Original Article

Association between Ambient Air Pollution and Outpatient Visits for Acute Bronchitis in a Chinese City*

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Abstract

Objective To investigate the short-term association between outdoor air pollution and outpatient visits for acute bronchitis, which is a rare subject of research in the mainland of China.

Methods A time-series analysis was conducted to examine the association of outdoor air pollutants with hospital outpatient visits in Shanghai by using two-year daily data (2010-2011).

Results Outdoor air pollution was found to be associated with an increased risk of outpatient visits for acute bronchitis in Shanghai. The effect estimates of air pollutants varied with the lag structures of the concentrations of the pollutants. For lag06, a 10 μg/m^3 increase in the concentrations of PM_{10}, SO_2, and NO_2 corresponded to 0.94% (95% CI: 0.83%, 1.05%), 11.12% (95% CI: 10.76%, 11.48%), and 4.84% (95% CI: 4.49%, 5.18%) increases in hospital visits for acute bronchitis, respectively. These associations appeared to be stronger in females (P<0.05). Between-age differences were significant for SO_2 (P<0.05), and between-season differences were also significant for SO_2 (P<0.05).

Conclusion Our analyses have provided the first evidence that the current air pollution level in China has an effect on acute bronchitis and that the rationale for further limiting air pollution levels in Shanghai should be strengthened.

Key words: Air pollution; Outpatient visits; Acute bronchitis; Time-series

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INTRODUCTION

Acute bronchitis is an inflammation of the large bronchi (medium-size airways) in the lungs that is usually caused by viruses, bacteria or chemicals and may last several days or weeks[1]. Acute bronchitis is one of the most common causes of hospital visits in large cities. Annually, acute bronchitis (AB) occurrence peaks during winter and is probably associated with air

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pollution[2]. Air pollution exposure has also been linked to increases in reports of respiratory symptoms and increases in the overall number of respiratory infections[3-6]. Many authors have previously found significant associations between the concentrations of air pollutants [i.e., particulate matter less than 10 μm in aerodynamic diameter (PM_{10}), sulfur dioxide (SO_2) and nitrogen dioxide (NO_2)] and adverse health effects. However, few studies have investigated the effects of air pollution on AB, which is the leading cause of infant morbidity. Moreover, the associations between outdoor air pollution and acute bronchitis have not been well documented in the mainland of China, as one of the largest developing countries. In this study, a time-series analysis was conducted to evaluate the effects of PM_{10}, SO_2, and NO_2 on daily hospital visits for acute bronchitis between 2010 and 2011 in urban areas of Shanghai, which is the largest city in China.

METHODS

Data

The daily numbers of outpatient visits for acute bronchitis between January 1, 2010 and December 31, 2011 (730 d) were obtained from the Shanghai Yangpu District Central Hospital (SYDCH), also known as the Yangpu Hospital of Tongji University. With medical services covering approximately 1.3 million residents, the SYDCH is regarded as an important hospital for the diagnosis and treatment of acute and complex diseases in urban areas of Shanghai. The hospital's out-patient and emergency department visits number approximately 1.5 million per year, and the in-patient services of this hospital amount to over 30,000 visits per year. Physicians must submit standard documents that include detailed information such as gender, age, and cause of disease by completing the outpatient visit cards. Then, these cards are sent to SYDCH through the internal computer network. Therefore, the information from the SYDCH database appears to be sufficiently complete and accurate for use in epidemiological studies.

Daily air pollution data, including PM_{10}, SO_2, and NO_2 levels, were obtained from the database of the Shanghai Environmental Monitoring Center (SEMC), which is a government agency responsible for collecting air pollution data in Shanghai. The environmental monitoring system in Shanghai has been certified by the China State Environmental Protection Agency. According to the relevant rules of the Chinese government, the locations of the stations recording pollution measurements should not be in the direct vicinity of traffic or industrial sources of pollution. Tapered element oscillating microbalance (TEOM), ultraviolet fluorescence and chemiluminescence methods were used to measure PM_{10}, SO_2, and NO_2, respectively. The daily (24-h) average concentrations of PM_{10}, SO_2, and NO_2 were collected. For the calculations of 24-h mean concentrations of PM_{10}, SO_2, and NO_2, a minimum of 75% of the 1-h values was required to be available for that particular day.

To adjust for the effects of weather on outpatient visits, meteorological data (i.e., daily mean temperature and relative humidity) were obtained from the database of the Shanghai Meteorological Bureau.

Statistical Analyses

Hospital visits, air pollution and weather were linked by date. Therefore, a time-series analysis was conducted to examine the associations between outdoor air pollutants (PM_{10}, SO_2, and NO_2) and hospital visits for acute bronchitis in Shanghai. Assuming that the Shanghai population changed little over the course of our study period, the daily hospital visit counts followed an approximately Poisson distribution. Quasi-Poisson regression generalized additive models (GAM) with natural spline-smoothing functions was adopted to adjust for long-term and seasonal trends and other time-varying covariates. According to the our previous PAPA[7-9] and CAPES[10-12] protocols, the following covariates were incorporated into the GAM: (1) a natural cubic smooth function of calendar time with seven degrees of freedom (df) per year that excluded unmeasured long-term and seasonal trends; (2) the naturally smooth functions of mean temperature and relative humidity to control for the potential nonlinear confounding effects of weather conditions, and (3) an indicator variable for 'day of the week'.

After the basic models were established, the pollutant variables were then introduced and their effects on hospital visits were analyzed. The lag effects of air pollutants were also considered in building the models because concentrations on a given day and on the several preceding days could affect outpatient counts on that given day[12-13]. The effects of outdoor air pollutants (PM_{10}, SO_2, and NO_2) were examined with different lag (L) structures that included both single-day lags (from L0 to L6) and multiday lag (L01, L02, L03, L04, L05, and L06). For example, in single-day lag models, a lag of zero days (L0) corresponds to the current-day pollutant concentration, and a lag of one day (L1) refers to the previous-day concentration; in multi-day lag models, L01 corresponds to a two-day moving average of pollutant concentration composed of the current and previous day, and L06 corresponds to seven-day moving average of pollutant concentration composed of the current and previous six days. The effects of air pollution were analyzed separately for the warm seasons (from April to September), cool seasons (from October to March), and the entire year. Both single-pollutant models and multi-pollutant models were fit to assess the stability of the effects of the pollutants. As the assumption of linearity between hospital visits and air pollution levels may not be justified, we used smoothing splines with 3 df for pollutant concentrations to graphically describe their relationships[13-15]. To examine the linearity of the curve, we compared the linear and spline models by computing the difference between the deviances of the fitted two models.

All analyses were conducted in R 2.8.1 using the MGCV package. The results are presented as percent changes in daily hospital visits per 10 μg/m^3 increase in pollutant concentration, consistent with the broad literature. The statistical significance of differences between effect estimates of the strata of a potential effect modifier (e.g., the difference between females and males) was tested by calculating the 95% confidence interval as $(\hat{Q}_1 - \hat{Q}_2) \pm 1.96\sqrt{S\hat{E}_1^{\,2} + S\hat{E}_2^{\,2}}$ where $\hat{Q}_1$ and $\hat{Q}_2$ are the estimates for the two categories, and $S\hat{E}_1$ and $S\hat{E}_2$ are their respective standard errors[16].

RESULTS

From 2010 to 2011 (730 d), a total of 58,740 hospital visits for acute bronchitis were recorded. On average, there were approximately 82 hospital visits for acute bronchitis per day in our study area (Table 1). There were few immigrants in our dataset. During our study period, the mean daily average concentrations were 79 μg/m^3 for PM_{10}, 30 μg/m^3 for SO_2, and 56 μg/m^3 for NO_2. The mean daily average temperature and humidity were 17 °C and 68%, reflecting the subtropical climate of Shanghai. Generally, PM_{10}, SO_2, and NO_2 had relatively higher correlation coefficients with each other and were negatively correlated with temperature and humidity (Table 2).

Table 3 shows the results from the single-lag day (L0-L6) and cumulative exposure models (L01, L02, L03, L04, L05, and L06) in terms of the percent increases in hospital visits for acute bronchitis per 10 μg/m^3 in pollution. The effect estimates varied for different lag structures of pollutant concentrations. Statistically significant relationships between hospital visits and PM_{10} pollution were observed in most lag day models (with the exceptions of L0, L1, L01, and L02). Hospital visits for acute bronchitis were significantly associated with SO_2 and NO_2 pollution at all lags we examined. For lag06, 10 μg/m^3 increases in the concentrations of PM_{10}, SO_2, and NO_2 corresponded to 0.94% (95% CI: 0.83%, 1.05%), 11.12% (95% CI: 10.76%, 11.48%), and 4.84% (95% CI: 4.49%, 5.18%) increases in hospital visits for acute bronchitis, respectively.

Table 1. Summary Statistics for the Daily Hospital Visits for Acute Bronchitis, Air Pollutant Concentrations and Weather Conditions in the Study Area (2010-2011)

Items	Mean±SD	Minimum	*P*(25)	Median	*P*(75)	Maximum
Acute bronchitis	94±72	0	42	82	125	579
Air pollutants concentrations (24-h average)						
PM_{10} (μg/m^3)	79±61	7	44	64	96	600
SO_2 (μg/m^3)	30±17	6	16	26	40	134
NO_2 (μg/m^3)	56±21	16	42	54	69	152
Meteorological measures (24-h average)						
Temperature (°C)	17±9	-2	9	18	25	36
Humidity (%)	68±13	23	60	69	78	95

Note. *P*(25): 25th percentile; *P*(75): 75th percentile.

Table 4 shows the results of the analyses stratified by age, sex, and season. The three outdoor air pollutants (PM_{10}, SO_2, and NO_2) had significant effects on acute bronchitis in residents aged 5-65 and those aged 66 or above; however, the differences in effect estimates were only statistically significant for SO_2. Significant associations between hospital visits and all three ambient pollutants were also observed in both males and females. Notably, the between-sex difference in hospital visit was not statistically significant for PM_{10}. In the season-specific analyses, significant associations between hospital visits and all three pollutants were generally observed during both the cool and warm seasons. Between-season differences were significant for SO_2, but not for PM_{10} and NO_2.

Table 2. Pearson Correlation Coefficients for the Association between Daily Air Pollutant Concentrations and Weather Conditions in Metropolitan Shanghai (2010-2011)

Items	SO_2	NO_2	Temperature	Relative Humidity
PM_{10}	0.55	0.55	-0.20	-0.32
SO_2	-	0.67	-0.41	-0.45
NO_2	-	-	-0.41	-0.19
Temperature	-	-	-	0.23

Table 3. Percent Increases (Means and 95% CI) in Daily Hospital Visits for Acute Bronchitis Associated with 10 μg/m^3 Increases in Pollutant Concentrations in Shanghai in 2010-2011

Lag (L)	PM_{10} (Means and 95% CI)	SO_2 (Means and 95% CI)	NO_2 (Means and 95% CI)
L0	-0.13 (-0.29, 0.13)	0.31 (0.04, 0.58)	0.30 (0.09, 0.53)
L1	-0.04 (-0.10, 0.03)	1.45 (1.20, 1.70)	0.46 (0.25, 0.68)
L2	0.31 (0.25, 0.38)	2.93 (2.69, 3.17)	1.19 (0.98, 1.41)
L3	0.36 (0.30, 0.42)	4.82 (4.58, 5.06)	2.55 (2.34, 2.77)
L4	0.31 (0.24, 0.38)	4.82 (4.57, 5.06)	2.18 (1.96, 2.40)
L5	0.65 (0.59, 0.72)	3.69 (3.45, 3.92)	1.85 (1.67, 2.07)
L6	0.51 (0.45, 0.58)	3.73 (3.49, 3.97)	1.15 (0.93, 1.36)
L01	-0.09 (-0.18, 0.07)	1.27 (0.97, 1.56)	0.52 (0.27, 0.76)
L02	0.01 (-0.16, 0.18)	2.88 (2.28, 3.49)	1.15 (0.62, 1.68)
L03	0.20 (0.02, 0.45)	7.28 (6.94, 7.61)	3.31 (3.00, 3.62)
L04	0.35 (0.25, 0.45)	7.28 (6.94, 7.61)	3.31 (3.00, 3.62)
L05	0.70 (0.50, 0.91)	9.28 (8.59, 9.96)	4.29 (3.65, 4.94)
L06	0.94 (0.83, 1.05)	11.12 (10.76, 11.48)	4.84 (4.49, 5.18)

Table 4. Age-, Gender-, and Season-Specific Percent Increases in Daily Hospital Visits for Acute Bronchitis Associated with 10 μg/m^3 Increases in Pollutant Concentrations (lag06) in Shanghai (Means and 95% CI)

Items	PM_{10}	SO_2	NO_2
Age group			
5-65	0.83 (0.69, 0.96)	12.66 (12.22, 13.09)*	4.44 (4.02, 4.85)
66-	1.14 (0.94, 1.34)	7.82 (7.15, 8.49)*	5.54 (4.92, 6.16)
Sex			
Male	0.89 (0.72, 1.06)	9.90 (9.33, 10.47)*	4.08 (3.55, 4.61)*
Female	0.99 (0.84, 1.13)	12.05 (11.58, 12.53)*	5.46 (5.00, 5.91)*
Season			
Cool[a]	1.13 (0.98, 1.29)	6.56 (6.13, 6.98)*	6.27 (5.78, 6.77)
Warm[b]	1.47 (1.30, 1.65)	17.19 (16.36, 18.02)*	5.75 (5.19, 6.31)

Note. [a]Cool season: from November to April. [b]Warm season: from May to October. *Significant between-group difference (P<0.05).

Table 5 compares the results of the single-pollutant and multiple-pollutant models. The effects of PM_{10} on hospital visits decreased after adding NO_2 into the models; however, following the addition of SO_2 the effects of PM_{10} became insignificant. Regarding SO_2, a significant association was observed in either the single or multi-pollutant model, and the effects were similar after the addition of PM_{10} and NO_2 into the models. The effects of NO_2 on hospital visits were altered little by the addition of PM_{10}; however, the effect of NO_2 decreased and became insignificant after adjusting for SO_2.

Figure 1 graphically illustrates the concentration-response relationships of the air pollutants (multi-day lag 6, L06) with hospital visits for acute bronchitis. Nearly linear relationships were observed for the three outdoor air pollutants (PM_{10}, SO_2, and NO_2). Significant differences were identified between the spline model and linear model; therefore, these curves were likely to be linear. Notably, we were able to observe apparent health effects of these pollutants in the curves even below the levels of the current air quality standards for residential areas of China.

DISCUSSION

These time-series analyses revealed that outdoor air pollution (PM_{10}, SO_2, and NO_2) was associated with hospital visits for acute bronchitis in Shanghai in 2010-2011. The three outdoor air pollutants (PM_{10}, SO_2, and NO_2) significantly affected acute bronchitis in both age groups. Moreover, we observed significant associations between hospital visits and these pollutants in both sexes and in both the cool and warm seasons. We also found significant effects of gaseous pollutants (SO_2 and NO_2) after adjusting for PM_{10}.

Ambient air pollution in large cities has changed from the conventional coal combustion type to the mixed coal combustion/motor vehicle emission type. In Shanghai, air pollution in the city is predominantly derived from coal smoke, and PM and SO_2 are the principal pollutants. Moreover, ambient air $NO_{(x)}$ levels have been increasing due to the increased number of motor vehicles[17]. We found that significant effects of air pollution were present below the levels of the current air quality standards for Shanghai. Our study may have implications for environmental and social policies in this metropolitan city, and may as well suggest that the local government should take steps to protect human health. Moreover, our findings emphasize the need for comprehensive information systems that include both health information and air pollution measurements to support the evaluation of environmental accountability.

Table 5. Percent Increases in Hospital Visits for Acute Bronchitis Associated with 10 μg/m^3 Increases in Pollutant Concentrations (lag06) for the Single- and Multiple-pollutant Models

Items	Adjustment	Total
PM_{10}	Without adjustment	0.94 (0.83, 1.05)
	Adjusting for SO_2	-0.07 (-0.21, 0.14)
	Adjusting for NO_2	0.19 (0.05, 0.33)
	Adjusting for SO_2+NO_2	-0.44 (-0.93, 0.05)
SO_2	Without adjustment	11.12 (10.76, 11.48)
	Adjusting for PM_{10}	10.24 (9.82, 10.66)
	Adjusting for NO_2	9.50 (9.06, 9.95)
	Adjusting for PM_{10}+NO_2	12.47 (11.57, 13.36)
NO_2	Without adjustment	4.84 (4.49, 5.18)
	Adjusting for PM_{10}	4.31 (3.88, 4.74)
	Adjusting for SO_2	-0.06 (-0.49, 0.36)
	Adjusting for PM_{10}+SO_2	-0.57 (-1.50, 0.36)

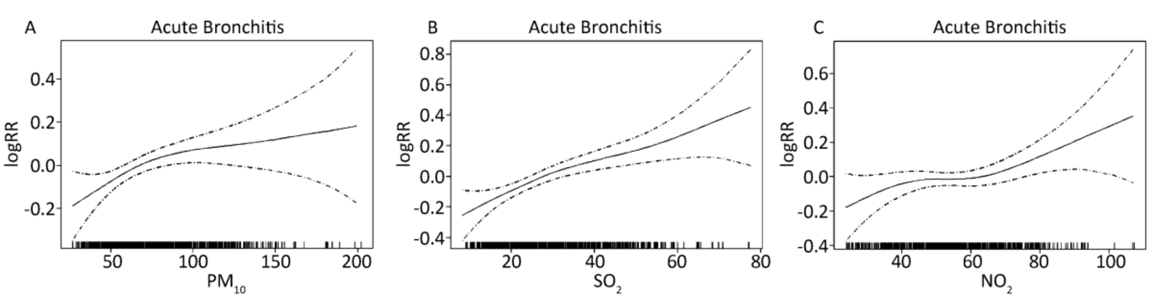

Figure 1. Smoothed plots of air pollutants against outpatient counts. The X-axes indicate the pollutant concentrations (μg/m^3) (multi-day lag, L06). The solid lines indicate the estimated mean percentage changes in daily outpatient counts, and the dotted lines represent twice the standard error. A: PM_{10}; B: SO_2; C: NO_2.

Our models indicated that the health effects of the various pollutants (PM_{10}, SO_2, and NO_2) followed different lag structures (Table 3); and these findings are consistent with those of previous air pollution morbidity studies in Asian countries[18]. Notably, we did not observe statistically significant associations in all pollutant concentration lag structures. More research is needed to clarify the lag structures and magnitudes of these effects[13]. Additionally, we observed greater effects with larger lags, which might be attributable to the fact that the government-provided healthcare system in Shanghai controls access to hospital facilities and requires more time to refer persons with severe diseases to hospitals[14].

In the US and Europe, many patients do not visit doctors in local clinics. Additionally, regular outpatient visits are often scheduled by appointment. As a result, the outpatient records from hospitals in the US and Europe may not reliably reflect the true morbidities. Notably, these two factors restrict the potential for epidemiologic studies of the acute effects of air pollution on outpatient visits in developed countries. However, in China, hospital visits are typically unscheduled and provided on a first-come, first-served basis. The present study takes advantage of China's medical system in which patients seek medical care in their designated local hospitals. Thus, the hospital records used in our study provided reliable morbidity information for a geographically defined population and offered the opportunity to evaluate the association between daily hospital outpatient visits and air pollution[13].

Recently, there have been many studies concerned with the potential mechanisms linking air pollution and respiratory diseases. Air pollutants can, through oxidant effects on the mitochondria, induce apoptosis or the necrosis of macrophages and respiratory epithelial cells, which may decrease the host’s defenses against respiratory infection or increase airway reactivity[19]. Karr and his colleagues evaluated the effects of several air pollutants and their sources on infant bronchiolitis and found that air pollutants from several sources might increase the incidence of infant bronchiolitis requiring clinical care. Moreover, traffic, local point source emissions, and wood smoke might contribute to this disease[6]. Cai and his colleagues reported that prior SO_2 exposure promoted airway inflammation and subepithelial fibrosis following repeated ovalbumin challenge[3]. Mehta and his colleagues evaluated and compared association lag structures between daily ambient levels of nitrogen dioxide (NO_2) and respiratory symptom-related doctor visits in adults with different patterns of underlying chronic respiratory disease. These authors found that hospital visits dramatically increased over the first week following a 10 μg/m^3 increase in NO_2 concentration[20]. These findings demonstrated that outdoor air pollution affected the respiratory system. Our analyses are consistent with these studies and provide the first evidence that outdoor air pollutants (PM_{10}, SO_2, and NO_2) affect hospital visits for acute bronchitis in China.

We found that the effects of SO_2 were more serious among female residents aged 5-65 and during the warm season. In contrast, the effects of NO_2 were greater among residents aged 66 or above and during the cool season. We also observed greater effects of outdoor air pollutants (PM_{10}, SO_2, and NO_2) in females than in males, although this difference was not statistically significant for PM_{10}. Previous studies have also reported greater effect estimates for PM in women than in men[7,21], although effect modification by sex remains inconclusive[22]. The observed vulnerability of women may be attributable to greater deposition of fine particles, greater airway hyper-responsiveness to oxidants, or relatively lower socioeconomic status[7,22].

Our findings that the associations among PM_{10}, SO_2, and hospital visits for acute bronchitis were stronger in the warm season are consistent with previous studies that reported greater air pollution effects during the warm season[18,23-24]. However, the effects of NO_2 were greater during the cool season; and this finding is also consistent with several other air pollution and health studies in Hong Kong[25-26] and Athens[27]. Because the concentrations of these three pollutants were highly correlated, the seasonal differences in the effect sizes of the examined pollutants may also have been due to other pollutants that were also elevated during a particular season. Exposure patterns may also have contributed to our season-specific observations. Nevertheless, the apparent effects of air pollution on acute bronchitis outcomes in Shanghai indicate that the interaction of air pollution exposure with season should be further studied.

Although the strongest evidence linking outdoor air pollutants to adverse health effects that is currently available is related to PM[15], we observed greater health effects of gaseous pollutants (SO_2 and

NO_2) compared to PM. The effects of SO_2 and NO_2 on hospital visits were altered little by the addition of PM_{10} (Table 5), which indicates that the other pollutants were also critical in Shanghai. It has been suggested that SO_2 and NO_2 may contribute to the formation of PM; however, our analyses have demonstrated that SO_2 and NO_2 are separately regulated pollutants that are independently related to adverse health effects. To our knowledge, there have been no studies examining the associations between ambient SO_2 and NO_2 concentrations and hospital visits for acute bronchitis in China. Nevertheless, the significant health effects of SO_2 and NO_2 observed in Shanghai suggest that the role of exposure to outdoor gaseous pollutants should be further investigated.

The shapes of the concentration-response relationships are crucial for public health assessment, and there has been a growing demand for researchers to provide these curves. The relationships may vary by location and depend on factors such as air pollution mixture, climate, and the health of the studied population[14,28]. In this Shanghai population, we found significant effects of outdoor air pollution at pollution levels that were below the levels of the air quality standards in China (150, 150, and 80 μg/m^3 for the daily average concentration of PM_{10}, SO_2, and NO_2, respectively) (Figure 1). Therefore, the current air quality standards might be insufficient for protecting public health in Shanghai. Further control of air pollution is likely to result in health benefits. Reductions in morbidity and mortality following the implementation of interventional programs will add support to the hypothesis that a causal link exists between air pollution and ill health[14].

Our study has several strengths. First, our study is the first in China to link air pollutants (PM_{10}, SO_2, and NO_2) with acute bronchitis. Second, most of the previous studies that have related air pollution exposure to acute bronchitis have been carried out in infants[6,29-30]. Thus, the results of these studies may not reflect the effects of pollutant exposure on acute bronchitis in the general population, particularly among healthy persons. Third, most prior studies have considered only hospital admissions or inpatients; outpatient visits had not been comprehensively analyzed, which may have resulted in selective bias. Fourth, we were able to obtain the age- and gender-specific data about the hospital visits for acute bronchitis, which enabled us to identify the subgroups that are susceptible to air pollution exposure.

Our study has several limitations. First, as in most previous time-series studies, we simply averaged the monitoring results across various stations as a proxy for population air pollution exposure levels. This simple averaging method may raise a number of issues given that pollutant measurements can differ between monitoring locations and that ambient monitoring results differ from personal air pollutant exposure levels[14,28]. Numerous factors, such as differences between indoor and outdoor air due to air conditioning and ventilation rates, may affect the validity of using monitoring results from fixed stations as proxies for personal exposure to air pollutants[13,31]. The differences between these proxy values and the true exposures may have substantial implications for interpreting time-series air pollution studies, although one study suggested that this measurement error would generally tend to bias estimates downwards[13,32]. Second, our analysis was restricted to a large Chinese city, and the health data were collected from a tertiary general hospital. Future studies of air pollutants should include a greater number of large cities in addition to small cities and rural areas. Third, the strong correlations between particle (PM_{10}) and gaseous pollutants (SO_2 and NO_2) concentrations in Shanghai limited our ability to separate the independent effect of each pollutant[14]. Fourth, the data on flu and allergy were not available in this study, which might have confounded our results.

In summary, short-term exposure to outdoor air pollution (PM_{10}, SO_2, and NO_2) was associated with hospital visits for acute bronchitis in Shanghai. These findings have provided information about the health effects of air pollution in Shanghai, China and might have implications for local environmental and social policies. Further research will be needed to disentangle the effects of the various pollutants and to gain insights into the differences in the effects of air pollutions on health due to individual socio-demographic characteristics and seasons.

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