

Acute Effect of Ambient Air Pollution on Stroke Mortality in the China Air Pollution and Health Effects Study

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Background and Purpose—There have been no multicity studies on the acute effects of air pollution on stroke mortality in China. This study was undertaken to examine the associations between daily stroke mortality and outdoor air pollution (particulate matter <10 μm in aerodynamic diameter, sulfur dioxide, and nitrogen dioxide) in 8 Chinese cities.

Methods—We used Poisson regression models with natural spline-smoothing functions to adjust for long-term and seasonal trends, as well as other time-varying covariates. We applied 2-stage Bayesian hierarchical statistical models to estimate city-specific and national average associations of air pollution with daily stroke mortality.

Results—Air pollution was associated with daily stroke mortality in 8 Chinese cities. In the combined analysis, an increase of 10 μg/m³ of 2-day moving average concentrations of particulate matter <10 μm in aerodynamic diameter, sulfur dioxide, and nitrogen dioxide corresponded to 0.54% (95% posterior intervals, 0.28–0.81), 0.88% (95% posterior intervals, 0.54–1.22), and 1.47% (95% posterior intervals, 0.88–2.06) increase of stroke mortality, respectively. The concentration–response curves indicated linear nonthreshold associations between air pollution and risk of stroke mortality.

Conclusions—To our knowledge, this is the first multicity study in China, or even in other developing countries, to report the acute effect of air pollution on stroke mortality. Our results contribute to very limited data on the effect of air pollution on stroke for high-exposure settings typical in developing countries. (*Stroke*. 2013;44:954-960.)

Key Words: air pollution ■ China ■ mortality ■ stroke

Stroke is a common cause of death and a leading cause of long-term severe disability in both developed and developing countries.¹ The World Health Organization estimated that in 2002 there were 15.3 million strokes worldwide, more than a third of which (5.5 million) resulted in death. Globally, stroke accounts for approximately 10% of all deaths.² Although most research and attention to prevention and intervention occurs in high-income countries, >85% of strokes occur in low- and middle-income countries. In China, the largest developing country, stroke burden is disproportionately high. For example, stroke mortality accounts for 19% of total mortality rate, whereas ischemic heart disease mortality only accounts for 8% of all deaths.³ Despite widespread concern and the great health burden imposed on the middle-aged and elderly, the relationship between stroke and environmental risk factors has not been studied adequately.

Air pollution is potentially one environmental risk factors for stroke.⁴ Recent studies conducted in North America, Europe, and Asia provide evidence of the acute effect of

ambient pollutants on stroke mortality and hospital admissions;^{5–12} however, most of these studies were conducted in developed countries, and only a small number of studies have been conducted in developing countries. There remains a need for studies in developing countries, where characteristics of outdoor air pollution (eg, air pollution level and mixture, transport of pollutants), and sociodemographic status of local residents (eg, disease pattern, age structure, and socioeconomic characteristics) may be different from developed countries.

China is currently facing the worst air pollution problem in the world.¹³ The objective of this article is to examine the association of air pollution with daily stroke mortality in 8 Chinese cities. This analysis is a component of the China Air Pollution and Health Effects Study.

Methods

Data Collection

The original China Air Pollution and Health Effects Study included 17 Chinese cities. In this analysis, we considered only 8 of these

Received August 7, 2012; final revision received December 14, 2012; accepted December 19, 2012.

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Stroke is available at <http://stroke.ahajournals.org>

DOI: 10.1161/STROKEAHA.111.673442

(Beijing, Fuzhou, Guangzhou, Hong Kong, Shanghai, Shenyang, Suzhou, Tangshan; Figure 1) because we were not able to obtain the stroke mortality data in the other cities. Our study area was restricted to the urban areas of these 8 cities because of inadequate air pollution monitoring stations in the suburban areas.

Daily numbers of stroke deaths were obtained from the Municipal Center for Disease Control and Prevention in each city. Stroke was defined according to the International Classification of Diseases, 10th Revision code I60-I69.

Air pollution data, including particulate matter <10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2), were collected from the National Air Pollution Monitoring System, which is certified by the Ministry of Environmental Protection of China. Each city had between 2 and 12 monitoring stations (Table 1). The Chinese Government has mandated detailed quality assurance and quality control programs at each monitoring station providing air pollution data. The daily (24-hour) average concentrations of PM_{10} , SO_2 , and NO_2 were measured using tapered element oscillating microbalance, ultraviolet fluorescence, and chemiluminescence methods, respectively. For the calculation of 24-hour mean concentrations, at least 75% of the 1-hour values had to be available on that particular day. If a station had >25% of the values missing for the whole period of analysis, the entire station was excluded. Per Chinese Government rules, the location of monitoring stations are mandated to not be in the direct vicinity of traffic or of industrial sources, and not be influenced by local pollution sources, and to avoid buildings, or those housing large emitters, such as coal-, waste-, or oil-burning boilers, furnaces, and incinerators. In each city, the daily air pollutants' concentrations were averaged from the available monitoring results across various stations.¹⁴

To allow adjustment for the effect of weather conditions on stroke mortality, meteorologic data (daily mean temperature and relative humidity) were obtained from each city.

Statistical Analysis

We applied 2-stage Bayesian hierarchical statistical models to estimate city-specific and national average associations of air pollution, with daily stroke mortality.¹⁵

In the first stage, we applied the generalized additive models with quasi-Poisson regression to examine the association between air pollution and stroke mortality. We incorporated natural cubic smooth functions of calendar time with 8 degrees of freedom (*df*) per year in the generalized additive models to control for the long-term and seasonal trends of daily stroke mortality. We also included day of the week as an indicator variable. To control for the confounding effects of weather conditions, we applied natural smooth functions with 6 *df*

for temperature and 3 *df* for humidity. After we established the basic models, we introduced the pollutant variables and analyzed their effects on stroke mortality. We fitted single-pollutant models and used 2-day moving average of current and previous day concentrations of air pollutants (lag 01) for our main analyses.

In the second stage, we used Bayesian hierarchical models to obtain the national average estimates of the association between air pollution and daily stroke mortality.¹⁶ This approach provides a flexible tool to pool risk estimates, whereas accounting for within-city statistical error and between-city variability (heterogeneity) of the true risks. The model generated a posterior probability distribution of the pooled mean estimates, from which we reported the combined log-relative risks as the posterior mean and 95% posterior interval (PI). We performed a χ^2 test to examine heterogeneity of the city-specified risks (Cochran *Q* test).¹⁷

Because the assumption of the linearity between the log of stroke mortality and air pollution level may not be justified, we used the same approach as the Air Pollution and Health—A European Approach project to combine the city-specific concentration–response relationship curves to get overall associations between air pollution and stroke mortality.¹⁸ We compared the linear and spline models by computing the difference between the deviances of the 2 fitted models.¹⁹

We performed 3 sensitivity analyses to examine the robustness of our findings. First, we fitted 2-pollutant models to assess the stability of the pollutants' effect. Second, we estimated air pollution's effects on stroke mortality using different lag structures, including both single-day lags (from lag 0 to lag 4) and multiday lags (lag 01 and lag 04). In single-day lag models, a lag of 0 days (lag 0) corresponded to the current-day air pollutants concentration, and a lag of 1 day (lag 1) referred to the previous-day concentration; in multiday lag models, lag 04 meant the 5-day moving average concentrations of current day and the previous 4 days. Third, we tested the impact of alternative *df* values for time trend on the association between air pollution and stroke mortality.

The first- and second-stage analyses were conducted in *R* 2.15.1 using the mixed GAM computation vehicle with GCV/AIC/REML smoothness estimation and two-level normal independent sampling estimation packages, respectively. All statistical tests were 2-sided and probability values of <0.05 were considered statistically significant. The results are presented as the percentage change in daily stroke mortality per 10 $\mu\text{g}/\text{m}^3$ increase of air pollutants' concentrations.

Results

Table 1 summarizes the study period, population, exposure (PM_{10} , SO_2 , and NO_2), outcome (daily stroke mortality), and

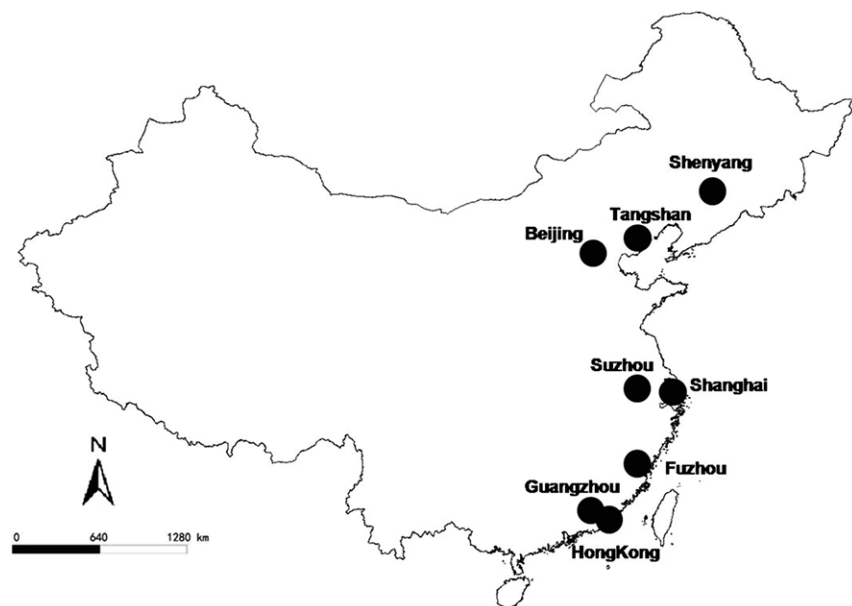


Figure 1. Location of 8 Chinese cities (Beijing, Fuzhou, Guangzhou, Hong Kong, Shanghai, Shenyang, Suzhou, Tangshan).

Table 1. Descriptive Statistics in This Study

City	Study Period	Population (Million)	No. of Air Monitors	Stroke Deaths Per Day	Air Pollutants' Concentrations (Mean and Standard Deviation, $\mu\text{g}/\text{m}^3$)			Mean Temperature ($^{\circ}\text{C}$)
					PM ₁₀	SO ₂	NO ₂	
Beijing	2007–2008	12.3	12	23	139 (87)	41 (43)	58 (25)	14.8
Fuzhou	2004–2006	1.8	4	4	72 (37)	16 (7)	45 (9)	20.7
Guangzhou	2007–2008	6.5	9	10	74 (40)	50 (33)	66 (32)	22.8
Hong Kong	1996–2002	6.7	7	9	52 (25)	18 (12)	56 (20)	23.7
Shanghai	2001–2004	8.5	9	26	102 (65)	45 (24)	67 (25)	17.7
Shenyang	2005–2008	6.4	2	15	114 (50)	55 (44)	37 (15)	8.2
Suzhou	2005–2008	4.1	8	7	90 (48)	45 (21)	45 (21)	17.2
Tangshan	2006–2008	1.9	6	4	98 (47)	84 (60)	41 (18)	12.6

NO₂ indicates nitrogen dioxide; PM₁₀, particulate matter <10 μm in aerodynamic diameter; and SO₂, sulfur dioxide.

mean temperature in 8 Chinese cities. The population size at each city varied from 1.8 to 12.3 millions, with a total population of 48.2 million. The daily mean number of stroke deaths varied according to the size of the city and ranged from 4 (Tangshan) to 26 (Shanghai). There were no missing data for the air pollution measurements. The averaged daily concentrations ranged from 52 $\mu\text{g}/\text{m}^3$ (Hong Kong) to 139 $\mu\text{g}/\text{m}^3$ (Beijing) for PM₁₀, from 16 $\mu\text{g}/\text{m}^3$ (Fuzhou) to 84 $\mu\text{g}/\text{m}^3$ (Tangshan) for SO₂, and from 37 $\mu\text{g}/\text{m}^3$ (Shenyang) to 67 $\mu\text{g}/\text{m}^3$ (Shanghai) for NO₂. Generally, the reported air pollution levels in these Chinese cities

were much higher than those reported in developed countries.^{20,21} The mean temperature ranged from 8.2 $^{\circ}\text{C}$ (Shenyang) to 23.7 $^{\circ}\text{C}$ (Hong Kong). The correlation coefficients between PM₁₀, SO₂, and NO₂ differed across cities, ranging from 0.51 to 0.87 (data not shown).

In the single-pollutant models, the associations of daily stroke mortality with air pollutants (lag 01) varied between cities (Figure 2). We observed statistically significant associations of daily stroke mortality with PM₁₀, SO₂, and NO₂ in most of the cities we examined. χ^2 tests showed the heterogeneity was

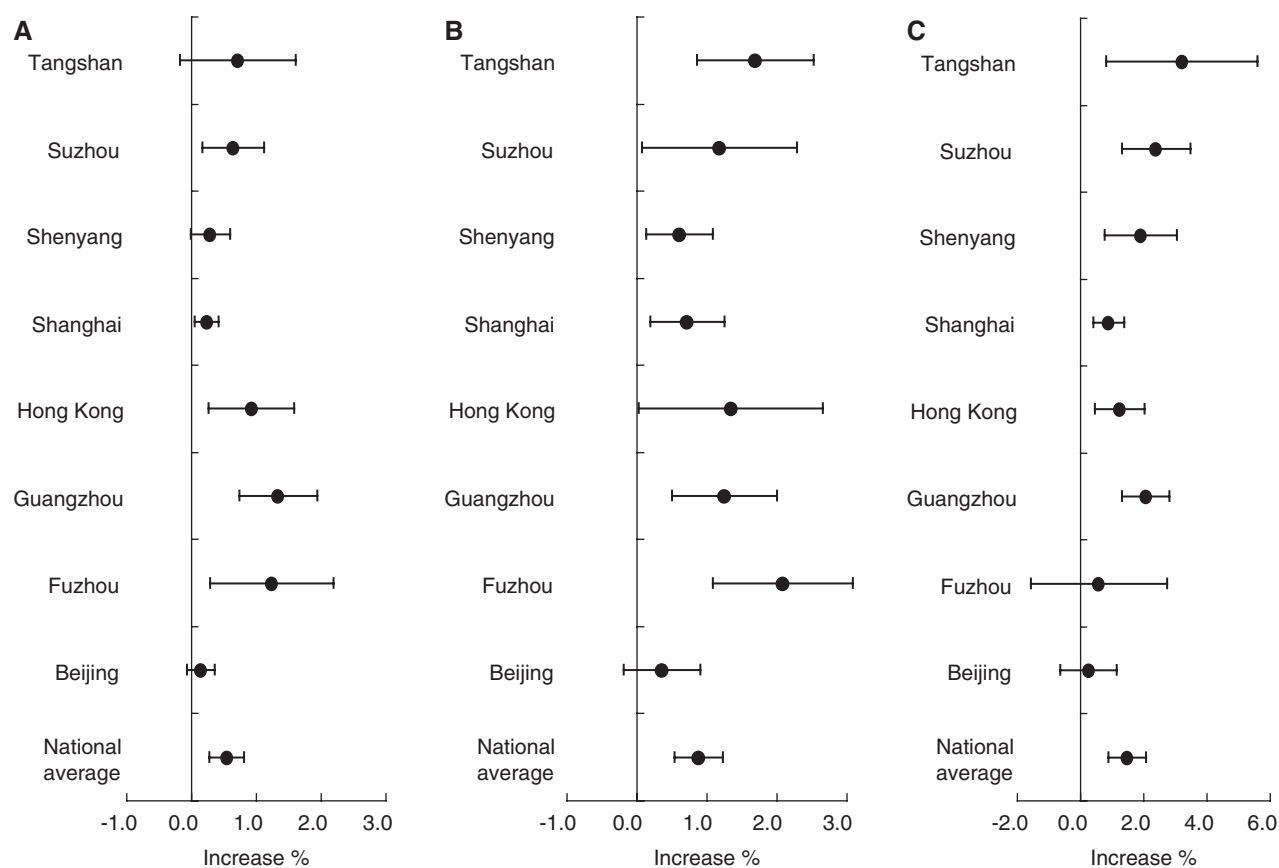


Figure 2. Percentage increase of stroke mortality associated with 10 $\mu\text{g}/\text{m}^3$ increase of 2-day moving average air pollutant concentrations in 8 Chinese cities—effect estimates of individual cities (mean and 95% confidence intervals) and national average (mean and 95% posterior intervals; **A**, PM₁₀; **B**, SO₂; **C**, NO₂). NO₂ indicates nitrogen dioxide; PM₁₀, particulate matter <10 μm in aerodynamic diameter; and SO₂, sulfur dioxide.

significant for all 3 pollutants ($P < 0.05$). When considering the national average associations, we estimated an increase of 0.54% (95% PI, 0.28–0.81), 0.88% (95% PI, 0.54–1.22), and 1.47% (95% PI, 0.88–2.06) in stroke mortality associated with a 10 $\mu\text{g}/\text{m}^3$ increase of PM_{10} , SO_2 , and NO_2 , respectively.

Figure 3 shows the combined concentration–response curves of stroke mortality with air pollution. For all 3 pollutants, we observed almost linear relationships. The differences in the deviance between the linear and spline models did not

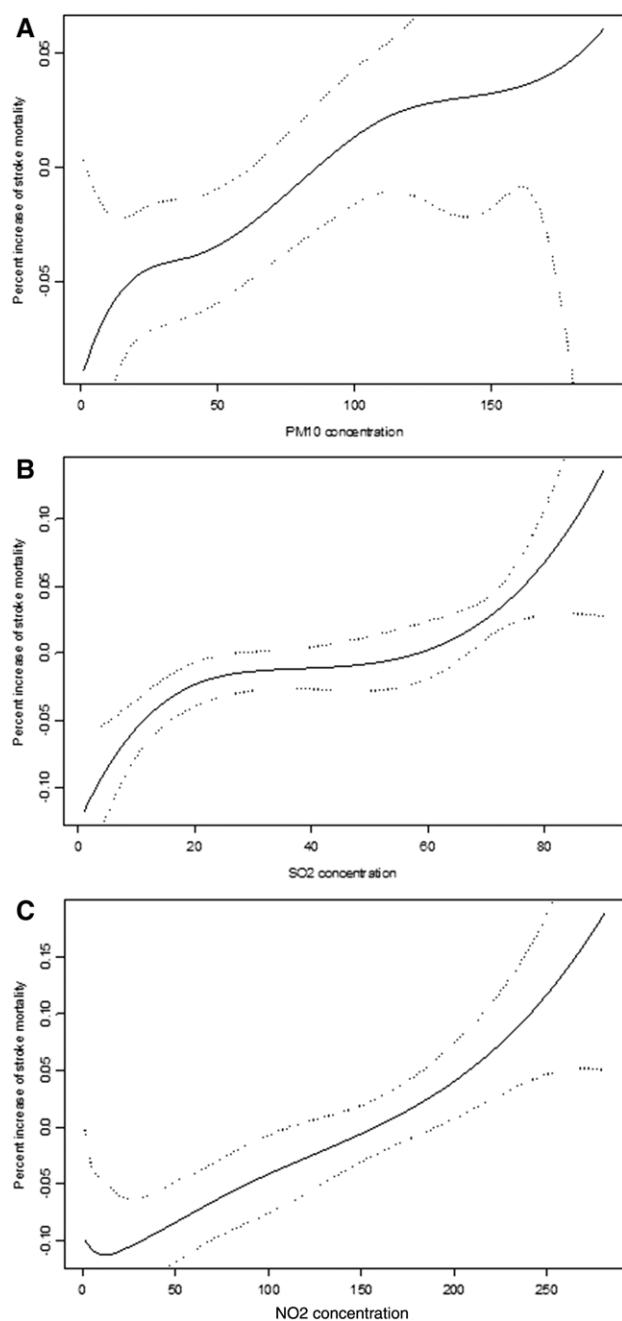


Figure 3. Pooled concentration–response curves of air pollutants and daily stroke mortality in 8 Chinese cities. X-axis is the 2-day average air pollutants' concentrations ($\mu\text{g}/\text{m}^3$; **A**, PM_{10} ; **B**, SO_2 ; **C**, NO_2). The black line is the mean estimate and the dotted lines are its 95% confidence intervals. NO_2 indicates nitrogen dioxide; PM_{10} , particulate matter $< 10 \mu\text{m}$ in aerodynamic diameter; and SO_2 , sulfur dioxide.

indicate a statistically significant improvement in the fit of the spline versus linear models.

PM_{10} , SO_2 , and NO_2 showed similar lag patterns for their effects on stroke mortality (Figure 4). For single-day lags, the risks of stroke mortality decreased between 0 and 4 days lag. Multiday exposures (lag 01 and lag 04) generally presented larger effect estimates than single-day exposure.

In the 2-pollutant model, the association of PM_{10} with stroke mortality decreased but remained statistically significant by adding SO_2 into the models; however, adjustment for NO_2 lessened the association and rendered it statistically insignificant (Table 2). Similarly, adjustment for NO_2 rendered the association for SO_2 insignificant. In contrast, the effects of NO_2 remained statistically significant, after controlling for PM_{10} or SO_2 in the models. For example, a 10 $\mu\text{g}/\text{m}^3$ increase in the 2-day moving average of NO_2 , after adjustment for PM_{10} and SO_2 , was associated with a 1.17% (95% PI, 0.47–1.88) and 1.35% (95% PI, 0.55–2.15) increase of stroke mortality, respectively.

Within the range of 4 to 10 *df* per year, changing its value for time trend control did not substantially affect the association of air pollution with stroke mortality (data not shown), suggesting that our findings are relatively robust in this aspect.

Discussion

Our multicity analysis found significant associations between major air pollutants (PM_{10} , SO_2 , and NO_2) and increased risk of death from stroke in 8 Chinese cities. The combined concentration–response curves indicated linear associations between air pollution and risk of stroke mortality. We found significant effects of air pollution even below the latest Air Quality Standard in China (24-hour average: 150 $\mu\text{g}/\text{m}^3$ for PM_{10} , 150 $\mu\text{g}/\text{m}^3$ for SO_2 , and 120 $\mu\text{g}/\text{m}^3$ for NO_2). To our knowledge, this is the first multicity study in China, or even in other developing countries, to report the acute effects of air pollution on stroke mortality. Our findings may have implications for primary prevention of stroke in China.

In the current analysis, a 10 $\mu\text{g}/\text{m}^3$ increase of PM_{10} , SO_2 , and NO_2 was associated with a 0.54%, 0.88%, and 1.47% increase of stroke mortality, respectively. These estimates were similar to our previous estimates on cardiovascular mortality, suggesting that air pollution may have comparable hazards on cardiac and cerebrovascular health. Generally, the magnitude of our estimates was comparable with previous findings worldwide.²² In the Netherlands, for example, Hoek et al reported that a 10 $\mu\text{g}/\text{m}^3$ increase of PM_{10} , SO_2 , and NO_2 was associated with 0.4%, 1.3%, and 1.6% increase of stroke mortality, though the associations were significant for SO_2 only.²³ In another study in Seoul, Korea, Hong et al estimated a 0.7% (95% confidence interval, 0.6–0.9) increase in stroke mortality per 10 $\mu\text{g}/\text{m}^3$ of PM_{10} .⁷ In Hong Kong, however, Wong et al did not find statistically significant association between air pollution and stroke mortality.²⁴ The heterogeneity of various findings may reflect differences in the analytic techniques used, aside from the different characteristics of the study sites. For instance, various statistical models, as well as the parameter setting in these models (eg, *df* selection and convergence criteria) can affect the effect estimates of time-series studies.²⁵ In addition, characteristics of the study sites,

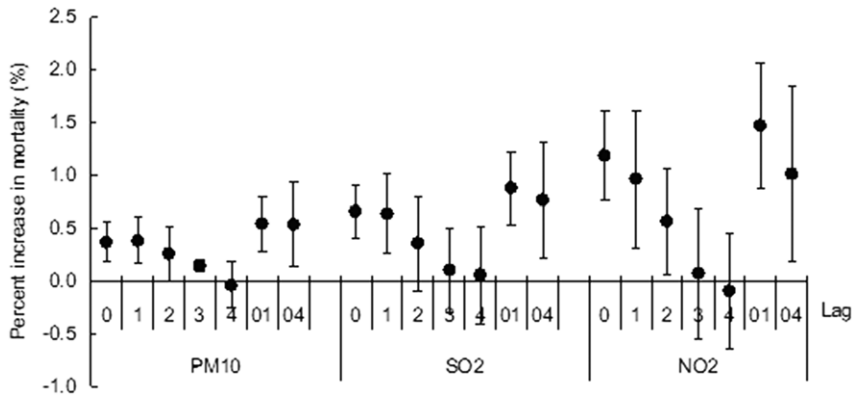


Figure 4. Percentage increase (mean and 95% posterior intervals [PI]) of stroke mortality associated with a $10 \mu\text{g}/\text{m}^3$ increase of air pollutants' concentrations, using different lag structures in 8 Chinese cities. NO_2 indicates nitrogen dioxide; PI, posterior intervals; PM_{10} , particulate matter $<10 \mu\text{m}$ in aerodynamic diameter; and SO_2 , sulfur dioxide.

such as indoor air pollution, weather patterns, sensitivity of local residents to air pollution, outdoor air pollution levels, and especially components of pollution mixture, may affect the magnitudes of exposure–response relationships.²⁶

We reported similar acute mortality risk of stroke as found in other parts of the world; however, the importance of this increased risk for stroke mortality is greater than in developed countries, not only because stroke burden is disproportionately high in China, but also because the air pollution level is much higher. It should be noted that we may have underestimated the stroke mortality burden from outdoor air pollution because we accounted only for the short-term effects.²⁷ Future research should focus on the long-term effects of outdoor air pollution on cerebrovascular health (eg, individual-level cohort study) in China.

We observed heterogeneity of the association between air pollution and stroke mortality in various Chinese cities (Figure 2). This difference may be explained by the characteristics of the study sites, such as indoor air pollution, weather patterns, housing types, sensitivity of local residents to air pollution (eg, socioeconomic status, age, and smoking rate), air pollution levels, and components of ambient particles. Different research periods in each city may also contribute to the heterogeneity we observed.

Among the pollutants we examined in the 8 Chinese cities, only NO_2 remained significantly associated with stroke

mortality after adjustment for copollutants (Table 2). Our findings for NO_2 are robust and consistent with a recent multicity analysis in Europe (Air Pollution and Health—A European Approach).²⁸ However, in the analysis of 20 US cities within the National Morbidity, Mortality and Air Pollution Study, no consistent pattern of association between stroke mortality and NO_2 was found.²⁹ The difference between National Morbidity, Mortality and Air Pollution Study and Air Pollution and Health—A European Approach findings may be attributed to the varying air pollution sources and mixture in the United States and Europe.²⁸ Most air pollution epidemiologic studies, including ours, use ambient pollutant concentrations as surrogates of personal exposure. Therefore, the observed health effects attributed to NO_2 might actually be a result of exposures to fine particles or traffic-related emissions.³⁰ For example, Seaton et al suggested NO_2 is a surrogate for ultrafine particle measures;³¹ therefore, there is a possibility that the effect of NO_2 we observed might be because of other unmeasured pollutant such as ultrafine particle. In Europe and North America, NO_2 is typically a traffic-related pollutant; in China, however, both vehicles and coal-fired plants are major sources of NO_2 . At present, we cannot conclude that NO_2 is a suitable proxy of particulate pollutant, or that it has direct effects on stroke mortality. The role of outdoor exposure to NO_2 should be investigated further.

The shape of exposure–response relationships is crucial for public health assessment, and there has been growing demand for studies to provide relevant curves. Previous multicity studies in the United States and Europe have explored the exposure–response relationship between air pollution and mortality, and generally supported a linear association without a threshold.¹⁸ In our study, we found significant effects of air pollution on stroke mortality, even below the current Air Quality Standard levels in China (Figure 3). Therefore, the current standards might not be sufficient to protect individuals from the negative cerebrovascular health effects in the country. Thus, further control of air pollution is likely to result in health benefits. A reduction in stroke morbidity and mortality after the implementation of an intervention program would add evidence to the hypothesis of a causal link between air pollution and cerebrovascular health.

The mechanisms by which air pollution affects the stroke deaths is still not clear, although some biological mechanisms have been proposed.³² For example, air pollution has been associated with increased plasma viscosity, changes in the

Table 2. Pooled Estimates (Mean and 95% PI) for the Increase in Stroke Mortality Associated With an Increase of $10 \mu\text{g}/\text{m}^3$ in 2-Day Moving Average Air Pollutant Concentrations, Using the Single- and Two-Pollutant Models

	Mean	95% PI
PM_{10}	0.54	0.28, 0.81
Adjusted for SO_2	0.38	0.10, 0.67
Adjusted for NO_2	0.14	−0.04, 0.31
SO_2	0.88	0.54, 1.22
Adjusted for PM_{10}	0.54	0.06, 1.01
Adjusted for NO_2	0.16	−0.41, 0.72
NO_2	1.47	0.88, 2.06
Adjusted for PM_{10}	1.17	0.47, 1.88
Adjusted for SO_2	1.35	0.55, 2.15

NO_2 indicates nitrogen dioxide; PI, posterior intervals; PM_{10} , particulate matter $<10 \mu\text{m}$ in aerodynamic diameter; and SO_2 , sulfur dioxide.

characteristics of the blood, and indicators of abnormal autonomic function of the cerebrovascular system.³² These findings provide possible pathways in which air pollution affects stroke deaths.

Our analysis has limitations. First, we were not able to differentiate the subtypes (ischemic versus hemorrhagic) of stroke because of data limitations.⁸ Second, as in most previous time-series studies, we simply averaged the results across various monitoring stations as the proxy for population exposure levels. This simple averaging method may raise a number of issues, given that pollutant measurements can differ from monitoring location to monitoring location, and these differ from personal air pollutant exposure levels.³⁰ Third, high correlation between PM₁₀, SO₂, and NO₂ in China limited our ability to separate the independent effect for each pollutant. Further research will be needed to disentangle the effects of the various pollutants on cerebrovascular health. Finally, we were not able to obtain the sex-, age-, and socioeconomic status-specific stroke mortality in these Chinese cities, which has limited our ability to examine potential modifiers of the association between air pollution and stroke mortality.

Conclusions

In summary, we found that short-term exposure to outdoor air pollution was associated with increased risk of death from stroke in China. To our knowledge, this is the first multicity study conducted in China, or in other even developing countries, to report the acute effect of air pollution on stroke mortality. Our results contribute to very limited data on the effect of air pollution on stroke for high-exposure settings typical in developing countries.

Acknowledgments

We sincerely thank those who participated in data collection and management.

Sources of Funding

The study was supported by the National Basic Research Program (973 program) of China (2011CB503802), National Natural Science Foundation of China (30800892), Gong-Yi Program of China Ministry of Environmental Protection (201209008), and Shanghai Municipal Committee of Science and Technology (12dz1202602).

Disclosures

None.

References

- Johnston SC, Mendis S, Mathers CD. Global variation in stroke burden and mortality: estimates from monitoring, surveillance, and modelling. *Lancet Neurol*. 2009;8:345–354.
- Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. *Lancet Neurol*. 2007;6:182–187.
- Kim AS, Johnston SC. Global variation in the relative burden of stroke and ischemic heart disease. *Circulation*. 2011;124:314–323.
- Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, et al.; American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378.
- Kan H, Jia J, Chen B. Acute stroke mortality and air pollution: new evidence from Shanghai, China. *J Occup Health*. 2003;45:321–323.
- Hong YC, Lee JT, Kim H, Kwon HJ. Air pollution: a new risk factor in ischemic stroke mortality. *Stroke*. 2002;33:2165–2169.
- Hong YC, Lee JT, Kim H, Ha EH, Schwartz J, Christiani DC. Effects of air pollutants on acute stroke mortality. *Environ Health Perspect*. 2002;110:187–191.
- Wellenius GA, Schwartz J, Mittleman MA. Air pollution and hospital admissions for ischemic and hemorrhagic stroke among medicare beneficiaries. *Stroke*. 2005;36:2549–2553.
- Lee JT, Kim H, Cho YS, Hong YC, Ha EH, Park H. Air pollution and hospital admissions for ischemic heart diseases among individuals 64+ years of age residing in Seoul, Korea. *Arch Environ Health*. 2003;58:617–623.
- Tsai SS, Goggins WB, Chiu HF, Yang CY. Evidence for an association between air pollution and daily stroke admissions in Kaohsiung, Taiwan. *Stroke*. 2003;34:2612–2616.
- Le Tertre A, Medina S, Samoli E, Forsberg B, Michelozzi P, Boumghar A, et al. Short-term effects of particulate air pollution on cardiovascular diseases in eight European cities. *J Epidemiol Community Health*. 2002;56:773–779.
- Villeneuve PJ, Chen L, Stieb D, Rowe BH. Associations between outdoor air pollution and emergency department visits for stroke in Edmonton, Canada. *Eur J Epidemiol*. 2006;21:689–700.
- Kan H, Chen R, Tong S. Ambient air pollution, climate change, and population health in China. *Environ Int*. 2012;42:10–19.
- Wong CM, Vichit-Vadakan N, Kan H, Qian Z. Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality. *Environ Health Perspect*. 2008;116:1195–1202.
- Chen R, Huang W, Wong CM, Wang Z, Thach TQ, Chen B, et al.; CAPES Collaborative Group. Short-term exposure to sulfur dioxide and daily mortality in 17 Chinese cities: the China air pollution and health effects study (CAPES). *Environ Res*. 2012;118:101–106.
- Dominici F, Peng RD, Bell ML, Pham L, McDermott A, Zeger SL, et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. *JAMA*. 2006;295:1127–1134.
- Sutton AJ, Higgins JP. Recent developments in meta-analysis. *Stat Med*. 2008;27:625–650.
- Samoli E, Analitis A, Touloumi G, Schwartz J, Anderson HR, Sunyer J, et al. Estimating the exposure-response relationships between particulate matter and mortality within the APHEA multicity project. *Environ Health Perspect*. 2005;113:88–95.
- Dominici F, Daniels M, Zeger SL, Samet JM. Air pollution and mortality: Estimating regional and national dose-response relationships. *J Am Stat Assoc*. 2002;97:100–111.
- Samet JM, Dominici F, Currier FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987–1994. *N Engl J Med*. 2000;343:1742–1749.
- Samoli E, Peng R, Ramsay T, Pipikou M, Touloumi G, Dominici F, et al. Acute effects of ambient particulate matter on mortality in Europe and North America: results from the APHENA study. *Environ Health Perspect*. 2008;116:1480–1486.
- Li XY, Yu XB, Liang WW, Yu N, Wang L, Ye XJ, et al. Meta-analysis of association between particulate matter and stroke attack. *CNS Neurosci Ther*. 2012;18:501–508.
- Hoek G, Brunekreef B, Fischer P, van Wijnen J. The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. *Epidemiology*. 2001;12:355–357.
- Wong TW, Tam WS, Yu TS, Wong AH. Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. *Occup Environ Med*. 2002;59:30–35.
- Peng RD, Dominici F, Louis TA. Model choice in time series studies of air pollution and mortality. *J R Stat Soc Ser A*. 2006;169:179–203.
- Kan H, London SJ, Chen G, Zhang Y, Song G, Zhao N, et al. Season, sex, age, and education as modifiers of the effects of outdoor air pollution on daily mortality in Shanghai, China: The Public Health and Air Pollution in Asia (PAPA) Study. *Environ Health Perspect*. 2008;116:1183–1188.
- Künzli N, Medina S, Kaiser R, Quénel P, Horak F Jr, Studnicka M. Assessment of deaths attributable to air pollution: should we use risk estimates based on time series or on cohort studies? *Am J Epidemiol*. 2001;153:1050–1055.
- Samoli E, Aga E, Touloumi G, Nisiotis K, Forsberg B, Lefranc A, et al. Short-term effects of nitrogen dioxide on mortality: an analysis within the APHEA project. *Eur Respir J*. 2006;27:1129–1138.

29. Samet JM, Zeger SL, Dominici F, Curriero F, Coursac I, Dockery DW, et al. The National Morbidity, Mortality, and Air Pollution Study. Part II: Morbidity and mortality from air pollution in the United States. *Res Rep Health Eff Inst.* 2000;94(Pt 2):5–70; discussion 71.
30. Sarnat JA, Brown KW, Schwartz J, Coull BA, Koutrakis P. Ambient gas concentrations and personal particulate matter exposures: implications for studying the health effects of particles. *Epidemiology.* 2005;16:385–395.
31. Seaton A, Dennekamp M. Hypothesis: ill health associated with low concentrations of nitrogen dioxide—an effect of ultrafine particles? *Thorax.* 2003;58:1012–1015.
32. Brook RD, Franklin B, Cascio W, Hong Y, Howard G, Lipsett M, et al.; Expert Panel on Population and Prevention Science of the American Heart Association. Air pollution and cardiovascular disease: a statement for health-care professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. *Circulation.* 2004;109:2655–2671.

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Stroke. 2013;44:954-960; originally published online February 7, 2013;

doi: 10.1161/STROKEAHA.111.673442

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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