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Short-term exposure to ambient particulate matter and mortality among HIV/AIDS patients: Case-crossover evidence from all counties of Hubei province, China

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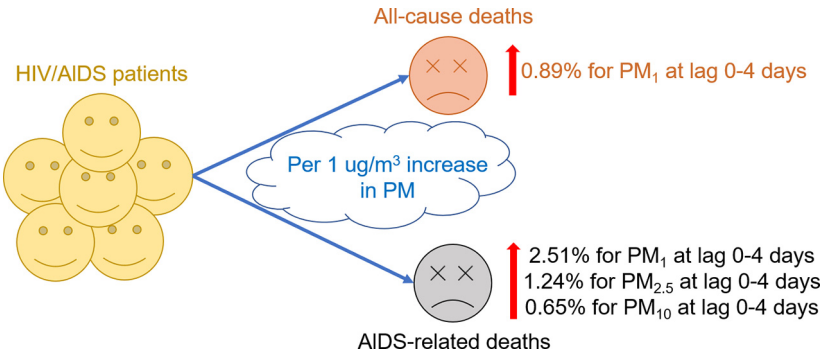
HIGHLIGHTS

- Short-term exposure to ambient particulate matter was associated with the risk of mortality among HIV/AIDS patients.
- The adverse impacts of PM_1 were stronger than $PM_{2.5}$ and PM_{10}.
- The effects of PM_1 and PM_{10} on AIDS-related deaths were significantly stronger in males than females

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) has been a worrisome public health problem in the world. However, evidence for associations between short-term exposure to particulate matter (PM) and mortality among HIV/AIDS patients is scarce.
Methods: We collected daily death records in people with HIV/AIDS from all counties (N = 103) of Hubei province, China from 2018 to 2019. The county-level daily concentrations of PM_1, $PM_{2.5}$ and PM_{10} in the same period were extracted from ChinaHighAirPollutants dataset. A time-stratified case-crossover design with conditional logistic regression analysis was performed to assess the associations between PM and mortality.
Results: Each 1 μg/m^3 increased in PM_1 corresponded with 0.89 % elevated in all-cause deaths (ACD) at lag 0–4 days. The largest effects of PM_1, $PM_{2.5}$ and PM_{10} on AIDS-related deaths (ARD) were detected at lag 0–4 days, and PM_1 [percent changes in odds ratio: 2.51 % (95 % CIs: 0.82, 4.22)] appeared greater health hazards than $PM_{2.5}$ [1.24 % (95 % CIs: 0.33, 2.15)] as well as PM_{10} [0.65 % (95 % CIs: 0.01, 1.30)]. In subgroup analyses, the significant associations of PM_1/$PM_{2.5}$ and ACD were only found in male and the cold season. We also observed the effects of PM_1 and PM_{10} on ARD were significantly stronger (*P* for interaction <0.05) in males than females. In addition, we caught sight of HIV/AIDS patients aged over 60 years old were more susceptible to ARD caused by PM than younger population.

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Conclusions: Our study suggested PM_1 was positively linked with the risk of ACD and ARD. Male patients with HIV/AIDS were more significantly susceptible to PM_1, $PM_{2.5}$ and PM_{10}. $PM_1/PM_{2.5}$ appeared stronger associations with ARD in HIV/AIDS patients aged over 60 years old and in the cold season.

1. Introduction

Acquired immunodeficiency syndrome (AIDS) is an infectious disease caused by the human immunodeficiency virus (HIV) (Sharp and Hahn, 2011). Experts estimated that there were 36.8 [95 % uncertainty interval (UI): 34.8–39.2] million people living with HIV, 1.94 (95 % UI: 1.63–2.29) million new cases of HIV and 0.95 (95 % UI: 0.91–1.01) million AIDS-related deaths worldwide in 2017 (Collaborators, 2019). HIV/AIDS has changed from the 33rd leading cause for global disability-adjusted life years (DALYs) in 1990 to the 11th in 2019, with an increase of 58.5 % (95 % UI: 37.1–89.2) in age-standardized DALY rates (GDaI Collaborators 2020). The prevalence of HIV/AIDS continually increases yearly in China, which has become a worrisome public health problem (Qiao et al., 2019). Therefore, there is an urgent need to identify new risk factors and take comprehensive measures to prevent deaths among HIV/AIDS people.

Ambient particulate matter (PM) is the fourth leading risk factor for global mortality and contributes a lot to deaths and DALYs, especially in developing countries with severe air pollution, such as China (Bu et al., 2021; GBDRF Collaborators 2020). Previous epidemiological studies found that long- or short-term exposure to PM was associated with the increment of all-cause and disease-specific (e.g. respiratory diseases, cardiovascular diseases, type-2 diabetes and cancers) deaths (Di et al., 2017; Liu et al., 2021; Wu et al., 2021; Yu et al., 2021; Zhang, 2021; Zhou et al., 2022). However, most of them focused mainly on the effects of $PM_{2.5}$ (PM with an aerodynamic diameter ≤ 2.5 μm) and PM_{10} (PM with an aerodynamic diameter ≤ 10 μm). In recent years, the harm of PM_1 (PM with an aerodynamic diameter ≤ 1 μm) to human health has gradually attracted research attention due to the smaller particle size (Cigankova et al., 2021; Li et al., 2021; Yang et al., 2019). Nevertheless, because PM_1 is not a routinely monitored pollutant in most parts of the world, a relatively small number of epidemiological studies investigated the associations between PM_1 and health (Song et al., 2022; Xiong et al., 2022). Even more scarce literature has provided evidence linking PM_1 and mortality among HIV/AIDS people. A previous animal experiment found that side-stream cigarette smoke led to further immunosuppress on the basis of the immune function decline caused by AIDS, which could make AIDS mice more susceptible to opportunistic infections and accelerate the progression of murine AIDS (Zhang et al., 2002). In addition, a study conducted in the USA pointed out that exposure to PM_{10} increased HIV host susceptibility to pulmonary infection by suppressing IgM response (Blount et al., 2013). The impact of air pollution on mortality might be mediated by changes in immunocompetence (Hertz-Picciotto et al., 2005). Therefore, in consideration of people with HIV/AIDS have some defects in their immune function (Salzer et al., 2018), we hypothesize that they are more vulnerable to ambient PM.

In this study, we aim to explore the associations between short-term exposure to PM (PM_1, $PM_{2.5}$, and PM_{10}) and mortality among HIV/AIDS patients in all counties of Hubei province (China) by conducting a time-stratified case-crossover design. We also performed subgroup analyses stratified by gender, age and season to identify potential vulnerable populations and periods. This study may add to the total body of knowledge on the relationship between PM and mortality among HIV/AIDS people and provide a valuable epidemiological reference for local government policy-making.

2. Methods

2.1. Study area

Hubei, the thoroughfare of nine provinces, is located in central China and governs 103 counties, with a total area of 185,900 km^2 and 58.3 million inhabitants. The terrain of Hubei Province is generally surrounded by mountains in the East, West and North, with a low and flat middle, which is an incomplete basin slightly open to the south. In the total area of the whole province, mountains account for 56 %, hills 24 % and plain lakes 20 %, belonging to the Yangtze River system. Most areas in Hubei province have a subtropical monsoon humid climate.

2.2. Data collection

The death data of AIDS patients during our study period were obtained from the HIV/AIDS Comprehensive Response Information Management System of Hubei Provincial Center for Disease Control and Prevention, including the main cause of death [AIDS-unrelated deaths and AIDS-related deaths (ARD)], gender, age, race, residential address (county-level), marriage status, educational level, occupation, route of infection, date of diagnosis and date of death, etc. The spatial distribution of the cases was shown in Fig. 1. During the same period, we collected daily data set of surface climate data in China (V3.0) from the National Meteorological Science Data Center (http://data.cma.cn/). There are a total of 27 weather stations that can generally cover the whole Hubei Province (Fig. S1). We linked the daily mean county-level temperature and relative humidity to the nearest weather station.

Daily mean concentrations of PM_1, $PM_{2.5}$ and PM_{10} were derived from ChinaHighAirPollutants (CHAP, available at https://weijing-rs.github.io/product.html), which is a series of long-term, full-coverage, high-resolution (1 km × 1 km), and high-quality datasets of ground-level air pollutants for China (Wei et al., 2019, 2020, 2021a, 2021b). Briefly, CHAP was generated from the big data (e.g., ground-based measurements, satellite remote sensing products, atmospheric reanalysis, and model simulations) using artificial intelligence by considering the spatiotemporal heterogeneity of air pollution. The cross-validation coefficient of determination (CV-R^2) and root-mean-square error (RMSE) of PM_1, $PM_{2.5}$ and PM_{10} were 0.77, 14.6 μg/m^3, 0.92, 10.76 μg/m^3, and 0.90, 21.12 μg/m^3 on a daily basis, respectively. Similar to the above methods, we extract daily county-level air pollution by overlapping the grid data of CHAP with the shapefile of the study areas.

2.3. Statistical analysis

To explore the associations between short-term exposure to PM and daily mortality, we performed a time-stratified case-crossover study design, which was widely used in environmental epidemiological studies (Chen et al., 2019; Gasparrini, 2021; Liu et al., 2021). The same calendar day of the week in the calendar year and month of deaths were used as fixed time strata. For instance, if a death occurred on the 9th of June 2019 (Sunday), the 9th of June 2019 was defined as the case day while all other Sundays in the same calendar year and month (2nd, 16th, 23rd, and 30th of June 2019) were regarded as the control days. Profiting by this study design, every person acted as self-control, and individual-level time-independent confounders (such as age, gender, education level, physical condition, treatment) can be controlled spontaneously (Khan et al., 2019). Moreover, the effect of week, seasonality and long-term trends could also be well automatically controlled (Levy et al., 2001).

Pearson correlation analysis was used to describe the relationships between environmental factors. After adjusting for temperature and relative humidity using a natural spline function with 6 degrees of freedom (df) and 3 df (Xu et al., 2022), respectively, conditional logistic regression models were applied to investigate the short-term health effects of PM on all-cause deaths (ACD) and ARD. To assess the lagged effects of PM, we also estimated PM-mortality relationships in single-day (lag 0 to lag 7 day) and cumulative lag days (lag 0–1 to lag 0–7 days). Subgroup analyses

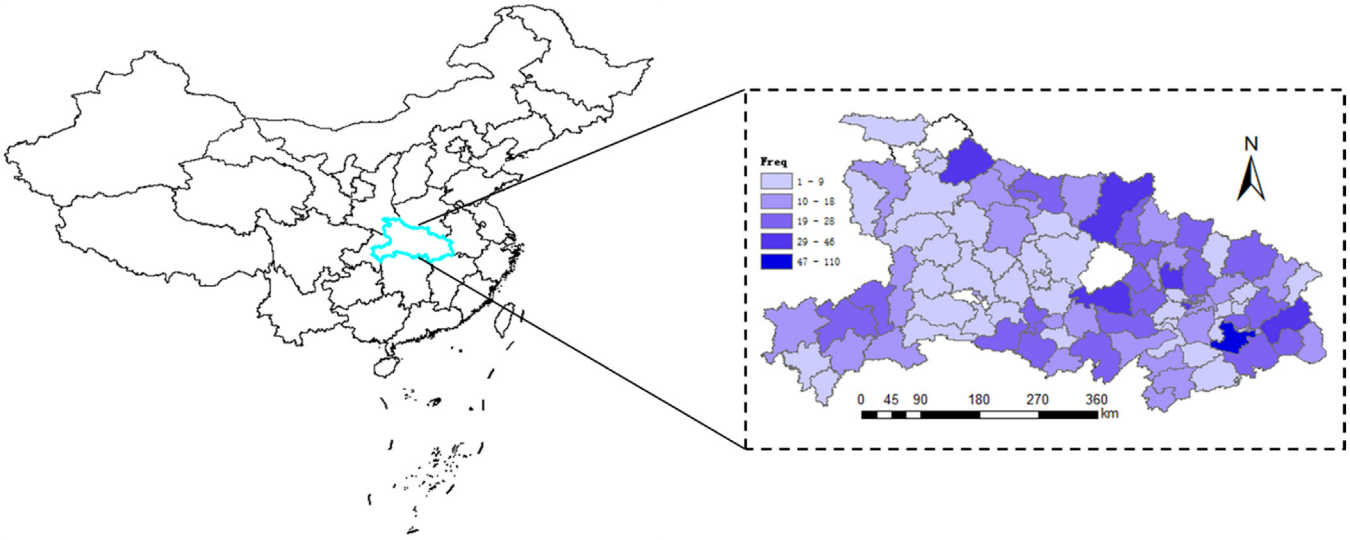

Fig. 1. The location of study area (Hubei province, China) and spatial distribution of the deaths.

were performed stratified by gender (male, female), age (0–59, 60+ years old) and season (warm: April to September, cold: October to March of the next year), and we identified potential interaction between subgroups by 2-sample z-test (Altman and Bland, 2003). After investigating the associations of PM-mortality in the initial model, two sensitivity analyses were conducted to check the robustness of the effects of PM on ACD and ARD: (1) establishing two-pollutant models; (2) changing the degrees of freedom of temperature and relative humidity from 6 to 5 or 7 and 3 to 2 or 4, respectively.

Consistent with prior studies, results in this study were reported as percent change in odds ratio [(OR − 1) × 100 %] and 95 % confidence intervals (CIs) corresponded to per 1 μg/m^3 increase in the daily concentrations of PM. All statistical analyzes were conducted in R software (version 4.1.1), and the "survival" and "splines" packages were utilized to fit the model. Results with a 2-sided and *P*-value < 0.05 were considered statistically significant.

3. Results

Table 1 summarizes the characteristics of the study population in Hubei province from 2018 to 2019. There were a total of 1505 ACD in HIV/AIDS patients, 389 (25.85 %) of them succumbed to opportunistic infections caused by AIDS. Males occupied about 80 % overall, and more than half of the whole deaths were aged <60 years old. Heterosexual transmission and Homosexual transmission involved 1122 and 297 individuals, accounting for 74.55 % and 19.73 % of the total, respectively. Table 2 shows the distribution of ambient particulate matter and meteorological conditions on case days and control days during the study period. Daily mean concentrations of PM_1 and $PM_{2.5}$ were 23.40 μg/m^3 and 41.99 μg/m^3 on case days, which were slightly higher than on control days. Fig. 2 illustrates the pairwise coefficients of Pearson correlation between daily average concentrations of environmental factors. We found higher positive correlations between PM, while slight or negative correlations between PM and meteorological factors.

Table 3 exhibits the percent changes in odds ratio (%) and 95 % confidence intervals (CIs) for ACD and ARD with per 1 μg/m^3 increase in particulate matter in single-pollutant models. For ACD, significant associations were only found in PM_1. Per 1 μg/m^3 increase in PM_1 corresponded with 0.89 % elevated in ACD at lag 0–4 days. For ARD, the largest effects of PM_1, $PM_{2.5}$ and PM_{10} on ARD were both detected at lag 0–4 days, and PM_1 [2.45 % (95 % CIs: 0.72, 4.21)] appeared greater health hazards than $PM_{2.5}$ [1.25 % (95 % CIs: 0.31, 2.20)] and PM_{10} [0.65 % (95 % CIs: 0.01, 1.30)]. Fig. S1 shows the exposure-response curves of ambient particulate matter and ACD as well as ARD. By and large, the odds ratio (OR) of ACD showed a very trifling upward trend as PM_1 concentration increased, while ARD was rapidly rising with the increasing concentration of PM_1, $PM_{2.5}$ and PM_{10}.

Fig. 3 displays the subgroup-specific percent changes in odds ratio (%) with 95 % CIs associated with per 1 μg/m^3 increase in particulate matter at lag 0–4 days. The significant effects of PM_1 and $PM_{2.5}$ on ACD were only found in males and the cold season. We also observed the effects of PM_1 and PM_{10} on ARD were significantly stronger (*P* for interaction <0.05) in male than in female, with corresponding percent changes in odds ratio of 3.13 % (1.33, 4.96) versus −3.51 % (−8.95, 2.26) for PM_1 and 0.95 % (0.27, 1.63) versus −2.07 % (−4.26, 0.17) for $PM_{2.5}$. In

Table 1
The characteristics of the study population in Hubei province, 2018 to 2019.

Characteristic	Count
Days	
Case days	1505
Control days	5098
Deaths (n, %)	
All-cause deaths	1505 (100.00)
AIDS-related deaths	389 (25.85)
Gender (n, %)	
Male	1227 (81.53)
Female	278 (18.47)
Age at death (n, %)	
<60 years	875 (58.14)
60+ years	630 (41.86)
Race (n, %)	
Han	1449 (96.28)
Minority	56 (3.72)
Marriage status (n, %)	
Married	615 (40.86)
Unmarried/divorced/widowed	880 (58.47)
Educational level (n, %)	
Primary school and blow	664 (44.12)
Junior high school	536 (35.61)
High school and above	302 (20.07)
Route of infection (n, %)	
Injecting drugs	30 (1.99)
Heterosexual transmission	1122 (74.55)
Homosexual transmission	297 (19.73)
Blood transmission	45 (2.99)
Other and unknown	11 (0.73)
Season at death (n, %)	
Warm	740 (49.17)
Cold	765 (50.83)

Table 2
The distribution of ambient particulate matter and meteorological conditions on case days and control days.

Variables	Min	P_{25}	P_{50}	P_{75}	Max	Mean	SD
On case days (n = 1505)							
Air pollutant							
PM_1 (μg/m^3)	5.41	13.58	19.27	28.12	100.73	23.40	14.43
$PM_{2.5}$ (μg/m^3)	8.06	25.11	34.93	49.65	167.62	41.99	24.48
PM_{10} (μg/m^3)	11.59	44.76	60.72	84.19	344.58	69.16	34.55
Meteorological factor							
Temperature (°C)	−4.40	9.15	17.70	25.40	33.60	17.21	9.19
Relative humidity (%)	32.00	67.00	75.00	84.00	99.00	74.72	13.15
On control days (n = 5098)							
Air pollutant							
PM_1 (μg/m^3)	5.02	13.50	19.23	27.77	143.23	23.21	14.55
$PM_{2.5}$ (μg/m^3)	7.17	25.17	34.52	49.54	299.89	41.67	24.78
PM_{10} (μg/m^3)	10.50	44.55	60.33	83.51	341.48	69.17	34.86
Meteorological factor							
Temperature (°C)	−5.50	9.10	18.30	25.40	33.80	17.37	9.31
Relative humidity (%)	28.00	66.00	75.00	84.00	100.00	74.40	12.90

Note: Min: minimum; Max: maximum; P: Percentile; SD: Standard deviation.

addition, although the difference between subgroups were not statistically significant, we caught sight of HIV/AIDS patients aged over 60 years old were more susceptible to PM_1, $PM_{2.5}$ and PM_{10} and lead to ARD than younger population, with the percent changes in odds ratio were 4.08 % (1.27, 6.96) versus 1.42 % (−0.78, 3.67) for PM_1, 2.06 % (0.59, 3.55) versus 0.63 % (−0.56, 1.85) for $PM_{2.5}$ and 1.21 % (0.11, 2.32) versus 0.33 % (−0.47, 1.14).

Table S1 exhibits the percent changes in odds ratio (95 % CIs) for ACD and ARD corresponded with each 1 μg/m^3 increase in ambient PM along 0–4 days in the sensitivity analyses. In the two-pollutant models, PM_1-ACD, PM_1-ARD and $PM_{2.5}$-ARD associations remain statistically significant after adjusting for PM_{10}. We also found the previously significant relationships of particulate matter and ACD as well as ARD still kept significant after changing the degrees of freedom of temperature and relative humidity from 6 to 5 or 7 and 3 to 2 or 4, respectively. The above results suggested that our main findings were robust.

4. Discussion

To the best of our knowledge, this is the first paper to comprehensively assess the acute effect of PM on mortality among HIV/AIDS patients in China. In this study, we applied a time-stratified case-crossover design to estimate the associations between short-term exposure to PM and ACD as well as ARD in all counties (N = 103) of Hubei province, China. Our results found that positive and significant links existed between PM_1 and ACD. Short-term exposure to PM_1, $PM_{2.5}$ and PM_{10} was associated with an increased risk of ARD, and PM_1 displayed a stronger effect value than $PM_{2.5}$ and PM_{10}. In addition, the approximately linear exposure-response curves of PM and ARD suggest that lower concentrations of PM would have the capacity to aggravate ARD. Information obtained from subgroup analyses for ARD also showed that males appeared to be more significantly vulnerable to PM_1 and PM_{10}. Furthermore, PM_1 and $PM_{2.5}$ were the risk factors for ARD in HIV/AIDS patients aged over 60 years old and in the cold season that deserved attention. All in all, our findings might help deepen the understanding of the relationships between short-term exposure

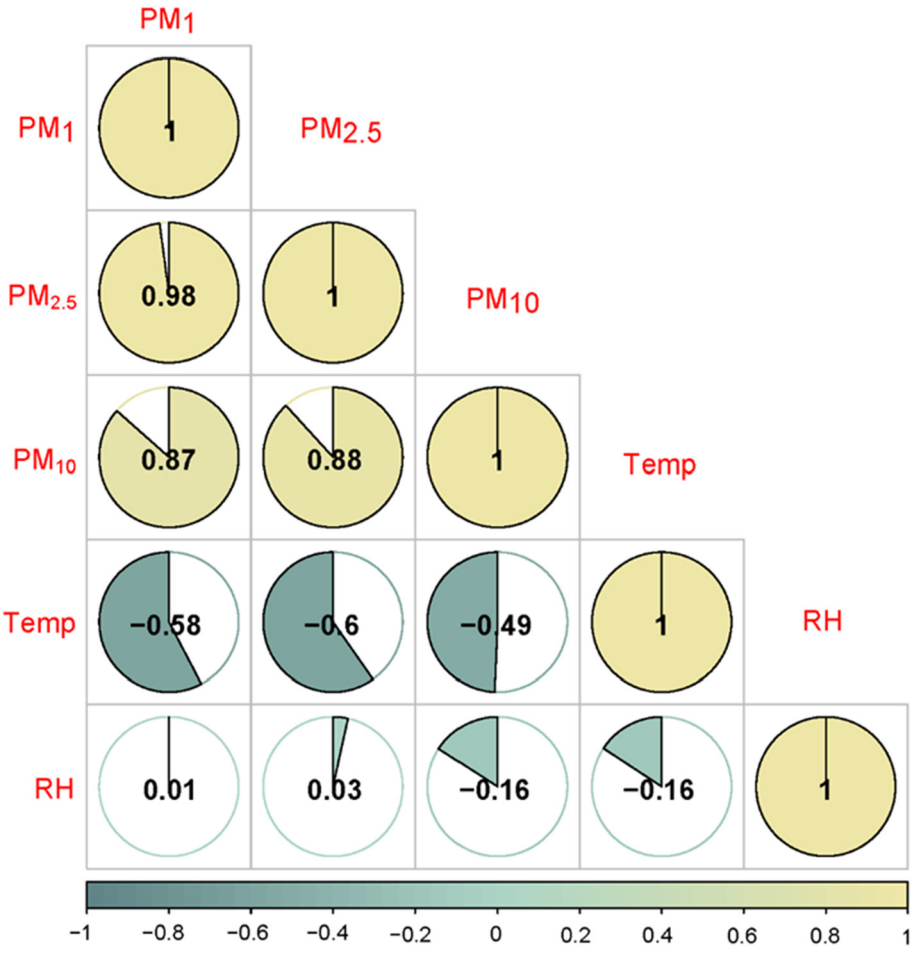

Fig. 2. The Pearson correlation coefficient between environmental factors.
Note: Temp: temperature; RH: relative humidity.

Table 3
The percent change in odds ratio (%) and 95 % CIs for ACD and ARD with per 1 μg/m^3 increase in ambient particulate matter in single-pollutant models.

Lag days (days)	All-cause deaths			AIDS-related deaths		
	PM_1	$PM_{2.5}$	PM_{10}	PM_1	$PM_{2.5}$	PM_{10}
Single-lag						
Lag 0	0.23 (−0.43, 0.90)	0.11 (−0.27, 0.50)	−0.01 (−0.27, 0.24)	1.14 (−0.09, 2.39)	0.69 (−0.04, 1.42)	0.34 (−0.13, 0.81)
Lag 1	0.56 (−0.11, 1.23)	0.26 (−0.12, 0.65)	0.19 (−0.05, 0.43)	**1.82 (0.55, 3.11)**	**0.98 (0.23, 1.73)**	**0.48 (0.03, 0.95)**
Lag 2	0.30 (−0.34, 0.95)	0.11 (−0.26, 0.48)	−0.01 (−0.24, 0.22)	**1.56 (0.34, 2.79)**	**0.75 (0.04, 1.45)**	0.38 (−0.08, 0.84)
Lag 3	0.57 (−0.05, 1.20)	0.33 (−0.03, 0.68)	0.00 (−0.24, 0.23)	1.00 (−0.18, 2.19)	0.58 (−0.11, 1.27)	0.17 (−0.28, 0.63)
Lag 4	**0.62 (0.01, 1.23)**	0.31 (−0.05, 0.66)	0.08 (−0.15, 0.31)	**1.14 (−0.03, 2.33)**	**0.71 (0.03, 1.40)**	0.31 (−0.14, 0.76)
Lag 5	0.23 (−0.36, 0.83)	0.08 (−0.27, 0.43)	0.02 (−0.21, 0.25)	0.20 (−0.94, 1.35)	0.03 (−0.64, 0.71)	0.01 (−0.43, 0.45)
Lag 6	−0.04 (−0.63, 0.55)	0.00 (−0.34, 0.34)	−0.05 (−0.28, 0.18)	−0.14 (−1.30, 1.02)	−0.09 (−0.75, 0.59)	−0.11 (−0.55, 0.34)
Lag 7	−0.20 (−0.80, 0.40)	−0.14 (−0.50, 0.22)	−0.13 (−0.37, 0.10)	−0.50 (−1.60, 0.61)	−0.32 (−0.98, 0.34)	−0.23 (−0.67, 0.22)
Cumulative lag						
Lag 0–1	0.48 (−0.25, 1.23)	0.23 (−0.19, 0.66)	0.12 (−0.15, 0.39)	**1.79 (0.41, 3.19)**	**1.03 (0.20, 1.85)**	0.50 (−0.01, 1.01)
Lag 0–2	0.53 (−0.27, 1.33)	0.24 (−0.22, 0.70)	0.08 (−0.20, 0.37)	**2.23 (0.71, 3.76)**	**1.21 (0.32, 2.12)**	**0.60 (0.03, 1.16)**
Lag 0–3	0.71 (−0.13, 1.56)	0.34 (−0.10, 0.79)	0.07 (−0.24, 0.38)	**2.33 (0.73, 3.97)**	**1.12 (0.26, 1.99)**	0.60 (−0.01, 1.21)
Lag 0–4	**0.89 (0.00, 1.78)**	0.42 (−0.05, 0.89)	0.10 (−0.23, 0.42)	**2.51 (0.82, 4.22)**	**1.24 (0.33, 2.15)**	**0.65 (0.01, 1.30)**
Lag 0–5	0.90 (−0.03, 1.84)	0.41 (−0.09, 0.90)	0.10 (−0.25, 0.44)	**2.38 (0.62, 4.18)**	**1.12 (0.16, 2.08)**	0.59 (−0.07, 1.26)
Lag 0–6	0.84 (−0.14, 1.83)	0.42 (−0.15, 0.98)	0.07 (−0.29, 0.44)	**2.20 (0.35, 4.09)**	**1.22 (0.13, 2.32)**	0.51 (−0.18, 1.21)
Lag 0–7	0.75 (−0.29, 1.80)	0.36 (−0.24, 0.97)	0.03 (−0.36, 0.42)	**1.96 (0.00, 3.94)**	1.08 (−0.08, 2.25)	0.42 (−0.31, 1.16)

Note: Bold results are statistically significant (*P*-value < 0.05).

to PM and mortality among HIV/AIDS patients and provide valuable evidence for the government to formulate strategies for ambient particulate matter control more reasonably, especially for PM_1.

Prior studies pointed out that air pollution played a role in the development of AIDS-unrelated and AIDS-related diseases among HIV/AIDS patients (Alvaro-Meca et al., 2015; Elf et al., 2017; North et al., 2015; Toe et al., 2022), which were similar with our results. A study conducted in Spain found that a higher concentration of PM_{10} was associated with pneumocystis pneumonia (PCP) admission and PCP-related deaths in HIV-positive patients from 1997 to 2011 (Alvaro-Meca et al., 2015). Toe and her colleagues reported that exposure to $PM_{2.5}$ might amplify carotid intima-media thickness (IMT) among adolescents with perinatally acquired HIV (PHIV) while not in HIV-uninfected teenagers (Toe et al., 2022). The underlying biological mechanism of elevated mortality caused by PM in HIV/AIDS patients was not completely clarified yet. The previous experimental, panel and large-scale epidemiological studies provided plenty of evidence to confirm that exposure to PM triggered oxidative stress and systemic inflammation which were linked with risks of mortality from respiratory and cardiovascular diseases (Andersson et al., 2009; Deng et al., 2013; Lin et al., 2017; Yang et al., 2020). In addition, exposure to PM could change the number of immunoglobulins and over-activate the Notch signaling pathway resulting in immunity disorder (Gu et al., 2017;

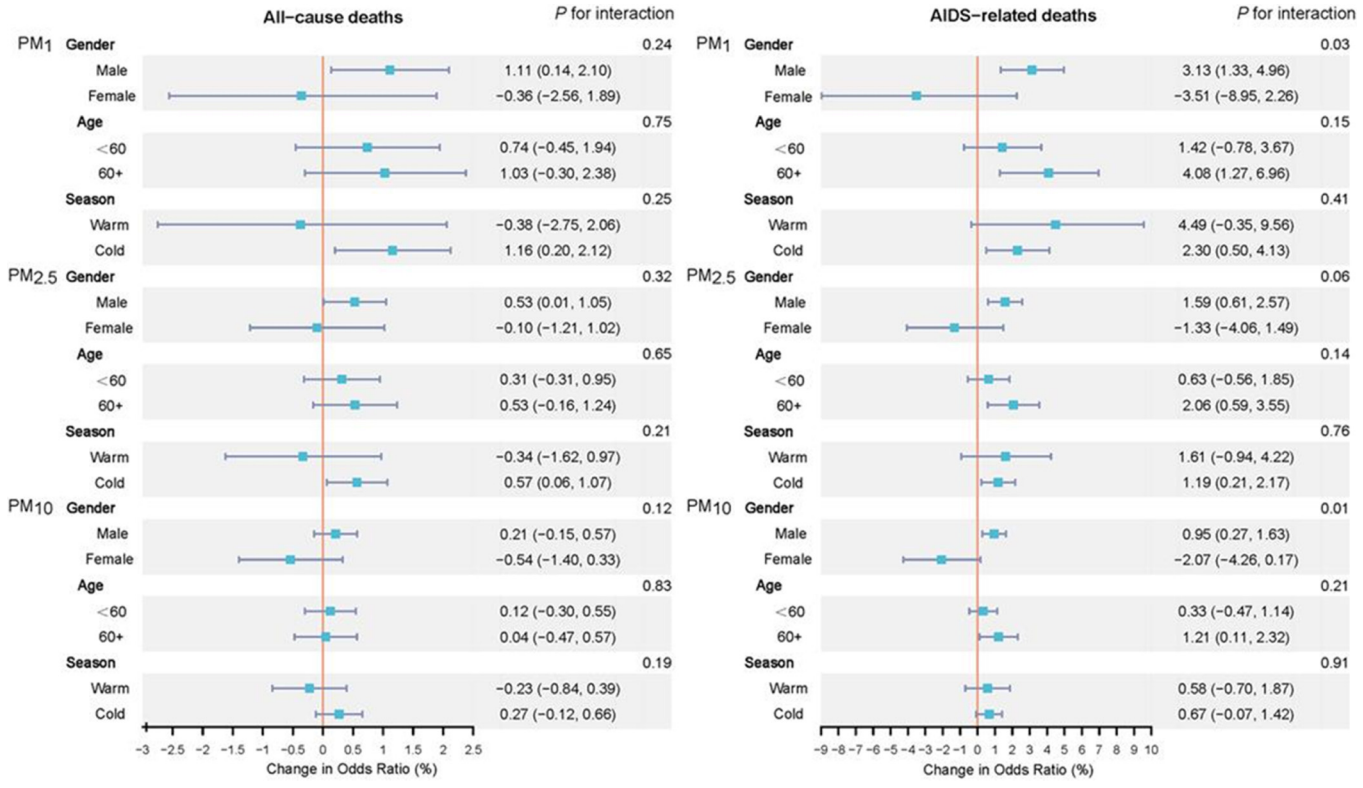

Fig. 3. The subgroup-specific percent changes in odds ratio (%) with 95 % CIs associated with per 1 μg/m^3 increased in ambient particulate matter at lag 0–4 days.

Zhao et al., 2013). Therefore, these clues suggested a reasonable hypothesis that the status of oxidative stress and systemic inflammation induced by exposure to PM reduced the ability of the body's immunity and increased the likelihood and harm of opportunistic infection among HIV/AIDS patients.

In the current study, we found larger effects of PM_1 on ACD and ARD than $PM_{2.5}$ and PM_{10} at the same lag days. For instance, the percent change (%, 95 % CIs) in odds ratio of per 1 μg/m^3 increased in PM_1, $PM_{2.5}$ and PM_{10} along 0–4 days were 0.89 % (95 % CIs: 0.00, 1.78), 0.42 % (95 % CIs: −0.05, 0.89) and 0.10 (95 % CIs: −0.23, 0.42) for ACD, respectively, and 2.51 % (95 % CIs: 0.82,4.22), 1.24 % (95 % CIs: 0.33, 2.15) and 0.65 (95 % CIs: 0.01, 1.30) for ARD, separately. Similar to previous researches, smaller aerodynamic diameters of ambient PM generally have more significant severe perniciousness for health, such as leading to an increase in mortality, emergency department visits and hospitalizations (Chen et al., 2017; Hu et al., 2018; Zhang et al., 2020). There were three possible explanations: (1) PM_1 with a smaller size could suspend in the air for a longer time, thus increasing the chance of exposure for people (Song et al., 2022); (2) the tinier PM had stronger penetration ability, for example, PM_{10} was capable of mainly reaching the throat, while $PM_{2.5}$/PM_1 could easily get to the alveoli of bronchioles and penetrate vascular barriers to enter the circulation of blood (Yang et al., 2018); (3) compared with $PM_{2.5}$ and PM_{10}, PM_1 had proportionally larger surface areas per unit mass, resulting in absorbing more highly concentrated toxic components such as heavy metal and microbes (Schraufnagel, 2020).

Our subgroup analysis found that significant associations of PM_1-ACD and PM-ARD were only observed in males. This result echoed with a cohort study focused on all-cause deaths conducted in China, with hazard ratios (HRs, 95 % CIs) of 1.097 (1.055, 1.140) for males but 0.986 (0.936, 1.038) for females corresponding to per 10 μg/m^3 increase in $PM_{2.5}$ (Zhang, 2021). An analysis of 22 European cohorts and a nationwide cohort study enrolling all Medicare beneficiaries in the continental United States also showed similar differences in gender analysis when exposed to PM (Beelen et al., 2014; Di et al., 2017). The susceptibility of adult men can be partly explained by the stronger work-related outdoor PM exposure and the higher prevalence of smoking and drinking behavior, which may increase the risk of PM-related death. However, there was a time-series study shows females were more sensitive to PM (Hu et al., 2018). Due to findings in air pollution epidemiology remained still being inconclusive, more comprehensive studies were warranted. In the age-stratified analysis, the pronounced links of PM_1/$PM_{2.5}$-ARD were only found in HIV/AIDS patients aged over 60 years old. Similar results were observed in prior studies (Hu et al., 2018; Zhou et al., 2022). Hu et.al found that per 10 μg/m^3 increased in PM_1 and $PM_{2.5}$ were associated with 0.70 % (95 % CIs: 0.34, 1.07) and 0.67 % (95 % CIs: 0.33, 1.01) increase for all-cause mortality in aged 65+ years group, higher than aged 0–64 years group, with excess relative risks of 0.44 % (95 % CIs: 0.06, 0.81) and 0.43 % (95 % CIs: 0.08, 0.78) for PM_1 and $PM_{2.5}$, respectively (Hu et al., 2018). A case-crossover study detected that associations of $PM_{2.5}$-mortality only existed in people aged over 80 years old, with per 76.3 μg/m^3 increase in $PM_{2.5}$ corresponding to 4.0 % (95 % CIs: 1.7, 6.5) increase in the excess risks of all-cause mortality (Zhou et al., 2022). The academic circle has reached a wide consensus that elderly people tended to suffer from higher risks of death associated with particulate pollution exposure because of their basic diseases and physical function decline (Qu et al., 2018; Tian et al., 2018; Yang et al., 2012; Zhang et al., 2016).

In this paper, we observed short-term exposure to PM_1 and $PM_{2.5}$ only elevated the risk of all-cause and AIDS-related mortality in the cold season, which was in agreement with the existing findings (Cox et al., 2013; Kan et al., 2008; Sui et al., 2021; Zhou et al., 2011). A study conducted in Hefei found that every 10 μg/m^3 increase of $PM_{2.5}$ would significantly raise cardiovascular mortality by 0.22 % (95 % CIs: 0.05, 0.39) at lag 0 day in the cold season, while not in the warm season [−0.37 % (95 % CIs: −1.36, 0.64)] (Cheng et al., 2019). There were several rational explanations for the seasonal differences in the role of PM: (1) the constituents of PM in the cold season was more harmful than in another season due to the different contribution source (Chen et al., 2013; Rodopoulou et al., 2015; Sanchez-Soberon et al., 2019), for example, plenty of coal, oil and natural gas was consumed for heating in the cold season while not in the warm season; (2) the daily concentrations of PM were usually pronounced higher in the cold season than in the warm season (Yang et al., 2005; Zhang et al., 2021). In addition, lower temperatures and wind delayed the diffusion of air pollution (Dai et al., 2013). Both of them aggravated people's PM exposure level; (3) the changes in hemoconcentration and immune resistance in the winter increased people's susceptibility to PM exposure (Callaly et al., 2013); (4) the prevailing peak period of pulmonary tuberculosis occurred in the late winter and early spring annually (Yu et al., 2020), which might increase the probability of opportunistic infection of AIDS in the same period.

There are two major strengths of this study. Firstly, this is the first study focused on the associations between short-term exposure to PM (PM_1, $PM_{2.5}$ and PM_{10}) and mortality among HIV/AIDS patients in China. Secondly, in case-crossover design, confounding factors such as age, gender, education, social-economic and disease status can be successfully controlled, which can accurately reflect the true links of PM and mortality. However, some limitations must be emphasized. First, since the specific residential address of each death case is not available, we used the county-level PM concentration as the individual exposure indicator, which may cause inevitable exposure misclassification (Goldman et al., 2011; Zhou et al., 2022). Second, our data did not contain information on the specific classification of ARD, so we were not able to estimate which opportunistic infections are more vulnerable to PM. Third, although the case-crossover design automatically controls time-independent confounding factors, residual confounding may still exist. Fourth, our results were only collected from a single province in China, therefore, our conclusions might not be well generalized to another and broader regions.

5. Discussion

In summary, we investigate the associations between short-term exposure to ambient PM (PM_1, $PM_{2.5}$ and PM_{10}) and mortality among HIV/AIDS patients in Hubei, China. Our study suggested that PM_1 was positively linked with the risk of ACD and ARD. Male patients with AIDS were more susceptible to PM_1, $PM_{2.5}$ and PM_{10}. PM_1/$PM_{2.5}$ appeared stronger effects on ARD in HIV/AIDS patients aged over 60 years old and in the cold season. Consequently, this study provided epidemiological evidence for public health departments to lay down more efficient preventive measures for AIDS HIV/patients.

Ethical approval

This study was approved by the Ethics Committee of Wuhan University.

Consent to participate

Not applicable.

Consent to publish

Not applicable.

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CRediT authorship contribution statement

Wei Zhu, Dejia Li and Jing Wei conceived and designed the study; Hen Tang and Tingyuan Zhao collected and cleaned the data; Faxue Zhang, Hen Tang and Tingyuan Zhao performed the data analysis and drafted the manuscript. Shijie Zhu, Xupeng Zhang, Xiaowei Zhang, Gaichan Zhao

and Tianzhou Li helped revise the manuscript. All authors read and approved the final manuscript.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.159410.

References

Altman, D.G., Bland, J.M., 2003. Interaction revisited: the difference between two estimates. BMJ 326, 219.

Alvaro-Meca, A., Palomares-Sancho, I., Diaz, A., Resino, R., De Miguel, A.G., Resino, S., 2015. Pneumocystis pneumonia in hiv-positive patients in Spain: epidemiology and environmental risk factors. J. Int. AIDS Soc. 18, 19906.

Andersson, H., Piras, E., Demma, J., Hellman, B., Brittebo, E., 2009. Low levels of the air pollutant 1-nitropyrene induce DNA damage, increased levels of reactive oxygen species and endoplasmic reticulum stress in human endothelial cells. Toxicology 262, 57–64.

Beelen, R., Raaschou-Nielsen, O., Stafoggia, M., Andersen, Z.J., Weinmayr, G., Hoffmann, B., et al., 2014. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 european cohorts within the multicentre escape project. Lancet 383, 785–795.

Blount, R.J., Djawe, K., Daly, K.R., Jarlsberg, L.G., Fong, S., Balmes, J., et al., 2013. Ambient air pollution associated with suppressed serologic responses to pneumocystis jirovecii in a prospective cohort of hiv-infected patients with pneumocystis pneumonia. Plos One 8, e80795.

Bu, X., Xie, Z., Liu, J., Wei, L., Wang, X., Chen, M., et al., 2021. Global pm2.5-attributable health burden from 1990 to 2017: estimates from the global burden of disease study 2017. Environ. Res. 197, 111123.

Callaly, E., Mikulich, O., Silke, B., 2013. Increased winter mortality: the effect of season, temperature and deprivation in the acutely ill medical patient. Eur. J. Intern. Med. 24, 546–551.

Chen, D.Y., Zhang, F.X., Yu, C.H., Jiao, A.Q., Xiang, Q.Q., Yu, Y., et al., 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.B., Li, S.S., Zhang, Y.M., Zhang, W.Y., Li, D.W., Wei, X.M., et al., 2017. Effects of ambient pm1 air pollution on daily emergency hospital visits in China: an epidemiological study. Lancet Planet. Health 1, E221–E229.

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.

Cheng, H., Zhu, F., Lei, R., Shen, C., Liu, J., Yang, M., et al., 2019. Associations of ambient pm2.5 and o3 with cardiovascular mortality: a time-series study in Hefei, China. Int. J. Biometeorol. 63, 1437–1447.

Cigankova, H., Mikuska, P., Hegrova, J., Krajcovic, J., 2021. Comparison of oxidative potential of pm1 and pm2.5 urban aerosol and bioaccessibility of associated elements in three simulated lung fluids. Sci. Total Environ. 800, 149502.

Collaborators GBDRF, 2020. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. Lancet 396, 1223–1249.

Collaborators GDaI, 2020. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the global burden of disease study 2019. Lancet 396, 1204–1222.

Collaborators, G.H., 2019. Global, regional, and national incidence, prevalence, and mortality of hiv, 1980–2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the global burden of diseases, injuries, and risk factors study 2017. Lancet Hiv 6, E831–E859.

Cox Jr., L.A., Popken Jr., D.A., Ricci Jr., P.F., 2013. Warmer is healthier: Effects on mortality rates of changes in average fine particulate matter (pm2.5) concentrations and temperatures in 100 U.S. cities. Regul Toxicol Pharmacol 66, 336–346.

Dai, W., Gao, J.Q., Cao, G., Ouyang, F., 2013. Chemical composition and source identification of pm2.5 in the suburb of Shenzhen, China. Atmos. Res. 122, 391–400.

Deng, X., Rui, W., Zhang, F., Ding, W., 2013. Pm2.5 induces nrf2-mediated defense mechanisms against oxidative stress by activating pik3/akt signaling pathway in human lung alveolar epithelial a549 cells. Cell Biol. Toxicol. 29, 143–157.

Di, Q., Wang, Y., Zanobetti, A., Wang, Y., Koutrakis, P., Choirat, C., et al., 2017. Air pollution and mortality in the medicare population. N. Engl. J. Med. 376, 2513–2522.

Elf, J.L., Eke, O., Rakgokong, M., Variava, E., Baliram, Y., Motlhaoleng, K., et al., 2017. Indoor air pollution from secondhand tobacco smoke, solid fuels, and kerosene in homes with active tuberculosis disease in South Africa. BMC Res. Notes 10, 591.

Gasparrini, A., 2021. The case time series design. Epidemiology 32, 829–837.

Goldman, G.T., Mulholland, J.A., Russell, A.G., Strickland, M.J., Klein, M., Waller, L.A., et al., 2011. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. Environ. Health-Glob. 10.

Gu, X.Y., Chu, X., Zeng, X.L., Bao, H.R., Liu, X.J., 2017. Effects of pm2.5 exposure on the notch signaling pathway and immune imbalance in chronic obstructive pulmonary disease. Environ. Pollut. 226, 163–173.

Hertz-Picciotto, I., Herr, C.E., Yap, P.S., Dostal, M., Shumway, R.H., Ashwood, P., et al., 2005. Air pollution and lymphocyte phenotype proportions in cord blood. Environ. Health Perspect. 113, 1391–1398.

Hu, K.J., Guo, Y.M., Hu, D.Y., Du, R.G., Yang, X.C., Zhong, J.M., et al., 2018. Mortality burden attributable to pm1 in Zhejiang province, China. Environ. Int. 121, 515–522.

Kan, H.D., London, S.J., Chen, G.H., Zhang, Y.H., Song, G.X., Zhao, N.Q., et al., 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., et al., 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.

Levy, D., Lumley, T., Sheppard, L., Kaufman, J., Checkoway, H., 2001. Referent selection in case-crossover analyses of acute health effects of air pollution. Epidemiology 12, 186–192.

Li, Q., Wang, Y.Y., Guo, Y., Zhou, H., Wang, Q.M., Shen, H.P., et al., 2021. Association between airborne particulate matter and renal function: an analysis of 2.5 million young adults. Environ. Int. 147, 106348.

Lin, Z., Niu, Y., Chen, R., Xu, W., Li, H., Liu, C., et al., 2017. Fine particulate matter constituents and blood pressure in patients with chronic obstructive pulmonary disease: a panel study in shanghai, China. Environ. Res. 159, 291–296.

Liu, Y., Pan, J., Fan, C., Xu, R., Wang, Y., Xu, C., et al., 2021. Short-term exposure to ambient air pollution and mortality from myocardial infarction. J. Am. Coll. Cardiol. 77, 271–281.

North, C., Hunt, P., Mocello, A., Martin, J., Boum, Y., Haberer, J., et al., 2015. Cooking fuel type and respiratory symptoms among a cohort of people living with hiv in rural Uganda. Chest 148.

Qiao, Y.C., Xu, Y., Jiang, D.X., Wang, X., Wang, F., Yang, J., et al., 2019. Epidemiological analyses of regional and age differences of hiv/aids prevalence in China, 2004–2016. Int. J. Infect. Dis. 81, 215–220.

Qu, Y., Pan, Y., Niu, H., He, Y., Li, M., Li, L., et al., 2018. Short-term effects of fine particulate matter on non-accidental and circulatory diseases mortality: a time series study among the elder in Changchun. Plos One 13, e0209793.

Rodopoulou, S., Samoli, E., Chalbot, M.G., Kavouras, I.G., 2015. Air pollution and cardiovascular and respiratory emergency visits in Central Arkansas: a time-series analysis. Sci. Total Environ. 536, 872–879.

Salzer, H.J.F., Schafer, G., Hoenigl, M., Gunther, G., Hoffmann, C., Kalsdorf, B., et al., 2018. Clinical, diagnostic, and treatment disparities between hiv-infected and non-hiv-infected immunocompromised patients with pneumocystis jirovecii pneumonia. Respiration 96, 52–65.

Sanchez-Soberon, F., Rovira, J., Sierra, J., Mari, M., Domingo, J.L., Schuhmacher, M., 2019. Seasonal characterization and dosimetry-assisted risk assessment of indoor particulate matter (pm10-2.5, pm2.5-0.25, and pm0.25) collected in different schools. Environ. Res. 175, 287–296.

Schraufnagel, D.E., 2020. The health effects of ultrafine particles. Exp. Mol. Med. 52, 311–317.

Sharp, P.M., Hahn, B.H., 2011. Origins of hiv and the aids pandemic. Cold Spring Harb. Perspect. Med. 1, a006841.

Song, J., Ding, Z., Zheng, H., Xu, Z., Cheng, J., Pan, R., et al., 2022. Short-term pm1 and pm2.5 exposure and asthma mortality in Jiangsu province, China: What's the role of neighborhood characteristics? Ecotoxicol. Environ. Saf. 241, 113765.

Sui, X., Zhang, J., Zhang, Q., Sun, S., Lei, R., Zhang, C., et al., 2021. The short-term effect of pm2.5/o3 on daily mortality from 2013 to 2018 in Hefei, China. Environ. Geochem. Health 43, 153–169.

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

Toe, S., Nagy, M., Albar, Z., Yu, J., Sattar, A., Nazzinda, R., et al., 2022. Ambient air pollution is associated with vascular disease in Ugandan HIV-positive adolescents. AIDS 36, 863–870.

Wei, J., Li, Z.Q., Guo, J.P., Sun, L., Huang, W., Xue, W.H., et al., 2019. Satellite-derived 1-km-resolution PM_1 concentrations from 2014 to 2018 across China. Environ. Sci. Technol. 53, 13265–13274.

Wei, J., Li, Z., Cribb, M., et al., 2020. Improved 1 km resolution $PM_{2.5}$ estimates across China using enhanced space-time extremely randomized trees. Atmos. Chem. Phys. 20 (6), 3273–3289.

Wei, J., Li, Z., Xue, W., Sun, L., Fan, T., Liu, L., et al., 2021a. The ChinaHighPM$_{10}$ dataset: generation, validation, and spatiotemporal variations from 2015 to 2019 across China. Environ. Int. 146, 106290.

Wei, J., Li, Z.Q., Lyapustin, A., Sun, L., Peng, Y.R., Xue, W.H., et al., 2021b. Reconstructing 1-km-resolution high-quality $PM_{2.5}$ data records from 2000 to 2018 in China: spatiotemporal variations and policy implications. Remote Sens. Environ. 252.

Wu, C., Yan, Y., Chen, X., Gong, J., Guo, Y., Zhao, Y., et al., 2021. Short-term exposure to ambient air pollution and type 2 diabetes mortality: a population-based time series study. Environ. Pollut. 289, 117886.

Xiong, J., Li, J., Wu, X., Wolfson, J.M., Lawrence, J., Stern, R.A., et al., 2022. The association between daily-diagnosed covid-19 morbidity and short-term exposure to pm1 is larger than associations with pm2.5 and pm10. Environ. Res. 210, 113016.

Xu, R.J., Wang, Q.Q., Wei, J., Lu, W.F., Wang, R., Liu, T.T., et al., 2022. Association of short-term exposure to ambient air pollution with mortality from ischemic and hemorrhagic stroke. Eur. J. Neurol. 29, 1994–2005.

Yang, B.Y., Guo, Y., Markevych, I., Qian, Z.M., Bloom, M.S., Heinrich, J., et al., 2019. Association of long-term exposure to ambient air pollutants with risk factors for cardiovascular disease in China. JAMA Netw. Open 2, e190318.

Yang, C.X., Peng, X.W., Huang, W., Chen, R.J., Xu, Z.C., Chen, B.H., et al., 2012. A time-stratified case-crossover study of fine particulate matter air pollution and mortality in Guangzhou, China. Int. Arch. Occup. Environ. Health 85, 579–585.

Yang, F., Ye, B., He, K., Ma, Y., Cadle, S.H., Chan, T., et al., 2005. Characterization of atmospheric mineral components of pm2.5 in Beijing and shanghai, China. Sci. Total Environ. 343, 221–230.

Yang, J., Zhou, M.G., Li, M.M., Yin, P., Hu, J.L., Zhang, C.L., et al., 2020. Fine particulate matter constituents and cause-specific mortality in China: a nationwide modelling study. Environ. Int. 143.

Yang, M., Chu, C., Bloom, M.S., Li, S., Chen, G., Heinrich, J., et al., 2018. Is smaller worse? New insights about associations of pm1 and respiratory health in children and adolescents. Environ. Int. 120, 516–524.

Yu, P., Guo, S., Xu, R., Ye, T., Li, S., Sim, M.R., et al., 2021. Cohort studies of long-term exposure to outdoor particulate matter and risks of cancer: a systematic review and meta-analysis. Innovation (Camb) 2, 100143.

Yu, Y., Wu, B., Wu, C., Wang, Q., Hu, D., Chen, W., 2020. Spatial-temporal analysis of tuberculosis in Chongqing, China 2011–2018. BMC Infect. Dis. 20, 531.

Zhang, F., Liu, X., Zhou, L., Yu, Y., Wang, L., Lu, J., et al., 2016. Spatiotemporal patterns of particulate matter (pm) and associations between pm and mortality in Shenzhen, China. BMC Public Health 16, 215.

Zhang, F., Zhang, H., Wu, C., Zhang, M., Feng, H., Li, D., et al., 2021. Acute effects of ambient air pollution on clinic visits of college students for upper respiratory tract infection in Wuhan, China. Environ. Sci. Pollut. Res. Int. 28, 29820–29830.

Zhang, J., Du Ester, E.J., Watson, R.R., 2002. Side-stream cigarette smoke accentuates immunomodulation during murine aids. Int. Immunopharmacol. 2, 759–766.

Zhang, Y., Ding, Z., Xiang, Q., Wang, W., Huang, L., Mao, F., 2020. 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.Q., 2021. All-cause mortality risk and attributable deaths associated with long-term exposure to ambient pm2.5 in Chinese adults. Environ. Sci. Technol. 55, 6116–6127.

Zhao, J., Gao, Z., Tian, Z., Xie, Y., Xin, F., Jiang, R., et al., 2013. The biological effects of individual-level pm(2.5) exposure on systemic immunity and inflammatory response in traffic policemen. Occup. Environ. Med. 70, 426–431.

Zhou, J.A., Ito, K., Lall, R., Lippmann, M., Thurston, G., 2011. Time-series analysis of mortality effects of fine particulate matter components in Detroit and Seattle. Environ. Health Perspect. 119, 461–466.

Zhou, P., Hu, J., Yu, C., Bao, J., Luo, S., Shi, Z., et al., 2022. Short-term exposure to fine particulate matter constituents and mortality: case-crossover evidence from 32 counties in China. Sci China. Life Sci. 65.