Temperature-Modified Acute Effects of Ozone on Human Mortality — Beijing Municipality, Tianjin Municipality, Hebei Province, and Surrounding Areas, China, 2013–2018

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Summary
What is already known about this topic?
Ozone (\(O_3\)) is a weather-driven photochemical ambient pollutant, and its harm to human health may be affected by meteorological factors such as temperature. However, there is conflicting evidence regarding whether temperature can modify the effects of ozone on health.

What is added by this report?
Short-term exposure to \(O_3\) in the Beijing Municipality, Tianjin Municipality, Hebei Province, and surrounding areas was associated with an increased risk of human mortality and that association was positive modified by relatively higher (>75th 24 h-average temperature) or extreme cold temperature (<10th 24 h-average temperature). Under extreme temperatures (>90th 24 h-average temperature) modification, the associations were further increased. Cardiopulmonary diseases, as vulnerable diseases of air pollution, their mortality risks associated with \(O_3\) were markedly strengthened by uncomfortable temperatures.

What are the implications for public health practice?
This study suggests that policymakers should pay attention to the synergistic effect between ozone and heat or extreme cold on human health, as well as provide evidence for establishing an integrated early-warning system to protect the public against both uncomfortable temperature and air pollution.

Short-term exposure to ambient ozone (\(O_3\)), a weather-driven photochemical pollutant, has been found to be associated with increased risk of mortality in previous epidemiological studies (1–2). Most of these studies analyzed \(O_3\)-mortality associations by controlling for meteorological factors in a model fitting process. Regarding the high correlation between \(O_3\) and temperature, a recent area of interest is whether the observed \(O_3\)-mortality associations can be modified by temperature. Jhun et al. found both high and low temperature could strengthen acute effects of \(O_3\) on mortality (3), while Chen et al. and Shi et al. reported that \(O_3\)-mortality associations were strengthened in high temperature but not in low temperature settings (4–5), and Liu et al. and Chen et al. only found modifications by low temperature (6–7). In summary, evidence on temperature-modification was inconsistent and needed to be supplemented by regional epidemiological studies involving various meteorological characteristics. Note that in the new air quality guidelines issued by the World Health Organization (WHO), \(O_3\) limits have been distinguished between warm and cold seasons. Beijing Municipality and Tianjin Municipality, along with 26 cities distributed in Hebei, Shandong, Shanxi and Henan Provinces, have formed the regional air pollution transmission channel, and experienced a challenge of regional \(O_3\) pollution increasing steadily. Therefore, additional efforts are needed to better quantify the local health risks of \(O_3\) by considering the influence of temperature in the Beijing, Tianjin, Hebei and surrounding areas.

This study used daily counts of deaths from the Disease Surveillance Point System of China CDC and included 39 counties in the Beijing, Tianjin, Hebei and surrounding areas from January 1, 2013 to December 31, 2018. Three major causes of deaths were classified according to the 10th Revision of the International Statistical Classification of Diseases (ICD-10): non-accidental disease (A00–R99), cardio-cerebrovascular disease (I00–I99), and respiratory disease (J00–J99). Daily ambient \(O_3\) concentrations were collected from the National Urban Air Quality Real-Time Release Platform and calculated to a daily 8-hour moving average maximum (\(O_3\) 8 h-average), 1-hour maximum (\(O_3\) 1 h-max), and 24 hour-average of \(O_3\) (\(O_3\) 24 h-average). Daily average temperature and relative humidity were obtained from the China Meteorological Data Network.

The study applied two time-series approaches with a two-stage statistical analysis to estimate whether and how temperature modified acute effects of \(O_3\) on mortality.
mortality in the Beijing, Tianjin, Hebei and surrounding areas. The first approach, a temperature-adjusted approach, aimed to control the cumulative temperature impacts with a cross-basis function using a generalized linear model (GLM) and analyze associations between O₃ and death without considering interactions.

The second approach, a temperature-stratified approach by a Pick-A-Point technique centering on changes of the conditional effect of O₃ across the designated levels of the modifier (8), aimed to construct interaction terms between O₃ and a stratification variable of temperature in the GLM and analyze differences of associations under three different temperature levels: low, moderate, and high temperature. In this model, we used three cutoffs to categorize daily average temperature, including the 10th and 90th (P₁₀/P₉₀), 20th and 80th (P₂₀/P₈₀), and 25th and 75th (P₂₅/P₇₅) percentiles. The model of the temperature-stratified approach was set up as follows:

\[
\log(E(Y_t)) = \text{intercept} + \beta O₃ + \beta₁ Tem + \beta₂ O₃ : Temstrata + n₁(RH, df) + dow + n(time, df)
\]

Where was the expected value of death on day t; Tem represented the daily value of temperature; \(O₃ : Temstrata\) was the interaction term between O₃ and temperature, in which temperature was divided into low, moderate, and high levels of the categorical variable by cutoffs. Both approaches estimated effects of the 2-day average of current and previous-day concentrations (lag 01) of O₃ 8 h-average and controlled for seasonal and time trends [time, natural smoothing function of 8 degrees of freedom (df)], day of the week (dow), and relative humidity (RH, natural smoothing function of 5 df). The effect estimate was expressed as a percent increase (PI) in mortality risk per 10 μg/m³ increase in O₃ exposure.

This study examined the sensitivity of key findings for non-accidental mortality with respect to using the following: 1) the specification of df in the smoothing functions of time trend (df=6 or 7/year) and relative humidity (df=3) in the temperature-adjusted approach to observe model stability; 2) the other two metrics (O₃ 1 h-max and O₃ 24 h-average) with different lagged exposure [the same day as deaths (lag 0), the previous day (lag 1), and lag 01] in the temperature-adjusted approach to observe impacts from different exposure assessments for the study population; and 3) O₃ 1 h-max and O₃ 24 h-average with lag 01 exposure in the temperature-stratified approach to observe whether the modification effect of temperature on different ozone metrics was robust. Statistical analyses were conducted in the R Statistical Software (version 4.0.2, the Free Software Foundation’s GNU Public License, Vienna, Austria). Statistical significance was considered at a P-value <0.05.

From 2013 to 2018, residents in the Beijing, Tianjin, Hebei and surrounding areas were exposed to a concentration of O₃ 8 h-average of (95.2±61.4) μg/m³. Approximately 11 deaths for non-accidental disease, 6 for cardio-cerebrovascular disease, and 1 for respiratory disease per day per county were recorded (Table 1).

Based on the temperature-adjusted approach without considering interactions, a per 10 μg/m³ increase in exposure to O₃ 8 h-average would increase daily mortality risks of non-accidental [PI=0.15%, 95% Confidence Interval (CI): 0.06%–0.24%], cardio-cerebrovascular (PI=0.20%, 95% CI: 0.07%–0.33%), and respiratory diseases (PI=0.08%, 95% CI: -0.42%–0.25%) in the Beijing, Tianjin, Hebei and surrounding areas. Based on temperature-stratified approach, relatively higher temperature (>75th 24 h-average temperature) significantly strengthened O₃-mortality associations, with a 0.57% risk increase of

| Variable                          | Mean±SD     | P₉₅ | P₃₀ | P₅₀ |
|-----------------------------------|-------------|-----|-----|-----|
| O₃ 24 h-average (μg/m³)           | 56.3±38.7   | 25.3| 49.5| 80.2|
| O₃ 8 h-average (μg/m³)            | 95.2±61.4   | 48.2| 83.8| 135.4|
| O₃ 1 h-max (μg/m³)                | 111.0±71.5  | 59.7| 95.0| 155.0|
| Temperature (°C)                  | 13.3±11.1   | 2.8 | 14.6| 23.4|
| Humidity (%)                      | 0.6±0.2     | 0.4 | 0.6 | 0.7 |
| Non-accidental diseases           | 11±8        | 6   | 9   | 14  |
| Cardio-cerebrovascular diseases   | 6±4         | 3   | 5   | 7   |
| Respiratory diseases              | 1±1         | 0   | 1   | 2   |

Abbreviations: SD=standard deviation; P₉₅=25th percentile; P₅₀=50th percentile; P₇₅=75th percentile.
non-accidental disease, 0.64% risk increase of cardio-cerebrovascular disease, and 1.17% risk increase of respiratory disease (Figure 1). Under extreme temperature (>90th 24 h-average temperature) modification, the associations between O₃ and human mortality has further increased: a 0.98% risk increase of non-accidental disease, 1.19% risk increase of cardio-cerebrovascular disease, and 1.76% risk increase of respiratory disease (Figure 1). Moreover, extreme low temperature (<10th 24 h-average temperature) was also found to strengthen the acute effects of O₃ on mortality (Figure 1).

Associations between short-term exposure to O₃ 8 h-average and mortality peaked at Lag 01 exposure. Analyses with different metrics of O₃ exposure and more or less stringent time trends and relative
humidity controlled by varying $d_f$ did not meaningfully change our findings (Table 2). For the three cutoffs of $P_{10}/P_{90}$, $P_{20}/P_{80}$, and $P_{25}/P_{75}$, the associations between the other two $O_3$ metrics and mortality were both increased under high temperature levels (Table 3). The extreme low temperature was found to only significantly modify the association between $O_3$ 24 h-average and mortality.

## DISCUSSION

We used two time-series approaches to explore the effects of short-term exposure to $O_3$ on mortality across temperature levels in the Beijing, Tianjin, Hebei and surrounding areas throughout a six-year period. Both the temperature-adjusted and temperature-stratified approaches indicated that short-term exposure to $O_3$ was associated with an increased risk of mortality, and that the association was positive modified by high-temperature levels, especially modified by extreme heat. These findings were consistent with epidemiological evidence from several previous national-level studies (3,5,9). From an exposure standpoint, it may be because ground-level $O_3$ is usually formed by photochemical reactions of precursor pollutants under the presence of light; as the temperature increases, the formation of $O_3$ accelerates, and the emission of precursor pollutants increases, resulting in an increase in effect size of $O_3$ along with increased pollution.

The study also found that the $O_3$-mortality risks of cardiopulmonary diseases, as vulnerable diseases of air pollution, were further strengthened in the presence of high temperature. However, studies in some southern cities in China (6–7) have not observed this modification effect. For example, a study conducted by Chen et al. in Jiangsu showed that $O_3$ has a higher impact on death from cardiovascular diseases in a low temperature environment. The conflicting results indicated that the modification may vary considerably.
provide evidence for establishing an integrated early-warning system for protecting the public against both unsuitable temperature and air pollution.

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