44), asthma (J45–J46) and lung cancer (C33–C34) were identified when the underlying cause of death had been recorded.

The individuals were monitored from 1 January 1 2009 until either the date of death or the end of the study (31 December 2016).

Study population for the burden of mortality due to $PM_{2.5}$

To calculate the burden of mortality due to long-term exposure to $PM_{2.5}$, the elderly population and mortality data were collected from the KOSIS [11] (Supplementary Text S1, Tables S1 and S2, and Figure S1, available as Supplementary data at *IJE* online). In addition to the seven cities (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon and Ulsan) used to estimate the long-term $PM_{2.5}$ exposure HRs, additional nine provinces were also considered (Kyunggi, Kwangwon, Choongbuk, Choongnam, Jeonbuk, Jeonnam, Kyungbuk, Kyungnam and Jeju) to estimate nationwide health impacts on the elderly. Residents in seven cities and nine provinces were exclusively included in the study (i.e. those living in one of the seven cities are not resident in any of the provinces).

This study was exempted for review by the Institutional Review Board of the Seoul National University Hospital (E-1807-038-956) because the identification of individuals was decoded by the NHID and the KOSIS before the authors had access to the datasets.

Exposure assessment

Three different $PM_{2.5}$ concentration moving average values (12-, 24- and 36-month) were computed by averaging daily $PM_{2.5}$ concentrations of the concurrent month and the 11, 23 and 35 previous months of exposure, respectively, for each district. District-level 12-, 24- and 36-month moving average $PM_{2.5}$ concentrations in monthly time intervals were assigned to the individuals based on the residential address in the NHID during the follow-up. Description of the exposure modelling can be found in previous studies,[13,14] and is summarized in Supplementary Text S2, available as Supplementary data at *IJE* online. We obtained daily meteorological data from the Korea Meteorological Administration and computed annual average temperatures in summer (i.e. June–August) and winter (i.e. December–February) for each district.

Individual- and district-level covariates

We garnered individual- (sex, age and annual income- and wealth-based insurance premiums) and district-level variables [current smoking rate (%), monthly average income (KRW), the proportion of the population with a high-school diploma (%) and the population-standardized elderly mortality rate per 100 000 people]. Age and sex (male or female) data were obtained from the NHID. Data on age and insurance premiums were obtained at the end of each year and therefore generated for individuals in annual time intervals. Description of the covariates is detailed in the Supplementary Text 3, available as Supplementary data at *IJE* online.

Statistical analysis

Time-varying Cox proportional hazards models were used to estimate HRs for all-cause and cause-specific mortality associated with $PM_{2.5}$ levels. The individuals were monitored from the baseline (1 January 2009) to the date of death or 31 December 2016 (i.e. whichever was earlier). Moving average $PM_{2.5}$ concentration (12-, 24- and 36-month) levels were assigned to individuals in monthly time intervals, and age, insurance premiums and temperatures were assigned in annual time intervals. Sex and district-level covariates were considered to be time-invariant in the model. We estimated linear HRs of the association between the long-term exposure to $PM_{2.5}$ and cause-specific mortality. In the base model, we adjusted for each individual's sex, age, annual income- and wealth-based insurance premiums (low or high), region (one of seven cities) and annual average summer and winter temperatures. In the full model, we additionally considered district-level covariates, including current smoking rate (%), monthly average income (KRW), the proportion of the population with a high-school diploma (%) and population-standardized elderly mortality rate per 100 000 people. We also compared the HRs for the mortality associated with the 36-month moving average $PM_{2.5}$ by sex. In a sensitivity analysis, we applied a random intercept to account for the correlation between districts within cities.

The burden of all-cause mortality due to long-term exposure to $PM_{2.5}$ in 16 regions in South Korea was estimated based on four $PM_{2.5}$ concentration scenarios, annual elderly population and mortality rates between 2015 and 2045 with an assumption of linearity of $PM_{2.5}$-associated health effects. Scenario 1 considered the same $PM_{2.5}$ exposure levels as those in 2015, which assumes that $PM_{2.5}$ levels and HRs will remain the same in 2015–45. Scenarios 2, 3 and 4 accounted for linear reductions of $PM_{2.5}$ levels by 2045 to 15 , 10 and 5 $\mu g/m^3$, respectively.

Considering the HRs of $PM_{2.5}$, a growing ageing population, and the four scenarios for $PM_{2.5}$ levels, the burden of mortality due to long-term exposure to $PM_{2.5}$ was computed for 2015, 2020, 2025, 2030, 2035, 2040 and 2045 in South Korea (seven cities and nine provinces), as follows:

$$\triangle M_i = P_i \times I_i \times \left(\frac{HR-1}{HR}\right) \times \Delta PM$$

where ΔM_i is the mortality burden due to long-term exposure to $PM_{2.5}$ for each region i, P_i is the population aged $\geq$65 years in each region (i), I_i is the average annual mortality rate in the population aged $\geq$65 years in each region (i), ΔPM is the concentration of $PM_{2.5}$ levels, and HR represents the all-cause or cause-specific HRs for the elderly.

All analyses were conducted using SAS (v 9.4; Cary, NC, USA) and the R software for statistical computing (v 3.6.0).

Results

In the enrolment year (2008), data on 1 720 230 elderly adults ($\geq$65 years old) residing in seven cities were analysed in the study. During the follow-up period (2009–16), a total of 421 100 elderly subjects died. Of the deceased, 29.6% ($n = 124 650$) died due to cancer, followed by cardiovascular-related diseases (29.6%, $n = 124 491$) and respiratory diseases (13.0%, $n = 54 658$). Cause-specific mortality counts due to IHD, stroke, COPD, asthma and lung cancer were 29 458 (7.0%), 53 929 (12.8%), 11 384 (2.7%), 3168 (0.8%) and 32 009 (7.6%), respectively (Table 1). Cancer (including lung cancer) mortality occurred at relatively younger ages, whereas older adults died due to cardiovascular and respiratory diseases (Supplementary Figure S2, available as Supplementary data at *IJE* online). In particular, 39.6 and 35.8% of individuals aged between 65 and 74 years died due to cardiovascular and respiratory diseases, whereas 61.6% died due to cancer (Supplementary Table S3, available as Supplementary data at *IJE* online). The proportions of the population with a high-school diploma and men who were current smokers were >60 and 40% in the seven cities, respectively (Supplementary Text 1, Table S4, available as Supplementary data at *IJE* online).

$PM_{2.5}$ concentration levels decreased until 2012 and peaked in 2014 (for Seoul only) or 2013 (for other areas) (Supplementary Figure S3, available as Supplementary data at *IJE* online). Mean annual $PM_{2.5}$ concentrations in 2006–16 ranged between 21.1 (Kyungbuk) and 31.9 $\mu g/m^3$ (Seoul), except in Jeju island (11.3 $\mu g/m^3$) (Table 2 and Supplementary Figure S4, available as Supplementary data at *IJE* online). The median level of the mean $PM_{2.5}$ concentration in the seven cities was 27.4 $\mu g/m^3$.

A plot of the relationship between all-cause elderly mortality and $PM_{2.5}$ is illustrated in Figure 1. Our results showed non-linear relationships between all-cause, IHD and lung cancer mortality, whereas asthma and COPD mortality showed linear relationships with $PM_{2.5}$. Risks of IHD, COPD and asthma mortality attributable to long-term exposure to $PM_{2.5}$ levels were higher than those of stroke and lung cancer mortality (Supplementary Figure S5, available as Supplementary data at *IJE* online).

HRs for the links between $PM_{2.5}$ and all-cause mortality showed strong associations when the elderly were exposed to $PM_{2.5}$ levels equivalent to the 36-month moving average: 1.030 [with 95% confidence interval (CI) values of 1.014, 1.045] per 10 $\mu g/m^3$ increase in $PM_{2.5}$ in the base model. After controlling for district-level covariates in the full model, the HR was slightly attenuated to 1.024 (95% CI: 1.009, 1.039). Furthermore, random intercept models did not alter our main findings (data not shown). Cardiovascular-related and IHD mortality also showed positive associations with increases in the 36-month moving average $PM_{2.5}$: 1.090 (95% CI: 1.060, 1.121) and 1.306 (95% CI: 1.233, 1.383), respectively, in the full model (Table 3). The HR of the female mortality due to

Table 1. Characteristics of numbers of deaths among National Health Insurance policyholders ≥ 65 years old in 2008 residing in seven cities in South Korea ($n = 1\,720\,230$)

Characteristic	ICD-10 Code	No. of deaths and cause of death (%)	No. (%) of subpopulation among total deaths			Time (months, mean ± SD)
			Female	75+ years old	Low income	
Baseline participants			987 137	465 199	930 396	
All-cause deaths	A00–Y99	421 100 (100.0)	214 946 (51.0)	238,966 (56.7)	228 560 (54.3)	57.6 ± 30.5
All cardiovascular disease	I00–I99	124 491 (29.6)	71 803 (57.7)	75 151 (60.4)	68 521 (55.0)	61.3 ± 33.4
Ischaemic heart disease	I20–I25	29 458 (7.0)	15 908 (54.0)	17 193 (58.4)	16 425 (55.8)	60.6 ± 33.3
Stroke	I60–I69	53 929 (12.8)	29 684 (55.0)	31 092 (57.7)	29 517 (54.7)	58.1 ± 33.3
Haemorrhagic stroke	I60–I62	11 940 (2.8)	5895 (49.4)	6971 (58.4)	6560 (54.9)	58.5 ± 34.0
Ischaemic stroke	I63–I66	23 200 (5.5)	14 505 (62.5)	12 532 (54.0)	12 970 (55.9)	57.5 ± 33.4
All respiratory disease	J00–J99	54 658 (13.0)	24 501 (44.8)	35 117 (64.2)	28 858 (52.8)	68.2 ± 32.5
COPD	J40–J44	11 384 (2.7)	3479 (30.6)	7107 (62.4)	6168 (54.2)	60.0 ± 33.3
Asthma	J45–J46	3168 (0.8)	1944 (61.4)	2317 (73.1)	1812 (57.2)	55.6 ± 33.8
All cancer	C00–C99	124 650 (29.6)	48 044 (38.5)	47 819 (38.4)	67 477 (54.1)	61.1 ± 33.0
Lung cancer	C33–C34	32 009 (7.6)	8677 (27.1)	11 174 (34.9)	17 899 (55.9)	60.4 ± 33.2

Table 2. Descriptive statistics of $PM_{2.5}$ concentrations during the 2006–16 period

City/province	Surface area (km^2)	$PM_{2.5}$ concentration				
		Mean	SD	25%	50%	75%
City						
Seoul	605	31.9	20.2	19.4	28.0	39.2
Busan	770	26.1	14.8	17.2	23.1	31.8
Daegu	884	27.4	16.7	17.2	24.2	33.9
Incheon	1049	30.3	18.1	18.9	26.7	37.4
Gwangju	501	26.2	16.7	15.6	22.9	32.6
Daejeon	539	29.3	19.3	16.7	25.6	36.9
Ulsan	1061	26.0	16.8	15.8	22.7	32.5
Province						
Kyunggi	10 175	30.1	17.6	19.0	27.0	37.0
Kwangwon	16 826	22.6	12.9	13.7	20.2	28.4
Choongbuk	7407	30.1	17.9	18.1	26.7	38.1
Choongnam	8214	28.0	16.8	17.6	25.1	34.4
Jeonbuk	8067	28.5	16.4	17.7	25.4	35.3
Jeonnam	12 313	21.8	12.6	13.7	19.2	26.4
Kyungbuk	19 031	21.1	13.3	13.0	18.9	26.7
Kyungnam	10 539	24.4	13.9	16.0	21.8	29.5
Jeju	1849	11.3	9.4	5.7	9.1	14.1

IHD was greater than that of the male mortality: 1.163 (95% CI: 1.066, 1.270) for male and 1.302 (95% CI: 1.201, 1.413) for female mortality per 10 $\mu g/m^3$ increase in the 36-month moving average $PM_{2.5}$ (Supplementary Figure S6, available as Supplementary data at *IJE* online). Shorter $PM_{2.5}$ exposure windows (12- and 24-month moving average) were associated with an increased risk of cardiovascular-related and IHD mortality. However, the effect sizes were attenuated compared with the longer exposure window (36-month) (Supplementary Table S5, available as Supplementary data at *IJE* online). Specific causes of respiratory and cancer mortality also showed strong associations with $PM_{2.5}$. HRs of COPD, asthma and lung cancer mortality were respectively 1.097 (95% CI: 1.001, 1.202), 1.230 (95% CI: 1.038, 1.458) and 1.069 (95% CI: 1.012, 1.129) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ concentration in the full model (Table 3). The associations of COPD with the 36-month moving average $PM_{2.5}$ were more pronounced in the case of female mortality than in the case of male mortality. However, shorter $PM_{2.5}$ exposure windows were not associated with COPD (12- and 24-month moving averages) and lung cancer (12-month moving average).

We estimated that 11 833 all-cause deaths of the elderly were attributable to long-term exposure to $PM_{2.5}$ in 2015. Among these attributable deaths, 6820, 2143 and 1191 deaths were due to IHD, lung cancer and COPD, respectively. Moreover, 4693 all-cause deaths occurred in the seven cities, whereas 7139 deaths occurred across the nine provinces (Table 4). Given the predicted increase in the elderly population and decrease in mortality rate over the coming years (Supplementary Table S1; Figure S1, available as Supplementary data at *IJE* online), projected

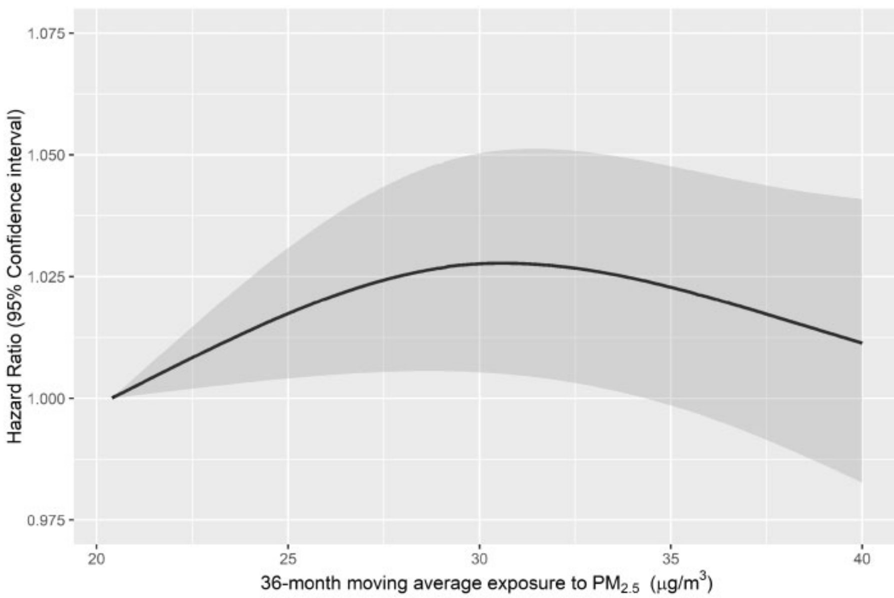

Figure 1. Hazard ratio plot for all-cause mortality. Models controlled for age, sex, average annual summer and winter temperature in the year before death, individual income- and wealth-based monthly insurance premiums (low or high), region (seven cities), district-level current smoking rate (%), monthly average income (KRW), proportion of population with a high-school diploma (%) and population-standardized elderly mortality rate per 100 000 people

Table 3. Hazard ratio for all-cause and cause-specific mortality associated with 10 μg/m^3 increases in 36-month moving average exposure to $PM_{2.5}$ in seven cities in South Korea, 2008–16 (95% confidence intervals in parenthesis)

	Base model[a]		Full model[b]	
All-cause deaths	1.030 (1.014, 1.045)*	0.0002	1.024 (1.009, 1.039)*	0.002
All cardiovascular disease	1.067 (1.038, 1.097)*	<0.0001	1.090 (1.060, 1.121)*	<0.0001
Ischaemic heart disease	1.251 (1.181, 1.325)*	<0.0001	1.306 (1.233, 1.383)*	<0.0001
Stroke	1.026 (0.980, 1.075)	0.224	1.016 (0.973, 1.061)	0.4655
Haemorrhagic stroke	0.965 (0.878, 1.060)	0.4562	0.951 (0.863, 1.049)	0.3173
Iscahemic stroke	0.995 (0.933, 1.062)	0.8868	1.000 (0.934, 1.071)	0.9941
All respiratory disease	0.968 (0.927, 1.011)	0.1444	0.974 (0.933, 1.018)	0.2425
COPD	1.166 (1.060, 1.282)*	<0.0001	1.097 (1.001, 1.202)*	0.0481
Asthma	1.243 (1.044, 1.480)*	0.0147	1.230 (1.038, 1.458)*	0.0168
All cancer	1.024 (0.996, 1.053)	0.095	1.028 (1.000, 1.058)	0.0539
Lung cancer	1.038 (0.982, 1.097)	0.1858	1.069 (1.012, 1.129)*	0.0162

*P-value < 0.05 for testing a null hypothesis that a hazard ratio equals to one with an increase in $PM_{2.5}$ concentration.

[a]Base models controlled for age, sex, average annual summer and winter temperature of the year before death, individual income- and wealth-based monthly insurance premiums (low or high) and region (seven cities).

[b]In the full model, we additionally controlled for district-level current smoking rate (%), monthly average income (KRW), the proportion of the population with a high-school diploma (%) and population-standardized elderly mortality rate per 100 000 people.

$PM_{2.5}$-associated mortality in South Korea, including the seven cities and nine provinces, was 17 948, assuming that $PM_{2.5}$ levels remain constant until 2045. However, with gradual reductions in $PM_{2.5}$ concentrations to 15, 10 and 5 μg/m^3 by 2045, the attributable all-cause mortality would decrease to 10 900, 7293 and 3647, respectively, by 2045 (Figure 2 and Supplementary Table S6, available as Supplementary data at *IJE* online).

Discussion

The present study revealed long-term adverse effects of mid-range $PM_{2.5}$ concentrations on elderly mortality in South Korea (mean levels ranged between 21.1 and 31.9 μg/m^3 with a median level of 27.4 μg/m^3 in the seven metropolitan cities). To fill the knowledge gap of the health effects of mid-range $PM_{2.5}$ concentrations, we estimated linear HRs for the all-cause and cause-specific

Table 4. Cause-specific deaths attributable to long-term exposure to $PM_{2.5}$ in 2015 (95% confidence intervals in parenthesis)

	Nation	Cities[a]	Provinces[b]
All-cause deaths	11 832.9 (4331.1, 19099.4)	4693.5 (1717.9, 7575.7)	7139.4 (2613.2, 11523.7)
All cardiovascular disease	10 057.2 (6860.9, 13169.5)	4025.4 (2746.1, 5271.0)	6031.8 (4114.9, 7898.4)
Ischaemic heart disease	6820.3 (5496.8, 8060.5)	2758.7 (2223.3, 3260.3)	4061.7 (3273.5, 4800.2)
Stroke	788.3 (−1374.0, 2877.2)	316.7 (−551.9, 1155.8)	471.6 (−822.0, 1721.4)
Haemorrhagic stroke	−592.7 (−1824.2, 536.2)	−254.7 (−784.1, 230.5)	−337.9 (−1040.1, 305.8)
Ischaemic stroke	0.0 (−1459.8, 1374.1)	0.0 (−645.8, 607.9)	0.0 (−814.0, 766.2)
All respiratory disease	−1682.9 (−4554.1, 1101.6)	−625.3 (−1692.1, 409.3)	−1057.6 (−2861.9, 692.3)
COPD	1190.7 (10.6, 2261.0)	392.9 (3.5, 746.0)	797.8 (7.1, 1514.9)
Asthma	640.8 (126.0, 1077.1)	191.8 (37.7, 322.5)	448.9 (88.3, 754.7)
All cancer	3518.0 (−59.9, 7037.0)	1451.0 (−24.7, 2902.4)	2067.0 (−35.2, 4134.6)
Lung cancer	2143.4 (408.7, 3800.8)	851.6 (162.4, 1510.1)	1291.8 (246.3, 2290.7)

[a]Cities (7) included Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon and Ulsan.
[b]Provinces (9) included Kyunggi, Kwangwon, Choongbuk, Choongnam, Jeonbuk, Jeonnam, Kyungbuk, Kyungnam and Jeju.

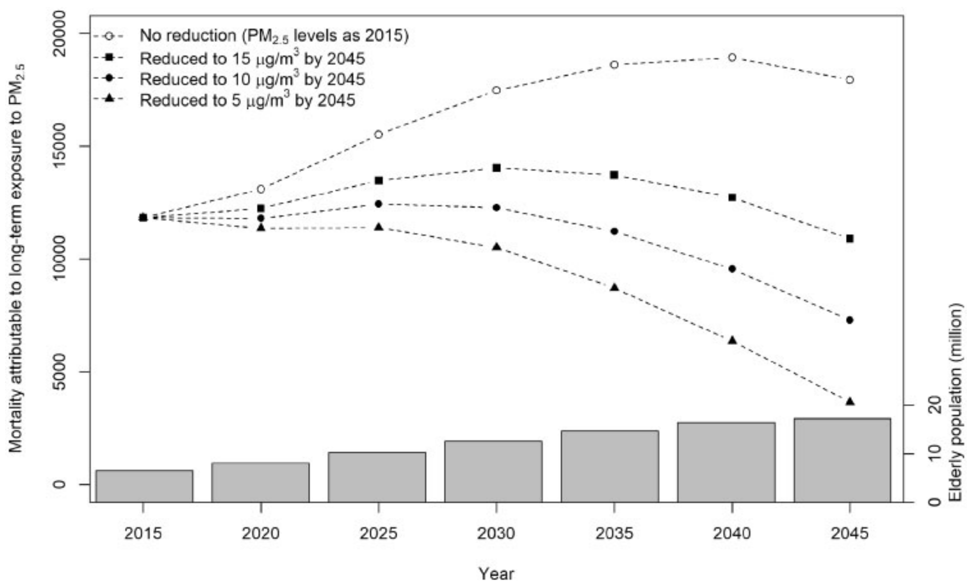

Figure 2. Projected mortality attributable to long-term exposure to $PM_{2.5}$ in South Korea (2015–45). Different curves show different projections based on varying reductions in $PM_{2.5}$ concentration; elderly population numbers are represented by grey bars

mortality, as conducted in previous cohort studies,[2,3,15–22] despite the non-linear relationship of the long-term exposure to $PM_{2.5}$ and some cause-specific mortalities. The present study showed a lower level of HR for the all-cause mortality among the elderly (1.024, 95% CI: 1.009, 1.039) compared with previous studies (ranged between 1.020[18] and 1.231[20]).[2,3,15–22] As shown in the Supplementary Table S7, available as Supplementary data at *IJE* online, regions with lower levels of $PM_{2.5}$ concentrations in the USA are more likely to have higher HRs compared with regions with higher levels. For example, HRs for elderly mortality associated with a 10 $\mu g/m^3$ increase in $PM_{2.5}$ were 1.065, 1.231, 1.132, 1.188, 1.073, 1.068 and 1.020 in the regions with median or mean $PM_{2.5}$ levels of 8.2, 10.7, 10.7, 11.3, 11.5, 14.0 and 15.0 $\mu g/m^3$, respectively[16–20,22] (Supplementary Table S7, available as Supplementary data at *IJE* online). The pooled results of previous cohort studies revealed that the risk of all- or natural-cause mortality among the elderly associated with an increase in $PM_{2.5}$ was lowered in regions with higher levels of $PM_{2.5}$. The present study, with mid-range $PM_{2.5}$ concentrations, contributed to the less steep slope of the pooled results below a $PM_{2.5}$ of 35 $\mu g/m^3$ (Supplementary Figure S7, available as Supplementary data at *IJE* online). Given that the IER functions are based on data with low or high levels of $PM_{2.5}$ [1], the results of the present study may contribute to reducing the uncertainties in the estimation of the long-term health effects of wide $PM_{2.5}$ concentrations.

The CVD-related mortality due to $PM_{2.5}$ in our study was also lower. The HRs for CVD mortality among the elderly in the USA and Hong Kong were estimated to range between 1.105 and 1.221 per 10 μg/m^3 increase in $PM_{2.5}$ levels, respectively,[2,3,18] whereas the present study observed an HR for CVD mortality of 1.09 per 10 μg/m^3 increase in $PM_{2.5}$ levels.

Although the evidence for an overall higher respiratory mortality among the elderly associated with $PM_{2.5}$ was not convincing in the present study,[18] strong linear associations between long-term exposure to $PM_{2.5}$ and mortality due to asthma and COPD were observed. In particular, given the small number of deaths related to asthma [$n = 3168$ (0.8% of all-cause mortality)], the HR for asthma mortality was surprisingly high (1.23 per 10 μg/m^3). Whereas short-term exposure to $PM_{2.5}$ was thought to increase the risk of mortality or hospitalization due to asthma,[23–25] increasing evidence suggests that long-term exposure to $PM_{2.5}$ is also linked to incident asthma,[26–29] but sparsely to asthma mortality.[30] In the present study, the investigation of a susceptible population (the elderly) in areas with moderately high levels of $PM_{2.5}$ enabled us to detect a strong relationship between long-term exposure to $PM_{2.5}$ and asthma mortality. Although we observed consistently strong associations between 12-, 24- and 36-month exposure to $PM_{2.5}$ and asthma mortality in fully adjusted models, more substantial effect sizes were observed in the 36-month moving average of $PM_{2.5}$ exposure on COPD and lung cancer compared with shorter window periods (12- or 24-months). Because COPD and lung cancer are both chronic diseases with slow disease progression, relatively acute exposure to $PM_{2.5}$ (12- or 24-months) may not show strong associations.

Whereas short-term exposure to $PM_{2.5}$ showed associations with stroke mortality in South Korea,[31] we did not observe an association between the long-term effects of $PM_{2.5}$ and stroke mortality in the elderly. Since we were unable to control for personal level risk factors (e.g. alcohol consumption and individual smoking habits), further studies are needed to elucidate the risk of stroke mortality associated with long-term $PM_{2.5}$ exposure.

The use of different CR functions, exposure modelling and mortality data may result in different attributable mortality estimations. The IER functions estimated ~15 900 attributable deaths in 2016 in South Korea.[32,33] Using the HR derived from a cohort study in the USA in conjunction with satellite and chemical transport modelling, attributable deaths were estimated higher (17 203 deaths) [5] than the estimate using the IER functions of the health risk and the Community Multiscale Air Quality (CMAQ) of exposure modeling (11 872 deaths) [4] (Supplementary Table S8, available as Supplementary data at *IJE* online). The present study estimated 11 833 all-cause elderly ($\geq$ 65 years old) deaths, including 10 943 deaths caused by COPD, IHD, stroke and lung cancer using the nation-specific HRs and CMAQ of exposure modelling. Therefore, one should be cautious when comparing the results between the present and previous studies.

The present study has several merits. We incorporated data from 1 720 230 eligible elderly adults across seven cities (32% of the entire elderly population in 2008) in South Korea to estimate HRs. Compared with a previous study that used sampling data that covered 2% of the national health insurance claims in a city (Seoul),[34] the results of the present study constitute more reliable estimates of $PM_{2.5}$ effects. Moreover, our results demonstrate the effects of long-term exposure to moderately high levels of $PM_{2.5}$ on mortality, which helps to fill the current knowledge gap. Furthermore, we projected the burden of mortality attributable to long-term exposure to $PM_{2.5}$ to future years (up to 2045) under various scenarios, considering an increasingly susceptible ageing population. We found compelling evidence that demonstrates the health benefits of continuing to reduce $PM_{2.5}$ concentrations, which has significant future policy implications.

The present study also had several limitations. First, we estimated the burden of mortality attributable to the long-term exposure to $PM_{2.5}$ in 16 regions (seven cities and nine provinces) based on HRs derived from city-level data. Cities and provinces may have different $PM_{2.5}$ concentrations and compositions and different socio-economic conditions. Additionally, we estimated the burden of mortality due to the long-term exposure to $PM_{2.5}$ in future years up to 2045 by assuming a linear mortality HR across all $PM_{2.5}$ concentration ranges. However, several studies have suggested that HR is non-linear, occasionally showing higher effects in areas with lower $PM_{2.5}$ levels.[35] Because we estimated future scenarios of $PM_{2.5}$ reduction to lower levels (5, 10 or 15 μg/m^3), our calculation for 2020–45 could have been underestimated. Therefore, caution should be exercised in the interpretation of the derived burden of mortality in the nine provinces and future years. Furthermore, given that only 75% of mortality occurs in individuals aged $\geq$65 years in South Korea, results based purely on mortality of elderly adults under-represent the burden of mortality for all age groups in South Koreans. Moreover, the development of diseases leading to death differed by cause of death. Specific causes of cardiovascular (except stroke) and respiratory deaths responded to the 3-year moving average of $PM_{2.5}$ levels, whereas stroke mortality did not show associations. Thus, further research with detailed disease pathogenesis in relation to $PM_{2.5}$ exposure is needed.

Additionally, we were not able to obtain individual-level risk factors, including smoking (e.g. ever-smoking, age at which smoking began and the amount of smoking), which may confound the association. Instead, we controlled for the district-level smoking rate in the model, as described in previous analyses of administrative cohorts in the USA and Canada.[16,36,37] Alternatively, we compared the association by sex because men showed a higher current smoking rate than women (Supplementary Table S4, available as Supplementary data at *IJE* online). However, we did not observe particularly higher HRs for the mortality of men compared with that of women across the cause-specific deaths (Supplementary Figure S6, available as Supplementary data at *IJE* online). Although a previous study suggested that ecological information on the smoking rate can be informative in estimating HRs,[37] further studies with individual-level characteristics are warranted to estimate a more representative number of attributable deaths due to chronic $PM_{2.5}$ exposure. Finally, we projected the burden of mortality with various scenarios of gradual $PM_{2.5}$ reductions by 2045. However, linear reductions in $PM_{2.5}$ levels may not be realistic enough to reflect future reductions. Furthermore, when we projected the burden of mortality attributable to $PM_{2.5}$, we did not consider changes in $PM_{2.5}$ emission sources and composition over time, which may have influenced the HRs.

Conclusion

This study revealed the health effects of long-term exposure to moderately high $PM_{2.5}$ levels on all-cause and cause-specific mortality in the elderly population of South Korea. Furthermore, the projection of mortality attributable to long-term exposure to $PM_{2.5}$ explicitly indicated the urgent need for emission controls and reductions in $PM_{2.5}$ concentration levels in South Korea over the coming decades to safeguard the vulnerable ageing population.

Supplementary data

Supplementary data are available at *IJE* online.

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This study used customized health insurance data based on the health insurance claim-related data in Korea. The aim and conclusion of this study are irrelevant to the National Health Insurance Service, Republic of Korea. The research number of this study is NHIS-2019-1-023.

Conflict of interest

None declared.

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