Acute effects of ambient air pollution on daily neurology clinic visits for vertigo: a time-series study in Wuhan, China

Jiachen Zheng (2018302130050@whu.edu.cn)
Zhongnan Hospital of Wuhan University https://orcid.org/0000-0001-8782-5467
Min Xu
Wuhan University Zhongnan Hospital: Zhongnan Hospital of Wuhan University
Haoyue Xu
Wuhan University Zhongnan Hospital: Zhongnan Hospital of Wuhan University
Fei Ye
Central Hospital of Wuhan: The Central Hospital of Wuhan
Xiaozhou Li
Central Hospital of Wuhan: The Central Hospital of Wuhan
Yumin Liu
Wuhan University Zhongnan Hospital: Zhongnan Hospital of Wuhan University
Xiaoqing Jin
Wuhan University Zhongnan Hospital: Zhongnan Hospital of Wuhan University https://orcid.org/0000-0002-2571-3512

Research Article

Keywords: air pollution, air pollutants, vertigo, neurology clinic visits (NCVs), a time-series study

Posted Date: January 26th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2454814/v1

Version of Record: A version of this preprint was published at Environmental Science and Pollution Research on March 27th, 2023. See the published version at https://doi.org/10.1007/s11356-023-26575-4.

Abstract

Objective: This study aimed to disclose the relationship between ambient air pollution and neurology clinic visits (NCVs) for vertigo.

Methods: A time-series study was conducted to examine relationships between different air pollutants (SO_2, NO_2, $PM_{2.5}$, PM_{10}, CO, and O_3) and daily NCVs for vertigo in Wuhan, China from January 1st 2017 to November 31th 2019. Stratified analyses were computed according to gender, age and season.

Results: 14,749 records of NCVs for vertigo were enrolled in the study. Data demonstrated daily NCVs for vertigo significantly corresponded to per increase of 10μg/m^3 for SO_2, NO_2 and O_3. Males were more susceptible in acute SO_2 and NO_2 exposure, while females were more vulnerable to O_3. Acute SO_2, NO_2, and O_3 exposure correlated with daily NCVs for vertigo significantly stronger in individuals aged less than 50 years old. Acute $PM_{2.5}$ exposure associated with daily NCVs for vertigo more obviously in cool seasons, whereas the correlation was conversely stronger in warm seasons between O_3 exposure and daily NCVs for vertigo.

Conclusion: Our study demonstrated acute exposure to ambient NO_2 and O_3 positively associated with daily NCVs for vertigo. Acute effects of air pollution on daily NCVs for vertigo varied according to gender, age and season.

Introduction

Air pollution is recognized as one of the top five risks for developing diseases according to the Global Burden of Disease study and the World Health Organization (Collaborators, 2018; Health Effects Institute., 2017). Exposure to air pollutants leads to more emergency room visits, outpatient service, hospitalizations and decreased productivity(Ma et al., 2016). As the metropolitan city with a large population in central China, Wuhan also suffers from severe air pollution(Zeng et al., 2018). Thus, it is important to understand potential health risks of ambient air pollution, serving to be helpful in health policy-making.

Vertigo is a common complaint in outpatient neurology clinic visits (NCVs), which varied in etiology according to Bárány Society's Committee for the Classification of Vestibular Disorders.(Bisdorff et al., 2015) In the last decade, studies showed that exposure to some air pollutants contributed to the occurrence of different neurological consequences, leading increased outpatient service of neurological clinics(Block and Calderon-Garciduenas, 2009; Costa et al., 2020; Loane et al., 2013; Salvi and Salim, 2019).These associated neurological disorders and symptoms, included but not limited to vertigo(Mariani et al., 2008; Yuan et al., 2021), depression(Braithwaite et al., 2019), migraines(Elser et al., 2021), and epilepsy(Chiang et al., 2021). However, the reported associations are mainly studied in developed countries or vulnerable populations such as the elderly and pregnant women. Data in this area conducted in general population or developing countries is scared, and relations between ambient air pollution and daily NCVs for vertigo are still unclear.

Air pollution is complex for its multiple components (e.g sulfides, nitrogen oxides, particulate matter, carbon monoxide, and ozone etc.) and meteorological influence factors (e.g temperature, humidity, barometric pressure etc.). In this study, we conducted time-series analyses to examine relationships between different ambient air pollutants (SO_2, NO_2, $PM_{2.5}$, PM_{10}, CO, and O_3) and daily NCVs for vertigo. Meanwhile, we incorporated a two-pollutant model to assess the robustness of effect estimates after adjusting for the effects of co-pollutants. Furthermore, sensitivity analyses were also computed according to season, gender and age. Our findings should be applicable on health policy-making in cities with similar emission condition.

Materials And Methods

Wuhan is the capital of Hubei Province situating in Central China (latitude 30°35'N and longitude 114°17'E). It is a large metropolitan city with a population over 10 million, and 13 districts covering about 8494.41km^2(http://www.wuhan.gov.cn).As an important industrial base and transportation hub in China, the main sources of air pollution in Wuhan are automobile exhaust and industrial emissions(Liu et al., 2022). Wuhan has a subtropical monsoon climate with warm and rainy summers, cold and dry winters. The average ambient temperature of Wuhan is 30.1°C in July and 4.1°C in January. Due to the monsoon from the north where two seriously polluted provinces are located (Henan and Hebei), the air pollution in Wuhan is more severe in winter.(Mao et al., 2018)

Neurology clinic visits (NCVs) data

Outpatient records of NCVs for vertigo were extracted from the hospital information system of Zhongnan Hospital, Wuhan University for the study period between January 1st 2017 and November 30th 2019. NCVs for vertigo of Zhongnan Hospital are local outpatients mainly from Wuchang district of Wuhan, where the hospital is located. Wuchang district contains 19% population of the whole urban are and 12% population of Wuhan(Liu et al., 2022). A total of 14749 outpatient records of NCVs with a chief complaint of vertigo were enrolled in the study (N = 14749). The dataset included dates of NCVs for vertigo and related demographic information of gender, age and residential address of enrolled participants. Non-Wuhan permanent residents and cases who had previously recurrently visited for vertigo in Zhongnan hospital were excluded from the study. Disorders of vestibular function(H81),Dizziness and giddiness (R42) were coded according to the tenth version of International Classification of Diseases (ICD-10). This study protocol was approved by the Medical Ethics Committee of Zhongnan Hospital (IRB number: 2022142K).

Environmental and meteorological data

Daily ambient air pollution data for the study period between January 1st 2017 and November 30th 2019 were obtained from the website of Wuhan Ecological Environment Bureau (http://hbj.wuhan.gov.cn/). The daily average concentrations of air pollutants (SO_2, NO_2, $PM_{2.5}$, PM_{10}, CO, and O_3) were calculated by averaging hourly values of each air pollutant from ten fixed-site monitoring stations, which cover the urban areas of Wuhan. All the stations are far from industrial, residential and vehicular sources, ensuring the monitoring data reflects overall urban background air conditions without uncertain interference. Data of the following meteorological parameters (daily average ambient temperature [°C], relative humidity [%], and barometric pressure [KPa]) for the study period were obtained from the meteorological data sharing service of the China Meteorological Administration (Beijing, China). Seven days (0.66%) of environmental and meteorological data were missing, and data with missing information were eliminated from the study.

Statistical analysis

An over-dispersive generalized additive model (GAM) for time series analyses(Song et al., 2018a)was chosen in the exploration of acute effects of ambient air pollutants on daily NCVs for vertigo. Data of daily NCVs for vertigo followed an over-dispersed Poisson distribution, so quasi-Poisson regression was used in the above model. Meanwhile, distributional lag models were applicated in the deduction of both cumulative exposure effects and displacement effects of air pollutants on daily NCVs for vertigo(Song et al., 2018b).

Several covariates were imported in the GAM model to control both time-invariant and time-varying confounding effects. First, a natural cubic regression smoothing function for calendar time with 7 degrees of freedom (df) per year excluded long-term and seasonal trends over 2 months. Second, natural smooth functions of daily average ambient temperature (6 df), relative humidity (3 df) and barometric pressure (3 df) were incorporated to control for the non-linear confounding effect of meteorological factors. Third, other covariates such as public holidays (Holiday) and days of the week (DOW) were adjusted as dummy variables in the GAM model.

The core model is described as follows:

$$logE\left(Yt\right)=\beta Z_t+DOW+ns\left(time,df\right)+ns\left(temperture,6\right)+ns\left(huamidity,3\right)+ns\left(pressure,3\right)+intercept$$

where$E\left(Yt\right)$represents numbers of daily NCVs for vertigo on day t; β denotes the log-relative rate of daily NCVs for vertigo associated with unit increase of each air pollutant; $Z_t$denotes concentrations of each air pollutant on day t; *DOW* is a dummy variable for days of the week; and *ns* refers to the natural cubic regression smoothing function. We derived the exposure-response (E-R) relationship curves between each air pollutant and daily NCVs for vertigo by importing 3 df as natural spline function into the above model.

Three sensitivity analyses were subsequently performed to ensure the stability of this model. First, an alternative proxy of 4–10 df per year was selected for the smoothness of temporal time trend. Second, a two-pollutant model was used to assess the robustness of effect estimates after adjusting for co-pollutants with correlation coefficients inferior to 0.7. Third, two different lag time constructions were examined for each air pollutant: the single-day lags algorithm (lag0 to lag7) and the multi-days algorithm of moving average lags (lag0-1 to lag0-7). And three statistics methods of Akaike Information Criterion (AIC), Generalized Cross Validation (GCV) and Partial Autocorrelation Function (PACF) were applied to determine the optimal lag structure for this model.

In addition, stratification analyses were computed according to season (warm: April to September; cool: October to March), age (< 50 years; ≥50 years), and gender (females; males) to explore the potential vulnerable factors related to short-term effects of ambient air pollution on daily NCVs for vertigo. The statistical significance of the differences between the strata effect estimates by calculating 95% confidence intervals as $\left(\widehat{Q}_1-\widehat{Q}_2\right) \pm 1.96\sqrt{\left(S\widehat{E}_1\right)^2+\left(S\widehat{E}_2\right)^2}$ where $\widehat{Q}_1$ and $\widehat{Q}_2$ are the estimates for two categories, and $S\widehat{E}_1$ and $S\widehat{E}_2$ are their respective standard errors.

All the statistical analyses were performed in R software (version 4.1.0) using the MGCV package. A two-tailed $p < 0.05$ was used to determine the statistical significance. Effects were described as changes of percentage and 95% CI in numbers of daily NCVs for vertigo per 10 μg/m3 increase of each air pollutant (SO_2, NO_2, $PM_{2.5}$, PM_{10}, CO, and O_3).

Results

As shown in **Table 1**, a total of 14,749 records of NCVs for vertigo were enrolled in the present study for the period between January 1st 2017 and November 30th 2019. Total NCVs for vertigo in warm seasons was slightly greater than in cold seasons(50.9% vs 49.1%). The proportion of females were higher than males in total NCVs for vertigo (58.9% vs 41.1%); while elders aged more than 50 years old presented more frequently than young individuals aged less than 50 years old in NCVs for vertigo(65.0% vs 35%). In addition, the average ambient temperature, relative humidity and barometric pressure was 17.7 °C, 78.76% and 101.51 KPa respectively during the study period in Wuhan. Annual average levels of air pollutants were 9.04 μg/m^3 for SO_2, 46.22 μg/m^3 for NO_2, 46.76 μg/m^3 for $PM_{2.5}$, 76.89 μg/m^3 for PM_{10}, 996.56 μg/m^3 for CO, and 99.25 μg/m^3 for O_3 respectively.

Figure 2 demonstrated moderate to strongly positive correlations among short-term exposure to SO_2, NO_2, $PM_{2.5}$, PM_{10}, and CO, with Spearman's correlation coefficients ranged from 0.52 to 0.87. However, the association between O_3 and other air pollutants was weak with correlation coefficients ranged merely from − 0.24 to 0.09. Furthermore, Short-term exposures to SO_2, NO_2, $PM_{2.5}$, PM_{10} were all negatively correlated with ambient temperature and relative humidity, whereas O_3 and CO exposure was positively associated with ambient temperature (Spearman's correlation coefficient:0.66) and relative humidity (Spearman's correlation coefficient:0.13). Meanwhile, short-term exposure to SO_2, NO_2, $PM_{2.5}$, PM_{10} and O_3 all showed moderate positive correlations with atmospheric pressure, while CO exposure was negatively associated with atmospheric pressure with correlation coefficient of -0.55.

Figure 3 further illustrated percentage changes of daily NCVs for vertigo (mean concentrations and 95% CI) associated with per 10μg/m^3 increase of each air pollutant using the single-day lags algorithm (lag0 to lag7) and multi-days algorithm of moving average lags (lag0-1 to lag0-7). As shown in **Table 2**, lag1 for SO_2, lag07 for NO_2, lag2 for $PM_{2.5}$, lag4 for CO, lag01 for PM_{10}, lag0 for O_3 were chosen as the optimal lag structures to get the smallest AIC/GCV/PACF values according to the model fitting statistics. It exhibited that percentage changes of daily NCVs for vertigo respectively corresponded to per 10 μg/m^3 increase of SO_2 (-7.60%; 95% CI: -14.25% to -0.44%), NO_2 (3.14%; 95% CI: 0.23–6.13%), $PM_{2.5}$ (0.53%; 95% CI: -0.66–1.74%), PM_{10} (1.32%; 95% CI: -0.36–3.06%), CO (0; 95% CI: -0.12–0.13%) and O_3 (0.90%; 95% CI: -0.01–1.83%). Furthermore, short-term NO_2 and O_3 exposure positively correlated to daily NCVs for vertigo, whereas the association between SO_2 exposure and daily NCVs for vertigo was conversely negative. Correlations remained significantly robust after adjusting for co-pollutants in two-pollutant model (**Table 2**). Sensitivity analysis further demonstrated that an alternative proxy of 4–10 df did not significantly affect the real-world effects of air pollutants on daily NCVs for vertigo (**Figure S1**).

Table 3 demonstrated different estimated effect of air pollutants on daily NCVs for vertigo stratified by seasons, gender and age. It showed that short-term exposure to $PM_{2.5}$ was positively associated with daily NCVs for vertigo in cool seasons (1.62; 95% CI: 0.15 to 3.12); however, CO exposure and daily NCVs for vertigo showed positive association in warm seasons (0.21; 95% CI: 0.05 to 0.38). Males were more susceptible to short-term NO_2 exposure compared to females in daily NCVs for vertigo (NO_2: 3.95; 95% CI: 0.05 to 8); whereas negative correlation was conversely observed between short-term SO_2 exposure and daily NCVs for vertigo in males (SO_2: -11.91; 95% CI: -20.42 to -2.42). Meanwhile, females presented more vulnerabilities than males when short-termly exposed to

O_3 (O_3: 0.94; 95% CI:0.03 to 1.86). In addition, short-term exposure to NO_2 (4.55; 95% CI: 0.15 to -9.13) and O_3 (1.27; 95% CI: 0.07 to 2.48) were positively correlated with daily NCVs for vertigo among individuals aged less than 50 years old. Conversely, effects of short-term SO_2 exposure to were significantly but negatively associated with daily NCVs for vertigo in the same subgroup (-12.75; 95% CI: -22.05 to -2.34).

Figure 4 graphically illustrated the exposure-response (E-R) relationship curves between short-term exposure to air pollutants and daily NCVs for vertigo. (1) SO_2 exposure: with the increasing concentration of ambient SO_2, daily NCVs for vertigo showed a sustained declining trend firstly and then maintained in a steady state at more than 20 μg/m3. (2) NO_2 exposure: The E-R graph presented a flattened sine curve twisted in two opposite directions at the concentration of around 35μg/m3. (3) $PM_{2.5}$ exposure: The E-R graph firstly maintained in a flatten trend within the interval of 0–40 μg/m^3 followed by an inverted flatten U-shaped curve, of which the turning point of was at the concentration of 100 μg/m^3. (4) PM_{10} exposure: with the increasing concentration of PM_{10}, daily NCVs for vertigo sharply rise within the interval of 0–70 μg/m^3, but then maintained in approximately flatten state at more than 70 μg/m^3. (5) CO exposure: An approximately straight flatten curve was observed from the E-R relationship curve between short-term CO exposure and daily NCVs for vertigo. (6) O_3 exposure: The E-R graph presented a U-shaped curve symmetrically twisted into two opposite parts at the concentration of 70 μg/m^3.

Discussion

During the study period, annual average concentrations of ambient NO_2, $PM_{2.5}$ and PM_{10} in Wuhan were obviously exceeded the Chinese National Ambient Air Quality Standards (https://www.mee.gov.cn). Conversely, the annual average level of ambient SO_2 in Wuhan was well below the above standards and other air pollutants in our study.

Our study demonstrated that short-term exposure to ambient NO_2 presented statistically significant correlations with daily NCVs for vertigo. As we know, NO_2 is asphyxiating odorous gas characterized as one of environmental irritants. Studies showed that airborne NO_2 could penetrate into the inner ear through the round window membrane(Aguilera et al., 2013; Sasa et al., 1989) and then dissolved in the perilymph and endolymph, which resulting in the elevated peri-lymphatic and endolymphatic acidity (Mun et al., 2021). It is reported that acidic surrounding environment facilitated the degeneration of otoconia, leading to the detachement of otoconia (Walther et al., 2014). The above findings underline plausible explanations for the onset of Benign paroxysmal positional Vertigo(BPPV)and Meniere's disease related to ambient NO_2 exposure. On the other hand, inhaled NO_2 exerts deleterious effects on brain via olfactory epithelium triggering neuroinflammation, and transfers inflammation to distal brain regions by damaging the permeability of blood-brain barrier(Adams et al., 2016). From cellular and animal levels, pathways of neuroinflammatory activation, impaired neurogenesis and neurodegeneration highlight mechanisms of vertigo of central origin related to air pollution(Li and Xin, 2013).

In our study, short-term exposure to O_3 also positively correlated with daily NCVs for vertigo, which is consistent with previous studies. One study conducted in Korea revealed that O_3 exposure was associated with high incidence of Ménière's disease. Ground-level O_3 in Wuhan is mainly produced by photochemical reactions of nitrogen oxides and volatile organic compounds(Choi et al., 2021). As the powerful inhaled oxidizing agent, studies showed that oxidative stress induced by O_3 exposure intimately linked with brain lipid peroxidation, neuroinflammation and subsequent neuron damage and impaired cerebral vascular endothelial injury(Cai et al., 2016; Yang et al., 2019). Moreover, the microglial activation in response to air pollutants and inflammatory cytokines or cells was also shown to be engaged in the neuron and cerebral vasculature damage(Block and Calderon-Garciduenas, 2009; Costa et al., 2020). The above evidence provided implications for the observed association between O_3 exposure and increased daily NCVs for vertigo in our study.

Nevertheless, a significantly negative correlation was observed between acute exposure to SO_2 and daily NCVs for vertigo. In Wuhan, ambient SO_2 is mainly from burning coal and sulfur containing fossil fuels in energy-intensive industries. Since exogenous SO_2 is known as toxic irritant gas with detrimental effects on human bodies,

Chinese government has instituted strict emission policy of SO_2 in the last decade. In our study, the annual average level of ambient SO_2 in Wuhan was well below the Chinese National Ambient Air Quality Standards and other air pollutants (NO_2, $PM_{2.5}$ and PM_{10}), ascribing to the environmental policy-tightening in China. Thus, it is difficult to determine the exact mechanism through which ambient O_3 exposure reduce the daily NCVs for vertigo. We speculated that human bodies might deal with inhaled SO_2 through conversion in a certain threshold range(Wang et al., 2017). It is reasonable that people will reduce outdoor activities when confronted extreme air pollution. Animal studies showed that low levels of inhaled SO_2 could be converted to sulfur-containing amino acids(Wang et al., 2017) and the endogenous derivatives through a series of physiological changes, resulting in significant anti-inflammatory, antioxidant and maintenance of cerebrovascular normalcy(Du et al., 2008; Wang et al., 2017), neuroprotective effects(Ohtani and Nishimura, 2020), and may have suppressed depression and anxiety(Shi et al., 2020). On the other hand, it is possible that chronic high level exposure to SO_2 in the past would led to behavioral adaptations in the body and enhanced tolerance to SO_2(Jun and Min, 2019). To date, the potential roles of environmental sulfur dioxide in brain homeostasis remains elusive and quantitative evidence is still in deficiency, which requires further research.

In our study, correlations between daily NCVs for vertigo and acute exposure to NO_2 and SO_2 were stronger in males and young individuals aged less than 50 years old. This may be linked to the fact that males and young people are more likely to undertake outdoor activities with more exposure to environmental pollution(Gu et al., 2020). The same reasoning also applies to the negative correlation between acute O_3 exposure and daily NCVs for vertigo with stronger coefficient in young people. Conversely, females were found to be more susceptible to O_3 exposure in daily NCVs for vertigo. This phenomenon has also been shown in the respiratory and cardiovascular systems, which is attributed to greater airway reactivity and smaller airways in females(Mao et al., 2018). Moreover, the correlation between daily NCVs for vertigo and short-term exposure to $PM_{2.5}$ was stronger in cool seasons, which is consistent with previous studies(Song et al., 2018b). Due to the special geographical location and unfavorable meteorological conditions of Wuhan, it is difficult for the dispersion of air pollutants in weak winter monsoons. And it is possible that the spreading velocities might vary among air pollutants of different molecular weight. However, the acute effect of CO on daily NCVs for vertigo was more pronounced in warm seasons. We speculated that the inconsistence of season differences among different air pollutants might attribute to the diversity of air pollutant mixtures in different seasons(Tsai et al., 2019). For example, the monsoon in warm season leads to less particulate matter but more opportunities of O_3 exposure, just like that frequent window openings lead to increased exposure in warm season(Tsai et al., 2019). Taken together, the stratification analysis of this study helped to figure out the vulnerable influence factors in daily NCVs for vertigo when confronted extremely air pollutions.

The exposure-response (E-R) curve is critical for the public health assessment. In the study, we observed that both NO_2 and O_3 exposure in a low range were not associated with daily NCVs for vertigo. This might be related to the fact that the E-R relationship is influenced by various factors, such as air pollution mixtures, climatic conditions and population sensitivity. However, the E-R curve of NO_2 exposure smoothed out at higher levels, which referred to the "harvest effect". Due to the "harvest effect", vulnerable population will emerge before levels of air pollutant reach reasonably high levels(Chen et al., 2017). Absence of significant thresholds in the E-R curve of O_3 can be explained by the limited availability of single city data(Song et al., 2018c) and enhanced effects of high-level O_3 on other air pollutants(Win-Shwe et al., 2013). Similarly, the E-R curves for SO_2 exposure smoothed out at higher levels, which may be related to limited outdoor activities in higher-level exposure to SO_2. Thus, it is suggested to tailor emission policies of air pollutants according to local conditions, of which scientific rationality of each air pollutant threshold warrants further exploration with larger samples.

Our study has several limitations. First, we used average concentrations of air pollutants measured by stationary site monitoring to represent individual exposures, which may lead to inevitable exposure misclassification. Second, although we have considered some possible confounding effects of co-pollutants and meteorological factors (temperature, relative humidity and pressure), there may be other factors that affect the onset of vertigo and impair a person’s tolerance to air pollutants, such as pre-existing diseases and unhealthy factors. Third, we only collected data from one hospital in a highly polluted city, resulting in the possible selection bias. Therefore, further studies are needed to confirm our results, and molecular biology or animal experiments are necessary to explore the exact mechanisms between air pollution and the onset of dizziness and vertigo.

Conclusions

Our study demonstrated that acute exposure to ambient NO_2 and O_3 positively correlated with daily NCVs for vertigo in Wuhan, China. The acute effects of air pollution on daily NCVs for vertigo varied according to season, gender and age. Our findings could be helpful in health policy-making when confronted extreme air pollution in cities with similar emission condition.

Declarations

Funding

None

Competing interests

The authors declare no competing interests.

Authors’ contributions

All authors contributed to the study conception and design. Jiachen Zheng: Methodology, Software,Visualization,Writing-Original Draft. Min Xu: Writing-Reviewing and Editing. Haoyue Xu: Software,investigation. Fei Ye: investigation. Xiaozhou Liu: investigation. Yumin Liu: Supervision, Project administration, Funding acquisition. Xiaoqing Jin: Supervision, Project administration, Funding acquisition. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The research protocol was approved by the Medical Ethics Committee of Zhongnan Hospital. (IRB 262 number: 2022142K)

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgements

We would like to thank all the participants who made this study possible.

References

1. Adams, D.R., Ajmani, G.S., Pun, V.C., Wroblewski, K.E., Kern, D.W., Schumm, L.P., McClintock, M.K., Suh, H.H., Pinto, J.M., 2016. Nitrogen dioxide pollution exposure is associated with olfactory dysfunction in older US adults. International Forum of Allergy & Rhinology, 6(12): 1245-1252.
2. Aguilera, I., Pedersen, M., Garcia-Esteban, R., Ballester, F., Basterrechea, M., Esplugues, A., Fernandez-Somoano, A., Lertxundi, A., Tardon, A., Sunyer, J., 2013. Early-life exposure to outdoor air pollution and respiratory health, ear infections, and eczema in infants from the INMA study. Environ Health Perspect, 121(3): 387-92.
3. Bisdorff, A.R., Staab, J.P., Newman-Toker, D.E., 2015. Overview of the International Classification of Vestibular Disorders. Neurologic Clinics, 33(3): 541-+.
4. Block, M.L., Calderon-Garciduenas, L., 2009. Air pollution: mechanisms of neuroinflammation and CNS disease. Trends Neurosci, 32(9): 506-16.
5. Braithwaite, I., Zhang, S., Kirkbride, J.B., Osborn, D.P.J., Hayes, J.F., 2019. Air Pollution (Particulate Matter) Exposure and Associations with Depression, Anxiety, Bipolar, Psychosis and Suicide Risk: A Systematic Review and Meta-Analysis. Environ Health Perspect, 127(12): 126002.
6. Cai, Y., Zhang, B., Ke, W., Feng, B., Lin, H., Xiao, J., Zeng, W., Li, X., Tao, J., Yang, Z., Ma, W., Liu, T., 2016. Associations of Short-Term and Long-Term Exposure to Ambient Air Pollutants With Hypertension: A Systematic Review and Meta-Analysis. Hypertension, 68(1): 62-70.

7. Chen, R., Yin, P., Meng, X., Liu, C., Wang, L., Xu, X., Ross, J.A., Tse, L.A., Zhao, Z., Kan, H., Zhou, M., 2017. Fine Particulate Air Pollution and Daily Mortality. A Nationwide Analysis in 272 Chinese Cities. Am J Respir Crit Care Med, 196(1): 73-81.
8. Chiang, K.L., Lee, J.Y., Chang, Y.M., Kuo, F.C., Huang, C.Y., 2021. The effect of weather, air pollution and seasonality on the number of patient visits for epileptic seizures: A population-based time-series study. Epilepsy Behav, 115: 107487.
9. Choi, H.G., Lee, C.H., Yoo, D.M., Min, C., Park, B., Kim, S.Y., 2021. Effects of short- and long-term exposure to air pollution and meteorological factors on Meniere's disease. Sci Rep, 11(1): 16063.
10. Collaborators, G.B.D.R.F., 2018. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet, 392(10159): 1923-1994.
11. Costa, L.G., Cole, T.B., Dao, K., Chang, Y.C., Coburn, J., Garrick, J.M., 2020. Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders. Pharmacol Ther, 210: 107523.
12. Du, S.X., Jin, H.F., Bu, D.F., Zhao, X., Geng, B., Tang, C.S., Du, J.B., 2008. Endogenously generated sulfur dioxide and its vasorelaxant effect in rats. Acta Pharmacol Sin, 29(8): 923-30.
13. Elser, H., Morello-Frosch, R., Jacobson, A., Pressman, A., Kioumourtzoglou, M.A., Reimer, R., Casey, J.A., 2021. Air pollution, methane super-emitters, and oil and gas wells in Northern California: the relationship with migraine headache prevalence and exacerbation. Environ Health, 20(1): 45.
14. Gu, J., Shi, Y., Zhu, Y., Chen, N., Wang, H., Zhang, Z., Chen, T., 2020. Ambient air pollution and cause-specific risk of hospital admission in China: A nationwide time-series study. PLoS Med, 17(8): e1003188.
15. Health Effects Institute., 2017 State of global air. Health Effects Institute, Boston, MA.
16. Jun, T., Min, I.S., 2019. Air pollution, respiratory illness and behavioral adaptation: Evidence from South Korea. PLoS One, 14(8): e0221098.
17. Li, H.Y., Xin, X.Y., 2013. Nitrogen dioxide (NO2) pollution as a potential risk factor for developing vascular dementia and its synaptic mechanisms. Chemosphere, 92(1): 52-58.
18. Liu, Y., Jiang, Y., Wu, M., Muheyat, S., Yao, D., Jin, X., 2022. Short-term effects of ambient air pollution on daily emergency room visits for abdominal pain: a time-series study in Wuhan, China. Environ Sci Pollut Res Int, 29(27): 40643-40653.
19. Loane, C., Pilinis, C., Lekkas, T.D., Politis, M., 2013. Ambient particulate matter and its potential neurological consequences. Rev Neurosci, 24(3): 323-35.
20. Ma, Y.X., Xiao, B.S., Liu, C., Zhao, Y.X., Zheng, X.D., 2016. Association between Ambient Air Pollution and Emergency Room Visits for Respiratory Diseases in Spring Dust Storm Season in Lanzhou, China. International Journal of Environmental Research and Public Health, 13(6).
21. Mao, M., Zhang, X., Yin, Y., 2018. Particulate Matter and Gaseous Pollutions in Three Metropolises along the Chinese Yangtze River: Situation and Implications. Int J Environ Res Public Health, 15(6).
22. Mariani, P., Pelagatti, M., Hahn, A., Alpini, D., 2008. Epidemiology of paroxysmal positioning vertigo: correlation with seasons, climate, and pollution. Int Tinnitus J, 14(2): 168-74.
23. Mun, S.K., Oh, S.R., Yang, B.R., Oh, S.H., Chang, M., 2021. Impact of air pollution on benign paroxysmal positional vertigo incidence: a retrospective study of the citizens of Seoul, South Korea. Environ Sci Pollut Res Int.
24. Ohtani, M., Nishimura, T., 2020. Sulfur-containing amino acids in aged garlic extract inhibit inflammation in human gingival epithelial cells by suppressing intercellular adhesion molecule-1 expression and IL-6 secretion. Biomed Rep, 12(3): 99-108.
25. Salvi, A., Salim, S., 2019. Neurobehavioral Consequences of Traffic-Related Air Pollution. Front Neurosci, 13: 1232.
26. Sasa, H., Nagahara, K., Yamashita, T., Kumazawa, T., 1989. Gas permeability of round window membrane. ORL J Otorhinolaryngol Relat Spec, 51(2): 88-93.
27. Shi, X.R., Gao, Y., Song, L., Zhao, P.H., Zhang, Y.P., Ding, Y.J., Sun, R.X., Du, Y.R., Gong, M., Gao, Q., Shi, Y., Guo, Q.J., Shi, H.S., 2020. Sulfur dioxide derivatives produce antidepressant- and anxiolytic-like effects in mice. Neuropharmacology, 176.
28. Song, J., Liu, Y., Zheng, L., Gui, L., Zhao, X., Xu, D., Wu, W., 2018a. Acute effects of air pollution on type II diabetes mellitus hospitalization in Shijiazhuang, China. Environ Sci Pollut Res Int, 25(30): 30151-30159.
29. Song, J., Lu, M., Zheng, L., Liu, Y., Xu, P., Li, Y., Xu, D., Wu, W., 2018b. Acute effects of ambient air pollution on outpatient children with respiratory diseases in Shijiazhuang, China. BMC Pulm Med, 18(1): 150.

30. Song, J., Zheng, L., Lu, M., Gui, L., Xu, D., Wu, W., Liu, Y., 2018c. Acute effects of ambient particulate matter pollution on hospital admissions for mental and behavioral disorders: A time-series study in Shijiazhuang, China. Sci Total Environ, 636: 205-211.
31. Tsai, S.S., Chiu, H.F., Yang, C.Y., 2019. Ambient Air Pollution and Hospital Admissions for Peptic Ulcers in Taipei: A Time-Stratified Case-Crossover Study. Int J Environ Res Public Health, 16(11).
32. Walther, L.E., Blodow, A., Buder, J., Kniep, R., 2014. Principles of calcite dissolution in human and artificial otoconia. PLoS One, 9(7): e102516.
33. Wang, X.B., Cui, H., Liu, X., Du, J.B., 2017. Sulfur dioxide: foe or friend for life? Histol Histopathol, 32(12): 1231-1238.
34. Win-Shwe, T.T., Fujitani, Y., Sone, H., Furuyama, A., Nitta, H., Hirano, S., 2013. Effects of acute single intranasal instillation of secondary organic aerosol on neurological and immunological biomarkers in the brain and lung of BALB/c mice. J Toxicol Sci, 38(1): 71-82.
35. Yang, H., Li, N., Han, J., Zhu, C.L., Tian, L., Lin, B.C., Xi, Z.G., Liu, X.H., Chu, N., 2019. [Injury of rat blood vessels caused by acute ozone exposure and its mechanism]. Zhongguo Ying Yong Sheng Li Xue Za Zhi, 35(3): 193-198.
36. Yuan, H., Liu, H., Huangfu, H., Zhou, L., Li, Y., Yang, J., Wu, J., Wang, X., Chen, G., 2021. [Climatic variations and vertigo diseases in outpatients clinic of ENT]. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi, 35(2): 101-104.
37. Zeng, P., Lyu, X.P., Guo, H., Cheng, H.R., Jiang, F., Pan, W.Z., Wang, Z.W., Liang, S.W., Hu, Y.Q., 2018. Causes of ozone pollution in summer in Wuhan, Central China. Environ Pollut, 241: 852-861.

Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

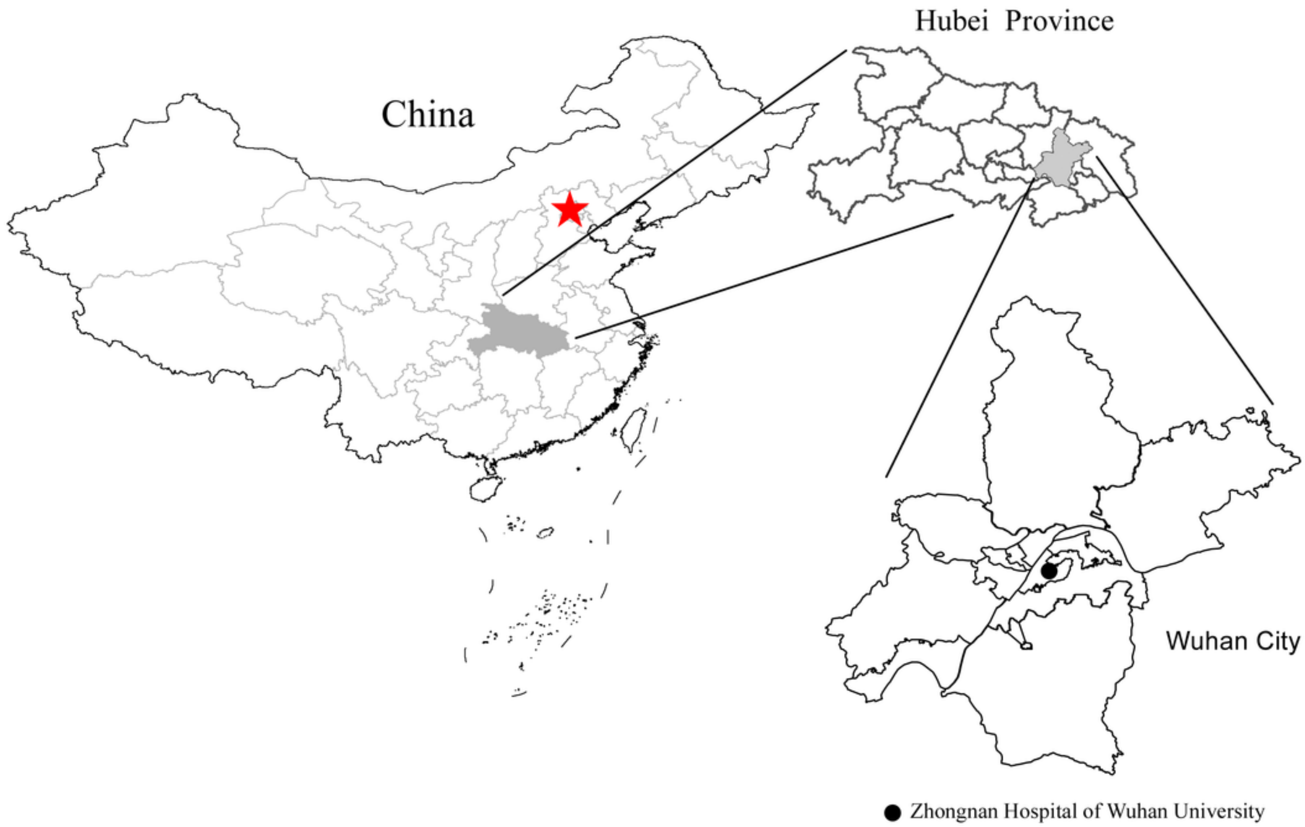

Figure 1

Legend not included with this version

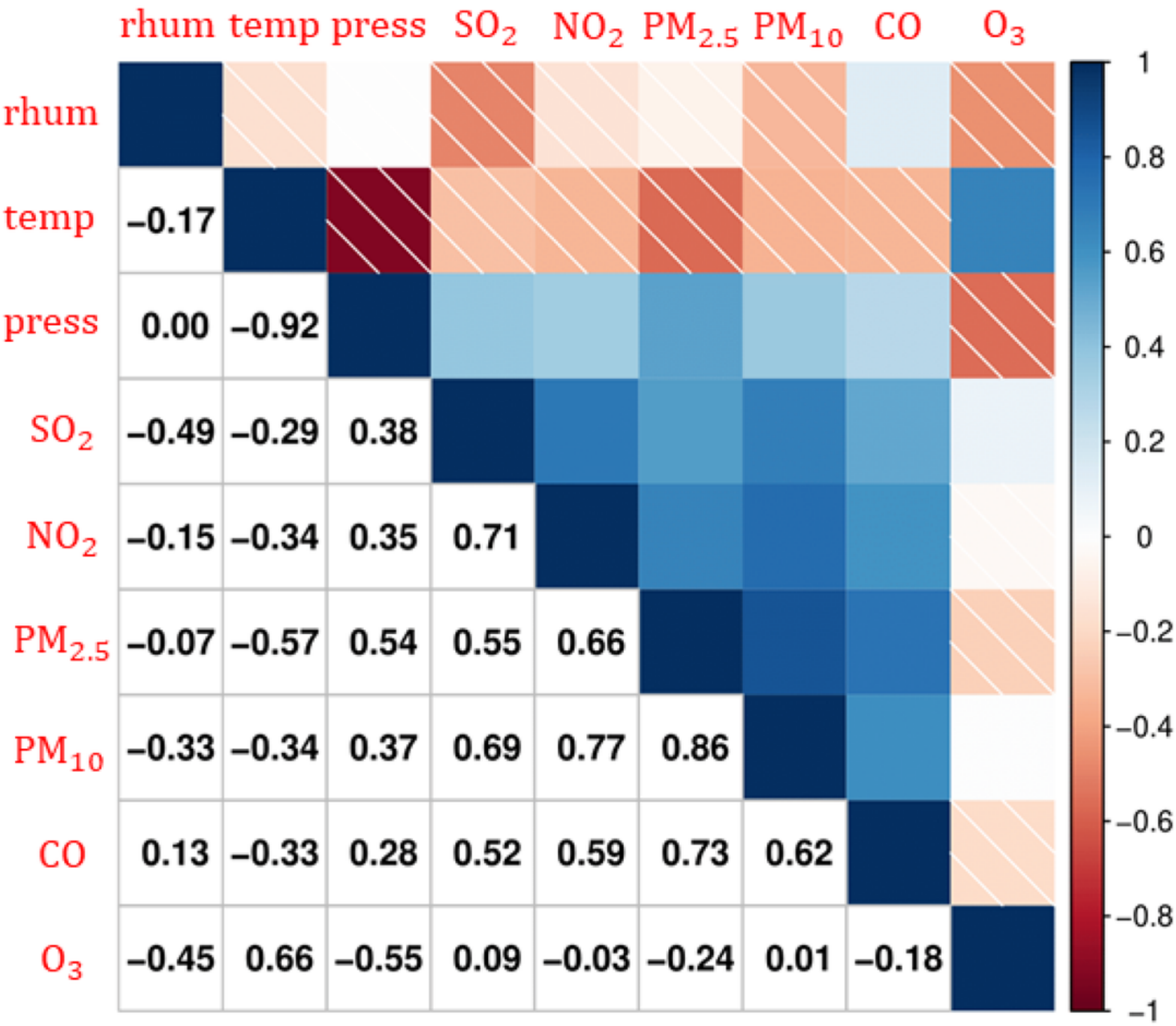

Figure 2

Legend not included with this version

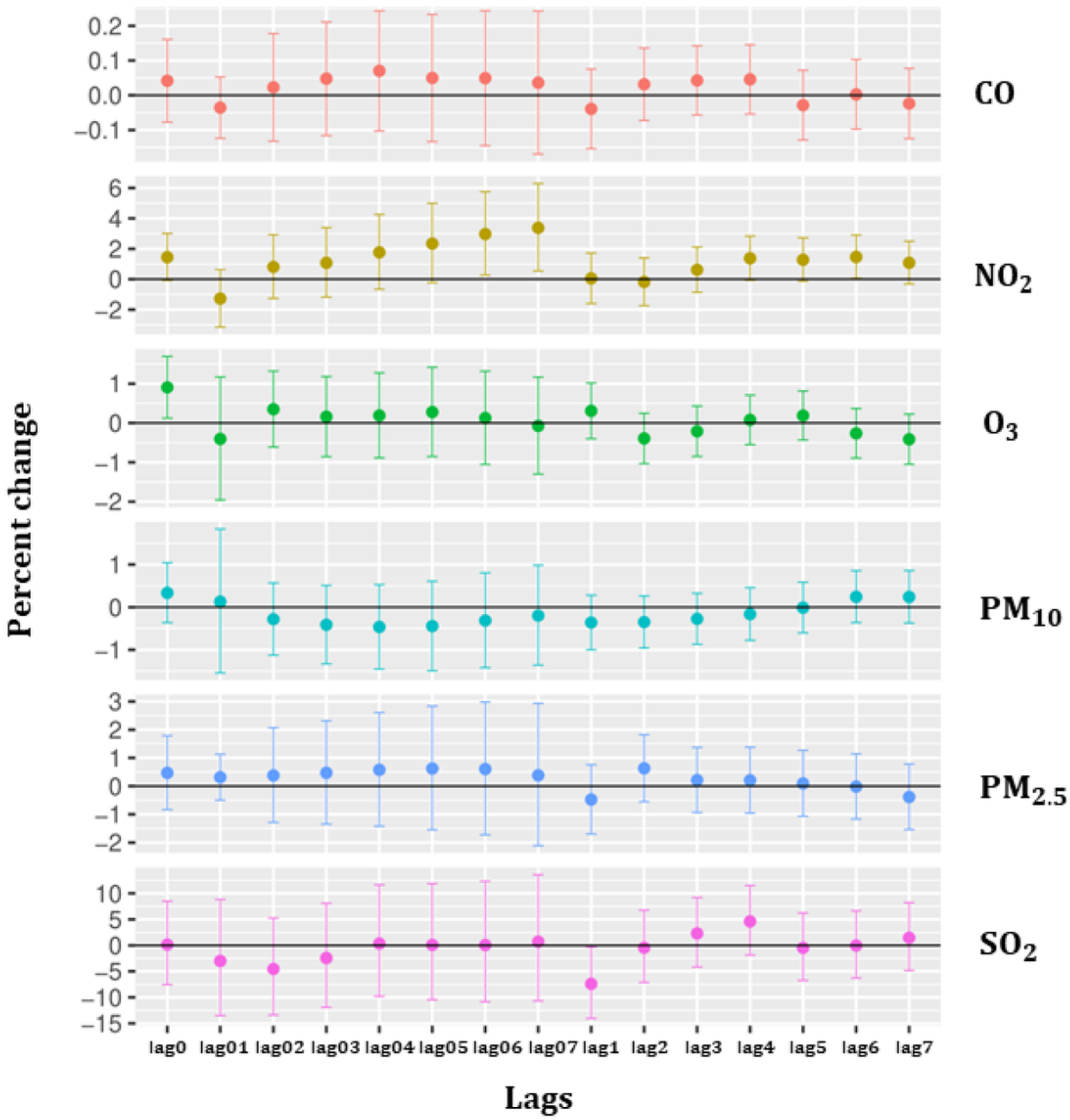

Figure 3

Legend not included with this version

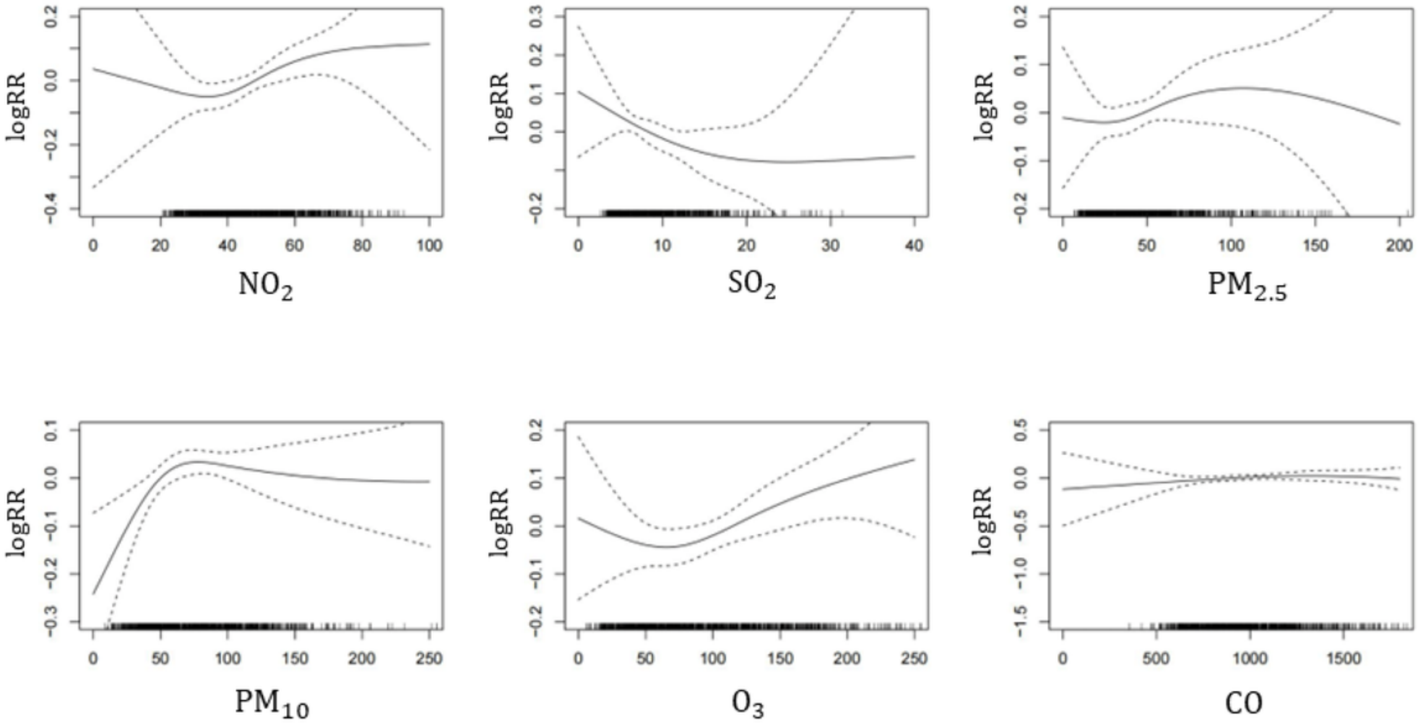

Figure 4

Legend not included with this version

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.pdf
- FigureS1.pdf