Association Between Ambient Air Pollution And Daily Hospital Visits For Cardiovascular Diseases In Wuhan, China: A Time-Series Analysis Based On Medical Insurance Data.

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Abstract

Although a large number of studies have proved the adverse effects of exposure to air pollution on cardiovascular disease, few studies have done such research focusing on the medically insured population, a group of relatively healthier people representing the working population. We used generalized additive model (GAM) to estimate the short-term effects of ambient air pollution on CVDs in Wuhan, China. We extracted daily air pollution data, meteorological data, and daily hospital visits for CVDs (including hypertension, coronary heart disease [CHD], and heart disease [HD]) from November 1^{st,} 2013 to October 31st, 2018. For each increase of 10 μg/m^3 in SO_2, NO_2, PM_{10}, and $PM_{2.5}$, the relative risks (RRs) of daily hospital visits for hypertension increased by 3.8% (95% confidence interval [CI]: 1.8%, 5.9%), 2.5% (95% CI: 1.9%, 3.2%), 0.5% (95% CI: 0.2%, 0.7%), and 0.7% (95% CI: 0.3%, 1.1%) at lag 0, respectively; For CHD, the RRs increased by 3.6% (95% CI: 1.8%, 5.5%), 2.6% (95% CI: 1.9%, 3.4%), 0.4% (95% CI: 0.1%, 0.7%), and 0.5% (95% CI: 0.1%, 0.9%) at lag 0, respectively; For HD, the RRs increased by 3.6% (95%CI: 1.4%, 5.8%), 2.1% (95%CI: 1.4%, 2.7%), 0.3% (95%CI: 0.1%, 0.6%), and 0.4% (95%CI: 0, 0.8%) at lag 0, respectively. We found that the influence of air pollution on daily hospital visits for CVDs is greater in the cold season than in the warm season. The results indicate that NO_2 and SO_2 may be potential confounders for co-pollutants in the multi-pollutant model. In conclusion, air pollutants including SO_2, NO_2, PM_{10}, and $PM_{2.5}$ may be associated with the risk of hypertension, CHD, and HD. Our findings not only can be used as reference for studying the financing and the allocation of medical resources in the future, but also served as a piece of evidence that supports the policymaking on air pollution and CVDs.

Introduction

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels, such as coronary heart disease (heart attack) and hypertension (increased blood pressure). According to a report from the World Health Organization (WHO, 2017), CVDs are major non-communicable diseases and the number one cause of death in the world. CVDs were estimated to cause 17.9 million deaths each year and are also responsible for the disability-adjusted life years at the national level. (Dimmeler 2011; Kayikcioğlu and Oto 2020; WHO 2017; Zhou et al. 2019). The incidence of CVDs has doubled since 1990, reaching nearly 94 million in 2016, and it will continue to increase in the next ten years in China (Liu et al. 2019; Weiwei et al. 2016). The increase in the incidence of CVDs has had a serious adverse effect on economy, posing a challenge to the healthcare system and the society as a whole (Wu et al. 2016). In low- and middle-income countries, given that 80% of cardiovascular deaths occur in low- and middle-income countries, a 10% reduction in CVD mortality from 2011 to 2025 is expected to reduce economic losses by $377 billion US dollars (Laslett et al. 2012). According to a report of the National Center for CVDs of China, the prevalence of CVDs in China is on a continuous rise. The report estimated that 290 million people are suffering from CVDs, of which 245 million are hypertension, 11 million are coronary heart disease, and 14 million are other types of heart disease such as congenital heart disease and rheumatic heart disease (Li et al. 2017; Ma et al. 2020; Zhu et al. 2016). The risk factors for CVDs include, but are

not limited to, unhealthy lifestyle, elevated blood pressure, hyperlipidemia, hyperglycemia, and air pollution (Lavie 2011; Shen and Ge 2018; Zhao et al. 2019).

Air pollution is a major environmental health problem worldwide. In 2016, 91% of the world's population lived in places that did not meet the WHO air quality guidelines (WHO 2018). Ambient air pollution causes more than seven million premature deaths globally each year, most of which occur in low- and middle-income countries (Landrigan et al. 2018; Orru et al. 2017; Yusuf et al. 2020). As one of the most polluted cities in China, Wuhan has experienced serious air pollution in the past decade (Mbululo et al. 2019). Evidence suggests that air pollution is a major risk factor for CVDs (Bai et al. 2019; Brook et al. 2010; Hadley et al. 2018; Nieuwenhuijsen 2018). In China, exposure to air pollution has been associated with an increase in the number of hospitalizations and deaths for CVDs (such as coronary heart disease [CHD] and hypertension) (Chen and Yang 2018; Dai et al. 2015; Phosri et al. 2019).

At present, China's epidemiological studies on air pollution and CVDs generally use disease data collected directly from hospitals, rather than medical insurance databases. As a result, the study focusing on the insured population is still a research gap. Since the population covered by basic medical insurance system mostly represents the working population that is considered healthier than the general population, research on this population has special public health significance. The basic medical insurance database that we extracted the data from is an important part of China's social insurance system. The outpatient, emergency, and hospitalization data contained in the database provide us with an opportunity to examine the relationship between air pollution exposure and CVDs.

Relying on data from the basic medical insurance database, this study used a generalized additive model (GAM) to explore the impact of short-term exposure to air pollution on hospital visits for hypertension, CHD and heart disease (HD) in Wuhan, China during 2013–2018.

Methods

Data collection

China's basic medical insurance system consists of three parts, namely basic medical insurance system for urban employees, basic medical insurance system for urban residents, and new rural cooperative medical care system. This study contains data collected at Wuhan city from the first two parts. We first randomly selected 1% of the total sample based on the ID number. Then, we selected the groups of diseases coded as CVDs. CVDs are a group of heart and blood vessel diseases, such as CHD, cerebrovascular disease, peripheral arterial vascular disease, and so on. We selected hypertension, CHD, and HD that belong to the category of CVDs as subgroups to analyze the relationship between CVD and air pollution. The data also includes the age, gender, and socioeconomic status (such as occupation) of patients with sensitive personal information removed.

Data on air pollution was collected from ten National Ambient Air Quality Monitoring Stations in Wuhan (Fig. 1). The daily concentration of each pollutant represents 24-h averages from all air quality monitoring

sites in this study. Five air pollutants were included in our research, namely, nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ground-level ozone (O_3), particulate matter (PM) with aerodynamic diameter ≤ 2.5 μm ($PM_{2.5}$), and PM with aerodynamic diameter ≤ 10 μm (PM_{10}). Data on meteorological factors including ambient temperature and relative humidity were obtained from the Hubei Meteorological Service Center.

Statistical analysis

We built a time-series database based on the date, air pollutant concentrations, meteorological factors, day of the week, and hospital visits for CVDs. We used descriptive analysis to show the characteristics of hospital visits for CVDs, air pollutants, and meteorological factors. The Spearman correlation was used to estimate the relationship between daily data of air pollutants and meteorological factors. A generalized additive Poisson regression model was established to explore the short-term impact of daily air pollutant levels on hospital visits for CVDs (Ravindra et al. 2019). In the GAM model, a smoothing spline function was selected to control the confounding effects of the long-term trend and meteorological factors. The Akaike Information Criterion for quasi-Poisson (Q-AIC) was conducted to determine the degrees of freedom (df) for time trend, relative humidity, and temperature. The model is as below:

$$Log\,[E(y_t)] = \beta X_t + DOW + ns\,(time, 8) + ns\,(temperature, 5) + ns\,(humidity, 3) + intercept$$

Where y_t is the number of hospital visits at day t; $E(yt)$ indicates the expected number of hospital visits for CVDs on day t; Xt represents the concentrations of air pollutants on day t; β indicates the regression coefficient, ns means a natural smoothing spline function, and DOW is an indicator variable meaning “day of the week”. According to the minimum value of Q-AIC, we selected a smooth function of 8 df to control for long-term effects, 5 df to control temperature, and 3 df to control relative humidity.

We conducted single-pollutant models to explore the short-term effects of each air pollutant on hospital visits for hypertension, CHD, and HD. We explored the effect by using different lag structures, including a single-day lag from the current day up to the previous 7 days (lag 0-lag 7) and moving averages of the current and previous days (lag 0–1 – lag0-7). Also, we performed the seasonal analysis by dividing the annual data into warm season (April-September) and cold season (October-March). If the correlation coefficient of two pollutants is less than 0.7, we put them in the two-pollutant model to explore the effect of each pollutant on hospital visits for hypertension, CHD, and HD.

We conducted four sensitivity analyses to verify the robustness of the results. Firstly, we modified the df values between 7 and 9 for calendar time to achieve the best model fit. Secondly, we conducted stratified analyses by gender (male and female), age (<65 and ≥ 65 years old), and socioeconomic status (blue-collar worker and white-collar worker) to further test the reliability of the results.

All statistical analyses were conducted by R-software (version 4.0.0) using “mgcv” and “nlme” packages. The results we obtained were reported as the relative risk (RR) and 95% confidence intervals (CIs) of hospital visits for CVDs associated with a 10 $\mu g/m^3$ increase in air pollutant concentrations. Effects with a p value<0.05 were considered statistically significant.

Results

The descriptive statistics of air pollutants, meteorological factors, hypertension, CHD, HD from November 2013 to October 2018 were shown in Table 1. During the five-year study period, 1,153,045 patients with hypertension, 180,777 patients with CHD, and 202,683 patients with HD were included in our analysis. The average daily hospital visits for hypertension, CHD, HD were 631, 98, and 110, respectively. There were more hospital visits for patients with hypertension in men than women, but the opposite is true for CHD. Hospital visits for hypertension, CHD, HD were higher in the elderly (≥ 65 years old) and blue-collar workers. The daily mean concentrations of SO_2, NO_2, O_3, PM_{10}, and $PM_{2.5}$ were 17.50 μg/m^3, 47.60 μg/m^3, 55.47 μg/m^3, 96.32 μg/m^3, and 63.31 μg/m^3, respectively. The average ambient temperature and relative humidity were 17.28℃ and 78.25% in the 1,827 days of observation during 2013–2018. The distribution of air pollutant concentrations, meteorological factors, and hospital visits for hypertension, CHD, and HD is presented in Fig. S1.

Table 1

The summary statistics of air pollutants, meteorological factors, and hospital visits for hypertension, coronary heart disease (CHD), and heart disease (HD) in Wuhan, China from November 1st, 2013 to October 31st, 2018.

Daily data	N	Mean	SD	Min	P25	Median	P75	Max
SO_2 (μg/m^3)	1817	17.50	16.23	2	7	13	22	112
NO_2 (μg/m^3)	1817	47.60	20.98	11	31	43	60	132
O_3 (μg/m^3)	1817	55.47	28.51	3	32	53	76	190
PM_{10} (μg/m^3)	1817	96.32	56.35	0	55	86	123	406
$PM_{2.5}$ (μg/m^3)	1817	63.31	45.13	5	32	51	80	298
Ambient temperature (°C)	1827	17.28	8.98	-3	9.5	18.4	24.9	34
Relative humidity (%)	1827	78.25	9.81	46	71.2	78.8	85.9	99
Hypertension (counts/day)								
Gender								
Female	560,919	307.02	309.52	18	129	200	313	1624
Male	592,119	324.09	380.99	13	115	176	299	2004
Age								
< 65	509,960	279.12	271.84	20	118	181	291	1429
≥ 65	643,081	351.99	419.56	13	124	199	325	2215
Socioeconomic factors								
Blue-collar worker	592,771	324.45	325.45	24	138	214	335	1756
White-collar worker	206,644	113.11	115.43	6	44	76	124	574
Total	1153,045	631.11	689.42	37	245	377	613	3628
CHD (counts/day)								
Gender								
Female	91,622	50.15	30.88	6	29	44	59	199
Male	89,154	48.80	34.80	2	26	422	55	226
Age								

CHD: Coronary heart disease; HD: Heart disease; SD: Standard deviation; Min: Minimum;

Daily data	N	Mean	SD	Min	P25	Median	P75	Max
<65	59,955	32.82	21.82	2	18	28	39	134
≥65	120,821	66.13	43.91	3	38	57	75	291
Socioeconomic factors								
Blue-collar worker	99,918	54.69	33.62	5	31	48	65	231
White-collar worker	31,050	17	10.88	0	9	15	22	69
Total	180,777	98.95	64.74	8	56	86	111	425
HD (counts/day)								
Gender								
Female	89,883	49.20	47.47	1	18	33	58	280
Male	112,798	61.74	72.59	2	18	36	64	469
Age								
<65	78,739	43.10	45.40	1	12	28	52	249
≥65	123,942	67.84	74.61	2	24	41	70	483
Socioeconomic factors								
Blue-collar worker	106,540	58.31	61.87	2	20	36	66	450
White-collar worker	35,673	19.53	19.86	0	6	13	24	118
Total	202,683	110.94	119.12	4	37	68	121	732
CHD: Coronary heart disease; HD: Heart disease; SD: Standard deviation; Min: Minimum;								

Table S1 shows the Pearson's correlation coefficients of air pollutants, ambient temperature, and relative humidity, which range from 0.007 (ambient temperature and relative humidity) to 0.740 ($PM_{2.5}$ and PM_{10}). SO_2, NO_2, PM_{10}, and $PM_{2.5}$ were all positively correlated with each other and were negatively correlated with ambient temperature and relative humidity. O_3 was positively correlated with ambient temperature (r = 0.659), while it was negatively correlated with the remaining four air pollutants and relative humidity.

Figure 2 shows the RRs and 95% CIs of hospital visits for hypertension, CHD, and HD associated with a 10 μg/m^3 increase in pollutant concentrations at lag 0, 1, 2, 3, 0–3 in the single pollutant model. The complete results regarding the single-day lag model and the cumulative day lag model were shown in Fig. S2. The effects of exposure to air pollution on hypertension, CHD, and HD have similar trends. SO_2, NO_2, PM_{10}, and $PM_{2.5}$ were significantly associated with daily hospital visits for CVDs. In the single-day lag model, the effects of the four air pollutants on daily hospital visits for CVDs is highest at lag 0 and then

shows a downward trend. For each 10 μg/m^3 increase in SO_2, NO_2, PM_{10}, and $PM_{2.5}$ concentrations, the RRs of daily hospital visits for hypertension increased by 3.8% (95%CI: 1.8%, 5.9%), 2.5% (95%CI: 1.9%, 3.2%), 0.5% (95%CI: 0.2%, 0.7%), and 0.7% (95%CI: 0.3%, 1.1%) at lag 0, respectively; the RRs of daily hospital visits for CHD increased by 3.6% (95%CI: 1.8%, 5.5%), 2.6% (95%CI: 1.9%, 3.4%), 0.4% (95%CI: 0.1%, 0.7%), and 0.5% (95%CI: 0.1%, 0.9%) at lag 0, respectively; the RRs of daily hospital visits for HD increased by 3.6% (95%CI: 1.4%, 5.8%), 2.1% (95%CI: 1.4%, 2.7%), 0.3% (95%CI: 0.1%, 0.6%), and 0.4% (95%CI: 0, 0.8%) at lag 0, respectively. In the multi-day lag model, the effects of SO_2 and NO_2 on hypertension, CHD, and HD remain significantly at lag 0–3.

The seasonal analysis shows the RRs and 95% CIs of hospital visits for hypertension, CHD, and HD associated with a 10 μg/m^3 increase in pollutant concentrations at different lag days during the cold and warm seasons (Fig. 3). In both the single-day lag model and the multi-day lag model, SO_2, NO_2, PM_{10}, and $PM_{2.5}$ have a stronger effect on hypertension, CHD, and HD in the cold season than in the hot season. On the contrary, O_3 has a stronger effect in the warm season than in the cold season.

The results of RR and 95% CIs of hospital visits for hypertension, CHD, and HD based on the single- and two-pollutant models were shown in Table 2. The results of multi-pollutant models were presented at Table S2. Considering the collinearity between pollutants, the correlation coefficient between the two pollutants has to be less than 0.7 in order to include them in the two-pollutant model, otherwise would be excluded from the analysis. The effect of PM_{10} and $PM_{2.5}$ on CHD and HD decreased after the adjustment for SO_2 in the two-pollutant model. Meanwhile, after adjusting for NO_2, the effects of SO_2 and $PM_{2.5}$ on hypertension, CHD, and HD become statistically insignificant. In addition, NO_2 can strengthen the effect of O_3 on CHD and HD.

Table 2
Estimated relative risks (RRs) and 95% confidence intervals (CIs) of hospital visits for a 10 μg/m^3 increase of pollutant concentrations based on the single- and two-pollutant models.

Pollutant		RR (95%CI)		
		Hypertension	CHD	HD
SO_2		1.038 (1.018–1.059)	1.036 (1.018–1.055)	1.036 (1.014–1.058)
	+NO_2	0.989 (0.966–1.014)	1.002 (0.980–1.023)	0.991 (0.965–1.018)
	+O_3	1.038 (1.018–1.058)	1.036 (1.018–1.055)	1.035 (1.013–1.058)
	+PM_{10}	1.027 (1.005–1.049)	1.030 (1.010–1.051)	1.028 (1.004–1.053)
	+$PM_{2.5}$	1.030 (1.009–1.052)	1.033 (1.014–1.052)	1.032 (1.009–1.055)
NO_2		1.025 (1.019–1.032)	1.026 (1.019–1.034)	1.021 (1.014–1.027)
	+ SO_2	1.027 (1.019–1.036)	1.026 (1.017–1.035)	1.023 (1.014–1.031)
	+O_3	1.025 (1.019–1.032)	1.026 (1.019–1.034)	1.021 (1.014–1.028)
	+$PM_{2.5}$	1.026 (1.018–1.033)	1.028 (1.019–1.037)	1.023 (1.015–1.030)
O_3		1.028 (0.982–1.077)	1.051 (0.993–1.112)	1.040 (0.994–1.089)
	+ SO_2	1.028 (0.981–1.076)	1.050 (0.993–1.112)	1.040 (0.993–1.088)
	+NO_2	1.038 (0.991–1.086)	1.059 (1.001–1.121)	1.048 (1.001–1.096)
	+PM_{10}	1.025 (0.979–1.074)	1.048 (0.990–1.109)	1.038 (0.991–1.087)
	+$PM_{2.5}$	1.027 (0.981–1.075)	1.050 (0.992–1.111)	1.039 (0.992–1.088)
PM_{10}		1.005 (1.002–1.007)	1.004 (1.001–1.007)	1.003 (1.001–1.006)
	+SO_2	1.003 (1.000-1.006)	1.002 (0.999–1.005)	1.002 (0.999–1.005)
	+O_3	1.005 (1.002–1.007)	1.004 (1.001–1.007)	1.003 (1.001–1.006)
$PM_{2.5}$		1.007 (1.003–1.011)	1.005 (1.001–1.009)	1.004 (1.000-1.008)
	+SO_2	1.005 (1.001–1.009)	1.002 (0.998–1.007)	1.002 (0.998–1.007)
	+NO_2	1.000 (0.995–1.004)	0.998 (0.994–1.003)	0.998 (0.993–1.002)
	+O_3	1.007 (1.003–1.011)	1.005 (1.001–1.009)	1.004 (1.000-1.008)

Table 3 shows the results of the stratified analysis by gender (male and female), age (<65 and ≥ 65 years old), and socioeconomic status (blue-collar worker and white-collar worker) at lag 0. We have not observed considerable differences in the effects of air pollution on CVDs in terms of age, gender, and socioeconomic status. All results regarding the stratified analysis are presented in Fig. S3 (gender), Fig. S4 (age), and Fig. S5 (socioeconomic status). Since the number of CVDs in late 2017 to the most of 2018 was significantly higher than the previous year (see Fig. S1), we compared the differences in the effects of air pollution on CVD in the months when the number of visits was high and the effects in the previous year (the months when the number of visits was low). The results show that similar trends were observed in both periods (Fig. S6).

Table 3. Estimated relative risks (RRs) and 95% confidence intervals (CIs) of hospital visits for a 10 μg/m^3 increase of pollutant concentrations by gender, age, and socioeconomic factors among patients had hypertension, coronary heart disease (CHD), and heart disease (HD).

Variables	Gender		Age		Socioeconomic factors	
	Female	Male	<65	≥65	Blue-collar worker	White-collar worker
Hypertension						
SO_2	1.044 (1.024-1.064)	1.032 (1.011-1.054)	1.036 (1.018-1.055)	1.040 (1.017-1.063)	1.036 (1.015-1.057)	1.028 (1.004-1.052)
NO_2	1.027 (1.021-1.034)	1.023 (1.017-1.030)	1.023 (1.017-1.029)	1.027 (1.020-1.034)	1.026 (1.019-1.033)	1.026 (1.018-1.034)
O_3	1.025 (0.977-1.075)	1.031 (0.984-1.081)	1.021 (0.977-1.066)	1.033 (0.982-1.087)	1.048 (0.996-1.103)	1.057 (0.999-1.119)
PM_{10}	1.005 (1.003-1.008)	1.004 (1.002-1.007)	1.004 (1.002-1.006)	1.005 (1.002-1.008)	1.005 (1.002-1.007)	1.005 (1.002-1.008)
$PM_{2.5}$	1.008 (1.004-1.012)	1.006 (1.002-1.011)	1.006 (1.003-1.010)	1.008 (1.003-1.012)	1.007 (1.003-1.011)	1.006 (1.002-1.011)
CHD						
SO_2	1.043 (1.024-1.062)	1.029 (1.009-1.049)	1.042 (1.021-1.063)	1.034 (1.015-1.053)	1.036 (1.017-1.056)	1.022 (0.997-1.048)
NO_2	1.027 (1.018-1.035)	1.026 (1.018-1.035)	1.023 (1.014-1.032)	1.028 (1.020-1.036)	1.026 (1.018-1.035)	1.022 (1.011-1.033)
O_3	1.046 (0.985-1.111)	1.056 (0.992-1.124)	1.077 (1.009-1.149)	1.038 (0.978-1.103)	1.051 (0.985-1.121)	1.059 (0.975-1.149)
PM_{10}	1.004 (1.001-1.007)	1.004 (1.001-1.007)	1.003 (0.999-1.006)	1.005 (1.002-1.008)	1.004 (1.001-1.008)	1.003 (0.999-1.008)
$PM_{2.5}$	1.005 (1.000-1.009)	1.005 (1.000-1.009)	1.003 (0.998-1.008)	1.006 (1.001-1.010)	1.005 (1.000-1.009)	1.005 (0.999-1.010)
HD						
SO_2	1.049 (1.025-1.074)	1.024 (0.999-1.049)	1.013 (0.998-1.040)	1.048 (1.025-1.072)	1.039 (1.015-1.065)	1.042 (1.010-1.074)
NO_2	1.023 (1.016-1.031)	1.019 (1.012-1.026)	1.016 (1.008-1.023)	1.024 (1.017-1.031)	1.024 (1.016-1.031)	1.021 (1.011-1.030)

O_3	1.034 (0.982-1.089)	1.046 (0.994-1.101)	1.047 (0.992-1.104)	1.036 (0.986-1.090)	1.051 (0.997-1.108)	1.078 (1.008-1.153)
PM_{10}	1.005 (1.002-1.007)	1.002 (1.000-1.005)	1.002 (0.999-1.005)	1.004 (1.002-1.007)	1.004 (1.002-1.007)	1.003 (0.999-1.007)
$PM_{2.5}$	1.005 (1.000-1.009)	1.004 (0.999-1.009)	1.003 (0.998-1.008)	1.005 (1.000-1.009)	1.006 (1.001-1.010)	1.007 (1.001-1.013)

Discussion

We conducted a time-series analysis to explore the association between air pollution and hospital visits for CVDs from 2013 to 2018 in Wuhan, China. We found that the short-term exposures to SO_2, NO_2, PM_{10}, and $PM_{2.5}$ were significantly associated with the risk of hypertension, CHD, and HD. Our results show that the largest effect of air pollution on CVDs occurred at lag 0 (single-day lag) and lag 0–3 (multi-day lag). We also found that the association is stronger in the cold season than in the warm season. As far as we know, this is the first study to explore the association between daily hospital visits for CVDs and air pollution in Wuhan based on medical insurance data.

In the past few decades, the environment in China has faced great challenges due to rapid industrial development and urbanization. The increase in the number of vehicles and energy consumption and the decrease in green coverage has affected air quality to varying degrees. Continuous haze weather is commonly seen in China, causing serious environmental hazards, especially in cities with large populations (Maji et al. 2018; Xu et al. 2019). Wuhan, the largest city in central China, has a population of 12 million and is one of the most polluted cities in China. Our study suggested that the 24-hour average concentrations of PM_{10} (96.09 μg/m^3) and $PM_{2.5}$ (63.03 μg/m^3) far exceeded the air quality standards set by the WHO (50 μg/m^3 and 25 μg/m^3, respectively). The impact of air pollution on the cardiovascular system is frequently reported worldwide. A study conducted in Ahvaz, Iran indicated that the risk of hospital admission for CVDs increased by 0.6% (95% CI: 0.1 to 1%) for every increase of 10 μg/m^3 of NO_2 at lag 0 (Dastoorpoor et al. 2019). Dai et al. (2015) reported that for every 10 μg/m^3 increase in the concentrations of PM_{10} and SO_2, the risk of out-of-hospital coronary deaths increased by 0.49% (95% CI: 0.11 to 0.88%) and 0.88% (95% CI: 0.14 to 1.62%) at lag 0, respectively. A time-series study by Zhang et al. (2017) found that exposures to SO_2, NO_2, and PM_{10} were associated with a 5.26% (95%CI: 3.31–7.23%), 2.71% (95%CI: 1.23–4.22%), and 0.68% (95%CI: 0.33–1.04%) increase in cardiovascular mortality at lag 0–3. Another study conducted by systematic review and meta-Analysis reported that short-term exposure to SO_2, $PM_{2.5}$, and PM_{10} is significantly associated with a 4.6% (1.2–8.1%), 6.9% (0.3–14.1%), and 2.4% (1.6–3.2%) increase in the risk of hypertension (Cai et al. 2016). Our findings are generally consistent with the results of past studies in two dimensions. One is the effects of air pollution on cardiovascular disease and the second is the time or moment when the strongest effects occur. However, some studies have also reported different findings. A time-series study conducted in Guangzhou, China

found that PM has no significant effect on CVDs (Ge et al. 2018). In addition, we did not observe a significant association between the short-term exposure to O_3 and the increased mortality of CVDs that many studies have already reported (Bero Bedada et al. 2016; Mazidi and Speakman 2018; Sicard et al. 2019; Zhang et al. 2019). This inconsistency may be due to the following reasons: 1) the statistical methods used in these studies are different from ours; 2) the different geographical location of the study may cause differences in results; 3) the demographic characteristics of the exposed population are different.

The latest scientific statement from the American Heart Association believes that there is a causal relationship between exposure to $PM_{2.5}$ and cardiovascular morbidity and mortality (Brook et al. 2010). The possible physiological and molecular mechanisms involved are still in the process of exploration. One of the possible mechanisms is that inhalation of particulate matter in the environment can cause the body to produce pro-oxidant substances (reactive oxygen species, etc.), pro-inflammatory biological mediators (interleukin 6, etc.), the acute phase reactants (C-reactive protein, etc.), and vasoactive hormones (endothelin, etc.), resulting in systemic inflammation and oxidative stress. These reactions in the lung will eventually affect the cardiovascular system through blood circulation (Gurgueira et al. 2002; Q Liu et al. 2019; Mannucci et al. 2019; Pope et al. 2016). Meanwhile, evidence suggests that particulate matter can pass through the lung epithelium into the circulatory system or interact with lung receptors (direct action) to induce an acute cardiovascular response (Fiordelisi et al. 2017; Nemmar et al. 2001; Nemmar et al. 2002). In addition, air pollutants can cause the body's autonomic nervous system to malfunction and activate pathways of the central nervous system, leading to increased blood pressure and heart rate variability. Due to inhalation of air pollutants, the nose, bronchus, and lung C nerve fiber subtypes will activate many receptors that can affect sensory nerves. (Franklin et al. 2015; Rajagopalan et al. 2018).

The seasonal analysis shows that the effect of most air pollutants on hospital visits for CVDs is stronger in the cold season than in the warm season except for O_3. The results are consistent with previous studies (Song et al. 2019; Tong et al. 2014; Ye et al. 2016). Like our study, a previous study (Brook and Kousha 2015) also found that the effect of O_3 on CVDs is also more pronounced in the warm season rather than in the cold season. One possible explanation for the different O_3 results between studies is that the chemical composition and source of air pollutants may vary by region and season (Krall et al. 2013).

We found that all pollutants except O_3 are statistically significant for cardiovascular disease in the single-pollutant model. However, in the two-pollutant model, after adjusting for SO_2 or NO_2, the effects of other pollutants on hypertension, CHD, and HD have been changed (intensified or weakened). This may suggest that they are confounding factors for other pollutants and cardiovascular disease. It may be due to the collinearity between air pollutants, given that the difference in correlation coefficients between pollutants is not obvious (VanderWeele 2009). Therefore, to avoid collinearity, we include two pollutants with a correlation coefficient of less than 0.7 into the two-pollutant model.

In addition to the single-pollutant models, we also constructed two-pollutant models to assess the effect of air pollution on CVDs. To avoid collinearity, two pollutants included in the model have to meet the criteria that their correlation coefficients must be less than 0.7. After including the second pollutant in the model, the results are not much different from those produced by the single-pollutant model. However, it should be noticed that after adjusting for SO_2 or NO_2, the effects of co-pollutants on CVDs are universally changed (intensified or weakened). This may indicate that these two pollutants are the major confounders between air pollutants and cardiovascular diseases.

This study has several limitations. First, we obtained the data on pollutants from air quality monitoring stations rather than personal exposure samplers. Also, we assume that everyone is exposed to the same level of air pollution each day. This may lead to exposure misclassification, an inevitable flaw in such type of ecological studies. Second, the findings of this study are based on data collected in a single city, so generalizing the conclusions to other cities or regions will produce bias. Third, our data comes from basic medical insurance data, so the conclusion does not apply to the general public. However, this is also an advantage of our study. People who are covered by medical insurance are generally healthier than the general public, so investigating the impact of air pollution on such a population has special public health significance.

Declarations

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Author's contributions YNM and ZHL made formal analysis, software analysis, data curation, conceptualization, and original draft. JYH made software analysis and validation. FXT and HHZ made validation and search resources. YHL made supervision. SYL made data curation, conceptualization, and reviewed the manuscript.

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Consent for publication Not applicable.

Availability of data and materials The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interests The authors declare no competing interests.

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Figures

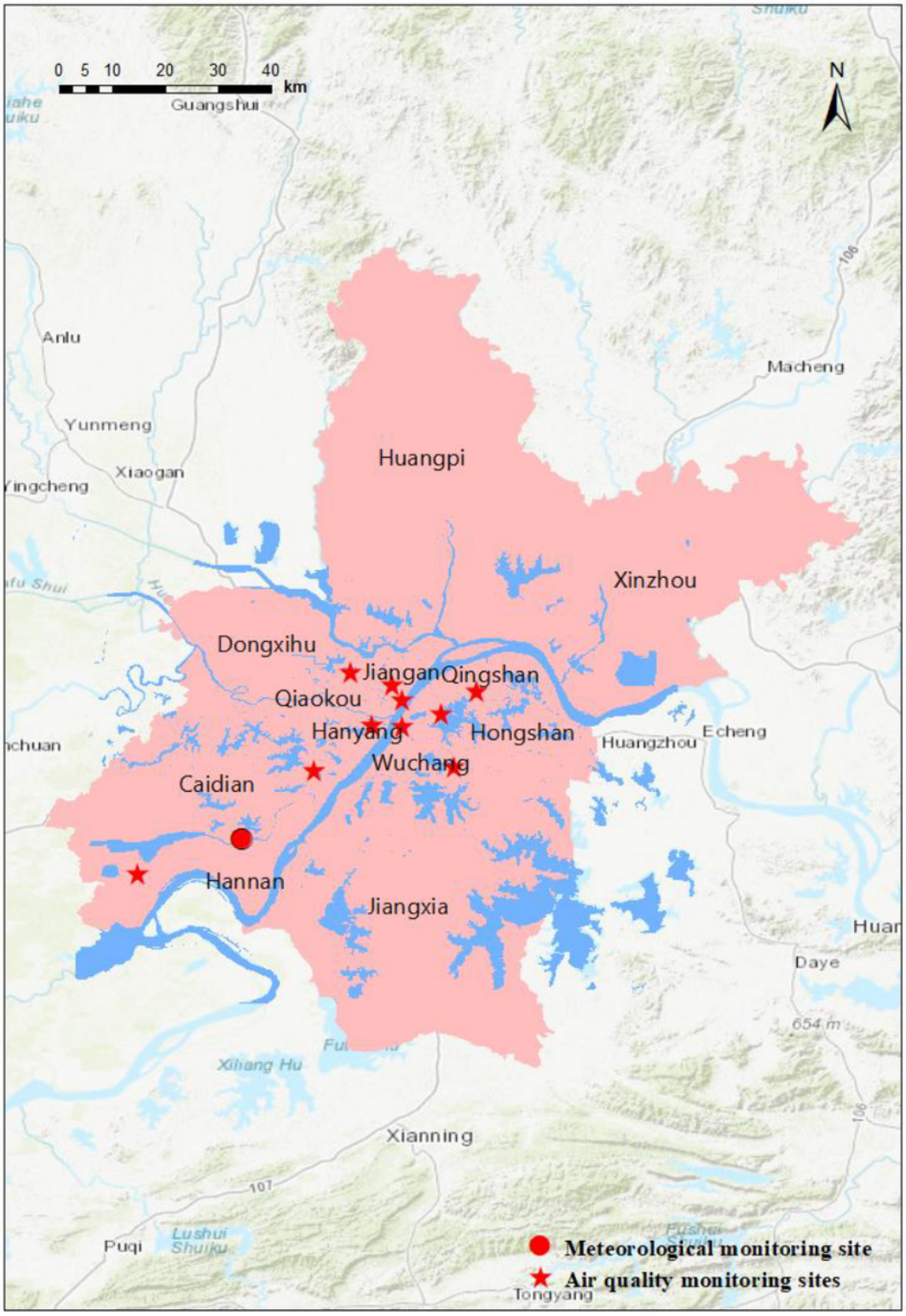

Figure 1

Map of Wuhan showing the location of weather and air quality monitoring sites.

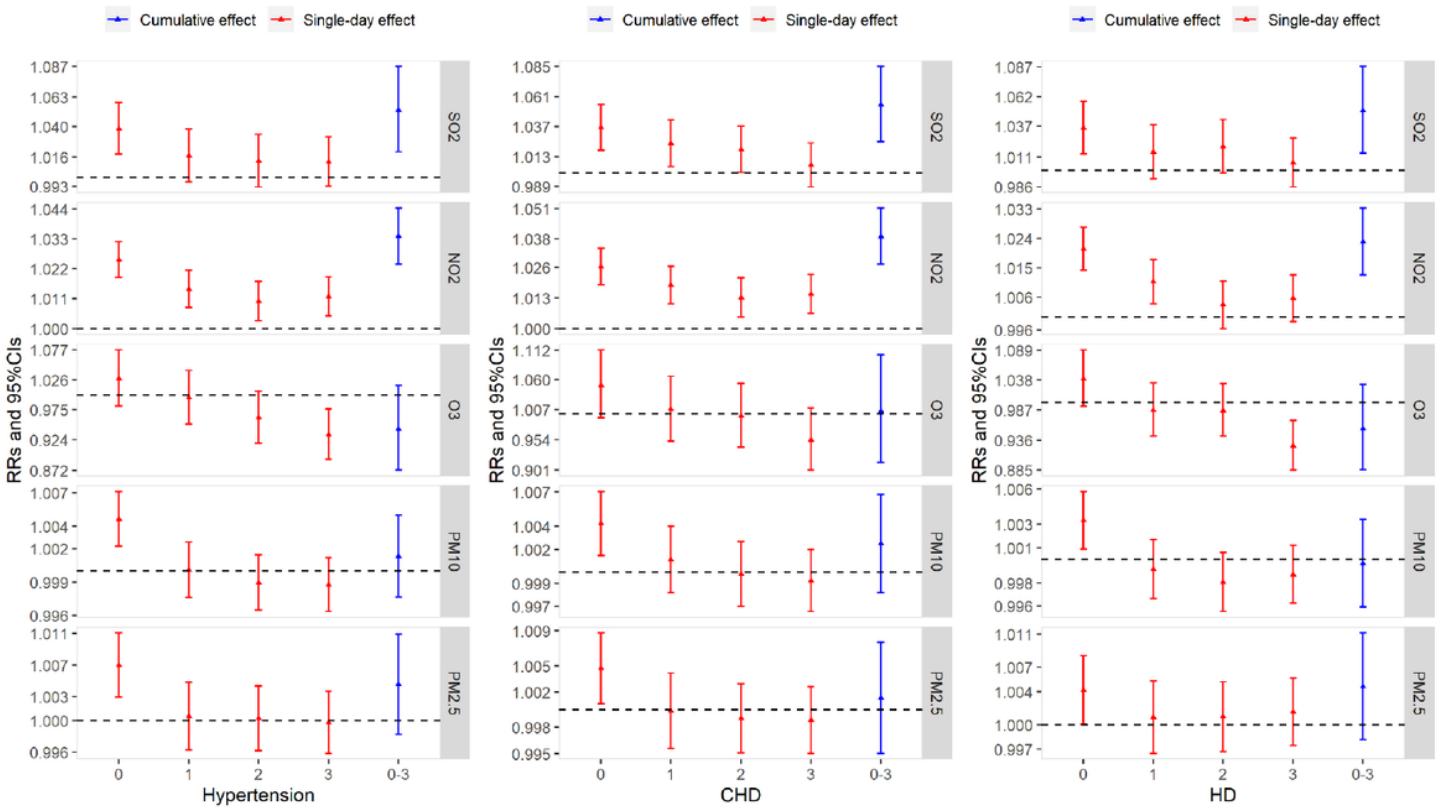

Figure 2

Estimated relative risks (RRs) and 95% confidence intervals (CIs) of hospital visits for selected Cardiovascular diseases (CVDs) associated with a 10 μg/m3 increase of pollutant concentrations on different lag days.

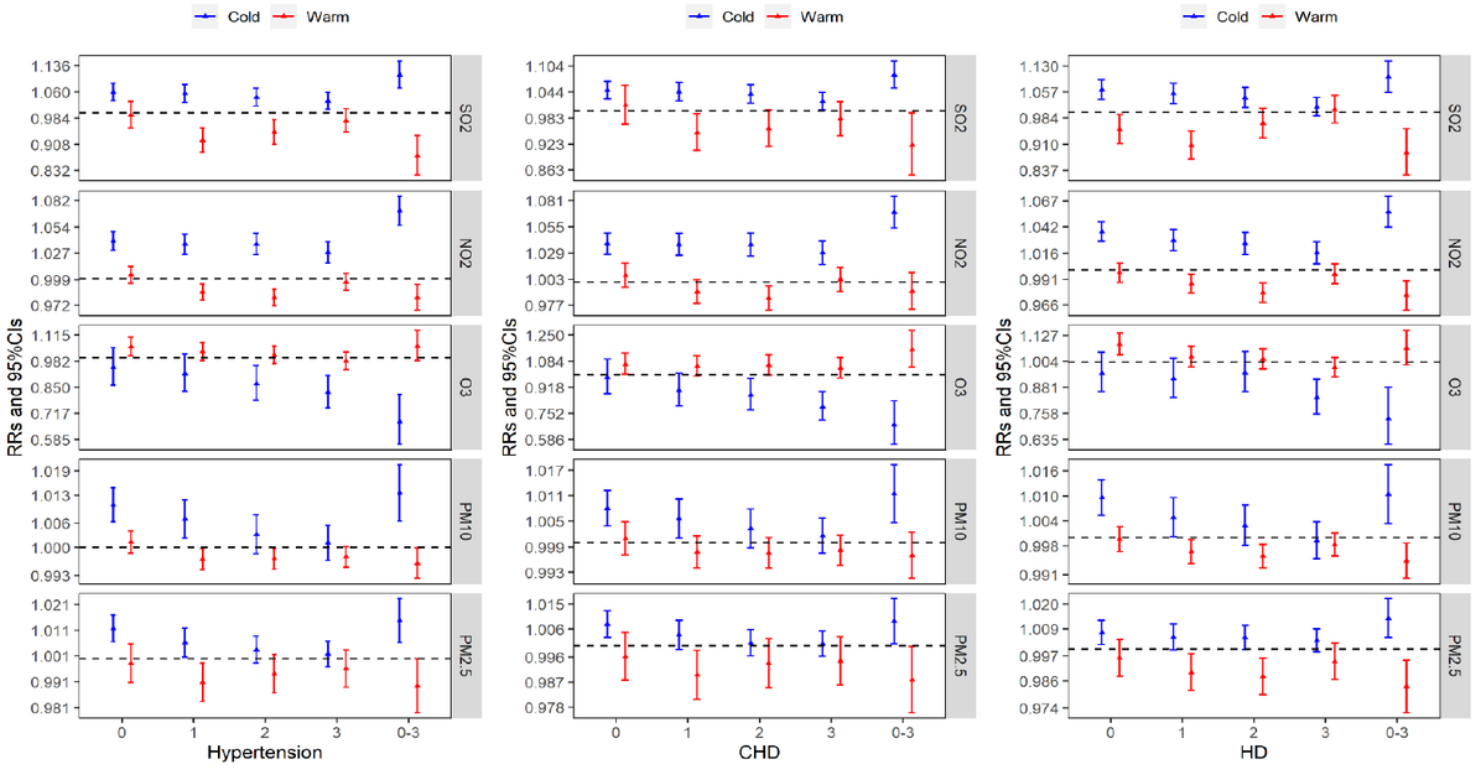

Figure 3

Estimated relative risks (RRs) and 95% confidence intervals (CIs) of hospital visits for selected Cardiovascular diseases (CVDs) associated with a 10 μg/m3 increase of pollutant concentrations on different lag days in the cold (October to March) and warm (April to September) seasons.

Supplementary Files

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- SupplementaryMaterial.docx