Long-term exposure to high particulate matter pollution and cardiovascular mortality: A 12-year cohort study in four cities in northern China

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A B S T R A C T

Epidemiologic studies have demonstrated that long-term exposure to relatively low levels of particulate air pollution is associated with adverse cardiovascular outcomes in Europe and North America. However, few studies have assessed the association with high level air pollutants. We aimed to assess the cardiovascular effects of long-term exposure to high level concentrations of inhalable particulate and to identify the characteristics of the Chinese population that are susceptible to the health effects. A retrospective cohort, containing 39,054 subjects from four cities in northern China, was followed for mortality of all cause and specific cardiovascular diseases from 1998 to 2009. Information on concentrations of PM10 (particulate matter ≤ 10 μm in aerodynamic diameter) was collected from the local Environmental Monitoring Centers. The estimated exposure for the study participants was the mean concentration of PM10 over their surviving years during the cohort period. Relative risk values were obtained using Cox proportional hazards regression models after adjusting for potential confounding factors. For each 10 μg/m³ increase in PM10, the relative risk ratios (RRs) of all-cause mortality, cardiovascular disease mortality, ischemic heart disease mortality, heart failure disease mortality, and cerebrovascular disease mortality were 1.24 (95% CI, 1.22–1.25), 1.23 (95% CI, 1.19–1.26), 1.37 (95% CI, 1.28–1.47), 1.11 (95% CI, 1.05–1.17), and 1.23 (95% CI, 1.18–1.28), respectively. Results from stratified analyses suggest that the effects of PM10 on cardiovascular mortality were more pronounced in males, smokers and people with a higher socioeconomic status. Long-term exposure to PM10 increases mortality from cardiovascular disease, especially from ischemic heart disease and this association seemed to be modified by other factors. Further research that focuses on exploring dose–response relationship and inter-population comparisons is warranted.

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1. Introduction

Epidemiologic studies have demonstrated that particulate air pollution is associated with many adverse health outcomes, including mortality and morbidity from heart and lung diseases and impaired lung function (Brunekreef and Holgate, 2002). Since the early 1990s, mounting evidence has linked long-term exposure to air pollution with the risk of cardiovascular mortality (Brook and Rajagopalan, 2010; Pope et al., 1995; Dockery et al., 1993; Filleul et al., 2005; Heinrich et al., 2013; Krewski et al., 2009; Miller et al., 2007; Nishiwaki et al., 2013; Pope, 2003). However, most of these studies were conducted in areas with relatively low levels of air pollution. For example, the annual average concentration of inhalable particles (PM10) was 28.8 (SD: 5.9) μg/m³ in Abbey et al. (1999) in the United States and 22.6 μg/m³ in Zemek et al. (2010) in Canada. Likewise, similar level of air pollution was also investigated in some European studies (Raaschou-Nielsen et al., 2013). In contrast, according to the China Ministry of Environmental Protection,
the annual average concentrations in 113 major Chinese cities in 2009 were 87 μg/m³ for PM₁₀ (SEPA 2010).

Although several health studies have examined the effects of higher concentrations of particulate air pollution on all-cause and cardiopulmonary mortality, hospitalizations and morbidity, most of these were either time-series, case-crossover, or short-term studies (Kan et al., 2008; Venners et al., 2003; Wong et al., 2008; Xu et al., 2000). Long term large population-based cohort studies are able to provide information in years of life lost, pollution's effects on long-term mortality and morbidity, and the role of pollution in both initiation and progression of chronic disease (Kunzli et al., 2001). Yet, few cohort studies have been conducted to demonstrate the associations between higher concentrations of air pollution and cardiovascular and cerebrovascular mortality (Cao et al., 2011; Zhang et al., 2011). Uncertainty still remains regarding the magnitude of these associations, particularly with long-term exposure to higher concentrations of PM₁₀. Further, little is known regarding whether the effect of PM₁₀ is modified by other factors.

In the past three decades, China has seen both rapid economic development and the resultant deteriorating environmental pollution. In fact, China is now experiencing one of the most serious air pollution problems in the world. In the present study, we reported a large population-based cohort study of 39,054 subjects from four cities in northern China and examined the associations between high particulate air pollution levels measured by PM₁₀ and all-cause and cardiovascular mortality. We further explored how other personal and socio-demographic factors may modify the health effects of PM₁₀ in the study population.

2. Methods

2.1. Study area and population

China has great regional variations in industrial activities and economic development. The northern part of China is traditionally known for its heavy and energy industries, such as steel, coal, and mining. Despite intra-regional variations, in general, air quality was worse in northern cities than that in southern cities (SEPA, 2006).

![Map of China showing the distribution of PM₁₀ concentrations in 108 Chinese cities in 2005 (μg/m³) (Reference: (SEPA, 2006))](Image)

The study population was from four cities in northern China: Tianjin, Shenyang, Taiyuan and Rizhao. These cities cover the full range of particulate air pollution levels in northern China (Fig. 1). Tianjin (longitude: 116°43′ to 118°04′; latitude: 38°34′ to 40°15′), comprising an area of 11917.3 km², lies southeast of Beijing with a population of 12.3 million in 2009. As one of the first cities with heavy industry in China, Tianjin consumes the majority of energy deriving from the combustion of coal. Shenyang (longitude: 122°25′ to 123°48′; latitude: 41°11′ to 43°2′) has a total area of 13,308 km² and a population of 7.9 million as of 2009. The major industries in Shenyang include steel manufacturing, nonferrous metals, machinery, chemical- and coke-related industries and electric power generation. Taiyuan (longitude: 110°30′ to 113°09′; latitude: 37°27′ to 38°25′) is the capital of Shanxi province, which is the largest coal-producing area in China. It is located on the eastern edge of the Loess Plateau, and the altitude of the residential area is 800 m above the mean sea level. The population was 3.5 million in 2009. Rizhao (longitude: 118°25′ to 119°39′; latitude: 35°04′ to 36°04′), located on the west coast of the Yellow China Sea, is an emerging coastal city. Its population was 2.7 million in 2009.

According to the design, our cohort included 10 thousand participants from each study site. The numbers of environmental monitor stations in each city was largely proportional to its geographical and population size and varied from 1 (Rizhao, the smallest city) to 7 (Tianjin, the largest city). Within a radius of 1 km from the monitoring stations, we randomly selected small neighborhoods, which were either apartment buildings or street blocks. Specifically, within the defined area around each environmental monitoring station, small neighborhoods were first numbered to form a sampling frame, from which random samples were drawn until a desired sample size was met. Approximately, each neighborhood has 500 to 700 households. To be eligible for this study, an individual had to be born before January 1st, 1975, and would have resided in the defined area for at least 10 years since January 1st, 1998.

The ethical committee of the coordinating center of Tianjin Medical University approved the study. Informed consent was obtained from all participants. There were a total of 48,114 people at the beginning of the study cohort. Because of budget constraints, we did not contact individual participants but only collected address, years of residence at present location, sex, age and ethnicity from local neighborhood offices
Table 1
Baseline characteristics of the cohort participants from four cities.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Tianjin</th>
<th>Shenyang</th>
<th>Taiyuan</th>
<th>Rizhao</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases</td>
<td>9663</td>
<td>9921</td>
<td>10,090</td>
<td>9380</td>
<td>39,054</td>
</tr>
<tr>
<td>Attrition ratea</td>
<td>20.80%</td>
<td>17.50%</td>
<td>17.69%</td>
<td>20.39%</td>
<td>18.83%</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>4661 (48.24)</td>
<td>4811 (48.50)</td>
<td>5051 (50.1)</td>
<td>4937 (52.63)</td>
<td>19,460 (49.83)</td>
</tr>
<tr>
<td>Females</td>
<td>5002 (51.76)</td>
<td>5110 (51.50)</td>
<td>5039 (49.9)</td>
<td>4443 (47.37)</td>
<td>19,594 (50.17)</td>
</tr>
<tr>
<td>Age</td>
<td>46.29 ± 13.00</td>
<td>47.30 ± 14.41</td>
<td>44.78 ± 14.00</td>
<td>38.53 ± 12.56</td>
<td>44.29 ± 13.95</td>
</tr>
<tr>
<td>BMI</td>
<td>22.93 ± 3.19</td>
<td>22.38 ± 3.36</td>
<td>22.87 ± 2.66</td>
<td>22.34 ± 2.52</td>
<td>22.63 ± 2.97</td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>4642 (48.04)</td>
<td>5966 (60.14)</td>
<td>4926 (48.8)</td>
<td>6631 (70.69)</td>
<td>22,165 (56.75)</td>
</tr>
<tr>
<td>High</td>
<td>5021 (51.96)</td>
<td>3955 (39.86)</td>
<td>5164 (51.2)</td>
<td>2749 (29.31)</td>
<td>16,889 (43.25)</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>6516 (67.43)</td>
<td>6470 (65.22)</td>
<td>7042 (69.79)</td>
<td>7207 (76.83)</td>
<td>27,235 (69.74)</td>
</tr>
<tr>
<td>Former</td>
<td>374 (3.87)</td>
<td>444 (4.48)</td>
<td>312 (3.09)</td>
<td>339 (3.61)</td>
<td>1469 (3.76)</td>
</tr>
<tr>
<td>Current</td>
<td>2624 (27.16)</td>
<td>2526 (25.46)</td>
<td>2401 (23.80)</td>
<td>1542 (16.44)</td>
<td>9093 (23.28)</td>
</tr>
<tr>
<td>Alcohol intake (%)</td>
<td>1997 (20.67)</td>
<td>2012 (20.28)</td>
<td>1812 (17.96)</td>
<td>1827 (19.75)</td>
<td>7008 (18.25)</td>
</tr>
<tr>
<td>Exercise (%)</td>
<td>5787 (59.89)</td>
<td>5217 (52.59)</td>
<td>5517 (54.68)</td>
<td>5206 (55.50)</td>
<td>21,727 (55.63)</td>
</tr>
<tr>
<td>Occupational exposure (%)</td>
<td>712 (7.37)</td>
<td>476 (4.80)</td>
<td>1256 (12.45)</td>
<td>381 (4.06)</td>
<td>2825 (7.23)</td>
</tr>
<tr>
<td>Meat consumption (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>3318 (34.37)</td>
<td>2582 (26.03)</td>
<td>1965 (19.47)</td>
<td>1853 (19.75)</td>
<td>9718 (24.88)</td>
</tr>
<tr>
<td>Middle</td>
<td>3480 (36.01)</td>
<td>3138 (33.44)</td>
<td>3526 (32.78)</td>
<td>3805 (40.57)</td>
<td>15,749 (40.33)</td>
</tr>
<tr>
<td>High</td>
<td>2620 (27.11)</td>
<td>3730 (37.60)</td>
<td>2464 (24.42)</td>
<td>3364 (35.86)</td>
<td>12,178 (31.81)</td>
</tr>
<tr>
<td>Vegetable and fruit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1131 (11.70)</td>
<td>1152 (11.61)</td>
<td>1279 (12.68)</td>
<td>1927 (20.54)</td>
<td>5489 (14.05)</td>
</tr>
<tr>
<td>Middle</td>
<td>1308 (13.54)</td>
<td>1251 (12.61)</td>
<td>2594 (25.71)</td>
<td>2338 (23.17)</td>
<td>7491 (19.18)</td>
</tr>
<tr>
<td>High</td>
<td>6975 (72.18)</td>
<td>7045 (71.01)</td>
<td>5883 (56.31)</td>
<td>4718 (46.76)</td>
<td>24,621 (63.04)</td>
</tr>
<tr>
<td>Total mortality (%)</td>
<td>234 (2.42)</td>
<td>501 (5.43)</td>
<td>386 (3.83)</td>
<td>314 (3.35)</td>
<td>1405 (3.67)</td>
</tr>
<tr>
<td>Cardiovascular disease (%)</td>
<td>143 (1.48)</td>
<td>236 (2.56)</td>
<td>168 (1.67)</td>
<td>130 (1.39)</td>
<td>677 (1.73)</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
<td>43 (0.44)</td>
<td>107 (1.16)</td>
<td>83 (0.82)</td>
<td>63 (0.67)</td>
<td>296 (0.76)</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>31 (0.32)</td>
<td>72 (0.78)</td>
<td>35 (0.35)</td>
<td>24 (0.26)</td>
<td>162 (0.41)</td>
</tr>
<tr>
<td>Dysrhythmias, heart failure, cardiac arrest (%)</td>
<td>49 (0.51)</td>
<td>41 (0.44)</td>
<td>28 (0.28)</td>
<td>33 (0.37)</td>
<td>153 (0.39)</td>
</tr>
</tbody>
</table>

The values are presented as percentages (%) or means ± SD. Some columns do not add up to 100% because of missing data.

a Attrition includes “moved out,” “nobody at home” and “refused to participate in the study” or “refused to complete the questionnaire.”

at baseline. In the retrospective follow-up, the interviewers contacted all selected participants to complete a standardized survey questionnaire, which contains socio-demographic information, lifestyle and diet. A total of 39,054 participants completed the study as shown in Table 1; the attrition rate was 18.83%.

2.2. Outcome assessment

For deceased subjects, their family members completed the questionnaire and were asked to provide information about the death, including time, place and cause of death. All mortality information collected from family members were crosschecked against death certificates kept at the local Center for Disease Control and Prevention (CDC). Causes of death were obtained for more than 98% of all known deaths. The cause of death was coded according to the International Classification of Diseases, tenth revision (ICD-10). In the current study, deaths attributed to cardiovascular diseases (I00–I09), ischemic heart disease (I20–I25), dysrhythmias/heart failure/cardiac arrest (I46–I51) and cerebrovascular diseases (I60–I69) were identified. The length of survival time was calculated from the date of study enrollment to the date of death from the afore-mentioned diseases. Patients who remained alive by the end of the follow-up were considered censored in the analyses.

2.3. PM10 exposure estimates

Data on air pollutants were acquired from the database of the local Environmental Monitoring Centers, the government agency in charge of collecting air pollution data. PM10 were measured by β-radiation attenuation and the concentrations were averaged from the available monitoring results of several stations in every city covered by China National Quality Control. To comply with the technical guidelines of the Chinese government, which require that the location of these monitoring stations be sufficiently far from any emission source, we selected seven monitoring stations in Tianjin, five in Shenyang, two in Taiyuan, and one in Rizhao, mixing residential and commercial areas. As a result, the monitoring data could reflect the general background urban particulate matter level in our study area. We calculated 24-hour average concentrations, from which annual average concentrations were further computed (Fig. 2). There were no adequately advanced ambient monitoring stations until 2000 in Rizhao city. Thus, the PM10 data for the first two missing years were converted from the concentrations of total suspended particles (TSP, PM10/TSP ≈ 0.5 (Qian et al., 2001)).

All study participants were followed until either the end of the study or a death occurred. The estimated exposure for the study participants was the monitoring station specific mean concentration of PM10 over their surviving years during the cohort period.

2.4. Statistical analyses

The statistical analyses comprised three parts: descriptive, overall, and stratified analyses. We first compared selected characteristics among the four study sites, based on which a Cox proportional hazards regression model was performed for the entire study cohort to determine the associations between PM10 and the relative risk of all-cause and cause-specific mortality. This involved the following two analytical steps. First, we included PM10 in the model without introducing other covariates (crude model). Then, we expanded the models by including hypothesized potential confounding variables (adjusted model). These variables included age at baseline, sex, smoking status, education attainment, household income, occupation BMI, alcohol consumption, and leisure exercise. Age was dichotomized to less than 60 and 60 years or older. Low education was defined as lower than high school and low income was defined as lower than the 50th percentile. A three level categorical variable was used to describe smoking behavior: never, former and current smokers. Based on self-reported information,
alcohol drinking and occupational exposure to harmful dust or gas were grouped into “yes” and “no”. On average, if individuals had two or more sessions of leisure physical activities per week (such as jogging, walking, and swimming) they were regarded as “active” and otherwise “non-active”. Study participants were asked to report the average frequency of meat and vegetable/fruit consumption in the past 10 years. Both of the dietary items were divided into three categories: less than once a week, two or three times a week, and greater than four times a week.

Heterogeneity in subgroup effects by PM$_{10}$ was first tested using stratified Cox proportional hazards regression models. Formal statistical interactions were further assessed by introducing multiplicative interaction terms to the Cox regression models. Potential effect modifiers that were examined in this study included age, sex, education level, personal income, smoking status and occupational exposure.

The data entry of the questionnaires was completed using EpiData (version 3.1, EpiData Association). Data management and statistical analyses were conducted using the PASW Statistics (Version 18.0, IBM). All tests of significance were two-sided and a 5% significance level was used throughout the analyses.

3. Results

3.1. Description of the study subjects

Table 1 shows the baseline characteristics of the study participants from the four cities. The mean age of the subjects was 44.29 years at the enrollment, and 49.83% were male. People of Han ethnicity comprised more than 97% of the sample, and the mean BMI was 22.63.

More than a quarter (male 45.77%, female 4.84%) were current smokers and one-fifth (male 38.20%, female 4.60%) were drinkers. A total of 1435 (3.67%) subjects died during the 12 years of follow up; of these, 677 (1.73%) died specifically from cardiovascular disease. As shown in Table 1, while the four study sites were comparable with respect to age, sex, smoking and drinking behavior, differences were evident for other characteristics (e.g. diet habits).

3.2. PM$_{10}$ pollution and exposure

Table 2 shows the mean annual levels of PM$_{10}$ in the 15 districts of four cities during the study period. The levels were highest in Taiyuan and Rizhao.

Table 2

<table>
<thead>
<tr>
<th>Cause-of-death groupings</th>
<th>ICD-10 codes</th>
<th>No. of deaths</th>
<th>RR (95% CI)$^a$</th>
<th>RR (95% CI)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause disease</td>
<td></td>
<td>1435</td>
<td>1.26 (1.24–1.29)</td>
<td>1.24 (1.22–1.27)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>100–199</td>
<td>677</td>
<td>1.24 (1.21–1.28)</td>
<td>1.23 (1.19–1.26)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>120–125</td>
<td>162</td>
<td>1.43 (1.33–1.53)</td>
<td>1.37 (1.28–1.47)</td>
</tr>
<tr>
<td>Dysrhythmias, heart failure, cardiac arrest</td>
<td>146–151</td>
<td>153</td>
<td>1.12 (1.07–1.18)</td>
<td>1.11 (1.05–1.17)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>160–169</td>
<td>295</td>
<td>1.24 (1.19–1.29)</td>
<td>1.23 (1.17–1.28)</td>
</tr>
</tbody>
</table>

$^a$ Crude model: adjusted no factors associated with all-cause and specific mortality and PM$_{10}$

$^b$ Adjusted model: adjusted for age, sex, smoking status (coded as never/former/current), education level (coded as below high school or high school and higher), personal income (divided into quartiles), BMI, alcohol consumption (yes/no), exercise (yes/no), occupational exposure (yes/no), meat consumption, and vegetable and fruit consumption (low, middle, high).
As reported in Table 2, PM$_{10}$ were associated with increased risks of all-cause mortality and cause-specific mortality in both crude and adjusted models. The adjusted relative risks (RRs) for all causes, cardiovascular disease, ischemic heart disease, heart failure disease, and cerebrovascular disease were 1.24 (95% CI, 1.22–1.27), 1.23 (95% CI, 1.19–1.26), 1.38 (95% CI, 1.28–1.47), 1.11 (95% CI, 1.05–1.17) and 1.23 (1.18–1.28) for each 10 μg/m$^3$ increase in PM$_{10}$ concentration, respectively.

Sex, BMI, personal income, and exercise were significantly associated with the two outcomes (Table 3). Older age, male sex, and smoking significantly increased the risks whereas high household income significantly reduced the risk of dying from cardiovascular disease. The relationships between the PM$_{10}$ and ischemic heart disease and cardiovascular disease mortality according to the characteristics of the study participants are summarized in Table 4. The effect heterogeneity (or interaction with PM$_{10}$) between strata of age, sex, education level, personal income, smoking status, and occupational exposure was statistically significant for both ischemic heart disease-specific and cardiovascular disease-specific mortality. Overall, the results in Table 4 suggest that the effect of PM$_{10}$ on cardiovascular-related death was stronger in older people, smokers, and those with occupational exposure and high income. For example, in people with low income the RR was 1.21 (95% CI: 1.13–1.30) for every μg/m$^3$ increase in PM$_{10}$, while the corresponding number was 2.30 (95% CI: 2.01–2.62) among those with high income.

### 4. Discussion

Our study contributes to the existing literature on PM$_{10}$ and adverse health outcomes in two ways. First, this large study offers an in-depth description of the largest and the longest published cohort study on this topic in China. We reported a significant association between long-term exposure to high PM$_{10}$ concentrations and the risk of all-cause and cardiovascular disease mortality. While the results are consistent with those reported in a previous Chinese study (Zhang et al., 2011), the magnitude of adverse health effects measured by RR per unit PM$_{10}$ increase was stronger than those reported in western countries (Cesaroni et al., 2013; Crouse et al., 2012; Jerret et al., 2009;...
Lepeule et al., 2012; Pope, 2003). For example, based on a population in Norway with relatively lower exposure, the RR with cardiovascular disease of per 10 μg/m³ increase of PM₁₀ was 1.09 (Naess et al., 2007) compared with 1.23 in our study. The higher RR in population with high PM₁₀ exposure may suggest that the dose–response relation between PM₁₀ and cardiovascular disease related mortality may not be a linear one. However, it is also possible that the chemical contents of PM₁₀ were responsible for the observed differences in RR across populations. This issue is of great importance and begs further investigation.

The mechanism by which long-term exposure to air pollution may increase the risk of cardiovascular mortality remains uncertain (Bhatnagar, 2006; Brook et al., 2004; Pope, 2003). Some studies have reported that the mechanisms may include pulmonary oxidative stress and inflammation in response to inhaled particles could lead to systemic oxidative damage and inflammation (Gurgueira et al., 2002) as well as consequent endothelial dysfunction (O’Neill et al., 2005), increased thrombosis (Ruckerl et al., 2006), and plaque vulnerability. Both human and animal studies suggest that long-term exposure to particulate air pollution enhances the progression and instability of underlying atherosclerosis via inflammatory processes, thereby promoting further ischemic events (Hoffmann et al., 2007; Kunzli et al., 2005; Sun et al., 2005). Our findings show stronger associations between particulate matter and ischemic heart disease than with other specific cardiovascular diseases that have supported the view of inflammatory hypothesis.

Second, ours was among the most comprehensive studies that systematically explored how the adverse health effects vary according to people’s characteristics. The results suggest that the effect of PM₁₀ on cardiovascular related death was stronger in older people, smokers, and those with occupational exposure and high income. With respect to age, sex, and smoking status, the findings were consistent with previous studies (Cesaroni et al., 2013; Naess et al., 2007; Abbey et al., 1999; Middleton et al., 2008; Zanobetti and Schwartz, 2005). However, in terms of how the effect varies by gender, the research evidence is not consistent. Some studies have indicated that the association between PM₂.₅ and cardiovascular mortality may be stronger in females than in males (Chen et al., 2005; Franklin et al., 2007).

The role of SES in relation to the association between PM₁₀ and adverse health outcome is unclear in the literature (Ostro et al., 2006, 2008; Zeka et al., 2006; Miller et al., 2007; Bateson and Schwartz, 2004). Ostro and Zeka reported an increased risk of mortality from exposure to PM in groups with lower educational level (Ostro et al., 2006, 2008; Zeka et al., 2006). However, results from other failed to demonstrate that SES could significantly modify the relationship between air pollution and cardiovascular disease (Miller et al., 2007; Kunzli et al., 2005; Bateson and Schwartz, 2004). Our study adds new evidence that people with higher SES in China may be more susceptible to PM₁₀. Despite its ubiquity and importance in epidemiological research, SES is often difficult to define and measure. Thus, it is not known to what extent the reported discrepancies in the literature could be explained by the differences in measuring SES. Further research is warranted in this regard.

Smoking is a major risk factor for an array of diseases; therefore we were not surprised to find that PM₁₀ was more harmful to smokers. Similar conclusions have been found in an extended follow-up of the Harvard Six Cities Study (Lepeule et al., 2012), ACS study (Pope, 2003) and JPHC study (Japanese Public Health Center) (Nishiwaki et al., 2013). There are several plausible pathways to describe the effects of smoking on the risk of cardiovascular disease, including elevated inflammatory markers, fibrinogen and white cell counts (Panagiotakos et al., 2004), blood viscosity (Frohlich et al., 2003), heart rate (Bolinder and de Faire, 1998), and oxidative stress (Guthikonda et al., 2004). Smoking has also been found to trigger acute vasoconstriction and thus enhance the development of atherosclerosis in the systemic vasculature (Kiechl et al., 2002). These pathways are similar to the mechanisms by which PM affects the population, and thus, these two factors would have a synergistic effect with each other. These findings suggest multiple biological mechanisms for the association between smoking and cardiovascular mortality.

Our study is subject to a number of limitations. Firstly, individual-level exposure was estimated from participants’ geographical residence, which assumed that PM₁₀ levels were relatively uniform in the area around the site. Thus, the exposure assessment in this study can only approximately reflect the exposure level at the subjects’ residences. Many factors, such as wind and wind-direction, temperature, humidity, individual outdoor activities and the use of a mask all affect actual individual exposure to air pollution. Future studies may benefit from a more detailed exposure assessment and the use of exposure bio-markers.

Secondly, the design of this study is a retrospective cohort design, which may introduce recall bias for certain information, such as diet habits and physical activities. In addition, the classification of some variables (including smoking habits) in the study was not time-dependent and did not differentiate between smokers with high and low daily tobacco consumption levels. Furthermore, we did not take secondhand smoking into account in the questionnaire.

Finally, PM₂.₅ concentration data were not available in China during the study period. To get a rough estimate, we used the conversion factors ranging from 0.5–0.7 for PM₂.₅/PM₁₀ developed in an air pollution study conducted in four cities in China (Qian et al., 2001). Yet, despite our efforts, we were unable to examine the health effects of PM₂.₅ in this study. The PM₂.₅ level monitoring started in 2010; thus we expect to assess its health impact in the second follow-up of this study cohort.

5. Conclusions

The findings of this study provide new evidence that long-term exposure to high levels of PM₁₀ is an important risk factor for cardiovascular mortality, especially for ischemic heart disease. Overall, the strength of association is stronger than those reported in North America and Europe with low PM concentration. We also found that males, smokers, and those with a higher SES were more susceptible to the effects of PM₁₀. Future studies with more robust assessment of both exposure level and content are needed to further confirm the results reported in this study.

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