

International Journal of Environmental Research and Public Health



# Article The Association between Air Pollution and Outpatient and Inpatient Visits in Shenzhen, China

Yachuan Liu <sup>1,†</sup>, Shanen Chen <sup>2,†</sup>, Jian Xu <sup>3</sup>, Xiaojian Liu <sup>4</sup>, Yongsheng Wu <sup>4,\*</sup>, Lin Zhou <sup>4</sup>, Jinquan Cheng <sup>4</sup>, Hanwu Ma <sup>4</sup>, Jing Zheng <sup>5</sup>, Denan Lin <sup>5</sup>, Li Zhang <sup>3</sup> and Lili Chen <sup>3,\*</sup>

- <sup>1</sup> Department of Statistics, University of California, Berkeley, CA 94720, USA; liuyachuan7119@hotmail.com
- <sup>2</sup> Department of Industrial Engineering and Management, Peking University, Beijing 100871, China; shanen.chen@pku.edu.cn
- <sup>3</sup> IBM Research China, Beijing 100193, China; xujianx@cn.ibm.com (J.X.); zhanglir@cn.ibm.com (L.Z.)
- <sup>4</sup> Shenzhen Center for Disease Control and Prevention, Shenzhen 518073, China; xjliu@szcdc.net (X.L.); zhoulin\_szcdc@163.com (L.Z.); cjinquan@szcdc.net (J.C.); szmhw@szcdc.net (H.M.)
- <sup>5</sup> Medical Information Center of Shenzhen Municipality, Shenzhen 518055, China; cnzhengj@163.com (J.Z.); ldn308@163.com (D.L.)
- \* Correspondence: cdc@szcdc.net (Y.W.); chenlili1002@126.com (L.C.); Tel.: +86-010-58748121 (L.C.)
- t These authors contributed equally in this work and they are co-first authors.

Received: 18 November 2017; Accepted: 17 January 2018; Published: 23 January 2018

**Abstract:** Nowadays, air pollution is a severe environmental problem in China. To investigate the effects of ambient air pollution on health, a time series analysis of daily outpatient and inpatient visits in 2015 were conducted in Shenzhen (China). Generalized additive model was employed to analyze associations between six air pollutants (namely SO<sub>2</sub>, CO, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>) and daily outpatient and inpatient visits after adjusting confounding meteorological factors, time and day of the week effects. Significant associations between air pollutants and two types of hospital visits were observed. The estimated increase in overall outpatient visits associated with each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant concentration ranged from 0.48% (O<sub>3</sub> at lag 2) to 11.48% (SO<sub>2</sub> with 2-day moving average); for overall inpatient visits ranged from 0.73% (O<sub>3</sub> at lag 7) to 17.13% (SO<sub>2</sub> with 8-day moving average). Our results also suggested a heterogeneity of the health effects across different outcomes and in different populations. The findings in present study indicate that even in Shenzhen, a less polluted area in China, significant associations exist between air pollution and daily number of overall outpatient visits.

Keywords: air pollution; health effects; time series analysis; generalized additive model

# 1. Introduction

Ambient air pollution was at least suspected to cause adverse health effects, which was estimated to be responsible for more than 2 million deaths annually and 6.4 years of lost life worldwide [1]. Exposures to air pollution increase risk in mortality, particularly in susceptible populations, and present enormous burden on existing public health system. Assessing the association between air pollution and diseases can allow a better coordination of mitigation and intervention resources.

A broad epidemiological studies have shown that increased ambient air pollutant concentrations are associated with excess daily mortality [2], hospital admissions [3] and emergency hospital visits [4]. These research studies were conducted to assess health impact of air pollution on specific diseases. For instance, associations have been observed between air pollution and emergency department visits for asthma [4–6], particularly for effects of nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>), sulfur dioxide (SO<sub>2</sub>) and particulate concentrations. Air pollutants including NO<sub>2</sub>, SO<sub>2</sub> and particulate matter less than 2.5 µm in aerodynamic diameter (PM<sub>2.5</sub>) have also been reported to be risk factors of hospital

admissions for cardiovascular diseases [7], hypertension [8] and respiratory infection [9]. For example, Xia et al. [9] found that acute respiratory infection hospital admission would significantly increase when people exposed to ambient air pollution in Shenzhen in 2013. However, few studies were devoted to pooled estimate of air pollution health effects using overall hospitalized outpatient and inpatient visits. The comprehensive estimate of health effects for air pollution is necessary for us to implement better disease control policy.

Furthermore, most previous studies focused on heavily polluted areas such as Beijing or Shanghai whereas associations between air pollutant concentrations and health effect metrics were less addressed, especially in China. For heavily polluted areas, Guo et al. [10,11] conducted health risk assessment of air pollution on hypertension and cardiovascular diseases in Beijing and Tianjin, respectively, where both cities were of high air pollutant concentrations. Similar studies that highlighted the air pollution health effects in heavily polluted areas could also be found in other literature [12]. On the other hand, relations between pollution and hospital visits for specific diseases have also been reported from areas with low-level air pollution concentration [13,14], although less frequently. Oudin et al. [14] investigated the health effects of daily O<sub>3</sub>, particulate matter less than 10  $\mu$ m in aerodynamic diameter (PM<sub>10</sub>), and NO<sub>x</sub> on hospital visits for stroke in Southern Sweden where pollutant concentrations were rather low. Increased risk for ischemic stroke hospital visits at certain level of PM<sub>10</sub> has been observed, whereas no consistent associations were found for ischemic stroke and O<sub>3</sub> or NO<sub>x</sub>. Consequently, particularly in China, there is evidence of associations between certain diseases and air pollutions where air pollution concentrations are high, whereas the studies on health effects of air pollutions in less polluted areas are insufficient.

Shenzhen, a less polluted city of China, is a part of the Pearl River Delta region. With the development of industrialization and urbanization, different severe air pollutants, such as  $PM_{10}$  and  $PM_{2.5}$  [15,16], NO<sub>2</sub> [17] and O<sub>3</sub> [18] have appeared in the Pearl River Delta region. The objective of the present study is to explore associations between ambient air pollution and overall hospital outpatient and inpatient visits at locations with comparatively low concentrations of pollution where air quality index is usually less than 100. Data including air pollutant concentrations, meteorological factors and inpatient and different hospitals in Shenzhen. The effects of air pollutants, namely SO<sub>2</sub>, carbon monoxide (CO), NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub> were analyzed with a time series analysis.

## 2. Materials and Methods

# 2.1. Data Collection for the Hospital Outpatient and Inpatient Visit

Situated at a degree south of the Tropic of Cancer, south of China, Shenzhen has a warm, humid subtropical climate, and is less polluted due to geographical location, climatological parameters and low degree of industrialization. To evaluate the health effect of air pollution in Shenzhen, data on daily hospital outpatient and inpatient visits from 1 January 2015 to 31 December 2015 were collected from Center for Disease Control and Prevention (CDC) of Shenzhen. 25,185 records of outpatient and inpatients visits for a total of 69 hospitals in Shenzhen, including a pediatric, an ophthalmological and a cardiovascular hospital, were obtained. Most of general hospitals in Shenzhen are open regularly all day from Monday to Sunday, however several special hospitals could be close on holidays, for which records of zero outpatient and inpatient visits could be observed. To improve the reliability of analysis, 17 hospitals that meet the following standards were removed for further analysis:

- The ratio of zero records was greater or equal to mean of that for all hospitals
- The ratio of outliers (records fall outside mean ±2 standard deviation) was greater or equal to mean ratio of outliers +2 standard deviations
- The coefficient of variation was greater or equal to mean ±2 standard deviations

Records of the remaining 52 hospitals was further filtered with mean  $\pm 2$  standard deviations criteria.

#### 2.2. Data Collection for Air Pollution and Weather Condition

The daily concentrations of ambient air pollutants in 2015 were obtained from Shenzhen Environmental Protection Bureau website. There are 19 fixed monitoring stations in the city, which are distributed in six administrative areas and four new areas in Shenzhen. Daily average concentrations of monitoring stations on SO<sub>2</sub>, CO, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub> were included in this study. If data of air pollutants were missed on a given day, the missing values would be calculated with the average concentration computed from the remaining data. Of note, the air pollution data was representative to analyze the exposure of city population. Daily temperature, humidity and barometric pressure data were also collected from Shenzhen Meteorological Bureau website to adjust the effects of air pollution.

#### 2.3. Statistical Analysis

In present study, Poisson regression using a generalized additive modeling technique was performed to analyze the associations between ambient air pollutant concentrations and outpatient and inpatient visits. The dependent variables were the overall hospital daily count of outpatient and inpatient visits. In most analyses, the 3-day moving average pollutant concentration (the average of concentrations today (lag 0), yesterday (lag 1), and 2 days ago (lag 2) were modeled [19]. To further describe the associations, this study examined the moving average concentrations from 2 to 8 days (lag 0~1, lag 0~2, ... , lag 0~7). Moreover, air pollutant concentrations at lag time of 1–7 days were tested for significance. The relevant daily data of air temperature (minimum, average and maximum), relative humidity, and barometric pressure were incorporated into the models as confounding factors. Regression models also accounted for time and day of the week with six dummy variables. Additionally, to assess the effect of air pollutants on specific population, this study performed separate analysis on data with regards to general hospitals, pediatric hospital, ophthalmological hospital and cardiovascular hospital.

The anti-log of the regression coefficients for the major pollutants in the generalized additive models is a rate ratio, also interpreted as relative risk (RR). Increased risk (RR–1 \* 100%) and the associated 95% confidence intervals (95% CI) for per 10  $\mu$ g/m<sup>3</sup> increase in air pollutants were further derived from estimated RRs, as observed during the study period. All statistical tests were two-sided. Only those independent variables with a test values of *p* < 0.05 were considered statistically significant. In addition, all the analysis was performed with R 3.2.3 on a Linux server.

# 3. Results

Table 1 shows the summary statistics of daily hospital visits for 49 hospitals, air pollution, and weather condition of Shenzhen in 2015.

Variable	Mean	Standard Deviation (SD)	Min	Max				
Hospital admission								
Outpatient visits	100,495.42	9752.35	70,167.00	122,731.00				
Inpatient visits	2540.69	336.90	1756.00	3348.00				
Air pollutants ( $\mu g/m^3$ )								
$SO_2$	8.33	2.45	4.12	21.32				
CO	850.45	168.41	551.62	1408.88				
NO <sub>2</sub>	33.36	11.50	13.67	101.58				
O <sub>3</sub>	55.53	23.56	16.00	162.53				
PM <sub>10</sub>	49.11	24.40	13.54	160.48				
PM <sub>2.5</sub>	29.87	17.09	7.00	100.71				
Weather conditions								
Relative Humidity (%)	71.93	11.05	28.00	93.00				
Pressure (hPa)	1005.97	6.45	990.60	1019.30				
Temperature (°C)	23.96	5.24	11.90	33.00				

**Table 1.** Summary statistics of outpatient/inpatient visits, air pollution and weather conditions (n = 365).

The average daily outpatient visits for 49 hospitals were 100,495 (maximum 122,731, minimum 70,167). The average daily inpatient visits were 2540 with a maximum of 3348 and a minimum of 1756. Air pollutant measurements were available for 365 days, of which the daily average concentrations of SO<sub>2</sub>, CO, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> were 8.33  $\mu$ g/m<sup>3</sup>, 850.45, 33.36, 55.53, 49.11, and 29.87  $\mu$ g/m<sup>3</sup>, respectively, wherein all the air pollutants were lower than the national primary ambient air quality standard in China (20  $\mu$ g/m<sup>3</sup>, 4000  $\mu$ g/m<sup>3</sup>, 40  $\mu$ g/m<sup>3</sup>, 100  $\mu$ g/m<sup>3</sup>, 50  $\mu$ g/m<sup>3</sup>, and 35  $\mu$ g/m<sup>3</sup>, respectively).

The increased risk and the associated 95% CI for each air pollutant (at different lags) were evaluated by controlling the influence of temperature, relative humidity, pressure and day of the week. Figure 1 displays increased risk for day-specific lags (lags 0–7), and day-specific moving average concentrations from 2 to 8 days (lag 0~1, lag 0~2, ... ..., lag 0~7) for association between ambient air pollutant concentrations and hospital visits (outpatient and inpatient visits).



**Figure 1.** Increased risk estimates and 95% CI between each pollutant and overall outpatient and inpatient visits under different day specific lag associated with a  $10 \,\mu\text{g/m}^3$  increase in air pollutants.

The overall association estimate for per  $10 \ \mu\text{g/m}^3$  increase in air pollutants at different lags were also summarized in Table 2. For overall outpatient visits, the highest increases in visits associated with each  $10 \ \mu\text{g/m}^3$  increase in air pollutants were 11.48% (95% CI: 6.32–16.89%) for SO<sub>2</sub>, 4.38% (95% CI: 2.25–6.56%) for NO<sub>2</sub>, 1.28% (95% CI: 0.76–1.80%) for O<sub>3</sub>, 1.52% (95% CI: 0.90–2.13%) for PM<sub>10</sub>, and 2.36% (95% CI: 1.45–3.28%) for PM<sub>2.5</sub>, respectively. Estimates from this distributed lag generalized additive model suggested that there were both immediate and lagged effects for these air pollutants.

 $0 \sim 4$ 

0~5

0~6

 $0 \sim 7$ 

 $12.3(3.62 \sim 21.7)$ 

14.24 (4.83~24.49)

15.99 (5.79~27.17)

17.13 (6.13~29.26)

 $0.05(-0.1 \sim 0.2)$ 

0.07 (-0.09~0.23)

 $0.05(-0.12 \sim 0.22)$ 

 $0.07(-0.11 \sim 0.25)$ 

For all pollutants except CO, the pollutant concentrations on the day of outpatient visits (lag 0) as well as within 5-day moving average concentrations were significantly associated with overall outpatient visits. Interestingly, marginally reduced risk has been observed between CO and overall outpatient visits. As for overall inpatient visits, increased health risk effects were found between air pollutants consisting of SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, PM<sub>2.5</sub> and inpatient visits, with highest increase in visits associated with each 10  $\mu$ g/m<sup>3</sup> increase in air pollutants being 17.13% (95% CI: 6.13–29.26%) for SO<sub>2</sub>, 3.66% (95% CI: 0.63–6.77%) for NO<sub>2</sub>, 1.70% (95% CI: 0.59–2.84%) for O<sub>3</sub>, 2.20% (95% CI: 1.01–3.41%) for PM<sub>10</sub>, and 3.27% (95% CI: 1.51–5.07%) for PM<sub>2.5</sub>. Among the above associations, the strongest associations between air pollutants and inpatient visits was found at 8-day moving average pollutant concentration. For the other associations (CO), the effects on hospital inpatient visits were not statistically significant at any lags of CO.

		1	1	1					
Lag (Dave)	% Changes (95% CI)—Outpatient Visits for All Hospitals								
Lag (Days)	SO <sub>2</sub>	СО	NO <sub>2</sub>	O <sub>3</sub>	PM <sub>10</sub>	PM <sub>2.5</sub>			
0	10.21 (5.75~14.86)	0 (-0.07~0.07)	1.21 (0.24~2.19)	1.03 (0.57~1.50)	1.24 (0.73~1.75)	1.85 (1.11~2.59)			
1	5.87 (1.4~10.54)	$-0.04(-0.11 \sim 0.04)$	0.65 (-0.32~1.63)	0.93 (0.46~1.4)	0.90 (0.38~1.42)	1.50 (0.74~2.26)			
2	2.31 (-2.06~6.88)	$-0.07(-0.14 \sim 0.01)$	1.09 (0.14~2.05)	0.48 (0.01~0.95)	0.65 (0.14~1.17)	1.01 (0.26~1.77)			
3	$-0.08(-4.19 \sim 0.21)$	$-0.05(-0.13 \sim 0.02)$	0.68 (-0.27~1.63)	0.34 (-0.13~0.81)	0.51 (-0.01~1.03)	$0.69(-0.08 \sim 1.46)$			
4	0.59 (-3.88~5.26)	$-0.09(-0.17 \sim 0.02)$	1.06 (0.07~2.06)	$0.04(-0.45 \sim 0.54)$	0.20 (-0.33~0.75)	$-0.06(-0.86 \sim 0.74)$			
5	$-1.55(-5.79 \sim 2.88)$	$-0.09(-0.16 \sim 0.02)$	$0.4(-0.55 \sim 1.35)$	$0.09(-0.41 \sim 0.60)$	0.15 (-0.39~0.69)	$-0.22(-1.02 \sim 0.58)$			
6	0.98 (-3.38~5.54)	$-0.05(-0.12 \sim 0.02)$	1.09 (0.12~2.07)	$-0.07(-0.53 \sim 0.40)$	$0.4(-0.12 \sim 0.94)$	0.12 (-0.67~0.92)			
7	0.90 (-3.46~5.47)	$-0.02(-0.09 \sim 0.05)$	1.23 (0.28~2.2)	$-0.26(-0.72 \sim 0.20)$	0.41 (-0.11~0.93)	$0.4(-0.39 \sim 1.18)$			
0~1	11.48 (6.32~16.89)	$-0.02(-0.1 \sim 0.06)$	1.39 (0.23~2.58)	1.28 (0.76~1.80)	1.41 (0.84~1.97)	2.23 (1.41~3.06)			
0~2	10.62 (4.87~16.69)	$-0.06(-0.15 \sim 0.03)$	1.86 (0.46~3.26)	1.11 (0.53~1.71)	1.52 (0.90~2.13)	2.36 (1.45~3.28)			
0~3	8.61 (2.34~15.26)	$-0.1(-0.2 \sim 0)$	2.13 (0.54~3.73)	0.99 (0.34~1.65)	1.43 (0.74~2.12)	2.19 (1.16~3.23)			
0~4	7.04 (0.30~14.23)	$-0.12(-0.23 \sim 0.02)$	3.05 (1.32~4.81)	0.77 (0.07~1.49)	1.28 (0.52~2.04)	2.04 (0.97~3.12)			
0~5	7.18 (0.46~14.34)	$-0.16(-0.27 \sim 0.04)$	2.84 (0.95~4.77)	0.65 (-0.12~1.42)	1.23 (0.41~2.05)	1.81 (0.66~2.97)			
0~6	6.56 (-1.35~15.11)	$-0.19(-0.31 \sim 0.07)$	3.4 (1.37~5.47)	0.61 (-0.22~1.44)	1.38 (0.49~2.28)	1.6 (0.29~2.93)			
0~7	6.85 (-1.68~16.12)	-0.19 (-0.32~0.07)	4.38 (2.25~6.56)	0.41 (-0.46~1.28)	1.45 (0.50~2.41)	1.64 (0.24~3.05)			
% Changes (95% CI)—Inpatient Visits for All Hospitals									
0	5.61 (-0.05~11.59)	0.05 (-0.04~0.15)	1.66 (0.36~2.98)	0.77 (0.10~1.43)	0.80 (0.06~1.54)	1.06 (-0.02~2.14)			
1	5.19 (-0.45~11.15)	$0.05(-0.05 \sim 0.14)$	$0.4(-0.88 \sim 1.70)$	$0.52(-0.1 \sim 1.14)$	0.61 (-0.08~1.31)	1.13 (0.12~2.15)			
2	6.11 (0.35~12.20)	0 (-0.10~0.10)	0.33 (-1.01~1.68)	$0.2(-0.48 \sim 0.89)$	0.96 (0.26~1.66)	1.64 (0.62~2.67)			
3	3.37 (-2.33~9.41)	0.03 (-0.07~0.13)	0.47 (-0.83~1.79)	0.77 (0.13~1.41)	0.89 (0.18~1.59)	1.26 (0.23~2.30)			
4	3.44 (-2.26~9.46)	0.01 (-0.08~0.11)	0.72 (-0.58~2.04)	0.53 (-0.11~1.17)	0.57 (-0.14~1.27)	0.95 (-0.07~1.99)			
5	4.26 (-1.43~10.28)	0.06 (-0.04~0.1)	0.87 (-0.42~2.19)	$0.45(-0.18 \sim 1.09)$	0.83 (0.14~1.52)	1.51 (0.51~2.53)			
6	2.61 (-3.01~8.56)	0 (-0.11~0.10)	0.96 (-0.34~2.28)	0.49 (-0.15~1.13)	0.63 (-0.07~1.33)	0.72 (-0.3~1.75)			
7	2.59 (-3.09~8.61)	0.09 (-0.02~0.19)	1.2 (-0.13~2.55)	0.73 (0.04~1.43)	1.02 (0.27~1.78)	0.79 (-0.27~1.86)			
0~1	7.29 (0.82~14.18)	0.05 (-0.06~0.16)	1.31 (-0.26~2.90)	0.74 (0.05~1.45)	0.75 (-0.04~1.53)	1.19 (0.04~2.34)			
0~2	10.22 (3.01~17.92)	0.06 (-0.07~0.18)	1.44 (-0.41~3.34)	0.90 (0.14~1.67)	1.19 (0.34~2.05)	1.93 (0.68~3.19)			
0~3	11.48 (3.55~20.01)	$0.05(-0.08 \sim 0.19)$	$1.72(-0.43 \sim 3.93)$	1.10 (0.26~1.93)	1.46 (0.54~2.38)	2.26 (0.90~3.63)			

 $2.30(-0.10 \sim 4.76)$ 

2.77 (0.17~5.43)

3.04 (0.24~5.92)

3.66 (0.63~6.77)

 $1\,14\,(0\,23\sim2\,05)$ 

1.34 (0.37~2.32)

1.63 (0.59~2.67)

1.70 (0.59~2.84)

 $1.54(0.54 \sim 2.54)$ 

1.83 (0.78~2.90)

2.05 (0.93~3.19)

2.20 (1.01~3.41)

2.42 (0.95~3.91)

2.97 (1.41~4.55)

3.18 (1.53~4.86)

3.27 (1.51~5.07)

**Table 2.** Increased risk and 95% confidence intervals for per 10  $\mu$ g/m<sup>3</sup> increase in air pollutants for associations between air pollutants and outpatient and inpatient visits.

A total of 49 hospitals have been divided into four categories, namely general hospitals, pediatric hospital, ophthalmological hospital and cardiovascular hospital. Generalized additive models have performed separately on data of four categories of hospitals. Thereafter, associations with each  $10 \ \mu g/m^3$  increase in air pollutant concentration and 95% CI were estimated similarly by controlling temperature, relative humidity, pressure, time and day of the week. This study also calculated increase estimates for day-specific lags (lags 0–7), and day-specific moving average concentrations from 2 to 8 days for different categories of hospitals to assess the health effects of ambient air pollution. For general hospitals, all the pollutants investigated in this study were significantly associated with outpatient visits, with a maximum of 13.65% (95% CI: 5.47–22.46%) increase in visits for each  $10 \ \mu g/m^3$  increase in 2-day moving average concentration of SO<sub>2</sub>. Meanwhile, air pollutants except CO significantly increased risk of inpatient visits, which confirmed to results of overall inpatient visits and air pollutants, while the risk estimates of pollutants except O<sub>3</sub> suggested strong relations between air pollution and inpatient visits. Increase in pediatric hospital inpatient visits associated with each  $10 \ \mu g/m^3$  increase in air pollutant concentrations ranged from 0.16% (95% CI: 0.005–0.31%, CO with

lag'7) to 27.94% (95% CI: 8.44–50.96%, SO<sub>2</sub> with 8-day moving average). The results also showed that SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub> displayed significant associations for both outpatient and inpatient visits of ophthalmological hospitals. CO increased risk for outpatient visits but did not significantly affect inpatient visits of ophthalmological hospitals. Analyses of outpatient and inpatient visits for cardiovascular hospital revealed that air pollutants except CO increased risk for outpatient visits, while only NO<sub>2</sub> were observed to be strongly associated with inpatient visits.

# 4. Discussion

The present study analyzed the hospital visits (outpatient and inpatient visits) data obtained from Shenzhen CDC to investigate associations between major air pollutants and hospital inpatient and outpatient visits over a period of 12 months. Significant associations between air pollutants including SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, as well as PM<sub>2.5</sub>, and two types of hospital visits were observed. The estimated increase in overall outpatient visits associated with each 10  $\mu$ g/m<sup>3</sup> increase in air pollutant concentrations ranged from 0.48% (O<sub>3</sub> at lag 2) to 11.48% (SO<sub>2</sub> with 2-day moving average); for overall inpatient visits ranged from 0.73% (O<sub>3</sub> at lag 7) to 17.13% (SO<sub>2</sub> with 8-day moving average). For general and ophthalmological hospitals, the strength of the associations is consistent with estimates of overall outpatient visits, while different results have been obtained for pediatric and cardiovascular hospitals.

While ambient air pollution consists of a complex mixture of compounds, the study focused on SO<sub>2</sub>, CO, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>. SO<sub>2</sub> is a traditional pollutant of industrial origin related to the combustion of coal and other fossil fuels. Consistent with the previous findings, our study demonstrated that the daily outpatient and inpatient visits were significantly associated with the concentration of SO<sub>2</sub> [20,21]. A list of studies provided evidence that hospital admission due to allergic rhinitis [22], asthma [18,23] and acute respiratory diseases [24,25] were related to exposure to SO<sub>2</sub>. Increases in various types of admission would elevate the overall hospital admission, which might explain the significant associations between SO<sub>2</sub> and overall outpatient and inpatient visits in our study.

Our study results shown that CO only had significant estimated associations with inpatient visits to the pediatric hospital, which partially agreed with the previous studies. Pan et al. [26] found that there were positive associations between CO levels and asthma. Bell et al. [27] shown that short term exposure to ambient CO, even at low ambient CO concentration, was associated with risk of cardiovascular disease hospitalizations. In addition, Fusco et al. [28] have evaluated the associations between CO and most of the respiratory conditions in all ages in Rome. They have found that CO was remained an independent predictor for respiratory admission. On the other hand, Villeneuve et al. [29] found that when CO increased by interquartile range of 5-day moving average, the risk of an asthma emergency department visit for children aged 2–4 would increase by 48%. Hajat et al. [30] identified that CO was significant associated with daily asthma visits and other lower respiratory disease in children. Compared with other age groups, children are more susceptible and they would not be affected by the confounders such as smoking, stress, emotional factors and systemic diseases, which may explain, at least in part, why ambient CO was only associated with inpatient visits in pediatric hospital in our study.

The main sources of ambient NO<sub>2</sub> emission are coal and oil fired power plants and gasoline powered motor vehicle engines. The results of this study shows that increase of NO<sub>2</sub> concentrations has a statistically significant association with outpatient and inpatient visits for all categories of hospitals. It is in agreement with studies that focused on hospital visits for specific diseases [31]. In both meta-analysis [32] and spatiotemporal analysis [33], robust associations were found for NO<sub>2</sub> elevation and asthma admission, which support our findings in this study.

 $O_3$  is a highly reactive gas which might induce bronchial inflammation, constriction of the airways and decrease lung function. The findings in our study have demonstrated strong associations between  $O_3$  and outpatient visits of general, ophthalmological and cardiovascular hospitals, while yielding inconsistent results for inpatient visits of pediatric and cardiovascular hospitals. Similarly, the previous studies have not yielded consistent results on associations between  $O_3$  and certain type of hospital admissions. Exposures to  $O_3$  have been previously reported to be associated with asthma admission and emergency department visits [33]. In contrast, admission due to asthma were not associated with  $O_3$  in North America [34]. For respiratory conditions, strong association of 10.00% increase in outpatient visits with per 10  $\mu$ g/m<sup>3</sup> increase in  $O_3$  has been reported for total respiratory disease after controlling for potential confounders [35]. However, daily general practice admission for respiratory conditions were unrelated to  $O_3$  in Taiwan [36]. The effect of  $O_3$  might be confounded by different types of admission to hospitals, which could explain the inconsistent results obtained in this study.

 $PM_{10}$  and  $PM_{2.5}$  are reported to be the major indicators of air pollutants which have direct negative bearings on human health. In our study,  $PM_{10}$ , and  $PM_{2.5}$  were associated with increased likelihood of hospital outpatient and inpatient visits with every 10 µg/m<sup>3</sup> increase in pollutant concentrations. Both  $PM_{10}$  and  $PM_{2.5}$  are heterogeneous mixture of small solid or liquid particles with varying compositions in the atmosphere, which would impact the outpatient and inpatient visits in a quite similar pattern. For specific disease risk evaluation, research studies found no consistent results between  $PM_{10}$  and asthma admissions [37]. Increase of the average levels of  $PM_{2.5}$  has been found to increase the daily outpatient visits in respiratory hospitals (per 10 µg/m<sup>3</sup> increase = 0.35%, 95% CI: 0.12–1.64%), while  $PM_{10}$  was not significantly associated with daily outpatient visits of the same hospital [38]. Pan et al. found levels of  $PM_{10}$  were associated with outpatient visits for asthma [27]. Hwang and Chan analyzed the data obtained from clinic records and environmental monitoring stations in Taiwan and reported a significant impact of  $PM_{10}$  on outpatient visits [36]. These results were consistent with our findings.

Most of previous studies have focused on air pollutants on specific diseases of certain hospitals. The analysis conducted in this study evaluated the associations between different air pollutants and overall outpatient and inpatient visits. A major strength of the study is the high-quality data obtained from the Shenzhen with a high coverage of all hospitalized outpatient and inpatient visits. Since the database includes various types of visits in multiple hospitals and different air pollutant data that are highly representative, we can rule out the possibility of selection bias. Particularly, since the data were obtained from a historical database and collected sufficient information, recall bias was avoided.

There were still several potential limitations in our study. First, though several potential confounders were adjusted in the generalized additive models, a bunch of possible confounding variables such as seasonal effect, family history, occupational exposures were not included in present study. Second, self-treatment with alternative services was not included. Therefore, the extent of the issue may have been considerably underestimated. Finally, potentially inaccurate data in the records could increase the estimation error in statistical analysis.

## 5. Conclusions

In conclusion, the present study provides evidence that ambient air pollution exerted increased health risk effects on health and increased certain types of hospital outpatient and inpatient visits. These findings reinforce the importance of air pollution controls and disease prevention in less polluted areas, and warn the public about the atmospheric factors that could impact public health. This study also provides insight into the planning of clinical services and emergency contingency response for air pollution exposures.

**Acknowledgments:** The authors would like to thank Shenzhen Environmental Protection Bureau and Shenzhen Meteorological Bureau for providing the open access to necessary data. This research was supported by supported by National High Technology Research and Development Program of China (2015AA020109).

**Author Contributions:** Yachuan Liu and Shanen Chen analyzed the data and wrote the results section; Jian Xu and Xiaojian Liu analyzed the data; Yongsheng Wu and Lin Zhou performed the data collection and interpretation; Jinquan Cheng, Hanwu Ma, Jing Zheng and Denan Lin designed research framework and wrote the discussion. Li Zhang and Lili Chen wrote the introduction and materials and method.

Conflicts of Interest: The authors declare no conflict of interest.

# References

- Chen, R.; Wang, X.; Meng, X.; Hua, J.; Zhou, Z.; Chen, B.; Kan, H. Communicating air pollution-related health risks to the public: An application of the Air Quality Health Index in Shanghai, China. *Environ. Int.* 2013, *51*, 168–173. [CrossRef] [PubMed]
- Goldberg, M.S.; Burnett, R.T.; Stieb, D.M.; Brophy, J.M.; Daskalopoulou, S.S.; Valois, M.F.; Brook, J.R. Associations between ambient air pollution and daily mortality among elderly persons in Montreal, Quebec. *Sci. Total Environ.* 2013, 463, 931–942. [CrossRef] [PubMed]
- 3. Chen, R.; Chu, C.; Tan, J.; Cao, J.; Song, W.; Xu, X.; Jiang, C.; Ma, W.; Yang, C.; Chen, B.; et al. Ambient air pollution and hospital admission in Shanghai, China. *J. Hazard. Mater.* **2010**, *181*, 234–240. [CrossRef] [PubMed]
- 4. Strickland, M.J.; Darrow, L.A.; Klein, M.; Flanders, W.D.; Sarnat, J.A.; Waller, L.A.; Sarnat, S.E.; Mulholland, J.A.; Tolbert, P.E. Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. *Am. J. Respir. Crit. Care Med.* **2010**, *182*, 307–316. [CrossRef] [PubMed]
- 5. Schwartz, J.; Slater, D.; Larson, T.V.; Pierson, W.E.; Koenig, J.Q. Particulate air pollution and hospital emergency room visits for asthma in Seattle. *Am. Rev. Respir. Dis.* **1993**, *147*, 826–831. [CrossRef] [PubMed]
- 6. Lavigne, E.; Villeneuve, P.J.; Cakmak, S. Air pollution and emergency department visits for asthma in Windsor, Canada. *Can. J. Public Health* **2012**, *103*, 4–8. [PubMed]
- 7. Schwartz, J.; Morris, R. Air pollution and hospital admissions for cardiovascular disease in Detroit, Michigan. *Am. J. Epidemiol.* **1995**, 142, 23–35. [CrossRef] [PubMed]
- Guo, Y.; Tong, S.; Zhang, Y.; Barnett, A.G.; Jia, Y.; Pan, X. The relationship between particulate air pollution and emergency hospital visits for hypertension in Beijing, China. *Sci. Total Environ.* 2010, 408, 4446–4450. [CrossRef] [PubMed]
- Xia, X.; Zhang, A.; Liang, S.; Qi, Q.; Jiang, L.; Ye, Y. The association between air pollution and population health risk for respiratory infection: A case study of Shenzhen, China. *Int. J. Environ. Res. Public Health* 2017, 14, 950. [CrossRef] [PubMed]
- Guo, Y.; Jia, Y.; Pan, X.; Liu, L.; Wichmann, H.E. The association between fine particulate air pollution and hospital emergency room visits for cardiovascular diseases in Beijing, China. *Sci. Total Environ.* 2009, 407, 4826–4830. [CrossRef] [PubMed]
- 11. Guo, Y.; Barnett, A.G.; Zhang, Y.; Tong, S.; Yu, W.; Pan, X. The short-term effect of air pollution on cardiovascular mortality in Tianjin, China: Comparison of time series and case-crossover analyses. *Sci. Total Environ.* **2010**, *409*, 300–306. [CrossRef] [PubMed]
- 12. Cao, J.; Li, W.; Tan, J.; Song, W.; Xu, X.; Jiang, C.; Chen, G.; Chen, R.; Ma, W.; Chen, B.; et al. Association of ambient air pollution with hospital outpatient and emergency room visits in Shanghai, China. *Sci. Total Environ.* **2009**, *407*, 5531–5536. [CrossRef] [PubMed]
- Lisabeth, L.D.; Escobar, J.D.; Dvonch, J.T.; Sanchez, B.N.; Majersik, J.J.; Brown, D.L.; Smith, M.A.; Morgenstern, L.B. Ambient air pollution and risk for ischemic stroke and transient ischemic attack. *Ann. Neurol.* 2008, 64, 53–59. [CrossRef] [PubMed]
- 14. Oudin, A.; Stromberg, U.; Jakobsson, K.; Stroh, E.; Bjork, J. Estimation of short-term effects of air pollution on stroke hospital admissions in southern Sweden. *Neuroepidemiology* **2010**, *34*, 131–142. [CrossRef] [PubMed]
- 15. Hagler, G.S.W.; Bergin, M.H.; Salmon, L.G.; Yu, J.Z.; Wan, E.C.H.; Zheng, M.; Zeng, L.M.; Kiang, C.S.; Zhang, Y.H.; Lau, A.K.H. Source areas and chemical composition of fine particulate matter in the Pearl River Delta region of China. *Atmos. Environ.* **2006**, *40*, 3802–3815. [CrossRef]
- Jahnet, H.J.; Schneider, A.; Breitner, S.; Eißner, R.; Wendisch, M.; Krämer, A. Particulate matter pollution in the megacities of the Pearl River Delta, China—A systematic literature review and health risk assessment. *Int. J. Hyg. Environ. Health* 2011, 214, 281–295. [CrossRef] [PubMed]
- 17. Richter, A.; Burrows, J.P.; Nuess, H.; Granier, C.; Niemeier, U. Increase in tropospheric nitrogen dioxide over China observed from space. *Nature* **2005**, *437*, 129–132. [CrossRef] [PubMed]
- 18. Tao, Y.B.; Huang, W.; Huang, X.L.; Zhong, L.J.; Lu, S.E.; Li, Y.; Dai, L.Z.; Zhang, Y.H.; Zhu, T. Estimated acute effects of ambient ozone and nitrogen dioxide on mortality in the Pearl River Delta of southern China. *Environ. Health Perspect.* **2012**, *120*, 393–398. [CrossRef] [PubMed]

- Peel, J.L.; Tolbert, P.E.; Klein, M.; Metzger, K.B.; Flanders, W.D.; Todd, K.; Mulholland, J.A.; Ryan, P.B.; Frumkin, H. Ambient air pollution and respiratory emergency department visits. *Epidemiology* 2005, *16*, 164–174. [CrossRef] [PubMed]
- 20. Lindgren, A.; Stroh, E.; Nihlen, U.; Montnemery, P.; Axmon, A.; Jakobsson, K. Traffic exposure associated with allergic asthma and allergic rhinitis in adults. A cross-sectional study in southern Sweden. *Int. J. Health Geogr.* **2009**, *8*, 25. [CrossRef] [PubMed]
- 21. Zhang, F.; Wang, W.; Lv, J.; Krafft, T.; Xu, J. Time-series studies on air pollution and daily outpatient visits for allergic rhinitis in Beijing, China. *Sci. Total Environ.* **2011**, 409, 2486–2492. [CrossRef] [PubMed]
- 22. Wood, S.N.; Augustin, N.H. GAMs with integrated model selection using penalized regression splines and applications to environmental modelling. *Ecol. Model.* **2002**, *157*, 157–177. [CrossRef]
- 23. Chan, T.C.; Chen, M.L.; Lin, I.F.; Lee, C.H.; Chiang, P.H.; Wang, D.W.; Chuang, J.H. Spatiotemporal analysis of air pollution and asthma patient visits in Taipei, Taiwan. *Int. J. Health Geogr.* **2009**, *8*, 26. [CrossRef] [PubMed]
- 24. Wong, C.M.; Thach, T.Q.; Chau, P.Y.; Chan, E.K.; Chung, R.Y.; Ou, C.Q.; Yang, L.; Peiris, J.S.; Thomas, G.N.; Lam, T.H.; et al. Interaction between air pollution and respiratory viruses: Time-series study of daily mortality and hospital admissions in Hong Kong. *Res. Rep. Health Eff. Inst.* **2010**, *154*, 283–362.
- 25. Li, R.; Jiang, N.; Liu, Q.; Huang, J.; Guo, X.; Liu, F.; Gao, Z. Impact of air pollutants on outpatient visits for acute respiratory outcomes. *Int. J. Environ. Res. Public Health* **2017**, *14*, 47. [CrossRef] [PubMed]
- Pan, H.H.; Chen, C.T.; Sun, H.L.; Ku, M.S.; Liao, P.F.; Lu, K.H.; Sheu, J.N.; Huang, J.Y.; Pai, J.Y.; Lue, K.H. Comparison of the effects of air pollution on outpatient and inpatient visits for asthma: A population-based study in Taiwan. *PLoS ONE* 2014, *9*, e96190. [CrossRef] [PubMed]
- Bell, M.L.; Peng, R.D.; Dominici, F.; Samet, J.M. Emergency hospital admissions for cardiovascular diseases and ambient levels of carbon monoxide: Results for 126 United States urban counties, 1999–2005. *Circulation* 2009, 120, 949–955. [CrossRef] [PubMed]
- Fusco, D.; Forastiere, F.; Michelozzi, P.; Spadea, T.; Ostro, B.; Arca, M.; Perucci, C.A. Air pollution and hospital admissions for respiratory conditions in Rome, Italy. *Eur. Respir. J.* 2001, *17*, 1143–1150. [CrossRef] [PubMed]
- Villeneuve, P.J.; Chen, L.; Rowe, B.H.; Coates, F. Outdoor air pollution and emergency department visits for asthma among children and adults: A case-crossover study in northern Alberta, Canada. *Environ. Health* 2007, *6*, 40. [CrossRef] [PubMed]
- Hajat, S.; Haines, A.; Goubet, S.A.; Atkinson, R.W.; Anderson, H.R. Association of air pollution with daily GP consultations for asthma and other lower respiratory conditions in London. *Thorax* 1999, 54, 597–605. [CrossRef] [PubMed]
- 31. Santos, U.P.; Terra-Filho, M.; Lin, C.A.; Pereira, L.A.; Vieira, T.C.; Saldiva, P.H.; Braga, A.L. Cardiac arrhythmia emergency room visits and environmental air pollution in Sao Paulo, Brazil. *J. Epidemiol. Community Health* **2008**, *62*, 267–272. [CrossRef] [PubMed]
- 32. Takenoue, Y.; Kaneko, T.; Miyamae, T.; Mori, M.; Yokota, S. Influence of outdoor NO<sub>2</sub> exposure on asthma in childhood: Meta-analysis. *Pediatr. Int.* **2012**, *54*, 762–769. [CrossRef] [PubMed]
- Winquist, A.; Klein, M.; Tolbert, P.; Flanders, W.D.; Hess, J.; Sarnat, S.E. Comparison of emergency department and hospital admissions data for air pollution time-series studies. *Environ. Health* 2012, *11*, 70. [CrossRef] [PubMed]
- Schildcrout, J.S.; Sheppard, L.; Lumley, T.; Slaughter, J.C.; Koenig, J.Q.; Shapiro, G.G. Ambient air pollution and asthma exacerbations in children: An eight-city analysis. *Am. J. Epidemiol.* 2006, 164, 505–517. [CrossRef] [PubMed]
- 35. Lin, Y.K.; Chang, S.C.; Lin, C.; Chen, Y.C.; Wang, Y.C. Comparing ozone metrics on associations with outpatient visits for respiratory diseases in Taipei Metropolitan area. *Environ. Pollut.* **2013**, *177*, *177–184*. [CrossRef] [PubMed]
- 36. Hwang, J.S.; Chan, C.C. Effects of air pollution on daily clinic visits for lower respiratory tract illness. *Am. J. Epidemiol.* **2002**, *155*, 1–10. [CrossRef] [PubMed]

- Slaughter, J.C.; Kim, E.; Sheppard, L.; Sullivan, J.H.; Larson, T.V.; Claiborn, C. Association between particulate matter and emergency room visits, hospital admissions and mortality in Spokane, Washington. *J. Expo. Anal. Environ. Epidemiol.* 2005, *15*, 153–159. [CrossRef] [PubMed]
- 38. Ma, G.P.; Zou, B.L.; Xu, Z.C.; Lv, J.C. Association of respiratory diseases outpatient visits and air pollution in a district, Guangzhou: A time-series study. *J. Environ. Health* **2012**, *29*, 526–528.



© 2018 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).