Temperature Enhanced Effects of Ozone on Cardiovascular Mortality in 95 Large US Communities, 1987-2000
-- Assessment Using the NMMAPS data

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Abstract

A few studies examined interactive effects between air pollution and temperature on health outcomes. This study is to examine if temperature modified effects of ozone and cardiovascular mortality in 95 large US cities. A nonparametric and a parametric regression models were separately used to explore interactive effects of temperature and ozone on cardiovascular mortality during May and October, 1987-2000. A Bayesian meta-analysis was used to pool estimates. Both models illustrate that temperature enhanced the ozone effects on mortality in the northern region, but obviously in the southern region. A 10-ppb increment in ozone was associated with 0.41 % (95% posterior interval (PI): -0.19 %, 0.93 %), 0.27 % (95% PI: -0.44 %, 0.87 %) and 1.68 % (95% PI: 0.07 %, 3.26 %) increases in daily cardiovascular mortality corresponding to low, moderate and high levels of temperature, respectively. We concluded that temperature modified effects of ozone, particularly in the northern region.

Recently, several large multi-site studies and meta-analyses have consistently shown that ambient ozone pollution is associated with adverse human health. [1-4] Ozone is one of the most toxic photochemical components of air pollution, and the level is driven by weather conditions in many places. It is well known that temperature is also associated with human health.[5-7] Temperature is usually considered as a confounder in air pollution studies. However, extreme temperatures can aggravate pre-existing medical conditions and therefore may modify effects of air pollution. Some studies have examined whether temperature modifies the effects of air pollution, such as ambient particles, ozone and sulphur dioxide on cardiovascular diseases. [8-10] Although recent studies added new evidence,[11-13] this critical issues is yet to be clarified.

Effect modification occurs when the effect of one factor changes with other factors. This has important implications for biological mechanisms and public health interventions. Many studies indicate that demographic characteristics, pre-existing medical conditions and season may modify health effects of air pollution.[14-16] Some studies have shown that the effects of ozone vary across season and region. [3, 17] For example, Levy et al.[3] reported that ozone adversely influenced mortality and this effect was stronger in summer than in winter. This suggests that temperature modifies the ozone effect. Ito et al.[17] conducted a meta-analysis and found that the effects of ozone were negatively associated with mean temperature in different regions. Therefore, a question arises as to whether the difference in ozone effects is due to different weather patterns. This study aimed to examine whether or not temperature modified ozone effects on cardiovascular mortality and whether such effect modification was heterogeneous across different climatic regions. This study uses the data collected from the National Morbidity, Mortality, and Air Pollution Study (NMMAPS).

Materials and methods

Study areas

This analysis was based on the NMMAPS database obtained from the website of the Internet-based Health and Air Pollution Surveillance System (http://www.ihapss.jssph.edu).[18] In order to examine whether there were ozone-mortality associations and whether such associations were modified by temperature heterogeneous across regions, this study included 95 communities in 7 US regions, ie, the Northeast (NE), Industrial Midwest (IM), Upper Midwest (UM), Northwest (NW) regions in the northern US and Southern California (SC), Southwest (SW) and Southeast (SE) regions in the southern US, based on the classification of the NMMAPS data.[18-19]

Data collection

The NMMAPS database consists of daily time series data on mortality, weather conditions, and air pollution assembled from publicly available sources in each community between January 1st, 1987, and December 31st, 2000 (5114 days in total). The daily cause-specific mortality counts included cardiovascular and respiratory diseases in each of 95 communities for three age groups (less than 65 years, between 65 and 75 years, and 75 years or older). The daily mortality counts were reported at the county level (either single or multiple neighbouring counties representing a metropolitan area). Cardiovascular deaths (CVD) were classified according to the International Classification of Disease (ICD). Cardiovascular diseases included ICD-9 codes 390-448 and ICD-10 I000-I799.

Daily maximum temperature and dew point temperature data were obtained from the National Climatic Data Center on the Earth-Info CD database. Air pollution data, obtained

from the US Environmental Protection Agency's (EPA) Aerometric Information Retrieval System database, included 24-h ozone (O_3). We used 10% trimmed means of ozone (average of monitoring measures by excluding 10% extreme values) to reduce the influence of outliers.[17] We restricted this analysis to the intervals between May and October, 1987-2000 for each community because over one-third of communities in the NMMAPS dataset, often in the northern areas, only measured ambient ozone values during this period. We separately estimated effect modifications between temperature and ozone on the current day, lag of 1 day and three-day moving averages.

Analytical protocol

S-Plus software version 6.2 was used for the analyses in this study.[20] Two models were applied to examine the interactive effects between ozone and temperature on cardiovascular mortality in the 95 communities and the models were described in detail in our previous studies.[11, 21] Briefly, we fitted a bivariate response model to explore a two-dimensional smooth response surface of temperature and ozone on CVD in each community (ie. Model 1~~A~~). [21, 22] This model is a flexible approach to examine an interactive effect [23] and allows us to visually examine the joint effects of both ozone and temperature as continuous functions on cardiovascular mortality. A Poisson generalized additive model (GAM) was used to explore the community-specific patterns.[23] For the joint term of ozone and temperature in the bivariate model, we used a LOESS smoothing function. We adjusted for other potential confounders, such as seasonality, long-term trends, short-term fluctuation and dew point temperature.[21, 22] We used maximum temperature as a temperature indicator. To be consistent with the following stratification model, we used the natural cubic spline function to adjust for corresponding potential continuous covariates. The model is described as the following:

$$Log(E(Y_t \mid X)) = \alpha + lo(ozone_t, temp_t, span = 0.25) + \lambda Age + ns(season_t, df = 7) + \gamma Dow_t + ns(year_t, df = 4) + ns(dptemp_t, df = 4) + \varepsilon_t \quad (1)$$

where the subscript *t* refers to the time of the observation; $E(Y_t \mid X)$ refers to daily expected cardiovascular deaths at time *t*; $ns(\cdot)$ and $lo(\cdot)$ separately denote natural cubic spline and LOESS smoothing spline. α is the intercept term; *temp* denotes temperature at time *t*. *dptemp* means dewpoint temperature at time *t*. *season* means seasonality at time *t*. *Dow* means the day of the week. ε_t is the residual at time *t*.

We used a natural cubic spline function of calendar time (days of the year) to adjust for seasonality.[24] Like other studies,[24, 25] we used 4 degrees of freedom (*df*) per year between May and October so that little information from time scales longer than two months was included. We adjusted for long-term trends using years (natural cubic spline, *df* = 4) and the potential confounding effect of weather by including dew point temperature (natural cubic spline, *df* = 4). We controlled for short-term fluctuations using the day of the week as a factor, and included age as a categorical factor (less than 65 years, between 65 and 75 years and 75 years or older). We also considered adjusting for particulate matter (PM) as a confounding variable. However, the EPA only requires measuring levels of PM every six days and the proportion of missing data for PM was high for most communities. Moreover, previous studies have shown that particulate matter less than 10 μm in diameter (PM_{10}) did not confound ozone effect estimates using the NMMAPS data.[1, 26] Therefore, we did not adjust for PM in this study. Because studies have shown that the default convergence criteria may result in bias, [25] we used a stricter criterion (ie, e-10) for the S GAM function in the three-dimensional response surface model.

A stratification model (Model 2) was used to quantitatively examine the heterogeneity of ozone effects across maximum temperature levels and regions. In this model, we categorized temperature into three levels (ie, the first and second tertiles as cut-offs), known as low, moderate and high temperature levels, in each community and then included parametric terms of both ozone and temperature and their interactive term in the Poisson regression model.

$$Log(E(Y_t \mid X)) = \alpha + \beta_1 ozone_t + \beta_2 (ozone_t : temp_{kt}) + \beta_3 temp_{kt} + \lambda Age + ns(season_t, df = 7) + \gamma Dow_t + s(year_t, df = 4) + ns(dptemp_t, df = 4) + \varepsilon_t \quad (2)$$

where $temp_{kt}$ signifies levels of the moving average of temperature at time t. β_1 denotes the main effect of ozone. β_2 is a vector for coefficients of the interactive term between ozone and temperature levels, and β_3 is a vector for coefficients of temperature levels. Others are the same as Model 1.

Then, we used a hierarchical model to estimate overall regional and national associations between short-term ambient ozone and cardiovascular mortality, adjusting for other potential confounders, such as seasonality and short-term fluctuations as in the above bivariate response surface model.

Firstly, we used a Poisson regression model to estimate community-specific relative rates of cardiovascular mortality associated with exposure to ozone across temperature levels. Because preliminary analyses showed that the convergences were not obtained in most communities with GAM using the S *gam.exact* function, [27, 28] we used a generalized linear

regression with Poisson distribution to quantitatively estimate community-specific relative rates of cardiovascular mortality associated with exposure to ozone across levels of temperature.[29] The generalized linear model (GLM) involves the maximum likelihood method and therefore avoids the convergence problem in GAM. [29] The same methods as in the bivariate response model were used to adjust for potential confounders.

Secondly, we estimated the overall relative rates of total mortality associated with short-term exposure to ambient ozone across temperature levels and regions. [30, 31] At the first stage, we obtained estimates $\hat{\beta}^c$ and variance (Var($\hat{\beta}^c$)) for each community *c* using Poisson regression as described above. At the second stage, we divided these estimates into seven regions (NE, IM, UM, NW, SC, SW, SE). Within each region *r* and level *l*, we assumed that $\hat{\beta}^c$ was normally distributed with mean effect β^c and variance σ^{2c} estimated by variance (Var($\hat{\beta}^c$)). In turn, we assumed the true β^c to be normally distributed with overall mean μ and variance τ^2. We used Bayesian meta-analysis to estimate the marginal posterior distribution of each pooled effect μ^{rl} by taking into account the within-community variance (σ^{2c}) and the between-community variance τ^2.[30] In addition, for each region, we calculated the community-specific differences of estimates between high- and low-temperature levels. At the third stage, we assessed the overall effect at the national level using the same methods as the second stage. We used the software WinBUGS to conduct Bayesian meta-analysis.[31, 32] We used non-informative prior distributions: that is $\mu \sim$N (0, 0.0001) and $1/\tau^2 \sim$Unif (0,100).

Results

The ninety-five communities covered a US population of over 108 million, and total cardiovascular deaths were over 4.3 million during the study period.[18] In order to examine relationships between ozone and temperature, we calculated Pearson's correlation coefficients between daily maximum temperature and ozone in specific communities. In general, ozone was highly correlated with temperature and the correlations varied slightly across communities in the northern, while the correlations were generally weaker and varied considerably in the southern (Table 1).

We separately fitted the bivariate response surface models using the current day, lags of one and two day, and three-day averages (the current day, lags of 1 and 2 days) of ozone, maximum temperature and dew point temperature. The bivariate response surfaces (Model A) indicate that ozone and temperature jointly affected cardiovascular mortality and that the combined effects varied substantially across communities and regions. In the northern region, in general, temperature positively modified the ozone-mortality associations, but negative effect modifications appeared in a few communities, such as Arlington, Providence. In the southern region, the situation varied considerably. Both positive and negative modifications appeared with similar frequency. Fig 1 provides the joint patterns of ozone and temperature on cardiovascular mortality in the 8 largest communities in the northern region and the 7 largest communities in the southern region using three-day averages of ozone, temperature and dew point temperature, respectively. Fig 1 shows that in the northern communities (A to H), ozone effects increased with temperature except for Oakland (E) and San Jose (G) where ozone effect changed little with rising temperature, but in the southern communities (I to O), ozone effects varied only slightly with temperature levels except for Houston (J) and Oklahoma City (L), where ozone effects were stronger at low temperature than at high temperature.

[Fig 1 about here]

To further quantitatively estimate the community-specific ozone-mortality associations across different temperature levels, we separately fitted the stratification model in each community (Model B) and then used Bayesian meta-analysis to estimate regional and national overall ozone effects across different temperature levels. Results show that ozone-mortality associations were substantially heterogeneous across communities, regions, and temperature levels. In general, temperature synergistically modified ozone-mortality associations in most northern, but not obvious in southern communities.

Table 2 provides quantitative Bayesian estimates and 95% posterior intervals (PIs) of the association between ozone and cardiovascular mortality at both regional and national levels across three temperature strata where both ozone and temperature are lagged to the same day, namely current day, lags of one and two day, and three-day averages. Results show that the associations between ozone and cardiovascular mortality increased with temperature in the northern areas except for the Upper Midwest, but not obvious in the southern region. There wereas a significant differences in overall associations between ozone and cardiovascular mortality for high and low temperature levels in the northern areas. For example, for per 10-ppb increase in average ozone concentration in the previous three days, relative risks (RR) of cardiovascular mortality increased 3.49 % (95 % PI: 2.19 %, 4.39 %), 2.46 % (95 % PI: 1.11 %, 3.74 %), 1.05 % (95 % PI: -0.82 %, 2.81 %), 2.77 % (95 % PI: 1.18 %, 4.41 %), 0.57 % (95 % PI: -0.14 %, 1.25 %), 0.76 % (95 % PI: -0.95 %, 2.35 %), 0.57 % (-0.80 %, 1.93 %), 1.68 % (95 % PI: 0.07 %, 3.26 %) in NE, IM, UM, NW, SE, SW, SC and all 95 communities (National), respectively when temperature was high; 0.43 % (95 %

PI: -0.28 %, 1.07 %), 0.47 % (95 % PI: -0.14 %, 1.06 %), 0.33 % (95 % PI: -0.77 %, 1.14 %), 0.35 % (95 % PI: 0.63 %, 1.06 %), 0.39 % (95 % PI: -0.27 %, 1.03 %), 0.42 % (95 % PI: -0.33 %, 1.17 %), 0.49 % (-0.13 %, 1.10 %), 0.41 % (95 % PI: -0.19 %, 0.93 %) in NE, IM, UM, NW, SE, SW, SC and National, respectively when temperature was low. The RR differences between high and low temperatures were 3.06 % (95 % PI: 1.58 %, 4.20 %), 1.99 % (95 % PI: 0.47 %, 3.42 %), 0.72 % (95 % PI: -1.36 %, 2.85 %), 2.42 % (95 % PI: 0.61 %, 4.26 %), 0.18 % (95 % PI: -0.77 %, 1.13 %), 0.34 % (95 % PI: -1.54 %, 2.12 %), 0.08 % (-1.38 %, 1.55 %), 1.27 % (95 % PI: -0.41 %, 2.92 %), respectively~~region~~.-The modification was stronger in lag 1 of day than on the current day and lag of two day. Three day average shows the strongest effect modification.

Discussion

This study used two time-series models to explore the associations between ozone and mortality across temperature levels in 95 large US communities in the summer throughout a 14-year period. Both the bivariate and stratification models indicate that ambient ozone was associated with cardiovascular mortality and that the associations were substantially heterogeneous across communities. Results indicate that rising temperature enhanced ozone-mortality association in the northern region, but such enhancement was not obvious in the southern region. Overall, the positive association between ozone levels and cardiovascular mortality was slightly greater at high temperature than at low temperature during the summer season.

Several previous studies have investigated whether or not temperature modified air pollution effects. Some studies found evidence that temperature modified the association of air pollution with human health [8, 9, 11], but others did not.[10] For example, Roberts [9] investigated two US county data between 1987 and 1994 and found that temperature might modify PM_{10} on mortality (Cook County, IL and Allegheny, PA). Our recent study also indicates that temperature modified the association between PM_{10} and morbidity/mortality in Brisbane between 1996 and 2000.[11, 12] This study shows that the modification varied considerately across communities and climatic regions. Therefore, single or several site studies might produce conflicting results. However, the joint effects between particulate matter and temperature are likely to be different from ones between ozone and temperature because ozone is highly related to temperature in many places.

One of our studies examined the effect modification of maximum ozone on the assessments of associations between maximum temperature and cardiovascular mortality in the same 95 large U.S. communities and found the associations between temperature and cardiovascular mortality were different across different ozone levels. Such effect modifications varied across different regions. In general, maximum ozone modified the associations between maximum temperature and cardiovascular mortality in the northern regions, but such effect modification was not obvious in the southern regions.[21] The current study examined the interactive effects between ozone and temperature on cardiovascular mortality in another perspectives, i.e., effect modification of daily temperature on the associations between daily ozone and cardiovascular mortality. Both studies found that temperature and ozone symmetrically modified their associations with cardiovascular mortality and such modifications were varied across different regions. However, the magnitudes of effect modifications were different, depending on which variable was considered as an effect modifier.

Our findings are consistent with previous studies showing that the ozone-mortality associations substantially varied across seasons or regions.[1-3, 12, 17] But these previous studies did not consider temperature as a modifier in their assessments. For example, Gryparis et al.[2] investigated the ozone-mortality relationship in 20 cities in Europe and found the pooled estimates were weak and not significant for the whole year; nevertheless, mortality increased by 0.33% (95% confidence interval (CI): 0.17%, 0.52%) and 0.31% (95% CI: 0.17%, 0.52%) per 10μg/m³ increment in 1-hour ozone and 8-hour ozone during the summer period (April to September), respectively. They also found geographic differences among the associations – viz., the effects were higher in southern European cities, compared with northwest and central eastern regions. Levy et al.[3] conducted a meta-analysis and found that the magnitudes of the

ozone-mortality relationships substantially differed across seasons (higher in summer). Huang et al.[26] examined the adverse effect of ozone in 19 large NMMAPS communities and found that a 10-ppb increase in the previous week's ozone during the summer season (June to September) was associated with a 1.25 % (95% PI: 0.47%, 2.03%) increase in daily cardiovascular mortality. Bell et al.[1] also conducted a multisite study to estimate overall relationship between ambient ozone and mortality during the previous days (up to 6 days) in the same 95 NMMAPS communities as we used here. They found the ozone-mortality associations were substantially heterogeneous across communities. Nationally, a 10-ppb increase in ozone over the previous week was associated with 0.64% (95% PI: 0.31%, 0.98%) and 0.52 % (95% PI: 0.27%, 0.77%) increases for daily cardiovascular and total non-external mortalities throughout the year, respectively. However, they did not consider seasonal factors, which might result in overestimates to some extent because more than one-third of the 95 communities, mainly in northern areas, only monitored ozone values during the warm season (April to October) and ozone effects may be nonlinear.[33]

This study found that temperature and ozone appeared to have synergistic effects on CVM. However, biomedical or physiological reasons for such interaction are very complex because causal ways for both risks are not completely clear and the biological or physiological reactions are complicated. A number of epidemiological and toxicological studies show that it is biologically plausible that temperature and ozone modify the effect of each other. Some experimental studies show that exposure to ozone has significant biological effects on the respiratory system, including acute and chronic effects.[34] Exposure to ozone can result in injuries to the nasal cavity, trachea and proximal bronchi, and central acinar bronchioles and alveolar ducts under three primary categories: cellular response, metabolic activity and physiological changes in respiratory function. [34] It is also known that marked changes in

ambient temperature can cause physiological stress and alter a person's physiological response to toxic agents.[35] Ulmer et al. [36] reported that the average blood pressure in a population fluctuates with season (more likely via temperature). In elderly persons, the ability to thermoregulate body temperatures is likely to reduce and sweating thresholds are generally elevated in comparison with young adults. [37, 38] When body heat production is greater than necessary to maintain a normal body temperature, blood flow from the body core to the skin increases, and heat is transferred more rapidly to the external environment. As a result, blood pressure may increase initially, and heart rates increase subsequently.[39] Sharma [40] reported that some hyperthermia deaths were related to profound brain swelling leading to compression of vital centres that could responsible for instant death. Therefore, hyperthermia, especially in susceptible groups, could make them more vulnerable to exposure to toxic agents. Therefore, high temperature can synergistically modify ozone-mortality associations.

The reasons why the modification effects of temperature on ozone-mortality associations varied with regions remain largely unknown. We postulate several possible explanations, but there is lack of supporting evidence so far . Firstly, the relationship between ozone and temperature varied across different climatic regions (Table 1). In general, ozone was highly correlated with temperature in the northern region. Therefore, high temperature and high ozone frequently appeared at the same period, increasing potential joint effects. In contrast, in the southern region, such correlation varied considerately and was generally weaker. Because of the weaker or sometimes negative correlation, high temperature and high ozone only occasionally appeared at the same time and therefore modification will be less likely to be observed. This difference may partly explain the variation of the effect modification across the regions. Secondly, other climatic differences may partially explained the variation of effect modification across different regions. For example, humidity and

rainfall are correlated to temperature and ozone. In the southern U.S. region, high humidity and more cloudy days or rainfall in summer may reduce the ozone generation. These situations are less happened in the northern U.S. region. Thirdly, physical adaptation of the residents to exposure to ozone may be another reason for the regional difference. Due to relatively high levels of ozone and temperature throughout the year in the southern region, residents may become adapted to high levels of ozone and temperature to some degree. Residents in the southern may become less sensitive to the variability of ozone and temperature. Some studies show that after prolonged exposure to ozone, pulmonary functions become adapted, but inflammation still exists.[41, 42] Therefore, the ozone effect changed little with temperature in the southern region. Finally~~Thirdly~~, misclassification of personal exposure to ozone may also contribute to the variation between different regions. Ozone is very reactive and its concentrations are much lower indoors than outdoors.[2] Due to high temperatures during the summer in the southern region, air conditioning use might encourage people to stay indoors, and their personal exposure to ozone may be much lower than the ambient measures. Yet, this influence may be weaker in the northern region due to relatively lower temperature or relatively shorter high-temperature periods during the summer. Several studies suggest that the prevalence of air conditioning is inversely associated with ozone effects.[2, 3]

In conclusion, this study found that ozone was consistently associated with cardiovascular mortality and the association was heterogeneous across the geographical regions of the US. Temperature modified the ozone-cardiovascular mortality association and the modification varied across different regions. Temperature synergistically modified the ozone effect on cardiovascular mortality in the northern region, but not obviously so in the southern region. These findings may have significant implications in the development of disease control and prevention programs in relation to air pollution and climate change.

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Table 1. Summary description for Pearson correlation coefficients between daily maximum temperature and ozone across different regions during the summer (May to October)

Region[1]	Number of communities	Correlation coefficients					
		Mean	Minimum	25 Pctl[2]	Median	75 Pctl	Maximum
NE	15	0.618	0.438	0.554	0.642	0.683	0.727
IM	19	0.644	0.589	0.651	0.663	0.695	0.709
UM	7	0.511	0.302	0.439	0.521	0.589	0.644
NW	12	0.399	-0.051	0.368	0.439	0.520	0.620
SE	26	0.279	-0.361	0.031	0.305	0.515	0.623
SW	9	0.218	-0.329	0.061	0.304	0.392	0.540
SC	7	0.350	-0.208	-0.026	0.515	0.728	0.754

1 NE, IM, UM, NW, SE, SW and SC represent the Northeast, Industrial Midwest, Upper Midwest, Northwest, Southeast, Southwest and Southern California, respectively.

2 Pctl denote percentile.

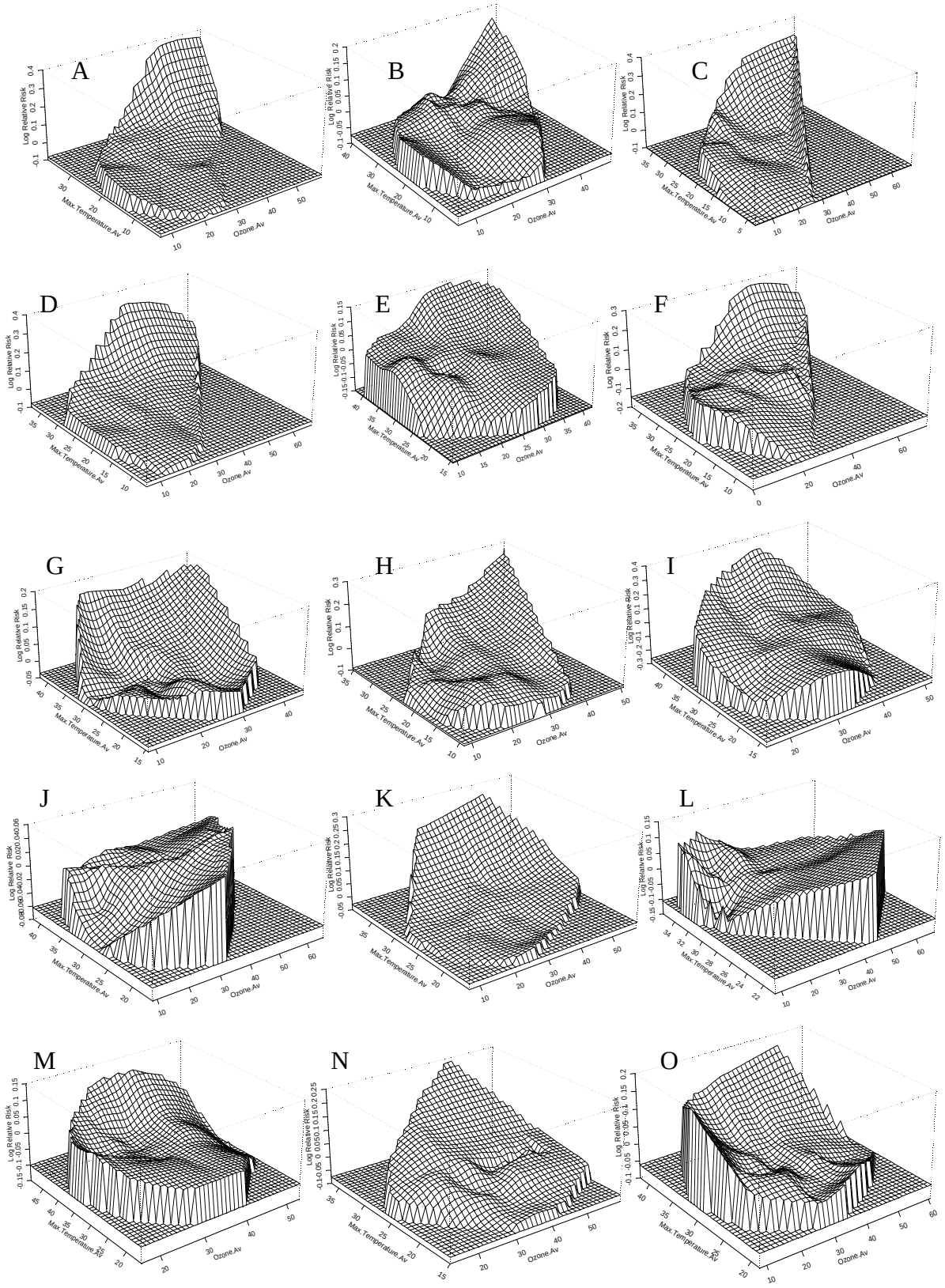
Table 2 Percentage changes in daily cardiovascular mortality per 10-ppb increase in ozone across regions and temperature levels during the summer using Bayesian meta-analysis (log relative rate)

		Low Temperature	Moderate Temperature	High Temperature	Difference (High-Low)*
Current Day	Northeast	0.63 (0.11,1.20)	0.67 (-0.15, 1.62)	1.23 (0.53, 1.87)	0.60 (-0.27, 1.44)
	Industrial Midwest	0.58 (0.07, 1.08)	0.66 (-0.01, 1.39)	1.22 (0.45, 2.10)	0.65 (-0.27, 1.66)
	Upper Midwest	0.50 (-0.46, 1.12)	0.43 (-0.80, 1.47)	1.11 (-0.04, 2.32)	0.62 (-0.72, 2.11)
	Northwest	0.46 (-0.52, 1.17)	0.22 (-1.05, 1.11)	1.66 (0.51, 3.35)	1.19 (-0.15, 3.04)
	Southeast	0.58 (0.01, 1.09)	0.59 (0.05, 1.21)	0.62 (0.03, 1.20)	0.04 (-0.73, 0.85)
	Southwest	0.64 (-0.01, 1.33)	0.26 (-0.75, 1.07)	0.69 (-0.50, 1.72)	0.05 (-1.26, 1.32)
	South California	0.63 (0.05, 1.25)	0.21 (-0.85, 1.03)	1.04 (0.22, 1.92)	0.41 (-0.61, 1.46)
	National	0.58 (0.07, 1.03)	0.43 (-0.30, 1.08)	1.08 (0.39, 1.89)	0.51 (-0.34, 1.45)
Lag 1	Northeast	0.20 (-0.33, 0.77)	0.42 (-0.10, 0.99)	2.17 (1.15, 2.92)	1.97 (0.82, 2.93)
	Industrial Midwest	0.22 (-0.31, 0.80)	0.36 (-0.25, 0.96)	1.83 (0.81, 2.81)	1.60 (0.47, 2.73)
	Upper Midwest	0.20 (-0.55, 0.91)	0.41 (-0.35, 1.29)	0.72 (-0.86, 2.31)	0.51 (-1.18, 2.13)
	Northwest	0.22 (-0.45, 0.88)	0.45 (-0.29, 1.38)	1.81 (0.39, 3.11)	1.60 (0.04, 3.09)
	Southeast	0.16 (-0.39, 0.68)	0.43 (-0.02, 0.93)	0.23 (-0.54, 0.82)	0.07 (-0.73, 0.86)
	Southwest	0.26 (-0.41, 1.02)	0.18 (-0.81, 0.85)	0.73 (-0.54, 1.92)	0.47 (-0.98, 1.85)
	South California	0.27 (-0.27, 0.92)	0.28 (-0.35, 0.87)	0.07 (-1.04, 1.24)	-0.20 (-1.49, 1.08)
	National	0.22 (-0.25, 0.72)	0.36 (-0.16, 0.85)	1.08 (-0.09, 2.22)	0.86 (-0.37, 2.07)
Lag 2	Northeast	0.13 (-0.43, 0.79)	0.20 (-0.34, 0.89)	1.20 (0.36, 2.16)	1.07 (-0.01, 2.17)
	Industrial Midwest	0.06 (-0.45, 0.59)	-0.04 (-0.64, 0.45)	1.15 (0.31, 2.14)	1.09 (0.10, 2.19)
	Upper Midwest	0.07 (-0.77, 0.98)	0.10 (-0.65, 0.99)	0.33 (-1.01, 1.34)	0.26 (-1.34, 1.62)
	Northwest	-0.04 (-0.83, 0.58)	0.00 (-0.83, 0.73)	0.51 (-0.61, 1.43)	0.54 (-0.75, 1.77)
	Southeast	-0.04 (-0.56, 0.40)	0.01 (-0.47, 0.45)	0.61 (-0.01, 1.25)	0.65 (-0.10, 1.40)
	Southwest	-0.04 (-0.80, 0.60)	-0.20 (-1.27, 0.45)	0.32 (-0.90, 1.26)	0.35 (-1.02, 1.55)
	South California	0.05 (-0.54, 0.68)	-0.02 (-0.73, 0.55)	0.52 (-0.39, 1.27)	0.47 (-0.64, 1.42)
	National	0.03 (0.47, 0.51)	0.01 (-0.53, 0.47)	0.66 (-0.14, 1.37)	0.64 (-0.35, 1.49)
Three – Day Average	Northeast	0.43 (-0.28, 1.07)	0.36 (-0.56, 1.29)	3.49 (2.19, 4.39)	3.06 (1.58, 4.20)
	Industrial Midwest	0.47 (-0.14, 1.06)	0.33 (-0.46, 1.12)	2.46 (1.11, 3.74)	1.99 (0.47, 3.42)
	Upper Midwest	0.33 (-0.77, 1.14)	0.26 (-0.80, 1.14)	1.05 (-0.82, 2.81)	0.72 (-1.36, 2.85)
	Northwest	0.35 (-0.63, 1.06)	0.23 (-0.95, 1.11)	2.77 (1.18, 4.41)	2.42 (0.61, 4.26)
	Southeast	0.39 (-0.27, 1.03)	0.39 (-0.22, 1.01)	0.57 (-0.14, 1.25)	0.18 (-0.77, 1.13)
	Southwest	0.42 (-0.33, 1.17)	0.05 (-1.28, 0.86)	0.76 (-0.95, 2.35)	0.34 (-1.54, 2.12)
	South California	0.49 (-0.13, 1.10)	0.24 (-0.54, 0.89)	0.57 (-0.80, 1.93)	0.08 (-1.38, 1.55)
	National	0.41 (-0.19, 0.93)	0.27 (-0.44, 0.87)	1.68 (0.07, 3.26)	1.27 (-0.41, 2.92)

* Differences of the estimates between high temperature level and low temperature levels. The values in the parentheses mean 95% posterior intervals (95% PI).

Figure 1 Legend

Figure 1 Joint response surfaces of ozone and temperature on cardiovascular mortality in Chicago(A), Denver(B), Detroit(C), New York(D), Oakland(E), Philadelphia(F), San Jose(G), Seattle(H) (the 8 largest northern communities) and El Paso(I), Houston(J), Los Angeles(K), Oklahoma City(L), Phoenix(M), San Diego(N) and Santa Ana/Anaheim(O) (the 7 largest southern communities) between May and October, 1987-2000.


A
B
C
D
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L
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O
Log Relative Risk
Max.Temperature.Av
Ozone.Av

Figure 1