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Acute effect of ozone exposure on daily mortality in seven cities of Jiangsu Province, China: No clear evidence for threshold

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Abstract

Background—Few multicity studies have addressed the health effects of ozone in China due to the scarcity of ozone monitoring data. A critical scientific and policy-relevant question is whether a threshold exists in the ozone-mortality relationship.

Methods—Using a generalized additive model and a univariate random-effects meta-analysis, this research evaluated the relationship between short-term ozone exposure and daily total mortality in seven cities of Jiangsu Province, China during 2013–2014. Spline, subset, and threshold models were applied to further evaluate whether a safe threshold level exists.

Results—This study found strong evidence that short-term ozone exposure is significantly associated with premature total mortality. A 10 $\mu\text{g}/\text{m}^3$ increase in the average of the current and previous days' maximum 8-h average ozone concentration was associated with a 0.55% (95% posterior interval: 0.34%, 0.76%) increase of total mortality. This finding is robust when considering the confounding effect of $\text{PM}_{2.5}$, PM_{10} , NO_2 , and SO_2 . No consistent evidence was found for a threshold in the ozone-mortality concentration-response relationship down to concentrations well below the current Chinese Ambient Air Quality Standard (CAAQS) level 2 standard (160 $\mu\text{g}/\text{m}^3$).

Conclusions—Our findings suggest that ozone concentrations below the current CAAQS level 2 standard could still induce increased mortality risks in Jiangsu Province, China. Continuous air pollution control measures could yield important health benefits in Jiangsu Province, China, even in cities that meet the current CAAQS level 2 standard.

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Conflict of interests

The authors have declared that no competing interests exist.

Keywords

ambient ozone; mortality; threshold; time-series; China

1. Introduction

Short-term exposure to ambient ozone has been found to be associated with numerous adverse health effects, including increased mortality, increased rates of respiratory hospital admissions and emergency room visits, and decreased lung function (Gryparis et al., 2004; Kinney et al., 1989; Lippmann, 1993; Schwartz, 1996). Recent multicity analyses pooling estimates from city-specific results provide further evidence supporting the causal relationship between short-term ozone exposure and total mortality (U.S. EPA, 2013). However, most of these studies were conducted in North America (Bell and Dominici, 2008; Smith et al., 2009), Latin America (Romieu et al., 2012), and Europe (Katsouyanni et al., 2009; Stafoggia et al., 2010). Few multicity studies have addressed health effects of ozone in large regions of China due to the scarcity of ozone monitoring data (Kan et al., 2012; Wong et al., 2008).

China currently experiences severe and complex ambient air pollution. In addition to particulate pollution, ozone pollution in China is already appearing with large increases during the past two decades (Brauer et al., 2015). Since air pollution characteristics, resident health conditions, population sensitivity, and life-styles in China differ from those in developed countries (Yan et al., 2013), the concentration-response coefficients observed in developed countries may not be applicable in China. Previous studies have noted stronger associations between short-term ozone exposure and daily mortality in mainland China than those in U.S., Canada, European countries (Liu et al., 2013; Wong et al., 2008), and Japan (Chen et al., 2014).

A key issue in assessing the acute effect of short-term ozone exposure on mortality is whether a threshold exists, which plays an important role in setting ozone air quality standard (U.S. EPA, 2013). No evidence of a threshold was found in most of studies in the North America and Europe (Bell et al., 2006; Katsouyanni et al., 2009; Peng et al., 2013; Smith et al., 2009). Previous studies in several Chinese cities also found a linear relationship between ozone and mortality, suggesting no evidence of an obvious threshold (Wong et al., 2008; Yang et al., 2012). On the contrary, a reanalysis in the U.S. reported apparent thresholds in nine major U.S. cities (Stylianou and Nicolich, 2009). A recent multicity study in Japan and Korea also found a nonlinear association with a clear threshold around 30 to 40 ppb (Bae et al., 2015). Whether a safe ozone threshold exists is also very critical in assessing the ozone-related health burden. Compared with a no threshold assumption, applying a relatively high concentration threshold (30 to 40 ppb) would greatly reduce the estimated ozone-related burden of premature mortality under both past and future climate change (Anenberg et al., 2010; Heal et al., 2013; Raquel et al., 2013). Given the increasing ambient ozone pollution in China and the importance of threshold assumption in assessing its health burden, more studies are needed to explore the possible presence of ozone threshold in the ozone-mortality relationship in China.

In this study, we aimed to evaluate the relationship between short-term ozone exposure and daily total mortality, and to explore the potential threshold in seven cities of Jiangsu Province, China during 2013–2014.

2. Methods

Our study area included the urban districts of seven cities in Jiangsu Province: Nanjing, Wuxi, Changzhou, Suzhou, Lianyungang, Yancheng, and Zhenjiang (Supplemental Material, Fig. S1). The total population in our study area is 25.51 million by the end of 2010.

2.1 Mortality Data

Daily mortality data for each city from January 1, 2013 to December 31, 2014 were obtained from the Jiangsu Provincial Center for Disease Prevention and Control. Daily total non-accidental deaths were identified based on the International Classification of Diseases, Revision 10 (ICD-10) using codes A00-R99 for all ages. Because the mortality cases were underreported in the last three days of the year 2014 in Nanjing, these days were excluded.

2.2 Air pollution and meteorological data

Air pollution data from January 18, 2013 to December 31, 2014 in each city of Jiangsu Province were collected from the official web site of the China Environmental Monitoring Center (<http://106.37.208.233:20035>). A total of 42 national air quality monitoring sites were located in the seven cities (Supplemental Material, Fig. S1). The daily average concentrations of maximum 8-h average (MDA8) ozone, particulate matter with an aerodynamic diameter of 2.5 μm or less ($\text{PM}_{2.5}$), particulate matter with an aerodynamic diameter of 10 μm or less (PM_{10}), nitrogen dioxide (NO_2), and sulphur dioxide (SO_2) were computed for each monitoring station from the hourly concentrations. Then, the daily concentrations from each stations within a city were averaged to derive the city-specific daily concentrations. For all seven cities during our study period, the percentage of days with missing data is 0.4% for MDA8 ozone, 6.2% for $\text{PM}_{2.5}$, 6.3% for PM_{10} , 6.2% for NO_2 , and 6.2% for SO_2 , respectively. Daily mean temperature (T_{mean}) and relative humidity (RH) values were obtained from the China Meteorological Data Sharing Service System. For urban districts without weather stations, temperature and RH data from nearest weather stations were used. There were no missing data for temperature and RH during our study period.

2.3 Statistical analysis

We used a 2-stage method to evaluate the association between short-term ozone exposure and daily total mortality in Jiangsu Province. First, estimates were calculated for each city using a time-series model; then, estimates were pooled to generate an overall effect.

Because daily mortality counts were very low, they were usually assumed to follow an over-dispersed Poisson distribution. Thus, we used a generalized additive model (GAM) with a quasi-Poisson regression to evaluate the association between ozone and total mortality in each city, while controlling the confounding effects of long-term trends, temperature, relative humidity, and day of week effect. Cubic regression spline (CRS) was used to

represent the smooth terms of time trend, temperature, and relative humidity. The GAM model used the following formula:

$$\text{Log}E(Y_t) = \beta \text{Ozone} + \gamma X + s(\text{time}, \text{df}) + s(\text{Tmean}, \text{df}) + s(\text{RH}, \text{df}) + \text{DOW} = \beta \text{Ozone} + \text{COVs}$$

[1]

where $E(Y_t)$ is the expected daily mortality count at day t with $\text{Var}(Y_t) = \phi E(Y_t)$, ϕ is the over-dispersion parameter; β and γ are the coefficients for ozone and pollutant X ; the smooth function s captures the nonlinear relationships between the covariates (time, Tmean, and RH) and mortality; and DOW is the dummy variable for day of the week. As in our previous study (Chen et al., 2013), 8 degree of freedom (df) per year for time trend, 6 df for temperature, and 3 df for relative humidity were selected. As in previous multicity studies (Chen et al., 2014; Wong et al., 2008), the moving average of current-day and previous day (lag0–1) was used to represent the lag effect of short-term ozone exposure. Ozone exposure at alternative single lag days (lag0–lag3) and a four-day moving average (lag0–3) were also examined. Since the effect of temperature on daily mortality may lagged over days or weeks (Gasparrini et al., 2015), we applied different lag structures for temperature: lag0–7 (the moving average of the current-day and the previous seven days); lag0–14 (the moving average of the current-day and the previous 2 weeks); lag0–21 (the moving average of the current-day and the previous 3 weeks); lag0–28 (the moving average of the current-day and the previous 4 weeks). In addition, we also applied two separate lag structures together in the model (lag0 and lag1–3) as used in a multicity study in the U.S. (Bell et al., 2006). To select the optimal temperature lag structure, the generalized cross-validation (GCV) values was computed.

In the second stage, city-specific estimates across seven cities were combined to estimate the average risk of ozone-related mortality using a univariate random-effects meta-analysis (Gasparrini et al., 2012). This approach can flexibly pool the risk estimates while accounting for variations across cities (heterogeneity). This approach generates posterior estimates (mean and 95% intervals) for the overall effect of short-term ozone exposure on daily total mortality in Jiangsu Province. Heterogeneity among cities was assessed by the I^2 statistic, which measures the percentage of variability due to the true heterogeneity (Higgins and Thompson, 2002). Heterogeneity was considered to be significant if $I^2 > 0.5$, moderately significant if $0.25 < I^2 < 0.5$, and nonsignificant if $I^2 < 0.25$ (Chen et al., 2014).

In addition to the full-year data analysis, the modifying effects of seasonality (warm and cold) on the ozone-mortality relationship were also analyzed. The df for the time trend in the seasonal analysis was half of those from the full-year analysis, while other parameters remained the same.

We applied three approaches to evaluate whether a threshold exists in the ozone-mortality concentration-response curve. Firstly, we explored the nonlinearity in the concentration-response curve for each city using a spline approach, which also allows for a visual

inspection of the existence of a safe ozone threshold. In this approach, the ozone variable in Equation [1] was replaced by a natural cubic spline of ozone with 3 df. To compare spline models with linear models, we computed the difference between the deviances of the fitted linear and spline models for each city, which follows a chi-square distribution with 2 (the difference in the df of the spline model and linear model) df (Samoli et al., 2005).

In addition, under a linear association assumption, we conducted a subset approach that only includes days that meet the standard in each city. Taking both sample size and the potential threshold reported in previous studies, we here performed the subset analyses using threshold ranging from 60 to 160 $\mu\text{g}/\text{m}^3$ with an increment of 10 $\mu\text{g}/\text{m}^3$.

Finally, we performed a threshold analysis applied in a previous study (Bell et al., 2006), assuming that a linear ozone-mortality relationship is only observed above the threshold (h) and not below it. The ozone variable in Equation [1] was thus replaced by the following term:

$$(Ozone - h)_+ = \begin{cases} (Ozone - h); & \text{if } Ozone > h \\ 0; & \text{otherwise} \end{cases} \quad [2]$$

We performed this threshold analysis for each city and each threshold ranging from 0 to 160 $\mu\text{g}/\text{m}^3$ with an increment of 10 $\mu\text{g}/\text{m}^3$. If a threshold exists, the model with an appropriate threshold value h should generate the best model fit (Bell et al., 2006). The Akaike Information Criterion for quasi-Poisson (Q-AIC) values for models was applied here to assess the best model fit minimizing the Q-AIC values (Akaike, 1998). Low Q-AIC values generally indicate better fitted models. If the difference in Q-AIC values between two models is larger than 2, there is likely difference in model fits (Burnham and Anderson, 2004).

All analyses were conducted with R software, version 3.2.1 (R Development Core Team, 2015), using the MGCV package (Wood, 2011) and mvmeta package (Gasparrini et al., 2012).

3. Results

From January 18, 2013 to December 31, 2014, there were 235.4 total non-accidental deaths occurred every day in the urban districts of seven Jiangsu cities (Table 1). Nanjing had the highest number of daily total deaths (67.3), while Lianyungang had the smallest number (12.2). The mean MDA8 ozone concentration during 2013–2014 was 90.5 $\mu\text{g}/\text{m}^3$, with a larger concentration in the warm season (106.8 $\mu\text{g}/\text{m}^3$) than in the cold season (72.3 $\mu\text{g}/\text{m}^3$). In general, the MDA8 ozone concentration peaked during April to June in our study area (Supplemental Material, Fig. S2). Nanjing had the largest number of days with MDA8 ozone concentration exceeding the Chinese Ambient Air Quality Standard (CAAQS) level 2 standard (160 $\mu\text{g}/\text{m}^3$), while Zhenjiang had the smallest number (Supplemental Material, Fig. S3). More than 95% of the exceeding days occurred in warm season.

Ozone was positively correlated with daily mean temperature and negatively correlated with relative humidity in the full year period (Table S1). A stronger correlation between ozone and temperature was found in the cold season than that in the warm season. The absolute values of the Spearman correlation coefficients between ozone and the co-pollutants (PM_{2.5}, PM₁₀, NO₂, and SO₂) were less than 0.2 in the full year period, indicating a lack of correlation between ozone and these four co-pollutants. In the warm season, the correlation coefficients between ozone and co-pollutants were less than 0.4. In the cold season, the correlations between ozone and co-pollutants were much weaker and became negative.

Table 2 shows the model fit parameters when using different lag structures. The smallest GCV was found in the moving average of the current-day and previous 14 days (lag0–14) for temperature. Thus, the lag0–14 was used to control the lag effect of temperature on daily mortality in this study. The I² statistics suggested that heterogeneity contributed 1.0%, 1.0% and 36.6% for full year, warm season, and cold season, respectively, of the total variability in ozone effects. Thus, nonsignificant heterogeneity was observed for the full year analysis and warm season analyses, but a moderate heterogeneity was noticed for the cold season analysis.

While the associations between ozone and total mortality varied somewhat between cities in Jiangsu Province (Fig. 1), in general, we observed positive associations in all seven cities. Nanjing, Suzhou, and Zhenjiang had significant associations. Lianyungang, Yancheng, and Zhenjiang had smaller population than the average of all seven cities (Table 1) and large error bars in the risk estimates (Fig. 1). On average, using the lag0–14 for temperature, a 10 µg/m³ increase in short-term exposure to MDA8 ozone was found to be associated with an increase of 0.55% (95% posterior interval (PI): 0.34%, 0.76%) in daily total mortality in the full year period, 0.38% (95%PI: 0.12%, 0.64%) in daily total mortality in the warm season, and 0.88% (95%PI: 0.26%, 1.51%) in daily total mortality in the cold season, respectively (Table 2).

Fig. 2 presents the pooled association of MDA8 ozone with total mortality in the single-pollutant and two-pollutant models in seven Jiangsu cities. Compared with the single-pollutant model, the estimated ozone effect on daily total mortality was robust when we controlled for PM_{2.5}, PM₁₀, NO₂, and SO₂. Sensitivity analysis of ozone lag structure indicated that the moving average of current-day and previous day (lag01) used in our model yielded larger estimates for ozone compared with single day lags (lag0, lag1, lag2, and lag3) and the moving average of current-day and previous three days (lag03) (Supplemental material, Fig. S4). Compared with the moving average of current-day and previous two days (lag02), using lag01 generated similar estimates. Risk estimates for single day lags became insignificant after lag1 (i.e., lag2 and lag3). Thus, lag01 was used in this study to represent the lag effect of short-term ozone exposure.

The estimated concentration-response (CR) curve between ozone and total mortality using the natural cubic spline approach for each city is shown in Supplemental material, Fig. S5. The linearity tests showed that the city-specific deviance between the linear and the spline models was not statistically significant (p-value > 0.05 for all cities), indicating no evidence for a non-linear model. The city-specific CR curves presented approximately linear

relationships over medium concentrations (80 to 160 $\mu\text{g}/\text{m}^3$). But evidence for an association were generally weaker at both low and high concentrations, where ozone data were sparse. The CR curves in Nanjing, Wuxi, and Suzhou were found to be near horizontal at low concentrations (below 80 $\mu\text{g}/\text{m}^3$), indicating the existence of potential thresholds. In Changzhou, Lianyungang, and Zhenjiang, no obvious threshold below which ozone has no effect on total mortality was found.

For days when MDA8 ozone met the CAAQS level 2 standard (160 $\mu\text{g}/\text{m}^3$), a significant ozone effect on total mortality was still observed: a 10 $\mu\text{g}/\text{m}^3$ increase in short-term exposure to MDA8 ozone was found to be associated with an increase of 0.68% (95%PI: 0.40%, 0.96%) in daily total mortality in seven cities of Jiangsu Province (Fig. 3). Significant ozone-mortality risk estimates were found when the threshold decreased from 160 to 110 $\mu\text{g}/\text{m}^3$, indicating that if a threshold for ozone-mortality relationship does exist, it should be smaller than 110 $\mu\text{g}/\text{m}^3$ in Jiangsu. Positive associations between ozone and mortality were still found for threshold decreasing from 110 to 60 $\mu\text{g}/\text{m}^3$ with a generally increasing 95% confidence interval, which is likely due to declining sample size.

The averaged Q-AIC was minimized at the threshold value of 90 $\mu\text{g}/\text{m}^3$ (Fig. 4), suggesting a potential threshold around 90 $\mu\text{g}/\text{m}^3$ in Jiangsu. The averaged Q-AICs for the threshold of 90 $\mu\text{g}/\text{m}^3$ was 4273.9 and smaller than those for 120 to 160 $\mu\text{g}/\text{m}^3$ by a value of 2, indicating better model fits (Burnham and Anderson, 2004). However, this difference in Q-AIC between 90 and 0 $\mu\text{g}/\text{m}^3$ (no threshold assumption) was smaller than 2 and only accounts 0.03% of the Q-AIC for the no threshold assumption (Q-AIC value: 4275.1).

4. Discussion

In summary, this multicity study over seven cities of Jiangsu Province provides strong evidence that short-term ozone exposure is significantly associated with premature total mortality. This finding is robust when considering the confounding effect of $\text{PM}_{2.5}$, PM_{10} , NO_2 , and SO_2 . No strong evidence was found to support a threshold in the ozone-mortality concentration-response relationship down to concentrations well below the current Chinese Ambient Air Quality Standard (CAAQS) level 2 standard (160 $\mu\text{g}/\text{m}^3$). To the best of our knowledge, this is the first multicity study in China to systematically examine the evidence of threshold in the concentration-response function for ozone and daily mortality.

Our estimates of the ozone-mortality relationship are generally consistent with previous multicity studies and meta-analyses in China (Chen et al., 2014; Shang et al., 2013; Tao et al., 2011; Yan et al., 2013). Per 10 $\mu\text{g}/\text{m}^3$ increase in MDA8 ozone concentrations, daily total mortality was increased by 0.55% (95%PI: 0.34%, 0.76%) in our study of seven cities in Jiangsu Province, 0.51% (95%CI: 0.24%, 0.78%) in four cities of mainland China (Chen et al., 2014), 0.54% (95%CI: 0.34%, 0.75%) in four cities of the Pearl River Delta after adjusted for PM_{10} (Tao et al., 2011), 0.48% (95%CI: 0.38%, 0.58%) in a meta-analysis of eight studies in China (Shang et al., 2013), and 0.42% (95%CI: 0.32%, 0.52%) in a meta-analysis of five studies in China (Yan et al., 2013). Our estimate was slightly higher than results from studies in the U.S. and Europe (Bell et al., 2004; Pascal et al., 2012; Peng et al.,

2013), where the mean estimates ranges from 0.18% to 0.39% increase of total mortality per $10 \mu\text{g}/\text{m}^3$ increase in MDA8 ozone concentrations.

Because $\text{PM}_{2.5}$ was not officially monitored nationally in China before 2013, previous studies assessing the relationship between ozone and mortality in China were unable to test for confounding by $\text{PM}_{2.5}$ (Chen et al., 2013; Chen et al., 2014; Kan et al., 2008; Liu et al., 2013; Yang et al., 2012). In this study, we found similar increments in total mortality associated with a $10 \mu\text{g}/\text{m}^3$ increase in MDA8 ozone concentrations before and after controlling for $\text{PM}_{2.5}$ (0.56% vs. 0.58%). Our finding confirms that ozone mortality risk estimates in China are robust to the inclusion of $\text{PM}_{2.5}$ in copollutant models, which is consistent with previous studies in the U.S. (Bell et al., 2007; Franklin and Schwartz, 2008).

We found an increased mortality risk of short-term ozone exposure during the cold season (Oct.–Mar.) in Jiangsu Province, China (Table 2). This finding is robust when adjusting for $\text{PM}_{2.5}$, PM_{10} , NO_2 , and SO_2 in the cold season analysis, though ozone risk estimates were slightly reduced in the two-pollutant models (Fig. 2). Consistently, recent studies in Asia revealed a significant ozone effect on daily mortality in cold or winter months in China (Chen et al., 2013; Kan et al., 2008; Li et al., 2015; Liu et al., 2013; Yang et al., 2012), Japan (Ng et al., 2013), and Thailand (Guo et al., 2014). The significant association between low level cold season ozone (mean level: $72.3 \mu\text{g}/\text{m}^3$) and daily mortality observed in this study suggests that there is no threshold or a very low threshold in the ozone-mortality relationship in Jiangsu Province, China. In accordance with previous single city studies in China (Chen et al., 2013; Kan et al., 2008; Li et al., 2015; Liu et al., 2013; Yang et al., 2012), we found a stronger mortality effects of short-term ozone exposure in cold season than in warm season (Apr.–Sept.). This finding is also in line with multicity studies in Japan (Ng et al., 2013) and Thailand (Guo et al., 2014), but contradicts many studies in North America and Europe (Katsouyanni et al., 2009; Pascal et al., 2012). The difference in seasonal pattern of acute ozone effect on mortality between China and western countries may be due to several factors such as ozone exposure patterns, demographic and socioeconomic conditions (Chen et al., 2013; Yan et al., 2013). Changes in indoor/outdoor activity patterns and window opening frequencies may increase residents' ozone exposure in Jiangsu Province during cold seasons (Chen et al., 2013).

Our finding provides evidence for a no-threshold, linear association concentration-response relationship between ozone and mortality. Using a spline approach, we did not find significant departures from linearity in the ozone-mortality relationship in all seven cities (Supplemental material, Fig. S5). In accordance with our finding, previous studies also supported the linear association between ozone and mortality in Chinese cities (Wong et al., 2008; Yang et al., 2012). In the subset approach, we found significant effects of short-term ozone exposure on total mortality at ozone concentrations below $110 \mu\text{g}/\text{m}^3$ (Fig. 4). We observed positive but insignificant ozone-mortality effects below $100 \mu\text{g}/\text{m}^3$, where data density is low in the subset approach. Using an alternative threshold approach to overcome the small sample size at low concentrations, we did not find a strong evidence for an apparent threshold at which the average Q-AIC value was smaller than that at $0 \mu\text{g}/\text{m}^3$ (no threshold) by more than 2 (Fig. 4). The association between thresholds and Q-AIC did not follow a U-shaped curve as a flat curve was observed at low thresholds. This indicates lack

of support for the presence of a threshold (Peng et al., 2013). This is consistent with previous time-series studies showing lack of evidence of ozone threshold in the U.S., Canada, and Europe (Bell et al., 2006; Katsouyanni et al., 2009).

On the contrary, recent studies found evidence of a threshold effect around 30 ppb (approximately $60 \mu\text{g}/\text{m}^3$) using the 24-hour average metric in U.S. (Moolgavkar et al., 2013; Stylianou and Nicolich, 2009), 30–40 ppb (approximately $60\text{--}80 \mu\text{g}/\text{m}^3$) using the 24-hour average metric in Korea and Japan (Bae et al., 2015), and $65 \mu\text{g}/\text{m}^3$ using the MDA8 metric in London, U.K. (Atkinson et al., 2012). In general, these reported thresholds were comparable to the background ozone levels at the Northern Hemisphere (approximately 20–45 ppb) (Vingarzan, 2004). In the present study, potential thresholds around $80 \mu\text{g}/\text{m}^3$ in the spline approach and $90 \mu\text{g}/\text{m}^3$ in the threshold approach were suggested, both of which are near the mean total background ozone level over China (44.1 ppb, approximately $88 \mu\text{g}/\text{m}^3$) (Wang et al., 2011). Our findings suggest even if a threshold exists for ozone-mortality relationship, it should be near the background ozone level in China. Any anthropogenic emission in Jiangsu, China will pose an increased risk of premature mortality.

The CAAQS level 2 standard should not be misinterpreted as a completely safe level for human health. The establishment of the CAAQS level 2 standard was a complex systematic process, which considered not only human health risk but also socio-economic and technical conditions. We found that the current CAAQS level 2 standard ($160 \mu\text{g}/\text{m}^3$) is not sufficient enough to protect public health in Jiangsu Province, China. Our combined evidence from spline, subset, and threshold approaches suggest that even if a threshold exists, it should be no higher than $100 \mu\text{g}/\text{m}^3$. This finding indicates that reduction in ambient ozone levels in Jiangsu Province, even in cities that meet the current CAAQS level 2 standard but, exceed the level of $100 \mu\text{g}/\text{m}^3$, should generate important health benefits.

There are several limitations in our study. First, exposure measurement error is inevitable as we used mean pollutant concentrations from several monitoring stations to represent population exposure levels. Since ambient pollutant concentrations could vary between different monitoring stations and are not highly associated with corresponding personal exposures (Sarnat et al., 2005), this exposure measurement error could thus bias the risk estimates, most likely towards the null. Second, the limited amount of data may lead to some uncertainty. However, we have found comparable risk estimates for ozone-mortality relationship compared with other time-series studies with at least three years of data (Chen et al., 2014; Tao et al., 2011). Third, the association between short-term ozone exposure and cause-specific mortality is not explored here, as our main focus was to quantify the association between ozone and total mortality and to explore whether this association diminished below a certain threshold. Finally, this study was only conducted in seven cities of Jiangsu Province and its results may not be applicable to other regions in China. Future studies in other provinces of China with similar methods should be performed to investigate the potential threshold in the ozone-mortality relationship in China.

5. Conclusion

Overall, we found significant associations between short-term ozone exposure and daily total mortality in seven cities of Jiangsu Province, even after adjusting for other air pollutants such as PM_{2.5}. No evidence of a threshold larger than background levels was found in this association, suggesting that ozone concentrations below the current CAAQS level 2 standard could still induce increased mortality risks in Jiangsu Province, China. Our finding shows that continuous air pollution control measures could yield important health benefits in Jiangsu Province, China, even if future ozone air quality meets the current CAAQS level 2 standard.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- We estimated the acute effect of ozone on total mortality in seven Jiangsu cities.
- Short-term ozone exposure was significantly associated with total mortality.
- Ozone-mortality relationship was not confounded by PM_{2.5}, PM₁₀, NO₂, and SO₂.
- No strong evidence for threshold in the ozone-mortality relationship.
- Current Chinese ozone standard is not 'safe' enough in Jiangsu Province.

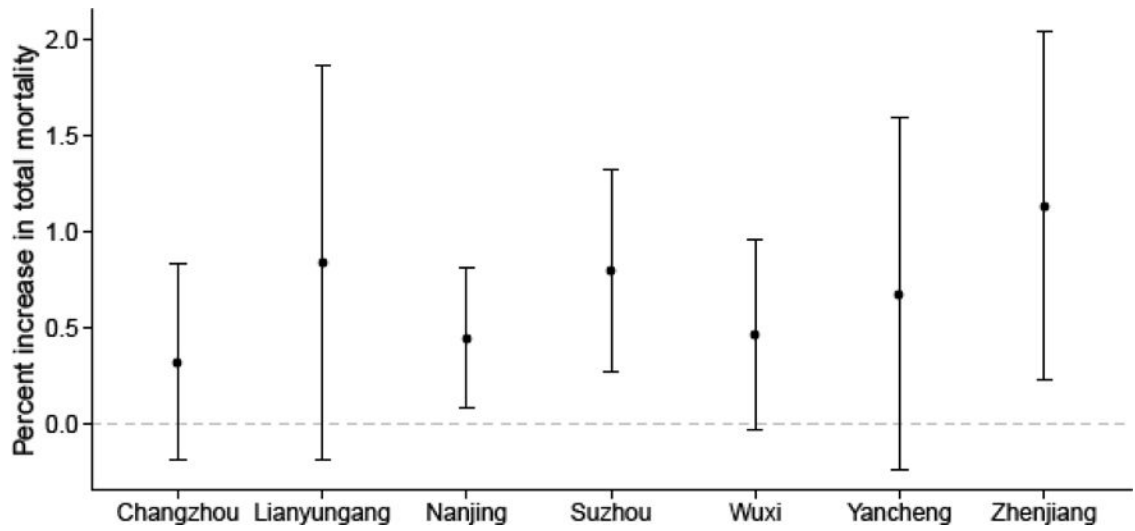


Fig. 1. Per cent increase (mean and 95% confidence intervals) of daily total mortality associated with a $10 \mu\text{g}/\text{m}^3$ increase of ozone concentration at lag01 in seven Jiangsu cities, 2013–2014.

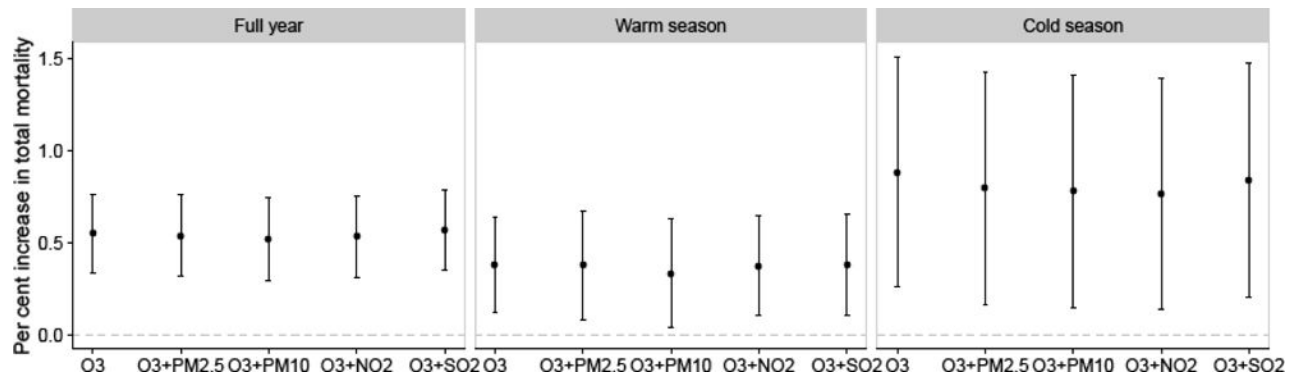


Fig. 2. Per cent increase (posterior mean and 95% posterior intervals) of daily total mortality associated with a $10 \mu\text{g}/\text{m}^3$ increase of ozone concentration based on single- and two-pollutant models by season in seven Jiangsu cities, 2013–2014.

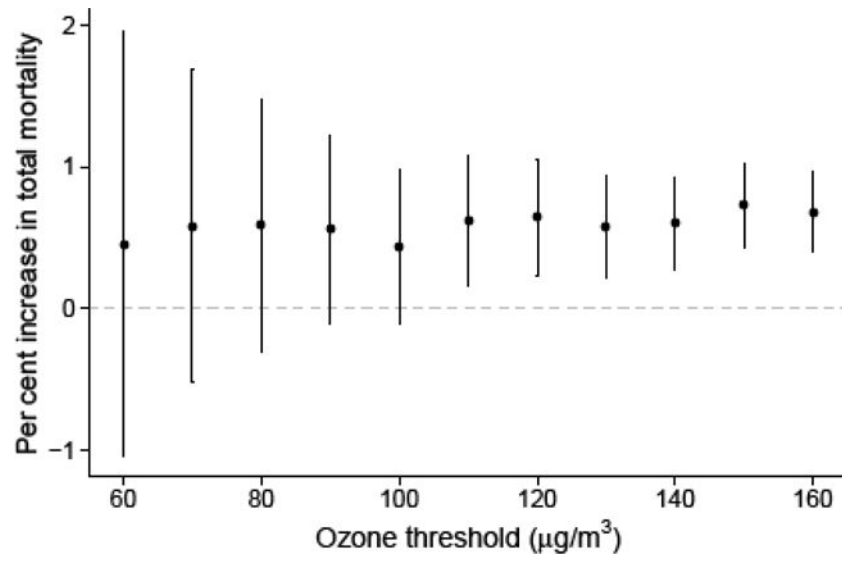


Fig. 3. Per cent increase (posterior mean and 95% posterior intervals) of daily total mortality associated with a $10 \mu\text{g}/\text{m}^3$ increase of ozone concentration by varying thresholds in seven Jiangsu cities, 2013–2014.

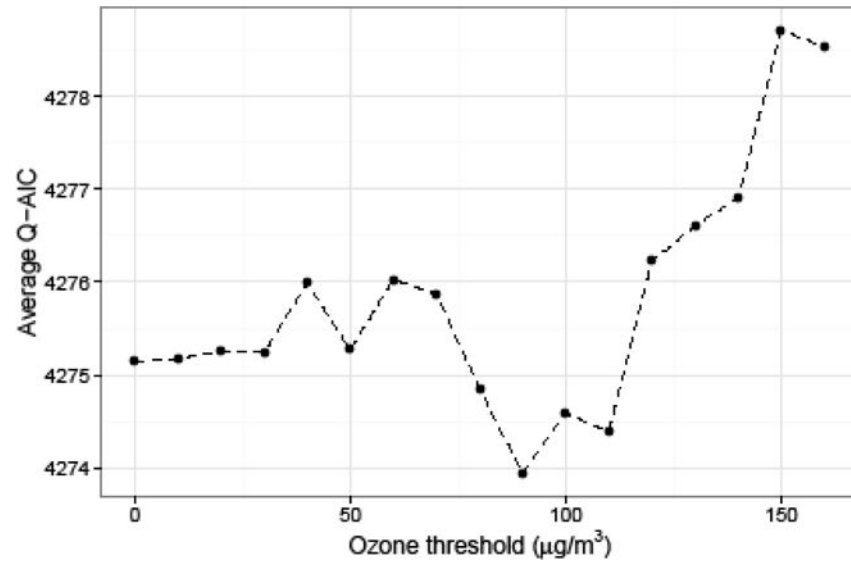


Fig. 4. Plot of average Q-AIC values versus threshold values from seven cities in Jiangsu Province using lag01 MDA8 ozone and total mortality.

Table 1
Descriptive statistics for daily total non-accidental deaths, air pollution, and weather conditions in urban districts of seven cities, Jiangsu Province, China (2013–2014).

City	Population (million)	Daily total deaths	Air pollutant concentration (µg/m ³)							Weather		
			Ozone	PM _{2.5}	PM ₁₀	NO ₂	SO ₂	Tmean (°C)	RH (%)			
<i>Full year</i>												
Nanjing	6.3	67.3	91.8	75.8	123.3	50.9	27.8	17.1	71.1			
Wuxi	3.5	38.4	89.4	71.7	103.4	42.1	32.0	17.5	70.6			
Changzhou	3.3	38.2	93.2	69.1	97.0	42.8	33.7	18.4	70.2			
Suzhou	4.1	36.8	93.4	67.6	93.6	51.8	25.8	17.7	71.4			
Lianyungang	1.1	12.2	93.8	67.0	110.9	33.0	29.2	14.7	73.5			
Yancheng	1.6	24.4	93.5	60.4	89.9	24.8	22.5	16.4	79.0			
Zhenjiang	1.2	18.1	78.7	70.0	114.3	40.9	25.0	17.1	70.4			
Average	3.0	33.6	90.5	68.8	104.6	40.9	28.0	17.0	72.3			
<i>Warm season (Apr.–Sep.)</i>												
Nanjing		62.4	107.9	59.8	106.4	44.6	23.5	23.9	72.8			
Wuxi		35.3	109.0	55.3	89.7	38.2	26.5	24.2	71.6			
Changzhou		35.5	112.3	55.2	86.2	42.9	31.8	24.2	71.5			
Suzhou		34.0	113.6	54.9	79.4	40.4	21.8	24.2	73.1			
Lianyungang		11.4	110.2	52.1	96.2	27.5	21.7	22.0	77.2			
Yancheng		22.8	104.3	45.6	78.5	21.7	20.4	22.3	81.4			
Zhenjiang		17.0	90.3	55.6	108.1	35.8	22.7	24.0	72.2			
Average		31.2	106.8	54.1	92.1	35.9	24.1	23.5	74.3			
<i>Cold season (Oct.–Mar.)</i>												
Nanjing		72.5	74.4	91.4	156	63.7	35.7	9.8	69.4			
Wuxi		41.5	68.7	87.6	130	51.3	41.5	10.4	69.6			
Changzhou		41.8	68.5	85.5	125	49.3	41.0	10.8	68.5			
Suzhou		39.9	72	79.9	107	62.7	29.6	10.89	69.5			
Lianyungang		13.1	76.3	81.4	140	42.8	40.5	6.9	69.7			
Yancheng		26.6	79.5	77.9	118	32.3	28.5	8.7	75.7			
Zhenjiang		19.2	66.4	83.8	136	50.9	30.4	9.9	68.6			

City	Population (million)	Daily total deaths	Air pollutant concentration ($\mu\text{g}/\text{m}^3$)						Weather	
			Ozone	PM _{2.5}	PM ₁₀	NO ₂	SO ₂	Tmean (°C)	RH (%)	
Average		36.4	72.3	83.9	130.3	50.4	35.3	9.6	70.1	

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Model fit parameters and estimated per cent increase of total mortality associated with a 10 $\mu\text{g}/\text{m}^3$ increase in short-term exposure to ozone in models adjusted for different temperature lag structures in seven Jiangsu cities, 2013–2014.

Table 2

Temperature lag	Model fit*		Full year			Warm season			Cold season			
	GCV	Mean	95% PI	Mean	95% PI	Mean	95% PI	Mean	95% PI	Mean	95% PI	
												Mean
0 & 1–3	1.230	0.37	0.14, 0.59	0.16	-0.10, 0.42	0.80	0.18, 1.43	0.63	0.41, 0.84	0.35	0.10, 0.61	
0–7	1.233	0.63	0.41, 0.84	0.38	0.12, 0.64	0.88	0.26, 1.51	0.55	0.34, 0.76	0.40	0.14, 0.67	
0–14	1.225	0.54	0.33, 0.75	0.51	0.29, 0.72	0.44	0.18, 0.71	1.227	0.54	0.33, 0.75	0.40	0.14, 0.67
0–21	1.240	0.51	0.29, 0.72	0.51	0.29, 0.72	0.44	0.18, 0.71	1.240	0.51	0.29, 0.72	0.51	0.29, 0.72
0–28	1.240	0.51	0.29, 0.72	0.51	0.29, 0.72	0.44	0.18, 0.71	1.240	0.51	0.29, 0.72	0.51	0.29, 0.72

* Model fit parameters using the full-year analysis.