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Association between Ambient Air Pollution and Hospital Admissions, Length of Hospital Stay and Hospital Cost for Patients with Cardiovascular Diseases and Comorbid Diabetes Mellitus: Base on 1,969,755 cases in Beijing, China, 2014–2019 †

Running title: Air pollution on daily admissions, hospital stay and cost for CVD with comorbid DM

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Abstract: *Background* Evidence on the effects of the air pollutants on the hospital admissions, hospital cost and length of stay (LOS) among patients with comorbidities remains limited in China, particularly for patients with cardiovascular diseases and comorbid diabetes mellitus (CVD-DM). *Methods* We collected daily data on CVD-DM patients from 242 hospitals in Beijing between 2014 and 2019. Generalized additive model was employed to quantify the associations between admissions, LOS, and hospital cost for CVD-DM patients and air pollutants. We further evaluated the attributable risk posed by air pollutants to CVD-DM patients, using both Chinese and WHO air quality guidelines as reference. *Results* Per 10 ug/m3 increase of particles with an aerodynamic diameter < 2.5 μm (PM2.5), particles with an aerodynamic diameter < 10 μm (PM10), sulfur dioxide (SO2), nitrogen dioxide (NO2), carbonic oxide (CO) and ozone (O3) corresponded to a 0.64% (95% CI: 0.57 to 0.71), 0.52% (95% CI: 0.46 to 0.57), 0.93% (95% CI: 0.67 to 1.20), 0.98% (95% CI: 0.81 to 1.16), 1.66% (95% CI: 1.18 to 2.14) and 0.53% (95% CI: 0.45 to 0.61) increment for CVD-DM patients' admissions. Among the six pollutants, particulate pollutants (PM2.5 and PM10) in most lag days exhibited adverse effects on LOS and hospital cost. For every 10 ug/m3 increase in PM2.5 and PM10, the absolute increase with LOS will increase 62.08 days (95% CI: 28.93 to 95.23) and 51.77 days (95% CI:22.88 to 80.66), respectively. The absolute increase with hospital cost will increase 105.04 Chinese Yuan (CNY) (95% CI: 49.27 to 160.81) and 81.76 CNY (95% CI: 42.01 to 121.51) in PM2.5 and PM10, respectively. Given WHO 2021 air quality guideline as the reference, PM2.5 had the maximum attributable fraction of 3.34% (95% CI: 2.94% to 3.75%), corresponding to an avoidable of 65,845 (95% CI: 57,953 to 73,812) patients with CVD-DM. Conclusion PM2.5 and PM10 are positively associated with hospital admissions, hospital cost and LOS for patients with CVD-DM. Policy changes to reduce air pollutants exposure may reduce CVD-DM admissions and substantial savings in health care spending and LOS..

Keywords: air pollutants, hospital admissions, length of stay, hospital cost, comorbidities

1. Introduction

As one of the leading causes of morbidity and mortality, cardiovascular disease (CVD) and diabetes mellitus (DM) have caused a huge health burden worldwide [1, 2]. According to the Global Burden of Disease (GBD) Study 2019, an estimated 523 million adults were living with CVD and 463 million adults were living with DM [3,4]. CVD often coexists with DM in clinical practice [5]. People with diabetes have a higher prevalence rate of CVD than people without diabetes [6], and the risk of CVD continues to increase as fasting plasma glucose levels rise, even before reaching levels sufficient for a diagnosis of diabetes [7]. CVD and comorbid DM imposes a tremendous burden on patients [8, 9]. To reduce the prevalence of comorbid CVD and DM, it is vital to examine modifiable risk factors to formulate appropriate measures for prevention and control. Ambient air pollutants are common modifiable risk factors for both CVD and DM [10, 11]. For example, growing evidence showed that particulate matters are associated with CVD and DM [12, 13]. Etiological studies found patients with diabetes mellitus can have reduced vascular elasticity due to the large amount of glucose adhering to the inner walls of blood vessels [14]. At the same time, most patients with cardiovascular disease develop atherosclerosis of small blood vessels, which exacerbates the damage to vascular endothelial function caused by air pollution [15]. However, few studies have estimated the effect of air pollution in patients with cardiovascular diseases and comorbid diabetes mellitus (CVD-DM) [16, 17], and could not completely reflect the burden of diseases using morbidity and mortality as indicators [18]. Recently, the effect of air pollution on length of stay (LOS) and hospital cost have attracted increasing attention [19]. CVD and DM are more common and frequently less well-controlled in China due to low use of cardio-protective and glucose-control medications [20]. Beijing, the capital of China, suffers from more serious air pollution than some cities in western developed countries, and studies have shown that the toxic composition of air pollutants varies from region to region [21]. Therefore, we aimed to estimate the association of air pollutants with hospital admissions, LOS and hospital cost for CVD-DM patients in Beijing, China. Furthermore, we also discussed the attributable fraction of CVD-DM due to exposure to air pollution under different Air Quality Guidelines (AQG), such as the WHO AQG 2021 which has tightened the recommendation on all air pollutants [22]. We hypothesized that air pollution would be positively associated with hospital admissions, LOS and hospital cost for CVD-DM patients.

2. Material and Methods

2.1. Data collection

2.1.1. Patient data

CVD-DM patients data between January, 1, 2014 and December, 31, 2019 from 242 Second-class hospital or higher across Beijing were collected from Beijing Municipal Health Commission Information Center (BMHCIC, http://www.phic.org.cn/) which is a government agency that implements the specific work of integrating health information resources in Beijing and is responsible for the statistics and analysis of relevant health information data (Figure S3). We have acquired a cooperation agreement with BMHCIC. During the cooperation period we are authorized to perform data analysis at the Information Statistics Department of BMHCIC. Due to the sensitivity of the data, the raw data can only be obtained and used on a dedicated computer at BMHCIC. The original database was individual data with patient ID, gender, age, date in hospital, length of stay, hospital cost and admission diagnosis. Then we reshaped the original database into time series data to get daily number of admissions, length of stay and hospital cost of CVD-DM patients with different demographic characteristics (e.g., age and gender). The admission diagnosis was determined by the International Classification of Diseases 10th Revision (ICD-10). The CVD-DM patient was defined as the admission diagnosis with an ICD-10 code between I00 and I99 and E12. More specific information about the data can be found in our previously published articles [23-25].

2.1.2. Air pollutants and meteorology factors data

We collected air pollution data from 35 fixed monitoring stations set up by Beijing Environmental Protection Bureau (BEPB, http://zx.bjmemc.com.cn/?timestamp=1621413941009), which is one of the first environmental professional monitoring institutions to obtain national-level metrological certification and a certificate of conformity for metrological certification granted by the China Technical Supervision Bureau. Air pollution data were monitored according to the standard methods specified in "Ambient Air Quality Standards GB3095-2012" [26]. All monitoring equipment follows the "Measures for On-site Supervision and Inspection of Pollution Source Automatic Monitoring Facilities" [27], and the air pollutant monitoring system was regularly calibrated dynamically using calibrators and analyzers certified by national metrology institutions. All the above documents were released by the Ministry of Ecological Protection of China. The variables include particulate matter less than 2.5 μm in diameter (PM2.5, μg/m3), particulate matter less than 10 μm in diameter (PM10, μg/m3), carbon monoxide (CO,mg/m3), ozone (O3, μg/m3), nitrogen dioxide (NO2, μg/m3) and sulfur dioxide (SO2,μg/m3) (Figure S3). Meteorology factors data including temperature (°C) and relative humidity (%) were collected from China Meteorological Data Sharing Service System online (CMDSSS, https://data.cma.cn/en). We matched the average data aggregated across all monitoring sites with total hospital admissions data from 242 hospitals by date.

2.2. Statistical Analysis

First, we used means, standard deviations (SD), quartiles, maximum, and minimum to describe the distribution of air pollutants and meteorology factors and used the calendar heat map to show the daily variation in the number of hospital admissions, LOS and hospital cost for CVD-DM patients. Then, we used generalized additive model (GAM) to explore the relationship between daily CVD-DM patients admissions, LOS, hospital cost and air pollutions, respectively. GAM model was proposed by Hastie and Tibshirani and can be used in time series analysis [28, 29]. It is an extension of the generalized linear model and can deal with the complex nonlinear relationship of various variables using smooth function. We determined the parameters of GAM model and then calculated the Percentage change (%, PC) for daily admissions and Absolute increase for LOS and hospital cost referred as previous study [30][31]. The process of building the GAM model and the calculation methods of PC and Absolute increase can be found in Section S1 and Section S2 in supplementary. We then explored the non-linear relationship using the plot.gam() function from mgcv package. Its requirement is that the link function of the model be a log function, so we only explored the nonlinear relationship between air pollution and hospital admissions. Next, we used two different lag structures to explore the delayed effect of air pollution [32]. Single lag is expressed as lag1, lag2, …, lag3. Cumulative lag is shown as lag01, lag02 lag03. Lag1 denotes the concentration of air pollutants on the previous day. Lag01 denotes the 2-day moving average concentration of air pollutants concentrations on the present day and previous day. Considering that we are focus on acute effect of air pollution, we chose a maximum lag period of 7 days both for single lag and moving lag. Following that, to better measure the burden of CVD-DM (e.g., admissions, LOS and hospital cost) attributable to air pollutants exposure, we used attributable number (AN) and population attributable fraction (PAF) based on the previous established GAM model. The method proposed by Lin et al. has been widely used in time series studies related to the assessment of the disease burden of air pollution [18, 30, 33]. Three different standards were obtained as the reference concentration, including China's air quality guideline (AQG), WHO's 2005 AQG and WHO's 2021 AQG. The detailed procedures are shown in Section S3 in supplementary. We also did subgroup analyses. Age and gender stratified subgroup analyses were used to explore differences in effect values across populations both in GAM model and attributable risk calculation. The Z test was adopted to test the differences between the different subgroups, where Z was calculated by the estimates of the two groups and compared to the standard normal distribution [34]. Finally, multiple sensitivity analyses were performed to confirm the stability of the results. For example, using single and multiple pollutant model, changing the df of time trend and excluding hospital that were far away from fixed air pollutant monitoring. All sensitivity analysis methods used in our study are shown in Section S4. All statistical analyses were conducted in R software (version 4.0.2) using the MGCV, DLNM and TERRA packages. Arcmap software (version 10.5) was used for spatial mapping. The statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Result

3.1. Basic descriptive results

A total of 1,969,755 CVD-DM patients were included in our study (Table S1), which related to 19.7 million length of hospital stay days and 24.7 billion CNY hospital cost. The daily range for CVD-DM admission, LOS and hospital cost were from 5 to 2,543 patients, 4,638.97 to 24,792.00 days and 6,714.65 to 36,588.83 thousand CNY, respectively. For the air pollutants, particulate pollutants had the widest concentration range which correspond to from 67.08 ug/m3 to 444.09 ug/m3 for PM2.5 and from 72.04 ug/m3 to 901.24 ug/m3 for PM10 (Table 1). Figure S2 indicates that there were positive correlations between PM2.5, PM10, SO2, CO and relative humidity among which PM2.5 and PM10, PM2.5 and CO had a strong correlation (correlation coefficient > 0.80). O3, average temperature and other pollutants showed a negative correlation.

3.2. Effect of air pollution on CVD-DM

Figure 1 shows the PC value in each air pollutants with different lag days in CVD-DM admissions in the multi-pollutant model. All six air pollutants show statistically different adverse effects. The best lag day varies among six pollutants for total population in which PM2.5 is 0.64% (95% CI: 0.57 to 0.71) at lag 06, PM10 is 0.52% (95% CI: 0.46 to 0.57) at lag 06, SO2 is 0.93% (95% CI: 0.67 to 1.20) at lag 01, NO2 is 0.98% (95% CI: 0.81 to 1.16) at lag 02, CO is 1.66% (95% CI: 1.18 to 2.14) at lag 03 and O3 is 0.53% (95% CI: 0.45 to 0.61) at lag 7. In age subgroup analysis, the effect is stronger in young adult than those over 65 years old. Figure 2 and Figure 3 show the absolute increase with LOS and hospital cost in six air pollutants, respectively. Among the six pollutants, particulate pollutants (PM2.5 and PM10) in most lag days exhibited adverse effects on LOS and hospital cost. More specifically, for every 10 ug/m3 of increase in PM2.5 and PM10 concentration, the absolute increase with LOS will increase 62.08 days (95% CI: 28.93 to 95.23) at lag 03 and 51.77 days (95% CI:22.88 to 80.66) at lag 06, respectively. The absolute increase with hospital cost will increase 105.04 CNY (95% CI: 49.27 to 160.81) and 81.76 CNY (95% CI: 42.01 to 121.51) in PM2.5 and PM10, respectively.

3.3. Attributable risk of CVD-DM due to air pollution

We further estimated the attributable risk of air pollutants on CVD-DM for admissions, LOS and hospital cost based on China's AQG, WHO's 2005 AQG and WHO's 2021 AQG. More admissions, LOS and hospital cost will be avoided, in using the latest WHO 2021 AQG as the standard (Table 2 to Table 4). Table 2 displays avoidable value and population attributable fraction for admissions in total population. The maximum attributable fraction in all pollutants is PM2.5 using WHO 2021 AQG as the reference which we estimated that about 3.34% (95% CI: 2.94% to 3.75%) corresponding to an avoidable of 65,845 (95% CI: 57,953 to 73,812) CVD-DM patients. Similar results were found in subgroup populations (Table S15 and Table S16). Table 3 and Table 4 displays avoidable value and population attributable fraction for LOS and hospital cost, respectively. Overall, PM10, PM2.5 and O3 will significantly avoid more LOS and hospital cost using WHO 2021 as the reference, compared to other air pollutants. However, the population attributable fraction of particulate pollutants is higher than that of O3. Subgroup analyses stratified by age and sex found similar results (Table 17 to Table S20).

3.4. The exposure-response curve between air pollution and hospital admissions

The exposure-response curve between six air pollutants and CVD-DM patient admissions are shown in Figure S23. Approximately U-shaped curves with different degrees of curvature were observed in each air pollutant, which indicated that the effect of air pollution on CVD-DM patient admissions tend to be nonlinear. For example, high risks were observed for high NO2 concentrations, with flat slopes at low concentrations and steeper slopes for concentrations ≥ 60 μg/m3.

3.5. Sensitivity analysis

Our sensitivity analyses by varying the time and air pollution degrees of freedom did not substantially change the effect estimates (Figure S8 to Figure S10), and the E- value calculated for the total population and each subpopulation did not exceed the original RR (Table S21). The results were very close between 6 air pollutants and 3 different outcomes (hospital admissions, length of stay and hospital cost) in single and multiple pollutant model using the screened hospital data and all hospital data (Figure S11 to Figure S16). The model results from CHAP data were mostly consistent with the results using 35 fixed monitoring stations (Figure S17 to Figure S22).

4. Discussion

Most previous studies have examined the separate associations between air pollutants and CVD or DM, and few studies have investigated the association between air pollutants and patients with CVD-DM. This is the first study, to our knowledge, to examine the relationship between the six air pollutants and hospital admissions, LOS and hospital cost among patients with CVD-DM, synchronously, as well as the burden of CVD-DM attributable to air pollutants exposure. We observed that daily air pollution especially particulate matter pollutants are associated with an increased risk of hospital admissions, LOS and hospital cost for patients with CVD-DM. For most air pollutants, the effects of air pollutants at lag 0 are already statistically significant for patients with CVD-DM and reached maximum effect at lag 03 or lag 06 in our study. However, Other epidemiological studies have found a general 2-6 days lag in the effect of air pollutants on patients with CVD or DM alone [35]. A study based on 8084 Italian municipalities reported that the effect of PM2.5 and PM10 on cardiovascular mortality is not statistically significant until at lag 6 averagely [36]. Mojtaba et al. found that there were a statistically significant effects on emergency hospital admissions of cardiovascular patients only at lag 2 for PM2.5 and lag 4 for CO [37]. Similar findings also have been found in other countries or other subpopulations [38, 39]. On the other hand, the effects of air pollutants on hospital admissions for patients with CVD-DM were stronger. For example, we found that increases of 10 ug/m3 in PM2.5 was associated with 0.64% (95% CI: 0.57 to 0.71) increases in hospital admissions for CVD-DM patients with best lag day in multiple pollutants model. A study based on a population of 28 million, also conducted in China, found that each 10 ug/m3 in PM2.5 was associated with 0.34% (95% CI: 0.20 to 0.48), which were slightly lower than the effect in the CVD-DM patients in our study [40]. There are several reasons to interpret the observed faster and stronger effects of air pollutants in patients with CVD-DM, comparing with the previous epidemiology studies. First, patients with CVD-DM have weaker immune systems. In patients with CVD, plasma lipoproteins are more likely to retain in the subendothelial wall of arteries triggering the formation of atherosclerotic plaques by T helper type 1 (Th1) cells and monocyte-derived macrophages, thereby weakening the immune system's resistance to other toxic substances, such as heavy metals carried in particulate matter [41]. Other studies have also shown that high glucose levels can also damage the immune system. These mechanisms include suppression of cytokine production, defects in phagocytosis, dysfunction of immune cells, and failure to kill microbials [42]. Second, our study site is still at high levels of air pollution. Compared to developed countries in Europe and the Americas, air pollutant levels in China, especially in the northern regions (e.g., Beijing), are still high. For example, the average PM2.5 concentration in a survey of air pollutant levels and population health conducted in Canada was only 8.9 ug/m3 [43], while the value in our study was 67.1 ug/m3, which is 7.5 times higher than the Canadian level. In addition, particulate matter is a complex mixture and the toxicology of each chemical component may vary by time and locations which shows different effect sizes in different regions [44]. We also observed in the age-stratified subgroup analysis that the effect of air pollutions on people older than 65 years were slightly lower than those younger adults. This may be related to the time spent outdoors. In China, outdoor physical activity has been a traditional practice [45], which makes young people more likely to inhale air pollutants compared to the elderly, thus showing a stronger effect of air pollutants on young people [46]. We observed that the relationship between six air pollutants and LOS and hospital cost were mainly significant in particulate pollutants for CVD-DM patients, which were in line with a few other studies. Xuyan et al. reported that after adjusting for multiple confounding factors, exposures to PM2.5 and PM10 were associated with increased LOS for all ischemic heart disease patients in both single- and multi-pollutant models [47]. In Shanghai, Voorhees et al. founded that avoided hospital admissions had an estimated value from 20 to 43 million yuan for PM10 [48]. One similar study conducted in Unites States reported that in multivariable analyses, a 1 mg/m3 increase in monthly PM2.5 led to a $47 increase in LOS [49]. The attributable risk estimated both using China's AQG and WHO's AQG in our study was in line with a few studies [50, 51]. And the associations remained similar when using WHO's AQG 2005 and WHO's AQG 2021, respectively. For example, when the recommended concentration of PM2.5 was reduced from 25 ug/m3 to 15 ug/m3, the population attributable fraction for hospital admissions in CVD-DM patients was only reduced from 3.1% to 3.34%. Although this is only a 0.24% reduction, if this ratio was applied to the global population of 7.6 billion, it would reduce hospital admissions for 18.24 million CVD-DM patients, which is a tremendous number. WHO proposed the new guideline to facilitate stepwise improvement in air quality and thus gradual, but meaningful, health benefits for the population, of which the greatest benefit would be observed in countries with high air pollution levels and large populations such as China [52]. In addition, the new guidelines could provide new evidence-informed tools for policymakers in each country to guide legislation and policies to reduce global air pollutant levels and reduce the burden of disease caused by exposure to air pollution. In our study, we employed multiple sensitivity analyses to confirm the stability of the results. The results of most sensitivity analyses were consistent. However, it is worth to be noted that the difference between the results of CHAP data and the results of Original data in the multi-pollutant model is slightly larger compared to the results of the single-pollutant model (For example, PM10 in Figure S17 vs. PM10 in Figure S20). We interpret this difference to be due to the different variables in the model. More specifically, in single-pollutant model, only the air pollutant of interest was included in the model in addition to the covariates, whether CHAP data or Original data were used. In multi-pollutant model, only PM10 and O3 were included when using CHAP data. However, when using Original data, in addition to the air pollutant of interest, the other 5 pollutants were also adjusted in multi-pollutant model in the form of principal components. All sensitivity analyses prove that our results are robust. There are several potential mechanisms to explain the adverse effects of air pollution for CVD-DM patients. Firstly, the inflammatory response induced in the lungs by inhaled air pollutants (e.g. SO2, CO) leads to the release of cytokines and other mediators that reach all parts of the body through the systemic circulation[53]. Secondly, pollutants may cross the alveolar wall and interact directly with the cardiovascular system [54]. Thirdly, for particulate pollutants, it may activate the autonomic nervous system through sensory receptors on the alveolar surface, which has been reported as a rapid way to affect cardiovascular function[53]. Finally, inhaled air pollutants could also damage endothelial dysfunction, hepatic insulin resistance, elevated hemoglobin level and alterations in autonomic tone which may increase insulin resistance [55, 56]. Our study encompasses several strengths. First, there was a large sample size, corresponding to nearly 2 million CVD-DM patients from 242 Second-class hospital or higher across Beijing were included in our study, which gives a good representation for the estimate. Second, we measured the relationship between air pollution and CVD-DM patients in several aspects, including hospital admissions, LOS and hospital cost which allows us for a more comprehensive view for the relationship between air pollutants and CVD-DM patients in terms of acute effects and disease burden. Third, we used multiple criteria including China's and WHO's AQG to estimate the attributable risk of pollutants. This is the first time the WHO's 2021 AQG has been applied to a real-world study since its publishing in September 2021. Several limitations should be noted. First, this study is an observational and ecological study, we cannot draw a causal inference although we used several methods to reduce the confounding bias. Second, We calculated air pollutant concentrations based on fixed monitoring stations, which may result in exposure measurement errors [57]. Third, Due to the expiration of the collaboration with BMHCIC, our study only focused on patients with total CVD comorbid with DM, and not all CVD subtypes are associated with air pollutants [36]. Meanwhile, we cannot check the number of hospital admission for CVD and DM respectively. We will continue to discuss with BMHCIC to obtain different types of CVD data for more detailed analysis in the future. Finally, we cannot adjust for confounding factors such as lifestyle habits, medication history, etc. for each individual, due to the aggregated time series data. Based on the findings of our present study and limitations, we propose the following points for future research. First, subsequent studies should be based on individual data with residential information for more in-depth exploration. We believe that data based on individual address information is more suitable for use in conjunction with satellite data such as AOD data [58] because it is possible to obtain accurate individual air pollution exposure through latitude and longitude information. Second, the specific components of particulate pollutants and the sources of gaseous pollutants vary from country to country, and subsequent studies should focus more on the effects of particular component. Finally, our study only preliminarily observed the effect of air pollution on total CVD comorbid with DM, and future studies should concentrate on the relationship between different subtypes of CVD comorbid with DM and air pollution to provide more precise findings.

5. Conclusion

In summary, air pollutants exposure especially PM2.5 and PM10 are associated with increased hospital admissions, hospital cost and length of hospital stay for CVD-DM patients. The effects of air pollutants are faster and stronger in patients with CVD-DM, compared to patients with CVD or DM alone. Policy changes to reduce air pollutants exposure may lead to improved CVD-DM admissions and substantial savings in health care spending and hospital stay.

Abbreviations

LOS: Length of hospital stay;
CVD-DM: Cardiovascular disease comorbid with diabetes;
PM2.5: particles with an aerodynamic diameter < 2.5 μm;
PM10: particles with an aerodynamic diameter < 10 μm ;
SO2: Sulfur dioxide;
NO2: Nitrogen dioxide;
O3: Ozone;
CO: Carbonic Oxide;
ICD-10: International Classification of Diseases 10th Revision;
BMHCIC: Beijing were collected from Beijing Municipal Health Commission Information Center
BEPB: Beijing Environmental Protection Bureau;
CMDSSS: China Meteorological Data Sharing Service System online;
GAM: Generalize additive model;
PC: Percentage change;
df: Degree of freedom;
AIC: Akaike information criterion;
CI: Confidence interval;
AN: Attributable number;
PAF: Population attributable fraction;
AQG: Air quality guideline;
AOD: aerosol optical depth;
LUR: Land use regression;

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Ethical Approval: The study protocol was approved by the Institutional Review Board at the School of Public Health, Capital Medical University.

Consent for publication: Our manuscript does not contain any individual person's data in any form (including any individual details, images or videos), so written informed consent was not required.

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Table 1 Distribution characteristics of daily cases of CVD-DM, air pollutants and meteorological factors in Beijing from 2014 to 2019.

Variables	Mean	SD	Min	P25	P50	P75	Max
Case number	899.02	475.60	5.00	386.00	975.00	1258.00	2543.00
LOS	8995.84	4638.97	77.00	3958.50	10081.00	12592.50	24792.00
Hospital cost (Thousand CNY)	13508.85	6714.65	33.68	5638.45	15071.67	18436.17	36588.83
PM2.5	67.08	60.24	4.31	26.09	49.53	87.62	444.09
PM10	99.08	72.04	5.63	51.98	81.80	123.84	901.24
SO2	45.91	21.25	8.55	31.29	41.62	55.59	146.00
NO2	11.17	13.82	2.03	3.34	6.34	12.36	127.79
CO	1.08	0.87	0.20	0.56	0.83	1.20	7.72
O3	59.99	36.58	3.26	31.01	55.00	82.06	189.24
Temperature	12.64	12.51	-31.99	1.36	14.20	23.74	38.06
Humidity	53.77	19.16	11.30	38.26	53.47	69.76	95.43

SD: Standard deviation ; LOS: length of hospital stay; The hospital cost data is only available for 2014 to 2018.

Table 2 The admission attributable risk for different population with different air quality guideline.

Type	Air Pollution	Guideline	Avoidable value	Population attributable fraction (%)
China	PM2.5	75	**24102 (21853, 26364)**	**1.22 (1.11, 1.34)**
	PM10	150	**11040 (9785, 12303)**	**0.56 (0.5, 0.62)**
	SO2	150	NA	NA
	NO2	80	**2194 (1814, 2577)**	**0.11 (0.09, 0.13)**
	CO#	4	**1123 (994, 1254)**	**0.06 (0.05, 0.06)**
	O3	160	NA	NA
WHO 2005	PM2.5	25	**46420 (42096, 50769)**	**2.36 (2.14, 2.58)**
	PM10	50	**38722 (34343, 43125)**	**1.97 (1.74, 2.19)**
	SO2	20	**3596 (2720, 4478)**	**0.18 0.14, 0.23)**

	O3*	100	259 (-290, 809)	0.01 (-0.01, 0.04)
WHO 2021	PM2.5	15	**50049 (45388, 54737)**	**2.54 (2.3, 2.78)**
	PM10	45	**44154 (39161, 49175)**	**2.24 (1.99, 2.5)**
	SO2	40	**1518 (1149, 1891)**	**0.08 (0.06, 0.10)**
	NO2	25	**37389 (30871, 43948)**	**1.9 (1.57, 2.23)**

#: China and WHO 2021 have the same standards for CO; *: WHO 2005 and WHO 2021 have the same standards for ozone; NA: The number of days over the recommended threshold during the study period was too small to calculate results.

Table 3 The LOS attributable risk for different population with different air quality guideline.

Type	Air Pollution	Guideline	Avoidable value	Population attributable fraction (%)
China	PM2.5	75	**177195.49 (75978.24, 278412.74)**	**0.9 (0.39, 1.41)**
	PM10	150	**89815.28 (35903.44, 143727.12)**	**0.46 (0.18, 0.73)**
	SO2	150	NA	NA
	NO2	80	14739.4 (-7613.16, 37091.97)	0.07 (-0.04, 0.19)
	CO#	4	**13063.45 (4405.52, 21721.38)**	**0.07 (0.02, 0.11)**
	O3	160	NA	NA
WHO 2005	PM2.5	25	**419641.49 (179934.72, 659348.27)**	**2.13 (0.91, 3.35)**
	PM10	50	**398975.18 (159489.37, 638460.98)**	**2.02 (0.81, 3.24)**
	SO2	20	32000.01 (-22137.04, 86137.07)	0.16 (-0.11, 0.44)
	O3*	100	12549.79 (-18025.09, 43124.67)	0.06 (-0.09, 0.22)
WHO 2021	PM2.5	15	**498172.26 (213607.3, 782737.22)**	**2.53 (1.08, 3.97)**
	PM10	45	**428844.34 (171429.5, 686259.18)**	**2.18 (0.87, 3.48)**
	SO2	40	11709.84 (-8100.66, 31520.34)	0.06 (-0.04, 0.16)
	NO2	25	250476.63 (-129375.59, 630328.86)	1.27 (-0.66, 3.2)

#: China and WHO 2021 have the same standards for CO; *: WHO 2005 and WHO 2021 have the same standards for ozone; NA: The number of days over the recommended threshold during the study period was too small to calculate results.

Table 4 The hospital cost attributable risk for different population with different air quality guideline.

Type	Air pollution	Guideline	Avoidable value	Population attributable fraction (%)
China	PM2.5	75	**227503.64 (90026.6, 364980.68)**	**0.92 (0.36, 1.48)**
	PM10	150	**128894.77 (55165.66, 202623.88)**	**0.52 (0.22, 0.82)**
	SO2	150	NA	NA
	NO2	80	9638.43 (-21977.47, 41254.33)	0.04 (-0.09, 0.17)
	CO#	4	**15167.92 (3133.07, 27202.78)**	**0.06 (0.01, 0.11)**
	O3	160	NA	NA
WHO 2005	PM2.5	25	**516354.94 (204329.38, 828380.51)**	**2.09 (0.83, 3.36)**
	PM10	50	**540872.22 (231487.86, 850256.58)**	**2.19 (0.94, 3.45)**
	SO2	20	13493.54 (-60767.08, 87754.15)	0.05 (-0.25, 0.36)
	O3*	100	12425.03 (-33207.45, 58057.51)	0.05 (-0.13, 0.24)
WHO 2021	PM2.5	15	**605586.53 (239639.66, 971533.4)**	**2.46 (0.97, 3.94)**
	PM10	45	**578711.69 (247682.77, 909740.61)**	**2.35 (1, 3.69)**
	SO2	40	4937.72 (-22236.64, 32112.08)	0.02 (-0.09, 0.13)
	NO2	25	150050.83 (-342144.83, 642246.48)	0.61 (-1.39, 2.6)

#: China and WHO 2021 have the same standards for CO; *: WHO 2005 and WHO 2021 have the same standards for ozone; NA: The number of days over the recommended threshold during the study period was too small to calculate results.

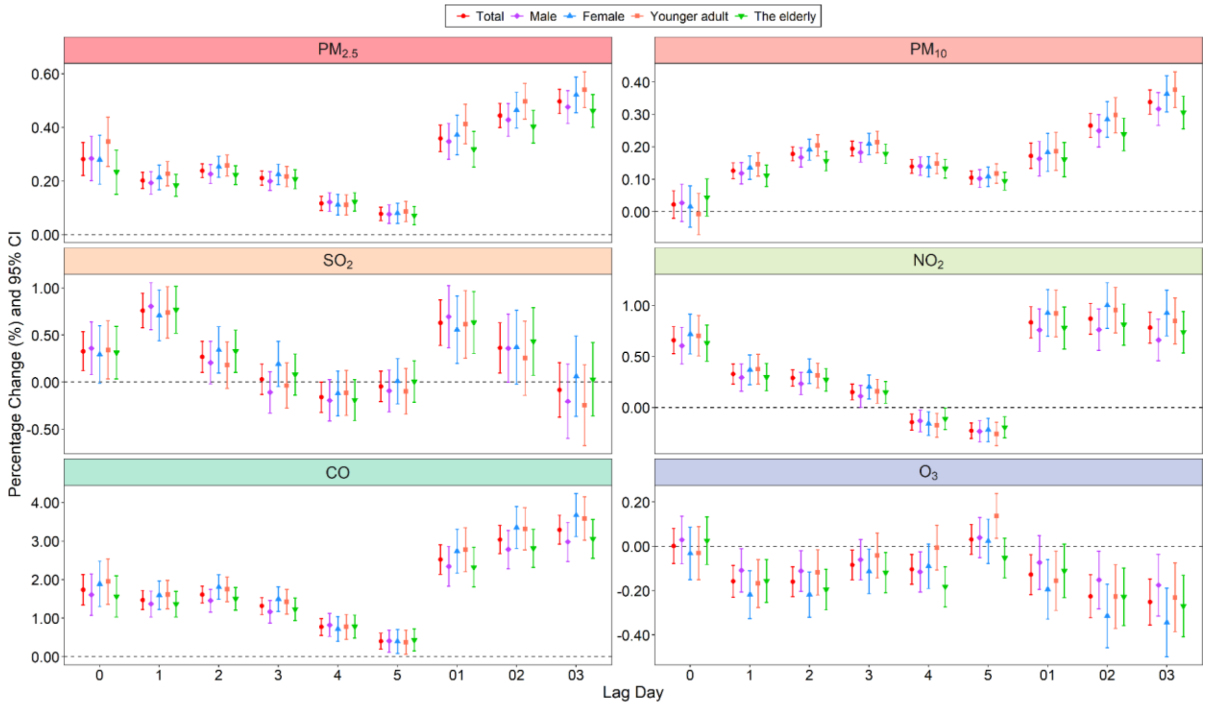

Figure 1 The effect of six air pollutants on admission with multiple pollutant model. (Note: Percentage Change for PM2.5, PM10, SO2, NO2 and O3 were per 10 ug/m3 increase and 1 mg/m3 for CO. Younger Adult: Age less than or equal to 65 years old. The elderly: Age over 65 years old.).

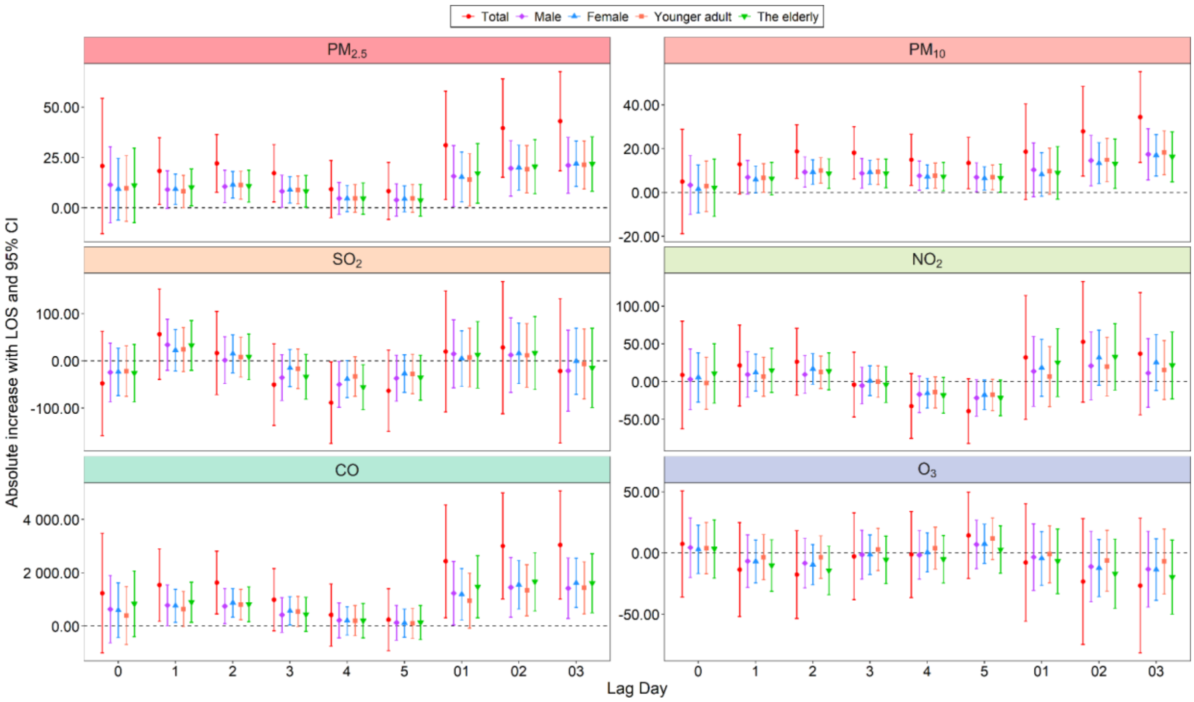

Figure 2 The effect of six air pollutants on LOS with multiple pollutant model.(Note: Absolute increase for PM2.5, PM10, SO2, NO2 and O3 were per 10 ug/m3 increase and 1 mg/m3 for CO. Younger Adult: Age less than or equal to 65 years old. The elderly: Age over 65 years old.).

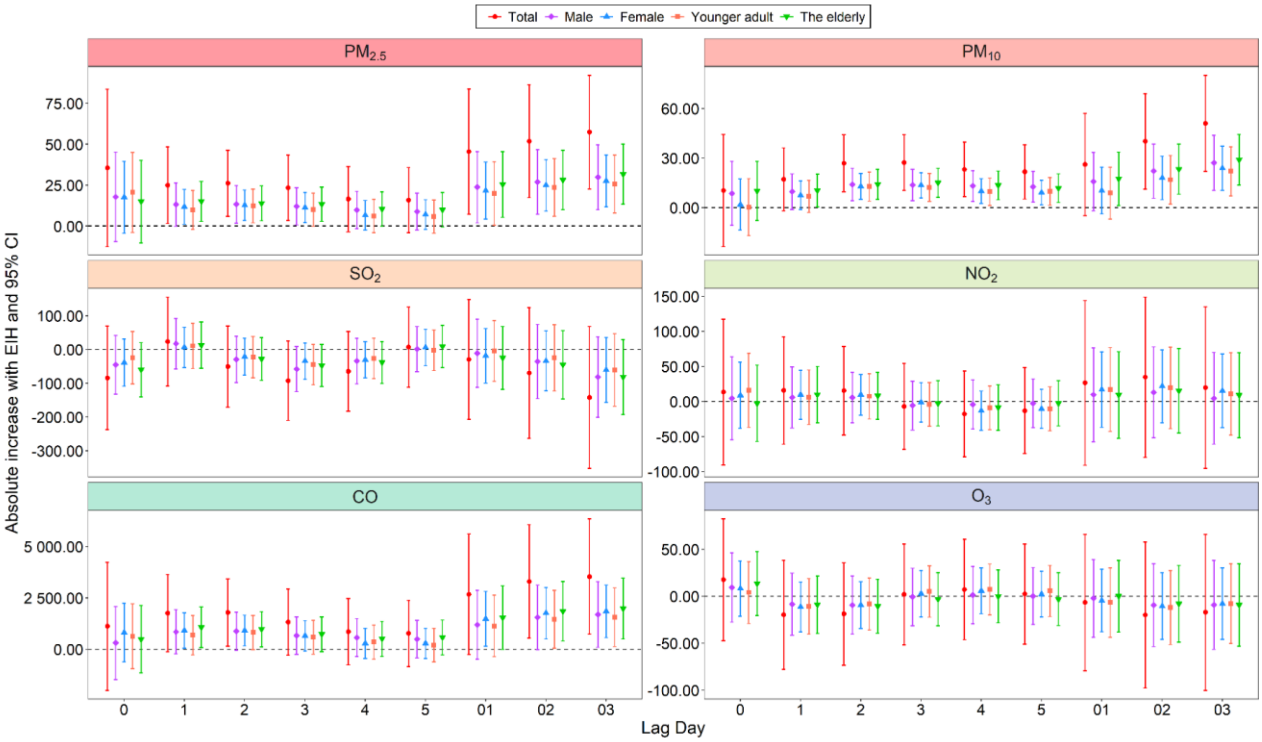

Figure 3 The effect of six air pollutants on hospital cost with multiple pollutant model. Note: Absolute increase for PM2.5, PM10, SO2, NO2 and O3 were per 10 ug/m3 increase and 1 mg/m3 for CO. Younger Adult: Age less than or equal to 65 years old. The elderly: Age over 65 years old.