

## Short Communication

### Acute Stroke Mortality and Air Pollution: New Evidence from Shanghai, China

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The association between air pollution and daily mortality, especially of respiratory and cardiovascular diseases, has been confirmed by numerous studies<sup>1</sup>. Recently, two studies conducted in Korea have identified air pollution as a new risk factor for ischemic stroke mortality<sup>2,3</sup>. Nevertheless, the results still need to be replicated in other areas of the world. In Shanghai, the largest city in China, stroke has become one of the leading causes of death; and the stroke mortality reached 79.2 per 100,000 in the 37–79 age group during 1991 to 1999 with 87.2 and 71.4 per 100,000 for males and females<sup>4</sup> respectively. Therefore, it is worthwhile to explore the relationship between air pollution and stroke mortality in Shanghai, since air pollution is a potentially preventive risk factor. In this study, we used a time-series approach to assess the relationship between air pollution and daily stroke mortality in one urban district of Shanghai, and we also explored the patterns of exposure-response relationship for the major air pollutants considered.

#### Materials and Methods

##### Data

We obtained stroke mortality data (International Classification of Diseases, 9th revision [ICD-9] code 430–438) in Zhabei District of Shanghai between January 1, 2001 and December 31 in 2002. Meteorological data (daily mean temperature, relative humidity, dew point) and air pollution data (daily PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> concentrations) during the study period were collected from Shanghai Meteorological Bureau and Shanghai Environmental Monitoring Center, respectively.

##### Statistical methods

The analysis followed a time-series procedure. We used log-linear models to estimate air pollution/stroke mortality relative risks (RRs), while controlling for longer-term trends, seasonality, weather and days of the

week. The core analysis was a semi-parametric generalized additive model (GAM). We first fitted nonparametric smoothing (by means of the smoothing spline function) terms for trend on days (1–730), temperature, relative humidity, dew point, and dummy variables for days of the week. After controlling for time, weather and day of the week, each pollutant was introduced into the model. We fitted models with a different combination of pollutants (up to three pollutants per model) to assess the stability of individual effects. In addition, we also considered the lag effects of weather and air pollution variables in building the models. To compare the relative quality of the mortality predictions across these models, Akaike's Information Criterion (AIC) was used as a measure of how well the model fit the data<sup>5</sup>. Smaller AIC values indicate the preferred model. Considering that the assumption of linearity between the log of stroke mortality and the air pollution level may not be accurate, we used the smoothing function to graphically analyze the relationship between air pollution and stroke mortality.

All analyses were carried out with S-PLUS 2000 software (Insightful Corp, Seattle, U.S.A). Considering that the default settings in the *gam* function of the S-Plus software package do not assure convergence of its iterative estimation procedures and can provide biased estimates of regression coefficients and standard errors<sup>6</sup>, we analyzed the data with more stringent convergence parameters than the default settings when using the *gam* function.

#### Results

A total of 2,426 stroke deaths were included in the analysis, accounting for 24.7% of the total non-accidental deaths in the study region. On average, approximately 3.32 people died from stroke each day during the study period. The average daily concentrations of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> meantime were 97.0, 48.4 and 37.2  $\mu\text{g}/\text{m}^3$  respectively.

Table 1 shows the correlation for daily values over the entire period among the air pollutants and weather variables. PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> had a strong positive correlation with one another and were negatively correlated with temperature, relative humidity and dew point.

In our time-series analysis, the relative risks (RRs) on the best statistical lagged day (the day with minimum AIC, lag=1 d) were significant for PM<sub>10</sub> and NO<sub>2</sub>, but not for SO<sub>2</sub> (Table 1). Each increase of 10  $\mu\text{g}/\text{m}^3$  in PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> corresponded to 1.008 (95%CI 1.000–1.016), 1.017 (95%CI 0.998–1.036) and 1.029 (95%CI 1.001–1.057) relative risks of stroke mortality, respectively. But in the multiple pollutant models, the introduction of other pollutants would weaken the effect on stroke mortality risk induced by each pollutant.

Figure 1 shows the exposure-response relationships between air pollutant levels and stroke mortality at the

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**Table 1.** Pearson correlation coefficients among daily air pollution and weather variables

	PM <sub>10</sub>	SO <sub>2</sub>	NO <sub>2</sub>	Temperature	Relative humidity	Dew point
PM <sub>10</sub>	1.00					
SO <sub>2</sub>	0.67	1.00				
NO <sub>2</sub>	0.65	0.73	1.00			
Temperature	-0.33	-0.30	-0.40	1.00		
Relative humidity	-0.39	-0.47	-0.22	0.25	1.00	
Dew point	-0.41	-0.40	-0.42	0.96	0.50	1.00

**Table 2.** Relative risks of stroke mortality for a 10 µg/m<sup>3</sup> increase of air pollutant concentrations under single and multiple pollutant models

	Mean	95%CI
PM <sub>10</sub>	1.008	1.000–1.016
adjusted for SO <sub>2</sub>	1.006	0.994–1.017
adjusted for NO <sub>2</sub>	1.004	0.993–1.015
adjusted for both SO <sub>2</sub> and NO <sub>2</sub>	1.004	0.993–1.016
SO <sub>2</sub>	1.017	0.998–1.036
adjusted for PM <sub>10</sub>	1.008	0.982–1.034
adjusted for NO <sub>2</sub>	1.004	0.975–1.033
adjusted for both PM <sub>10</sub> and NO <sub>2</sub>	0.999	0.968–1.030
NO <sub>2</sub>	1.029	1.001–1.057
adjusted for PM <sub>10</sub>	1.020	0.984–1.056
adjusted for SO <sub>2</sub>	1.025	0.983–1.067
adjusted for both PM <sub>10</sub> and SO <sub>2</sub>	1.021	0.977–1.064

best-lagged day (lag=1 day, df=5) in the single pollutant models.

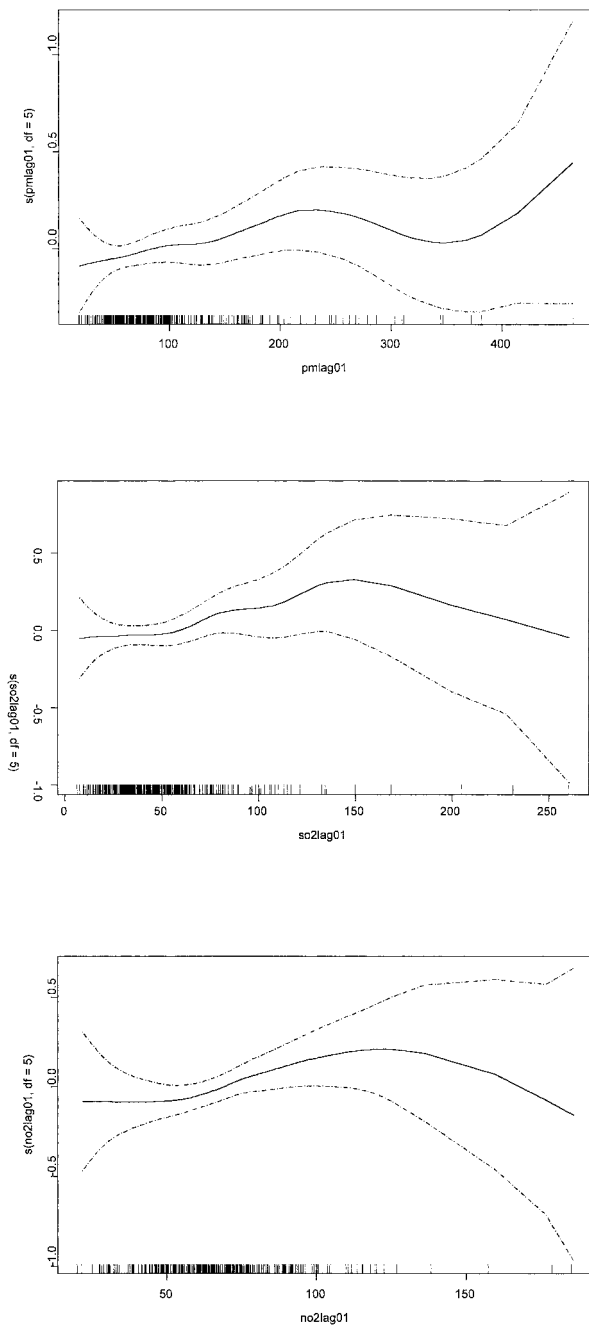
## Discussion

To the best of our knowledge, this is the first study to report an association between stroke mortality and air pollution outside Korea. During the past decade, Shanghai has undergone the most rapid development and urbanization in her history. The traditional coal combustion-related air pollution in Shanghai has improved substantially, although the vehicle-originated air pollution level is increasing rapidly. At the same time, the disease pattern of Shanghai residents has changed a lot, and non-communicable diseases (NCDs), such as stroke, diabetes etc, have placed much more of a disease burden on Shanghai residents than before. This background information raises interest in the study of an association between ambient air pollution and stroke. Evidence gained in this study showed that the current levels of PM<sub>10</sub> and NO<sub>2</sub> in Zhabei District of Shanghai were associated with the death rates from stroke. Due to the problems of co-linearity between air pollutants (high

correlation between pollutants) (see Table 1), it was difficult to separate the effect of individual pollutants on stroke mortality. The multiple pollutant models can increase the standard error of the results (see Table 2), which might lead to less statistical significance<sup>7)</sup>. Nevertheless, it seems clear that current air pollution level in Zhabei District of Shanghai have been related to increased daily stroke mortality.

Recently there have been many epidemiologic and toxicological studies concerned with the potential mechanisms linking air pollution and cardiovascular diseases, including stroke. For example, increased exposure to air pollution has been associated with causing myocardial infarction<sup>8)</sup>, initiation of life-threatening arrhythmias<sup>9)</sup>, changes in cardiac rhythm and autonomic function<sup>10)</sup>, endothelial dysfunction<sup>11)</sup>, increased plasma viscosity<sup>12)</sup>, and increased C-reactive protein<sup>13)</sup>. These findings provide possible pathways in which air pollutants, especially particulate matter, affect the incidence and death rate of stroke, but the underlying biological mechanisms still need to be further explored.

To date, although a number of studies have reported



**Fig. 1.** Smoothing plots of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> against stroke mortality risk (df=5) in the single pollutant model

an increased risk of cardiovascular mortality associated with air pollution, few studies have attempted to qualify the specific effects of air pollution on stroke mortality. The present study provides new evidence for the

association. By focusing on the preventive aspects of stroke, e.g. air pollution, we can reduce stroke-related health problems more significantly.

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