Association between ozone exposure and prevalence of mumps: a time-series study in a Megacity of Southwest China

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Abstract

In the present study, we aim to evaluate the delayed and cumulative effect of ozone (O₃) exposure on mumps in a megacity with high population density and high humidity. We took Chongqing, a megacity in Southwest China, as the research area and 2013–2017 as the research period. A total of 49,258 confirmed mumps cases were collected from 122 hospitals of Chongqing. We employed the distributed lag nonlinear models with quasi-Poisson link to investigate the relationship between prevalence of mumps and O₃ exposure after adjusting for the effects of meteorological conditions. The results show that the effect of O₃ exposure on mumps was mainly manifested in the lag of 0–7 days. The single-day lag effect was the most obvious on the 4th day, with the relative risk (RR) of mumps occurs of 1.006 (95% CI: 1.003–1.007) per 10 µg/m³ in the O₃ exposure. The cumulative RR within 7 days was 1.025 (95% CI: 1.013–1.038). Our results suggest that O₃ exposure can increase the risk of mumps infection, which fills the gap of relevant research in mountainous areas with high population density and high humidity.

Keywords Mumps · Air pollution · Distributed lag · O₃ · Cumulative exposure

Introduction

Respiratory diseases such as coronavirus (COVID-19) have been the hotspot of public health concern. Mumps caused by

the mumps virus (MuV) is one of the serious respiratory infections (Hviid et al. 2008). Patients often have symptoms such as parotid gland swelling and pain, which may lead to encephalitis, meningitis, orchitis, and other complications in severe cases (Betakova et al. 2013; Rubin et al. 2016). The number of mumps in China declined from 2013 to 2016 but rebounded from 2017 to 2018, which might be associated with the change in air quality (WHO 2020; Zhang et al. 2021). For example, urban O₃ pollution gradually increased from 2015 to 2017 in China (Guo et al. 2020). O₃ is harmful to human health, and short-term exposure to O₃ may increase morbidity, hospitalization, and mortality of cardiovascular and respiratory diseases (Yan et al. 2013). It is thus important to study the relationship between mumps and air quality for disease prevention.

The previous epidemiological studies have shown that air pollution would enhance the health risk from respiratory infections (Thurston et al. 2017). According to a report from the World Health Organization (WHO), acute pollution incidents in a number of cities around the world have led to an increase in morbidity and mortality (WHO 2016). The animal toxicology studies have shown that O₃ exposure can cause antioxidant depletion in mice and oxidation of lipids and proteins in respiratory tract lining fluid (RTLFL), which would exacerbate

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respiratory infections (Valacchi et al. 2004). However, the existing results on the association between the outbreak of mumps and environmental factors varied widely (Ho et al. 2015; Hu et al. 2018; Li et al. 2017). A study reported that the levels of sulfur dioxide (SO₂) and nitrogen dioxide (NO₂) were significantly associated with the prevalence of mumps at 2-day lag, but 23-day lag for SO₂, O₃, and respirable particulate matter (PM₁₀) (Hao et al. 2019). It is worth noting that these studies were all from plains and coastal areas, and more efforts are needed to evaluate the relationship in other geographical regions such as mountainous areas.

In environmental epidemiological analyzes, time-series regression models are widely used to quantify the effects of air pollution exposures (Bhaskaran et al. 2013; Modarres and Dehkordi 2005; Young and Minchin 1991). On the basis of the empirical exposure-response relationships, the relative risks of human health attributable to air pollution exposure were quantitatively evaluated (Onozuka and Hashizume 2011). In light of the advancement of epidemiological research methods, researchers have found that the effects of air pollution on human health tend to be hysteretic and/or nonlinear (Luo et al. 2018). In the distributed lag non-linear model (DLNM), the cross-basis functions of independent variables are constructed to evaluate the exposure-lag-effect relationship by accounting for the hysteresis and non-linear relationships (Gasparrini et al. 2010).

The purpose of this study is to evaluate the relationship between O₃ exposure and the prevalence of mumps. We selected Chongqing as the study area, which is a typical mountainous city located in Southwest China and the upper reaches

of the Yangtze River. Chongqing covers an area of 82,400 km² with a permanent population of approximately 31 million (NBSC 2019). Compared to the areas selected in the previous studies on mumps, Chongqing is a mountainous, humid, and densely populated area. We combined DLNM and the generalized additive model (GAM) to explore the exposure-lag-effect relationship and evaluate the relative risk (RR) (Gasparrini et al. 2010; Luo et al. 2018). The results from this study are expected to advance the understanding of the adverse effects of air pollution on mumps and to provide a basis for early warning with potential medical intervention.

Materials and methods

Study area

Chongqing (28°10'~32°13' North, 105°11'~110°11' East; Fig. 1) is a megacity of Southwest China. It has a humid subtropical monsoon climate. It's a typical mountainous, high-humidity, and high-population-density area, with annual average relative humidity (RH) of 75.1% and average temperature of 16.8°C during 2013–2017 (CMA 2020).

Data collection

A collection of daily diagnosed mumps cases was reported from 122 hospitals in Chongqing from January 1, 2013 to December 31, 2017. According to *International Classification of Diseases, the 10th Revision (ICD-10)*,

Fig. 1 Locations of air pollutants monitoring stations and hospitals in Chongqing

mumps is coded as B26. A total of 49,258 confirmed cases who lived in the study area were included. The daily concentrations of O₃, SO₂, NO₂, carbon monoxide (CO), fine particulate matter (PM_{2.5}), and PM₁₀ during 2013–2017 were monitored at 17 air quality stations in Chongqing, which were maintained by the Ministry of Ecology and Environment of China (MEEC 2020). The daily meteorological conditions, including relative humidity, precipitation, temperature, sunshine duration, atmospheric pressure, wind speed, and evaporation, were observed at 12 meteorological stations maintained by the China Meteorological Administration (CMA 2020). The daily concentrations of the air pollutants were calculated from the hourly concentrations. We excluded the days with >25% missing data of hourly concentrations (4 days during the study period), and then employed an iterative imputation method named *missForest* (Stekhoven and Bühlmann 2012) to fill the missing values.

Statistical analyzes

In this study, the DLNM was mainly employed to evaluate the association between O₃ exposure and the prevalence of mumps. We selected GAM as the workhorse model (Zeng et al. 2020) and the quasi-Poisson link as the connection function (Kim et al. 2015). With respect to the lag effects, we first constructed a single-day lag model, which however, might suffer the problem of temporal misalignment (Zhu et al. 2019). As cumulative exposure had a greater impact on human health (Lee et al. 2019; Samoli et al. 2013), we calculated the effect between cumulative O₃ exposure and the risk of mumps based on the single-day lag model. Considering the potential impact of meteorological factors on the prevalence of mumps, we modeled the meteorological factors as confounding variables with natural cubic spline functions. As the outbreak of mumps has a certain seasonal regularity, the indicator variable of month is added to the model (Qiu et al. 2019). The model is as follows:

$$Y_t = P(\mu_t) \quad (1)$$

$$E(Y_t) = \mu_t \quad (2)$$

$$\begin{aligned} \text{Log}(\mu_t) = & \alpha + \beta C_{x,l} + \sum s(\text{Meteorological factor}) \\ & + \text{ns}(\text{Time}, 5*7) + f(M) \end{aligned} \quad (3)$$

where Y_t is the number of mumps caused by exposure to air pollutants on day t ; μ_t is the average of Y_t ; α is the intercept; $C_{x,l}$ is the cross-basis function of exposure to O₃ for l day; β is the regression coefficient; $s()$ is natural cubic spline function; *Meteorological factors* include relative humidity, precipitation, temperature, sunshine hours, air pressure, wind speed, and evaporation; *Time* is a time series; *M* is a monthly variable. The degrees of freedom (df) of meteorological factors are determined by the Quasi-Poisson Information Criterion (Q-

AIC). We set the degrees of freedom to 7 per year for *Time* in order to address the long-term trend and seasonal fluctuation (Peng et al. 2006).

Considering the strong seasonality of mump outbreaks, we conducted subgroup analyses of season to evaluate the season-specific effects of O₃ exposure on mumps. A year was divided into a warm season (April to September) and a cool season (October to March).

Moreover, we developed two-pollutant models and performed subgroup analyzes to explore the potentially superimposing or synergistic effects of O₃ and other air pollutants, including SO₂, NO₂, PM_{2.5}, and PM₁₀. The formula of the two-pollutant model is as follows:

$$\begin{aligned} \text{Log}(\mu_t) = & \alpha + \beta C_{x,l} + \gamma C_{y,l} \\ & + \sum s(\text{Meteorological factor}) \\ & + \text{ns}(\text{Time}, 5*7) + f(M) \end{aligned} \quad (4)$$

where $C_{y,l}$ represents the cross-basis function of exposure to the second pollutant y (i.e., SO₂, NO₂, PM_{2.5}, or PM₁₀) and its lag e effects; γ is vector of coefficients; and please refer to Eq. (3) for the meanings of the other variables. For the subgroup analyzes, we divided the whole dataset into three groups (i.e., low, moderate, and high) according to the 1/3 and 2/3 quantiles of a second pollutant concentrations. For each group, we developed a separate DLNM model based on Eq. (3). The estimated RR for each group was then comparatively evaluated to examine potentially synergistic effect.

After obtaining the estimates of each regression coefficients K (e.g., β , γ), we then calculate the relative risks (RR) as follows:

$$RR = e^{K*C} \quad (5)$$

where C represents the increase of air pollution exposure (set to 10 $\mu\text{g}/\text{m}^3$ in the present study), the effects of air pollution exposure on mumps is expressed as RR with 95% confidence interval (95% CI). We then compared the RR under different conditions to illustrate the impact of O₃ on mumps and explored the potential synergistic effects between O₃ and other pollutants.

Moreover, we conducted sensitivity analyzes to evaluate the robustness of the modeling results. We first changed the number of lag-days of cross-basis function (5–30 days) to estimate the maximum lag days. We then changed the degrees of freedom of the time-series and temperature to smooth the effect of long-term trend. Finally, we randomly sampled 15% of the data to establish a validation data set, with the remaining 85% of the data for building the model.

All our analyzes were performed using R (version 4.0.2) with packages “dlnm” (Gasparrini 2011), “splines” (R Development Core Team 2012), and “mgcv” (Wood 2011).

Table 1 Description of air pollution and meteorological factors in Chongqing, 2013–2017

Variables ^a	Mean	SD ^b	Min	Percentiles			Max
				25%	50%	75%	
NO ₂ (μg/m ³)	41.4	12.2	13.1	32.6	40.0	48.6	91.9
SO ₂ (μg/m ³)	19.2	12.2	4.1	11.0	15.3	23.6	78.3
O ₃ (μg/m ³)	41.5	28.5	3.1	18.5	36.1	57.9	216.5
PM _{2.5} (μg/m ³)	55.9	34.6	7.5	31.9	45.6	69.1	214.5
PM ₁₀ (μg/m ³)	86.5	47.5	13.0	53.2	74.7	106.0	296.6
CO (mg/m ³)	1.0	0.3	0.3	0.8	1.0	1.2	2.8
Temperature (°C)	16.8	7.5	-0.4	10.0	17.3	22.8	32.0
Humidity (%)	75.1	9.5	41.3	68.7	75.0	82.0	98.0
Precipitation (mm)	3.2	7.5	0.0	0.0	0.2	2.7	65.5
Wind speed (m/s)	1.8	0.5	0.3	1.4	1.8	2.1	4.2
Evaporation (mm)	2.3	1.4	0.1	1.2	1.8	3.1	7.2
Pressure (hPa)	953.6	7.8	927.1	947.5	953.3	959.8	976.6
Sunshine duration (hour)	3.8	3.6	0.0	0.2	2.8	6.8	11.5

^a Daily average; ^b Standard deviation

Results and discussion

Correlational analysis

The average concentrations of NO₂, SO₂, O₃, PM_{2.5}, PM₁₀, and CO were 41.4 μg/m³, 19.2 μg/m³, 41.5 μg/m³, 55.9 μg/m³, 86.5 μg/m³, and 1.0 mg/m³, respectively. The average temperature was 16.8 °C, and the average relative humidity was 75.1% (Table 1). The spearman correlations between the prevalence of mumps, air pollutants, and meteorological factors are shown in Figure S1. Among them, the prevalence of

mumps was significantly positively correlated with O₃ and SO₂, with correlation coefficients of 0.17 and 0.05, respectively ($P < 0.05$). While, the prevalence of mumps was significantly negatively correlated with NO₂, CO, PM_{2.5}, and PM₁₀, with correlation coefficients of -0.07, -0.16, -0.08, and -0.03, respectively ($P < 0.05$).

Figure 2 shows the seasonal fluctuations of mumps cases, daily average O₃ concentration and daily average temperature. The daily prevalence of mumps showed a clear seasonality. We observed that the prevalence of mumps was the highest in summer, followed by winter. The O₃ concentrations showed a

Fig. 2 Time series of mumps cases, O₃ concentrations, and air temperature during 2013–2017

similar temporal pattern, which were the highest in hot seasons. We found a total of 49,258 confirmed cases of mumps during 2013–2017, consisting of 30,860 and 18,398 cases in the warm and cool seasons, respectively. The average number of cases per day was approximately 27. In 535 days of the study period, the number of cases exceeded 30 per day.

During the study period, the high levels of O₃ were due to photochemical reactions and elevated concentrations of volatile organic compounds (VOCs) and NO_x from industrial and transport emissions (Lee et al. 2019; Su et al. 2018). A plenty of previous studies have estimated the association between air pollution and respiratory infectious diseases. A study in South Korea found that the prevalence of tuberculosis was highly correlated with SO₂ exposure (Hu et al. 2018), and several studies reported that particulate matters could increase the risk of influenza (Clifford et al. 2015; DeFelice 2020; Feng et al. 2016).

Distributed lag non-linear models (DLNM)

Figure S2 summarizes the most prominent single-day lag effect of each air pollutant on the prevalence of mumps. Only O₃ exhibited significant effects on the prevalence of mumps ($P < 0.01$). Our results are inconsistent with the previous studies with respect to the adverse health effects from exposure to particulate matters. The previous studies on air pollutants and respiratory infectious diseases considered that atmospheric particles could carry viruses and hence aggregated the ability of viruses to infect respiratory tract (Chen et al. 2018; Cruz-Sanchez et al. 2013; Griffin 2007). More efforts such as meta-analyses are required to investigate the spatiotemporal heterogeneity of the associations.

Among different lags of days, we found that the increase in O₃ concentrations was significantly associated with the increased prevalence of mumps during the 7-day lag time window ($P < 0.01$).

The DLNM results show that the lag-effect of O₃ exposure on the prevalence of mumps is in a positive and nonlinear manner. The complete lag-curve shows a trend of rising in the first 4 days and then falling thereafter. The exposure-response effect was not statistically significant on the first day of exposure due to the lag effect. In the time lag of 4 days, the highest effect of the O₃ exposure emerged, with the maximum RR of 1.006 (95% CI: 1.003–1.007). The effect of O₃ exposure on the prevalence of mumps gradually decline afterwards and became negligible on the 7th day, with RR of 1.0001 (95% CI: 0.997–1.005; Fig. 3).

In the previous study from Wuhan, no significant effect of O₃ on the prevalence of mumps was found in the range of 7-day lag but a lag of 23 days (Hao et al. 2019). The difference in the lag days than our study might result from the large differences between Wuhan and Chongqing in geographical and climatic conditions, as well as local populations. A plenty

Fig. 3 Estimated relative risk (RR) and 95% CIs of mumps for a 10 µg/m³ increase of O₃ at lag-0 to lag-7 days

of studies found that temperature had an effect on prevalence of mumps (Ho et al. 2015; Onozuka and Hashizume 2011). A recent study from the western China indicated that precipitation and wind speed also had effect on the prevalence of mumps (Zha et al. 2020). Warm and humid weather would promote MuV reproduction and evolution, enhancing the infection risk (Nenna et al. 2017). More efforts are required to investigate the combination with MuV transmission mechanism, population immunity model, and more epidemiological evidence.

Considering the accumulated effects of air pollution exposure, we calculated the cumulative effect of O₃ exposure on mumps (Fig. 4). We found that the RR for the prevalence of mumps increased rapidly within 1–5 days, which was 1.022 (95% CI: 1.011–1.032), indicating that 10 µg/m³ increase in daily O₃ exposure during 5-day lag would lead to the increase in the prevalence of mumps by 2.2%. The cumulative effect caused by the O₃ exposure on the 6th to 7th days would gradually decline, while the growth rate of RR also gradually leveled off. There was no significant association between O₃ and the prevalence of mumps after 7-day lag, and the cumulative RR of O₃ short-term exposure within 7 days was 1.025 (95% CI: 1.013–1.038) for 10 µg/m³ increase in the daily O₃ concentration.

Figure 5 shows the results of subgroup analyses of season using the single-day-lag models. The effects of O₃ exposure on mumps were statistically insignificantly different between the warm and cool seasons, with cumulative RR of 1.034 (95% CI: 1.015–1.053) and 1.066 (95% CI: 1.029–1.103), respectively. The RR for each lag-day was insignificantly different between the cool and warm seasons neither. In the warm season, the RR first increased from lag-0 to lag-4 day, and then gradually decreased till lag-7 day. In the cool season, the RR remained steady from lag-0 to lag-6 day, followed by an increase till lag-7 day.

It should be noted that mumps outbreak occurred relatively more frequently in the warm season than the cold season (Fig. 2), which is consistent with the results of the previous study on mumps in China (Cui et al. 2014). The season-specific effects

Fig. 4 Cumulative Relative Risk (RR) and 95% CIs of mumps for a $10 \mu\text{g}/\text{m}^3$ increase in O_3 exposure

of O_3 exposure on mumps were comparable to those reported in the previous studies (Kai et al. 2018; Qing et al. 2020). Although the RR was insignificantly different between these two seasons, more pollens in spring and more infectious diseases in winter might exacerbate the risk of mumps (Qing et al. 2020). In addition, we found that the single-day RR became significant at lag-6 day in the cool season, compared to lag-2 day in the warm season. Warm conditions are suitable for virus survival and replication, causing people more susceptible to infection (Averett 2016; Hess et al. 2014).

In the results of the single-pollutant models, we found significant association of mumps with O_3 exposure, but none for all the other regularly monitored air pollutants (Figure S2). In order to evaluate the synergistic effects between the other pollutants and O_3 , we developed two-pollutant models and performed subgroup analyzes. Figure 6 shows the cumulative RR calculated by using the single- and two-pollutant models.

After inclusion of a second pollutant, the cumulative RR for O_3 did not change significantly. For the subgroup analyzes, while the RR for O_3 was slightly different among the three groups, the highly overlapped confidence intervals represent insignificant difference (Figure S3). Figure S4 shows the single-day RR for a $10 \mu\text{g}/\text{m}^3$ increase of a second pollutant (i.e., $\text{PM}_{2.5}$, PM_{10} , SO_2 and NO_2 , respectively) in the two-

pollutants models. The RR for the second pollutant was insignificant or marginally significant through the lag days. The analysis results therefore suggest negligibly synergistic effects between O_3 and other pollutants.

Currently, there still lacks research clearly explaining the mechanism of O_3 exposure affecting the pathogenesis of mumps. Virus transmissions mainly occur through inhalation of aerosol particles, respiratory droplets, and body contact (Meselson 2020; van Doremalen et al. 2020). People under enhanced oxidative stress are more vulnerable to virus infection (Ciencewicki et al. 2008). O_3 can react with unsaturated fatty lipids in the respiratory tract to produce reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), lipid ozonation products, and lipid peroxides. Furthermore, oxidative stress can cause DNA damage and protein adducts, as well as apoptosis induced by mitochondrial dysfunction (Jaspers et al. 2005). The fact that the increase in O_3 exposure associated with the onset of mumps might be due to immune damage. Exposure to O_3 can reacts directly with unsaturated fatty lipids in the respiratory tract to produce reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), lipid

Fig. 5 Estimated relative risk (RR) and 95% CIs of mumps for a $10 \mu\text{g}/\text{m}^3$ increase of O_3 at lag-0 to lag-7 days in the warm (April to September) and cool (October to March) seasons

Fig. 6 Cumulative relative risk (RR) of mumps for a $10 \mu\text{g}/\text{m}^3$ increase of O_3 . The RR for “ O_3 ” is estimated by using the one-pollutant model. The RR for “+X” (i.e., SO_2 , NO_2 , $\text{PM}_{2.5}$, and PM_{10}) is estimated by using the two-pollutant models (Eq. 4), i.e., the RR for O_3 in the presence of a second pollutant in the model

ozonation products, and lipid peroxides. It can cause oxidation of lipids and proteins in the lining fluid of the pulmonary airway (RTLFL) (Valacchi et al. 2004), as well as damage to the nasal cavity and oral mucosa (Carson et al. 1987; Kienast et al. 1994), thereby increasing the risk of MuV and respiratory diseases. As a consequence of the human upper respiratory tract infection, the respiratory immune system suffers certain damage, and the immune function of T cells to MuV become weakened, resulting in the spread of MuV from the lymph nodes (Rubin et al. 2015), increasing the risk of mumps.

Robustness of statistical estimates

In the validation analysis, the model showed reasonable predictive performance. The model parameterized with the training data set decently predicted the prevalence of mumps, with the correlation coefficient of 0.87 and the root mean square error of 9.63. In the sensitivity analysis, when we changed the degrees of freedom of time per year from 7 df to 6 df and 8 df, the model estimates remained steady, indicating robust modeling results (Table 2).

With respect to the models used in this study, GAM has been commonly used to investigate the relationship between air pollution exposure and respiratory infectious diseases (Chen et al. 2016; Wang et al. 2020; Zhu et al. 2019), while DLNM couples the hysteresis and nonlinear relationship. When simulating the association between air pollution and respiratory infectious diseases, this modeling method shows better goodness of fitting and can simultaneously describe the hysteresis and nonlinear effects, which compensates the lack of the hysteresis model in capturing the nonlinear relationship (Braga et al. 2001; Zeng et al. 2020).

Under the current air quality guideline in China, the safe thresholds are 160 and 200 $\mu\text{g}/\text{m}^3$ for the daily maximum 8-hour average concentration and hourly average concentration, respectively (Ministry of Ecology and Environment of the People's Republic of China 2012). Both thresholds are higher than those recommended by the WHO. In the 14th Five-Year plan of China (2021–2025), it is proposed to curb the increasing trend of O_3 through reducing the emissions of NO_x and VOCs (Central People's Government of the People's Republic of China. 2021). Given the adverse health effects of O_3 exposure reported in the present and previous studies (Kai et al. 2018; Niewiadomska et al. 2020), from a conservative

perspective, the air quality guideline in China may need to be refined for lowering health burden due to O_3 exposure. An early warning system can be established to issue notifications of reducing outdoor activities in O_3 pollution seasons.

This study has several limitations. Firstly, we used the average concentrations observed at the air quality stations in Chongqing to evaluate the exposure levels, without considering the variation personal exposure levels (Zeger et al. 2000). Most of these monitoring stations were located in the districts with high population densities, which reasonably represented the average ambient exposure levels of the local population. Nevertheless, the exposure levels of each individual might be considerably different from the average ambient exposure levels due to variation in personal daily activities and indoor-outdoor air exchange rates. The personal exposure levels could be validated and refined by using portable air quality monitors (Dessimond et al. 2021; Schmitz et al. 2019). Secondly, there existed time gaps between the onset of a patient and the patient's hospital visit. Some patients with mild symptoms might not visit hospitals, which would also introduce uncertainty to the exposure-response relationship (Chen et al. 2017; Feng et al. 2016). Finally, we were unable to collect individual information, including personal lifestyles (e.g., smoking and indoor ventilation frequency), age, and gender. For the elderly, pregnant women, and children, weaker respiratory immune systems tended to induce higher susceptibility to mumps when they were exposed to air pollution (Capraz et al. 2017; Chen et al. 2019). In future research, patients can be divided into various groups based on personal information to investigate the association between air pollution and the risk of mumps.

Conclusions

To the best of our knowledge, this is the first study of using DLNM to examine the association between O_3 exposure and prevalence of mumps in a populous and humid megacity. On the basis of the DLNM results, we found that the risk of mumps was significantly positively associated with the O_3 concentrations within a 7-day lag time window. The relative risk of mumps increased by 2.5% for 10 $\mu\text{g}/\text{m}^3$ increase in the O_3 concentrations. The results of this study advance the understanding of the impact of O_3 exposure on the risk of mumps, suggesting the importance of controlling O_3 pollution for protecting public health.

Table 2 Cumulative RR of mumps in different time-series in O_3 exposure

df	Cumulative RR	95% CI
6	1.018	1.006-1.029
7	1.025	1.013-1.038
8	1.027	1.015-1.039

Abbreviations O_3 , Ozone; MuV, Mumps Virus; RR, Relative Risk; WHO, World Health Organization; RTLFL, Respiratory Tract Lining Fluid; DLNM, Distributed Lag Non-linear Model; GAM, Generalized Additive Model; CI, Confidence Intervals; SO_2 , Sulfur Dioxide; NO_2 , Nitrogen Dioxide; CO, Carbon Monoxide; $\text{PM}_{2.5}$, Fine Particulate

Matter; PM₁₀, Respirable Particulate Matter; VOCs, Volatile Organic Compounds; df, degrees of freedom

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Data and materials availability The datasets used in this study can be provided by contacting the corresponding author.

Author contribution WX and WZ drafted the manuscript. HZ, CS, and BW provided extensive comments on this manuscript. WX and WZ participated in the data preparation and model coding. YZ designed research plan and revised manuscript. All authors had read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate As the data used in the present study included no personally identifiable information, individual informed consent was waived.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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