



Air pollutants and asthma patient visits: Indication of source influence

Huibin Guo^{a,*}, Sijing Huang^b, Minxuan Chen^a

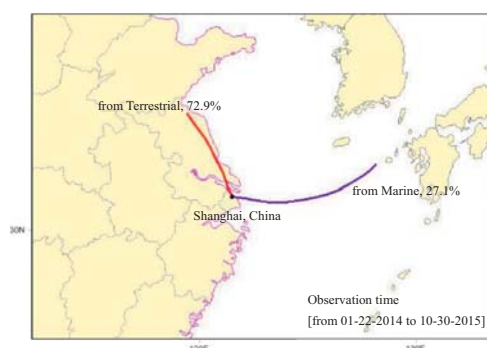
^a Department of Environmental Science and Engineering, Fudan University, Shanghai 200032, China

^b Department of Obstetrics and Gynecology, The First Affiliated Hospital of Xiamen University, Xiamen, China

HIGHLIGHTS

- All of the pollutants except O₃ mainly come from terrestrial during observation.
- All of the pollutants except NO₂ displayed the highest effect for relative risk of asthma in the spring.
- PM_{2.5} and CO are major pollutant affecting the relative risk of asthma patient visits in Shanghai.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:

Received 8 October 2017

Received in revised form 3 December 2017

Accepted 24 December 2017

Available online xxxx

Editor: SCOTT SHERIDAN

Keywords:

Terrestrial and marine source

Air pollutants

Asthma patient visits

Shanghai

ABSTRACT

Background: Sources of air pollutants are significant factors for adverse health effect. Few current studies explored the linking of sources influence and ambient pollutants to asthma patient visits in Shanghai, China.

Objectives: This study explored the associations between short-term exposures to ambient pollutants and asthma morbidity with terrestrial and marine source influence in Shanghai.

Methods: Generalized additive model (GAM) was used to explore the association of daily patient visits and ambient pollutants. These analyses were calculated in R statistical software in mgcv package. PSCF modeling was used to locate potential source areas contributing to the concentrations of pollutants.

Results: We found that per IQR of PM_{2.5}, PM₁₀, NO₂, SO₂, O₃ and CO in terrestrial source were associated with an increase of 6.63% (95% CI: −0.27% to 14%), 6.48% (95% CI: 0.06% to 13.3%), 1.68% (95% CI: −2.68% to 6.24%), 2.81% (95% CI: −1.42% to 7.22%), −0.60% (95% CI: −5.94% to 5.04%) and 16.6% (95% CI: 8.68% to 25.2%), respectively in asthma patient visits. Per IQR of PM_{2.5}, PM₁₀, NO₂, SO₂, O₃ and CO in marine source were associated with an increase of 5.34% (95% CI: 0.42% to 10.5%), 3.84% (95% CI: 0.08% to 7.74%), 3.21% (95% CI: −0.92% to 7.52%), 2.58% (95% CI: −1.02% to 6.30%), 1.42% (95% CI: −3.10% to 6.15%) and 8.81% (95% CI: 2.56% to 15.4%). The PSCF show all of the pollutants except O₃ mainly come from terrestrial during observation. We also found that all of the pollutants except NO₂ displayed the highest effect in the spring for relative risk of asthma morbidity.

Conclusions: Ambient air pollutants that cause an increase in asthma patient visits, such as PM_{2.5}, PM₁₀, NO₂, SO₂ and CO are mainly produced from terrestrial sources, while O₃ is primarily from marine sources. The association of ambient pollutants and asthma patient visits is closely related with seasons, especially with spring. PM_{2.5} and CO are major air pollutants increasing the relative risk of asthma patient visits in Shanghai.

© 2017 Published by Elsevier B.V.

* Corresponding author.

E-mail address: 16110740004@fudan.edu.cn (H. Guo).

1. Introduction

Exposure to ambient air pollution affects a range of clinical aspects of asthma from 2010 (Deng et al., 2016; Mirabelli et al., 2016). Acute exposure to particulate matter with an aerodynamic diameter $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) is linked to increase risk of asthma mortality, pneumothorax and respiratory failure exacerbation (Jouneau et al., 2014; Ko et al., 2007; Liu et al., 2016; Wang et al., 2016). Epidemiological studies also suggest that exposure to nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and ozone (O_3) may increase asthma morbidity (Bao et al., 2014; Dijkema et al., 2016; Wigenstam et al., 2016). The children, elderly and those with potential diseases, for example, asthma diseases, are particularly susceptible to affect the health of PM and gaseous pollutants (Cakmak et al., 2011; Ding et al., 2017). However, current evidences for the hazards of PM and gaseous pollutants from different sources on asthma patients are inconclusive (Guarnieri and Balmes, 2014).

Understanding the relative contributions to ambient air pollutants from anthropogenic and natural sources, as well as terrestrial and marine sources, is imperative to make realistic decisions about reducing their health impact on human health. Regarding terrestrial sources, recent literatures have showed a possible effect of the traffic emission on asthma morbidity (Delfino et al., 2014). For example, 348.19 million tons of coal equivalent was consumed by the transport sector in China in 2013, which led to serious air pollution (Lu et al., 2015). Specifically, the emissions of CO, NO_x and PM from passenger vehicles were 18.95, 18.89 and 0.12 million tons, respectively. Such emission levels exceed the global and national standards (Vahlsing and Smith, 2012). Empirical evidence suggests that transport-related air pollutants have serious effects on human health, by increasing the risk of lung cancer (Reungoat et al., 2003), respiratory (Ramos et al., 2016) and cardiovascular disease (Bonyadi et al., 2016). Accordingly, air pollution generated from traffic-related source is responsible for a significantly excessive number of deaths and hospital admissions. The emissions from the combustion of biomass and coal in the houses where people resides were also found to be caused high asthma morbidity (Jie et al., 2014). Other studies have evaluated the sources of exposure to air pollutants and found increase in asthma morbidity risk with thermal power plants (Li et al., 2011), industrial (Morin et al., 2012) and diffused biomass burning (Laumbach and Kipen, 2012). Regarding marine sources, they are also a major sources of air pollutants that affect the health of people living in the neighborhood of the source and also contribute to regional air pollution problems. Marine sources include marine vessels, locomotives, trucks etc. (Bailey and Solomon, 2004).

China, is the largest developing country, and its economic expansion has led to a dramatic increase in emissions of ambient air pollutants. As a result, China is now facing the worst air pollution levels, which cause public health problems (Tao et al., 2014). The inhabitants of some of the most developed and largest cities, most notably Beijing (Gao et al., 2015), Shenyang (Zhai et al., 2013), Shanghai (Shan et al., 2016) and other developed cities (Wu et al., 2016) are suffering from severe asthma. With the rapid industrialization and urbanization in China, some environmental troubles are becoming vital factors of asthma increase (Tan and Bernstein, 2014). Previous studies investigated the association of ambient air pollutants with hospital outpatient and emergency room visits (Pan et al., 2014), but the impact of the source variation in the association between asthma and air pollutants has not been studied in detail. To date, to the best of our knowledge, few studies have investigated the association between asthma patient visits and levels of air pollutants generated from both terrestrial sources and marine sources in Shanghai.

The aim focus of the present study was to investigate the correlation between sources of air pollutants and asthma patient visits in Shanghai, in particular terrestrial sources and marine sources.

2. Methods

2.1. Study area

Shanghai is the most famous city in China, and is located in the Yangtze River Delta in east China. The city has a moderate subtropical climate, with abundant rainfall and distinct seasons. The population of Shanghai at the end of 2014 was 24.26 million inhabitants, with an area of 6341 sq. km. The study areas comprise the eight urban districts of Shanghai (259 km²). These urban districts are Putuo, Yangpu, Luwan, Qingpu, Hongkou, Jing'an, Xuhui, and Pudong. The data of the cases of asthma in this study were obtained from Shanghai Pulmonary Hospital, the only a pulmonary hospital in Shanghai. These urban districts were selected to be investigated because of their adequate air pollutants monitoring data.

2.2. Asthma patient visits

The data of asthma patient visits were collected from Shanghai Pulmonary Hospital, including 7200 asthma patient visits. Asthma patient visits refer to all the clinic visits who related respiratory disease symptoms, which is suspected or confirmed in asthma. The cases were selected basing on the code in International Classification of Diseases (ICD). The basic information, including sex, date of admission, diagnostic and residential address was used in this study. According to the residential address, the patients who lived in Shanghai were included.

2.3. Environmental data

According to relevant rules of the Chinese government, these stations should not be in the neighborhood of industrial or traffic source. In addition, the local pollution should not affect the location and should avoid waste-burning boilers, furnaces and buildings. If a station had $>25\%$ of the values missing for the whole period of analysis, the whole data should be excluded from the analysis. The meteorological data were obtained from the Shanghai Meteorological Bureau, including daily mean temperature and relative humidity. The data were collected according to the World Meteorological Organization (WMO) standard. We testify that the data were representative and authentic.

2.4. Statistical analysis

From January 22, 2014 to October 30, 2015 (500 d of daily patient counts except weekend, around 647 d of air pollutants and meteorological data), a total of 7200 emergency room visits were recorded in the study population, including a mean male (~ 7) and female (~ 7) individuals per day. The association between air pollution and asthma patient visits were examined by GAM methods. Participants who have asthma are included. The data from the weekends and holidays were deleted because the collecting stations were not open on those days. Air pollutants data were obtained from the Shanghai Environmental Monitoring Center (SEMC), which provides representative data. Daily mean temperature and relative humidity were obtained from the Shanghai Meteorological Bureau in the study area.

In some developed countries, for example European countries and the US, some patient visits are usually scheduled by appointment. However, patient visits records from a hospital may not reliably reflect the real morbidity. In China, especially in Shanghai, hospital patient visits usually are unscheduled, and patient visits are first-come first-serve basis. Thus, it represents an advantageous approach for data collection.

The Pearson correlation coefficients were computed to study the association between air pollutants and asthma because they may influence the asthma morbidity. The Pearson correlation coefficients were used to assess the inter-relations between air pollutants. The daily asthma patient visits are attributed to small probability event, and they fit a Poisson distribution. In this study, GAM was used to explore the

association between daily patient visits and air pollutants. In order to better understand the association between asthma and air pollutants, there are two models that need to be established. First, the influence of air pollutants on asthma patient visits were studied based on the data of the asthma admissions in each season. The degree of freedom is 6 because of the data reduction. The corresponding model is described by Eq. (1).

$$\log(x) = \alpha + s(t, df = 4) + DOW + s(T, df = 6) + s(H, df = 3) \quad (1)$$

Where, α is patient visits ~ air pollution; s is smoothing parameter; t is time (d); T is temperature (K); H is humidity (%); df is degree of freedom; DOW is the day of the week;

Second, the influence of air pollutants on asthma patient visits were studied based on the data of asthma admissions and the marine and terrestrial sources, and the corresponding model is described by Eq. (2).

$$\log(x) = \alpha + s(t, df = 6) + DOW + s(T, df = 6) + s(H, df = 3) \quad (2)$$

All analyses were calculated using the R statistical software in the mgcv package. The corresponding equations were input into the R software.

The PSCF modeling was used to assess the potential contribution source of common air pollutants, which is given by following Eq. (3),

$$PSCF_{ij} = \frac{m_{ij}}{n_{ij}} \quad (3)$$

Where, n_{ij} is the sum of trajectory endpoints that fall in the ij th grid cell, and m_{ij} is a subclass of n_{ij} . The $PSCF_{ij}$ indicate regions of potential contribution for the pollutant. Generally, $PSCF_{ij}$ values are thought to be low (<0.5) and high (>0.5).

The weighting function W_{ave} was applied to minimize the uncertainties causing by small n_{ij} values, which is described as (4):

$$W_{ij} = \begin{cases} 1.0 & 3n_{ave} < n_{ij} \\ 0.7 & 1.5n_{ave} < n_{ij} < 3n_{ave} \\ 0.42 & 0.75n_{ave} < n_{ij} < 1.5n_{ave} \\ 0.17 & n_{ij} < 0.75n_{ave} \end{cases} \quad (4)$$

A 36-h backward trajectory was calculated every 5-h period (at 23, 18, 13, 08 and 03 o'clock) to identify potential regional contributors of common air pollutants. The analysis was initiated at an altitude of 500 m. the grid cells were split into $0.5^\circ \times 0.5^\circ$.

3. Results and discussions

3.1. Influence of air pollutants on asthma patient visits

The descriptive statistics for the number of asthma patients and environmental variables are summarized in Table 1. During the study period, the daily mean temperature and relative humidity were 18 °C and 70%, respectively, reflecting the subtropical climate of Shanghai. The daily mean concentration of PM_{10} , O_3 , SO_2 , NO_2 and CO were 68.3 $\mu g/m^3$, 106 $\mu g/m^3$ (8-hour average value), 16.5 $\mu g/m^3$, 43.7 $\mu g/m^3$ and 0.78 mg/ m^3 , respectively. Additionally, the daily mean $PM_{2.5}$ concentration is 50.5 $\mu g/m^3$, which is around 5 times higher than the Global Guideline (10 $\mu g/m^3$) established by the World Health Organization (WHO). The NO_2 concentration was higher than the Grade II national standard (40 $\mu g/m^3$). Recently, there have been many studies on the potential mechanisms linking air pollution and asthma (Poynter et al., 2006). For example, PM was found to cause lung damage and breathing problems and trigger asthma when it is inhaled (Mazzarella et al., 2012). Also, O_3 was shown to cause airway inflammation and damages lung tissues, which can lead to breathing problems including coughing, wheezing, and chest pain (Yoda et al., 2014). O_3 was also proven to increase the immune response to allergens in some individuals (Tenland

Table 1

Summary statistics of asthma patient visits and air pollutants.

	No.	Mean	Min	P(25)	Median	P(75)	Max
Daily patient counts							
Total	500	14.4	1	8	13	21	40
Male	500	7.1	0	3	7	10	24
Female	500	7.3	0	4	7	10	24
Air pollutants							
$PM_{2.5}$ ($\mu g/m^3$)	647	50.5	5	28	42	65.5	199
PM_{10} ($\mu g/m^3$)	644	68.3	6	42	57	85.2	261
O_3 ($\mu g/m^3$)	647	106	14	76	101	131	265
SO_2 ($\mu g/m^3$)	647	16.5	6	11	13	19	75
NO_2 ($\mu g/m^3$)	647	43.7	6	30	40	53	139
CO ($\mu g/m^3$)	647	780	360	600	700	900	2200
Meteorologic							
Temperature (°C)	647	18	−1	12	20	24	34
Humidity (%)	647	70	28	60	72	80	99

24-hour average for $PM_{2.5}$, PM_{10} , SO_2 , NO_2 , CO; 8-hour average for O_3 .

et al., 2016). In addition, NO_2 was found to irritate the lungs, causing bronchitis and pneumonia (Gamon et al., 2014). Exposure to SO_2 was demonstrated to cause breathing problems and lung damage, especially in those individuals with asthma, bronchitis, and emphysema (Yun et al., 2015). These findings revealed possible pathways whereby air pollutants can affect asthma patient visits. With increased industrialization and urbanization in Shanghai, the levels of ambient air pollutants have been increasing in recent years (Xie et al., 2016). Importantly, the highest rate of asthma in China was found in Shanghai at 7.6%. The data from Shanghai shows that asthma morbidity has increased from 2.1% in 1990 to 10.2% in 2013. This finding indicates that high air pollutants concentration ($PM_{2.5}$, PM_{10} , SO_2 , NO_2 , etc.) may induce an increase in asthma patient visits.

Table 2 presented Pearson correlation coefficients between air pollutants. $PM_{2.5}$, PM_{10} , SO_2 , NO_2 and CO had obvious correlations with each other; $PM_{2.5}$ and PM_{10} with $r = 0.90$, $P < 0.01$; $PM_{2.5}$ and SO_2 with $r = 0.73$, $P < 0.01$; $PM_{2.5}$ and NO_2 with $r = 0.69$, $P < 0.01$; $PM_{2.5}$ and CO with $r = 0.86$, $P < 0.01$; PM_{10} and SO_2 with $r = 0.79$, $P < 0.01$; PM_{10} and NO_2 with $r = 0.69$, $P < 0.01$; PM_{10} and CO with $r = 0.76$, $P < 0.01$; NO_2 and SO_2 with $r = 0.77$, $P < 0.01$; CO and SO_2 with $r = 0.74$, $P < 0.01$; and CO and NO_2 with $r = 0.75$, $P < 0.01$. Moreover, O_3 presented positive correlations with $PM_{2.5}$ ($r = 0.10$, $P < 0.01$) and PM_{10} ($r = 0.12$, $P < 0.01$), but negative correlations with gaseous compounds such as NO_2 ($r = -0.16$, $P < 0.01$), SO_2 ($r = -0.15$, $P < 0.01$), and CO ($r = -0.11$, $P < 0.01$). There is evidence that O_3 is involved in the formation of secondary particles, and elevates the number of aerosol particles (Hinks et al., 2016). Accordingly, there is a positive correlation between O_3 and PM. For example, a study of 23 normotensive patients found significant rises in diastolic blood pressure (6 mm Hg) after a two-hour exposure to $PM_{2.5}$ and O_3 (Koulova and Frishman, 2014). Similar findings have been made regarding a positive correlation between PM and O_3 in Hong Kong ($r = 0.469$ with $P < 0.01$) (Lin et al., 2010) and Beijing ($r = 0.12$ with $P < 0.1$) (Jonas et al., 2014). A possible explanation is that O_3 oxidation may dominate the process of secondary particle formation, which contributes significantly to the increase of PM (Meusinger et al., 2017). However, O_3 was strongly, negatively correlated with gaseous pollution (NO_2 , SO_2 , etc.), due to the ability of O_3 to oxidize NO_2 and SO_2 to produce SO_4^{2-} and NO_3^- (Yoon et al., 2016). In fact, O_3 can react with NO_2 , SO_2 and CO in the atmosphere to produce their oxidation product. The reaction process is as follows:

NO_2 :

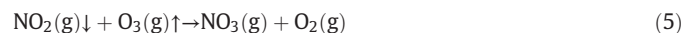
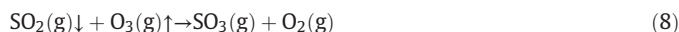


Table 2
Correlation coefficients between daily air pollutant concentrations in Shanghai.

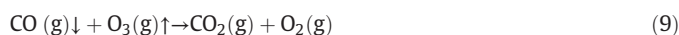
	PM _{2.5}	PM ₁₀	O ₃	SO ₂	NO ₂	CO	Temperature	Humidity
PM _{2.5}	1	0.91	0.08	0.74	0.69	0.86	0.49	−0.14
PM ₁₀		1	0.11	0.81	0.70	0.77	0.43	−0.17
O ₃			1	−0.14	−0.15	−0.09	0.02	0.01
SO ₂				1	0.76	0.74	0.37	−0.17
NO ₂					1	0.75	0.40	−0.14
CO						1	0.53	−0.17
Temperature							1	0.36
Humidity								1

Significant Pearson correlation coefficients ($r > 0.6$) are marked bold.

SO₂:



CO:



Through these chemical reactions the amount of NO₂, SO₂ and CO, would be decreased, especially in the condition of high O₃ concentration, which directly lead to negative correlations between these pollutants. Similar studies confirmed that O₃ reacts with precursors (NO₂, SO₂ et al.) to produce secondary particles, such as sulfate and nitrate particles (Tursic et al., 2001). Previous study also demonstrated that there existed negative correlation between O₃ and CO ($r = -0.23$, $P < 0.05$), O₃ and NO₂ ($r = -0.08$, $P < 0.05$), O₃ and SO₂ ($r = -0.05$, $P < 0.05$) in metropolitan Toronto, Canada (Stieb et al., 1996). There is also evidence that O₃ was strongly negatively correlated with NO₂ ($r = -0.304$, $P < 0.05$) and SO₂ ($r = -0.431$, $P < 0.05$) in Valencia, Spain (Alhanti et al., 2016).

The increase rate associated with higher concentration levels of air pollutants varied by sex or age (Table S1). The estimated effect of O₃ and PM among male were higher than those in female, although their between-sex difference was insignificant. The estimated effect of NO₂ on asthma morbidity was 5.83% (female) and 6.56% (male). The overall asthma morbidity for residents under 18 years of age was very low

and therefore these data were excluded from our analysis. We observed significant effects of air pollution in residents 18–60 years of age and >70 years of age. Among those 60–70 years of age, the estimated effect of NO₂ was 6.64% (95% CI: −2.21, 16.31), but it is insignificant.

3.2. Influence of four seasons on asthma patient visits

The association of O₃ with asthma patient visits did not show a significant seasonal variation in the combined analysis nor in Shanghai for any of the time exposures evaluated, as shown in Fig. 1. The association of asthma patient visits with CO was higher during the warm seasons (spring and summer). The seasonal variation in the levels of CO has been found not to be consistent among cities. For example, in California (Granados-Munoz and Leblanc, 2016), the effect on asthma patient visits was stronger in the warm season, while in Guangzhou (Xiao et al., 2014) and New York (Shmool et al., 2016), it was higher in the cold season (autumn and winter), although none of these differences were statistically significant ($P > 0.1$). NO₂ and SO₂ seasonal variation were not observed in the combined analysis. However, other studies found that the association between asthma patient visits and seasons was significantly stronger and weaker during the warm season in Delhi and Tirana, respectively (Pandey et al., 2015). Finally, in this study, PM_{2.5} and PM₁₀ levels were significantly associated with asthma patient visits and seasons. This may be due to the location of Shanghai in a transitional zone of the northern subtropical monsoon

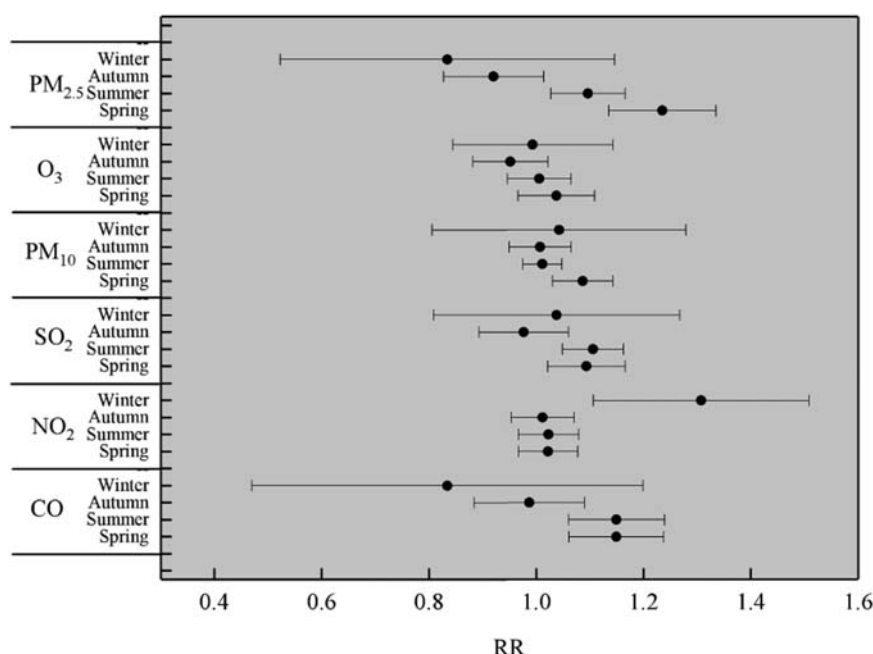
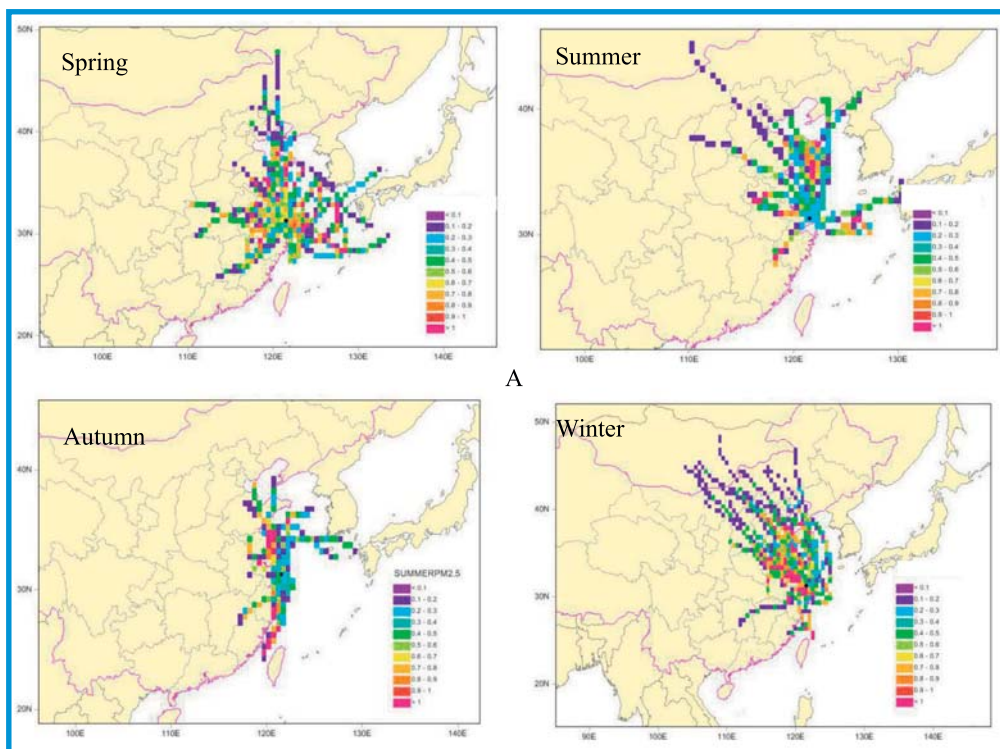


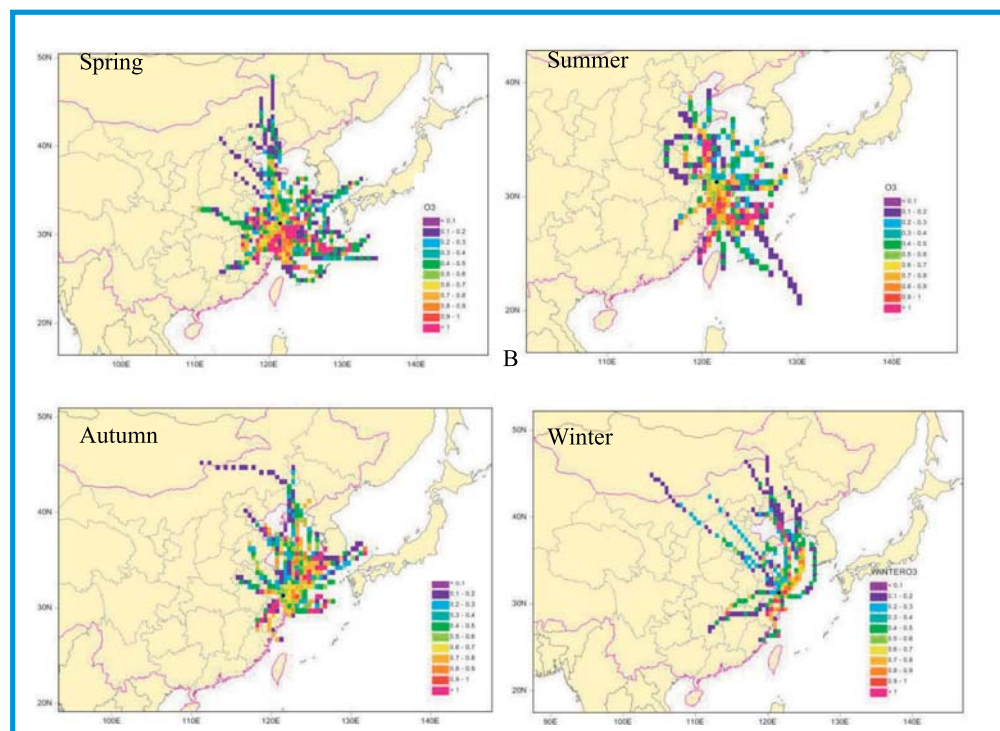
Fig. 1. Relative risk in asthma patient visits of air pollutants at lag 0 in spring and autumn, summer and winter, adjusted for meteorological factors.

system. In Shanghai, the northwesterly winter monsoon enters from mainland China, bringing pollutants generated from industries and other human activities in other places in China and increase the PM levels in the cold seasons. On the other hand, the southeasterly

summer monsoon enters from the Western Pacific Oceans in the warm seasons, which also may contribute to increase PM_{2.5} concentration in Shanghai through long-range transport from southeastern regions.



(A)



(B)

Fig. 2. Together with PSCF analysis for air mass backward trajectory of PM_{2.5} (A) and O₃ (B) in four seasons during observation.

As reported in previous studies (Guilleminault et al., 2016), there are usually high asthma morbidity in spring and autumn. We applied an alternative approach called PSCF to investigate the likely regional sources and transport routes of various $PM_{2.5}$ -associated and O_3 -associated speciation in these four seasons, as illustrated in Fig. 2. The seasonal analysis of the PSCF calculation revealed low PSCF values (<0.4) in the autumn, and high PSCF values (>0.6) in spring over Shanghai. All the pollutants, except NO_2 displayed the highest effect on asthma patient visits in the spring. The regions contributing to increase the level of $PM_{2.5}$ in Shanghai were mostly on the western terrestrial side, including most of the Jiangsu and Zhejiang provinces in spring, the Jiangsu province in autumn, except the local pollution. These findings indicated that pollutants may be emitted from local large stationary sources, such as fossil fuel fired power plants, smelters, industrial boilers, oil refineries and manufacturing facilities, as well as from adjacent areas and mobile sources. The regions contributing to increase level of O_3 in Shanghai were mostly on the eastern

marine side. All the pollutants except O_3 mainly come from the terrestrial sources during observation (Fig. 3). We can use the derived information and results to effectively evaluate the asthma patient visits in Shanghai, especially when the pollutant level exceeds the daily standard.

$PM_{2.5}$, PM_{10} , SO_2 , CO and NO_2 which increase asthma patient visits are mainly derived from terrestrial sources except O_3 that is primarily derived from marine source. The association for SO_2 , NO_2 and O_3 did not show a significantly seasonal variation. Association with CO was higher during the warm seasons. $PM_{2.5}$ and PM_{10} had significant association with seasons.

3.3. Influence of terrestrial sources and marine sources on asthma patient visits

The rate of increase in asthma patients associated with air mass routes is shown Table 3. Regarding the differences of marine and

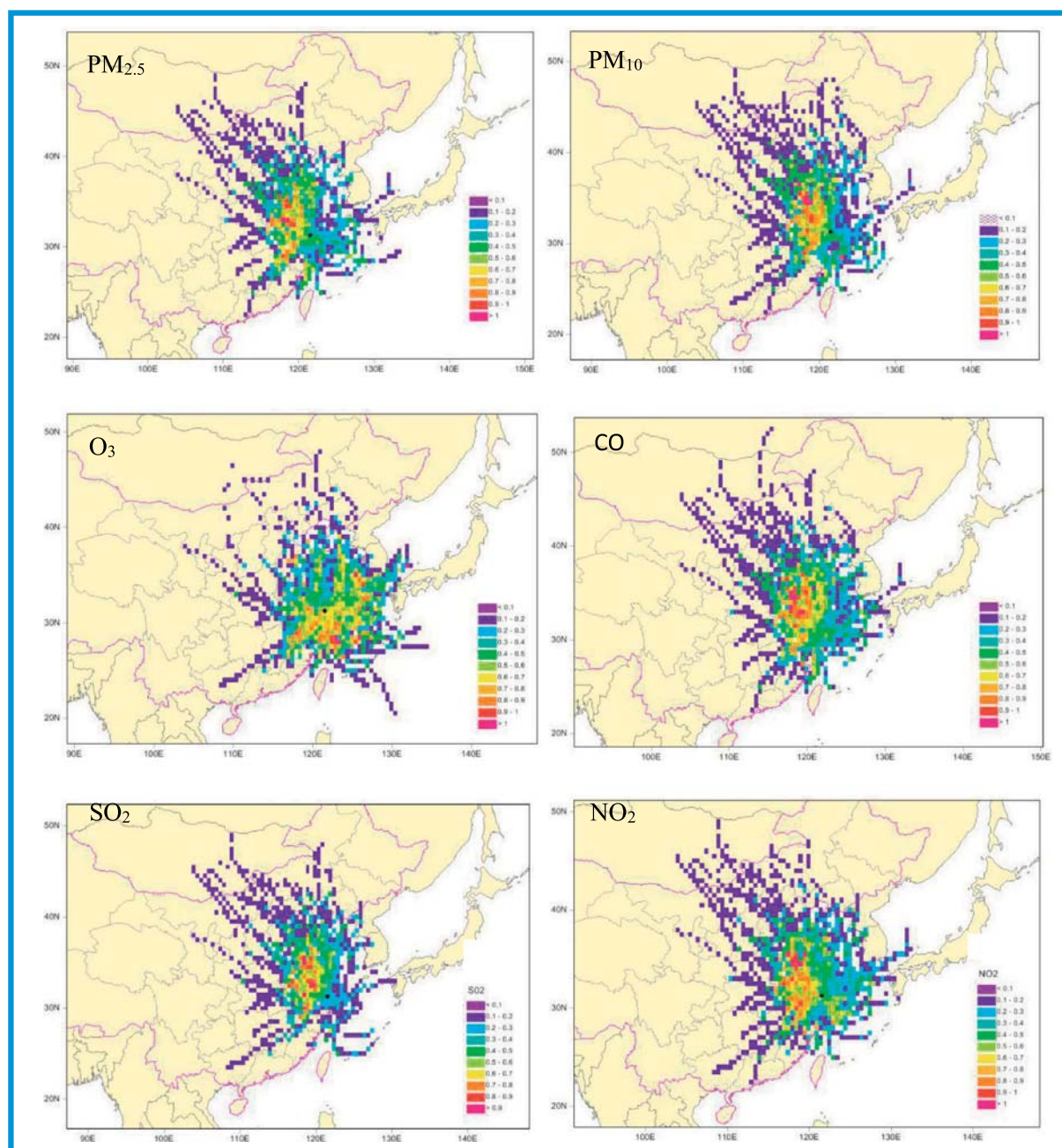


Fig. 3. PSCF analysis for air mass backward trajectory of $PM_{2.5}$, PM_{10} , O_3 , CO, SO_2 and NO_2 during observation in Shanghai.

terrestrial sources, we stratified the analyses for associations between the variations in the air pollutant levels and the asthma patient visits. For marine sources, per interquartile range (IQR) of PM_{2.5}, PM₁₀, O₃, NO₂, SO₂ and CO were associated with an increase of 5.34% (95% CI: 0.42% to 10.5%), 3.84% (95% CI: 0.08% to 7.74%), 3.21% (95% CI: −0.92% to 7.52%), 2.58% (95% CI: −1.02% to 6.30%), 1.42% (95% CI: −3.10% to 6.15%) and 8.81% (95% CI: 2.56% to 15.4%), respectively, in asthma patient visits. We found remarkable increases in the risk of asthma patient visits due to exposure to PM_{2.5}, PM₁₀, O₃, NO₂, SO₂ and CO, and the strongest positive associations were observed for CO. In contrast, no significant associations among NO₂ and asthma patient visits were found in terrestrial source (−0.60%, 95% CI: −5.94% to 5.04%). These effects could be due to the simultaneous shutdown of multiple pollutant sources, which made it difficult to differentiate effects of individual pollutants or pollutant source. For terrestrial source, per IQR of PM_{2.5}, PM₁₀, SO₂, O₃ and CO were associated with an increase of 6.63% (95% CI: −0.27% to 14%), 6.48% (95% CI: 0.06% to 13.3%), 1.68% (95% CI: −2.68% to 6.24%), 2.81% (95% CI: −1.42% to 7.22%) and 16.6% (95% CI: 8.68% to 25.2%), respectively, in asthma patient visits. By comparing the change in asthma patient visits, we found that terrestrial sources have a higher contribution than marine sources. This could be attributed to special geographic and socioeconomic levels in Shanghai, as determined by climate, economy, population and local or adjacent pollution levels, which are reported to be a factor for asthma diseases (D'Amato et al., 2013). Terrestrial sources usually have higher pollutant contribution than marine sources because of local emission and long-range transport, and result in increased asthma patient visits.

The PSCF trajectory statistical model coupled with the PM_{2.5}, PM₁₀, CO, NO₂, O₃ and SO₂ mass concentration data were adopted to identify potential sources of air pollutants in Shanghai, China. During the observation period between January 22, 2014 and October 31, 2015, stronger variations in air pollution loadings and concentrations at air quality monitoring station were observed (Fig. 3). From PSCF calculation, regions of high contribution to increase the air pollutant levels, except that of O₃ in Shanghai (PSCF > 0.5), were mostly contribution from the western terrestrial side including most of Jiangsu, part of Zhejiang and Anhui provinces, which form part of the biggest economic zone in China, namely the economic circle of the Yangtze river delta. The high intensity of industrial and construction activities generate abundant fine PM. Other regions that contributed to air pollutants in Shanghai, included the North China region and part of the Southwest China region. Noticeable, area from nearly all directions contributed to increase the air pollutants levels, despite having identified the region of high contribution as the northerly. At the same time, local emissions are prominent contributors as well due to local industrial pollution, construction etc. Environmental authorities can use the derived models and results for effectively reducing air pollution in Shanghai. Lastly, further work is still needed to gain a thorough understanding of the effects of air pollutants on asthma patients by using more sources and health outcomes.

Table 3
Percent increase of asthma patients increase associated with air mass pathways.

Pollutant	Asthma patient visit change					
	Marine source			Terrestrial source		
	% Change	95% CI		% Change	95% CI	
PM _{2.5}	5.34%	0.42%	–	10.5%	6.63%	−0.27%
PM ₁₀	3.84%	0.08%	–	7.74%	6.48%	0.06%
O ₃	3.21%	−0.92%	–	7.52%	1.68%	−2.68%
SO ₂	2.58%	−1.02%	–	6.30%	2.81%	−1.42%
NO ₂	1.42%	−3.10%	–	6.15%	−0.60%	−5.94%
CO	8.81%	2.56%	–	15.4%	16.6%	8.68%

CI: represents confidential interval.

PM_{2.5}, PM₁₀, O₃, SO₂, NO₂, CO per IQR for patient visit percent change.

4. Conclusions

In conclusions, exposure to common air pollutants derived from terrestrial sources (PM_{2.5}, PM₁₀, NO₂, SO₂) and marine sources (O₃) were closely associated with asthma patient visits in Shanghai from January 22, 2014 to October 31, 2015. Additionally, association of ambient pollutants and asthma patient visits were closely related with the seasons, especially with spring. Our findings showed that PM_{2.5}, PM₁₀, SO₂, CO and NO₂ which increase the asthma patient visits are mainly derived from terrestrial sources, but O₃ is primarily derived from marine sources. In addition, PM_{2.5} and CO are major pollutants that increase the relative risk of asthma patient visits in Shanghai. Improving air quality to prevent the increase of asthma patient visits not only requires the use of some prevention strategy by ourselves, but also strong governmental efforts to move economies from combustion of fossil fuels for energy production in regions where the terrestrial and marine sources are located. These information and suggestions are of particular significance for controlling the increase in asthma patient visits.

Appendix A. Supplementary data

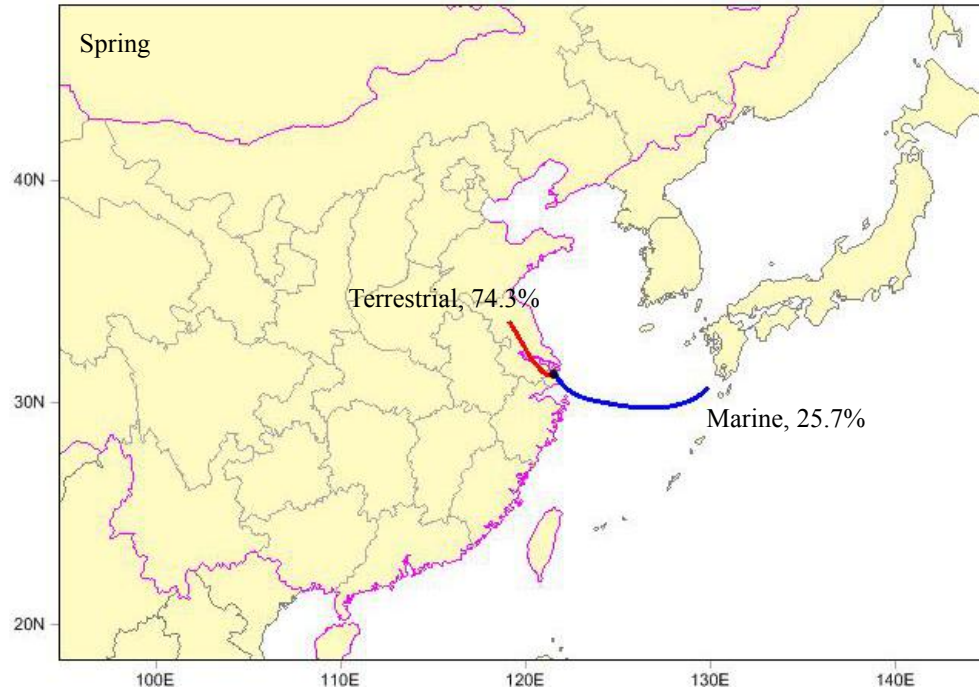
Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2017.12.298>.

References

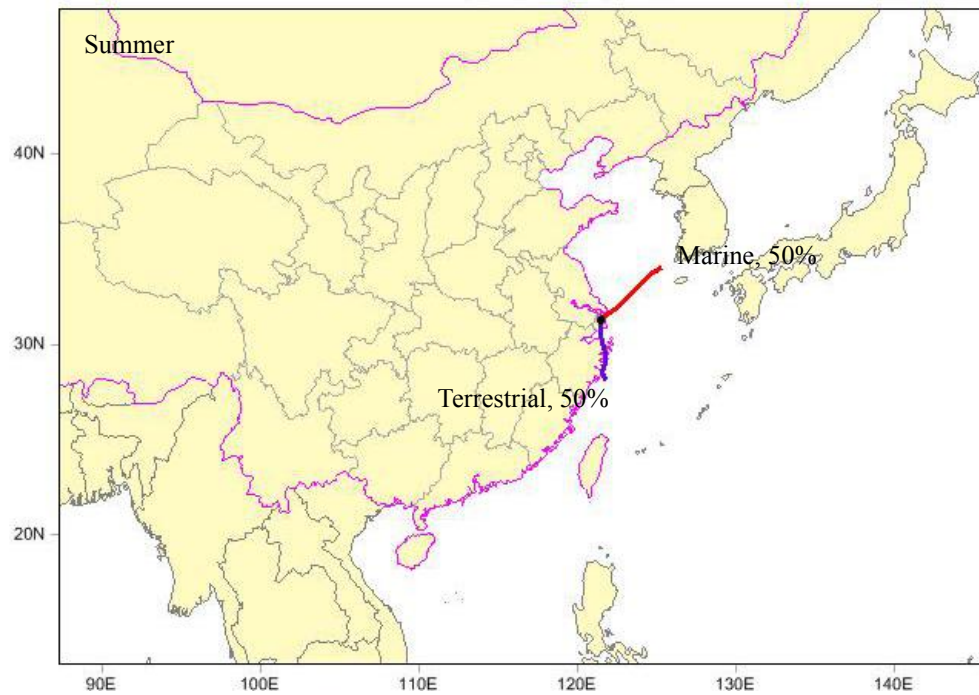
- Alhanti, B.A., Chang, H.H., Winquist, A., Mulholland, J.A., Darrow, L.A., Sarnat, S.E., 2016. Ambient air pollution and emergency department visits for asthma: a multi-city assessment of effect modification by age. *J. Expo. Sci. Environ. Epidemiol.* 26, 180–188.
- Bailey, D., Solomon, G., 2004. Pollution prevention at ports: clearing the air. *Environ. Impact Assess. Rev.* 24, 749–774.
- Bao, A.H., Li, F., Zhang, M., Chen, Y.Q., Zhang, P.Y., Zhou, X., 2014. Impact of ozone exposure on the response to glucocorticoid in a mouse model of asthma: involvements of p38 mapk and mkp^{−1}. *Respir. Res.* 15.
- Bonyadi, Z., Ehrampoush, M.H., Ghaneian, M.T., Mokhtari, M., Sadeghi, A., 2016. Cardiovascular, respiratory, and total mortality attributed to pm 2.5 in Mashhad, Iran. *Environ. Monit. Assess.* 188.
- Cakmak, S., Dales, R.E., Rubio, M.A., Vidal, C.B., 2011. The risk of dying on days of higher air pollution among the socially disadvantaged elderly. *Environ. Res.* 111, 388–393.
- D'Amato, G., Cecchi, L., Liccardi, G., Salzillo, A., Piccolo, A., Russo, M., et al., 2013. Climate change and allergic respiratory diseases. *Allergy, Asthma & Immunophysiology: From Basic Science to Clinical Management*, pp. 25–31.
- Delfino, R.J., Wu, J., Tjoa, T., Gullesterian, S.K., Nickerson, B., Gillen, D.L., 2014. Asthma morbidity and ambient air pollution effect modification by residential traffic-related air pollution. *Epidemiology* 25, 48–57.
- Deng, Q.H., Lu, C., Li, Y.G., Sundell, J., Norback, D., 2016. Exposure to outdoor air pollution during trimesters of pregnancy and childhood asthma, allergic rhinitis, and eczema. *Environ. Res.* 150, 119–127.
- Dijkema, M.B.A., van Strien, R.T., van der Zee, S.C., Mallant, S.E., Fischer, P., Hoek, G., et al., 2016. Spatial variation in nitrogen dioxide concentrations and cardiopulmonary hospital admissions. *Environ. Res.* 151, 721–727.
- Ding, L., Zhu, D.J., Peng, D.H., Zhao, Y., 2017. Air pollution and asthma attacks in children: a case-crossover analysis in the city of Chongqing, China. *Environ. Pollut.* 220, 348–353.
- Gamon, L.F., White, J.M., Wille, U., 2014. Oxidative damage of aromatic dipeptides by the environmental oxidants NO₂ center dot and O₃. *Org. Biomol. Chem.* 12, 8280–8287.
- Gao, M., Guttikunda, S.K., Carmichael, G.R., Wang, Y.S., Liu, Z.R., Stanier, C.O., et al., 2015. Health impacts and economic losses assessment of the 2013 severe haze event in Beijing area. *Sci. Total Environ.* 511, 553–561.
- Granados-Munoz, M.J., Leblanc, T., 2016. Tropospheric ozone seasonal and long-term variability as seen by lidar and surface measurements at the JPL-table mountain facility, California. *Atmos. Chem. Phys.* 16, 9299–9319.
- Guarnieri, M., Balmes, J.R., 2014. Outdoor air pollution and asthma. *Lancet* 383, 1581–1592.
- Guilleminault, L., Just, J., Humbert, M., Leroyer, C., Epaul, R., 2016. Seasonality in asthma: impact and treatments. *Presse Med.* 45, 1005–1018.
- Hinks, M.L., Brady, M.V., Lignell, H., Song, M.J., Grayson, J.W., Bertram, A.K., et al., 2016. Effect of viscosity on photodegradation rates in complex secondary organic aerosol materials. *Phys. Chem. Chem. Phys.* 18, 8785–8793.
- Jie, Y., Houjin, H., Xun, M., Kebin, L., Xuesong, Y., Jie, X., 2014. Relationship between pulmonary function and indoor air pollution from coal combustion among adult residents in an inner-city area of southwest china. *Braz. J. Med. Biol. Res.* 47, 982–989.
- Jonas, J.B., Wang, N.L., Wang, Y.X., You, Q.S., Xie, X.B., Yang, D.Y., et al., 2014. Body height, estimated cerebrospinal fluid pressure and open-angle glaucoma. The Beijing eye study 2011. *PLoS One* 9.
- Jouneau, S., Brinchault, G., Desrués, B., 2014. Management of copd exacerbations: from primary care to hospitalization. *Presse Med.* 43, 1359–1367.

- Ko, F.W.S., Tam, W., Wong, T.W., Lai, C.K.W., Wong, G.W.K., Leung, T.F., et al., 2007. Effects of air pollution on asthma hospitalization rates in different age groups in Hong Kong. *Clin. Exp. Allergy* 37, 1312–1319.
- Koulova, A., Frishman, W.H., 2014. Air pollution exposure as a risk factor for cardiovascular disease morbidity and mortality. *Cardiol. Rev.* 22, 30–36.
- Laumbach, R.J., Kipen, H.M., 2012. Respiratory health effects of air pollution: update on biomass smoke and traffic pollution. *J. Allergy Clin. Immunol.* 129, 3–13.
- Li, S., Batterman, S., Wasilevich, E., Elasaad, H., Wahl, R., Mukherjee, B., 2011. Asthma exacerbation and proximity of residence to major roads: a population-based matched case-control study among the pediatric Medicaid population in Detroit, Michigan. *Environ. Health* 10.
- Lin, C., Lin, P., Song, F., 2010. Property rights protection and corporate R&D: evidence from China. *J. Dev. Econ.* 93, 49–62.
- Liu, C.J., Liu, C.Y., Mong, N.T., Chou, C.C.K., 2016. Spatial correlation of satellite-derived pm 2.5 with hospital admissions for respiratory diseases. *Remote Sens.* 8.
- Lu, Z.Y., Li, W.H., Xie, B.C., Shang, L.F., 2015. Study on China's wind power development path-based on the target for 2030. *Renew. Sust. Energ. Rev.* 51, 197–208.
- Mazzarella, G., Esposito, V., Bianco, A., Ferraraccio, F., Prati, M.V., Lucariello, A., et al., 2012. Inflammatory effects on human lung epithelial cells after exposure to diesel exhaust micron sub particles (pm 1.0) and pollen allergens. *Environ. Pollut.* 161, 64–69.
- Meusinger, C., Bluhme, A.B., Ingemar, J.L., Feilberg, A., Christiansen, S., Andersen, C., et al., 2017. Treatment of reduced sulphur compounds and SO₂ by gas phase advanced oxidation. *Chem. Eng. J.* 307, 427–434.
- Mirabelli, M.C., Vaidyanathan, A., Flanders, W.D., Qin, X.T., Garbe, P., 2016. Outdoor pm 2.5, ambient air temperature, and asthma symptoms in the past 14 days among adults with active asthma. *Environ. Health Perspect.* 124, 1882–1890.
- Morin, A., Brook, J.R., Duchaine, C., Laprise, C., 2012. Association study of genes associated to asthma in a specific environment, in an asthma familial collection located in a rural area influenced by different industries. *Int. J. Environ. Res. Public Health* 9, 2620–2635.
- Pan, H.H., Chen, C.T., Sun, H.L., MS, Ku, Liao, P.F., KH, Lu, et al., 2014. Comparison of the effects of air pollution on outpatient and inpatient visits for asthma: a population-based study in Taiwan. *PLoS One* 9.
- Pandey, A.K., Kumar, R.P., Kumar, K., 2015. Satellite and ground-based seasonal variability of NO₂ and SO₂ over New Delhi, India. In: Comeron, A., Kassianov, E.I., Schafer, K., Picard, R.H., Weber, K. (Eds.), *Remote Sensing of Clouds and the Atmosphere*. vol. 9640 xx.
- Poynter, M.E., Persinger, R.L., Irvin, C.G., Butnor, K.J., van Hirtum, H., Blay, W., et al., 2006. Nitrogen dioxide enhances allergic airway inflammation and hyperresponsiveness in the mouse. *Am. J. Phys. Lung Cell. Mol. Phys.* 290, L144–L152.
- Ramos, C.A., Wolterbeek, H.T., Almeida, S.M., 2016. Air pollutant exposure and inhaled dose during urban commuting: a comparison between cycling and motorized modes. *Air Qual. Atmos. Health* 9, 867–879.
- Reungoat, P., Chiron, M., Gauvin, S., Le Moullec, Y., Momas, I., 2003. Assessment of exposure to traffic pollution using the extra index: study of validation. *Environ. Res.* 93, 67–78.
- Shan, W.J., Y.M., Lu, Guo, Y.S., Li, Y.Q., LY, Xu, Cao, L.F., 2016. Short-term association between particular matter air pollution and pediatric clinical visits for wheezing in a subarea of Shanghai. *Environ. Sci. Pollut. Res.* 23, 19201–19211.
- Shmool, J.L.C., Kinnee, E., Sheffield, P.E., Clougherty, J.E., 2016. Spatio-temporal ozone variation in a case-crossover analysis of childhood asthma hospital visits in New York City. *Environ. Res.* 147, 108–114.
- Stieb, D.M., Burnett, R.T., Beveridge, R.C., Brook, J.R., 1996. Association between ozone and asthma emergency department visits in Saint John, New Brunswick, Canada. *Environ. Health Perspect.* 104, 1354–1360.
- Tan, J., Bernstein, J.A., 2014. Occupational asthma: an overview. *Curr Allergy Asthma Rep* 14.
- Tao, Y., Mi, S., Zhou, S., Wang, S., Xie, X., 2014. Air pollution and hospital admissions for respiratory diseases in Lanzhou, China. *Environ. Pollut.* 185, 196–201.
- Tenland, E., Hakansson, G., Alaridah, N., Lutay, N., Ronnholm, A., Hallgren, O., et al., 2016. Innate immune responses after airway epithelial stimulation with mycobacterium bovis bacille-calmette guerin. *PLoS One* 11.
- Tursic, J., Grgic, I., Bizjak, M., 2001. Influence of NO₂ and dissolved iron on the s(iv) oxidation in synthetic aqueous solution. *Atmos. Environ.* 35, 97–104.
- Vahlsing, C., Smith, K.R., 2012. Global review of national ambient air quality standards for pm 10 and SO₂ (24 h). *Air Qual. Atmos. Health* 5, 393–399.
- Wang, T.Y., Jerrett, M., Sinsheimer, P., Zhu, Y.F., 2016. Estimating pm 2.5-associated mortality increase in California due to the Volkswagen emission control defeat device. *Atmos. Environ.* 144, 168–174.
- Wigenstam, E., Elfsmark, L., Bucht, A., Jonasson, S., 2016. Inhaled sulfur dioxide causes pulmonary and systemic inflammation leading to fibrotic respiratory disease in a rat model of chemical-induced lung injury. *Toxicology* 368, 28–36.
- Wu, Y.S., Zhang, F.Y., Shi, Y., Pilot, E., Lin, L.Y., YB, Fu, et al., 2016. Spatiotemporal characteristics and health effects of air pollutants in Shenzhen. *Atmos. Pollut. Res.* 7, 58–65.
- Xiao, Y.H., Liu, S.R., Tong, F.C., Kuang, Y.W., Chen, B.F., Guo, Y.D., 2014. Characteristics and sources of metals in tsp and pm 2.5 in an urban forest park at Guangzhou. *Atmos.* 5, 775–787.
- Xie, Y.J., Zhao, L.J., Xue, J., QM, Hu, Xu, X., Wang, H.B., 2016. A cooperative reduction model for regional air pollution control in china that considers adverse health effects and pollutant reduction costs. *Sci. Total Environ.* 573, 458–469.
- Yoda, Y., Otani, N., Sakurai, S., Shima, M., 2014. Acute effects of summer air pollution on pulmonary function and airway inflammation in healthy young women. *J. Epidemiol.* 24, 312–320.
- Yoon, H.J., Park, H.W., Park, D.W., 2016. Simultaneous oxidation and absorption of NO_x and SO₂ in an integrated O₃ oxidation/wet atomizing system. *Energy Fuel* 30, 3289–3297.
- Yun, Y., Gao, R., Yue, H.F., Li, G.K., Zhu, N., Sang, N., 2015. Synergistic effects of particulate matter (pm 10) and SO₂ on human non-small cell lung cancer a549 via ros-mediated nf-kappa b activation. *J. Environ. Sci.* 31, 146–153.
- Zhai, L., Zhao, J., Xu, B., Deng, Y., Xu, Z., 2013. Influence of indoor formaldehyde pollution on respiratory system health in the urban area of Shenyang, China. *Afr. Health Sci.* 13, 137–143.

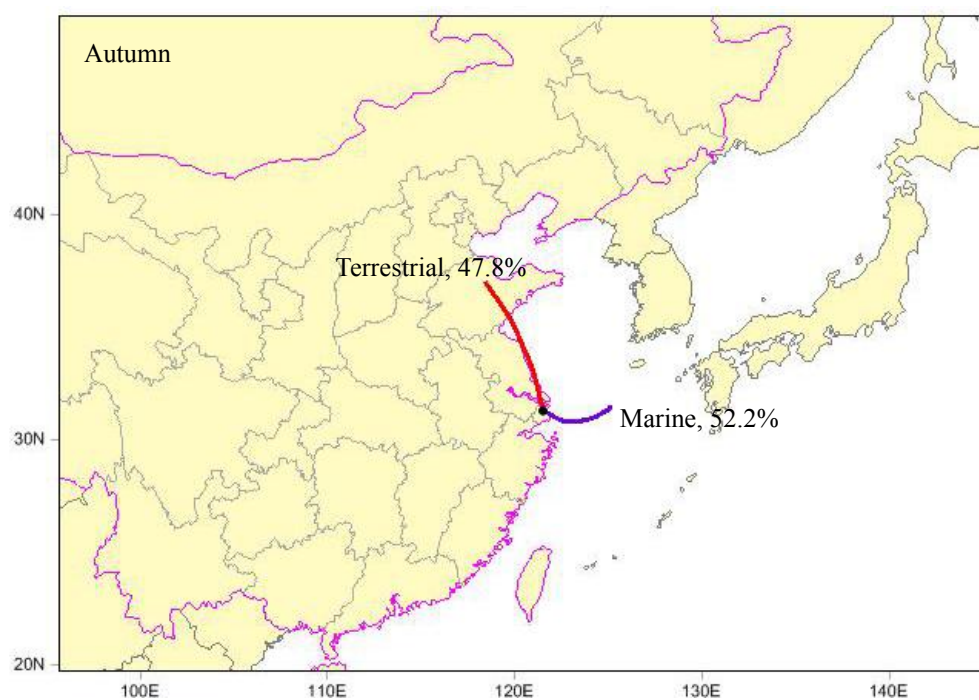
Supporting Information



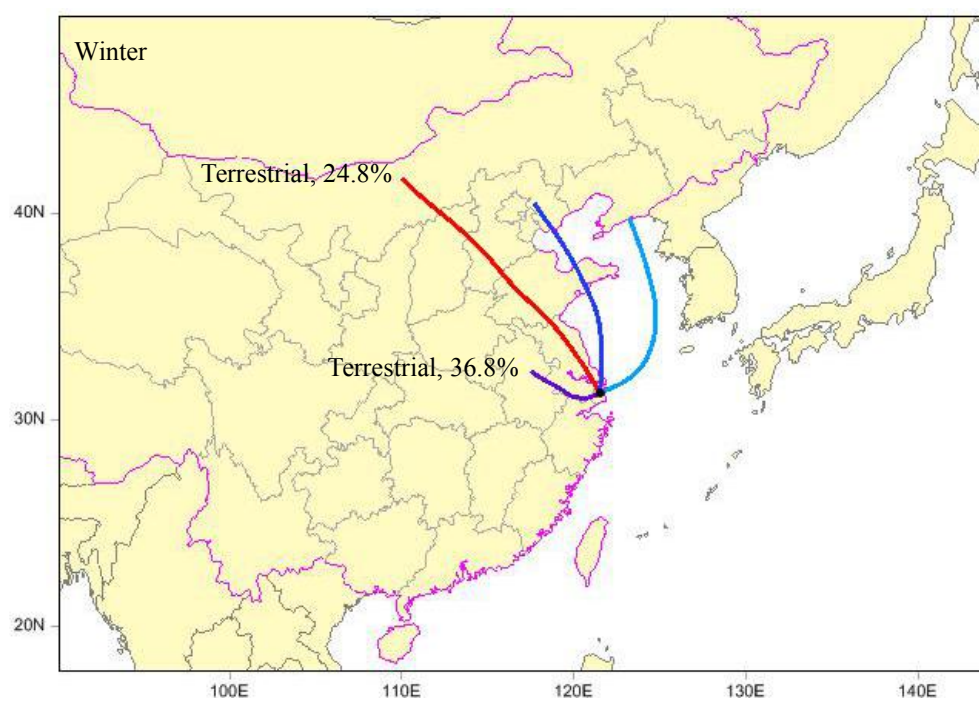
(A)



(B)



(C)



(D)

Figure S1. Source distribution proportion of air pollutants during observation in Shanghai.

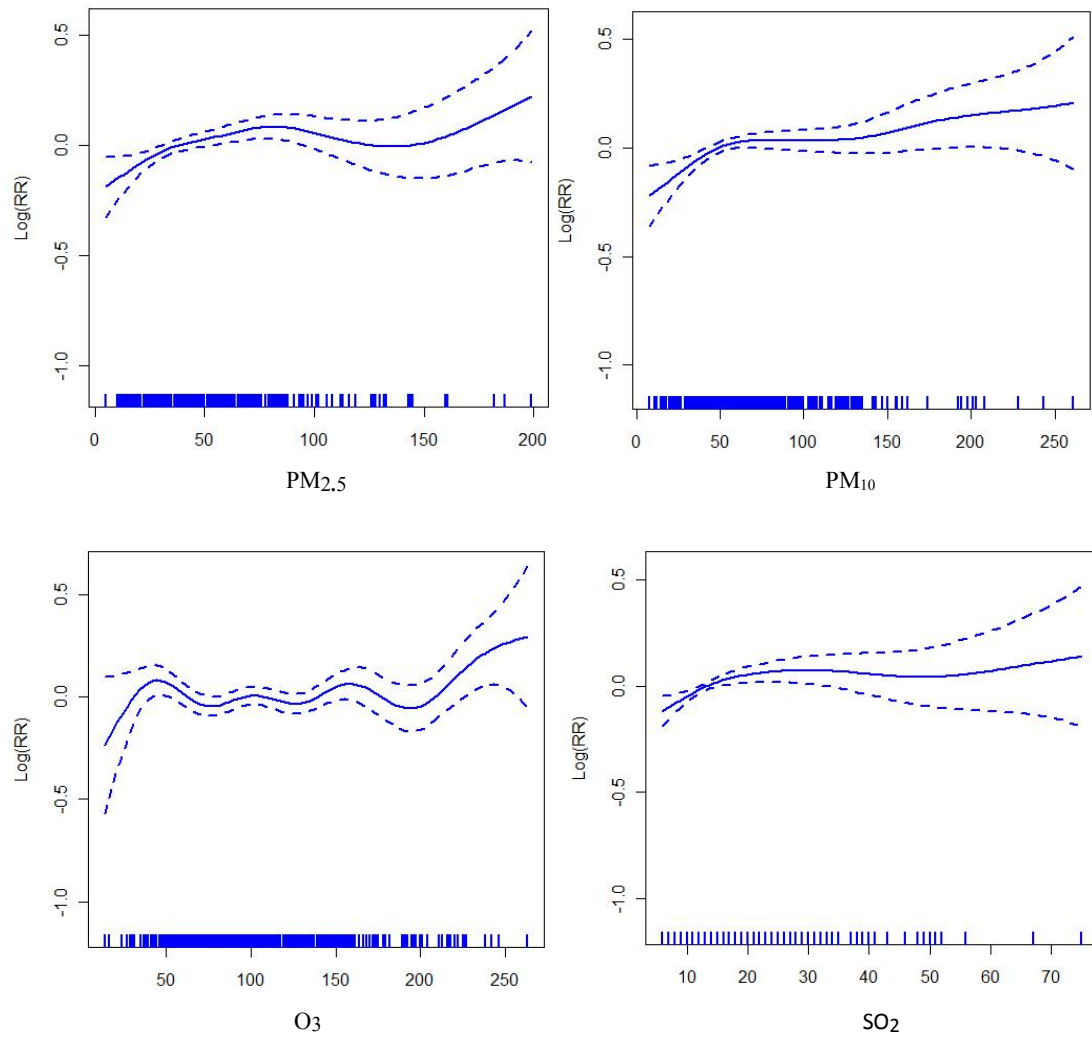


Figure. S2. Smoothing plots of pollutants against asthma patient visits. X-axis is pollutants concentrations. The estimated mean percent change in asthma patient visits is shown by the solid line, and the dotted lines represent twice the point-wise standard error. Current-day temperature and relative humidity were used with a df of 6 and 3, respectively.

Table S1. Percent increase (95% CI) in total asthma morbidity of Shanghai residents associated with per IQR increase in air pollutant concentrations by sex and age.

	Pollutant					
	PM _{2.5}	PM ₁₀	O ₃	CO	SO ₂	NO ₂
Sex						
Female (15.7%)	-2.04 (-21.45,17.21)	-2.15 (-6.71,2.63)	-0.81 (-5.94,4.59)	-0.85 (-5.15,3.64)	2.00 (-2.23,6.42)	*5.83 (0.80,11.11)
Male (84.3%)	0.73 (-9.83,12.53)	1.88 (-1.78,5.69)	0.51 (-12.18,14.76)	1.71 (-8.60, 13.51)	2.78 (-6.71,13.47)	*6.56 (1.57,11.80)
Age (years)						
18-60 (48.9%)	6.61 (-0.39,14.11)	4.93 (-1.87,12.22)	-6.03 (-13.74,2.34)	6.02 (-0.68,13.18)	2.20 (-3.89,8.68)	*11.88 (4.26,20.05)
60-70 (32.9%)	-4.30 (-12.28,4.41)	-3.34 (-11.14,5.14)	-6.27 (-15.60,4.09)	-1.70 (-9.32,6.55)	0.91 (-6.28,8.66)	6.64 (-2.21,16.31)
>70 (17.7%)	6.27 (-5.20,19.13)	5.13 (-6.09,17.71)	-5.02 (-16.99,8.67)	5.13 (-5.65,17.15)	7.13 (-2.94,18.26)	14.01 (1.51,28.04)

*** P < 0.05**