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Supplemental Information

Ambient air pollution and low temperature associated with case fatality of COVID-19: A nationwide retrospective cohort study in China

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Table S1. The univariate analysis of risk factors for COVID-19 fatality in China.

Variables	Univariate Analysis						
	Coefficient	SE	HR (95% CI)	Likelihood-ratio	Wald	Score (log rank)	*P* Value *
Age group				25624	21357	31939	
< 25 years			1.00 (Ref)				
25-65 years	2.57	0.17	1.87 (1.26, 2.76)				<0.01
≥ 65 years	4.64	0.17	5.64 (3.88, 8.23)				<0.01
Sex				1853	1780	1829	
Male			1.00 (Ref)				
Female	-0.57	0.01	0.56 (0.54, 0.58)				<0.01
Occupation				8072	5111	6507	
Medical-related			1.00 (Ref)				
Service-related	0.09	0.14	1.10 (0.83, 1.44)				0.51
Office worker	0.59	0.09	1.82 (1.52, 2.18)				<0.01
Home worker	2.30	0.09	10.04 (8.42, 11.96)				<0.01
Others	1.75	0.09	2.91 (1.59, 5.35)				<0.01
Residence				627.9	649.5	655.9	
Local			1.00 (Ref)				
Migrant	0.34	0.01	1.41 (1.37, 1.45)				<0.01
Severity				32715	39291	72970	
Mild/asymptomatic			1.00 (Ref)				
Moderate	-0.30	0.02	0.73 (0.71, 0.77)				0.89
Severe	1.44	0.01	4.24 (4.09, 4.39)				< 0.01

Critical	3.02	0.02	20.47 (19.74, 21.23)				< 0.01
Hospital transfer				15.62	15.48	15.48	
No			1.00 (Ref)				
Yes	-0.06	0.01	0.94 (0.91, 0.97)				< 0.01
Location				6333	5126	5756	
Non-Wuhan			1.00 (Ref)				
Wuhan	1.19	0.02	3.27 (3.17, 3.38)				< 0.01
Province				6119	2941	4225	
Inside Hubei			1.00 (Ref)				
Outside Hubei	-2.12	0.04	0.12 (0.11, 0.13)				< 0.01
Lockdown †				1270	1396	1432	
Before			1.00 (Ref)				
After	-0.55	0.01	0.57 (0.56, 0.59)				< 0.01
GDP Per Capita	-0.06	0.005	0.94 (0.93, 0.95)	115	109.5	109	< 0.01
Hospital Beds per 1000 Persons	1.13	0.03	3.11 (2.95, 3.28)	2691	1729	1852	< 0.01

Note: HR, hazard ratio; GDP, gross domestic product.

* *P* values were calculated by χ^2 test or Fisher's exact test, as appropriate.

† Lockdown: On 23 January 2020, the central government of China imposed a lockdown in Wuhan and other cities in Hubei.

Table S2. Characteristics of study participants by survival status in China using resampling approach.

Variable	Deceased (n=3,934)	Alive (n=3,934) §		*P* -value †
		Resampling value	95% CI	
Environmental factors				
Exposure window I *				
Temperature (°C)	5.90 ± 2.24	6.27 ± 0.06	6.17, 6.37	<0.001
Relative humidity (%)	80.13 ± 5.75	78.09 ± 0.13	77.87, 78.31	<0.001
$PM_{2.5}$ (μg/m^3)	53.71 ± 15.52	51.03 ± 0.03	50.50, 51.57	<0.001
PM_{10} (μg/m^3)	62.02 ± 16.93	59.76 ± 0.04	59.18, 60.42	<0.001
O_3 (μg/m^3)	54.31 ± 9.03	56.02 ± 0.01	55.77, 56.27	<0.001
SO_2 (μg/m^3)	7.33 ± 2.11	7.68 ± 0.01	7.58, 7.77	<0.001
NO_2 (μg/m^3)	22.88 ±6.61	19.81 ± 0.01	19.63, 19.99	<0.001
Exposure window II *				
Temperature (°C)	7.41 ± 2.76	6.27 ± 0.06	6.18, 6.36	<0.001
Relative humidity (%)	79.66 ± 6.53	78.20 ± 0.13	78.00, 78.41	<0.001
$PM_{2.5}$ (μg/m^3)	45.11 ± 17.32	51.11 ± 0.03	50.58, 51.69	<0.001
PM_{10} (μg/m^3)	49.85 ± 18.66	59.93 ± 0.04	59.21, 60.46	<0.001
O_3 (μg/m^3)	54.73 ± 9.01	55.97 ± 0.02	55.70, 56.22	<0.001
SO_2 (μg/m^3)	7.41 ± 2.10	7.65 ± 0.01	7.57, 7.74	<0.001
NO_2 (μg/m^3)	19.54 ± 6.17	19.91 ± 0.01	19.74, 20.08	<0.001
Age group (n, %)				<0.001
< 25 years	6 (0.15)	203 (5.16)	179, 226	
25-64 years	1146 (29.13)	2905 (73.84)	2860, 2949	
≥ 65 years	2782 (70.72)	826 (21.00)	785, 867	
Sex (n, %)				<0.001
Male	2515 (63.93)	1983 (50.41)	1932, 2033	
Female	1419 (36.07)	1951 (49.59)	1899, 2000	
Occupation (n, %)				<0.001
Medical-related	21 (0.53)	152 (3.86)	132, 171	
Service-related	15 (0.38)	99 (2.52)	83, 115	
Office worker	226 (5.74)	895 (22.75)	849, 937	
Homemaker	3226 (82.00)	2238 (56.89)	2189, 2290	
Others	446 (11.34)	550 (13.98)	515, 588	

Residence (n, %)				<0.001
Permanent	2476 (62.94)	2785 (70.79)	2738, 2833	
Temporarily	1458 (37.06)	1149 (29.21)	1101, 1196	
Severity (n, %)				<0.001
Mild	806 (20.49)	1627 (41.36)	1576, 1678	
Moderate	597 (15.18)	1635 (41.56)	1585, 1683	
Severe	1285 (32.66)	585 (14.87)	548, 619	
Critical	1246 (31.67)	87 (2.21)	72, 103	
Hospital transfer				0.092
No	2927 (74.40)	2886 (73.36)	2839, 2928	
Yes	1007 (25.60)	1048 (26.64)	1006, 1095	

Note: $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤ 10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

[*] Exposure window I represents the mean exposure value from the date of symptom onset to the date of diagnosis; Exposure window II represents the mean exposure value from the date of diagnosis to the date of death or the end of the study.

[†] *P*-value were calculated by χ^2 test or Fisher's exact test, as appropriate.

[§] The results of the alive were based on the 1000 times random resampling.

Table S3. Spearman's correlation coefficients among meteorological variables and air pollutants during the different exposure windows. *

Variables	**Temperature**	**Relative humidity**	**$PM_{2.5}$**	**PM_{10}**	**O_3**	**NO_2**	**SO_2**
Exposure I †							
Temperature	1.00						
Relative humidity	-0.14	1.00					
$PM_{2.5}$	0.36	-0.16	1.00				
PM_{10}	0.35	-0.17	0.96	1.00			
NO_2	0.19	0.02	0.45	0.43	1.00		
SO_2	0.43	-0.39	0.34	0.38	0.31	1.00	
O_3	0.01	-0.59	0.23	0.22	-0.21	0.18	1.00
Exposure II †							
Temperature	1.00						
Relative humidity	-0.34	1.00					
$PM_{2.5}$	0.45	-0.30	1.00				
PM_{10}	0.29	-0.58	0.76	1.00			
NO_2	-0.12	-0.13	0.15	0.23	1.00		
SO_2	0.16	-0.25	0.28	0.37	0.31	1.00	
O_3	-0.06	-0.28	0.01	0.14	-0.16	0.08	1.00

Note: $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 μm; PM_{10}, particulate matter with an aerodynamic diameter ≤ 10 μm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

* All pairwise correlation coefficients were statistically significant ($P < 0.05$).

† Exposure window I represents the mean exposure value from the date of symptom onset to the date of diagnosis; Exposure window II represents the mean exposure value from the date of diagnosis to the date of death or the end of the study.

Table S4. Sensitivity analyses for the hazard ratios of COVID-19 fatality associated with each 10 μg/m^3 increase in $PM_{2.5}$, PM_{10}, SO_2, NO_2, and O_3 in different model parameters.

Models †	**$PM_{2.5}$***	**PM_{10}***	**NO_2***	**SO_2***	**O_3***
df=2 for temperature	1.11 (1.09, 1.13)	1.10 (1.08, 1.12)	1.25 (1.16, 1.34)	1.10 (0.95, 1.27)	1.08 (1.02, 1.14)
df=4 for temperature	1.10 (1.07, 1.13)	1.10 (1.07, 1.12)	1.27 (1.19, 1.35)	1.10 (0.95, 1.26)	1.09 (1.03, 1.15)
df=5 for relative humidity	1.11 (1.08, 1.13)	1.10 (1.08, 1.12)	1.27 (1.18, 1.35)	1.11 (0.95, 1.27)	1.09 (1.03, 1.14)
df=2 for relative humidity	1.10 (1.08, 1.13)	1.10 (1.08, 1.13)	1.26 (1.19, 1.36)	1.10 (0.95, 1.27)	1.12 (1.03, 1.20)
df=4 for relative humidity	1.11 (1.08, 1.14)	1.10 (1.08, 1.12)	1.27 (1.19, 1.35)	1.09 (0.95, 1.25)	1.09 (1.03, 1.14)
df=5 for relative humidity	1.09 (1.07, 1.12)	1.10 (1.08, 1.13)	1.26 (1.18, 1.36)	1.10 (0.95, 1.27)	1.09 (1.03, 1.14)
df=6 for relative humidity	1.11 (1.08, 1.14)	1.10 (1.08, 1.12)	1.27 (1.19, 1.35)	1.10 (0.96, 1.27)	1.10 (1.05, 1.15)

*Effect estimated using Window I, and exposure window I represents the mean exposure value from the date of symptom onset to the date of diagnosis.

† Multivariate model, adjusted for age, sex, occupation, residence, severity of the illness, location, and transfer history, temporal trend, lockdown, city-level GDP, hospital beds per 1000 persons, temperature (only for the pollutants) and relative humidity.

Table S5. Hazard ratios of COVID-19 fatality mortality associated with 10 μg/m^3 increase in $PM_{2.5}$, PM_{10}, NO_2, and O_3 in the two-pollutant models.

Pollutants	Models	Hazard Ratios	*P*-value[†]
$PM_{2.5}$	Single pollutant model	1.11 (1.09, 1.13)	
	Two- pollutant model		
	Adjust for O_3	1.11 (1.09, 1.14)	0.99
	Adjust for NO_2	1.10 (1.07, 1.13)	0.58
	Adjust for SO_2	1.13 (1.11, 1.16)	0.22
PM_{10}	Single pollutant model	1.10 (1.08, 1.13)	
	Two- pollutant model		
	Adjust for O_3	1.10 (1.08, 1.13)	0.99
	Adjust for NO_2	1.09 (1.07, 1.12)	0.58
	Adjust for SO_2	1.13 (1.10, 1.15)	0.09
NO_2	Single pollutant model	1.27 (1.19, 1.35)	
	Two- pollutant model		
	Adjust for $PM_{2.5}$	1.08 (0.99, 1.17)	<0.01
	Adjust for PM_{10}	1.06 (0.98, 1.16)	<0.01
	Adjust for O_3	1.28 (1.19, 1.36)	0.86
	Adjust for SO_2	1.32 (1.23, 1.43)	0.44
O_3	Single pollutant model	1.09 (1.03, 1.14)	
	Two- pollutant model		
	Adjust for $PM_{2.5}$	1.01 (0.95, 1.06)	0.04
	Adjust for PM_{10}	1.01 (0.96, 1.06)	0.04
	Adjust for NO_2	1.09 (1.04, 1.15)	0.99
	Adjust for SO_2	1.09 (1.04, 1.14)	0.99

[*]Effect estimated using Window I.

[†] Estimated using likelihood ratio test by comparing the single-pollutant model and each nested two-pollutant model.

Table S6. Hazard ratios and 95% CI of case fatality of COVID-19 associated with environmental factors of overall exposure windows in China [*].

Variables	**Hazard Ratios (95% CI)**	
	Crude [§]	**Adjusted** [‡]
Temperature	1.30 (1.28, 1.32)	2.34 (2.30, 2.39)
$PM_{2.5}$	1.22 (1.14, 1.30)	1.31 (1.26, 1.37)
PM_{10}	1.20 (1.18, 1.22)	1.29 (1.15, 1.44)
NO_2	1.32 (1.13, 1.51)	1.52 (1.23, 1.80)
SO_2	0.75 (0.52, 0.99)	1.06 (0.83, 1.29)
O_3	0.93 (0.73, 1.11)	1.32 (1.14, 1.51)

Note: $PM_{2.5}$, particulate matter with an aerodynamic diameter ≤ 2.5 µm; PM_{10}, particulate matter with an aerodynamic diameter ≤ 10 µm; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

[*] Exposure window represents the exposure window of whole infection course (from the symptom onset to death/recovery or end of the study)

[§] Crude model, with no adjustment.

[‡] Multivariate model, adjusted for age, sex, occupation, residence, severity of the illness, location, and transfer history, temporal trend, lockdown, city-level GDP, hospital beds per 1000 persons, temperature (only for the pollutants) and relative humidity.

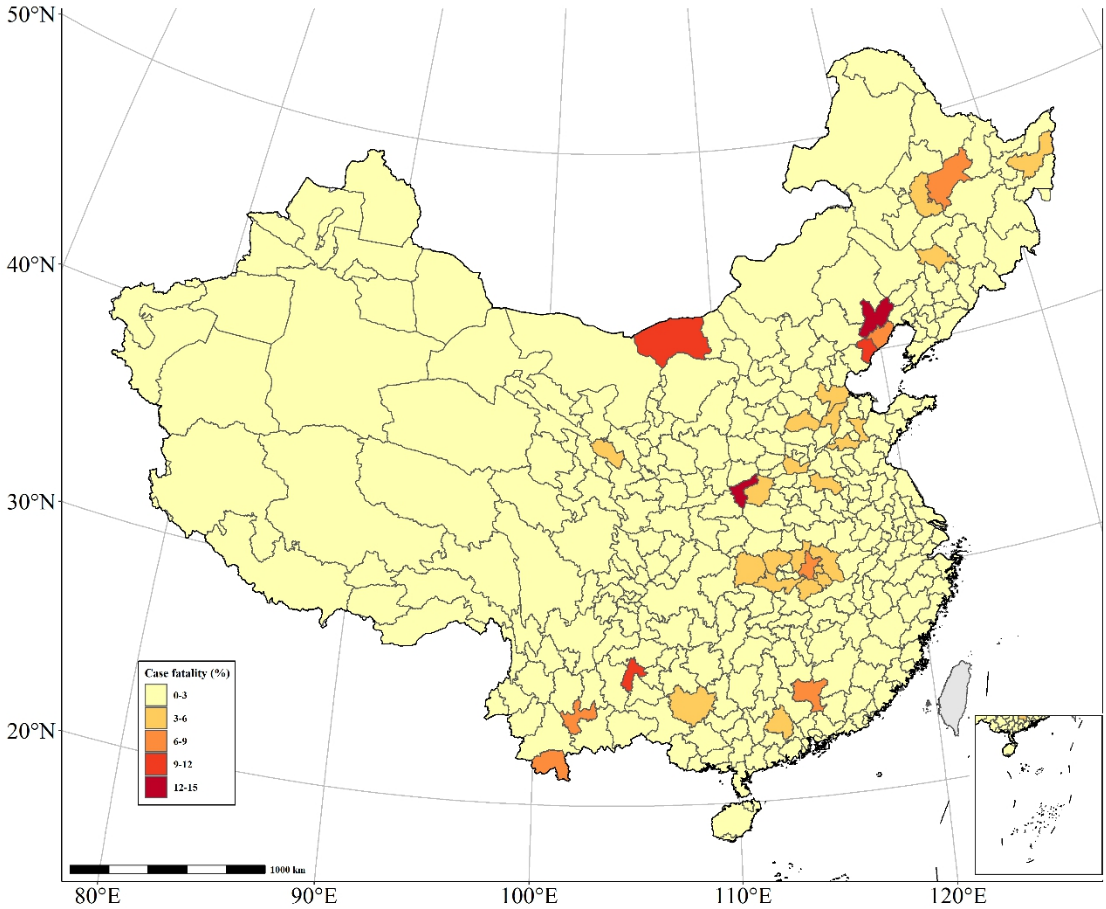

Figure S1. The distribution of fatality rates across the 321 cities in China.

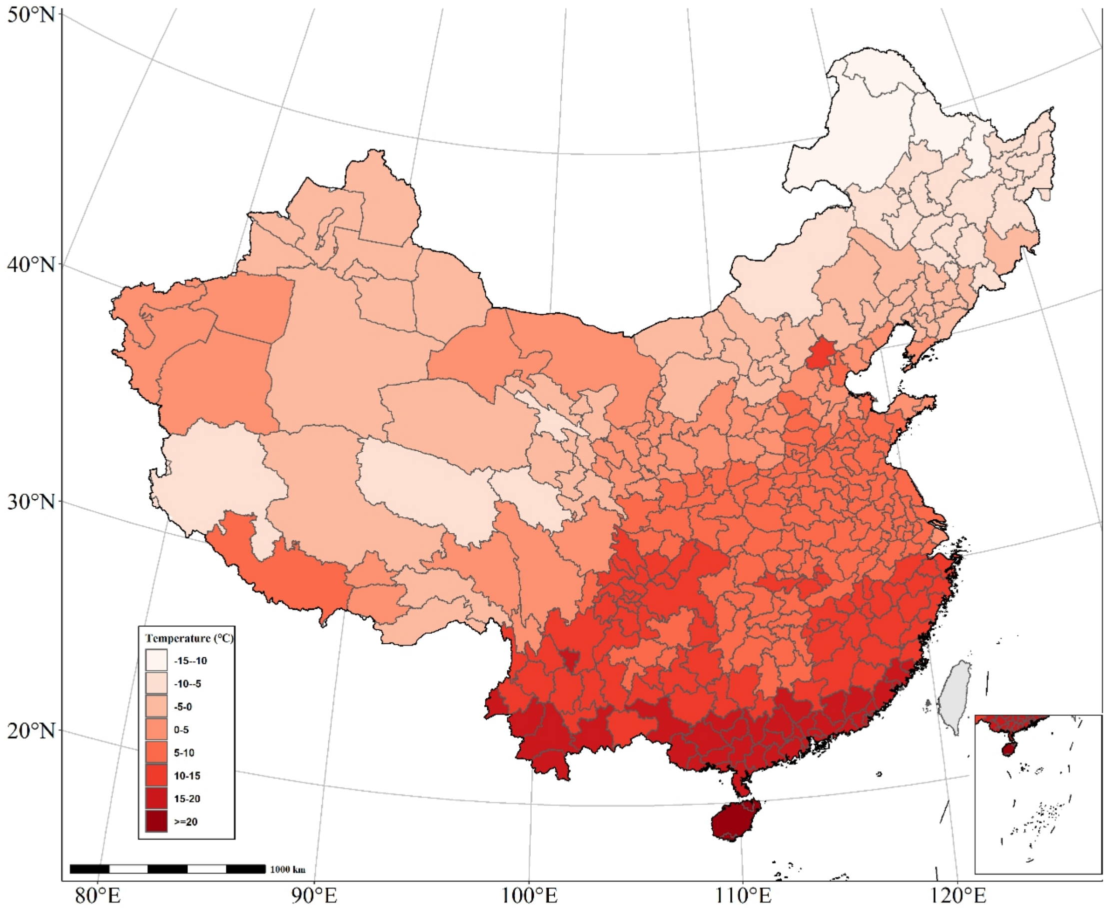

Figure S2. The distribution of the average temperature during the COVID-19 epidemic in China.

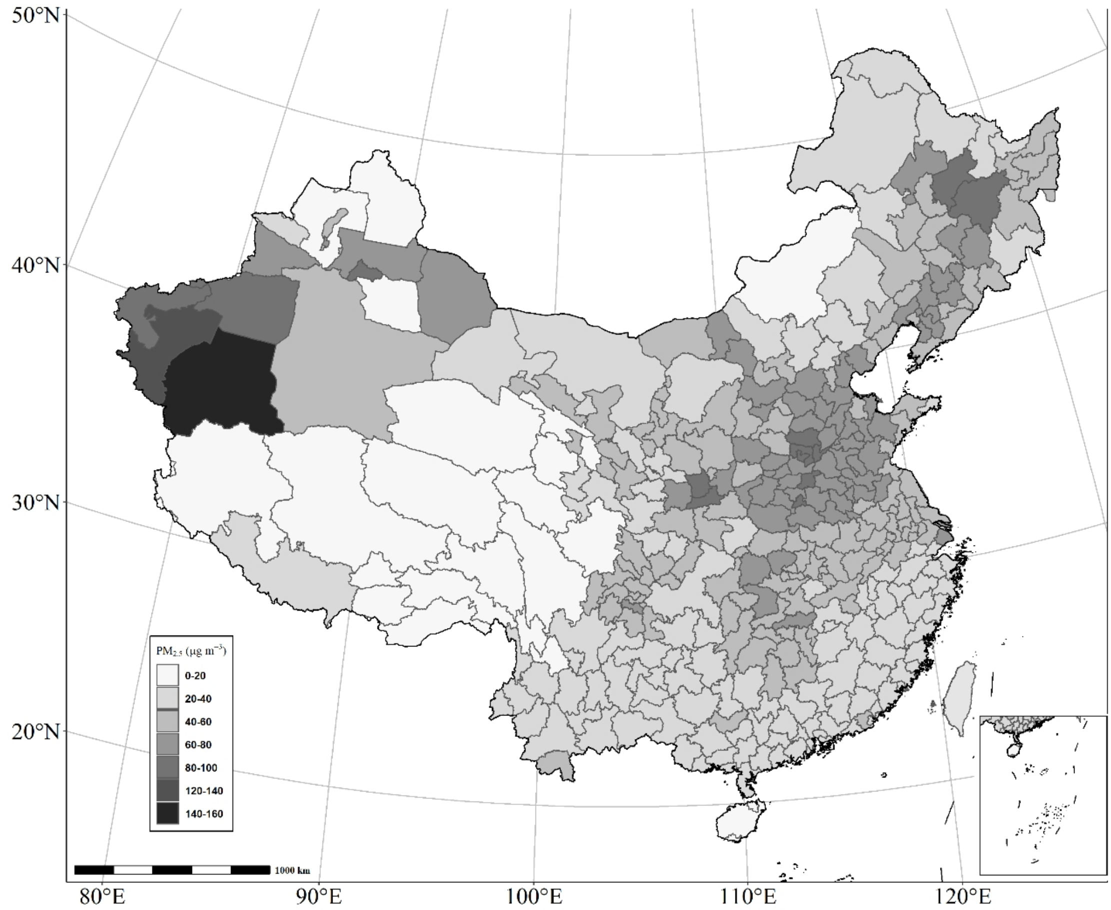

Figure S3. The distribution of the average concentration of $PM_{2.5}$ during the COVID-19 epidemic in China.

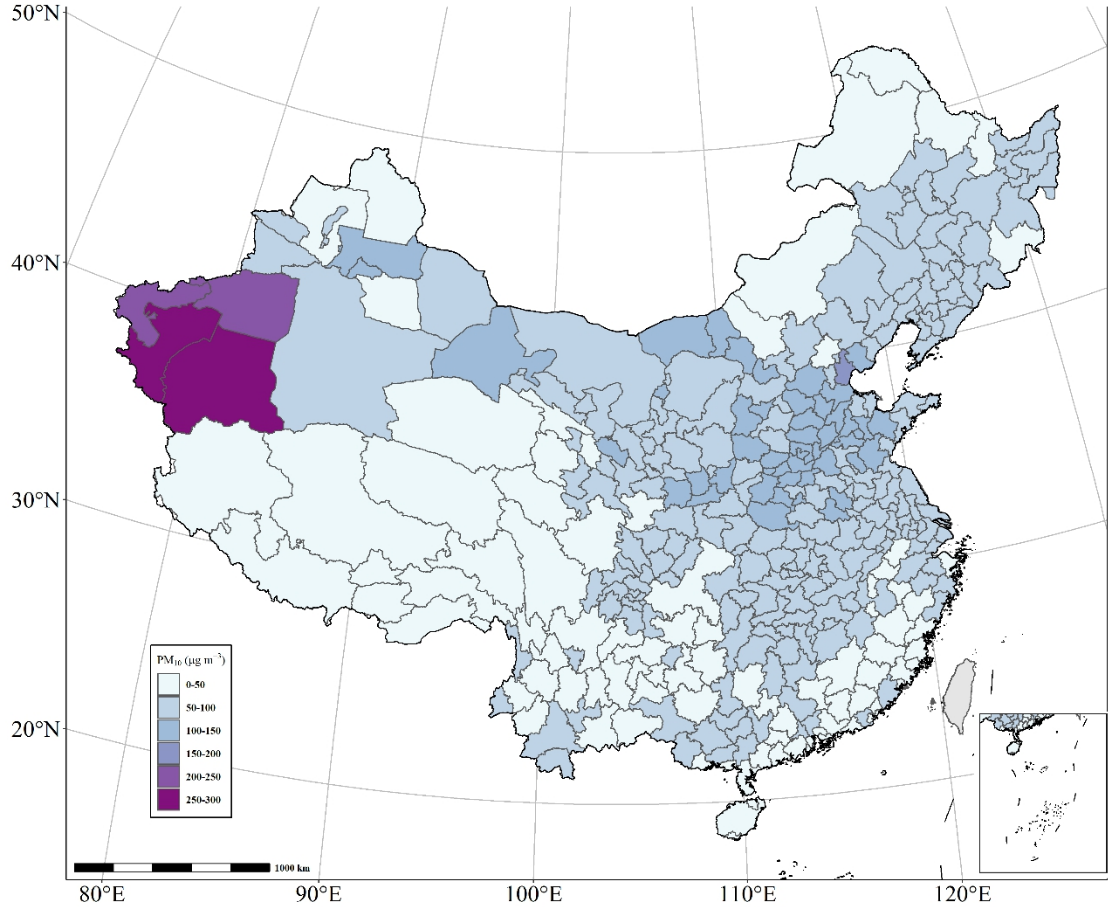

Figure S4. The distribution of the average concentration of PM_{10} during the COVID-19 epidemic in China.

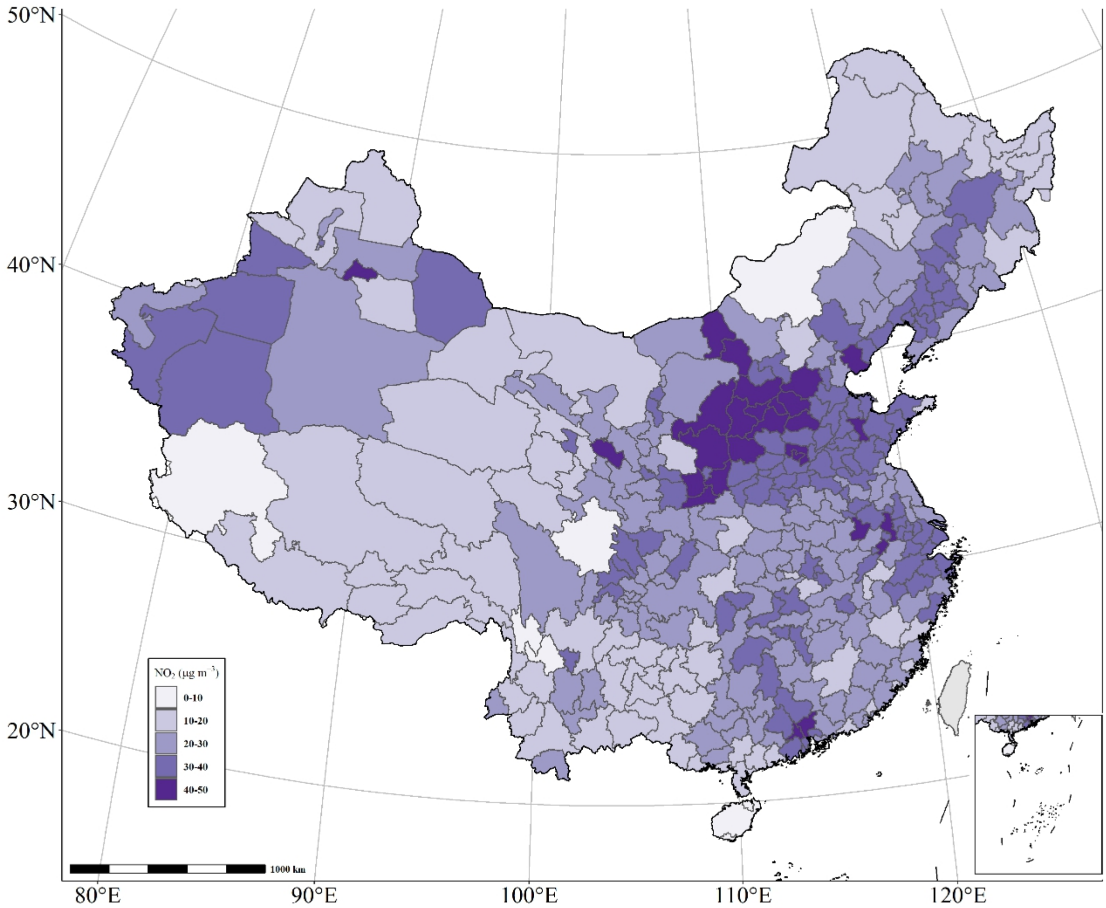

Figure S5. The distribution of the average concentration of NO_2 during the COVID-19 epidemic in China.

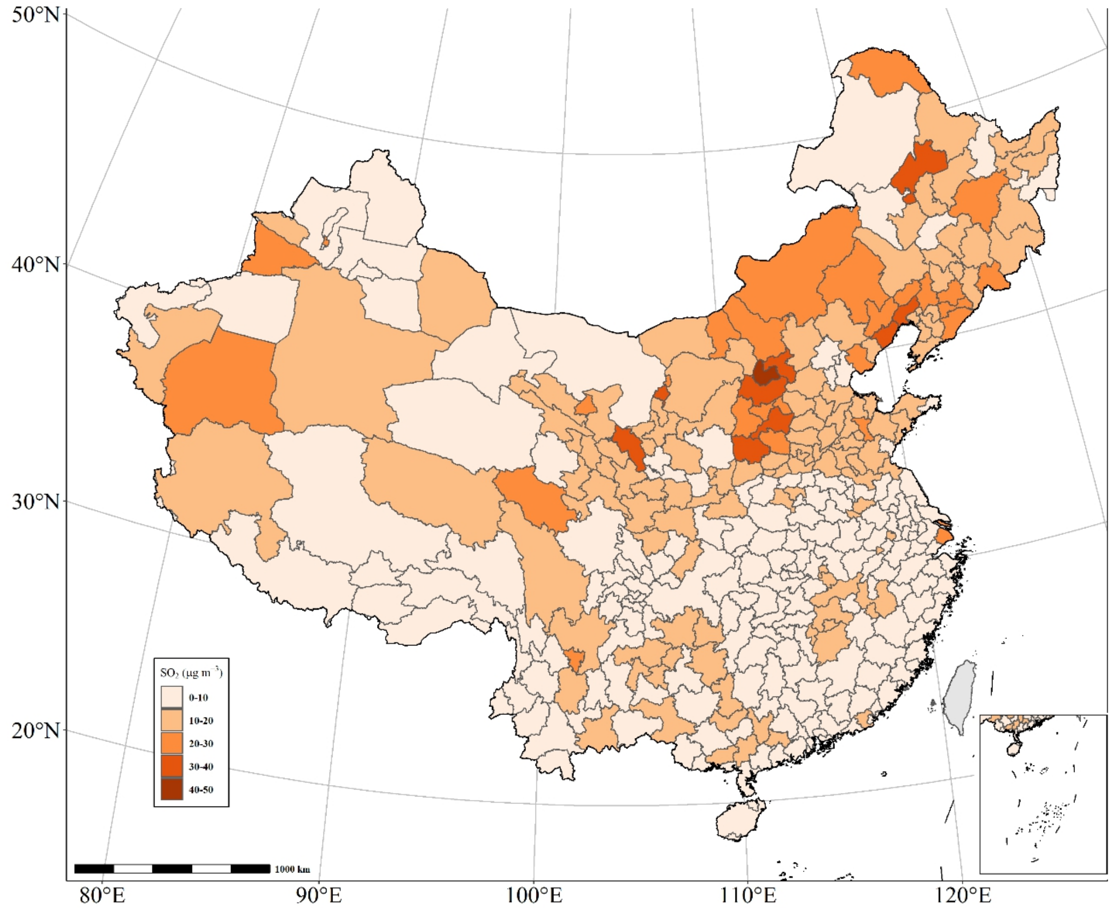

Figure S6. The distribution of the average concentration of SO_2 during the COVID-19 epidemic in China.

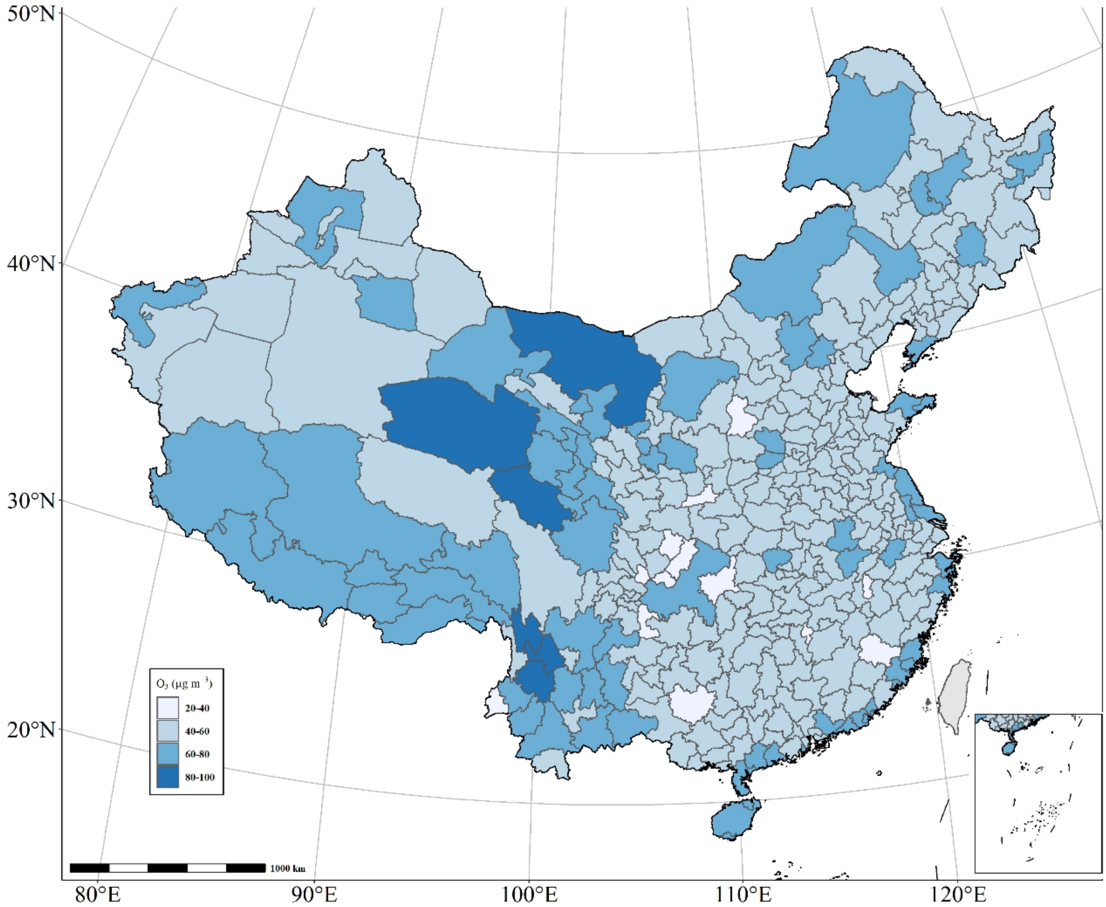

Figure S7. The distribution of the average concentration of O_3 during the COVID-19 epidemic in China.

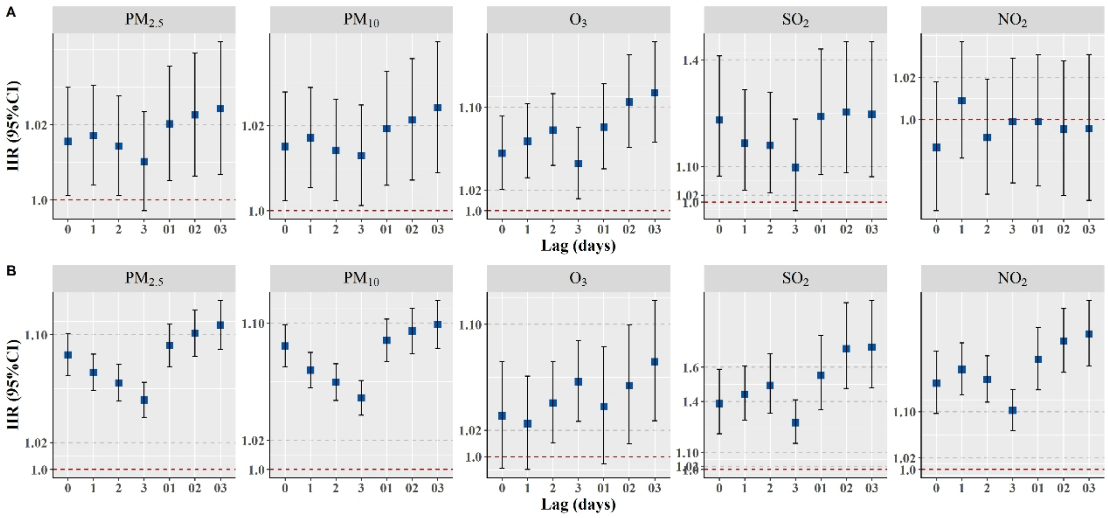

Figure S8. Hazard ratios (HRs) and 95% CIs of COVID-19 case-fatality associated with each 10 μg/m^3 increase in air pollutant concentrations at different lags in China.

Effect estimation using the date of symptom onset (A) and the date of diagnosis (B) are shown.

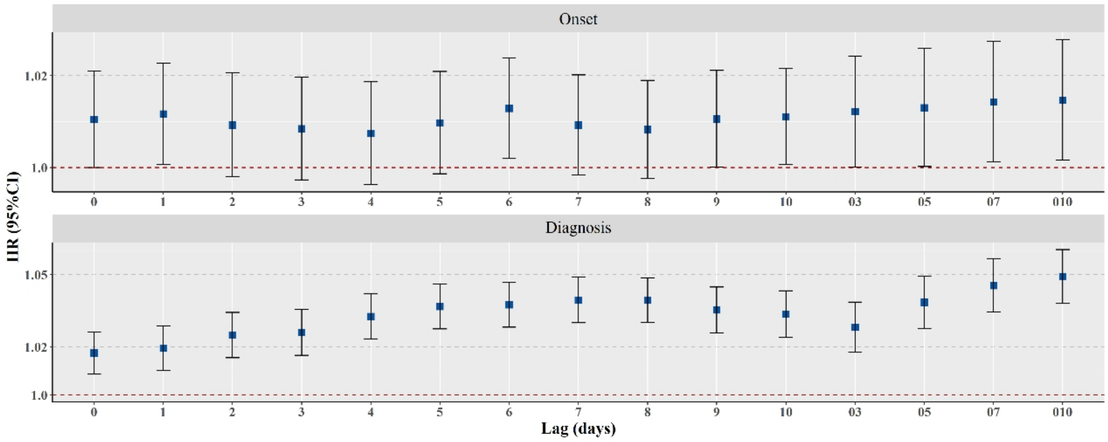

Figure S9. Hazard ratios (HRs) and 95% CIs of case-fatality of COVID-19 associated with each 1 ℃ decrease in temperature at different lag days in China. Effect estimatations using the date of onset and diagnosis are shown.

Text S1. Regression equations for Cox regression model III for ambient air pollution.

$$h(t) = h_0 * exp(\beta_j X_j + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + \beta_9 X_9 + \beta_{10} X_{10} + \beta_{11} X_{11} + \beta_{12} X_{12} + \beta_{13} X_{13} + \beta_{14} X_{14})$$

where:

t represents the survival time;

$h(t)$ is the hazard function determined by a set of variates ($X_j, X_2, \ldots X_{14}$);

The term h_0 is called the baseline hazard. It corresponds to the value of the hazard if all the X_i are equal to zero. The 't' in $h(t)$ reminds us that the hazard may vary over time.

The coefficients (β_j, β_2,... β_{14}) = effects parameter estimates;

X_j = gaseous pollutants ($PM_{2.5}$, PM_{10}, NO_2 SO_2, and O_3);

X_2 = sex (female or male);

X_3 = age group (<25 years, 25-65 years, and ≥65 years);

X_4 = residence (local or migrant);

X_5 = occupation (medical-related, service-related, office worker, home worker, and others);

X_6 = severity of the illness (mild/asymptomatic, moderate, severe, critical);

X_7 = location (Wuhan or Non-Wuhan);

X_8 = transfer to a better hospital or not (yes or no);

X_9 = time trend;

X_{10} = temperature;

X_{11} = relative humidity;

X_{12} = lockdown (before or after);

X_{13} = city-level GDP;

X_{14} = hospital beds per 1000 persons.

Text S2. Regression equations for Cox regression model III for ambient temperature.

$$h(t) = h_0 * exp(\beta_t X_t + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \beta_6 X_6 + \beta_7 X_7 + \beta_8 X_8 + \beta_9 X_9 + \beta_{10} X_{10} + \beta_{11} X_{11} + \beta_{12} X_{12} + \beta_{13} X_{13})$$

where:

t represents the survival time;

$h(t)$ is the hazard function determined by a set of variates $(X_t, X_2, \ldots X_{13})$;

The term h_0 is called the baseline hazard. It corresponds to the value of the hazard if all the X_i are equal to zero. The 't' in $h(t)$ reminds us that the hazard may vary over time.

The coefficients (β_t, β_2,... β_{13}) = effects parameter estimates;

X_t = temperature;

X_2 = sex (female or male);

X_3 = age group (<25 years, 25-65 years, and ≥65 years);

X_4 = residence (local or migrant);

X_5 = occupation (medical-related, service-related, office worker, home worker, and others);

X_6 = severity of the illness (mild/asymptomatic, moderate, severe, critical);

X_7 = location (Wuhan or Non-Wuhan);

X_8 = transfer to a better hospital or not (yes or no);

X_9 = time trend;

X_{10} = relative humidity;

X_{11} = lockdown (before or after);

X_{12} = city-level GDP;

X_{13} = hospital beds per 1000 persons.