

Modification Effects of Ambient Temperature on Ozone-Mortality Relationships in Chengdu, China

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Abstract

A multitude of epidemiological studies have demonstrated that both ambient temperatures and air pollution are closely related to health outcomes. However, whether temperature has modification effects on the association between ozone and health outcomes is still debated. In this study, Three parallel time-series Poisson generalized additive models (GAMs) were used to examine the effects of modifying ambient temperatures on the association between ozone and mortality (including non-accidental, respiratory, and cardiovascular mortality) in Chengdu, China, from 2014 to 2016. The results confirmed that the ambient high temperatures strongly amplified the adverse effects of ozone on human mortality; specifically, the ozone effects were most pronounced at $>28^{\circ}\text{C}$. Without temperature stratification conditions, a $10\text{-}\mu\text{g}/\text{m}^3$ increase in the maximum 8-hour average ozone ($\text{O}_{3-8\text{hmax}}$) level at lag01 was associated with increases of 0.40% (95% confidence interval [CI]: 0.15%, 0.65%), 0.61% (95%CI: 0.27%, 0.95%) and 0.69% (95%CI: 0.34%, 1.04%) in non-accidental, respiratory, and cardiovascular mortality, respectively. On days during which the temperature exceeded 28°C , a $10\text{-}\mu\text{g}/\text{m}^3$ increase in $\text{O}_{3-8\text{hmax}}$ led to increases of 2.22% (95%CI: 1.21%, 3.23%), 2.67% (95%CI: 0.57%, 4.76%), and 4.13% (95%CI: 2.34%, 5.92%) in non-accidental, respiratory, and cardiovascular mortality, respectively. Our findings validated that high temperature could further aggravate the health risks of $\text{O}_{3-8\text{hmax}}$, thus mitigating ozone exposure will be brought into the limelight especially under the context of changing climate.

1. Introduction

It is universally acknowledged that air pollution has adverse effects on human health; among all air pollutants, particles with aerodynamic diameters less than $2.5\ \mu\text{m}$ ($\text{PM}_{2.5}$) and ground-level ozone are considered to be most extraordinarily associated with morbidity and mortality (Dimakopoulou et al., 2017; Vicedo-Cabrera et al., 2020; Zhang et al., 2019a, 2020b; Cohen et al., 2017). China, the largest developing country, is currently facing a serious situation regarding air pollution, and $\text{PM}_{2.5}$ and ozone are the first and second major pollutants, respectively (Kan et al., 2012; Wang, 2021). Over the past decades, most studies have focused on the health risks of $\text{PM}_{2.5}$; subsequently, a series of corresponding policies regarding $\text{PM}_{2.5}$ control and intervention measures have been implemented based on these research results, leading to the $\text{PM}_{2.5}$ level being effectively controlled in China (Lu et al., 2019; Maji et al., 2017). However, evidence concerning the adverse effects of ozone on health outcomes has been limited due to a lack of ozone data availability. No data were published concerning ozone before 2008. The Ministry of Ecology and Environment of the People's Republic of China set the subsequent ozone air quality standards, and ground-level ozone data have been available online since 2013 (<http://www.cnenc.cn/>). Compared with other countries, it is difficult to evaluate ozone standards in China due to the lack of sufficient evidence regarding the health effects of ozone. Recently, environmental monitoring observations have indicated that the concentration of $\text{PM}_{2.5}$ in the Sichuan Basin of China is decreasing yearly, whereas the concentration of surface ozone is increasing (Ning et al., 2017); these results aroused our concern regarding the health risks caused by ozone in this area.

The ambient temperature is another important health risk factor. Substantial epidemiological and toxicological literature has been published showing a clear and consistent association between exposure to adverse ambient temperature, especially in cases of hypothermia and hyperpyrexia, both of which can cause a series of acute health effects, including respiratory tract injury, chronic cardiovascular conditions, systemic inflammation, premature mortality and so on (Wang, 2021; Dimakopoulou et al., 2019; Qian et al., 2020). At the same time, the spatiotemporal distribution of ambient pollutants is affected by meteorological conditions, especially the ambient temperature (Zhang et al., 2019b); hence, ambient temperature and air pollution are generally highly correlated in many places and may symmetrically interact to affect health outcomes (Bae et al., 2020; Chen et al., 2014). Nonetheless, related studies about the modification effects of the ambient temperature on ozone-mortality relationships are rare, and published results have been inconsistent: some researchers have claimed a strong enhancement of ozone risks on health outcomes only under high temperature levels, whereas others have found outstandingly increases only under low temperature conditions, and some have validated relatively high ozone risks for both high and low temperatures (Iny et al., 2014; Kai et al., 2018; Ren et al., 2007). These inconsistencies may correspond to the different climate and topographic conditions, ozone distribution characteristics, demographic compositions, people's lifestyles, and education levels of diverse areas (Li et al., 2018). As the capital city of Sichuan Province, the population of Chengdu exceeded 16.04 million as of June 2018, and the city suffers serious ozone pollution, especially in summer (Yang et al., 2021). The modulatory effects of ambient temperatures on ozone-mortality relationships in this area are still unclear.

In the present study, we assessed ozone mortality risks on non-accidental, respiratory, and cardiovascular mortality in Chengdu, China, from 2014 to 2016. In addition, we explored whether the associations between ozone and non-accidental mortality as well as cause-specific mortality were modified by ambient temperature. To achieve this aim, three parallel time-series Poisson generalized additive models (GAMs) were used to estimate how the air temperature modulates the health risks of ozone on the three analyzed kinds of mortality.

2. Data And Methods

2.1 Data collection

We collected daily mortality data of Chengdu, China, for years 2014 through 2016 from the Chinese Centers for Disease Control and Prevention (CDC). Data were collected for non-accidental mortality [International Classification of Diseases, 10th revision (ICD-10) codes: A00-R99], cardiovascular mortality (ICD-10 codes: I00-I99), and respiratory mortality (ICD-10 codes: J00-J99).

The air pollution data used to obtain the ozone concentrations were retrieved from the Chengdu Environmental Monitoring Center. Previous studies have indicated that the daily maximum 8-hour average ozone ($O_{3-8hmax}$) concentration is more strongly associated with health outcomes than other metrics, such as the 1-hour maximum ozone concentration or the daily average ozone concentration (Yang et al., 2012). Consistent with the preceding studies, we therefore chose the daily $O_{3-8hmax}$ as the

ozone concentration indicator. $O_{3-8hmax}$ was averaged from the available monitoring results of six monitoring stations in Chengdu including three urban environmental monitoring stations (Jinquan Lianghe, Sanwayao and Shahepu), two traffic pollution monitoring stations (Shilidian, Liangjiaxiang), and one suburban environmental monitoring station (Lingyansi).

Daily meteorological data recorded during the same time period were retrieved from the China Meteorological Data Sharing Service System (<http://data.cma.cn/>). The daily surface meteorological data of Chengdu were obtained through station averages, mainly including the daily average temperature ($^{\circ}C$), daily average relative humidity (RH) (%), and daily average wind speed (m/s).

2.2 Statistical methods

We utilized three GAMs to assess how the air temperature modulates the health risks of $O_{3-8hmax}$ on health outcomes: an independent model, a nonparametric bivariate response surface model, and a stratification parametric model (Zhang et al., 2020b). First, we used an independent GAM to investigate the adverse health effects of $O_{3-8hmax}$ on non-accidental mortality, as well as cause-specific (respiratory and cardiovascular) mortality at different lag days. Model 1 can be expressed as follows:

$$\begin{aligned} \log[E(Y_t|X)] &= NS(Time, 3 * 7) + NS(RH, 3) + NS(Wind, 3) + NS(Temp, 3) + \text{as.factor}(DOW) \\ &+ \text{as.factor}(Holiday) + O_{3-8hmax,i} + \alpha \\ &= NS(Temp, 3) + O_{3-8hmax,i} + COVs \end{aligned}$$

(2)

where subscript t is the day of the observation; $E(Y_t|X)$ indicates the expected death counts on day t , and $NS(\cdot)$ denotes the natural cubic spline function. According to the preceding study (Yang et al., 2012), the Time variable was controlled with 7 degrees of freedom (df) per year to express a long-term trend. We also changed the df from 4 to 10 per year to test the robustness of the model in sensitivity analyses. At the same time, ($df=3$) was also used to control the current day's average relative humidity (RH) and mean wind speed ($Wind$), as well as the moving average daily mean temperature of the current and the previous day (lag01) (Zhang et al., 2020b). DOW and $Holiday$ are two categorical variables that represent the day of the week and the presence of a public holiday, respectively. The subscript i represent different lag days. We explored the adverse health effects of $O_{3-8hmax}$ on three types of mortality at different lag days which include both a single-day lag (from lag0 to lag4) and cumulative lags (using moving averages of the current day and the previous 1, 2, 3, or 4 days [lag01 to lag04]). α represents the intercept. In addition, $COVs$ is all other covariates.

Second, a nonparametric bivariate response surface model was adopted to visually examine the combining effects of both the ambient average temperature and $O_{3-8hmax}$ on three types of mortality. The model is described as follows:

$$\log[E(Y_t|X)] = ST(Temp, O_{3-8hmax}) + COVs \quad (1)$$

where $ST(\bullet)$ indicates the thin-plate spline functions. Statistics revealed that the adverse health risks of $O_{3-8hmax}$ on three types of mortality were strongest between the current and previous day (lag01) (as is described later in this study). Therefore, the daily $O_{3-8hmax}$ at lag01 was used in the follow-up research to effectively capture the overall effects. The $COVs$ are the same as those used in model 1.

Finally, we adopted a temperature-stratified parametric model to examine the heterogeneity of $O_{3-8hmax}$ risks across different temperature ambient temperature strata. Temperatures were categorized into high and low temperature levels and then to determine whether the $O_{3-8hmax}$ risks varied across different temperature strata. However, there is by no means uniform standard for choosing temperature cutoff points so far (Meng et al., 2012; Zhang et al., 2020b). According to previous research results, people feel more comfortable when the daily average temperature is near approximately 24°C and begin to feel uncomfortable due to heat when the daily average is >28°C (Ssl et al., 2019). Therefore, we chosen temperature cutoff points corresponding to the transition from comfort to discomfort with increasing heat (i.e., 24°C, 26°C, and 28°C), as outlined by Zhang et al. (2020b). Finally, we divided the temperature data into two strata, including high temperatures (above the cutoffs) and low temperatures (below the cutoffs). Then, we assessed how the $O_{3-8hmax}$ mortality risks varied among the different temperature levels using varied temperature cutoff points. Model 3 is given as follows:

$$\log[E(Y_t|X)] = \beta_1 O_{3-8hmax} + \beta_2 Temp_k + \beta_3 (O_{3-8hmax} : Temp_k) + COVs \quad (3)$$

where $Temp_k$ is the k -th temperature strata; β_1 and β_2 denote the main independent effects of $O_{3-8hmax}$ levels and daily average temperature, respectively; and β_3 refers to a vector of coefficients reflecting the conjunction effects between $O_{3-8hmax}$ and daily average temperatures; this vector was also adjusted for temperature $Temp_k$ within each temperature strata. The $COVs$ are the same as those used in model 1.

All statistical analyses were conducted with R 4.1.2. The estimated modulating effects and corresponding 95% confidence interval (CI) were showed as percentage changes in health outcomes with each 10- $\mu\text{g}/\text{m}^3$ increment in the $O_{3-8hmax}$ mass concentration.

3. Results

Table 1 summarizes the distributions of three types of mortality, meteorological factors, and $O_{3-8hmax}$ concentrations during the study period. There were considerable variations in the three mortality types, ranging from 144 to 430 non-accidental mortalities, 35 to 136 cardiovascular mortalities, and 23 to 121 respiratory mortalities. During the study period, the average temperature in Chengdu was $16.6 \pm 7.2^\circ\text{C}$, the average RH was $81.7 \pm 8.2\%$, and the average wind speed was 1.3 ± 0.5 m/s. Notably, the average daily $O_{3-8hmax}$ concentration was $119.9 \mu\text{g}/\text{m}^3$ that quite higher than those reported in some developed countries (Tao et al., 2016; Nyssanbayeva et al., 2019; Winiewski et al., 2021) and in other Chinese cities (Sui, et al., 2021; Zhang et al., 2006). According to the National Ambient Air Quality Standard (GB3095-

2012), the $O_{3-8hmax}$ concentrations exceeded the primary ($100 \mu\text{g}/\text{m}^3$) and secondary ($160 \mu\text{g}/\text{m}^3$) standard limits in 611 days and 280 days, respectively, and the corresponding over standard rates were 55.75% and 25.55%, respectively.

Table 1

Summary statistics of three types of mortality, meteorological factors, and $O_{3-8hmax}$ concentrations in Chengdu, China, from 2014~2016

Variable	Mean \pm SD	Minimum	Percentile			Maximum	Interquartile range
			25%	50%	75%		
Mortality							
Non-accidental	222 \pm 37	144	195	217	244	430	73
Cardiovascular	70 \pm 15	35	58	68	80	136	22
Respiratory	54 \pm 15	23	43	51	64	121	21
Meteorology							
Temperature ($^{\circ}\text{C}$)	16.6 \pm 7.2	-1.9	10.1	17.7	22.8	29.8	11.3
Relative humidity (%)	81.7 \pm 8.2	42.0	77.0	83.0	88.0	98.0	11.0
Wind speed (m/s)	1.3 \pm 0.5	0.3	1.0	1.2	1.5	3.4	0.5
Air pollution							
$O_{3-8hmax}$ ($\mu\text{g}/\text{m}^3$)	119.9 \pm 60.6	13.2	72.9	109.2	161.0	331.1	88.1
SD: standard deviation; $O_{3-8hmax}$: 8-hour maximum ozone concentration.							

Figure 1 illustrates the effects of percentage changes in $O_{3-8hmax}$ on three types of mortality at different lags. The most significant effects of $O_{3-8hmax}$ on the three types of mortality all appeared at a cumulative lag of one day (lag01). Therefore, lag01 $O_{3-8hmax}$ was used as the research object in subsequent studies. After the calculations, a $10\text{-}\mu\text{g}/\text{m}^3$ increase in $O_{3-8hmax}$ was found to lead to 0.40% (95% CI: 0.15%, 0.65%), 0.61% (95% CI: 0.27%, 0.95%) and 0.69% (95% CI: 0.34%, 1.04%) increases in non-accidental, respiratory and cardiovascular mortality, respectively.

Figure 2 graphically depicts the combined effects of the daily average temperature and $O_{3-8hmax}$ on non-accidental, cardiovascular, and respiratory mortality using three-dimensional visualization graphs. It is apparent that the combined effects were extremely complex. It is interesting to note that the non-accidental, cardiovascular and respiratory mortality all reached their maxima when high-temperature and high-concentration $O_{3-8hmax}$ coexisted, thus indicating that the high-temperature exacerbated/amplified the mortality risks of $O_{3-8hmax}$.

Table 2 summarizes the modulating effects of low/high temperatures on $O_{3-8hmax}$ -mortality relationships using varied temperature cutoff points. It should also be noted that the modulation effects of temperature on $O_{3-8hmax}$ -mortality were more pronounced in the high-temperature section than in the low-temperature section, and these effects were stronger than those obtained in the independent effect model. Furthermore, the higher the temperature cutoff points were, the greater the health risks of $O_{3-8hmax}$ were on the same kind of mortality at a high temperature level, indicating that high temperatures significantly aggravated the health risk of $O_{3-8hmax}$ on mortality compared to low temperatures.

Table 2

Percentage changes (%; 95% CI) in non-accidental, respiratory, and cardiovascular mortality per $10\text{-}\mu\text{g}/\text{m}^3$ increase in $O_{3-8hmax}$ under high/low temperature conditions using varied temperature cutoff points

Temperature Cut-offs	Temperature	Non-accidental	Respiratory	Cardiovascular
24°C	High	0.52 (0.28, 0.76) ^a	0.65 (0.14, 1.16) ^a	1.15 (0.71, 1.59) ^a
	Low	0.17 (0.00, 0.34) ^a	0.18 (0.14, 0.22) ^a	0.22 (-0.08, 0.52)
26°C	High	0.74 (0.37, 1.11) ^a	0.81 (0.37, 1.25) ^a	1.30 (0.62, 1.97) ^a
	Low	0.25 (0.10, 0.41) ^a	0.60 (-0.18, 1.39)	0.44 (0.17, 0.72) ^a
28°C	High	2.22 (1.21, 3.23) ^a	2.67 (0.57, 4.76) ^a	4.13 (2.34, 5.92) ^a
	Low	0.27 (0.12, 0.42) ^a	0.30 (-0.01, 0.60)	0.47 (0.20, 0.73) ^a
^a $P < 0.05$.				

The sensitivity analyses turned out that the $O_{3-8hmax}$ mortality risks kept robust to changing the *df* of the temporal smoothness per year (Fig. 3). The percentage changes derived per $10\text{-}\mu\text{g}/\text{m}^3$ increment in $O_{3-8hmax}$ significantly increased from 0.35% (95% CI: 0.24%, 0.46%) to 0.40% (95% CI: 0.27%, 0.53%) for non-accidental mortality, 0.48% (95% CI: 0.26%, 0.70%) to 0.61% (95% CI: 0.35%, 0.87%) for respiratory mortality, and 0.62% (95% CI: 0.39%, 0.85%) to 0.69% (95% CI: 0.46%, 0.92%) for cardiovascular mortality when the *df* was changed from 4-10 per year.

4. Discussion

Ground-level ozone has become a compelling environmental problem that has drawn substantial attention worldwide (Stocker et al., 2013). Assessing ground-level ozone health effects could provide additional evidences for policymaking on the topic of ozone control measures, particularly under the background of climate change (Madaniyazi et al., 2016). Our findings proved that exposure to ground-level $O_{3-8hmax}$ were positively associated with non-accidental mortality as well as cardiovascular and respiratory mortality in Chengdu, China, during the study period. Furthermore, our study further validated

that high-temperature significantly amplified $O_{3-8hmax}$ mortality risks on the three analyzed mortality types. In particular, there existed a consistent pattern of increasing $O_{3-8hmax}$ mortality risks as we progressively adopted higher cutoffs for high-temperature category.

It is worth noting that the average daily $O_{3-8hmax}$ concentration was $119.9 \mu\text{g}/\text{m}^3$ and has a high ozone exceeding standard rate in Chengdu during the study period. From the perspective of air-pollution meteorology, there exist two key factors leading to air pollution: one is the excessive emission of air pollutants and secondary transformation, and the other is the dilution and diffusion of air pollutants by the unfavorable meteorological conditions (Cai et al., 2017). As we all known, ozone, as a secondary pollutant, is widespread in the atmospheric troposphere and mainly produced by photochemical reactions of precursors [nitrogen oxides and volatile organic compounds (VOCs)]; the concentration of ground-level ozone are influenced by anthropogenic and natural emissions and by chemical, physical, and biological processes (Lamarque et al., 2013). The anthropogenic VOCs are mainly come from incomplete combustion in motor vehicle exhaust, the volatilization of oil and gas coatings, and industrial emissions (Rd et al., 2021). As of June 2018, motor vehicle ownership had exceeded 3.89 million in Chengdu, and these vehicles produce plenty of nitrogen oxides and VOCs, which are conducive to the formation of ozone. On the other hand, Chengdu is located in the Sichuan Basin and is thus affected by the topography of the Qinghai-Tibetan Plateau; the average wind speed in the Sichuan Basin is low year-round, and the frequency of static and stable weather is high. These conditions are unfavorable to the diffusion or dilution of ground-level ozone (Zhang et al., 2019b). These high precursor concentrations and poor air diffusion conditions ultimately synergistically lead to high ozone pollution concentrations in Chengdu. Therefore, Chengdu should strengthen its air quality control, reduce its emission of ozone precursors and formulate corresponding motor vehicle control and dispatching policies according to the changing meteorological conditions.

The temperature stratification results showed that the health risks of $O_{3-8hmax}$ were more prominent at high temperature levels than at low temperature levels. For instance, one days where temperatures exceeded 24°C , a $10\text{-}\mu\text{g}/\text{m}^3$ increment in $O_{3-8hmax}$ increased mortality risks of non-accidental, respiratory, and cardiovascular by 0.52%, 0.65%, and 1.15%, respectively. The corresponding risks were 0.17%, 0.18%, and 0.22%, respectively, under low-temperature conditions ($<24^\circ\text{C}$). These results keep consistent with some previous findings that $O_{3-8hmax}$ mortality risks were more prominent in warm season (or summer half year) than in cold season (or winter half year) (Gryparis et al., 2004; Sun et al., 2018). Some previous studies considered the exposure pattern to be an important factor affecting the results (Bell and Michelle et al., 2004). Chengdu city is located in southwestern China and has a subtropical climate. In Chengdu, the warm season is relatively mild, and few extreme weather events occur. For instance, the average warm-season temperature is 20.93°C . People therefore have passion for staying outdoors and open windows in these mild temperatures, which might increase the exposure of the population to ambient ozone (Wong et al., 2001). In contrast, people prefer stay at home rather than go out in cold season, especially in winter, due to the bitter cold outdoor temperatures and poor air quality, ultimately reducing human exposure to ambient ozone in this season.

Although the independent health risks of adverse temperatures or $O_{3-8hmax}$ on human health have been studied extensively and expounded in numerous studies, the interactions between temperature and $O_{3-8hmax}$ have been explored only in fragments, and the results remain controversial (Ren et al., 2007; Shi, et al., 2020; Rainham et al., 2003). Only some studies have found interactive effects, while others have not. These discrepancies mainly result from environmental and climatic conditions, acclimatization, education attainment, infrastructures, etc (Zhang et al., 2020b). Furthermore, the analytical methods used in various studies would lead to the inconsistency of results. Compared with previous studies, we divided temperatures into two levels (low and high temperatures) by using different temperature thresholds corresponding to comfort and discomfort. Our findings further support the notion that high concentration ozone and high temperatures mutually interact to affect public health. The evidence from our study indicated the higher the temperature cutoff points were, the greater the health risks of $O_{3-8hmax}$ were on the same kind of mortality at a high temperature level. Therefore, heat exposure may exacerbate physiological responses to short-term ozone exposure. For instance, each $10\text{-}\mu\text{g}/\text{m}^3$ increase in $O_{3-8hmax}$ concentration increased mortality risks by 0.74%, 0.81% and 1.30% in non-accidental, respiratory, and cardiovascular mortality under high-temperature ($>26^\circ\text{C}$) conditions; the corresponding risks were 2.22%, 2.67% and 4.13% when chosen 28°C as the temperature cutoff. As a warmer climate will likely increase individual susceptibility to ambient ozone exposure. As a result, it will become even more important to mitigate ozone exposure in the future (Tao et al., 2012; Vicedo-Cabrera et al., 2020).

The mechanisms by which the ambient temperature causes modulation effects on the relationships of ozone on human health remain unclear. There are several possible underlying mechanisms that explain this phenomenon. High temperatures are a well-known cause of heat-related mortality and can thus affect the physiological and psychological stress of the human body and aggravate many pre-existing diseases (Rainham et al., 2003). Furthermore, high temperatures are a necessary meteorological condition for ozone generation. Extreme high temperatures may further aggravate the generation rate of ozone and subsequently increase the health risks posed by ozone to the population. Ozone is a potent oxidant capable of generating reactive oxygen species/free radicals in lung cells, thus leading to the promotion of oxidative stress, inducing acute airway inflammation and damaging biomolecules (Lodovici and Bigagli., 2011; Ahmad et al., 2005). The inflammation of pulmonary tissues could further induce a spectrum of mediators and alter cardiac functions or the irritant receptor-mediated stimulation of parasympathetic pathways (Watkinson et al., 2001), making people more vulnerable to the effects of ozone variability. Therefore, both high-temperature and high-concentration ozone may interact to synergistically affect people health.

Some limitations of this study should be acknowledged. First, we utilized mortality data from only a 3-year period, and the statistical power was thus reduced. Second, we had no access to sub-categorical mortality characteristics, such as age, sex, educational background, work status, or the air conditioning utilization rate. Iny et al. (2014) proved that air conditioning can mitigate the mortality risks caused by ozone exposure in 97 US cities, especially during the warm season. Unfortunately, we did not collect the relevant data mentioned above, and this limited our ability to link potentially sensitive subpopulations.

Third, similar to most previous time-series studies (Bae et al., 2020; Shin et al., 2020), we only collected available outdoor monitoring data to represent personal exposure to ambient ozone, but not collected ozone concentration information in the indoor environments where people spend more time, and this omission could have biased the assessment accuracy obtained for ozone risks, resulting in a large exposure measurement error (Maji et al., 2021).

5. Conclusions

In conclusion, high temperatures strongly amplified the adverse health risks of $O_{3-8hmax}$ on non-accidental mortality as well as cause-specific mortality (including respiratory and cardiovascular mortality) in Chengdu, China. The results validated that reducing $O_{3-8hmax}$ emissions, especially in hot weather, would benefit public health. These findings improve our cognition for the short-term health risks of ozone and offer substantial reference information for policymaking regarding ground-level ozone control and adaptation strategies with the aim of protecting public health.

Declarations

Conflicts of Interest:

The authors declared that they have no conflicts of interest to this work.

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Ethical Approval

Not applicable

Consent to Participate

Not applicable

Consent to Publish

Not applicable

Author contributions

Q.T. and S.W. designed the research; C.Z., W.H., and X.F. collected and analyzed the data; Y.Z., J.X. and P.M. wrote the paper.

Availability of data and materials

Not applicable

References

1. Ahmad S, Ahmad A, McConville G et al (2005) Lung epithelial cells release ATP during ozone exposure: signaling for cell survival. *Free Radic Biol Med* 39(2):213–226
2. Bae S, Lim YH, Hong YC (2020) Causal association between ambient ozone concentration and mortality in Seoul, Korea. *Environmental research*, 182(Mar.):109098.1-109098.5
3. Bell ML (2004) Ozone and short-term mortality in 95 US urban communities, 1987-2000. *JAMA* 292(19):2372–2378
4. Cai W, Li K, Liao H et al (2017) Weather conditions conducive to Beijing severe haze more frequent under climate change. *Nature Climate Change* 7(4):257–262
5. Chen L, Shi M, Gao S et al (2017) Response to comment on "Assessment of population exposure to PM 2.5 for mortality in China and its public health benefit based on BenMAP". *Environmental Pollution*, 221(FEB.):311
6. Renjie C, Jing C, Xia M et al Ozone and Daily Mortality Rate in 21 Cities of East Asia: How Does Season Modify the Association?. *American Journal of Epidemiology* 2014: 180(7):729–736
7. Cohen AJ, Brauer B et al (2017) Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 389(10082):1907–1918
8. Dimakopoulou K, Grivas G, Samoli E et al (2017) Determinants of personal exposure to ozone in school children. Results from a panel study in Greece. *Environ Res* 154:66–72
9. Gryparis A, Forsberg B, Katsouyanni K et al (2004) Acute Effects of Ozone on Mortality from the "Air Pollution and Health. *American Journal of Respiratory & Critical Care Medicine* 170(10):1080–1087
10. Iny J (2014) Effect modification of ozone-related mortality risks by temperature in 97 US cities. *Environ Int* 73(1):128–134
11. Zhang J, Qi C, Wang Q et al (2019a) The acute health effects of ozone and PM2.5 on daily cardiovascular disease mortality: A multi-center time series study in China. *Ecotoxicol Environ Saf* 174(15):218–223
12. Kan H, Chen R, Tong S (2012) Ambient air pollution, climate change, and population health in China. *Environ Int* 42(none):10–19
13. Kai C, Wolf K, Hampel R et al (2018) Does temperature-confounding control influence the modifying effect of air temperature in ozone–mortality associations? *Environmental Epidemiology* 2(1):1–7

14. Li Y, Shang Y, Zheng C et al (2018) Estimated Acute Effects of Ozone on Mortality in a Rural District of Beijing, China, 2005–2013: A Time-Stratified Case-Crossover Study. *Int J Environ Res Public Health* 15(11):2460
15. Ssl A, Aha B, Es A (2019) Using simulation methods to investigate the impact of urban form on human comfort. Case study: Coast of Baltim, North Coast, Egypt. *Alexandria Engineering Journal* 58(1):273–282
16. Lodovici M, Bigagli E, Luceri C et al (2011) Protective Effect of Resveratrol against Oxidation Stress Induced by 2-Nitropropane in Rat Liver, vol 02. *Pharmacology & Pharmacy*, pp 228–234. 3
17. Lu X, Lin C, Li W et al (2019) Analysis of the adverse health effects of PM_{2.5} from 2001 to 2017 in China and the role of urbanization in aggravating the health burden. *Sci Total Environ* 652(20):683–695
18. Madaniyazi L, Nagashima T, Guo Y et al (2016) Projecting ozone-related mortality in East China. *Environ Int* 92–93:165–172
19. Maji KJ, Dikshit AK, Arora M et al (2017) Estimating premature mortality attributable to PM_{2.5} exposure and benefit of air pollution control policies in China for 2020. *Sci Total Environ* 612:683
20. Maji KJ, Namdeo A (2021) Continuous increases of surface ozone and associated premature mortality growth in China during 2015-2019. *Environ Pollut* 269C:116183
21. Xia M, Zhang Y, Zhao Z et al (2012) Temperature modifies the acute effect of particulate air pollution on mortality in eight Chinese cities. *Sci Total Environ* 435–436:215–221
22. Ning G, Wang S, Ma M et al (2017) Characteristics of air pollution in different zones of Sichuan Basin, China. *Sci Total Environ* 612:975
23. Nyssanbayeva AS, Cherednichenko AV, Cherednichenko AV et al (2019) Temporal dynamics of ground-level ozone and its impact on morbidity in Almaty city in comparison with Astana city, Kazakhstan. *Int J Biometeorol* 63(17):1381–1392
24. Qian X, Zbs B, Yan TA et al (2020) Impacts of urbanization on the temperature-cardiovascular mortality relationship in Beijing, China. *Environ Res* 191:110234
25. Rainham D, Smoyer-Tomic KE (2003) The role of air pollution in the relationship between a heat stress index and human mortality in Toronto. *Environ Res* 93(1):9–19
26. Ren C, Williams G, Morawska L et al (2007) Ozone modifies associations between temperature and cardiovascular mortality: analysis of the NMMAPS data. *Epidemiology* 18(4):255–260
27. Rd A, Hong LB, Yu FC (2020) Quantifying the anthropogenic and meteorological influences on summertime surface ozone in China over 2012–2017. *Science of The Total Environment*,754
28. Shi W, Sun Q, Du P et al (2020) Modification Effects of Temperature on the Ozone-Mortality Relationship: A Nationwide Multicounty Study in China. *Environ Sci Technol* 54(5):2859–2868
29. Shin HH, Parajuli RP, Maquiling A et al (2020) Temporal trends in associations between ozone and circulatory mortality in age and sex in Canada during 1984–2012. *Sci Total Environ* 724:137944

30. Church J, Clark P, Cazenave A et al (2013) Sea Level Change: Chapter 13. *Encyclopedia of Ocean Sciences*, :179–184
31. Stocker TF, Qin D, Plattner GK et al (2014) *Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of IPCC the Intergovernmental Panel on Climate Change.*
publications_ipcc_fourth_assessment_report_wg1_report_the_physical_science_basis htm 18(2):95–123. http://www.ipcc.ch/publications_and_data/
32. Sui X, Zhang J, Zhang Q et al (2021) The short-term effect of PM_{2.5}/O₃ on daily mortality from 2013 to 2018 in Hefei, China. *Environ Geochem Health* 43(2):153–169
33. Sun Q, Wang W, Chen C et al (2018) Acute effect of multiple ozone metrics on mortality by season in 34 Chinese counties in 2013–2015. *J Intern Med* 283(5):481–488
34. Tao L, Zeng W, Lin H et al (2016) Tempo-Spatial Variations of Ambient Ozone-Mortality Associations in the USA: Results from the NMMAPS Data. *International Journal of Environmental Research & Public Health* 13(9):851
35. Tao Y, Huang W, Huang X et al (2021) Estimated acute effects of ambient ozone and nitrogen dioxide on mortality in the Pearl River Delta of southern China. *Environ Health Perspect* 120(3):393–398
36. Vicedo-Cabrera AM, Sera F, Liu C et al (2020) Short term association between ozone and mortality: global two stage time series study in 406 locations in 20 countries. *BMJ*,
37. Wang Q, He Y, Hajat S et al (2021) Temperature-sensitive morbidity indicator: consequence from the increased ambulance dispatches associated with heat and cold exposure. *International Journal of Biometeorology*, :1–10
38. Wang P (2021) China's air pollution policies: Progress and challenges. *Current Opinion in Environmental Science & Health* 19:100227
39. Watkinson WP, Campen MJ, Nolan JP et al (2001) Cardiovascular and systemic responses to inhaled pollutants in rodents: effects of ozone and particulate matter. *Environ Health Perspect* 109(Suppl 4):539–546
40. Winiewski O, Kozak W, Winiewski M (2021) The ground-level ozone concentration is inversely correlated with the number of COVID-19 cases in Warsaw, Poland. *Air Quality Atmosphere & Health* 14(8):1169–1173
41. Wong C, Ma S, Hedley A et al (2001) Effect of air pollution on daily mortality in Hong Kong. *Environ Environmental Health Perspectives* 109(4):335–340
42. Yang C, Yang H, Guo S et al (2012) Alternative ozone metrics and daily mortality in Suzhou: The China Air Pollution and Health Effects Study (CAPES). *Sci Total Environ* 426:83–89
43. Yang X, Wu K, Lu Y et al (2021) Origin of regional springtime ozone episodes in the Sichuan Basin, China: Role of synoptic forcing and regional transport. *Environ Pollut* 278(4):116845
44. Zhang Y, Huang W, London SJ et al (2006) Ozone and Daily Mortality in Shanghai, China. *Environ Health Perspect* 114(8):1227–1232

45. Zhang Y, Wang S, Zhang X et al (2020a) Temperature modulation of the adverse consequences on human mortality due to exposure to fine particulates: A study of multiple cities in China. Environ Res 185:109353
46. Zhang Y, Zhang X, Fan X et al (2020b) Modifying effects of temperature on human mortality related to black carbon particulates in Beijing, China. Atmospheric Environment, 243(JAN):117845
47. Zhang Y, Wang S, Fan X et al (2019b) A temperature indicator for heavy air pollution risks (TIP).Science of The Total Environment,678

Figures

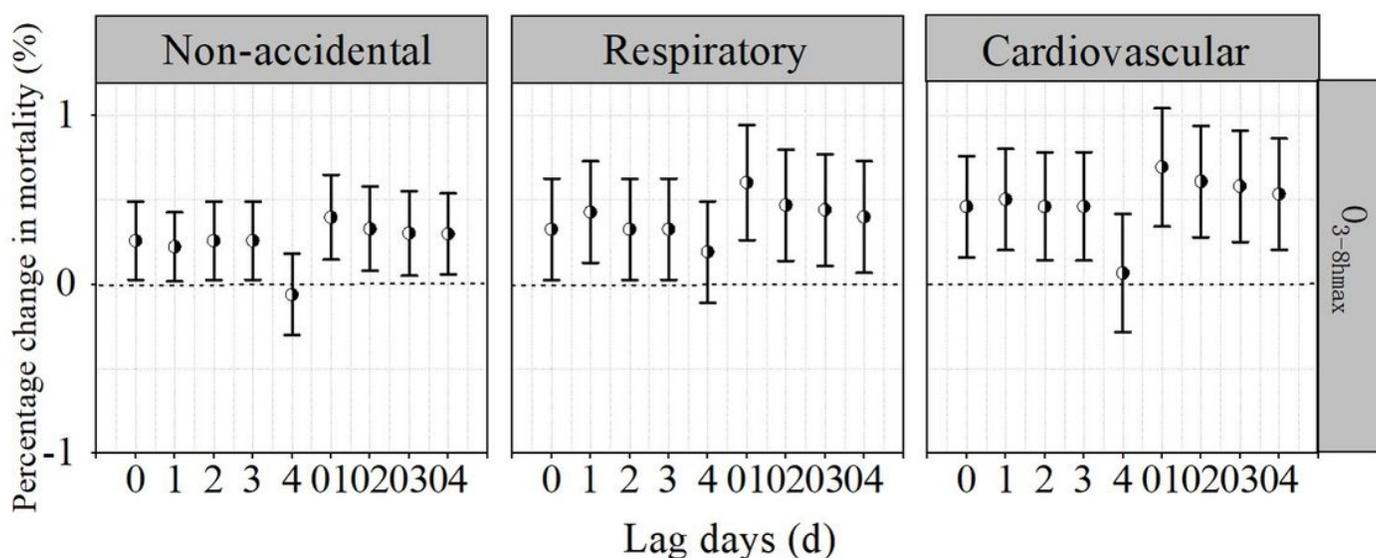


Figure 1

Percentage changes (%) in mortality for every 10- $\mu\text{g}/\text{m}^3$ increase in $\text{O}_{3-8\text{hmax}}$ at both single lag times of 0~4 days and cumulative lag times of 01~04 days

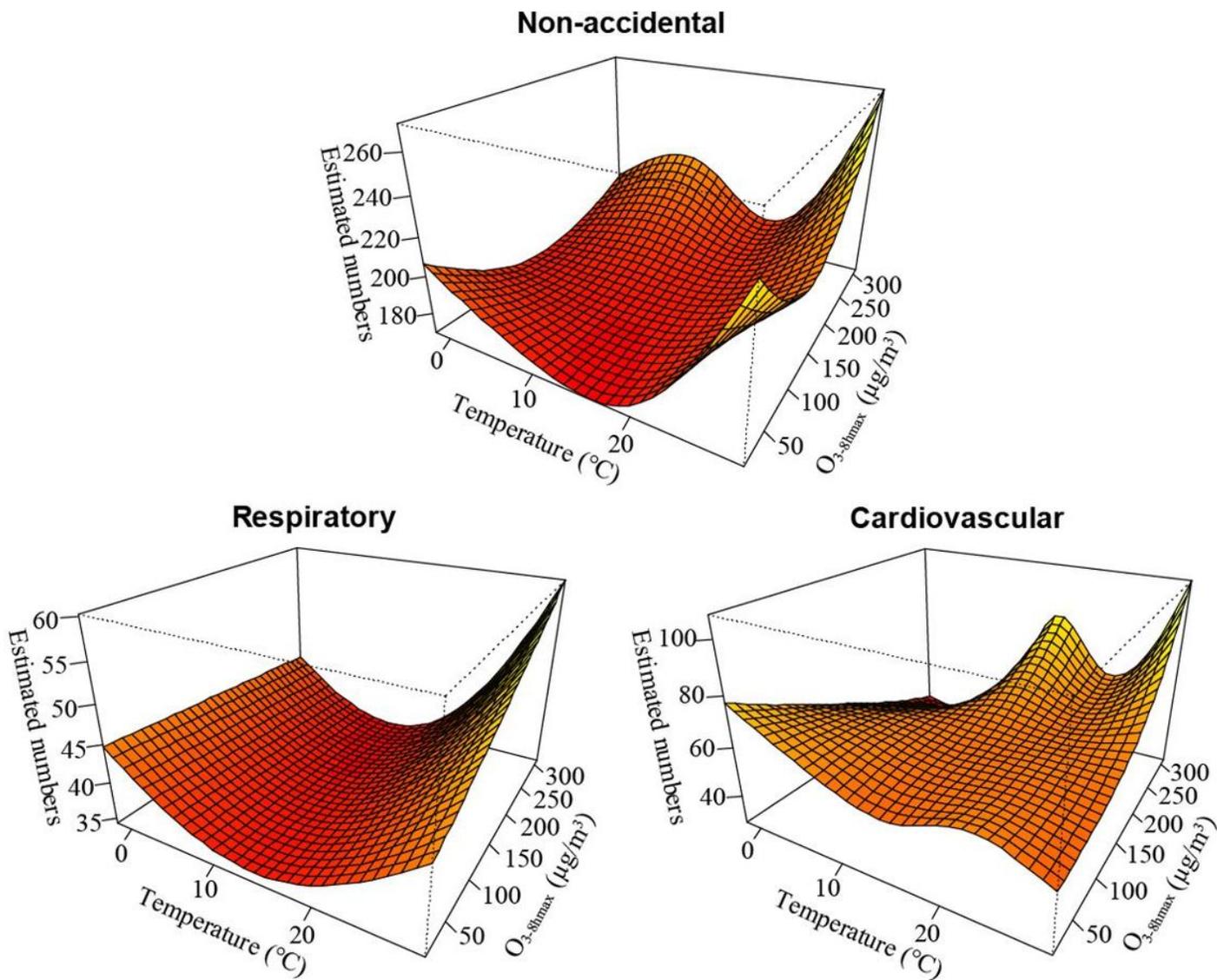


Figure 2

Bivariate response surfaces of air temperature and O_{3-8hmax} on health outcomes

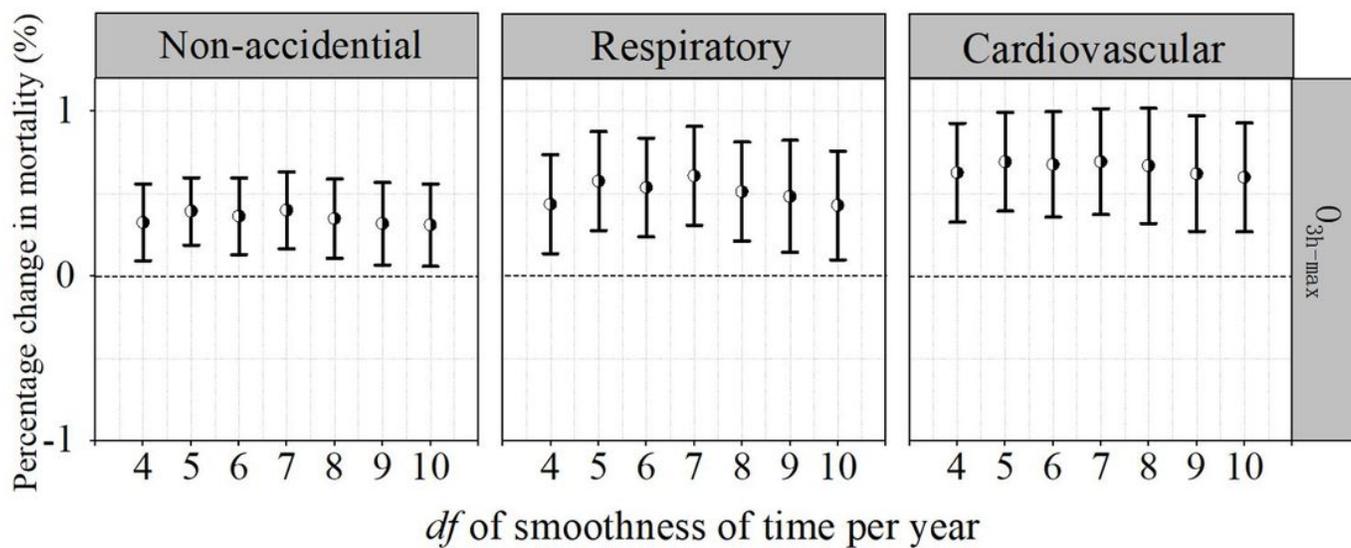


Figure 3

Sensitivity analyses of the health risks of $O_{3-8hmax}$ on three mortality types with different df values of the temporal smoothness per year.