Assessment of interactive effects of temperature and air pollution on mortality in Mexico City

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Abstract

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Environmental conditions such as air pollution and ambient temperature, can pose increased risk of premature mortality. In Mexico City, despite recent improvements in reducing air pollution, ozone and particulate matter continue to contribute to thousands of deaths each year, with mounting evidence of interactive effects (synergy) between temperature and air pollution on mortality. As global temperatures rise and become more volatile, there is a growing need to untangle these relationships in order to mitigate future pollution-related mortality. This study investigated potential interactions between temperature and air pollution, specifically ozone and $PM_{2.5}$, on all-cause, cardiovascular disease, and respiratory disease mortality. Daily mortality counts were modelled using generalized additive models (GAMs), adjusting for long term and seasonal trends in mortality. Bivariate response surface models and parametric models indicate interaction between air pollution and temperature. In particular, risk of mortality due to $PM_{2.5}$ was significantly heightened at colder temperatures. This study highlights the importance of reducing air pollution exposure, particularly during periods of anomalously cold temperature.

Introduction

Air pollution contributed to over 2,600 deaths in Mexico City in 2016, and contributed to over 4 million deaths globally[1]. Air pollution causes death and disease through a range of causes including respiratory illness, ocular disease, cardiovascular disease, and diabetes[2]. Most air pollution related deaths in Mexico City are due to particulate matter less than 2.5 microns in diameter ($PM_{2.5}$), with a smaller subset of deaths due to ambient ozone[1]. Over the past few decades, Mexico City officials and policymakers have made strides in reducing pollution by improving public transportation, requiring emissions test, and mandating factories to reduce greenhouse gas emissions[3]. In spite of these improvements, the city continues to struggle to reduce pollution. In 2014, Mexico City reported average annual particulate matter concentration two times higher than guidelines set by the World Health Organization at 20 $\mu g/m^3$, and higher than other Latin American mega-cities such as Buenos Aires and São Paulo[4].

There is abundant evidence that ambient temperature contributes to health loss[5]. Generally, extreme heat and cold are associated with increased mortality risk, although multi-country analyses have found these relationships to vary across space and time[6]. Proposed biological mechanisms through which extreme temperatures act to harm health include reduced immune system capacity for respiratory diseases and increased vasoconstriction and blood pressure for cardiovascular diseases[7–9]. However, finding what range or ranges of temperature pose the greatest threat has been difficult and substantial research has suggested relative temperature appears to be more predictive of mortality than absolute temperature[10]. A location's minimum mortality temperature, or the temperature at which the lowest all-cause mortality is observed, appears to be related to its annual average temperature, suggesting populations adapt to thermal conditions[10]. To capture all these complex components, assessments of the direct effects of temperature on mortality require geographically resolved data, and must stratify analyses over increasingly granular cause of death categories.

The climate of Mexico City is classified as subtropical highland due to its unique combination of tropical latitude and high elevation[11]. The city generally experiences temperate weather with an annual average temperature of 17°C. Rainfall in Mexico City is substantially higher in summer months from June to October; however, there is substantial intra-city variation in temperature and precipitation, with the lower, northern municipalities experiencing drier, warmer climate than its higher, southern peers. Mexico City exhibits large variation in diurnal temperatures and there is evidence of increasing average diurnal temperature range elsewhere in Mexico[12]. Previous studies have investigated the effects of diurnal temperature range, however, mean daily temperature was chosen as the primary temperature metric due to its interpretability and proven relationship with mortality[10].

There is growing evidence of air pollution modifying the effect of temperature in Australia, western Europe, and the United States[13–15]. Most recently, high temperatures were found to modify the effect of specific pollutants (particulate matter with aerodynamic diameter <10 μm, sulfur dioxide, and nitrogen dioxide) on mortality in China[16]. However, these relationships may be location-specific as some studies have found little interaction between temperature and air pollution[17]. Heterogeneous and at time conflicting findings across geography from previous research further emphasizes the motivation for conducting an independent analysis in Mexico City. Additionally, there is strong evidence indicating a delayed effect of both

temperature and air pollution on health, in addition to immediate effects[18]. In warmer, subtropical climates, the health effects of these atmospheric variables can last 14 to 25 days[19].

We sought to assess the individual effects of temperature and air pollution on mortality in Mexico City, and describe how temperature and air pollution interact as it relates to mortality in Mexico City. While previous studies have investigated individual effects of air pollution and temperature on mortality in Mexico City, this is the first study to assess of interactive effects of air pollution and temperature on mortality in Mexico City[20,21]. Both short and long-term effects were assessed using moving averages of each of atmospheric variable across 2 days and 14 days. We used parametric and non-parametric regression models to characterize relationships between atmospheric conditions and mortality. Non-parametric models were visually investigated for trends, while parametric models were statistically assessed for strength of effects. Analyses were conducted on all-cause mortality, respiratory illness mortality, and cardiovascular disease mortality to assess how risk functions change across broad cause of death groups.

Materials and Methods

Mortality data

Individual level mortality data from 1998-2016 were downloaded from National Institute of Statistics and Geography (INEGI), an institute that compiles death certificate information and publishes these data online[22]. INEGI reports mortality data back to 1990, however, lack of data availability in the temperature and air pollution database restricted the analysis to 1998-2016. Since the goal of the analysis was to characterize temperature and air pollution effect on mortality in Mexico City, data were geographically restricted to include 14 of the 16 municipalities of Mexico City (two municipalities did not contain temperature or pollution data) and collapsed to represent daily all-cause mortality count for each municipality. Daily mortality datasets for respiratory diseases (ICD-10 codes J00–J99) and cardiovascular diseases (ICD-10 codes I00–I99) were prepped by restricting the dataset to include deaths under the corresponding international classifications of disease (ICD) code[23](Table S1-S2).

Temperature and Air Pollution data

Hourly measurements of ozone, $PM_{2.5}$ concentration, and ambient temperature were downloaded from Mexico City System of Atmospheric Monitoring for 1998-2016[24]. The data were subsetted to only include weather stations located in Mexico City and included a total of 28 monitoring stations located within 14 municipalities of Mexico City. Each of these monitoring stations are biennially or triennially audited to ensure measurement and reporting accuracy. A map of the location of each monitoring station is shown in Figure 1. Each of the monitoring stations were linked to one of the 14 municipalities. Daily average values for temperature and pollutants were calculated by taking the arithmetic mean across the hourly measurements for each day. For municipalities with multiple monitoring stations, daily averages were the arithmetic mean across stations for a given day. Two-day average temperature and pollutant values were a moving average across the day of and the day previous. Fourteen-day average temperature and pollutant values were a moving average across the day of and the 13 days previous. Considerable proportion of the full daily time series from 1998-2016 across municipalities contained missing values for ozone (~8.5%), temperature (~34%), and $PM_{2.5}$ (~39%). From 2003-2013, monitoring stations added the capacity to report $PM_{2.5}$ information. Since by 2013, 25 out of the 28 monitoring stations began reporting pollutant data, we conducted

a sensitivity analysis using data post-2013 to assess the influence of the missing values. No imputation was performed on missing temperature or air pollution values and information for those days were presumed to be missing at random.

Statistical Analysis

Due to the inherent stochasticity of daily temperature and air pollution variables, it was necessary to adopt a modeling framework that could reliably capture the non-linear, short-term effects of predictor variables on mortality. Generalized additive models (GAMs) have been shown to perform well in these circumstances as they enable smoothed predictors to enter the model and support flexible, non-linear relationships necessary to describe epidemiologic pathways[25]. Thus, GAMs were employed to estimate, predict, and visualize the effects of temperature and air pollution on mortality.

To control for seasonal confounding and long-term changes in mortality, each model included a categorical season variable and a trend variable, which was a complete enumeration from 1 to the end of the time series for each municipality. The trend variable was modeled as a penalized spline with 4 degrees of freedom (df) per year. Sensitivity analyses to test the degrees of freedom on trend variable revealed little change in overall dose-response relationship and generalized cross validation (GCV) statistic. Day of the week variable proved to be insignificant and did not improve GCV, thus, was not included in the models. Random intercepts were placed on municipality and a population exposure term was included to control for differences in underlying mortality between municipalities. Daily mortality data were modeled assuming a Quasi-Poisson distribution as daily mortality data tends to contain extra-Poisson variation[26]. For the response surface models, the joint function between temperature and a given pollutant were parameterized using a tensor product, which is a bivariate cubic spline. All data preparation, cleaning, and modeling was conducted in R statistical software[27].

Results

Temperature and Air Pollution Summary

The following results only present daily mean temperature findings since alternative temperature metrics (daily minimum or maximum) were found to be less predictive of mortality, as indicated in the Methods section. The minimum and maximum mean daily temperature in the analyzed dataset was 3°C and 26°C, respectively. On average, the coldest month in the dataset was January at 13°C and the warmest month was May at 20°C. Seasonal averages from 1998-2016 is shown in Figure 2. Mean daily temperature was highly correlated with daily minimum and daily maximum temperature but showed little correlation with diurnal temperature range. Pearson correlation coefficients are provided in Table S3.

The annual average concentrations of ozone and $PM_{2.5}$ in Mexico City were 31 ppb and 25 ppb, respectively. Seasonal variation in the daily mean concentration for both pollutants was marked and followed similar trends, with highest average monthly concentrations occurring in May and the lowest in September. Seasonal averages over the study time period are shown in Figure 2. The minimum and maximum daily mean concentrations for ozone was 0 and 101 ppb. The minimum and maximum daily mean concentrations for $PM_{2.5}$ was 2 and 130 ppb. Bivariate distributions of the daily mean counts for temperature and each pollutant are shown in Figure 3. Correlation between temperature and the pollutants of interest was modest and correlation

coefficients are provided in Table 1. Inter-station correlation of pollutant variable was calculated to assess whether the stations were representative of daily variations in Mexico City, as opposed to station-specific variation. Monitoring stations proved to be highly correlated across both ozone and $PM_{2.5}$ measurements (Tables S4-S5).

Mortality data summary

The analysis included 576,549 deaths from 1998-2016 in Mexico City, with 151,137 cardiovascular disease deaths and 50,749 respiratory disease deaths. Stark seasonal variation in mortality was observed, with a crude all-cause mortality rate of 7.3 deaths per 1000 person-years in winter months and 6.2 deaths per 1000 during summer months. Substantial intra-city heterogeneity in mortality was also observed, with some municipalities such as Cuauhtémoc experiencing 3-4 times higher mortality than Iztacalco. The average annual mortality rate across Mexico City from 1998-2016 was 6.7 deaths per 1000 (Table 2).

Individual effects

Two-day average (lag-2) temperature was associated with increased all-cause mortality on anomalously cold and hot days, and visual inspection of the plot shown in Figure 4 indicates a minimum mortality temperature (mmt) of 17°C. Almost exclusively cold effects were observed for temperature with a 14-day lag period (lag-14), with temperatures lower than 17°C resulting in increased mortality. Mortality exhibited a monotonically increasing relationship with lag-2 ozone, while lag-14 average ozone showed little increased risk apart from exceptionally high concentrations. Mortality and lag-2 $PM_{2.5}$ were positively associated, whereas mortality exhibited little relationship with lag-14 $PM_{2.5}$.

Both cardiovascular disease and respiratory disease mortality showed little association with lag-2 temperature, shown in Figures 5 and 6, respectively. However, cold effects were observed across lag-14 temperature for both specific cause of death categories. Cause-specific mortality was positively associated with short-term ozone (lag-2), while respiratory disease deaths were attenuated with increases in lag-14 ozone. The effect of lag-2 $PM_{2.5}$ on cardiovascular mortality was positive and statistically significant (Figure 5). Both short-term and mid-term $PM_{2.5}$ appeared to trigger increases in respiratory mortality, however, the splines were not significant (Figure 6).

Response Surfaces

Bivariate response surface models are shown in Figures 7-9. Consistent across all-cause and cause-specific models, the effect of lag-2 ozone was greater at warmer (greater than 20°C) temperatures. Response surfaces were less consistent across causes for lag-14 ozone and lag-14 temperature. Heat appears to enhance risk of cardiovascular mortality at high ozone concentrations (Figure 8), while very little temperature-ozone synergy is observed for respiratory mortality (Figure 9). We observed little effect modification on all-cause and cardiovascular mortality of $PM_{2.5}$ by temperature for either lag period. Generally, the all-cause (Figure 7) and cardiovascular (Figure 8) lag-2 model reveals a greater overall $PM_{2.5}$ effect while the lag-14 model shows a greater overall cold effect, irrespective of $PM_{2.5}$ level. We observed the strongest effect modification between $PM_{2.5}$ and temperature in the models predicting risk of respiratory disease mortality (Figure 9), where increases in $PM_{2.5}$ strongly potentiated the effect of cold temperatures.

Interaction Models

Results of interaction models between temperature quantiles and corresponding pollutant are shown in Figures 10-12. Confidence intervals on interaction coefficients were notably wide but many of the coefficients indicate significant interactions between temperature and pollution within particular temperature quantile. The effect of ozone on all-cause mortality was greatest at the highest temperature quantiles across both lag periods (Figure 10). We observed minimal variation in the effect of ozone on cardiovascular and respiratory mortality across temperature quantiles. The effect of lag-2 $PM_{2.5}$ on all-cause mortality increased with warmer temperatures, while this relationship was not observed for lag-14 $PM_{2.5}$. Lag-2 $PM_{2.5}$ had a stronger effect on cardiovascular (Figure 11) and respiratory (Figure 12) deaths at colder temperatures but no indication of effect modification was observed in lag-14 $PM_{2.5}$ across temperature quantiles.

Discussion

General

Temperature and air pollution show complex, non-linear associations with mortality. In this analysis, we sought to untangle those complex associations and characterize individual short-term effects of atmospheric conditions on mortality and potential interactive effects between them in Mexico City. The effect of warm temperatures (heat effects) on mortality was stronger over a lag period of 2 days, while cold effects were observed more strongly over a lag period of 14 days. This finding further corroborates previous analyses conducted in Europe, China, and the United States[15,28]. In Mexico City, the effect of cold appeared more pronounced compared to European settings, while the effect of heat was largely attenuated, suggesting that Mexico City residents have better adapted (structurally or behaviorally) to heat. Structural adaptation could include widespread air-conditioning penetration-a protective measure against heat-related deaths, while behavioral adaptation could entail enacting early warning signs for predicted heatwaves [29,30]. Indications of local adaptation to temperature have also been observed in the United States, where stronger cold effects have been observed in southern cities, while northern cities experience stronger heat effects in relation to mortality[31].

In general, a monotonically increasing relationship was observed between both ozone and $PM_{2.5}$ with mortality. Response surface models indicated some degree of interaction between temperature and both of the pollutants at multiple lag periods. Short-term heat (2-day lag) exacerbating the effect of ozone on mortality was a robust finding that was observed across different causes of death and multiple models. Relationships between short-term temperature and $PM_{2.5}$ were less consistent across causes and response surfaces showed minor interaction. Response surfaces indicated interaction between cold temperature and mid-term (14-day lag) $PM_{2.5}$, particularly for respiratory disease mortality. Similar results have been found elsewhere in Shanghai, China and Brisbane, Australia-two locations that share the relatively warm climate of Mexico City and add further evidence that cold temperature in warm climates pose substantial risk[13,32].

As low and middle income countries industrialize and grow economically, these populations will face rising exposure to air pollution due to increased carbon and nitrogen emissions unless strict air quality regulations are implemented[33]. Rapidly developing urban areas in particular, with dense population and concentrated sources of pollution, will face the greatest challenges in reducing air pollution-related death and disease. The rise of global temperatures

and persistence of air pollution emphasizes the importance of understanding how these factors act individually and in tandem will become increasingly critical for at-risk populations and emboldened policymakers. Findings from this analysis suggest that Mexico City policymakers should, in general, work to mitigate ozone exposure during hot days and mitigate $PM_{2.5}$ exposure on cold days. Health care facilities should be particularly cognizant of the effects harmful atmospheric conditions can have on the most vulnerable populations-children and the elderly[34].

Limitations

Missingness among the atmospheric variables was a notable limitation that restricted the power of the findings. Specifically, only 3 of the 14 municipalities contained monitoring stations that contributed a full time series of pollutant and temperature data. Many of the remaining municipalities began reporting pollutant data regularly from 2003-2013. While missing values reduced the statistical power of analysis, the introduction of bias due to missingness in pollutant variables would have required monitoring stations to selectively report as a function of pollutant concentration. To test this possibility, we performed a sensitivity analysis by restricting the analysis to post-2013 data- when nearly all temperature and pollutant observations were available. The results of individual effects and response surfaces for all-cause mortality are generally similar, indicating minimal bias was introduced by missingness. Comprehensive results of the sensitivity analysis can be found in Figures S1-S3.

Exposure classification in this analysis is not straightforward and misclassification is a possibility with an ecological exposure metric. For example, individuals were mapped to the municipality of residence in order to link temperature and pollutant values but there was no guarantee that every individual was actually in that municipality in the days leading up to their death. For some deaths, it is possible that municipality of residence does not accurately capture the individual's location and actual exposure to atmospheric conditions. This form of non-differential exposure misclassification would dilute the strength of the estimated effect, leading to a bias toward the null.

Future directions

Daily average temperature, ozone, and $PM_{2.5}$ were the primary metrics investigated in this study. They were chosen for interpretability and based on past precedent in the literature, however, there are other components of temperature and pollution that should be investigated in setting-specific manners. Metrics such as diurnal temperature or maximum daily temperature may be a strong predictor of mortality in settings such as Mexico City, where the daily temperature range is particularly sizable. This study stratified analysis on broad categories of causes of death, yet, future studies should investigate the role of atmospheric conditions on even more granular categories of causes of death. It is important to evaluate not only how risk functions for respiratory illness and cardiovascular diseases differ but also how risk of ischemic heart disease and stroke may differ in relation to atmospheric conditions. Furthermore, age-specific analyses will be crucial to identifying biologically vulnerable populations, which can be used to inform policy and infrastructure decisions. Finally, as more complete time series of atmospheric conditions become available and estimation techniques are refined, future research should include analysis of health effects of lesser studied pollutants such as sulfur dioxide and nitrogen dioxide.

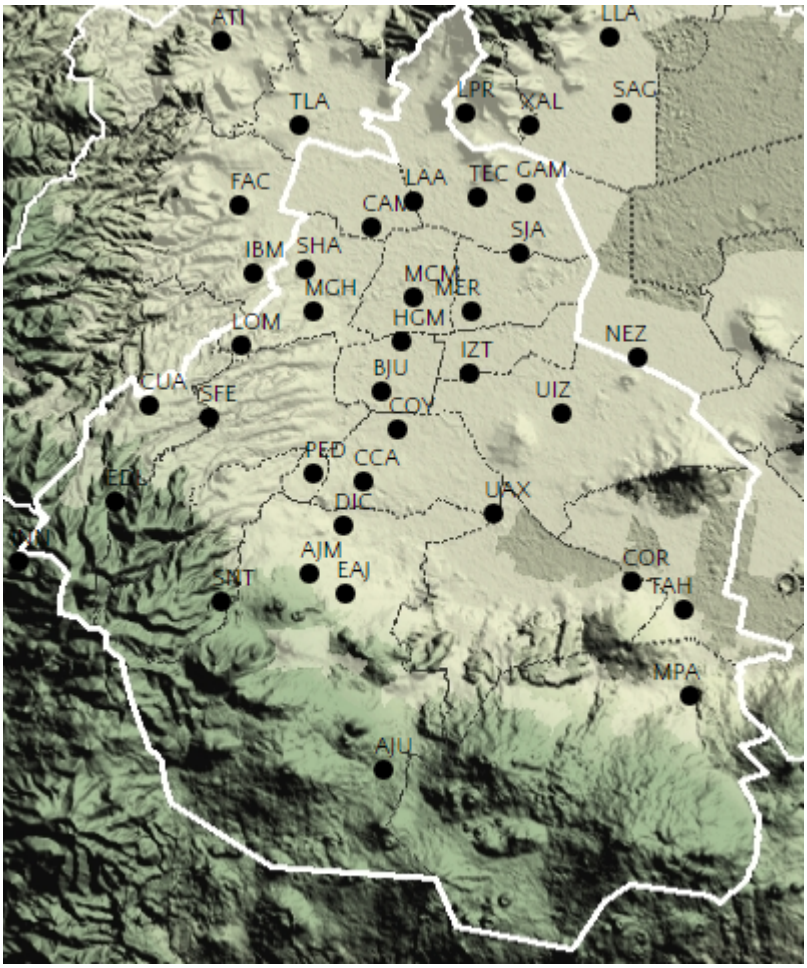


Figure 1. Locations of each monitoring station reporting pollutant and temperature in Mexico City (within white border). Map provided by Mexico City Atmospheric Monitoring[24].

Table 1. Pearson correlation coefficients across atmospheric variables.

	Temperature	Ozone	PM 2.5
Temperature	1	0.23	0.05
Ozone		1	0.17
PM 2.5			1

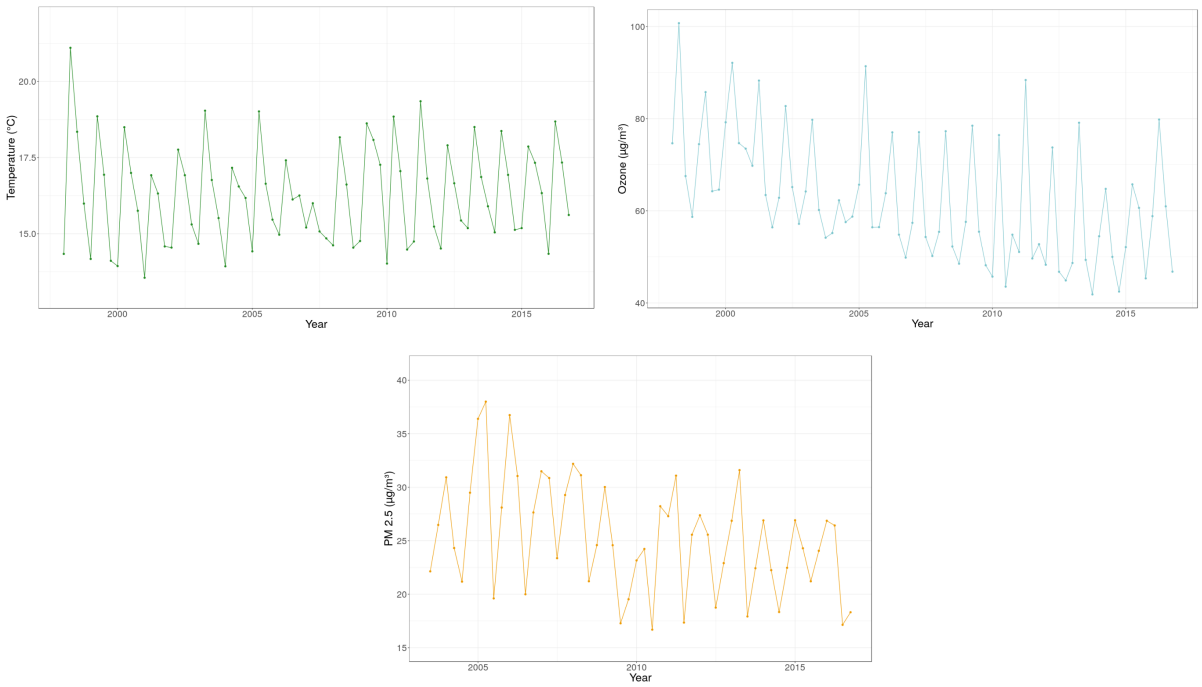


Figure 2. Seasonal averages for temperature, ozone, and $PM_{2.5}$ from 1998-2016 (2003-2016 for $PM_{2.5}$).

Table 2. Summary measures of Mexico City mortality data.

	All Cause	Cardiovascular	Respiratory
Deaths	576,549	151,137	50,794
Mortality	6.71/1000	1.76/1000	0.59/1000
Winter Mortality	7.32/1000	1.96/1000	0.78/1000
Summer Mortality	6.25/1000	1.61/1000	0.47/1000

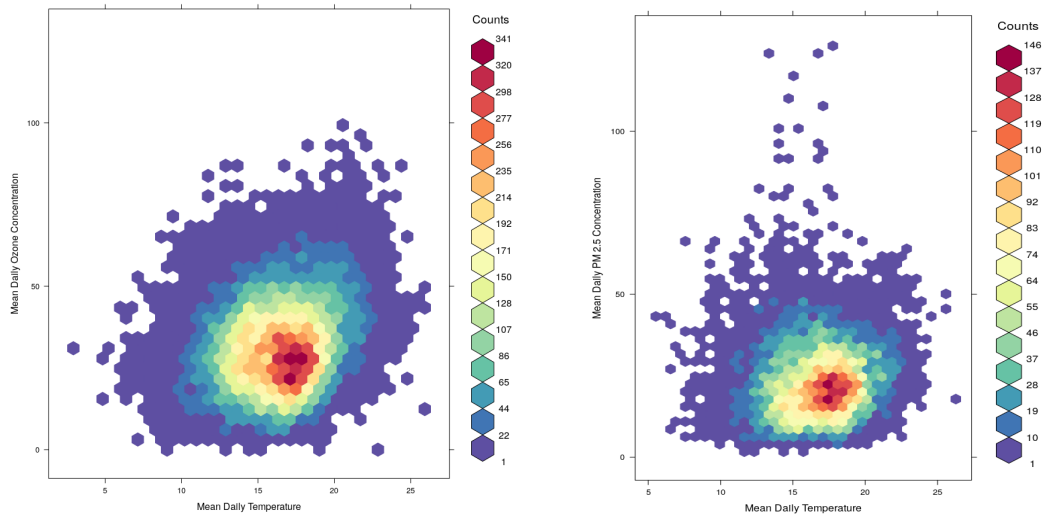


Figure 3. Bivariate distributions of daily counts between temperature and ozone (left) and temperature and $PM_{2.5}$ (right).

Individual Relationships

All-cause Mortality

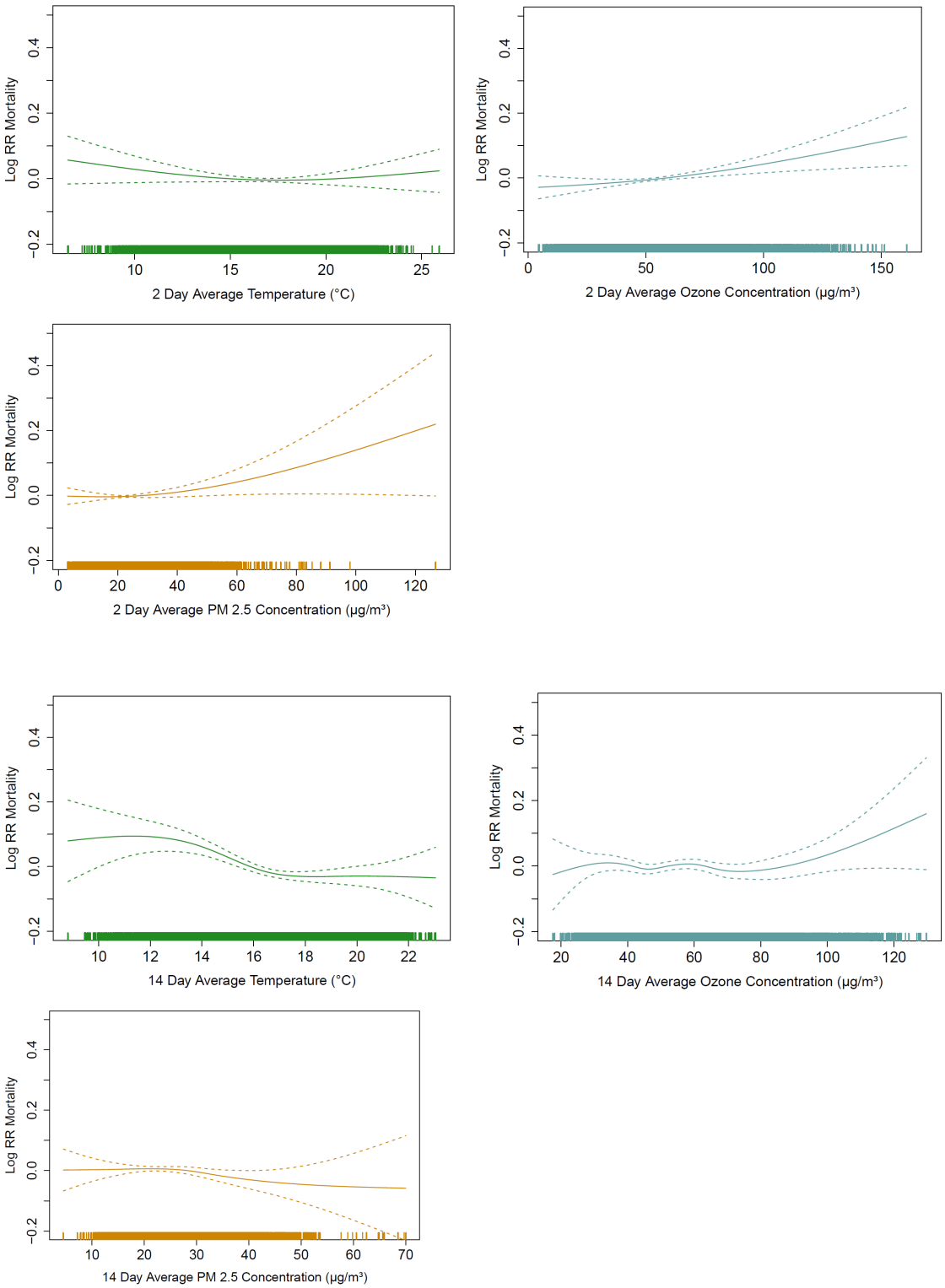


Figure 4. Refer to Table S6 for F statistic and p-values for each spline.

Cardiovascular Disease Mortality

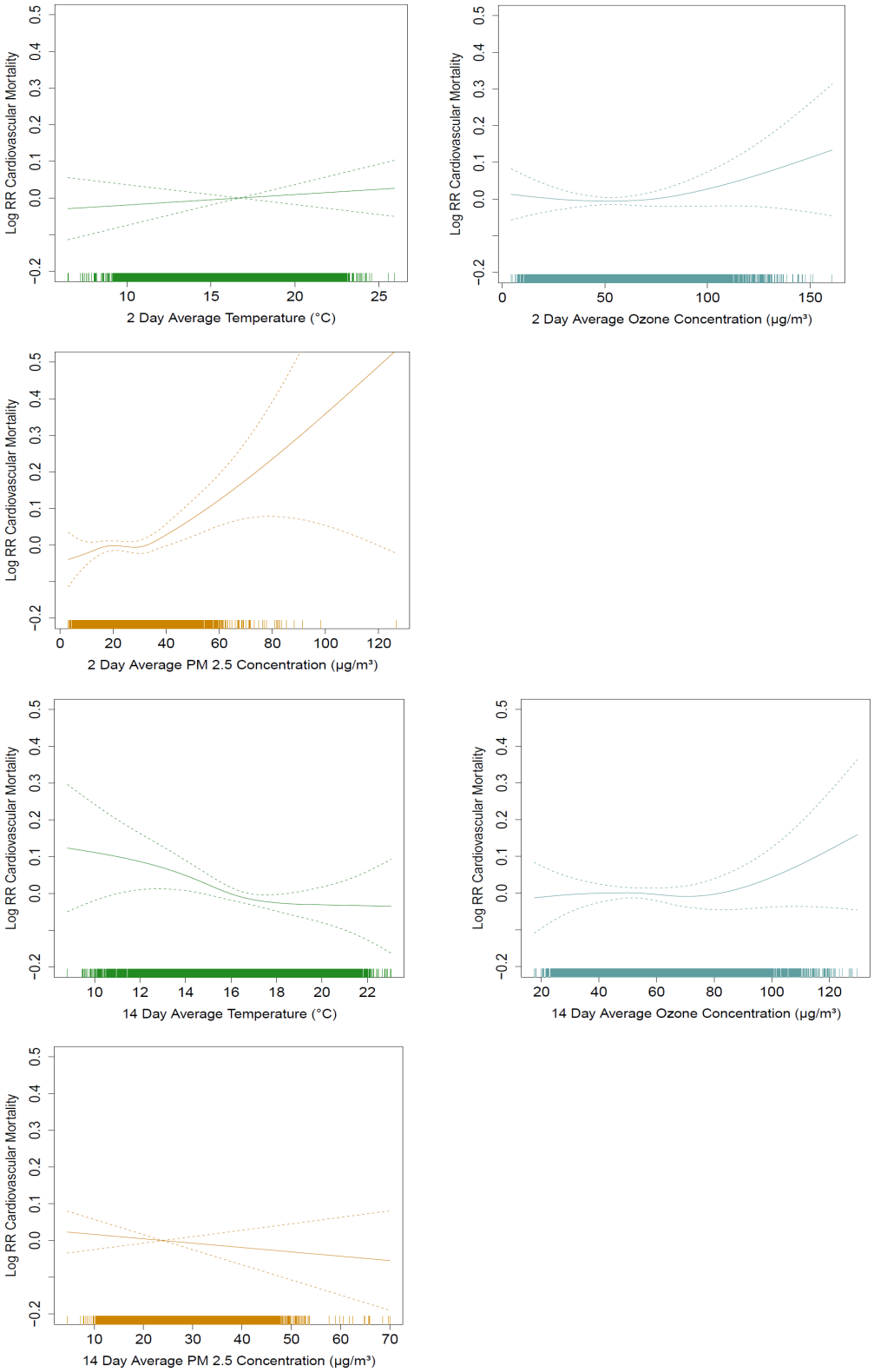


Figure 5. Refer to Table S6 for F statistic and p-values for each spline.

Respiratory Disease Mortality

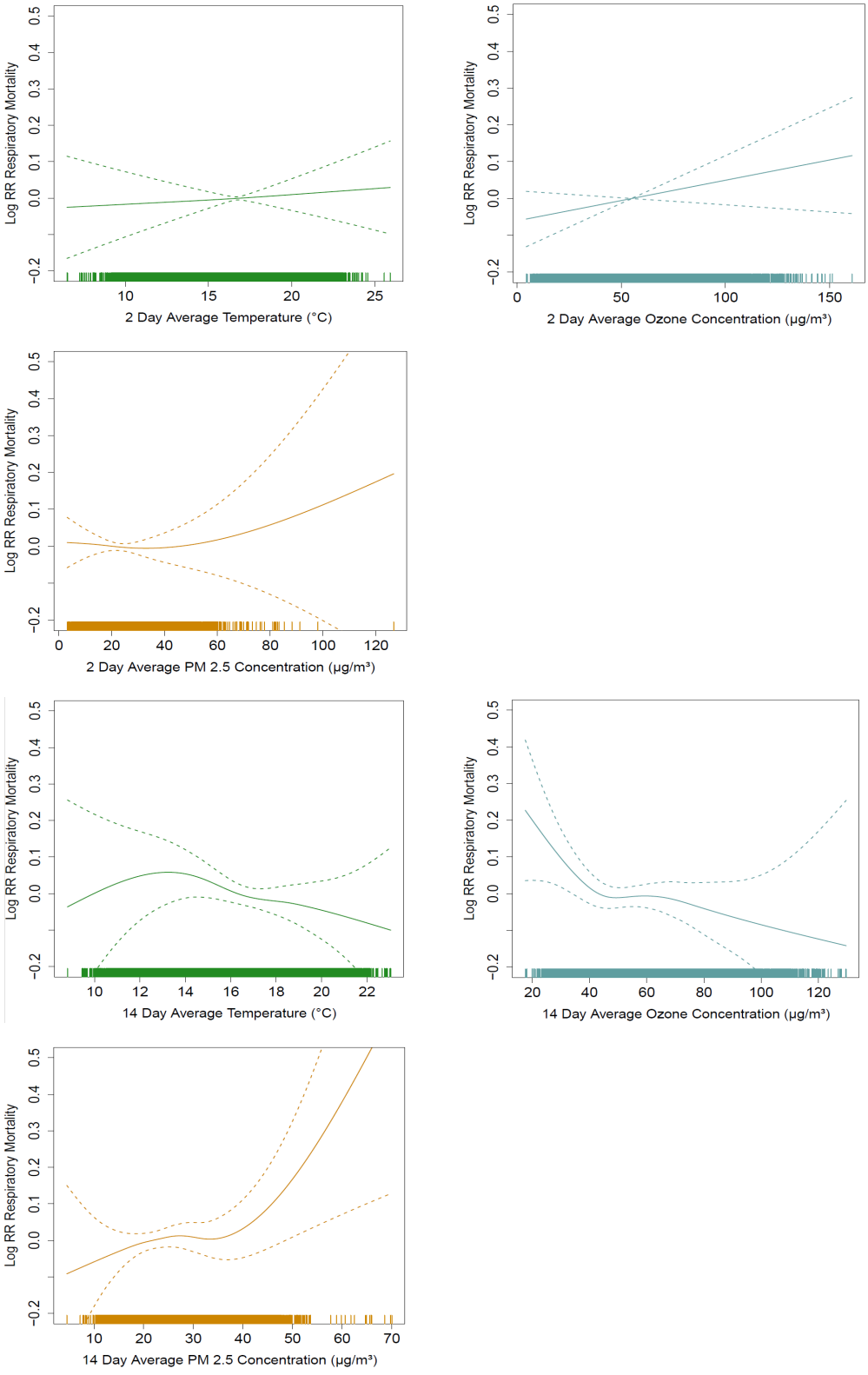


Figure 6. Refer to Table S6 for F statistic and p-values for each spline.

Response Surfaces

All-cause Mortality

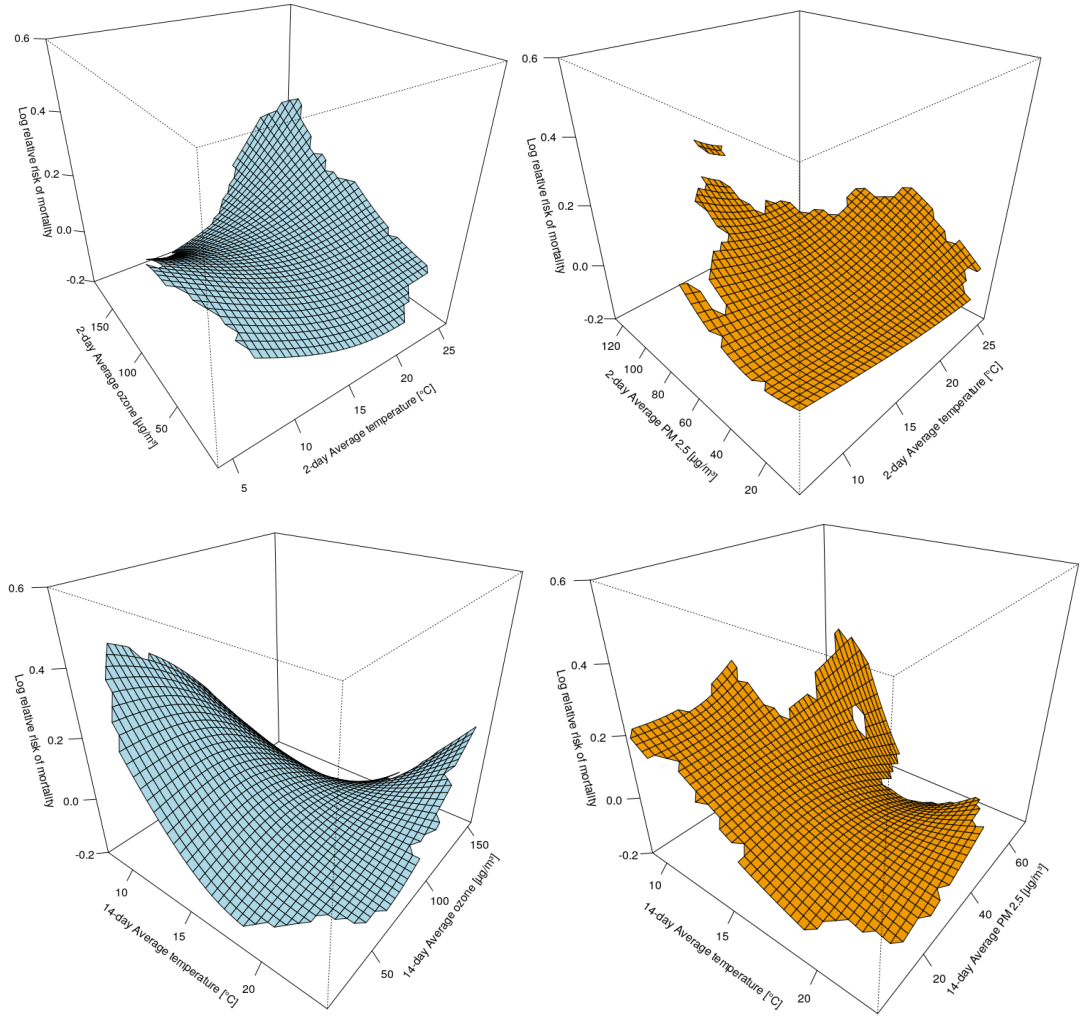


Figure 7.

Cardiovascular Disease Mortality

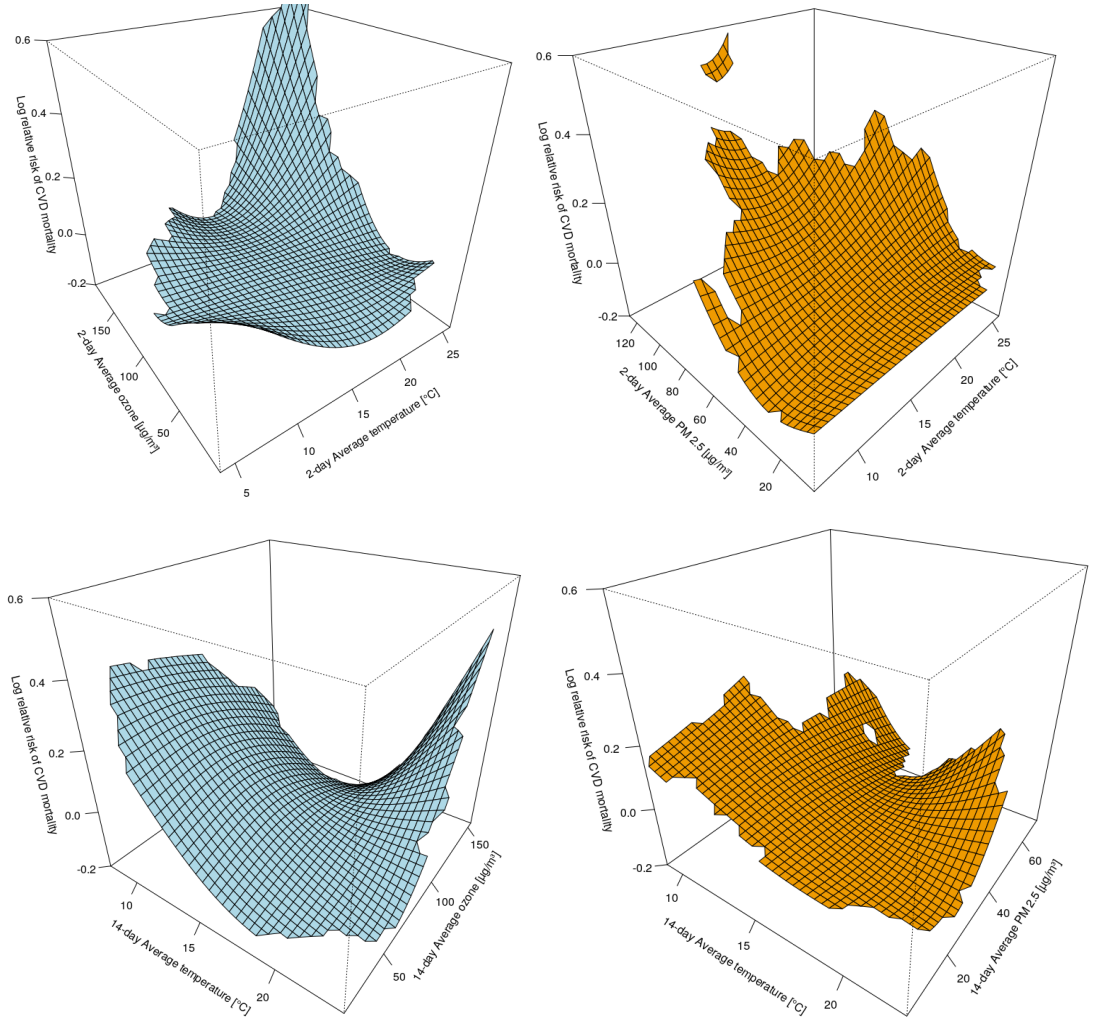


Figure 8.

Respiratory Disease Mortality

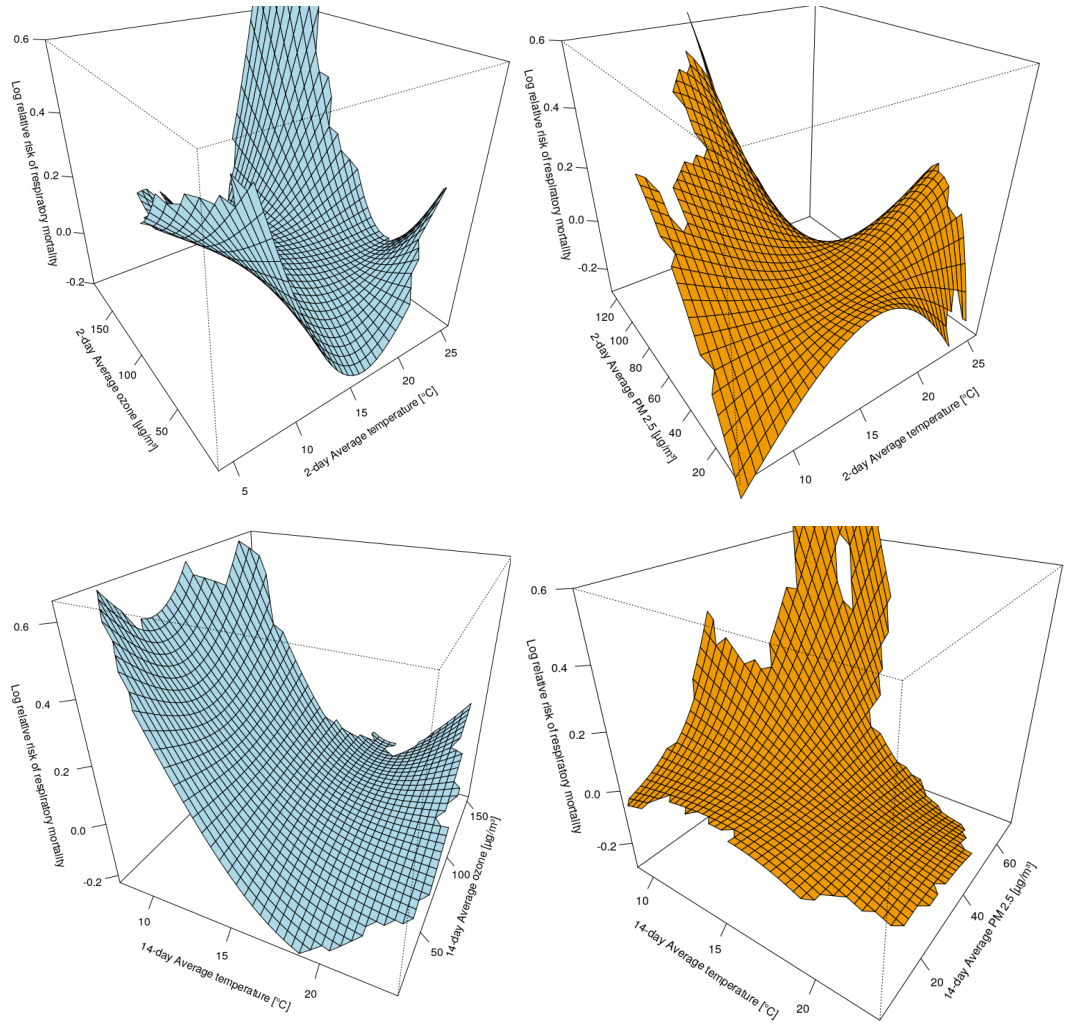
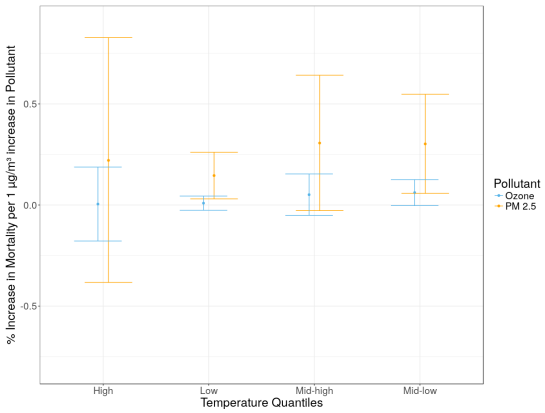


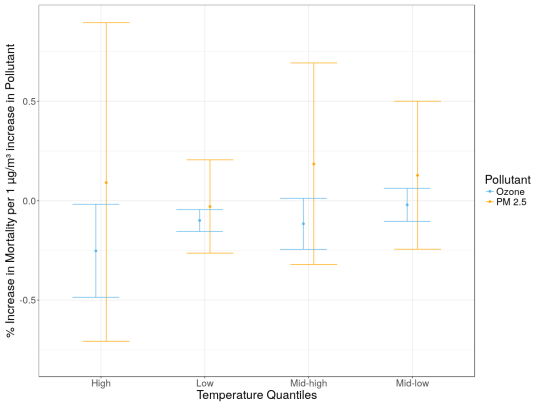
Figure 9.

Interaction Models

All-cause Mortality



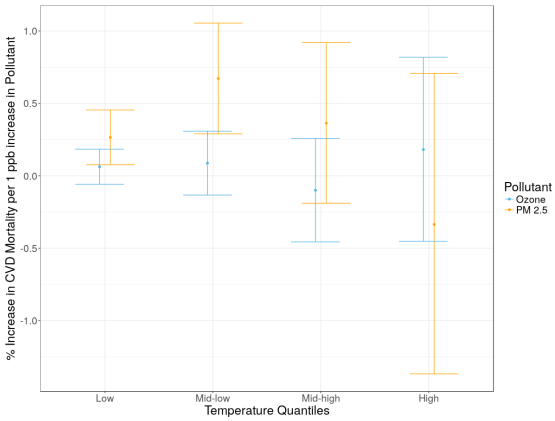
Interaction on 2-day average pollutant



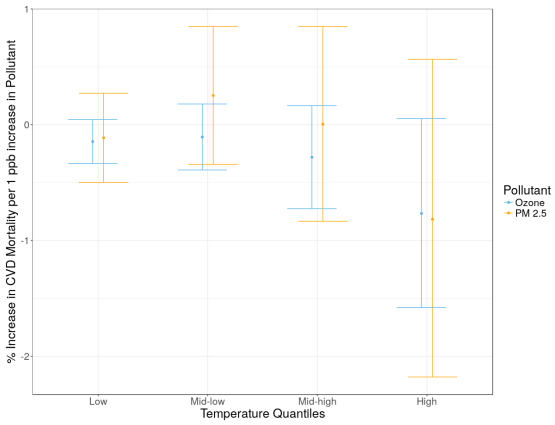
Interaction on 14-day average pollutant

Figure 10.

Cardiovascular Disease Mortality



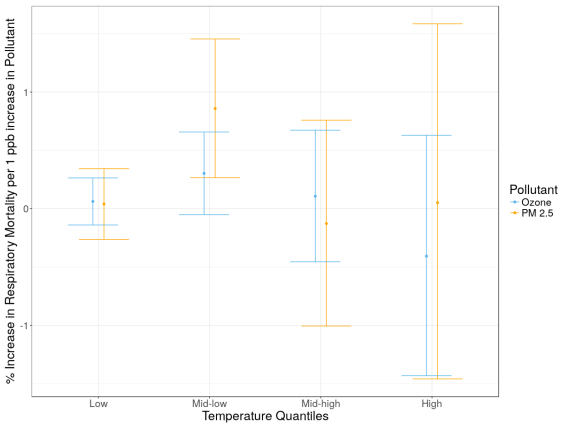
Interaction on 2-day average pollutant



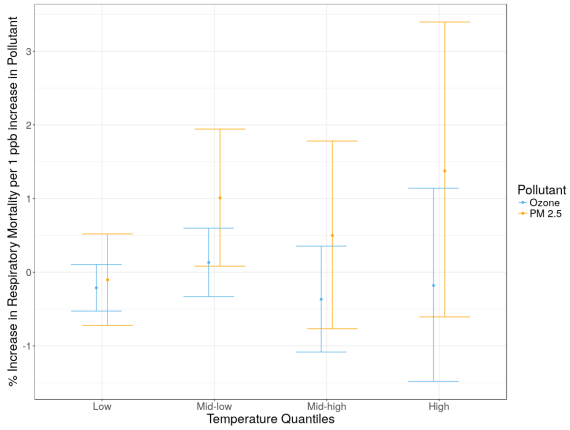
Interaction on 14-day average pollutant

Figure 11.

Respiratory Disease Mortality



Interaction on 2-day average pollutant



Interaction on 14-day average pollutant

Figure 12.

Citations

1. Institute for Health Metrics and Evaluation (IHME). GBDCompareDataVisualization. Seattle, WA: IHME, University of Washington, 2016. Available from http:// vizhub.healthdata.org/gbd-compare. (Accessed [December 1, 2017]).
2. Dominici, F. et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA 295, 1127–34 (2006).
3. Cesar, H., Borja-Aburto, V. H., Cicero-Fernandez, P. & Dorland, K. Improving Air Quality in Metropolitan Mexico City. (2002).
4. WHO | WHO Global Urban Ambient Air Pollution Database (update 2016). (2016).
5. Song, X. et al. Impact of ambient temperature on morbidity and mortality: An overview of reviews. Sci. Total Environ. 586, 241–254 (2017).
6. Gasparrini, A. et al. Temporal Variation in Heat–Mortality Associations: A Multicountry Study. Environ. Health Perspect. 123, (2015).
7. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. The Eurowinter Group. Lancet (London, England) 349, 1341–6 (1997).
8. Yang, L. et al. Outdoor temperature, blood pressure, and cardiovascular disease mortality among 23 000 individuals with diagnosed cardiovascular diseases from China. Eur. Heart J. 36, 1178–1185 (2015).
9. Keatinge, W. R. et al. Winter mortality in relation to climate. Int. J. Circumpolar Health 59, 154–9 (2000).
10. Guo, Y. et al. Global variation in the effects of ambient temperature on mortality: a

systematic evaluation. Epidemiology 25, 781–9 (2014).

11. Volken, E. & Onnimann, S. B. MetZet Classic Papers The thermal zones of the Earth according to the duration of hot, moderate and cold periods and to the impact of heat on the organic world WLADIMIR OPPEN translated from German and edited. Meteorol. Zeitschrift 20, 351–360 (2011).

12. Brito-Castillo, L., Castro, S. C. D. & Ulloa Herrera, R. S. Observed tendencies in maximum and minimum temperatures in Zacatecas, Mexico and possible causes. Int. J. Climatol. Int. J. Clim. 29, 211–221 (2009).

13. Ren, C., Williams, G. M. & Tong, S. Does particulate matter modify the association between temperature and cardiorespiratory diseases? Environ. Health Perspect. 114, 1690–6 (2006).

14. Roberts, S. Interactions between particulate air pollution and temperature in air pollution mortality time series studies. Environ. Res. 96, 328–337 (2004).

15. Burkart, K. et al. Interactive short-term effects of equivalent temperature and air pollution on human mortality in Berlin and Lisbon. (2013). doi:10.1016/j.envpol.2013.06.002

16. Qin, R. X. et al. The interactive effects between high temperature and air pollution on mortality: A time-series analysis in Hefei, China. Sci. Total Environ. 575, 1530–1537 (2017).

17. Samet, J., Zeger, S., Kelsall, J., Xu, J. & Kalkstein, L. Does Weather Confound or Modify the Association of Particulate Air Pollution with Mortality?: An Analysis of the Philadelphia Data, 1973–1980. Environ. Res. 77, 9–19 (1998).

18. Gao, H., Lan, L., Yang, C., Wang, J. & Zhao, Y. The Threshold Temperature and Lag Effects on Daily Excess Mortality in Harbin, China: A Time Series Analysis. Int. J. Occup. Environ. Med. 8, 85–95 (2017).

19. Huang, J., Wang, J. & Yu, W. The Lag Effects and Vulnerabilities of Temperature Effects on Cardiovascular Disease Mortality in a Subtropical Climate Zone in China. Int. J. Environ. Res. Public Health 11, 3982–3994 (2014).

20. Bell, M. L. et al. Vulnerability to heat-related mortality in Latin America: a case-crossover study in Sao Paulo, Brazil, Santiago, Chile and Mexico City, Mexico. Int. J. Epidemiol. 37, 796–804 (2008).

21. Loomis, D. P., Borja-Aburto, V. H., Bangdiwala, S. I. & Shy, C. M. Ozone exposure and daily mortality in Mexico City: a time-series analysis. Res. Rep. Health. Eff. Inst. 1-37; discussion 39-45 (1996).

22. Estadística de defunciones generales. (2016).

23. International Statistical Classification of Diseases and Related Health Problems, 10th revision. (2008).

24. Cuidad de Mexico Gobierno. Dirección de Monitoreo Atmosférico. (2018). Available at: http://www.aire.cdmx.gob.mx/default.php?opc=%27aKBhnmI=%27&opcion=Zg==.

(Accessed: 25th May 2018)

25. Dominici, F., Mcdermott, A., Zeger, S. L. & Samet, J. M. On the Use of Generalized Additive Models in Time-Series Studies of Air Pollution and Health. Am. J. Epidemiol. 156,

26. Aylin, P., Best, N., Bottle, A. & Marshall, C. Following Shipman: a pilot system for monitoring mortality rates in primary care. Lancet 362, 485–491 (2003).

27. R Core Team & R Foundation for Statistical Computing. R: A Language and Environment for Statistical Computing. (2018).

28. Luís, A., Braga, F., Zanobetti, A. & Schwartz, J. The Time Course of Weather-Related Deaths. Epidemiology 662–667 (2001).

29. Bouchama, A. et al. Prognostic Factors in Heat Wave–Related Deaths<subtitle>A Meta-analysis</subtitle> Arch. Intern. Med. 167, 2170 (2007).

30. Ebi, K. L., Kovats, R. S. & Menne, B. An approach for assessing human health vulnerability and public health interventions to adapt to climate change. Environ. Health Perspect. 114, 1930–4 (2006).

31. Curriero, F. C. et al. Temperature and Mortality in 11 Cities of the Eastern United States. 155, (2018).

32. Cheng, Y. & Kan, H. Effect of the Interaction Between Outdoor Air Pollution and Extreme Temperature on Daily Mortality in Shanghai, China. J. Epidemiol. 22, 28–36 (2012).

33. Selden, T. M. & Song, D. Environmental Quality and Development: Is There a Kuznets Curve for Air Pollution Emissions? J. Environ. Econ. Manage. 27, 147–162 (1994).

34. Bunker, A. et al. Effects of Air Temperature on Climate-Sensitive Mortality and Morbidity Outcomes in the Elderly; a Systematic Review and Meta-analysis of Epidemiological Evidence. EBioMedicine 6, 258–268 (2016).