

Particulate Matter and Hospital Admissions for Stroke in Beijing, China: Modification Effects by Ambient Temperature

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Background—The impact of particulate matter (PM) on stroke may vary by particle size, stroke subtype, and patient characteristics and temperature. We examined the association of stroke admissions with PM in different subgroups in Beijing, China, during 2013–2014.

Methods and Results—A time-stratified case-crossover design was used to assess the relation between PM of different particle sizes and hospital admissions for ischemic and hemorrhagic stroke. Stratified analyses were performed by age, sex, and temperature. In total, there were 147 624 stroke admissions during the study period. In the whole-period analysis, both PM_{2.5} and PM₁₀ were positively associated with ischemic stroke admissions on the day of hospital admission and negatively associated with ischemic stroke at lag2 and lag3 day. In warm days (>13.5°C), the odds ratios of ischemic stroke admissions were 2.071 (95% CI 1.959–2.190), 1.470 (95% CI 1.391–1.554), and 1.590 (95% CI 1.493–1.694) per IQR increase in the same-day PM_{2.5} (82.0 µg/m³), PM_{2.5–10} (36.6 µg/m³), and PM₁₀ (93.5 µg/m³), respectively. For hemorrhagic stroke, the corresponding values were 1.941 (95% CI 1.658–2.273), 1.590 (95% CI 1.366–1.851), and 1.527 (95% CI 1.278–1.826). The positive associations were also observed in the other lag structures and were higher than in cold days (≤13.5°C).

Conclusions—This study suggests that the associations of PM_{2.5}, PM_{2.5–10}, and PM₁₀ with stroke admissions differed across levels of temperature. Short-term exposure to PM_{2.5}, PM_{2.5–10}, and PM₁₀ was positively associated with hospital admissions for ischemic and hemorrhagic stroke on warm days (>13.5°C). (*J Am Heart Assoc.* 2016;5:e003437 doi: 10.1161/JAHA.116.003437)

Key Words: air pollution • hospital admission • particulate matter • stroke

There is increasing evidence for an association of short-term exposure to particulate matter (PM) with elevated risk of cardiovascular disease, including stroke.^{1–3} Stroke is listed as the second leading cause of death in the Global Burden of Disease 2010, and the incidence of stroke is

increasing, particularly in low- and middle-income countries, which account for two-thirds of all strokes.^{4,5} To enhance primary prevention efforts, the relationship of PM with stroke requires further investigation given the high stroke burden in terms of mortality and disability worldwide.

Previous reports examining the effect of PM on stroke have shown inconsistent results.^{1,6–8} Moreover, toxicological studies suggest that fine particles may be more harmful to the circulation system than coarse particles.⁹ Indeed, coarse particles are mostly deposited in the upper respiratory tract, whereas fine particles can be inhaled deep into the lung and translocated via the circulation to other organs.^{10,11} However, only limited epidemiological studies have examined the relationship between stroke and PM of different particle sizes.^{1,12,13}

Regarding the various subtypes of stroke, most prior reports have focused on cerebrovascular disease or ischemic stroke, while a few studies have examined ischemic and hemorrhagic stroke separately but reported inconsistent results.^{12,14,15} Further, some studies reported that the risk of stroke associated with air pollution differed by ambient temperature or season, although there are contrasting findings.^{16–19} Additional studies are therefore required to

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Table 1. Summary Statistics of Stroke Admissions in Beijing, China, 2013–2014

Variable	No.
Disease	147 624 (100.0%)
Stroke subtype	
Ischemic stroke	130 744 (88.6%)
Hemorrhagic stroke	16 880 (11.4%)
Sex	
Men	90 502 (61.3%)
Women	57 122 (38.7%)
Age, mean y (SD)	68.2 (12.8)
>65	85 800 (58.1%)
≤65	61 824 (41.9%)

improve our understanding of the biological mechanism of the association and develop specific interventions for specific groups and days.

The aims of this study were to examine the association of PM with stroke admissions in Beijing, China, during 2013–2014 and to determine whether the association differed across particle size, stroke subtype, patient characteristics, and ambient temperature, by using a time-stratified case-crossover design.

Methods

Data Collection

The air pollution data, including PM that is ≤ 2.5 μm in diameter ($\text{PM}_{2.5}$), PM that is ≤ 10 μm in diameter (PM_{10}), carbon monoxide (CO), and nitrogen dioxide (NO_2), were obtained from the Centre of City Environmental Protection Monitoring Website Platform (www.bjmemc.com.cn) from January 1, 2013, through December 31, 2014, in Beijing. There were 35 monitoring stations located in 16 districts of Beijing. PM in the size range of >2.5 to ≤ 10 μm in diameter ($\text{PM}_{2.5-10}$) was not measured directly. We estimated $\text{PM}_{2.5-10}$ concentrations by subtracting $\text{PM}_{2.5}$ from PM_{10} at collocated monitoring stations.²⁰ The daily mean concentration of air pollutants for each district was calculated by averaging the concentrations of all stations in that district. Meteorological data, including daily mean temperature ($^{\circ}\text{C}$) and relative humidity (%) in the 16 districts, were obtained from the Chinese Meteorological Bureau over the same period.

Daily data for stroke admissions from January 1, 2013, through December 31, 2014, were obtained from the medical record database for cardiovascular and cerebrovascular disease in Beijing. The database contained 63 hospitals, with the capability to diagnose and treat cardiovascular and cerebrovascular disease in Beijing.

Table 2. Summary Statistics of Air Pollutants and Meteorological Variables in Beijing, China, 2013–2014

Variables	Mean	SD	Min	P25	Med	IQR	P75	Max
Air pollutants								
All days								
$\text{PM}_{2.5}$, $\mu\text{g}/\text{m}^3$	89.8	73.2	4.0	37.0	71.4	82.0	119.0	685.5
$\text{PM}_{2.5-10}$, $\mu\text{g}/\text{m}^3$	42.1	37.6	0.0	18.4	34.1	36.6	55.0	447.0
PM_{10} , $\mu\text{g}/\text{m}^3$	122.5	86.1	5.4	62.7	105.4	93.5	156.2	677.0
CO, mg/m^3	1.7	1.2	0.0	1.0	1.3	1.0	2.0	11.5
NO_2 , $\mu\text{g}/\text{m}^3$	52.5	28.1	1.0	31.7	48.3	36.3	68.0	196.8
Warm days ($>13.5^{\circ}\text{C}$)								
$\text{PM}_{2.5}$, $\mu\text{g}/\text{m}^3$	81.8	56.9	4.0	38.7	69.0	40.0	109.0	372.9
$\text{PM}_{2.5-10}$, $\mu\text{g}/\text{m}^3$	46.9	36.7	0.0	24.5	41.0	20.0	61.0	405.5
PM_{10} , $\mu\text{g}/\text{m}^3$	111.9	65.1	5.4	65.0	105.0	40.3	145.3	506.0
Cold days ($\leq 13.5^{\circ}\text{C}$)								
$\text{PM}_{2.5}$, $\mu\text{g}/\text{m}^3$	98.5	85.9	4.3	35.1	75.3	55.4	130.7	685.5
$\text{PM}_{2.5-10}$, $\mu\text{g}/\text{m}^3$	38.2	37.9	0.0	15.1	28.5	20.5	49.0	447.0
PM_{10} , $\mu\text{g}/\text{m}^3$	131.4	98.9	6.0	60.5	106.0	64.6	170.6	677.0
Meteorological variables								
Temperature, $^{\circ}\text{C}$	11.9	11.2	-13.3	1.5	13.5	20.7	22.2	31.1
Relative humidity (%)	56.1	17.5	12.8	42.8	56.5	27.2	70.0	96.0

CO indicates carbon monoxide; Max, maximum value; Med, median; Min, minimum value; NO_2 , nitrogen dioxide; P25, 25th percentile; P75, 75th percentile; PM_{10} , particulate matter that is ≤ 10 μm in diameter; $\text{PM}_{2.5}$, particulate matter that is ≤ 2.5 μm in diameter; $\text{PM}_{2.5-10}$, particulate matter in the size range of >2.5 to ≤ 10 μm in diameter.

Table 3. Spearman Correlation Coefficients Among the Exposure Variables

Variables	PM _{2.5}	PM _{2.5-10}	PM ₁₀	CO	NO ₂	T	RH
PM _{2.5}	1.00	0.18*	0.81*	0.68*	0.61*	-0.05*	0.40*
PM _{2.5-10}	—	1.00	0.56*	0.04*	0.25*	0.23*	-0.04*
PM ₁₀	—	—	1.00	0.60*	0.63*	-0.03†	0.24*
CO	—	—	—	1.00	0.60*	-0.23*	0.13*
NO ₂	—	—	—	—	1.00	-0.42*	0.18*
T	—	—	—	—	—	1.00	0.36*
RH	—	—	—	—	—	—	1.00

CO indicates carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter that is ≤10 μm in diameter; PM_{2.5}, particulate matter that is ≤2.5 μm in diameter; PM_{2.5-10}, particulate matter in the size range of >2.5 to ≤10 μm in diameter; RH, relative humidity; T, temperature.

*P<0.001.

†P<0.05.

The medical record database included the information of age, sex, date of hospital admission, and address of residence. The diagnosis of disease was coded using the *International Classification of Diseases, 10th Revision* (ICD-10). Hospital admissions because of ischemic stroke (ICD-10: I63) and hemorrhagic stroke (ICD-10: I61–62) were extracted based on the discharge diagnosis. We calculated daily count of hospital admissions for each district.

The protocol of this study was approved by the School of Public Health, Capital Medical University Institutional Review Board (IRB00009511). Informed consent was not required because we used aggregated data. The patient information was anonymized and deidentified prior to analysis.

Statistical Analysis

A time-stratified case-crossover design was used to examine the association of short-term exposure to PM (PM_{2.5}, PM_{2.5-10}, and PM₁₀) with hospital admissions for ischemic and hemorrhagic stroke. The case period was defined as the day of hospital admission. Control periods were defined as the same days of the week in the same month of the same year in the same district as the case period. Three or 4 control periods for each case period were chosen. This design allowed for controlling of the effects of day of week, season, and slowly varying confounders.

Conditional logistic regression was used to perform the time-stratified case-crossover design. The statistical model was adjusted by temperature and relative humidity, given that these meteorological variables are reported to be associated with the risk of stroke.²¹ We used natural cubic splines with 3 df to model the nonlinear effects of temperature and relative humidity on the concurrent day of hospital admission.¹⁵ Because prior research has found that fewer strokes occur on holidays,²² we controlled for public holidays using binary

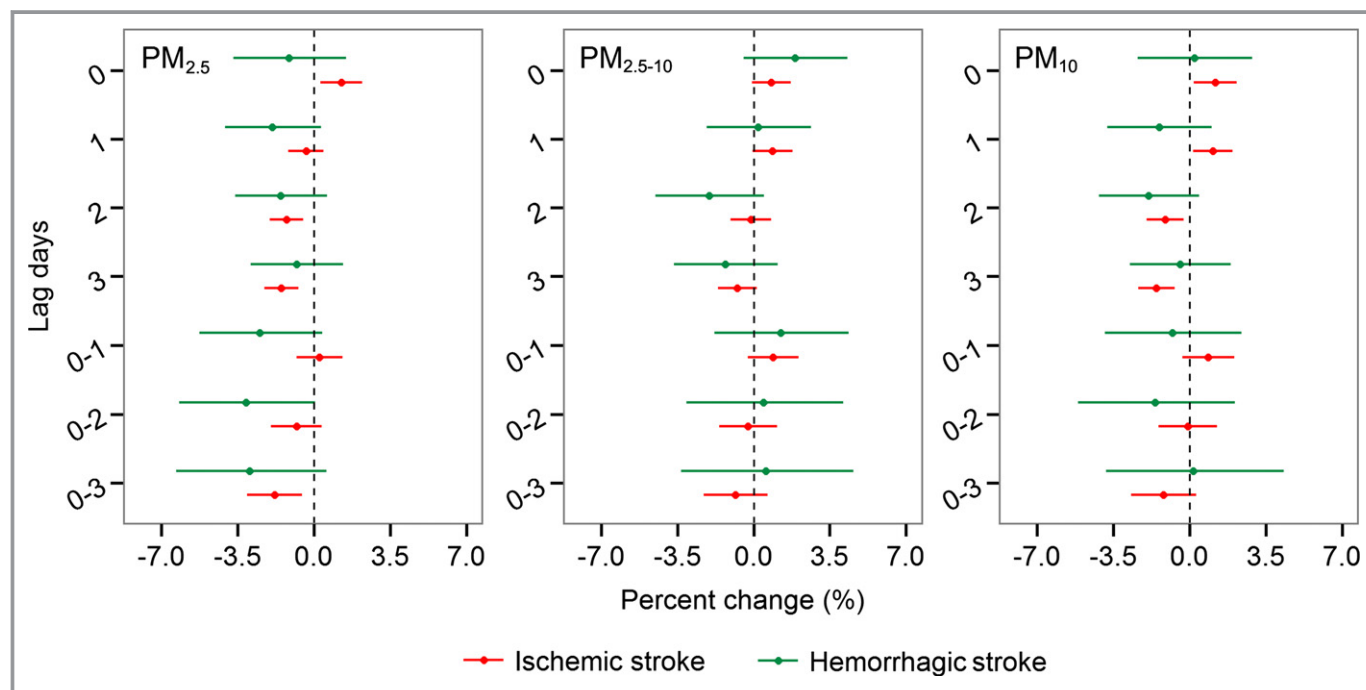


Figure. Percentage change (95% CI) in hospital admissions for ischemic stroke and hemorrhagic stroke associated with a 1-IQR increase in PM_{2.5} (82.0 μg/m³), PM_{2.5-10} (36.6 μg/m³), and PM₁₀ (93.5 μg/m³) in Beijing, China, 2013–2014. PM_{2.5}, particulate matter that is ≤2.5 μm in diameter; PM_{2.5-10}, particulate matter in the size range of >2.5 to ≤10 μm in diameter; PM₁₀, particulate matter that is ≤10 μm in diameter.

Table 4. Percentage Change (95% CI) in Ischemic Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 μg/m³), PM_{2.5-10} (36.6 μg/m³), and PM₁₀ (93.5 μg/m³) Stratified by Age and Sex in Beijing, China, 2013–2014

Variables	Age				Sex			
	Age >65 y	Age ≤65 y	Z Value*	P Value*	Men	Women	Z Value*	P Value*
PM_{2.5}								
Lag0	1.37 (0.12 to 2.63)	1.11 (−0.40 to 2.64)	0.26	0.795	1.23 (0.00 to 2.48)	1.30 (−0.24 to 2.86)	−0.07	0.945
Lag1	0.25 (−0.81 to 1.31)	−1.26 (−2.54 to 0.03)	1.78	0.076	−0.11 (−1.15 to 0.95)	−0.77 (−2.07 to 0.55)	0.77	0.439
Lag2	−1.19 (−2.19 to −0.18)	−1.36 (−2.57 to −0.14)	0.22	0.828	−1.49 (−2.48 to −0.50)	−0.90 (−2.13 to 0.35)	−0.74	0.460
Lag3	−1.41 (−2.41 to −0.40)	−1.61 (−2.82 to −0.39)	0.25	0.801	−1.46 (−2.45 to −0.46)	−1.53 (−2.77 to −0.28)	0.09	0.929
Lag0–1	0.84 (−0.53 to 2.23)	−0.6 (−2.25 to 1.08)	1.30	0.193	0.40 (−0.95 to 1.77)	0.03 (−1.66 to 1.74)	0.34	0.737
Lag0–2	−0.39 (−1.89 to 1.13)	−1.39 (−3.2 to 0.45)	0.83	0.407	−0.77 (−2.24 to 0.73)	−0.85 (−2.70 to 1.02)	0.07	0.941
Lag0–3	−1.57 (−3.2 to 0.09)	−2.14 (−4.11 to −0.14)	0.44	0.663	−1.76 (−3.36 to −0.12)	−1.89 (−3.90 to 0.16)	0.10	0.918
PM_{2.5-10}								
Lag0	1.04 (−0.10 to 2.19)	0.48 (−0.93 to 1.91)	0.60	0.546	0.93 (−0.19 to 2.07)	0.64 (−0.80 to 2.09)	0.32	0.750
Lag1	0.94 (−0.23 to 2.12)	0.74 (−0.71 to 2.21)	0.21	0.835	1.28 (0.11 to 2.46)	0.21 (−1.25 to 1.68)	1.11	0.265
Lag2	−0.61 (−1.78 to 0.58)	0.59 (−0.88 to 2.08)	−1.24	0.214	−0.20 (−1.37 to 0.99)	−0.02 (−1.50 to 1.48)	−0.18	0.856
Lag3	−1.04 (−2.15 to 0.09)	−0.27 (−1.70 to 1.17)	−0.82	0.412	−0.48 (−1.61 to 0.66)	−1.14 (−2.53 to 0.27)	0.71	0.477
Lag0–1	0.94 (−0.55 to 2.45)	0.83 (−1.03 to 2.72)	0.09	0.927	1.29 (−0.20 to 2.80)	0.27 (−1.59 to 2.17)	0.83	0.408
Lag0–2	−0.39 (−2.07 to 1.32)	−0.02 (−2.13 to 2.14)	−0.27	0.789	0.21 (−1.49 to 1.93)	−0.95 (−3.04 to 1.19)	0.83	0.404
Lag0–3	−1.22 (−3.07 to 0.66)	−0.19 (−2.54 to 2.23)	−0.67	0.500	−0.39 (−2.26 to 1.52)	−1.50 (−3.80 to 0.85)	0.73	0.466
PM₁₀								
Lag0	1.25 (−0.02 to 2.53)	1.08 (−0.46 to 2.64)	0.17	0.866	1.46 (0.20 to 2.73)	0.73 (−0.83 to 2.32)	0.70	0.483
Lag1	1.55 (0.39 to 2.72)	0.35 (−1.06 to 1.77)	1.28	0.201	1.44 (0.29 to 2.60)	0.47 (−0.96 to 1.92)	1.04	0.301
Lag2	−1.07 (−2.16 to 0.03)	−1.19 (−2.52 to 0.15)	0.13	0.894	−1.15 (−2.23 to −0.06)	−1.07 (−2.42 to 0.30)	−0.09	0.927
Lag3	−1.64 (−2.73 to −0.54)	−1.36 (−2.69 to −0.01)	−0.32	0.751	−1.53 (−2.60 to −0.44)	−1.52 (−3.05 to 0.04)	−0.01	0.988
Lag0–1	1.38 (−0.15 to 2.93)	0.06 (−1.79 to 1.95)	1.06	0.288	1.43 (−0.09 to 2.96)	−0.07 (−1.94 to 1.84)	1.20	0.230
Lag0–2	0.50 (−1.23 to 2.27)	−0.97 (−3.08 to 1.17)	1.05	0.294	0.60 (−1.12 to 2.36)	−1.20 (−3.32 to 0.98)	1.27	0.203
Lag0–3	−0.78 (−2.69 to 1.16)	−1.81 (−4.12 to 0.56)	0.66	0.507	−0.63 (−2.52 to 1.30)	−2.11 (−4.45 to 0.28)	0.96	0.339

PM₁₀ indicates particulate matter that is ≤10 μm in diameter; PM_{2.5}, particulate matter that is ≤2.5 μm in diameter; PM_{2.5-10}, particulate matter in the size range of >2.5 to ≤10 μm in diameter.

*Z test was used to test the statistical significance of the subgroup difference and the P value was the interaction P value.

variable (coded as public holiday = 1 and no public holiday = 0) in the model.

We fitted the models with different lag structures from the current day (lag0) up to 3 lag days (lag3), and we used 2-day, 3-day, and 4-day moving averages of current day and previous 1, 2, and 3 days PM concentrations (lag0–1, lag0–2, and lag0–3, respectively) for our main analyses.

Stratified analyses were conducted to examine whether the association differed by age (>65 years and ≤65 years), sex (men and women), and temperature (greater than median and median or less). In both warm (greater median) and cold days (median or less), temperature in linear form and the interaction of temperature and PM in product form were adjusted in the model. We tested the statistical significance of subgroup differences through Z test.²³

Sensitivity analyses and multipollutant models were performed to check the robustness of the results. Degrees of freedom were changed for meteorological variables. We also used temperature and relative humidity lagged by up to 2 weeks to control the potentially lagged effects of meteorological variables. The 1-, 2-, and 3-pollutant models adjusting CO and NO₂ were fitted.

The association between PM and stroke admissions was assessed by adjusted odds ratio (OR) and 95% CI per IQR increase in PM concentration. The results were also expressed by percentage change in stroke admissions per IQR increase in PM concentration. We used the Akaike information criterion to determine the goodness of the model fit. The conditional logistic regression was performed by using the PHREG procedure in SAS statistical software

Table 5. Percentage Change (95% CI) in Hemorrhagic Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 μg/m³), PM_{2.5-10} (36.6 μg/m³), and PM₁₀ (93.5 μg/m³) Stratified by Age and Sex in Beijing, China, 2013–2014

Variables	Age				Sex			
	Age >65 y	Age ≤65 ys	Z Value*	P Value*	Men	Women	Z Value*	P Value*
PM_{2.5}								
Lag0	-1.63 (-5.52 to 2.42)	-0.74 (-4.07 to 2.71)	-0.33	0.738	-0.80 (-4.07 to 2.57)	-1.68 (-5.68 to 2.49)	0.33	0.744
Lag1	-3.33 (-6.66 to 0.13)	-0.92 (-3.79 to 2.03)	-1.05	0.292	-1.94 (-4.74 to 0.94)	-1.83 (-5.29 to 1.76)	-0.05	0.960
Lag2	-2.37 (-5.57 to 0.95)	-0.95 (-3.69, 1.87)	-0.65	0.517	-1.04 (-3.70 to 1.70)	-2.32 (-5.67 to 1.14)	0.58	0.563
Lag3	-2.32 (-5.52 to 0.98)	0.29 (-2.46 to 3.11)	-1.19	0.233	-0.67 (-3.33 to 2.06)	-1.03 (-4.38 to 2.43)	0.16	0.871
Lag0-1	-4.42 (-8.62 to -0.02)	-1.05 (-4.73 to 2.77)	-1.15	0.249	-2.06 (-5.63 to 1.64)	-3.11 (-7.49 to 1.48)	0.36	0.722
Lag0-2	-6.29 (-10.89 to -1.47)	-2.19 (-6.22 to 2.02)	-1.28	0.199	-3.45 (-7.36 to 0.63)	-4.64 (-9.44 to 0.41)	0.37	0.712
Lag0-3	-6.21 (-11.27 to -0.85)	-1.98 (-6.41 to 2.67)	-1.20	0.231	-3.83 (-8.10 to 0.64)	-3.62 (-8.97 to 2.04)	-0.06	0.953
PM_{2.5-10}								
Lag0	1.82 (-1.70 to 5.47)	2.01 (-1.13 to 5.25)	-0.08	0.939	1.82 (-1.21 to 4.94)	2.00 (-1.70 to 5.84)	-0.07	0.943
Lag1	-1.28 (-4.84 to 2.42)	1.33 (-1.81 to 4.56)	-1.06	0.291	0.57 (-2.48 to 3.71)	-0.33 (-4.03 to 3.50)	0.36	0.718
Lag2	-2.23 (-5.86 to 1.54)	-1.83 (-5.13 to 1.58)	-0.16	0.875	-1.15 (-4.29 to 2.09)	-3.44 (-7.33 to 0.61)	0.88	0.380
Lag3	-0.51 (-3.99 to 3.10)	-1.94 (-5.08 to 1.30)	0.59	0.556	0.09 (-2.88 to 3.15)	-3.70 (-7.48 to 0.23)	1.51	0.131
Lag0-1	-0.59 (-5.08 to 4.12)	2.71 (-1.35 to 6.95)	-1.04	0.297	2.21 (-1.71 to 6.29)	-0.22 (-4.92 to 4.71)	0.76	0.447
Lag0-2	-1.41 (-6.60 to 4.07)	2.03 (-2.73 to 7.02)	-0.93	0.352	1.22 (-3.32 to 5.97)	-0.79 (-6.30 to 5.05)	0.54	0.592
Lag0-3	0.32 (-5.42 to 6.42)	0.84 (-4.34 to 6.30)	-0.13	0.899	1.92 (-3.09 to 7.19)	-1.74 (-7.73 to 4.63)	0.89	0.373
PM₁₀								
Lag0	-0.29 (-4.23 to 3.80)	0.65 (-2.77 to 4.20)	-0.35	0.728	1.04 (-2.32 to 4.52)	-1.11 (-5.15 to 3.09)	0.79	0.430
Lag1	-2.36 (-5.95 to 1.37)	-0.80 (-3.89 to 2.39)	-0.63	0.526	-1.09 (-4.14 to 2.04)	-1.85 (-5.53 to 1.97)	0.31	0.760
Lag2	-1.63 (-5.12 to 1.98)	-2.12 (-5.10 to 0.96)	0.20	0.839	-0.94 (-3.86 to 2.08)	-3.44 (-7.01 to 0.27)	1.04	0.298
Lag3	-1.03 (-4.51 to 2.56)	-0.08 (-3.08 to 3.02)	-0.40	0.687	0.64 (-2.28 to 3.65)	-2.28 (-5.88 to 1.47)	1.21	0.227
Lag0-1	-2.56 (-7.20 to 2.30)	0.53 (-3.56 to 4.79)	-0.96	0.339	0.25 (-3.76 to 4.42)	-2.34 (-7.10 to 2.66)	0.79	0.427
Lag0-2	-3.45 (-8.75 to 2.16)	-0.22 (-4.89 to 4.67)	-0.87	0.384	0.03 (-4.58 to 4.86)	-3.99 (-9.38 to 1.71)	1.08	0.280
Lag0-3	-1.93 (-7.93 to 4.47)	1.57 (-3.70 to 7.13)	-0.83	0.406	2.59 (-2.65 to 8.12)	-3.54 (-9.58 to 2.91)	1.45	0.147

PM₁₀ indicates particulate matter that is ≤10 μm in diameter; PM_{2.5}, particulate matter that is ≤2.5 μm in diameter; PM_{2.5-10}, particulate matter in the size range of >2.5 to ≤10 μm in diameter;

*Z test was used to test the statistical significance of the subgroup difference and the P value was the interaction P value.

(version 9.2; SAS Institute, Inc), and the TIES=BRESLOW option was used to account for the grouped data. Spearman correlation coefficients were calculated to examine the associations among exposure variables. All statistical tests were 2-sided, and P<0.05 values were considered statistically significant.

Results

There were 147 624 stroke admissions in 2013–2014 that formed the basis for this study (130 744 for ischemic stroke and 16 880 for hemorrhagic stroke) (Table 1). There were 61.3% male patients, and 58.1% patients were >65 years old. The mean (SD) age of the stroke patients was 68.2 (12.8) years.

The descriptive statistics of air pollutants and meteorological variables are shown in Table 2. The means (SD) of air pollutants were 89.8 (73.2) μg/m³ for PM_{2.5}, 42.1 (37.6) μg/m³ for PM_{2.5-10}, 122.5 (86.1) μg/m³ for PM₁₀, 1.7 (1.2) mg/m³ for CO, and 52.5 (28.1) μg/m³ for NO₂. The means (SD) of temperature and relative humidity were 11.9°C (11.2°C) and 56.1% (17.5%), respectively. In warm days (>13.5°C), the means (SD) of PM_{2.5}, PM_{2.5-10}, and PM₁₀ were 81.8 (56.9), 46.9 (36.7), and 111.9 (65.1) μg/m³, respectively. In cold days (≤13.5°C), the corresponding values were 98.5 (85.9), 38.2 (37.9), and 131.4 (98.9) μg/m³.

Spearman correlation coefficients for correlation among the exposure variables are presented in Table 3. PM₁₀ was highly correlated with PM_{2.5} (correlation coefficient, r=0.81, P<0.001) and moderately correlated with PM_{2.5-10} (r=0.56, P<0.001).

Table 6. OR (95% CI) of Ischemic Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 μg/m³), PM_{2.5–10} (36.6 μg/m³), and PM₁₀ (93.5 μg/m³) Stratified by Temperature in Beijing, China, 2013–2014

Variables	Temperature >13.5°C		Temperature ≤13.5°C		Z Test*	
	OR	95% CI	OR	95% CI	Z Value	P Value
PM_{2.5}						
Lag0	2.071	1.959–2.190 [†]	1.006	0.993–1.018	24.72	<0.001
Lag1	1.839	1.738–1.946 [†]	1.015	1.005–1.025 [‡]	20.24	<0.001
Lag2	1.271	1.204–1.340 [†]	0.988	0.978–0.997 [‡]	9.10	<0.001
Lag3	0.970	0.923–1.020	0.968	0.959–0.977 [†]	0.09	0.928
Lag0–1	2.415	2.261–2.578 [†]	1.009	0.995–1.023	25.49	<0.001
Lag0–2	2.507	2.323–2.707 [†]	1.002	0.987–1.017	23.07	<0.001
Lag0–3	2.118	1.948–2.302 [†]	0.982	0.966–0.998 [‡]	17.67	<0.001
PM_{2.5–10}						
Lag0	1.470	1.391–1.554 [†]	1.054	1.041–1.067 [†]	11.48	<0.001
Lag1	1.093	1.042–1.147 [†]	1.042	1.029–1.055 [†]	1.90	0.058
Lag2	1.099	1.039–1.162 [†]	1.037	1.024–1.050 [†]	1.99	0.047
Lag3	1.071	1.011–1.135 [‡]	1.007	0.995–1.019	2.07	0.038
Lag0–1	1.387	1.298–1.482 [†]	1.050	1.034–1.066 [†]	8.03	<0.001
Lag0–2	1.264	1.177–1.357 [†]	1.056	1.037–1.075 [†]	4.81	<0.001
Lag0–3	1.261	1.162–1.369 [†]	1.034	1.014–1.054 [†]	4.63	<0.001
PM₁₀						
Lag0	1.590	1.493–1.694 [†]	1.055	1.042–1.067 [†]	12.50	<0.001
Lag1	1.354	1.274–1.439 [†]	1.051	1.040–1.062 [†]	8.03	<0.001
Lag2	1.259	1.176–1.346 [†]	1.009	0.999–1.019	6.35	<0.001
Lag3	1.050	0.985–1.121	0.969	0.960–0.979 [†]	2.40	0.016
Lag0–1	1.679	1.555–1.812 [†]	1.066	1.051–1.081 [†]	11.49	<0.001
Lag0–2	1.848	1.685–2.028 [†]	1.054	1.037–1.070 [†]	11.74	<0.001
Lag0–3	1.857	1.660–2.077 [†]	1.010	0.993–1.028	10.51	<0.001

OR indicates odds ratio; PM₁₀, particulate matter that is ≤10 μm in diameter; PM_{2.5}, particulate matter that is ≤2.5 μm in diameter; PM_{2.5–10}, particulate matter in the size range of >2.5 to ≤10 μm in diameter.

*Z test was used to test the statistical significance of the subgroup difference and the P value was the interaction P value.

[†]P<0.001.

[‡]P<0.05.

Correlations of PM_{2.5–10} with PM_{2.5}, CO, and NO₂ were low (r=0.04–0.25, P<0.001). Moderate correlations (r=0.60–0.68, P<0.001) were observed for PM_{2.5} and PM₁₀ with CO and NO₂.

In the whole-period analyses, an IQR increase in the same-day concentration of PM_{2.5} (82.0 μg/m³) and PM₁₀ (93.5 μg/m³) corresponded to a 1.26% (95% CI 0.30–2.23%) and 1.18% (95% CI 0.19–2.17%) increase in ischemic stroke admissions, respectively (Figure). PM₁₀ was also positively associated with ischemic stroke on the previous day of hospital admission (1.06%, 95% CI 0.17–1.97). Meanwhile, both PM_{2.5} and PM₁₀ were negatively associated with ischemic stroke admissions at lag2 (–1.26%, 95% CI –2.03% to –0.49%, and –1.12%, 95% CI –1.96% to –0.27%,

respectively) and lag3 (–1.49%, 95% CI –2.26% to –0.71% and –1.53%, 95% CI –2.37% to –0.68%) day. For hemorrhagic stroke, no statistically significant associations were found in any lag structures.

Stratified analyses showed that the associations with PM were not different between patients >65 years and ≤65 years old or between male and female patients, for both ischemic and hemorrhagic stroke (Tables 4 and 5).

ORs for the associations with ischemic and hemorrhagic stroke admissions per IQR increase in PM concentration in different temperature levels are shown in Tables 6 and 7. For both ischemic and hemorrhagic stroke, the associations with PM_{2.5}, PM_{2.5–10} and PM₁₀ were higher on warm days (>13.5°C) than on cold days (≤13.5°C) in all lag structures.

Table 7. OR (95% CI) of Hemorrhagic Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 µg/m³), PM_{2.5–10} (36.6 µg/m³), and PM₁₀ (93.5 µg/m³) Stratified by Temperature in Beijing, China, 2013–2014

Variables	Temperature >13.5°C		Temperature ≤13.5°C		Z Test*	
	OR	95% CI	OR	95% CI	Z Value	P Value
PM_{2.5}						
Lag0	1.941	1.658–2.273 [†]	0.986	0.954–1.018	8.24	<0.001
Lag1	1.839	1.566–2.159 [†]	1.001	0.975–1.029	7.32	<0.001
Lag2	1.315	1.129–1.532 [†]	0.981	0.957–1.006	3.71	<0.001
Lag3	1.029	0.897–1.182	0.977	0.953–1.002	0.73	0.466
Lag0–1	2.310	1.917–2.783 [†]	0.987	0.953–1.023	8.78	<0.001
Lag0–2	2.511	2.018–3.125 [†]	0.972	0.934–1.011	8.37	<0.001
Lag0–3	2.323	1.828–2.952 [†]	0.970	0.929–1.014	7.03	<0.001
PM_{2.5–10}						
Lag0	1.590	1.366–1.851 [†]	1.056	1.024–1.089 [†]	5.17	<0.001
Lag1	1.108	0.967–1.269	1.029	0.998–1.061	1.04	0.299
Lag2	1.102	0.942–1.289	1.009	0.976–1.044	1.07	0.283
Lag3	1.283	1.095–1.503 [‡]	0.998	0.968–1.030	3.04	0.002
Lag0–1	1.401	1.170–1.678 [†]	1.041	1.002–1.081 [‡]	3.17	0.002
Lag0–2	1.304	1.070–1.589 [‡]	1.047	1.000–1.097	2.11	0.035
Lag0–3	1.321	1.056–1.652 [‡]	1.030	0.980–1.083	2.12	0.034
PM₁₀						
Lag0	1.527	1.278–1.826 [†]	1.045	1.013–1.079 [‡]	4.10	<0.001
Lag1	1.293	1.086–1.540 [‡]	1.021	0.993–1.050	2.62	0.009
Lag2	1.250	1.032–1.516 [‡]	0.989	0.962–1.016	2.37	0.018
Lag3	1.169	0.982–1.391	0.981	0.955–1.007	1.96	0.051
Lag0–1	1.558	1.252–1.937 [†]	1.039	1.003–1.078 [‡]	3.59	<0.001
Lag0–2	1.736	1.331–2.265 [†]	1.023	0.981–1.066	3.86	<0.001
Lag0–3	1.913	1.391–2.632 [†]	1.020	0.974–1.068	3.83	<0.001

OR indicates odds ratio; PM₁₀, particulate matter that is ≤10 µm in diameter; PM_{2.5}, particulate matter that is ≤2.5 µm in diameter; PM_{2.5–10}, particulate matter in the size range of >2.5 to ≤10 µm in diameter.

*Z test was used to test the statistical significance of the subgroup difference and the P value was the interaction P value.

[†]P<0.001.

[‡]P<0.05.

In warm days (>13.5°C), ORs of ischemic stroke admissions were 2.071 (95% CI 1.959–2.190), 1.470 (95% CI 1.391–1.554), and 1.590 (95% CI 1.493–1.694) per IQR increase in the same-day concentration of PM_{2.5} (82.0 µg/m³), PM_{2.5–10} (36.6 µg/m³), and PM₁₀ (93.5 µg/m³), respectively. For hemorrhagic stroke, the corresponding values were 1.941 (95% CI 1.658–2.273), 1.590 (95% CI 1.366–1.851), and 1.527 (95% CI 1.278–1.826), respectively. The positive and statistically significant associations were also observed at some lag days and all average lag days.

On cold days (≤13.5°C), ORs of ischemic stroke admissions were 1.054 (95% CI 1.041–1.067), 1.055 (95% CI 1.042–1.067), and 1.015 (95% CI 1.005–1.025) per IQR increase in the same-day PM_{2.5–10} (36.6 µg/m³) and PM₁₀

(93.5 µg/m³) and the previous day PM_{2.5} (82.0 µg/m³). Meanwhile, negative associations were observed with PM_{2.5} at lag2, lag3, lag0–3 day, and with PM₁₀ at lag3 day. For hemorrhagic stroke, ORs were 1.056 (95% CI 1.024–1.089) and 1.045 (95% CI 1.013–1.079) for the same-day PM_{2.5–10} and PM₁₀, respectively. There were no statistically significant associations between hemorrhagic stroke admissions and PM_{2.5} in cold days (≤13.5°C).

Sensitivity analyses showed that changing the degrees of freedom and the lag days of temperature and relative humidity did not change the main findings (Table 8). Two- and 3-pollutant models showed that adjustment for other copollutants had no obvious impact on the associations of PM with stroke admissions (Table 9).

Table 8. Percentage Change (95% CI) in Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 µg/m³), PM_{2.5–10} (36.6 µg/m³), and PM₁₀ (93.5 µg/m³) in Sensitivity Analyses

Variables	Main Model	Sensitivity Analysis I*	Sensitivity Analysis II†
PM_{2.5}			
Lag0	0.98 (0.07 to 1.89)	0.96 (0.06 to 1.88)	0.74 (0.00 to 1.49)
Lag1	-0.53 (-1.30 to 0.24)	-0.55 (-1.32 to 0.22)	-0.23 (-0.97 to 0.51)
Lag2	-1.27 (-1.99 to -0.54)	-1.29 (-2.02 to -0.56)	-0.93 (-1.68 to -0.17)
Lag3	-1.39 (-2.11 to -0.65)	-1.45 (-2.18 to -0.72)	-1.19 (-1.95 to -0.41)
Lag0-1	-0.06 (-1.05 to 0.94)	-0.09 (-1.09 to 0.91)	0.20 (-0.67 to 1.07)
Lag0-2	-1.15 (-2.23 to -0.06)	-1.19 (-2.27 to -0.09)	-0.49 (-1.49 to 0.51)
Lag0-3	-2.00 (-3.18 to -0.81)	-2.08 (-3.27 to -0.88)	-1.18 (-2.30 to -0.04)
PM_{2.5–10}			
Lag0	0.95 (0.12 to 1.79)	0.92 (0.08 to 1.76)	1.26 (0.44 to 2.10)
Lag1	0.78 (-0.07 to 1.64)	0.76 (-0.10 to 1.61)	0.78 (-0.08 to 1.64)
Lag2	-0.37 (-1.23 to 0.50)	-0.39 (-1.26 to 0.48)	-0.32 (-1.20 to 0.56)
Lag3	-0.82 (-1.65 to 0.01)	-0.79 (-1.62 to 0.04)	-0.54 (-1.38 to 0.30)
Lag0-1	0.94 (-0.15 to 2.04)	0.89 (-0.20 to 1.99)	0.98 (-0.10 to 2.08)
Lag0-2	-0.16 (-1.40 to 1.10)	-0.34 (-1.58 to 0.92)	-0.15 (-1.39 to 1.11)
Lag0-3	-0.67 (-2.03 to 0.72)	-0.72 (-2.09 to 0.67)	-0.76 (-2.14 to 0.63)
PM₁₀			
Lag0	1.08 (0.16 to 2.00)	1.06 (0.13 to 1.99)	0.85 (0.04 to 1.67)
Lag1	0.78 (-0.06 to 1.63)	0.75 (-0.09 to 1.60)	0.65 (-0.15 to 1.47)
Lag2	-1.20 (-1.99 to -0.40)	-1.25 (-2.05 to -0.45)	-0.95 (-1.76 to -0.12)
Lag3	-1.39 (-2.18 to -0.59)	-1.46 (-2.25 to -0.66)	-1.11 (-1.94 to -0.28)
Lag0-1	0.67 (-0.43 to 1.79)	0.61 (-0.50 to 1.74)	0.45 (-0.53 to 1.44)
Lag0-2	-0.24 (-1.50 to 1.03)	-0.36 (-1.62 to 0.92)	-0.14 (-1.30 to 1.03)
Lag0-3	-1.01 (-2.40 to 0.40)	-1.20 (-2.59 to 0.22)	-0.76 (-2.09 to 0.60)

CI indicates confidence interval; PM₁₀, particulate matter that is ≤10 µm in diameter; PM_{2.5}, particulate matter that is ≤2.5 µm in diameter; PM_{2.5–10}, particulate matter in the size range of >2.5 to ≤10 µm in diameter.

*Changing the temperature and relative humidity degrees of freedom to 4 instead of 3.

†Adjusting temperature and relative humidity lagged by up to 2 weeks.

Discussion

This study found that PM_{2.5} and PM₁₀ were positively associated with ischemic stroke during the whole study period on the concurrent day or previous day of hospital admissions, generally consistent with prior studies.^{15,24–26} There are numerous toxicological and epidemiological studies that support our findings. For example, exposure to PM was suggested to adversely affect vascular endothelial function, increase systemic inflammation and platelet activation, and decrease antioxidant enzyme activity.^{27–31} These responses may increase blood clotting and thrombosis, impair vascular function and blood flow, and elevate blood pressure, which may ultimately cause stroke.^{32,33}

Other studies have also reported nonsignificant trends for delayed effects of PM_{2.5} and PM₁₀ on stroke.^{15,24–26,34} In the

present study, PM_{2.5} and PM₁₀ were negatively associated with ischemic stroke admissions at lag2 and lag3 days, which can be explained by a displacement of hospital admissions or a harvesting effect.^{35,36} However, the phenomenon was not observed on warm days (>13.5°C) when stratified by temperature, indicating that the association may still have public health importance, especially on warm days (>13.5°C).

There were no statistically significant associations of hemorrhagic stroke admissions with PM_{2.5}, PM_{2.5–10}, and PM₁₀ during the whole study period, consistent with most previous studies.^{14,15} In addition to the difference in the mechanisms between hemorrhagic and ischemic stroke, the fewer hospital admissions of hemorrhagic stroke, reflecting the lower incidence of this subtype, might result in wider CIs for the estimate.³⁷ Notably, when stratified by temperature,

Table 9. Percentage Change (95% CI) in Stroke Admissions for per-IQR Increase in Concentration of PM_{2.5} (82.0 µg/m³), PM_{2.5-10} (36.6 µg/m³), and PM₁₀ (93.5 µg/m³) in Different Pollutant Models

Variables	Adjust CO	Adjust NO ₂	Adjust CO and NO ₂
PM_{2.5}			
Lag0	1.37 (0.19 to 2.57)	0.47 (−0.72 to 1.67)	1.10 (−0.19 to 2.42)
Lag1	−0.88 (−1.71 to −0.04)	−0.81 (−1.62 to 0.00)	−0.88 (−1.72 to −0.05)
Lag2	−1.56 (−2.32 to −0.80)	−1.44 (−2.19 to −0.68)	−1.48 (−2.24 to −0.71)
Lag3	−1.46 (−2.21 to −0.71)	−1.38 (−2.13 to −0.63)	−1.41 (−2.17 to −0.66)
Lag0−1	−0.09 (−1.26 to 1.10)	−0.67 (−1.80 to 0.47)	−0.29 (−1.50 to 0.92)
Lag0−2	−1.28 (−2.48 to −0.06)	−1.59 (−2.75 to −0.42)	−1.33 (−2.54 to −0.11)
Lag0−3	−1.99 (−3.26 to −0.71)	−2.20 (−3.43 to −0.95)	−1.97 (−3.24 to −0.68)
PM_{2.5-10}			
Lag0	0.82 (−0.03 to 1.67)	0.60 (−0.25 to 1.45)	0.62 (−0.23 to 1.48)
Lag1	0.39 (−0.49 to 1.27)	0.36 (−0.51 to 1.23)	0.23 (−0.65 to 1.12)
Lag2	−0.63 (−1.50 to 0.26)	−0.55 (−1.42 to 0.33)	−0.72 (−1.59 to 0.17)
Lag3	−0.78 (−1.62 to 0.06)	−0.93 (−1.76 to −0.08)	−0.77 (−1.61 to 0.08)
Lag0−1	0.64 (−0.46 to 1.76)	0.49 (−0.62 to 1.60)	0.44 (−0.67 to 1.56)
Lag0−2	−0.56 (−1.81 to 0.70)	−0.67 (−1.92 to 0.60)	−0.76 (−2.02 to 0.51)
Lag0−3	−0.99 (−2.36 to 0.41)	−0.87 (−2.24 to 0.53)	−0.99 (−2.37 to 0.41)
PM₁₀			
Lag0	0.65 (−0.46 to 1.78)	−0.34 (−1.52 to 0.85)	−0.17 (−1.39 to 1.06)
Lag1	−0.04 (−0.93 to 0.85)	0.08 (−0.79 to 0.95)	−0.12 (−1.01 to 0.78)
Lag2	−1.32 (−2.14 to −0.51)	−1.27 (−2.07 to −0.46)	−1.28 (−2.10 to −0.46)
Lag3	−1.25 (−2.06 to −0.43)	−1.31 (−2.11 to −0.49)	−1.23 (−2.05 to −0.42)
Lag0−1	−0.50 (−1.78 to 0.80)	−0.72 (−2.00 to 0.56)	−0.91 (−2.23 to 0.42)
Lag0−2	−1.27 (−2.62 to 0.10)	−1.33 (−2.67 to 0.04)	−1.47 (−2.84 to −0.08)
Lag0−3	−1.65 (−3.09 to −0.18)	−1.57 (−3.00 to −0.11)	−1.68 (−3.13 to −0.20)

CO indicates carbon monoxide; NO₂, nitrogen dioxide; PM₁₀, particulate matter that is ≤10 µm in diameter; PM_{2.5}, particulate matter that is ≤2.5 µm in diameter; PM_{2.5-10}, particulate matter in the size range of >2.5 to ≤10 µm in diameter.

statistically significant and positive associations with PM_{2.5}, PM_{2.5-10}, and PM₁₀ were observed for both ischemic and hemorrhagic stroke on warm days (>13.5°C). Further studies are needed to explore whether the association truly varies with stroke subtype.

In the present study, the positive associations of PM_{2.5}, PM_{2.5-10}, and PM₁₀ with hospital admissions for both ischemic and hemorrhagic stroke were higher on warm days (>13.5°C) than on cold days (≤13.5°C), as reported in prior studies of stroke admissions and cause-specific mortality in Taipei,¹⁶ Tianjin, China,¹⁷ and Edmonton, Canada.¹⁸ Several explanations have been proposed to explain the higher associations on warm days. High temperature plays important roles in determining air pollution emission, transport, dilution, chemical transformation, and eventual deposition of the air pollutants.³⁸ In addition, Villeneuve et al reported that adults spent a greater portion of their time indoors during cold days

with very low temperatures,¹⁸ and that there will be more infiltration into homes as ventilation is different on warm days.

Our results indicate that PM_{2.5-10} was positively associated with hospital admissions for ischemic and hemorrhagic stroke when stratified by temperature, although there was no statistically significant association during the whole study period. Epidemiological studies have found positive associations of PM_{2.5-10} with hospital admissions and mortality for cardiovascular disease, rather than for cerebrovascular disease.^{1,39} However, increasing stroke mortality at higher PM_{2.5-10} concentrations was reported.^{12,13} Given the similarities in the pathophysiology of cardiovascular and cerebrovascular disease, it is plausible that PM_{2.5-10} is also an important and modifiable risk factor of stroke.

There are several strengths of this study. First, the medical record database for cardiovascular and

cerebrovascular disease contains all hospitals with the capability to diagnose and treat cardiovascular and cerebrovascular disease in Beijing. Thus, the results likely reflect the real effects of PM on the population in the study area. Second, district daily-level air pollutants and weather conditions were used in this study, which can provide better control of measurement error than use of data from 1 monitoring site. Third, whether the associations of stroke admissions with PM differed across particle size, stroke subtype, individual characteristics, and ambient temperature was examined. This is helpful to develop specific interventions for specific groups and specific days (eg, heatwave days with serious air pollution).

There are also several limitations of our study. First, the admission date may result in temporal misalignment between exposure and outcome, as the onset of stroke symptoms often began in the days before admission. Second, district-level concentration of PM rather than individual exposure was used as the exposure concentration. This exposure estimation method may lead to spatial misalignment and loss of precision. Third, the unknown sensitivity and specificity of administrative data to determine the occurrence of stroke were also important sources of bias in this study. These sources of bias can result in a marked bias toward the null and minimize the potential impact of PM on stroke incidence.

Conclusions

This study suggests that the associations of PM_{2.5}, PM_{2.5–10}, and PM₁₀ with stroke admissions differed across levels of temperature. Short-term exposure to PM_{2.5}, PM_{2.5–10}, and PM₁₀ was positively associated with hospital admissions for ischemic and hemorrhagic stroke on warm days (>13.5°C).

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Disclosures

None.

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