

# Association Between Ambient Air Pollution and Mortality From Chronic Obstructive Pulmonary Disease in Wuhan, China: a Population-based Time-series Study

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## Research

**Keywords:** air pollution, short-term effects, COPD mortality, time-series

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## Abstract

**Background:** Previous studies have mainly focused on the associations between air pollution and total respiratory disease mortality. However, evidence on the short-term effects of air pollution on chronic obstructive pulmonary disease (COPD) mortality is still not conclusive to date. The aim of this study was to investigate the short-term effects of ambient air pollution on COPD mortality in Wuhan China.

**Methods:** Daily death numbers, concentrations of air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub>) and meteorological characteristics in Wuhan between January 1, 2014 to December 31, 2019 were collected. Time-series analysis using generalized additive model was applied to evaluate the association between ambient air pollution and daily COPD mortality. Subgroup analysis by age (<65 and ≥65 year) and sex (male and female) were also conducted.

**Results:** During the study period, we observed a total of 16150 deaths (7.37 deaths per day) from COPD. The daily average concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub> were 59.03, 90.48, 12.91, 48.84 and 91.77 µg/m<sup>3</sup>, respectively. In single pollutant model, for every increase of 10 µg/m<sup>3</sup> in PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> levels, COPD mortality increased by 0.581% (95CI:0.054%-1.111%), 4.316%(95CI:1.002%-7.738%) and 1.815%(95CI:0.523%-3.125%) at lag03, respectively. No significant associations were found for PM<sub>2.5</sub> and O<sub>3</sub>. Subgroup analysis demonstrated that females were more susceptible to PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub>, in addition the concentrations of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> were significantly associated with COPD mortality for older adults. In two-pollutant models, the significantly positive associations between SO<sub>2</sub> as well as NO<sub>2</sub> and COPD mortality remained after adjusting for PM<sub>2.5</sub> or O<sub>3</sub>.

**Conclusions:** Short-term exposure to PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> are significantly associated with a higher risk of COPD mortality. Female or elderly are more susceptible to air pollution. Further research is required to reveal the underlying mechanisms. The implementation of the environmental protection policy has become urgent.

## Background

With the rapid development of modern industry and social economy, air pollution has become a common global problem that cannot be neglected in recent years. China is a developing country and the magnitude is quite different from developed countries. Especially in several megacities, air pollution has become a major threat to public health. In 2010, air pollution is the fourth burden of disease in China, which lead to 1.234 million deaths and 250 million disability adjusted life yeas (DALY)[1]. Wuhan, as the capital city of Hubei province, has a large population of about 11.21 million. The air pollution is severe because of the drastic urbanization and industrial expansion. During 2013 to 2017, average annual limit of PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub> were 1.3 ~ 1.8, 1.5 ~ 2.7 and 1.2 ~ 1.5 times higher than the annual average acceptable limit, respectively[2]. Therefore, exploring the associations between air pollution and health in Wuhan is of great importance.

Since 1990s, numerous evidences have found that short term exposure to ambient air pollution can increase the risk of adverse health effects, ranging from sub-health status to death, especially respiratory disorders[3–6]. It is accepted that air pollution can disturb the function of respiratory system. Particulate matter may exert oxidative stress on cells in the lung by presenting or by stimulating the cells to produce reactive oxygen species (ROS) and inflammatory factors, and these play important roles in lung tissue injury[7–9]. Chronic respiratory diseases represent a substantial health-care burden in China, and chronic obstructive pulmonary disease (COPD) is the third most common causes of mortality, with 910809 deaths in 2013[1]. Cohort and case crossover studies have shown that ambient air pollution has contributed to increased incidence and prevalence of COPD[10]. Among individuals with COPD, the air pollutants are associated with loss of lung function and increase respiratory symptoms[11]. So ambient air pollutants are also associated with COPD exacerbations and mortality. The World Health Organization (WHO) estimates that ambient air pollution is responsible for 3.7 million premature death worldwide in 2012 and 14% of these deaths are due to COPD or acute lower respiratory infections[12]. It is urgent to further investigate the effects of ambient air pollution exposure on COPD mortality.

Many researches have explored the health effects of air pollution with time-series methods[13–17], but few studies specific measured the association between ambient air pollution and COPD mortality. Furthermore, the characteristics of air pollution in different regions vary substantially. Hence, the aim of this study was to investigate the associations between the concentrations of ambient PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub> and COPD mortality in Wuhan, China.

## Methods

### Data collection

Death counts between January 1, 2014 to December 31, 2019 were obtained from Mortality Register System in Wuhan Center for Disease Control and Prevention. For this analysis, we selected the deaths due to COPD, which were classified according to the International Statistical Classification of Disease, 10th Revision codes (ICD-10: J40-J44, I27.9). In view of the vast majority of pulmonary heart diseases (I27.9) were caused by chronic bronchitis and emphysema, few were caused by pulmonary embolism, primary pulmonary hypertension, kyphoscoliotic heart disease and so on, all pulmonary heart disease would be included in COPD. Date of death, cause of death, sex and age were collected. Because the death data were surveillance data, there was no requirement for informed consent. This study was approved by the Ethical committee of Wuhan Center for Disease Control and Prevention, and was conducted in compliance with the tenets of the Declaration of Helsinki. The results were reported according to the STORBE statement.

Wuhan is located in central China (29°58'-31°22'N, 113°41'-115°05'E), with an area of 8,569 km<sup>2</sup>. 10 national air quality monitoring stations have been established. In this study, daily average concentrations of air pollutants including PM<sub>2.5</sub> (mass of particles with aerodynamic diameter < 2.5 μm), PM<sub>10</sub> (mass of particles with aerodynamic diameter < 10 μm), SO<sub>2</sub> (sulfur dioxide), NO<sub>2</sub> (nitrogen dioxide) and O<sub>3</sub> (ground-level ozone) during January 1, 2014 to December 31, 2019 were obtained from Wuhan Ecology and Environmental Bureau.

Daily meteorological data, including daily mean temperature, atmospheric pressure and relative humidity during the same period, were obtained from Wuhan Meteorological Administration.

### Statistical analysis

Daily COPD mortality, air pollutants and meteorological data were described as mean, standard deviation (SD) and quartile. Spearman's correlation was used to estimated the associations between air pollutants and meteorological factors.

For the time-series analysis, daily COPD mortality data was low, belonging to small probability event and approximately followed the Poisson distribution. Therefore, generalized additive Poisson regression with a log-link function was conducted to assess the association between daily counts of COPD mortality and air pollutants concentrations. The model is as below:

$$\log[E(Y_t)] = \alpha + \beta X_t + DOW + s(\text{time}, df) + s(Z_t, df)$$

In this equation,  $t$  refers to the day of the observation;  $Y_t$  is the observed daily death counts on day  $t$ ;  $E(Y_t)$  is the expected daily death count on day  $t$ ;  $\alpha$  is the intercept of the model,  $\beta$  represents the regression coefficient for each air pollutant;  $X_t$  is the air pollutant concentrations at day  $t$ ;  $Z_t$  represents meteorological data at day  $t$ ;  $DOW$  is the dummy variable for day of the week;  $s$  is the smoothing spline function for the nonlinear variables such as temperature, humidity, atmospheric pressure and calendar time. We used the value of Akaike information criterion (AIC) to determine the degrees of freedom ( $df$ ) and the smaller AIC value indicating the preferred model. Finally, we selected 7  $df$  per year for the time to adjust the time trend and seasonality, and 3  $df$  were used for temperature, humidity and atmospheric pressure. Regarding the concentrations of air pollutants, we estimated the associations with different lag structures using single lag from the current day up to the previous 5 days (lag0-lag5), as well as moving averages of the current and previous days (lag01-lag05). After the working model containing all control variables was built, the air pollutants were included separately. Subgroup analyses by age (< 65, ≥ 65) and sex (males, females) were also conducted. Elderly was defined as older than 65 years old. Furthermore, we used two-pollutant models for all pollutants without interactions to determine the possible role of single pollutants.

The association between air pollutants and COPD mortality was reported as excess relative risk (ERR) with 95% confidence interval (CI) for 10 µg/m<sup>3</sup> increase in PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub> concentrations. All statistical analysis were performed using R (version 4.0.2) packages “mgcv” and “nlme”. Statistical significance was defined as a two-tailed  $P < 0.05$ .

## Results

Table 1 presented the descriptive statistics for daily number of COPD death, air pollutants and meteorological data from January 1, 2014 to December 31, 2019. During the 6-year period, there were 16150 deaths (7.37 deaths per day) from COPD in Wuhan. Daily death counts were higher in males than females (4.81 vs. 2.56 deaths per day). Death among elderly (older than 65 years old) accounted for 92.28% and the daily mean was 6.80. The daily mean concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub> were 59.03, 90.48, 12.91, 48.84 and 91.77 µg/m<sup>3</sup>, respectively. And the average of atmospheric pressure, relative humidity and daily temperature were 1013.10 kPa, 79.42% and 17.18°C.

Table 1  
Descriptive statistics of daily mortality counts, air pollutants concentrations and meteorological parameters in Wuhan, China, during 2014–2019.

Variables	Mean(SD)	Min	P25	P50	P75	Max
Number of COPD deaths						
Total	7.37(3.56)	0	5	7	9	21
Males	4.81(2.57)	0	3	4	6	16
Females	2.56(1.88)	0	1	2	4	12
< 65 years	0.57(0.79)	0	0	0	1	4
≥ 65 years	6.80(3.35)	0	4	6	9	21
Air Pollutants						
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	59.03(40.20)	5.00	31.23	48.62	75.62	300.89
PM <sub>10</sub> (µg/m <sup>3</sup> )	90.48(50.28)	7.56	53.00	81.56	117.78	532.00
SO <sub>2</sub> (µg/m <sup>3</sup> )	12.91 (10.23)	2.33	6.22	10.00	15.56	101.33
NO <sub>2</sub> (µg/m <sup>3</sup> )	48.84(20.60)	9.78	32.93	45.00	61.20	125.33
O <sub>3</sub> (µg/m <sup>3</sup> )	91.77(50.43)	5.33	51.00	85.33	128.00	261.50
Meteorological variables						
Air pressure (kPa)	1013.10(9.40)	993.50	1004.90	1013.10	1020.40	1043.00
Relative humidity (%)	79.42(10.27)	41.00	73.00	80.00	87.00	100.00
Temperature(°C)	17.18(9.16)	-3.80	9.10	18.15	24.90	33.90

The daily concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> were strongly and positively correlated with each other, as shown in Table 2. In contrast, the daily concentrations of O<sub>3</sub> was moderately and negatively correlated with those of the other pollutants. In addition, air pressure was positively and temperature was negatively correlated with all air pollutants except for O<sub>3</sub> ( $r_{hpa-O_3} = -0.55$ ,  $P < 0.001$ ;  $r_{tem-O_3} = 0.68$ ,  $P < 0.001$ ). Relative humidity was negatively correlated with the five air pollutants ( $P < 0.01$ ).

Table 2  
Spearman's correlation between air pollutants and meteorological factors in Wuhan, China, during 2013–2019

	PM <sub>2.5</sub>	PM <sub>10</sub>	SO <sub>2</sub>	NO <sub>2</sub>	O <sub>3</sub>	Air pressure	Relative humidity	Temperature
PM <sub>2.5</sub>	1.00							
PM <sub>10</sub>	0.84 <sup>a</sup>	1.00						
SO <sub>2</sub>	0.68 <sup>a</sup>	0.73 <sup>a</sup>	1.00					
NO <sub>2</sub>	0.70 <sup>a</sup>	0.77 <sup>a</sup>	0.72 <sup>a</sup>	1.00				
O <sub>3</sub>	-0.22 <sup>a</sup>	-0.08 <sup>a</sup>	-0.03	-0.07 <sup>b</sup>	1.00			
Air pressure	0.49 <sup>a</sup>	0.29 <sup>a</sup>	0.41 <sup>a</sup>	0.38 <sup>a</sup>	-0.55 <sup>a</sup>	1.00		
Relative humidity	-0.07 <sup>b</sup>	-0.36 <sup>a</sup>	-0.37 <sup>a</sup>	-0.15 <sup>a</sup>	-0.44 <sup>a</sup>	-0.04	1.00	
Temperature	-0.53 <sup>a</sup>	-0.26 <sup>a</sup>	-0.37 <sup>a</sup>	-0.38 <sup>a</sup>	0.68 <sup>a</sup>	-0.91 <sup>a</sup>	-0.12 <sup>a</sup>	1.00
<sup>a</sup> $P < 0.001$ , <sup>b</sup> $P < 0.01$								

Figure 1 showed the time trends for air pollutants and all showed relatively stable seasonal trends annually. The concentrations of PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> had similar characteristics of periodic fluctuation, which were higher in the cold season and lower in the warm season. However, the concentrations of O<sub>3</sub> showed an inverses trend. The daily concentrations of PM<sub>2.5</sub> and SO<sub>2</sub> during 2017 to 2019 were lower than previous years. COPD mortality in the study period also showed a seasonal pattern with higher counts in winter and lower counts in summer.

Table 3 illustrated the EER of COPD mortality with every 10 µg/m<sup>3</sup> increase of air pollutant concentrations with different lag days in single pollutant models. All the five pollutants were positively associated with COPD mortality. However, for the single-day lag effects, positive significant associations were observed only for SO<sub>2</sub> at lag1 and lag 2, NO<sub>2</sub> at lag 1 and lag2, and O<sub>3</sub> at lag 3. The estimates of the effects of the five pollutants on COPD mortality were highest at lag0 for PM<sub>2.5</sub> (ERR: 0.475%, 95%CI: -0.056 ~ 1.008), at lag 1 for PM<sub>10</sub> (ERR: 0.384%, 95%CI: -0.002 ~ 0.772) and SO<sub>2</sub> (ERR: 2.962%, 95%CI:0.673 ~ 5.303), at lag 2 for NO<sub>2</sub> (ERR: 1.327%, 95%CI: 0.366 ~ 2.296) and at lag3 for O<sub>3</sub> (ERR: 0.494%, 95%CI:0.027 ~ 0.962).

Table 3

Estimated excess relative risks (ERRs) and 95% confidence intervals (95%CI) of daily death from chronic obstructive pulmonary disease for a 10 µg/m<sup>3</sup> increase in air pollutant's concentrations with different lag days in single pollutant models.

Lag Days	PM <sub>2.5</sub>	PM <sub>10</sub>	SO <sub>2</sub>	NO <sub>2</sub>	O <sub>3</sub>
Lag0	0.475(-0.056,1.008)	0.263(-0.135,0.663)	0.998(-1.339,3.391)	0.570(-0.335,1.484)	-0.119(-0.649,0.414)
Lag1	0.287(-0.239,0.817)	0.384(-0.002,0.772)	2.962(0.673,5.303) b	1.037(0.069,2.015) b	0.210(-0.298,0.720)
Lag2	0.148(-0.376,0.658)	0.319(-0.054,0.695)	2.673(0.458,4.938) b	1.327(0.366,2.296) a	0.284(-0.191,0.761)
Lag3	0.316(-0.198,0.832)	0.228(-0.140,0.596)	1.469(-0.705,3.690)	0.847(-0.074,1.776)	0.494(0.027,0.962) b
Lag4	-0.259(-0.769,0.254)	-0.134(-0.496,0.230)	-0.849(-2.965,1.313)	-0.165(-1.058,0.736)	-0.143(-0.604,0.320)
Lag5	-0.481(-0.997,0.037)	-0.105(-0.467,0.258)	-0.858(-2.972,1.302)	0.164(-0.724,1.061)	-0.035(-0.497,0.428)
Lag01	0.469(-0.139,1.081)	0.423(-0.026,0.875)	2.770(0.048,5.572) b	1.011(-0.034,2.066)	0.061(-0.567,0.692)
Lag02	0.430(-0.245,1.108)	0.536(0.045,1.029) b	4.010(0.967,7.145) a	1.558(0.378,2.752) a	0.255(-0.424,0.939)
Lag03	0.518(-0.219,1.261)	0.581(0.054,1.111) b	4.316(1.002,7.738) b	1.815(0.523,3.125) a	0.485(-0.234,1.210)
Lag04	0.368(-0.426,1.168)	0.464(-0.094,1.025)	3.480(-0.034,7.118)	1.608(0.224,3.010) b	0.321(-0.435,1.082)
Lag05	0.154(-0.695,1.011)	0.386(-0.201,0.977)	2.865(-0.854,6.724)	1.563(0.095,3.052) b	0.267(-0.526,1.067)
a <i>P</i> < 0.01, b <i>P</i> < 0.05					

The effects of moving average lags were higher than single lags in different period. For the moving averages, positive significant associations were observed for PM<sub>10</sub> at lag02 and lag03, SO<sub>2</sub> at lag01-lag03, NO<sub>2</sub> at lag02-lag05. All pollutants showed the strongest estimates at lag03. For each increase of 10 µg/m<sup>3</sup> in PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub> concentrations, COPD mortality increased by 0.518% (95%CI: -0.219 ~ 1.261), 0.581% (95%CI: 0.054 ~ 1.111), 4.316% (95%CI: 1.002 ~ 7.738), 1.815% (95%CI: 0.523 ~ 3.215) and 0.458% (95%CI: -0.234 ~ 1.210) at lag03, respectively.

The effects of the individual air pollutants on subjects by sex and age were performed in Fig. 2. SO<sub>2</sub> had the greatest impact on each subgroup analysis. PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> estimates of females were higher than those for males, except for PM<sub>2.5</sub> at lag5, SO<sub>2</sub> at lag 3, and NO<sub>2</sub> at lag 1, lag2 as well as lag01-lag03. In contrast, the associations of O<sub>3</sub> was higher for males than females, except at lag2. In general, except for O<sub>3</sub>, all pollutants estimates of < 65 year group was higher than those for older adults, but the estimates of < 65 year group were almost nonsignificant (except for PM<sub>2.5</sub> at lag2, SO<sub>2</sub> at lag2 and lag3, and NO<sub>2</sub> at lag3). For older adults, significant positive associations were observed for PM<sub>10</sub> at lag1 and lag01-lag03, SO<sub>2</sub> at lag1, lag2 as well as lag01-03, and NO<sub>2</sub> at lag1, lag2 as well as lag02-lag04.

Figure 3 summarized the ERRs for COPD mortality associated with every 10 µg/m<sup>3</sup> increase of air pollutant concentrations in two pollutant models at lag03. The estimates for SO<sub>2</sub> and NO<sub>2</sub> were the most stable across all two-pollutant models. In contrast, the estimates of PM<sub>2.5</sub>, PM<sub>10</sub> and O<sub>3</sub> decreased after the inclusion of SO<sub>2</sub> or NO<sub>2</sub>. Additionally, the estimates of PM<sub>2.5</sub> decreased

after the inclusion of PM<sub>10</sub>. The significant positive associations between SO<sub>2</sub> as well as NO<sub>2</sub> and COPD mortality remained after adjusting for PM<sub>2.5</sub> or O<sub>3</sub>.

## Discussion

In our study, a population-based time-series model was used to investigate the association between short-term air pollutants (PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> and O<sub>3</sub>) exposure and COPD mortality in Wuhan, China, during January 1, 2014 to December 31, 2019. The results showed that the concentrations of PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> were significantly positively associated with COPD mortality. As far as we know, this was the first time-series study assessed the adverse effects of air pollutants on COPD mortality in China.

During 2014 to 2019, the levels of ambient air pollution were relatively high in Wuhan, China. The daily mean concentrations of PM<sub>2.5</sub> (59.03 µg/m<sup>3</sup>), PM<sub>10</sub> (90.48 µg/m<sup>3</sup>) and NO<sub>2</sub> (48.84 µg/m<sup>3</sup>) exceeded the values of WHO Air Quality Guidelines (10, 20, 40 µg/m<sup>3</sup> respectively). And the daily mean concentrations of SO<sub>2</sub> and O<sub>3</sub> were 12.91 and 91.77 µg/m<sup>3</sup>, which were within the Air Quality Guidelines values (20, 100 µg/m<sup>3</sup> respectively). The concentrations of air pollutants showed relatively stable trends. PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> peaked in winter. It was probable that coal-burning was still the important source of heat and energy in China. Furthermore, in winter, the dispersion of pollutants was poor. However, O<sub>3</sub> was mostly formed by the conversion of nitrogen oxides and volatile organic compounds under high temperature, sufficient sunshine and low humidity, which finally led to the peak values of O<sub>3</sub> in summer. By the end of 2019, the number of motor vehicles exceed 3.3 million in Wuhan, and vehicle emission also became one of the major sources of environmental air pollution.

Our results showed that ambient air pollutants were positively associated with COPD mortality in single pollutant models. The effects on COPD mortality peaked within 4 day (lag03) and the strongest association estimated were observed for SO<sub>2</sub>. An increase of 10 µg/m<sup>3</sup> of PM<sub>10</sub> was associated with a 0.581%(95%CI:0.054%-1.111%) increase in COPD mortality. Moogavkar et.al reported a significantly positive association between PM<sub>10</sub> and the risk of COPD mortality with a increase of 2.66% (95%CI:0.12%-5.20%) in COPD mortality per 25 µg/m<sup>3</sup> increase in PM<sub>10</sub> [18]. And a meta-analysis by Zhu et al. also concluded that a 10 µg/m<sup>3</sup> increase in PM<sub>10</sub> was associated with a 1.1% (95%CI:0.8%-1.4%) increase in COPD mortality [19]. While, a case-crossover study in Cook city showed a lack of association between PM<sub>10</sub> and the risk of mortality for COPD [20]. We did not found significantly association between the concentrations of PM<sub>2.5</sub> and COPD mortality, consistent with the results of a large population-based cohort study in Metropolitan Vancouver, Canada [21]. But a meta-analysis concluded that a 10 µg/m<sup>3</sup> increase in daily PM<sub>2.5</sub> was associated with a 2.5%(95%CI:1.5%-3.5%) increase in COPD mortality[22]. And in a COPD cohort, Faustini et al found that effects on respiratory mortality among COPD subjects were particularly elevated 11.6%(95%CI:2.0%-22.2%) from PM<sub>2.5</sub> per 11 µg/m<sup>3</sup> increase[23].

Interestingly, our findings demonstrated that gaseous pollutants had stronger effects on COPD mortality than particulate matter. Similarly, other studies also suggested that compared to particulate matter, gaseous pollutant had stronger effects on COPD exacerbation and daily outpatient visits of respiratory diseases[24, 25]. Our estimates showed that a 10 µg/m<sup>3</sup> of NO<sub>2</sub> was significantly associated with a 1.815%(95%CI:0.523%-3.125%) increase in COPD mortality. In a 6-year cohort study including all residents aged 51–90 years in Oslo, Norway, the results found that the concentrations of NO<sub>2</sub> on COPD mortality appeared to have significantly linear effects[26]. While Hart et al found positive but nonsignificant associations of COPD mortality with NO<sub>2</sub>, PM<sub>2.5</sub> and SO<sub>2</sub> exposure in industry workers[27].

SO<sub>2</sub> mainly came from burning of fossil fuels, with the promotion of clean fuels in Wuhan recently, the concentration of SO<sub>2</sub> gradually decreased. The mean concentrations of SO<sub>2</sub> in Wuhan was 12.91 µg/m<sup>3</sup>, which could be considered as low-level compared with many other Chinese cities[5, 28, 29]. But our results showed that every increase of 10 µg/m<sup>3</sup> of SO<sub>2</sub> was associated with 4.316%(95%CI:1.002%-7.738%) increase in COPD mortality, which was higher than the estimated reported in several previous studies[30]. And Zhang et al also demonstrated that SO<sub>2</sub> had a stronger effect on cardiovascular mortality in Hefei, China[28]. The reason for this phenomenon was still unclear, but Samoli et al found that when the concentration of SO<sub>2</sub> at

a lower level, the impact of SO<sub>2</sub> to mortality is greater than the high concentration[31], which might partially explain the effects of SO<sub>2</sub> in our study. Furthermore, similar with the results of a meta-analysis, we did not find significant association between the concentrations of O<sub>3</sub> and COPD mortality[25]. To sum up, the inconformity with our findings might due to the different chemical compositions of PM<sub>10</sub> or PM<sub>2.5</sub> in different areas, which could result in different effects on COPD mortality. In addition, the meteorological factors might influent the effects of air pollutants, but the compositions of air pollutants and meteorological conditions varied in different regions[32]. Moreover, the age, socioeconomic status and education level and so on were able to modify the effects of air pollutants.

Although the mechanical explanation of adverse effects of ambient air pollution on COPD mortality remains unclear, identifying the associations of ambient air pollution in different exposure windows is of great importance in the estimation of health risk. In our study, we found that exposure to air pollutants at lag03 yielded the strongest estimates on COPD mortality. Another time-series study in Hefei, China also found the similar phenomenon in the associations between ambient air pollution and cardiovascular mortality[28].

Subgroup analysis showed that females seemed to suffer more risk of COPD mortality from ambient air pollution. In addition, the results showed that the air pollution estimates of < 65 year group were higher than those for older adults, though the estimates were almost nonsignificant. Only 7.2% in our study were < 65 year group, the sample size might be a strong confounder. A population based cohort study also showed that the relative risks for COPD mortality associated with a 0.78 µg/m<sup>3</sup> elevation in black carbon concentrations were 1.06 (95%CI:0.97–1.15) and 1.08 (95%CI:0.97–1.20) for males and females, and 1.31 (95%CI:1.07–1.60) and 1.04 (95%CI:0.97–1.12) for < 65 and ≥ 65 year groups[21]. Similar with the results from a population based UK Biobank study, it concluded that the adverse effects of PM<sub>2.5</sub> and NO<sub>2</sub> on COPD prevalence were stronger in females[33]. However, Naess et al documented that males were more susceptible to air pollution (PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>2</sub>) than females[26]. The reasons for our gender-specific findings were still unclear and needed further investigation. Furthermore, the concentrations of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> were significantly associated with COPD mortality for older adults, effective public health prevention policies specified for older adults should be made to reduce the burden of COPD.

Two-pollutant models were implemented in our study to explore the possible role of single pollutants. We concluded that the estimates of PM<sub>2.5</sub>, PM<sub>10</sub> and O<sub>3</sub> decreased after the inclusion of SO<sub>2</sub> or NO<sub>2</sub>, consistent with the previous studies[29, 34]. These results revealed the relatively independent associations of SO<sub>2</sub> and NO<sub>2</sub>. The associations of SO<sub>2</sub> and NO<sub>2</sub> on COPD mortality might better reflect the associations between air pollution and COPD mortality in Wuhan compared with other pollutants.

Though this study was a population-based time-series study which covered all population in Wuhan, there were some limitations. Firstly, the average of ten fixed sited monitoring data of air pollutant concentrations were used to infer exposures of individuals, which might lead to potential misclassification exposure and ignore the spatial impact of air pollution on COPD. Secondly, due to data unavailability, some factors including personal social information (such as tobacco use, body mass index and so on) that could affect the effects were not controlled. Thirdly, we could not rule out the non-relevant death records due to obesity or other reasons than air pollution.

## Conclusions

The results of this study suggested that exposure to PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> were significantly positively associated with a higher risk of COPD mortality in Wuhan, China. Moreover, female and elderly are more susceptible to air pollution. Our findings could provide evidence to help understand the adverse health effects of air pollution, which might have important implications for policy makers to curb and reduce ambient air pollution in Wuhan.

## Declarations

**Ethics approval and consent to participate:**



The death data were surveillance data, there was no requirement for informed consent. This study was approved by the Ethical committee of Wuhan Center for Disease Control and Prevention

**Consent for publication:**

Not applicable.

**Availability of data and materials:**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests:**

The authors declare that they have no competing interests.

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**Authors' contributions:**

YY: Conceptualization, Methodology, Funding acquisition. LS: Formal analysis, Writing-Original draft preparation. YG: Software, Funding acquisition. YZ: Data curation. PZ: Software. BX: Validation. JZ: Data curation. MY: Writing-Reviewing and Editing, Conceptualization, Funding acquisition. LW: Conceptualization. All authors read and approved the final manuscript.

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## References

1. Yang, G., et al., Rapid health transition in China, 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet*, 2013. 381(9882): 1987-2015.
2. Mbululo, Y., et al., Boundary layer perspective assessment of air pollution status in Wuhan city from 2013 to 2017. *Environ Monit Assess*, 2019. 191(2): 69.
3. Khilnani, G.C. and P. Tiwari, Air pollution in India and related adverse respiratory health effects: past, present, and future directions. *Curr Opin Pulm Med*, 2018. 24(2): 108-16.
4. Schraufnagel, D.E., et al., Health Benefits of Air Pollution Reduction. *Ann Am Thorac Soc*, 2019. 16(12): 1478-87.
5. Guan, W.J., et al., Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet*, 2016. 388(10054): 1939-51.
6. Brugha, R. and J. Grigg, Urban air pollution and respiratory infections. *Paediatr Respir Rev*, 2014. 15(2): 194-9.
7. Tao, F., B. Gonzalez-Flecha and L. Kobzik, Reactive oxygen species in pulmonary inflammation by ambient particulates. *Free Radic Biol Med*, 2003. 35(4):327-40.
8. Goldsmith, C.A., et al., Alveolar macrophage interaction with air pollution particulates. *Environ Health Perspect*, 1997. 105 Suppl 5: 1191-5.

9. Ghio, A.J., et al., Metals associated with both the water-soluble and insoluble fractions of an ambient air pollution particle catalyze an oxidative stress. *Inhal Toxicol*, 1999. 11(1): 37-49.
10. Song, Q., et al., The global contribution of outdoor air pollution to the incidence, prevalence, mortality and hospital admission for chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Int J Environ Res Public Health*, 2014. 11(11): 11822-32.
11. Doiron, D., et al., Air pollution, lung function and COPD: results from the population-based UK Biobank study. *The European respiratory journal*, 2019. 54(1): 1802140.
12. World Health Organization, WHO fact sheet on ambient (outdoor) air quality guidelines: includes key facts, definition, health effects, guideline values and WHO response. 2014.
13. Astudillo-Garcia, C.I., et al., Air Pollution and Suicide in Mexico City: A Time Series Analysis, 2000-2016. *Int J Environ Res Public Health*, 2019. 16(16).
14. Guo, Y., et al., Time series analysis of ambient air pollution effects on daily mortality. *Environ Sci Pollut Res Int*, 2017. 24(25): 20261-72.
15. Katsouyanni, K., et al., Short-term effects of air pollution on health: a European approach using epidemiological time-series data. The APHEA project: background, objectives, design. *European Respiratory Journal*, 1995. 8(6): 1030-8.
16. Luo, L., et al., Time series analysis of ambient air pollution effects on dynamic stroke mortality. *Int J Health Plann Manage*, 2020. 35(1): 79-103.
17. Mokoena, K.K., et al., Ambient air pollution and respiratory mortality in Xi'an, China: a time-series analysis. *Respir Res*, 2019. 20(1): 139.
18. Moolgavkar, S.H., Air pollution and daily mortality in three U.S. counties. *Environ Health Perspect*, 2000. 108(8): 777-84.
19. Zhu, R., et al., The relationship between particulate matter (PM10) and hospitalizations and mortality of chronic obstructive pulmonary disease: a meta-analysis. *COPD*, 2013. 10(3): 307-15.
20. Bateson, T.F. and J. Schwartz, Who is sensitive to the effects of particulate air pollution on mortality? A case-crossover analysis of effect modifiers. *Epidemiology*, 2004. 15(2): 143-9.
21. Gan, W.Q., et al., Associations of ambient air pollution with chronic obstructive pulmonary disease hospitalization and mortality. *Am J Respir Crit Care Med*, 2013. 187(7): 721-7.
22. Li, M.H., et al., Short-term Exposure to Ambient Fine Particulate Matter Increases Hospitalizations and Mortality in COPD: A Systematic Review and Meta-analysis. *Chest*, 2016. 149(2): 447-458.
23. Faustini, A., et al., Short-term effects of air pollution in a cohort of patients with chronic obstructive pulmonary disease. *Epidemiology*, 2012. 23(6): 861-79.
24. Cheng, Y., et al., Health Impacts of Exposure to Gaseous Pollutants and Particulate Matter in Beijing-A Non-Linear Analysis Based on the New Evidence. *Int J Environ Res Public Health*, 2018. 15(9).
25. Li, J., et al., Major air pollutants and risk of COPD exacerbations: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis*, 2016. 11: 3079-91.
26. Naess, O., et al., 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): 435-43.
27. Hart, J.E., et al., Long-term ambient multipollutant exposures and mortality. *Am J Respir Crit Care Med*, 2011. 183(1): 73-8.
28. Zhang, C., et al., Association between air pollution and cardiovascular mortality in Hefei, China: A time-series analysis. *Environ Pollut*, 2017. 229: 790-797.
29. Wang, J., et al., Associations between ambient air pollution and mortality from all causes, pneumonia, and congenital heart diseases among children aged under 5 years in Beijing, China: A population-based time series study. *Environ Res*, 2019. 176: 108531.
30. Kan, H. and B. Chen, A case-crossover analysis of air pollution and daily mortality in Shanghai. *J Occup Health*, 2003. 45(2): 119-24.

31. Samoli, E., et al., Investigating regional differences in short-term effects of air pollution on daily mortality in the APHEA project: a sensitivity analysis for controlling long-term trends and seasonality. *Environ Health Perspect*, 2001. 109(4): 349-53.
32. Sunyer, J. and X. Basagana, Particles, and not gases, are associated with the risk of death in patients with chronic obstructive pulmonary disease. *Int J Epidemiol*, 2001. 30(5): 1138-40.
33. Doiron, D., et al., Air pollution, lung function and COPD: results from the population-based UK Biobank study. *Eur Respir J*, 2019. 54(1).
34. Nhung, N.T.T., et al., Acute effects of ambient air pollution on lower respiratory infections in Hanoi children: An eight-year time series study. *Environment International*, 2018. 110(jan.): 139-48.

## Figures

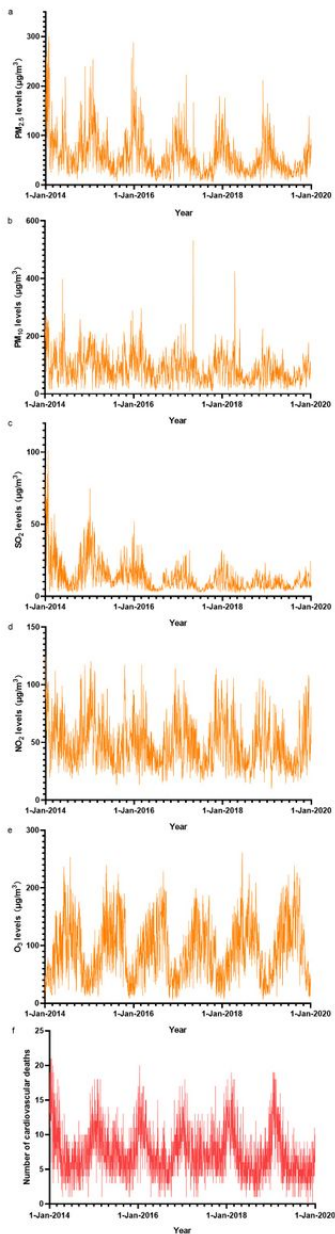


Figure 1

Time series of PM<sub>2.5</sub> (a), PM<sub>10</sub> (b), SO<sub>2</sub> (c), NO<sub>2</sub>(d), O<sub>3</sub>(e) and chronic obstructive pulmonary disease mortality(f) in Wuhan, China, during 2014-2019.

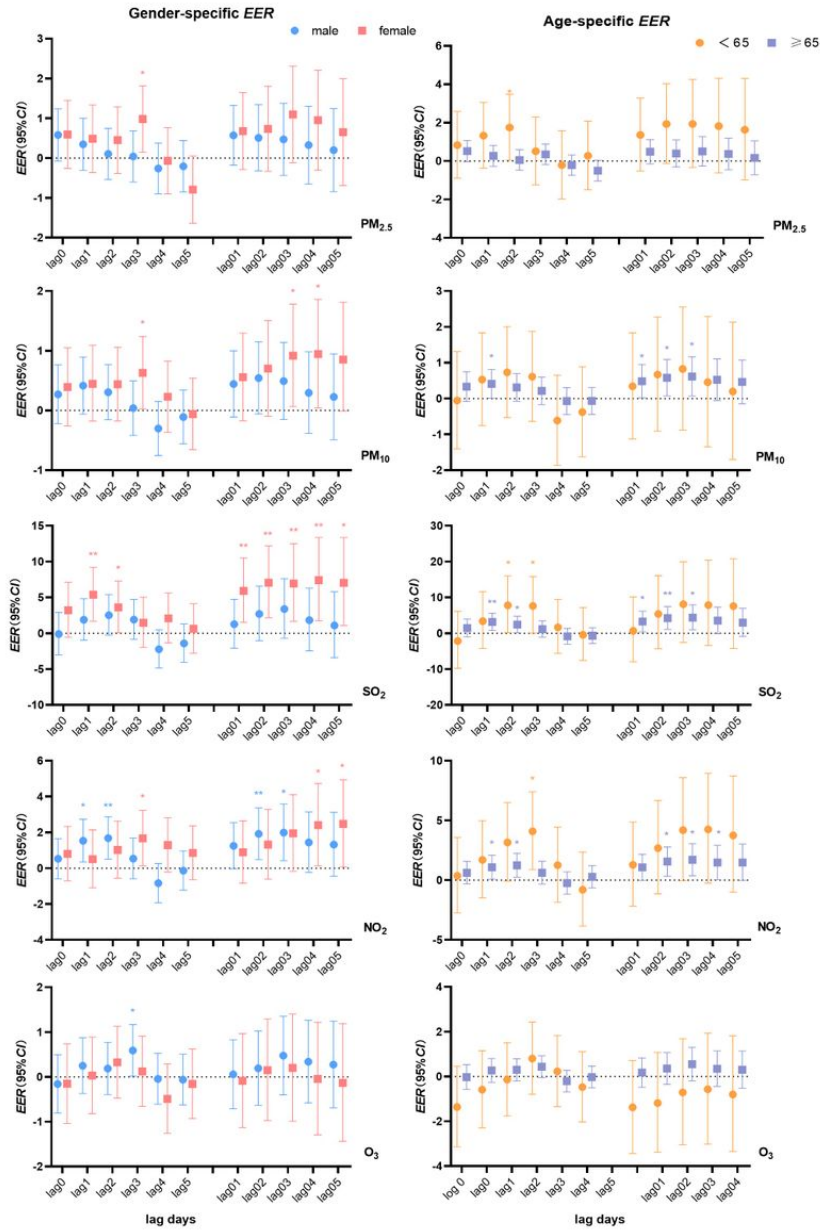
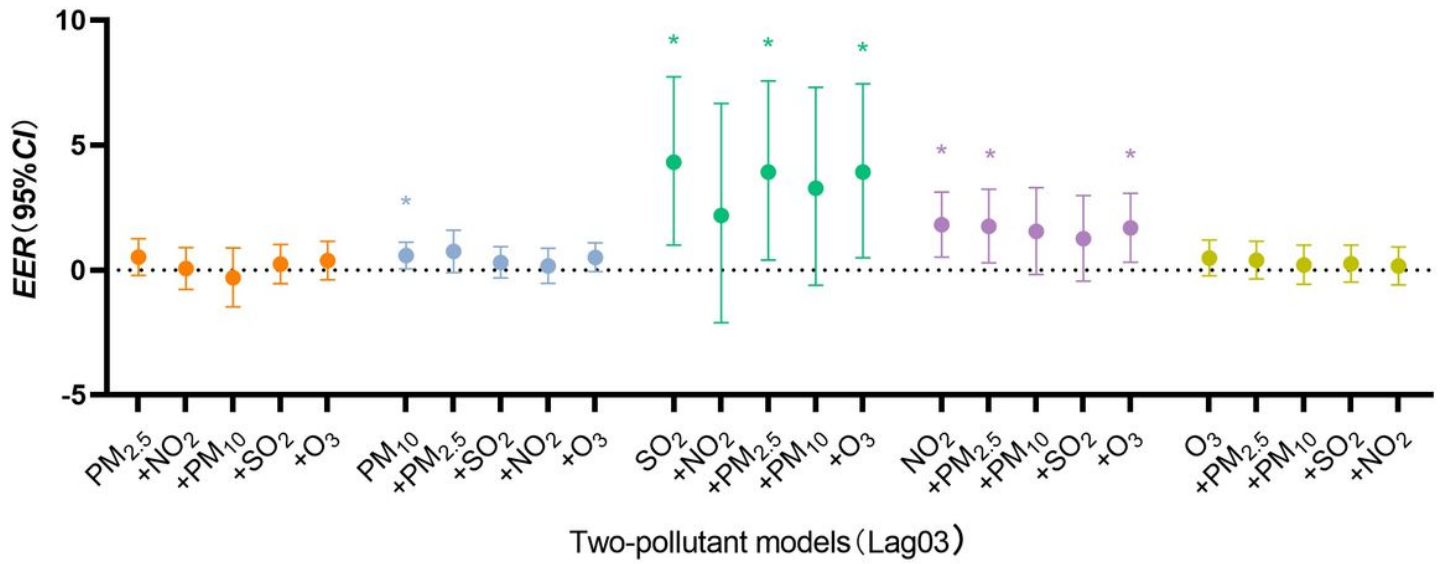


Figure 2

Age- and gender-specific estimated excess relative risks (ERRs) and 95% confidence intervals (95%CI) for daily deaths from chronic obstructive pulmonary disease with a 10 $\mu$ g/m<sup>3</sup> increase in air pollutants using different lag days.



**Figure 3**

Estimated excess relative risks (ERRs) and 95% confidence intervals (95%CI) for daily deaths from chronic obstructive pulmonary disease with a 10 $\mu\text{g}/\text{m}^3$  increase in air pollutants using single- and two-pollutant models. Lag03 were used.