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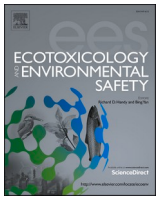

Is COPD mortality in South China causally linked to the long-term PM_1 exposure? Evidence from a large community-based cohort

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ABSTRACT

Background: Long-term ambient particulate matter (PM) exposure has been found associated with chronic obstructive pulmonary disease (COPD) mortality in an increasing body of research. However, limited evidence was available on the potential causal links between PM_1 and COPD mortality, especially in highly exposed areas.
Objectives: To examine the COPD mortality risk following long-term ambient PM_1 exposure in south China.
Methods: The cohort included 580,757 participants recruited during 2009–2015. Satellite-based annual concentrations of PM_1 were estimated at a spatial resolution of 1 km × 1 km and assigned to each participant based on their residential addresses. We analyzed the potential causal links between time-varying PM_1 exposure and COPD mortality using marginal structural cox models within causal frameworks. Stratified analyses were also performed to identify the potential susceptible groups.
Results: The annual average PM_1 concentration continuously decreased over time. After adjusting for confounders, each 1 $\mu g/m^3$ increase in PM_1 concentration corresponded to an 8.1 % (95% confidence interval: 6.4–9.9 %) increment in the risk of COPD mortality. The impact of PM_1 was more pronounced among the elderly and those with low exercise frequency, with a 1.9–6.9 % higher risk than their counterparts. We further observed a 0.1–9.7 % greater risk among those who lived in lower greenness settings. Additionally, we observed higher effect estimates in participants with long-term low PM_1 exposure compared to the general population.
Conclusions: COPD mortality risk significantly increased following long term ambient PM_1 exposure, particularly among groups with certain demographics or long-term low exposure.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a type of obstructive lung disease which is characterized by persistent limitation to airflow (Ritchie and Wedzicha, 2020). As one of the leading health concerns worldwide, COPD was estimated to affect 544.9 million people globally in 2017, and according to the Global Burden of Disease study, caused 3.28 million deaths and 74.43 million disability-adjusted life years in 2019 (Christenson et al., 2022; Zou et al., 2022). In China, 99.9 million adults aged over 20 years were suffering from spirometry-defined COPD, accounting for approximately 8.6 % of the general adult population in 2015 (Wang et al., 2018).

Ambient air pollution is recognized as one of the major environmental health concerns worldwide, with extensive epidemiological

Abbreviations: COPD, chronic obstructive pulmonary disease; PM, particulate matter; PM1, particulate matter with an aerodynamic diameter ≤ 1 μm; IPW, inverse probability weighting; HR, hazard ratio; CI, confidence interval; GPS, generalized propensity score; LM, linear model; GEE, generalized estimating equation; ML, machine learning; NDVI, normalized difference vegetation index.

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studies providing evidence linking particulate matter (PM) exposure to the COPD mortality. For instance, a recent meta-analysis on top of 11 cohort studies estimated an 11 % increased risk of COPD mortality following each 10 μg/m^3 increase in long-term $PM_{2.5}$ exposure (Chen and Hoek, 2020). Although the health impact of regular-sized particles such as $PM_{2.5}$ is still of a great public concern, the impact of smaller particles has attracted a growing attention over recent years (Hu et al., 2022). PM_1 is one of the most important fine particles and a major component of the regular-sized particles (Chen et al., 2018). It is very likely and biologically plausible that PM_1 may impose a greater risk of chronic respiratory diseases than larger particles as the smaller size and larger surface area of the particles may result in a deeper invasion, prolonged internal stay, and more pulmonary inflammation (Chen et al., 2015; Valavanidis et al., 2008). However, limited evidence is available on PM_1 exposure and the risk of COPD. High-quality evidence, especially based on large cohorts, would be critical to expanding our understanding of the respiratory effects of PM exposures.

Furthermore, existing evidence assessing the respiratory effects of PMs exposure generally relies on traditional association analysis and prone to the residual confounding issues which potentially leads to a biased estimation (Pang et al., 2016; Robinson and Jewell, 1991). Recent advances in the theory of causal inference based on the observational data make it possible to investigate the health effect that could be specifically attributed to a certain exposure under a counterfactual framework (Danesh Yazdi et al., 2021; Robins et al., 2000; Wu et al., 2020). The causal clues generally are considered more significant for decision-makings relative to the traditional association information. However, evidence on the potential causal links of PM_1 exposure and COPD mortality is even more scarce.

To fill the research gaps in the area of PM_1-COPD mortality research, we first used causal inference models to investigate the potential causal links of long-term PM_1 exposure with the COPD mortality using data from a community-based cohort study in south China, and then performed stratified analyses to identify the potential susceptible groups.

2. Materials and methods

2.1. Study design and population

Participants for the current study were recruited from Guangzhou area, China between 2009 and 2015, as part of the national project of community-based collaborative innovation hepatitis B virus (Ruan et al., 2019). In the present study, we included all the residents in the community who signed health service contract (for physical checkup) with the community healthcare centers. These residents were identified through official residential records and were simultaneously enrolled in China's basic public health service project, with a long-standing residential history in the local area. This study recruited a total of 654,115 participants, the locations of whom have been described elsewhere (Zhang et al., 2023). After excluding 72,330 participants who were younger than 18 years of age and 1028 individuals who died from unknown causes, the number of participants analyzed was 580,757. This study was approved by the Institutional Review Board (IRB) Committee at Sun Yat-sen University. We collected information on demographic characteristics, behavioral factors, a detailed assessment of body mass index, and other variables during the baseline survey.

2.2. Outcome definition

Information on survival status of each participant and the cause of death for those who died during January 2009 through December 2020 were obtained from the Death Registry System of the Guangzhou Center for Disease Control and Prevention. In the current study, the outcome was the COPD mortality (International Classification of Diseases, 10th revision: J40-J44, J47). Each participant was followed from enrollment until either the occurrence of the outcome or the end of the follow-up, whichever occurred first.

2.3. Exposure assessment

Annual average PM_1 concentrations for the period of 2009–2020 were obtained from the ChinaHighAirPollutants data set at a spatial resolution of 1 km × 1 km. The predictive model of daily PM_1 concentrations displayed a satisfactory performance with a 10-fold cross-validation R^2 (root mean square error) value of 0.77 (14.6 μg/m^3). Detail on the simulation process and model validation can be found elsewhere (Wei et al., 2019). In the present study, annual average PM_1 concentrations were calculated and linked to participants' residential address. During the follow-up period, we matched the annual average PM_1 concentration for participants who died before June, with the last exposure value being the annual concentration of the previous year. For participants who died after June, the last exposure value was the annual concentration of the mortality year.

Given the existing evidence suggesting an association of greenness with both air pollution and respiratory diseases, we examined the potential confounding effect of greenness exposure (Twohig-Bennett and Jones, 2018). The normalized difference vegetation index (NDVI) is a widely used for evaluating vegetation coverage, which is obtained from the Land Processing Distributed Active Archive Center(Huete et al., 2002). The annual average NDVI value within a 500-meter radius buffer around the residential address was computed for each participant.

2.4. Potential confounders

In order to select potential confounders, we utilized a directed acyclic graph which integrated both evidence synthesis strategies and causality principles (Ferguson et al., 2020). The potential confounders included in this study were age, sex, ethnicity (Han Chinese and ethnic minorities), education (illiterate or semiliterate, elementary school, middle school, high school, and college or above), marital status (never married, married, widowed, and divorced), medical insurance (medical insurance for urban workers, medical insurance for urban residents, the new rural cooperative medical insurance, and others), smoking (never, former and current), exercise frequency (low, moderate, and high), and NDVI (Fig. S1). More details have been described elsewhere (Wang et al., 2023a).

2.5. Statistical analysis

Marginal structural models with inverse probability weighting (IPWs) that combined time-varying Cox model was used to evaluate the risk of COPD mortality following each 1 μg/m^3 increase in PM_1 concentrations, providing hazard ratio (HR) and 95 % confidence interval (CI). The marginal structural models took into account time-varying covariates, such as the annual average PM_1 concentrations and NDVI (500 m), that changed during the follow-up period. The main idea of the model is to establish a pseudo-population in which the covariates are balanced between different exposure groups. With this method, a generalized propensity score (GPS) is first computed using three different methods which included the linear model (LM), generalized estimating equation (GEE), and gradient boosting machine learning (ML). Then, following the approach by Robins et al. (Robins et al., 2000), stabilized inverse probability weights (IPW) of exposure were constructed using the inverse of the GPS to weigh the observations. These weights were assigned to each participant, creating a weighted pseudo-population that balances the potential confounding effects across exposure groups. The optimal model with the best performance in confounding balancing was identified based on the average absolute correlation (AC) values, and the LM weighting method was chosen for the marginal structural model (Fig. S2). More methodological details have been described elsewhere (Wang et al., 2023b; Wu, et, 2020).

Model 0 was the crude model under time-varying Cox model. In

multivariable analyses (model 1), adjusted for sex, age, demographic characteristics, behavioral factors, and time-varying NDVI. Model 2 was assessed using the marginal structural model, with the same covariates employed in Model 1. The main findings in the present study were presented as the results from Model 2.

In addition, stratified analyses were performed by the demographic characteristics, behavioral factors, and NDVI. Multiple imputations using chained equations were utilized to fill in missing data for confounding variables (van Buuren and Groothuis-Oudshoorn, 2011). Moreover, the previous studies have shown that participants in the same region but exposed to lower PM concentrations tended to have a higher susceptibility (Danesh Yazdi et al., 2021; Di et al., 2017). To explore the potential impact of low exposure on human susceptibility, the analysis was further restricted to participants with annual PM_1 concentrations of were generally under the 75th percentile among all the annual concentration of all the participants.

Multiple sensitivity analyses were conducted. First, the effect of NDVI buffer option was evaluated by defining NDVI exposure using buffers of varying sizes (i.e., 250 m and 1000 m). Second, the impact of missing data imputation was evaluated by conducting a complete case analysis only including participants without missing data.

Third, we additionally adjusted for alcohol consumption and BMI in our model. Fourth, the effect of using different IPW construction methods was also assessed (i.e., LM vs GEE vs ML). In addition, the potential impact of unmeasured confounders was evaluated by calculating the *E*-value (VanderWeele and Ding, 2017), with a higher E-value indicating that the results are less likely to be affected by unmeasured confounders bias. All statistical analysis was conducted in R version 4.1.3.

3. Results

A total of 580,757 participants [mean (standard deviation (SD)) age= 48.3 (17.6 years; 305,081 (52.53 %) women] were included in the present analysis. During an average of 8.0 years (SD=3.3) follow-up, 2250 COPD deaths occurred. The average concentration of PM_1 from 2009–2020 was 19.56 $\mu g/m^3$ (SD=4.48), and the annual average PM_1 concentration decreased during this period (Fig. S3). Table 1 shows that participants who were minorities, never married, or had a lower education level had higher average PM_1 concentrations (all $P < 0.001$). Moreover, participants who were never smokers, never alcohol uses, had low exercise frequency, lower NDVI exposure, and higher BMI levels tended to have higher average PM_1 concentrations (all $P < 0.001$). Table S1 displays the characteristics of the complete case dataset.

Fig. 1 shows a significant association between long-term PM_1 exposure and COPD mortality. For each 1 $\mu g/m^3$ increase in PM_1 concentration, the HR of COPD mortality was 1.084 (95 % CI:1.067–1.101) in the crude model. In the marginal structural Cox model, the HR and 95 % CI were 1.081 (95 % CI:1.064–1.099) per 1 $\mu g/m^3$ increase in PM_1 concentration after adjustment for sex, age, demographic characteristics, behavioral factors and NDVI. The results obtained from the fully adjusted time-varying Cox model were similar, with the HR and 95 % CI being 1.090 (95 % CI:1.071–1.109).

Results of stratified analyses were showed in Fig. 2. The older participants (above 65 years) showed greater susceptibility to the impacts of PM_1 exposure on mortality due to COPD (HR: 1.110, 95 % CI: 1.092–1.128) than younger participants (HR: 1.091, 95 % CI: 1.013–1.175). We also found that participants with low exercise frequency may be more susceptible to the impact of PM_1, compared to participants with a moderate exercise frequency, with the HRs being

Table 1
Baseline characteristics by quartiles of long-term PM_1 concentrations in 2009–2020.

Characteristics	long-term PM_1 concentrations					*P*
	Overall (N = 580,757)	Quartile 1 (N = 147,433)	Quartile 2 (N = 159,475)	Quartile 3 (N = 148,608)	Quartile 4 (N = 125,241)	
Demographics						
Age (mean (SD))	48.33 (17.55)	47.75 (17.27)	49.91 (17.64)	49.12 (17.71)	46.05 (17.28)	<0.001
Sex (men %)	275,676 (47.47)	71,246 (48.32)	73,852 (46.31)	69,804 (46.97)	60,774 (48.53)	<0.001
Ethnicity (minority %)	10,953 (1.89)	249 (0.17)	702 (0.44)	1953 (1.31)	8049 (6.43)	<0.001
Marital status (%)						<0.001
Never married	108,424 (18.67)	23,059 (15.64)	31,538 (19.78)	27,107 (18.24)	26,720 (21.34)	
Married	448,138 (77.16)	120,227 (81.55)	119,018 (74.63)	114,151 (76.81)	94,742 (75.65)	
Widowed	17,262 (2.97)	2926 (1.99)	6618 (4.15)	5093 (3.43)	2625 (2.09)	
Divorced	6933 (1.20)	1221 (0.82)	2301 (1.44)	2257 (1.52)	1154 (0.92)	
Education level (%)						<0.001
Illiterate or semiliterate	6603 (1.14)	418 (0.28)	1986 (1.25)	2563 (1.72)	1636 (1.31)	
Elementary school	67,247 (11.58)	11,891 (8.07)	19,643 (12.32)	19,046 (12.82)	16,667 (13.31)	
Middle school	131,394 (22.62)	22,424 (15.21)	34,341 (21.53)	43,647 (29.37)	30,982 (24.74)	
High school	266,467 (45.88)	65,259 (44.26)	74,885 (46.96)	64,242 (43.23)	62,081 (49.57)	
College or above	109,046 (18.78)	47,441 (32.18)	28,620 (17.94)	19,110 (12.86)	13,875 (11.07)	
Medical insurance (%)						<0.001
Medical insurance for urban workers	354,396 (61.02)	92,203 (62.54)	93,971 (58.93)	89,455 (60.20)	78,767 (62.89)	
Medical insurance for urban residents	164,213 (28.28)	44,994 (30.52)	48,186 (30.22)	42,476 (28.58)	28,557 (22.80)	
The new rural cooperative medical insurance	6439 (1.11)	239 (0.16)	613 (0.38)	2398 (1.61)	3189 (2.55)	
Others	55,709 (9.59)	9997 (6.78)	16,705 (10.47)	14,279 (9.61)	14,728 (11.76)	
Lifestyle behaviors						
Exercise frequency (%)						<0.001
Low	322,225 (55.48)	97,255 (65.97)	74,599 (46.78)	79,267 (53.34)	71,104 (56.78)	
Moderate	141,938 (24.44)	27,672 (18.77)	40,802 (25.58)	40,697 (27.38)	32,767 (26.16)	
High	116,594 (20.08)	22,506 (15.26)	44,074 (27.64)	28,644 (19.28)	21,370 (17.06)	
Smoking status (%)						<0.001
Non-smoker	505,385 (87.02)	134,765 (91.41)	123,080 (77.18)	132,249 (88.99)	115,291 (92.06)	
Ever smoker	6716 (1.16)	1343 (0.911)	2385 (1.49)	1943 (1.31)	1045 (0.83)	
Current smoker	68,656 (11.82)	11,325 (7.68)	34,010 (21.33)	14,416 (9.70)	8905 (7.11)	
Alcohol consumption (%)						<0.001
Never	515,205 (88.71)	135,802 (92.11)	128,778 (80.75)	135,020 (90.86)	115,605 (92.31)	
Ever	65,552 (11.29)	11,631 (7.89)	30,697 (19.25)	13,588 (9.14)	9636 (7.69)	
Body mass index (mean (SD))	22.07 (2.45)	21.82 (2.23)	22.10 (2.57)	22.189 (2.50)	22.17 (2.47)	<0.001
NDVI (500), mean (SD)	0.214 (0.04)	0.251 (0.033)	0.217 (0.041)	0.191 (0.025)	0.194 (0.024)	<0.001

Abbreviations: SD, standard deviation; PM1, particulate matter with an aerodynamic diameter $\leq$ 1 μm, NDVI, normalized difference vegetation index.

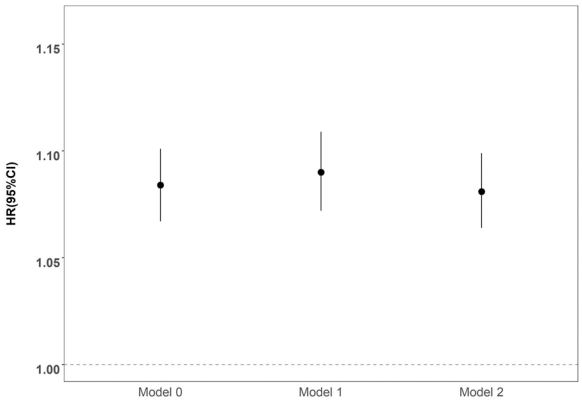

Fig. 1. Association between 1-μg/m^3 increase in long-term PM_1 exposure and mortality due to COPD under two different statistical approaches (traditional approach and causal inference approach). Note: 1) Model 0 was a crude model under time-varying Cox model. 2) Model 1: model 0 adjusted for sex, age, ethnicity, education, marital status, medical insurance, smoking status, exercise frequency and normalized difference vegetation index (500 m). 3) Model 2: refitted with the marginal structural Cox model based on the same co-variates in the model 1. Abbreviations: HR, hazard ratio; CI, confidence interval; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm;.

1.114 (95 % CI: 1.076–1.154), and 1.045 (95 % CI: 1.011–1.080), respectively. Regarding the modification of NDVI, participants with low NDVI exposure were more susceptible to the influence of PM_1 than those with higher NDVI exposure.

Fig. 3 showed the relationships between COPD mortality and long-term PM_1 exposure among individuals who were generally exposed to low PM_1 concentrations (Fig. S4). We found the estimated HR for COPD mortality was larger among those who were always exposed to lower levels of PM_1 (HR: 1.382, 95 % CI: 1.234–1.548) concentrations in comparison to the entire population.

Our sensitivity analysis yielded consistent results across different buffer sizes of NDVI (250 m, 1000 m), between data with and without imputation, additional adjustments for alcohol consumption and BMI, as well as across three different approaches for IPW computation (LM, ML, and GEE) (Table S2). Our conclusions were considered robust with regards to unmeasured confounding bias, based on the *E* values. (Table S3).

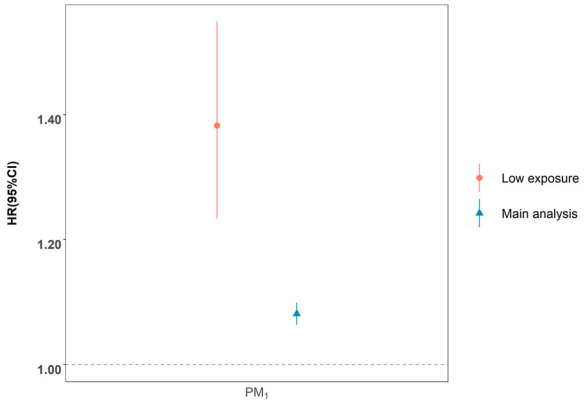

Fig. 3. Association between 1-μg/m^3 increase in long-term PM_1 exposure and mortality due to COPD under causal inference approach among all participants and participants who always exposed to low concentrations. Abbreviations: HR, hazard ratio; CI, confidence interval; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm;.

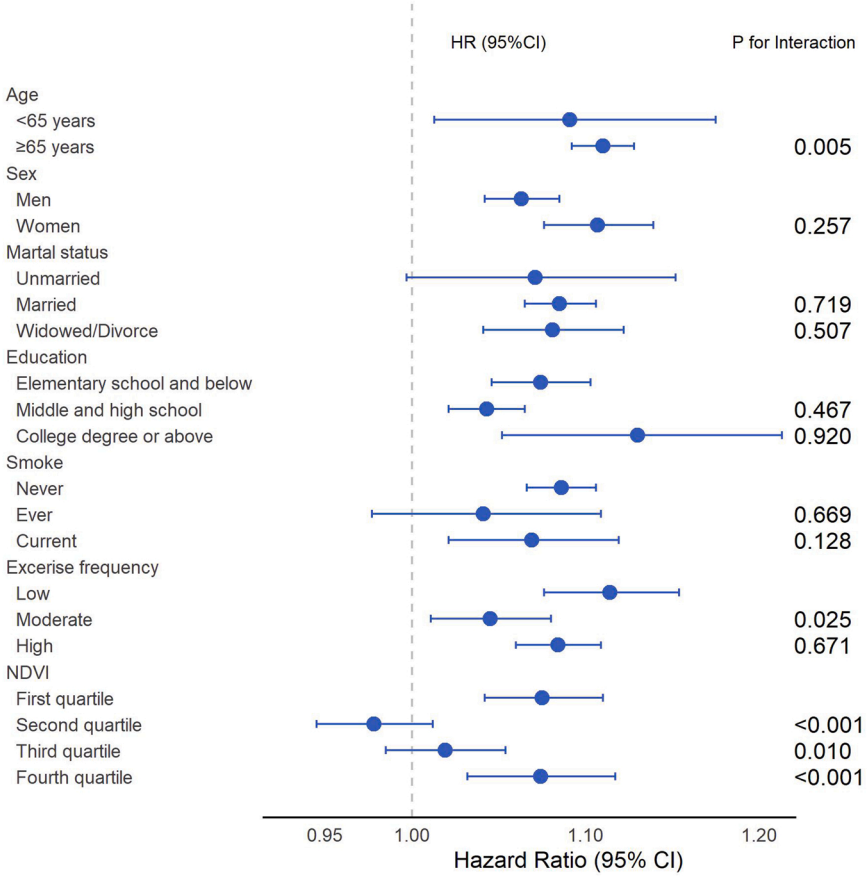

Fig. 2. The modification effect of basic participant characteristics on the association between PM_1 concentrations and mortality due to COPD.
Note: The effects were estimated under causal inference model with adjustment for sex, age, ethnicity, education, marital status, medical insurance, smoking status, exercise frequency and normalized difference vegetation index (500 m). All stratified estimates were adjusted for the remaining covariates. Abbreviations: HR, hazard ratio; CI, confidence interval; PM_1, particulate matter with an aerodynamic diameter ≤ 1 μm;.

4. Discussion

In a general population cohort study, the findings of our study demonstrated an elevated risk of about 8.1 % in COPD mortality for each 1 μg/m^3 increase in long-term PM_1 concentration after adjusting for confounding factors. The impact of PM_1 was more pronounced among the elderly, people with lower exercise frequency, and lower residential greenness than their counterparts. Furthermore, we observed a higher effect estimate in participants with long-term low PM_1 exposure compared to the general population. This is the first study utilizing the causal inference approaches to provide robust evidence clarifying the potential causal relationship between long-term PM_1 exposure and COPD mortality in China.

Although numerous epidemiological studies, including our previous research (Wang et al., 2023a), have shown the relationship between $PM_{2.5}$ and PM_{10} and COPD mortality, the risk from long-term PM_1 exposure remains understudied. Our study highlights the importance of elevated long-term PM_1 exposure concentration as a risk factor for COPD mortality. Previously, limited research has investigated the impact of PM_1 on health outcomes, primarily assessing short-term effects or using cross-sectional study design (Hu et al., 2018; Lin et al., 2016; Perez et al., 2009). A study using case-crossover design in China found that per 10 μg/m^3 increase of PM_1 concentration was linked to a 9 % elevated risk of respiratory diseases admission at lag 0–2 days (Zhang et al., 2020). Another time-series study in China revealed that for each 10 μg/m^3 increase in short-term PM_1 exposure, the risk of mortality due to COPD increased by 0.7 % at lag 0–2 days (Hu et al., 2018). These findings include our research underscoring the benefits of reducing exposure to PM_1 for improving health outcomes.

Interestingly, compared with the effects of $PM_{2.5}$ and PM_{10} reported (Wang et al., 2023a). we observed that the impact of PM exposure on COPD mortality differs with the particle size, with the long term PM_1 exposure being observed with a greater risk. The previous research on the health effects of PM exposure of different sizes have not reached a consistent conclusion. Several potential mechanisms may explain the higher effects of PM_1. PM_1 is more likely to be inhaled into deeper regions of the lungs compared to larger particle size and can access the alveoli and bronchioles, leading to inflammation and other harmful reactions, while $PM_{2.5}$ and PM_{10} mainly settle in the upper respiratory tract and could be cleared by self-cleaning mechanisms, such as the mucociliary clearance system (Filep et al., 2016). The smaller the particles are, the relatively larger amounts of toxic organic compounds they may contain (Agudelo-Castan~eda et al., 2015). For example, the PM_1 particles were reported to contain about 86 % of the carcinogenic potential when comparing the total carcinogenic potency in $PM_{2.5}$ and PM_1 (Pehnec and Jakovljević, 2018). In addition, the smaller particles are more likely to trigger gene variations, causing greater health risk (Frydas et al., 2020). Overall, more in-depth mechanistic research on the sources and composition of PM is necessary to advise better control and preventive strategies.

In subgroup analyses, participants who were older than 65 years and those with lower exercise frequency had an increased risk of COPD mortality due to PM_1 exposure. Aging is among the most frequently investigated demographic features that could increase the vulnerability to the health effects of PM exposures (Katsouyanni et al., 2001). In a case-crossover study in China, the excess fractions of cardiovascular disease (CVD) mortality attributable to short-term PM_1 exposure were higher in participants over 80 years old than in the younger ones (Xu et al., 2022). The vulnerability of the elderly may be partly due to their decreased immune function and the higher prevalence of chronic diseases, and other underlying health conditions. The current evidence on the modification effect of physical activity on air pollution is limited and controversial (Qin et al., 2019). Our study agrees with prior research in suggesting that the benefit of physical activities, even in highly polluted areas (Nocon et al., 2008; Sun et al., 2020; Tainio et al., 2016). One potential explanation is that only a small proportion of the inhaled air pollutants can be attributed to air pollutants from physical activity, and the health benefits of high-intensity exercise exceed the harmful consequences due to ambient air pollution (Qin et al., 2019). Further mechanistic studies clarifying the modification effects of physical activity on the relationship between air pollution and human health are warranted.

Our findings suggested a beneficial effect of a greater residential green space against the deleterious effect of PM exposure, corresponding to previous findings (Son et al., 2021). There are several major factors that can be suggested in order to explain these protective associations. Green plants can adsorb PM and gaseous pollutants from the air leading to a decrease in its concentration and inhalation (Markevych et al., 2017; Trivedi et al., 2018). In addition, green space can reduce the harm of PM through enhancing the performance of the immune system, providing chances for physical exercise, promoting psychological restoration, and other factors (Li, 2010; McMorris et al., 2015; Pun et al., 2018). This finding further demonstrates the importance of residential green space in mitigating the harmful consequences of ambient air pollution on human health, meaning that greening could prove to be a valuable approach to ease the burden of diseases linked to environmental air pollution.

Furthermore, the low-exposure group exhibited a higher risk of COPD mortality at the same PM concentration compared to the participants of the entire cohort. Our findings were consistent with the results of a 652-city study which suggested a stronger association between PM exposure and daily all-cause, CVD and respiratory mortality in areas with lower $PM_{2.5}$ concentrations (Liu et al., 2019). Another study conducted in the United States showed that each 10 μg/m^3 increase in $PM_{2.5}$ may increase the risk of death by 7.3 % for the entire population, whereas by 13.6 % for participants with low exposure (Di et al., 2017). The results may be partly due to that participants living in high-pollution areas may have developed certain defenses or adaptive mechanisms that make them less susceptible to PM exposure, compared to those living in low-pollution areas. Taken together, vulnerable populations may have a higher risk of COPD mortality at the same PM concentration, which underlines the problem of environmental pollution inequity and highlights the importance of considering susceptibility and environmental justice when formulating environment-related policies.

Our study has several strengths. First, the study has a large sample size, which yields significant statistical power to detect the effects of PM_1 on COPD mortality and identify the potential susceptible groups. Second, the study takes into account the temporal variation of PM_1 exposure during follow-up and constructed the causal inference models to obtain accurate effect estimates of long-term PM exposure. Third, the prospective design and the participants with a wide range of demographic backgrounds ensured the reliability and the generalizability of the results. Currently, the air pollution standards do not include PM_1 regulations, and this study has made an important contribution to establish long-term PM_1 standards for the government, providing empirical support of the harmful effects of prolonged PM_1 exposure on human health.

This study also has some limitations. First, participant mobility during the follow-up period may be a possible cause of exposure misclassification since we did not have the updated addresses. However, the Death Registry System covers all the permanent residents in the entire area of Guangzhou. Although we could not rule out the possibility of some residents moving out and loss of following, the percentage should be quite small in this large cohort as the research was carried out in old urban areas with less migration. And this issue should be further minimized as the status of all the permanent resident, even outside the area, would be regularly checked by the community mangers responsible for the resident resignation information and reported to the Death Registry database. Second, some individual factors such as occupational history, cooking habits and indoor pollution may also be potential confounding factors. However, these individual-level details were not

collected. Future studies are warranted to fill this gap. Third, our study lacked information on personal income and occupation, which are indicators of individual socioeconomic status, although some surrogate factors such as educational level and medical insurance status were included. However, common confounding factors such as education and occupational exposure are unlikely to reverse the effect estimates (Pope et al., 2002), and our conclusions were considered robust with regards to unmeasured confounding bias, based on the *E* values. Third, the effect estimates may be affected by missing values. However, the sensitivity analysis showed that the results from the complete-case analysis and multiple imputation analysis were similar.

5. Conclusion

This study provides new evidence that long term PM_1 exposure is associated with an elevated risk of COPD mortality in China. In addition, the elderly, participants with low exercise frequency, lower residential greenness, or in low-exposure areas are more sensitive to the effect of PM_1. The findings of our research may have implications for the development of environmental policies, and prompt the adoption of more rigorous measures to mitigate the hazards posed by fine particles.

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CRediT authorship contribution statement

Ying Wang: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization. **Jie Jiang:** Conceptualization, Formal analysis, Investigation, Data curation, Writing – review & editing. **Liufu Chen:** Conceptualization, Methodology, Writing – original draft. **Tong Guo:** Formal analysis, Investigation, Data curation. **Shimin Chen:** Formal analysis, Investigation. **Zhicheng Du:** Conceptualization, Methodology, Software, Writing – review & editing. **Jing Wei:** Conceptualization, Methodology, Software, Validation. **Wangjian Zhang:** Conceptualization, Validation, Formal analysis, Investigation, Data curation, Writing – review & editing, Funding acquisition, Resources, Supervision, Project administration. **Yuantao Hao:** Conceptualization, Validation, Formal analysis, Investigation, Data curation, Writing – review & editing, Funding acquisition, Resources, Supervision, Project administration.

Declaration of Competing Interest

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

Data availability

Data are available upon reasonable request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2023.115299.

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