Atmospheric Environment 251 (2021) 118271

Contents lists available at ScienceDirect

Atmospheric Environment

journal homepage: http://www.elsevier.com/locate/atmosenv

Size-specific particulate air pollution and hospitalization for cardiovascular diseases: A case-crossover study in Shenzhen, China

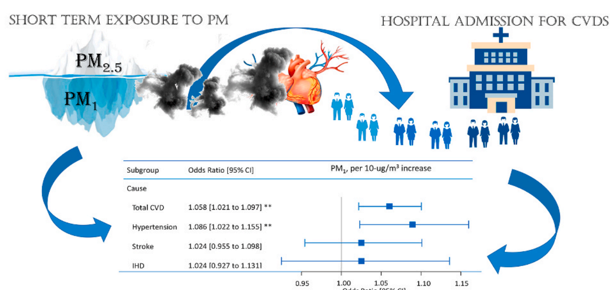
Yuanyuan Zhang [a], Liansheng Zhang [a,**], Jing Wei [b,c], Linjiong Liu [a], Yaqi Wang [a], Jiaxin Liu [a], Peixuan Zhou [a], Lu Wang [d], Zan Ding [e], Yunquan Zhang [a,f,*]

[a] *Department of Epidemiology and Biostatistics, School of Public Health, Wuhan University of Science and Technology, Wuhan, 430065, China*
[b] *State Key Laboratory of Remote Sensing Science, College of Global Change and Earth System Science, Beijing Normal University, Beijing, China*
[c] *Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, MD, USA*
[d] *Department of Nursing, Medical College, Wuhan University of Science and Technology, Wuhan, 430065, China*
[e] *The Institute of Metabolic Diseases, Baoan Central Hospital of Shenzhen, The Fifth Affiliated Hospital of Shenzhen University, Shenzhen, 518102, China*
[f] *Hubei Province Key Laboratory of Occupational Hazard Identification and Control, Wuhan University of Science and Technology, Wuhan, 430065, China*

HIGHLIGHTS

- PM_1 exhibited relatively stronger effects on CVDs than $PM_{2.5}$ and PM_{10}.
- Detected impacts from size-specific PMs on hypertension but not IHD and stroke.
- PM-associated effects on IHD were only identified in cold months.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
PM_1
Fine particulate matter
Cardiovascular diseases
Short-term impact
Case-crossover study

ABSTRACT

Background: Despite contributing to the majority of ambient fine particles ($PM_{2.5}$), PM_1 (particulate matter [PM] with aerodynamic diameter ≤ 1 μm) remains poorly studied in terms of its acute effects on cardiovascular diseases (CVDs) in China. This study aims to evaluate the short-term associations of size-specific PMs (i.e., PM_1, $PM_{2.5}$, and PM_{10}) exposures with hospital admissions for CVDs in a southern Chinese metropolis.

Methods: We collected 5,969 records of hospital admissions for CVDs and daily average concentrations of air pollutants and weather conditions in Shenzhen from January 1st 2015 to December 31st 2017. We adopted a time-stratified case-crossover design and conditional logistic regression models to assess short-term associations between size-specific PMs and CVD hospitalizations along different exposure days.

Results: During the study period, annual average concentrations of PM_1, $PM_{2.5}$, and PM_{10} were 18.7, 27.8, and 45.4 μg/m^3, respectively. Compared to $PM_{2.5}$ and PM_{10}, PM_1 exhibited a generally stronger association with CVD hospitalizations. Hospital admissions for CVDs increased by 6.7% (95% confidence interval: 1.2–12.5%), 4.5% (0.4–8.7%), and 3.4% (0.5–6.3%), corresponding to per 10-μg/m^3 rise in exposure to PM_1, $PM_{2.5}$, and PM_{10} at lag

* Corresponding author. Department of Epidemiology and Biostatistics, School of Public Health, Wuhan University of Science and Technology, Wuhan, 430065, China.

** Corresponding author.

E-mail addresses: zhangliansheng@wust.edu.cn (L. Zhang), YunquanZhang@wust.edu.cn (Y. Zhang).

https://doi.org/10.1016/j.atmosenv.2021.118271
Received 31 August 2020; Received in revised form 25 January 2021; Accepted 11 February 2021
Available online 17 February 2021

03 days. In our stratified analyses by CVD sub-causes, size-specific PMs showed consistent effects on hypertension but no evident association with ischemic heart disease (IHD) and stroke. Seasonal analysis revealed significantly larger PM-associated risks among IHD patients in cold months (October–March). Nevertheless, in warm months (April–September), the older group (aged 65+ years) was more prone to adverse effects of PM_1 exposure at lag 0 day.

Conclusion: Short-term exposure to size-specific PMs, PM_1 in particular, may trigger incidences of CVD hospitalization. To effectively mitigate adverse effects of particulate pollution, evidence-based PM_1 standards should be developed as well in Chinese less-polluted megacities.

1. Introduction

According to the Global Burden of Disease Study, cardiovascular diseases (CVDs) have remained the top leading cause of health loss globally until now (Roth et al., 2017, 2018). The all-age number of deaths due to CVDs was estimated to be achieved upwards 17.8 million worldwide in 2017, with counting around 330.2 million years of life lost (Roth et al., 2018). Over the past couple of decades, plenty of epidemiological research has investigated the adverse effects of short-term and lifelong exposure to ambient particulate matter on cardiovascular health (Cohen et al., 2017; Khan et al., 2019; Pope et al., 2004; Rajagopalan et al., 2018; Saber et al., 2013). Derived from the burning of biomass and fossil fuels (Heal, 2014), ambient $PM_{2.5}$, particle mass with aerodynamic diameter less than 2.5 μm, is widely deemed to be the main hazardous component to cardiovascular health in particulate pollutants (Achilleos et al., 2017; Chang et al., 2015; Chen and Hoek, 2020; Khan et al., 2019; Requia et al., 2017).

The authoritative scientific statement from the American Heart Association summarized that exposure to $PM_{2.5}$ over a few hours to weeks could trigger CVD-related mortality and nonfatal events such as hospital admission (Brook et al., 2004, 2010). To date, PM-related evidence for CVDs is mainly concentrated on fine and coarse particulate matters across the globe (Chang et al., 2015; Crichton et al., 2016; Dominici et al., 2006; Gu et al., 2020; Liu et al., 2017). Nevertheless, emerging studies suggested smaller particles may induce stronger toxic effects on the cardiovascular system (Chen et al., 2015; Kwon et al., 2020; Yang et al., 2019). For instance, a Milan research regarding PM_1-associated adverse effects on mice cardiovascular system found that inhaled PM_1 could sustain the adhesion of platelets to endothelia and considerably increase thrombosis and myocardial infarction risks (Farina et al., 2013). However, due to a wide lack of monitoring data for submicron particulate matter, PM_1-CVD evidence has been very sparse worldwide, particularly in developing countries.

Compared with developed states, China suffers more greatly from burden of disease attributed to ambient fine particulate pollution (Maji et al., 2018; Wang et al., 2020). According to ground measurements across over 90 stations in mainland China during 2013–2014, the ratios of PM_1 to $PM_{2.5}$ ranged from 60% to 90% across regions and seasons (Chen et al., 2018; Wang et al., 2015). PM_1-associated effects on hospitalizations for cause-specific CVDs remain unknown, although several studies have demonstrated that PM_1 was strongly associated with hospital admissions in China (Chen et al., 2020a; Liu et al., 2021; Zhang et al., 2020a). In this study, we employed a time-stratified case-crossover design to examine the effect of short-term exposure to size-specific PMs (i.e., PM_1, $PM_{2.5}$ and PM_{10}) on hospital admissions for major cardiovascular subcategories in Shenzhen, China. The susceptible populations and seasonal patterns were further identified by subgroup analysis by sex, age, and season.

2. Materials and methods

2.1. Study site

Shenzhen (coordinates: 22°24′ to 22°52′ N, 113°43′ to 114°38′ E), a coastal metropolis bordering on Hong Kong, is a primary node in the global economic network. It has an area of around 1997 km^2 and a permanent resident population of about 11.4 million in 2016 (Meng et al., 2020). Baoan Central Hospital of Shenzhen is a large-scale general hospital located in the central Baoan District. Among 10 district-level jurisdictions of Shenzhen, Baoan district has the broadest area (384 km^2) and the largest population (3.34 million people), accounting for more than a quarter of Shenzhen's total population (http://tjj.sz.gov.cn/). Besides, Shenzhen has a subtropical maritime monsoon climate and a relatively low level of ambient particulate pollution compared with other Chinese megacities. But as one of the primary air pollutants in Shenzhen, the concentration of $PM_{2.5}$ still exceeds the annual standard (10 $\mu g/m^3$) recommended by the World Health Organization.

2.2. Data collection

2.2.1. Daily records of hospital admissions for CVDs

We collected 5,969 cases of CVD hospitalizations in the Baoan Central Hospital of Shenzhen during January 1st 2015–December 31st 2017. For each patient, we extracted its admission date, disease code, and demographic information such as sex, age, marital status, and ethnicity. According to the Tenth Revision of the International Classification of Diseases (ICD-10), CVD sub-causes were coded as follows: CVDs (I00–I99), hypertension (I10–I15), ischemic heart disease (IHD, I20–I25), and stroke (I60–I69). The dates of hospitalizations are further divided into cold months (October–March) and warm months (April–September), and other sub-categories are classified by sex (male and female), and age (0–17, 18–44, 45–64, and 65+ years).

2.2.2. Ground measurements of air pollutants and meteorological data

Daily concentrations of $PM_{2.5}$ and PM_{10}, recorded in Shenzhen Environmental Monitoring Center (SEMC), were average ground measurements across 11 air quality monitoring stations. These reliable monitoring measurements have been widely used to estimate atmospheric pollution exposures in China (Lee et al., 2019; Maji et al., 2018). For restrictions of measuring technology in SEMC, PM_1 levels were not considered into routine monitoring work. We gleaned daily mean concentrations of PM_1 in Shenzhen from China Atmosphere Watch Network (CAWNET), which is an adjunct of the Chinese Academy of Meteorological Sciences (Wang et al., 2019; Zang et al., 2018). Details of the measurement technique have been reported previously (Wang et al., 2015). Briefly, with two quality-control procedures in sampling ambient air, we used an optical particle counter (OPC) and environmental dust monitors (GRIMM 180, Grimm 180 Multi-channel Aerosol Spectrometer; Ainring, Germany) to acquire information regarding particle number size distribution and daily ambient PM_1 levels (Chen et al., 2017a; Zang et al., 2018). During the study period (1096 days), there is complete data for PM_1 and around 2.0% missing data for $PM_{2.5}$ and PM_{10} (22 days). Given sporadic days of missing data, we did not perform missing data imputation in statistical analysis (Tian et al., 2019).

We also collected monitoring data of four gaseous pollutants (sulfur dioxide [SO_2], nitrogen dioxide [NO_2], carbon monoxide [CO], and ozone [O_3]) from SEMC. Over the same period, daily meteorological covariates were shared on the China Meteorological Network (http://data.cma.cn). Meteorological factors included temperature (°C), relative humidity (%), sunshine duration (hour), wind speed (m/s), and atmospheric pressure (hPa). Hospital admission information, ground measurements of air pollutants, and meteorological data were matched by date for each hospitalized case for CVDs.

2.3. Study design

A case-crossover design was proposed to identify risk factors of acute events (Maclure, 1991), and its theoretical framework is to compare the exposure of the same research subject in the period time before the event with the exposure without the incident. In this design, self-matching of cases could increase experimental efficiency and control time-invariant individual-level confounders such as behavioural and metabolic factors (Carracedo-Martínez et al., 2010). To deal with the potential confounding effects by long-term trend, seasonality and day of week, Lumley and Levy introduced a time-stratified case-crossover (TSCC) design (Lumley and Levy, 2000). Our study used a TSCC design to assess the risk of hospital admissions for CVDs associated with short-term exposure to particulate pollution. For each admission date of CVD patient, time could be stratified by month and day of week in the same year to create partitions with three or four referent days (Liu et al., 2019; Lumley and Levy, 2000; Zhang et al., 2020a).

2.4. Statistical analysis

The Spearman correlation coefficient was adopted to measure the correlation between air pollutants and meteorological conditions (Liu et al., 2019). Our study applied conditional logistic regression (CLR) models, a standard method to tackle the matched case-control study, to evaluate the short-term effects of ambient exposures to PM_1, $PM_{2.5}$, and PM_{10} on hospital admissions for CVDs. CLR model can be implemented using a Cox proportional hazards regression model in R software (Ding et al., 2017). Our main analytic model was shown as below:

$$\ln(\mathrm{h}(t, X)) = \ln(\mathrm{h}_0(\mathrm{t})) + \beta(PMs) + ns(\text{temperature},\ df = 3) + ns(\text{relative humidity},\ df = 3)$$

Where t = the day; X = the hospital admission; ln (h (t, X)) = risk function; ln (h_0 (t)) = baseline risk function; β = the coefficient for PMs to be estimated; ns = natural cubic spline function; and df = degrees of freedom (Chen et al., 2019; Di et al., 2017).

Using maximum likelihood estimation (MLE) method, we estimated odds ratios (ORs) and their 95% confidence intervals (CIs) for CVD admission associated with per 10-μg/m^3 increase in PM exposure. The exposure-response relationship curves were plotted to examine linearity hypothesis between PM concentrations and CVD hospitalizations. In brief, we replaced the linear term of PMs in the main analytic model with ns smoothers (3 df for PM_1, $PM_{2.5}$ and PM_{10}), as was done in previous studies (Bell et al., 2006; Gu et al., 2020).

To explore delayed or cumulative effects of particulate pollutants, we used different lag structures, including single-day lag (lag 0–lag 4 day) and moving-average lag (lag 01–lag 04 days) (Wang et al., 2020; Zhang et al., 2020a). For instance, lag 2 day's exposure was assigned the PM concentration measured at 2 days prior to admission, while lag 02 days' exposure was the average concentration recorded on the day of admission, 1 day and 2 days before hospitalization.

Meanwhile, we conducted subgroup analyses stratified by cause of admission (total CVDs, hypertension, stroke, and IHD), sex (male, female), and age (18-44, 45-64, and 65+ years) (Amsalu et al., 2019; Organization, 2010). According to date for admissions, we further divided each subgroup into warm season and cold season to identify the seasonal pattern of PM-hospitalization associations. In line with prior research (Guo, 2017; Zhang et al., 2020b), a meta-regression (MR) method was applied to differentiate PM-associated effect estimates between subgroups (cause, gender, and age) and seasons. For example, treating the cause of CVD admission as a meta-predictor (total CVDs as the reference), we regarded cause-specific effect estimates as the dependent variable in the MR model. We utilized the likelihood ratio test to assess whether the effects estimated for sub-causes statistically varied from that for total CVDs.

2.5. Sensitivity analysis

A range of sensitivity analyses were conducted to check the robustness of our findings by changing the regression modelling parameters. Specifically, we (1) changed df of temperature (3–6 df) and relative humidity (3–6 df) for natural cubic spline methods; (2) performed two-pollutant models by additionally adjusting for gaseous pollutants (i.e., SO_2, NO_2, CO, and O_3); (3) included the natural cubic spline term of other meteorological factors (i.e., atmospheric pressure, wind speed, and sunshine duration); (4) excluded CVD cases under the age of 18 years (only 42 inpatients, 0.7%).

All analyses were conducted using R software (version 3.6.3). We used (1) the “ggcorrplot” package for Spearman' correlation analysis; (2) the “survival” and “splines” package for CLR analysis; (3) the “mvmeta” package for meta-regression analysis. For all statistical tests, the two-sided effect of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Summary description

Table 1 presents the statistical characteristics of hospital admission cases for CVDs included in analysis, 2015–2017. There was a total of 5969 patients, with a mean age of 53.7 (standard deviation [SD], 16.3). The group aged 18–64 years accounted for about three quarters (73.4%), while the group aged 0–17 only shared a proportion of <1%. Three CVD sub-cause groups having over one-tenth were hypertension (31.9%), stroke (29.2%) and IHD (12.1%), respectively. The vast majority of people are married and Han, and approximately half CVD hospitalizations occurred in warm season.

Table 1
Basic characteristics of hospital admission cases for cardiovascular diseases in Shenzhen, China, 2015–2017.

Characteristics	Value
Total cardiovascular diseases, No. (%)	5,969 (100)
Case day, No.	5,969
Control day, No.	20,355
Cause, No. (%)	
Hypertension	1,905 (31.9)
Stroke	1,744 (29.2)
Ischemic heart disease	722 (12.1)
Sex, No. (%)	
Male	3,599 (60.3)
Female	2,370 (39.7)
Age of admission, years	
Mean (SD)	53.7 (16.3)
Median (IQR)	52.0 (22.0)
Age, No. (%)	
0–17	42 (0.7)
18–44	1,707 (28.6)
45–64	2,667 (44.7)
65+	1,553 (26.0)
Marital status, No. (%)	
Never married	323 (5.4)
Married	5,372 (90.0)
Divorced or widowed	216 (3.6)
Undefined	58 (1.0)
Ethnicity, No. (%)	
Han	5,954 (99.7)
Other	15 (0.3)
Season of admission, No. (%)	
Warm	2,914 (48.8)
Cold	3,055 (51.2)

Abbreviation: SD, standard deviation; IQR, interquartile range; Warm, April to September; Cold, October to March of the next year.

Table 2 depicts distribution characteristics of particulate and gaseous pollutants and meteorological factors. During the study period, mean concentrations of PM_1, $PM_{2.5}$, and PM_{10} were 18.7 (interquartile range [IQR] = 16.3) μg/m^3, 27.8 (21.0) μg/m^3, and 45.4 (29.0) μg/m^3, respectively. Fig. 1 shows Spearman's correlation coefficients (r) between air pollution and meteorological conditions. PMs and gaseous pollutants are positively correlated, with r ranging from 0.43 to 0.63. Meanwhile, PMs had a positive association with atmospheric pressure and were negatively correlated with temperature and relative humidity, while not significantly associated with wind speed and sunshine duration. PM levels showed a clear seasonal pattern with higher concentrations in cold months (Fig. S1).

3.2. Main findings

Fig. 2 shows season-specific ORs (95% CIs) for CVD hospitalizations associated with per 10-μg/m^3 increase in PM_1, $PM_{2.5}$, and PM_{10} exposure along several lag days. The corresponding estimates were detailed in Table S1. In full-year analysis, for each 10-μg/m^3 rise in exposures, the estimated ORs (95% CIs) at lag 03 days were 1.067 (1.012–1.125) for PM_1, 1.044 (1.004–1.087) for $PM_{2.5}$, and 1.034 (1.005–1.063) for PM_{10}, respectively. Fig. 3 displayed exposure-response curves smoothed by ns function, suggesting generally linear relationship between CVD admissions and concentrations of size-specific PMs. In season-stratified analysis, significant PM-hospitalization associations were all found in cold season, with an exception of PM_1-associated CVD risk (1.009, 1.003–1.016) at lag 0 day in warm season.

3.3. Subgroups analyses

Fig. 4 displays subgroup-specific OR estimates for associations between CVD hospitalizations and ambient exposures to PM_1, $PM_{2.5}$, and PM_{10}, stratified by CVD sub-cause, sex, and age. The pattern of associations stratified by CVD sub-cause and sex were broadly similar when using different fraction-specific PMs as the exposure, and the intensity of associations with PM_1 was relatively stronger than those with $PM_{2.5}$ and PM_{10}. For a 10-μg/m^3 increase in exposures to PM_1, $PM_{2.5}$ and PM_{10}, effect estimates for hypertension admissions were 1.086 (1.022–1.155), 1.083 (1.036–1.133), and 1.056 (1.025–1.089), respectively. For IHD and stroke, no evident associations with size-specific PMs were observed during full year. Risks of CVD admissions for male associated with per 10-μg/m^3 rise in exposures to particulate air pollutant increased by 8.8% (95% CI, 4.0–13.0%) for PM_1, 3.7% (0.1–7.4%) for $PM_{2.5}$, and 3.2% (0.7–5.8%) for PM_{10}, respectively. No significant adverse effects of PMs were seen among female patients with CVDs. Additionally, no clear evidence was identified for risk vulnerability among subpopulations stratified by CVD sub-cause, sex, and age.

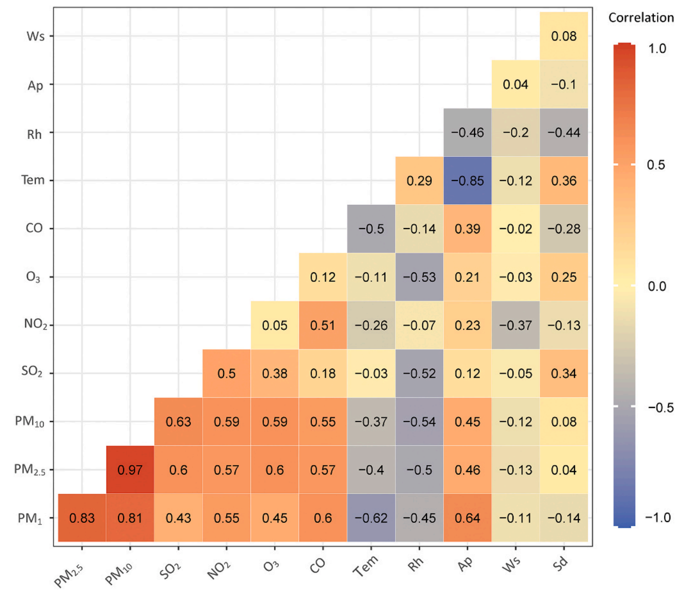


Fig. 1. Spearman correlation matrix between levels of ambient air pollutants and meteorological conditions in Shenzhen, China, 2015–2017. Abbreviations: PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone; Tem, temperature; Rh, relative humidity; Ap, atmospheric pressure; Ws, wind speed; Sd, sunshine duration.

3.4. Seasonal analyses

Fig. 5 manifests seasonal differences between aforementioned subgroups in PM_1-CVD associations. PM_1-hospitalization associations of most subgroups (i.e., total CVD, hypertension, IHD, male, and 45–64 years) were exclusively exhibited in cold season, while significant difference was only identified for IHD with a p-value of 0.014 for between-season effects. Similar IHD findings were also observed for $PM_{2.5}$ (OR = 1.016, 1.001–1.031, Fig. S2) and PM_{10} (OR = 1.012, 1.002–1.022, Fig. S3) in cold season. Specifically, among patients aged 65+ years, we detected a converse seasonal pattern ($p = 0.026$), with PM_1-associated ORs of 1.018 (1.004–1.031) in warm months versus 1.000 (0.991–1.008) in cold months. Season-stratified estimates for subgroups by cause (Tables S2), gender (Table S3), and age groups (Table S4) were detailed in the supplementary material.

Table 2
Summary statistics of ambient air pollutants and meteorological factors in Shenzhen, China, 2015–2017.

Variable	Mean ± SD	Min	P_{25}	P_{50}	P_{75}	Max
Particulate pollutants, μg/m^3						
PM_1	18.7 ± 11.9	1.9	9.1	16.6	25.4	82.7
$PM_{2.5}$	27.8 ± 15.3	5.0	16.0	25.0	37.0	100.0
PM_{10}	45.4 ± 22.4	10.0	29	40.0	58.0	160.0
Gaseous pollutants						
SO_2, μg/m^3	7.7 ± 2.2	3.0	6.0	7.0	9.0	18.0
NO_2, μg/m^3	31.5 ± 10.9	12.0	23.0	30.0	37.0	102.0
CO, mg/m^3	0.8 ± 0.2	0.5	0.7	0.8	0.9	1.6
O_3, μg/m^3	58.7 ± 24.8	12.9	37.9	53.5	75.5	144.0
Meteorological factors						
Temperature, °C	23.6 ± 5.4	3.5	19.2	25.0	28.2	33.0
Relative humidity, %	76 ± 12.4	28.0	70.0	78.0	85.0	100.0
Atmospheric pressure, hPa	1005.8 ± 6.5	986.8	1000.9	1005.3	1010.6	1027.3
Wind speed, m/s	1.9 ± 0.7	0.4	1.3	1.7	2.2	5.9
Sunshine duration, hour	5.1 ± 3.8	0.0	1.3	5.2	8.7	12.3

Abbreviation: SD, standard deviation; PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; CO, carbon monoxide; O_3, ozone.

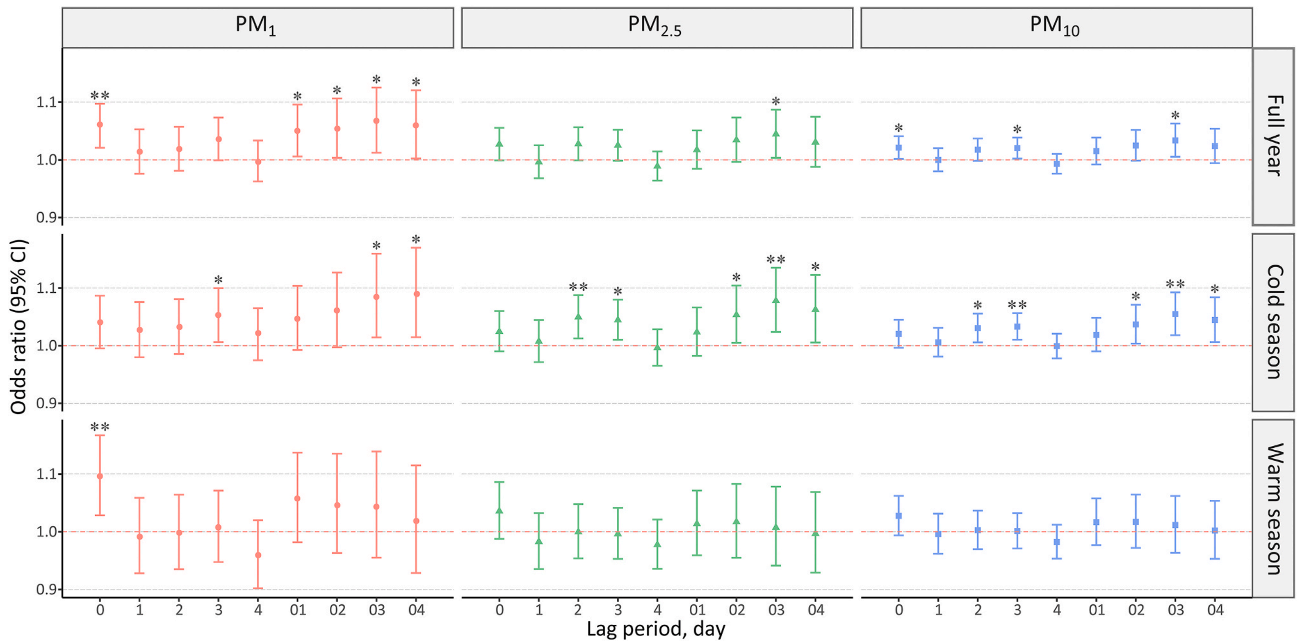


Fig. 2. Season-specific odds ratios (95% CIs) of hospitalization for total cardiovascular diseases associated with per 10-μg/m^3 increase in exposure to PM_1, $PM_{2.5}$, and PM_{10} at various lag days. Notes: *$p < 0.05$, **$p < 0.01$. Abbreviations: CI, confidence interval; PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm.

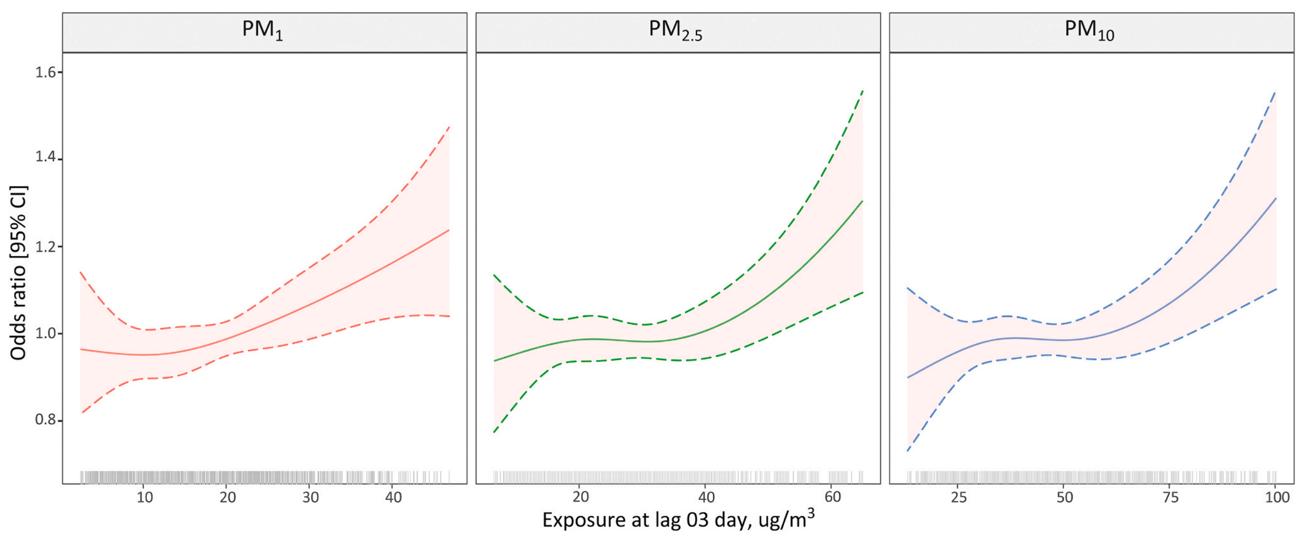


Fig. 3. Exposure-response curves for PM_1, $PM_{2.5}$ and PM_{10} associated with hospital admission for total cardiovascular diseases at lag 03 days, respectively. Abbreviations: CI, confidence interval; PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm.

3.5. Sensitivity analysis

Table S5 presents the results of the sensitivity analyses, suggesting that the PM-CVD associations were consistently observed after changing the above-mentioned regression modelling parameters. For instance, for each 10-μg/m^3 rise in PM_1, ORs of CVD hospitalizations ranged only from 1.063 to 1.082.

4. Discussion

To the best of our knowledge, PM_1-associated health effects were little known in China owing to lack of ground PM_1 measurements. In this case-crossover study, we evaluated short-term effects of ambient size-specific PMs (i.e., PM_1, $PM_{2.5}$ and PM_{10}) on hospital admissions for CVDs. Compared with $PM_{2.5}$ and PM_{10}, PM_1 exhibited a generally stronger association with hypertension but not with IHD and stroke during full year. Seasonal analysis revealed significantly larger PM-associated risks among IHD patients in cold months. Moreover, PM-hospitalization associations varied slightly among sex- and age-specific subpopulations.

Our results support the hypothesis that hospital admissions for CVDs are associated with short-term exposure to ambient fraction-specific PMs, especially PM_1. This finding was highly consistent with many time-series and case-crossover studies study in China (Amsalu et al., 2019; Chen et al., 2020a; Li et al., 2019; Liu et al., 2018, 2020). Besides, a rigorously controlled study on particulate air pollution and circulating biomarkers reported that size fractions with the strongest associations were <1 and 0.25–0.40 μm for aerodynamic diameters (Chen et al.,

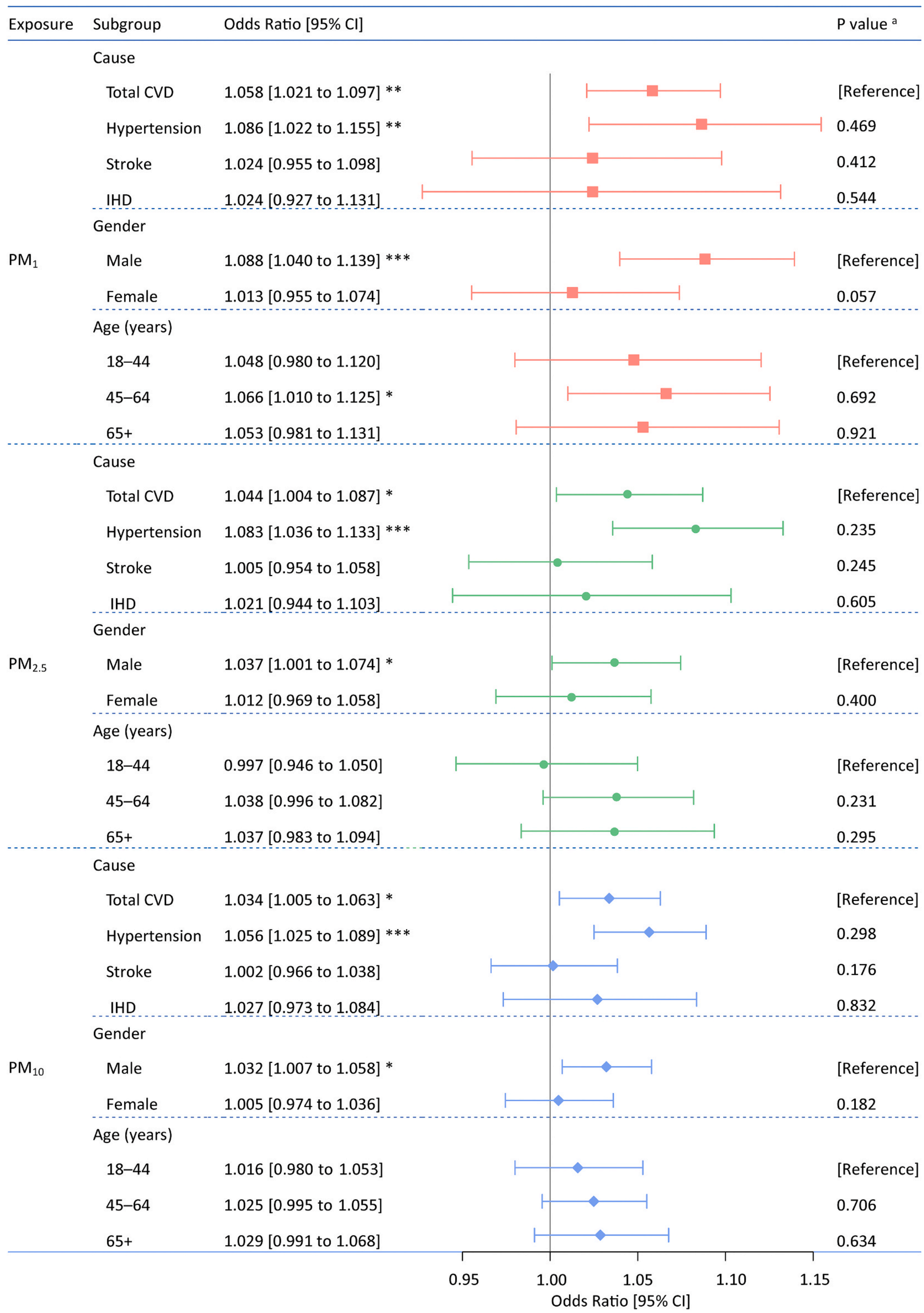


Fig. 4. Odds ratios (95% CIs) for hospitalization associated with per 10-μg/m^3 increase in exposure to PM_1, $PM_{2.5}$ and PM_{10} among subgroups stratified by cause, gender, and age. Notes: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; a p-value for difference between subgroups. Abbreviations: CI, confidence interval; PM_1, particulate matter with aerodynamic diameter ≤1 μm; $PM_{2.5}$, particulate matter with aerodynamic diameter ≤2.5 μm; PM_{10}, particulate matter with aerodynamic diameter ≤10 μm.

2015). The biological mechanisms of short-term particulate effects on circulatory system might be indirect inflammatory responses induced by inhaled pollutants (Brook et al., 2004, 2010). Given that smaller particles may have higher order of magnitudes in particle surface area, particulate number concentration, and level of adsorbed or condensed toxic air pollutants per unit mass (Caggiano et al., 2019; Kwon et al., 2020), they were easier to enter lung-based cells and systemic circulation, causing more obvious adverse effects on CVD patients (Farina et al., 2013; Filep et al., 2016).

The magnitude of evidence supporting associations between $PM_{2.5}$ and CVDs has grown substantially in past decades (Chang et al., 2015; Liu et al., 2017; Rajagopalan et al., 2018). In our study, the estimated

Subgroup	Odds Ratio [95% CI]	P value [a]
Total CVD	1.001 [0.995 to 1.007] 1.005 [1.001 to 1.010] *	0.263
Hypertension	1.005 [0.995 to 1.016] 1.010 [1.003 to 1.018] **	0.465
Stroke	0.999 [0.986 to 1.011] 1.004 [0.995 to 1.012]	0.531
IHD	0.984 [0.966 to 1.003] 1.013 [1.000 to 1.025] *	0.014
Male	1.002 [0.994 to 1.010] 1.006 [1.000 to 1.012] *	0.406
Female	0.999 [0.989 to 1.009] 1.003 [0.996 to 1.011]	0.455
18–44	0.993 [0.977 to 1.009] 1.010 [0.997 to 1.023]	0.094
45–64	1.004 [0.991 to 1.017] 1.011 [1.001 to 1.021] *	0.395
65+	1.018 [1.004 to 1.031] ** 1.000 [0.991 to 1.008]	0.026

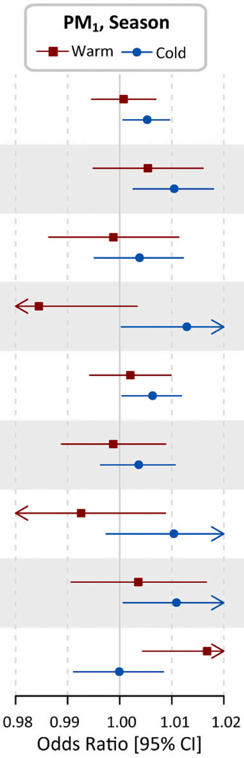


Fig. 5. Season-specific odds ratios (95% CIs) for hospital admission associated with per 10-μg/m^3 increase in exposure to PM_1, stratified by cause, sex and age. Notes: *p < 0.05; **p < 0.01; [a] p-value for difference between the effects in warm and cold season. Abbreviations: CI, confidence interval; PM_1, particulate matter with aerodynamic diameter ≤1 μm.

effects associated with a 10-μg/m^3 increment of $PM_{2.5}$ concentrations was 4.4% at lag 03 days for CVD hospitalizations, and 8.3% at lag 3 days for hypertension admissions, respectively. Similarly, for per 10-μg/m^3 rise in $PM_{2.5}$ at lag 0 day, a 0.26% and a 0.80% increase for CVD hospitalizations were reported by a nationwide investigation in 184 major Chinese cities (Tian et al., 2019) and by a study of 202 US counties (Bell et al., 2008), respectively. In Canada, research using the same case-crossover design with time-stratified strategy linked a 7% increase in the risk of emergency department visits for hypertension with an IQR (6.2 μg/m^3) rise in $PM_{2.5}$ concentrations (Szyszkowicz et al., 2012). Maybe because of the variations in study population, levels of $PM_{2.5}$, meteorological factors, socioeconomic status, and geographical conditions, the intensity of $PM_{2.5}$-CVD associations varied by studies and locations (Basu et al., 2019; Chen et al., 2017b; Dominici et al., 2006).

The associations between particulates pollutants and CVD sub-cause groups are inconsistent, with lots of controversy regarding stroke (Crichton et al., 2016; Gu et al., 2020; Shah et al., 2015). In this study, no associations between size-specific PMs and stroke admission were observed. Two possible explanations for the finding are as follows. First and foremost, on account of pathogenesis, stroke can be divided into hemorrhagic and ischaemic stroke (Liu et al., 2017). The short-term exposure to ambient particulate pollutants have been reported to be associated with ischaemic stroke but not with hemorrhagic stroke (Gu et al., 2020; Liu et al., 2017; Tian et al., 2019). In our study, due to the insufficient number of stroke patients, we did not distinguish the type of stroke, which may lead to much weaker or null effects. Additionally, the characteristics of study population and location might partly affect PM-stroke association in this study (Newell et al., 2017; Yusuf et al., 2020). For instance, Shenzhen has a large number of migrant residents with a young age structure (Yang et al., 2015), giving rise to inconspicuous effects of PMs on human health (Chen et al., 2017b; Yang et al., 2019).

Many PM-CVD epidemiologic experiments have widely explored the threats of sex and age to the effects (Brook et al., 2010; George et al., 2015), which suggested elderly individual is at higher risk of short-term particle exposure but modification by sex is not well consistent (Clougherty, 2010; Hu et al., 2018). In our study, PM-CVD associations were more robust among the elderly and male, but we did not identify a significant heterogeneity between these subpopulations. There is a consensus that pre-existing diseases (e.g., diabetes) and the degradation of cardiovascular function in the elderly may elevate PM-associated risk of hospitalization for CVDs (Brook et al., 2004; Yang et al., 2018; Zhang et al., 2020b). Our sex-stratified results were echoed in several previous studies, such as time-series analysis in China (Chen et al., 2020b) and Cyprus (Middleton et al., 2008), and population-based survival research in Canada (Bai et al., 2019). Conversely, two single-city investigations in Shanghai and Beijing reported slightly stronger effects of particle pollution for females compared with males (Kan et al., 2008; Tian et al., 2018). Overall, sex-specific effects may vary by experimental design and study locations. Further research is needed to explore the source of sex discrepancy in particulate effects.

Coincided with many prior studies (Bell et al., 2008; Chang et al., 2015; Kan et al., 2008), our seasonal analysis also observed positive PM-hospitalization associations in cold season. This may be due to the reasons as follows. First, the relatively high $PM_{2.5}$ concentrations and $PM_1/PM_{2.5}$ ratios existed in cold months (Chen et al., 2018; Jiao et al., 2020). Besides, the sources and constituents of particles may vary by season and region (Peng et al., 2005; Wei et al., 2019), and the most toxic ambient PM had a winter or summer maximum in southern China (Chen et al., 2013). Notably, we observed a higher PM_1-induced risk in warm months (April–September) among CVD patients aged 65+ years, which was in agreement with a provincial study in Zhejiang, China suggesting stronger associations of PM_1 with CVD mortality in June–September (Hu et al., 2018). Due to complex composition of atmospheric particulates and data unavailability, our study cannot analyze the relationship in detail. Research on PM changes over time is warranted in the future to explain the seasonal variations comprehensively.

We acknowledged our study had several limitations. First, owing to lack of residential address, we could not confirm that all admissions lived in the study area, which would cause exposure measurement error. However, hospital admission has been validated as an effective outcome in assessing PM-associated health effects in previous epidemiological studies (Dominici et al., 2006; Lanzinger et al., 2016; Son et al., 2013; Tian et al., 2019). Second, we used station-based PM measurements instead of individual exposures because data on patients' addresses were not available. Such an assignment method could inevitably result in exposure misclassification (Zhang et al., 2020b), however, which tends to be random and generally biases the effect estimates downward (Tian et al., 2019; Zhang et al., 2020a). Third, the confounding effects of time-invariant covariates (e.g., obesity status, smoking history) could have been commendably controlled through the TSCC study design. But, the TSCC design may allow for selection bias and confounding by time-varying factors. Additionally, our CVD cases were originated from one single hospital, which might hinder the extrapolation of the results to other regions.

5. Conclusions

In summary, our study provided case-crossover evidence that short-term exposure to size-specific PMs, PM_1 in particular, may trigger the incidence of CVD hospitalization as well in Chinese less-polluted megacities. PM_1-associated risk may vary by season and among subpopulations. Given the sparse evidence of sub-micrometric particles, more PM_1-health investigations are thus needed in the future to better depict health impacts associated with ambient fine particulate air pollution.

CRediT authorship contribution statement

Yuanyuan Zhang: performed the data analysis and drafted the original manuscript, All authors read and approved the final manuscript. **Liansheng Zhang:** helped revise the manuscript. **Jing Wei:** collected and cleaned the data. **Linjiong Liu:** helped revise the manuscript. **Jiaxin Liu:** collected and cleaned the data. **Peixuan Zhou:** collected and cleaned the data. **Lu Wang:** collected and cleaned the data. **Zan Ding:** collected and cleaned the data. **Yunquan Zhang:** conceived and designed the study, performed the data analysis and drafted the original manuscript.

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.

Acknowledgments

This study was supported by Science and Technology Research Project of Hubei Provincial Department of Education (Grant No. Q20201104), Open Fund Project of Hubei Province Key Laboratory of Occupational Hazard Identification and Control (Grant No. OHIC2020Y01), the Key Research Center for Humanities and Social Sciences in Hubei Province (Hubei University of Medicine) (Grant No. 2020ZD001), Outstanding Young and Middle Aged Technology Innovation Team Project of Hubei Provincial Department of Education (Grant No. T2020003), and Scientific Research Project of Wuhan Health Committee (Grant No. EG20C05).We thank Shenzhen Environmental Monitoring Center for providing air pollution data and the China Meteorological Data Network for providing meteorological data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.atmosenv.2021.118271.

References

Achilleos, S., Kioumourtzoglou, M.A., Wu, C.D., Schwartz, J.D., Koutrakis, P., Papatheodorou, S.I., 2017. Acute effects of fine particulate matter constituents on mortality: a systematic review and meta-regression analysis. Environ. Int. 109, 89–100.

Amsalu, E., Wang, T., Li, H., Liu, Y., Wang, A., Liu, X., Tao, L., Luo, Y., Zhang, F., Yang, X., Li, X., Wang, W., Guo, X., 2019. Acute effects of fine particulate matter (PM2.5) on hospital admissions for cardiovascular disease in Beijing, China: a time-series study. Environ. Health 18, 70.

Bai, L., Shin, S., Burnett, R.T., Kwong, J.C., Hystad, P., van Donkelaar, A., Goldberg, M. S., Lavigne, E., Copes, R., Martin, R.V., Kopp, A., Chen, H., 2019. Exposure to ambient air pollution and the incidence of congestive heart failure and acute myocardial infarction: a population-based study of 5.1 million Canadian adults living in Ontario. Environ. Int. 132, 105004.

Basu, S., Tian, Y., Liu, H., Si, Y., Cao, Y., Song, J., Li, M., Wu, Y., Wang, X., Xiang, X., Juan, J., Chen, L., Wei, C., Gao, P., Hu, Y., 2019. 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.

Bell, M.L., Ebisu, K., Peng, R.D., Walker, J., Samet, J.M., Zeger, S.L., Dominici, F., 2008. Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999–2005. Am. J. Epidemiol. 168, 1301–1310.

Bell, M.L., Peng, R.D., Dominici, F., 2006. The exposure–response curve for ozone and risk of mortality and the adequacy of current ozone regulations. Environ. Health Perspect. 114, 532–536.

Brook, R.D., Franklin, B., Cascio, W., Hong, Y., Howard, G., Lipsett, M., Luepker, R., Mittleman, M., Samet, J., Smith, S.C., Tager, I., 2004. Air pollution and cardiovascular disease. Circulation 109, 2655–2671.

Brook, R.D., Rajagopalan, S., Pope 3rd, C.A., Brook, J.R., Bhatnagar, A., Diez-Roux, A.V., Holguin, F., Hong, Y., Luepker, R.V., Mittleman, M.A., Peters, A., Siscovick, D., Smith Jr., S.C., Whitsel, L., Kaufman, J.D., American Heart Association Council on, E., Prevention, C.o.t.K.i.C.D, Council on Nutrition, P.A., Metabolism, 2010. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. Circulation 121, 2331–2378.

Caggiano, R., Sabia, S., Speranza, A., 2019. Trace elements and human health risks assessment of finer aerosol atmospheric particles (PM1). Environ. Sci. Pollut. Control Ser. 26, 36423–36433.

Carracedo-Martínez, E., Taracido, M., Tobias, A., Saez, M., Figueiras, A., 2010. Case-crossover analysis of air pollution health effects: a systematic review of methodology and application. Environ. Health Perspect. 118, 1173–1182.

Chang, C.C., Chen, P.S., Yang, C.Y., 2015. Short-term effects of fine particulate air pollution on hospital admissions for cardiovascular diseases: a case-crossover study in a tropical city. J. Toxicol. Environ. Health 78, 267–277.

Chen, D., Zhang, F., Yu, C., Jiao, A., Xiang, Q., Yu, Y., Mayvaneh, F., Hu, K., Ding, Z., Zhang, Y., 2019. Hourly associations between exposure to ambient particulate matter and emergency department visits in an urban population of Shenzhen, China. Atmos. Environ. 209, 78–85.

Chen, G., Li, S., Zhang, Y., Zhang, W., Li, D., Wei, X., He, Y., Bell, M.L., Williams, G., Marks, G.B., Jalaludin, B., Abramson, M.J., Guo, Y., 2017a. Effects of ambient PM1 air pollution on daily emergency hospital visits in China: an epidemiological study. Lancet Planet Health 1, e221–e229.

Chen, G., Morawska, L., Zhang, W., Li, S., Cao, W., Ren, H., Wang, B., Wang, H., Knibbs, L.D., Williams, G., Guo, J., Guo, Y., 2018. Spatiotemporal variation of PM1 pollution in China. Atmos. Environ. 178, 198–205.

Chen, J., Hoek, G., 2020. Long-term exposure to PM and all-cause and cause-specific mortality: a systematic review and meta-analysis. Environ. Int. 105974.

Chen, L., Zhang, Y., Zhang, W., Chen, G., Lu, P., Guo, Y., Li, S., 2020a. Short-term effect of PM1 on hospital admission for ischemic stroke: a multi-city case-crossover study in China. Environ. Pollut. 260, 113776.

Chen, R., Gao, Q., Sun, J., Yang, H., Li, Y., Kang, F., Wu, W., 2020b. Short-term effects of particulate matter exposure on emergency room visits for cardiovascular disease in Lanzhou, China: a time series analysis. Environ. Sci. Pollut. Res. Int. 27, 9327–9335.

Chen, R., Peng, R.D., Meng, X., Zhou, Z., Chen, B., Kan, H., 2013. Seasonal variation in the acute effect of particulate air pollution on mortality in the China Air Pollution and Health Effects Study (CAPES). Sci. Total Environ. 450–451, 259–265.

Chen, R., Yin, P., Meng, X., Liu, C., Wang, L., Xu, X., Ross, J.A., Tse, L.A., Zhao, Z., Kan, H., Zhou, M., 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, R., Zhao, Z., Sun, Q., Lin, Z., Zhao, A., Wang, C., Xia, Y., Xu, X., Kan, H., 2015. Size-fractionated particulate air pollution and circulating biomarkers of inflammation, coagulation, and vasoconstriction in a panel of young adults. Epidemiology 26, 328–336.

Clougherty, J.E., 2010. A growing role for gender analysis in air pollution epidemiology. Environ. Health Perspect. 118, 167–176.

Cohen, A.J., Brauer, M., Burnett, R., Anderson, H.R., Frostad, J., Estep, K., Balakrishnan, K., Brunekreef, B., Dandona, L., Dandona, R., Feigin, V., Freedman, G., Hubbell, B., Jobling, A., Kan, H., Knibbs, L., Liu, Y., Martin, R., Morawska, L., Pope, C.A., Shin, H., Straif, K., Shaddick, G., Thomas, M., van Dingenen, R., van Donkelaar, A., Vos, T., Murray, C.J.L., Forouzanfar, M.H., 2017. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. Lancet 389, 1907–1918.

Crichton, S., Barratt, B., Spiridou, A., Hoang, U., Liang, S.F., Kovalchuk, Y., Beevers, S.D., Kelly, F.J., Delaney, B., Wolfe, C.D.A., 2016. Associations between exhaust and non-exhaust particulate matter and stroke incidence by stroke subtype in South London. Sci. Total Environ. 568, 278–284.

Di, Q., Dai, L., Wang, Y., Zanobetti, A., Choirat, C., Schwartz, J.D., Dominici, F., 2017. Association of short-term exposure to air pollution with mortality in older adults. J. Am. Med. Assoc. 318, 2446–2456.

Ding, L., Zhu, D., Peng, D., Zhao, Y., 2017. Air pollution and asthma attacks in children: a case-crossover analysis in the city of Chongqing, China. Environ. Pollut. 220, 348–353.

Dominici, F., Peng, R.D., Bell, M.L., Pham, L., McDermott, A., Zeger, S.L., Samet, J.M., 2006. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. J. Am. Med. Assoc. 295, 1127–1134.

Farina, F., Sancini, G., Longhin, E., Mantecca, P., Camatini, M., Palestini, P., 2013. Milan PM1 induces adverse effects on mice lungs and cardiovascular system. BioMed Res. Int. 2013, 583513.

Filep, A., Fodor, G.H., Kun-Szabo, F., Tiszlavicz, L., Razga, Z., Bozso, G., Bozoki, Z., Szabo, G., Petak, F., 2016. Exposure to urban PM1 in rats: development of bronchial inflammation and airway hyperresponsiveness. Respir. Res. 17, 26.

George, J., Rapsomaniki, E., Pujadesrodriguez, M., Shah, A.D., Denaxas, S., Herrett, E., Smeeth, L., Timmis, A., Hemingway, H., 2015. How does cardiovascular disease first present in women and men? Incidence of 12 cardiovascular diseases in a contemporary cohort of 1 937 360 people. Circulation 132 (14), 1320–1328.

Gu, J., Shi, Y., Chen, N., Wang, H., Chen, T., 2020. Ambient fine particulate matter and hospital admissions for ischemic and hemorrhagic strokes and transient ischemic attack in 248 Chinese cities. Sci. Total Environ. 715, 136896.

Guo, Y., 2017. Hourly associations between heat and ambulance calls. Environ. Pollut. 220, 1424–1428.

Heal, M.R., 2014. The application of carbon-14 analyses to the source apportionment of atmospheric carbonaceous particulate matter: a review. Anal. Bioanal. Chem. 406, 81–98.

Hu, K., Guo, Y., Hu, D., Du, R., Yang, X., Zhong, J., Fei, F., Chen, F., Chen, G., Zhao, Q., Yang, J., Zhang, Y., Chen, Q., Ye, T., Li, S., Qi, J., 2018. Mortality burden attributable to PM1 in Zhejiang province, China. Environ. Int. 121, 515–522.

Jiao, A., Xiang, Q., Ding, Z., Cao, J., Ho, H.C., Chen, D., Cheng, J., Yang, Z., Zhang, F., Yu, Y., 2020. Short-term impacts of ambient fine particulate matter on emergency department visits: comparative analysis of three exposure metrics. Chemosphere 241, 125012.

Kan, H., London, S.J., Chen, G., Zhang, Y., Song, G., Zhao, N., Jiang, L., Chen, B., 2008. Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: the Public Health and Air Pollution in Asia (PAPA) Study. Environ. Health Perspect. 116, 1183–1188.

Khan, R., Konishi, S., Ng, C.F.S., Umezaki, M., Kabir, A.F., Tasmin, S., Watanabe, C., 2019. Association between short-term exposure to fine particulate matter and daily emergency room visits at a cardiovascular hospital in Dhaka, Bangladesh. Sci. Total Environ. 646, 1030–1036.

Kwon, H.S., Ryu, M.H., Carlsten, C., 2020. Ultrafine particles: unique physicochemical properties relevant to health and disease. Exp. Mol. Med. 52, 318–328.

Lanzinger, S., Schneider, A., Breitner, S., Stafoggia, M., Erzen, I., Dostal, M., Pastorkova, A., Bastian, S., Cyrys, J., Zscheppang, A., medicine, c.c., 2016. Ultrafine and fine particles and hospital admissions in Central Europe. Results UFIREG Study 194, 1233–1241.

Lee, S., Park, H., Kim, S., Lee, E.K., Lee, J., Hong, Y.S., Ha, E., 2019. Fine particulate matter and incidence of metabolic syndrome in non-CVD patients: a nationwide population-based cohort study. Int. J. Hyg Environ. Health 222, 533–540.

Li, N., Chen, G., Liu, F., Mao, S., Liu, Y., Hou, Y., Lu, Y., Liu, S., Wang, C., Xiang, H., Guo, Y., Li, S., 2019. Associations of long-term exposure to ambient PM1 with hypertension and blood pressure in rural Chinese population: the Henan rural cohort study. Environ. Int. 128, 95–102.

Liu, L., Song, F., Fang, J., Wei, J., Ho, H., Song, Y., Zhang, Y., Wang, L., Yang, Z., Hu, C., Zhang, Y., 2021. Intraday effects of ambient PM1 on emergency department visits in Guangzhou, China: a case-crossover study. Sci. Total Environ. 750, 142347.

Liu, H., Tian, Y., Xiang, X., Juan, J., Song, J., Cao, Y., Huang, C., Li, M., Hu, Y., 2018. Ambient particulate matter concentrations and hospital admissions in 26 of China's largest cities: a case-crossover study. Epidemiology 29, 649–657.

Liu, H., Tian, Y., Xu, Y., Zhang, J., 2017. Ambient particulate matter concentrations and hospitalization for stroke in 26 Chinese cities: a case-crossover study. Stroke 48, 2052–2059.

Liu, S., Wang, L., Zhou, L., Li, W., Pu, X., Jiang, J., Chen, Y., Zhang, L., Qiu, H., 2020. Differential effects of fine and coarse particulate matter on hospitalizations for ischemic heart disease: a population-based time-series analysis in Southwestern China. Atmos. Environ. 224.

Liu, Y., Pan, J., Zhang, H., Shi, C., Li, G., Peng, Z., Ma, J., Zhou, Y., Zhang, L., 2019. Short-term exposure to ambient air pollution and asthma mortality. Am. J. Resp. Crit Care 200, 24–32.

Lumley, T., Levy, D., 2000. Bias in the case-crossover design: implications for studies of air pollution. Environmetrics 11, 689–704.

Maclure, M., 1991. The case-crossover design: a method for studying transient effects on the risk of acute events. Am. J. Epidemiol. 133, 144–153.

Maji, K.J., Dikshit, A.K., Arora, M., Deshpande, A., 2018. Estimating premature mortality attributable to PM2.5 exposure and benefit of air pollution control policies in China for 2020. Sci. Total Environ. 612, 683–693.

Meng, L., Sun, Y., Zhao, S., 2020. Comparing the spatial and temporal dynamics of urban expansion in Guangzhou and Shenzhen from 1975 to 2015: a case study of pioneer cities in China's rapid urbanization. Land Use Pol. 97, 104753.

Middleton, N., Yiallouros, P., Kleanthous, S., Kolokotroni, O., Schwartz, J., Dockery, D. W., Demokritou, P., Koutrakis, P., 2008. A 10-year time-series analysis of respiratory and cardiovascular morbidity in Nicosia, Cyprus: the effect of short-term changes in air pollution and dust storms. Environ. Health 7, 39.

Newell, K., Kartsonaki, C., Lam, K.B.H., Kurmi, O.P., 2017. Cardiorespiratory health effects of particulate ambient air pollution exposure in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Planetary Health 1, e368–e380.

Organization, W.H., 2010. Global Recommendations on Physical Activity for Health. World Health Organization.

Peng, R.D., Dominici, F., Pastor-Barriuso, R., Zeger, S.L., Samet, J.M., 2005. Seasonal analyses of air pollution and mortality in 100 US cities. Am. J. Epidemiol. 161, 585–594.

Pope 3rd, C.A., Burnett, R.T., Thurston, G.D., Thun, M.J., Calle, E.E., Krewski, D., Godleski, J.J., 2004. Cardiovascular mortality and long-term exposure to particulate air pollution: epidemiological evidence of general pathophysiological pathways of disease. Circulation 109, 71–77.

Rajagopalan, S., Al-Kindi, S.G., Brook, R.D., 2018. Air pollution and cardiovascular disease: JACC state-of-the-art review. J. Am. Coll. Cardiol. 72, 2054–2070.

Requia, W.J., Adams, M.D., Koutrakis, P., 2017. Association of PM2.5 with diabetes, asthma, and high blood pressure incidence in Canada: a spatiotemporal analysis of the impacts of the energy generation and fuel sales. Sci. Total Environ. 584–585, 1077–1083.

Roth, G.A., Abate, D., Abate, K.H., Abay, S.M., Abbafati, C., Abbasi, N., Abbastabar, H., Abd-Allah, F., Abdela, J., Abdelalim, A.J.T.L., 2018. Global, Regional, and National Age-sex-specific Mortality for 282 Causes of Death in 195 Countries and Territories, 1980–2017: a Systematic Analysis for the Global Burden of Disease Study, vol. 392, pp. 1736–1788, 2017.

Roth, G.A., Johnson, C., Abajobir, A., Abd-Allah, F., Abera, S.F., Abyu, G., Ahmed, M., Aksut, B., Alam, T., Alam, K., Alla, F., Alvis-Guzman, N., Amrock, S., Ansari, H., Arnlov, J., Asayesh, H., Atey, T.M., Avila-Burgos, L., Awasthi, A., Banerjee, A., Barac, A., Barnighausen, T., Barregard, L., Bedi, N., Belay Ketema, E., Bennett, D., Berhe, G., Bhutta, Z., Bitew, S., Carapetis, J., Carrero, J.J., Malta, D.C., Castaneda-Orjuela, C.A., Castillo-Rivas, J., Catala-Lopez, F., Choi, J.Y., Christensen, H., Cirillo, M., Cooper Jr., L., Criqui, M., Cundiff, D., Damasceno, A., Dandona, L., Dandona, R., Davletov, K., Dharmaratne, S., Dorairaj, P., Dubey, M., Ehrenkranz, R., El Sayed Zaki, M., Faraon, E.J.A., Esteghamati, A., Farid, T., Farvid, M., Feigin, V., Ding, E.L., Fowkes, G., Gebrehiwot, T., Gillum, R., Gold, A., Gona, P., Gupta, R., Habtewold, T.D., Hafezi-Nejad, N., Hailu, T., Hailu, G.B., Hankey, G., Hassen, H.Y., Abate, K.H., Havmoeller, R., Hay, S.I., Horino, M., Hotez, P.J., Jacobsen, K., James, S., Javanbakht, M., Jeemon, P., John, D., Jonas, J., Kalkonde, Y., Karimkhani, C., Kasaeian, A., Khader, Y., Khan, A., Khang, Y.H., Khera, S., Khoja, A. T., Khubchandani, J., Kim, D., Kolte, D., Kosen, S., Krohn, K.J., Kumar, G.A., Kwan, G.F., Lal, D.K., Larsson, A., Linn, S., Lopez, A., Lotufo, P.A., El Razek, H.M.A., Malekzadeh, R., Mazidi, M., Meier, T., Meles, K.G., Mensah, G., Meretoja, A., Mezgebe, H., Miller, T., Mirrakhimov, E., Mohammed, S., Moran, A.E., Musa, K.I., Narula, J., Neal, B., Ngalesoni, F., Nguyen, G., Obermeyer, C.M., Owolabi, M., Patton, G., Pedro, J., Qato, D., Qorbani, M., Rahimi, K., Rai, R.K., Rawaf, S., Ribeiro, A., Safiri, S., Salomon, J.A., Santos, I., Santric Milicevic, M., Sartorius, B., Schutte, A., Sepanlou, S., Shaikh, M.A., Shin, M.J., Shishehbor, M., Shore, H., Silva, D.A.S., Sobngwi, E., Stranges, S., Swaminathan, S., Tabares-Seisdedos, R., Tadele Atnafu, N., Tesfay, F., Thakur, J.S., Thrift, A., Topor-Madry, R., Truelsen, T., Tyrovolas, S., Ukwaja, K.N., Uthman, O., Vasankari, T., Vlassov, V., Vollset, S.E., Wakayo, T., Watkins, D., Weintraub, R., Werdecker, A., Westerman, R., Wiysonge, C. S., Wolfe, C., Workicho, A., Xu, G., Yano, Y., Yip, P., Yonemoto, N., Younis, M., Yu, C., Vos, T., Naghavi, M., Murray, C., 2017. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J. Am. Coll. Cardiol. 70, 1–25.

Saber, A.T., Lamson, J.S., Jacobsen, N.R., Ravn-Haren, G., Hougaard, K.S., Nyendi, A.N., Wahlberg, P., Madsen, A.M., Jackson, P., Wallin, H., Vogel, U., 2013. Particle-induced pulmonary acute phase response correlates with neutrophil influx linking inhaled particles and cardiovascular risk. PloS One 8, e69020.

Shah, A.S., Lee, K.K., McAllister, D.A., Hunter, A., Nair, H., Whiteley, W., Langrish, J.P., Newby, D.E., Mills, N.L., 2015. Short term exposure to air pollution and stroke: systematic review and meta-analysis. BMJ 350, h1295.

Son, J.-Y., Lee, J.-T., Park, Y.H., Bell, M.L.J.E., 2013. Short-term Effects of Air Pollution on Hospital Admissions in Korea, pp. 545–554.

Szyszkowicz, M., Rowe, B.H., Brook, R.D., 2012. Even low levels of ambient air pollutants are associated with increased emergency department visits for hypertension. Can. J. Cardiol. 28, 360–366.

Tian, L., Liang, F., Guo, Q., Chen, S., Xiao, S., Wu, Z., Jin, X., Pan, X., 2018. The effects of interaction between particulate matter and temperature on mortality in Beijing, China. Environ. Sci.: Processes Impacts 20, 395–405.

Tian, Y., Liu, H., Wu, Y., Si, Y., Song, J., Cao, Y., Li, M., Wu, Y., Wang, X., Chen, L., Wei, C., Gao, P., Hu, Y., 2019. 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, C., Zhu, G., Zhang, L., Chen, K., 2020. Particulate matter pollution and hospital outpatient visits for endocrine, digestive, urological, and dermatological diseases in Nanjing, China. Environ. Pollut. 261, 114205.

Wang, W., Mao, F., Zou, B., Guo, J., Wu, L., Pan, Z., Zang, L., 2019. Two-stage model for estimating the spatiotemporal distribution of hourly PM1.0 concentrations over central and east China. Sci. Total Environ. 675, 658–666.

Wang, Y.Q., Zhang, X.Y., Sun, J.Y., Zhang, X.C., Che, H.Z., Li, Y., 2015. Spatial and temporal variations of the concentrations of PM10, PM2.5 and PM1 in China. Atmos. Chem. Phys. 15, 13585–13598.

Wei, J., Li, Z., Guo, J., Sun, L., Huang, W., Xue, W., Fan, T., Cribb, M., 2019. Satellite-derived 1-km-resolution PM1 concentrations from 2014 to 2018 across China. Environ. Sci. Technol. 53, 13265–13274.

Yang, B., Guo, Y., Morawska, L., Bloom, M.S., Markevych, I., Heinrich, J., Dharmage, S. C., Knibbs, L.D., Lin, S., Yim, S.H.L., 2019. Ambient PM1 air pollution and cardiovascular disease prevalence: insights from the 33 Communities Chinese Health Study. Environ. Int. 123, 310–317.

Yang, W., Li, H., Fu, X., Lu, J., Xue, Z., Wu, C.a., 2015. Inequalities in cardiovascular health between local and migrant residents: a cross-sectional study of 6934 participants in Longhua District, Shenzhen. Medicine 94.

Yang, Y., Guo, Y., Qian, Z.M., Ruan, Z., Zheng, Y., Woodward, A., Ai, S., Howard, S.W., Vaughn, M.G., Ma, W., Wu, F., Lin, H., 2018. Ambient fine particulate pollution associated with diabetes mellitus among the elderly aged 50 years and older in China. Environ. Pollut. 243, 815–823.

Yusuf, S., Joseph, P., Rangarajan, S., Islam, S., Mente, A., Hystad, P., Brauer, M., Kutty, V. R., Gupta, R., Wielgosz, A., AlHabib, K.F., Dans, A., Lopez-Jaramillo, P., Avezum, A., Lanas, F., Oguz, A., Kruger, I.M., Diaz, R., Yusoff, K., Mony, P., Chifamba, J., Yeates, K., Kelishadi, R., Yusufali, A., Khatib, R., Rahman, O., Zatonska, K., Iqbal, R., Wei, L., Bo, H., Rosengren, A., Kaur, M., Mohan, V., Lear, S.A., Teo, K.K., Leong, D., O'Donnell, M., McKee, M., Dagenais, G., 2020. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 395, 795–808.

Zang, L., Mao, F., Guo, J., Gong, W., Wang, W., Pan, Z., 2018. Estimating hourly PM1 concentrations from Himawari-8 aerosol optical depth in China. Environ. Pollut. 241, 654–663.

Zhang, Y., Ding, Z., Xiang, Q., Wang, W., Huang, L., Mao, F., 2020a. Short-term effects of ambient PM1 and PM2.5 air pollution on hospital admission for respiratory diseases: case-crossover evidence from Shenzhen,China. Int. J. Hyg Environ. Health 224, 113418.

Zhang, Y., Fang, J., Mao, F., Ding, Z., Xiang, Q., Wang, W., 2020b. Age- and season-specific effects of ambient particles (PM1, PM2.5, and PM10) on daily emergency department visits among two Chinese metropolitan populations. Chemosphere 246, 125723.