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RESEARCH ARTICLE

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Short-term effects of ambient (outdoor) air pollution on cardiovascular death in Tehran, Iran – a time series study

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ABSTRACT

The aim of this study was to estimate the effect of ambient air pollutants on cardiovascular deaths in Tehran, Iran. In this time series study, air pollutant data were acquired from the Environmental Protection Agency. Meteorological data were acquired from the meteorological organization, and death data were acquired from the Tehran's cemetery registration. Generalized Additive Models (GAM) were used for estimating the Rate Ratio. NO_2, SO_2 and PM_{10} were associated with total cardiovascular deaths. PM_{10} and NO_2 showed stronger relations with deaths in the elder age group. The result of this study showed that NO_2, SO_2, PM_{10} and O_3 are probably responsible for part of the cardiovascular deaths that happen daily in Tehran.

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Introduction

Air pollution is composed of a heterogeneous mixture of compounds including carbon monoxide (CO), ozone (O3), nitrogen oxides (NOx), sulfur dioxide (SO2), particulate matter (PM) and liquids (Sun *et al.* 2010).

Air pollution is a main environmental hazard and a threat to human health. The rising health consequences of air pollution have attracted the attention of researchers in the last decades. In 2014, 91% of the global population lived in places where the levels of air pollutants failed to meet the World Health Organization's air quality standards. The World Health Organization (WHO) reported that in 2016 around 4.2 million people lost their lives because of inhaling outdoor polluted air. These facts confirm that air pollution is now the world's largest single environmental health risk (WHO, 2018).

Air pollution in developing countries is mainly related to their increased population, wrong ways of regulating vehicles, vast usage of fossil fuels, urban sprawl, immigration to big cities and inappropriate expansion of industries without appropriate site selection (Roushan *et al.* 2009, Rezaei *et al.* 2016).

Numerous epidemiological studies across the world, especially in developed countries have reported a relation between short-term changes in air pollution, and cardiovascular diseases and death especially in America, Europe and China (Wong *et al.* 2002, Stieb *et al.* 2003, Zhang *et al.* 2006, Lopez-Villarrubia *et al.* 2010, Sun *et al.* 2010, Yu *et al.* 2012, Yamamoto *et al.* 2014). A number of studies have also been conducted in Iran (Hosseinpoor *et al.* 2005, Shahi *et al.* 2014, Hashemi *et al.* 2014, Dadbakhsh *et al.* 2016, Hashemi and Khanjani 2016, Vahedian *et al.* 2017, Dastoorpoor *et al.* 2018, Dastoorpoor *et al.* 2019).

Although the Rate Ratio of mortality caused by air pollution is low, the proportion of deaths related to air pollution is high because of the high number of exposed and sensible populations (Qorbani and Yunesian 2010). Air pollution shows a nations environmental health and quality control problems. Although there are many studies done in the world about air

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pollution and its health effects, but there have been fewer studies from developing countries; and, therefore, studying the various aspects of air pollution in developing countries is essential (Santus *et al.* 2012).

Tehran is the capital and the biggest city of Iran, with a population of about 8.5 million people, from the 80 million people who live in Iran. The area of Tehran is 1500 km^2. This city is very densely populated and suffers from air pollution due to its specific geographical conditions (topography and meteorology), social and cultural problems (population distribution, traffic), urban development and abundant consumption of energy in transportation and industry. Controlling air pollution has been complicated in Tehran and investigation about the different aspects of air pollution and its health effects is still necessary (Hosseinpoor *et al.* 2005, Khalilzadeh *et al.* 2009).

Given the importance of air pollution in Tehran, this time series study was carried out to find about the short-term effects of air pollution on deaths due to cardiovascular disease in this city.

Methods

This was a time series and population-based study conducted in Tehran, Iran. Tehran is geographically located in a valley and surrounded by medium to high mountains on its north, northwest, east, and southeast.

Air pollution, meteorological and death data

Data on ambient air pollutants (CO, O_3, NO_2, SO_2, and PM_{10}) from 2005 to 2014 were collected from the Tehran Department of Environment and Tehran Air Quality Control Company. Tehran has 22 municipality districts and there are one or more air pollution monitoring stations in each district (36 in total). In all monitoring stations, the concentrations of air pollutants are registered hourly. In this study, the outlier observations were identified with spatio-temporal screening tools. In this method the mean and standard deviation of each observation in a specific hour, and 1 and 2 h before and after it, in each station and the neighboring stations were computed. Then observation which were more than ±3 SD away from the mean were recognized as outliers (Shamsipour *et al.* 2014, Dehghan *et al.* 2018).

Missing air pollution data was estimated using the Expectation-Maximization (EM) algorithm in SPSS20 software. This approach was proposed by Dempster *et al.* (1977). This method is an algorithm for nonlinear optimization and is appropriate for time series applications involving unknown components (Anava *et al.* 2015). EM is a repetitive and effective process that uses maximum likelihood estimation in estimating missing data. Each repetition of the algorithm consists of two steps: the mathematical expectation stage (E-Step) and the maximization step (M-Step). In the mathematical expectation step, missing data is estimated based on observed data and the current estimation of the model parameters. In the maximization step, the likelihood function is maximized with the assumption that the missing data is known. Here, the estimates of missing data from the E-step are placed instead of missing values. By repeating the algorithm, the missing value is corrected at each step, and convergence can be assured (Afshari Safavi *et al.* 2015).

After missing imputation was done, the daily averages of pollutants in selected stations were computed. Then the average of included stations was computed and one value was generated for the whole city in all days. The included stations were the Aghdasiyeh, Azadi, Poonak, Pardisan, Razi, Park-e-roz and Shahr-e-rey stations.

The data of cardiovascular deaths were collected from the Tehran's Cemetery (Behesht-e Zahra) Organization. Cardiovascular deaths included deaths from heart attacks, strokes, heart diseases related to blood pressure, kidney diseases related to blood pressure, pulmonary embolism, embolism and arterial thrombosis, aortic aneurysm, other vascular diseases, other heart diseases, other cardiovascular diseases, non-rheumatic disorders in the mitral and aortic valves, acute and sub-acute endocarditis, acute pericarditis, acute myocarditis, cardiomyopathy, cardiac failure, and congenital abnormality of the cardiovascular system. The daily count of cardiovascular deaths was entered in the GAM model as the outcome variable.

The daily average of meteorological data (temperature and relative humidity), were inquired from the Tehran Meteorological Organization as potential confounder variables; because some studies have reported that cardiovascular disease mortality may change with fluctuations in temperature (Khanjani and Bahrampour 2013), although other studies have denied a relation (Dadbakhsh *et al.* 2018).

Data analysis

The mean, standard deviation, median, 25^{th} and 75^{th} percentiles of air pollutants, meteorological variables and the frequency of cardiovascular deaths were computed.

A time-series regression analysis was used to assess the short-term association between air pollutant exposures and count of cardiovascular deaths. Generalized Additive Models (GAM) were used to estimate Rate Ratio (RR). GAM models have been widely used in studies about air pollution and health outcomes; because they are able to adjust for the effect of non-linear confounding variables such as seasonal changes, trends and meteorological variables (Dominici *et al.* 2002, Guisan *et al.* 2002, Dehghan *et al.* 2018).

The degree of freedom for the smoothers was determined by Generalized Cross Validation (GCV) using the "mgcv" package in R i386 3.2.2 software.

Multivariate GAM models were also run for the same outcome and in subgroups. Relative humidity, temperature, season and weekdays were entered into the model as potential confounding variables. Then the strongest lag for pollutants was reported.

The formula of the GAM model is as follows (Wang and Pham 2011).

$$Y_t \sim \text{Poisson}\ (\mu_t)$$
$$Log\ \mu_t = \alpha + \beta_i(X_i) + \sum S_j(X_j) + yS\ (season) + \eta D(dow)$$

In this formula Y_t is the frequency of the incidence of cardiovascular deaths. β_i is the coefficient for air pollutants (X_i) and indicates the logarithm of Risk Ratio (RR) for 10 unit increase in all pollutants (10 µg/m^3 for PM_{10} and 10 ppb for O_3, SO_2 and NO_2), except CO which it is for 1 ppm increase. Furthermore, $S_j(X_j)$ is a smoothing function for meteorological variables (relative humidity and temperature) and trend. S(season) are indicator variables for Spring, Summer, Autumn and Winter. D(dow) are indicator variables for weekdays. Season and weekdays were added to the model as categorical variables.

In this study, due to the correlation between pollutants, one pollutant models were performed. But, we also used two pollutant models to assess the stability of the results from the one pollutant models.

Result

During the 10-year study period, 215 373 cardiovascular deaths occurred in Tehran which included 122 911 (57.07%) male and 92 462 (42.93%) female deaths. The frequencies of cardiovascular deaths are shown in Table 1 by year and gender. Figure 1 shows the trend of cardiovascular deaths.

Table 1. Count of deaths due to cardiovascular disease in Tehran during 2005–2014 by sex and year.

Year	Male	Female	Male/Female	Total	ASR*
2005	12,724	9449	1.34	22,173	277.99
2006	11,757	8767	1.34	20,524	258.96
2007	11,975	8894	1.34	20,869	259.03
2008	12,916	9567	1.35	22,483	269.63
2009	12,190	9100	1.34	21,290	256.58
2010	12,393	9332	1.32	21,725	257.31
2011	12,281	9279	1.32	21,560	253.72
2012	11,358	8629	1.31	19,987	238.01
2013	12,426	9526	1.30	21,952	252.89
2014	12,891	9919	1.29	22,810	258.1
Total	122,911	92,462	1.32	215,373	–

*Age- standardized cardiovascular rate per 100,000 population.

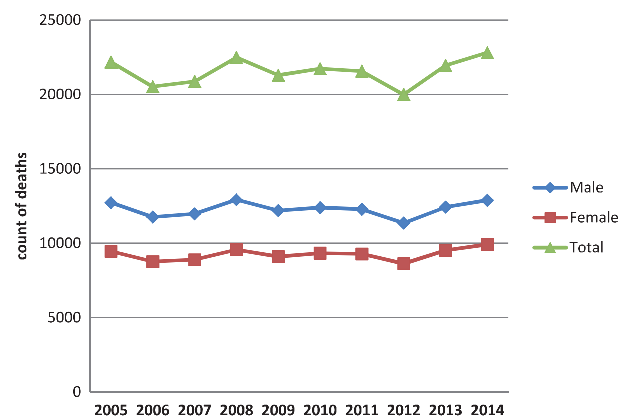

Figure 1. The frequency of cardiovascular deaths between 2005 and 2014.

Figure 2 shows the scatter plot of air pollutants and death during 2005 to 2014 in Tehran.

The descriptive statistics of air pollutants, humidity, temperature and death during 2005–2014 in Tehran are showed in Table 2. These results show the annual average of PM_{10} was over the WHO 2014 annual thresholds guidelines (20 µg/m^3). The average of SO_2 concentrations was higher than the standard values as well.

Table 3 shows the Mean ± SD of pollutants and number of cardiovascular deaths by season in Tehran, during 2005–2014. The highest concentration of O_3 was in summer, CO and PM_{10} was in fall, and NO_2 and SO_2 was in winter and spring respectively. Also most cardiovascular deaths occurred in winter (29.03%) and the lowest number of deaths was in summer (21.34%).

Table 4 shows the correlation between different pollutants. All pollutants had a significant correlation with each other; except O_3 that showed a direct correlation only with PM_{10}, and an inverse correlation with CO. The highest correlation was found between nitrogen dioxide and sulfur dioxide ($r = 0.696$, $p = <.001$).

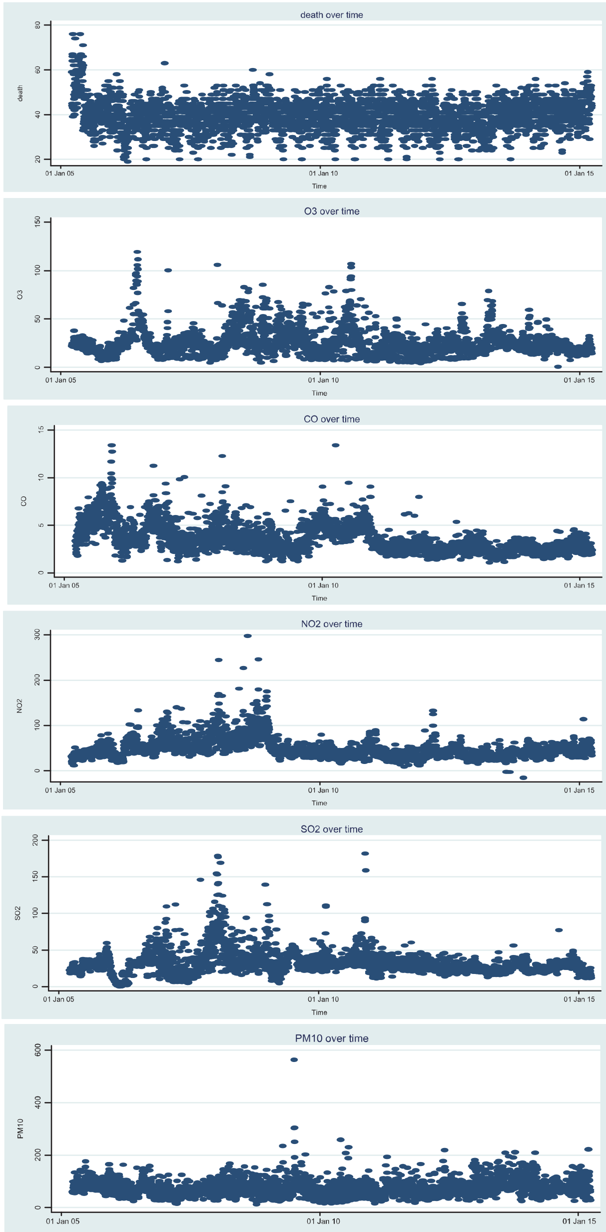

Figure 2. Scatter plot of total cardiovascular deaths and air pollutants during the study period (2005–2014).

Table 2. Mean, median, SD, min and max of daily air pollutants, meteorological and death variables in Tehran, 2005–2014.

	Mean	SD	Median	Minimum	Maximum
CO (ppm)	3.30	0.97	3.14	1	11
O3 (ppb)	24.66	9.12	23.30	6.88	77
SO2 (ppb)	33.46	10.47	32.05	9	119
NO2 (ppb)	53.48	16.52	49.84	12	154
PM10 ($\mu g/m^3$)	69.75	20.61	68.04	12	331
Relative humidity (%)	43.73	18.37	39.50	10	89
Temperature (°C)	16.49	9.52	16.80	−9	34
Male deaths (N)	33.66	7.09	34.00	12	56
Female deaths (N)	25.32	5.54	26.00	10	41
Overal deaths (N)	58.97	9.36	59.00	30	94
Under 18 years (N)	0.93	1.12	1	0	6
18 to 60 years (N)	18.89	3.94	19	9	30
Over 60 years (N)	39.16	6.25	38	19	63

Table 5 shows the GAM results of air pollutants and total cardiovascular death. After adjusting for confounders including temperature, relative humidity, trend, season and DOW; total deaths were significantly associated with NO_2 in lag 0 to lag 4 in the one pollutant model and lag 0 to 3 in the two pollutant model. But the strongest relation was seen in lag 3 in the one pollutant and lag 1 in the two pollutant model. SO_2 in the one pollutant model showed significant associations with total death in lag 0 and 1. But in the two pollutant model no significant relation was seen. PM_{10} showed a significant association with total death in lag 0 to 3 in both models (one and two pollutant). But the strongest relation was seen in lag 0.

Table 6 shows the RR of air pollutants and cardiovascular deaths in men. In men, NO_2, SO_2 and PM_{10} had the strongest direct relation with cardiovascular death in lag 3, 0 and 0 respectively, in the one pollutant model. But in the two pollutant model, the strongest relation for NO_2 and PM_{10} was seen in lag 0; and SO_2 did not show a significant relation with death.

Table 7 shows the RR of air pollutants and cardiovascular deaths in women. In women, O_3 showed a significant direct relation with deaths, in lag 0–3 in the one pollutant and lag 0–4 in the two pollutant models. NO_2 in lag 6 (one pollutant model) and lag 5 (two pollutant model) had a significant relation with death. PM_{10} had a relation with cardiovascular deaths in lag 0–2 in the one and two pollutant models.

No pollutant was related to cardiovascular deaths in people under 18 years old (Table 8). In people 18–60 years, NO_2, SO_2 and PM_{10} showed a strong relation with death in lag 1, 0 and 0 (day) respectively, in the one pollutant model. But in the two pollutant model, NO_2 and PM_{10} showed the strongest relation in lag 3 (Table 9).

NO_2 and PM_{10} in people over 60 years had the strongest relation with cardiovascular deaths in 1, and 0 day lags respectively in the one and two pollutant models. SO_2 showed a direct relation only in the one pollutant model (Table 10).

Discussion

This study showed a probable association between high levels of NO_2, SO_2, and PM_{10} with cardiovascular mortality.

In this study, with a 10 mg/m^3 increase in PM_{10} on the same day, total cardiovascular deaths increased 0.57% (95% CI: 0.34–0.79%) in the one pollutant model and 0.59% (95% CI: 0.28–0.84%) in the two pollutant model. PM_{10} was also related with cardiovascular death

Table 3. Mean ± SD of pollutant and number of cardiovascular death by season in Tehran, 2005–2014.

	CO	O_3	NO_2	SO_2	PM_{10}	Cont(%) of death
Spring	2.95 ± 0.80	28.30 ± 7.34	48.21 ± 14.16	36.58 ± 14.04	66.40 ± 21.62	52056 (24.17)
Summer	3.28 ± 0.89	29.03 ± 9.58	51.22 ± 12.74	36.39 ± 9.05	68.74 ± 18.12	45961 (21.34)
Fall	3.59 ± 1.13	19.88 ± 6.46	56.99 ± 16.60	32.57 ± 7.74	76.88 ± 20.42	54834 (25.46)
winter	3.40 ± 0.94	21.13 ± 8.81	57.78 ± 19.94	28.51 ± 7.75	66.82 ± 20.39	62522 (29.03)

Table 4. Pearson correlation coefficients between air pollutants.

	O3	CO	NO_2	SO_2	PM_{10}
O_3	1				
CO	−0.162**	1			
NO_2	0.019	0.414**	1		
SO_2	0.067	0.473**	0.696**	1	
PM_{10}	0.249**	0.205**	0.056*	0.263**	1

*$p < .01$.
**$p < .001$.

Table 5. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on total cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	2.57	0.998 (0.991–1.005)	.577	2.48	0.996 (0.989–1.003)	.289
	1	1.88	1.002 (0.999–1.009)	.564	2.21	1.002 (0.994–1.009)	.679
	2	2.60	0.998 (0.992–1.005)	.658	4.82	0.998 (0.991–1.005)	.582
	3	5.64	0.995 (0.988–1.002)	.191	6	0.994 (0.987–1.001)	.112
	4	6.4	0.996 (0.989–1.003)	.174	7.02	0.992 (0.984–0.998)	.02
	5	6.67	0.994 (0.987–1.001)	.121	7.27	0.991 (0.984–0.998)	.015
	6	1	0.992 (0.985–0.999)	.040	2.84	0.994 (0.987–1.002)	.134
	7	2.53	0.995 (0.988–1.002)	.206	1	0.993 (0.986–1.001)	.094
O_3 (ppb)	0	7.99	0.996 (0.990–1.002)	.212	8.06	1.004 (0.992–0.998)	.591
	1	3.39	0.999 (0.993–1.006)	.965	3.18	1.008 (0.996–1.002)	.450
	2	3.47	0.999 (0.993–1.005)	.838	2.93	1.007 (0.995–1.002)	.629
	3	3.74	0.998 (0.992–1.004)	.549	3.15	1.006 (0.994–1.000)	.892
	4	4.05	0.998 (0.992–1.005)	.326	3.69	0.994 (0.988–1.001)	.101
	5	4.7	0.991 (0.985–0.997)	.003	4.44	0.995 (0.989–1.002)	.199
	6	5.74	0.992 (0.985–0.999)	.008	4.8	0.996 (0.989–1.002)	.218
	7	4.85	0.993 (0.986–0.998)	.021	5.7	0.994 (0.988–1.001)	.091
NO_2 (ppb)	0	2.83	1.007 (1.003–1.010)	<.001	2.37	1.005 (1.002–1.008)	.003
	1	1.59	1.007 (1.004–1.011)	<.001	1	1.005 (1.002–1.009)	.001
	2	1	1.006 (1.003–1.009)	<.001	1	1.005 (1.001–1.008)	.004
	3	1.28	1.008 (1.003–1.009)	<.001	1.59	1.004 (1.001–1.008)	.006
	4	4.29	1.007 (1.004–1.011)	<.001	4.66	1.009 (0.998–1.013)	.165
	5	2.32	1.008 (0.999–1.018)	.128	3.8	1.003 (0.999–1.006)	.286
	6	1.76	1.004 (0.995–1.013)	.255	1	1.002 (0.998–1.005)	.275
	7	1.33	1.007 (1.003–1.010)	.306	1.02	1.001 (0.998–1.005)	.246
SO_2 (ppb)	0	8.50	1.009 (1.004–1.014)	<.001	8.18	1.001 (0.995–1.007)	.681
	1	8.41	1.007 (1.002–1.012)	.009	1	0.997 (0.992–1.004)	.483
	2	8.32	1.005 (0.999–1.010)	.069	1	0.998 (0.992–1.004)	.596
	3	1	1.004 (0.999–1.009)	.095	1	1.001 (0.994–1.006)	.818
	4	4.05	1.002 (0.997–1.007)	.283	1	1.003 (0.997–1.009)	.253
	5	1	1.005 (0.999–1.010)	.059	1	1.002 (0.995–1.007)	.678
	6	1	1.004 (0.998–1.009)	.153	1	0.999 (0.993–1.005)	.913
	7	1	1.004 (0.999–1.009)	.164	1	1.002 (0.996–1.008)	.356
PM_{10} ($\mu g/m^3$)	0	1.88	1.005 (1.003–1.008)	<.001	2.53	1.006 (1.002–1.008)	<.001
	1	1.69	1.006 (1.003–1.008)	<.001	2.54	1.005 (1.003–1.007)	<.001
	2	7.44	1.004 (1.001–1.006)	.001	7.38	1.003 (1.001–1.005)	.002
	3	6.83	1.002 (1.000–1.005)	.043	6.39	1.003 (0.999–1.005)	.043
	4	6.20	1.002 (0.997–1.006)	.389	6.38	1.000 (0.997–1.003)	.838
	5	6.95	1.001 (0.998–1.003)	.467	2.27	1.001 (0.999–1.004)	.25
	6	6.83	1.002 (0.999–1.004)	.078	6.66	1.002 (0.999–1.004)	.091
	7	6.84	1.002 (0.999–1.004)	.051	6.44	1.017 (0.994–1.041)	.134

in men, women, and in the 18–60 and over 60 years old age groups. Similar to these results, in Wuhan, China, the maximum effect of PM_{10} on cardiovascular deaths occurred on the same day, and was a 0.51% increase for every 10 $\mu g/m^3$ increase in PM_{10} (95% CI 0.28–0.75%) (Qian *et al.* 2007). In a meta-analysis, the

Table 6. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on male cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	2.34	1.005 (0.995–1.014)	.319	2.56	0.999 (0.989–1.008)	.846
	1	2.30	1.009 (0.999–1.018)	.06	2.64	1.002 (0.993–1.012)	.628
	2	3.06	1.006 (0.996–1.015)	.239	3.8	0.996 (0.986–1.005)	.413
	3	2.69	0.999 (0.990–1.009)	.948	4.43	0.991 (0.981–1.000)	.059
	4	4.99	0.999 (0.992–1.007)	.473	5.64	0.984 (0.975–0.993)	.001
	5	3.65	0.996 (0.987–1.005)	.433	5.52	0.988 (0.979–0.997)	.014
	6	2.92	0.989 (0.979–0.998)	.023	2.96	0.986 (0.977–0.995)	.004
	7	2.44	0.992 (0.983–1.002)	.113	4.09	1.005 (0.995–1.014)	.294
O_3 (ppb)	0	7.81	0.982 (0.974–0.991)	<.001	7.88	0.986 (0.978–0.994)	.001
	1	6.80	0.987 (0.979–0.996)	.002	2.46	0.991 (0.983–1.000)	.051
	2	2.95	0.988 (0.980–0.996)	.003	2.90	0.991 (0.983–0.999)	.049
	3	3.35	0.991 (0.981–1.000)	.36	3.17	0.991 (0.983–0.999)	.031
	4	4.32	0.991 (0.981–1.000)	.619	4.09	0.984 (0.976–0.992)	.001
	5	5.06	0.991 (0.981–1.001)	.226	4.72	0.986 (0.978–0.994)	.001
	6	5.84	0.954 (0.944–0.963)	<.001	6.15	0.987 (0.979–0.996)	.003
	7	6.25	0.983 (0.975–0.991)	<.001	5.73	1.002 (0.996–1.007)	.526
NO_2 (ppb)	0	2.85	1.009 (1.005–1.014)	<.001	2.64	1.010 (1.005–1.015)	<.001
	1	2.56	1.011 (1.006–1.015)	<.001	2.97	1.009 (1.005–1.014)	<.001
	2	2.57	1.010 (1.005–1.014)	<.001	2.8	1.011 (1.006–1.016)	<.001
	3	2.41	1.011 (1.006–1.015)	<.001	7.43	1.012 (1.007–1.017)	<.001
	4	2.25	1.008 (1.003–1.014)	<.001	7.41	1.004 (0.999–1.006)	.126
	5	1.81	1.010 (1.005–1.015)	<.001	1.76	1.003 (0.998–1.008)	.276
	6	1.35	1.001 (0.996–1.005)	.542	1	1.002 (0.999–1.005)	.143
	7	1.05	1.004 (0.995–1.012)	.289	1	1.003 (0.998–1.007)	.052
SO_2 (ppb)	0	8.22	1.014 (1.007–1.021)	<.001	7.71	0.998 (0.990–1.006)	.640
	1	8.17	1.009 (1.003–1.016)	.006	7.81	0.993 (0.986–1.002)	.119
	2	8.06	1.008 (1.001–1.015)	.018	1.91	0.994 (0.986–1.002)	.144
	3	8.29	1.007 (1.001–1.014)	.032	1.79	0.995 (0.988–1.004)	.305
	4	1	1.004 (0.995–1.013)	.114	1	0.995 (0.988–1.003)	.285
	5	1	1.006 (0.999–1.013)	.09	1	0.993 (0.985–1.001)	.083
	6	1	1.004 (0.996–1.011)	.275	1	0.995 (0.987–1.003)	.229
	7	1	1.006 (0.998–1.013)	.057	1	0.995 (0.987–1.003)	.212
PM_{10} ($\mu g/m^3$)	0	7.12	1.005 (1.002–1.008)	<.001	6.68	1.006 (0.708–1.428)	.001
	1	1.95	1.005 (1.002–1.008)	<.001	2.54	1.005 (1.002–1.007)	.003
	2	6.16	1.003 (1.000–1.006)	.025	5.51	1.003 (0.999–1.006)	.072
	3	6.42	1.002 (0.999–1.005)	.142	2.35	1.002 (0.999–1.005)	.145
	4	6.68	1.002 (0.998–1.005)	.146	1	1.001 (0.997–1.004)	.562
	5	7.35	1.000 (0.997–1.004)	.587	7.22	1.003 (0.999–1.006)	.059
	6	6.68	1.002 (0.999–1.005)	.146	6.17	1.002 (0.999–1.006)	.071
	7	6.68	1.002 (0.999–1.005)	.111	6.15	1.002 (0.999–1.005)	.132

pooled results of studies analyzed by the GAM method showed that PM_{10} was associated with increased mortality from cardiovascular diseases, and for each 1 $\mu g/m^3$ increase in the concentration of PM_{10}, cardiovascular death increased by 2.2% (CI 95%: 1.6 to 2.8%), but the pooled results of another study that did not use the GAM model, showed the increase in cardiovascular death was 1.3% (CI 95%: 0.8–1.9%) (Stieb *et al.* 2003). In a study done by Dastoorpoor et al. in Ahvaz, Iran; 10 $\mu g/m^3$ increase in PM_{10}, increased cardiovascular deaths by 1.012% (95% CI:1.001–1.023%) (Dastoorpoor *et al.* 2018). In a study done by Middleton et al. in Nicosia, Cyprus, every 10 mg/m^3 increase in PM_{10} concentration increased hospital admissions because of cardiovascular diseases by 1.2% (95%CI: −0.0%, 2.4%) (Middleton *et al.* 2008). In Vahedian et al.'s study conducted in Arak, Iran; for every 10 $\mu g/m^3$ increase in PM_{10}, hospital admissions for cardiovascular diseases increased 0.7% (95% CI: 0.02–1.2%) (Vahedian *et al.* 2017).

However, in some studies, the results were inconsistent with our results, for example in studies from Mashhad, Iran (Ghorbani *et al.* 2017), Shiraz, Iran (Dadbakhsh *et al.* 2016), and Kerman, Iran (Hashemi *et al.* 2014), PM_{10} did not have a significant direct relation with cardiovascular mortality; although, in these three studies the concentration of PM_{10} was more than the PM_{10} concentration in Tehran. One reason for these different results may be that negative binomial regression models were used in these previous studies, which are different and less advanced than the GAM models. Also the time unit in the Kerman (Hashemi *et al.* 2014) and Shiraz (Dadbakhsh *et al.* 2016) study was month, and in the Mashhad study (Ghorbani *et al.* 2017) no confounder variable was used in the model.

Table 7. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on female cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	1.04	0.989 (0.978–1.000)	.051	1	0.992 (0.981–1.003)	.177
	1	1	0.992 (0.981–1.003)	.16	1	0.997 (0.986–1.008)	.58
	2	2.84	0.989 (0.979–1.001)	.068	2.07	0.992 (0.982–1.003)	.174
	3	3.34	0.991 (0.981–1.002)	.111	1.68	0.992 (0.981–1.003)	.141
	4	4.27	0.994 (0.983–1.005)	.231	1	0.989 (0.982–1.004)	.179
	5	6.16	0.993 (0.983–1.004)	.236	6.38	0.998 (0.987–1.009)	.753
	6	1	0.998 (0.987–1.009)	.782	1	1.001 (0.990–1.012)	.844
	7	1	1.001 (0.989–1.011)	.923	1	1.001 (0.990–1.012)	.826
O_3 (ppb)	0	2.37	1.015 (1.005–1.024)	.002	2.11	1.012 (1.003–1.022)	.012
	1	2.69	1.016 (1.007–1.026)	<.001	2.53	1.016 (1.007–1.026)	.001
	2	4.31	1.016 (1.006–1.025)	<.001	1.57	1.015 (1.005–1.024)	.002
	3	1.59	1.013 (1.004–1.023)	.005	1	1.013 (1.004–1.023)	.005
	4	1.25	1.003 (0.994–1.013)	.078	1.2	1.012 (1.005–1.019)	.014
	5	1.93	1.006 (0.996–1.015)	.203	2.21	1.006 (0.996–1.015)	.203
	6	3.35	1.005 (0.996–1.015)	.277	3.62	1.007 (0.997–1.016)	.154
	7	2.56	1.006 (0.998–1.016)	.193	2.11	1.006 (0.997–1.016)	.188
NO_2 (ppb)	0	1	1.002 (0.997–1.008)	.38	1	0.999 (0.994–1.005)	.858
	1	1.01	1.004 (0.998–1.009)	.142	3.68	1.000 (0.995–1.006)	.927
	2	2.73	1.003 (0.997–1.008)	.269	2.75	0.998 (0.993–1.004)	.526
	3	3.55	1.004 (0.999–1.009)	.111	3.79	0.999 (0.994–1.005)	.981
	4	1	1.003 (0.997–1.008)	.238	4.15	1.003 (0.997–1.008)	.33
	5	3.95	1.005 (0.999–1.010)	.065	4.27	1.006 (1.000–1.011)	.034
	6	1.10	1.006 (1.001–1.011)	.023	1	0.999 (0.994–1.005)	.916
	7	1	1.003 (0.998–1.008)	.207	1	1.004 (0.998–1.009)	.182
SO_2 (ppb)	0	7.93	1.003 (0.995–1.011)	.444	7.77	1.005 (0.996–1.015)	.241
	1	7.82	1.004 (0.996–1.012)	.297	1	1.003 (0.993–1.012)	.556
	2	1	1.002 (0.993–1.009)	.701	1	1.002 (0.993–1.012)	.587
	3	5.98	1.002 (0.993–1.010)	.632	1	1.005 (0.996–1.014)	.256
	4	1	1.001 (0.992–1.009)	.783	1	1.004 (0.995–1.013)	.264
	5	6.64	1.005 (0.997–1.013)	.197	6.12	1.009 (0.999–1.018)	.056
	6	7.53	1.005 (0.997–1.014)	.182	7.84	1.003 (0.994–1.012)	.401
	7	8.09	1.007 (0.999–1.015)	.081	7.77	1.008 (0.998–1.017)	.087
PM_{10} ($\mu g/m^3$)	0	1.05	1.008 (1.001–1.018)	<.001	1	1.006 (1.003–1.010)	<.001
	1	1	1.007 (1.003–1.010)	<.001	1	1.006 (1.003–1.007)	<.001
	2	6.46	1.005 (1.001–1.008)	.008	6.6	1.004 (1.001–1.008)	.011
	3	3.90	1.003 (0.999–1.006)	.094	4.39	1.003 (0.999–1.006)	.126
	4	3.37	1.003 (0.999–1.006)	.083	2.48	1.001 (0.997–1.004)	.66
	5	5.18	1.001 (0.997–1.004)	.576	5.35	1.001 (0.997–1.004)	.444
	6	3.34	1.002 (0.998–1.005)	.269	4.35	1.002 (0.998–1.005)	.302
	7	3.34	1.002 (0.999–1.006)	.173	1	1.025 (0.986–1.055)	.242

Ambient particulate matter may cause heart disease and cardiovascular death through increase in blood clotting, impaired heart function, increased blood viscosity and changes in heart rate (Qian *et al.* 2007).

The World Health Organization guidelines state that reduction of particulate matter (PM_{10}) from 70 to 20 $\mu g/m^3$ can decrease air pollution-related deaths by around 15%. In this study, the annual average of PM_{10} was higher than the WHO recommended 2014 guideline.

Another pollutant that showed a significant relation with cardiovascular deaths in this study was Nitrogen dioxide. NO_2 was associated with all cardiovascular deaths, and with each 10 ppb increase in NO_2, total cardiovascular deaths increased (0.88%, 95% CI: 0.3–0.99%) in lag 3 in the one pollutant; and (0.57%, 95% CI: 0.23–0.92%) in lag 1, in two pollutant models. In this study, NO_2 showed relations with cardiovascular death in men, women and elder age groups, as well. Ghorbani et al. study's in Mashhad, Iran, also showed that by 1 ppb increase in NO_2, all cardiovascular deaths increased by 1% (95% CI:0.6 to 1.4) (Ghorbani *et al.* 2017). In one study in 8 Chinese cities, each 10 $\mu g/m^3$ increase in NO_2, related to 1.3% (95%CI: 0.45–2.14) increase in coronary heart disease mortality after 2 days lag (Li *et al.* 2015). In a study from Shiraz NO (RR = 1.00229, 95% CI: 1.00031–1.00426) and NO_x (RR = 1.00187, 95% CI: 1.00016–1.003) were related to cardiovascular disease mortality, but NO_2 had no relation with cardiovascular deaths (RR = 1.00429, 95% CI: 0.99637–1.01228) (Dadbakhsh *et al.* 2016).

NO_2 is a gas with a red-orange (almost brown) color. It has a boiling point of 21.2 °C. The toxicity of NO_2 is several times higher than NO in humans. NO_2

Table 8. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on under 18 years old cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	1	1.013 (0.957–1.072)	.654	1.31	0.946 (0.827–1.083)	.424
	1	1.35	1.027 (0.971–1.086)	.357	1.49	0.991 (0.866–1.133)	.891
	2	1	1.009 (0.953–1.069)	.744	1	0.962 (0.838–1.104)	.583
	3	1	1.027 (0.971–1.088)	.341	1.49	0.926 (0.803–1.067)	.291
	4	1	1.021 (0.969–1.076)	.404	1.12	0.959 (0.837–1.099)	.551
	5	1	1.039 (0.982–1.100)	.175	2.21	0.936 (0.817–1.072)	.340
	6	1	1.049 (0.992–1.109)	.059	1	0.951 (0.832–1.087)	.465
	7	1	1.014 (0.958–1.074)	.623	1	1.072 (0.934–1.231)	.322
O_3 (ppb)	0	5.75	0.985 (0.937–1.036)	.564	5.96	1.072 (0.959–1.197)	.221
	1	1.33	0.995 (0.949–1.044)	.854	1	1.081 (0.976–1.198)	.134
	2	1	0.971 (0.923–1.022)	.254	1	1.021 (0.917–1.136)	.702
	3	1.36	0.967 (0.921–1.015)	.179	1	0.966 (0.870–1.073)	.618
	4	1	0.969 (0.923–1.018)	.215	1	0.976 (0.879–1.084)	.492
	5	7.49	0.969 (0.921–1.019)	.229	7.34	0.924 (0.828–1.030)	.154
	6	4.65	0.981 (0.931–1.033)	.464	1	1.019 (0.915–1.134)	.735
	7	1	0.981 (0.932–1.031)	.445	4.5	1.030 (0.927–1.144)	.576
NO_2 (ppb)	0	1	1.011 (0.983–1.039)	.428	1	1.023 (0.955–1.096)	.505
	1	1.01	1.026 (0.998–1.054)	.068	1	1.015 (0.951–1.083)	.429
	2	1	1.011 (0.983–1.039)	.44	1	0.997 (0.931–1.068)	.942
	3	2.57	1.014 (0.986–1.043)	.314	1	1.022 (0.954–1.093)	.537
	4	2.02	1.004 (0.977–1.032)	.321	1.6	1.021 (0.958–1.089)	.295
	5	2.07	1.007 (0.979–1.035)	.625	1.13	1.128 (0.996–1.278)	.342
	6	1	1.015 (0.987–1.044)	.284	1.08	0.997 (0.927–1.065)	.857
	7	1.46	1.007 (0.979–1.035)	.628	1	1.065 (0.996–1.139)	.063
SO_2 (ppb)	0	1.67	1.029 (0.987–1.074)	.172	1.82	0.947 (0.826–1.085)	.434
	1	1.20	1.041 (0.998–1.085)	.061	1.83	1.126 (0.989–1.282)	.071
	2	1.02	1.055 (0.998–1.114)	.163	1.1	1.058 (0.929–1.204)	.086
	3	1.01	1.049 (0.982–1.123)	.219	1	1.023 (0.896–1.168)	.736
	4	2.14	1.061 (0.978–1.149)	.228	7.55	1.012 (0.887–1.156)	.849
	5	2.23	1.027 (0.946–1.114)	.312	1	1.005 (0.882–1.145)	.943
	6	1.05	1.076 (0.980–1.181)	.621	1	1.035 (0.908–1.179)	.871
	7	1	1.038 (0.955–1.128)	.369	1.06	0.997 (0.874–1.137)	.964
PM_{10} ($\mu g/m^3$)	0	1	0.994 (0.975–1.012)	.508	1	0.994 (0.956–1.034)	.782
	1	1	0.999 (0.981–1.017)	.916	1	0.985 (0.946–1.025)	.461
	2	1	1.000 (0.982–1.019)	.965	2.06	1.013 (0.974–1.052)	.520
	3	1.01	0.994 (0.976–1.013)	.543	1	0.996 (0.958–1.035)	.829
	4	1	0.995 (0.973–1.017)	.691	1	0.995 (0.961–1.031)	.618
	5	1	1.002 (0.985–1.021)	.785	1	1.014 (0.976–1.053)	.467
	6	1	1.003 (0.985–1.021)	.744	1	1.012 (0.975–1.051)	.511
	7	1	1.011 (0.993–1.029)	.236	1	0.995 (0.959–1.032)	.813

at 15 ppm concentration can damage human kidney, liver and heart tissues after just 2 h contact (Bahrami Asl *et al.* 2014). The main mechanism of toxicity of NO_2 is intervening with the peroxidation of lipids in cell membranes. Its free radicals have various adverse effects on structural and functional molecules (Kelly *et al.* 1996). According to the World Health Organization's guideline the mean annual threshold for NO_2 is 40 $\mu g/m^3$.

In this study, sulfur dioxide showed a significant relation with cardiovascular deaths in the one pollutant model, and for 10 ppb increase in SO_2, total death increased by 0.89% (95%CI: 0.36–1.62%). According to a study done by Hong et al. in Korea, sulfur dioxide showed a relation with ischemic stroke as well; and the Rate Ratio was 1.04 (95% CI, 1.01 to 1.08) (Hong *et al.* 2002). In a study from Shiraz, a relation was observed between SO_2 and cardiovascular mortality in women, and the IRR was 1.00089 (95%CI: 1.00008–1.00171) for each 1 ppb increase in SO_2 (Dadbakhsh *et al.* 2016). In a study done in Brazil, the 7-day moving average of SO_2 was significantly related with mortality due to circulatory diseases and the RR was 1.04 (95%CI = 1.01–1.06), after adjusting for ozone (Amancio and Nascimento, 2012). Zeng et al showed that SO_2 per 10 $\mu g/m^3$ increase and after one day lag, increased cardiovascular deaths by 0.48% (95% CI: 0.11–0.85%) (Zeng *et al.* 2015).

Researchers think sulfur dioxide exacerbates cardiovascular complications and causes death. But many questions about the effects of sulfur dioxide on human health remain unanswered. Sulfur oxides

Table 9. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on 18 to 60 years old cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (Adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	7.3	0.997 (0.985–1.010)	.666	7.45	0.996 (0.983–1.008)	.49
	1	1.7	1.002 (0.989–1.014)	.783	2.12	1.001 (0.988–1.014)	.857
	2	2.44	0.998 (0.986–1.011)	.802	3.3	0.997 (0.985–1.010)	.727
	3	5.88	0.996 (0.983–1.008)	.509	6.15	0.994 (0.982–1.007)	.391
	4	6.76	0.997 (0.983–1.010)	.526	7.2	0.992 (0.979–1.005)	.208
	5	7.37	0.995 (0.982–1.007)	.433	7.6	0.991 (0.978–1.003)	.139
	6	1	0.993 (0.981–1.006)	.286	2.29	0.991 (0.980–1.002)	.096
	7	2.51	0.995 (0.983–1.008)	.471	4.78	0.993 (0.980–1.005)	.255
O_3 (ppb)	0	7.73	0.995 (0.984–1.006)	.382	7.81	0.997 (0.986–1.008)	.658
	1	3.20	0.999 (0.988–1.009)	.855	3	1.002 (0.991–1.013)	.729
	2	3.04	0.999 (0.988–1.010)	.858	2.53	1.002 (0.991–1.012)	.785
	3	3.21	0.997 (0.987–1.008)	.675	2.77	1.001 (0.989–1.012)	.916
	4	3.78	0.998 (0.986–1.011)	.375	3.54	0.993 (0.982–1.004)	.232
	5	4.34	0.990 (0.979–1.001)	.077	4.22	0.994 (0.984–1.005)	.316
	6	5.35	0.991 (0.980–1.002)	.099	4.12	0.996 (0.985–1.007)	.448
	7	4.49	0.992 (0.982–1.003)	.177	5.34	0.996 (0.985–1.007)	.457
NO_2 (ppb)	0	2.04	1.007 (1.001–1.013)	.019	1.95	1.008 (1.000–1.016)	.044
	1	1	1.008 (1.002–1.014)	.01	1	1.008 (1.001–1.016)	.035
	2	1	1.007 (1.001–1.013)	.03	1	1.005 (1.001–1.013)	.026
	3	1	1.007 (1.001–1.013)	.019	1	1.013 (1.005–1.021)	.002
	4	1.07	1.006 (0.999–1.013)	.152	4.65	1.092 (1.001–1.017)	.020
	5	1.74	1.007 (0.999–1.014)	.128	3.5	1.009 (1.002–1.017)	.016
	6	1.19	1.007 (0.999–1.014)	.216	1	1.008 (0.999–1.015)	.051
	7	1	1.006 (0.999–1.012)	.193	1	1.006 (0.998–1.014)	.109
SO_2 (ppb)	0	8.45	1.009 (1.000–1.019)	.04	8.12	1.002 (0.989–1.014)	.769
	1	8.37	1.008 (0.998–1.017)	.099	1	0.998 (0.983–1.008)	.512
	2	8.33	1.005 (0.996–1.015)	.249	8.02	0.996 (0.983–1.008)	.505
	3	8.24	1.005 (0.995–1.014)	.267	1	0.998 (0.985–1.011)	.771
	4	1	1.004 (0.994–1.014)	.333	1	0.997 (0.985–1.009)	.434
	5	1	1.006 (0.997–1.015)	.195	1	1.000 (0.988–1.013)	.957
	6	1	1.005 (0.995–1.014)	.325	7.39	0.996 (0.983–1.008)	.521
	7	1	1.007 (0.997–1.016)	.14	1	1.001 (0.988–1.016)	.858
PM_{10} ($\mu g/m^3$)	0	1.99	1.006 (1.002–1.010)	.004	2.78	1.005 (1.001–1.009)	.007
	1	1.96	1.005 (1.002–1.009)	.004	2.44	1.005 (1.001–1.009)	.007
	2	7.48	1.004 (0.999–1.007)	.082	7.49	1.003 (0.999–1.007)	.101
	3	6.95	1.002 (0.998–1.006)	.223	6.6	1.002 (0.998–1.006)	.281
	4	6.34	1.001 (0.997–1.005)	.264	5.37	1.000 (0.996–1.004)	.834
	5	7.07	1.001 (0.997–1.005)	.601	6.77	1.002 (0.997–1.005)	.491
	6	6.79	1.002 (0.998–1.006)	.298	6.36	1.002 (0.998–1.006)	.322
	7	7.78	1.002 (0.998–1.006)	.252	6.27	1.018 (0.978–1.059)	.378

tends to be present in polluted air containing suspended solids and severe moisture and as a result, few epidemiologic studies are able to distinguish the effects of these pollutants separately (Goudarzi *et al.* 2014).

In this study, O_3 showed no significant relation with cardiovascular deaths in males and in total. In some other studies, similar results have been seen (Wong *et al.* 2002, Hashemi *et al.* 2014, Dadbakhsh *et al.* 2016, Ghorbani *et al.* 2017). But in women, after a 1 day lag, with 10 ppb increase of O_3, cardiovascular deaths increased 1.66% (95%CI: 0.73–2.61%) in the one pollutant and 1.65% (0.71–2.61%) in the two pollutant model. Some other studies have shown a relation between O_3 with cardiovascular death as well. Zhang *et al.* showed that for each 10 $\mu g/m^3$ increase in O_3 concentration, cardiovascular deaths increased by 0.45% (CI 95%: 0.16–0.73) in Shanghai (Zhang *et al.* 2006). In a meta-analysis done in 2005, the short-term effects of exposure to ozone and cardiovascular and respiratory mortality were analyzed. The pooled results showed that a 10 ppb increase in daily ozone, in lags 0, 1, or 2 days was associated with a 0.87% (95% CI = 0.55–1.18) increase in overall (male and female) mortality. But in some studies ozone had no significant relation with cardiovascular deaths (Dadbakhsh *et al.* 2016). Kan et al. reported that the effect of O_3 on total mortality in females was higher than males; and gender was an effect modifier in Shanghai, China (Kan *et al.* 2008). However, the mechanism of effect of ozone on cardiovascular deaths is still not known and requires further investigation (Ghanbari Ghozikali *et al.* 2014).

Table 10. Results of Adjusted Generalized Additive Model, about the effect of air pollutants on over 60 years old cardiovascular death, for 1 unit increase in CO and 10 units increase in all other pollutants (Adjusted for relative humidity, temperature, trend, season and day of week).

		One pollutant			Two pollutant		
	lag	df	RR (95% CI)	*p*	df	RR (95% CI)	*p*
CO (ppm)	0	7.17	0.998 (0.989–1.007)	.663	2.28	0.996 (0.987–1.005)	.388
	1	1	1.002 (0.993–1.011)	.623	1.89	1.002 (0.993–1.011)	.709
	2	2.54	0.998 (0.989–1.007)	.738	4.32	0.998 (0.989–1.007)	.653
	3	5.47	0.995 (0.987–1.004)	.319	5.83	0.994 (0.985–1.003)	.211
	4	6.41	0.995 (0.985–1.006)	.461	7	0.991 (0.983–1.000)	.058
	5	7.03	0.994 (0.986–1.003)	.273	7.42	0.989 (0.981–0.999)	.023
	6	4.1	0.992 (0.984–1.001)	.091	1	0.994 (0.984–1.002)	.149
	7	1	0.995 (0.986–1.004)	.303	1	0.992 (0.984–0.999)	.031
O_3 (ppb)	0	7.86	0.996 (0.988–1.003)	.315	7.92	0.998 (0.991–1.006)	.672
	1	3.2	1.000 (0.992–1.007)	.997	2.72	1.003 (0.995–1.010)	.475
	2	3.24	0.999 (0.992–1.008)	.846	2.54	1.001 (0.994–1.000)	.711
	3	3.48	0.998 (0.991–1.005)	.614	2.84	1.001 (0.993–1.008)	.863
	4	3.82	0.999 (0.992–1.007)	.546	3.55	0.993 (0.986–1.001)	.089
	5	4.37	0.990 (0.983–0.998)	.016	4.24	0.995 (0.987–1.002)	.175
	6	5.46	0.997 (0.984–0.999)	.029	4.22	0.995 (0.988–1.003)	.25
	7	4.46	0.993 (0.985–1.000)	.056	5.38	0.996 (0.988–1.003)	.288
NO_2 (ppb)	0	2.54	1.006 (1.002–1.011)	.002	1.7	1.006 (1.001–1.011)	.031
	1	1.29	1.007 (1.003–1.012)	<.001	1	1.012 (1.006–1.017)	<.001
	2	1	1.006 (1.002–1.010)	.005	1	1.007 (1.001–1.012)	.012
	3	1	1.006 (1.002–1.011)	.002	1	1.007 (1.002–1.013)	.007
	4	4.17	1.004 (1.000–1.008)	.001	4.54	1.006 (1.003–1.009)	<.001
	5	1.96	1.007 (1.003–1.012)	<.001	3.25	1.009 (1.004–1.015)	<.001
	6	1.49	1.008 (1.004–1.013)	<.001	1	1.008 (1.002–1.013)	.005
	7	1	1.008 (1.004–1.012)	.002	1	1.006 (0.996–1.015)	.176
SO_2 (ppb)	0	8.43	1.009 (1.003–1.015)	.006	8.18	1.002 (0.993–1.010)	.731
	1	1	1.007 (1.001–1.013)	.033	1	0.996 (0.987–1.005)	.373
	2	8.25	1.005 (0.998–1.011)	.131	7.9	0.997 (0.988–1.005)	.452
	3	1	1.005 (0.998–1.011)	.139	1	0.999 (0.994–1.004)	.226
	4	1	1.003 (0.995–1.009)	.377	1	0.999 (0.990–1.007)	.825
	5	7.84	1.005 (0.998–1.012)	.11	1	1.000 (0.992–1.009)	.923
	6	1.01	1.004 (0.997–1.010)	.234	7.39	0.996 (0.987–1.005)	.384
	7	7.84	1.006 (0.999–1.013)	.059	7.38	1.001 (0.992–1.009)	.871
PM_{10} ($\mu g/m^3$)	0	1.84	1.005 (1.003–1.008)	.001	2.17	1.005 (1.002–1.008)	<.001
	1	1.57	1.005 (1.0025–1.008)	.001	1	1.005 (1.002–1.008)	<.001
	2	7.49	1.003 (1.001–1.006)	.017	7.48	1.003 (1.000–1.006)	.023
	3	6.9	1.002 (0.999–1.005)	.138	6.52	1.000 (0.997–1.003)	.198
	4	6.21	1.001 (0.996–1.006)	.124	1.98	1.004 (0.998–1.009)	.154
	5	6.94	1.001 (0.997–1.003)	.658	6.63	1.001 (0.998–1.004)	.509
	6	6.81	1.002 (0.999–1.004)	.196	6.45	1.002 (0.999–1.005)	.063
	7	6.82	1.002 (0.999–1.005)	.149	6.32	1.002 (0.999–1.005)	.054

CO was not related with cardiovascular deaths in this study, and Dastoorpoor et al. did not see a relation between CO and cardiovascular deaths in Ahwaz either (Dastoorpoor *et al.* 2018). But some studies have shown a relation between this pollutant and cardiovascular deaths. In Hong et al.'s study in Korea, carbon monoxide was related to ischemic stroke and the Rate Ratio was 1.04 (95% CI = 1.01–1.07) (Hong *et al.* 2002). One of the reasons for these controversial results may be that in our study and in the Ahvaz study, all cardiovascular deaths have been included, but Hong et al only included deaths from ischemic stroke. More investigation is needed about the effects of air pollutants on specific cardiovascular diseases.

In this present study, NO_2, SO_2 and PM_{10} in people over 60 years had a stronger relation with cardiovascular deaths than the younger age group. This finding shows the stronger effects of NO_2, SO_2 and PM_{10} pollutants on the elderly people. Maheswaran et al, in south London also showed a higher risk of ischemic stroke in the 65 to 79-year old age group, and the RR for NO_2 and PM_{10} were respectively 1.86 (95% CI: 1.10–3.13) and 1.23 (95% CI: 0.99–1.53) (Maheswaran *et al.* 2012). The elderly are probably more susceptible to air pollution due to the consequences of natural aging (Bentayeb et al. 2012).

In some cases air pollutants may show significant negative relations with cardiovascular deaths. But this is usually due to the harvesting effect. In this study the RR for the effect of pollutants on cardiovascular deaths in percentiles above the 95^{th} percentile were compared to the 5^{th} percentile. Result showed that the ratio of count of deaths in the above the 95^{th} percentile range on the count of deaths in the under the 5^{th} percentile range were greater than 1. And this shows that the harvesting effect has probably happened. Spix et al. have introduced methods for identifying the harvesting effect (Spix *et al.* 1993).

Ambient air pollutants may cause cardiovascular death through numerous mechanisms, such as accelerated atherosclerosis, changes in heart function, increased inflammatory cytokines in the heart, increased blood clotting, increased blood viscosity, increased plasma fibrinogen and changes in heart rate, lung inflammation and aggravation of lung disease (Brook *et al.* 2010).

Several studies have shown that ambient air pollutants are related to cardiovascular deaths. But, the different results between studies may be related to differences in the concentration of pollutants in different parts of the world, the statistical models use for data analysis, and adjusting for different confounders.

Mobile and stationary sources are both responsible for the air pollution crisis in Tehran. Motor vehicles are the main source for especially CO, NO_2 and PM_{10} in Tehran. Tehran also has a lot of factories and is an industrial hub. According to Mazaheri et al, mobile sources of air pollution are more important than stationary sources in making and emitting NO_2 and CO in Tehran (Mazaheri Tehrani *et al.* 2015). Therefore, efforts to reduce pollutants released from mobile resources are essential.

Strengths and limitations

The strength of this study was that air pollution and cardiovascular death data from a ten-year period was used; and air pollution and meteorological data were obtained from reliable sources. Also as studies have shown that meteorological data, do not have a linear relation with health outcomes (Bhaskaran *et al.* 2009), in this study, we used Generalized Additive Models (GAM) for nonlinear confounder variables.

A limitation of this study was that about 8% of the air pollution data was missing. However, they were estimated using the EM algorithm method. Analysis was done separately for completed cases and imputed cases and the results were almost the same. But, in most cases analysis by EM imputed data produced higher precision.

Another limitation was that the impact of other potential confounding variables such as the concentrations of other pollutants, and wind direction were not investigated. We did not do variable interactions in this study either, but it can be an interesting topic for future researchers.

Conclusion

The results of this study showed that air pollution in Tehran may be responsible for some part of the cardiovascular deaths that happen in this city. Further efforts to control air pollutants, especially PM_{10}, and NO_2 in Tehran are essential. These efforts can include reducing emissions in the industrial and transport sector and strict regulations for using low sulfur gasoline or diesel filters. It is also recommended that elderly people with cardiovascular diseases avoid outdoor work and activity and use approved masks on days when air pollution is higher than the WHO standard guidelines.

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Ethical approval

This project was approved by the Standing Committee of Ethics in Research of Kerman University of Medical Sciences (Ethics code: IR.KMU.REC.1395.267).

Disclosure statement

No potential conflict of interest was reported by the authors.

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