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Research Article

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Posted Date: July 15th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10216536/v1>

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Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at BMC Public Health on October 12th, 2026.
See the published version at <https://doi.org/10.1186/s12889-026-29901-w>.

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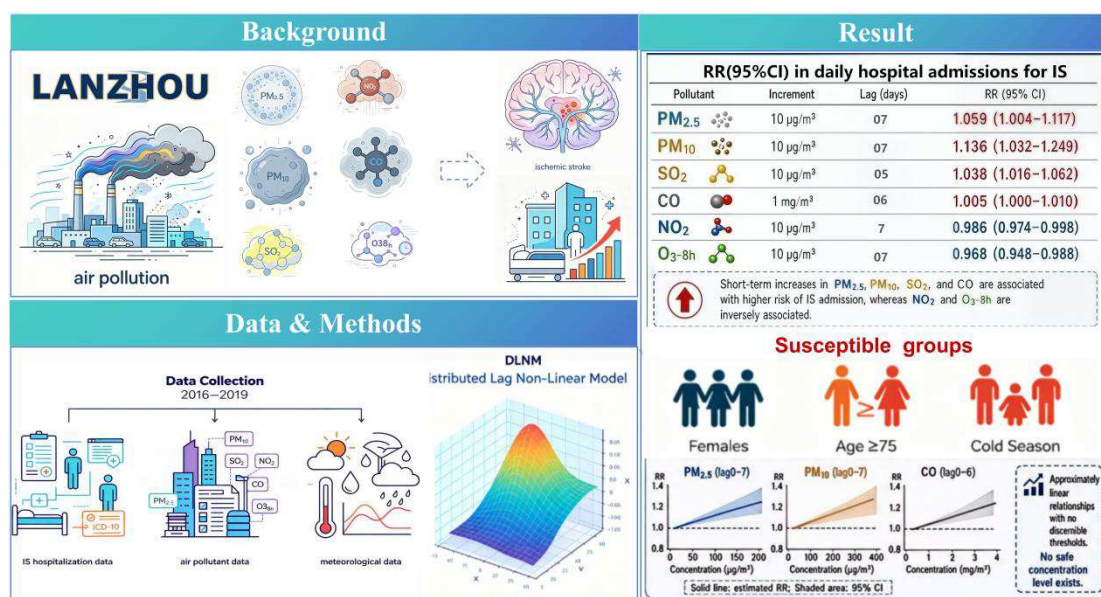
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Abstract

Ambient air pollution has been increasingly recognized as a modifiable risk factor for cerebrovascular disease; however, evidence from heavily polluted valley cities remains limited. This study aimed to investigate the associations between short-term exposure to six ambient air pollutants (PM_{2.5}, PM₁₀, SO₂, NO₂, O₃8h, and CO) and daily hospital admissions for ischemic stroke (IS) in Lanzhou, a typical river-valley city in northwestern China, and to identify vulnerable subpopulations by

gender, age, and season. Daily IS hospital admissions from all public hospitals, concurrent air pollutant concentrations, and meteorological data in Lanzhou were obtained from January 1, 2016 to December 31, 2019. A time-series analysis using a quasi-Poisson generalized linear model coupled with a distributed lag non-linear model (DLNM) was employed to quantify the pollutant–IS associations, adjusting for long-term temporal trends, day-of-week effects, and meteorological confounders. Stratified analyses were performed by gender, age group, and season. Exposure-response (E-R) relationships were characterized, and robustness was assessed through two-pollutant models and sensitivity analyses with varying degrees of freedom. Over the four-year study period, 53,489 IS admissions were recorded, averaging 37 cases per day. In single-pollutant models, each 10 $\mu\text{g}/\text{m}^3$ increment in $\text{PM}_{2.5}$ (lag07), PM_{10} (lag07), and SO_2 (lag05), and each 1 mg/m^3 increment in CO (lag06) were associated with significantly elevated risks of IS admission, with cumulative RRs of 1.059 (95% CI: 1.004–1.117), 1.136 (95% CI: 1.032–1.249), 1.038 (95% CI: 1.016–1.062), and 1.005 (95% CI: 1.000–1.010), respectively. Notably, NO_2 (lag7) and O_3 -8h (lag07) exhibited inverse associations, with RRs of 0.986 (95% CI: 0.974–0.998) and 0.968 (95% CI: 0.948–0.988). Subgroup analyses revealed heightened susceptibility among females, individuals aged ≥ 75 years (particularly for particulate matter), and during the cold season. The E-R curves for $\text{PM}_{2.5}$, PM_{10} , and CO demonstrated approximately linear relationships with no discernible thresholds, suggesting that no safe concentration level exists for these pollutants. This study provides robust evidence that short-term elevations in $\text{PM}_{2.5}$, PM_{10} , SO_2 , and CO significantly increase the risk of IS hospital admissions in a topographically constrained, heavily polluted urban environment. The observed effect modification by gender, age, and season underscores the need for differentiated public health strategies. These findings carry important implications for local policymakers in developing season-specific air quality interventions and targeted early-warning systems to protect vulnerable populations from pollution-related cerebrovascular events.

Keywords: Air pollution; Ischemic stroke; Hospital admissions; Distributed lag non-linear model; Time-series study

1. Introduction

Ischemic stroke (IS) refers to brain tissue necrosis caused by narrowing or occlusion of the cerebral blood-supplying arteries, including the carotid and vertebral arteries[1]. Stroke is one of the leading causes of death and disability worldwide, ranking as the third most fatal disease globally. Approximately 15 million people suffer from stroke each year worldwide[4]. As the most prevalent subtype, IS accounts for over 80% of all stroke cases[5], and has become the second leading cause of death and the third leading cause of disability globally[6]. The risk factors for IS are multifactorial, encompassing smoking, alcohol consumption, obesity, genetic predisposition, and dietary patterns. Notably, environmental factors, particularly ambient air pollution, have been increasingly recognized as important contributors to the onset and progression of IS[7].

With the deterioration of global air quality, growing attention has been paid to the association between ambient air pollution and stroke. A number of epidemiological studies have demonstrated significant associations between air pollutant exposure and stroke risk in various countries, including Korea[8], Canada[9], and the United States[10], as well as in several Chinese cities such as Shenzhen[7], Chengdu[11], Wuhan[12], Changsha[13], and Hangzhou[14]. However, given the substantial geographic variations in air pollution profiles, climatic conditions, and population characteristics, findings from these studies may not be directly generalizable to other regions.

Lanzhou, an important heavy industrial city in northwest China, is one of the largest cities situated in the upper reaches of the Yellow River. Characterized by a valley basin topography and unfavorable atmospheric dispersion conditions, Lanzhou has long been confronted with severe air pollution challenges. With rapid economic development and lifestyle changes, the burden of IS has been increasing in this region. However, most existing studies have focused on high-income countries or

economically developed regions, and limited evidence is available regarding the impact of air pollution on IS hospital admissions in Lanzhou.

The distributed lag non-linear model (DLNM) is a well-established statistical approach for evaluating the health effects of short-term exposure to air pollution[15, 16]. DLNM employs cross-basis functions to simultaneously capture both linear and non-linear exposure-response relationships, while allowing for a comprehensive quantitative assessment of pollutant effects across different lag days and cumulative lag periods, thereby offering higher model flexibility and accuracy compared with conventional methods. Therefore, we collected daily IS hospital admissions, ambient air pollutant concentrations, and meteorological data in Lanzhou from 2016 to 2019, and employed DLNM to investigate the short-term effects of air pollutants on IS hospital admissions. This study aims to provide scientific evidence for the development of targeted prevention strategies and air quality control policies to reduce the IS burden and protect population health in Lanzhou.

2. Materials and Methods

2.1. Study area

Lanzhou, the capital of Gansu Province, is located in northwest China (36°03'N, 103°40'E), with a permanent resident population exceeding 3.3 million and a total administrative area of 13,100 square kilometers in 2019. The city features a typical temperate continental climate and is characterized by a river valley topography nestled between canyons and basins.



Figure 1. Geographic location of Lanzhou City and the distribution of air pollution monitoring stations

2.2. Data collection

Daily IS hospital admission data were obtained from the Health Statistics Information Network Direct Reporting System of the Health Statistics Information Center of Gansu Province for the period from January 1, 2016 to December 31, 2019. The database contains information on each inpatient's gender, age, residential address, disease coding, and dates of admission and discharge extracted from electronic hospitalization records. IS cases were identified using the International Classification of Diseases, 10th Revision (ICD-10) code I63.

Daily concentrations of six air pollutants during 2016–2019 were obtained from the China Air Quality Online Monitoring and Analysis Platform (<https://www.aqistudy.cn/>). Hourly air pollution data were collected from three state-controlled monitoring stations located in the main urban area of Lanzhou (Figure 1). The 24-hour average concentrations of PM_{2.5}, PM₁₀, SO₂, NO₂, and CO, as well as

the maximum daily 8-hour average ozone concentration (O₃8h), were then calculated. The completeness and consistency of the monitoring data met the requirements of the national Ambient Air Quality Monitoring Specification. Daily meteorological data, including mean temperature (°C) and relative humidity (%), were obtained from the China Meteorological Data Service Center (<http://data.cma.cn>).

2.3. Statistical analysis

Given that daily IS hospital admissions are rare events relative to the total population, the data approximate a Poisson distribution. Therefore, a quasi-Poisson generalized linear regression model combined with the DLNM was employed to estimate the short-term effects of air pollutants on daily IS hospital admissions, which served as the dependent variable. Natural spline (ns) functions were applied to control for confounding factors, including long-term temporal trends, temperature, and relative humidity. The day-of-the-week effect and public holiday effect were incorporated as dummy variables. The model was constructed as follows:

$$\text{Log}[E(Y_t)] = \alpha + \beta \text{Pollution} + \text{ns}(T_t, \text{df}) + \text{ns}(\text{Temperature}_t, \text{df}) + \text{ns}(\text{Humidity}_t, \text{df}) + \text{as.factor}(\text{holiday}) + \text{as.factor}(\text{dow})$$

where t denotes the observation day; Y_t represents the number of hospital admissions for IS on day t ; $E(Y_t)$ is the expected number of hospital admissions on day t ; α is the intercept; β is the regression coefficient of air pollutants; Pollution _{t} is the concentration of air pollutants on day t ; ns denotes the natural spline smoothing function; df represents the degrees of freedom; T_t is the time variable for long-term trends; Temperature _{t} is the daily mean temperature on day t ; Humidity _{t} is the relative humidity on day t ; holiday is a dummy variable for public holidays; and dow is a dummy variable for the day-of-the-week effect. The degrees of freedom for each smoothing term were determined using the Quasi Akaike Information Criterion (QAIC)[17]. The optimal degrees of freedom for the time trend, temperature, and relative humidity were 7 per year, 3, and 3, respectively.

Previous studies have suggested that the health effects of air pollution may exhibit a lag period typically not exceeding 7 days[18]. Accordingly, in this study,

both single-day lag structures (lag0–lag7) and cumulative multi-day lag structures (lag01–lag07) were constructed to assess the effects of air pollutants on daily IS hospital admissions. Stratified analyses were performed by gender (male and female), age (<65, 65–74, and ≥ 75 years), and season (warm season: April to September; cold season: October to March of the following year). Exposure-response relationship curves were also fitted to visualize the concentration-response patterns. Finally, sensitivity analyses were conducted by applying two-pollutant models and varying the degrees of freedom for the time trend ($df = 6-10$) to evaluate the robustness of the results. All statistical analyses were performed using the "dlnm" package in R software (version 4.1.1), with a two-sided significance level of 0.05.

3. Results

3.1. Data description

A total of 53,489 IS hospital admissions in Lanzhou City were included in this study. Table 1 presents the descriptive statistics of daily hospital admissions, air pollutant concentrations, and meteorological factors during the study period. From January 1, 2016 to December 31, 2019, the daily average number of IS admissions was 37, of which 21 were males and 16 were females. Among the three age groups, the 65–74 years group had the highest daily admissions with an average of 13 cases per day. The daily mean concentrations of PM_{2.5}, PM₁₀, SO₂, NO₂, O₃8h, and CO were 46.47 $\mu\text{g}/\text{m}^3$, 114.10 $\mu\text{g}/\text{m}^3$, 19.00 $\mu\text{g}/\text{m}^3$, 50.12 $\mu\text{g}/\text{m}^3$, 97.02 $\mu\text{g}/\text{m}^3$, and 1.15 mg/m^3 , respectively, none of which exceeded the Chinese National Ambient Air Quality Standards (GB 3095-2012)[19]. The daily mean temperature was 11.36°C and the mean relative humidity was 51.03%.

3.2. Spearman correlation analysis

Figure 2 presents the Spearman correlation matrix among air pollutants and meteorological factors. In this figure, the color and size of the circles represent the magnitude of the correlation coefficient, with blue indicating positive correlations and orange indicating negative correlations; crosses denote statistically non-significant correlations ($P > 0.05$). Temperature was negatively correlated with PM_{2.5} ($r = -0.60$),

PM₁₀ ($r = -0.44$), SO₂ ($r = -0.70$), NO₂ ($r = -0.37$), CO ($r = -0.57$), and O₃8h ($r = -0.76$). Similarly, relative humidity was negatively correlated with PM_{2.5} ($r = -0.20$), PM₁₀ ($r = -0.41$), SO₂ ($r = -0.28$), NO₂ ($r = -0.20$), CO ($r = -0.06$), and O₃8h ($r = -0.28$). In addition, moderate to strong inter-pollutant correlations were observed among the six air pollutants. These findings indicated the necessity of adjusting for meteorological confounders in the regression models and employing two-pollutant models to assess the independence of pollutant effects.

Table 1. Distribution of daily IS admissions, air pollutant concentrations, and meteorological factors in Lanzhou, China (2016–2019).

	$\bar{X}\pm S$	Minimum	Percentage			Maximum
			P_{25}	P_{50}	P_{75}	
CI hospital admissions						
Total	37.00±35.00	2.00	17.00	26.00	43.00	210.00
Male	21.00±18.00	1.00	9.00	15.00	25.00	124.00
Female	16.00±15.00	1.00	6.00	11.00	19.00	91.00
<65	12.00±11.00	1.00	4.00	8.00	15.00	81.00
65-74	13.00±9.00	1.00	6.00	10.00	15.00	67.00
≥75	12.00±11.00	1.00	4.00	8.00	14.00	83.00
Air pollutants						
PM _{2.5} (μg/m ³)	46.47±26.87	9.00	28.21	40.00	56.00	278.00
PM ₁₀ (μg/m ³)	114.10±93.85	16.00	66.00	94.88	132.98	1484.54
SO ₂ (μg/m ³)	19.00±13.52	3.54	9.00	14.00	25.00	81.87
N0 ₂ (μg/m ³)	50.12±19.18	13.21	37.00	47.89	58.75	146.60
O ₃ 8h(μg/m ³)	97.02±39.79	11.00	65.00	92.00	126.00	222.00
CO(mg/m ³)	1.15±0.70	0.20	0.70	0.90	1.37	4.65
Meteorological factors						
Mean temperature (°C)	11.36±9.99	-12.30	2.25	12.70	20.06	30.40
Relative humidity (%)	51.03±14.95	11.71	40.00	51.46	61.62	96.09

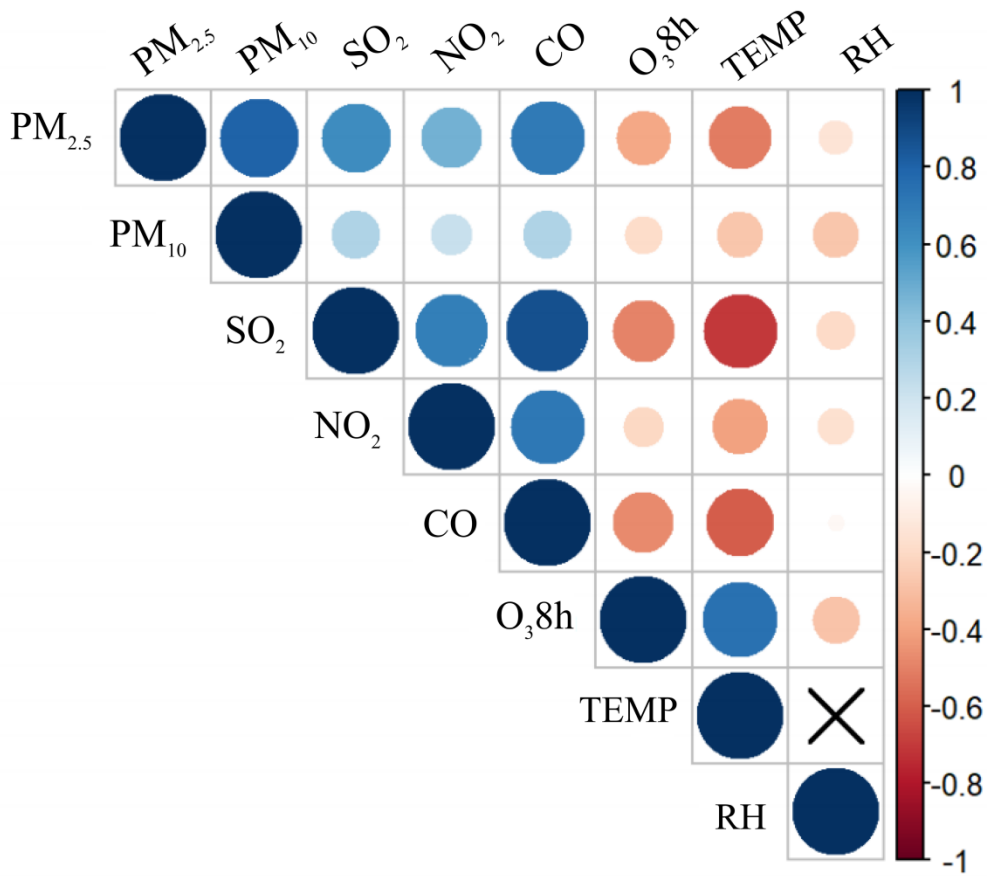


Figure 2. Spearman correlation coefficients among air pollutants and meteorological factors

3.3. DLNM analysis

Figure 3 presents the three-dimensional plots of the lag-response relationships between concentrations of six air pollutants and daily IS hospital admissions in single-pollutant models. The results revealed non-linear associations between all six pollutants (PM_{2.5}, PM₁₀, SO₂, NO₂, O₃8h, and CO) and daily IS hospital admissions, with evident lag patterns in the effect estimates. The relative risks exhibited a trend of initial increase followed by decline as lag days progressed. Specifically, PM_{2.5}, NO₂, and CO showed the strongest associations at lag day 1, while SO₂ and O₃8h peaked at lag day 4, and the effects of PM₁₀ remained relatively stable across lag days 5 to 6.

Table 2 presents the RR and 95% CI for the associations between air pollutant concentrations and daily IS hospital admissions in single-pollutant models. Significant positive associations were observed for PM_{2.5} (lag6, lag04–lag07), PM₁₀ (lag5, lag6,

and lag07), SO₂ (lag05, lag06), and CO (lag02–lag07). The strongest cumulative effects for each 10 µg/m³ increase in PM_{2.5}, PM₁₀, and SO₂, and each 1 mg/m³ increase in CO were identified at lag07 for PM_{2.5} (RR: 1.038, 95% CI: 1.016–1.062), lag07 for PM₁₀ (RR: 1.005, 95% CI: 1.000–1.010), lag05 for SO₂ (RR: 1.059, 95% CI: 1.002–1.117), and lag06 for CO (RR: 1.136, 95% CI: 1.032–1.249). In contrast, protective effects were detected for NO₂ and O₃8h, with significant negative associations observed at NO₂ (lag6–lag7) and O₃8h (lag2, lag02–lag07). The lowest risks of daily IS admissions were found at lag7 for NO₂ (RR: 0.986, 95% CI: 0.974–0.998) and lag07 for O₃8h (RR: 0.968, 95% CI: 0.948–0.988).

Figure 4 presents the results of stratified analyses by gender. Overall, females exhibited greater susceptibility to air pollution-related IS hospital admissions. Significant positive associations were observed among females for PM_{2.5} at lag07, PM₁₀ at lag07, SO₂ at lag05, and CO at lag06, with RRs of 1.047 (95% CI: 1.022–1.072), 1.006 (95% CI: 1.000–1.012), 1.070 (95% CI: 1.009–1.134), and 1.164 (95% CI: 1.046–1.294) for each 10 µg/m³ increase in PM_{2.5}, PM₁₀, and SO₂ and each 1 mg/m³ increase in CO, respectively. In contrast, NO₂ and O₃8h showed stronger protective effects among males, with the lowest RRs observed at lag7 for NO₂ (RR: 0.986, 95% CI: 0.973–0.999) and lag07 for O₃8h (RR: 0.971, 95% CI: 0.950–0.992).

Figure 5 presents the results of stratified analyses by age group. The effects of PM_{2.5} and PM₁₀ were most pronounced in patients aged ≥75 years at lag07, with corresponding RRs of 1.051 (95% CI: 1.022–1.080) and 1.007 (95% CI: 1.000–1.013), respectively. For the <65 years group, the strongest effects were observed at lag06 for SO₂, lag1 for NO₂, and lag07 for CO, with corresponding RRs of 1.069 (95% CI: 1.000–1.143), 1.025 (95% CI: 1.002–1.149), and 1.162 (95% CI: 1.027–1.314), respectively. In contrast, O₃8h exhibited the strongest protective effect in the 65–74 years group, with the lowest RR observed at lag07 (RR: 0.962, 95% CI: 0.942–0.982).

Table 3 presents the results of stratified analyses by season. Overall, the effects of PM_{2.5}, PM₁₀, SO₂, NO₂, and CO on IS hospital admissions were more pronounced during the cold season. The strongest effects were observed at lag02 for PM_{2.5}, lag07 for PM₁₀, lag05 for SO₂, lag04 for NO₂, and lag05 for CO. For each 10 µg/m³ increase

in PM_{2.5}, PM₁₀, SO₂, and NO₂, and each 1 mg/m³ increase in CO, the corresponding RRs were 1.039 (95% CI: 1.013–1.065), 1.006 (95% CI: 1.002–1.010), 1.075 (95% CI: 1.010–1.145), 1.085 (95% CI: 1.052–1.118), and 1.264 (95% CI: 1.136–1.408), respectively. Similarly, the protective effect of O₃8h was also more significant during the cold season, with the lowest RR observed at lag07 (RR: 0.933, 95% CI: 0.903–0.963).

Figure 6 illustrates the exposure-response (E-R) curves depicting the relationships between air pollutant concentrations at lag07 and the relative risks of daily IS hospital admissions. The E-R curves for PM_{2.5}, PM₁₀, and CO exhibited approximately linear relationships without apparent thresholds, indicating that the risk of IS hospital admissions increased steadily with rising pollutant concentrations. The curve for SO₂ also displayed a linear trend, but the association was not statistically significant. Negative concentration-response relationships were observed for NO₂ and O₃8h with daily IS hospital admissions, suggesting protective effects at higher concentrations. However, the curve for NO₂ did not reach statistical significance, whereas the protective effect of O₃8h was statistically significant.

3.4. Stability analysis

Table S1 presents the results of two-pollutant models. The models were constructed by incorporating the pollutant pairs at their respective most significant lag days. Due to the high collinearity between PM_{2.5} and PM₁₀, these two pollutants were not included in the same model simultaneously. After adjusting for co-pollutants, the associations of PM_{2.5}, PM₁₀, SO₂, NO₂, O₃8h, and CO with daily IS hospital admissions remained robust, indicating that the effects of individual pollutants were independent of one another.

Table S2 presents the results of sensitivity analyses examining model stability at the strongest lag days (lag07 for PM_{2.5}, lag07 for PM₁₀, lag05 for SO₂, lag01 for NO₂, lag4 for O₃8h, and lag06 for CO). The models were refitted by varying the degrees of freedom for the time trend from 6 to 10 per year. The RR estimates and 95% CIs did not change substantially across different specifications, confirming the robustness and stability of the models.

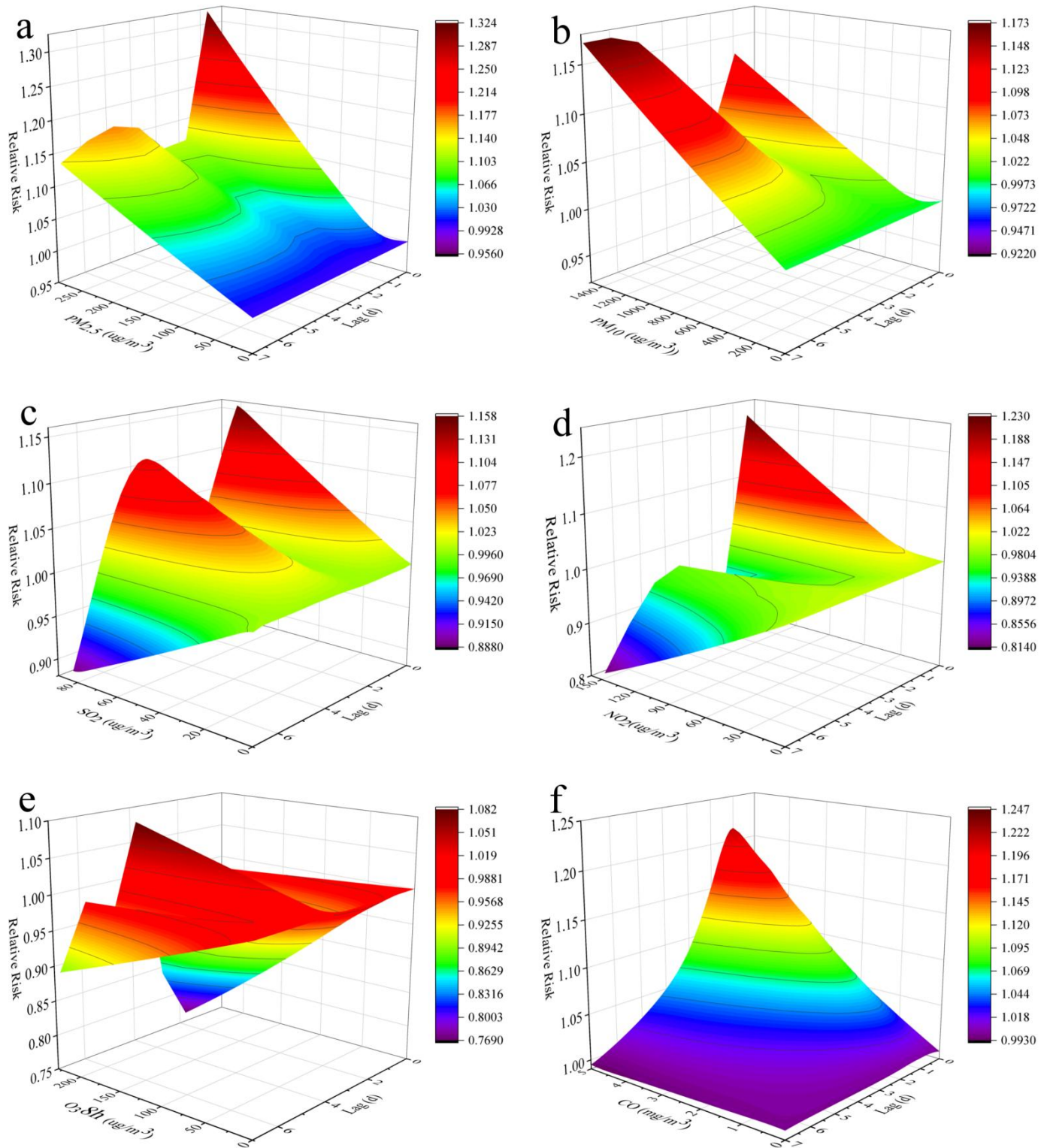


Figure 3. Three-dimensional plots of exposure-lag-response relationships between air pollutants and daily IS hospital admissions. (a) PM_{2.5}, (b) PM₁₀, (c) SO₂, (d) NO₂, (e) O₃ 8h, (f) CO.

Table 2. Relative risks (95% CIs) for daily IS hospital admissions associated with a 10 µg/m³ increase in air pollutant concentrations (1 mg/m³ for CO) at different lag days

Lag days	PM _{2.5}		PM ₁₀		SO ₂		NO ₂		O ₃ 8h		CO	
	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
lag0	0.998	(0.983,1.014)	0.999	(0.996,1.003)	1.018	(0.981,1.057)	1.002	(0.984,1.020)	0.999	(0.989,1.010)	1.024	(0.958,1.095)
lag1	1.010	(0.995,1.025)	1.001	(0.997,1.004)	1.009	(0.970,1.049)	1.014	(0.995,1.034)	0.991	(0.979,1.002)	1.045	(0.975,1.121)
lag2	1.004	(0.994,1.015)	1.000	(0.998,1.003)	1.000	(0.973,1.027)	0.995	(0.982,1.008)	0.988	(0.977,1.000)	1.027	(0.979,1.077)
lag3	1.004	(0.997,1.011)	1.001	(0.999,1.002)	1.008	(0.990,1.026)	0.995	(0.986,1.003)	0.993	(0.982,1.005)	1.016	(0.984,1.049)
lag4	1.005	(0.998,1.012)	1.001	(0.999,1.002)	1.014	(0.995,1.032)	0.998	(0.990,1.007)	1.003	(0.991,1.015)	1.010	(0.978,1.042)
lag5	1.006	(0.999,1.012)	1.001	(1.000,1.003)	1.010	(0.993,1.027)	0.997	(0.989,1.005)	0.998	(0.987,1.010)	1.005	(0.976,1.036)
lag6	1.005	(1.000,1.011)	1.001	(1.000,1.004)	0.999	(0.987,1.011)	0.992	(0.986,0.998)	0.999	(0.987,1.010)	1.002	(0.981,1.023)
lag7	1.005	(0.994,1.015)	1.001	(0.999,1.004)	0.986	(0.961,1.011)	0.986	(0.974,0.998)	0.995	(0.985,1.005)	0.999	(0.955,1.045)
lag01	1.009	(0.993,1.024)	1.000	(0.997,1.004)	1.027	(0.985,1.071)	1.016	(0.997,1.035)	0.990	(0.976,1.004)	1.071	(0.996,1.150)
lag02	1.013	(0.997,1.028)	1.001	(0.997,1.004)	1.027	(0.983,1.072)	1.011	(0.991,1.030)	0.979	(0.963,0.995)	1.099	(1.020,1.184)
lag03	1.017	(0.999,1.035)	1.001	(0.997,1.005)	1.035	(0.986,1.086)	1.005	(0.983,1.028)	0.972	(0.955,0.989)	1.117	(1.028,1.214)
lag04	1.022	(1.004,1.041)	1.002	(0.998,1.006)	1.049	(0.998,1.102)	1.003	(0.980,1.027)	0.975	(0.957,0.993)	1.128	(1.035,1.229)
lag05	1.028	(1.008,1.048)	1.003	(0.999,1.007)	1.059	(1.004,1.117)	1.000	(0.974,1.026)	0.973	(0.954,0.993)	1.134	(1.033,1.244)
lag06	1.034	(1.013,1.055)	1.004	(0.999,1.009)	1.058	(1.002,1.117)	0.992	(0.965,1.020)	0.972	(0.952,0.992)	1.136	(1.032,1.249)
lag07	1.038	(1.016,1.062)	1.005	(1.000,1.010)	1.043	(0.986,1.104)	0.978	(0.949,1.008)	0.968	(0.948,0.988)	1.134	(1.026,1.253)

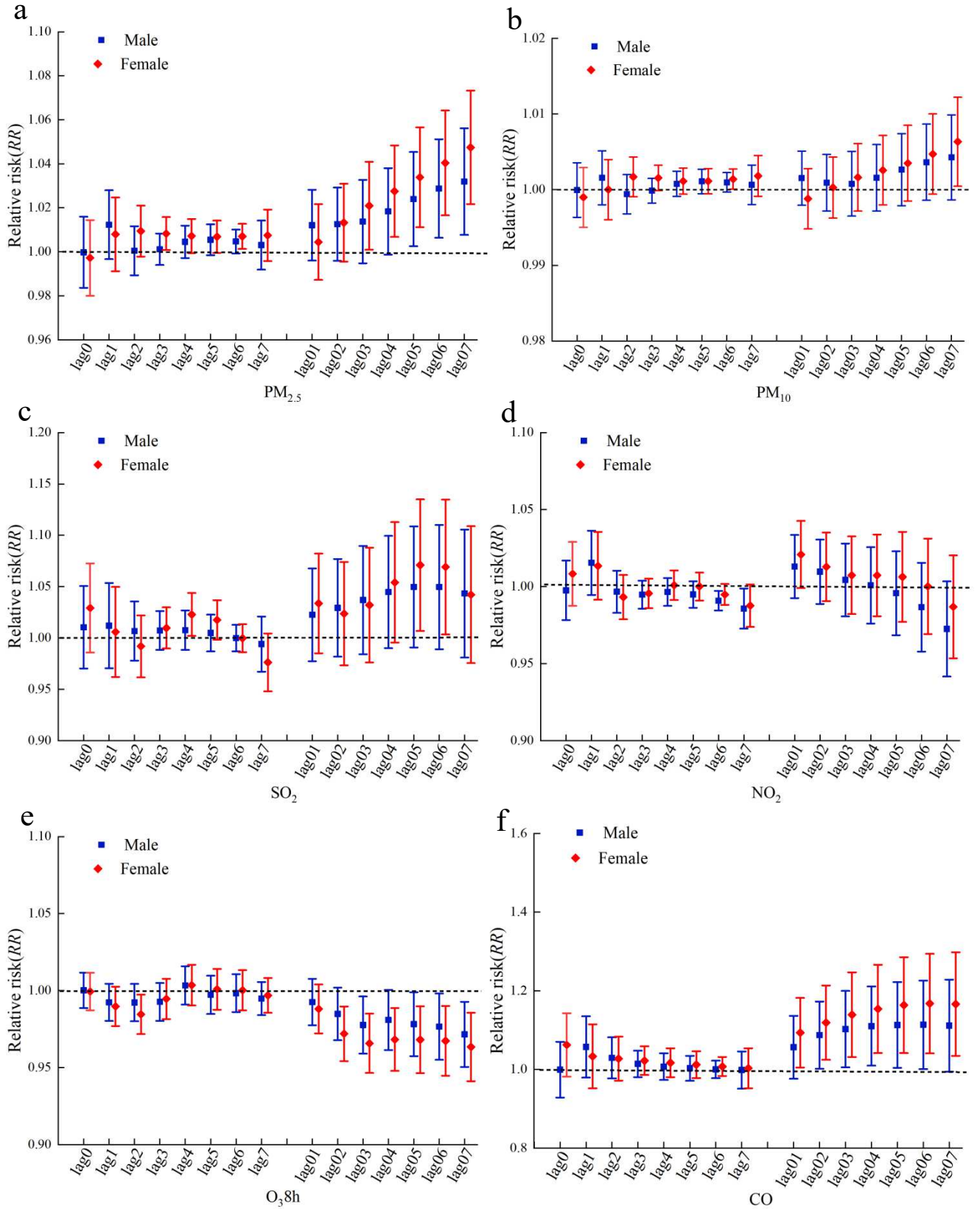


Figure 4. Relative risks (95% CIs) for daily IS hospital admissions associated with a 10 µg/m³ increase in air pollutant concentrations (1 mg/m³ for CO) stratified by gender in single-pollutant models. (a) PM_{2.5}, (b) PM₁₀, (c) SO₂, (d) NO₂, (e) O₃ 8h, (f) CO.

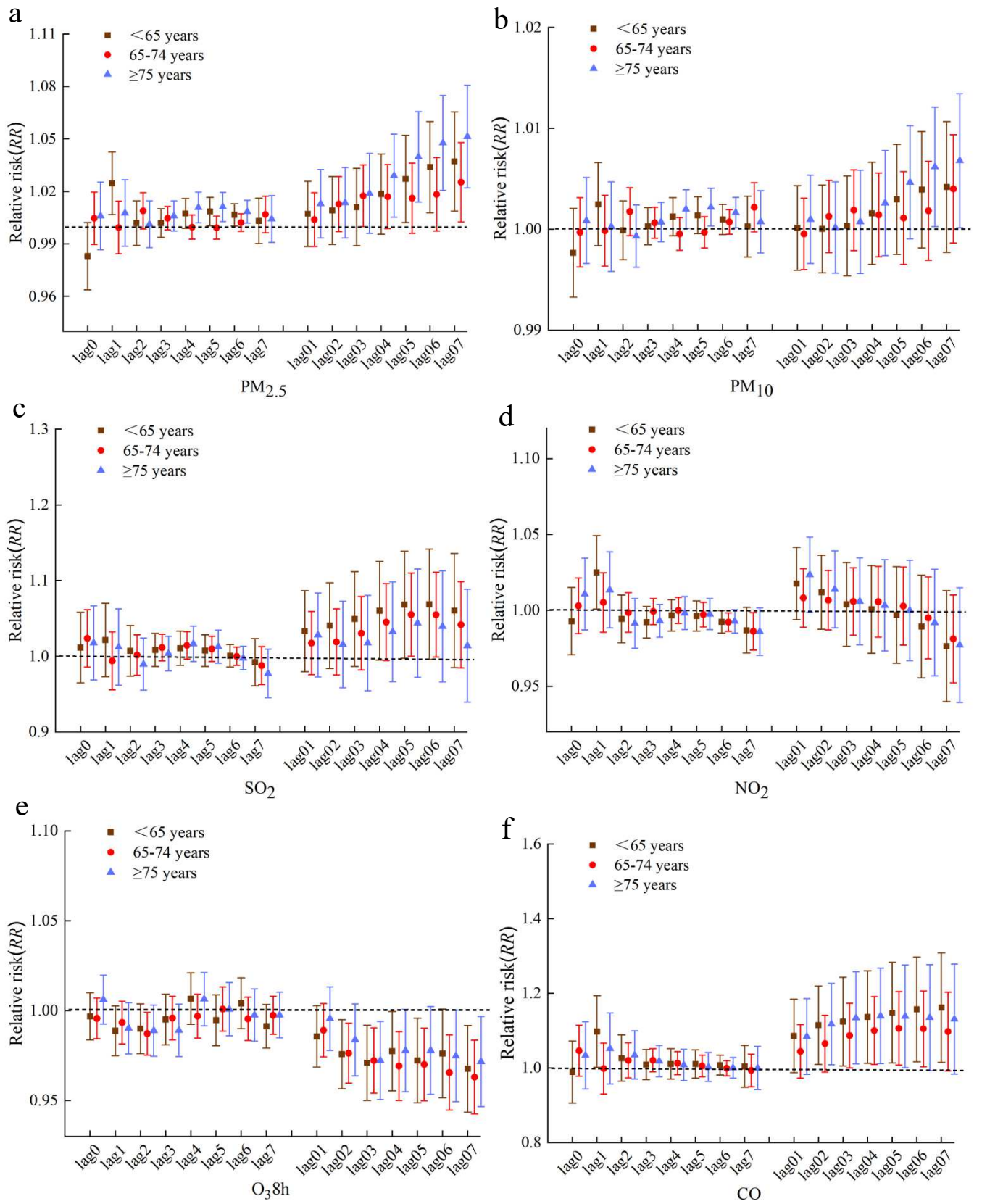


Figure 5. Relative risks (95% CIs) for daily IS hospital admissions associated with a 10 µg/m³ increase in air pollutant concentrations (1 mg/m³ for CO) stratified by age in single-pollutant models. (a) PM_{2.5}, (b) PM₁₀, (c) SO₂, (d) NO₂, (e) O₃ 8h, (f) CO.

Table 3 . Relative risks (95% CIs) for daily IS hospital admissions associated with a 10 µg/m³ increase in air pollutant concentrations (1 mg/m³ for CO) stratified by season in single-pollutant models.

	Lag days	PM _{2.5}		PM ₁₀		SO ₂		NO ₂		O ₃ 8h		CO	
		RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
Cold	lag0	1.01	(0.994,1.031)	1.00	(0.999,1.007)	0.98	(0.943,1.029)	1.01	(0.994,1.041)	0.98	(0.964,1.004)	1.01	(0.945,1.085)
		2		3		5		7		4		3	
	lag1	1.01	(0.997,1.039)	1.00	(0.997,1.006)	1.01	(0.969,1.056)	1.02	(1.000,1.049)	0.99	(0.971,1.012)	1.07	(1.001,1.161)
		8		1		2		4		1		8	
	lag2	1.00	(0.990,1.019)	1.00	(0.998,1.005)	1.03	(1.003,1.066)	1.02	(1.005,1.040)	0.99	(0.977,1.018)	1.06	(1.011,1.121)
		4		1		4		2		7		5	
	lag3	0.99	(0.990,1.008)	0.99	(0.997,1.001)	1.02	(1.007,1.049)	1.01	(1.002,1.025)	0.97	(0.953,0.993)	1.04	(1.010,1.083)
		9		9		8		4		3		6	
	lag4	0.99	(0.990,1.007)	0.99	(0.996,1.000)	1.01	(0.993,1.035)	1.00	(0.994,1.017)	0.99	(0.978,1.019)	1.02	(0.992,1.066)
		8		8		4		5		8		8	
	lag5	1.00	(0.991,1.008)	0.99	(0.996,1.000)	1.00	(0.983,1.022)	0.99	(0.988,1.009)	0.99	(0.976,1.017)	1.01	(0.978,1.046)
		0		8		2		8		6		1	
	lag6	1.00	(0.996,1.008)	1.00	(0.999,1.002)	0.99	(0.978,1.005)	0.99	(0.986,1.001)	1.00	(0.987,1.029)	0.99	(0.971,1.019)
		2		0		1		3		8		5	
	lag7	1.00	(0.992,1.018)	1.00	(1.000,1.006)	0.98	(0.954,1.010)	0.98	(0.974,1.004)	0.98	(0.965,1.003)	0.97	(0.933,1.026)
		5		3		2		9		4		9	
	lag01	1.03	(1.010,1.050)	1.00	(1.000,1.009)	0.99	(0.945,1.050)	1.04	(1.013,1.071)	0.97	(0.951,1.000)	1.09	(1.004,1.187)
		0		5		6		2		5		2	
	lag02	1.03	(1.016,1.054)	1.00	(1.002,1.010)	1.03	(0.975,1.088)	1.06	(1.036,1.094)	0.97	(0.945,1.000)	1.16	(1.064,1.269)
		5		6		0		5		2		2	
	lag03	1.03	(1.012,1.055)	1.00	(1.001,1.010)	1.05	(0.999,1.122)	1.07	(1.048,1.112)	0.94	(0.917,0.976)	1.21	(1.105,1.338)

		4		5		9		9		6		6	
	lag04	1.03 2	(1.010,1.054)	1.00 3	(0.998,1.008)	1.07 3	(1.012,1.138)	1.08 5	(1.052,1.118)	0.94 4	(0.914,0.975)	1.25 0	(1.132,1.380)
	lag05	1.03 2	(1.008,1.056)	1.00 2	(0.996,1.007)	1.07 5	(1.010,1.145)	1.08 3	(1.047,1.120)	0.94 0	(0.909,0.972)	1.26 4	(1.136,1.408)
	lag06	1.03 4	(1.009,1.059)	1.00 2	(0.996,1.008)	1.06 6	(1.000,1.136)	1.07 6	(1.038,1.114)	0.94 8	(0.916,0.980)	1.25 8	(1.126,1.405)
	lag07	1.03 9	(1.013,1.065)	1.00 5	(0.999,1.011)	1.04 6	(0.980,1.117)	1.06 3	(1.025,1.103)	0.93 3	(0.903,0.963)	1.23 1	(1.100,1.377)
	Lag days	PM _{2.5}		PM ₁₀		SO ₂		NO ₂		O ₃ 8h		CO	
		RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI	RR	95%CI
Warm	lag0	0.99 7	(0.978,1.017)	1.00 0	(0.995,1.005)	0.99 0	(0.926,1.058)	0.98 1	(0.954,1.009)	0.99 8	(0.987,1.008)	0.90 3	(0.759,1.074)
	lag1	1.01 3	(0.998,1.028)	1.00 3	(1.000,1.007)	0.95 2	(0.894,1.014)	0.99 9	(0.971,1.027)	0.99 4	(0.983,1.005)	0.97 3	(0.818,1.159)
	lag2	1.00 2	(0.990,1.014)	1.00 0	(0.998,1.003)	0.95 2	(0.908,0.999)	0.97 4	(0.956,0.993)	0.99 2	(0.982,1.003)	0.92 3	(0.809,1.053)
	lag3	1.00 2	(0.994,1.010)	1.00 1	(0.999,1.003)	0.98 2	(0.950,1.015)	0.99 0	(0.977,1.004)	0.99 2	(0.982,1.003)	1.01 9	(0.932,1.114)
	lag4	1.00 4	(0.996,1.013)	1.00 1	(0.999,1.003)	1.00 2	(0.967,1.037)	1.00 7	(0.994,1.021)	1.00 1	(0.991,1.012)	1.10 0	(1.005,1.203)
	lag5	1.00 2	(0.994,1.010)	1.00 1	(0.999,1.003)	0.99 8	(0.966,1.032)	1.00 7	(0.994,1.020)	0.99 6	(0.985,1.007)	1.08 3	(0.995,1.179)
	lag6	0.99 7	(0.990,1.005)	1.00 0	(0.998,1.001)	0.98 0	(0.955,1.005)	0.99 4	(0.985,1.003)	1.00 3	(0.992,1.013)	1.00 3	(0.941,1.070)

lag7	0.99 1	(0.978,1.005)	0.99 8	(0.995,1.001)	0.95 4	(0.912,0.997)	0.97 6	(0.960,0.992)	1.00 1	(0.991,1.010)	0.90 1	(0.804,1.010)
lag01	1.01 0	(0.990,1.031)	1.00 3	(0.998,1.008)	0.94 2	(0.863,1.029)	0.98 0	(0.946,1.015)	0.99 2	(0.978,1.005)	0.87 9	(0.704,1.098)
lag02	1.01 2	(0.989,1.035)	1.00 3	(0.998,1.009)	0.89 7	(0.816,0.988)	0.95 5	(0.919,0.992)	0.98 4	(0.969,1.000)	0.81 2	(0.640,1.029)
lag03	1.01 4	(0.988,1.041)	1.00 4	(0.998,1.010)	0.88 1	(0.793,0.979)	0.94 6	(0.907,0.986)	0.97 7	(0.960,0.993)	0.82 7	(0.636,1.076)
lag04	1.01 9	(0.990,1.047)	1.00 5	(0.999,1.012)	0.88 3	(0.789,0.988)	0.95 3	(0.911,0.996)	0.97 8	(0.960,0.996)	0.90 9	(0.688,1.203)
lag05	1.02 1	(0.990,1.053)	1.00 6	(0.999,1.014)	0.88 1	(0.781,0.995)	0.95 9	(0.914,1.006)	0.97 4	(0.955,0.993)	0.98 5	(0.728,1.333)
lag06	1.01 8	(0.986,1.052)	1.00 6	(0.998,1.014)	0.86 3	(0.762,0.978)	0.95 3	(0.907,1.002)	0.97 7	(0.957,0.997)	0.98 9	(0.724,1.350)
lag07	1.00 9	(0.973,1.046)	1.00 4	(0.995,1.013)	0.82 3	(0.726,0.934)	0.93 0	(0.885,0.978)	0.97 7	(0.958,0.997)	0.89 1	(0.651,1.218)

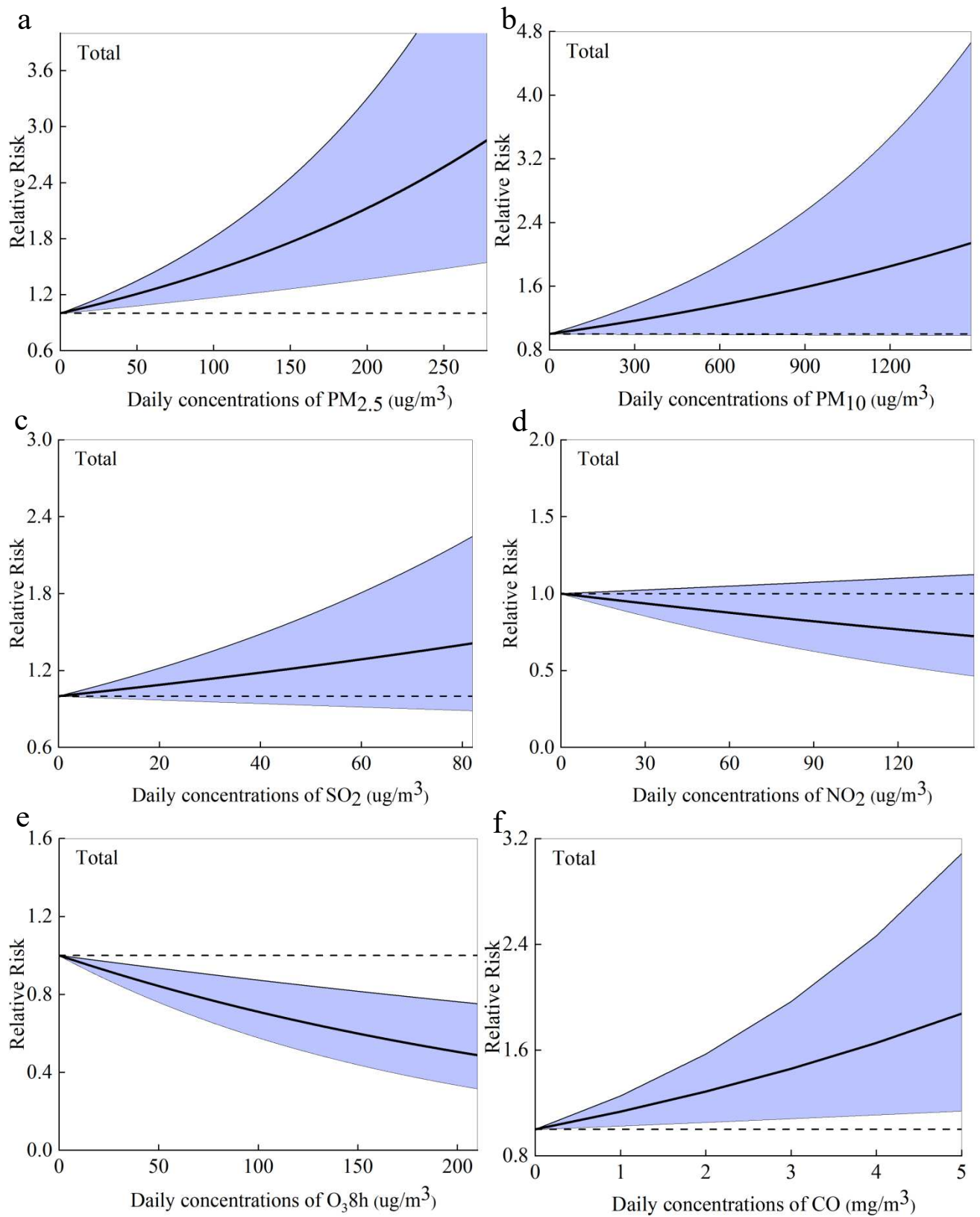


Figure 6. Exposure-response curves for the associations between air pollutants and daily IS hospital admissions at lag 07.

4. Discussion

This study employed a quasi-Poisson generalized linear regression model combined with the distributed lag non-linear model (DLNM) to investigate the short-term effects of ambient air pollutants on daily ischemic stroke (IS) hospital admissions in Lanzhou from 2016 to 2019. Our findings revealed significant positive associations between IS admissions and ambient concentrations of PM_{2.5}, PM₁₀, SO₂, and CO, whereas NO₂ and O₃8h exhibited protective associations. These effects were modified by gender, age, and season. The exposure-response curves for PM_{2.5}, PM₁₀, and CO demonstrated approximately linear relationships without apparent thresholds, while O₃8h displayed a negative concentration-response relationship with IS admissions.

4.1 Lag Patterns and Regional Heterogeneity

The strongest cumulative effects on daily IS admissions were observed at lag07 for PM_{2.5} and PM₁₀, lag05 for SO₂, and lag06 for CO. These lag patterns differ from those reported in other Chinese cities. In Beijing[20], PM_{2.5} and PM₁₀ exhibited the most significant effects on cerebrovascular disease emergency visits at lag6, while in Wuhan[21], PM_{2.5} peaked at lag0 and PM₁₀ and SO₂ at lag1. A nationwide study across 172 Chinese cities[22] demonstrated consistent significant associations at lag0 for PM_{2.5}, SO₂, and CO. These discrepancies likely reflect regional differences in geographic and climatic conditions, pollutant compositions and concentrations, and population susceptibility, suggesting that the precise window of exposure vulnerability is region-specific and warrants further investigation.

4.2 Positive Associations with PM_{2.5}, PM₁₀, SO₂, and CO

Each 10 µg/m³ increase in PM_{2.5} and PM₁₀ was associated with elevated IS admission risks. These findings are consistent with studies conducted in Yancheng[23], Shenzhen[7], Beijing[20], and Hangzhou[14]. The biological plausibility of these associations is well-established: particulate matter exposure can

dysregulate cardiac autonomic function, elevate and destabilize blood pressure[24], stimulate oxidative stress, promote systemic inflammatory cytokine release, and impair vascular endothelial function, collectively enhancing peripheral thrombosis and coagulation[25, 26].

SO₂ exposure was significantly associated with increased IS admissions, consistent with findings from Wuhan[21], Guangzhou[27], and Chongqing[28]. Similarly, CO demonstrated a significant positive association with IS admissions, corroborating results from Canada[9] and a nationwide Chinese study[29]. The underlying mechanisms for both pollutants likely involve alterations in cardiac autonomic function, enhanced oxidative stress, and increased blood coagulation and thrombosis[30, 31]. Notably, the health effects of CO on IS remain relatively understudied compared with particulate matter, and further investigation is warranted.

4.3 Protective Associations with NO₂ and O₃8h

Our finding of a protective association between NO₂ and IS admissions contrasts with most previous studies, which have reported either positive associations in Korea[32], Chongqing[28], and Guangzhou[27], or null associations in Sweden[33]. Similarly, O₃8h exhibited a protective effect on IS admissions in Lanzhou, differing from the adverse effects reported in Chengdu[34] and Shenzhen[7], though consistent with the uncertain or null associations observed in Japan[35] and Wuhan[21]. The discrepancies for both pollutants may be attributable to differences in ambient concentration levels, meteorological conditions, and population characteristics. Regarding O₃, it is important to note that strong solar radiation and elevated temperatures during summer facilitate photochemical ozone formation, resulting in substantially higher O₃ concentrations during the warm season[36]. Given that IS incidence is characteristically higher during the cold season—when O₃ concentrations are typically lowest—the observed negative association may reflect seasonal co-variation rather than a direct biological protective mechanism. These findings warrant cautious interpretation and further investigation.

4.4 Effect Modification by Gender

The associations between air pollutants and IS admissions were more pronounced in females, consistent with findings from Chengdu[37], Beijing[20], Wuhan[21], Shenzhen[7], and other studies. The greater susceptibility of females may be partially explained by anatomical and physiological differences in the respiratory system: females tend to have smaller and more reactive airways, and the deposition of coarse particles in proximal airways results in a greater local tissue burden, potentially leading to enhanced systemic inflammatory responses[38, 39]. However, this finding is not universal, as no significant gender modification was detected in Chongqing[28]. The role of gender in modifying air pollution effects on IS requires further investigation, as physiological differences, lifestyle behaviors, occupational exposure patterns, and immune function may all contribute to the observed heterogeneity.

4.5 Effect Modification by Age

Patients aged ≥ 75 years were more susceptible to PM_{2.5} and PM₁₀, while those aged < 65 years were more vulnerable to SO₂, NO₂, and CO, and the protective effect of O₃8h was most pronounced in the 65–74 years age group. The heightened susceptibility of older adults to particulate matter is supported by studies in Yancheng[23], Beijing[20], and the United States[40], and may be related to age-related declines in respiratory and cardiovascular function, compromised immune defenses, and a higher prevalence of underlying comorbidities. The differential age-specific vulnerability to gaseous pollutants across studies—including findings from Chengdu[34] and Shenyang[41]—likely reflects differences in exposure assessment methodologies, population activity patterns, and pollutant source characteristics.

4.6 Seasonal Variation

Statistically significant associations between air pollutants and IS admissions were predominantly observed during the cold season, consistent with studies in Shenzhen[7], Yancheng[23], Changzhou[42], and Chongqing[28]. Several factors

may explain this pattern in Lanzhou. The city's river valley topography inherently limits atmospheric pollutant dispersion, and cold-season subsidence air currents further suppress vertical mixing. Additionally, extensive fossil fuel combustion for residential heating leads to substantially elevated pollutant concentrations. Cold temperatures themselves may exacerbate physiological vulnerability by inducing vasoconstriction, altering fibrinogen levels and plasma viscosity, and increasing cholesterol and triglyceride concentrations[43]. The compounded effects of higher pollutant concentrations and increased physiological susceptibility underscore the need for enhanced protective measures during the cold season.

4.7 Exposure-Response Relationships

The approximately linear exposure-response relationships without apparent thresholds observed for PM_{2.5}, PM₁₀, and CO are consistent with findings from Yancheng[23], Wuhan[21], and Chongqing. These results suggest that no safe concentration level exists below which these pollutants pose no cerebrovascular risk, underscoring the importance of continuous air quality improvement. The negative concentration-response relationship observed for O₃8h differs from findings in other cities, potentially reflecting regional differences in O₃ concentration levels and seasonal confounding as discussed above.

5. Conclusions

In conclusion, this study demonstrated that PM_{2.5}, PM₁₀, SO₂, and CO were significantly and positively associated with IS hospital admissions in Lanzhou, with the effects being more pronounced during the cold season. Females appeared to be more susceptible to the adverse effects of PM_{2.5}, PM₁₀, SO₂, and CO. Regarding age-specific vulnerability, patients aged ≥ 75 years were more vulnerable to PM_{2.5} and PM₁₀, while those aged < 65 years were more vulnerable to SO₂, NO₂, and CO. The exposure-response curves for PM_{2.5}, PM₁₀, and CO at lag07 exhibited approximately linear relationships without apparent thresholds, suggesting that no safe concentration level exists for these pollutants with respect to IS risk. Based on these findings, we

recommend that local authorities implement targeted measures to improve air quality, strengthen health protection advisories for susceptible populations—particularly females, the elderly, and residents during the cold season—and establish early warning systems to mitigate the cerebrovascular health risks associated with air pollution exposure.

Acknowledgments

The authors would like to express sincere gratitude to Jiyuan Dong for invaluable guidance on research methodology, to Jinwen Yao for generously providing access to the medical record data, and to Yongcong Chen and Yongmei He for their dedicated assistance with manuscript preparation and proofreading.

Author Contributions Statement

Sixuan Chen: Acquisition, analysis, or interpretation of data for the work, Writing-Original draft preparation, Methodology, Software, Revised the manuscript .

Yongmei He: Data curation, proofreading article.

Yongcong Chen: Writing assistance and proofreading the article

Funding declaration

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics, Consent to Participate, and Consent to Publish declarations

Ethics approval and consent to participate:

This study was approved by the Ethics Committee of the School of Public Health, Lanzhou University (approval number: IRB21122501). The requirement for informed consent was waived because anonymized individual-level data were used.

Consent for publication: Not applicable.

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