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RESEARCH ARTICLE

The effect of ambient air pollution on circulatory mortality: a short-term exposure assessment in Xi'an, China

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Abstract
Various studies have illustrated that exposure to ambient air pollution has negative impacts on health. However, little evidence exists on the effects of ambient air pollution on circulatory mortality in Xi'an, China. This study aims to investigate and ascertain the association between short-term exposure to ambient air pollutants and circulatory mortality in Xi'an, China. Daily average concentrations of $PM_{2.5}$, SO_2, and O_3, meteorological data (temperature and relative humidity) and daily counts of circulatory mortality were obtained between January 2014 and June 2016. Mortality was stratified by gender and age group (≤ 64 years and ≥ 65 years). A generalized additive model (GAM) with natural splines (NS) was constructed to analyze the relationship between ambient air pollutants and daily circulatory mortality. There were 57,570 cases of circulatory mortality, with cerebrovascular and ischemic heart diseases accounting for 48.5% and 43.5%, respectively. All ambient air pollutants displayed different seasonal patterns. In the single pollutant model, 10 $\mu g/m^3$ increase in 2-day moving average concentrations of $PM_{2.5}$, SO_2, and O_3 was associated with relative risk of 1.288(1.198, 1.388), 1.360(0.877, 2.331), and 1.324(1.059, 1.705) in circulatory mortality, respectively. After adjusting for collinearity in the multi-pollutant model, the effects remained statistically significant. The ≥ 65 years and female sub-groups were associated with a higher risk of circulatory mortality. Short-term exposure to ambient air pollutants plays a pivotal role in the genesis of circulatory mortality in Xi'an. Responses to ambient air pollutants exposure in relation to circulatory mortality are different when analyzed by sub-groups.

Keywords Ambient air pollution · Circulatory diseases · Cardiovascular diseases · Mortality · Time-series · Public health

Introduction

Air pollution is recognized as the single and foremost critical environmental health hazard, a problem affecting developed and developing countries alike. The impact of air pollution dates back to the 1952 London Smog where approximately 12,000 people died prematurely due to unusually high levels of air pollution, an occurrence that led to the development of environmental protection policies globally (Bell and Davis 2001). Air pollution epidemiology continues to play a fundamental role in identifying the hazards of air pollution as well as re-forming guidelines and policies that govern air quality standards (Fann et al. 2011). Consequently, in the past three decades, there has been a surge of air pollution epidemiological and clinical studies to ascertain the links between exposure to ambient air pollution and the possible risk of an array of adverse health consequences (Lee et al. 2014; Yang et al. 2013). Although awareness on the adverse health effect associated with exposure to air pollution has improved, the World Health Organization (WHO) reports that about 98% of cities in low- and middle-income countries with populations more than 100,000 people still do not meet the WHO Air Quality Guidelines (WHO 2016a).

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China has an ongoing challenge of increased air pollution, with concentration levels substantially higher than in other developing countries. In 2014, China was the world's most populous country with a population of over 1.36 billion people, subsequently accounting for a significant portion of the world's health burden. Consequently, this rapid growth has led to major changes in the environmental and public's health. Over the past few years, air pollution levels in Asia have been high and consistently above the upper limits of the WHO Ambient Air Quality Guidelines, leading to an epidemic of cardiovascular diseases. In 2016, the Ministry of Environmental Protection reported only 84 cities out of the 338 prefecture-level were in line with the ambient air quality standard in China (China Daily 2017). Substantial epidemiological and clinical studies suggest that short-term exposure to ambient air pollution has significant adverse effects on health (Shang et al. 2013). These studies have established a clear and robust relationship between short-term exposure to ambient air pollution and cardiovascular diseases in China; however, most studies are conducted in the metropolis and not smaller cities or rural areas.

Globally, cardiovascular diseases continue to be among the leading causes of mortality with approximately 3.7 million deaths in people below the ages of 60 years (Shang et al. 2013). Between 1990 and 2013, cardiovascular diseases increased by 41% (climbing from 12.3 million deaths), and were responsible for approximately 17.3 million deaths (i.e., 30% of total deaths), a figure that increased to 17.92 million cardiovascular deaths in 2015. Cardiovascular diseases are projected to escalate to 25 million deaths by the year 2020 (Lozano et al. 2012; Global Burden of Diseases 2014). With half of the world's population found in Asia, the global burden of cardiovascular diseases weighs more on the continent than other parts of the world. In East Asia (which includes China), 40% of the deaths were attributed to cardiovascular diseases in 2013 (Roth et al. 2015). In China, cardiovascular diseases have become a significant public health problem having surpassed infectious diseases to become the leading cause of morbidity and mortality in both urban and rural areas (Zhou et al. 2016). Cardiovascular-related morbidity and mortality have increased rapidly with the age of affected Chinese residents decreasing which is an alarming concern (Li and Ge 2015). Approximately 3.5 million cases of deaths due cardiovascular diseases have been reported annually accounting for about 40% of all annual deaths in China, suggesting that on average, at least 9590 Chinese people die due to cardiovascular-related diseases daily (i.e., about 400 deaths per hour and 1 death every 10 s) and consistently on the rise (Li and Ge 2015). Moreover, in 2014, approximately 290 million people were reported to be affected by cardiovascular diseases in China, an increase of 60 million from 2010 where 1 in 5 people were affected by cardiovascular disease, with mortality reported to have increased from 223.5 per 100,000 people to 239.5 per 100,000 people between 2004 and 2010 (World Health Organization 2018; Li and Ge 2015; Weiwei et al. 2016; National Center for Cardiovascular Disease China 2016). With China experiencing rapid economic development, the disease burden of cardiovascular diseases has also increased, with at least 43% of the total deaths in 2016 attributed to cardiovascular diseases (World Health Organization 2018). The National Center for Cardiovascular Disease China (2016) and the World Health Organization (2018) have projected that cardiovascular diseases in China will increase by approximately 50% between 2010 and 2030 based on population age and growth alone.

Although China has seen a growing interest in cardiovascular mortality related to short-term ambient air pollution exposure, the association remains poorly characterized in cities like Xi'an. Studies focusing precisely on the effects of $PM_{2.5}$, SO_2, and O_3 remain limited in most small Chinese cities (Shang et al. 2013). To determine the circulatory mortality risk associated with short-term exposure to ambient air pollution, we conducted a time-series analysis, applying the generalized additive model (GAM) to evaluate associations between short-term exposure to ambient air pollutants ($PM_{2.5}$, SO_2, and O_3) and daily circulatory mortality in Xi'an. Gender and age stratifications were used to examine the adverse health effects of air pollution on different subgroups.

Materials and methods

Study area and population

The study population was local residents in the Household Register of Xi'an (13 districts). Xi'an with an area of 9983 km^2 and a population of about 8,705,600 million inhabitants is the largest city in central north-western China's Shaanxi Province. Located at 34° 15′ 44″ north latitude and 108° 56′ 16″ east longitude, Xi'an is situated in the middle of the Yellow River's Guangzhong Plain, with Weihe River to the north and Qinling Mountains to the south. Xi'an's climate has a distinct pattern of four seasons per year, corresponding to the sub-humid, warm, and temperate continental monsoon climate. Xi'an is an essential industrial epicenter of the central north-western region of mainland China, consequently carrying the burden of poor air quality in the region. As of 2016, the number of motor vehicles in Xi'an had astonishingly reached 2.5 million and continues to grow at an average annual growth rate of 14.3%, a factor that is possibly contributing to the soaring air pollution levels (Li et al. 2016). Xi'an experiences severe air pollution problems in China (Cao et al. 2005), something that can be attributed to the prevalence and continued industrial coal burning and road traffic.

Study design

The study was conducted using a time-series study design, typically suitable in epidemiology and used to assess the mortality risks associated with transient exposures to ambient air pollution based on the daily aggregate date, and also controls for both time-invariant and time-varying confounders by design (Fung et al. 2003). The population of Xi'an was assessed with reference to change over time in the rate of circulatory mortality and the corresponding changes in the short-term exposure ambient air pollutants ($PM_{2.5}$, SO_2, and O_3) including meteorological parameters during the same period.

Data collection

Circulatory mortality cases were obtained from the Shaanxi Centre for Disease Control and Prevention (CDC) in Xi'an, China (from January 2014 to June 2016). To obtain a representative sample of the population, publicly funded hospitals ranging from primary to tertiary level were used to monitor circulatory events in the city continuously. Patients' data were derived from the computerized medical system in the hospitals and validated by Shaanxi CDC. Information on the death records included nationality, age, gender, diagnosis, the onset of disease, visit date, date of death, and the causes of death coded according to the "*International Classification of Diseases, Tenth Revision* (ICD-10), chapter IX, (I00-99)" (WHO 2016b). The total circulatory mortality cases were stratified by gender (male and female) and age (≤ 64 years and ≥ 65 years) (Kan et al. 2008). Meteorological parameters (relative humidity and temperature) were obtained from the Xi'an Meteorological Bureau during the study period. Daily ambient air pollution 24-h average data for $PM_{2.5}$, SO_2, and 8-h average for O_3 were collected from the Xi'an Environmental Monitoring Centre. The data was available in averages derived from state-controlled monitoring stations across Xi'an.

Statistical methods

Daily circulatory mortality, ambient air pollution, and environmental parameters were linked by date and analyzed employing a time-series approach. A generalized additive model (GAM) with natural splines (NS) was constructed in R software version 3.2.2 with "mgcv" package to analyze the relationship of daily levels of ambient air pollutants and circulatory mortality as well as other covariates (R 2015; Yang et al. 2013). Following Wood's detailed introduction of GAM, a basic model was firstly constructed for circulatory mortality without analyzing the ambient air pollution variables; after that, ambient air pollutant variables were introduced into the model, and their effects on circulatory mortality were examined (Wood 2006). Considering the confounding effects, we incorporated the NS functions of time and meteorological parameters, which provide lodgings for both non-linear and monotonic links between mortality with time and meteorological parameters, offering a more flexible modeling tool (Hastie and Tibshirani 1990). To verify the stability of the model, various sensitivity analyses were conducted and various degrees of freedom (df) per year were used (4 df/year, 8 df/year, and 12 df/year) for the time trend. For meteorological parameters, 3 df was used for temperature and relative humidity (Dominici et al. 2006; Samet et al. 2000). Furthermore, the day of week (DOW) was included as a dummy variable in the basic model. The following log-linear GAM model was fit to obtain the estimated pollution log-relative rate β:

$$\log[E(Y_t)] = \propto_0 + \sum_{i=1}^{q} \beta_i(X_i) + \sum_{j=1}^{p} f_j\left(Z_j, df\right) + W_t(\text{week})$$

where $E(Y_t)$ represents the expected number of deaths at day t, β represents the log-relative rate of mortality associated with a unit increase of ambient air pollutants, X_i indicates the concentration of ambient air pollutants at day t, W_t(week) is the dummy variable for day of the week, Z_j is the predictor variables other than ambient air pollutants (i.e., time, mean daily temperature, and relative humidity), and fj is a smooth function of these variables. Single-day lag models are known to possibly underestimate the cumulative effect of air pollution on mortality; 2-day moving averages of current-day and previous-day concentrations of air pollutants (lag01) were used in our main analysis with current-day (lag 0 day) temperature and relative humidity (Bell et al. 2004; Braga et al. 2001). Sensitivity analyses were conducted to examine the impact of air pollutants on mortality with lag structures, including single-day lag (lag 0 to 4) and multi-day lag (lag 01 to 04).

In order to exclude the impacts of collinearity in the multi-pollutant model, a "principal component" was introduced into the study where we established a dose-response model of multiple ambient air pollutants' health effects (Zhao et al. 2011). Suitable information of primary ambient air pollutants was substituted by composite latent variables (principal components) in the GAM. Meanwhile, we transformed the regression coefficient β of the principal components into the regression coefficient b of the primary ambient air pollutants. Then, relative risks and their confidence intervals (CIs) were estimated to quantify the influence of each ambient air pollutant on daily mortality in the multivariate model. Lastly, stratified analyses by gender (male and female) and age group (≤ 64 years and ≥ 65 years) were conducted to examine potential effect modifications. The statistical significance of the differences between the effect estimates of the strata of a potential effect modifier was tested by calculating the 95%CI and expressed as:

$$\left(\hat{Q}_1 - \hat{Q}_2\right) \pm 1.96\sqrt{\widehat{SE_1} + \widehat{SE_2}}$$

In which $\hat{Q}_1$ and $\hat{Q}_2$ are the estimates for the two aforementioned sub-groups, and $\hat{SE}_1$ and $\hat{SE}_2$ were the respective standard errors (SEs) (Altman and Bland 2003). In order to compare the results of our study with others, all results were presented as the relative risk of daily circulatory mortality and 95%CI associated with each 10 μg/m^3 increase in ambient air pollutant concentration. The statistical significance was defined as $P < 0.05$.

Results

Descriptive statistics

Descriptive statistics summary is presented in Table 1. A total of 57,570 cases of circulatory mortality (ICD-10: I00-99) occurred in Xi'an between January 2014 and June 2016; of this, 48.5% were cerebrovascular diseases (ICD 10: I60-69), 43.5% being ischemic heart diseases (ICD-10: I20-25), and 8% being other forms of circulatory diseases. During the study, the daily number of circulatory mortality cases ranged from 16 to 164 with an average of 65.09. The mortality rate was 220.3 per 100,000 people, and the proportional mortality rate was 43.2 per 1000 people. Daily averages for the meteorological parameters were 13.48 °C for temperature and 65.43% for relative humidity. The annual mean concentration of $PM_{2.5}$, SO_2, and O_3 were 66.63 μg/m^3, 26.38 μg/m^3, and 39.62 μg/m^3, respectively. Based on the GB3095-2012, $PM_{2.5}$ was higher than the accepted annual average in China (MEP 2012).

Correlation analysis

Spearman correlation coefficients between ambient air pollutant concentrations and meteorological parameters are presented in Table 2. $PM_{2.5}$ and SO_2 had a high positive correlation with each other with Spearman's r of 0.67. However, a negative correlation was observed between O_3 and all the other ambient air pollutants. Temperature showed negative correlations with all ambient air pollutants, except for O_3, which showed a high positive correlation with Spearman's r of 0.778. Humidity was negatively correlated with only SO_2 and O_3. No significant correlation was observed between humidity and temperature.

Table 2 Spearman correlation coefficients between daily ambient air pollutant and meteorological parameters

	SO_2	O_3	Temperature	Humidity
$PM_{2.5}$	0.670**	− 0.441**	− 0.431**	0.041
SO_2		− 0.666**	− 0.786**	− 0.248**
O_3			0.778**	− 0.240**
Temperature				0.058

** $P < 0.01$

Graphical representation of mortality and air pollutants data

Based on seasonal characteristics of Xi'an, ambient air pollutants were considered according to their levels in order to determine the most polluted seasons (Fig. 1a). The categorization of each pollutants' concentration per season demonstrated obvious and expected seasonal differences. $PM_{2.5}$ and SO_2 levels were high in the cold seasons (i.e., autumn and winter), while O_3 was higher in the warm seasons (i.e., spring and summer). $PM_{2.5}$ concentration levels for all seasons except winter were below the daily

Table 1 Descriptive statistics of daily mortality counts, air pollutant concentrations, and meteorological parameters ($n = 57{,}570$)

	Mean ± SD	Min	P25	P50	P75	Max
Mortality						
Circulatory diseases	65.09 ± 17.01	16	52	64	76	164
Male	40.65 ± 11.2	8	32	40	48	105
Female	33.44 ± 9.79	8	26	32	40	73
≤ 64 years	14.94 ± 4.88	2	11	15	18	34
≥ 65 years	59.05 ± 16.58	3	46	58	70	155
Air pollutant concentration (μg/m^3)						
$PM_{2.5}$	66.63 ± 50.13	11	36	53	77.25	527
SO_2	26.38 ± 21.55	2	12	19	35	145
O_3	39.62 ± 24.45	5	20	33	56	117
Meteorological parameters						
Temperature (°C)	13.48 ± 9.60	− 8	5	14	22	34
Humidity (%)	65.43 ± 15.8	21	55	65	78	99

SD, standard deviation; *Px*, xth percentiles

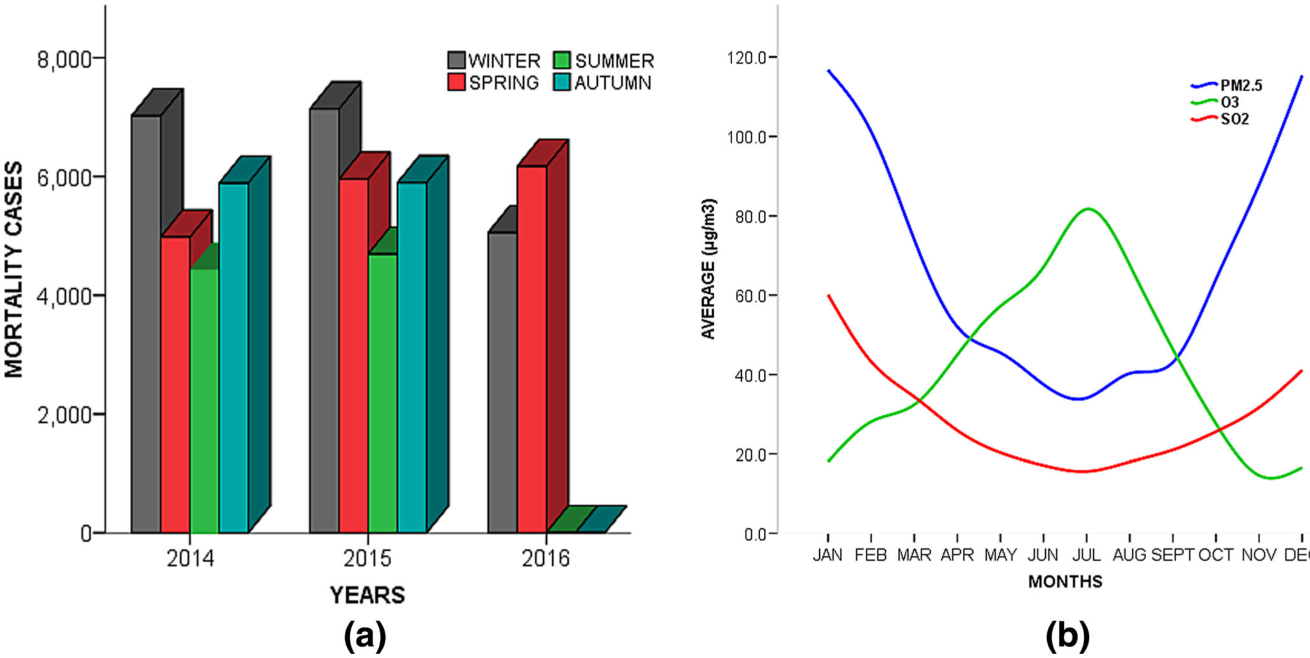

Fig. 1 Seasonal distribution of circulatory mortality (**a**) and variation of ambient air pollutants (**b**) in Xi'an between 2014 and 2016

ambient air quality limit (75 μg/m^3), while O_3 and SO_2 concentrations for all seasons were below the daily ambient air quality limits (150 μg/m^3 and 160 μg/m^3), respectively (MEP 2012). Seasonal distributions of circulatory mortality are illustrated in Fig. 1b. Circulatory mortality was highest in the winter season and lowest in the summer season.

Statistical analysis results

Table 3 summarizes the relative risk of daily circulatory mortality with 10 μg/m^3 increase in the 2-day moving average air pollutant levels. Estimated effects of all pollutants on circulatory mortality were all statistically significant ($P < 0.05$). After adjusting for collinearity by principal component, the estimated effects decreased with the exception of $PM_{2.5}$, however, remained statistically significant ($P < 0.05$), presumably as a result of increasing degrees of freedom.

In epidemiological studies associating ambient air pollution and mortality, gender and age are known to be effect modifiers. In this study, the relative risk for circulatory mortality at 10 μg/m^3 increments in each ambient air pollutant concentrations varied by gender and age with effect estimates for both males and females statistically significant ($P < 0.05$) for all three pollutants (Table 4). In regard to age, the ≥ 65 years category presented statistically significant effect estimates for all ambient air pollutants. However, only $PM_{2.5}$ effects at 1.293(1.062, 1.596) were statistically significant for the ≤64 years group, and no significant effects were observed for both SO_2 and O_3.

Table 3 Relative risk of daily circulatory mortality associated with 10 μg/m^3 increase in air pollutant concentration

Single model	RR(95% CI)	*P* value
$PM_{2.5}$	1.288(1.198, 1.388)	0.027
O_3	1.360(0.877, 2.331)	0.045
SO_2	1.324(1.059, 1.705)	0.012
After adjusting for collinearity by principal component analysis		
$PM_{2.5}$	1.290(1.215, 1.373)	0.036
O_3	1.292(1.142, 1.464)	0.018
SO_2	1.278(1.163, 1.408)	0.023

$P < 0.05$

Sub-groups lag analysis

Table 5 shows the estimated relative risk in circulatory mortality for each 10 μg/m^3 increment in ambient air pollutants using single-day and cumulative lags. Statistically significant associations were observed for $PM_{2.5}$ and SO_2 in lags 2 and 3, respectively ($P < 0.05$), while for O_3, statistical significance was observed in lags 2 and 04 ($P < 0.05$). After adjusting for collinearity, only $PM_{2.5}$ remained statistically significant associations at lags 3, 4, and 02 ($P < 0.05$).

Gender and age-stratified lag-response patterns of the effects of ambient air pollutants on circulatory mortality are presented in Fig. 2. Stratified lag effects in the single lag model had a narrow range which was assumed to be indicative of the association's precision in comparison with the

Table 4 Gender and age-specific relative risk of daily circulatory mortality associated with 10 μg/m^3 increase in air pollutant concentration

Category	$PM_{2.5}$	O_3	SO_2
Male	1.301(1.155, 1.472)*	1.358(0.849, 2.429)*	1.296(0.989, 1.777)*
Female	1.296(1.143, 1.479)*	1.439(0.759, 3.261)*	1.293(0.972, 1.815)*
≤64 years	1.293(1.062, 1.596)*	1.331(0.624, 3.772)	1.629(0.998, 2.961)
≥65 years	1.294(1.174, 1.430)*	1.389(0.892, 2.374)*	1.274(1.015, 1.653)*

* $P < 0.05$

cumulative lag model which presented a wider range. In males, the highest risk of circulatory mortality was observed for $PM_{2.5}$ in the single lag model at lag 2 ($P = 0.00570$) and lag 3 ($P = 0.00989$), and at lag 01 ($P = 0.02966$) and lag 02 ($P = 0.00296$) for the cumulative lag model. Ozone presented significant associations in the single lag model at lag 0 and lag 4 ($P = 0.02853$; $P = 0.01241$) for males, and no cumulative lag model was statistically significant. In females, the strongest risk for circulatory mortality was observed at lag 2 ($P = 0.00024$) and lag 3 ($P = 0.01527$) for $PM_{2.5}$ and O_3, respectively for the single lag model, while no lag was statistically significant for the cumulative lag model. Generally, women had a more statistically significant risk to circulatory mortality than men for $PM_{2.5}$ in the single lag model at lag 2 ($P = 0.00024$). For the age categories, in the ≤64 years group, significant associations were observed for SO_2 (lags 2, 3, 03, and 04) with P values ranging between 0.00821 and 0.036996. Ozone (lag 4, $P = 0.040472$) presented statistically significant associations in the ≤ 64 years group. In the ≥65 years group, statistically significant associations were observed for all pollutants with $PM_{2.5}$ having an increase at lag 2 ($P = 0.000620$) and lag 02 ($P = 0.035599$) and O_3 at lags 3 and 4 ($P = 0.006980$, $P = 0.025898$), while SO_2 was at lag 3 ($P = 0.000156$).

Discussions

Air pollution and temperature have been shown to have adverse effects on circulatory mortality. Similar to other past studies, the results of the present study showed clear seasonal differences in air pollutant concentration. Concentrations of $PM_{2.5}$ and SO_2 displayed comparatively stable trends and peaked in winter, while O_3 was higher during the warm season, findings similar to those previously reported in other studies across China (Teng et al. 2017).

Table 5 Relative risk for significant associations between air pollutants and daily circulatory mortality due to lag effects

	Lag	$PM_{2.5}$	O_3	SO_2
Single model	Lag 0	0.9999(0.999, 1.001)	1.0026(0.9968, 1.0084)	0.9965(0.9904, 1.0028)
	Lag 1	0.9995(0.9987, 1.000)	0.9991(0.9932, 1.0051)	0.9979(0.9928, 1.003)
	Lag 2	1.001(1.000, 1.002)*	0.998(0.9928, 1.0032)	1.005(1.002, 1.008)*
	Lag 3	0.9993(0.999, 1.000)	0.995(0.9895, 0.9996)*	0.9978(0.9954, 1.0001)
	Lag 4	1.000(0.999, 1.001)	0.9975(0.9931, 1.002)	0.9988(0.9963, 1.0012)
	Lag 01	1.002(0.999, 1.005)	0.9979(0.983, 1.013)	1.0049(0.9903, 1.0197)
	Lag 02	0.9977(0.994, 1.002)	0.9862(0.9658, 1.007)	1.0018(0.983, 1.0209)
	Lag 03	0.9988(0.995, 1.003)	1.0224(0.9944, 1.0512)	0.9775(0.9543, 1.0012)
	Lag 04	1.002(0.9987, 1.005)	1.0028(0.9825,1.0236	1.022(1.005, 1.039)*
After adjusting for collinearity	Lag 0	1.0002(0.9998, 1.0006)	1.0022(0.9995, 1.005)	0.9987(0.9964, 1.0009)
	Lag 1	0.9998(0.9991, 1.0004)	0.9999(0.9967, 1.0031)	0.9976(0.9951, 1.0001)
	Lag 2	1.0006(0.9999, 1.0012)	1.0004(0.9973, 1.0036)	1.0005(0.9981, 1.0029)
	Lag 3	0.999(0.998, 0.9998)*	1.0005(0.9971, 1.0039)	0.9991(0.9963, 1.0018)
	Lag 4	1.001(1.001, 1.002)*	0.9986(0.9954, 1.0017)	1.0003(0.9977, 1.0029)
	Lag 01	0.9983(0.9964, 1.0003)	0.9999(0.9975, 1.0022)	1.0019(0.9982, 1.0055)
	Lag 02	1.005(1.0006, 1.008)*	1.000(0.9953, 1.0047)	0.9994(0.9923, 1.0065)
	Lag 03	0.9972(0.9936, 1.0009)	0.9975(0.9919, 1.0031)	1.0026(0.9942, 1.011)
	Lag 04	0.9991(0.9974, 1.0009)	1.0019(0.9982, 1.0055)	0.9974(0.9922, 1.0027)

* $P < 0.05$

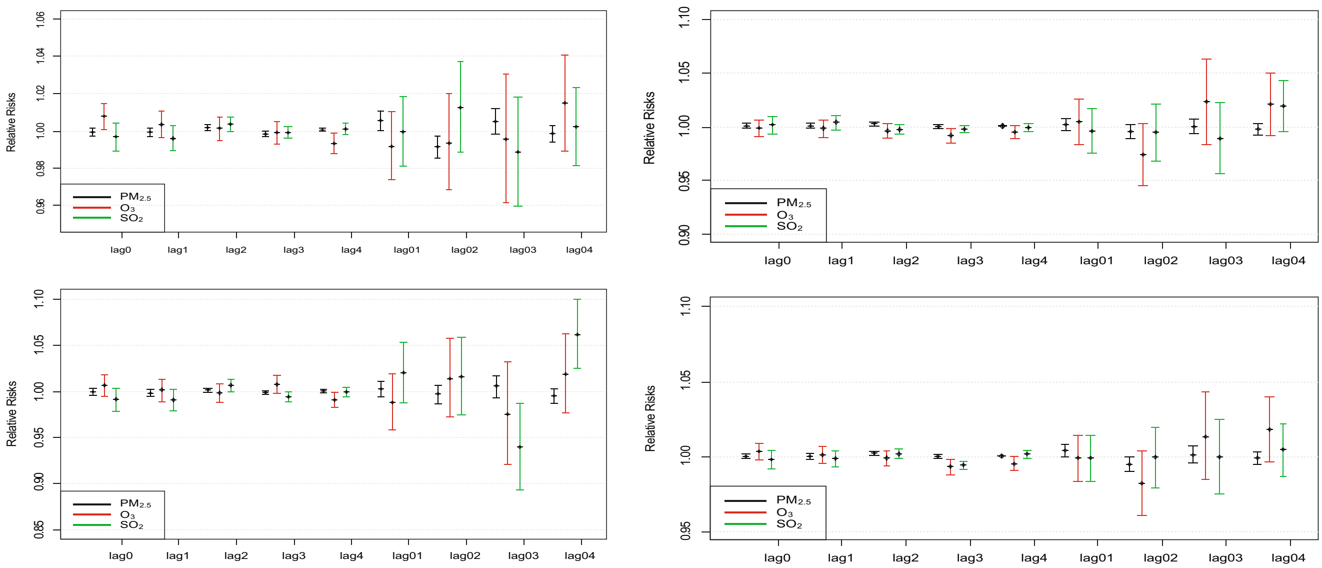

Fig. 2 Gender and age lag-response relationship associated with 10 μg/m^3 increase of ambient air pollutants

Moreover, ambient air pollutants in Xi'an during the period of the study were well within the ambient air quality standards (annual limit) in China, with the exception of $PM_{2.5}$ (75 μg/m^3) during the cold season (i.e., autumn and winter) (MEP 2012).

With Xi'an being the economic, industrial, and transportation hub of the northwestern region of China, the number of motor vehicles in the city was recently reported to have reached 2.5 million and further projected to have an annual growth rate of about 14.3%, subsequently impacting on the levels of $PM_{2.5}$ and SO_2 pollution in Xi'an (Cao et al. 2005; Huang et al. 2015). Additionally, Xi'an relies largely on coal-powered energy (for household and industrial use) and as a semi-humid region, it experiences a dry and dusty weather haze, often coupled with emissions from motor vehicles and burning of fossil fuels for heat in winter (Huang et al. 2015), causing the city to suffer from smog and haze annually. Therefore, it is safe to assume that the ambient air pollution problem in Xi'an is mainly caused by motor vehicle and industrial emissions, combustion of fossil fuels, smog and haze, and the dust from the desert as well as from construction activities in the city, which are known to contribute to elevated levels of O_3 (Cao et al. 2005; Li et al. 2016). Consistent with other studies, circulatory mortality in the present study was generally higher in winter and autumn seasons and lower during the summer and spring seasons (Peng et al. 2005).

Exposure to ambient air pollution is known to be associated with adverse health outcomes. Several studies have reported the effect of short-term exposure to ambient air pollutants on cardiovascular mortality (Burroughs Peña and Rollins 2017; Braga et al. 2001; Fung et al. 2003). The results of our study showed that $PM_{2.5}$, O_3, and SO_2 in the single pollutant model were strongly associated with circulatory mortality, with risk estimates of 1.288(1.198, 1.388), 1.360(0.877, 2.331), and 1.324(1.059, 1.705), respectively for every 10 μg/m^3 increments in each ambient air pollutant; our findings were consistent with those reported in various studies (Yang et al. 2013; Zhang et al. 2017a). A study in Jinan, China, reported an increase of 10 μg/m^3 in $PM_{2.5}$, and SO_2 was associated with an increased risk of cardiovascular mortality in the single pollutant model at 1.14(0.98, 1.30) and 1.69(1.56, 1.83), respectively, a finding consistent with that of the current study (Zhang et al. 2017a).

Although a lot of epidemiological and clinical studies have been conducted to determine the effect of individual air pollutants and their association with various adverse health effects, the likelihood of adverse health occurring due to exposure to a mixture of pollutants remains highly plausible as various pollutants tend to be inter-related. Subsequently, collinearity among pollutants in multi-pollutant models remains a problem. In the current study, the effect of pollutant interactions on circulatory mortality was evaluated to understand the effects of air pollution mixture better. Moreover, all three pollutant ($PM_{2.5}$, O_3, and SO_2) effect estimates remained statistically significant after adjusting for collinearity of different air pollutants in the multi-pollutant model at 1.290(1.215, 1.373), 1.292(1.142, 1.464), and 1.278(1.163, 1.408), respectively, a finding consistent with that found in a study conducted in Beijing, China, after the 2008 Olympics (Yang et al. 2013). With all the effect estimates remaining statistically significant after adjusting for collinearity, the results of the present study showed that the associations between air pollutants and circulatory mortality were relatively robust. Generally, our effect estimate levels for all ambient air pollutants were comparable with those reported in previous studies conducted in China and globally (Burroughs Peña and Rollins 2017; Zhang et al. 2006; Zhang et al. 2017a; Zhang et al. 2017b). For instance, one systematic review and meta-analysis of 110 peer-reviewed time-series studies conducted in China reported pooled effect estimates for each 10 μg/m^3 increment of $PM_{2.5}$ and mortality to range between 0.25 and 2.08% based on WHO region (Atkinson et al. 2014). A study conducted by Shang et al. (2013) reported effect estimates of 0.44(0.33, 0.54), 1.46(1.27, 1.64), and 0.45(0.29, 0.60) for each 10 μg/m^3 increment of $PM_{2.5}$, NO_2, and O_3, respectively. Interestingly, gaseous pollutants (SO_2 and O_3) in our study demonstrated slightly higher effects on circulatory mortality for every 10 μg/m^3 increment compared with $PM_{2.5}$, findings consistent to that reported in other studies in China (Shang et al. 2013; Zhang et al. 2017b). However, our reports showed slightly lower effect estimates compared with those reported in Hefei by Zhang et al. (2017b). Our study confirmed previous findings suggesting that associations exist between short-term exposure to ambient pollution and the increased risk of cardiovascular diseases mortality (Atkinson et al. 2014; Bell et al. 2004; Dominici et al. 2006; Fung et al. 2003; Samet et al. 2000; Zhang et al. 2017a). In the current study, several sub-group analyses were carried out.

Numerous epidemiological studies on the association of air pollution and health have consistently reported that air pollution affects population sub-groups (gender and age) differently, making certain individuals more vulnerable (Kan et al. 2008; WHO 2004). As a result of different socio-economic status, environmental factors, demographic, and hereditary characteristics, people can be exposed to the same air pollutants but may experience different effects on health. These effects may also manifest differently, making the susceptibility to ambient air pollution complex. In the current study, both males and females were vulnerable to ambient air pollutants, with age being a fundamental factor in the vulnerability of the groups. For the age sub-group, the ≥ 65 years group were more vulnerable to all ambient air pollutants than the group aged ≤ 64 years, as they were only vulnerable to $PM_{2.5}$. The susceptibility of the ≥ 65 years and women was previously reported by numerous authors to be as a result of underlying conditions, associated with cardiovascular and respiratory diseases (Dominici et al. 2006; Kan et al. 2008). The increased susceptibility of the ≥ 65 years and women to cardiovascular mortality in relation to short-term exposure to ambient air pollution can be linked to the fact that the more elderly and women are exposed to domestic sources of air pollution via combustion of solid bio-fuels, exposing them to more increased inhalation of smoke in comparison with men (Bell et al. 2013; Zhang et al. 2017b). Furthermore, the elderly are known to most likely suffer from circulatory system aging (commonly known as "cardiovascular aging") and chronic diseases with evidence indicating that exposure to ambient air pollutants may worsen underlying circulatory conditions possibly resulting in fatalities (Bateson and Schwartz 2004; Goldberg et al. 2013).

Given the fact that the effects of some environmental stressors on health have been noted to occur over time and not always instantaneously, it was worthwhile to investigate the effect of lag on ambient air pollutants as well as on stratified sub-groups for circulatory mortality. The results of the current study revealed that cumulative effect (lag 01 to 04) was slightly wider in range for every 10 μg/m^3 increase for all pollutants (except for $PM_{2.5}$) suggesting that time was of importance in indicating the delayed effects of circulatory mortality. The narrow lag effect estimates for all significant $PM_{2.5}$ associations in the cumulative model were indicative of the accuracy of the association. Moreover, the overall stratified lag-response on analysis on the short-term exposure to ambient air pollutants (per 10 μg/m^3 increment) in relation to circulatory mortality showed significant effects on both gender and age sub-groups.

Conclusion

In conclusion, this study demonstrated that the burden of ambient air pollution was as severe as that of the conventional risk factors associated with circulatory mortality in Xi'an. The findings of our study were in agreement with previous studies, which further provided evidence that ambient air pollution is a significant risk factor of circulatory mortality especially in the elderly. Therefore, there is a need to investigate further the associations considering the average age of the population, continued high levels of pollution, and increasing numbers of circulatory mortality cases. Additionally, more multi-pollutant analyses in relation to adverse health effects are needed in Xi'an and China at large.

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Author contributions Kingsley Katleho Mokoena and Yu Yan conceived the idea for the study. Feng Liu provided mortality data. Yameng Fan and Jie Rong translated the mortality data. Kingsley Katleho Mokoena and Crystal Jane Ethan were responsible for sourcing of the other data, running data analysis, and writing the manuscript. Yu Yan and Shale Karabo were responsible for cross-checking results and the manuscript.

Compliance with ethical standards

Ethics statement The study protocol for this research was accepted and approved by the Institutional Review Board at the School of Public Health, Health Science Centre, in Xi'an Jiaotong University. Written informed consent was not necessary or required, since aggregated data was used in the current study, and not individualized data. Patient information was anonymized before analysis.

Competing interests The authors declare that they have no competing interests.

Strengths and limitations The main strengths of our study are as follows: (1) assessing more pollutants in relation to circulatory mortality and (2) stratification of results by pollutant, gender, and age concerning circulatory mortality. In carrying out this time-series study, some limitations were encountered, and include the following: (1) As a proxy for personal exposure measurement, background ambient air pollutant levels were used in the current study. Consequently, this was expected to result in exposure measurement error which could possibly result in bias in terms of the risk estimates precision and strength.

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