



## Ambient air pollution and hospital admission in Shanghai, China

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### ABSTRACT

No prior studies exist in Mainland China examining the association of outdoor air pollution with hospital admissions. In this study, we conducted a time-series analysis to examine the association of outdoor air pollutants (PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub>) with both total and cause-specific hospital admission in Shanghai, using three years of daily data (2005–2007). Hospital admission and air pollution data were collected from the Shanghai Health Insurance Bureau and Shanghai Environmental Monitoring Center. Natural spline model was used to analyze the data. We found outdoor air pollution was associated with increased risk of total and cardiovascular hospital admission in Shanghai. The effect estimates of air pollutants varied by lag (L) structures of pollutants' concentrations. For lag 5, a 10 μg/m<sup>3</sup> increase in concentration of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> corresponded to 0.18% (95% CI: -0.15%, 0.52%), 0.63% (95% CI: 0.03%, 1.23%), and 0.99% (95% CI: 0.10%, 1.88%) increase of total hospital admission; and 0.23% (95% CI: -0.03%, 0.48%), 0.65% (95% CI: 0.19%, 1.12%), and 0.80% (95% CI: 0.10%, 1.49%) increase of cardiovascular hospital admission. The associations appeared to be more evident in the cool season (from November to April) than in the warm season (from May to October). We found significant effects of gaseous pollutants (SO<sub>2</sub> and NO<sub>2</sub>) after adjustment for PM<sub>10</sub>. Our analyses provide the first evidence in China that the current air pollution level has an effect on hospital admission and strengthen the rationale for further limiting air pollution levels in Shanghai.

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## 1. Introduction

Associations between outdoor air pollution and adverse health effects are well documented in North America and Europe [1–4] with fewer studies in Asia [5]. In Mainland China, the largest developing country, daily mortality has been associated with particulate and gaseous ambient air pollution in both single-city [6–10] and multi-city analyses [11]. However, data on the association between air pollution and morbidity are quite scarce in the country [12]. In these limited morbidity studies, the air pollution and health data were measured in the early 1990s [13–15], in which the levels of particulate matter (PM) and sulphur dioxide (SO<sub>2</sub>) were much higher than those in current years. Also, the total suspended particle (TSP), rather than inhalable particle (PM with aerodynamic diameter less than 10 μm, PM<sub>10</sub>), was used as the indicator for PM in these studies. No air pollution morbidity studies in China assess

hospital admissions, although hospital outpatient visits [13,14] and emergency-room visits [15] have been examined.

Previously, associations between ambient air pollution and hospital admission have been extensively reported in North America [16,17] and Europe [18,19]. There remains a need for replicating the findings of developed countries in China, where characteristics of outdoor air pollution (e.g. air pollution level and mixture, transport of pollutants), and socio-demographic status of local residents (e.g. disease pattern, age structure, and socioeconomic characteristics), may be different.

The present study aims at examining the associations between ambient air pollution and daily hospital admissions between 2005 and 2007 in Shanghai, China.

## 2. Methods

### 2.1. Data

Shanghai comprises urban/sub-urban districts and counties, with a total area of 6341 square kilometres (km<sup>2</sup>), and had a population of 13.2 millions at the end of 2000, representing 1% of

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China's total. Our study area includes the nine urban Districts only (289 km<sup>2</sup>). The target population includes all permanent residents living in the area, around 6.4 millions in 2005. We excluded the sub-urban districts and counties from our analysis due to inadequate air pollution monitoring stations in that area.

Daily hospital admission counts of residents living in the nine urban Districts from January 1, 2005 to December 31, 2007 (1095 days) were collected from the database of Shanghai Health Insurance Bureau (SHIB). SHIB is the government agency in charge of the Shanghai Health Insurance System. The Shanghai Health Insurance System, which provides compulsory universal health insurance, covers most of the fixed residents in Shanghai (the coverage rate was 95% in 2008). In Shanghai, all hospitals are contracted with the SHIB. Computerized records of daily hospital admissions are available for each contracted hospital. All hospitals must submit standard claim documents for medical expenses on a computerized form that includes the date of admission and discharge, identification number, gender, birthday, and the diagnostic for each admission. Therefore, the information from the SHIB database appears to be sufficiently complete and accurate for use in epidemiological studies. The causes of hospital admission were coded according to International Classification of Diseases, Revision 10 (ICD 10): all non-accidental causes (A00–R99), cardiovascular diseases (I00–I99), and respiratory diseases (J00–J98).

Daily air pollution data, including PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub>, were obtained from the database of Shanghai Environmental Monitoring Center (SEMC), the government agency in charge of collection of air pollution data in Shanghai. The daily concentrations for each pollutant were averaged from the available monitoring results of six fixed-site stations (Hongkou, Jin'an, Luwan, Putuo, Xuhui, and Yangpu) under China National Quality Control for Air Monitoring. The monitoring system in Shanghai has been certified by the China State Environmental Protection Agency. According to relevant rules of Chinese government, the location of these stations should not be in the direct vicinity of traffic or of industrial sources. Moreover, the locations should not be influenced by local pollution sources and should also avoid buildings, or housing large emitters such as coal-, waste-, or oil-burning boilers, furnaces, and incinerators. Thus the monitoring results reflect the general background urban air pollution level in our study area rather than local sources such as traffic or industrial combustion. Automatic continuous monitoring system was set up at each station to measure the air pollutant concentrations. The methods based on Tapered Element Oscillating Microbalance (TEOM), ultraviolet fluorescence, and chemiluminescence were used for the measurement of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub>, respectively. We collected the daily (24-h) average concentrations for PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub>. For the calculation of 24-h mean concentrations of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub>, at least 75% of the 1-h values must be available on that particular day. If a station had more than 25% of the values missing for the whole period of analysis, the whole data of that station were excluded from the analysis. When data were available from more than one monitoring station, we used a simple filling-in procedure to improve data completeness. Missing values were replaced with the mean of values from those stations with available data. The pollutant measures from all stations providing data were then averaged to provide city-wide daily estimates. Actually we have the monitoring results of PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>2</sub> from all six monitoring stations during our study period.

To allow adjustment for the effect of weather on hospital admission, meteorological data (daily mean temperature and relative humidity) were obtained from the database of Shanghai Meteorological Bureau. The weather data were measured at a fixed-site station located in Xuhui District of Shanghai.

Chinese government has mandated detailed quality assurance (QA) and quality control (QC) programs at those Institutions providing the hospital admission, air pollution and weather data. In

addition, staffs from Fudan University also went back to the raw databases to validate the daily values supplied before data analysis. For air pollution data, they focused on the implementation of 75% criteria and exclusion of potential abnormal values in the raw station-specific hourly data; for hospital admission data, they traced back to the raw database to validate some randomly selected daily numbers of hospital admission; all the selected daily numbers were successfully reproduced from the raw database.

## 2.2. Statistical analysis

Because counts of daily mortality data approximately follow a Poisson distribution and the relations between mortality and explanatory variables are mostly nonlinear [20], we used overdispersed generalized linear Poisson models (quasi-likelihood) with natural spline (ns) smoothers to analyze the hospital admission, air pollution, and covariates data.

First, we built the basic models for hospital admission excluding the air pollution variables. We incorporated the ns smoothers of time trend and weather conditions, which can accommodate nonlinear and non-monotonic relationships of hospital admissions with calendar time and weather variables. We used the partial autocorrelation function (PACF) to guide the selection of model parameters [21]. Specifically, we used 4–6 degrees of freedom (df) per year for time trend. When the absolute magnitude of the PACF plot was less than 0.1 for the first two lag days, the basic model was regarded as adequate; if this criteria was not met, auto-regression (AR) terms for lag up to 7 days was introduced to improve the model [21]. For weather conditions, we used 3 df (whole period of study) for both temperature and humidity because this has been shown to control well for their effects on health outcomes [22]. Day of the week (DOW) was included as dummy variable in the basic models. Residuals of the basic models were examined to check whether there were discernable patterns and autocorrelation by means of residual plots and PACF plots.

After we established the basic models, we introduced the pollutant variables and analyzed their effects on hospital admission. Briefly, we fit the following log-linear models to obtain the estimated pollution log-relative rate  $\beta$  in Shanghai:

$$\log E(Y_t) = \beta Z_t + \text{DOW} + \text{ns}(\text{time}, \text{df}) \\ + \text{ns}(\text{temperature/humidity}, 3)$$

Here  $E(Y_t)$  represents the expected number of hospital admission at day  $t$ ;  $\beta$  represents the log-relative rate of hospital admission associated with a unit increase of air pollutants;  $Z_t$  indicates the pollutant concentrations at day  $t$ ; DOW is dummy variable for day of the week;  $\text{ns}(\text{time}, \text{df})$  is the natural spline function of calendar time; and  $\text{ns}(\text{temperature/humidity}, 3)$  is the natural spline function for temperature and humidity with 3 df.

Both total non-accidental and cause-specific hospital admissions were assessed. We examined the effect of air pollutants with different lag (L) structures including both single-day lag (from L0 to L6) and multi-day lag (L01 and L06). For example, in single-day lag models, a lag of 0 day (L0) corresponds to the current-day pollutant concentration, and a lag of 1 day (L1) refers to the previous-day concentration; in multi-day lag models, L01 corresponds to 2-day average of pollutant concentration of the current and previous day, and L06 corresponds to 7-day average of pollutant concentration of the current and previous 6 days. We analyzed effects of air pollution separately for the warm season (from May to October) and cool season (from November to April) as well as for the entire year. We tested the statistical significance of differences between the seasons by calculating the 95% confidence interval (95% CI) as  $(\hat{Q}_1 - \hat{Q}_2) \pm 1.96 \sqrt{SE_1 + SE_2}$ , where  $\hat{Q}_1$  and  $\hat{Q}_2$  are the estimates

**Table 1**  
Summary statistics of daily hospital admission, air pollutant concentrations and weather conditions in the study area (2005–2007).

	Mean $\pm$ SD	Minimum	P(25) <sup>a</sup>	Median	P(75) <sup>a</sup>	Maximum
Daily hospital admissions						
Total	1555 $\pm$ 655	126	1206	1759	1970	4123
Cardiovascular	340 $\pm$ 159	13	262	369	440	1008
Respiratory	123 $\pm$ 55	8	94	134	158	334
Air pollutants concentrations (24-h average)						
PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	87 $\pm$ 55	12	50	74	108	600
SO <sub>2</sub> ( $\mu\text{g}/\text{m}^3$ )	56 $\pm$ 31	8	33	49	72	235
NO <sub>2</sub> ( $\mu\text{g}/\text{m}^3$ )	57 $\pm$ 22	13	43	54	70	146
Meteorologic measures (24-h average)						
Temperature ( $^{\circ}\text{C}$ )	18 $\pm$ 9	−3.2	10	19	25	34
Humidity (%)	70 $\pm$ 12	32	63	70	78	95

<sup>a</sup> P(25): 25th percentile; P(75): 75th percentile.

for the two seasons, and  $SE_1$  and  $SE_2$  are their respective standard errors [23]. We fitted both single-pollutant models and models with a different combination of pollutants (up to two pollutants per model) to assess the stability of pollutants' effect. Because the assumption of the linearity between hospital admission and air pollution level may not be justified, we used the smoothing splines, with 3 df for pollutant concentrations, to graphically describe their relationships.

All analyses were conducted in R 2.8.1 using the MGCV package [24]. The results are presented as the percent change in daily hospital admission per 10  $\mu\text{g}/\text{m}^3$  increase of pollutant concentrations.

### 3. Results

From 2005 to 2007 (1095 days), a total of 1,702,180 hospital admissions were recorded. On average, there were approximately 1555 hospital admissions per day in our study area, among which 340 were due to cardiovascular diseases and 123 were due to respiratory disease (Table 1). During our study period, the mean daily average concentrations were 87  $\mu\text{g}/\text{m}^3$  for PM<sub>10</sub>, 56  $\mu\text{g}/\text{m}^3$  for SO<sub>2</sub> and 57  $\mu\text{g}/\text{m}^3$  for NO<sub>2</sub>. Meanwhile, the mean daily average temper-

**Table 2**  
Pearson correlation coefficients between daily air pollutant concentrations and weather conditions in Metropolitan Shanghai (2005–2007).

	SO <sub>2</sub>	NO <sub>2</sub>	Temperature	Relative humidity
PM <sub>10</sub>	0.72	0.70	−0.18	−0.27
SO <sub>2</sub>		0.76	−0.37	−0.37
NO <sub>2</sub>			−0.39	−0.17
Temperature				0.11

ature and humidity were 18  $^{\circ}\text{C}$  and 70%, reflecting the subtropical climate in Shanghai. Generally, PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> had relatively higher correlation coefficients with each other, and were negatively correlated with temperature and humidity (Table 2).

Table 3 shows results from the single-lag day (L0–L6) and cumulative exposure models (L01 and L06) for the percent increase in hospital admission per 10  $\mu\text{g}/\text{m}^3$  in pollution. Statistically significant relationships were observed for total hospital admission with 4-day lagged pollution for NO<sub>2</sub>, and 5-day lagged pollution for both SO<sub>2</sub> and NO<sub>2</sub>. Cardiovascular hospital admission was associated

**Table 3**  
Percent increase (mean and 95% CI) of daily hospital admission associated with 10  $\mu\text{g}/\text{m}^3$  increase of pollutant concentrations in Shanghai in 2005–2007.

	Lag (L)	PM <sub>10</sub>	SO <sub>2</sub>	NO <sub>2</sub>
Total	L0	−0.28 (−0.62, 0.06)	−0.60 (−1.26, 0.06)	−0.32 (−1.26, 0.63)
	L1	−0.07 (−0.42, 0.28)	0.03 (−0.62, 0.69)	0.14 (−0.84, 1.11)
	L2	−0.24 (−0.59, 0.11)	−0.02 (−0.66, 0.62)	−0.36 (−1.30, 0.59)
	L3	−0.06 (−0.39, 0.27)	−0.22 (−0.84, 0.40)	0.14 (−0.79, 1.07)
	L4	0.16 (−0.16, 0.49)	0.39 (−0.21, 1.00)	<b>0.97 (0.07, 1.87)<sup>*</sup></b>
	L5	0.18 (−0.15, 0.52)	<b>0.63 (0.03, 1.23)<sup>*</sup></b>	<b>0.99 (0.10, 1.88)<sup>*</sup></b>
	L6	−0.05 (−0.39, 0.29)	−0.19 (−0.81, 0.43)	0.04 (−0.87, 0.95)
	L01	−0.28 (−0.67, 0.11)	−0.41 (−1.16, 0.34)	−0.15 (−1.25, 0.95)
	L06	−0.19 (−0.76, 0.37)	0.08 (−0.92, 1.08)	0.90 (−0.61, 2.41)
	Cardiovascular	L0	−0.15 (−0.41, 0.12)	−0.31 (−0.83, 0.21)
L1		0.08 (−0.19, 0.36)	0.33 (−0.17, 0.84)	0.57 (−0.19, 1.32)
L2		−0.22 (−0.49, 0.06)	−0.17 (−0.67, 0.33)	−0.14 (−0.88, 0.61)
L3		−0.01 (−0.27, 0.24)	−0.10 (−0.59, 0.39)	0.72 (−0.01, 1.44)
L4		<b>0.25 (0.00, 0.50)<sup>*</sup></b>	<b>0.64 (0.17, 1.11)<sup>*</sup></b>	<b>1.23 (0.53, 1.93)<sup>*</sup></b>
L5		0.23 (−0.03, 0.48)	<b>0.65 (0.19, 1.12)<sup>*</sup></b>	<b>0.80 (0.10, 1.49)<sup>*</sup></b>
L6		−0.11 (−0.37, 0.16)	−0.11 (−0.59, 0.37)	−0.06 (−0.77, 0.64)
L01		−0.06 (−0.37, 0.25)	0.03 (−0.56, 0.61)	0.37 (−0.49, 1.22)
L06		0.07 (−0.37, 0.51)	0.51 (−0.26, 1.28)	<b>1.54 (0.38, 2.69)<sup>*</sup></b>
Respiratory		L0	0.29 (−0.18, 0.76)	0.27 (−0.27, 0.80)
	L1	0.16 (−0.12, 0.44)	0.17 (−0.35, 0.69)	0.17 (−0.60, 0.94)
	L2	0.15 (−0.33, 0.63)	0.30 (−0.21, 0.81)	0.41 (−0.35, 1.16)
	L3	0.16 (−0.11, 0.42)	0.28 (−0.22, 0.78)	0.02 (−0.71, 0.76)
	L4	0.02 (−0.24, 0.28)	0.40 (−0.09, 0.88)	0.39 (−0.33, 1.12)
	L5	0.01 (−0.26, 0.28)	0.35 (−0.13, 0.83)	0.01 (−0.70, 0.73)
	L6	0.25 (−0.02, 0.52)	0.26 (−0.24, 0.75)	0.47 (−0.25, 1.18)
	L01	0.35 (−0.16, 0.87)	0.28 (−0.32, 0.88)	0.29 (−0.58, 1.16)
	L06	0.72 (−0.12, 1.56)	0.30 (−0.49, 1.09)	0.37 (−0.82, 1.55)

<sup>\*</sup>  $p < 0.05$ .

**Table 4**  
Percent increase of hospital admission of Shanghai residents associated with 10  $\mu\text{g}/\text{m}^3$  increase in air pollutants concentrations by season in 2005–2007.<sup>a</sup>

		Cool season <sup>b</sup>	Warm season <sup>c</sup>
Total	PM <sub>10</sub>	0.16 (−0.22, 0.53)	0.00 (−0.39, 0.38)
	SO <sub>2</sub>	0.58 (−0.08, 1.24)	0.11 (−0.60, 0.81)
	NO <sub>2</sub>	1.12 (1.00, 1.23) <sup>*</sup>	0.06 (−0.80, 0.92)
Cardiovascular	PM <sub>10</sub>	0.35 (0.03, 0.68)	−0.05 (−0.46, 0.37)
	SO <sub>2</sub>	0.92 (0.34, 1.50)	0.03 (−0.72, 0.78)
	NO <sub>2</sub>	1.66 (0.68, 2.63) <sup>*</sup>	−0.26 (−1.17, 0.66)
Respiratory	PM <sub>10</sub>	0.09 (−0.25, 0.43)	0.13 (−0.30, 0.57)
	SO <sub>2</sub>	0.65 (0.04, 1.25)	0.24 (−0.56, 1.03)
	NO <sub>2</sub>	0.65 (−0.37, 1.68)	0.05 (−0.91, 1.02)

<sup>a</sup> Single-day lag 5 (L5) pollutants concentrations were used.  
<sup>b</sup> Cool season: from November to April.  
<sup>c</sup> Warm season: from May to October.  
<sup>\*</sup> The difference between warm season and cool season was significant ( $p < 0.05$ ).

with all three pollutants at lag 4 days, SO<sub>2</sub> and NO<sub>2</sub> at lag day 5, and NO<sub>2</sub> at lag day L06. For lag 5, a 10  $\mu\text{g}/\text{m}^3$  increase in concentration of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> corresponded to 0.18% (95% CI: −0.15%, 0.52%), 0.63% (95% CI: 0.03%, 1.23%), and 0.99% (95% CI: 0.10%, 1.88%) increase of total hospital admission; and 0.23% (95% CI: −0.03%, 0.48%), 0.65% (95% CI: 0.19%, 1.12%), and 0.80% (95% CI: 0.10%, 1.49%) increase of cardiovascular hospital admission. Respiratory hospital admission did not exhibit any statistically significant relationships with any pollutants.

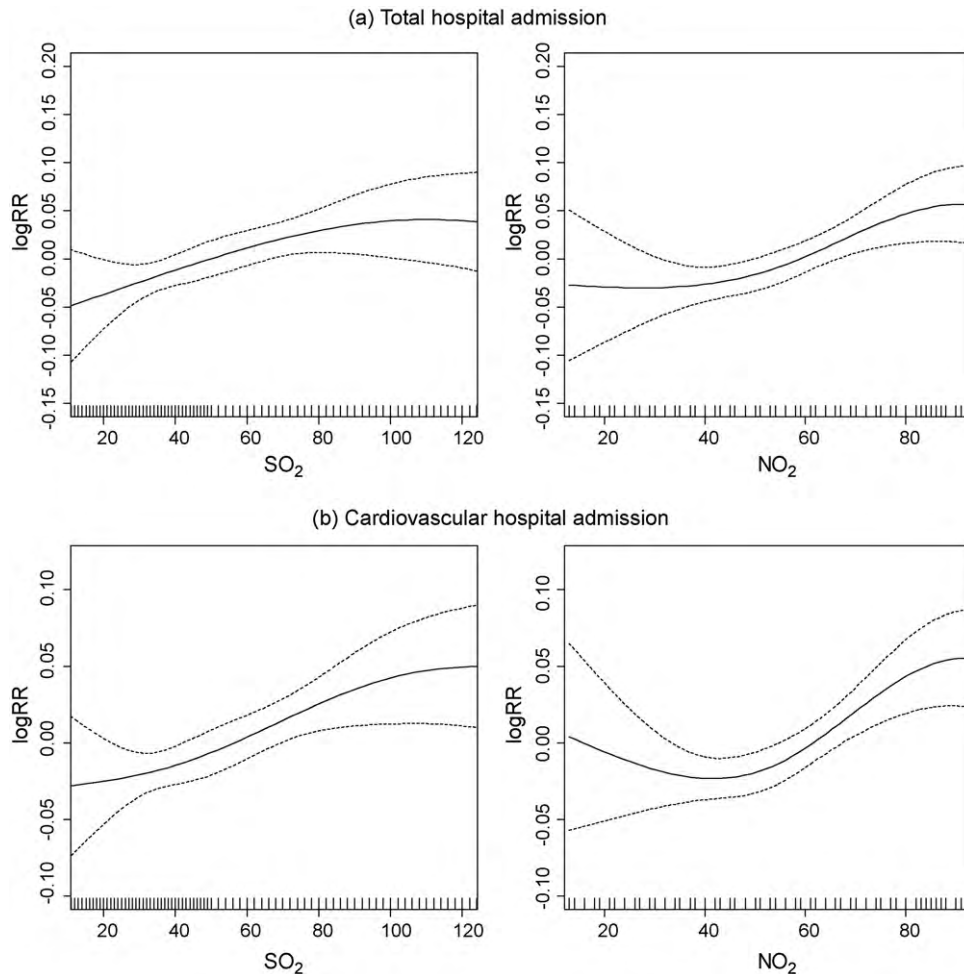
**Table 5**  
Percent increase of hospital admission from all and cardiovascular causes associated with 10  $\mu\text{g}/\text{m}^3$  increase of pollutant concentrations with single and multiple-pollutant models.<sup>a</sup>

		Total	Cardiovascular
PM <sub>10</sub>	Without adjustment	0.18 (−0.15, 0.52)	0.23 (−0.03, 0.48)
	Adjusted for SO <sub>2</sub>	−0.11 (−0.62, 0.39)	−0.04 (−0.43, 0.36)
	Adjusted for NO <sub>2</sub>	−0.14 (−0.63, 0.34)	0.04 (−0.33, 0.42)
SO <sub>2</sub>	Without adjustment	<b>0.63 (0.03, 1.23)<sup>†</sup></b>	<b>0.65 (0.19, 1.12)<sup>†</sup></b>
	Adjusted for PM <sub>10</sub>	<b>0.79 (0.07, 1.50)<sup>†</sup></b>	<b>0.70 (0.05, 1.35)<sup>†</sup></b>
	Adjusted for NO <sub>2</sub>	0.24 (−0.65, 1.13)	0.50 (−0.19, 1.20)
NO <sub>2</sub>	Without adjustment	<b>0.99 (0.10, 1.88)<sup>†</sup></b>	<b>0.80 (0.10, 1.49)<sup>†</sup></b>
	Adjusted for PM <sub>10</sub>	<b>1.27 (0.17, 2.37)<sup>†</sup></b>	<b>0.71 (0.00, 1.41)<sup>†</sup></b>
	Adjusted for SO <sub>2</sub>	0.74 (−0.59, 2.07)	0.28 (−0.76, 1.32)

<sup>a</sup> Single-day lag 5 was used.  
<sup>†</sup>  $p < 0.05$ .

In the season-specific analysis, we generally observed strong associations in the cool season than in the warm season (Table 4). In the cool season, we observed significant associations for total hospital admission with NO<sub>2</sub>, cardiovascular hospital admission with all three pollutants, and respiratory hospital admission with SO<sub>2</sub>. In the warm season, however, we did not find any significant associations. Between-season differences were significant for total and cardiovascular hospital admission with NO<sub>2</sub>.

Table 5 compares the results of the single-pollutant and multiple-pollutant models. For PM<sub>10</sub>, we did not observe significant



**Fig. 1.** Smoothing plots of SO<sub>2</sub> and NO<sub>2</sub> against hospital admission (df = 3). X-axis is the pollutants concentrations ( $\mu\text{g}/\text{m}^3$ ) (single-day lag, L5). The solid lines indicate the estimated mean percentage of change in daily hospital admission, and the dotted lines represent twice the standard error.



associations in both single and multi-pollutant models. The effects of SO<sub>2</sub> on total and cardiovascular hospital admission did not alter much after adding PM<sub>10</sub> into the models; however, when adding NO<sub>2</sub>, the effects of SO<sub>2</sub> decreased and became insignificant. For NO<sub>2</sub>, the effects on hospital admission did not alter much by adding PM<sub>10</sub>; however, its effect became insignificant after adjustment for SO<sub>2</sub>.

Fig. 1 graphically shows the exposure–response relationships for SO<sub>2</sub> and NO<sub>2</sub> (single-day lag 5, L5) with total and cardiovascular hospital admission. For SO<sub>2</sub>, we observed almost linear relationships. For NO<sub>2</sub>, we observed J-shaped exposure–response relationships. It should be noted that even below the levels of current air quality standard in residential area of China (24-h average: 150 µg/m<sup>3</sup> for SO<sub>2</sub> and 80 µg/m<sup>3</sup> for NO<sub>2</sub>), we were still able to observe apparent health effects of SO<sub>2</sub> and NO<sub>2</sub> from the curves.

#### 4. Discussion

Our work showed that outdoor air pollution was associated with both total and cardiovascular hospital admission in Shanghai in 2005–2007. The associations between air pollution and hospital admission appeared to be more evident in the cool season than in the warm season. We found significant effects of gaseous pollutants (SO<sub>2</sub> and NO<sub>2</sub>) after adjustment for PM<sub>10</sub>. We found significant effects of air pollution below the levels of current air quality standard in China. These findings may have implications for environmental and social policies in Shanghai, and for the local government to take steps to protect human health. Our study also emphasizes the need for comprehensive information systems, including both air pollution monitoring and health information sectors, to support such environmental accountability evaluation.

The health effects implicated different lag structures for various pollutants in our study (Table 3), which is consistent with other air pollution morbidity studies in the Asian region [25]. It should be noted that we observed statistically significant associations for some, but not all, lag structures of pollutant concentrations. Further research is needed to clarify the lag structure and magnitude of such effects. We observed greater effects with later lags; this could be explained by the fact that government-provided health care system in Shanghai controls access to hospital facilities and takes more time in referral to hospital of persons with severe disease. Different causes of disease for cardiovascular and respiratory hospital admission may account for the various effect estimates and lag patterns of pollutants on these two morbidity outcomes.

Levels of outdoor air pollution in China are among the highest in the world. In Shanghai, coal accounts for approximately 70% of all energy sources; consequently, air pollution in the city predominantly derives from coal smoke, with PM and SO<sub>2</sub> as the principal pollutants [26]. However, with the rapid increase in the number of motor vehicles in recent years, outdoor air pollution in Shanghai has gradually changed from the conventional coal combustion type to the mixed coal combustion/motor vehicle emission type. In addition, the composition of the motor vehicle fleet in developed countries may differ from that in Shanghai. This, together with other differences such as the widespread use of coal in the city, implies that the air pollution mixture may differ between Shanghai and the developed areas where most air pollution health studies were conducted.

Our finding of stronger association between air pollution and hospital admission in the cool season is consistent with a prior study on air pollution and mortality in Shanghai [6] and several other air pollution health studies in Hong Kong [27,28] and Athens [29], but in conflict with others reporting greater air pollution effects in the warm season [30–31]. In Shanghai, the concentrations of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub> were higher and more variable in the

cool season than in the warm season. Because these three pollutants were highly correlated, greater effects observed during the cool season may also be due to other pollutants that were also at higher levels during that season. Exposure patterns may contribute to our season-specific observation. During the warm season, Shanghai residents use air conditioning (AC) more frequently due to the relatively higher temperature and humidity, thus probably reducing their exposure indoors. For example, in a survey of 1106 families in Shanghai, 32.7% of the families in the winter versus 3.7% in the summer never turn on AC [32]. A previous study in the US shows that higher AC prevalence was associated with lower health effect estimates for PM [33]. In addition, frequent rain in the warm season may reduce time outdoors and thus personal exposure. In contrast, the cool season in Shanghai is drier and less variable, so people are more likely to go outdoors and open the windows. Nevertheless, the fact that more apparent effects of air pollution on both mortality [6] and morbidity outcomes were observed in the cool season in Shanghai suggests that the interaction of air pollution exposure and season should be studied further.

The shape of exposure–response relationships are crucial for public health assessment and there has been growing demand for providing the relevant curves. The relationships may vary by locations, depending on factors such as the air pollution mixture, climate and the health of the studied population [34]. In this Shanghai population, we found significant effects of outdoor air pollution even below the levels of air quality standard in China (150, 150, and 80 µg/m<sup>3</sup> for daily average concentration of PM<sub>10</sub>, SO<sub>2</sub> and NO<sub>2</sub>) (Fig. 1). Therefore, current air quality standards might not be sufficient to protect the public health in Shanghai. Further control of air pollution is likely to result in health benefits. A reduction in morbidity and mortality after the implementation of an intervention program will add evidence to the hypothesis of a causal link between air pollution and ill health.

Although the strongest evidence linking outdoor air pollutants with adverse health effects thus far is for PM [2], this study found stronger health effects of gaseous pollutants (SO<sub>2</sub> and NO<sub>2</sub>) than PM. Moreover, the estimates for SO<sub>2</sub> and NO<sub>2</sub> remained significant after adjustment for PM<sub>10</sub> (Table 5), suggesting that factors other than particle indicators are important for the air pollution mixture in Shanghai. Although it is well-known that SO<sub>2</sub> and NO<sub>2</sub> contribute to PM formation, the current analysis suggests that they are also separately regulated pollutants independently related with adverse health effects. Previously, the independent health effects of SO<sub>2</sub> and NO<sub>2</sub> were extensively reported in China. For example, Xu et al. found that it was SO<sub>2</sub>, not TSP, that was associated with daily mortality in Beijing [9]. Similarly, in Chongqing, Venners et al. found that SO<sub>2</sub> had significant effects on daily mortality even after adjustment for PM<sub>2.5</sub>, while the effect of PM<sub>2.5</sub> diminished after adjustment for SO<sub>2</sub> [8]. Zhang et al. found that concentration of SO<sub>4</sub><sup>2-</sup> in the air was closely associated with chronic disease mortality in Beijing [35]. Similar independent effects of SO<sub>2</sub> were also presented in a European multi-city analysis [36]. The most convincing evidence of the independent health effects of SO<sub>2</sub> thus far is from an intervention study in Hong Kong which showed SO<sub>2</sub> resulting from sulphur-rich fuels had a direct impact on cardiorespiratory deaths [37]. In Shanghai, Chen et al. reported that of all pollutants they examined only NO<sub>2</sub> remained significantly associated with total and cardiovascular mortality after adjustment for any co-pollutants [38]. Most air pollution epidemiologic studies use ambient pollutant concentrations as surrogates of personal exposure; therefore, the observed health effects attributed to SO<sub>2</sub> and NO<sub>2</sub> might actually be a result of exposures to fine particles or traffic-related emissions [39,40]. There may be more misclassification of the average population exposure to PM<sub>10</sub> compared to that of gaseous pollutants. Also, some authors have suggested that the pollutants measured might be better interpreted as indi-

cators of the biologically relevant pollutant mixture and that the best indicators might vary in different geographic areas [40]. To our knowledge, there have been no studies in China examining the associations between ambient SO<sub>2</sub>/NO<sub>2</sub> concentrations, personal exposure to SO<sub>2</sub>/NO<sub>2</sub> and personal PM exposure. At present, we cannot conclude these gaseous pollutants are proxies of particulate pollutant, or they have direct health effects. Nevertheless, a consistent, significant health effect of SO<sub>2</sub> and NO<sub>2</sub> observed in China suggests that the role of outdoor exposure to gaseous pollutants should be investigated further.

Our study has several limitations. We were not able to obtain the age- and gender-specific data for hospital admissions, thus limiting our ability to identify subgroups susceptible to air pollution exposure. As in most previous time-series studies, we simply averaged the monitoring results across various stations as the proxy for population exposure level to air pollution. The simple averaging method may raise a number of issues given that pollutant measurements can differ from monitoring location to monitoring location and that ambient monitoring results differ from personal exposure level to air pollutants [34]. Numerous factors, such as air conditioning and ventilation rate between indoor and outdoor air, may affect the monitoring results from fixed stations as surrogates of personal exposure to air pollutants [41]. The differences between these proxy values and the true exposures are an inherent and unavoidable type of measurement error. We were not able to obtain the monitoring data of ozone, which is an important component of photochemical air pollution. Our assessment of weather conditions was derived entirely from one monitoring station; however, the variability of weather across Metropolitan Shanghai is small, and there would be little reason to expect temperatures or humidity to vary within the city limits. Also, compared with other air pollution morbidity studies in Europe and North America, the data we collected was limited in being only one city, in sample size and in duration. In addition, high correlation between particle (PM<sub>10</sub>) and gaseous pollutants (SO<sub>2</sub> and NO<sub>2</sub>) in Shanghai limited our ability to separate the independent effect for each pollutant.

In summary, short-term exposure to outdoor air pollution was associated with total and cardiovascular hospital admission in Shanghai. As the first air pollution hospital admission study in China, our findings may supplement key scientific information on air pollution-related health effects in China, thereby providing local decision-makers with information needed to set priority of air pollution control measures with the largest health benefits. Further research will be needed to disentangle the effects of the various pollutants and to gain insights into the modification of individual socio-demographic characteristics and season on air pollution health effects.

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## References

- [1] B. Brunekreef, Health effects of air pollution observed in cohort studies in Europe, *J. Expo. Sci. Environ. Epidemiol.* 17 (Suppl. 2) (2007) S61–65.
- [2] M.L. Bell, J.M. Samet, F. Dominici, Time-series studies of particulate matter, *Annu. Rev. Public Health* 25 (2004) 247–280.
- [3] D.W. Dockery, Health effects of particulate air pollution, *Ann. Epidemiol.* 19 (2009) 257–263.
- [4] C.A. Pope, D.W. Dockery, Health effects of fine particulate air pollution: lines that connect, *J. Air Waste Manag. Assoc.* 56 (2006) 709–742.
- [5] Health Effects Institute, Health effects of outdoor air pollution in developing countries of Asia: a literature review, Boston, MA, USA, 2004.
- [6] H. Kan, S.J. London, G. Chen, Y. Zhang, G. Song, N. Zhao, L. Jiang, B. Chen, 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.* 116 (2008) 1183–1188.
- [7] Z. Qian, Q. He, H.M. Lin, L. Kong, D. Liao, J. Dan, C.M. Bentley, B. Wang, Association of daily cause-specific mortality with ambient particle air pollution in Wuhan, China, *Environ. Res.* 105 (2007) 380–389.
- [8] S.A. Venners, B. Wang, Z. Xu, Y. Schlatter, L. Wang, X. Xu, Particulate matter, sulfur dioxide, and daily mortality in Chongqing, China, *Environ. Health Perspect.* 111 (2003) 562–567.
- [9] X. Xu, J. Gao, D.W. Dockery, Y. Chen, Air pollution and daily mortality in residential areas of Beijing, China, *Arch. Environ. Health* 49 (1994) 216–222.
- [10] Z. Xu, D. Yu, L. Jing, X. Xu, Air pollution and daily mortality in Shenyang, China, *Arch. Environ. Health* 55 (2000) 115–120.
- [11] C.M. Wong, N. Vichit-Vadakan, H. Kan, Z. Qian, Public Health and Air Pollution in Asia (PAPA): a multicity study of short-term effects of air pollution on mortality, *Environ. Health Perspect.* 116 (2008) 1195–1202.
- [12] K. Aunan, X.C. Pan, Exposure-response functions for health effects of ambient air pollution applicable for China—a meta-analysis, *Sci. Total Environ.* 329 (2004) 3–16.
- [13] J.W. Dong, X.P. Xu, D.W. Dockery, Association of air pollution with unscheduled outpatient visits in Beijing Longfu Hospital, 1991, *Zhonghua Liu Xing Bing Xue Za Zhi* 17 (1996) 13–16 (in Chinese).
- [14] X. Xu, D.W. Dockery, D.C. Christiani, B. Li, H. Huang, Association of air pollution with hospital outpatient visits in Beijing, *Arch. Environ. Health* 50 (1995) 214–220.
- [15] X. Xu, B. Li, H. Huang, Air pollution and unscheduled hospital outpatient and emergency room visits, *Environ. Health Perspect.* 103 (1995) 286–289.
- [16] F. Dominici, R.D. Peng, M.L. Bell, L. Pham, A. McDermott, S.L. Zeger, J.M. Samet, Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases, *JAMA* 295 (2006) 1127–1134.
- [17] M.L. Bell, K. Ebisu, R.D. Peng, J. Walker, J.M. Samet, S.L. Zeger, F. Dominici, Seasonal and regional short-term effects of fine particles on hospital admissions in 202 US counties, 1999–2005, *Am. J. Epidemiol.* 168 (2008) 1301–1310.
- [18] R.W. Atkinson, H.R. Anderson, J. Sunyer, J. Ayres, M. Baccini, J.M. Vonk, A. Boumgahar, F. Forastiere, B. Forsberg, G. Touloumi, J. Schwartz, K. Katsouyanni, Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. Air Pollution and Health: a European Approach, *Am. J. Respir. Crit. Care Med.* 164 (2001) 1860–1866.
- [19] J. Sunyer, F. Ballester, A.L. Tertre, R. Atkinson, J.G. Ayres, F. Forastiere, B. Forsberg, J.M. Vonk, L. Bisanti, J.M. Tenias, S. Medina, J. Schwartz, K. Katsouyanni, The association of daily sulfur dioxide air pollution levels with hospital admissions for cardiovascular diseases in Europe (The Aphea-II study), *Eur. Heart J.* 24 (2003) 752–760.
- [20] F. Dominici, A. McDermott, T.J. Hastie, Improved semi-parametric time series models of air pollution and mortality, *J. Am. Stat. Assoc.* 468 (2004) 938–948.
- [21] B.A. Brumback, L.M. Ryan, J. Schwartz, L.M. Neas, P.C. Stark, H.A. Burge, Transitional regression models with application to environmental time series, *J. Am. Stat. Assoc.* 449 (2000) 16–28.
- [22] J.M. Samet, F. Dominici, S.L. Zeger, J. Schwartz, D.W. Dockery, The National Morbidity, Mortality, and Air Pollution Study. Part I: Methods and methodologic issues, *Res. Rep. Health Eff. Inst.* (2000) 5–14 (discussion 75–84).
- [23] A. Zeka, A. Zanobetti, J. Schwartz, Individual-level modifiers of the effects of particulate matter on daily mortality, *Am. J. Epidemiol.* 163 (2006) 849–859.
- [24] R Development Core Team, R: A Language and Environment for Statistical Computing, Version 2.8.1, R Foundation for Statistical Computing, Vienna, 2008.
- [25] M.L. Bell, J.K. Levy, Z. Lin, The effect of sandstorms and air pollution on cause-specific hospital admissions in Taipei, Taiwan, *Occup. Environ. Med.* 65 (2008) 104–111.
- [26] B. Chen, C. Hong, H. Kan, Exposures and health outcomes from outdoor air pollutants in China, *Toxicology* 198 (2004) 291–300.
- [27] C.M. Wong, R.W. Atkinson, H.R. Anderson, A.J. Hedley, S. Ma, P.Y. Chau, T.H. Lam, A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared, *Environ. Health Perspect.* 110 (2002) 67–77.
- [28] C.M. Wong, S. Ma, A.J. Hedley, T.H. Lam, Does ozone have any effect on daily hospital admissions for circulatory diseases? *J. Epidemiol. Commun. Health* 53 (1999) 580–581.
- [29] G. Touloumi, E. Samoli, K. Katsouyanni, Daily mortality and “winter type” air pollution in Athens, Greece—a time series analysis within the APHEA project, *J. Epidemiol. Commun. Health* 50 (Suppl. 1) (1996) s47–s51.
- [30] H.R. Anderson, A. Ponce de Leon, J.M. Bland, J.S. Bower, D.P. Strachan, Air pollution and daily mortality in London: 1987–92, *BMJ* 312 (1996) 665–669.
- [31] T.S. Nawrot, R. Torfs, F. Fierens, S. De Henauw, P.H. Hoet, G. Van Kersschaever, H. Kan, Stronger associations between daily mortality and fine particulate air pollution in summer than in winter: evidence from a heavily polluted region in western Europe, *J. Epidemiol. Commun. Health* 61 (2007) 146–149.
- [32] W. Long, T. Zhong, B. Zhang, China: the issue of residential air conditioning, 2007. <http://www.iifir.org/en/doc/1056.pdf>.
- [33] M.L. Bell, K. Ebisu, R.D. Peng, F. Dominici, Adverse health effects of particulate air pollution: modification by air conditioning, *Epidemiology* 20 (2009) 682–686.

- [34] E. Samoli, A. Analitis, G. Touloumi, J. Schwartz, H.R. Anderson, J. Sunyer, L. Bisanti, D. Zmirou, J.M. Vonk, J. Pekkanen, P. Goodman, A. Paldy, C. Schindler, K. Katsouyanni, Estimating the exposure–response relationships between particulate matter and mortality within the APHEA multicity project, *Environ. Health Perspect.* 113 (2005) 88–95.
- [35] J. Zhang, H. Song, S. Tong, L. Li, B. Liu, L. Wan, Ambient sulfate concentration and chronic disease mortality in Beijing, *Sci. Total Environ.* 262 (2000) 63–71.
- [36] K. Katsouyanni, G. Touloumi, C. Spix, J. Schwartz, F. Balducci, S. Medina, G. Rossi, B. Wojtyniak, J. Sunyer, L. Bacharova, J.P. Schouten, A. Ponka, H.R. Anderson, Short-term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. *Air Pollution and Health: a European Approach*, *BMJ* 314 (1997) 1658–1663.
- [37] A.J. Hedley, C.M. Wong, T.Q. Thach, S. Ma, T.H. Lam, H.R. Anderson, Cardiorespiratory and all-cause mortality after restrictions on sulphur content of fuel in Hong Kong: an intervention study, *Lancet* 360 (2002) 1646–1652.
- [38] G. Chen, G. Song, L. Jiang, Y. Zhang, N. Zhao, B. Chen, H. Kan, Short-term effects of ambient gaseous pollutants and particulate matter on daily mortality in Shanghai, China, *J. Occup. Health* 50 (2008) 41–47.
- [39] J.A. Sarnat, K.W. Brown, J. Schwartz, B.A. Coull, P. Koutrakis, Ambient gas concentrations and personal particulate matter exposures: implications for studying the health effects of particles, *Epidemiology* 16 (2005) 385–395.
- [40] J.A. Sarnat, J. Schwartz, P.J. Catalano, H.H. Suh, Gaseous pollutants in particulate matter epidemiology: confounders or surrogates? *Environ. Health Perspect.* 109 (2001) 1053–1061.
- [41] N.A. Janssen, J. Schwartz, A. Zanobetti, H.H. Suh, Air conditioning and source-specific particles as modifiers of the effect of PM(10) on hospital admissions for heart and lung disease, *Environ. Health Perspect.* 110 (2002) 43–49.