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Air Pollution and Hospital Admission for Epilepsy in Kerman, Iran

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Abstract

Background: This study aimed to investigate the relation between air pollution and epilepsy admissions in Kerman, Iran.
Methods: In this ecological study, the concentrations of ambient air pollutants and meteorological data were obtained from Kerman Environmental Protection Agency and Kerman Meteorology Organization, respectively. Additionally, epilepsy admission data were obtained from Kerman's Shafa hospital epilepsy registry. Generalized additive models with lags up to 7 days were used to estimate rate ratios (RRs).
Results: Within 2008 to 2020, 894 epilepsy admissions occurred in Kerman, 498 cases (55.7%) of whom were male. The strongest relations of epilepsy admission were observed in the over 59-year group for carbon monoxide (CO) in lag 0 (RR = 2.1455, 95% CI: 1.5823 - 2.9091), nitrogen dioxide (NO_2) in lag 0 (RR = 1.0409, 95% CI: 1.0282 - 1.0537), and particulate matter under 2.5 microns ($PM_{2.5}$) in lag 5 (RR = 1.0157, 95% CI: 1.0062 - 1.0252). There were also significant associations for particulate matter under 10 microns (PM_{10}) in the under 18-year group in lag 2 (RR = 1.0064, 95% CI: 1.0029 - 1.0098), ozone in lag 0 (RR = 0.9671, 95% CI: 0.9581 - 0.9761), and sulfur dioxide in lag 5 (RR = 0.9937, 95% CI: 0.9891 - 0.9983).
Conclusions: Exposure to CO, NO_2, $PM_{2.5}$, or PM_{10} air pollutants might be a risk factor for epilepsy admissions in Kerman. Epilepsy patients should better stay away from exposure to polluted air. Staying at home on polluted days or residing in areas with less air pollution might be an option.

Keywords: Air Pollution, Epilepsy, Kerman

1. Background

Epilepsy is one of the most common neurological diseases and affects individuals of all ages (1). Air pollution might cause central nervous system (CNS) damage and neurodegenerative disorders (2). The occurrence of seizures might be affected by the interaction of internal and pathologic factors and extrinsic factors, including medication and environmental factors (3, 4). Studies have shown that Parkinson's disease, Alzheimer's disease, multiple sclerosis, and stroke might be related to ambient air pollution (5, 6). Calderon et al. conducted a study in Mexico and reported that exposure to air pollutants could seriously affect children's CNS (7). Another study in China also showed the possible relation between air pollution and neurodegenerative diseases (8). Fluegge and Fluegge reported hospitalization for epilepsy associated with changes in the concentrations of various pollutants, including nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2), ozone (O_3), and particulate matter (PM). Additionally, Fluegge and Fluegge showed that air pollutants might be a risk factor for epilepsy hospital admissions (9).

However, the effect of air pollution on the CNS has not been thoroughly studied. Kerman has a population of about 740,000 individuals according to the 2016 census and is located in Kerman province in southeastern Iran (10). In addition to human-made air pollution, Kerman faces sandstorms and increased ambient dust in specific seasons. The prevalence of epilepsy in Kerman was 7.87 per 1000 individuals in 2011 (1). A recent review estimated that there are about 840,000 individuals with active epilepsy living in Iran, and epilepsy prevalence in Iran is 1% (11).

2. Objectives

The present study aimed to evaluate hospital admissions in Kerman for epilepsy and its possible relation with air pollution.

3. Methods

In this ecological study, the concentrations of ambient air pollutants (i.e., CO, O_3, NO_2, SO_2, and particulate matter under 10 and 2.5 microns [PM_{10} and $PM_{2.5}$]) were obtained from Kerman Environmental Protection Agency within September 2008 to March 2020. The meteorological data, including temperature and relative humidity, were obtained from Kerman Meteorological Organization. The aforementioned variables were adjusted as confounders.

The epilepsy hospitalization data were obtained from Kerman's Shafa hospital epilepsy registry and according to the International Classification of Diseases 10th Revision, which was code G40. The data were investigated regarding gender and age subgroups (under 18, within 18-59, and over 59 years). The data of all epilepsy patients that had stayed in the hospital for more than one day were included.

3.1. Statistical Analysis

Generalized additive models (GAMs) similar to the equation below were used to estimate the rate ratios (RRs) with lags up to 7 days. The time unit used was the day. The GAM has been used in numerous air pollution and health studies. This method can adjust for nonlinear confounding effects, such as seasonal changes and meteorological variables (12).

$$Y_t \sim Poisson\,(\mu_t) \quad (1)$$

$$log\mu_t = \alpha + \sum \beta_i\,(X_i) + \sum S_j\,(X_j) \quad (2)$$

Where Y_t denotes the daily number of epilepsy relapses in total, male, female, and age groups. β_i is the coefficient for air pollutants (X_i) and denotes the log of the RR. S_j and (X_j) are the smoothing functions of meteorological variables (i.e., temperature and relative humidity).

Several studies have shown that meteorological factors, such as temperature, are associated with hospital admissions for epilepsy attacks (3, 13-16). Therefore, the models were adjusted for average daily temperature and relative humidity. The time unit used in the analysis was the day. Microsoft Office Excel software (version 2010) and SPSS software (version 22) were used for the primary analysis. Then, the 'mgcv' package in R i386 4.0.3 software was used for GAM analysis.

4. Results

In the less than 12-year period under study, 894 epilepsy admissions occurred in Kerman, 498 (55.7%) and 396 (44.3%) cases of whom were male and female, respectively. Table 1 shows the number of epilepsy admissions within 2008 to 2020 in different population subgroups. Table 2 shows descriptive statistics of daily air pollution and meteorological variables within 2008-2020. The findings showed that the mean daily concentrations of PM_{10}, $PM_{2.5}$, and SO_2 were higher than the World Health Organization daily thresholds reported as 50, 25, and 20 μg/m^3, respectively (17).

Table 3 shows the results of the adjusted GAM about the effect of air pollutants on overall epilepsy admissions in male, female, and age groups adjusted for average daily relative humidity and temperature. Increased epilepsy admissions in the total population were observed in various lags for CO, NO_2, PM_{10}, and $PM_{2.5}$. Additionally, CO, NO_2, PM_{10}, and $PM_{2.5}$ had a direct association with epilepsy admissions in male subjects. The strongest relations were observed in lag 4 for CO (RR = 1.2352, 95% CI: 1.0298 - 1.4815), lag 0 for NO_2 (RR = 1.0409, 95% CI: 1.0282 - 1.0537), lag 2 for $PM_{2.5}$ (RR = 1.0066, 95% CI: 1.0014 - 1.0118), and lag 0 for PM_{10} (RR = 1.0057, 95% CI: 1.0039 - 1.0075). PM_{10} and $PM_{2.5}$ also had a direct association with epilepsy admissions in female subjects. The strongest relations were observed in lag 2 for $PM_{2.5}$ (RR = 1.0071, 95% CI: 1.0015 - 1.0128) and lag 6 for PM_{10} (RR = 1.0031, 95% CI: 1.0011 - 1.0050).

In all age groups, CO, NO_2, PM_{10}, and $PM_{2.5}$ showed direct relations with epilepsy admissions. The strongest relation between CO and epilepsy admissions was observed in the over 59-year group in lag 0 (RR = 2.1455, 95% CI: 1.5823 - 2.9091), NO_2 in the over 59-year group in lag 0 (RR = 1.0407, 95% CI: 1.0139 - 1.0681), $PM_{2.5}$ in the over 59-year group in lag 5 (RR = 1.0157, 95% CI: 1.0062 - 1.0252), and PM_{10} in the under 18-year group in lag 2 (RR = 1.0064, 95% CI: 1.0029 - 1.0098).

5. Discussion

This study showed significant relations between short-term exposure to air pollutants CO, NO_2, PM_{10}, and $PM_{2.5}$ with epilepsy admissions in Kerman, Iran. In this study, CO increased epilepsy admissions. Consistent with the results of this study, Bao et al.'s study in China showed an association between CO and increased epilepsy hospitalization (1.1%, 95% CI: 0.1 - 2.1%) (18). In addition, in Mexico, there was an association between ambient CO and epilepsy admissions (RR = 1.098, 95% CI: 1.045 - 1.155) (19).

In this study, NO_2 had a significant relation with epilepsy admissions in total and several different age groups, and the strongest relation was observed in male subjects. Automobile exhaust is one of the most important sources of NO_2. Wang et al.'s study in China demonstrated a significant association between the NO_2 of automobile exhaust and neurobehavioral function in school-age children. In the aforementioned study, two primary

Table 1. Number of Epilepsy Admissions within 2008 to 2020 in Different Population Subgroups

Year	Male	Female	Male/Female Ratio	< 18 years	18 - 59 years	> 59 years
2008	17	10	1.7	5	20	2
2009	61	52	1.17	21	69	23
2010	53	37	1.43	20	59	11
2011	39	40	0.97	27	47	5
2012	37	35	1.05	11	56	5
2013	54	38	1.42	18	61	13
2014	52	36	1.44	14	64	10
2015	31	18	1.72	15	28	6
2016	41	41	1	16	57	9
2017	33	21	1.57	6	39	9
2018	25	21	1.19	7	27	12
2019	54	47	1.14	10	67	24
2020 (only 3 months)	1	0	-	0	0	1
Total	498	396	1.25	170	594	130

Table 2. Descriptive Statistics of Daily Air Pollution and Meteorological Variables

	Mean ± SD	Median	Minimum	Maximum
O_3 (ppb)	30.21 ± 11.91	29.72	1.92	79
CO (ppm)	1.07 ± 0.69	0.92	0.03	12.27
NO_2 (ppb)	15.82 ± 7.96	15.41	0	78.45
SO_2 (ppb)	26.12 ± 20.64	21	0	128.46
PM_{10} ($\mu g/m^3$)	71.11 ± 47.45	63.48	0	382.76
$PM_{2.5}$ ($\mu g/m^3$)	27.47 ± 16.18	24.20	0	112
Temperature (°C)	16.75 ± 8.10	17.2	0	41
Humidity (%)	31.15 ± 17.30	27	3.5	100

schools were chosen. One school was located in a clear area and the other in a traffic dense and polluted area. NO_2 had been monitored for the effect of traffic-related air pollution on the school campuses and classrooms. Children participated in assisted neurobehavioral testing to assess neurobehavioral performance (20).

A systematic review in 2017 concluded that high concentrations of NO_2 in polluted air significantly affect the CNS in children and adults and represent a significant risk factor for human health (21). A study in China showed a significant relation between the increasing concentration of NO_2 with epilepsy attacks (2%, 95% CI: 0.5 - 3.6%) (18). Furthermore, in Mexico, an ecological study showed a significant relation between NO_2 and epilepsy attacks (RR = 1.083, 95% CI: 1.038 - 1.13) (19). In a cohort study in Denmark, residential exposure to road traffic and air pollution was associated with a higher risk for febrile seizures (IRR = 1.05, 95% CI: 1.02 - 1.07) (22). A study in southern Spain showed that even low levels of NO_2 exposure and traffic-related air pollution had adverse effects on children's neurodevelopment (23). Xu et al.'s study in China showed that the RR for epilepsy attacks was 3.17 (95% CI: 1.41 - 4.93) per 10 $\mu g/m^3$ increase of NO_2 (13). However, a study in the USA showed a protective effect for N_2O on epilepsy (IRR = 0.85, 95% CI: 0.74 - 0.97) (9). N_2O is a different compound and is derived mainly from agricultural fertilizers and natural sources; nonetheless, NO_2 is mainly produced by vehicles.

Another pollutant evaluated in this study was PM_{10}, which had a significant relation with epilepsy admissions in total and several subgroups, with the strongest relation observed in the under 18-year subgroup. Several studies have shown relations between ambient PM_{10} and epilepsy attacks (19, 24, 25). Consistent with the results of this study, Cakmak et al. in Mexico showed an association between PM_{10} and hospital admissions for epilepsy (RR = 1.083, 95% CI: 1.038 - 1.13) (19). A study in six cities in Italy demonstrated positive associations between PM_{10} exposure and total emergency calls within 2002 to 2006 (26). Additionally, increased emergency calls for epilepsy attacks were observed with exposure to PM_{10} in China (RR = 1.5, 95% CI: 1.1 - 2.0) (24). Radmanesh et al.'s study in Iran showed that patients with different types of headaches and epilepsy increased on dusty days, compared to clean days, and there were significant associations between increased concentrations of ambient PM_{10} and hospital admissions for these problems (25). Another study from Iran showed that exposure to PM_{10} increased oxidative stress and the expression of inducible nitric oxide synthase messenger ribonucleic acid levels and reduced the concentrations of antioxidant enzymes (27).

In this study, $PM_{2.5}$ had a significant relation with epilepsy admissions in total, and several subgroups, with the strongest relation, observed in the over 59-year subgroup. Consistent with the results of this study, a significant association was observed between $PM_{2.5}$ and epilepsy attacks in Mexico (RR = 1.065, 95% CI: 1.002 - 1.132) (19). Other studies have shown that oxidative stress, neuroinflammation, glial activation, and cerebrovascular damage are the primary pathways for inducing brain pathology by air pollution (28). Oxidative stress, changes in autonomous function, and progression of atherosclerosis can be exacerbated by exposure to ambient PM (29).

In this study, O_3 and SO_2 were inversely related to epilepsy admissions. In an ecological study in China, Xu et al. also reported negative associations between ambient O_3 and epilepsy attacks (-0.84%, 95% Cl: -1.58 - 0.09%) (13). An interventional study showed that O_3 could be protective against pentylenetetrazole-induced epilepsy attacks (30). However, in another study conducted in Mexico, a significant direct association was observed between O_3 and hospital admissions for epilepsy attacks (RR = 1.100, 95% CI: 1.025 - 1.181) (19). In Fluegge and Fluegge's study in the USA, no significant relation was observed between O_3 and epilepsy attacks (9). In the current study the average concentration of O_3 was 30.21 ± 11.19 ppb, which is less that Xu et al.'s study (mean = 100 ± 63 ppb) (13) which showed a negative association, and Cakmak et al.'s study (mean = 93.26 ppb) (19). Further research is needed to clarify the effect of O_3 exposure on epilepsy.

Some of the strengths of this study included about 12-year data on air pollution and epilepsy admissions and the use of GAMs to adjust for nonlinear confounder variables. However, given the ecological nature of this study, the results cannot be easily inferred at the individual level.

5.1. Conclusions

Exposure to ambient CO, NO_2, PM_{10}, and $PM_{2.5}$ might be related to epilepsy admissions in Kerman. This study further emphasizes the necessity to control and reduce ambient air pollutants. Additionally, epilepsy patients should better stay away from exposure to polluted air. Staying at home on polluted days or residing in areas with less air pollution might be an option.

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Footnotes

Authors' Contribution: NK conceptualized the idea and helped in writing and editing the manuscript. MAF acquired, cleaned, and analyzed the data and wrote the initial manuscript. HAE reviewed the manuscript and provided scientific advice for neurological diseases. MM supervised data analysis and provided statistical consultation. All the authors read and approved the final manuscript.

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Data Reproducibility: The data are available from the first author upon reasonable request.

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Table 3. Results of Adjusted Generalized Additive Models about the Effect of Air Pollutants on Epilepsy Admissions in Total, Male, Female, and Age Groups Adjusted for Relative Humidity and Temperature

Pollutant	RR	95% CI	P-Value
		Lag 0	
Total			
O_3	0.9816	0.9756 - 0.9877	0.0001
CO	0.9008	0.7906 - 1.0263	0.315
NO_2	1.0266	1.0168 - 1.0364	0.001
SO_2	0.9978	0.9945 - 1.0011	0.178
PM_{10}	1.0037	1.0024 - 1.0050	0.0001
$PM_{2.5}$	1.0017	0.9977 - 1.0057	0.402
Male			
O_3	0.9942	0.9854 - 1.0029	0.718
CO	0.9543	0.8015 - 1.1360	0.598
NO_2	1.0409	1.0282 - 1.0537	0.001
SO_2	0.9967	0.9923 - 1.0012	0.234
PM_{10}	1.0057	1.0039 - 1.0075	0.001
$PM_{2.5}$	1.0001	0.9949 - 1.0054	0.581
Female			
O_3	0.9671	0.9581 - 0.9761	0.001
CO	0.8665	0.7119 - 1.0547	0.240
NO_2	1.0049	0.9894 - 1.0206	0.533
SO_2	0.9988	0.9938 - 1.0038	0.560
PM_{10}	1.0023	1.0002 - 1.0044	0.015
$PM_{2.5}$	1.0042	0.9981 - 1.0104	0.215
< 18 years			
O_3	1.0062	0.9913 - 1.0212	0.089
CO	0.5803	0.4138 - 0.8139	0.001
NO_2	1.0213	1.0000 - 1.0435	0.004
SO_2	0.9985	0.9906 - 1.0064	0.510
PM_{10}	1.0051	1.0021 - 1.0081	0.0001
$PM_{2.5}$	1.0007	0.9915 - 1.0099	0.510
18 - 59 years			
O_3	0.9812	0.9736 - 0.9888	0.0001
CO	0.8188	0.6961 - 0.9632	0.015
NO_2	1.0243	1.0123 - 1.0365	0.0001
SO_2	0.9963	0.9922 - 1.0004	0.520
PM_{10}	1.0039	1.0022 - 1.0056	0.0001
$PM_{2.5}$	1.0005	0.9956 - 1.0053	0.540
> 59 years			
O_3	0.9545	0.9404 - 0.9689	0.0001
CO	2.1455	1.5823 - 2.9091	0.0001

NO_2	1.0407	1.0139 - 1.0681	0.002
SO_2	1.0031	0.9948 - 1.0115	0.151
PM_{10}	1.0022	0.9990 - 1.0054	0.216
$PM_{2.5}$	1.0148	1.0038 - 1.0259	0.0001
	Lag 1		
Total			
O_3	0.9908	0.9844 - 0.9972	0.0002
CO	1.0280	0.9148 - 1.1551	0.570
NO_2	1.0083	1.0000 - 1.0178	0.001
SO_2	0.9961	0.9928 - 0.9995	0.0201
PM_{10}	1.0027	1.0010 - 1.0040	0.0001
$PM_{2.5}$	1.0049	1.0010 - 1.0089	0.013
Male			
O_3	0.9950	0.9864 - 1.0037	0.141
CO	1.0052	0.8471 - 1.1927	0.580
NO_2	1.0080	0.9959 - 1.0203	0.713
SO_2	0.9958	0.9913 - 1.0003	0.998
PM_{10}	1.0033	1.0016 - 1.0050	0.026
$PM_{2.5}$	1.0052	0.9999 - 1.0106	0.717
Female			
O_3	0.9854	0.9759 - 0.9951	0.001
CO	1.0130	0.8486 - 1.2093	0.245
NO_2	1.0068	0.9927 - 1.0211	0.107
SO_2	0.9959	0.9909 - 1.0010	0.309
PM_{10}	1.0022	1.0002 - 1.0042	0.020
$PM_{2.5}$	1.0050	0.9990 - 1.0111	0.362
< 18 years			
O_3	0.9955	0.9807 - 1.0105	0.650
CO	0.9933	0.7675 - 1.2856	0.591
NO_2	1.0138	0.9953 - 1.0326	0.256
SO_2	0.9940	0.9960 - 1.0021	0.250
PM_{10}	1.0047	1.0013 - 1.0080	0.0002
$PM_{2.5}$	1.0012	0.9915 - 1.0110	0.550
18 - 59 years			
O_3	0.9936	0.9857 - 1.0015	0.315
CO	0.9894	0.8504 - 1.1512	0.510
NO_2	1.0063	0.9944 - 1.0182	0.123
SO_2	0.9954	0.9912 - 0.9996	0.013
PM_{10}	1.0024	1.0008 - 1.0041	0.003
$PM_{2.5}$	1.0046	0.9999 - 1.0095	0.050
> 59 years			
O_3	0.9707	0.9542 - 0.9875	0.0008
CO	1.2834	1.0073 - 1.6351	0.006

NO_2	1.1013	0.9868 - 1.0405	0.112
SO_2	1.0015	0.9931 - 1.0100	0.051
PM_{10}	1.0022	0.9992 - 1.0053	0.255
$PM_{2.5}$	1.0131	1.0003 - 1.0231	0.0006
	Lag 2		
Total			
O_3	0.9882	0.9819 - 0.9947	0.0001
CO	1.1044	0.9748 - 1.2511	0.195
NO_2	1.0099	1.0008 - 1.0192	0.012
SO_2	0.9964	0.9931 - 0.9998	0.009
PM_{10}	1.0028	1.0014 - 1.0042	0.0001
$PM_{2.5}$	1.0066	1.0028 - 1.0104	0.0001
Male			
O_3	0.9919	0.9833 - 1.0006	0.610
CO	1.1010	0.9261 - 1.3088	0.133
NO_2	1.0119	1.0001 - 1.0239	0.006
SO_2	0.9960	0.9915 - 1.0051	0.112
PM_{10}	1.0029	1.0011 - 1.0048	0.018
$PM_{2.5}$	1.0066	1.0014 - 1.0118	0.009
Female			
O_3	0.9834	0.9739 - 0.9930	0.0001
CO	1.1324	0.9459 - 1.3557	0.209
NO_2	1.0066	0.9926 - 1.0207	0.103
SO_2	0.9963	0.9913 - 1.0014	0.224
PM_{10}	1.0027	1.0008 - 1.0047	0.0003
$PM_{2.5}$	1.0071	1.0015 - 1.0128	0.009
< 18 years			
O_3	0.9996	0.9848 - 1.0146	0.580
CO	0.9128	0.6928 - 1.2026	0.710
NO_2	1.0144	0.9962 - 1.0329	0.308
SO_2	0.9958	0.9880 - 1.0036	0.126
PM_{10}	1.0064	1.0029 - 1.0098	0.003
$PM_{2.5}$	1.0038	0.9945 - 1.0132	0.187
18 - 59 years			
O_3	0.9891	0.9813 - 0.9970	0.0001
CO	1.1089	0.9513 - 1.2925	0.197
NO_2	1.0083	0.9971 - 1.0197	0.253
SO_2	0.9955	0.9913 - 0.9997	0.009
PM_{10}	1.0020	1.0003 - 1.0036	0.005
$PM_{2.5}$	1.0049	1.0003 - 1.0096	0.010
> 59 years			
O_3	0.9653	0.9489 - 0.9818	0.0001
CO	1.0768	0.8739 - 1.3267	0.175

NO_2	1.0100	0.9849 - 1.0358	0.284
SO_2	1.0017	0.9932 - 1.0101	0.520
PM_{10}	1.0030	0.9998 - 1.0062	0.30
$PM_{2.5}$	1.0182	1.0088 - 1.0276	0.007
	Lag 3		
Total			
O_3	0.9900	0.9836 - 0.9965	0.003
CO	1.1138	0.9875 - 1.2562	0.200
NO_2	1.0083	1.0001 - 1.0176	0.002
SO_2	0.9969	0.9935 - 1.0002	0.220
PM_{10}	1.0030	1.0016 - 1.0045	0.0001
$PM_{2.5}$	1.0042	1.0002 - 1.0082	0.0001
Male			
O_3	0.9899	0.9813 - 0.9986	0.025
CO	1.1553	0.9787 - 1.3638	0.110
NO_2	1.0095	0.9973 - 1.0220	0.291
SO_2	0.9964	0.9919 - 1.0010	0.283
PM_{10}	1.0038	1.0019 - 1.0057	0.0001
$PM_{2.5}$	1.0048	0.9995 - 1.0102	0.220
Female			
O_3	0.9895	0.9800 - 0.9992	0.011
CO	1.0374	0.8942 - 1.2036	0.580
NO_2	1.0058	0.9924 - 1.0194	0.630
SO_2	0.9970	0.9919 - 1.0020	0.149
PM_{10}	1.0022	0.9999 - 1.0044	0.400
$PM_{2.5}$	1.0036	0.9976 - 1.0097	0.155
< 18 years			
O_3	1.0039	0.9893 - 1.0188	0.610
CO	0.9110	0.6910 - 1.2008	0.172
NO_2	1.0068	0.9881 - 1.0259	0.177
SO_2	0.9964	0.9887 - 1.0042	0.199
PM_{10}	1.0060	1.0027 - 1.0093	0.0002
$PM_{2.5}$	1.0010	0.9912 - 1.0108	0.343
18 - 59 years			
O_3	0.9878	0.9800 - 0.9957	0.002
CO	1.1581	0.9906 - 1.3539	0.302
NO_2	1.0077	0.9964 - 1.0193	0.203
SO_2	0.9963	0.9921 - 1.0004	0.100
PM_{10}	1.0034	1.0015 - 1.0052	0.0001
$PM_{2.5}$	1.0042	0.9994 - 1.0090	0.110
> 59 years			
O_3	0.9817	0.9653 - 0.9983	0.014
CO	1.3500	0.9461 - 1.3615	0.213

NO_2	1.0092	0.9862 - 1.0328	0.185
SO_2	1.0026	0.9942 - 1.0110	0.168
PM_{10}	1.0022	0.9989 - 1.0055	0.202
$PM_{2.5}$	1.0111	1.0004 - 1.0218	0.008
	Lag 4		
Total			
O_3	0.9923	0.9859 - 0.9988	0.032
CO	1.1114	0.9834 - 1.2561	0.110
NO_2	1.0098	1.0008 - 1.0190	0.012
SO_2	0.9965	0.9932 - 0.9999	0.006
PM_{10}	1.0024	1.0010 - 1.0038	0.0001
$PM_{2.5}$	1.0019	0.9978 - 1.0059	0.102
Male			
O_3	0.9929	0.9844 - 1.0016	0.325
CO	1.2352	1.0298 - 1.4815	0.022
NO_2	1.0111	0.9993 - 1.0231	0.300
SO_2	0.9954	0.9909 - 1.0000	0.500
PM_{10}	1.0027	1.0010 - 1.0045	0.001
$PM_{2.5}$	1.0015	0.9959 - 1.0071	0.610
Female			
O_3	0.9909	0.9814 - 1.0005	0.151
CO	1.0568	0.9836 - 1.2497	0.170
NO_2	1.0068	0.9936 - 1.0202	0.118
SO_2	0.9971	0.9921 - 1.0022	0.134
PM_{10}	1.0030	1.0008 - 1.0052	0.0001
$PM_{2.5}$	1.0026	0.9965 - 1.0087	0.193
< 18 years			
O_3	1.0008	0.9862 - 1.0156	0.155
CO	1.0455	0.7878 - 1.3874	0.151
NO_2	1.0121	0.9938 - 1.0309	0.188
SO_2	0.9969	0.9895 - 1.0043	0.188
PM_{10}	1.0047	1.0015 - 1.0080	0.0008
$PM_{2.5}$	1.0007	0.9910 - 1.0104	0.141
18 - 59 years			
O_3	0.9917	0.9839 - 0.9996	0.007
CO	1.0844	0.9349 - 1.2579	0.129
NO_2	1.0103	1.0001 - 1.0219	0.002
SO_2	0.9956	0.9914 - 0.9998	0.007
PM_{10}	1.0021	1.0004 - 1.0038	0.009
$PM_{2.5}$	1.0009	0.9959 - 1.0058	0.151
> 59 years			
O_3	0.9826	0.9664 - 0.9991	0.008
CO	1.1031	0.8878 - 1.3705	0.197

NO_2	1.0045	0.9829 - 1.0265	0.153
SO_2	1.0015	0.9931 - 1.0099	0.151
PM_{10}	1.0004	0.9999 - 1.0038	0.155
$PM_{2.5}$	1.0090	0.9988 - 1.0193	0.200
	Lag 5		
Total			
O_3	0.9925	0.9861 - 0.9989	0.025
CO	1.0090	0.8982 - 1.1336	0.878
NO_2	1.0123	1.0023 - 1.0225	0.015
SO_2	0.9953	0.9918 - 0.9987	0.007
PM_{10}	1.0026	1.0011 - 1.0042	0.0001
$PM_{2.5}$	1.0024	0.9983 - 1.0065	0.235
Male			
O_3	0.9956	0.9868 - 1.0044	0.349
CO	1.0078	0.8475 - 1.1984	0.932
NO_2	1.0155	1.0022 - 1.0290	0.027
SO_2	0.9937	0.9891 - 0.9983	0.012
PM_{10}	1.0029	1.0011 - 1.0047	0.001
$PM_{2.5}$	1.0007	0.9949 - 1.0065	0.849
Female			
O_3	0.9885	0.9793 - 0.9978	0.015
CO	1.1199	0.9404 - 1.3337	0.180
NO_2	1.0037	0.9891 - 1.0184	0.616
SO_2	0.9972	0.9480 - 1.0489	0.285
PM_{10}	1.0021	1.0000 - 1.0042	0.045
$PM_{2.5}$	1.0046	0.9986 - 1.0107	0.291
< 18 years			
O_3	1.0119	0.9972 - 1.0267	0.331
CO	0.7856	0.5749 - 1.0737	0.282
NO_2	1.0058	0.9860 - 1.0260	0.563
SO_2	0.9927	0.9849 - 1.0000	0.072
PM_{10}	1.0060	1.0028 - 1.0093	0.0002
$PM_{2.5}$	0.9990	0.9890 - 1.0092	0.855
18 - 59 years			
O_3	0.9920	0.9841 - 0.9998	0.053
CO	1.0189	0.8838 - 1.1747	0.795
NO_2	1.0110	0.9988 - 1.0234	0.072
SO_2	0.9955	0.9913 - 0.9997	0.036
PM_{10}	1.0019	1.0002 - 1.0036	0.018
$PM_{2.5}$	0.9993	0.9942 - 1.0045	0.808
> 59 years			
O_3	0.9726	0.9577 - 0.9877	0.001
CO	1.2800	0.9305 - 1.3672	0.167

NO_2	1.0073	0.9821 - 1.0332	0.569
SO_2	0.9994	0.9908 - 1.0081	0.908
PM_{10}	1.0007	0.9971 - 1.0044	0.671
$PM_{2.5}$	1.0157	1.0062 - 1.0252	0.001
		Lag 6	
Total			
O_3	0.9936	0.9871 - 1.0000	0.054
CO	1.0437	0.9369 - 1.1628	0.436
NO_2	1.0096	0.9999 - 1.0195	0.051
SO_2	0.9959	0.9925 - 0.9993	0.018
PM_{10}	1.0027	1.0013 - 1.0040	0.0001
$PM_{2.5}$	1.0022	0.9981 - 1.0064	0.278
Male			
O_3	0.9973	0.9886 - 1.0062	0.560
CO	1.0608	0.8948 - 1.2575	0.496
NO_2	1.0143	1.0011 - 1.0277	0.033
SO_2	0.9955	0.9909 - 1.0001	0.053
PM_{10}	1.0021	1.0003 - 1.0039	0.019
$PM_{2.5}$	0.9995	0.9937 - 1.0053	0.807
Female			
O_3	0.9879	0.9787 - 0.9972	0.011
CO	1.0555	0.9220 - 1.2083	0.433
NO_2	1.0099	0.9956 - 1.0244	0.211
SO_2	0.9966	0.9915 - 1.0017	0.186
PM_{10}	1.0031	1.0011 - 1.0050	0.001
$PM_{2.5}$	1.0055	0.9994 - 1.0116	0.072
< 18 years			
O_3	1.0100	0.9952 - 1.0250	0.201
CO	0.9225	0.9090 - 0.9361	0.586
NO_2	1.0005	0.9803 - 1.0211	0.958
SO_2	0.9923	0.9842 - 1.0005	0.068
PM_{10}	1.0053	1.0023 - 1.0082	0.0001
$PM_{2.5}$	1.0036	0.9940 - 1.0132	0.461
18 - 59 years			
O_3	0.9939	0.9860 - 1.0019	0.137
CO	1.0478	0.9168 - 1.1976	0.492
NO_2	1.0123	1.0005 - 1.0242	0.039
SO_2	0.9961	0.9920 - 1.0003	0.071
PM_{10}	1.0018	1.0001 - 1.0036	0.037
$PM_{2.5}$	0.9985	0.9932 - 1.0037	0.577
> 59 years			
O_3	0.9728	0.9560 - 0.9898	0.001
CO	1.1216	0.9217 - 1.3648	0.251

NO_2	1.0021	0.9770 - 1.0278	0.866
SO_2	1.0011	0.9926 - 1.0098	0.784
PM_{10}	1.0020	0.9988 - 1.0052	0.182
$PM_{2.5}$	1.0148	1.0051 - 1.0245	0.003
	Lag 7		
Total			
O_3	0.9911	0.9848 - 0.9975	0.006
CO	1.0272	0.9233 - 1.1427	0.621
NO_2	1.0102	1.0002 - 1.0203	0.043
SO_2	0.9947	0.9913 - 0.9982	0.001
PM_{10}	1.0031	1.0017 - 1.0045	0.0001
$PM_{2.5}$	1.0026	0.9638 - 1.0429	0.190
Male			
O_3	0.9967	0.9879 - 1.0056	0.494
CO	1.1097	0.9176 - 1.3420	0.272
NO_2	1.0148	1.0015 - 1.0283	0.016
SO_2	0.9950	0.9905 - 0.9996	0.045
PM_{10}	1.0031	1.0012 - 1.0050	0.001
$PM_{2.5}$	0.9998	0.9943 - 1.0054	0.951
Female			
O_3	0.9874	0.9779 - 0.9971	0.011
CO	1.0615	0.9289 - 1.2129	0.377
NO_2	1.0041	0.9890 - 1.0193	0.838
SO_2	0.9952	0.9901 - 1.0003	0.062
PM_{10}	1.0030	1.0010 - 1.0049	0.002
$PM_{2.5}$	1.0049	0.9990 - 1.0109	0.096
< 18 years			
O_3	1.0074	0.9925 - 1.0225	0.112
CO	0.8833	0.6405 - 1.2179	0.449
NO_2	0.9990	0.9786 - 1.0197	0.925
SO_2	0.9925	0.9843 - 1.0007	0.075
PM_{10}	1.0055	1.0023 - 1.0087	0.0001
$PM_{2.5}$	1.0102	1.0017 - 1.0187	0.018
18 - 59 years			
O_3	0.9914	0.9836 - 0.9993	0.035
CO	1.0565	0.9242 - 1.2079	0.420
NO_2	1.0109	0.9998 - 1.0229	0.067
SO_2	0.9942	0.9900 - 0.9984	0.007
PM_{10}	1.0025	1.0009 - 1.0041	0.001
$PM_{2.5}$	0.9980	0.9928 - 1.0032	0.453
> 59 years			
O_3	0.9707	0.9540 - 0.9877	0.0001
CO	1.0964	0.8781 - 1.3690	0.416

NO_2	1.0074	0.9792 - 1.0364	0.790
SO_2	1.0025	0.9938 - 1.0114	0.560
PM_{10}	1.0014	0.9981 - 1.0046	0.396
$PM_{2.5}$	1.0110	1.0009 - 1.0212	0.030

Abbreviations: RR, rate ratio; CI, confidence interval.