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Examining the Relationships Between Air Pollutants and the Incidence of Acute Aortic Dissection with Electronic Medical Data in a Moderately Polluted Area of Northwest China

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Abstract

This paper explored whether air pollutants influenced acute aortic dissection (AAD) incidence in a moderately polluted area. A total of 494 AAD patients' data from 2013 to 2016 were analyzed. The results showed that AAD had the strongest associations with PM_{10}, SO_2, NO_2, CO, and O_3 on the day before an AAD incident (lag1) and with $PM_{2.5}$ two days before an incident (lag2) in single-pollutant model. In the three-pollutant model, PM_{10} was associated with the highest risk of adverse effects (RR = 1.37, 95% CI: 1.22, 1.53), whereas $PM_{2.5}$ was associated with the lowest risk (RR = .83, 95% CI: .79, .88). Both $PM_{2.5}$ and PM_{10} were affected by season, and SO_2 was significantly different between heating and non-heating seasons as well. This study revealed significant associations between short-term $PM_{2.5}$, PM_{10}, and SO_2 exposure and daily AAD incidence, showing that PM_{10} and SO_2 were strong predictors of AAD incidence in a moderately polluted area.

Keywords

air pollution, moderately pollution, seasonal difference, acute aortic dissection, incidence risk

Introduction

Environmental pollution is an increasingly critical health threat worldwide. Air pollution has been demonstrated to be one of the major influencing factors of cardiovascular disease. For instance, $PM_{2.5}$ exposure has an adverse effect on congenital heart disease,[1] ischemic heart disease,[2] and hypertension.[3] However, few studies have investigated the association between air pollution and acute aortic dissection (AAD), a fatal cardiovascular disease.

Acute aortic dissection is an uncommon cardiovascular disease. According to existing study and Chinese Cardiovascular Health and Disease Report, the estimated annual incidence rate of AAD was .028%, far below that of CHD (3.3%).[4,5] However, AAD is fatal. Blood from the aortic lumen enters the aortic media from a tear in the aortic intima, disconnects the media and expands along the long axis of the aorta to produce a true-and-false lumen separation state in the aortic wall. Acute aortic dissection has an extremely high mortality rate, with as high as 1% per hour direct mortality rate at initial onset.[6] Since AAD usually has no apparent symptoms before onset, it is usually diagnosed after aortic rupture or the onset of other AAD complications. Accordingly, identifying potential risk factors is crucial in the prevention of AAD.

To date, the cause of AAD is not yet clear. Previous studies have reached consensus on a few clinical risk factors, such as hypertension, congestive heart failure, hyperlipidemia, and other underlying diseases.[3,7] Some studies have found that meteorological factors have an impact on AAD incidence. For example, Takagi et al.[8] found that AAD incidence reached the

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What We Already Know

1. Air pollutions had adverse effects on cardiovascular disease in heavily polluted areas, while evidence showed low-level air pollution exposure is also harmful.
2. Acute aortic dissection is fatal but no apparent symbols before onset, and prevention of aortic dissection can save lives.
3. The associations between air pollutants and acute aortic dissection incidence are not fully understood.

What This Article Adds

1. This paper focuses on air pollution in a moderately polluted area and provides evidence for adverse effects of low-level air pollutant exposure on cardiovascular diseases.
2. This paper reveals significant associations between short-term air pollutants exposure and daily AAD incidence, helping cardiovascular patients to prevent the occurrence of AAD in their daily life.
3. This paper emphasizes the adverse effects of PM_{10} and SO_2 on the incidence of AAD, complementing the existing literature that mainly focused on $PM_{2.5}$ and ignored other pollutants.

Implication of This Article Towards Theory, Practice, or Policy

1. The results of this paper supplement the literature on the health effects of moderately polluted areas.
2. This paper gives a new idea for the daily prevention of AAD in cardiovascular patients that they should pay more attention to the possibility of onset with high concentrations of PM_{10} and SO_2.

highest (28.2%) in winter and lowest (20.6%) in summer. However, few studies have considered air pollution as a potential risk factor for AAD. Xie et al. studied 345 patients from Chengdu city, and found that the air quality index (AQI) and $PM_{2.5}$ concentration were important risk factors for AAD incidence.[9] Chen et al found a significant and robust association between short-term $PM_{2.5}$ exposure and increased AAD hospitalizations in Shanghai, China.[10] However, evidence of AAD risk associated with short-term exposure to air pollution in different areas is limited.

Most studies have focused on the impacts of air pollutants in heavily polluted areas, such as Beijing,[11] Shenzhen,[12] and Delhi.[13] Relationships between moderate levels of pollutants and AAD incidence have been rarely studied. Since more and more evidence estimated the associations between low-level air pollution exposure and increased mortality, it is necessary to fill the gaps in this area.[14] Our study aimed to identify the impacts of moderate pollution on AAD in Northwest China by studying residents in Xi'an city, expanding the data to a new study area. Meanwhile, existing research found AAD incidence had seasonal variation,[8] while others showed no predictive power of season on AAD events.[15] Since Xi'an belongs to the winter heating zone, and the concentrations of air pollutions are different between heating season and non-heating season (Figure A-1), this paper also analyzed the impact of seasonal variation on AAD incidence.

Material and Methods

Study Area

This study was carried out in Xi'an, the capital of China's northwestern Shaanxi province. Xi'an, with a population of more than 7 million, has a sub-humid continental monsoon climate. The mean annual temperature in Xi'an is 15.6 °C, with relatively moderate humidity (60.8% ± 16.4%). Xi'an is bordered by the Weihe River and the Loess Plateau to the north and the Qinling Mountains to the south, resulting in the dominant wind direction to the northeast. The unique nature of the terrain makes Xi'an highly susceptible to the accumulation of air pollution. Airborne dust, coal burning, traffic, and industrial pollution are main sources of $PM_{2.5}$ in Xi'an.[16] Since the Chinese Action Plan for Air Pollution Prevention and Control was implemented in 2013, Xi'an's air quality has improved significantly. During the study period, there were more than 50% of the days per quarter were classified as mildly polluted, and more than 30% of the days were classified as moderately polluted according to both China and U.S. AQI standards[17,18] (Figure A-2). Therefore, it is reasonable to designate Xi'an as a moderately polluted area.

Daily AAD Incidence Data

Hospital admissions were used to represent the AAD incidence in our model. The electronic medical records (EMRs) of patients with AAD admitted to the target hospital in Xi'an were collected from December 1, 2013 to December 31, 2016. The target hospital is one of the largest hospitals in Northwestern China, with 3.26 million outpatients and emergency visits in 2019, accounting for nearly 26% of the total number of general hospital outpatients in Xi'an according to Xi'an Statistical Yearbook (2018–2019). Therefore, our collected data are reasonably representative of the patient population in Xi'an.

Acute aortic dissection patients were identified according to the International Classification of Diseases Revision 10 (ICD-10) I71.0 diagnosis code. Each EMR record included length of hospitalization, sex, age, date of birth, address, time of admission, time of discharge, and medical diagnosis. The exclusion criteria were as follows: (1). permanent residence outside of Xi'an; (2). endophytic aortic disease due to prior cardiac surgery or interventional repair; and (3). patients with chronic aortic dissection. In total, 494 AAD patients were enrolled in our study. The protocol of study and accessing the hospital admission data was approved by the ethics committee of First Affiliated Hospital of Xi'an Jiaotong University (Number XJTU1AF2021LSK-2021-114).

Air Quality and Meteorological Data

Hourly averaged concentrations of six criteria air pollutants ($PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3) from December 1, 2013 to December 31, 2016 were downloaded from website of China Ministry of Ecology and Environment (http://datacenter.mee.gov.cn). The data were collected from 13 monitoring stations in Xi'an (Figure A-3). Selected pollutants included fine particles with a diameter of 2.5 μm or less ($PM_{2.5}$, $\mu g/m^3$), coarse particles with a diameter of 10 μm or less (PM_{10}, $\mu g/m^3$), sulfur dioxide (SO_2, $\mu g/m^3$), nitrogen dioxide (NO_2, $\mu g/m^3$), carbon monoxide (CO, mg/m^3), and ozone (O_3, $\mu g/m^3$). The missing measure rate was .2%. Missing data were imputed by linear interpolation.

Meteorological data were obtained from the Xi'an Meteorological Service Center. For each day, the following parameters were assessed: minimum temperature (°C), maximal temperature (°C), diurnal temperature range (°C), mean relative humidity (RH, %), AQI, and daily temperature, which was calculated by averaging the maximum temperature and minimum temperature.

Statistical Analysis

Acute aortic dissection incidence data, daily air pollution concentrations, and weather data were linked through calendar data and then analyzed for exposure-response associations. Discrete variables are presented as percentages. Continuous variables are presented as means ± standard deviations (SD). Categorical variables are expressed as total numbers and percentages. The RR and its 95% confidence interval (CI) were calculated for each 10-unit increase in each pollutant. Since the daily number of AAD incidents had a quasi-Poisson distribution, a generalized additive model (GAM) was adopted to capture the short-term effects of air pollutants on AAD incidence.[19,20] All statistical tests were two-sided, and a P-value < .05 was considered statistically significant. R software version 3.6.1 was used to perform all statistical analyses. R package mgcv V1.8-33 was used to build the GAM.

Since some of the pollutants had obvious non-normal distributions, the correlations between weather conditions and air pollution factors were evaluated by the Spearman correlation test. Locally weighted scatter plot smoothing (LOWESS) curves with 95% CIs were used to present the seasonal, monthly, and daily variations in the incidence of AAD.

Generalized additive models can reveal nonlinear relationships between health effects and environmental factors.[20] The natural cubic spline function was used to adjust for long-term trends of date and season. Dummy variables were used to adjust for confounder variables such as seasonal trends, day of the week, and public holidays. Single-pollutant models were used to explore the individual effects of each pollutant. A multiple-pollutant model was used to explore the joint effects of all the pollutants. Degrees of freedom (df) were selected by the Akaike information criterion (AIC). The GAM model in our study was as follows:

$$\begin{aligned} Log[E(y_t)] = \alpha + \beta X_t + s(calendartime, df_1) \\ + s(temperature, df_2) \\ s(humidity, df_3) + factor(season) + factor(DOW) \\ + factor(holiday) + \varepsilon \end{aligned} \qquad [1]$$

where $E(y_t)$ represented the expected number of AAD incidences on day t; X_t represented the concentration of pollutants at day t; β was the regression coefficient and represented the relative risk (RR) of AAD incidence associated with a 10-unit increase in each pollutant concentration; DOW was a dummy variable representing the day of the week (Monday to Sunday) used to control for short-term fluctuations in daily AAD incident number; function s was a natural cubic spline function; df_1, df_2, and df_3 represented the DF for the long-term trend of calendar time in the non-parametric function to adjust for daily average temperature in the smoothing function, and to adjust for daily RH in the smoothing function, respectively; and ε represented the residual error.[21,22] The basic model used 1–20 df, which was selected with the AIC. Finally, we selected 9 df for the time variable, 5 df for the temperature variable, and 5 df for the RH variable.

Since the relationship between air pollution exposure and the incidence of AAD indicated an "exposure-lag-response" relationship,[23] we selected a 4-phase lag (lag0 to lag4) to estimate the short-term effects of air pollutants on AAD incidence. We also took into account moving average lags (i.e., lag 0:1, lag 0:2, and lag 0:3) to be consistent with previous studies.[19,24] Lag0 indicates that the exposure and incident occurred on the same day. Lag1 indicates that the effect of exposure on incidence was delayed by one-day. Similarly, lag2, lag3 and lag4 represented 2-day, 3-day, and 4-day delays, respectively. A moving average lag of 0:1 was the average concentration of the present day and previous day. Correspondingly, lag 0:2, lag 0:3, and lag 0:4 were the averages of the present day and previous 2 days, previous 3 days, and previous 4 days, respectively.

As Xi'an is a typic central heating city and air quality varies from non-heating season to heating season,[16] we also analyzed the association between heating/non-heating season and AAD incidence. According to the central heating policy,[25] heating season begins from November 15th to March 15th next year and non-heating season begins from March 16th to November 14th.

Results

Descriptive Statistics

Time series trend of air pollutants and meteorological parameters. Table A-1 presents the summary statistics of air pollutants and weather conditions in Xi'an during the study period. Based on the Chinese National Ambient Air Quality Standards (CNAAQ) Class I ($\boldsymbol{PM}_{2.5}$ (35 $\mu g/m^3$), $\boldsymbol{PM}_{10}$ (50 $\mu g/m^3$), $\boldsymbol{SO}_2$ (50 $\mu g/m^3$), $\boldsymbol{NO}_2$ (80 $\mu g/m^3$), $\boldsymbol{O}_3$ (100 $\mu g/m^3$), and $\boldsymbol{CO}$ (4 mg/m^3)), $\boldsymbol{PM}_{10}$ and $\boldsymbol{PM}_{2.5}$ accounted for the majority of pollutants on 75.8% and 96.7% of the polluted days (973 days and 1183 days, respectively), followed by $\boldsymbol{NO}_2$ (55.6%) and $\boldsymbol{SO}_2$ (46.9%). Obviously, $\boldsymbol{PM}_{10}$ and $\boldsymbol{PM}_{2.5}$ were the dominant pollutants in Xi'an. $\boldsymbol{NO}_2$ and $\boldsymbol{SO}_2$ also accounted for heavy pollution due to residential heating and industrial production. The seasonal variation in air pollutants is shown in Figure A-4, in which all pollutants except $\boldsymbol{O}_3$ had higher concentrations in spring and winter than in fall and summer, whereas $\boldsymbol{O}_3$ peaked in summer. One potential reason for the $\boldsymbol{O}_3$ trend was the presence of strong solar radiation and its formation mechanism.[26]

The results of the Spearman correlation analyses between air pollutants and meteorological parameters showed that $PM_{2.5}$ and PM_{10} were highly correlated with each other (r = .91); SO_2 and CO were both weakly negatively correlated with O_3 (r = −.66 and −.61, respectively); both SO_2 and CO had moderate correlations with daily average temperature (r = −.76, and −.72, respectively); $PM_{2.5}$, PM_{10}, and NO_2 had relatively weak negative correlations with daily average temperature (r = −.46, −.45, and −.37, respectively); O_3 was moderately correlated with average temperature (r = .79), which was consistent with the formation mechanism of O_3; and all pollutants except $PM_{2.5}$ and CO were negatively correlated with RH (Table A-2).

Study population and AAD incidence trend. The study enrolled 494 AAD patients, including 372 males (75.42%) and 122 females (24.58%). The average age was 55 ± 13 years. The average length of hospital stay (LOS) was 12.42 ± 9.6 hours, indicating that AAD patient's hospital stay was shorter than other cardiovascular diseases (e.g., 6 days for congenital heart disease[27]), and implying that AAD was developing rapidly given the high lethality.

Figure A-5 shows the hourly, daily, and monthly trends of AAD incidence. It is clearly that the AAD incidence had a seasonal trend, with a high occurrence in cool weather (i.e., the heating season) and a low occurrence in warm weather (i.e., the non-heating season). The monthly variation shows a clear "V"-shaped pattern, with a tendency to moderately increase from January to May and sharply decrease from June to August, followed by a rapid increase from summer to winter. Specifically, AAD incidence was 1.7 times lower in July than in the rest of the year, and the difference was significant (P = .03). For 24-hour incidence, AAD incidents mostly occurred between 10 AM and 2 PM.

The diurnal temperature range and AAD incidence followed an inverted U-shaped pattern (Figure A-6). As the LOWESS curve shows, AAD incidence increased when the daily temperature was 5-9 °C , remained steady when the daily temperature was 9–13 °C, and then dropped sharply when the daily temperature reached 12–15 °C. This trend suggests that both small and large daily temperature differences did not significantly affect the incidence of AAD.

Table A-3 shows the differences in meteorological conditions between the days with AAD and without AAD incidents. The average temperature and diurnal temperature range were both significantly lower on the days with AAD incidents than on those without AAD incidents. In contrast, $PM_{2.5}$, PM_{10}, and SO_2 were all significantly higher on the days with AAD incidents. RH CO, NO_2, and O_3 were not significantly different between the two groups.

Single-Pollutant Models

Figure 1 shows the lagged effects of the air pollutants on AAD incidence. The RR for AAD associated with $PM_{2.5}$ peaked on lag2 (RR = 1.2, 95% CI: 1.19, 1.21). The RRs for AAD-associated PM_{10}, SO_2, NO_2, CO, and O_3 were statistically significant on the day of exposure (i.e., lag0), increased on lag1, and attenuated substantially from lag2 onward. Among all the pollutants, SO_2 was associated with the highest RR at lag1 (RR = 1.43, 95% CI: 1.14, 1.72), followed by PM_{10} (RR = 1.21, 95% CI: 1.05, 1.35). The increase in every 10-unit concentration of PM_{10}, SO_2, CO, and O_3 on lag1 corresponded to 1.15% (95% CI: .25%, 2.05%), .84% (95% CI: .26%, 1.41%), .51% (95% CI: .19, .83), and .87% (95% CI: .33%, 1.41%) increases in AAD incidence, respectively, and every 10-unit increase in $PM_{2.5}$ on lag2 led to a 1.07% (95% CI: .17%, 1.97%) increase in AAD incidence (Table A-4).

Multi-Pollutant Models

The single-pollutant models revealed significant associations between air pollutants and the daily incidence of AADs. The combined influence of air pollutants was tested with multi-pollutant models. Since $PM_{2.5}$, PM_{10} and SO_2 were associated with the highest RRs (Figure 1) and were also the major pollutants of Xi'an (Table A-1), our research focused on the combined effect of these 3 pollutants.

Figure 2 presents the RRs associated with $PM_{2.5}$, PM_{10}, and SO_2 in the single-pollutant, two-pollutant, and three-pollutant models. Figure 2(a)–(c) show that (1) adding either PM_{10} or SO_2 decreased the effect of $PM_{2.5}$ on AAD incidence and (2) there was no fundamental distinction between the effects of PM_{10} and SO_2 on $PM_{2.5}$. Conversely, Figure 3(d) and (e) show that the RR for AAD associated with SO_2 increased from 1.2 to 1.39 when SO_2 was added. Figure 2(c), (e), and (f) show that after adding $PM_{2.5}$ and PM_{10} , the RRs

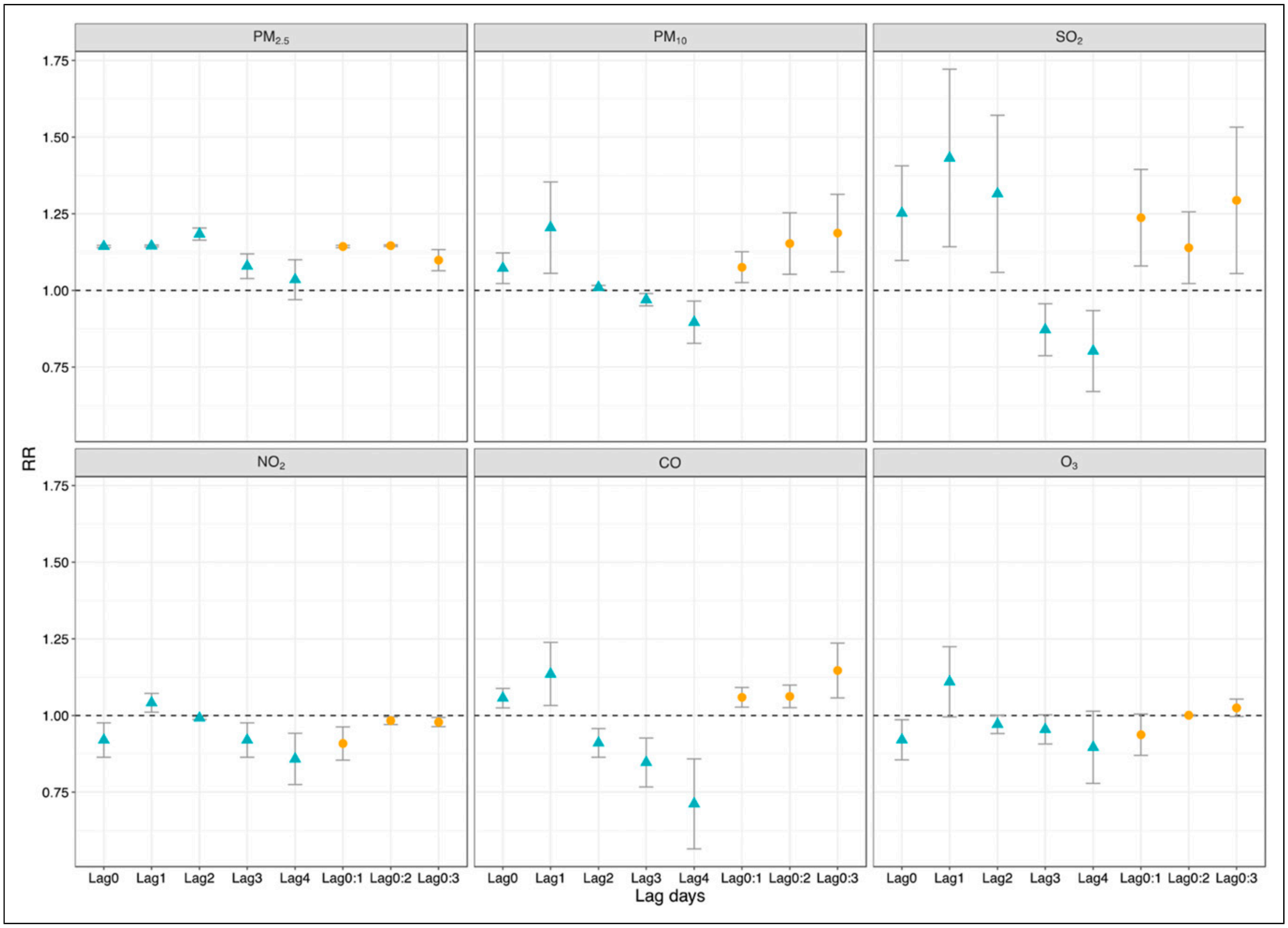

Figure 1. RR (with 95% CIs) for AAD incidence per 10-unit increases in $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO and O_3 on different lag days.

associated with SO_2 decreased from 1.43 to 1.38 and .94, respectively. Finally, Figure 2(g) shows that when all 3 pollutants were introduced into the model simultaneously, the effect of $PM_{2.5}$ declined sharply, and PM_{10} dominated the combined adverse effect (RR = 1.37, 95% CI: 1.22, 1.53) (Table A-4).

Comparison Between the Heating Season and Non-heating Season

Xi'an's AQIs in the heating season and non-heating seasons varied. This section discusses the different influences of $PM_{2.5}$, PM_{10}, and SO_2 on AAD incidence in both the heating and non-heating seasons. As shown in Figure 3, the RRs for AAD associated with $PM_{2.5}$ showed the greatest change between the heating and non-heating seasons, peaking on lag1 in the non-heating season and on lag0 in the heating season. The influence on other lag days was also greater than that in the non-heating season ($P < .05$). In contrast, the RRs associated with PM_{10} did not change drastically between the heating season and non-heating season. The RR associated with SO_2 in the heating season was significantly higher than that in non-heating season ($P < .05$), but there were no critical differences among other lag days.

Discussion

Based on the data of 495 AAD patients in Xi'an from December 2013 to December 2016, the present study analyzed the relationships between 6 air pollutants and daily AAD incidents in a moderately polluted area. The largest group of patients was farmers, followed by retirees (176 and 118, respectively) (Table A-5). Potential reasons are that farmers are more accustomed to physical discomfort due to the nature of their work, and elderly individuals (including retirees) are a major source of cardiovascular disease.[28]

The results showed that both air pollutants and temperatures affected AAD incidence. In general, the incidence of AAD showed a seasonal trend. The incidence rate was higher in heating season than in non-heating season. One possible reason is that the concentration of air pollutants is higher in heating season than in non-heating season due to central heating. The 24-hour incidence rate showed an inverted "U" pattern, where the incidence gradually increased from 6 AM to

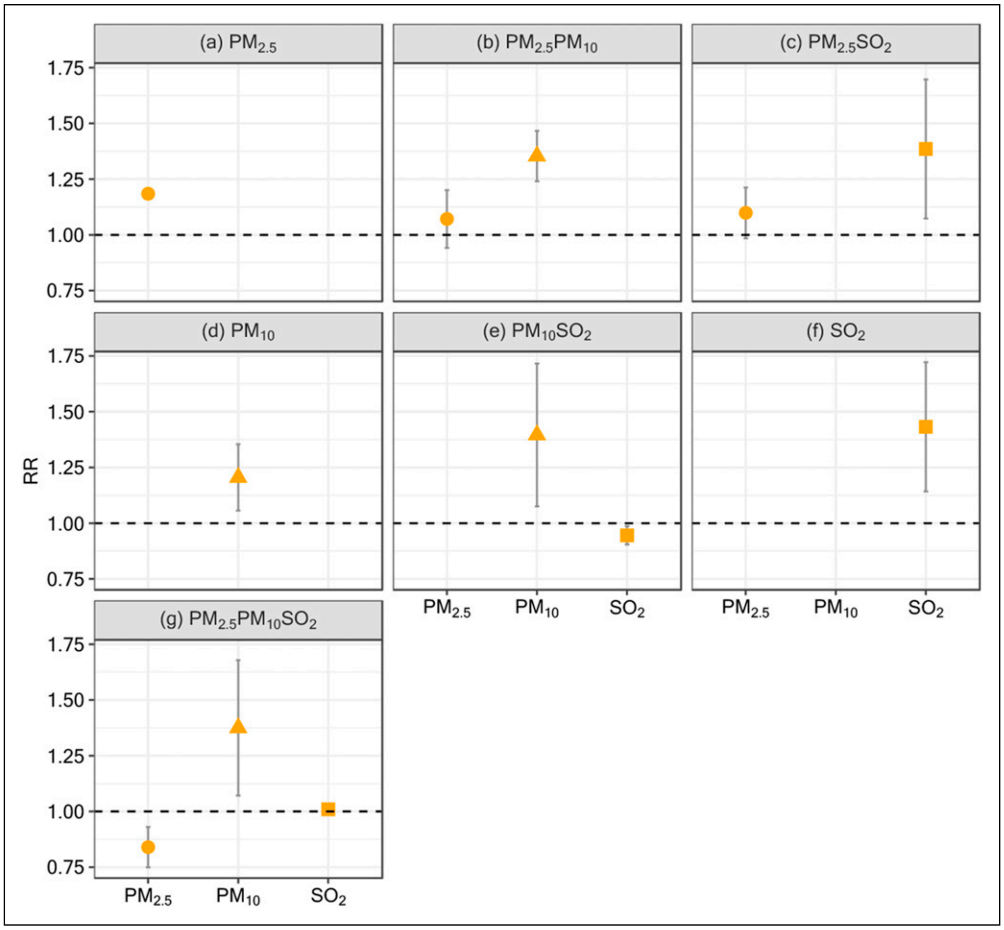

Figure 2. RRs (with 95% CIs) for AAD incidence with a $10-\mu g/m^3$ increase in $PM_{2.5}$ on lag2, PM_{10} and SO_2 on lag1 in the single- and multi-pollutant models.

11 AM, peaked at noon, decreased subsequently, and valleyed at night, in line with existing research. Suárez-Barrientos et al. found that patients who suffered from heart attacks between 6 AM and noon had higher blood pollutant levels than those who had heart attacks later in the day.[29] We speculate that this was because the patients' blood pressures increased quickly in the morning to prepare them for the day; moreover, the blood vessels were thick, stiff, and difficult to bend, which increased the risk of arterial plaque formation. Arterial plaque along with high blood pressure in the morning resulted in a ruptured artery.

The single-pollutant models showed that $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 had transient lag effects on the incidence of AAD. The highest RR associated with $PM_{2.5}$ exposure occurred on lag2, and the highest RRs occurred on lag1 for the other pollutants. Similar to previous studies, our findings showed that $PM_{2.5}$ had a significant association with the incidence of AAD after controlling for confounding factors, such as long-term trends, weather conditions, and other gaseous pollutants.[9] It was also found that in areas with the same pollution and temperature conditions as Xi'an, both SO_2 and PM_{10} had more significant effects on the increase in AAD incidence than $PM_{2.5}$. The three-pollutant model showed that PM_{10} had a stronger association with adverse effect than the other 2 pollutants, indicating that serious attention should be given to PM_{10} when considering the overall effects of pollutants in moderately polluted areas. The research results are biologically credible since recent literature has shown that short-term exposure to $PM_{2.5}$, PM_{10}, and SO_2 is a risk factor for hypertension,[30] and elevated blood pressure is an important cause of AAD.[7]

This study has three limitations. First, this was a retrospective study with data selection bias. Second, this work used hospital admissions to reflect morbidity, so those who died before arriving at the hospital were excluded, which may cause data deviation. Third, the air pollutant monitoring sites were fixed, leading to regional limitations, and the impact of air pollution may be underestimated.

Our research makes the following contributions to the prevention of AAD. First, residents of a moderately polluted

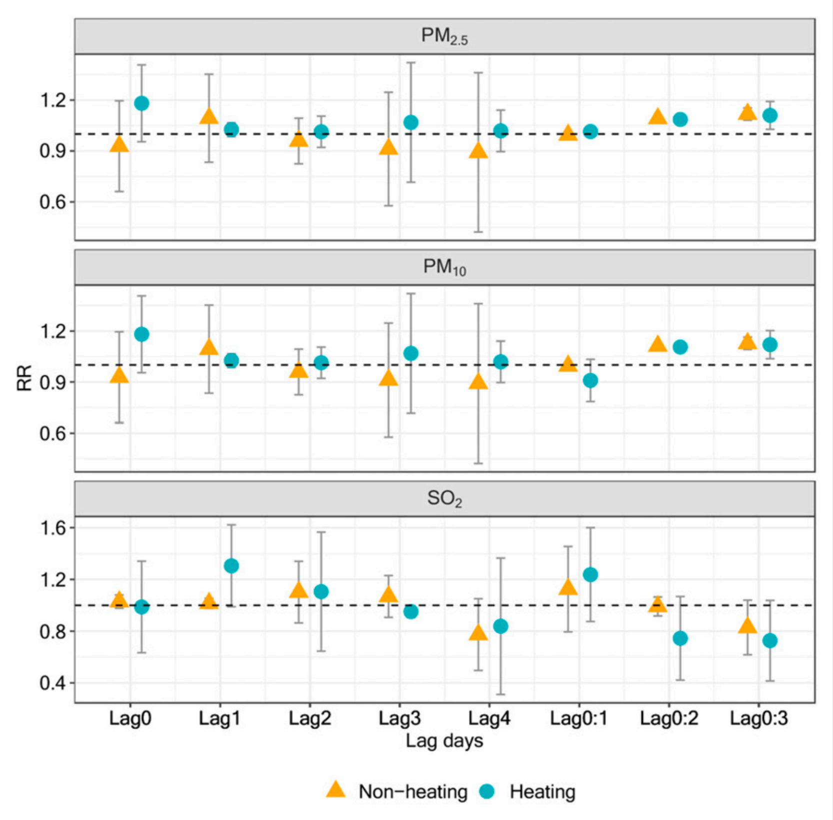

Figure 3. RRs (with 95% CIs) for AAD incidence in association with $PM_{2.5}$, PM_{10}, and SO_2 on different lag days in the heating season and the non-heating season.

city/area with basic cardiovascular diseases, such as high blood pressure, should take preventive measures when the daily temperature difference is 9–13 °C. Second, during the heating season, patients should reduce outdoor activities, practice indoor air purification, and wear masks to protect themselves from air pollution. These measures have been proven to be effective in reducing the impact of air pollution on cardiovascular disease.[31] Third, during the heating season or when the daily temperature difference is relatively large, hospitals need to increase their manpower dedicated to cardiovascular disease and outpatient services to address the potential increase in patients. Fourth, this research provides supporting evidence that Xi'an city may not need to spend billions in the winter season each year to replace the use of coal for heating with gas. Instead, the saved money could be used to further support the city government's existing policies and regulations to reduce vehicle exhaust emissions and encourage the use of new energy-efficient vehicles. In a large city with a population of more than 7 million, these measures could benefit hundreds of thousands of residents.

Conclusion

This retrospective cohort study explored the adverse effects of air pollutants on AAD incidence in the moderately polluted city of Xi'an. The results provide evidence that cold atmospheric temperatures and relatively large daily temperature changes significantly increase the risk of AAD. The results demonstrated that increased $PM_{2.5}$, PM_{10}, and SO_2 were significantly associated with increased risks of AAD in the multi-pollutant models, in which PM_{10} and SO_2 had greater influences than $PM_{2.5}$. The research further found that the associations between $PM_{2.5}$, PM_{10}, SO_2 and AAD incidence were stronger in the heating season than in the non-heating season and that $PM_{2.5}$, PM_{10}, and SO_2, especially PM_{10} and SO_2, could be strong predictors of AAD incidence.

Appendix

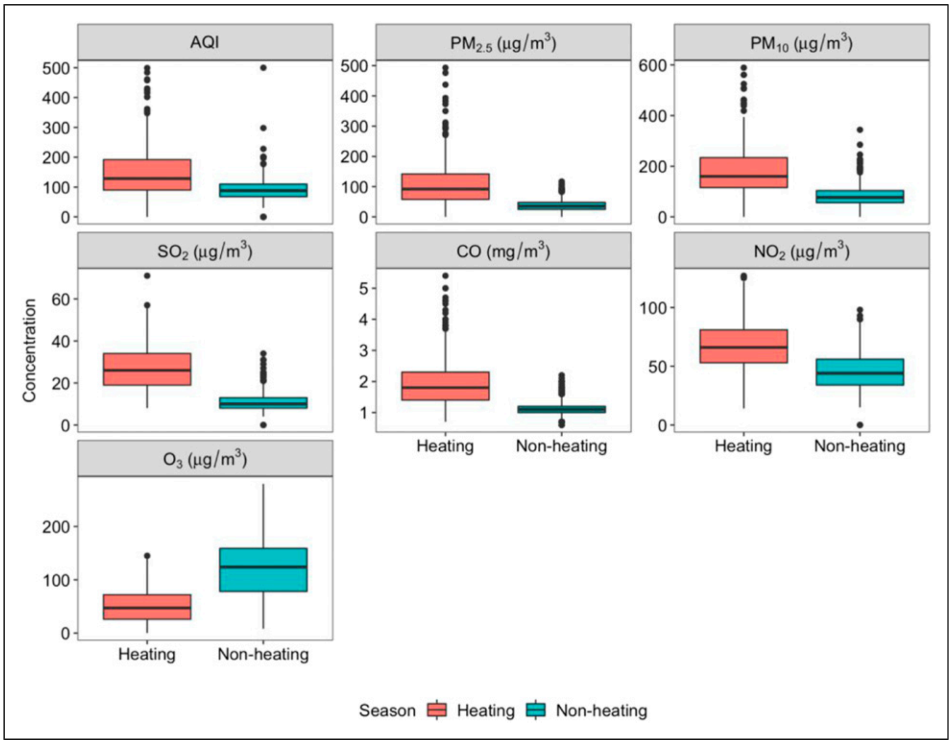

Figure A-1. Boxplot of AQI and air pollutants between heating season and non-heating season during study period.

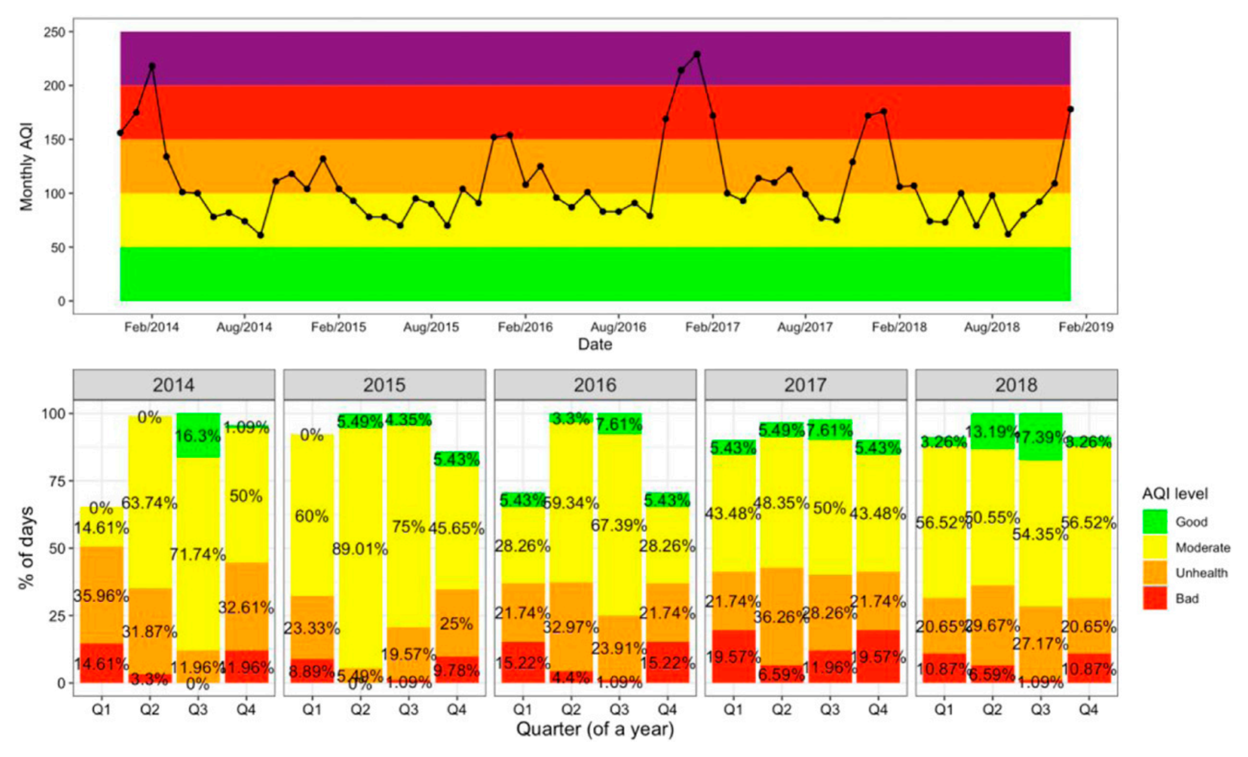

Figure A-2. Monthly AQI trend and quarterly AQI range from 2013 to 2018 in Xi'an. Green: AQI 0∼50, good; yellow: AQI 51∼100, moderate; orange: AQI 101∼150, unhealthy for sensitive groups; red: AQI 151∼200, unhealthy; purple: AQI 200∼250, very unhealthy.

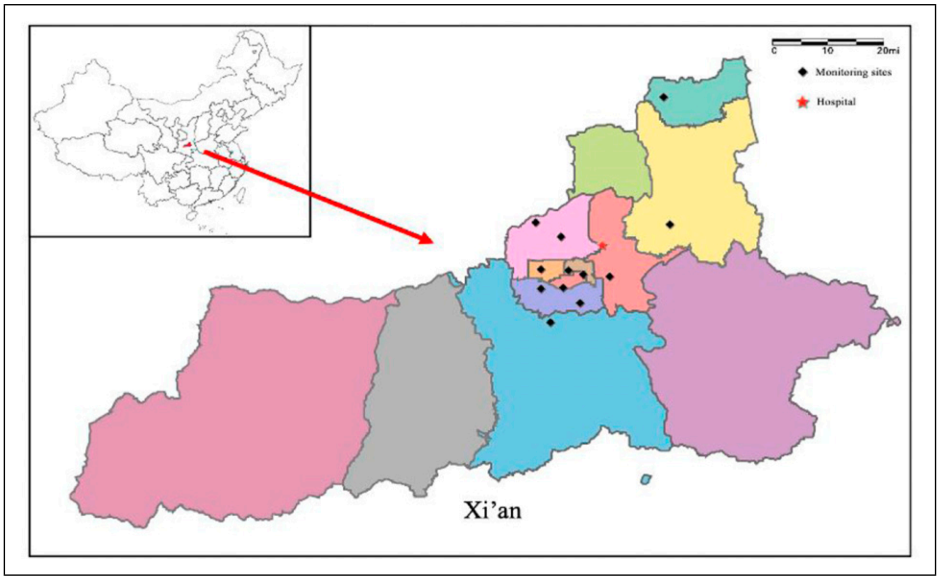

Figure A-3. Distribution of air quality monitoring sites and location of the target hospital in Xi'an.

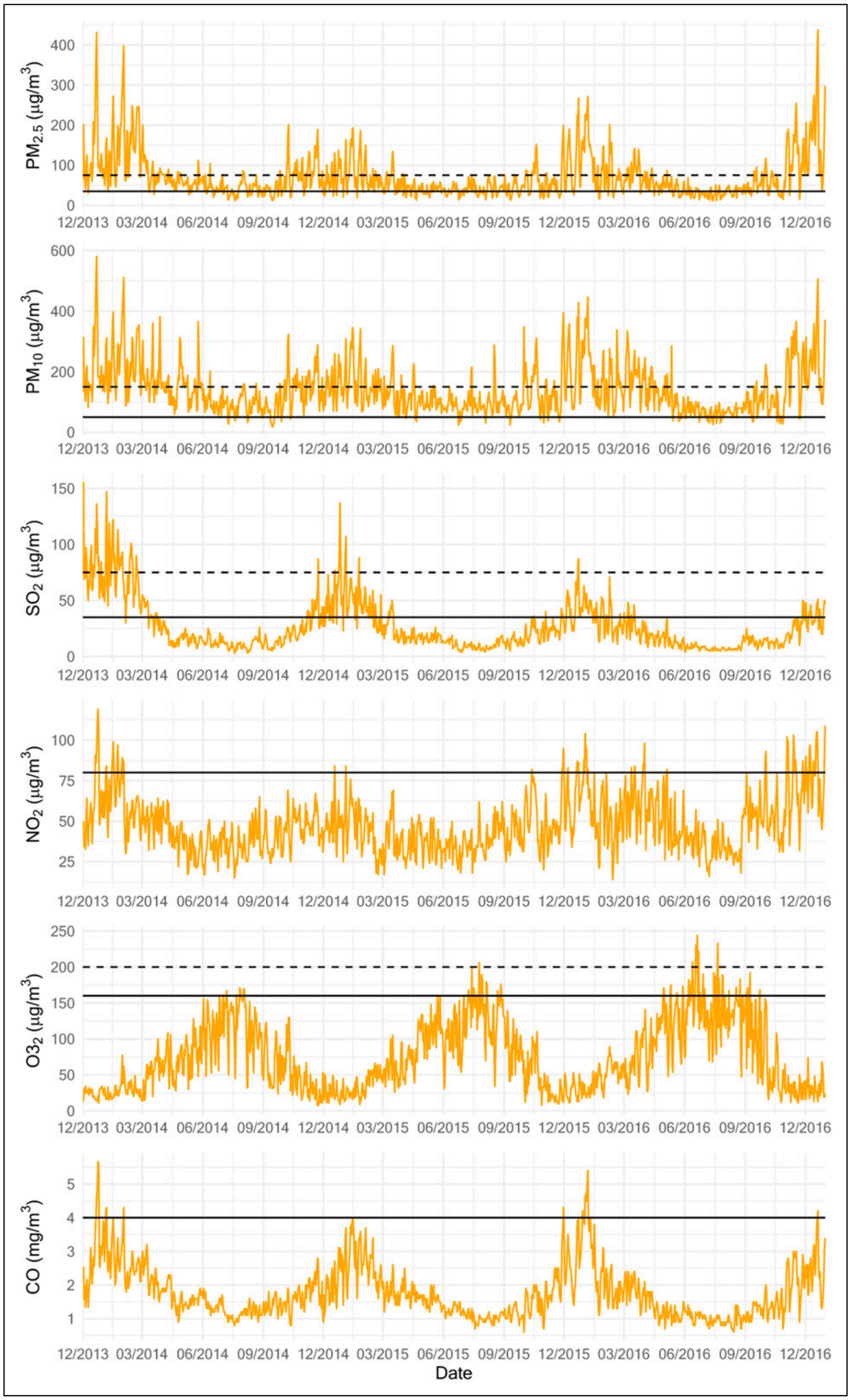

Figure A-4. Time series distribution of pollutants in Xi'an from 2013–2016. Solid line: Class I standard of air pollutant concentration according to the CNAAQS; dashed line: Class II standard of air pollutant concentration according to the CNAAQS.

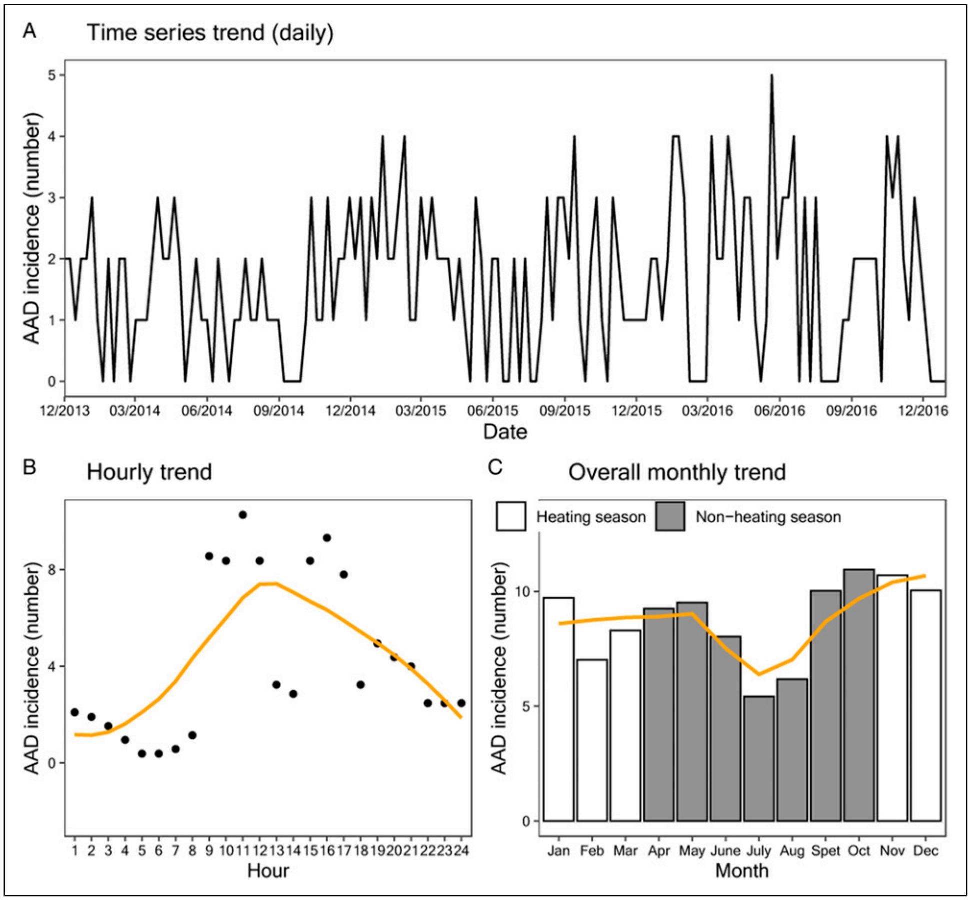

Figure A-5. Daily, hourly, and monthly AAD incidence trends from December 2013 to December 2016.

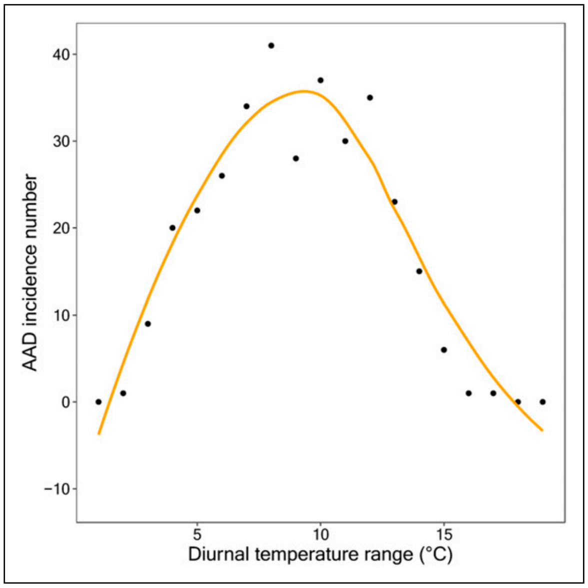

Figure A-6. LOWESS regression curve of AAD incidence based on diurnal temperature range.

Table A-1. Summary statistics of annual air pollutants and meteorological conditions in Xi'an from December 2013 to December 2016.

Variables	Mean ± SD	Min	P25	Median	P75	Max	C1 (%)	C2 (%)
$PM_{2.5}$, $\mu g/m^3$	70.0 ± 53.8	12	36	53	82	437	75.8	29.8
PM_{10}, $\mu g/m^3$	138.4 ± 80.4	18	82	118	173	581	96.7	83.2
SO_2, $\mu g/m^3$	26.8 ± 22.1	3	12	19	34	155	46.9	8.2
NO_2, $\mu g/m^3$	43.8 ± 20.8	0.8	32	43	56	109	55.6	19.6
O_3, $\mu g/m^3$	71.3 ± 48.5	7	31	57	107	244	28.2	4.7
CO, mg/m^3	5.3 ± 12.4	0.6	1.2	1.6	2.4	81	9.2	9.2
Average temp C	15.3 ± 9.5	−6	6.5	16.3	23.5	33.5	—	–
Diurnal temp C	9.2 ± 3.1	1	7.9	10	11	19	—	–
RH (%)	60.9 ± 16.5	18	49	60	73	97	—	–

*C1, C2: the ratio of the number of days when concentration exceed the Class I/II standard to the number of total study days.

*P25, P75: 25th percentile and 75th percentile.

*Class I 24-hour average value standard: $PM_{2.5}$ (35 $\mu g/m^3$), PM_{10} (50 $\mu g/m^3$), SO_2 (50 $\mu g/m^3$), NO_2 (80 $\mu g/m^3$), O_3 (100 $\mu g/m^3$, 8-hour average), and CO (4 mg/m^3).

*Class II 24-hour average value standard: $PM_{2.5}$ (75 $\mu g/m^3$), PM_{10} (150 $\mu g/m^3$), SO_2 (150 $\mu g/m^3$), NO_2 (200 $\mu g/m^3$), O_3 (160 $\mu g/m^3$, 8-hour average), and CO (4 mg/m^3).

Table A-2. Results of spearman correlation analyses between air pollutants and meteorological conditions.

Variables	**$PM_{2.5}$**	**SO_2**	**CO**	**NO_2**	**O_3**	Average Temp	RH
$PM_{2.5}$	.91*	.69*	.73*	.65*	−.46*	−.46*	.03
PM_{10}		.71*	.72*	.67*	−.39*	−.45*	−.19*
SO_2			.80*	.62*	−.66*	−.76*	−.27*
CO				.59*	−.61*	−.72*	−.04
NO_2					−.29*	−.37*	−.14*
O_3						.79*	−.23*
Average temp							.02*

*: P value < .05; RH: relative humidity.

Table A-3. Comparisons of the meteorological conditions on days with and without AAD incidents.

Variables	Days with AAD (n = 275)	Days without AAD (n = 949)	P value
$PM_{2.5}$, $\mu g/m^3$	83.16 ± 49.73	66.27 ± 56.56	<.01*
PM_{10}, $\mu g/m^3$	130 ± 79.68	110.56 ± 86.19	<.05*
SO_2, $\mu g/m^3$	25.68 ± 21.18	21.18 ± 20.02	.03*
CO, mg/m^3	2.77 ± 7.34	3.12 ± 8.81	.1
NO_2, $\mu g/m^3$	45.23 ± 18.93	42.95 ± 21.58	.14
O_3, $\mu g/m^3$	67.75 ± 48.12	69.37 ± 51.11	.53
Ave. tempC	19.35 ± 10.07	20.09 ± 10.09	.03*
Diurnal temp C	9.80 ± 8.72	11 ± 9.31	<.05*
RH, %	60.79 ± 17.36	60.94 ± 16.14	.75

*: $P<.05$; RH: relative humidity.

Table A-4. RRs (with 95% CIs) for AAD incidence with a 10-$\mu g/m^3$ increase in $PM_{2.5}$ on lag2, PM_{10} and SO_2 on lag1 in the single- and multi-pollutant models.

Model	RR	95% CI
$PM_{2.5}$		
Single model	1.18*	(1.12, 1.25)
$+PM_{10}$	1.07*	(1.00, 1.14)
$+SO_2$	1.10**	(1.04, 1.15)
$+ PM_{10} + SO_2$	.83*	(.79, .88)
PM_{10}		
Single model	1.20**	(1.05, 1.35)
$+PM_{2.5}$	1.35*	(1.29, 1.41)
$+SO_2$	1.39	(1.07, 1.71)
$+ PM_{2.5} + SO_2$	1.37*	(1.22, 1.53)
SO_2		
Single model	1.43*	(1.14, 1.72)
$+ PM_{2.5}$	1.38*	(1.22, 1.54)
$+ PM_{10}$	.94*	(.90, .98)
$+ PM_{2.5} + PM_{10}$	1.01*	(1.00, 1.01)

*: $P < .05$, **: $P < .01$.

Table A-5. Basic characteristics of the AAD patients included in the study.

Variables	Total (n = 494)
Age (year)	55 ± 13.4
Gender (male/female)	372/122
LOS (hour)	12.42 ± 9.6
Marriage (married/ spinsterhood/divorce & widowhood)	473/11/10
Occupation (peasant/ retirees/workers/other)	176/118/68/132

LOS: length of stay.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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