



Short-term exposure to reduced specific-size ambient particulate matter increase the risk of cause-specific cardiovascular disease: A national-wide evidence from hospital admissions

Yaohua Tian^{a,b,1}, Junhui Wu^{e,1}, Yiqun Wu^b, Mengying Wang^b, Siyue Wang^b, Ruotong Yang^b, Xiaowen Wang^b, Jiating Wang^b, Huan Yu^b, Dankang Li^a, Tao Wu^b, Jing Wei^{c,*,2}, Yonghua Hu^{b,d,**,2}

^a Ministry of Education Key Laboratory of Environment and Health, and State Key Laboratory of Environmental Health (Incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, No.13 Hangkong Road, 430030 Wuhan, China

^b Department of Epidemiology and Biostatistics, School of Public Health, Peking University, No.38 Xueyuan Road, 100191 Beijing, China

^c Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, MD, USA

^d Medical Informatics Center, Peking University, No.38 Xueyuan Road, 100191 Beijing, China

^e School of Nursing, Peking University, No. 38 Xueyuan Road, Beijing 100191, China

ARTICLE INFO

Edited by Dr. RENJIE CHEN

Keywords:

PM₁
Fine particulate matter
Air pollution
Cardiovascular disease
Time-series

ABSTRACT

Evidence for the health effects of ambient PM₁ (particulate matter with an aerodynamic diameter $\leq 1 \mu\text{m}$) pollution is limited, and it remains unclear whether a smaller particulate matter has a greater impact on human health. We conducted a time-series study in 184 major cities by extracting daily hospital data on admissions for ischemic heart disease, heart failure, heart rhythm disturbances, and stroke between 2014 and 2017 from a medical insurance claims database of 0.28 billion beneficiaries. City-specific associations were estimated with over-dispersed generalized additive models. A random-effects meta-analysis was used to estimate regional and national average associations. We conducted stratified and meta-regression analyses to explore potential effect modifiers of the association. We recorded 8.83 million cardiovascular admissions during the study period. At the national-average level, a $10\text{-}\mu\text{g}/\text{m}^3$ increase in same-day PM₁, PM_{2.5} (particulate matter with an aerodynamic diameter $\leq 2.5 \mu\text{m}$) and PM₁₀ (particulate matter with an aerodynamic diameter $\leq 10 \mu\text{m}$) concentrations corresponded to a 1.14% (95% confidence interval 0.88–1.41%), 0.55% (0.40–0.70%), and 0.45% (0.36–0.55%) increase in cardiovascular admissions, respectively. PM₁ exposure was also positively associated with all cardiovascular disease subtypes, including ischemic heart disease (1.28% change; 0.99–1.56%), heart failure (1.30% change; 0.70–1.91%), heart rhythm disturbances (1.11% change; 0.65–1.58%), and ischemic stroke (1.29% change; 0.88–1.71%). The associations between PM₁ and cardiovascular admissions were stronger in cities with lower PM₁ levels, higher air temperatures and relative humidity, as well as in subgroups with elder age (all $P < 0.05$). This study provides robust evidence of short-term associations between PM₁ concentrations and increased hospital admissions for all major cardiovascular diseases in China. Our findings suggest a greater short-term impact on cardiovascular risk from PM₁ in comparison to PM_{2.5} and PM₁₀.

1. Introduction

Epidemiological studies have demonstrated close, quantitative

associations between short-term exposure to ambient particulate matter (PM) pollution and increased risk of mortality and morbidity from cardiovascular disease (CVD) (Brook et al., 2010; Liu et al., 2019). The

* Corresponding author.

** Corresponding author at: Department of Epidemiology and Biostatistics, School of Public Health, Peking University, No.38 Xueyuan Road, 100191 Beijing, China.

E-mail addresses: weijing_rs@163.com (J. Wei), yhhu@bjmu.edu.cn (Y. Hu).

¹ Yaohua Tian and Junhui Wu contributed equally to this work.

² Yonghua Hu and Jing Wei contributed equally as corresponding authors.

majority of previous studies have used PM with an aerodynamic diameter $\leq 10 \mu\text{m}$ (PM_{10}) or $\leq 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) as PM measurements. Size is a critical determinant of health effects of PM (Nel, 2005). Recently, a growing body of research is focusing on the health effect of PM_1 (PM with an aerodynamic diameter $\leq 1 \mu\text{m}$), a major component of $\text{PM}_{2.5}$. Monitoring and modeling data suggested that PM_1 comprises considerable proportion of $\text{PM}_{2.5}$ mass (Samek et al., 2018; Zhao et al., 2014). Compared with $\text{PM}_{2.5}$, PM_1 has higher pulmonary deposition efficiency and surface area. In addition, evidence from both toxicological and epidemiological studies indicated that smaller PMs induced stronger cytotoxic and inflammatory responses, as well as subclinical cardiovascular effects (Chen et al., 2015; Yang et al., 2023). Therefore, it is of great importance to study which specific size fraction below $\text{PM}_{2.5}$ has greater health impact from both a scientific viewpoint and a public health perspective (Kan, 2017). However, to date, evidence for the health effects of ambient PM_1 pollution is quite limited worldwide because of the unavailability of air monitoring data.

In China, a handful of studies have evaluated the health effects of PM_1 , and reported increased risk of emergency department visits (Chen et al., 2017a; Wang et al., 2021), mortality (Hu et al., 2018), and hospital admissions (Chen et al., 2020) following short-term exposure to PM_1 pollution. A key scientific issue in assessing the PM-associated health impacts is which specific size fractions that dominate the health effects. Some studies reported that PM_1 was more hazardous than $\text{PM}_{2.5}$ (Chen et al., 2020; Fang et al., 2022; Yang et al., 2020; Zhang et al., 2021), while others indicated similar associations for PM_1 and $\text{PM}_{2.5}$ with health outcomes (Chen et al., 2017a; Hu et al., 2018; Yang et al., 2018). However, previous estimations were primarily based on one or several cities or several hospitals. Moreover, spatial variation of PM_1 pollution in China has been demonstrated (Chen G and Zhang, 2018). Differences in the exposure estimation and statistical analysis may also contribute to inconsistent results. Therefore, a large nationwide study would offer greater statistical power with limited selection bias, especially in view of the evidence for heterogeneity in effect estimates across individual cities.

No studies to date have examined the relation between PM_1 exposure and CVD hospital admissions on a national scale. Motivated by this, we conducted a national analysis to investigate the associations between short-term exposures to PM_1 , $\text{PM}_{2.5}$ and PM_{10} and hospital admissions for cause-specific major cardiovascular diseases in China.

2. Methods

2.1. Study population

There are three main health insurance programs in China: The Urban Employee Basic Medical Insurance (UEBMI) for urban working and retired people, the Urban Resident Basic Medical Insurance for urban residents without formal employment, and the New Rural Cooperative Medical Scheme for rural residents. According to Chinese policy, a claim for billable health care should be submitted for reimbursement on a standardized electronic form. The claims include individuals' basic information, dates of medical services, diagnoses, treatments, and expenses. We extracted daily hospital admission data for 2014–2017 from the UEBMI database. At the end of 2016, more than 0.28 billion people were enrolled in the UEBMI program. Cardiovascular reasons for admission included ischemic heart disease, heart failure, heart rhythm disturbances, and stroke (Dominici et al., 2006; Tian et al., 2019b). Hospital admissions for each health outcome were identified from the primary diagnosis (International Classification of Diseases [ICD] code or text in the disease diagnosis field). We considered the time of the day of admission for patients with a confirmed primary diagnosis to be the time of illness onset. In this analysis, we excluded cities with no data on disease diagnosis. Data on city-specific counts of individuals recorded in the database, residents, and population with UEBMI coverage appear in our previous publications (Dominici et al., 2006; Tian et al., 2019a; Tian

et al., 2019b).

PM pollution characteristics and geographical and meteorological conditions differ between southern and northern China, which is divided by the Qinling Mountains-Huai River line. Therefore, we separately estimated the effects of PM in the southern and northern regions ($n = 94$ and 90 cities, respectively). Stratified analyses were carried out to evaluate possible effect modification by sex and age (18–64, 65–74, and ≥ 75 years).

2.2. Environmental data

The air pollution data are collected from the ChinaHighAirPollutants (CHAP) dataset (available at: <https://weijing-rs.github.io/product.html>, accessed data: August 10, 2021), which is generated using our developed space-time extremely randomized trees (STET) model from big data including ground-based measurements, satellite remote sensing products, meteorology, land use and topographical properties, and model simulations (Jing Wei et al., 2021; Jing Wei et al., 2022; Wei et al., 2019; Wei et al., 2021). Here, daily full-coverage three particulate matters with different particle sizes (PM_1 , $\text{PM}_{2.5}$ and PM_{10}) and four ground-level gaseous pollutants (NO_2 , SO_2 , CO , and O_3) at a 10-km spatial resolution are employed. Cross-validation results illustrated that the predicted air pollutants are reliable with small uncertainties (Jing Wei et al., 2021; Jing Wei et al., 2022; Wei et al., 2019; Wei et al., 2021). In addition, we collected city-specific meteorological monitoring data (daily mean air temperature and relative humidity) from the China Meteorological Data Sharing Service System.

2.3. Statistical analysis

We applied a two-stage analytic approach to estimate the associations of PM with daily admissions for CVDs following a previously developed method (Liu et al., 2019; Tian et al., 2019b; Yin et al., 2017). In the first stage, we fitted over-dispersed generalized additive models to obtain city-specific estimates. The outcome measure in the model is a city-specific daily count of admissions for each outcome. Consistent with previous studies (Liu et al., 2019; Tian et al., 2019b; Yin et al., 2017), several covariates were incorporated into the model: (1) a natural cubic spline function of time with 7 degrees of freedom (df) per year to accommodate seasonality and time trends; (2) natural cubic spline functions with 6 df for temperature and 3 df for relative humidity to allow the adjustment of the potential nonlinear effects of meteorology; (3) two indicator variables for day of week and public holidays to control the possible variations for each day. To study the temporal pattern of PM effects on daily admissions, we assessed the associations at different lag days: the present day (lag 0), 1 day prior (lag 1), 2 days prior (lag 2), and the average of days 0–1 (lag 0–1). In the second stage, we performed random-effects meta-analyses to produce regional- and national-average estimates (Liu et al., 2019; Yin et al., 2017).

We assessed the role of potential effect modifiers on the associations of PM with CVD admissions. We performed subgroup analyses by region, sex, and age. We calculated P -values for differences between subgroups using Z-tests (Altman and Bland, 2003). We also fitted multivariable meta-regression models to assess potential effect modifications by city-level characteristics such as annual-average mean PM_1 concentrations, temperature and relative humidity, $\text{PM}_1/\text{PM}_{2.5}$ ratio, gross domestic product per capita, average age, smoking rate, and the UEBMI coverage rate (Tian et al., 2019b; Yin et al., 2017).

We then conducted four sensitivity analyses. First, we fitted two-pollutant models with adjustment for NO_2 , SO_2 , CO , and O_3 . Second, we assessed the sensitivity of the associations concerning the degree of freedom in the smoothing function of calendar time (df values 6–10 per year), temperature (3–6), and humidity (3–6). Third, we used penalized spline functions for time and meteorological variables. Finally, Poisson modelling was applied instead of quasi-Poisson regression.

All first-stage analyses were carried out with R software, version

3.2.2. We performed meta-analyses in Stata statistical software, version 12 (StataCorp, College Station, TX, USA). The results are expressed as percentage changes and 95% confidence intervals (CIs) in daily hospital admissions per 10- $\mu\text{g}/\text{m}^3$ increase in PM concentrations. Percentage change equals relative risk minus 1 and then multiplied by 100.

3. Results

Data from 184 cities were included in the analysis (Fig. 1). More than 8.83 million cardiovascular admissions were included in this study. Table 1 summarizes environmental and hospital admission data for 2014–2017 in 184 cities. On average, we identified 47 (SD, 74) admissions for CVD, 26 (53) for ischemic heart disease, one (5) for heart failure, two (4) for heart rhythm disturbances, and 14 (28) for ischemic stroke per day across cities. The average annual mean PM₁, PM_{2.5} and PM₁₀ concentrations for the 184 cities during the study period was 27 $\mu\text{g}/\text{m}^3$ (SD 8), 48 $\mu\text{g}/\text{m}^3$ (15), and 86 $\mu\text{g}/\text{m}^3$ (35). The PM₁/PM_{2.5} ratio varied between cities, with a range from 0.30 (Kashi) to 0.68 (Haikou). Table S1 lists city-specific annual-average PM₁ concentrations, PM₁/PM_{2.5} ratio, annual-average temperature and relative humidity, and other city-level characteristics. At the national level, daily PM₁ concentrations were highly positively correlated with the concentrations of PM_{2.5} ($r = 0.97$) and PM₁₀ ($r = 0.84$), and moderately correlated with SO₂, NO₂, and CO ($r = 0.64$ – 0.75) (Table S2).

Fig. 2 presents the national-average estimates of the associations between PM₁, PM_{2.5} and PM₁₀ concentrations and hospital admissions for CVD and its subtypes at different lag structures. We observed significant associations between same-day PM concentrations (lag 0) and almost all health outcomes. At the national average level, an increase of 10 $\mu\text{g}/\text{m}^3$ in concurrent day PM₁, PM_{2.5} and PM₁₀ was associated with a 1.14% (95% confidence interval 0.88–1.41%), 0.55% (0.40–0.70%), and 0.45% (0.36–0.55%) increase in CVD admissions, respectively. PM₁

Table 1

Summary statistics on daily hospital admissions for all CVD as well as cause-specific major cardiovascular diseases, PM levels, and weather conditions in 184 Chinese cities by region, 2014–2017.

Variable	Nationwide	South	North
Number of cities	184	94	90
Annual-average PM ₁ (mean \pm SD, $\mu\text{g}/\text{m}^3$)	27 (8)	25 (6)	29 (9)
Annual-average PM _{2.5} (mean \pm SD, $\mu\text{g}/\text{m}^3$)	48 (15)	45 (10)	52 (17)
Annual-average PM ₁₀ (mean \pm SD, $\mu\text{g}/\text{m}^3$)	86 (35)	71 (16)	102 (42)
Annual-average temperature (mean \pm SD, $^{\circ}\text{C}$)	14 (5)	18 (3)	10 (4)
Annual-average relative humidity (mean \pm SD, %)	68 (12)	77 (5)	57 (8)
Daily hospital admissions (mean \pm SD)			
All CVD	47 (74)	33 (56)	51 (87)
Ischemic heart disease	26 (53)	20 (35)	33 (66)
Heart failure	1 (5)	1 (1)	1 (7)
Heart rhythm disturbances	2 (4)	1 (1)	2 (6)
Ischemic stroke	14 (28)	12 (26)	17 (29)

SD: standard deviation; CVD: cardiovascular disease.

exposure was associated with all CVD subtypes. A 10 $\mu\text{g}/\text{m}^3$ increase in PM₁ concentrations was associated with increases in hospital admissions of 1.28% (0.99–1.56%) for ischemic heart disease, 1.30% (0.70–1.91%) for heart failure, 1.11% (0.65–1.58%) for heart rhythm disturbances, and 1.29% (0.88–1.71%) for ischemic stroke on the same day (Fig. 2). We further estimated the associations between PM₁ concentrations and hospital admissions for all CVDs in six geographical regions (mid-south, east, southwest, northwest, north, and northeast). We observed consistent associations in all six regions except for the northwest and

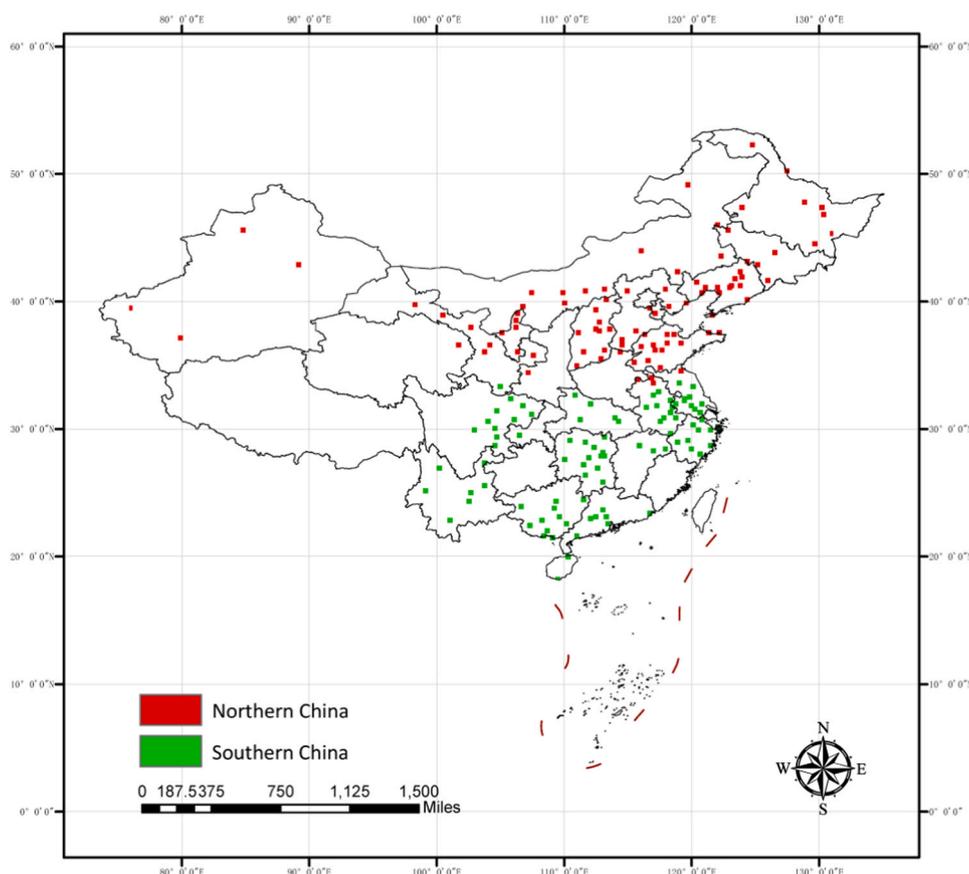


Fig. 1. The locations of 184 cities analyzed in this study. The most populous city in each province was marked.

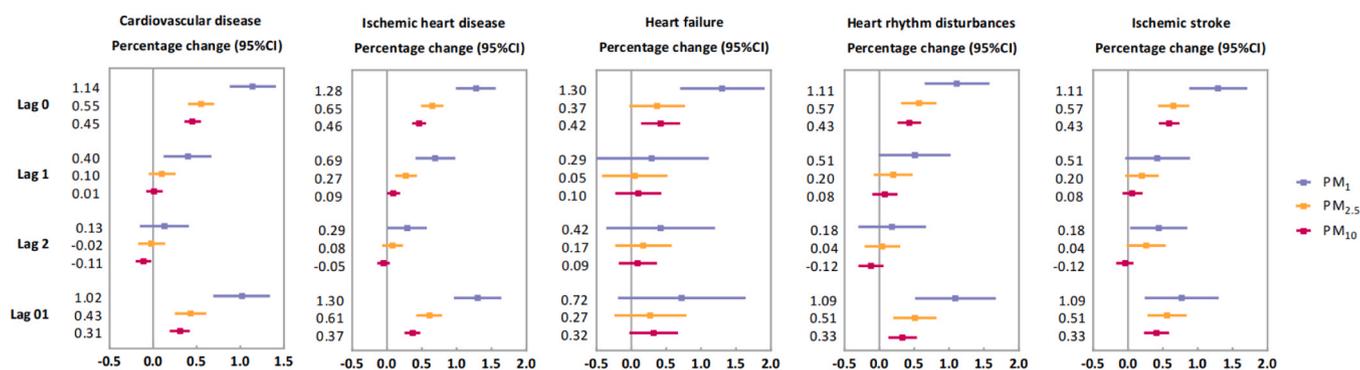


Fig. 2. National-average percentage changes (with 95% confidence intervals) in daily hospital admissions for cause-specific cardiovascular diseases per 10-µg/m³ increase in concentrations of PM₁, PM_{2.5}, and PM₁₀ on different lag days in 184 Chinese cities, 2014–2017.

southwest (Table 2).

Fig. 3 shows the results of stratified analyses by sex, age, and region on the associations between PM concentrations (lag day 0) and hospital admissions for all CVDs. PM₁, PM_{2.5} and PM₁₀ significantly increased the CVD admissions in different sex and age groups. The differences in the estimates between males and females were not statistically significant (all *P* > 0.05). The estimates were consistently higher in individuals aged 65–74 years or ≥ 75 years than in those aged 18–64 years for all CVDs. The estimates were consistently greater in the southern region than in the northern region (all *P* < 0.05).

Table 3 shows the results of meta-regression analyses of the relationships of PM₁ (lag day 0) with CVD admissions by city characteristics. Annual-average mean PM₁ concentrations reduced the PM₁ effect (*P* = 0.038). Annual-average temperature (*P* = 0.001) and relative humidity (*P* = 0.005), and average age (*P* = 0.024) enhanced the PM₁ effect. The association was not modified by cities’ PM₁/PM_{2.5} ratio (*P* = 0.309), gross domestic product per capita (*P* = 0.837), smoking rate (*P* = 0.452), or UEBMI coverage rate (*P* = 0.084).

Table 4 lists the results of two-pollutant models. The relationships of PM₁ (lag day 0) with CVD admissions were weakened but remained significant after adjustment for SO₂ (0.52% change; 0.16–0.87%), CO (0.81% change; 0.46–1.16%), and O₃ (1.09% change; 0.81–1.37%).

Table 2

Regional-average percentage change with 95% confidence interval in daily hospital admissions for cardiovascular disease associated with 10 µg/m³ increase in concurrent day PM₁ (lag 0) concentrations in 184 Chinese cities, 2014–2017.

Region	Percentage change (95% confidence interval) ^a	<i>P</i>
PM ₁		
East	1.21 (0.85–1.58)	< 0.001
Middle-south	2.37 (1.48–3.28)	< 0.001
Southwest	1.10 (–1.00 to 3.26)	0.307
Northwest	0.53 (–1.21 to 2.30)	0.552
North	0.51 (0.18–0.84)	0.002
Northeast	0.80 (0.11–1.50)	0.022
PM _{2.5}		
East	0.49 (0.31–0.67)	< 0.001
Middle-south	1.25 (0.75–1.75)	< 0.001
Southwest	0.92 (–0.31 to 2.17)	0.144
Northwest	0.42 (–0.53 to 1.38)	0.385
North	0.31 (0.11–0.50)	0.002
Northeast	0.38 (–0.02 to 0.78)	0.059
PM ₁₀		
East	0.41 (0.29–0.54)	< 0.001
Middle-south	1.13 (0.75–1.52)	< 0.001
Southwest	0.97 (0.12–1.84)	0.025
Northwest	0.10 (–0.24 to 0.44)	0.582
North	0.25 (0.14–0.36)	< 0.001
Northeast	0.44 (0.20–0.68)	< 0.001

^a Adjusted for temperature, relative humidity, calendar time, day of week, and public holiday.

However, the estimated effect turned out to be statistically insignificant after adjustment of NO₂ (0.22% change; –0.11% to 0.55%). Table 5 presents the results of the sensitivity analyses. The estimates remained stable when using alternative *df* values for time, temperature, and humidity. Applying penalized spline functions (1.19% change; 0.89–1.48%) or Poisson modelling (1.19% change; 0.93–1.45%) only slightly change the estimates.

4. Discussion

In this nationwide analysis in China, we observed significant associations of PM₁, PM_{2.5} and PM₁₀ concentrations with increased CVD admissions in 184 major cities. PM₁ had the greatest effect on CVD admissions, followed by PM_{2.5} and PM₁₀. The associations between PM₁ and CVD hospitalizations varied between cities by PM₁ concentrations, air temperature, and relative humidity, as well as by age group. Furthermore, we noted consistent associations between PM₁ concentrations and all major cause-specific CVDs. To our knowledge, this is the first study in China or even worldwide to report associations between PM₁ concentrations and CVD hospital admissions on a national scale.

In contrast with previous studies using data obtained from just one or a few cities, we analyzed national data with the same approach, thus avoiding potential publication bias and having greater statistical power to observe a significant association of PM₁ with daily CVD admissions. In addition, we included 184 major Chinese cities involving great diversity in PM₁ levels, meteorological conditions, geography, and socioeconomic status, which provided a unique opportunity to explore the potential effect modification by these characteristics. The present study is therefore a source of more representative and stable estimates of the association between PM₁ and CVD hospital admissions than prior studies.

Although the adverse effects of PM_{2.5} and PM₁₀ on CVD risk have been examined in numeric studies in China and worldwide (Brook et al., 2010; Chen et al., 2017b; Tian et al., 2019b), far less scientific evidence is available for PM₁. Overall, we found a significant association between short-term exposure to PM₁ and CVD admissions in China, in line with several previous reports (Chen et al., 2020; Hu et al., 2018; Lin et al., 2016; Yin et al., 2017). A critical issue about the associations of PM with health outcomes is which specific size fractions that dominate the health effects. Previous studies have reported mixed results on this issue. For example, Lin et al. (Lin et al., 2016) and Yin et al. (Yin et al., 2017) demonstrated stronger associations between PM₁ and CVD mortality than PM_{2.5} in China. A multicity study in Zhejiang province demonstrated that PM₁ had slightly higher effect on CVD mortality than PM_{2.5} (Hu et al., 2018). In contrast, Chen et al. (Chen et al., 2017a) reported similar associations of PM₁ and PM_{2.5} with all-cause hospital visits in 28 hospitals. However, a time-series study indicated that PM₁ had a higher risk for emergency department visits than PM_{2.5} in 19 hospitals in Beijing (Wang et al., 2021). The discrepancy in the findings might be explained by the variations in the study outcomes, exposure assessment

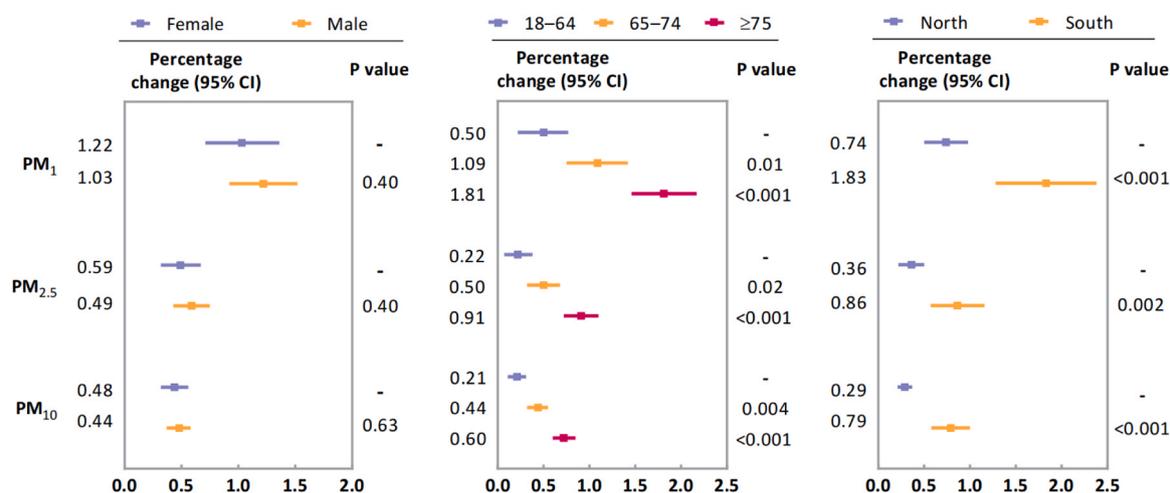


Fig. 3. National-average percentage changes (with 95% confidence intervals) in daily hospital admissions for cardiovascular disease per 10-µg/m³ increase in concentrations of PM₁, PM_{2.5}, and PM₁₀ (lag 0) stratified by sex, age, and geographical region.

Table 3

Multivariable meta-regression results of the modification effects of city-level characteristics on the associations between concurrent day PM₁ (lag 0) and daily hospital admissions for cardiovascular disease in 184 cities in China, 2014–2017.

Variables	Percentage change (95% CI)	P value
Annual-average mean PM ₁ levels (10 µg/m ³)	-0.462 (-0.898 to -0.025)	0.038
PM ₁ /PM _{2.5} ratio (0.10)	-0.386 (-1.133 to 0.361)	0.309
Temperature (°C)	0.146 (0.065–0.228)	0.001
Relative humidity (%) ^a	0.045 (0.014–0.075)	0.005
GDP per capita (¥10,000)	-0.019 (-0.202 to 0.164)	0.837
Average age (year)	0.112 (0.015–0.210)	0.024
Smoking rate (%)	-0.057 (-0.205 to 0.092)	0.452
Coverage rate by UEBMI (%)	-0.023 (-0.049 to 0.003)	0.084

¥10,000 (£1169; \$1456; €1377).

CI: confidence interval; SD: standard deviation; GDP: gross domestic product.

The primary meta-regression model was multivariable including annual-average mean PM₁ levels, PM₁/PM_{2.5} ratio, temperature, GDP per capita, average age of the city, smoking rate, and population coverage rate by UEBMI.

^a Percentage change of the relative humidity was adjusted for all the variables in the primary meta-regression model except the temperature due to the collinearity between the two variables.

Table 4

Percentage change with 95% confidence interval in daily hospital admissions for cardiovascular disease associated with 10 µg/m³ increase in concurrent day PM₁ concentrations (lag 0) in two-pollutant models in 184 Chinese cities, 2014–2017.

Variables	Percentage change (95% CI) ^a	P-value
Adjust SO ₂	0.52 (0.16–0.87)	0.004
Adjust NO ₂	0.22 (-0.11 to 0.55)	0.190
Adjust CO	0.81 (0.46–1.16)	< 0.001
Adjust O ₃	1.09 (0.81–1.37)	< 0.001
Adjust PM _{2.5}	2.81 (1.76–3.87)	< 0.001
Adjust PM ₁₀	1.31 (1.04–1.57)	< 0.001

^a Adjusted for temperature, relative humidity, calendar time, day of week, and public holiday.

methods, air pollution levels, economic and demographic patterns, and meteorological conditions across studies. In this nationwide study, we observed that PM₁ posed a greater impact on CVD admissions than did PM_{2.5} and PM₁₀, strengthening the evidence that a smaller PM may be a higher health risk factor.

Table 5

Results of sensitivity analyses on the association between concurrent day PM₁ concentrations (lag 0) and cardiovascular admissions in 184 Chinese cities, 2014–2017.

Variables	Percentage change (95% CI)	P
df for calendar time		
6	1.08 (0.80–1.36)	< 0.001
7	1.14 (0.88–1.41)	< 0.001
8	1.14 (0.88–1.41)	< 0.001
9	1.22 (0.94–1.49)	< 0.001
10	1.28 (1.01–1.55)	< 0.001
df for temperature		
3	1.12 (0.84–1.40)	< 0.001
4	1.16 (0.88–1.43)	< 0.001
5	1.17 (0.90–1.44)	< 0.001
6	1.14 (0.88–1.41)	< 0.001
df for relative humidity		
3	1.14 (0.88–1.41)	< 0.001
4	1.14 (0.87–1.41)	< 0.001
5	1.13 (0.86–1.40)	< 0.001
6	1.13 (0.86–1.40)	< 0.001
Spline function		
Penalized spline function	1.19 (0.89–1.48)	< 0.001
Poisson regression	1.19 (0.93–1.45)	< 0.001

Note: 95%CI (95% confidence interval), df (Degree of freedom).

The heterogeneity in the association of PM₁ concentrations with CVD admissions may be caused by variations in city characteristics. We observed a downward trend for PM₁ effects in cities with higher long-term PM₁ levels, which were supported by two national studies in China that reported lower estimates of the associations between PM_{2.5} concentrations and CVD risk in cities with higher annual mean PM_{2.5} levels (Chen et al., 2017b; Wei et al., 2019). This finding was also complemented by the negative effect modification of PM₁ concentrations on CVD risk as shown in the meta-regression analyses. In addition, positive effects modifications of air temperature and relative humidity were observed in this study. Our findings were consistent with previous demonstrations of stronger PM_{2.5} impacts in cities with higher temperatures (Chen et al., 2017b; Wei et al., 2019). Previous studies suggested that there were synergistic effects of air pollution with high temperature (Li et al., 2017).

Identification of potentially sensitive subpopulations has significant implications for public health and policy-making. Consistent with most prior studies on PM₁ and other air pollutants (Chen et al., 2017b; Di et al., 2017; Hu et al., 2018), we found that the association between PM₁ and CVD admissions was stronger in elderly people. Changes in the

structure of respiratory system, reductions in biological function, or declined resistance to infection may explain the higher risk estimate in elderly. In addition, the effect estimate was slightly larger in men than in women, but the difference was not statistically significant.

Our study has several limitations. First, outdoor monitoring data were used to represent population exposure; the resulting exposure measurement error would tend to bias effect estimates downward. Second, the effects of PM_{0.1} were not explored due to the lack of monitoring data. PM_{0.1} are ultrafine particles with a diameter of less than 0.1 μm that penetrate deep into the lungs and may enter the bloodstream, causing health effects (Kuwayama et al., 2013). Therefore, future studies are needed to examine the effect of PM_{0.1}. Third, information on several patient characteristics were not available, limiting our ability to control individual-level confounding variables and identify potentially susceptible populations. However, the time-series analysis was in fact a self-controlled design to adjust for the confounding by slowly varying individual-level risk factors where participants were compared with themselves at differing levels of air pollution. In addition, this study should be interpreted with caution because the finding is based on hospitalization data for CVD, and future exploration of effect using incident data is needed. Finally, we were not able to study the constituents of the particulates that may have influenced regional biological effects for lack of information.

5. Conclusion

Using the hospital admission data in 184 major cities during 2014–2017, our study presented for the first time national estimation of the relations between short-term exposure to ambient PM₁ pollution and hospital admissions for cause-specific major cardiovascular diseases in China or even in the world. Transient elevations in PM₁, PM_{2.5} and PM₁₀ concentrations were associated with increased hospital admissions for all major CVDs. Meanwhile, our findings suggested greater effect of PM₁ on CVD admissions than PM_{2.5} and PM₁₀.

Funding

This work was supported by the National Natural Science Foundation of China (No. 81872695) and China Postdoctoral Science Foundation (No.2022TQ0017 and No.2022M720303). The funders were not involved in the research and preparation of the article, including study design; collection, analysis, and interpretation of data; writing of the article; no in the decision to submit it for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

Acknowledgements

None.

Authors' contributions

Y.H.H., Y.H.T., J.H.W., and J.W. contributed to the study concept. Y.H.H. J.H.W., had full access to all the data in the study and take responsibility for the integrity of the data. Y.H.T., J.H.W. and Y.Q.W. contributed to the statistical analysis and tables' development of this article. Y.H.T., J.H.W., Y.Q.W., M.Y.W., S.Y.W., R.T.Y., X.W.W., J.T.W., H.Y., D.K.L., T.W., J.W., and Y.H.H. interpreted the findings and drafted

the article. All the authors contributed to the critical revision of the article for important intellectual content. Y.H.H. is the guarantor. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2023.115327.

References

- Altman, D.G., Bland, J.M., 2003. Interaction revisited: the difference between two estimates. *Bmj* 326, 219.
- Brook, R.D., et al., 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation* 121, 2331–2378.
- Chen, G., et al., 2017a. Effects of ambient PM(1) air pollution on daily emergency hospital visits in China: an epidemiological study. *Lancet Planet Health* 1, e221–e229.
- Chen, L., et al., 2020. Short-term effect of PM(1) on hospital admission for ischemic stroke: a multi-city case-crossover study in China. *Environ. Pollut.* 260, 113776.
- Chen, R., et al., 2015. Size-fractionated particulate air pollution and circulating biomarkers of inflammation, coagulation, and vasoconstriction in a panel of young adults. *Epidemiology* 26, 328–336.
- Chen, R., et al., 2017b. Fine particulate air pollution and daily mortality. A nationwide analysis in 272 Chinese cities. *Am. J. Respir. Crit. Care Med* 196, 73–81.
- Chen G, M.L., Zhang, W., 2018. Spatiotemporal variation of PM1 pollution in China. *Atmos. Environ.* 178, 198–205.
- Di, Q., et al., 2017. Association of short-term exposure to air pollution with mortality in older adults. *JAMA* 318, 2446–2456.
- Dominici, F., et al., 2006. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *JAMA* 295, 1127–1134.
- Fang, J., et al., 2022. Associations of ultrafine and fine particles with childhood emergency room visits for respiratory diseases in a megacity. *Thorax* 77, 391–397.
- Hu, K., et al., 2018. Mortality burden attributable to PM(1) in Zhejiang province. *China Environ. Int* 121, 515–522.
- Jing Wei, Z.L., Lyapustin, Alexei, Sun, Lin, Peng, Yiran, Xue, Wenhao, Su, Tianning, Cribb, Maureen, 2021. Reconstructing 1-km-resolution high-quality PM2.5 data records from 2000 to 2018 in China: spatiotemporal variations and policy implications. *Remote Sens. Environ.* 252, 112136.
- Jing Wei, Z.L., Li, Ke, Dickerson, Russell R., Pinker, Rachel T., Wang, Jun, Liu, Xiong, Sun, Lin, Xue, Wenhao, Cribb, Maureen, 2022. Full-coverage mapping and spatiotemporal variations of ground-level ozone (O3) pollution from 2013 to 2020 across China. *Remote Sens. Environ.* 270, 112775.
- Kan, H., 2017. The smaller, the worse? *Lancet Planet Health* 1, e210–e211.
- Kuwayama, T., et al., 2013. Daily trends and source apportionment of ultrafine particulate mass (PM0.1) over an annual cycle in a typical California city. *Environ. Sci. Technol.* 47, 13957–13966.
- Li, J., et al., 2017. Modification of the effects of air pollutants on mortality by temperature: A systematic review and meta-analysis. *Sci. Total Environ.* 575, 1556–1570.
- Lin, H., et al., 2016. Particle size and chemical constituents of ambient particulate pollution associated with cardiovascular mortality in Guangzhou, China. *Environ. Pollut.* 208, 758–766.
- Liu, C., et al., 2019. Ambient particulate air pollution and daily mortality in 652 cities. *N. Engl. J. Med.* 381, 705–715.
- Nel, A., 2005. Atmosphere. Air pollution-related illness: effects of particles. *Science* 308, 804–806.
- Samek, L., et al., 2018. Seasonal contribution of assessed sources to submicron and fine particulate matter in a Central European urban area. *Environ. Pollut.* 241, 406–411.
- Tian, Y., et al., 2019a. Association between temperature variability and daily hospital admissions for cause-specific cardiovascular disease in urban China: a national time-series study. *PLoS Med* 16, e1002738.
- Tian, Y., et al., 2019b. Association between ambient fine particulate pollution and hospital admissions for cause specific cardiovascular disease: time series study in 184 major Chinese cities. *Bmj* 367, l6572.
- Wang, H., et al., 2021. Associations between PM(1) exposure and daily emergency department visits in 19 hospitals, Beijing. *Sci. Total Environ.* 755, 142507.
- Wei, J., et al., 2019. Satellite-Derived 1-km-Resolution PM(1) Concentrations from 2014 to 2018 across China. *Environ. Sci. Technol.* 53, 13265–13274.
- Wei, J., et al., 2021. The ChinaHighPM(10) dataset: generation, validation, and spatiotemporal variations from 2015 to 2019 across China. *Environ. Int* 146, 106290.
- Yang, M., et al., 2018. Is smaller worse? New insights about associations of PM(1) and respiratory health in children and adolescents. *Environ. Int* 120, 516–524.
- Yang, M., et al., 2020. Is PM(1) similar to PM(2.5)? A new insight into the association of PM(1) and PM(2.5) with children's lung function. *Environ. Int* 145, 106092.
- Yang, M., et al., 2023. Sources, chemical components, and toxicological responses of size segregated urban air PM samples in high air pollution season in Guangzhou, China. *Sci. Total Environ.* 865, 161092.

Yin, P., et al., 2017. Particulate air pollution and mortality in 38 of China's largest cities: time series analysis. *Bmj* 356, j667.

Zhang, Y., et al., 2021. Early-life exposure to submicron particulate air pollution in relation to asthma development in Chinese preschool children. *J. Allergy Clin. Immunol.* 148, 771-782.e12.

Zhao, C.X., et al., 2014. [Temporal and spatial distribution of PM2.5 and PM10 pollution status and the correlation of particulate matters and meteorological factors during winter and spring in Beijing]. *Huan Jing Ke Xue.* 35, 418–27.