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Ambient particulate matter and in-hospital case fatality of acute myocardial infarction: A multi-province cross-sectional study in China

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ABSTRACT

The acute myocardial infarction (AMI) outcomes have been extensively linked with ambient particulate matter (PM). However, whether a smaller particle has greater impact and the consequent attributable burden associated with PM of different sizes remain unclear. We conducted a multi-province cross-sectional study among AMI patients using the inpatient discharge datasets from four Chinese provinces (Shanxi, Sichuan, Guangxi, and Guangdong) from 2014 to 2019. Ambient PM exposure for each patient was assessed using the ChinaHigh-AirPollutants dataset. We employed the mixed-effects logistic regression models to evaluate the association of PM of different sizes (PM_1, $PM_{2.5}$, PM_{10}) on in-hospital case fatality. The potential reducible fractions in in-hospital case fatality were estimated through counterfactual analyses. Of 177,749 participants, 125,501 (70.6 %) were male and the in-hospital case fatality rate was 4.9%. For short-term (7-day average) exposure, the odds ratios (ORs) for PM_1, $PM_{2.5}$, and PM_{10} (per 10 μg/m^3) were 1.052 (95 % confidence interval [CI], 1.032–1.071), 1.026 (95 % CI, 1.014–1.037), and 1.016 (95% CI, 1.008–1.024), respectively. The estimated ORs for long-term exposure (annual average) were 1.303 (95 % CI, 1.252–1.356) for PM_1, 1.209 (95 % CI, 1.178–1.241) for $PM_{2.5}$, 1.157 (95 % CI, 1.134–1.181) for PM_{10}. Short-term exposure to PM_1 showed the highest potential reducible fraction (8.5 %, 95 % CI, 5.0–11.7 %), followed by $PM_{2.5}$ and PM_{10}, while the greatest potential reducible fraction of long-term exposure was observed in PM_{10} (30.9 %, 95 % CI, 27.2–34.4%), followed by $PM_{2.5}$ and PM_1. In summary, PM with smaller size had a more pronounced impact on in-hospital AMI case fatality, with PM_1 exhibiting greater effects than $PM_{2.5}$ and PM_{10}. Substantial health benefits for AMI patients could be achieved by mitigating ambient PM exposure.

1. Introduction

Cardiovascular diseases (CVDs) are a leading cause of death globally in 2019, accounting for approximately 18.6 million deaths (Roth et al., 2020). About 80 % of CVD deaths occur in low- and middle-income countries (Prabhakaran et al., 2018), and acute myocardial infarction (AMI) is the major contributor to CVD death (Dani et al., 2022). In China, AMI has been one of major public health concerns (Li et al., 2015). According to the estimates of the World Bank (2011), the quantity of individuals with AMI in China is expected to rise to 23 million by the year 2030. The National Center for Cardiovascular Diseases in China (2022) reported that the AMI mortality rate has continued

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to climb in the past decade. For instance, in rural China, this rate has doubled, rising from 38.09 deaths per 100,000 population in 2010 to 78.24 deaths per 100,000 population in 2019. This stands in stark contrast to the declining trend reported in developed countries like the United States (Ariss et al., 2022).

Numerous studies have linked AMI mortality to ambient exposure to particulate matter (PM) with diameter of ≤2.5 μm ($PM_{2.5}$) or ≤ 10 μm (PM_{10}) (Chen et al., 2016; Cramer et al., 2020; Liu et al., 2021). However, limited research has explored such associations concerning PM with smaller size, such as PM that are 1 μm or less in diameter (PM_1). To date, the evidence linking ambient exposure to PM of different sizes with the risk of AMI case fatality remain scarce, particularly in developing countries like China, where both severe air pollution and elevated AMI case fatality rates are widespread concerns (Cai et al., 2022b; National Center for Cardiovascular Diseases, China, 2022). Hence, a deeper understanding of how ambient PM of different sizes is associated with AMI case fatality could have significant implications for public health, offering opportunities to improve patient outcomes and reduce the disease burden, particularly in developing countries facing air pollution challenge.

In this study, we utilized the inpatient discharge datasets from four provinces in China to explore the links between in-hospital AMI case fatality risk and ambient exposure to PM_1, $PM_{2.5}$, and PM_{10}. Furthermore, we sought to estimate the burden of in-hospital AMI case fatality (fraction of in-hospital AMI case fatality) attributable to ambient PM exposure.

2. Materials and methods

2.1. Study population

Our study obtained de-identified inpatient discharge datasets from the provincial health commission of four provinces in China: Shanxi (spanning from 2014 to 2017), Sichuan (from 2017 to 2019), Guangxi (from 2014 to 2016), and Guangdong (specifically Zhanjiang City, from 2014 to 2016). The inpatient discharge dataset is routinely reported by hospitals using a national template with standardized coding and covers the entire population within each province. It contains over 100 variables related to hospitalisation, including patients' demographic and socioeconomic details, residential address, primary and secondary diagnoses, procedures, medical expenditure information, and discharge status of patients. In addition to textual descriptions of primary and secondary diagnoses, these diagnoses were coded using the International Classification of Diseases, Tenth Revision (ICD-10).

The patients with primary diagnosis of AMI were eligible for inclusion. Following previous studies (Cai et al., 2022b; Lin et al., 2017, 2020), we identified AMI patients from the inpatient discharge datasets based on the ICD-10 code of their primary diagnosis (I21). AMI subtypes were also identified for further stratified analyses, including ST-segment elevation myocardial infarction (STEMI, I21.0-I21.3), non-ST-segment elevation myocardial infarction (NSTEMI, I21.4), and unspecified myocardial infarction (I21.9). To address potential concerns related to ICD-10 miscoding, we employed a text matching algorithm utilizing regular expressions within clinical diagnosis descriptions (Cai et al., 2022b). Based on the ICD-10 code and text description of primary diagnosis, we initially included 190,029 AMI cases.

We excluded patients younger than 18 years old or those with missing data on age, sex, ethnicity, or insurance status (n = 6877, 3.6 %). We also excluded patients without residential address information (n = 4812, 2.5 %) and those lacking pollution exposure data (n = 591, 0.3 %). A final sample of 177,749 AMI cases from the four provinces were included in our study (Supplementary Fig. S1).

2.2. Exposure

We obtained grid data (10 km × 10 km) for daily average ambient PM concentrations in four provinces in China from the publicly available ChinaHighAirPollutants (CHAP) dataset for the period of 2013–2019 (Wei et al., 2021, 2020, 2019). The CHAP dataset is a product of diverse data sources (e.g., air quality data from ground monitoring stations, remote sensing data from satellite, model simulations results, and atmospheric reanalysis), providing long-term ground-level air pollutants (including PM_1, $PM_{2.5}$, and PM_{10}) across China. The details of CHAP dataset, as well as the cross-validation results for PM_1, $PM_{2.5}$, and PM_{10} are introduced in previous work (Wei et al., 2021, 2020, 2019).

To assess individual-level exposure to air pollutants, we obtained the coordinates (longitudes and latitudes) of patients' residential addresses using the *amapR* package in R software (version 4.1.2). Based on the four closest grids in proximity to their residential address, we calculated a weighted average PM concentration for each patient by employing a bilinear interpolation approach. The detailed techniques of the bilinear interpolation approach can be found in our previous study (Cai et al., 2022b). For each patient, we calculated 7-day (short-term) and 365-day (long-term) average exposure levels to PM preceding the day of hospitalisation (Cai et al., 2022b, 2023b; Wang et al., 2014). In sensitivity analyses, we used alternative exposure windows to measure short-term PM exposure levels (e.g., 3-day average PM exposure levels).

2.3. Outcome

In-hospital case fatality, an important index to reflect the prognosis of AMI, was defined as all-cause case fatality within time of hospitalisation. Due to the details on follow-up outcomes after discharge were not available in the inpatient discharge dataset, we were not able to analyse other outcomes such as 30-day case fatality or 90-day case fatality.

2.4. Statistical analyses

Considering the hierarchical characteristics of the pooled inpatient discharge data (patients were nested in province), mixed-effects logistic regression models were used to investigate the association of ambient exposure to PM_1, $PM_{2.5}$, and PM_{10} with the risk of in-hospital AMI case fatality, with random intercepts capturing the province-specific heterogeneity. Odds ratios (ORs) per 10 μg/m^3 increment in PM pollution and its 95 % confidence intervals (CIs) were reported. Following the procedures outlined in our previous research on stroke case fatality (Cai et al., 2022b, 2023b), we controlled the potential confounders associated with in-hospital case fatality, including patients' demographic and socioeconomic characteristics (e.g., age, sex, ethnicity, marital status, occupation), insurance status, a set of comorbidities, hospital level (tertiary hospital and non-tertiary hospital), and meteorological conditions (seven-day average temperature and relative humidity prior to the day of hospitalisation). We also incorporated adjustments for percutaneous coronary intervention (PCI) procedure, hospital volume and weekend admission in our study, as these factors have demonstrated strong predictive capabilities in assessing AMI mortality among Chinese patients (Cai et al., 2022a; Lin et al., 2020; Ni et al., 2019). To address the concern arising from unmeasured confounders, E-value was computed to assess the potential impact of an unobserved confounder in attenuating the observed associations (VanderWeele and Ding, 2017). The prevalence of outcome (in-hospital case fatality) in our study was less than 15% (rare event), we therefore calculated the E-value for OR: $E-\text{value}=OR+\sqrt{OR*(OR-1)}$, and E-value for 95 % CI: $E-\text{value}=LCI+\sqrt{LCI*(LCI-1)}$, where LCI indicates the lower confidence interval ($LCI>1$). We also depicted the exposure-response relationship curves using restricted cubic spline models (3 knots). To identify potential susceptible populations, we performed stratified analyses by AMI subtype (STEMI, NSTEMI), age (<65 years, ≥65 years), sex (male, female), and season of admission (warm, cold). We conducted interaction analyses to assess whether the associations were significantly modified by these factors of interest.

To assess the potential reducible fraction linked to PM exposure, we separately calculated the population attributable fractions (PAFs) for PM_1, $PM_{2.5}$, and PM_{10} within a counterfactual scenario. In this scenario, we hypothetically reduced the concentrations of ambient PM to a specified target exposure level, except when the observed concentrations were already lower than this target level (Cai et al., 2023b). Given the unavailability of guideline level for PM_1, we opted for the fifth percentile of observed PM concentration as the target exposure level. The PAF for each PM within the counterfactual scenario was calculated by two steps. Firstly, we estimated the expected number of fatalities ($fatality_{exp}$) using the fitted models in main analyses. Second, we employ the formula of subtracting the expected number of fatalities ($fatality_{exp}$) from the observed number of fatalities ($fatality_{obs}$), dividing this difference by the observed number of fatalities, and subsequently multiplying the outcome by 100% ($PAF = (fatality_{obs} - fatality_{exp})/fatality_{obs} * 100\%$). The 95% CIs based on 1000 bootstrap replicated samples were calculated for the PAFs.

We conducted several sensitivity analyses. First, we introduced each of the other pollutants (SO_2, NO_2, CO) individually into our main model to fit a two-pollutant model (Liu et al., 2019, 2021). The likelihood ratio test was used to compare our main model and the two-pollutant models. Ozone was not involved in two-pollutant models due to insufficient data quality. Additionally, because PM_1, $PM_{2.5}$ and PM_{10} were strongly correlated (Supplementary Fig. S3), we did not include them in the same model to avoid multicollinearity issues (Cai et al., 2023c; Chen et al., 2021). Second, we used alternative measures of short-term exposure assessment and re-estimated the associations. Third, we selected the time to fatality during hospitalisation as the primary outcome of interest and fitted Cox proportional hazard models to assess the associations. Fourth, to comprehensively capture the influence of comorbidity, we incorporated the Elixhauser comorbidity score into our analysis. The Elixhauser comorbidity score is a composite measure of 31 individual comorbidities, showing a strong predictive performance for in-hospital mortality within Chinese patient populations (Cai et al., 2020). Fifth, we re-estimated the associations within each province. Sixth, as the study periods differed across provinces, we re-estimated our results in the subsample of 71,016 hospitalisations from Shanxi, Guangxi, and Guangdong (Zhanjiang City) from January 2014 to December 2016. Seventh, the threshold setting of fifth percentile in the counterfactual scenario might be arbitrary, we therefore calculated the PAFs and its 95% CIs using alternative thresholds (ranging from the 10th to the 25th percentiles of PM concentrations).

3. Results

3.1. Patient characteristics and pollutant exposures

This study included 177,749 AMI cases, of which 82,766 (46.6%) were from Sichuan Province, 77,099 (43.4%) were from Shanxi Province, 11,456 (6.5%) were from Guangxi Province, and 6428 (3.6%) were from Zhanjiang City, Guangdong Province. The geographic distributions of all AMI cases are presented in Supplementary Fig. S2. Table 1 presents the descriptive statistics of our study populations. Of the 177,749 AMI cases, median age was 67 years (IQR: 56–76), 125,501 (70.6%) were male, 5763 (3.2%) were non-Han Chinese, 73,528 (41.4%) were involved in agricultural work, and 86,535 (48.7%) were admitted with STEMI. A total of 8725 in-hospital fatalities were observed during the study period, showing a case fatality rate of 4.9%. Patients were more likely to experience in-hospital fatalities if they were older, female, retired, unmarried or widowed, admitted on weekends; had unspecified MI and comorbidities; had not undergone PCI.

As shown in Table 2, the median (IQR) level of short-term (7-day average) exposure to ambient PM preceding the day of hospitalisation was 28.50 (21.63–41.83) μg/m^3 for PM_1, 44.18 (31.38–61.77) μg/m^3 for

Table 1
Descriptive statistics of study populations.

Characteristics	Overall	Case fatality		P-value
	N = 177,749	No (n = 169,024 [95.1%])	Yes (n = 8725 [4.9 %])	
Patient characteristics				
Age, y, median [IQR]	67 [56,76]	66 [55,75]	76 [68,82]	<0.001
Sex				
Female	52,248 (29.39)	48,804 (28.87)	3444 (39.47)	<0.001
Male	125,501 (70.61)	120,220 (71.13)	5281 (60.53)	
Ethnicity				
Han	171,986 (96.76)	163,675 (96.84)	8311 (95.26)	0.018
non-Han	5763 (3.24)	5349 (3.16)	414 (4.74)	
Occupation				
Public sector	9600 (5.40)	9298 (5.50)	302 (3.46)	<0.001
Private sector	16,705 (9.40)	16,190 (9.58)	515 (5.90)	
Agriculture	73,528 (41.37)	70,730 (41.85)	2798 (32.07)	
Unemployed	6402 (3.60)	6079 (3.60)	323 (3.70)	
Retired	26,102 (14.68)	24,082 (14.25)	2020 (23.15)	
Other	45,412 (25.55)	42,645 (25.23)	2767 (31.71)	
Marital status				
Married	157,380 (88.54)	150,429 (89)	6951 (79.67)	<0.001
Unmarried	4306 (2.42)	3919 (2.32)	387 (4.44)	
Widowed	8226 (4.63)	7450 (4.41)	776 (8.89)	
Divorced	2814 (1.58)	2481 (1.47)	333 (3.82)	
Other	5023 (2.83)	4745 (2.81)	278 (3.19)	
Insurance status				
UEBMI	49,108 (27.63)	46,035 (27.24)	3073 (35.22)	<0.001
URBMI	45,597 (25.65)	43,157 (25.53)	2440 (27.97)	
NRCMS	53,435 (30.06)	51,883 (30.70)	1552 (17.79)	
Self-payment	16,548 (9.31)	15,700 (9.29)	848 (9.72)	
Other	13,061 (7.35)	12,249 (7.25)	812 (9.31)	
Comorbidities				
Hypertension	78,912 (44.40)	75,212 (44.50)	3700 (42.41)	<0.001
Diabetes	38,218 (21.50)	35,830 (21.20)	2388 (27.37)	<0.001
Congestive heart failure	82,904 (46.64)	79,026 (46.75)	3878 (44.45)	<0.001
Cardiac arrhythmias	31,453 (17.70)	29,183 (17.27)	2270 (26.02)	<0.001
Pulmonary circulation disorders	3001 (1.69)	2529 (1.50)	472 (5.41)	<0.001
Peripheral vascular disorders	18,709 (10.53)	18,256 (10.80)	453 (5.19)	<0.001
Chronic pulmonary disease	18,377 (10.34)	16,949 (10.03)	1428 (16.37)	<0.001
Renal failure	7512 (4.23)	6483 (3.84)	1029 (11.79)	<0.001
Liver disease	18,383 (10.34)	17,599 (10.41)	784 (8.99)	<0.001
Elixhauser comorbidity score, median [IQR]	8 [4,12]	8 [4,12]	9 [4,15]	<0.001
AMI subtype				
STEMI	86,535 (48.68)	83,096 (49.16)	3439 (39.42)	<0.001
NSTEMI	42,196 (23.74)	40,834 (24.16)	1362 (15.61)	

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Table 1 (*continued*)

Characteristics	Overall	Case fatality		P-value
	N = 177,749	No (n = 169,024 [95.1%])	Yes (n = 8725 [4.9 %])	
Unspecified	49,018 (27.58)	45,094 (26.68)	3924 (44.97)	
Weekend admission	44,302 (24.92)	42,030 (24.87)	2272 (26.04)	0.015
PCI procedure	56,653 (31.87)	55,828 (33.03)	825 (9.46)	<0.001
Hospital characteristics				
Hospital level				
Tertiary	138,216 (80.13)	131,995 (80.45)	6221 (73.92)	<0.001
Non-tertiary	34,271 (19.87)	32,076 (19.55)	2195 (26.08)	
Hospital volume, cases/y, median [IQR]	382 [123,696]	395 [127,705]	187 [44,466]	<0.001

Notes: AMI, acute myocardial infarction; IQR, interquartile range; NRCMS, new rural cooperative medical scheme; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PM_1, ambient particulate matter with diameter ≤ 1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤ 2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤ 10 μm in aerodynamic diameter; STEMI, ST-segment elevation myocardial infarction; UEBMI, urban employee basic medical insurance; URBMI, urban resident basic medical insurance.

Table 2
Ambient concentrations of particulate matter, temperature, and relative humidity during study period.

Variable	Mean	SD	Percentile			IQR
			25 %	50 %	75 %	
Short-term exposure (7-day average prior to hospitalization, μg/m^3)						
PM_1	34.24	19.16	21.63	28.50	41.83	20.20
$PM_{2.5}$	50.35	28.31	31.38	44.18	61.77	30.39
PM_{10}	86.08	43.17	54.01	78.98	109.05	55.04
Long-term exposure (annual average prior to hospitalization, μg/m^3)						
PM_1	33.46	9.76	26.86	32.22	39.79	12.93
$PM_{2.5}$	51.65	14.52	41.28	50.03	62.37	21.10
PM_{10}	87.97	26.70	67.13	84.68	109.99	42.86
Meteorologic factors (7-day average prior to hospitalization)						
Temperature (°C)	14.28	9.20	7.80	15.47	21.90	14.10
Relative humidity (%)	65.78	16.28	54.97	70.25	78.35	23.39

Notes: IQR, interquartile range; PM_1, ambient particulate matter with diameter ≤ 1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤ 2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤ 10 μm in aerodynamic diameter; SD, standard deviation.

$PM_{2.5}$, 78.98 (54.01–109.05) μg/m^3 for PM_{10}. Similarly, the median (IQR) level of long-term (annual average) exposure was 32.22 (26.86–39.79) μg/m^3 for PM_1, 50.03 (41.28–62.37) μg/m^3 for $PM_{2.5}$, 84.68 (67.13–109.99) μg/m^3 for PM_{10}. The 7-day average temperature and relative humidity were 14.28 °C and 65.78%, respectively.

3.2. Associations of ambient PM exposure with in-hospital AMI Case fatality

As shown in Table 3, the greatest impact of short-term PM exposure on in-hospital AMI case fatality was associated with for PM_1 (OR, 1.052 [95% CI, 1.032–1.071]), followed by $PM_{2.5}$ (OR, 1.026 [95% CI, 1.014–1.037]) and PM_{10} (OR, 1.016 [95% CI, 1.008–1.024]). We observed similar patterns of ORs for long-term PM exposure: 1.303 (95% CI, 1.252–1.356) for PM_1, 1.209 (95% CI, 1.178–1.241) for $PM_{2.5}$, 1.157 (95% CI, 1.134–1.181) for PM_{10}. The E-values quantifying the potential effect of unmeasured confounders were relatively large, particularly for long-term PM exposure (greater than 1.58).

Table 3
Estimated odds ratios of in-hospital AMI case fatality associated with exposure to each 10 μg/m^3 increase in PM_1, $PM_{2.5}$, and PM_{10}.

Air pollution	OR (95% CI)	E-value for OR	E-value for 95% CI
Short-term exposure (7-day average)			
PM_1	1.052 (1.032–1.071)	1.284	1.215
$PM_{2.5}$	1.026 (1.014–1.037)	1.189	1.135
PM_{10}	1.016 (1.008–1.024)	1.143	1.095
Long-term exposure (annual average)			
PM_1	1.303 (1.252–1.356)	1.932	1.815
$PM_{2.5}$	1.209 (1.178–1.241)	1.712	1.635
PM_{10}	1.157 (1.134–1.181)	1.584	1.524

Notes: Models accounted for age, sex, ethnicity, occupation, marital status, insurance status, comorbidities (hypertension, diabetes, congestive heart failure, cardiac arrhythmias, pulmonary circulation disorders, peripheral vascular disorders, chronic pulmonary disease, renal failure, liver disease), acute myocardial infarction subtypes, weekend admission, percutaneous coronary intervention procedure, hospital level, hospital annual volume, the splines of seven-day average temperature and relative humidity (five degrees of freedom), year of admission, and province random effect. The E-values were computed for the scenarios of odds ratios with the prevalence of outcomes <15% (rare events), quantifying the strength of an unmeasured confounder to explain away the observed association. AMI, acute myocardial infarction; CI, confidence interval; OR, odds ratio; PM_1, ambient particulate matter with diameter ≤1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤10 μm in aerodynamic diameter.

Table 4 presents the ORs for the association of PM exposure with the risk of in-hospital AMI case fatality by AMI subtype, age group, sex, and season. The association between short-term PM exposure and in-hospital AMI case fatality was slightly stronger in patients with STEMI. We observed a different pattern for long-term PM exposure. When stratified by age group, we observed significantly greater ORs of in-hospital AMI case fatality associated with long-term PM exposure among patients aged 65 years and older, as compared with those younger than 65 years. The association of long-term exposure to $PM_{2.5}$ and PM_{10} with in-hospital AMI case fatality was stronger in females. The association between long-term PM_{10} exposure and in-hospital AMI case fatality were enhanced during the warm season.

Fig. 1. presented the exposure–response curves depicting the non-linear relationships between ambient PM exposure and in-hospital case fatality. The concave-down trend of the nonlinear relationship between short-term PM exposure and in-hospital case fatality were consistently observed for PM_1, $PM_{2.5}$, and PM_{10} (Fig. 1a.). For the long-term exposure, a concave-down trend was observed for PM_1, while the trends for $PM_{2.5}$ and PM_{10} showed a slightly concave-up relationship (Fig. 1b.).

3.3. Potential reducible fractions of in-hospital fatalities

For the short-term exposure, PM_1 exhibited the highest potential reducible fraction (8.5%, 95% CI, 5.0–11.7%), followed by $PM_{2.5}$ (6.9%, 95% CI, 3.6–10.1%) and PM_{10} (6.7%, 95% CI, 2.9–10.2%). In contrast, for the long-term exposure, the largest potential reducible fraction was observed in PM_{10} (30.9%, 95% CI, 27.2–34.4%), followed by $PM_{2.5}$ (26.8%, 95% CI, 23.2–30.1%) and PM_1 (24.8%, 95% CI, 21.2–27.8%).

Table 4

Estimated odds ratios of in-hospital AMI case fatality associated with exposure to each 10 μg/m^3 increase in PM_1, $PM_{2.5}$, and PM_{10} stratified by AMI subtype, age group, sex, and season.

Subgroups	Sample size	PM_1		$PM_{2.5}$		PM_{10}	
		OR (95% CI)	P for interaction	OR (95% CI)	P for interaction	OR (95% CI)	P for interaction
Short-term exposure (7-day average)							
AMI subtype							
STEMI	86,535	1.030 (1.001–1.060)	0.024	1.011 (0.993–1.028)	0.003	1.008 (0.995–1.021)	0.027
NSTEMI	42,196	1.095 (1.049–1.143)		1.064 (1.038–1.091)		1.040 (1.021–1.059)	
Age group							
Elderly	98,753	1.056 (1.034–1.078)	0.535	1.029 (1.016–1.042)	0.551	1.019 (1.010–1.029)	0.157
Non-elderly	78,996	1.038 (0.997–1.081)		1.015 (0.990–1.041)		1.004 (0.985–1.023)	
Sex							
Male	125,501	1.053 (1.029–1.078)	0.975	1.024 (1.010–1.039)	0.725	1.015 (1.004–1.025)	0.376
Female	52,248	1.047 (1.016–1.079)		1.027 (1.009–1.046)		1.017 (1.003–1.030)	
Season							
Warm	84,966	1.100 (1.042–1.161)	0.071	1.063 (1.023–1.105)	0.133	1.031 (1.009–1.053)	0.362
Cold	92,783	1.052 (1.029–1.074)		1.023 (1.011–1.036)		1.015 (1.006–1.025)	
Long-term exposure (annual average)							
AMI subtype							
STEMI	86,535	1.319 (1.245–1.398)	0.263	1.220 (1.172–1.269)	0.737	1.165 (1.130–1.201)	0.816
NSTEMI	42,196	1.327 (1.202–1.466)		1.219 (1.144–1.299)		1.150 (1.097–1.206)	
Age group							
Elderly	98,753	1.325 (1.267–1.386)	0.007	1.229 (1.193–1.267)	<0.001	1.179 (1.152–1.206)	<0.001
Non-elderly	78,996	1.241 (1.139–1.352)		1.146 (1.082–1.213)		1.086 (1.039–1.135)	
Sex							
Male	125,501	1.290 (1.227–1.357)	0.309	1.190 (1.151–1.230)	0.042	1.145 (1.116–1.175)	0.037
Female	52,248	1.320 (1.237–1.408)		1.238 (1.186–1.293)		1.175 (1.137–1.215)	
Season							
Warm	84,966	1.287 (1.208–1.372)	0.356	1.230 (1.180–1.282)	0.099	1.193 (1.154–1.234)	0.024
Cold	92,783	1.305 (1.238–1.376)		1.194 (1.152–1.237)		1.133 (1.103–1.164)	

Notes: AMI, acute myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PM_1, ambient particulate matter with diameter ≤1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤10 μm in aerodynamic diameter; STEMI, ST-elevation myocardial infarction.

3.4. Sensitivity analyses

Comparing the results of two-pollutant models with our main results, the magnitude of associations mostly decreased, but the overall pattern of these associations was largely unchanged: PM_1 showed the largest ORs, followed by $PM_{2.5}$ and PM_{10} (Supplementary Table S1). Notably, the ORs for both short- and long-term PM exposure in the two-pollutant models exhibited a significant decrease following adjustment for nitrogen dioxide ($P < 0.001$). We also found that our main findings were robust (1) using alternative measures of short-term exposure, (2) using Cox proportional hazard models, and (3) using Elixhauser comorbidity score as a composite measure of comorbidities (Supplementary Tables S2-S4). When we re-estimated the associations by province, we observed consistent patterns of the associations between exposure to PM and in-hospital fatality, except for the statistical insignificance of several estimates for short-term exposure in Sichuan, Guangxi, and Zhanjiang (Supplementary Table S5). We re-estimated the associations using the subsample of patients in Shanxi, Guangxi, and Zhanjiang in 2014–2016, yielding very similar results (Supplementary Table S6). We re-calculated the PAFs and its 95% CIs in additional counterfactual scenarios, showing consistent patterns (Supplementary Fig. S4).

4. Discussion

Using the inpatient discharge datasets from four Chinese provinces, our study established a consistent and positive association between in-hospital AMI case fatality risk and ambient exposure to PM_1, $PM_{2.5}$, and PM_{10}. Our results suggest that ambient PM_1 exposure exhibited a stronger association compared to $PM_{2.5}$ and PM_{10}. Furthermore, counterfactual analyses suggested that long-term ambient PM_{10} exposure had the largest potential reducible fraction of in-hospital AMI case fatality.

The size of particles may be crucial in determining the adverse health impacts of PM exposure (Chen et al., 2015; Kan, 2017). In comparison to larger particles, smaller particles such as PM_1 are more prone to adhere toxic components on their surface, deposit within the lungs, and even penetrate into bloodstream, thereby causing vascular dysfunction and endothelial damage. These characteristics may explain their stronger effects on cardiovascular outcomes (Kan, 2017). Our study suggested that PM_1 exhibited a greater effect on elevating the in-hospital AMI case fatality risk than $PM_{2.5}$ and PM_{10}, which aligns with the results of prior research (Ma et al., 2023; Yang et al., 2019; Zhang et al., 2021). For example, Yang et al. (2019) examined the impact of exposure to PM_1 and $PM_{2.5}$ (three-year average) on the prevalence of cardiovascular disease in a large sample of 24,845 adults from 33 communities in China, and they found that PM_1 exposure exhibits a larger association. A recent time-series study using 36,235 myocardial infarction death from Qingdao, China also demonstrated that short-term exposure PM_1 had higher impact on myocardial infarction mortality than $PM_{2.5}$ (Ma et al., 2023). Our findings, combined with existing evidence, consistently reinforce the long-standing hypothesis that exposure to PM with smaller size poses a greater health hazard than exposure to PM with larger size (Polichetti et al., 2009). Previous toxicological studies indicated that PM exposure may contribute to the development of cardiovascular diseases via multiple pathways, including oxidative stress, inflammation, coagulation, and vasoconstriction (Al-Kindi et al., 2020; Chen et al., 2015; Delfino et al., 2011; Hassanvand et al., 2017; Li et al., 2016). A few studies explored the impact of PM size on the circulating biomarkers of oxidative stress or inflammation, and indicated that smaller particles exhibit greater toxicity compared to larger particles (Chen et al., 2015; Hassanvand et al., 2017). However, the potential biological mechanism for the association we observed among patients hospitalised with AMI remains unclear and requires further investigation.

In counterfactual analyses, long-term PM_{10} exposure has the largest PAFs, followed by $PM_{2.5}$ and PM_1, in contrast to the patterns of associations observed in primary analyses. Furthermore, the pattern of PAFs for short-term PM exposure was contrary to that observed for long-term PM exposure. These seemingly contradictory results could be explained by the differences in estimation methods and statistical distribution of

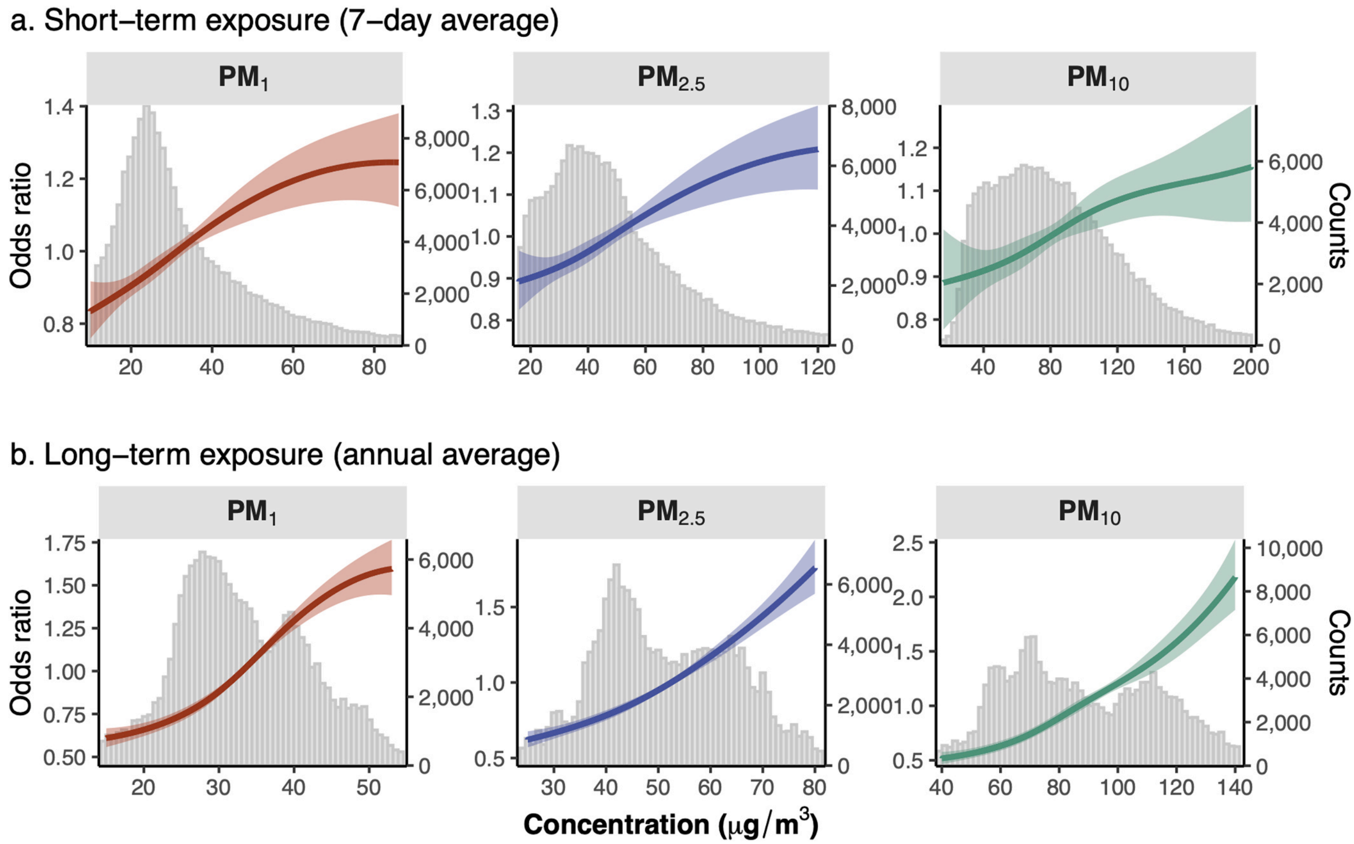

Fig. 1. Exposure–response relationships between ambient exposure to PM_1, $PM_{2.5}$, and PM_{10} and in-hospital AMI case fatality. Exposure-response relationships of (a) short-term and (b) long-term exposure to particulate matter (including PM_1, $PM_{2.5}$, and PM_{10}) with in-hospital AMI case fatality for were assessed separately. The solid lines with shaded regions indicate the changes in odds of in-hospital AMI case fatality and their corresponding 95% confidence intervals, respectively. The gray bars show the statistical distribution of particulate matter in the study sample. AMI, acute myocardial infarction; PM_1, ambient particulate matter with diameter ≤ 1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤ 2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤ 10 μm in aerodynamic diameter.

PM. Our primary analyses estimated the impact of exposure to PM of different sizes on in-hospital case fatality using a predefined increment of 10 μg/m^3, while the counterfactual analyses estimated the PAFs using the fifth percentile of PM exposure levels which depends on the statistical distributions of PM. The statistical distribution of PM_{10} was more dispersed than that of $PM_{2.5}$ and PM_1 (Fig. 2.), indicating a higher potential for reducing PM_{10} levels in the hypothetical scenario at the fifth percentile. Moreover, short-term PM exposure had a right-skewed unimodal distribution, while long-term exposure had a bimodal distribution, suggesting greater potential for reduction in long-term PM exposure. The target levels we selected in counterfactual analyses for $PM_{2.5}$ (29.8 μg/m^3) and PM_{10} (49.7 μg/m^3) were much higher than the air quality guideline (AQG) levels (5 μg/m^3 for $PM_{2.5}$ and 15 μg/m^3 for PM_{10}) set by the World Health Organization (WHO), which means achieving WHO AQG levels in China's air quality holds the potential for substantial public health benefits in terms of reducing in-hospital AMI case fatality.

In stratified analyses, we observed a stronger association of PM exposure with in-hospital fatality in patients aged 65 years and older. On one hand, elderly patients are more susceptible to accumulating adverse cardiovascular effects caused by PM exposure due to their relatively longer exposure periods (Yang et al., 2018). On the other hand, respiratory or cardiovascular conditions tend to be more common among the elderly population, which may serve to exacerbate the adverse consequences of PM exposure (Kan et al., 2008). Additionally, a more pronounced impact of long-term PM exposure on in-hospital case fatality was observed among females when compared to males. One possible explanation is that females generally possess a lower count of red blood cells in comparison to males, which might render them more susceptible to air pollution (Sørensen et al., 2003). Another likely explanation is that females typically engaged in more frequent cooking activities than males (Wolfson et al., 2021), which may increase their exposure to PM due to the use of solid fuels (Chen and Kan, 2020).

Our findings hold significant implications for environmental regulation in China and other rapidly developing countries grappling with similar air pollution challenges, such as India. First, reducing ambient PM concentration could yield substantial public health benefits, even when only the potential benefit of lowing AMI in-hospital case fatality is considered. Continuous investment and extensive efforts on reducing ambient PM concentration are warranted. Given the pronounced health benefits of reducing long-term PM_{10} exposure, mitigating ambient PM_{10} air pollution should receive higher priority than other PM pollution within the context of Chinese policymaking. Meanwhile, as the PM pollution characteristics and source compositions exhibit regional and seasonal variations (Zhang et al., 2023, 2018), the formulation and implementation of environmental policies must be carefully attuned to localized conditions (e.g., sources of PM pollution, energy and industry structure, government management level). Second, our results suggest that the adverse health effects of ambient PM exposure appear to be more pronounced among vulnerable populations, particularly among older individuals and female patients. For policymakers in other parts of the world, this study necessitates an augmented focus on environmental health disparity stemming from air pollution, especially gender- and age-related dimensions of environmental health equity. Recognizing these dimensions as the determinants of vulnerability to air pollution-induced health risks highlights the need for targeted

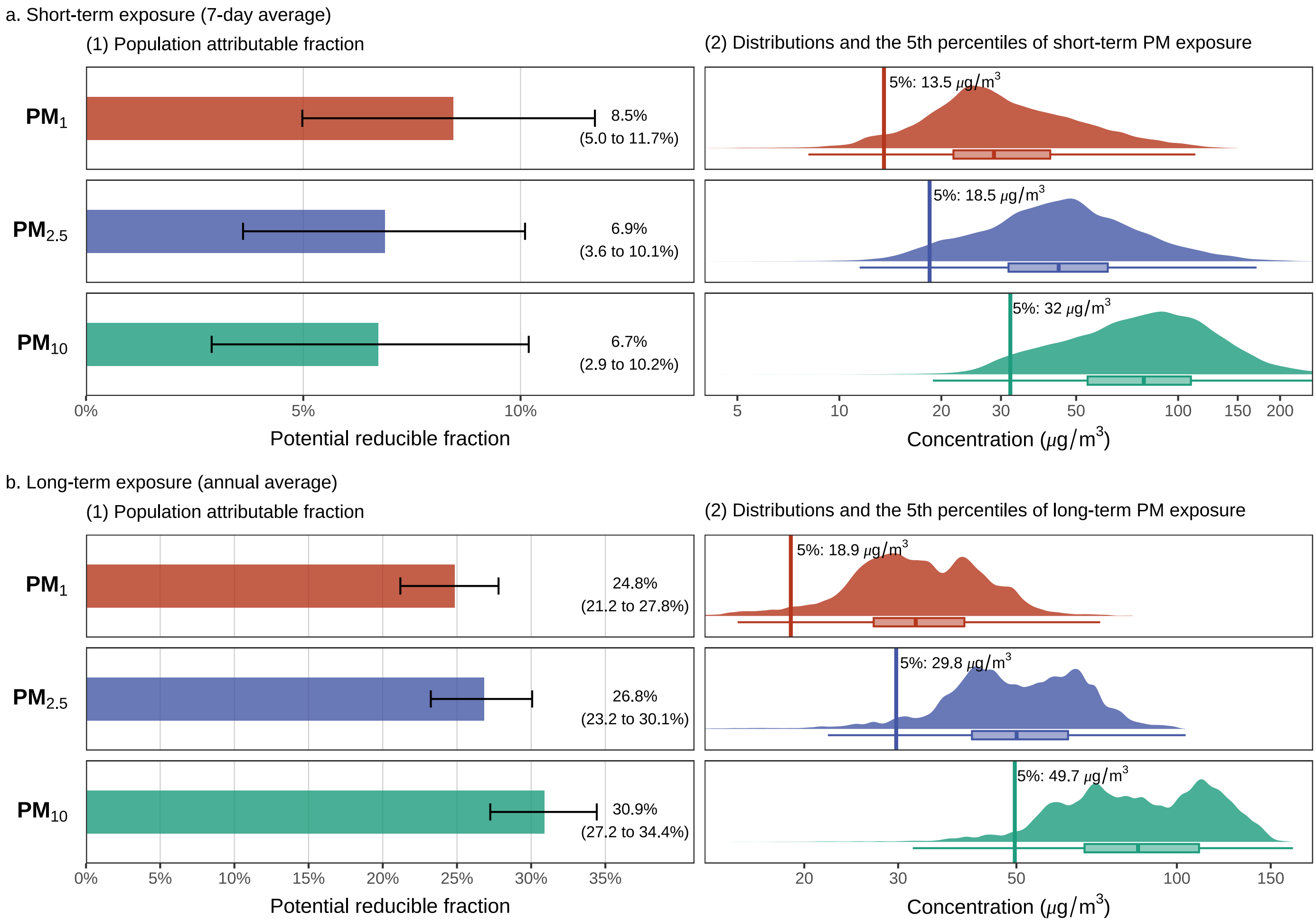

Fig. 2. Potential reducible fraction of in-hospital AMI case fatality based on a counterfactual scenario and statistical distribution of ambient PM exposure. The population attributable fractions of in-hospital AMI case fatality attributable to (a) short-term and (b) long-term exposure to ambient PM_1, $PM_{2.5}$, and PM_{10} were calculated based on a counterfactual scenario of the 5th percentiles of air pollutant distributions. The error bars in Fig. a1. and Fig. b1. are the 95% confidence intervals calculated based on 1000 bootstrap samples. The vertical lines in Fig. a2. and Fig. b2. are the 5th percentiles of the distributions of ambient PM_1, $PM_{2.5}$, and PM_{10}. AMI, acute myocardial infarction; PM_1, ambient particulate matter with diameter ≤ 1 μm in aerodynamic diameter; $PM_{2.5}$, ambient particulate matter with diameter ≤ 2.5 μm in aerodynamic diameter; PM_{10}, ambient particulate matter with diameter ≤ 10 μm in aerodynamic diameter.

interventions and inclusive policy frameworks on a global scale (Al-Aly, 2022; Cai et al., 2023a).

Our study has several strengths. We utilized the full-coverage and high-quality CHAP dataset and patients' residential addresses recorded in the inpatient discharge dataset to assess the individual-level PM exposure. Furthermore, China experienced a significant burden of heavy air pollution during our study period, allowing us to investigate the PM exposure–fatality association across a wide spectrum of air pollutant concentrations. Additionally, we analysed a considerable large sample size (n = 177,749), enabling us to reach more nuanced understandings of the PM exposure–fatality association.

Nevertheless, our study has the following limitations. First, we acknowledge that we cannot measure and adjust for all potential confounders associated with in-hospital AMI case fatality (e.g., body mass index, smoking status, and traffic noise). However, the large size of the E-values obtained in our main analyses suggest that the observed association is less likely to be neutralized by the unmeasured confounders. Second, our study samples were gathered from four specific provinces in China based on data availability, potentially constraining the applicability of our findings to a broader geographic scope. Future studies involving larger sample sizes or encompassing more regions would be necessary to verify our findings. Additionally, it is worth noting that the utilization rate of PCI in China remains relatively lower than that in developed countries such as the United States and Japan (Inohara et al., 2020). Thus, our findings may have limited generalizability to other countries or regions with high PCI use rates. Third, the CHAP dataset exclusively offers outdoor air pollution exposure data, making it unfeasible for us to estimate the association of indoor air pollution with in-hospital AMI case fatality. The outcomes after patient discharge were not recorded by the inpatient discharge database, and thus we were unable to further estimate the impact of PM exposure on other AMI-related outcomes such as 30-day case fatality.

5. Conclusions

By leveraging a large sample of AMI hospitalisations across four Chinese provinces, our study revealed that a higher level of ambient PM exposure was associated with an elevated risk of in-hospital AMI case fatality, with PM_1 exhibiting the largest effects, followed by $PM_{2.5}$ and PM_{10}. Our results highlighted the potential health benefits for AMI patients by mitigating ambient PM exposure, especially in the case of long-term PM_{10} exposure, which presents a significant opportunity for reduction.

CRediT authorship contribution statement

Tan Kun: Data curation, Investigation, Resources. **Cai Miao:** Conceptualization, Data curation, Methodology, Software, Visualization, Writing – original draft. **Lin Xiaojun:** Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing – original draft. **Pan Jay:** Conceptualization, Resources, Supervision, Writing – review & editing. **Lin Hualiang:** Conceptualization, Resources, Supervision, Writing – review & editing. **Wang Xiuli:** Writing – review & editing. **Liu Echu:** Methodology, Writing – review & editing. **Wei Jing:** Data curation, Resources, Writing – review & editing. **Song Chao:** Writing – review & editing.

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

The authors do not have permission to share data.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2023.115731.

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