

Association between ambient fine particulate matters and chronic obstructive pulmonary disease (COPD) mortality: an analysis in Southeastern China

Zhijian Chen

Zhejiang Provincial Center for Disease Control and Prevention

Qiuli Fu

Zhejiang University School of Medicine Second Affiliated Hospital

Guangming Mao

Zhejiang Provincial Center for Disease Control and Prevention

Lizhi Wu

Zhejiang Provincial Center for Disease Control and Prevention

Peiwei Xu

Zhejiang Provincial Center for Disease Control and Prevention

Dandan Xu

Zhejiang Provincial Center for Disease Control and Prevention

Zhifang Wang

Zhejiang Provincial Center for Disease Control and Prevention

Xuejiao Pan

Zhejiang Provincial Center for Disease Control and Prevention

Yuan Chen

Zhejiang Provincial Center for Disease Control and Prevention

Xiaoming Lou

Zhejiang Provincial Center for Disease Control and Prevention

Xiaofeng Wang

Zhejiang Provincial Center for Disease Control and Prevention

Zhe Mo (✉ zhmo@cdc.zj.cn)

Zhejiang Provincial Center for Disease Control and Prevention <https://orcid.org/0000-0003-0375-509X>

Research

Keywords: air pollution, chronic obstructive pulmonary disease, PM, mortalities

Posted Date: July 20th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-44330/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background: The objective of this study was to investigate the association between ambient particulate matters (PMs) and chronic obstructive pulmonary disease (COPD) mortality.

Methods: Generalized Additive Mixed Model was employed to investigate the effects of ambient fine and coarse PMs on COPD mortality using 13,066 deaths from 2014 to 2016 among six cities in Zhejiang Province in Southeastern China.

Results: The daily average death count due to COPD was 3, varying from 1 to 7 among six cities. The daily 24-hour mean concentrations were diverse among cities, from 29.7 to 56.8 $\mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5}$, 16.7 to 30.3 $\mu\text{g}/\text{m}^3$ for $\text{PM}_{2.5-10}$, and 50.3 to 87.1 $\mu\text{g}/\text{m}^3$ for PM_{10} , respectively. The analysis showed that daily exposure to $\text{PM}_{2.5}$ and PM_{10} was associated with increased mortality due to COPD and that weak effects were observed between $\text{PM}_{2.5-10}$ and COPD mortality.

Conclusions: Our results provided evidence that the fine particles in air pollution have stronger functions on adverse health effects other than coarser particles in Southeastern China, which may be considered as a potential clinic target in PM-associated COPD.

Highlights

- To investigate the association between PMs and COPD mortality
- Generalized Additive Mixed Model was employed
- Daily exposure to PMs was associated with increased mortality due to COPD
- $\text{PM}_{2.5}$ have stronger functions on adverse health effects other than $\text{PM}_{2.5-10}$

Background

Chronic obstructive pulmonary disease (COPD), including emphysema and chronic bronchitis, is a serious public health issue. Approximately 174.5 million individuals worldwide suffer with COPD, which causes airflow blockage and a series of breathing problems [1, 2]. It was reported that more than 3 million people died of COPD each year, among whom about 30% died in China [3]. Although both internal and external risk factors have been proven to play crucial roles in COPD, evidence shows that external risk factors not only breakdown the functions of the lung and trachea but also are able to stimulate internal risk factors like susceptibility genes [2, 4–6]. Recently, investigations of effects of external risk factors like smoking and air pollution on COPD have gained increasing attention from both the public and government [4, 7, 8]. Although epidemiologic studies have revealed a solid boundary between smoking and COPD, 20% of COPD patients were still nonsmokers, suggesting the importance of the environment in COPD [9]. Therefore, understanding the effects of air pollution on COPD is of great value for its prevention and treatment.

Particulate matters (PMs), a complex of small particles and liquid droplets, are the main composition in air pollution. Increasingly evidence shows that PMs of different sizes exercise different functions on adverse health effects [10]. The effects of PMs in the respiratory system, for example, involve fine particles (with a diameter $\leq 2.5 \mu\text{m}$, $\text{PM}_{2.5}$) that are able to deposit deeper in the lung and bronchus, while coarser particles (with a diameter between 2.5 μm to 10 μm , $\text{PM}_{2.5-10}$) usually attach to the upper respiratory tract [11, 12]. Particle size may also influence the physicochemical properties of individual particles, which result in different outcomes [12–14]. Although the significant association between PM and COPD has been reported by many investigators worldwide, only a few studies focused on the diverse adverse health effect of $\text{PM}_{2.5}$ versus $\text{PM}_{2.5-10}$ [12, 13, 15]. Chen's study, which analyzed data in 272 cities throughout China, showed a significant association between daily cardiopulmonary mortality and short-term $\text{PM}_{2.5}$ or $\text{PM}_{2.5-10}$ exposure, respectively, providing useful insight of $\text{PM}_{2.5}$ versus $\text{PM}_{2.5-10}$ on adverse health effects, especially in a developing country like China [12, 15].

Zhejiang Province, located in southeastern China, is one of the top rapidly developing regions in China. It not only has big cities like Hangzhou (HZ) with air pollution because of industrialization, but also has smaller cities like Zhoushan (ZS) with better air quality, and other cities with environmental conditions in between. In our previous study, significant associations between $\text{PM}_{2.5}$ and respiratory diseases (RDs) were observed between HZ and ZS on mortality rates and outpatient visits [16]. In the present study, mortality cases from regions other than HZ and ZS in Zhejiang province were recruited to investigate the effects of $\text{PM}_{2.5}$, $\text{PM}_{2.5-10}$, and PM_{10} (particles with diameters $\leq 2.5 \mu\text{m}$).

Methods

Study area

Zhejiang Province is located in the Yangtze River Delta (YRD) region, which is considered one of the most rapidly developing regions in China. Due to its urbanized and industrialized processes, Zhejiang Province has severe PM pollution like many Chinese areas [17, 18]. We selected Hangzhou (HZ), Jinhua (JH), Lishui (LS), Ningbo (NB), Taizhou (TZ), and Zhoushan (ZS), all cities from Zhejiang Province, as survey cities, which account for 54.6% (6/11) of its total cities. The locations of the cities are shown in Fig. 1. The urban areas of each city were selected as survey areas due to the same cover of air-quality monitors and mortality.

Mortality data

Data on mortality were collected from the local mortality register of the Zhejiang Provincial Center for Disease Prevention and Control. Based on the 10th revision of the international classification of diseases and related health problems (ICD-10), the deaths due to RDs (RD: ICD-10 codes J00-99) and COPD (COPD: ICD-10 codes J40-44) were selected from January 1, 2014, to December 31, 2016, in HZ and ZS; January 1, 2015, to December 31, 2016, in JH and LS; and January 1, 2016, to December 31, 2016, in NB and TZ. Since deaths due to COPD accounted for 64.8% (13,066/20,168) of mortality due to RD according to the collected data, we selected COPD as the target disease in our study.

PM pollution and weather variables

Concentrations of $PM_{2.5}$, $PM_{2.5-10}$, and PM_{10} were monitored by ten environmental monitoring stations in urban areas of HZ, three urban areas of JH, three urban areas of LS, eight urban areas of NB, three urban areas of TZ, and one urban area of ZS during the study period. Twenty-four-hour means were applied for both air pollutants. The average of fixed monitoring stations in each city was used as the daily concentrations of $PM_{2.5}$, $PM_{2.5-10}$, and PM_{10} . To allow for the adjustment of weather conditions on mortality, we obtained daily mean temperature, atmospheric pressure, relative humidity, wind speed, and precipitation measurements for each city from the Zhejiang Meteorological Administration.

Statistical analyses

The descriptive statistics were calculated for COPD mortality, PM pollutants, and meteorological factors. The ANOVA test was used to compare the differences among cities with those variables, and the Spearman's correlation was used to evaluate the correlations among those variables.

We examined the acute effects of PM pollutants ($PM_{2.5}$, $PM_{2.5-10}$, and PM_{10}) on COPD mortality using the Generalized Additive Mixed Model, which was used to account for the random effect of a city to the additive predictor [19, 20]. A quasi-Poisson distribution was applied to account for overdispersion of daily deaths from COPD. In our model, several confounders were considered. Firstly, we adjusted possible variations in a week using dummy variables for day of the week (DOW). Then time trends, seasonal patterns, and weather conditions were controlled using penalized smoothing splines to exclude potential nonlinear effects on health [15, 21]. The degrees of freedom (df) for the splines were determined via generalized cross validation (GCV) [22, 23]. To examine the association with lag effect, we used the concentrations of PM pollutants from the current day (lag0) to the previous six days (lag6), as well as moving the average of current and previous 1, 2, and 3 day: lag01, lag02, lag03. We presented the results as Excess Risk (ER) with a 95% confident interval (CI) for COPD mortality per 10 $\mu\text{g}/\text{m}^3$ increase of PM pollutants. The model used appeared as follows:

$$\text{Log}[E(Y_t)] = \alpha + \beta PM_{t-i} + s(\text{time}, \text{df}) + s(X_t, \text{df}) + \text{re}(\text{city}) + \text{DOW}$$

where $E(Y_t)$ is the expectation of the number of daily COPD mortality at day t ; α is the intercept; PM_{t-i} is the concentration of PM pollutants in lag(i) day, $i = 0$ to 6 and 01 to 03; β is the regression coefficient; $s()$ refers to the function based on penalized smoothing splines; df is degrees of freedom; time represents temporal trend; X_t refers to the meteorological factors, such as daily mean temperature, atmospheric pressure, relative humidity, wind speed and precipitation; $\text{re}(\text{city})$ represents the random effect of city using categorical variables. DOW represents the dummy variables for the day of the week.

We further examined the nonlinear associations between PM pollutants and COPD mortality [24]. The lag time was selected according to the minimum values of AIC in the single lag model. To exhibit the nonlinear response more clearly, we generated expose-response curves to visualize the effects of PM pollutants on COPD mortality using the natural splines.

We used R software (version: 3.5.1; R Foundation for Statistical Computing, Vienna, Austria) to analyze the data in all analyses. The mgcv packages in R software were used to fit the GAMM model [25] (Wood and Scheipl, 2014). All statistical tests were two-sided, and the significance level was set at 0.05.

Results

Table 1 summarizes the daily COPD mortality, PM pollution, and weather conditions from 2014–2016 in Zhejiang Province. In the present study, the daily average death count due to COPD was 3, varying from 1 to 7 among six cities. The daily 24-hour mean concentrations of PM_{2.5}, PM_{2.5-10}, and PM₁₀ were 41.9, 22.3, and 64.1 µg/m³, respectively. The daily 24-hour mean concentrations among six cities were 29.7 to 56.8 µg/m³ for PM_{2.5}, 16.7 to 30.3 µg/m³ for PM_{2.5-10}, and 50.3 to 87.1 µg/m³ for PM₁₀, respectively. The daily mean temperature, pressure, relative humidity, wind speed and precipitation were 18.3°C, 1011 hpa, 77.3%, 1.88 m/s, and 5.08 mm, respectively. There were significant differences in COPD mortality, PM pollution, and weather conditions ($p < 0.01$) among six cities except precipitation ($p > 0.05$).

Table 1
Summary statistics of daily COPD mortality, PM pollutants, and weather conditions in Zhejiang Province, 2014–2016

City	Days	Year	COPD (death/day)	PM _{2.5} (µg/m ³)	PM _{2.5-10} (µg/m ³)	PM ₁₀ (µg/m ³)	Temperature (°C)	Pressure (hpa)	Relative humidity (%)	Wind speed (m/s)	Precipitation (mm)
All	4385	2014– 2016	3 ± 3	41.9 ± 27.1	22.3 ± 15.8	64.1 ± 38.0	18.3 ± 8.2	1011 ± 9	77.3 ± 13.0	1.88 ± 0.89	5.08 ± 12.2
HZ	1096	2014– 2016	7 ± 3	56.8 ± 31.5	30.3 ± 19.0	87.1 ± 44.7	17.8 ± 8.4	1011 ± 9	74.4 ± 13.9	2.15 ± 0.81	5.68 ± 11.8
JH	731	2015– 2016	1 ± 1	48.9 ± 26.8	16.7 ± 13.2	65.4 ± 34.8	18.8 ± 8.4	1009 ± 9	75.4 ± 14.0	1.70 ± 0.56	5.08 ± 11.6
LS	731	2015– 2016	1 ± 1	35.5 ± 21.4	16.8 ± 9.2	52.2 ± 26.9	19.4 ± 8.1	1009 ± 9	75.5 ± 11.3	1.05 ± 0.44	4.65 ± 10.9
NB	366	2016	3 ± 2	38.5 ± 22.9	23.4 ± 12.5	61.9 ± 33.1	18.3 ± 8.5	1015 ± 9	77.6 ± 11.2	2.55 ± 1.25	5.00 ± 14.1
TZ	366	2016	3 ± 2	35.7 ± 19.4	24.6 ± 13.0	60.3 ± 29.6	19.1 ± 8.2	1015 ± 9	81.9 ± 12.9	1.97 ± 0.75	4.99 ± 10.8
ZS	1095	2014– 2016	2 ± 1	29.7 ± 20.5	20.7 ± 15.8	50.3 ± 31.7	17.4 ± 7.7	1012 ± 9	81.1 ± 11.6	2.01 ± 0.85	4.84 ± 13.6
<i>F</i>			1272.24	157.83	108.65	145.47	7.87	60.86	47.33	261.56	0.80
<i>P</i>			0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.551

Table 2 shows the Spearman's correlation. COPD mortality was significantly correlated with the concentrations of PM_{2.5} ($r = 0.302, p < 0.01$), PM_{2.5-10} ($r = 0.282, p < 0.01$), PM₁₀ ($r = 0.323, p < 0.01$), wind speed ($r = 0.308, p < 0.01$), temperature ($r = -0.163, p < 0.01$), pressure ($r = 0.161, p < 0.01$), and relative humidity ($r = -0.0683, p < 0.01$), but not correlated with precipitation ($p > 0.05$). In addition, PM_{2.5} and PM_{2.5-10}, PM_{2.5} and PM₁₀, and PM₁₀ and PM_{2.5-10} were highly correlated ($r = 0.524, p < 0.01$, $r = 0.933, p < 0.01$, and $r = 0.772, p < 0.01$). Given that results obtained by combined effects of PM₁₀ with PM_{2.5} and PM_{2.5-10} may bring the multicollinearity, we did not select those in the multipollutant model.

Table 2

Spearman's correlation coefficients between daily COPD mortality, PM pollutants, and weather conditions in Zhejiang Province, 2014–2016

Variable	COPD (death/day)	PM _{2.5} ($\mu\text{g}/\text{m}^3$)	PM _{2.5-10} ($\mu\text{g}/\text{m}^3$)	PM ₁₀ ($\mu\text{g}/\text{m}^3$)	Temperature ($^{\circ}\text{C}$)	Pressure (hpa)	Relative humidity (%)	Wind speed (m/s)	Precipitation (mm)
COPD (death/day)	1								
PM _{2.5} ($\mu\text{g}/\text{m}^3$)	0.302**	1							
PM _{2.5-10} ($\mu\text{g}/\text{m}^3$)	0.282**	0.523**	1						
PM ₁₀ ($\mu\text{g}/\text{m}^3$)	0.323**	0.933**	0.772**	1					
Temperature ($^{\circ}\text{C}$)	-0.163**	-0.345**	-0.170**	-0.333**	1				
Pressure (hpa)	0.161**	0.294**	0.289**	0.342**	-0.869**	1			
Relative humidity (%)	-0.0683**	-0.309**	-0.471**	-0.423**	0.109**	-0.216**	1		
Wind speed (m/s)	0.308**	-0.159**	-0.010	-0.111**	-0.0486**	0.114**	-0.122**	1	
Precipitation (mm)	0.0256	-0.247**	-0.408**	-0.348**	-0.0157	-0.147**	0.637**	0.030	1
** $P < 0.01$									

Table 3 and Fig. 2 show the short-term associations between PM pollutants and COPD mortality over different lag days. We observed significant associations between COPD mortality and PM_{2.5} in lags of 1, 2, 3, 5, 7, 0–1, 0–2, and 0–3 days (ER = 1.03%, 95% CI: 0.361%, 1.70%; ER = 1.09%, 95% CI: 0.427%, 1.75%; ER = 0.868%, 95% CI: 0.214%, 1.53%; ER = 0.671%, 95% CI: 0.015%, 1.33%; ER = 0.751%, 95% CI: 0.096%, 1.41%; ER = 1.10%, 95% CI: 0.299%, 1.91%; ER = 1.55%, 95% CI: 0.668%, 2.44%; and ER = 1.85%, 95% CI: 0.895%, 2.82%, respectively). We also observed a significant association between COPD mortality and PM_{2.5-10} in lags of 2, 0–2, and 0–3 days (ER = 1.09%, 95% CI: 0.0680%, 2.13%; ER = 1.54%, 95% CI: 0.164%, 2.93%; ER = 1.50%, 95% CI: 0.058%, 2.95%, respectively). We also observed a significant association between COPD mortality and PM₁₀ in lags of 1, 2, 3, 5, 0–1, 0–2, and 0–3 days (ER = 0.711%, 95% CI: 0.236%, 1.19%; ER = 0.797%, 95% CI: 0.333%, 1.26%; ER = 0.504%, 95% CI: 0.0440%, 0.966%; ER = 0.495%, 95% CI: 0.0370%, 0.955%; ER = 0.764%, 95% CI: 0.189%, 1.34%; ER = 1.09%, 95% CI: 0.468%, 1.71%; and ER = 1.22%, 95% CI: 0.559%, 1.89%, respectively). Table 4 gives the adjusted effects of PM pollutant on COPD mortality. We found that the effects of PM_{2.5-10} on COPD mortality were not significant after they were adjusted for PM_{2.5} in either single or multiple lag models.

Table 3
Excess risk (95% confident intervals) of COPD mortality associated with a 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutants along different lags in Zhejiang Province, 2014–2016

Lag	PM _{2.5}	PM _{2.5-10}		PM ₁₀		
	ER(95% CI)	P	ER(95% CI)	P	ER(95% CI)	P
0	0.566(-0.152-1.29)	0.123	0.518(-0.713-1.76)	0.411	0.399(-0.129-0.930)	0.139
1	1.03(0.361-1.70)	0.002	0.815(-0.255-1.90)	0.136	0.711(0.236–1.19)	0.003
2	1.09(0.427–1.75)	0.001	1.09(0.0680–2.13)	0.037	0.797(0.333–1.26)	0.001
3	0.868(0.214–1.53)	0.009	0.165(-0.851-1.19)	0.752	0.504(0.044–0.97)	0.032
4	0.418(-0.237-1.08)	0.212	0.050(-0.957-1.07)	0.923	0.238(-0.220-0.698)	0.309
5	0.671(0.0150–1.33)	0.045	0.683(-0.321-1.70)	0.183	0.495(0.037–0.955)	0.034
6	0.625(-0.0310-1.29)	0.062	0.072(-0.932-1.09)	0.889	0.331(-0.128-0.792)	0.158
7	0.751(0.096–1.41)	0.025	-0.091(-1.09-0.92)	0.860	0.345(-0.113-0.805)	0.140
01	1.10(0.299–1.91)	0.007	0.992(-0.311-2.31)	0.136	0.764(0.189–1.34)	0.009
02	1.55(0.668–2.44)	0.001	1.54(0.164–2.93)	0.028	1.09(0.468–1.71)	0.001
03	1.85(0.895–2.82)	0.000	1.50(0.058–2.95)	0.041	1.22(0.559–1.89)	0.000

Table 4
Excess risk (95% confident intervals) of COPD mortality associated with a 10 $\mu\text{g}/\text{m}^3$ increase in PM pollutants with multipollutant model in Zhejiang Province, 2014–2016

Pollutants	Lag	ER(95% CI)	P
PM _{2.5} (Adjusted PM _{2.5-10})	2	0.908(0.164–1.66)	0.017
	03	1.71(0.634–2.79)	0.002
PM _{2.5-10} (Adjusted PM _{2.5})	2	0.604(-0.558-1.78)	0.310
	02	0.482(-1.04-2.02)	0.536

Figure 3 revealed the exposure-response curves for daily concentrations of PM pollutants associated with COPD mortality. According to the AIC values of each lag model, we selected lag 2 for single-day and lag 03 for multiple-day as lag time, except PM_{2.5-10}, in which we selected lag 02 for multiple-day. A visual inspection suggested nonlinear effects on COPD mortality both in PM_{2.5} and PM₁₀ for lag 2 were more obvious than those for lag03. As shown in Fig. 3, the nonlinear effects on COPD mortality for PM_{2.5} and PM₁₀ in lag03 and PM_{2.5-10} in lag2 and lag02 were negligible.

Discussions

In the present study, investigation using 13,066 deaths from 2014 to 2016 among six cities in Zhejiang Province revealed that daily exposure to PM_{2.5} and PM₁₀ was associated with increased mortality due to COPD, and that fewer effects were observed between PM_{2.5-10} and COPD mortality, suggesting that the fine particles in air pollution have stronger functions on adverse health effects other than coarser particles, which may be considered as a potential clinic target in PM-associated COPD.

Our previous study provided evidence that both the mortality rates and outpatient visits for RDs were significantly associated with air pollution among which PM_{2.5} plays a crucial role in two typical cities (HZ and ZS) in Zhejiang Province [16]. In order to further investigate the effects of particulates with different diameters, more data with a longer period from six cities with different air conditions in Zhejiang Province were collected. Our results showed that the average death rate due to COPD varied sharply among the six cities, which may be due to differences in economic level, medical level, or population size of those cities, although differences in PM pollutants among six cities may contribute to the change in health effects to some extent. Therefore, we compared the death counts in the same cover of air-quality monitors stratified by the city and applied the GAMM to account for the random effects from a different city. The positive correlation between COPD mortality and the concentrations of PM_{2.5}, PM_{2.5-10}, and PM₁₀ preliminarily indicated the increase in concentrations of PM pollutants may result in the increase

in mortality counts due to COPD. The significant effects of meteorological factors on COPD mortality were also found. Thus, we controlled the effects of weather conditions in our model with covariates.

Both $PM_{2.5}$ and PM_{10} significantly affected the COPD mortality in this study, which was similar to some previous epidemiologic studies. The significant association with COPD mortality was observed in two cohort studies from 34 cities in the United States (ER:22% for PM_{10}) [26] and Norway (Male ER: 29% for PM_{10} and 27% for $PM_{2.5}$; Female ER: 6% for PM_{10} and 9% for $PM_{2.5}$) [27]. A case-crossover study from Barcelona found increased PM_{10} associated with the higher mortality of COPD (ER:11%) [28]. Another time series study from 10 US cities [29] and Hong Kong [30] also found the increased COPD mortality risk was associated with PM_{10} (ER: 1.7% for the United States and 1.0% for Hong Kong). On the other side, several studies only observed significant associations in specific groups. A time series study in Netherlands reported the effect of PM_{10} on COPD mortality was found in some age groups [31]. Moreover, a cross-sectional study in Japan also only observed the significant association between $PM_{2.5}$, PM_{10} pollutants, and COPD mortality in females [22]. Compared with the ER values in previous studies, we found the values in cohort and case-crossover studies were largely higher than those in a time series design, which was in part due to the bigger power of the test in cohort and case-crossover design. Meanwhile, the ER values in this time series study were consistent with the results from other time series studies [29, 30]. Best lags for $PM_{2.5}$ and PM_{10} were lag 2 for single-day and lag 03 for multiple-day, respectively. Those were similar to the Hong Kong study [30], and differ from the US study [29], which suggested delay effects are varied in different regions partly owing to spatial variation of pollutants.

The particulate air pollution problem is one of the severest problems that a country normally would be facing during an industrialization process and social development. As one of the largest developing countries in the world, China is going through this particular process, and Zhejiang Province is China in miniature in a sense, as it is located in Yangtze River Delta (YDR) region, one of the fastest developing areas in the country. Therefore, analysis using data from six cities with varying environment conditions in Zhejiang Province may provide solid evidence to estimate the relationship between particulate air pollution and health problems in China to a certain extent.

As we all know, $PM_{2.5}$ was the most widely used risk indicator when the disease burden of ambient air pollution was estimated, but adverse health effects of exposure to $PM_{2.5-10}$ were not well understood. So far, only a few epidemiologic studies focus on the effects of $PM_{2.5-10}$ [11, 32–36], most of which were conducted in developed countries, not the part facing severe air pollution in the world. Powell et al. [35] found statistically significant evidence that daily variation in $PM_{2.5-10}$ was associated with emergency hospitalizations for cardiovascular diseases among Medicare enrollees ≥ 65 years of age, which was after adjusting for $PM_{2.5}$ [35]. A meta-analysis showed that short-term $PM_{2.5-10}$ exposure was related to increased mortality of respiratory and cardiovascular diseases, but the relationship became weaker and yielded less precise effect estimates after adjustment for $PM_{2.5}$ and publication bias [13]. These results are consistent with our finding that COPD mortality was associated to $PM_{2.5}$ and PM_{10} , but weak and less association between $PM_{2.5-10}$ and COPD mortality was observed after adjustment for $PM_{2.5}$, indicating that fine particulates rather than coarser ones may have stronger effects on COPD patients. Similar results were also observed in another study based on data from 272 cities throughout China. It found significant associations between short-term $PM_{2.5-10}$ exposure and daily non-accidental and cardiopulmonary mortality, but a city-specific situation was observed [12].

The limitations of the present analysis should also be noted. One limitation of our study was that although Zhejiang Province is a good representative area in China, only six cities in Zhejiang Province were recruited. Therefore, more cities in Zhejiang Province and even more provinces should be included in further studies. Another limitation was that the study period in each city was not identical due to the data system of each city. Therefore, data from longer periods are better to be used as the basis of analysis. Additionally, data of morbidity rate and outpatient visits should also be analyzed in future studies.

Conclusions

In conclusion, significant and strong associations between COPD mortality and $PM_{2.5}$ as well as PM_{10} were observed using data from six cities in Zhejiang Province in the present study. $PM_{2.5-10}$ was also significantly related to COPD mortality but with much weaker effects. Our results provided evidence that fine particulate matter has worse adverse health effects on respiratory disease from an epidemiologic point of view.

Declarations

Availability of data and materials

The dataset used and/or analyzed in this study are available under requested at public institutions: Zhejiang Environmental Institute (<http://sthjt.zj.gov.cn>) and Zhejiang Meteorological Administration (<http://zj.cma.gov.cn>).

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval was obtained from the ethics committee of the Zhejiang Provincial Centre for Disease Prevention and Control

Competing interests

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.

Funding

This work has been supported by National Natural Science Foundation of China (81300641, 81502786, 81670833), Medical Scientific Research Foundation of Zhejiang Province, China (2019KYA053, 2020KY093, 2020KY514, 2020KY516), Science and Technology Program of Zhejiang (2014C03025), Natural Science Foundation of Zhejiang Province (LQ14H260003), Zhejiang Province Key Research and Development Program(2015C03042, 2019C03091), the Fundamental Research Funds for the Central Universities (2019QNA7026).

Authors' contributions

Zhijian Chen, Qiuli Fu, Zhe Mo: Conceptualization, Methodology, Software, Data curation, Writing-Original draft preparation. Zhifang Wang, Xuejiao Pan: Data curation, Writing- Original draft preparation. Guangming Mao, Peiwei Xu, Dandan Xu: Visualization, Investigation. Xiaoming Lou, Xiaofeng Wang: Supervision. Lizhi Wu: Software, Validation. Yuan Chen: Writing- Reviewing and Editing.

Acknowledgments

The authors would like to acknowledge the Zhejiang Environmental Institute and Zhejiang Meteorological Administration for providing the dataset.

References

1. Collaborators: Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med* 2017, 5(9):691-706.
2. Hart JE, Grady ST, Laden F, Coull BA, Koutrakis P, Schwartz JD, Moy ML, Garshick E: Effects of Indoor and Ambient Black Carbon and [Formula: see text] on Pulmonary Function among Individuals with COPD. *Environ Health Perspect* 2018, 126(12).
3. Li J, Qin C, Lv J, Guo Y, Bian Z, Zhou W, Hu J, Zhang Y, Chen J, Cao W *et al*: Solid Fuel Use and Incident COPD in Chinese Adults: Findings from the China Kadoorie Biobank. *Environ Health Perspect* 2019, 127(5).
4. Rich DQ, Kipen HM, Huang W, Wang G, Wang Y, Zhu P, Ohman-Strickland P, Hu M, Philipp C, Diehl SR *et al*: Association between changes in air pollution levels during the Beijing Olympics and biomarkers of inflammation and thrombosis in healthy young adults. *Jama* 2012, 307(19):2068-2078.
5. Chen ZH, Wu YF, Wang PL, Wu YP, Li ZY, Zhao Y, Zhou JS, Zhu C, Cao C, Mao YY *et al*: Autophagy is essential for ultrafine particle-induced inflammation and mucus hyperproduction in airway epithelium. *Autophagy* 2016, 12(2):297-311.
6. Chen S, Gu Y, Qiao L, Wang C, Song Y, Bai C, Sun Y, Ji H, Zhou M, Wang H *et al*: Fine Particulate Constituents and Lung Dysfunction: A Time-Series Panel Study. *Environ Sci Technol* 2017, 51(3):1687-1694.
7. Huang W, Wang G, Lu SE, Kipen H, Wang Y, Hu M, Lin W, Rich D, Ohman-Strickland P, Diehl SR *et al*: Inflammatory and oxidative stress responses of healthy young adults to changes in air quality during the Beijing Olympics. *Am J Respir Crit Care Med* 2012, 186(11):1150-1159.
8. Comer DM, Kidney JC, Ennis M, Elborn JS: Airway epithelial cell apoptosis and inflammation in COPD, smokers and nonsmokers. *Eur Respir J* 2013, 41(5):1058-1067.

9. Lamprecht B, McBurnie MA, Vollmer WM, Gudmundsson G, Welte T, Nizankowska-Mogilnicka E, Studnicka M, Bateman E, Anto JM, Burney P *et al*: COPD in never smokers: results from the population-based burden of obstructive lung disease study. *Chest* 2011, 139(4):752-763.
10. Zhou T, Hu Y, Wang Y, Sun C, Zhong Y, Liao J, Wang G: Fine particulate matter (PM_{2.5}) aggravates apoptosis of cigarette-inflamed bronchial epithelium in vivo and vitro. *Environ Pollut* 2019, 248:1-9.
11. Peng RD, Chang HH, Bell ML, McDermott A, Zeger SL, Samet JM, Dominici F: Coarse particulate matter air pollution and hospital admissions for cardiovascular and respiratory diseases among Medicare patients. *Jama* 2008, 299(18):2172-2179.
12. Chen R, Yin P, Meng X, Wang L, Liu C, Niu Y, Liu Y, Liu J, Qi J, You J *et al*: Associations between Coarse Particulate Matter Air Pollution and Cause-Specific Mortality: A Nationwide Analysis in 272 Chinese Cities. *Environ Health Perspect* 2019, 127(1).
13. Adar SD, Filigrana PA, Clements N, Peel JL: Ambient Coarse Particulate Matter and Human Health: A Systematic Review and Meta-Analysis: *Curr Environ Health Rep*. 2014 Aug 8;1(3):258-274. doi: 10.1007/s40572-014-0022-z. eCollection 2014.; 2014.
14. Kim KH, Kabir E, Kabir S: A review on the human health impact of airborne particulate matter. *Environ Int* 2015, 74:136-143.
15. Chen R, Yin P, Meng X, Liu C, Wang L, Xu X, Ross JA, Tse LA, Zhao Z, Kan H *et al*: Fine Particulate Air Pollution and Daily Mortality. A Nationwide Analysis in 272 Chinese Cities. *Am J Respir Crit Care Med* 2017, 196(1):73-81.
16. Mo Z, Fu Q, Zhang L, Lyu D, Mao G, Wu L, Xu P, Wang Z, Pan X, Chen Z *et al*: Acute effects of air pollution on respiratory disease mortalities and outpatients in Southeastern China. *Sci Rep* 2018, 8(1):018-19939.
17. Zhang Y-L, Cao F: Fine particulate matter (PM 2.5) in China at a city level. *Scientific reports* 2015, 5:14884-14884.
18. Wang J, Zhao B, Wang S, Yang F, Xing J, Morawska L, Ding A, Kulmala M, Kerminen VM, Kujansuu J *et al*: Particulate matter pollution over China and the effects of control policies. *Sci Total Environ* 2017, 585:426-447.
19. Yang L, Qin G, Zhao N, Wang C, Song G: Using a generalized additive model with autoregressive terms to study the effects of daily temperature on mortality. *BMC Med Res Methodol* 2012, 12(165):1471-2288.
20. Li W, Cao Y, Li R, Ma X, Chen J, Wu Z, Xu Q: The spatial variation in the effects of air pollution on cardiovascular mortality in Beijing, China. *J Expo Sci Environ Epidemiol* 2018, 28(3):297-304.
21. Peng RD, Dominici F, Louis TA: Model choice in time series studies of air pollution and mortality. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 2006, 169(2):179-203.
22. Iwai K, Mizuno S, Miyasaka Y, Mori T: Correlation between suspended particles in the environmental air and causes of disease among inhabitants: cross-sectional studies using the vital statistics and air pollution data in Japan. *Environ Res* 2005, 99(1):106-117.
23. Wood S: mgcv: Mixed GAM Computation Vehicle with GCV/AIC/REML smoothness estimation. In.; 2012.
24. Shen Y, Wu Y, Chen G, Van Grinsven HJM, Wang X, Gu B, Lou X: Non-linear increase of respiratory diseases and their costs under severe air pollution. *Environ Pollut* 2017, 224:631-637.
25. Wood S, Scheipl F: Gamm4: Generalized additive mixed models using mgcv and lme4. In.; 2014.
26. Zanobetti A, Bind MA, Schwartz J: Particulate air pollution and survival in a COPD cohort. *Environ Health* 2008, 7(48):7-48.
27. Naess Ø, Nafstad P, Aamodt G, Claussen B, Rosland P: Relation between concentration of air pollution and cause-specific mortality: four-year exposures to nitrogen dioxide and particulate matter pollutants in 470 neighborhoods in Oslo, Norway. *Am J Epidemiol* 2007, 165(4):435-443.
28. Sunyer J, Basagaña X: Particles, and not gases, are associated with the risk of death in patients with chronic obstructive pulmonary disease. *Int J Epidemiol* 2001, 30(5):1138-1140.
29. Braga AL, Zanobetti A, Schwartz J: The lag structure between particulate air pollution and respiratory and cardiovascular deaths in 10 US cities. *J Occup Environ Med* 2001, 43(11):927-933.
30. Wong TW, Tam WS, Yu TS, Wong AH: Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. *Occup Environ Med* 2002, 59(1):30-35.
31. Fischer P, Hoek G, Brunekreef B, Verhoeff A, van Wijnen J: Air pollution and mortality in The Netherlands: are the elderly more at risk? *Eur Respir J Suppl* 2003, 40(10):00402503.
32. Zanobetti A, Schwartz J: The effect of fine and coarse particulate air pollution on mortality: a national analysis. *Environ Health Perspect* 2009, 117(6):898-903.
33. Chen R, Li Y, Ma Y, Pan G, Zeng G, Xu X, Chen B, Kan H: Coarse particles and mortality in three Chinese cities: the China Air Pollution and Health Effects Study (CAPES). *Sci Total Environ* 2011, 409(23):4934-4938.
34. Samoli E, Stafoggia M, Rodopoulou S, Ostro B, Declercq C, Alessandrini E, Díaz J, Karanasiou A, Kelessis AG, Le Tertre A *et al*: Associations between fine and coarse particles and mortality in Mediterranean cities: results from the MED-PARTICLES project. *Environ Health Perspect* 2013, 121(8):932-938.

35. Powell H, Krall JR, Wang Y, Bell ML, Peng RD: Ambient Coarse Particulate Matter and Hospital Admissions in the Medicare Cohort Air Pollution Study, 1999-2010. *Environ Health Perspect* 2015, 123(11):1152-1158.
36. Yorifuji T, Kashima S, Doi H: Associations of acute exposure to fine and coarse particulate matter and mortality among older people in Tokyo, Japan. *Sci Total Environ* 2016, 542(Pt A):354-359.

Figures

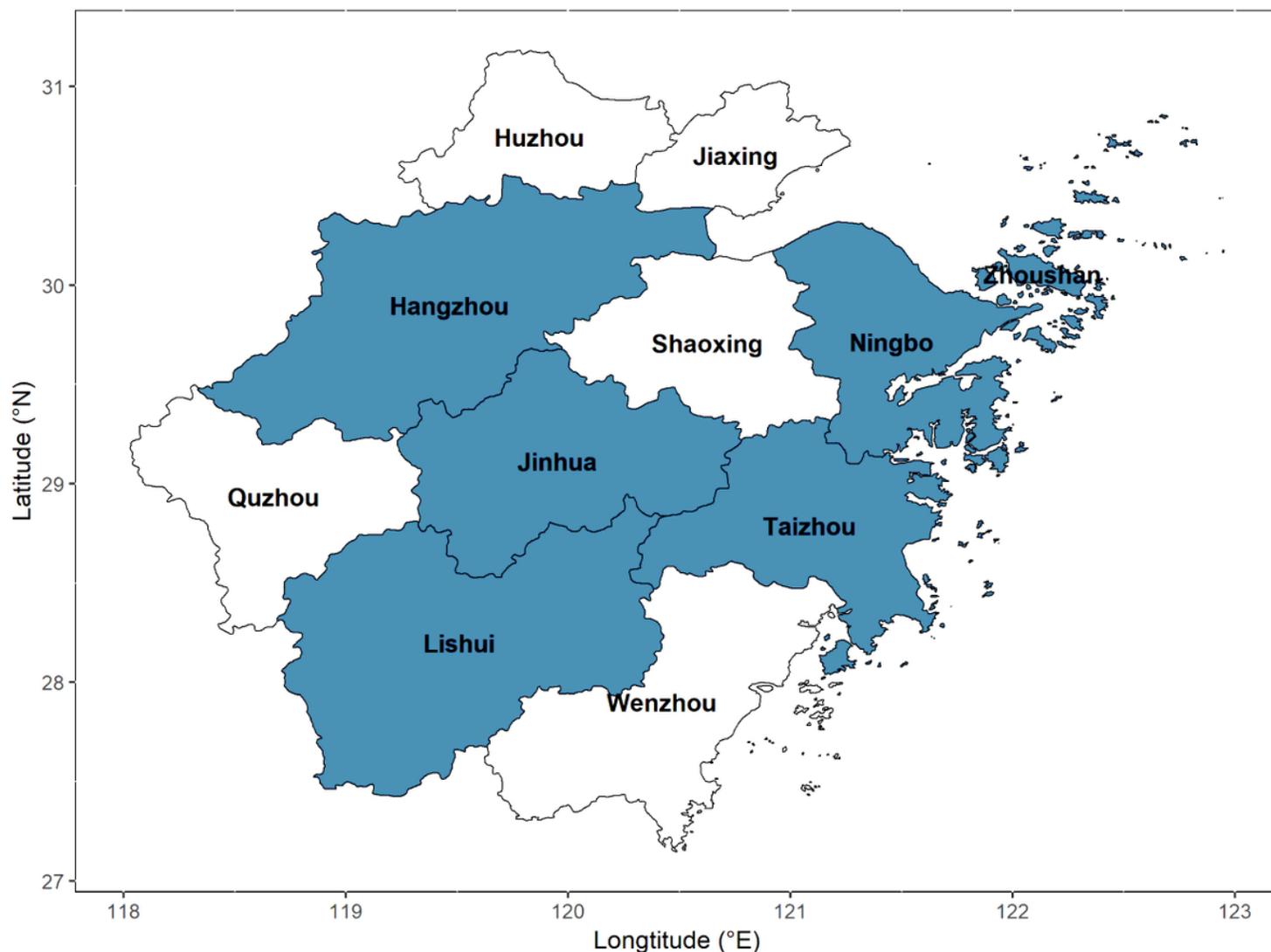


Figure 1

Map of Zhejiang Province, China, highlighting the cities of Hangzhou, Jinhua, Lishui, Ningbo, Taizhou, and Zhoushan as survey areas. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

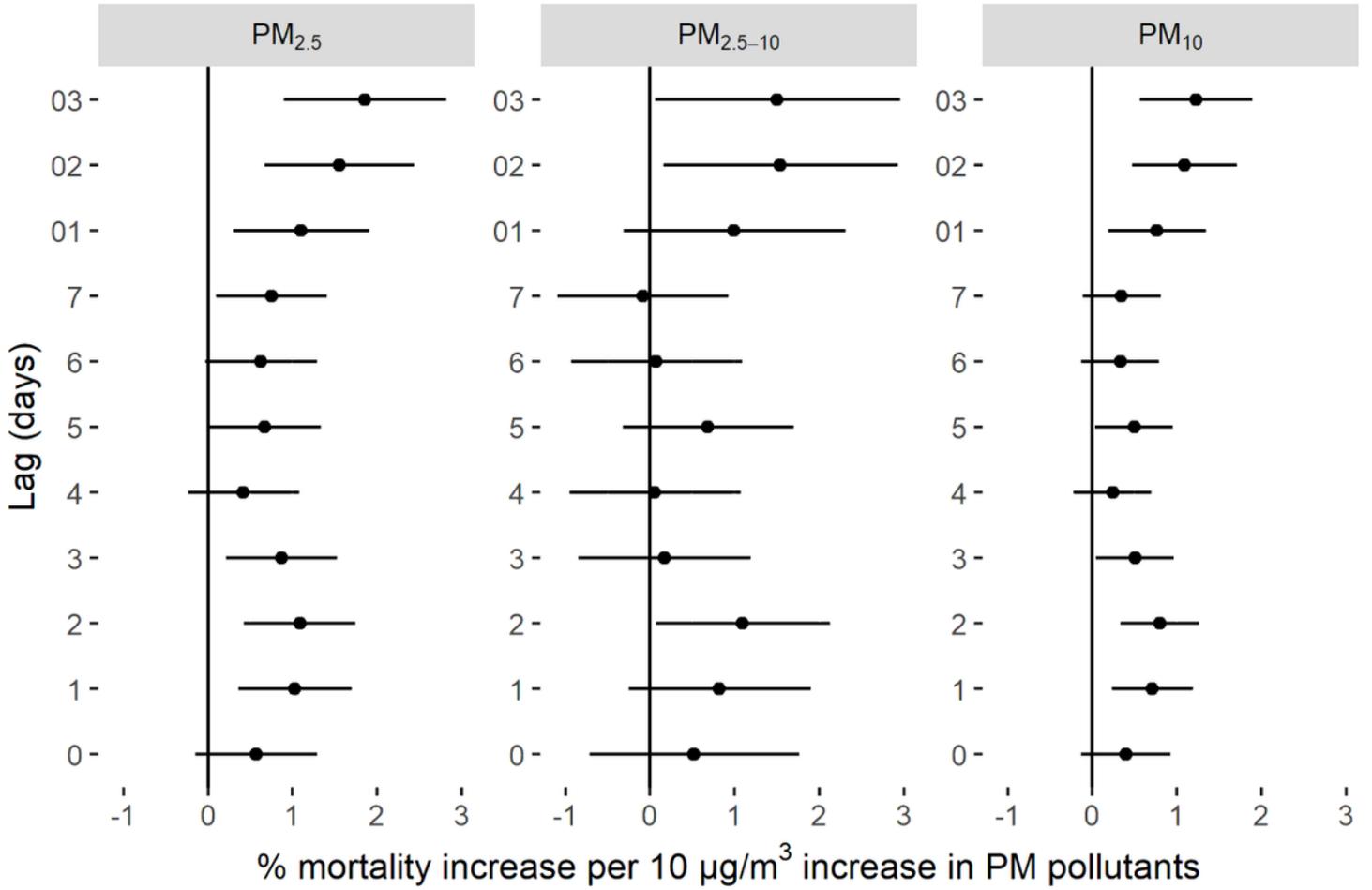


Figure 2

Excess risk (95% confident intervals) of COPD mortality associated with a 10 µg/m³ increase in PM pollutants in Zhejiang Province, 2014-2016.

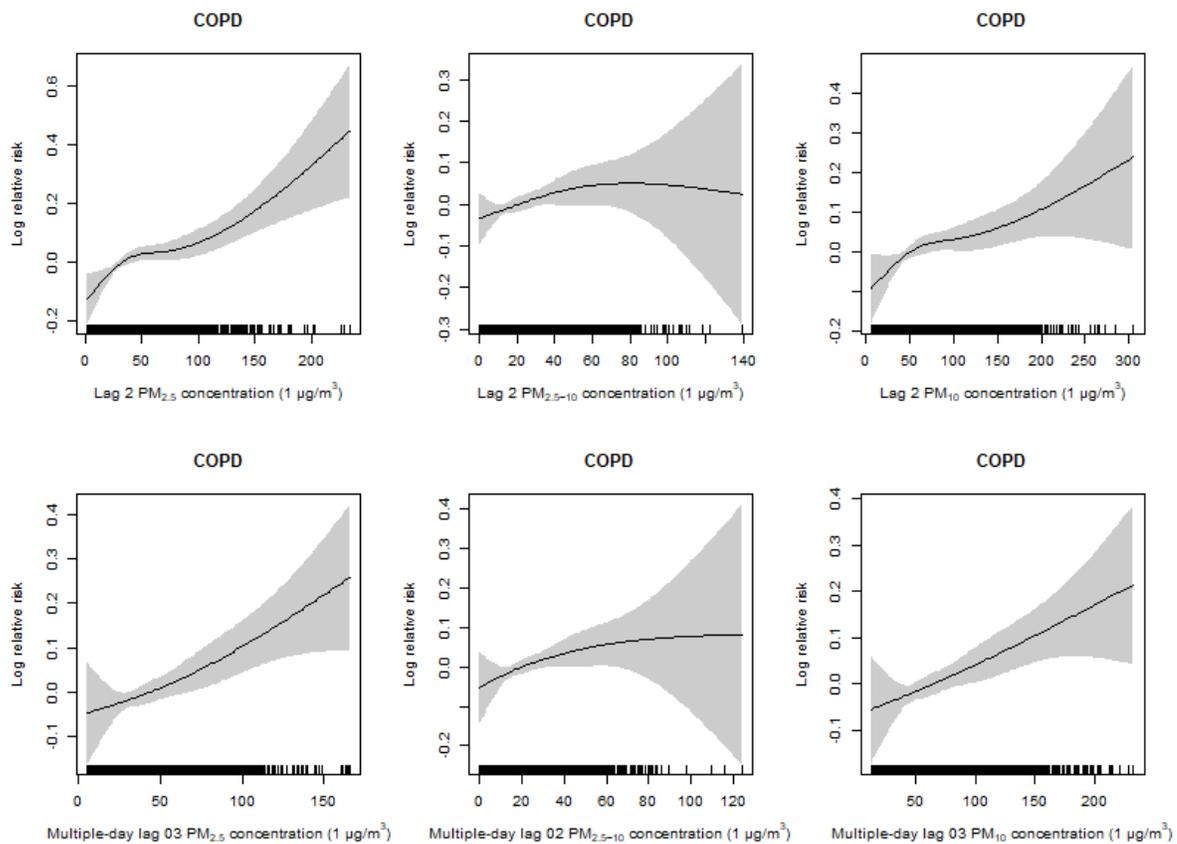


Figure 3

Exposure-response curves for daily concentrations of PM pollutants associated with COPD mortality in Zhejiang Province, 2014–2016