

Effects of Short-term Exposure to Ambient Airborne Pollutants on COPD-related Mortality Among the Elderly Residents of Chengdu City in Southwest China

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Research

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) has become a severe global burden in terms of both health and the economy. Few studies, however, have thoroughly assessed the influence of air pollution on COPD-related mortality among elderly people in higher elevation areas. This study is the first to examine the association between short-term exposure to ambient airborne pollutants and COPD-related mortality among elderly people in the central Sichuan Basin of southwestern China.

Methods: Data on COPD-related mortality among elderly people aged 60 and older were obtained from the Population Death Information Registration and Management System (PDIRMS). Data on airborne pollutants comprised of particulate matter < 2.5 μm in aerodynamic diameter ($\text{PM}_{2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) were derived from 23 municipal environmental monitoring sites. Data on weather conditions, including daily mean temperature and relative humidity, were obtained from the Chengdu Meteorological Bureau. All data were collected from January 1, 2015, to December 31, 2018. A quasi-Poisson general additive model (GAM) was utilized to assess the effects of short-term exposure to airborne pollutants on COPD-related mortality among elderly people.

Results: A total of 61,058 COPD-related deaths of people aged 60 and older were obtained. Controlling the influences of daily temperature and relative humidity, interquartile range (IQR) concentration increases of $\text{PM}_{2.5}$ (43 $\mu\text{g}/\text{m}^3$), SO_2 (8 $\mu\text{g}/\text{m}^3$), NO_2 (18 $\mu\text{g}/\text{m}^3$), CO (0.4 mg/m^3), and O_3 (78 $\mu\text{g}/\text{m}^3$) were associated with 1.9%, 3.4%, 2.7%, 2.5%, and 3.8% increases in COPD-related mortality in people aged 60 and older, respectively. The exposure-response curves between each pollutant and the log-relative risk of COPD-related mortality exhibited linear relationships. Statistically significant associations between COPD-related mortality and pollutants in the 60–69 age group were not observed but were observed in the ≥ 90 age group, with the exception of CO. Correspondingly, statistically significant associations between COPD-related mortality and $\text{PM}_{2.5}$ were only observed in the ≥ 90 age group. Statistically significant differences in the associations between pollutants and COPD-related mortality were not observed between males and females or between married individuals and those with alternative marital statuses (widowed, divorced, or never married). The effects of O_3 remained steady after adjusting for $\text{PM}_{2.5}$, SO_2 , NO_2 , and CO each time in the two-pollutant models.

Conclusions: Increased concentrations of ambient airborne pollutants composed of $\text{PM}_{2.5}$, SO_2 , NO_2 , O_3 , and CO were significantly and positively associated with COPD-related mortality in the central Sichuan Basin of southwestern China, which has an elevation of 500 meters. Susceptibilities to COPD-related mortality associated with ambient airborne pollutants may increase with age. The adverse effects of O_3 were stable, a finding that should receive more attention.

Background

Chronic obstructive pulmonary disease (COPD) is characterized as a group of conditions that affect the structures within the lungs in various ways, including emphysema, asthma, chronic bronchitis, and others [1]. Recently, COPD has become a severe global burden in terms of both health and the economy and had become the fifth leading cause of mortality worldwide by the early 21st century [2]. Ambient air pollution, as another severe health burden, now accounts for 1.2% of premature deaths and 0.5% of lost years of life worldwide [3]. Previous studies have reported air pollution and COPD incidences, hospital admissions, and mortality [4–7]. In China, most previous investigations concerning air pollution and COPD-related mortality were conducted in lower elevation areas, including eastern coast regions, as well as Beijing and its surrounding areas [8, 9].

It is known that oxygen concentration is very closely associated with the health conditions of COPD patients [10], and elevation is a crucial factor in determining the oxygen concentration in ambient air. For elevations above 500 meters in China, there have been few previous studies concerning the effects of ambient airborne pollutants on COPD-related mortality [8, 11]. Accordingly, there remains a lack of information regarding the influence of air pollution on COPD-related mortality in higher elevation areas. In light of previous research, we conducted this study to (1) explore the effects of short-term exposure to ambient airborne pollutants ($PM_{2.5}$, SO_2 , NO_2 , CO , and O_3) on COPD mortality among elderly people living on a plateau with an elevation > 500 meters and (2) determine the sociodemographic factors (e.g., age, gender, and marital status) that modify the effects of pollutants on COPD-related mortality.

We conducted our study in Chengdu City, located in the center of the Sichuan Basin in southwestern China, which has an average elevation of 500 meters [12]. Chengdu experiences severe air pollution [13]. In addition, being the bottom of a basin, the diffusion of airborne pollutants in Chengdu differs from that of the plains in which previous studies were carried out in China. Chengdu is densely populated, with more than 16 million residents in 2017 [14]. The aforementioned advantages make Chengdu a suitable location for a time-series study. To our knowledge, no similar reports concerning the associations between short-term exposure to ambient airborne pollutants and COPD-related mortality in this area have been presented. Thus, our study may add some limited evidence to this knowledge gap. An epidemiologically designed time series was conducted to assess the effects of short-term exposure to ambient airborne pollutants on COPD-related mortality among elderly people in Southwest China.

Methods

Data collection

Mortality data were obtained from the Population Death Information Registration and Management System (PDIRMS), which covers all the mortality information of residents in Chengdu City. After a resident was confirmed to have died by doctors in a hospital or at the resident's home, his or her personal information regarding the death would be recorded in the system. The personal information consists of ID number, name, gender, age, date of birth, date of death, marital status, residential address, primary death diagnosis, secondary death diagnosis, underlying cause of death diagnosis, and other data. Private

personal data that could be associated with a particular person, such as name and residential address, were omitted, while age, gender, marital status, primary death diagnosis, secondary death diagnosis, underlying cause of death diagnosis were maintained. All records from January 1, 2015, to December 31, 2018, were obtained from PDIRMS. A death record was maintained for further analysis when it fulfilled the following two criteria: (1) the age of the resident was 60 or older, (2) the death diagnosis was COPD. The International Classification of Diseases, 10th Revision (ICD-10) was used to diagnose COPD (ICD-10 code J40-J44).

Data on airborne pollutants comprised of particulate matter < 2.5 μm in aerodynamic diameter ($\text{PM}_{2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) were derived from 23 municipal environmental monitoring sites which operated continuously from January 1, 2015, to December 31, 2018, in Chengdu. These 23 sites were distributed almost evenly, covering both urban and rural areas in Chengdu (Fig. 1). The daily mean concentrations of $\text{PM}_{2.5}$, SO_2 , NO_2 , and CO were obtained daily, along with the daily 8-hour mean concentrations of O_3 , from each of the 23 sites. The daily mean concentrations of each pollutant were calculated using data from all the sites. If the data from a given site were missing on a given day, data from the remaining sites were used to calculate the mean concentrations. The missing data for each day and each site were recorded for use in calculating the missing data rate of each pollutant. Weather conditions, including daily mean temperature and relative humidity, were obtained from the Chengdu Meteorological Bureau. These conditions were considered to be confounding factors, and controlled in the models. Daily data on airborne pollutants and weather conditions were collected from January 1, 2015, to December 31, 2018.

Statistical analysis

The correlations between airborne pollutants and weather conditions were explored using Spearman's correlation test. Daily mortality, concentrations of airborne pollutants, and weather conditions were linked by date, correspondingly conforming to the design of the time series. Therefore, a quasi-Poisson general additive model (GAM) was utilized to assess the effects of airborne pollutants on COPD-related mortality. Daily mortality was set as the response variable, while the concentrations of airborne pollutants were the predictor variables in the model. A natural cubic spline function (NS) with degrees of freedom (DFs) was used to control the influence of time trends and potential nonlinear effects of confounding variables, including daily mean temperature and relative humidity. Based on previous studies [15], a total of seven DFs per year was selected for the time trends, while six DFs and three DFs were selected for daily mean temperature and relative humidity, respectively. An indicator day-of-week (DOW) was included for weekly variations.

Prior research has revealed that delays exist between air pollutant exposure and respiratory system health effects [16, 17]. Exposure to ambient air pollutants may eventually lead to COPD-related mortality. Single-day lag models with different lag periods were used to assess the delay effects, including the case day (lag0), and the previous one to three case days (lag1, lag2, and lag3, respectively). The exposure-response curves were plotted in order to graphically depict the relationship between each pollutant and the log-

relative risk of COPD-related mortality. The curves corresponded to the days of greatest effect for each pollutant.

Z-tests were utilized for testing the statistically significant differences of effect estimates between effect modifiers of sociodemographic factors (e.g., the difference between “marriage” and “alternative marital status”). The equation is as follows:

$$Z = (\hat{Q}_1 - \hat{Q}_2) / \sqrt{S\hat{E}_1^2 + S\hat{E}_2^2},$$

where \hat{Q}_1 and \hat{Q}_2 are the estimates for the two categories, and $S\hat{E}_1$ and $S\hat{E}_2$ are their respective standard errors.

Three types of sensitivity analyses were conducted in order to test the robustness of the results. First, two-pollutant models were run for each pollutant by adding the remaining pollutant each time into the model. Second, alternative degrees of freedom (DFs) for time trends ranging from 5–9 were used in the models. Third, multi-day lag models with different lag periods were employed, including the moving average of the case day and previous day (lag01), and the moving average of the case day and previous 3 days (lag03).

The results were calculated as relative risk (RR) with a 95% confidence interval (CI) for an interquartile range (IQR) increase in each pollutant. The “MGCV” package in the R programming language (version 3.5.1) was used for fitting the time series model.

Results

A total of 61,058 COPD-related deaths of people aged 60 and older were obtained from January 1, 2015, to December 31, 2018. Among these, 33,731 deaths were males and 27,327 were females. 31,948 of the deceased were married, while 29,110 had some sort of alternative marital status (including divorced, widowed, and never married). Deaths in the 60–69, 70–79, 80–89, and ≥ 90 age groups were 6,527, 16,916, 27,781, and 9,834, respectively. The mean value and IQR for each type of air pollutant, weather condition, and COPD-related death are listed in Table 1.

Table 1

Data for ambient air pollutants, weather conditions, and COPD-related deaths in Chengdu from 2015 to 2018

	Mean	SD	Min.	25%	50%	75%	Max.	IQR
PM _{2.5} (µg/m ³)	58.7	38.9	8.0	31.0	47.0	74.0	254.0	43.0
SO ₂ (µg/m ³)	14.5	6.3	4.0	10.0	14.0	18.0	41.0	8.0
NO ₂ (µg/m ³)	40.5	13.1	13.0	31.0	38.0	49.0	92.0	18.0
CO (mg/m ³)	0.9	0.3	0.4	0.7	0.9	1.1	2.2	0.4
O ₃ -8 h (µg/m ³)	98.8	51.8	11.0	59.0	88.0	137.0	279.0	78.0
Temperature (°C)	16.7	7.3	-1.9	9.9	17.3	23.0	29.8	13.1
RH (%)	80.8	8.9	41.0	75.0	81.0	88.0	99.0	13.0
COPD-related deaths	41.8	14.9	14.0	32.0	38.0	49.0	114.0	17.0
Age group (year)								
60–69	4.5	2.5	0	3.0	4.0	6.0	16.0	3.0
70–79	11.6	5.0	1.0	8.0	11.0	14.0	37.0	6.0
80–89	19.0	7.5	4.0	14.0	18.0	23.0	60.0	9.0
≥ 90	6.7	3.5	0	4.0	6.0	9.0	22.0	5.0
Gender								
Male	23.1	8.8	7.0	17.0	21.0	27.0	62.0	10.0
Female	18.7	7.5	4.0	13.0	17.0	23.0	61.0	10.0
Marital status								
Married	21.9	8.4	5.0	16.0	20.0	26.0	62.0	10.0
Alternative statuses ^a	19.9	7.9	4.0	14.0	19.0	24.0	55.0	10.0

^a Alternative marital statuses include widowed, divorced, and never married.

Abbreviations: PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; CO, carbon monoxide; O₃-8 h, daily eight-hour mean concentration of ozone; RH, relative humidity; COPD, chronic obstructive pulmonary disease; SD, standard deviation; IQR, interquartile range.

The concentrations of the PM_{2.5}, SO₂, NO₂, CO, and O₃ ambient air pollutants exhibited typical seasonal tendencies. The concentrations of PM_{2.5}, NO₂, and CO were considerably higher during winter, and lower during summer each year, while the seasonal variations of the O₃ concentrations were the opposite. The concentrations of SO₂ exhibited weaker seasonal tendencies than the other pollutants, although the pattern of higher in winter and lower in summer was also apparent (Figure S1).

As shown in Table 2, correlations were observed among ambient air pollutants and weather conditions, except between SO₂ and temperature, and between temperature and relative humidity.

Table 2
Spearman's correlation coefficients of air pollutants and weather conditions

	PM _{2.5}	SO ₂	NO ₂	CO	O ₃ -8 h	Temperature	RH
PM _{2.5}	1						
SO ₂	0.540 ^a	1					
NO ₂	0.799 ^a	0.435 ^a	1				
CO	0.820 ^a	0.450 ^a	0.712 ^a	1			
O ₃ -8 h	-0.215 ^a	0.092 ^a	-0.227 ^a	-0.368 ^a	1		
Temperature	-0.511 ^a	-0.028	-0.478 ^a	-0.551 ^a	0.712 ^a	1	
RH	-0.109 ^a	-0.254 ^a	-0.118 ^a	0.064 ^a	-0.510 ^a	-0.037	1
^a <i>P</i> < 0.05.							
Abbreviations: PM _{2.5} , particulate matter < 2.5 μm in aerodynamic diameter; SO ₂ , sulfur dioxide; NO ₂ , nitrogen dioxide; CO, carbon monoxide; O ₃ -8 h, daily eight-hour mean concentration of ozone; RH, relative humidity.							

Associations were apparent between COPD-related mortality and IQR increases in the concentrations of PM_{2.5} (43 μg/m³), SO₂ (8 μg/m³), NO₂ (18 μg/m³), CO (0.4 mg/m³), and O₃ (78 μg/m³) after the influences of weather conditions (i.e., daily mean temperature and relative humidity) were controlled. The days corresponding to the greatest effects of PM_{2.5} (RR = 1.019, 95% CI: 1.006–1.033), SO₂ (RR = 1.034, 95% CI: 1.016–1.053), NO₂ (RR = 1.027, 95% CI: 1.011–1.043), CO (RR = 1.025, 95% CI: 1.006–1.044), and O₃ (RR = 1.038, 95% CI: 1.015–1.061) were one-day, one-day, one-day, zero-day, and two-day lags in the single-day lag models, respectively. The estimate results calculated from the multi-day lag models were similar, although a small amount higher than the results from the single-day lag models for each pollutant. The days corresponding to the greatest estimate results for PM_{2.5}, SO₂, NO₂, CO, and O₃ were lag03, lag01, lag03, lag01, and lag03 in the multi-day lag models, respectively (Fig. 2). The exposure-

response curves exhibited linear relationships between each pollutant and the log-relative risk of COPD-related mortality (Fig. 3).

Statistically significant associations between COPD-related mortality and pollutants in the 60–69 age group were not observed but were observed in the ≥ 90 age group, with the exception of CO. Statistically significant associations between COPD-related mortality and $PM_{2.5}$ were only observed in the ≥ 90 age group. The greatest effects of SO_2 , NO_2 , and O_3 in the 70–79 age group were at lag1 (RR = 1.051, 95% CI: 1.018–1.085), lag0 (RR = 1.029, 95% CI: 1.002–1.057), and lag1 (RR = 1.054, 95% CI: 1.009–1.101), respectively, while the greatest effects of NO_2 , and O_3 in the 80–89 age group were both at lag0 (RR for NO_2 = 1.029, 95% CI: 1.007–1.051, RR for O_3 = 1.029, 95% CI: 1.003–1.056), and the greatest effects of $PM_{2.5}$, SO_2 , NO_2 , and O_3 in the ≥ 90 age group were at lag1 (RR = 1.036, 95% CI: 1.004–1.069), lag1 (RR = 1.055, 95% CI: 1.011–1.102), lag1 (RR = 1.048, 95% CI: 1.010–1.088), and lag2 (RR = 1.071, 95% CI: 1.016–1.129), respectively (Figure 4).

The RRs for $PM_{2.5}$, SO_2 , NO_2 , and O_3 in males were 1.018 (95% CI: 1.001–1.035), 1.037 (95% CI: 1.013–1.062), 1.026 (95% CI: 1.006–1.047), 1.040 (95% CI: 1.008–1.074), respectively, corresponding to zero-day, one-day, zero-day, and one-day lags. The RRs for $PM_{2.5}$, SO_2 , NO_2 , and O_3 in females were 1.023 (95% CI: 1.003–1.042), 1.030 (95% CI: 1.004–1.057), 1.034 (95% CI: 1.011–1.058), and 1.051 (95% CI: 1.018–1.086), respectively, corresponding to one-day, one-day, one-day, and two-day lags. The RRs for CO were not observed in either males or females. The RRs for $PM_{2.5}$, SO_2 , NO_2 , CO, and O_3 in married individuals were 1.022 (95% CI: 1.004–1.040), 1.041 (95% CI: 1.016–1.066), 1.036 (95% CI: 1.016–1.058), 1.032 (95% CI: 1.007–1.058), and 1.040 (95% CI: 1.007–1.075), respectively, corresponding to two-day, one-day, zero-day, zero-day, and one-day lags. The RRs for $PM_{2.5}$, SO_2 , and O_3 in alternative marital status individuals (including divorced, widowed, and never married) were 1.019 (95% CI: 1.001–1.038), 1.026 (95% CI: 1.001–1.053), and 1.050 (95% CI: 1.008–1.095), respectively, corresponding to zero-day, one-day, and zero-day lags. Statistically significant differences for the effects of airborne pollutants on COPD-related mortality were not observed between males and females, nor were they found between married individuals and alternative marital status individuals (Figure 5).

By adding the remaining pollutants each time as covariates into the models, two-pollutant model simulations were conducted for each pollutant corresponding to their greatest effective days. The effects of O_3 remained steady after adjusting for $PM_{2.5}$, SO_2 , NO_2 , and CO each time in the models. The effects of $PM_{2.5}$, SO_2 , and NO_2 remained after adjusting for CO and O_3 , respectively, while attenuating to zero after adjusting for each other. The effects of CO remained after adjusting for O_3 , while attenuating to zero after adjusting for $PM_{2.5}$, SO_2 , and NO_2 (Table 3).

Table 3

RRs for two-pollutant models including PM_{2.5}, SO₂, NO₂, CO, and O₃^b

Airborne pollutant	RR	RR 95% CI	
		Lower	Upper
PM _{2.5}	1.019 ^a	1.006	1.033
	+SO ₂	1.006	0.989
	+NO ₂	1.006	0.987
	+CO	1.023 ^a	1.003
	+O ₃	1.016 ^a	1.003
SO ₂	1.034 ^a	1.016	1.053
	+PM _{2.5}	1.001	0.9978
	+NO ₂	1.024	0.998
	+CO	1.036 ^a	1.014
	+O ₃	1.030 ^a	1.011
NO ₂	1.027 ^a	1.011	1.043
	+PM _{2.5}	1.022	0.9997
	+SO ₂	1.012	0.989
	+CO	1.033 ^a	1.011
	+O ₃	1.024 ^a	1.007
CO	1.025 ^a	1.006	1.044
	+PM _{2.5}	1.012	0.983
	+SO ₂	1.011	0.987

Abbreviations: PM_{2.5}, particulate matter < 2.5 μm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; CO, carbon monoxide; O₃, ozone; RR, relative risk; CI, confidence interval.

^a $P < 0.05$.

^b RRs for PM_{2.5}, SO₂, NO₂, CO, and O₃ were from one-day, one-day, one-day, zero-day, and two-day lags, respectively.

Airborne pollutant	RR	RR 95% CI		
		Lower	Upper	
	+NO ₂	1.002	0.975	1.029
	+O ₃	1.020 ^a	1.001	1.040
O ₃		1.038 ^a	1.015	1.061
	+PM _{2.5}	1.034 ^a	1.011	1.057
	+SO ₂	1.035 ^a	1.011	1.059
	+NO ₂	1.035 ^a	1.012	1.058
	+CO	1.038 ^a	1.015	1.061
Abbreviations: PM _{2.5} , particulate matter < 2.5 µm in aerodynamic diameter; SO ₂ , sulfur dioxide; NO ₂ , nitrogen dioxide; CO, carbon monoxide; O ₃ , ozone; RR, relative risk; CI, confidence interval.				
^a <i>P</i> < 0.05.				
^b RRs for PM _{2.5} , SO ₂ , NO ₂ , CO, and O ₃ were from one-day, one-day, one-day, zero-day, and two-day lags, respectively.				

Discussion

In this investigation, we employed a time-series study design to determine the associations between airborne pollutants and COPD-related mortality among elderly individuals aged 60 and above. After confounders consisting of daily mean temperature and relative humidity were controlled, IQR increases in the concentrations of PM_{2.5} (43 µg/m³), SO₂ (8 µg/m³), NO₂ (18 µg/m³), CO (0.4 mg/m³), and O₃ (78 µg/m³) were associated with 1.9, 3.4, 2.7, 2.5, and 3.8% increases in COPD-related mortality among elderly individuals aged 60 and above, respectively. The exposure-response curves for the aforementioned pollutants and COPD-related mortality were nearly linear, which is consistent with previous studies [18]. Some prior research reported adverse effects from gaseous pollutants composed of SO₂, NO₂, CO, and O₃ on COPD-related mortality higher than that from fine particulates [19], while some reported the opposite results [4, 20]. In our study, COPD-related mortality exhibited stronger associations with gaseous pollutants than with fine particulates.

The adverse effects of SO₂ on COPD-related mortality in our study were significantly higher than those in previous studies while the effects of PM_{2.5}, NO₂, CO, and O₃ were in accordance with the findings of prior research. A study of four Chinese cities revealed that 10 µg/m³ increases in concentrations of PM₁₀, SO₂, and NO₂ were related to 0.78, 1.38, and 1.85% increases in COPD mortality, respectively [18]. A time-series

study in Barcelona from 1985 to 1989 indicated that 50 $\mu\text{g}/\text{m}^3$ increases in NO_2 concentrations were associated with 14.5% increases in COPD mortality, while non-statistically significant associations existed between SO_2 and O_3 and COPD mortality [21]. The follow-up of the aforementioned study in Barcelona for the period 1985–1995 observed no effects of SO_2 , NO_2 , and CO gases on COPD mortality [4]. A case-crossover study in Shanghai indicated that 10 $\mu\text{g}/\text{m}^3$ increases in PM_{10} , SO_2 , and NO_2 concentrations could increase COPD mortality risks by 0.6, 3.3, and 4.2%, respectively [22]. A cohort study in the United States using hospital discharge data of patients aged 65 and older with a diagnosis of COPD revealed a 22% increase in the risk of COPD mortality for a 10 $\mu\text{g}/\text{m}^3$ increase in PM_{10} over the previous four years [23]. In a time series study in the Netherlands from 1992 to 2006, the excess risks of COPD mortality due to the effects of 10 $\mu\text{g}/\text{m}^3$ increases in the concentrations of $\text{PM}_{2.5}$, NO_2 , and O_3 were 0.9, 0.7, and 0.5%, respectively [16]. An extended follow-up of the Harvard Six Cities Study found non-statistically significant associations between $\text{PM}_{2.5}$ and COPD mortality [24]. The effect estimates for SO_2 on COPD-related mortality calculated in our study were approximately two to three times those in previous studies. Despite the fact that the individuals in our study were aged 60 and older, while the results in previous studies were mostly based on the entire population, the effect estimates for SO_2 in our study could be still considered higher than those in previous studies. The influences of other airborne pollutants, including $\text{PM}_{2.5}$, NO_2 , CO, and O_3 , on COPD-related mortality were similar to those in previous research.

Age, as a sociodemographic factor, modified the effect estimates for airborne pollutants on COPD-related mortality in our study. In general, the risks from airborne pollutants on COPD-related mortality increased with age, which is consistent with previous studies [23, 25]. Non-statistically significant effects on COPD-related mortality in individuals aged 60–69 were observed for ambient airborne pollutants in our study. Adverse effect estimates for $\text{PM}_{2.5}$ were only observed in individuals aged 90 and older, and those for CO were in individuals aged 80–89. Our investigation indicated that the health of older individuals was more likely to be adversely affected by ambient airborne pollutants than the health of younger individuals.

In this study, different effects of airborne pollutants on COPD-related mortality were not observed between different genders, nor among individuals with different marital statuses. Previous studies have reported that airborne pollutants had larger impacts on COPD in males than in females [9, 20, 25], raising the suspicion that smoking played a synergistic role that enhanced the influences of airborne pollutants. Simultaneously, some investigations have reported the opposite results [26, 27]. Therefore, future research is still needed on the modified effects of sociodemographic factors, including age and gender, with regard to air pollution and COPD-related mortality.

The associations between $\text{PM}_{2.5}$, SO_2 , and NO_2 and COPD-related mortality became non-statistically significant after adjusting for each other in our study, with some previous research reporting similar results [28, 29]. There were probable interactions among $\text{PM}_{2.5}$, SO_2 , and NO_2 . Conversely, O_3 exerted very stable influences on COPD-related mortality in our study, which was in accordance with previous research

[30, 31]. Adjusting for the remaining airborne pollutants did not alter the values of the effect estimates for O₃, suggesting that O₃ might be a more important exposure indicator than other ambient airborne pollutants when it comes to ambient air pollution and COPD-related mortality. CO exhibited unstably adverse effects according to our study. After adjusting for the remaining pollutants each time, the effects of CO were attenuated. Previous studies also reported unstable associations between ambient CO and COPD occurrences, hospitalizations, and emergency visits [32–34]. The effects of ambient CO on COPD-related mortality require further confirmation in future research.

Ambient airborne pollutants mostly originate from industrial emissions, traffic emissions, and the combustion of fuel [35–37]. The concentrations of airborne pollutants exhibited typical seasonal tendencies in our study. The concentrations of PM_{2.5}, SO₂, NO₂, and CO were relatively high during the winter, and lower during the summer. This was probably due to the reduction of airflow in winter and increased fuel consumption for heat. The concentration of O₃ was significantly higher in summer, which may be due to the increased sunlight. The influences of the seasonal tendencies were controlled using a natural cubic spline function in the models.

Airborne pollutants, including fine particulate matter and gaseous pollutants, could induce airway cellular injuries and cause airway epithelial cell apoptosis, which stimulates airway inflammation [38–40]. Progressive inflammatory disease in airways, alveoli, and microvasculature could induce COPD [41]. This represents a probable mechanism for airborne pollutants exacerbating COPD-related mortality. Another potential explanation is that individuals with COPD may be more susceptible to the acute cardiopulmonary effects of airborne pollutant exposure, thereby resulting in the higher risk of death [42].

The robustness of the models was tested using sensitivity analyses. The RRs calculated via different degrees of freedom for time trends ranging from 5 to 9 in the models were similar (Table S1). Hence, the results calculated from the models were reliable.

This study has three main strengths. First, it is the first to utilize a time-series study to examine the associations between ambient airborne pollutants and COPD-related mortality in the Sichuan Basin at an elevation over 500 meters. Second, the mortality data were derived from the PDIRMS, and were thus authentic and reliable. Third, the large and dense population and comparatively poor air conditions of Chengdu City made the area advantageous for conducting such an environmental study of the adverse effects of airborne pollutants on health. There are also some limitations, however. First, the exposure data were derived from 23 fixed monitoring sites, while personal exposure data were not obtained. Second, our study was conducted in the Sichuan Basin of southwestern China, where the characteristics of airborne pollutants and meteorological conditions may differ from those of other areas. Therefore, the results should be extrapolated with caution.

Conclusions

This study found that the ambient airborne pollutants PM_{2.5}, SO₂, NO₂, O₃, and CO were associated with COPD-related mortality in the central Sichuan Basin of southwestern China, which has an elevation of 500 meters. Susceptibilities to COPD-related mortality associated with ambient airborne pollutants may increase with age. The adverse effects of O₃ were stable. This study adds limited evidence to air pollution and health outcomes. Further research on personal exposure and the components of the particulate matter is needed to more accurately analyze air pollution and COPD-related mortality.

Abbreviations

PM_{2.5}, particulate matter < 2.5 µm in aerodynamic diameter; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; CO, carbon monoxide; O₃-8 h, daily eight-hour mean concentration of ozone; RH, relative humidity; COPD, chronic obstructive pulmonary disease; SD, standard deviation; IQR, interquartile range; RR, relative risk; CI, confidence interval.

Declarations

Ethics approval and consent to participate

Not applicable. This study does not involve experimental animals or individual information on human subjects.

Consent for publication

Not applicable.

Availability of data and material

The datasets used in this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JYC coordinated the study, performed data analysis, and drafted the manuscript; CLS, YL, HZN, and JZ contributed to the statistical analyses; RL assisted in obtaining air pollution and health data; and LZ organized and coordinated the study and edited the manuscript. All authors have read and approved the final manuscript.

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References

1. Rennard SI. COPD: Overview of Definitions, Epidemiology, and Factors Influencing Its Development. *Chest*. 1998;113(4, Supplement):235S–241S.
2. Pauwels RA, Rabe KF. Burden and clinical features of chronic obstructive pulmonary disease (COPD). *The Lancet*. 2004;364(9434):613–20.
3. Cohen AJ, Ross Anderson H, Ostro B, Pandey KD, Krzyzanowski M, Künzli N, Gutschmidt K, Pope A, Romieu I, Samet JM, et al. The Global Burden of Disease Due to Outdoor Air Pollution. *Journal of Toxicology Environmental Health Part A*. 2005;68(13–14):1301–7.
4. 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):1138–40.
5. Schikowski T, Sugiri D, Ranft U, Gehring U, Heinrich J, Wichmann HE, Krämer U. Long-term air pollution exposure and living close to busy roads are associated with COPD in women. *Respir Res*. 2005;6(1):152.
6. VIEGI G, MAIO S, PISTELLI F, BALDACCI S, CARROZZI L. Epidemiology of chronic obstructive pulmonary disease: Health effects of air pollution. *Respirology*. 2006;11(5):523–32.
7. Arbex MA, de Souza Conceição GM, Cendon SP, Arbex FF, Lopes AC, Moysés EP, Santiago SL, Saldiva PHN, Pereira LAA, Braga ALF. Urban air pollution and chronic obstructive pulmonary disease-related emergency department visits. *J Epidemiol Community Health*. 2009;63(10):777–83.
8. Hu G, Zhong N, Ran P. Air pollution and COPD in China. *J Thorac Dis*. 2015;7(1):59–66.
9. Peng L, Xiao S, Gao W, Zhou Y, Zhou J, Yang D, Ye X. Short-term associations between size-fractionated particulate air pollution and COPD mortality in Shanghai, China. *Environ Pollut*. 2020;257:113483.
10. Allardet-Servent J, Sicard G, Metz V, Chiche L. Benefits and risks of oxygen therapy during acute medical illness: Just a matter of dose! *La Revue de Médecine Interne*. 2019;40(10):670–6.
11. Li M-H, Fan L-C, Mao B, Yang J-W, Choi AMK, Cao W-J, Xu J-F. Short-term Exposure to Ambient Fine Particulate Matter Increases Hospitalizations and Mortality in COPD: A Systematic Review and Meta-analysis. *Chest*. 2016;149(2):447–58.
12. Yang Y, Chan C-y, Tao J, Lin M, Engling G, Zhang Z, Zhang T, Su L. Observation of elevated fungal tracers due to biomass burning in the Sichuan Basin at Chengdu City, China. *Science of The Total Environment*. 2012;431:68–77.
13. Han L, Zhou W, Li W, Li L. Impact of urbanization level on urban air quality: A case of fine particles (PM_{2.5}) in Chinese cities. *Environ Pollut*. 2014;194:163–70.

14. Resident Population (Year-end) by region. Sichuan Statistical Yearbook. <http://web.sctjj.cn/tjcbw/tjnj/2018/zk/indexch.htm>.
15. Liu C, Chen R, Sera F, Vicedo-Cabrera AM, Guo Y, Tong S, Coelho MSZS, Saldiva PHN, Lavigne E, Matus P, et al. Ambient Particulate Air Pollution and Daily Mortality in 652 Cities. *N Engl J Med*. 2019;381(8):705–15.
16. Fischer PH, Marra M, Ameling CB, Janssen N, Cassee FR. Trends in relative risk estimates for the association between air pollution and mortality in The Netherlands, 1992–2006. *Environ Res*. 2011;111(1):94–100.
17. Raji H, Riahi A, Borsi SH, Masoumi K, Khanjani N, AhmadiAngali K, Goudarzi G, Dastoorpoor M. Acute Effects of Air Pollution on Hospital Admissions for Asthma, COPD, and Bronchiectasis in Ahvaz, Iran. *Int J Chron Obstruct Pulmon Dis*. 2020;15:501–14.
18. Meng X, Wang C, Cao D, Wong C-M, Kan H. Short-term effect of ambient air pollution on COPD mortality in four Chinese cities. *Atmos Environ*. 2013;77:149–54.
19. Gan WQ, FitzGerald JM, Carlsten C, Sadatsafavi M, Brauer M. Associations of Ambient Air Pollution with Chronic Obstructive Pulmonary Disease Hospitalization and Mortality. *Am J Respir Crit Care Med*. 2013;187(7):721–7.
20. Næss 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):435–43.
21. Garcia-Aymerich J, Tobías A, Antó JM, Sunyer J. Air pollution and mortality in a cohort of patients with chronic obstructive pulmonary disease: a time series analysis. *J Epidemiol Community Health*. 2000;54(1):73–4.
22. Kan H, Chen B. A Case-crossover Analysis of Air Pollution and Daily Mortality in Shanghai. *J Occup Health*. 2003;45(2):119–24.
23. Zanobetti A, Bind M-AC, Schwartz J. Particulate air pollution and survival in a COPD cohort. *Environ Health*. 2008;7(1):48.
24. Lepeule J, Laden F, Dockery D, Schwartz J. Chronic Exposure to Fine Particles and Mortality: An Extended Follow-up of the Harvard Six Cities Study from 1974 to 2009. *Environ Health Perspect*. 2012;120(7):965–70.
25. Xu M, Sbihi H, Pan X, Brauer M. Modifiers of the effect of short-term variation in PM_{2.5} on mortality in Beijing, China. *Environ Res*. 2020;183:109066.
26. Li X, Xiao J, Huang M, Liu T, Guo L, Zeng W, Chen Q, Zhang J, Ma W. Associations of county-level cumulative environmental quality with mortality of chronic obstructive pulmonary disease and mortality of tracheal, bronchus and lung cancers. *Science of The Total Environment*. 2020;703:135523.
27. Doiron D, de Hoogh K, Probst-Hensch N, Fortier I, Cai Y, De Matteis S, Hansell AL. Air pollution, lung function and COPD: results from the population-based UK Biobank study. *Eur Respir J*. 2019;54(1):1802140.

28. 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. *Environmental health perspectives*. 2019;127(1):17008.
29. Burney P, Amaral AFS. Air pollution and chronic airway disease: is the evidence always clear? *The Lancet*. 2019;394(10215):2198–200.
30. Lim CC, Hayes RB, Ahn J, Shao Y, Silverman DT, Jones RR, Garcia C, Bell ML, Thurston GD. Long-Term Exposure to Ozone and Cause-Specific Mortality Risk in the United States. *Am J Respir Crit Care Med*. 2019;200(8):1022–31.
31. Kazemiparkouhi F, Eum K-D, Wang B, Manjourides J, Suh HH. Long-term ozone exposures and cause-specific mortality in a US Medicare cohort. *J Expo Sci Environ Epidemiol* 2019.
32. Pothirat C, Chaiwong W, Liwsrisakun C, Bumroongkit C, Deesomchok A, Theerakittikul T, Limsukon A, Tajarennmuang P, Phetsuk N. Acute effects of air pollutants on daily mortality and hospitalizations due to cardiovascular and respiratory diseases. *J Thorac Dis*. 2019;11(7):3070–83.
33. Qu F, Liu F, Zhang H, Chao L, Guan J, Li R, Yu F, Yan X. Comparison of air pollutant-related hospitalization burden from AECOPD in Shijiazhuang, China, between heating and non-heating season. *Environ Sci Pollut Res*. 2019;26(30):31225–33.
34. Hendryx M, Luo J, Chojenta C, Byles JE. Air pollution exposures from multiple point sources and risk of incident chronic obstructive pulmonary disease (COPD) and asthma. *Environ Res*. 2019;179:108783.
35. Guan W-J, Zheng X-Y, Chung KF, Zhong N-S. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *The Lancet*. 2016;388(10054):1939–51.
36. Chen T-M, Kuschner WG, Gokhale J, Shofer S. Outdoor Air Pollution: Nitrogen Dioxide, Sulfur Dioxide, and Carbon Monoxide Health Effects. *Am J Med Sci*. 2007;333(4):249–56.
37. Li J, Wang Z, Akimoto H, Yamaji K, Takigawa M, Pochanart P, Liu Y, Tanimoto H, Kanaya Y. Near-ground ozone source attributions and outflow in central eastern China during MTX2006. *Atmos Chem Phys*. 2008;8(24):7335–51.
38. Ayyagari VN, Januszkiewicz A, Nath J. Effects of Nitrogen Dioxide on the Expression of Intercellular Adhesion Molecule-1, Neutrophil Adhesion, and Cytotoxicity: Studies in Human Bronchial Epithelial Cells. *Inhalation Toxicol*. 2007;19(2):181–94.
39. Song A, Liao Q, Li J, Lin F, Liu E, Jiang X, Deng L. Chronic exposure to sulfur dioxide enhances airway hyperresponsiveness only in ovalbumin-sensitized rats. *Toxicol Lett*. 2012;214(3):320–7.
40. Abramson MJ, Wigmann C, Altug H, Schikowski T. Ambient air pollution is associated with airway inflammation in older women: a nested cross-sectional analysis. *BMJ Open Respiratory Research*. 2020;7(1):e000549.
41. Rabe KF, Watz H. Chronic obstructive pulmonary disease. *The Lancet*. 2017;389(10082):1931–40.
42. Chen X, Wang T, Qiu X, Que C, Zhang H, Zhang L, Zhu T. Susceptibility of individuals with chronic obstructive pulmonary disease to air pollution exposure in Beijing, China: A case-control panel study (COPDB). *Science of The Total Environment*. 2020;717:137285.

Figures

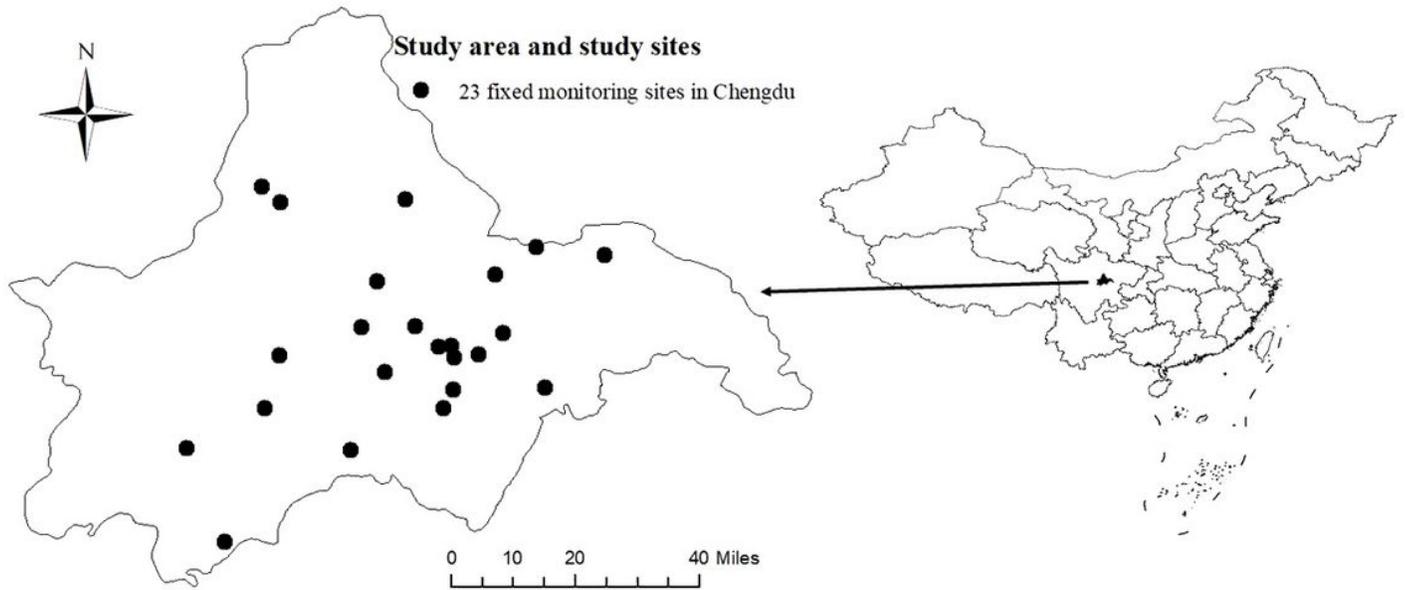


Figure 1

Location of study area in Chengdu City, southwestern China. The enlarged area on the left depicts the spatial distribution of 23 fixed monitoring sites throughout Chengdu City.

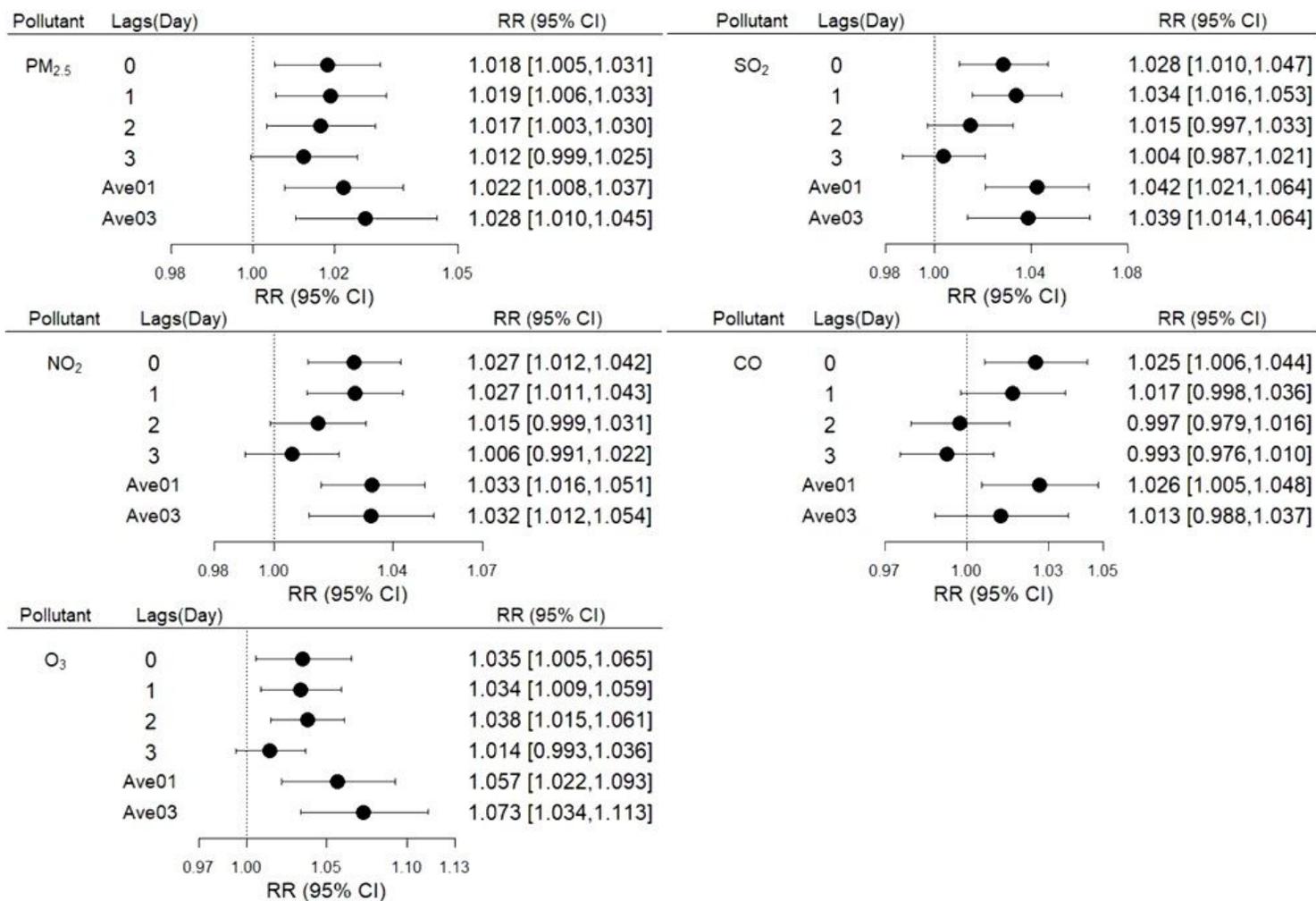


Figure 2

Associations between IQR increases in PM_{2.5}, SO₂, NO₂, CO, and O₃ and COPD-related mortality among elderly people at lag0, lag1, lag2, lag3, lag01, and lag03 days, respectively. All models were adjusted for daily temperature and relative humidity.

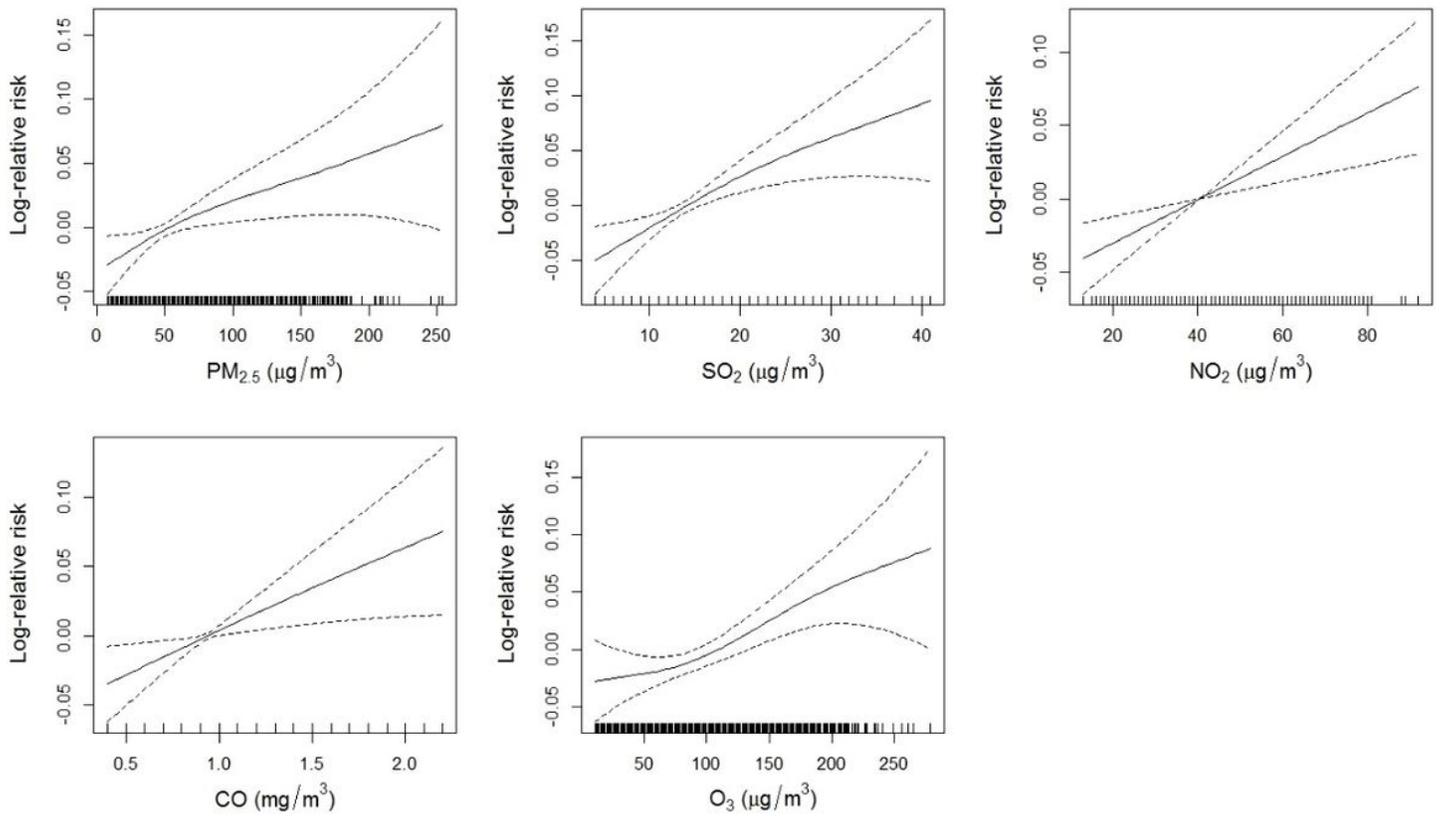


Figure 3

Exposure-response curves for associations between concentration increases in each ambient airborne pollutant and COPD-related mortality. Curves for PM_{2.5}, SO₂, NO₂, CO, and O₃ corresponded to one-day, one-day, one-day, zero-day, and two-day lags, respectively.

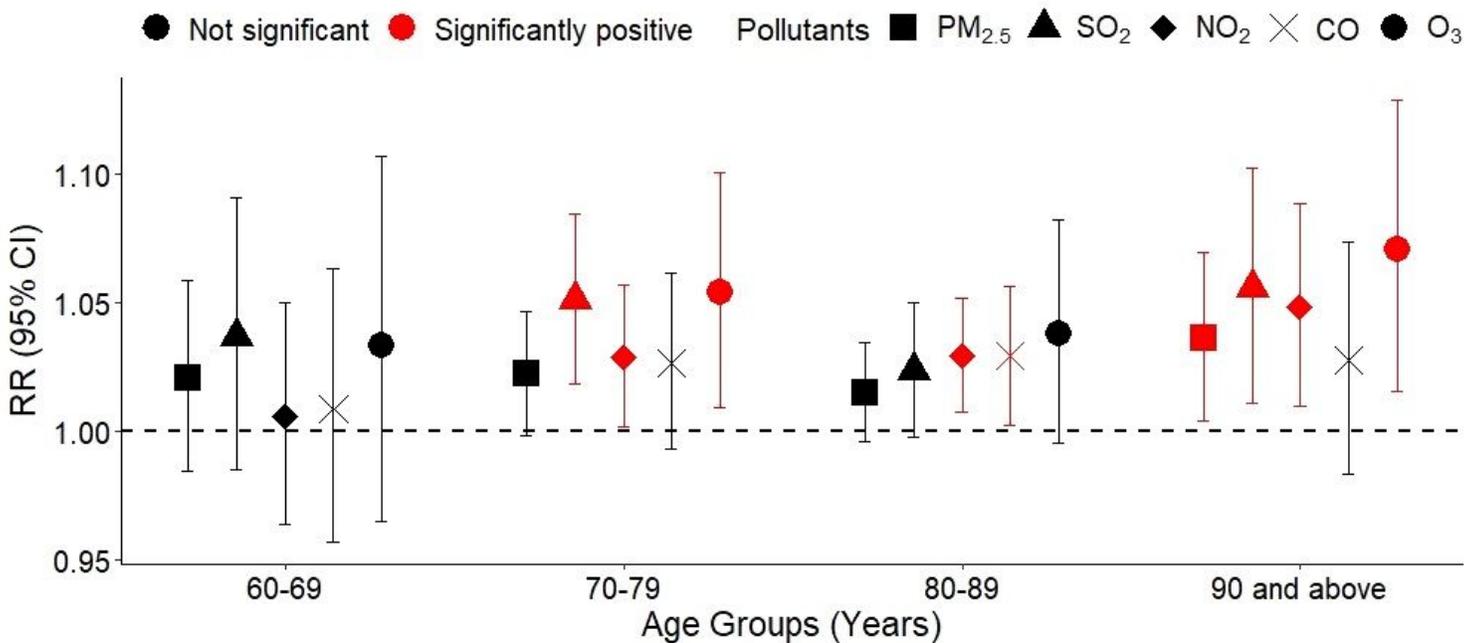


Figure 4

Associations between IQR increases in PM_{2.5}, SO₂, NO₂, CO, and O₃ and COPD-related mortality among different age groups

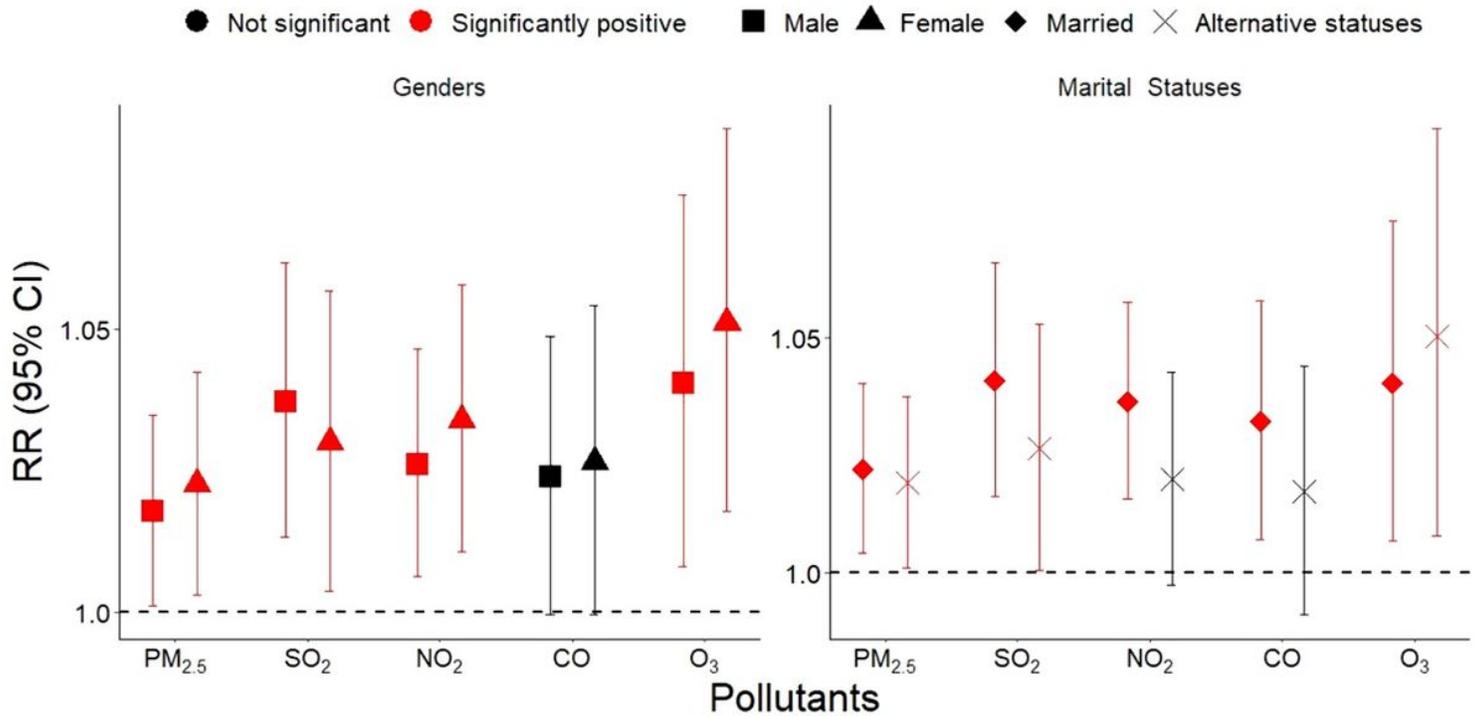


Figure 5

Associations between IQR increases in PM_{2.5}, SO₂, NO₂, CO, and O₃ and COPD-related mortality between different genders, and between different marital statuses

Supplementary Files

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