Preplanned Studies

Assessment of the Respiratory Disease Mortality Risk from Single and Composite Exposures to $PM_{2.5}$ and Ozone — Guangzhou City, Guangdong Province, China, 2018–2021

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Summary

What is already known about this topic?

Fine particulate matter ($PM_{2.5}$) and ozone (O_3) are prevalent pollutants in the atmosphere, which threaten human health, especially the respiratory system. Typically, people are exposed to a mixture of various pollutants in the environment. Thus, the single and combined effects of both pollutants need to be investigated.

What is added by this report?

$PM_{2.5}$ and O_3 increase the risk of death from lung cancer, chronic obstructive pulmonary disease (COPD), and respiratory diseases, with their lagged and cumulative effects analyzed, indicating an acute effect. In addition, combined exposure to both pollutants can significantly affect disease deaths.

What are the implications for public health practice?

This study provides further evidence of the single and combined effects of $PM_{2.5}$ and O_3 on respiratory diseases, emphasizing the need for sustained efforts in air pollution control, with greater attention to the synergistic management of air pollutants.

Air pollution continues to be a significant risk factor for disability and is associated with approximately 6.67 million global deaths annually (*1*). According to the 2018 Guangdong Ecological Environment Report, ozone (O_3) and fine particulate matter ($PM_{2.5}$), accounting for 55.5% and 17.0% of primary pollutants, respectively, are the predominant contaminants in the Pearl River Delta region's 9 cities (*2*). It has been established that $PM_{2.5}$ and O_3 are positively associated with the incidence and mortality rates of respiratory diseases, which may also have interaction effects between O_3 and $PM_{2.5}$ on population health (*3*).

In this study, we employed a generalized additive model (GAM) to analyze the associations between O_3 and $PM_{2.5}$ concentrations and mortality rates from respiratory diseases, chronic obstructive pulmonary disease (COPD), and lung cancer in Guangzhou. Additionally, we applied the quantile g-computation (QG-C) model to assess the combined effects of these pollutants on mortality related to respiratory conditions. Our findings contribute to a more comprehensive environmental health risk assessment and support the formulation of integrated prevention and control strategies.

Meteorological data, the daily maximum 8-hour average concentration of O_3 and the 24-hour average concentration of $PM_{2.5}$, during 2018–2021, were sourced from the Guangdong Multi-Trigger Smart Early Warning System. Respiratory diseases, COPD, and lung cancer, which are attributed to death, were classified using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) codes with J00-J99, J40-J47, and C34, respectively.

R (version 4.2.2; R Core Team, Vienna, Austria) equipped with the "mgcv" and "dlnm" packages was utilized to develop GAMs to investigate the non-linear relationships between pollutant exposure and mortality from selected diseases. Both lagged concentrations and moving averages of pollutants were integrated into the models to consider delayed and cumulative effects. The QG-C method, utilizing the "qgcomp" package, estimated the joint effects of $PM_{2.5}$ and O_3 exposure, with the lowest quantile serving as the reference point (*4*). Subgroup analyses were performed based on age (less than 85 years and 85 years or older), sex, seasonal variations (April to September as warm and October to March as cold), and the coronavirus disease 2019 (COVID-19) pandemic periods (2018–2019 and 2020–2021).

The outcomes of the single-pollutant exposure analysis are presented as excess risk (*ER*) with a 95%

confidence interval (*CI*) corresponding to every 10 μg/m^3 increment in pollutant levels. For combined exposure effects, relative risks (*RR*s) and their 95% *CI*s are reported per quartile increase in pollutant concentration. Z tests were employed to assess differences between subgroups, with a *P* less than 0.05 denoting statistical significance.

During 2018 and 2021, Guangzhou recorded 29,258 deaths from respiratory diseases, 11,036 from COPD, and 16,901 from lung cancer (Supplementary Table S1, available at https://weekly.chinacdc.cn/). The mortality rates for respiratory diseases and COPD declined in both genders, whereas lung cancer mortality rates varied throughout the period (Supplementary Table S2, available at https://weekly.chinacdc.cn/).

The average daily concentrations were 29.34 μg/m^3 for $PM_{2.5}$ and 90.63 μg/m^3 for O_3. O_3 levels exhibited a slight increase, whereas $PM_{2.5}$ levels showed a significant decline (Supplementary Figure S1A–B, available at https://weekly.chinacdc.cn/). The monthly trends in O_3 and $PM_{2.5}$ concentrations in Guangzhou varied significantly. According to the meteorological data, the daily average temperature was 22.71 °C, and the average relative humidity was 79.14% in Guangzhou. (Supplementary Figure S1C–D). $PM_{2.5}$ levels showed a distinct seasonal pattern, peaking in winter and reaching the lowest levels in summer. Autocorrelation analysis revealed a non-stationary sequence, indicating a decrease in pollutant concentrations over time. Unlike $PM_{2.5}$, O_3 concentrations did not exhibit any annual variability; however, they still displayed a seasonal pattern, with the highest levels of pollution from April to September (Supplementary Figure S1E–F).

As demonstrated in Table 1 and Supplementary Figure S2 (available at https://weekly.chinacdc.cn/), the highest and most statistically significant increased risk was observed on the first day (lag0) for both O_3 and $PM_{2.5}$ (P<0.05). As the lag time extended, the correlations between these pollutants and mortality rates gradually diminished and were no longer significant after three days (lag3), suggesting that O_3 and $PM_{2.5}$ primarily have acute impacts on respiratory diseases. Both $PM_{2.5}$ and O_3 exhibited cumulative effects on mortality from all selected diseases. The maximum cumulative effects of $PM_{2.5}$ and O_3 on all-cause mortality were seen at lag03, except that of O_3 on respiratory disease occurred at lag04. However, when $PM_{2.5}$ was set as a covariate, no significant association was observed between O_3 exposure and lung cancer mortality (Supplementary Table S3, available at https://weekly.chinacdc.cn/).

The results of the subgroup analysis assessing the impact of O_3 and $PM_{2.5}$ on mortality from selected diseases across various demographics and the COVID-19 pandemic period are presented (Figure 1, and Supplementary Table S4, available at https://weekly.chinacdc.cn/). The analysis revealed minimal significant differences in the effects across age groups, sexes, and throughout the COVID-19 pandemic, suggesting that these factors may not significantly modify the association between O_3/$PM_{2.5}$ exposure and mortality risk from selected diseases. Notably, the

TABLE 1. Excess risk associated with exposure to $PM_{2.5}$ or O_3 on respiratory disease mortality.

Lag time	$PM_{2.5}$, *ER* (95% *CI*) (%)			O_3, *ER* (95% *CI*) (%)		
	Respiratory diseases	COPD	Lung cancer	Respiratory diseases	COPD	Lung cancer
Lag0	1.08 (0.62, 1.55)*	1.00 (0.26, 1.74)*	1.42 (0.81, 2.04)*	0.37 (0.19, 0.55)*	0.50 (0.20, 0.79)*	0.34 (0.12, 0.57)*
Lag1	0.86 (0.49, 1.23)*	0.77 (0.18, 1.36)*	1.09 (0.61, 1.58)*	0.30 (0.16, 0.44)*	0.39 (0.16, 0.62)*	0.26 (0.08, 0.44)*
Lag2	0.63 (0.35, 0.92)*	0.54 (0.09, 1.00)*	0.76 (0.38, 1.13)*	0.23 (0.12, 0.33)*	0.29 (0.11, 0.46)*	0.17 (0.04, 0.31)*
Lag3	0.41 (0.18, 0.63)*	0.32 (−0.05, 0.68)	0.43 (0.13, 0.73)*	0.15 (0.07, 0.23)*	0.18 (0.04, 0.32)*	0.09 (−0.02, 0.19)
Lag4	0.18 (−0.04, 0.40)	0.09 (−0.26, 0.44)	0.10 (−0.19, 0.38)	0.08 (−0.00, 0.16)	0.07 (−0.06, 0.20)	0.00 (−0.09, 0.10)
Lag5	−0.04 (−0.30, 0.21)	−0.14 (−0.54, 0.27)	−0.23 (−0.57, 0.11)	0.00 (−0.09, 0.10)	−0.03 (−0.19, 0.13)	−0.08 (−0.20, 0.04)
Lag01	2.65 (1.47, 3.82)*	2.51 (0.62, 4.39)*	3.65 (2.10, 5.20)*	0.77 (0.30, 1.23)*	1.14 (0.37, 1.91)*	0.72 (0.13, 1.31)*
Lag02	3.06 (1.78, 4.34)*	2.61 (0.55, 4.67)*	3.83 (2.15, 5.52)*	1.03 (0.54, 1.52)*	1.40 (0.59, 2.22)*	0.79 (0.16, 1.41)*
Lag03	3.28 (1.91, 4.66)*	2.72 (0.51, 4.93)*	3.90 (2.08, 5.71)*	1.12 (0.61, 1.64)*	1.46 (0.61, 2.32)*	0.85 (0.20, 1.51)*
Lag04	3.15 (1.69, 4.62)*	2.70 (0.35, 5.04)*	3.42 (1.48, 5.35)*	1.14 (0.60, 1.68)*	1.41 (0.52, 2.31)*	0.77 (0.08, 1.46)*
Lag05	2.77 (1.23, 4.31)*	2.32 (−0.15, 4.80)	2.92 (0.88, 4.96)*	1.07 (0.50, 1.63)*	1.23 (0.29, 2.17)*	0.64 (−0.08, 1.36)*

Abbreviation: *ER*=excess risk; *CI*=confidence interval; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=fine particulate matter; O_3=ozone.

* *P*<0.05.

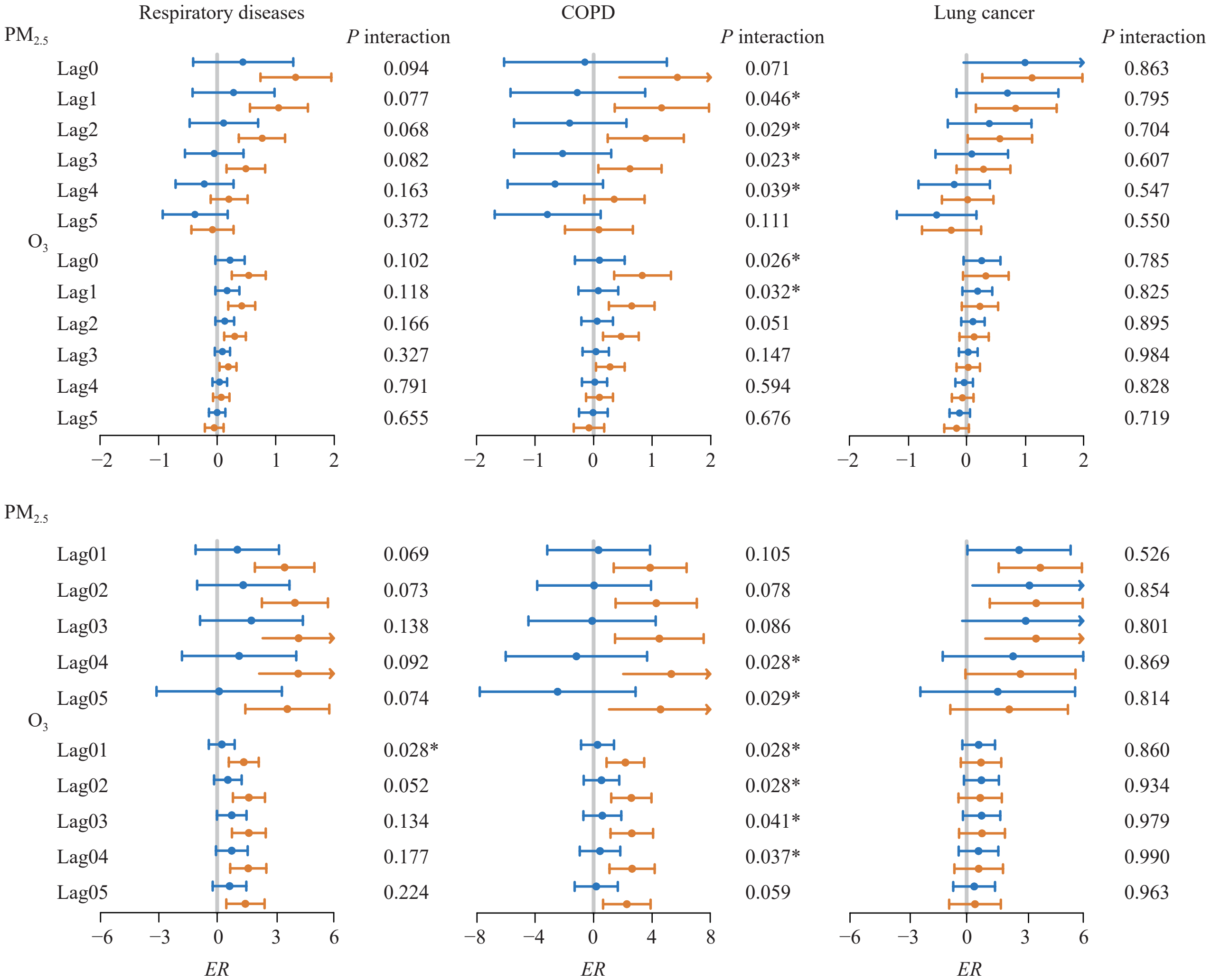

FIGURE 1. Effects of changes in $PM_{2.5}$ and O_3 concentrations on mortality across cool and warm season subgroups under various lag conditions.

Note: Single lags lag0 to lag5 and cumulative lags lag01 to lag05. Blue represents the cold group; yellow represents the warm group.

Abbreviation: *ER*=excess risk; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=fine particulate matter; O_3=ozone.

* P<0.05.

warm season exhibited a higher *ER* for mortality from COPD associated with exposure to O_3 or $PM_{2.5}$ (Figure 1). Furthermore, $PM_{2.5}$ exposure demonstrated a more pronounced effect on COPD mortality in males compared to females, whereas the reverse was observed for lung cancer. In terms of age, $PM_{2.5}$ exposure had a stronger impact on individuals aged above 85 years, whereas O_3 showed greater effects on those under 85 years.

Spearman correlation analysis revealed positive correlations between $PM_{2.5}$ and O_3, indicating potential interactions between these pollutants. In terms of meteorological factors, O_3 showed a positive correlation with temperature and a negative correlation with relative humidity. Conversely, $PM_{2.5}$ exhibited negative correlations with both temperature and relative humidity (Supplementary Table S5, available at https://weekly.chinacdc.cn/).

The QG-C model demonstrated that combined exposure to $PM_{2.5}$ and O_3 was significantly associated with increased mortality due to all selected diseases, of which the weights of two pollutants were presented in Supplementary Figure S3 (available at https://weekly.chinacdc.cn/). For females and individuals aged below 85, this combined exposure was identified as a risk factor for mortality. Among males, concurrent exposure to $PM_{2.5}$ and O_3 was also linked to an increased risk of mortality from lung cancer.

Furthermore, during the warm seasons, the correlation between combined exposure to $PM_{2.5}$ and O_3 and mortality from all examined diseases was evident, suggesting that higher temperatures may significantly influence respiratory-related diseases (Table 2).

DISCUSSION

In recent years, public concern over air pollution in China, specifically regarding $PM_{2.5}$ and O_3 exposure, has escalated. Standards set by the Chinese Ambient Air Quality Standards (AAQSs) reveal that from 2018 to 2021, only 68.99% of days met the $PM_{2.5}$ criteria. Furthermore, the compliance for O_3 was even lower, with just 35.25% of days meeting the AAQSs. This data underscores the persistent air pollution threat facing residents of Guangzhou and highlights the urgent need for enhanced pollution control measures.

It has been found that higher concentrations of $PM_{2.5}$ and O_3 were positively correlated with an increased risk of death from respiratory diseases in this study by using a time-series design. Many epidemiological studies have consistently demonstrated significant correlations between $PM_{2.5}$ and O_3 exposure and both the incidence and mortality of respiratory conditions, particularly lung-related diseases (*5*). The associations found in this study seem to be stronger than those reported elsewhere. This discrepancy could be attributed to Guangzhou's unique geographical characteristics (*6*), such as its extended warm seasons and elevated temperatures, which may enhance respiratory rates and lung ventilation, thereby heightening vulnerability to air pollutants.

Our findings indicate a positive association between combined exposure to $PM_{2.5}$ and O_3, and increased mortality from all selected diseases. This association may be mechanistically supported by the ability of particulate matter to reduce ultraviolet radiation penetration, thus interfering with O_3 photochemical reactions. Additionally, exposure to both $PM_{2.5}$ and O_3 can stimulate oxidative stress in lung tissues, suggesting there are biological interactions and combined effects between these pollutants (*7*).

This study also presents several limitations. First, it assumes that air pollutant concentrations from monitoring stations reflect the population exposures. Second, the dataset only includes Guangzhou, which limits the generalizability of the findings. Lastly, the study's time-series analysis design is unable to assess the long-term risks associated with air pollution.

Exposure to $PM_{2.5}$ and O_3 in the atmosphere is linked to an increased risk of respiratory diseases, COPD, and lung cancer mortality. The combined effects of $PM_{2.5}$ and O_3 further exacerbate mortality rates associated with these conditions. Given that the current levels of $PM_{2.5}$ and O_3 continue to pose health risks, it is crucial to enhance health protection and disease control strategies for the population in

TABLE 2. Association of combined $PM_{2.5}$ and O_3 exposure with mortality risk according to the QG-C model.

Group	Died of respiratory diseases	Died of COPD	Died of lung cancer
Total population	1.03 (1.01, 1.05)†	1.03 (1.00, 1.07)*	1.05(1.02, 1.08)†
Age group (years)			
≥85	1.03 (1.00, 1.06)*	1.03 (0.99, 1.08)	1.02 (0.95, 1.09)
<85	1.04 (1.01, 1.06)†	1.04 (0.99, 1.08)	1.05 (1.03, 1.08)†
Sex			
Male	1.01 (0.99, 1.04)	1.03 (0.99, 1.07)	1.05 (1.02, 1.08)†
Female	1.06 (1.03, 1.1)†,§	1.04 (0.98, 1.10)	1.06 (1.01, 1.11)*
Season			
Cold	1.00 (0.97, 1.03)	0.99 (0.95, 1.04)	1.02 (0.99, 1.06)
Warm	1.04 (1.02, 1.07)†,§	1.04 (1.00, 1.08)*	1.04 (1.00, 1.07)*
Time			
COVID-19	1.02 (0.99, 1.05)	1.03 (0.99, 1.07)	1.02 (0.99, 1.05)
non-COVID-19	1.01 (0.99, 1.04)	1.02 (0.98, 1.06)	1.06 (1.02, 1.09)†

Abbreviation: COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019.

* P<0.05;

† P<0.01;

§ statistically significant compared to males or cold group.

Guangzhou.

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SUPPLEMENTAL MATERIAL

The GAMs Model Equation

$$Log[E(Y_t)] = X + s\left(time, \frac{7df}{year}\right) + s(hum, \upsilon) + s(temp, \upsilon) + DOW + PH + intercept \quad (1)$$

where $E(Y_t)$ denotes the expected number of daily deaths from respiratory diseases, chronic obstructive pulmonary disease (COPD), or lung cancer on day t;

X represents O_3 (or $PM_{2.5}$);

s represents a smooth basis function;

time represents a time series.

df represents degrees of freedom. Drawing from prior research, a natural cubic spline function was employed with seven degrees of freedom per year to account for natural variations in mortality rates over time.

hum represents the daily average relative humidity;

temp represents the daily average temperature;

υ represents degrees of freedom;

DOW (day of the week) represents weekday variables;

PH (public holiday) represents holiday variables.

According to the AIC criterion, the value of υ for humidity was set at 2, and υ for temperature was set at 3.

Multiple Sensitivity Analyses

We performed several sensitivity analyses to assess the stability of the relationship between air pollutants and mortality due to respiratory diseases, COPD, and lung cancer. Initially, besides the aforementioned single-pollutant models, dual-pollutant models were employed to adjust for potential confounders from co-existing pollutants.

SUPPLEMENTARY TABLE S1. Descriptive analysis of disease-related deaths in Guangzhou City, 2018–2022.

Type of diseases	Subgroups	Number of diseases	$\bar{x}\pm s$
	Sex		
	Male	18,318	12.54±4.40
	Female	10,940	7.49±3.22
Respiratory diseases	Age, years		
	≥85	13,460	9.21±3.55
	<85	15,798	10.81±3.89
	Total	29,258	20.03±6.08
	Sex		
	Male	8,062	5.52±2.79
	Female	2,974	2.04±1.57
COPD	Age, years		
	≥85	4,915	3.36±2.08
	<85	6,121	4.19±2.35
	Total	11,036	7.55±3.47
	Sex		
	Male	11,635	7.96±2.93
	Female	5,266	3.60±1.93
Lung cancer	Age, years		
	≥85	2,065	1.41±1.19
	<85	14,836	10.15±3.32
	Total	16,901	11.57±3.56

Note: $\bar{x}$=the daily average mortality of each subgroup during 2018 to 2021 in Guangzhou; *s*=standard deviation.
Abbreviation: COPD=chronic obstructive pulmonary disease.

SUPPLEMENTARY TABLE S2. Gender-standardized mortality rates in Guangzhou City from 2018 to 2021 (per 100,000).

Disease type	Gender	2018	2019	2020	2021
Respiratory diseases	Male	50.23	53.37	43.11	47.94
	Female	29.49	30.66	25.02	24.77
COPD	Male	24.88	22.37	18.60	19.97
	Female	9.17	7.76	6.75	6.28
Lung cancer	Male	31.91	29.26	30.28	32.02
	Female	13.11	12.57	13.46	13.58

Abbreviation: COPD=chronic obstructive pulmonary disease.

SUPPLEMENTARY TABLE S3. Sensitivity analysis of the dual-pollutant model in Guangzhou from 2018 to 2021.

Lag time	$PM_{2.5}$, *ER* (95% *CI*) (%)			O_3, *ER* (95% *CI*) (%)		
	Respiratory diseases	COPD	Lung cancer	Respiratory diseases	COPD	Lung cancer
Lag0	1.15 (0.63, 1.67)*	0.98 (0.16, 1.82)*	1.49 (0.80, 2.18)*	0.31 (0.11, 0.52)*	0.48 (0.14, 0.82)*	0.16 (−0.10, 0.42)
Lag1	0.91 (0.50, 1.32)*	0.76 (0.10, 1.42)*	1.14 (0.59, 1.69)*	0.25 (0.09, 0.41)*	0.37 (0.11, 0.64)*	0.11 (−0.09, 0.32)
Lag2	0.67 (0.35, 0.99)*	0.53 (0.03, 1.04)*	0.79 (0.37, 1.22)*	0.19 (0.07, 0.31)*	0.27 (0.07, 0.47)*	0.07 (−0.08, 0.22)
Lag3	0.43 (0.19, 0.68)*	0.31 (−0.08, 0.70)	0.45 (0.13, 0.78)*	0.13 (0.04, 0.22)*	0.17 (0.02, 0.32)*	0.03 (−0.09, 0.14)
Lag4	0.19 (−0.03, 0.41)	0.09 (−0.27, 0.44)	0.11 (−0.19, 0.40)	0.07 (−0.01, 0.15)	0.07 (−0.06, 0.20)	−0.02 (−0.12, 0.08)
Lag5	−0.05 (−0.30, 0.21)	−0.14 (−0.54, 0.27)	−0.23 (−0.58, 0.11)	0.01 (−0.09, 0.11)	−0.03 (−0.19, 0.13)	−0.06 (−0.18, 0.06)
Lag01	2.75 (1.34, 4.17)*	2.41 (0.14, 4.69)*	4.18 (2.3, 6.06)*	0.4 (−0.18, 0.97)	0.88 (−0.07, 1.83)	−0.08 (−0.81, 0.66)
Lag02	3.3 (1.82, 4.78)*	2.73 (0.35, 5.11)*	4.37 (2.4, 6.34)*	0.67 (0.09, 1.25)*	1.23 (0.26, 2.2)*	0.05 (−0.69, 0.80)
Lag03	3.55 (2.01, 5.09)*	2.83 (0.36, 5.31)*	4.36 (2.32, 6.41)*	0.87 (0.28, 1.46)*	1.41 (0.43, 2.39)*	0.18 (−0.57, 0.93)
Lag04	3.47 (1.88, 5.07)*	2.84 (0.27, 5.40)*	3.89 (1.77, 6.02)*	0.96 (0.36, 1.56)*	1.42 (0.43, 2.41)*	0.24 (−0.53, 1.00)
Lag05	3.11 (1.45, 4.76)*	2.42 (−0.24, 5.08)	3.32 (1.12, 5.53)*	0.94 (0.33, 1.55)*	1.24 (0.23, 2.25)*	0.2 (−0.57, 0.98)

Abbreviation: *ER*=excess risk; *CI*=confidence interval; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=fine particulate matter; O_3=ozone.
* *P*<0.05.

SUPPLEMENTARY TABLE S4. Effect modification by different subgroups on the associations between exposure at lag 0–5 to $PM_{2.5}$/O_3 and respiratory-related diseases.

Subgroup	Lag time	$PM_{2.5}$, *ER* (95% *CI*) (%)			O_3, *ER* (95% *CI*) (%)		
		Respiratory diseases	COPD	Lung cancer	Respiratory diseases	COPD	Lung cancer
<85 years	Lag0	1.06 (0.46, 1.67)*	0.80 (−0.18, 1.78)	1.46 (0.81, 2.12)*	0.43 (0.20, 0.66)*	0.52 (0.13, 0.91)*	0.36 (0.12, 0.60)*
	Lag1	0.86 (0.39, 1.34)*	0.61 (−0.16, 1.40)	1.13 (0.61, 1.65)*	0.36 (0.17, 0.54)*	0.44 (0.13, 0.75)*	0.27 (0.08, 0.46)*
	Lag2	0.67 (0.30, 1.04)*	0.43 (−0.17, 1.03)	0.80 (0.40, 1.20)*	0.29 (0.15, 0.43)*	0.36 (0.13, 0.59)*	0.19 (0.04, 0.33)*
	Lag3	0.47 (0.17, 0.76)*	0.24 (−0.24, 0.73)	0.47 (0.15, 0.79)*	0.22 (0.11, 0.32)*	0.28 (0.10, 0.46)*	0.10 (−0.01, 0.22)
	Lag4	0.27 (−0.01, 0.55)	0.06 (−0.40, 0.52)	0.15 (−0.16, 0.45)	0.14 (0.04, 0.25)*	0.20 (0.03, 0.37)*	0.02 (−0.09, 0.12)
	Lag5	0.07 (−0.26, 0.41)	−0.12 (−0.67, 0.42)	−0.18 (−0.54, 0.18)	0.07 (−0.05, 0.20)	0.12 (−0.08, 0.33)	−0.07 (−0.20, 0.06)
	Lag01	2.76 (1.23, 4.28)*	1.70 (−0.80, 4.20)	3.91 (2.26, 5.56)*	1.04 (0.43, 1.64)*	1.37 (0.36, 2.38)*	0.79 (0.16, 1.42)*
	Lag02	3.28 (1.61, 4.94)*	1.97 (−0.75, 4.70)	4.06 (2.26, 5.85)*	1.28 (0.65, 1.92)*	1.66 (0.58, 2.73)*	0.85 (0.19, 1.52)*
	Lag03	3.59 (1.81, 5.38)*	2.33 (−0.59, 5.25)	4.22 (2.28, 6.15)*	1.47 (0.80, 2.14)*	1.92 (0.80, 3.05)*	0.92 (0.22, 1.62)*
	Lag04	3.42 (1.52, 5.33)*	2.19 (−0.92, 5.3)	3.78 (1.72, 5.84)*	1.50 (0.80, 2.20)*	1.99 (0.80, 3.17)*	0.85 (0.12, 1.58)*
	Lag05	3.13 (1.12, 5.13)*	1.79 (−1.5, 5.07)	3.29 (1.12, 5.47)*	1.48 (0.75, 2.22)*	1.88 (0.65, 3.12)*	0.74 (−0.03, 1.51)
≥85 years	Lag0	1.12 (0.46, 1.77)*	1.25 (0.20, 2.31)*	1.17 (−0.55, 2.92)	0.31 (0.06, 0.56)*	0.47 (0.05, 0.90)*	0.25 (−0.38, 0.88)
	Lag1	0.86 (0.34, 1.38)*	0.97 (0.13, 1.81)*	0.81 (−0.56, 2.19)	0.23 (0.03, 0.43)*	0.33 (−0.00, 0.67)	0.16 (−0.33, 0.66)
	Lag2	0.59 (0.19, 1.00)*	0.69 (0.04, 1.34)*	0.44 (−0.61, 1.51)	0.15 (0.00, 0.30)	0.19 (−0.06, 0.45)	0.07 (−0.30, 0.45)
	Lag3	0.33 (0.01, 0.66)*	0.41 (−0.11 ,0.93)	0.08 (−0.77, 0.93)	0.08 (−0.04, 0.19)	0.05 (−0.15, 0.25)	−0.01 (−0.30, 0.28)
	Lag4	0.07 (−0.23, 0.38)	0.13 (−0.36, 0.62)	−0.28 (−1.09, 0.53)	−0.00 (−0.11, 0.11)	−0.09 (−0.28, 0.10)	−0.10 (−0.37, 0.17)
	Lag5	−0.18 (−0.55, 0.18)	−0.15 (−0.73, 0.43)	−0.64 (−1.61, 0.33)	−0.08 (−0.21, 0.06)	−0.23 (−0.46, −0.00)	−0.19 (−0.52, 0.15)
	Lag01	2.6 (0.93, 4.27)*	3.6 (0.9, 6.29)*	2.19 (−2.22, 6.6)	0.45 (−0.21, 1.11)	0.85 (−0.27, 1.96)	0.22 (−1.42, 1.87)
	Lag02	2.91 (1.09, 4.73)*	3.48 (0.55, 6.41)*	2.75 (−2.03, 7.53)	0.72 (0.03, 1.42)*	1.09 (−0.09, 2.26)	0.34 (−1.38, 2.07)
	Lag03	3.04 (1.09, 4.99)*	3.29 (0.14, 6.45)*	2.15 (−2.99, 7.3)	0.72 (−0.01, 1.45)	0.89 (−0.34, 2.12)	0.39 (−1.43, 2.20)
	Lag04	2.95 (0.88, 5.02)*	3.43 (0.09, 6.77)*	1.22 (−4.26, 6.69)	0.72 (−0.04, 1.48)	0.70 (−0.59,1.99)	0.22 (−1.68,2 .12)
	Lag05	2.45 (0.27, 4.63)*	3.07 (−0.45, 6.6)	0.64 (−5.13, 6.4)	0.58 (−0.22, 1.38)	0.43 (−0.93,1.78)	−0.05 (−2.03, 1.94)
Female	Lag0	1.42 (0.68, 2.17)*	0.43 (−0.91, 1.78)	1.90 (0.82, 3.00)*	0.56 (0.27, 0.85)*	0.38 (−0.16, 0.93)	0.40 (0.00, 0.80)*
	Lag1	1.11 (0.52, 1.70)*	0.28 (−0.78, 1.36)	1.54 (0.68, 2.41)*	0.43 (0.21, 0.66)*	0.28 (−0.15, 0.71)	0.33 (0.02, 0.65)*
	Lag2	0.79 (0.34, 1.25)*	0.14 (−0.69, 0.97)	1.17 (0.51, 1.84)*	0.30 (0.13, 0.47)*	0.17 (−0.15, 0.50)	0.26 (0.02, 0.50)*
	Lag3	0.48 (0.12, 0.85)*	−0.01 (−0.67, 0.66)	0.81 (0.28, 1.34)*	0.18 (0.04, 0.31)*	0.07 (−0.19, 0.32)	0.19 (0.01, 0.38)*
	Lag4	0.17 (−0.18, 0.52)	−0.16 (−0.78, 0.48)	0.44 (−0.06, 0.95)	0.05 (−0.08, 0.17)	−0.04 (−0.28, 0.20)	0.12 (−0.05, 0.30)
	Lag5	−0.14 (−0.55, 0.27)	−0.30 (−1.04, 0.45)	0.08 (−0.52, 0.69)	−0.08 (−0.23, 0.07)	−0.15 (−0.44 ,0.15)	0.05 (−0.16, 0.26)
	Lag01	3.7 (1.81, 5.58)*	1.83 (−1.6, 5.27)	4.39 (1.65, 7.14)*	1.21 (0.47, 1.96)*	1.83 (−1.6, 5.27)	1.03 (−0.01, 2.07)*
	Lag02	3.86 (1.81, 5.91)*	1.01 (−2.75, 4.76)	5.52 (2.53, 8.51)*	1.47 (0.69, 2.25)*	1.01 (−2.75, 4.76)	1.15 (0.06, 2.25)*
	Lag03	3.84 (1.64, 6.05)*	0.62 (−3.42, 4.65)	6.25 (3.05, 9.46)*	1.45 (0.62, 2.27)*	0.62 (−3.42, 4.65)	1.34 (0.20, 2.49)*
	Lag04	3.7 (1.35, 6.05)*	0.2 (−4.08, 4.49)	6.02 (2.61, 9.44)*	1.36 (0.50, 2.23)*	0.2 (−4.08, 4.49)	1.34 (0.13, 2.54)*
	Lag05	3.3 (0.82, 5.78)*	−0.31 (−4.83, 4.22)	5.55 (1.94, 9.16)*	1.27 (0.36, 2.17)*	−0.31 (−4.83, 4.22)	1.28 (0.02, 2.55)*

Continued

Subgroup	Lag time	$PM_{2.5}$, *ER* (95% *CI*) (%)			O_3, *ER* (95% *CI*) (%)		
		Respiratory diseases	COPD	Lung cancer	Respiratory diseases	COPD	Lung cancer
Male	Lag0	0.90 (0.32, 1.48)*	1.22 (0.36, 2.09)*	1.21 (0.48, 1.96)*	0.26 (0.04, 0.49)*	0.54 (0.19, 0.89)*	0.32 (0.04, 0.59)*
	Lag1	0.72 (0.26, 1.18)*	0.96 (0.27, 1.65)*	0.89 (0.31, 1.48)*	0.22 (0.04, 0.40)*	0.43 (0.16, 0.71)*	0.23 (0.01, 0.44)*
	Lag2	0.54 (0.19, 0.90)*	0.70 (0.17, 1.24)*	0.58 (0.12, 1.03)*	0.18 (0.05, 0.31)*	0.33 (0.12, 0.53)*	0.13 (−0.03, 0.30)
	Lag3	0.37 (0.08, 0.65)*	0.44 (0.02, 0.87)*	0.26 (−0.10, 0.62)	0.14 (0.03, 0.24)*	0.22 (0.06, 0.38)*	0.04 (−0.08, 0.17)
	Lag4	0.19 (−0.08, 0.46)	0.18 (−0.22, 0.59)	−0.06 (−0.40, 0.29)	0.10 (−0.00, 0.19)	0.12 (−0.03, 0.27)	−0.05 (−0.17, 0.07)
	Lag5	0.01 (−0.31, 0.34)	−0.07 (−0.55, 0.41)	−0.37 (−0.79, 0.04)	0.05 (−0.07, 0.17)	0.01 (−0.17, 0.20)	−0.14 (−0.29, 0.01)
	Lag01	2.08 (0.6, 3.56)*	2.8 (0.59, 5.01)*	3.41 (1.54, 5.29)*	0.50 (−0.09, 1.09)	1.33 (0.43, 2.22)*	0.58 (−0.14, 1.30)
	Lag02	2.67 (1.05, 4.28)*	3.27 (0.86, 5.67)*	3.2 (1.15, 5.24)*	0.76 (0.14, 1.38)*	1.61 (0.66, 2.56)*	0.62 (−0.13, 1.38)
	Lag03	3.05 (1.32, 4.78)*	3.58 (1, 6.16)*	2.97 (0.77, 5.17)*	0.93 (0.28, 1.58)*	1.69 (0.70, 2.69)*	0.63 (−0.16, 1.43)
	Lag04	2.93 (1.09, 4.77)*	3.71 (0.97, 6.46)*	2.36 (0.02, 4.7)*	1.00 (0.32, 1.68)*	1.67 (0.63, 2.72)*	0.52 (−0.32, 1.35)
	Lag05	2.55 (0.61, 4.49)*	3.39 (0.49, 6.28)*	1.85 (−0.63, 4.32)	0.95 (0.24, 1.66)*	1.52 (0.43, 2.62)*	0.35 (−0.52, 1.22)
During the COVID-19 pandemic	Lag0	0.97 (0.02, 1.93)*	1.02 (−0.55, 2.62)	1.02 (−0.18, 2.24)	0.41 (0.14, 0.68)*	0.65 (0.19, 1.10)*	0.10 (−0.23, 0.43)
	Lag1	0.71 (−0.06, 1.49)	0.82 (−0.45, 2.11)	0.76 (−0.21, 1.73)	0.31 (0.09, 0.52)*	0.48 (0.12, 0.85)*	0.06 (−0.20, 0.33)
	Lag2	0.45 (−0.16, 1.07)	0.63 (−0.39, 1.66)	0.49 (−0.27, 1.27)	0.20 (0.04, 0.37)*	0.32 (0.04, 0.60)*	0.02 (−0.18, 0.23)
	Lag3	0.20 (−0.32, 0.71)	0.43 (−0.43, 1.29)	0.23 (−0.41, 0.87)	0.10 (−0.03, 0.24)	0.16 (−0.07, 0.39)	−0.02 (−0.18, 0.15)
	Lag4	−0.06 (−0.57, 0.45)	0.23 (−0.61,1.08)	−0.03 (−0.66, 0.60)	0.00 (−0.13, 0.13)	−0.00 (−0.22, 0.22)	−0.06 (−0.22, 0.10)
	Lag5	−0.32 (−0.90, 0.27)	0.04 (−0.93, 1.01)	−0.29 (−1.02, 0.44)	−0.10 (−0.25, 0.05)	−0.16 (−0.42, 0.09)	−0.10 (−0.28, 0.09)
	Lag01	3.03 (0.54, 5.51)*	3.7 (−0.43, 7.84)	3.35 (0.22, 6.49)*	0.81 (0.09, 1.53)*	1.54 (0.33, 2.75)*	0.16 (−0.73, 1.04)
	Lag02	3.29 (0.57, 6.01)*	3.97 (−0.54, 8.48)	3.55 (0.13, 6.98)	1.14 (0.37, 1.9)*	1.96 (0.67, 3.24)*	0.22 (−0.72, 1.16)
	Lag03	2.87 (−0.06, 5.81)	3.09 (−1.79, 7.96)	3.32 (−0.37, 7.01)	1.12 (0.31, 1.94)*	1.85 (0.49, 3.21)*	0.25 (−0.74, 1.25)
	Lag04	2.42 (−0.72, 5.57)	3.12 (−2.11, 8.36)	2.48 (−1.47, 6.44)	1.01 (0.15, 1.87)*	1.61 (0.16, 3.05)*	0.11 (−0.95, 1.16)
	Lag05	1.47 (−1.92, 4.85)	3.00 (−2.64, 8.64)	1.75 (−2.49, 5.99)	0.78 (−0.14, 1.69)	1.11 (−0.42, 2.65)	−0.07 (−1.19, 1.05)
Before the COVID-19 pandemic	Lag0	1.11 (0.53, 1.69)*	0.82 (−0.11, 1.76)	1.26 (0.48, 2.06)*	0.28 (0.02, 0.54)*	0.34 (−0.08, 0.77)	0.50 (0.15, 0.84)*
	Lag1	0.86 (0.39, 1.33)*	0.59 (−0.17, 1.36)	0.95 (0.31, 1.59)	0.23 (0.02, 0.44)*	0.28 (−0.06, 0.62)	0.38 (0.10, 0.65)*
	Lag2	0.61 (0.23, 0.99)*	0.36 (−0.26, 0.98)	0.63 (0.12, 1.15)	0.18 (0.02, 0.34)*	0.21 (−0.06, 0.49)	0.25 (0.03, 0.47)*
	Lag3	0.36 (0.05, 0.68)*	0.13 (−0.38, 0.64)	0.32 (−0.11, 0.75)	0.13 (−0.00, 0.26)	0.15 (−0.07, 0.37)	0.13 (−0.05, 0.31)
	Lag4	0.12 (−0.18, 0.42)	−0.10 (−0.58, 0.38)	0.00 (−0.40, 0.41)	0.08 (−0.04, 0.20)	0.09 (−0.12, 0.29)	0.01 (−0.16, 0.17)
	Lag5	−0.13 (−0.46, 0.20)	−0.33 (−0.86, 0.20)	−0.31 (−0.76, 0.15)	0.03 (−0.11, 0.17)	0.02 (−0.22, 0.26)	−0.12 (−0.31, 0.08)
	Lag01	2.50 (1.06, 3.95)	2.13 (−0.22, 4.48)	3.62 (1.65, 5.59)*	0.52 (−0.16, 1.2)	0.94 (−0.2, 2.08)	1.18 (0.26, 2.10)*
	Lag02	3.04 (1.42, 4.66)	2.08 (−0.55, 4.71)	3.70 (1.5, 5.89)*	0.77 (0.03, 1.5)*	1.11 (−0.11, 2.34)	1.2 (0.21, 2.18)*
	Lag03	3.60 (1.82, 5.38)	2.53 (−0.37, 5.43)	3.78 (1.36, 6.20)*	0.99 (0.21, 1.77)*	1.33 (0.02, 2.63)*	1.31 (0.26, 2.35)*
	Lag04	3.54 (1.59, 5.48)	2.71 (−0.46, 5.87)	3.17 (0.53, 5.80)*	1.11 (0.28, 1.94)*	1.45 (0.06, 2.84)*	1.21 (0.09, 2.32)*
	Lag05	3.05 (0.96, 5.13)	1.61 (−1.79, 5.00)	2.61 (−0.22, 5.44)	1.08 (0.21, 1.96)*	1.32 (−0.15, 2.79)	1.03 (−0.14, 2.21)

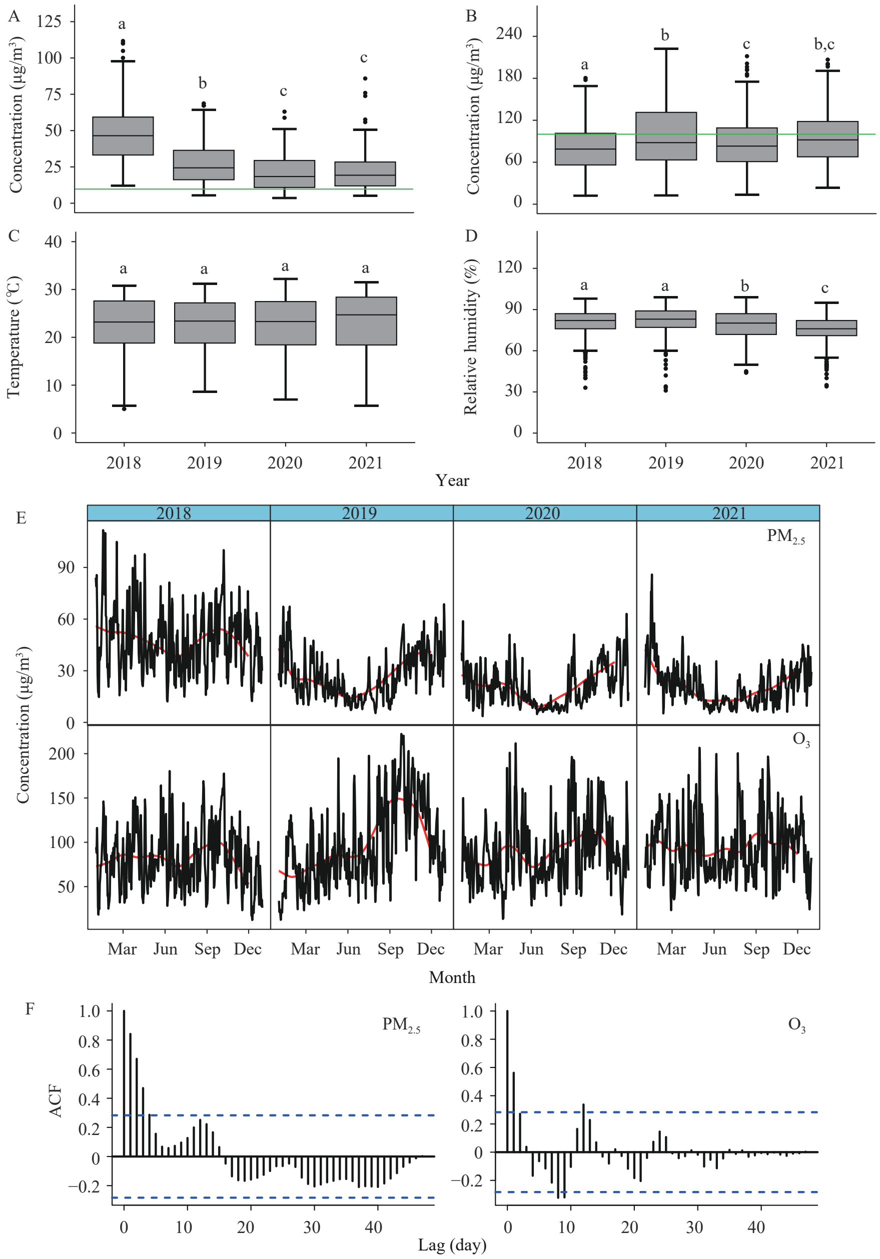
Abbreviation: *ER*=excess risk; *CI*=confidence interval; COPD=chronic obstructive pulmonary disease; COVID-19=coronavirus disease 2019; $PM_{2.5}$=fine particulate matter; O_3=ozone.

* *P*<0.05.

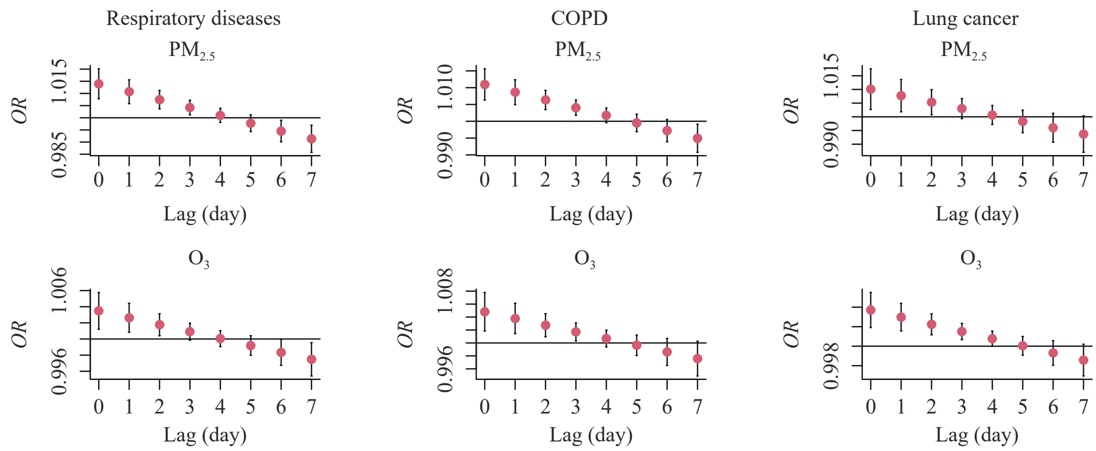
SUPPLEMENTARY TABLE S5. Spearman correlation test between O_3, $PM_{2.5}$, and meteorological factors.

Pollutants	O_3	$PM_{2.5}$	Temperature	Humidity
O_3	1.00			
$PM_{2.5}$	0.40*	1.00		
Temperature	0.17*	−0.34*	1.00	
Humidity	−0.44*	−0.22*	0.17*	1.00

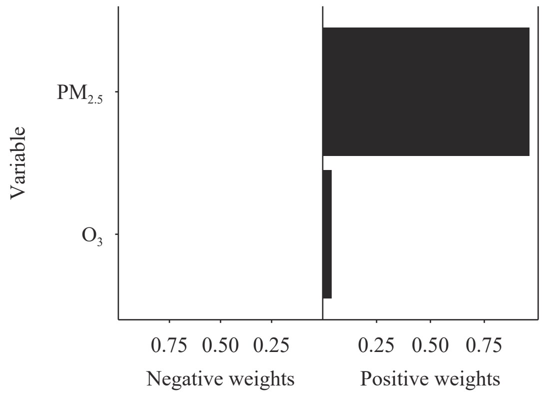
Abbreviation: *ER*=excess risk; *CI*=confidence interval; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=fine particulate matter of 2.5 micrometers; O_3=ozone.
* *P*<0.05.



SUPPLEMENTARY FIGURE S1. Concentrations of (A) $PM_{2.5}$ and (B) O_3, (C) distributions of temperature and (D) relative humidity, and (E) time series of $PM_{2.5}$ and (F) O_3 with autocorrelation in Guangzhou City, China, from 2018 to 2021.
Note: The green line represents the threshold value for each pollutant, while the red line shows the 7-day average concentration of each pollutant. The different letters (A, B, C, and D) signify statistically significant differences (*P*<0.05) between years.
Abbreviation: $PM_{2.5}$=fine particulate matter; O_3=ozone; ACF=autocorrelation function.



SUPPLEMENTARY FIGURE S2. Daily effects of $PM_{2.5}$ and O_3 on the number of deaths from respiratory diseases, COPD, and lung cancer in Guangzhou, 2018–2021.
Abbreviation: *OR*=odds ratio; COPD=chronic obstructive pulmonary disease; $PM_{2.5}$=fine particulate matter; O_3=ozone.



SUPPLEMENTARY FIGURE S3. The weights of $PM_{2.5}$ and O_3 in the QG-C model.
Abbreviation: $PM_{2.5}$=fine particulate matter; O_3=ozone.