The Effect of Climate Change and Air Pollution on Public Health

THE EFFECT OF CLIMATE CHANGE AND AIR POLLUTION ON PUBLIC HEALTH

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A Dissertation Submitted to the Faculty of

The Harvard School of Public Health

in Partial Fulfillment of the Requirements

for the Degree of Doctor of Science

in the Department of Environmental Health

Harvard University

Boston, Massachusetts.

March, 2015

PREFACE

The effects of temperature and air pollution on public health are comprehensive and ubiquitous. Therefore, this dissertation deals with the comprehensive topic of climate change and air pollution and their effects on public health.

The first chapter examines the effect of temperature on mortality in 148 cities in the U.S. from 1973 through 2006. We focused on the timing of exposure to unseasonal temperature and temporal and spatial acclimation.

The second chapter incorporated AOD data from satellite imagery with other predictors such as meteorological variables, land use regression, and spatial smoothing to predict the daily concentration of $PM_{2.5}$ at a 1 km^2 resolution across the southeastern United States, covering the seven states of Georgia, North Carolina, South Carolina, Alabama, Tennessee, Mississippi, and Florida for the years from 2003 through 2011.

As the sequel of the result from the second chapter, the last chapter investigated the acute effect of $PM_{2.5}$ on mortality in the entire population of North Carolina, South Carolina, and Georgia between 2007 and 2011 using the predictions from the second topic as $PM_{2.5}$ exposure.

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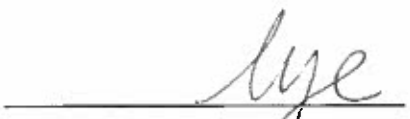
Acknowledgements

I would first like to thank my advisor, Dr. Joel Schwartz, for his support and guidance over the past five years. He has shared his wealth of experience and knowledge and it has been an absolute pleasure and privilege to have been mentored by him.

Next I thank my dissertation research committee. Dr. Petros Koutrakis was instrumental in shaping the direction of this dissertation work. I have been amazed by the insightful comments and suggestions. Dr. Brent Coull provided statistical guidance which is the important part of my research and also provided much great inputs. Both members were very understanding and eager to help me through this dissertation.

I thank my co-authors, classmates, and the faculty and staff at HSPH for their support on this journey. I dedicate this dissertation to my wonderful, loving family. I thank my mother and father, Malsun Ko and Sangyoo Lee, for their unconditional love and support of all my endeavors. My sister, Jihye Lee and my lovely nephews Sewon Park, Jiwon Park, have been my loudest cheerleader. Lastly, I thank my husband, Sunghyun Jung, for encouraging me to follow my dreams and for supporting me throughout my academic career.



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CHAPTER I

Acclimatization across space and time in the effects of temperature on mortality: a time-series analysis*

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* This chapter has been originally published in 'Environmental Health' 2014, 13:89.

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Abstract

Climate change has increased the days of unseasonal temperature. Although many studies have examined the association between temperature and mortality, few have examined the timing of exposure where whether this association varies depending on the exposure month even at the same temperature. Therefore, we investigated monthly differences in the effects of temperature on mortality in a study comprising a wide range of weather and years, and we also investigated heterogeneity among regions.

We analyzed 38,005,616 deaths from 148 cities in the U.S. from 1973 through 2006. We fit city specific Poisson regressions with penalized spline terms to examine the effect of temperature on mortality separately for each month of the year, using penalized splines. We used cluster analysis to group cities with similar weather patterns, and combined results across cities within clusters using meta-smoothing.

There was substantial variation in the effects of the same temperature by month. Heat effects were larger in the spring and early summer and cold effects were larger in late fall. In addition, heat effects were larger in clusters where high temperatures were less common, and vice versa for cold effects.

The effects of a given temperature on mortality vary spatially and temporally based on how unusual it is for that time and location. This suggests changes in variability of temperature may be

more important for health as climate changes than changes of mean temperature. More emphasis should be placed on warnings targeted to early heat/cold temperature for the season or month rather than focusing only on the extremes.

INTRODUCTION

The effects of temperature on public health are comprehensive and ubiquitous. Meanwhile, climate change is shifting the distribution of daily temperature upward, and may be increasing episodes of unseasonal temperature (Hartmann, D.L., A.M.G. Klein Tank, M. Rusticucci, L.V. Alexander, S. Brönnimann, Y. Charabi, F.J. Dentener, E.J. 2013).

Many studies have attempted to understand how extreme temperature affects human health and mortality (Braga, Zanobetti, and Schwartz 2002, 859-863; Analitis et al. 2008, 1397-1408; Zanobetti and Schwartz 2008, 563-570; Curriero et al. 2002, 80-87; Kaiser et al. 2007, S158-62). Generally, those approaches focused on dose-response relationships over an entire year. Other studies have suggested that temperature effects vary geographically with different threshold temperatures due to acclimatization to local weather (Curriero et al. 2002, 80-87; Ye et al. 2012, 19-28; Anderson and Bell 2009, 205-213). This raises the question of whether temporal acclimatization to temperature matters as well as spatial acclimatization. That is, does the dose-response vary by time of the year?

There have also been some studies implying that timing of exposure to excessive heat matters for the magnitude of the adverse health outcome (Anderson and Bell 2011, 210-218; Baccini et al. 2008, 711-719). They have found that early exposure to a heat wave has more impact than the same event later. However, those studies focused only on extreme events, early heat waves were not generally comparable in terms of the intensity and duration to later ones, and the definition of timing was descriptive. In this study, we investigated in a systematic way the effect of timing of exposure to both warm and cold temperatures treated as continuous predictors. Specifically, we examined the dose-response relationship separately in each city in each month, using sufficient years (1973-2006) to ensure stability of the estimates.

To further stabilize results we started with 148 US cities, and clustered them by similarity in seasonal mean and variance of temperature to obtain clusters of cities with similar weather. Results from cities belonging to the same cluster were combined to obtain a more robust estimate of how temperature effect varies by month, and the resulting exposure-response curves were compared among clusters. We also examined how the dose response curves varied by cluster, and the effect of timing by cluster.

DATA

We obtained the data from 211 cities with complete mortality and weather variables for the study. In most cases, a city was contained by a single county. However, we used multiple counties where the city's population extends beyond the boundaries of one county.

Among those cities, we restricted our analysis to cities with a daily average of 5 deaths per day or more for statistical robustness. As a result, we ended up with 148 cities.

Meteorological data were downloaded from the National Oceanic and Atmospheric Administration (NOAA) website and measured by airport weather stations. Since the data are from the airport weather stations, the measurements included visibility in meters as well as daily mean temperature, wind speed, sea level pressure, and dew point. Therefore, relative humidity was calculated with the following formula:

$$\text{Relative humidity (RH)} = 100 \times \left(\frac{112 - 0.1T_a + T_d}{112 + 0.9T_a}\right)^8$$

where T_a and T_d denote air temperature and dew point temperature, respectively (Wanielista, Kersten, and Eaglin 1997).

Among weather monitoring stations, the closest one in distance was assigned to each city for ambient temperature and relative humidity. Since the weather stations were located in airports, the difference in altitude didn't play a role. In case a monitor has missing data, we used the values of the nearest monitor within 60 kilometers. To remove erroneous readings without deleting true extreme events, temperatures out of the 8 standard deviation range were eliminated.

Daily mortality data, including the number of deaths for each day and cause of death, were obtained from the National Center for Health Statistics (NCHS), from the year 1973 through 2006 (Zanobetti and Schwartz 2008, 563-570; Zanobetti and Schwartz 2009, 898-903). We used deaths from any natural cause except for accidental causes (ICD-code 10th revision: V01-Y98, ICD-code 9th revision: 1-799), of persons who resided within the city where they died.

METHOD

Considering the huge variations in the climate of the United States, we categorized the 148 cities into 8 statistical clusters by seasonal temperatures and their seasonal variances. By doing this, we aimed to maximize the similarity within the cluster and dissimilarity between clusters at the same time. Specifically, we employed an agglomerative hierarchical approach where, we started by defining each data point to be a cluster and then combined existing clusters at each step through the single linkage method. PROC CLUSTER in SAS 9.2 (Copyright © 2012 SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA) was implemented based on the mean and standard deviation of the temperature for four seasons in each city.

The statistical analysis consists of two phases. In the first stage, separate daily Poisson time-series analyses were fit for each city and month of the year to evaluate the effect of

temperature on mortality. Because we had 34 years of data for each month, we had sufficient power to estimate these effects. The effect of heat seems to primarily manifest within a day, whereas the effect of cold temperatures is spread out over more days. To accommodate this we fit two temperature variables, temperature on the day of death (lag 0), and the average temperature for the five previous days (lags 1-5). For consistency, temperatures were centered to 18 °C. Since the association of temperature with mortality can be nonlinear, we used a penalized spline to estimate it. The model also controlled for the time trend of mortality and temperature over the 34 years by adding a linear term on the sequence of days. To check the collinearity between the lag 0 lag 1-5, the correlation coefficients were calculated. Day of week was also controlled. Specifically, we assumed:

$$\ln(\lambda)_{ijt} = \beta_{0ij} + \beta_{1i}\text{Time}_i + s(\text{TMP0}_{ijt}) + s(\text{TMP15}_{ijt}) + \beta_{2ij}\text{RH}_{ijt} + \beta_3\text{DOW}_t,$$

where λ denotes the expected number of deaths on day t for city i in month j; Time_i is the sequence of days which counts within month and also increments with the calendar year in city i; TMP0 is the ambient temperature in Celsius on the same day of death in city i; s is the penalized spline function for the temperature effects, estimated with cubic regression splines with 10 knots; TMP15 is the moving average of 1-5 previous days from the death day; RH is the relative humidity; DOW is the indicator variable for day of week on day t. We assumed a quasi-Poisson distribution for λ to account for any over-dispersion.

In the second stage, we combined the curves from the previous model into a curve representing each month for each cluster. Doing this by cluster assured that the overlap in temperature range between cities was large, and that the dose-response curves were similar. Since the splines in the city specific models choose knot points based on the city specific distribution of temperature, a meta-analysis of the spline coefficients is not possible. To avoid this problem, we

used meta-smoothing, a method introduced by Schwartz and Zanobetti to incorporate varying smooth curves into one overall curve (Schwartz and Zanobetti 2000, 666-672). It is based on the idea that predicted curves can be represented by using their predicted values for a dense range of points. Using the predicted values at those points, and their variance, we can do a point-wise meta-analysis.

In this study, we estimated predictions (and their confidence intervals) for each city/month for each 2 °C interval. Next, we applied random effects meta-analyses for each temperature. Finally, by connecting the points, meta-curves were completed. We confined the meta-smoothing to the 99.9^{th} percentile temperature range to avoid extreme values with only one city contributing to the estimate. In the subgroup analysis, mortality due to respiratory disease was examined.

Humidity is a key factor for regulating the body temperature since it modifies the evaporation of sweat in hot weather. As a sensitivity analysis to examine the effect of relative humidity control, we reran the model without the relative humidity term.

Temperature effects may also be confounded by air pollution effects such as PM_{10} or $PM_{2.5}$. Since these were never measured in some cities, and only in later years in others, we analyzed visibility instead as a surrogate for particles. Horizontal visibility is a sensitive indicator of fine particle concentrations (Ozkaynak et al. 1986). And we repeated the meta-smoothing to compare the results with one from the original model.

RESULTS

38,005,616 deaths occurred in 148 cities between 1973 and 2006. Figure I-1 and Table I-1. show the location of 148 cities by cluster and the descriptive statistics of the temperature and

mortality. The first cluster consists of 36 cities mainly located along the northern Atlantic coast area (New York City, Philadelphia, Boston, etc.) but also including some cities in the west (Spokane, Salt Lake City, and Albuquerque). The second cluster (27 cities) was the coldest region with cities such as Chicago, Detroit, and Minneapolis. The third cluster (16 cities), the secondly coldest area, had cities such as Cleveland, Pittsburgh, and St. Louis. Cluster 4 is comprised of 20 warm cities with mild winter temperature such as Atlanta, Charlotte, and Dallas. Cluster 5 contains 16 cities along the west coast (Los Angeles, San Francisco, and Seattle). The sixth cluster consists of 8 cities with very hot and dry weather such as Las Vegas and Phoenix. The seventh cluster is a hot and humid area including 10 cities such as New Orleans, Austin, Houston, etc. Lastly, the eighth cluster is made up of 15 tropical cities such as Miami and Honolulu.

Figure I-2 shows the monthly effects of heat on mortality (i.e. lag 0 temperature) in cluster 1. We present the results from this cluster because it is the one of the most seasonal cluster and also takes the largest number of cities among clusters. Each curve represents a month from April to September and shows the percent increase in mortality at each temperature compared to the mortality at 18 °C. The results clearly differ by month, with the same temperature having the largest effect on excess of mortality when it occurs in April, progressively lower relative impacts as summer develops, and increasing again in fall. Specifically, mortality increases by 8.69 % at 25 °C compared to 18 °C in April, by 6.77 % in May, and by only 2.98 % in June, which shows the decrease in the increment of mortality. In July, the midst of summer, the increase in mortality at 25 °C hits its minimum, which is 0.72 %. It recovers in August to 1.23 % and increases further to 3.51 % until September. This pattern was consistently observed in other clusters as well except cluster 5 (results not shown). In Figure I-3, the monthly trajectories of the increase in mortality at 25 °C are shown by clusters. In almost every cluster, the increases in mortality at 25 °C peak at

April, and decrease until they hit bottom in July (or August in cluster 5). The effect then rebounds into the fall. Those V-shaped curves demonstrate that exposure timing defined by month played a significant role in the relationship between temperature and mortality. That is, at the same temperature, the excess mortality response differed depending on when people were exposed to it. Table I-2. suggests the 95% confidence intervals for Figure I-3. The confidence intervals for cluster 1 which has the greatest number of cities (36) don't overlap implying that these trends are statistically significant. Due to the lack of number of cities, the confidence intervals from other clusters display a degree of overlaps. It also shows the amount of increase in mortality was not symmetric between the early season and the late season. It showed a smaller increase in mortality in September than in May. In addition, it illustrates the statistically substantial differences in the mortality effect by cluster.

Figure I-4 shows a similar pattern during the cold months. The effects of cold temperatures (lag 1-5) are the smallest in January and February and larger in December, November, and March. We present the results from cluster 2 since it has the next largest number of cities and to show the results from other than cluster. We observed that the early season effect occurred even in the coldest region, cluster 2. The increase in mortality at -10 °C is much higher in December compared to other months in the middle of winter at the same temperature. Again, there seemed to be an asymmetry in effects over the cold season, as the effect in March was lower than the effect of the same temperature in November. For reference, correlation between lag 0 and lag 1-5 was the average of 0.53.

We also found the geographic differences in the response to temperature, when investigated by cluster. Figure I-5 shows how heat effects differ by region in July. At 30 °C, cluster 5 shows

the highest mortality, followed by clusters 2, 1, 3, which are located in cold regions. Mortality at that temperature was lowest in the desert and tropical clusters (6 and 8). Looking at the percentile of temperature that corresponds to 30 °C tells the same story. In cluster 5, 30 °C is the 99.1th percentile, and is associated with the largest percentage increase in mortality amongst the clusters. The same temperature ranks as the 98.6 percentile in the second cluster leading to the second highest increase in mortality and so forth.

Regional differences in mortality were also observed for the cold effect (shown in Figure I-6) and the difference was more drastic than for the heat effects. As the region moves from cold to hot, the increase in mortality at a given temperature increases rapidly. While for the heat effects, the dose-response curves were generally parallel, with similar slopes but different intercepts, for cold temperature, the slopes change substantially between regions. As with the heat effect, the percentile of temperature was generally identical to the rank of increase in mortality by clusters. Cluster 8, the tropical cluster, was the most vulnerable region to cold.

The sensitivity analysis controlling for visibility had little effect. Rather, the addition of the visibility variable has increased the effect estimates slightly (Table I-3 and Figure I-7).

DISCUSSION

In this study, we demonstrated that the response to a given temperature depends on the month it occurs in, and that the response varies across clusters defined by similar temperature and humidity patterns. Furthermore, it appears that the earlier people are exposed to extreme temperatures for the season the higher the increase in mortality. This finding within each cluster is paralleled by the finding across cluster that at a given temperature in a given month (e.g. 30 °C

in July) the mortality response by cluster depends on the degree to which the temperature is unusual. This finding is consistent with other studies that found higher effects of early season exposure (Baccini et al. 2008, 711-719; Anderson and Bell 2011, 210-218; Ha and Kim 2013, 535-544). This phenomenon might be explained by mortality displacement, where the vulnerable population dies off in the first heat wave. However, that does not explain phenomena in Figure I-2 showing the constant pattern of monthly effects because if the vulnerable population dies off in earlier season such as April, the deceasing pattern of mortality will stop at the next month such as May or June at the same temperature of 25 ℃. It also does not explain the bounce back of the increase in mortality in Figure I-3. Again, if the vulnerable population dies off, the mortality will keep decreasing until September, not recover at the same temperature. Moreover, mortality displacement (Kovats and Hajat 2008, 41-55) after the depletion of susceptible persons is usually observed in a period of a week (Baccini et al. 2008, 711-719). Therefore, a monthly difference may not be explainable solely by the harvesting effect. This still applies even if the depletion of the susceptible takes longer than a week based on the phenomenon in Figure I-2 and Figure I-3.

Another plausible explanation would be the temporal acclimation over the course of a season. This can be due to physiological adaptation or behavioral change. Physiological acclimation develops over the course of seasons. For example, as summer progresses, the sweat glands expand and cardiac output increases to sweat, and the concentration of sodium in the same amount of sweat becomes diluted (Cheung, McLellan, and Tenaglia 2000, 329-359). Exposure to heat before such acclimation completes can be more hazardous, and the risk of illness is greatest during the first week of unusual heat (Sandstrom et al. 2008, 169-175; TAYLOR 2006, 331-344). Meanwhile, physiological adaptation doesn't last long and can decay within a few days or weeks after removal from heat (Garrett et al. 2009, 659-670; Taylor 2000, 11-22; Makinen 2010, 1047-

1067). This may explain the bounce back of mortality in Figure I-3. The non-symmetry in the amount of the increase in mortality between the early season and the late season may be explained by the remaining effects of acclimation. Behavioral adaptation such as wearing more clothes or the use of air conditioners is another key factor for lowering mortality. However, early exposure to heat/cold might occur before behavioral adaptation. The public may neglect to prepare themselves for early heat or cold, compared to those in the middle of season. The public should be notified that 25 °C in May can be as harmful to health as 29 °C in July.

For cold, there were more cumulative effects defined by lag 1 through lag 5. This could be because mortality due to cold is indirect, through illnesses such as pneumonia and influenza (McGeehin and Mirabelli 2001, 185-189). Mortality due to respiratory causes also showed a huge difference between the induction of the season (December) and the middle of the season (February). And it appears that the retention of acclimation lasts longer for cold than heat, considering that February showed the lowest mortality whereas July had the lowest mortality effect in summer.

Our findings suggest that if the effects of temperature are highly time dependent (i.e., differ by specific month), investigating temperature by season or only by year effectively averages over diverse months. Therefore, summing up temperature effects and ignoring the timing would dilute the effects of ambient temperature, reducing the estimated change in mortality per unit change in temperature.

We also found that spatial differences in the temperature effect on mortality. Cluster 6, characterized by a hot and dry climate, showed the strongest resistance to the heat. The first possible hypothesis is that the low relative humidity in those dry areas contributed to this high resistance to the heat. It appears that heat acclimation remains longer for dry heat compared to

humid heat (Pandolf 1998, S157-60). It could also be due to the prevalence of air conditioning. Lastly, compared to cluster 8, which is a tropical region, a wider range of heat temperature may have provoked the adaptation to the variability of temperature. For cold, the regional difference was greater than the heat effects. This suggests that human adapt better to cold than to heat.

Removal of the relative humidity from the model made estimates for early summer decrease but increases estimates for late season and winter. This might imply the adaptation is also going on for humidity as well as temperature.

Our results were not confounded by visibility, which is a surrogate measurement of particulate matter such as PM_{10} and $PM_{2.5}$. Rather, the addition of visibility increased the model estimates for temperature. Other studies also state that the relationship between temperature-mortality is robust to air pollution control (Zanobetti and Schwartz 2008, 563-570; Anderson and Bell 2009, 205-213).

The main limitation of the study is the use of ambient temperature as a surrogate for personal exposure. Personal exposure to ambient temperature is modified by adaptive mechanisms such as use of air conditioning. Actual outdoor temperature also can be altered from the airport monitoring stations due to the distance from the monitors and the difference in topography and elevation. Nevertheless, our results are conservative, because the measurement error is non-differential to the outcome. With an ongoing attempt to precisely predict temperature (Kloog et al. 2012, 85-92), exposure measurements will be improved.

Since cardiovascular stability is critical in heat acclimation and is also affected by cold, compromises in this ability will pose more severe burdens on the elderly and the ill. In future studies, subgroup analyses for these populations will reveal more about the impact of monthly temperature anomalies.

Our study has many policy implications. The monthly effects of temperature suggest that more warnings should be given to the public for hot and cold events early in the season as they occur before acclimation has developed. The media and many studies are interested in peak temperatures such as 40°C in the middle of summer. Yet our findings indicate that the impact of early events of less extreme temperature may be greater. Also, warnings could be provided based on a relative scale, such as a percentile, as well as the absolute scale of temperature. In July, 25°C is merely the 49th percentile, whereas the same temperature is the 86th percentile in May, and it poses more harm to the public in the earlier season. To the extent that climate change increases the occurrence of early season warm or cold days, this may be an important health consequence of such changes.

To our knowledge, this is the first study to examine the dependence on month of the effects of temperature on mortality. Timing of exposure to extreme temperature should be given more attention in terms of acclimation. Early heat and cold pose a higher risk, as people are not prepared for them. Furthermore, due to climate change, it is projected that unseasonal days will be increasing and arriving earlier. It is necessary to prepare for these hazards.

Bibliography

Alston, E. J., I. N. Sokolik, and O. V. Kalashnikova. 2012. "Characterization of Atmospheric Aerosol in the US Southeast from Ground- and Space-Based Measurements Over the Past Decade." Atmospheric Measurement Techniques 5 (7): 1667-1682.

Analitis, A., K. Katsouyanni, A. Biggeri, M. Baccini, B. Forsberg, L. Bisanti, U. Kirchmayer, et al. 2008. "Effects of Cold Weather on Mortality: Results from 15 European Cities within the PHEWE Project." American Journal of Epidemiology 168 (12): 1397-1408.

Anderson, B. G. and M. L. Bell. 2009. "Weather-Related Mortality: How Heat, Cold, and Heat Waves Affect Mortality in the United States." Epidemiology (Cambridge, Mass.) 20 (2): 205-213.

Anderson, G. B. and M. L. Bell. 2011. "Heat Waves in the United States: Mortality Risk during Heat Waves and Effect Modification by Heat Wave Characteristics in 43 U.S. Communities." Environmental Health Perspectives 119 (2): 210-218.

Armstrong, B. G. 1998. "Effect of Measurement Error on Epidemiological Studies of Environmental and Occupational Exposures." Occupational and Environmental Medicine 55 (10): 651-656.

Baccini, M., A. Biggeri, G. Accetta, T. Kosatsky, K. Katsouyanni, A. Analitis, H. R. Anderson, et al. 2008. "Heat Effects on Mortality in 15 European Cities." Epidemiology (Cambridge, Mass.) 19 (5): 711-719.

Barnett, A. G., G. M. Williams, J. Schwartz, T. L. Best, A. H. Neller, A. L. Petroeschevsky, and R. W. Simpson. 2006. "The Effects of Air Pollution on Hospitalizations for Cardiovascular Disease in Elderly People in Australian and New Zealand Cities." Environmental Health Perspectives 114 (7): 1018-1023.

Beckerman, Bernardo S., Michael Jerrett, Randall V. Martin, Aaron van Donkelaar, Zev Ross, and Richard T. Burnett. 2013. "Application of the Deletion/Substitution/Addition Algorithm to Selecting Land use Regression Models for Interpolating Air Pollution Measurements in California." Atmospheric Environment 77 (0): 172-177.

Boldo, Elena, Sylvia Medina, Alain Le Tertre, Fintan Hurley, Hans-Guido MÃ¼cke, FerrÃ¡n Ballester, and Inmaculada Aguilera. 2006. "Apheis: Health Impact Assessment of Long-Term Exposure to PM2.5 in 23 European Cities." European Journal of Epidemiology 21 (6): 449-458.

Braga, A. L., A. Zanobetti, and J. Schwartz. 2002. "The Effect of Weather on Respiratory and Cardiovascular Deaths in 12 U.S. Cities." Environmental Health Perspectives 110 (9): 859-863.

Brenner, H., D. A. Savitz, K. H. Jockel, and S. Greenland. 1992. "Effects of Nondifferential Exposure Misclassification in Ecologic Studies." American Journal of Epidemiology 135 (1): 85-95.

Cheung, S. S., T. M. McLellan, and S. Tenaglia. 2000. "The Thermophysiology of Uncompensable Heat Stress. Physiological Manipulations and Individual Characteristics." Sports Medicine (Auckland, N.Z.) 29 (5): 329-359.

Cormier, S. A., S. Lomnicki, W. Backes, and B. Dellinger. 2006. "Origin and Health Impacts of Emissions of Toxic by-Products and Fine Particles from Combustion and Thermal Treatment of Hazardous Wastes and Materials." Environmental Health Perspectives 114 (6): 810-817.

Curriero, F. C., K. S. Heiner, J. M. Samet, S. L. Zeger, L. Strug, and J. A. Patz. 2002. "Temperature and Mortality in 11 Cities of the Eastern United States." American Journal of Epidemiology 155 (1): 80-87.

de Hoogh, Kees, Meng Wang, Martin Adam, Chiara Badaloni, Rob Beelen, Matthias Birk, Giulia Cesaroni, et al. 2013. "Development of Land use Regression Models for Particle Composition in Twenty Study Areas in Europe." Environmental Science & Technology 47 (11): 5778-5786.

Dockery, D. W. 2009. "Health Effects of Particulate Air Pollution." Annals of Epidemiology 19 (4): 257-263.

Dockery, Douglas W., C. A. Pope, Xiping Xu, John D. Spengler, James H. Ware, Martha E. Fay, Benjamin G. Ferris, and Frank E. Speizer. 1993. "An Association between Air Pollution and Mortality in Six U.S. Cities." N Engl J Med 329 (24): 1753-1759.

Franklin, Meredith, Ariana Zeka, and Joel Schwartz. 2006. "Association between PM2.5 and all-Cause and Specific-Cause Mortality in 27 US Communities." J Expos Sci Environ Epidemiol 17 (3): 279-287.

Garrett, A. T., N. G. Goosens, N. J. Rehrer, M. J. Patterson, and J. D. Cotter. 2009. "Induction and Decay of Short-Term Heat Acclimation." European Journal of Applied Physiology 107 (6): 659-670.

Goldman, G. T., J. A. Mulholland, A. G. Russell, M. J. Strickland, M. Klein, L. A. Waller, and P. E. Tolbert. 2011. "Impact of Exposure Measurement Error in Air Pollution Epidemiology: Effect of Error Type in Time-Series Studies." Environmental Health : A Global Access Science Source 10: 61-069X-10-61.

Greenland, S. 1992. "Divergent Biases in Ecologic and Individual-Level Studies." Statistics in Medicine 11 (9): 1209-1223.

Ha, J. and H. Kim. 2013. "Changes in the Association between Summer Temperature and Mortality in Seoul, South Korea." International Journal of Biometeorology 57 (4): 535-544.

Hartmann, D.L., A.M.G. Klein Tank, M. Rusticucci, L.V. Alexander, S. Brönnimann, Y. Charabi, F.J. Dentener, E.J. 2013. 2013: Observations:
Atmosphere and Surface. in: Climate Change 2013: The Physical Science Basis. Contribution of Working Group
I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Stocker, T.F., D. Qin, G.-K.
Plattner, M. Tignor, S.K. Allen, J. Boschung, A. Nauels, Y. Xia, V. Bex and P.M. Midgley (Eds.)]. Cambridge, United Kingdom and New York, NY, USA: Cambridge University.

Hu, Xuefei, Lance A. Waller, Alexei Lyapustin, Yujie Wang, Mohammad Z. Al-Hamdan, William L. Crosson, Maurice G. Estes Jr., et al. 2014. "Estimating Ground-Level PM2.5 Concentrations in the Southeastern United States using MAIAC AOD Retrievals and a Two-Stage Model." Remote Sensing of Environment 140 (0): 220-232.

Jin, Suming, Limin Yang, Patrick Danielson, Collin Homer, Joyce Fry, and George Xian. 2013. "A Comprehensive Change Detection Method for Updating the National Land Cover Database to Circa 2011." Remote Sensing of Environment 132 (0): 159-175.

Kaiser, R., A. Le Tertre, J. Schwartz, C. A. Gotway, W. R. Daley, and C. H. Rubin. 2007. "The Effect of the 1995 Heat Wave in Chicago on all-Cause and Cause-Specific Mortality." American Journal of Public Health 97 Suppl 1: S158-62.

Kloog, I., A. Chudnovsky, P. Koutrakis, and J. Schwartz. 2012. "Temporal and Spatial Assessments of Minimum Air Temperature using Satellite Surface Temperature Measurements in Massachusetts, USA." The Science of the Total Environment 432: 85-92.

Kloog, I., F. Nordio, A. Zanobetti, B. A. Coull, P. Koutrakis, and J. D. Schwartz. 2014. "Short Term Effects of Particle Exposure on Hospital Admissions in the Mid-Atlantic States: A Population Estimate." PloS One 9 (2): e88578.

Kloog, Itai, Petros Koutrakis, Brent A. Coull, Hyung Joo Lee, and Joel Schwartz. 2011. "Assessing Temporally and Spatially Resolved PM2.5 Exposures for Epidemiological Studies using Satellite Aerosol Optical Depth Measurements." Atmospheric Environment 45 (35): 6267-6275.

Kovats, R. S. and S. Hajat. 2008. "Heat Stress and Public Health: A Critical Review." Annual Review of Public Health 29: 41-55.

Lee, H. J., Y. Liu, B. A. Coull, J. Schwartz, and P. Koutrakis. 2011. "A Novel Calibration Approach of MODIS AOD Data to Predict PM$_2.5$ Concentrations." Atmospheric Chemistry and Physics 11 (15): 7991-8002.

Li, Xia, Xiangao Xia, Shengli Wang, Jietai Mao, and Yan Liu. 2012. "Validation of MODIS and Deep Blue Aerosol Optical Depth Retrievals in an Arid/Semi-Arid Region of Northwest China." Particuology 10 (1): 132-139.

Lyapustin, A., Y. Wang, I. Laszlo, R. Kahn, S. Korkin, L. Remer, R. Levy, and J. S. Reid. 2011. "Multiangle Implementation of Atmospheric Correction (MAIAC): 2. Aerosol Algorithm." Journal of Geophysical Research: Atmospheres 116 (D3): - D03211.

Maclure, M. 1991. "The Case-Crossover Design: A Method for Studying Transient Effects on the Risk of Acute Events." American Journal of Epidemiology 133 (2): 144-153.

Makinen, T. M. 2010. "Different Types of Cold Adaptation in Humans." Frontiers in Bioscience (Scholar Edition) 2: 1047-1067.

Mar, Therese F., Kazuhiko Ito, Jane Q. Koenig, Timothy V. Larson, Delbert J. Eatough, Ronald C. Henry, Eugene Kim, et al. 2005. "PM Source Apportionment and Health Effects. 3. Investigation of Inter-Method Variations in Associations between Estimated Source Contributions of PM2.5 and Daily Mortality in Phoenix, AZ." J Expos Sci Environ Epidemiol 16 (4): 311-320.

McGeehin, M. A. and M. Mirabelli. 2001. "The Potential Impacts of Climate Variability and Change on Temperature-Related Morbidity and Mortality in the United States." Environmental Health Perspectives 109 Suppl 2: 185-189.

Medina-Ramon, M. and J. Schwartz. 2007. "Temperature, Temperature Extremes, and Mortality: A Study of Acclimatisation and Effect Modification in 50 US Cities." Occupational and Environmental Medicine 64 (12): 827-833.

Ostro, B. D., R. Broadwin, and M. J. Lipsett. 2000. "Coarse and Fine Particles and Daily Mortality in the Coachella Valley, California: A Follow-Up Study." Journal of Exposure Analysis and Environmental Epidemiology 10 (5): 412-419.

Pandolf, K. B. 1998. "Time Course of Heat Acclimation and its Decay." International Journal of Sports Medicine 19 Suppl 2: S157-60.

Pope, C. A.,3rd. 2000. "Epidemiology of Fine Particulate Air Pollution and Human Health: Biologic Mechanisms and Who's at Risk?" Environmental Health Perspectives 108 Suppl 4: 713-723.

Pope, C. A.,3rd, R. T. Burnett, M. J. Thun, E. E. Calle, D. Krewski, K. Ito, and G. D. Thurston. 2002. "Lung Cancer, Cardiopulmonary Mortality, and Long-Term Exposure to Fine Particulate Air Pollution." JAMA : The Journal of the American Medical Association 287 (9): 1132-1141.

Rhomberg, L. R., J. K. Chandalia, C. M. Long, and J. E. Goodman. 2011. "Measurement Error in Environmental Epidemiology and the Shape of Exposure-Response Curves." Critical Reviews in Toxicology 41 (8): 651-671.

Risom, L., P. Moller, and S. Loft. 2005. "Oxidative Stress-Induced DNA Damage by Particulate Air Pollution." Mutation Research 592 (1-2): 119-137.

Ruchirawat, M., D. Settachan, P. Navasumrit, J. Tuntawiroon, and H. Autrup. 2007. "Assessment of Potential Cancer Risk in Children Exposed to Urban Air Pollution in Bangkok, Thailand." Toxicology Letters 168 (3): 200-209.

Ryan, P. H. and G. K. LeMasters. 2007. "A Review of Land-use Regression Models for Characterizing Intraurban Air Pollution Exposure." Inhalation Toxicology 19 Suppl 1: 127-133.

Samet, J. M., F. Dominici, F. C. Curriero, I. Coursac, and S. L. Zeger. 2000. "Fine Particulate Air Pollution and Mortality in 20 U.S. Cities, 1987-1994." The New England Journal of Medicine 343 (24): 1742-1749.

Sandstrom, M. E., J. C. Siegler, R. J. Lovell, L. A. Madden, and L. McNaughton. 2008. "The Effect of 15 Consecutive Days of Heat-Exercise Acclimation on Heat Shock Protein 70." Cell Stress & Chaperones 13 (2): 169-175.

Schwartz, J. and A. Zanobetti. 2000. "Using Meta-Smoothing to Estimate Dose-Response Trends Across Multiple Studies, with Application to Air Pollution and Daily Death." Epidemiology (Cambridge, Mass.) 11 (6): 666-672.

TAYLOR, Nigel A. S. 2006. "Challenges to Temperature Regulation when Working in Hot Environments." Industrial Health 44 (3): 331-344.

Taylor, Nigel A. S. 2000. "Principles and Practices of Heat Adaptation." Journal of the Human-Environment System 4 (1): 11-22.

Valavanidis, A., K. Fiotakis, and T. Vlachogianni. 2008. "Airborne Particulate Matter and Human Health: Toxicological Assessment and Importance of Size and Composition of Particles for Oxidative Damage and Carcinogenic Mechanisms." Journal of Environmental Science and Health.Part C, Environmental Carcinogenesis & Ecotoxicology Reviews 26 (4): 339-362.

Wang, Rongrong, Sarah B. Henderson, Hind Sbihi, Ryan W. Allen, and Michael Brauer. 2013. "Temporal Stability of Land use Regression Models for Traffic-Related Air Pollution." Atmospheric Environment 64 (0): 312-319.

Wanielista, Martin P., Robert Kersten, and Ron Eaglin. 1997. Hydrology : Water Quantity and Quality Control. 2nd ed. New York: John Wiley & Sons.

Whitworth, K. W., E. Symanski, D. Lai, and A. L. Coker. 2011. "Kriged and Modeled Ambient Air Levels of Benzene in an Urban Environment: An Exposure Assessment Study." Environmental Health : A Global Access Science Source 10: 21-069X-10-21.

Wichmann, H. E., C. Spix, T. Tuch, G. WÃ¶lke, A. Peters, J. Heinrich, W. G. Kreyling, and J. Heyder. 2000. "Daily Mortality and Fine and Ultrafine Particles in Erfurt, Germany Part I: Role of Particle Number and Particle Mass." Research Report (Health Effects Institute) (98): 5-86; discussion 87-94.

Ye, X., R. Wolff, W. Yu, P. Vaneckova, X. Pan, and S. Tong. 2012. "Ambient Temperature and Morbidity: A Review of Epidemiological Evidence." Environmental Health Perspectives 120 (1): 19-28.

Zanobetti, A. and J. Schwartz. 2009. "The Effect of Fine and Coarse Particulate Air Pollution on Mortality: A National Analysis." Environmental Health Perspectives 117 (6): 898-903.

———. 2008. "Temperature and Mortality in Nine US Cities." Epidemiology (Cambridge, Mass.) 19 (4): 563-570.

TABLES

Table I-1. Descriptive Statistics of Temperature and Mortality by Cluster

Cluster	Season	Temperature (°C)		Relative Humidity (%)		Daily Death (Count)	
		Mean	S.D.*	Mean	S.D.	Mean	S.D.
1	Spring-Summer	16.83	8.00	63.55	16.84	22.63	33.08
	Fall-Winter	7.03	8.53	66.20	15.41	24.29	35.57
2	Spring-Summer	15.12	8.63	65.12	14.97	19.00	28.11
	Fall-Winter	4.13	9.56	69.76	14.33	20.22	29.88
3	Spring-Summer	18.04	8.16	65.77	13.43	17.29	13.67
	Fall-Winter	7.03	9.38	69.47	13.18	18.43	14.56
4	Spring-Summer	21.10	6.74	65.86	13.92	12.33	9.07
	Fall-Winter	11.58	8.14	66.82	15.52	13.20	9.70
5	Spring-Summer	16.79	4.93	66.56	13.83	29.16	33.50
	Fall-Winter	12.83	5.65	70.42	17.25	31.16	36.35
6	Spring-Summer	23.67	7.09	37.35	17.40	13.50	12.50
	Fall-Winter	14.76	7.36	52.66	21.91	14.51	13.40
7	Spring-Summer	23.93	5.01	70.99	12.20	13.47	11.58
	Fall-Winter	16.69	6.99	71.13	14.42	14.34	12.28
8	Spring-Summer	25.29	3.63	71.52	9.69	15.61	11.76
	Fall-Winter	21.02	5.44	73.13	10.87	16.39	12.22

*S.D. is the standard deviation

Table I-2. Percent increase in Mortality at 25 °C by Cluster and Month

April	May	June	July	August	September
8.69 (7.16, 10.25)	6.77 (5.52, 8.04)	2.98 (2.57, 3.39)	0.72 (0.48, 0.96)	1.23 (0.90, 1.57)	3.51 (2.77, 4.26)
6.58 (4.63, 8.56)	6.19 (4.94, 7.46)	4.26 (3.53, 4.99)	2.20 (1.78, 2.62)	2.92 (2.29, 3.56)	4.74 (3.67, 5.81)
5.09 (3.21, 7.01)	3.60 (2.70, 4.51)	1.39 (0.99, 1.80)	-0.02 (-0.13, 0.09)	0.70 (0.46, 0.94)	2.13 (1.30, 2.97)
2.89 (1.68, 4.12)	1.87 (1.10, 2.65)	0.19 (0.04, 0.35)	-2.10 (-2.87, -1.33)	-0.82 (-1.16, -0.48)	0.82 (0.31, 1.33)
5.35 (1.34, 9.51)	6.40 (4.07, 8.79)	7.33 (4.89, 9.82)	6.52 (5.21, 7.85)	4.82 (2.99, 6.69)	5.93 (3.95, 7.95)
2.74 (1.03, 4.49)	0.88 (0.36, 1.39)	-1.31 (-2.06, -0.54)	-3.19 (-6.26, -0.02)	-2.14 (-3.57, -0.70)	-0.49 (-0.77, -0.21)
1.62 (0.38, 2.87)	0.39 (0.04, 0.75)	-1.54 (-2.25, -0.81)	-2.8 (-4.30, -1.26)	-0.74 (-2.06, 0.61)	-0.02 (-0.25, 0.20)
0.61 (0.11, 1.11)	-0.36 (-0.62, -0.10)	-2.22 (-3.12, -1.31)	-2.63 (-4.05, -1.20)	-2.30 (-3.73, -0.85)	-1.59 (-2.61, -0.56)

Estimate is percent increase in mortality at 25 °C compared to mortality at 18 °C
Negative value means lower mortality than the reference temperature of 18 °C.
() is 95% confidence interval

Table I-3. Sensitivity Analysis – Percent Increase in Mortality at 25 °C by Cluster and Month

April	May	June	July	August	September
9.04 (7.42, 10.68)	7.02 (5.60, 8.47)	2.79 (2.27, 3.32)	0.66 (0.41, 0.91)	1.25 (0.92, 1.59)	3.45 (2.69, 4.21)
6.48 (4.56, 8.43)	6.00 (4.78, 7.24)	4.08 (3.25, 4.92)	1.98 (1.53, 2.44)	2.63 (1.94, 3.31)	4.38 (3.19, 5.58)
4.88 (2.98, 6.82)	3.72 (2.80, 4.65)	1.50 (1.06, 1.94)	-0.03 (-0.15, 0.09)	0.61 (0.33, 0.88)	2.08 (1.15, 3.02)
2.93 (1.75, 4.13)	1.65 (0.80, 2.52)	0.22 (0.05, 0.38)	-1.93 (-2.70, -1.15)	-0.74 (-1.14, -0.35)	0.77 (0.27, 1.28)
5.58 (1.22, 10.14)	6.69 (4.41, 9.02)	7.24 (4.74, 9.79)	6.29 (4.90, 7.69)	4.33 (2.80, 5.88)	6.18 (4.17, 8.23)
2.82 (0.60, 5.10)	0.64 (0.06, 1.22)	-1.43 (-2.21, -0.65)	-3.91 (-6.76, -0.97)	-2.40 (-3.84, -0.94)	-0.51 (-0.78, -0.24)
1.64 (0.13, 3.18)	0.38 (0.01, 0.74)	-1.48 (-2.25, -0.70)	-2.74 (-4.25, -1.20)	-0.64 (-1.98, 0.72)	-0.04 (-0.27, 0.19)
0.65 (0.09, 1.21)	-0.38 (-0.62, -0.14)	-2.05 (-2.95, -1.14)	-2.56 (-3.96, -1.15)	-2.40 (-3.90, -0.88)	-1.42 (-2.30, -0.52)

Sensitivity analysis for the addition of visibility.
Estimate is percent increase in mortality at 25 °C compared to mortality at the mean of each cluster and month
Negative value means lower mortality than the reference temperature of 18 °C.
() is 95% confidence interval

FIGURES

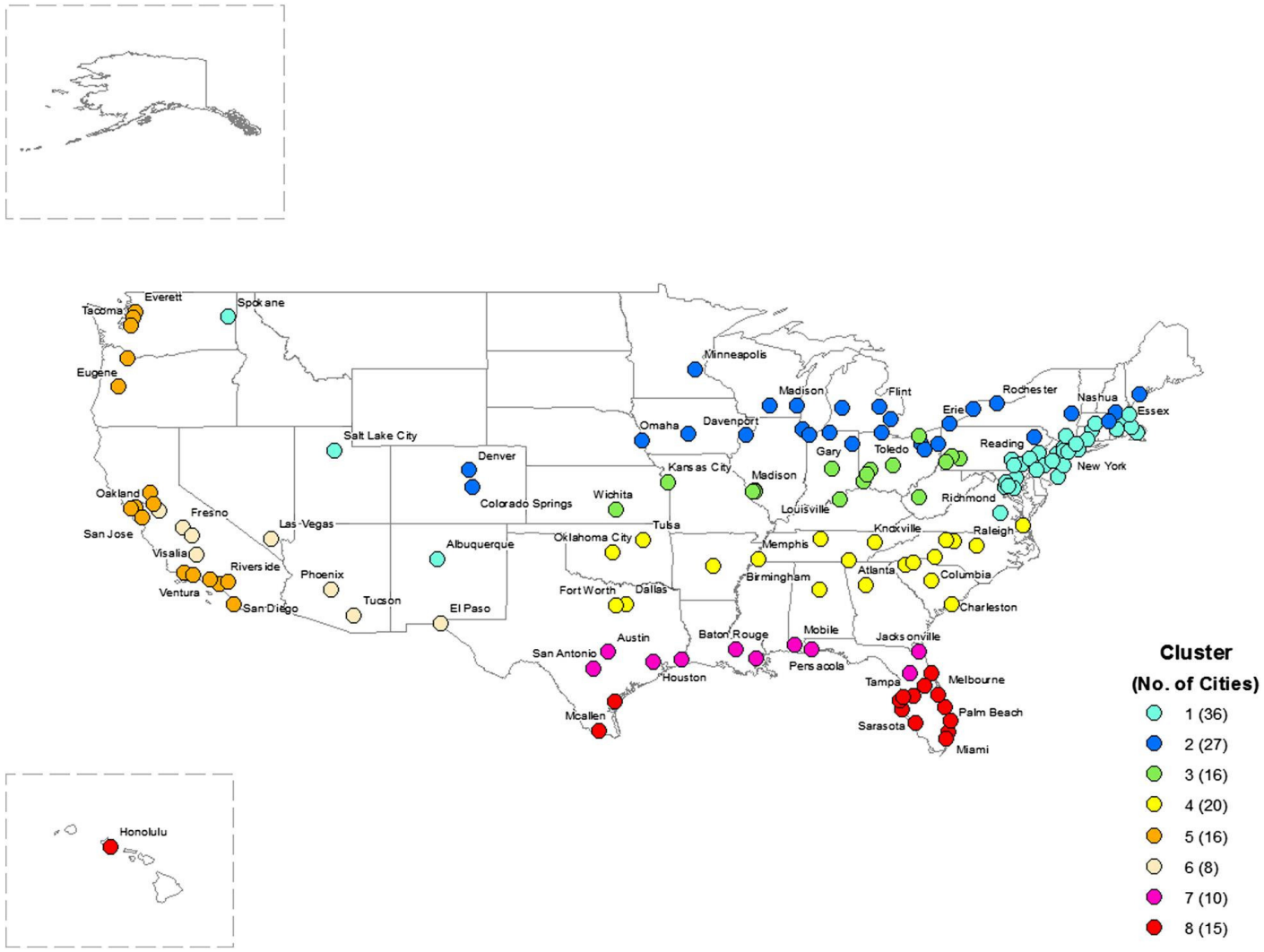

Figure I-1. Distribution of study area by cluster

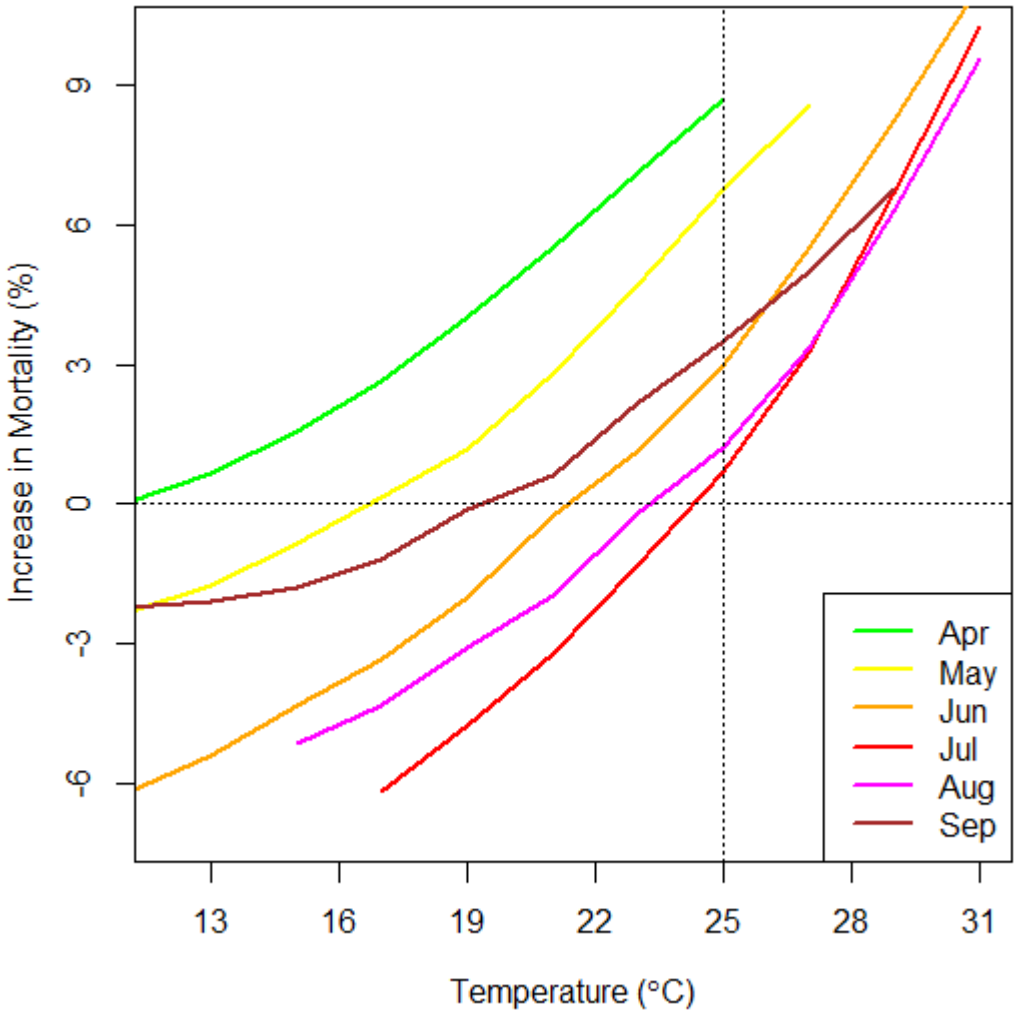

Figure I-2. Heat effects by month in cluster 1

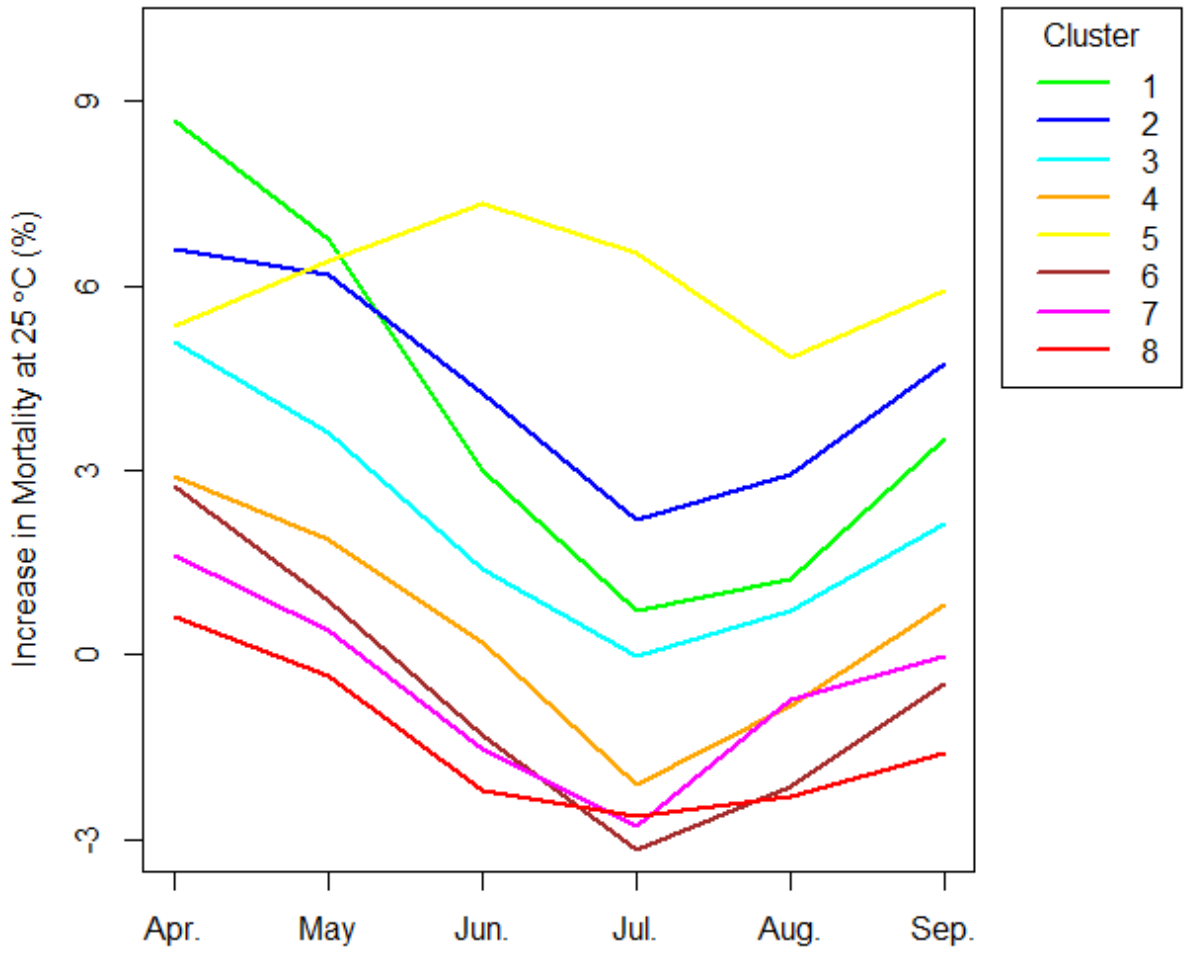

Figure I-3. monthly trend of mortality at 25 °C by cluster

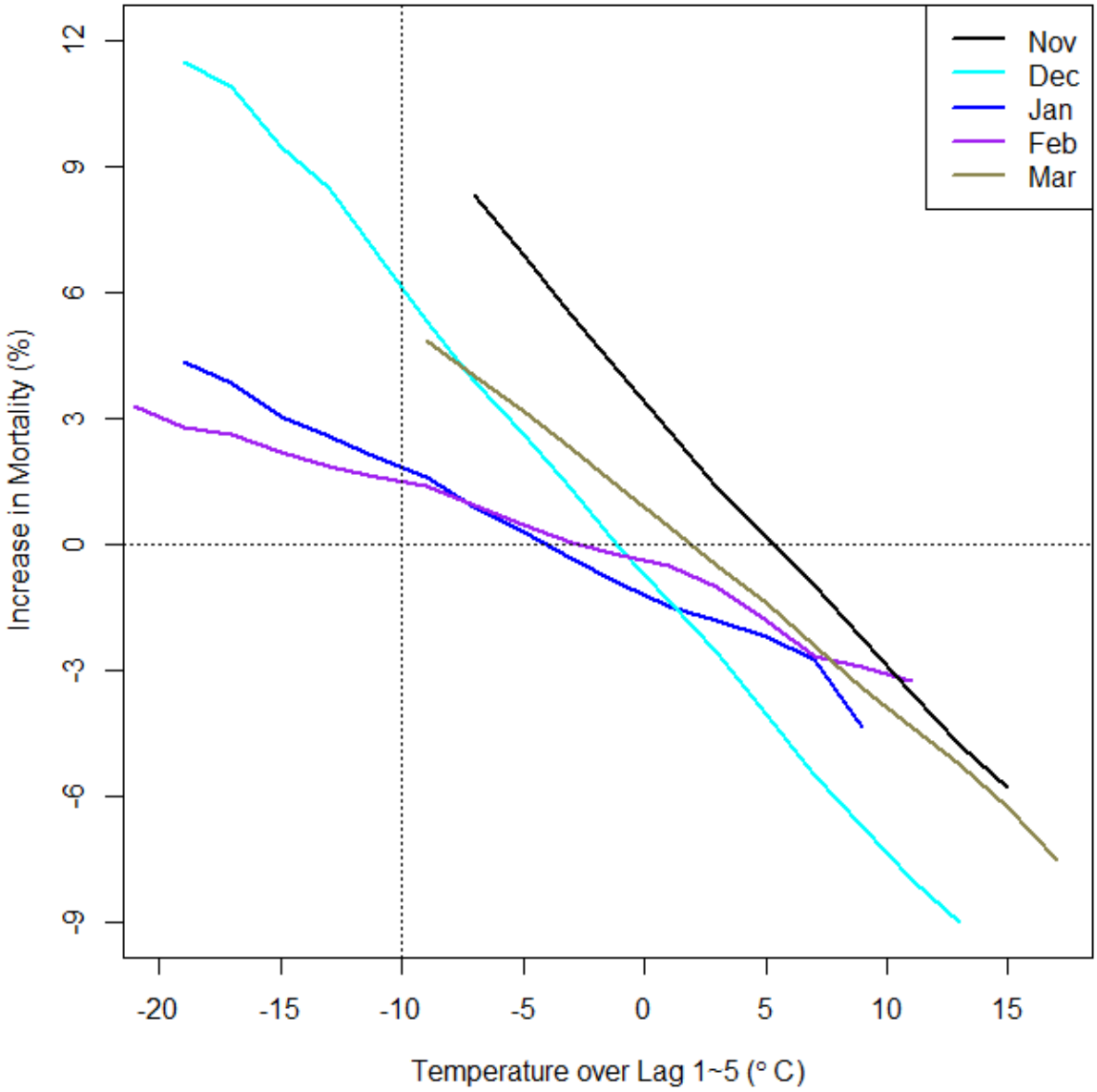

Figure I-4. Cold effects by month in cluster 2

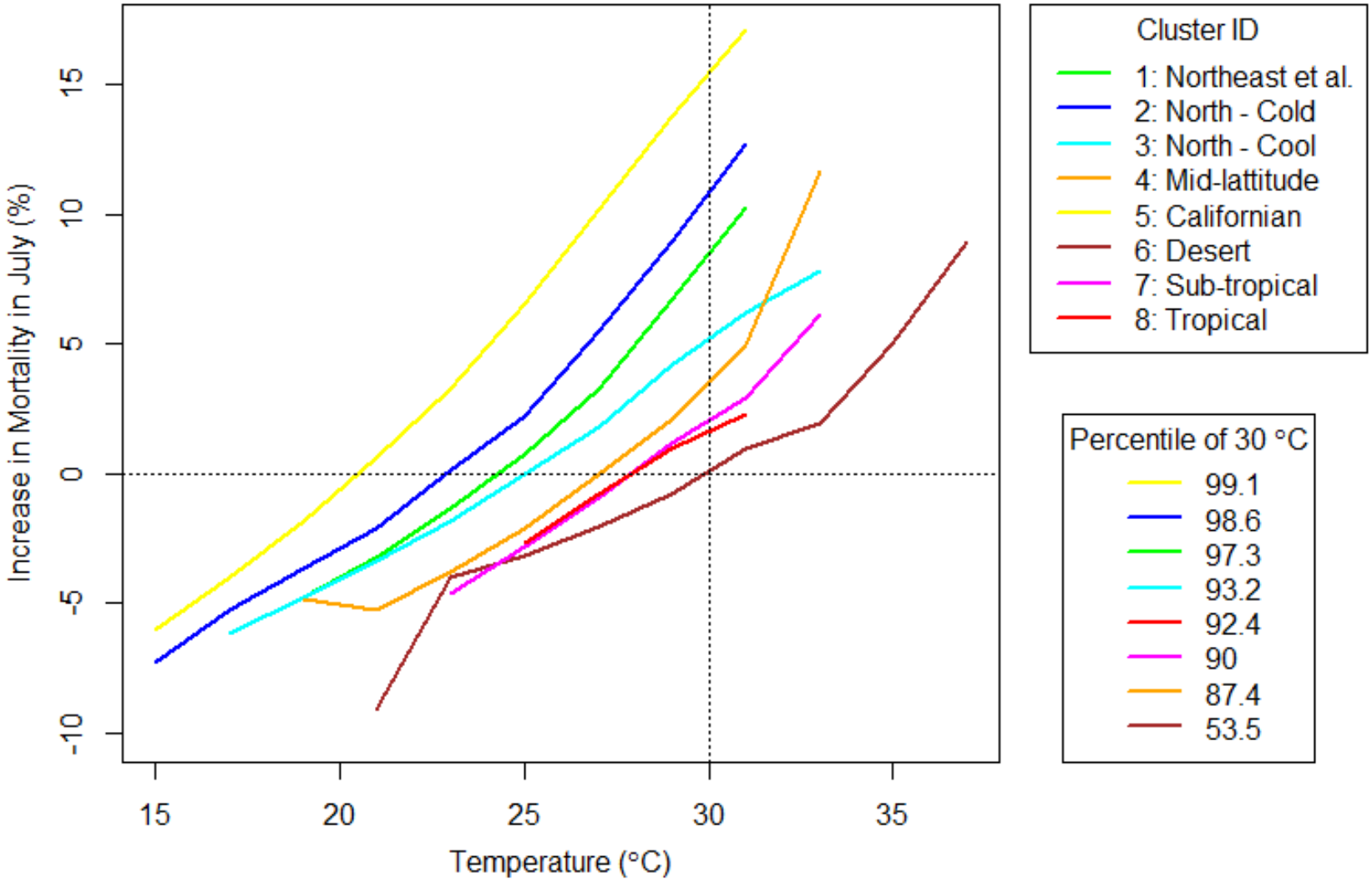

Figure I-5. Heat effects in July by cluster

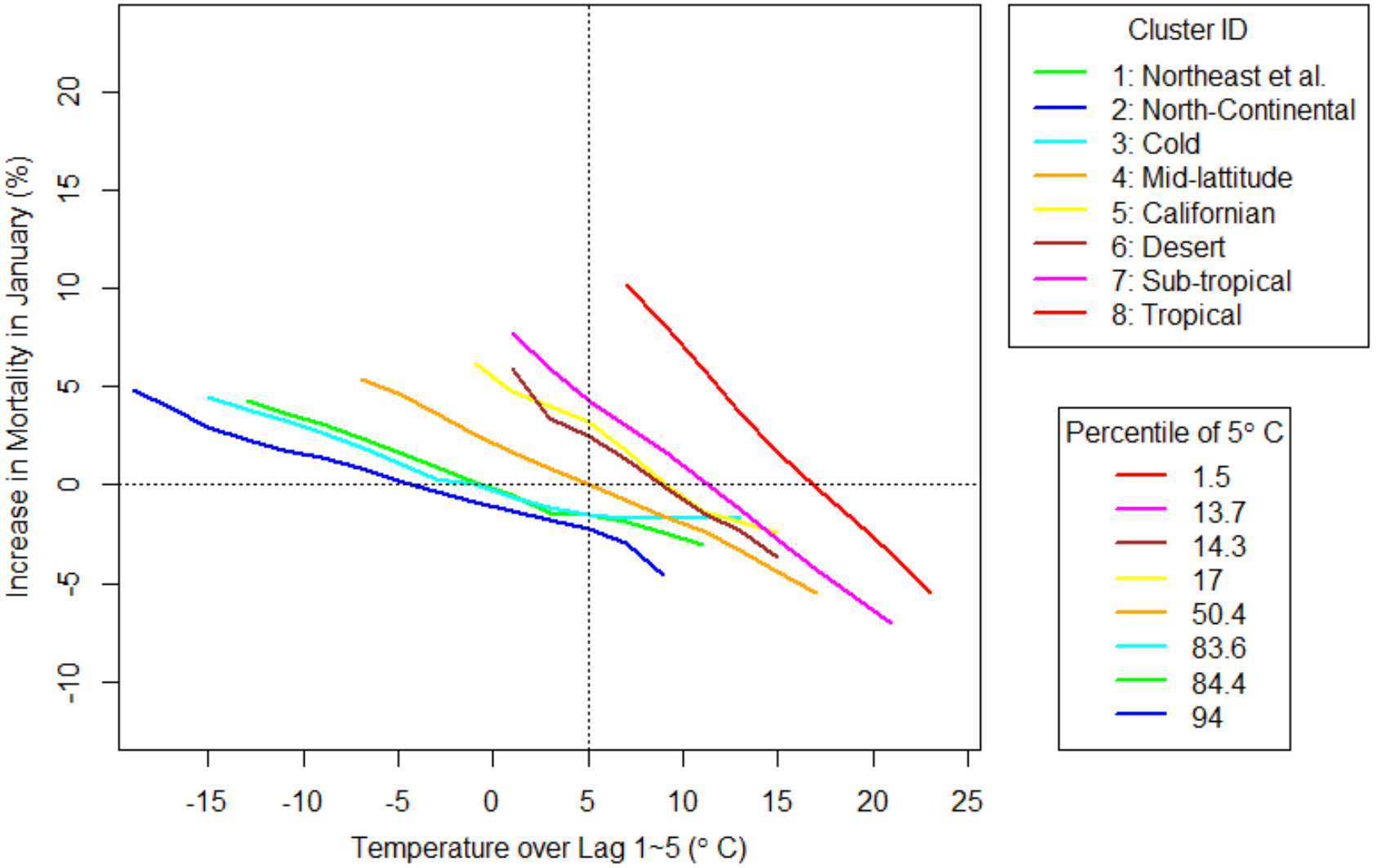

Figure I-6. Cold effects in January by cluster

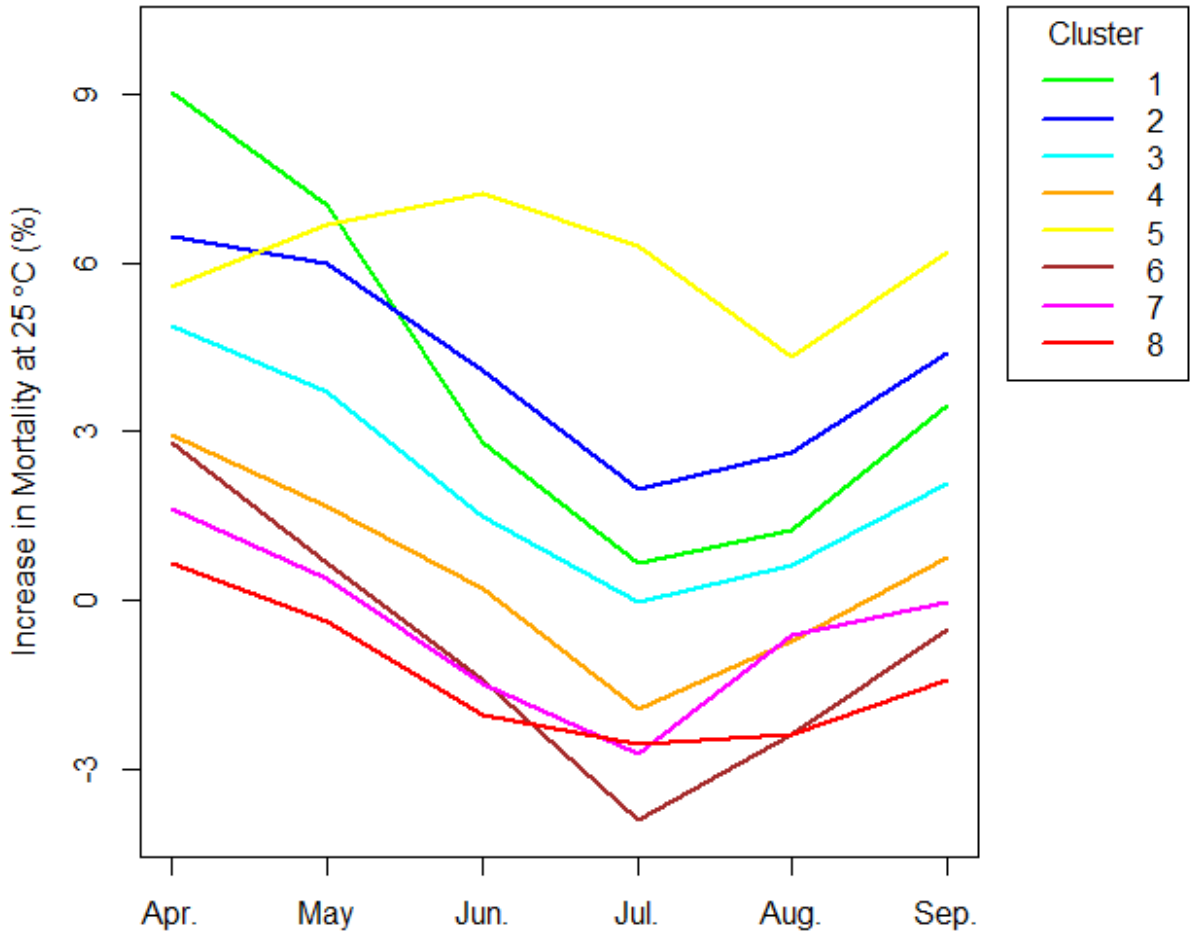

Figure I-7. Sensitivity analysis on visibility

CHAPTER II

Spatiotemporal prediction of fine particulate matter using high resolution satellite images in the southeastern U.S 2003-2011

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Spatiotemporal prediction of fine particulate matter

using high resolution satellite images in the southeastern U.S 2003-2011

Abstract

Most studies have demonstrated that fine particulate matter ($PM_{2.5}$, particles smaller than 2.5 μm in aerodynamic diameter) is associated with adverse health outcomes. The use of ground monitoring stations of $PM_{2.5}$ to approximate personal exposure however, induces measurement error. Land use regression provides spatially resolved predictions but land use terms do not vary temporally. Meanwhile, the advent of satellite-retrieved aerosol optical depth (AOD) products have made spatiotemporally-resolved $PM_{2.5}$ predictions possible.

In this paper, we incorporated AOD satellite measurements with other predictors such as meteorological variables, land use regression, and spatial smoothing to predict the daily concentration of $PM_{2.5}$ at a 1 km^2 resolution across the southeastern United States covering the seven states of Georgia, North Carolina, South Carolina, Alabama, Tennessee, Mississippi, and Florida for the years from 2003 through 2011. We divided the extensive study area into 3 regions and applied separate mixed-effect models to calibrate AOD values to $PM_{2.5}$ with other spatiotemporal predictors.

Using 10-fold cross-validation, we obtained out of sample R^2 of 0.77, 0.81, and 0.70 with the square root of the mean squared prediction errors (RMSPE) of 2.89 $\mu g/m^3$, 2.51 $\mu g/m^3$, and

2.82 $\mu g/m^3$ for regions 1, 2, and 3, respectively. The slopes of the relationships between predicted $PM_{2.5}$ and held out measurements were near 1 indicating no bias in the prediction model.

In conclusion, satellite AOD measurements can be combined with traditional land use terms to provide spatiotemporal predictions of $PM_{2.5}$ at a 1 km scale. These predictions can be used in epidemiological studies investigating the effects of both acute and chronic exposures to $PM_{2.5}$. Our model results will also extend the existing studies on $PM_{2.5}$ which are generally targeted to largely urban areas due to the availability of monitoring, into areas not previously studied such as rural areas.

INTRODUCTION

Particulate matter (PM) is particles or aerosols suspended in the atmosphere in various forms such as smoke, dust, or water droplets. The source of those aerosols are diverse including natural sources such as wild fire, sea particles, natural dust, and anthropogenic sources such as vehicles, houses, power plants or industrial factories. Among the various sizes of particulate matter, fine particulate matter (particulate matter with aerodynamic diameter < 2.5 μm, $PM_{2.5}$) poses the greatest health risks since it mainly originates from incomplete combustion and its small size allows it to penetrate through the human defense system, and into the systematic circulation system (Cormier et al. 2006, 810-817).

Since the Six Cities study (Dockery et al. 1993, 1753-1759), which showed a strong linear relationship between $PM_{2.5}$ and mortality between cities that differed by pollution level, a body of literature has developed reporting associations between $PM_{2.5}$ and adverse health effects ranging from respiratory or cardiovascular diseases to increases in hospital admissions and death (Pope 2000, 713-723; Pope et al. 2002, 1132-1141; Barnett et al. 2006, 1018-1023). In many of those studies, the assignment of $PM_{2.5}$ exposures to the study population has been based on the use of a central ground monitor by jurisdiction or within a specified distance. However, this approach induces information bias, and thus leads to attenuation of the magnitude of effects of air pollution or increases the variance of estimate (Rhomberg et al. 2011, 651-671; Armstrong 1998, 651-656; Goldman et al. 2011, 61-069X-10-61). Many studies have tried to resolve this issue and to produce $PM_{2.5}$ concentrations for locations distant from the monitors (Ryan and LeMasters 2007, 127-133; de Hoogh et al. 2013, 5778-5786; Beckerman et al. 2013, 172-177). This includes predicting $PM_{2.5}$ levels using regression models based on geographic covariates such as land use regressions or geostatistical interpolation methods such as kriging (Wang et al. 2013, 312-319; Ryan and

LeMasters 2007, 127-133; Whitworth et al. 2011, 21-069X-10-21). However, predictions from a land-use regression are limited to long-term exposures for chronic health effects studies, since the geographic covariates are generally not time varying (Kloog et al. 2011, 6267-6275). Moreover, if the amount of pollution due to a geographic predictor, e.g. traffic density, changes over time because of control technology, this is not easily incorporated into land use regression. Geostatistical methods also have limitations because the density of monitoring stations are too low compared to the area of the land, rendering the results unreliable especially in rural areas. Meanwhile, the aerosol optical depth (AOD) values from the Moderate-Resolution Imaging Spectroradiometer (MODIS) satellite provide daily measurements for the entire earth. AOD is a measure of particles in a column of air and is related to $PM_{2.5}$ (Alston, Sokolik, and Kalashnikova 2012, 1667-1682). With the advent of a new processing algorithm called Multi-Angle Implementation of Atmospheric Correction (MAIAC) (Lyapustin et al. 2011, - D03211), the spatial resolution of AOD has further improved from 10×10 km^2 to 1×1 km^2. Since the relationship between the AOD measurement and $PM_{2.5}$ is affected by various factors such as the optical properties of particulates, mixing height, and humidity, which vary daily, we used a mixed-effect model with daily random slopes for daily calibration rather than a general regression. This provides better predictive performance than other studies using the satellite imagery for the $PM_{2.5}$ prediction without daily calibration (Lee et al. 2011, 7991-8002).

In this paper, we incorporated those AOD satellite with other predictors such as meteorological variables, land use regression, and spatial smoothing to predict the daily concentration of $PM_{2.5}$ at a 1 km^2 resolution across the southeastern United States, covering the seven states of Georgia, North Carolina, South Carolina, Alabama, Tennessee, Mississippi, and Florida for the years from 2003 through 2011.

DATA

Ground particulate matter measurements

We obtained $PM_{2.5}$ mass concentration data from the U.S. Environmental Protection Agency (EPA) Air Quality System (AQS) database and the Interagency Monitoring of Protected Visual Environments (IMPROVE) network. The data covered the seven southeastern states (North Carolina, Tennessee, South Carolina, Georgia, Alabama, Mississippi, and Florida) for 2003-2011. A total of 257 monitoring sites were used.

Aerosol optical depth data

The MAIAC data were obtained from the National Aeronautics and Space Administration (NASA) at the resolution of 1 km^2. AOD data were delivered by tiles, which is the unit of spatial domain of MODIS image with an area of 10×10 degree at the equator. Our study used tiles h00v03, h01v02, h01v03, h01v04, h02v02, h02v03. The variables in the AOD data include the latitude and longitude in the WGS84 coordinate system, and its corresponding AOD values and quality flag. We deleted AOD values over 1.5 as it likely reflecting cloud contamination. We deleted AOD values over water bodies since the water reflects light and affects the reliability of AOD readings. The AOD value which was the closest in distance within a 1 km buffer was assigned to each $PM_{2.5}$ measurement.

Meteorological data

We downloaded weather data from the website of the National Climatic Data Center (NCDC, 2010). Weather variables include temperature, relative humidity, wind speed, visibility, and sea level pressure. A total of 144 weather stations were used and we assigned the weather readings based on the closest distance on a specific data.

Normalized difference vegetation index

NASA provides normalized difference vegetation index (NDVI) data from the MODIS sensor. We aggregated NDVI measurements to a 1 km grid and a one month average. Specifically we used the terra satellite product ID of MOD13A3.

Planetary boundary layer

We obtained planetary boundary layer (PBL) data from the National Oceanic and Atmospheric Administration (NOAA) Reanalysis Data. The spatial resolution of PBL data was 32×32 km on a daily basis.

Land use variables

Emissions of $PM_{2.5}$, PM_{10}, and NO_x from point sources and county area level emissions, were downloaded from national emission inventory data for 2005 from the website of the environmental protection agency (EPA 2005 NEI). To produce the percentage of urbanism for each satellite grid cell at 1 km^2 resolution, we used the national land cover database for 2011 (NLCD 2011) data at 30 meter resolution (Jin et al. 2013, 159-175). We reclassified land cover

codes 22 (Developed, Low Intensity), 23 (Developed, Medium Intensity), and 24 (Developed, High Intensity) to 1 as an urban cell and assigned 0 for the rest of codes. The mean of binary vales was calculated for each 1 km grid cell. For the location of geographical predictors such as roads, major buildings, ports, airports, and water bodies, spatial data from ESRI Data & Maps 2004 were used (ArcGIS® and ArcMap™ by Esri, Copyright © Esri).

METHOD

Date preparation

For each day, we assigned the closest AOD readings within a 1 km buffer of PM monitors. We confined our analysis to $PM_{2.5}$ less than 80 $\mu g/m^3$ to avoid influential outliers (25 observations among the total of 260,476 $PM_{2.5}$ measurements for 9 years). We also restricted our analysis to the cells greater or equal in population to 10, since the southeastern U.S. includes less populated areas. The pair of AOD over 0.5 and $PM_{2.5}$ less than 10 $\mu g/m^3$ were removed because we decided it likely reflects cloud contamination. The pair of AOD less than 0.15 and $PM_{2.5}$ over 25 $\mu g/m^3$ were removed because we decided it is likely on those days that low PBL moved particles closer to ground level, deteriorating the relationship between AOD and ground-level $PM_{2.5}$ measurements.

The aim of our model lies in high-performance predication, not associational inference between the exposure and outcome such as in the epidemiological studies. Hence our strategy was to eliminate observations with high residuals (over 10 $\mu g/m^3$) as too likely to distort our predictions for most observations, and to choose a model based on maximizing cross-validated (CV) R^2. Because AOD values are not missing at random (for example there are more missing in the winter) the missingness is non-ignorable and can distort the predictions. Hence we used inverse probability

weighting to account for this selection bias. Finally, the calibration between AOD and $PM_{2.5}$ can vary spatially, and daily. The daily variation is due to changes in particle size distribution, color, and vertical profile, and we address this by daily calibration and by using PBL data in the model. Since the number of monitors is limited, we used a random slope for each day, rather than a fixed one. To account for spatial differences in these daily slopes, we nested them within sub-regions, and to account for more permanent differences between locations, we included land use terms in our model. Specifically, we fitted the following model:

$$E\left(PM_{2.5_{ij}}\right) = \left(\beta_0 + b_{0j} + b_{0jk}\right) + \left(\beta_1 + b_{1j} + b_{2jk}\right)AOD_{ij} + \left(\beta_2 + b_{2j}\right)temp_{ij}$$

$$+ \sum_{m=1}^{7} \beta_{1m} X_{1m_{ij}} + \sum_{n=1}^{15} \beta_{2n} X_{2n_i} + \beta_{25} AOD \times PBL$$

where $PM_{2.5_{ij}}$ is the $PM_{2.5}$ measurements at the monitoring site i on day j. β_0 is the fixed effect intercept term (population intercept) and b_{0j} is the overall random intercept which varies from one day to another. b_{0jk} is the random intercept for day nested in each sub-region. Similarly, β_1 is the slope for the fixed effect of AOD, b_{1i} is the overall slope for the random effect of AOD for each day, and b_{2jk} is the random slope for each day nested in each sub-region. β_2 and b_{2j} represent the slopes for the fixed effect and the random effect of temperature, respectively. X_{1mij} is the matrix of m^{th} spatiotemporal covariates on the site i and day j other than temperature and consists of 7 variables: dew point temperature, sea level pressure, visibility, wind speed, absolute humidity; NDVI in the corresponding month; and PBL. X_{2ni} is the matrix of 15 spatial covariates for the i^{th} site which includes the percentage of urbanness, elevation, the density of major roads, population within 10 km diameter, $PM_{2.5}$ emissions at county level, $PM_{2.5}$ emissions from point sources, PM_{10} emission from point sources, NOx emission from point sources, the canopy surface in 2001, distance to the closest A1 roads, distance to the closest airport, distance to the closest port,

the distance to the closest railroad, and distance to a closest road, the distance to the major building. Observations with residuals over 10 $\mu g/m^3$ were re-visited and we determined their validity by comparing $PM_{2.5}$ readings from the surrounding monitors and the previous day and the next day. If we determined them to be erroneous, we assigned the readings from the closest monitoring station within 15 km.

Model

Due to the vast area of the study area, a single model was not able to achieve the best performance in prediction. The southeastern area consists of various topography, climate (tropical in Florida), and geographic features such as swamps and forests. Therefore, we decided to split the study area into three regions and to fit separate models for each region and implement nested random coefficients for sub-regions within each region (Figure II-1). Region 1 consist of Tennessee, Mississippi, Alabama, and Georgia. Region 2 covers North Carolina, South Carolina, and Georgia. Lastly, region 3 covers Florida, Mississippi, Alabama, Georgia, and South Carolina.

To adjust the non-random missingness of AOD, we modeled inverse probability weights (IPW) and applied them to the first stage models. Specifically, we fitted the following logistic model for the missingness of AOD measurements using meteorological and spatiotemporal factors.

$$\mathrm{E}\big(logit(p)\big) = \beta_0 + \beta_1 temp_{ij} + \beta_2 WS_{ij} + \beta_3 SLP_{ij} + \beta_4 elev_i + \beta_5 mon_j,$$

where temp is temperature of cell i on day j, WS_{ij} is wind speed of cell i on day j, SLP_{ij} is the sea level pressure of cell i on day j, elev is the elevation of cell i, and mon is the corresponding month that day j falls in.

Then we computed the inverse probability as, $\frac{1}{p}$. Finally, we normalized IPW by dividing each IPW by the mean. These were applied as a weight in the subsequent model.

To finalize the model by region, we used 10 fold cross-validation by region. To avoid over-fitting, we performed site-based 10-fold cross-validation (that is, we left out 10% of the monitoring sites for each validation sample) and used its R^2 in finalizing the models rather than modeled R^2. The rationale behind this was that the R^2 from the cross-validation by stations was more appropriate since it better assesses the ability to predict spatial variability. As a result, we ended up the following models based on the highest R^2 from the 10-fold cross-validation.

In region 1, we fitted the following model for each year with the IPW:

$$\mathrm{E}\left(PM_{2.5_{ij}}\right) = \left(\beta_0 + b_{0j} + b_{0jk}\right) + \left(\beta_1 + b_{1j} + b_{1jk}\right)AOD_{ij} + \beta_2 temp_{ij} + \beta_3 dewp_{ij} + \beta_4 slp_{ij} + \beta_5 wdsp_{ij} + \beta_6 visib_{ij} + \beta_7 ah_{ij} + \beta_8 NDVI + \beta_9 elev_i + \beta_{10} pbl + \beta_{11} urb_i + \beta_{12} emission + \beta_{13} PM10 + \beta_{14} NOX$$

where $PM_{2.5_{ij}}$ is the $PM_{2.5}$ measurements at the monitoring site i on day j. β_0 denotes the fixed effect intercept term (population intercept) and b_{0j} is the random effect intercept varies randomly from one day to another. b_{0jk} is the random intercept for day nested in each sub-region. Similarly, β_1 is the slope for the fixed effect of AOD, b_{1i} is the slope for the random effect of AOD for each day, and b_{2jk} is the random slope for each day nested in each sub-region.

In region 2, we fitted the following model for each year with the IPW:

$$\mathrm{E}\left(PM_{2.5_{ij}}\right) = \left(\beta_0 + b_{0j} + b_{0jk}\right) + \left(\beta_1 + b_{1j} + b_{1jk}\right)AOD_{ij} + \beta_2 temp_{ij} + \beta_3 dewp_{ij} + \beta_4 slp_{ij} + \beta_5 wdsp_{ij} + \beta_6 visib_{ij} + \beta_7 ah_{ij} + \beta_8 NDVI + \beta_9 elev_i + \beta_{10} pbl + \beta_{11} urb_i + \beta_{12} emission$$

For region 3, we fitted the following model for each year with the IPW:

$$\mathrm{E}\left(PM_{2.5_{ij}}\right) = \left(\beta_0 + b_{0j} + b_{0jk}\right) + \left(\beta_1 + b_{1j} + b_{1jk}\right)AOD_{ij} + \beta_2 temp_{ij} + \beta_3 dewp_{ij} + \beta_4 slp_{ij} + \beta_5 wdsp_{ij} + \beta_6 visib_{ij} + \beta_7 ah_{ij}$$

Besides the overall R^2 from the 10-fold cross-validation, we assessed the model performance from the spatial and temporal perspectives. We defined a spatial R^2 by regressing the annual mean of $PM_{2.5}$ against that of predicted $PM_{2.5}$ for each site. To assess the precision of the predictions, root mean squared prediction error (RMSPE) was generated by taking the square root of the mean of squared prediction residuals. A temporal R^2 was calculated by regressing the difference between the actual $PM_{2.5}$ measurement on a specific day and the annual mean for each site against the equivalent for the predicted values from the model.

Once we finalized the calibration models by three regions as above, we predicted $PM_{2.5}$ level based on the derived relationship between AOD values and other temporal and spatial variables.

For the areas that didn't have the AOD measurements on a specific day, we applied smoothing using surrounding AOD cells with the IPW.

$$\left(PredPM_{2.5_{ij}}\right) = \left(\beta_0 + b_{0j} + b_{0jk}\right) + (\beta_1 + b_{1ik})MPM_{ij} + \beta_2 bimon_{ij} + \beta_3 pbl_{ij} + \beta_4 ah\_gm3_{ij} + \beta_5 elev_{ij} + \beta_6 mpm \times bimon_{ij} + \beta_7 mpm \times pblh_{ij},$$

where $PredPM_{ij}$ is the predicted $PM_{2.5}$ level at a grid cell i on a day j. MPM_{ij} is the mean $PM_{2.5}$ measured at monitoring stations within a 100 km buffer for the cell i on day j.

To extract the AOD readings from the raw satellite image in the HDF format, Matlab was used. We used ArcGIS Desktop 10.2.2 along with python scripting for data preparation. Models were implemented by using the R 3.02 and SAS 9.3 (Statistical Analysis System).

RESULTS

A total of 257 monitoring stations were used for the study. Figure II-1 shows the study area and the locations of $PM_{2.5}$ monitors. The study area with the thick boundary line covers most of the seven states except for the small area of western Mississippi due to the lack of the total spatial domain consisting of AOD tiles. The numbers from 1 to 3 in big bold font indicate the study area region. Region 1 mainly consists of the states of Tennessee, and the upper part of Mississippi, Alabama, and Georgia, and contains 61 monitoring stations (0.0003 monitor/km^2). Region 2 covers most of North Carolina, the major part of South Carolina, and the part of Georgia with 88 monitors. Region 2 is most densely populated by PM monitoring stations (0.00038 monitor/km^2). Region 3 covers the most southern part, including Florida and the southern part of Mississippi, Alabama, Georgia, and South Carolina. Although region 3 has the largest number of monitors of 108, due to its vast area, the spatial distribution of PM monitoring stations is most scattered among the three regions (0.00026 monitor/km^2).

Table II-1 shows the descriptive statistics for $PM_{2.5}$ and AOD measurements in the southeastern U.S. by year from 2003 through 2011. The annual average of $PM_{2.5}$ has steadily decreased from 12.2 $\mu g/m^3$ in 2003 to 9.8 $\mu g/m^3$ in 2011. The standard deviation has also decreased from 6.5 $\mu g/m^3$ to 5.3 $\mu g/m^3$, implying less variation of $PM_{2.5}$ level around the mean. The AOD readings varied around 0.20 (unitless) over 9 years.

Our model showed a highly significant association between $PM_{2.5}$ and AOD controlling for other covariates and spatiotemporal predictors. Table II-2 presents results from the stage 1 model where the calibration of AOD and other spatiotemporal predictors were done by each year and region. The R^2 numbers are from the 10-fold cross-validation based on the sampling of monitors. The predictive powers of the models differed by region. Region 2 showed the highest

overall R^2 of 0.81 with the year-to-year variation ranging from 0.78 in 2008 to 0.85 in 2007. Region 3 showed the lowest performance with the average cross-validated R^2 of 0.70 (the minimum CV R^2 of 0.63 occurred in 2011 and the maximum CV R^2 of 0.75 occurred in 2003 and 2005). Region 1 had an average cross-validated R^2 of 0.77 ranging from 0.65 in 2010 to 0.83 in 2005. The slopes between the observed $PM_{2.5}$ versus the modeled $PM_{2.5}$ were almost 1 for all the regions, implying good agreement between the model results and actual measurements and the least bias. Region 2 exhibited the lowest average root mean square prediction error (RMSPE) of 2.51 $\mu g/m^3$, followed by region 3 with 2.82 $\mu g/m^3$ and region 1 with 2.87 $\mu g/m^3$. The RMSPE for the spatial component was much lower at 0.82 $\mu g/m^3$ in region 2. Generally speaking, the models performed better temporally than spatially. The temporal R^2 results were higher than spatial R^2 values except for region 3. For the temporal result, the mean R^2 was 0.80, 0.82, and 0.69 for regions 1, 2, 3, respectively. For the spatial model the mean R^2 was 0.69, 0.63, and 0.76 by region order.

The output prediction model based on the third model gave very similar results (Table II-3). The third column represents the R^2 for the prediction from stage 2 (prediction for the gird cells and days that AOD readings were available) and the last column illustrates those for the comparison with actual $PM_{2.5}$ observations. The final prediction showed high predictive power, from 0.89 (region 2) to 0.86 (region 3).

To graphically represent the predictions, Figure II-2 displays the prediction results in the form of annual average in 2003. Visual inspection reveals that the distribution of predicted $PM_{2.5}$ level follows the distribution of highways and the main cities and there was no systematic spatial patterns of residuals (Figure II-3).

DISCUSSION

In this paper, we predicted $PM_{2.5}$ levels across the southeastern U.S. at 1 km resolution using the MODIS satellite imagery derived by the newly developed algorithm, MAIAC. We expect these results to facilitate epidemiological studies to evaluate the association between $PM_{2.5}$ and adverse health effects with reduced measurement error in exposure. We also anticipate these results may extend to rural areas in the southeastern U.S., which were formerly restricted to urban areas due to the distance to monitoring stations. Considering that $PM_{2.5}$ measurements are not always daily, our model interpolates the temporal break using the daily satellite imagery and a smoothing technique as well as spatial predictions. This approach enables epidemiological studies on the acute effects of $PM_{2.5}$ in short time periods as well as chronic effects for long term exposure.

Our model performance varied by region. Region 2 mainly covering North Carolina revealed the highest performance (0.81) and region 3, covering the most southern part, such as Florida, had the lowest performance (0.70). One possible explanation would be that the spatial density of monitoring stations affects the performance of modeled calibration between actual $PM_{2.5}$ and AOD. Region 2 has the most abundant monitoring stations compared to its area, whereas region 3 lacks monitoring stations for its extensive area. This appeared to affect the results by providing fewer pairs to fit the model. Another explanation can be that region 2 is relatively more urbanized compared to region 3 with more land use factors which could be taken into account. This suggestion parallels with our experience during the analysis that the calibration model based on the highest R^2 for region 2 has more land use variables than that for region 3. Lastly, the quality of AOD from the MODIS instrument and the MAIAC algorithm can be factored in. Visual analysis (data not present) by AOD swath revealed that the performance of AOD differed by tile of satellite imagery. Tiles of h01v02 that overlapped with North Carolina showed the best performance and

tiles around Alabama (h00v03 and h01v03) showed the poorest performance. To resolve this, other AOD products from other algorithms such as AOD data from Deep Blue algorithm (Li et al. 2012, 132-139) at 10 km resolution can be incorporated since it is specialized for bright surfaces. More studies are needed to determine which factors play a role in the prediction of $PM_{2.5}$ using satellite imagery and to further improve the performance.

Nevertheless, our study still shows its superiority over other studies. Hu et al. (Hu et al. 2014, 220-232) have published a study predicting $PM_{2.5}$ concentrations for similar regions around Alabama and Mississippi in a single year of 2003. They adopted a mixed effect model calibrating the daily relationship between $PM_{2.5}$ and AOD controlling for meteorological variables and land use parameters. The results were an R^2 of 0.67 and RMSPE of 3.88 $\mu g/m^3$. In our model, even the lowest R^2 in 2003 was 0.72 with RMSPE 3.51 $\mu g/m^3$. Moreover, Hu et al.'s model predictions didn't extend the use of available AOD data. In contrast, our approach produced daily predictions for every grid cell. Collectively, our model is in a more advanced form in terms of the direct application to the actual epidemiological studies regardless of time and space.

In conclusion, we have demonstrated that the use of satellite imagery and other land use variables with a mixed-effect model produces reliable predictions of daily $PM_{2.5}$ for the extensive area of the southeastern United States. By incorporating land use terms and spatial smoothing, our models perform much better than previous studies. Therefore, our model results can be used in various epidemiological studies investigating the effects of $PM_{2.5}$ allowing one to assess both acute and chronic exposures with the implication of a new application. Our model results will extend the existing studies on $PM_{2.5}$ mainly targeted only for urban areas tied to the lack of monitors into new areas which used not to be studied such as rural areas.

REFERENCES

1. Cormier SA, Lomnicki S, Backes W, Dellinger B. Origin and health impacts of emissions of toxic by-products and fine particles from combustion and thermal treatment of hazardous wastes and materials. Environ Health Perspect. 2006;114(6):810-817.

2. Dockery DW, Pope CA, Xu X, et al. An association between air pollution and mortality in six U.S. cities. N Engl J Med. 1993;329(24):1753-1759. doi: 10.1056/NEJM199312093292401.

3. Pope CA,3rd. Epidemiology of fine particulate air pollution and human health: Biologic mechanisms and who's at risk?. Environ Health Perspect. 2000;108 Suppl 4:713-723.

4. Pope CA,3rd, Burnett RT, Thun MJ, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA. 2002;287(9):1132-1141.

5. Barnett AG, Williams GM, Schwartz J, et al. The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in australian and new zealand cities. Environ Health Perspect. 2006;114(7):1018-1023.

6. Rhomberg LR, Chandalia JK, Long CM, Goodman JE. Measurement error in environmental epidemiology and the shape of exposure-response curves. Crit Rev Toxicol. 2011;41(8):651-671. doi: 10.3109/10408444.2011.563420 [doi].

7. Armstrong BG. Effect of measurement error on epidemiological studies of environmental and occupational exposures. Occup Environ Med. 1998;55(10):651-656.

8. Goldman GT, Mulholland JA, Russell AG, et al. Impact of exposure measurement error in air pollution epidemiology: Effect of error type in time-series studies. Environ Health. 2011;10:61-069X-10-61. doi: 10.1186/1476-069X-10-61 [doi].

9. Ryan PH, LeMasters GK. A review of land-use regression models for characterizing intraurban air pollution exposure. Inhal Toxicol. 2007;19 Suppl 1:127-133. doi: 782016666 [pii].

10. de Hoogh K, Wang M, Adam M, et al. Development of land use regression models for particle composition in twenty study areas in europe. Environ Sci Technol. 2013;47(11):5778-5786. doi: 10.1021/es400156t.

11. Beckerman BS, Jerrett M, Martin RV, van Donkelaar A, Ross Z, Burnett RT. Application of the deletion/substitution/addition algorithm to selecting land use regression models for interpolating air pollution measurements in california. Atmos Environ. 2013;77(0):172-177. doi: http://dx.doi.org/10.1016/j.atmosenv.2013.04.024.

12. Wang R, Henderson SB, Sbihi H, Allen RW, Brauer M. Temporal stability of land use regression models for traffic-related air pollution. Atmos Environ. 2013;64(0):312-319. doi: http://dx.doi.org/10.1016/j.atmosenv.2012.09.056.

13. Whitworth KW, Symanski E, Lai D, Coker AL. Kriged and modeled ambient air levels of benzene in an urban environment: An exposure assessment study. Environ Health. 2011;10:21-069X-10-21. doi: 10.1186/1476-069X-10-21 [doi].

14. Kloog I, Koutrakis P, Coull BA, Lee HJ, Schwartz J. Assessing temporally and spatially resolved PM2.5 exposures for epidemiological studies using satellite aerosol optical depth measurements. Atmos Environ. 2011;45(35):6267-6275. doi: http://dx.doi.org.ezp-prod1.hul.harvard.edu/10.1016/j.atmosenv.2011.08.066.

15. Alston EJ, Sokolik IN, Kalashnikova OV. Characterization of atmospheric aerosol in the US southeast from ground- and space-based measurements over the past decade. Atmospheric Measurement Techniques. 2012;5(7):1667-1682. doi: 10.5194/amt-5-1667-2012.

16. Lyapustin A, Wang Y, Laszlo I, et al. Multiangle implementation of atmospheric correction (MAIAC): 2. aerosol algorithm. Journal of Geophysical Research: Atmospheres. 2011;116(D3):- D03211. doi: 10.1029/2010JD014986.

17. Lee HJ, Liu Y, Coull BA, Schwartz J, Koutrakis P. A novel calibration approach of MODIS AOD data to predict PM$_2.5$ concentrations. Atmospheric Chemistry and Physics. 2011;11(15):7991-8002. doi: 10.5194/acp-11-7991-2011.

18. Jin S, Yang L, Danielson P, Homer C, Fry J, Xian G. A comprehensive change detection method for updating the national land cover database to circa 2011. Remote Sens Environ. 2013;132(0):159-175. doi: http://dx.doi.org/10.1016/j.rse.2013.01.012.

19. Li X, Xia X, Wang S, Mao J, Liu Y. Validation of MODIS and deep blue aerosol optical depth retrievals in an arid/semi-arid region of northwest china. Particuology. 2012;10(1):132-139. doi: http://dx.doi.org/10.1016/j.partic.2011.08.002.

20. Hu X, Waller LA, Lyapustin A, et al. Estimating ground-level PM2.5 concentrations in the southeastern united states using MAIAC AOD retrievals and a two-stage model. Remote Sens Environ. 2014;140(0):220-232. doi: http://dx.doi.org/10.1016/j.rse.2013.08.032.

21. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med. 2000;343(24):1742-1749. doi: 10.1056/NEJM200012143432401 [doi].

22. Wichmann HE, Spix C, Tuch T, et al. Daily mortality and fine and ultrafine particles in erfurt, germany part I: Role of particle number and particle mass. Res Rep Health Eff Inst. 2000(98):5-86; discussion 87-94.

23. Mar TF, Ito K, Koenig JQ, et al. PM source apportionment and health effects. 3. investigation of inter-method variations in associations between estimated source contributions of PM2.5 and daily mortality in phoenix, AZ. J Expos Sci Environ Epidemiol. 2005;16(4):311-320.

24. Boldo E, Medina S, Le Tertre A, et al. Apheis: Health impact assessment of long-term exposure to PM2.5 in 23 european cities. Eur J Epidemiol. 2006;21(6):449-458. doi: 10.1007/s10654-006-9014-0.

25. Ostro BD, Broadwin R, Lipsett MJ. Coarse and fine particles and daily mortality in the coachella valley, california: A follow-up study. J Expo Anal Environ Epidemiol. 2000;10(5):412-419. doi: 10.1038/sj.jea.7500094.

26. Franklin M, Zeka A, Schwartz J. Association between PM2.5 and all-cause and specific-cause mortality in 27 US communities. J Expos Sci Environ Epidemiol. 2006;17(3):279-287.

27. Ruchirawat M, Settachan D, Navasumrit P, Tuntawiroon J, Autrup H. Assessment of potential cancer risk in children exposed to urban air pollution in bangkok, thailand. Toxicol Lett. 2007;168(3):200-209. doi: S0378-4274(06)01323-3 [pii].

28. Risom L, Moller P, Loft S. Oxidative stress-induced DNA damage by particulate air pollution. Mutat Res. 2005;592(1-2):119-137. doi: S0027-5107(05)00246-0 [pii].

29. Dockery DW. Health effects of particulate air pollution. Ann Epidemiol. 2009;19(4):257-263. doi: 10.1016/j.annepidem.2009.01.018 [doi].

30. Valavanidis A, Fiotakis K, Vlachogianni T. Airborne particulate matter and human health: Toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2008;26(4):339-362. doi: 10.1080/10590500802494538 [doi].

31. Brenner H, Savitz DA, Jockel KH, Greenland S. Effects of nondifferential exposure misclassification in ecologic studies. Am J Epidemiol. 1992;135(1):85-95.

32. Greenland S. Divergent biases in ecologic and individual-level studies. Stat Med. 1992;11(9):1209-1223.

33. Maclure M. The case-crossover design: A method for studying transient effects on the risk of acute events. Am J Epidemiol. 1991;133(2):144-153.

34. Medina-Ramon M, Schwartz J. Temperature, temperature extremes, and mortality: A study of acclimatisation and effect modification in 50 US cities. Occup Environ Med. 2007;64(12):827-833. doi: 10.1136/oem.2007.033175 [doi].

35. Schwartz J, Coull B, Laden F, Ryan L. The effect of dose and timing of dose on the association between airborne particles and survival. Environ Health Perspect. 2008;116(1):64-69. doi: 10.1289/ehp.9955 [doi].

36. Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: An extended follow-up of the harvard six cities study from 1974 to 2009. Environ Health Perspect. 2012;120(7):965-970. doi: 10.1289/ehp.1104660 [doi].

37. Kloog I, Nordio F, Zanobetti A, Coull BA, Koutrakis P, Schwartz JD. Short term effects of particle exposure on hospital admissions in the mid-atlantic states: A population estimate. PLoS One. 2014;9(2):e88578. doi: 10.1371/journal.pone.0088578 [doi].

TABLES

Table II-1. Descriptive statistics of $PM_{2.5}$ ($\mu g/m^3$) and AOD

Year	Mean PM (S.D.)	Mean AOD (S.D.)
2003	12.2 (6.5)	0.18 (0.18)
2004	12.6 (6.6)	0.18 (0.17)
2005	13.1 (7.3)	0.20 (0.19)
2006	12.6 (6.6)	0.20 (0.19)
2007	12.4 (7.5)	0.21 (0.21)
2008	10.8 (5.6)	0.18 (0.16)
2009	9.4 (4.6)	0.17 (0.15)
2010	10.2 (4.9)	0.17 (0.15)
2011	9.8 (5.3)	0.20 (0.18)

S.D., standard deviation

Table II-2. 10-fold cross-validated R^2 from stage 1 model

Year	Region	R^2 (CV)	Slope (CV)	RMSPE ($\mu g/m^3$)	Spatial R^2	Temporal R^2	Spatial RMSPE
	1	0.72	0.93	3.51	0.50	0.78	1.86
2003	2	0.83	0.98	2.67	0.59	0.84	1.03
	3	0.75	1.01	2.62	0.81	0.74	0.93
	1	0.79	0.97	2.92	0.94	0.80	1.07
2004	2	0.80	0.99	2.77	0.52	0.81	0.79
	3	0.74	0.99	2.83	0.77	0.74	0.86
	1	0.83	0.99	3.23	0.86	0.84	1.12
2005	2	0.80	0.97	3.12	0.81	0.81	0.93
	3	0.75	0.99	3.10	0.73	0.75	1.19
	1	0.80	0.98	2.99	0.53	0.83	1.26
2006	2	0.84	0.99	2.70	0.70	0.85	0.86
	3	0.74	1.00	2.69	0.67	0.75	1.15
	1	0.79	0.98	3.19	0.67	0.82	1.34
2007	2	0.85	0.99	2.54	0.59	0.86	0.84
	3	0.70	1.02	3.29	0.77	0.69	1.25
	1	0.78	0.99	2.71	0.74	0.80	0.99
2008	2	0.78	0.98	2.48	0.60	0.79	0.79
	3	0.69	1.00	2.74	0.85	0.65	0.99
	1	0.76	0.98	2.30	0.81	0.78	0.83
2009	2	0.78	0.99	2.05	0.81	0.79	0.78
	3	0.66	1.02	2.60	0.80	0.64	0.87
	1	0.65	0.95	2.80	0.33	0.71	1.33
2010	2	0.80	0.99	2.09	0.46	0.81	0.68
	3	0.66	1.00	2.51	0.69	0.66	1.11
	1	0.79	0.98	2.40	0.80	0.80	0.86
2011	2	0.78	0.98	2.21	0.55	0.79	0.69
	3	0.63	0.99	2.97	0.75	0.61	0.98
	1	0.77	0.97	2.89	0.69	0.80	1.18
Mean	2	0.81	0.99	2.51	0.63	0.82	0.82
	3	0.70	1.00	2.82	0.76	0.69	1.04

Table II-3. R^2 from stage 3 model

Year	Region	R^2 Pred2	R^2 PM_{25}
	1	0.83	0.90
2003	2	0.86	0.91
	3	0.61	0.85
	1	0.83	0.88
2004	2	0.84	0.90
	3	0.64	0.85
	1	0.83	0.91
2005	2	0.84	0.90
	3	0.65	0.87
	1	0.86	0.89
2006	2	0.87	0.91
	3	0.59	0.86
	1	0.83	0.90
2007	2	0.84	0.91
	3	0.62	0.88
	1	0.83	0.87
2008	2	0.82	0.88
	3	0.65	0.90
	1	0.81	0.86
2009	2	0.80	0.86
	3	0.61	0.83
	1	0.75	0.83
2010	2	0.81	0.89
	3	0.60	0.85
	1	0.85	0.89
2011	2	0.81	0.88
	3	0.61	0.87
	1	0.82	0.88
Mean	2	0.83	0.89
	3	0.62	0.86

FIGURES

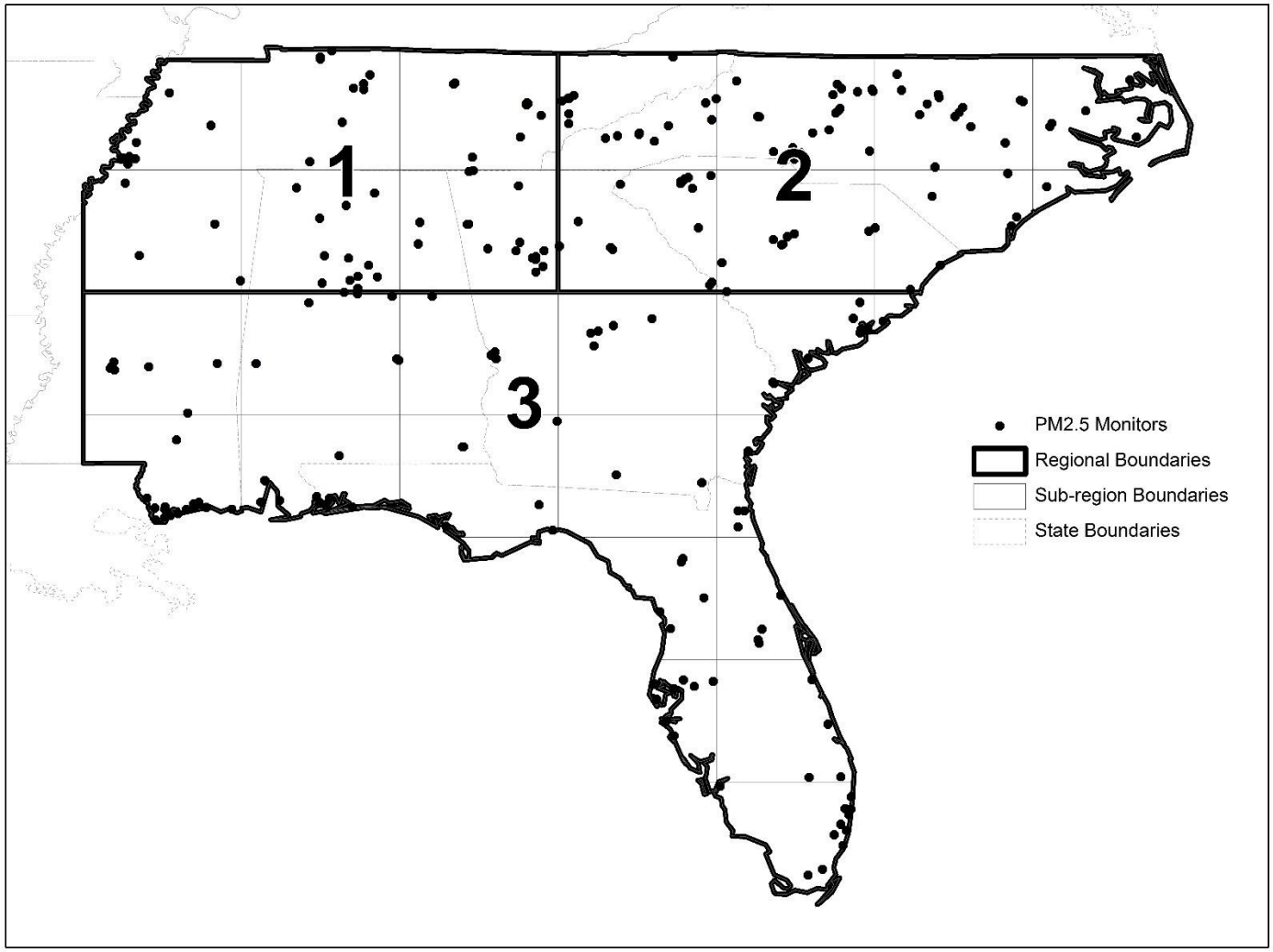

Figure II-1. Study area and the locations of $PM_{2.5}$ monitoring stations

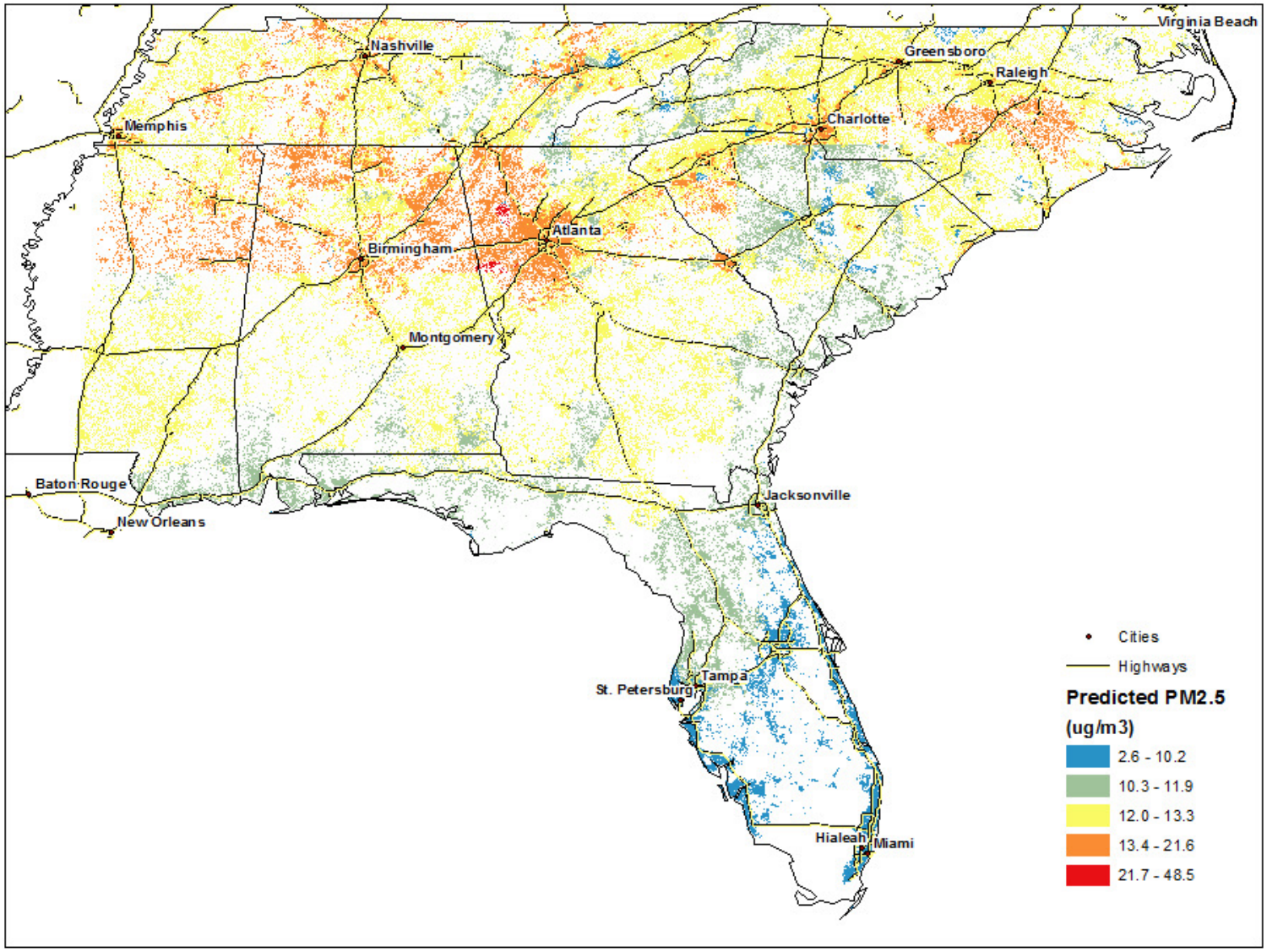

Figure II-2. Predicted $PM_{2.5}$ level in 2003

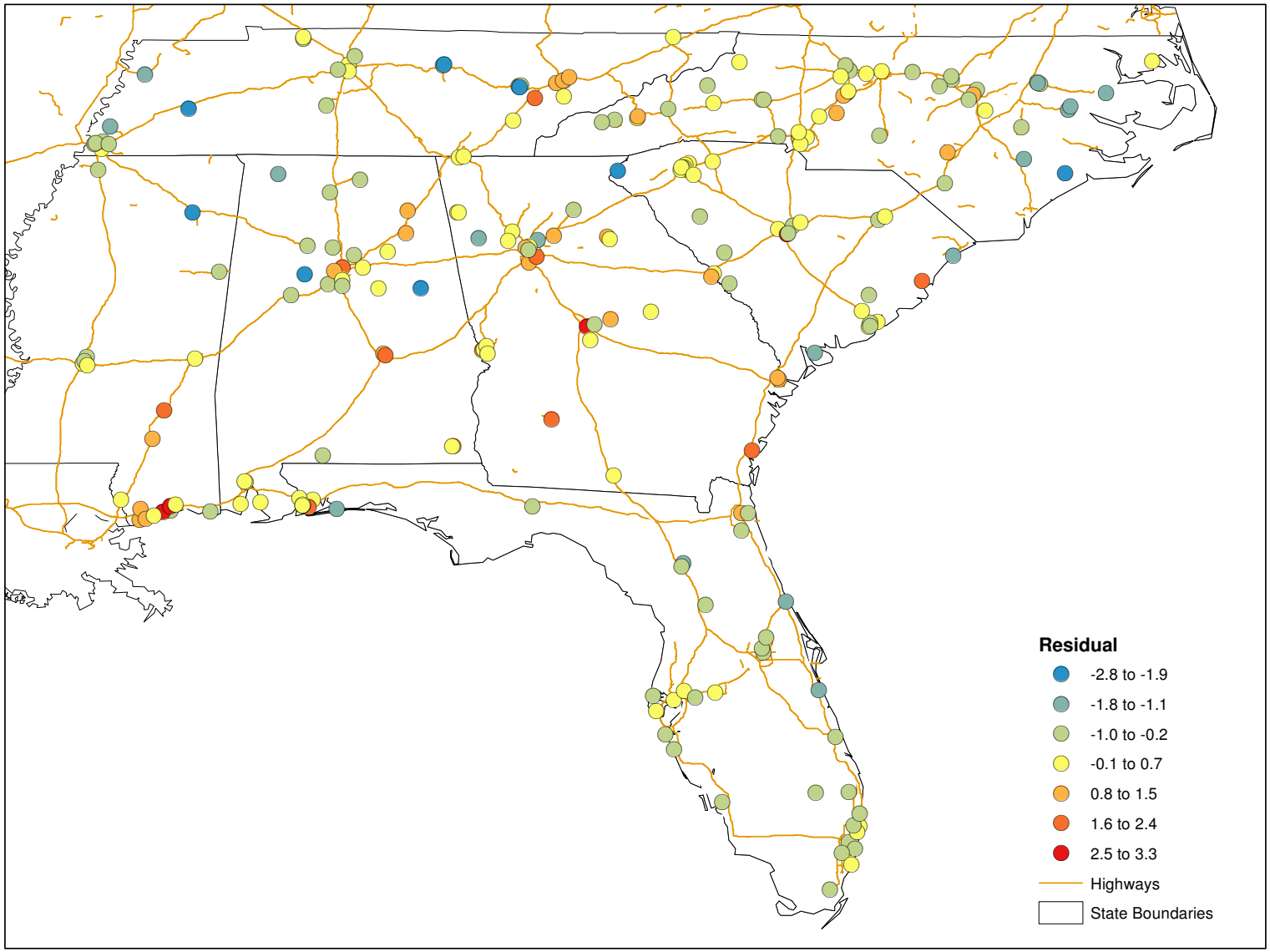

Figure II-3. Residual Map

CHAPTER III

Acute effect of fine particulate matter on mortality in three southeastern states 2007-2011: statewide analysis

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Acute effect of fine particulate matter on mortality in three southeastern states 2007-2011: statewide analysis

Abstract

Many studies, both time series and case-crossover analyses, have examined the acute effects of air pollution on mortality. However, they have generally been limited to larger cities, because that is where the air pollution monitors are, and have assigned all residents of those cities the same exposure, introducing exposure error. We have developed a spatiotemporal model to predict daily $PM_{2.5}$ level at a 1 km×1km resolution for the Southeastern United States between 2003 through 2011. We have also obtained zip-code level mortality data in three of those states: North Carolina, South Carolina, and Georgia between 2007 and 2011. This allows us to examine the acute effect of $PM_{2.5}$ on mortality in the entire population using finer resolution exposure.

We acquired mortality data from the departments of public health in the three states. Modeled $PM_{2.5}$ level from our prediction model were assigned to the zip code of residence of each decedent. We used a case-crossover study design rather than a time series because it allowed easier examination of effect size modification. We examined modification by age, sex, race, education, the primary cause of death, and residence in urban or rural areas. We also compared results based on our modeled $PM_{2.5}$ with the one from using the nearest monitor.

848,270 non-accidental death records were analyzed and we found each 10 $\mu g/m^3$ increase in $PM_{2.5}$ (mean lag0 and lag1) was associated with a 1.56 % (1.19, 1.94) increase in daily deaths.

Cause-specific analyses revealed that cardiovascular disease (2.32 %, 1.57-3.07) and specifically congestive heart failure (3.64 %, 1.35-5.99) showed the highest effect estimate. Blacks (2.19 %, 1.43-2.96) and persons with education ≤ 8 yr (3.13 %, 2.08-4.19) were the most vulnerable populations. Compared to monitoring measurement, our results showed more power and suggested that the $PM_{2.5}$ effects on rural populations have been underestimated due to selection bias and information bias.

We have demonstrated that our AOD-based exposure models can be successfully applied to epidemiologic studies investigating the acute effects of $PM_{2.5}$. This will add a new study population in rural areas, and by doing this, the result from those analyses will be generalizable to a larger population.

INTRODUCTION

Numerous epidemiologic studies have reported a positive relationship between acute exposures to fine particles (particles less than 2.5 micrometers in diameter, $PM_{2.5}$) and mortality ranging from all-cause deaths to respiratory or cardiovascular death (Samet et al. 2000, 1742-1749; Wichmann et al. 2000, 5-86; discussion 87-94; Mar et al. 2005, 311-320; Boldo et al. 2006, 449-458; Ostro, Broadwin, and Lipsett 2000, 412-419; Franklin, Zeka, and Schwartz 2006, 279-287; Ruchirawat et al. 2007, 200-209). $PM_{2.5}$ is believed to increase mortality by producing inflammation and oxidative stress (Risom, Moller, and Loft 2005, 119-137), in part because its small size allows it to penetrate into the alveoli and be retained in the lung parenchyma (Dockery 2009, 257-263). Toxicological research have shown that the components of $PM_{2.5}$ such as metals, sulfate, nitrate, or organic compounds also elicit reactive oxygen species (ROS), inflammatory injury, oxidative DNA damage, and other biological effects (Valavanidis, Fiotakis, and Vlachogianni 2008, 339-362).

Traditionally, $PM_{2.5}$ measurements from ground monitoring stations centrally located in the study domain have been used as surrogates for individual-level exposures to $PM_{2.5}$. Ecological exposure assignment is more subject to biases than individual-level exposure measurement, and the increased measurement error generally makes the risk estimates attenuated (Brenner et al. 1992, 85-95) and results in less statistical power (Greenland 1992, 1209-1223). The use of the existing monitoring stations imposes temporal limitations as well as spatial. Many monitors in the U.S. operate only every third or even sixth day.

As a result, a majority of studies are done in cities or urban areas close to the location of those monitors. Restriction in study population imposes a problem in generalizability of those epidemiologic studies.

However, the characteristics of rural populations are different from urban populations including factors such as education, housing, and the accessibility to health care facilities, and this may lead to a different response to environmental stimuli. Therefore, there have been a lot of uncertainties about acute $PM_{2.5}$ effects outside of large cities.

Recently, we have developed a spatiotemporal model to predict daily $PM_{2.5}$ level at a 1 km×1km resolution for the Southeastern United States between 2003 through 2011. It allowed us to estimate spatially resolved $PM_{2.5}$ on a daily basis throughout the 7 states located in the Southeastern U.S: North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, and Florida. We have also obtained zip-code level mortality data in three of those states: North Carolina, South Carolina, and Georgia between 2007 and 2011. Therefore, we use our model generated predictions to study the acute effect of $PM_{2.5}$ on mortality in the entire population of North Carolina, South Carolina, and Georgia between 2007 and 2011.

DATA AND METHODS

Outcome

We acquired mortality data from the departments of public health in Georgia, North Carolina, and South Carolina. Data was available between 2007 through 2011. The data variables include the date of death, age, sex, race, education, primary cause of death in ICD-code 10^{th} version, and residential zip code. We restricted our analyses to deaths from internal causes by excluding ICD codes V01 through Y98. Specific causes were derived from the ICD code for the underlying cause of death: respiratory disease (ICD codes J00 through J99), cardiovascular disease (ICD codes I01 through I52), and stroke (ICD codes I60 through J69).

As a result, we used 848,270 non-accidental deaths occurring in the study area from 2007 through 2011. Mortality data were unidentifiable, therefore, our research was exempted by the Harvard School of Public Health's Human Subjects Committee.

Exposure

Daily $PM_{2.5}$ exposures were assessed using our recently developed prediction models that incorporate satellite AOD (Aerosol Optical Depth) data for the years 2007–2011 in the Southeastern United States at a 1 × 1 km resolution. The prediction dataset covers virtually the entire areas of North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, and Florida. We used ground $PM_{2.5}$ measurements from 277 monitoring sites from the Environmental Protection Agency (EPA) and Interagency Monitoring of Protected Visual Environments (IMPROVE) monitoring networks to calibrate our model. Our predictors were AOD data from the Moderate Resolution Imaging Spectroradiometer (MODIS) on the Aqua satellite (at a 1km resolution), land use terms (elevation, distance to major roads, percent of open space, point emissions and area emissions) and meteorological variables (temperature, wind speed, relative humidity and visibility). Firstly, we calibrated the AOD grid-level observations to the $PM_{2.5}$ monitoring data collected within 1 km of a $PM_{2.5}$ measurement using a mixed model for observed $PM_{2.5}$ (containing both fixed and day-specific random effects), the AOD slopes with additional spatiotemporal predictors. In doing so, we applied inverse probability weights (IPW) to the first stage model to adjust for the non-random missingness of AOD. To accommodate the fact that the PM-AOD calibration factors can vary spatially between large regions, we divided the Southeastern area into 3 regions and each region has its sub-regions. The intercept, AOD, and temperature random effects in the model are nested within regions of the study. In stage 2 of the model, we

simply predicted $PM_{2.5}$ concentrations to grid cells without monitors using the model fit. We also predicted for the location- days that were missing AOD observations using regressions against nearby monitors and interpolation with a smoothing function. Specifically, for each region in the Southeast, we used the $PM_{2.5}$ predictions for the days when AOD was not missing, and estimated a smooth function of latitude and longitude with a random intercept for each cell and a slope for the mean of $PM_{2.5}$ monitors within 100 km of the grid cell on that day. The results of this model were used to estimate the $PM_{2.5}$ for gridcell-days where AOD was missing. To validate our model, we performed 10-fold cross-validation and chose our model to maximize cross-validated R^2. As a result, we obtained reasonable and reliable $PM_{2.5}$ predictions for the study area (mean cross-validated R^2 of 0.77, 81, 0.70 for region 1, 2, 3, respectively) with modest daily predictions errors (RMSPE -Root of the mean squared prediction errors = 2.89, 2.51, 2.82 $\mu g/m^3$ for region 1, 2, 3, respectively). Among the regions, Region 2 displayed best fit, and includes North Carolina, South Carolina, and part of Georgia. Furthermore, the slopes between observed vs. predicted were close to 1, indicating no bias. $PM_{2.5}$ exposure estimates were generated by our prediction models. For more detailed information on the prediction model, refer to Lee et al.

For this study, the daily predictions of $PM_{2.5}$ at a 1 km^2 resolution were aggregated into the zip code level. Then they were assigned to the zip code of each descendent on each day.

Ground particulate matter measurements

To compare the result from modeled $PM_{2.5}$ with the one from measured $PM_{2.5}$, we used the monitored $PM_{2.5}$ mass concentration from the EPA and IMPROVE monitors described previously. We assigned the resident zip code of the deceased to the nearest monitor. 62,467 observations from 96 $PM_{2.5}$ monitoring stations which operated in the three states between 2007 and 2011 were used.

Covariates

We downloaded daily temperature data from the Climate Data Online website hosted by NOAA's National Data Centers (NNDC) at The National Oceanic and Atmospheric Administration (NOAA) National Climate Data Center (NCDC, 2010). To fully exploit the temperature data, we selected stations regardless of the operation period. Therefore, the stations that had only partially run from 2007 to 2011 were also used. As a result, 26 stations were used. Grid cells were matched to the closest weather station on a specific day with available meteorological variables (24-hour means).

To classify zip codes into urban versus rural areas, we downloaded the 2004 ZIP Rural-Urban Commuting Area Codes (RUCAs) from the website of the WWAMI (WWAMI states: Washington, Wyoming, Alaska, Montana, and Idaho) Rural Health Research Center RHRC. RUCAs are a census tract-based classification scheme to characterize all of the nation's Census tracts regarding their rural and urban status. It was based on 2000 Census work commuting information, and Census Bureau defined Urbanized Areas (cities of 50,000 and greater population) and Urban Clusters (cities/towns with populations from 2,500 through 49,999) and a ZIP Code RUCA approximation has been developed. We utilized that data to classify zip codes in the study area as being urban or rural. RUCA version 2 was used. When the RUCA code is 1.0 or 1.1 which stands for the metropolitan area core, the corresponding zip code area was defined as an urban area. The spatial distribution of urbaneness by zip code is given by Figure III-1.

Statistical analyses

Zip code-specific deaths were matched with our exposure estimates for each grid cell. For monitoring data, we assigned the closest monitoring stations on a specific day. Since many monitoring stations operate on every third or sixth day, we found the next closest monitoring station, if the closest monitoring station didn't run on a specific day.

We used a case-crossover design (Maclure 1991, 144-153), which is a variant of the matched case-control design to study the effects of acute exposures on the acute outcome without carry-over effect. In this design, each case subject (a decedent) serves as his or her own control on days when no event (death) occurs. Since each subject serves as his or her own control, it provides perfect matching on all subject characteristics that do not vary over time. To avoid seasonal confounding, control days are only chosen within the same month of the same year that death occurred. Control days are chosen bi-directionally and we chose every third day from the case day in that month to reduce serial correlation in the exposure variable, given that in the US weather fronts generally pass through a location every 3–4 days (Medina-Ramon and Schwartz 2007, 827-833).

We defined the relevant exposure time window as the mean exposure on the day of and day before the decedent's death. Temperature was chosen as a potential confounder. Specifically, a conditional logistic regression was fitted as follows,

$$\text{logit}\,(p_i) = \beta_{0i} + \beta_1 PredPM_{2.5_{ij}} + \beta_2 Temp_{ij} + \beta_3 \text{Tuesday} + \cdots + \beta_8 \text{Sunday},$$

where $PredPM_{2.5_{ij}}$ is the predicted two day mean $PM_{2.5}$ level in zip code i on day j, $Temp_{ij}$ is the temperature for zip code i on day j, and the remaining are the indicator variables for day of the week.

For stratified analysis, we performed separate analyses to generate the effect estimate but used the interaction term with the exposure and the effect modifier to test for significant modification. For those sub-region analyses, we used the same exposure window as in the main analysis. Various stratified analyses were conducted: we examined effect modification by age, sex, race, education, and the primary cause of death. We also conducted analyses to compare the results that used modeled $PM_{2.5}$ with those using actual $PM_{2.5}$ measurement data.

The data analysis for this paper was generated using the PROC PHREG procedure in Base SAS software, version 9.3 of the SAS system for windows (Copyright © 2014 SAS Institute Inc., Cary, NC, USA).

RESULTS

Figure III-1 shows the study area. Zip codes are divided by being urban or rural. Main cities in the study areas were Atlanta (GA), Charlotte (NC), Raleigh (NC), and Columbia (SC). Most of the $PM_{2.5}$ monitors operated in urban areas. Figure III-2 presents one of the examples from our $PM_{2.5}$ prediction models, which is aggregated into a zip code level. It shows the spatial distribution of the average of modeled $PM_{2.5}$ in the study area in 2011 by zip code. The spatial distribution of $PM_{2.5}$ was relatively high in Georgia among three states and urban areas showed higher $PM_{2.5}$ level compared to the surrounding rural areas.

We used 848,270 non-accidental death records in three states of North Carolina, South Carolina, and Georgia between 2007 and 2011 (Table III-1). By state, 42% of the total record was collected from North Carolina, 37% of data from Georgia, and 21% was from South Carolina. The average age of the decedents was 73 years old with a standard deviation of 17 years. Therefore,

most of the decedents were aged over 65 (71 %) and about the half of the deceased died at 75 or over. The sex ratio was almost 1:1 with a slight excess of females (52 %). By race, whites accounted for 75 % of deaths, blacks for 24 %, and other races for 1 %. The percentage of whites was highest in North Carolina (78 %). For education level, less than high school education (years less than 12 years) occurred with the highest frequency (27 %). However 24 % of the education records were missing and most of that originated from data collected from Georgia (63% of Georgia records). 53 % of the population resided in urban areas and the proportion was highest in Georgia (59%). It is worth noting that the 4,339 (0.5 %) missing data on being urban or not includes true missing data as well as those with a residential zip code outside the study area.

Table III-1 also shows a summary of the modeled $PM_{2.5}$ level for rural/urban areas and temperature. The average $PM_{2.5}$ level was 11.1 $\mu g/m^3$ (S.D.=4.4 $\mu g/m^3$) from 2007 through 2011 and the average $PM_{2.5}$ in Georgia was slightly higher than the other states.

Table III-2 presents the estimated percent increase in mortality for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ by lag period and its comparison with the results from measurement data. For all non-accidental deaths, we found a 1.56 % increase in mortality (95% CI = 1.19 to 1.94). Compared to the result from our prediction model, the estimate from the existing monitoring stations showed a lower effect estimate, which was 1.21 % increase. The mean distance to the assigned monitors was around 55 km. It is worth noting the distances were different between lag 0 and lag 1, because many monitoring stations don't operate on a daily basis.

We conducted various sub-region analyses (Figure III-3). There was no significant effect modification by age, sex or race. However, we found that black population showed substantially higher risk (2.19%, 95% CI=1.43-2.96) than white population (1.40 %). While not significant, a 50% difference in effect size is noteworthy, and the significance may have been affected by the

small percentage of deaths that were blacks. For education level, the region less than 8 years of education showed more than double the risk (3.13%) compared to the more educated regions (1.43 %), and that difference was marginally significant.

The impact of $PM_{2.5}$ on CVD and CHF death rates was larger than for all natural causes; we found a 2.32 percent increase (95% CI =1.57 to 3.07) and a 3.64 % (1.35, 5.99) respectively. In contrast, the impact on deaths from MI (1.12 %) and stroke (0.55 %) was lower. We did not see significant associations with pulmonary deaths, perhaps because of small numbers.

We found differences (albeit not significant based on the p-value of the interaction term) in the $PM_{2.5}$ associations with mortality between people living in urban areas and those in rural areas and those results were reversed between modeled $PM_{2.5}$ and measured $PM_{2.5}$ (Figure III-4). Rural areas showed the higher risk for mortality (1.86 %; 1.75, 1.98) than the urban areas (1.38 %; 1.28, 1.47) in our analyses. Conversely, results based on the existing monitoring stations, showed a higher increase in mortality in urban areas (1.43 %; 1.36, 1.50) than rural areas (0.96 %; 0.88, 1.03).

DISCUSSION

In this paper we examine associations between $PM_{2.5}$ exposures generated by our prediction model and increased mortality in the three states of Georgia, North Carolina, and South Carolina between 2007 through 2011.

Compared to the effect estimate from our modeled $PM_{2.5}$, monitor-based estimates tended to be attenuated, and have wider confidence intervals. The use of the modeled $PM_{2.5}$ levels enabled us to investigate the entire region, with more power to conduct stratified analyses. We found

differences in effect size by race and education level, with blacks and less educated people having higher risk. While some studies using central monitoring sites have identified such effect modification before, the nature of the study design made it impossible to determine whether these effects were due to differential exposure or differential response. Our results, using 1km resolution exposure estimates strongly suggest that in addition to any differential exposure, there is differential response. This makes particulate air pollution a key environmental justice issue, since it is ubiquitous, and associated with more harm than most environmental exposures. Whether these differences relate to psychosocial stress, housing, or other factors needs further investigation.

In the stratified analyses for the primary cause of death, CVD and CHF exhibited the highest increase in mortality in response to $PM_{2.5}$. Other causes were not significant, likely due to the very small number of observations (Figure III-3).

We also found differences in the $PM_{2.5}$ associations between people living in rural areas and urban areas. Interestingly, the effects of acute $PM_{2.5}$ exposure appeared stronger in rural areas than urban areas. Kloog et al. (Kloog et al. 2014, e88578) reported results consistent with this in his paper where he used a similar model for $PM_{2.5}$ in the mid-Atlantic region of U.S. In contrast, using the nearest monitor we failed to find this result. Since that exposure overall produces lower effect size estimates, a result consistent with larger exposure error, the difference using this exposure likely reflects the higher measurement error in exposure in rural areas, because most residents live further from a monitor.

Another consequence of this finding is that the acute effects of particulate matter may have been underestimated because an important part of the population was excluded from most prior epidemiologic studies due to the lack of monitoring sites.

A possible explanation for the higher risk in rural areas can be sought in the socioeconomic characteristics of rural populations who tend to be in low income and education level compared to the population in urban areas (Kloog et al. 2014, e88578). Alternatively, these differences may be related to differences in the amount of outdoor time such as farmers, accessibility to hospitals or the prevalence of smoking.

We don't expect any problem in the exposure history, since we evaluated acute exposure with the history of exposure only within 1 previous day and used the zip codes for residence. Therefore, discrepancy in the record and the actual exposure is very low.

There are still limitations in our study. The resident location of the deceased was in an aggregated form of zip codes, not individual addresses which were not available due to privacy and confidentiality issues. This ecological attribute in exposure measurement still lends more measurement error than individual-level studies. With 1 km resolution exposure day, once we obtain the street-level address from study subjects, our research question will be better served. Yet, considering the area of zip code is much smaller than a city or a county, the magnitude of such error seems much smaller than the existing studies that used the sparse network of monitoring stations.

We also expect further improvements of the prediction. With an advent of finer satellite remote sensing and processing algorithms, we will be able to produce more reliable and accurate predictions of $PM_{2.5}$.

The same issue also exists for the covariate, temperature. Temperature was controlled as a possible confounder and its measurement was not based on the individual-level as well. The residual confounding in temperature is expected.

To the best of our knowledge, this is the first study that included the entire population in the three states in the Southeastern U.S. to assess the relationship between short-term $PM_{2.5}$ exposures and mortality.

In conclusion, our findings indicate that increased mortality especially for CVD and CHF were associated with $PM_{2.5}$ exposures. In addition, we have demonstrated that our AOD-based exposure models can be successfully applied to epidemiologic studies investigating the acute effects of $PM_{2.5}$. This has been possible because these models make it possible to estimate spatially-resolved $PM_{2.5}$ exposures for specific zip codes on a daily basis. This will add a new study population in rural areas, and in doing so, the result from those analyses will be more generalizable to other populations and areas.

REFERENCES

1. Samet JM, Dominici F, Curriero FC, Coursac I, Zeger SL. Fine particulate air pollution and mortality in 20 U.S. cities, 1987-1994. N Engl J Med. 2000;343(24):1742-1749. doi: 10.1056/NEJM200012143432401 [doi].

2. Wichmann HE, Spix C, Tuch T, et al. Daily mortality and fine and ultrafine particles in erfurt, germany part I: Role of particle number and particle mass. Res Rep Health Eff Inst. 2000(98):5-86; discussion 87-94.

3. Mar TF, Ito K, Koenig JQ, et al. PM source apportionment and health effects. 3. investigation of inter-method variations in associations between estimated source contributions of PM2.5 and daily mortality in phoenix, AZ. J Expos Sci Environ Epidemiol. 2005;16(4):311-320.

4. Boldo E, Medina S, Le Tertre A, et al. Apheis: Health impact assessment of long-term exposure to PM2.5 in 23 european cities. Eur J Epidemiol. 2006;21(6):449-458. doi: 10.1007/s10654-006-9014-0.

5. Ostro BD, Broadwin R, Lipsett MJ. Coarse and fine particles and daily mortality in the coachella valley, california: A follow-up study. J Expo Anal Environ Epidemiol. 2000;10(5):412-419. doi: 10.1038/sj.jea.7500094.

6. Franklin M, Zeka A, Schwartz J. Association between PM2.5 and all-cause and specific-cause mortality in 27 US communities. J Expos Sci Environ Epidemiol. 2006;17(3):279-287.

7. Ruchirawat M, Settachan D, Navasumrit P, Tuntawiroon J, Autrup H. Assessment of potential cancer risk in children exposed to urban air pollution in bangkok, thailand. Toxicol Lett. 2007;168(3):200-209. doi: S0378-4274(06)01323-3 [pii].

8. Risom L, Moller P, Loft S. Oxidative stress-induced DNA damage by particulate air pollution. Mutat Res. 2005;592(1-2):119-137. doi: S0027-5107(05)00246-0 [pii].

9. Dockery DW. Health effects of particulate air pollution. Ann Epidemiol. 2009;19(4):257-263. doi: 10.1016/j.annepidem.2009.01.018 [doi].

10. Valavanidis A, Fiotakis K, Vlachogianni T. Airborne particulate matter and human health: Toxicological assessment and importance of size and composition of particles for oxidative damage and carcinogenic mechanisms. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2008;26(4):339-362. doi: 10.1080/10590500802494538 [doi].

11. Brenner H, Savitz DA, Jockel KH, Greenland S. Effects of nondifferential exposure misclassification in ecologic studies. Am J Epidemiol. 1992;135(1):85-95.

12. Greenland S. Divergent biases in ecologic and individual-level studies. Stat Med. 1992;11(9):1209-1223.

13. Maclure M. The case-crossover design: A method for studying transient effects on the risk of acute events. Am J Epidemiol. 1991;133(2):144-153.

14. Medina-Ramon M, Schwartz J. Temperature, temperature extremes, and mortality: A study of acclimatisation and effect modification in 50 US cities. Occup Environ Med. 2007;64(12):827-833. doi: 10.1136/oem.2007.033175 [doi].

15. Schwartz J, Coull B, Laden F, Ryan L. The effect of dose and timing of dose on the association between airborne particles and survival. Environ Health Perspect. 2008;116(1):64-69. doi: 10.1289/ehp.9955 [doi].

16. Lepeule J, Laden F, Dockery D, Schwartz J. Chronic exposure to fine particles and mortality: An extended follow-up of the harvard six cities study from 1974 to 2009. Environ Health Perspect. 2012;120(7):965-970. doi: 10.1289/ehp.1104660 [doi].

17. Kloog I, Nordio F, Zanobetti A, Coull BA, Koutrakis P, Schwartz JD. Short term effects of particle exposure on hospital admissions in the mid-atlantic states: A population estimate. PLoS One. 2014;9(2):e88578. doi: 10.1371/journal.pone.0088578 [doi].

TABLES

Table III-1. Characteristics of mortality and modeled $PM_{2.5}$, 2007-2011

	Total	GA	NC	SC
Deaths (%)	848,270	311,831 (37)	357,915 (42)	178,524 (21)
Age, mean (SD), y	73 (17)	72 (18)	73 (17)	73 (17)
> 65, No. (%)	603,600 (71)	216,416 (69)	260,544 (73)	126,640 (71)
> 75, No. (%)	438,728 (52)	156,805 (50)	190,724 (53)	91,199 (51)
Missing	43 (≤ 1)	0 (0)	0 (0)	43 (≤ 1)
Sex, No. (%)				
Male	409,408 (48)	149,790 (48)	172,171 (48)	87,447 (49)
Female	438,847 (52)	162,041 (52)	185,739 (52)	91,067 (51)
Missing	15 (≤ 1)	0 (0)	5 (≤ 1)	10 (≤ 1)
Race, No. (%)				
White	631,701 (75)	223,727 (72)	279,375 (78)	128,599 (73)
Black	206,226 (24)	85,020 (27)	73,812 (21)	47,394 (27)
Other	9,202 (1)	3,084 (1)	4,728 (1)	1,390 (1)
Missing	1141 (≤ 1)	0 (0)	0 (0)	1,141 (1)
Education, No. (%)				
≤ 8 yrs	118,283 (14)	18,915 (6)	66,198 (19)	33,170 (19)
≤ 11	112,699 (13)	17,580 (6)	67,463 (19)	27,656 (16)
≤ 12	227,791 (27)	44,535 (14)	118,816 (33)	64,440 (37)
≤ 15	109,018 (13)	27,698 (9)	53,576 (15)	27,744 (16)
≥ 16	77,187 (9)	8,201 (3)	46,645 (13)	22,341 (13)
Missing	203,292 (24)	194902 (63)	5217 (1)	3,173 (2)
Residence, No. (%)				
Urban	445,393 (53)	182,461 (59)	174,830 (49)	88,102 (49)
Rural	398,538 (47)	129,095 (41)	179,381 (51)	90,062 (51)
Missing	4,339 (0.5)	275 (≤ 1)	3,704 (1)	360 (≤ 1)
Cause of Death, No. (%)				
CVD	194,180 (55)	71,643 (55)	81,604 (55)	40,933 (55)
Stroke	46,535 (13)	16,252 (12)	20,116 (13)	10,167 (14)
CHF	23,119 (7)	10,364 (8)	8,180 (5)	4,575 (6)
MI	42,371 (5)	13,686 (4)	18,105 (5)	10,580 (6)
Respiratory	89,280 (25)	32,475 (25)	38,791 (26)	18,014 (24)
Missing	38 (≤ 1)	38 (≤ 1)	0 (0)	0 (0)
$PM_{2.5}$ mean (SD), $\mu g/m^3$	11.1 (4.4)	11.6 (4.5)	10.7 (4.3)	10.9 (4.2)
Range (min, max)	0.02, 86.2	0.8, 80.2	0.02, 86.2	0.5, 70.99

Table III-2. Comparison of effect estimates between modeled and measured $PM_{2.5}$

LAG	Modeled $PM_{2.5}$	Measured $PM_{2.5}$	Mean Distance
0	1.12 (0.80, 1.43)	0.85 (0.63, 1.07)	54.96 km
1	1.19 (0.86, 1.52)	0.90 (0.68, 1.13)	54.93 km
0-1	1.56 (1.19, 1.94)	1.21 (0.94, 1.47)	N/A

Increase in mortality in percentage and (95% confidence intervals)

FIGURES

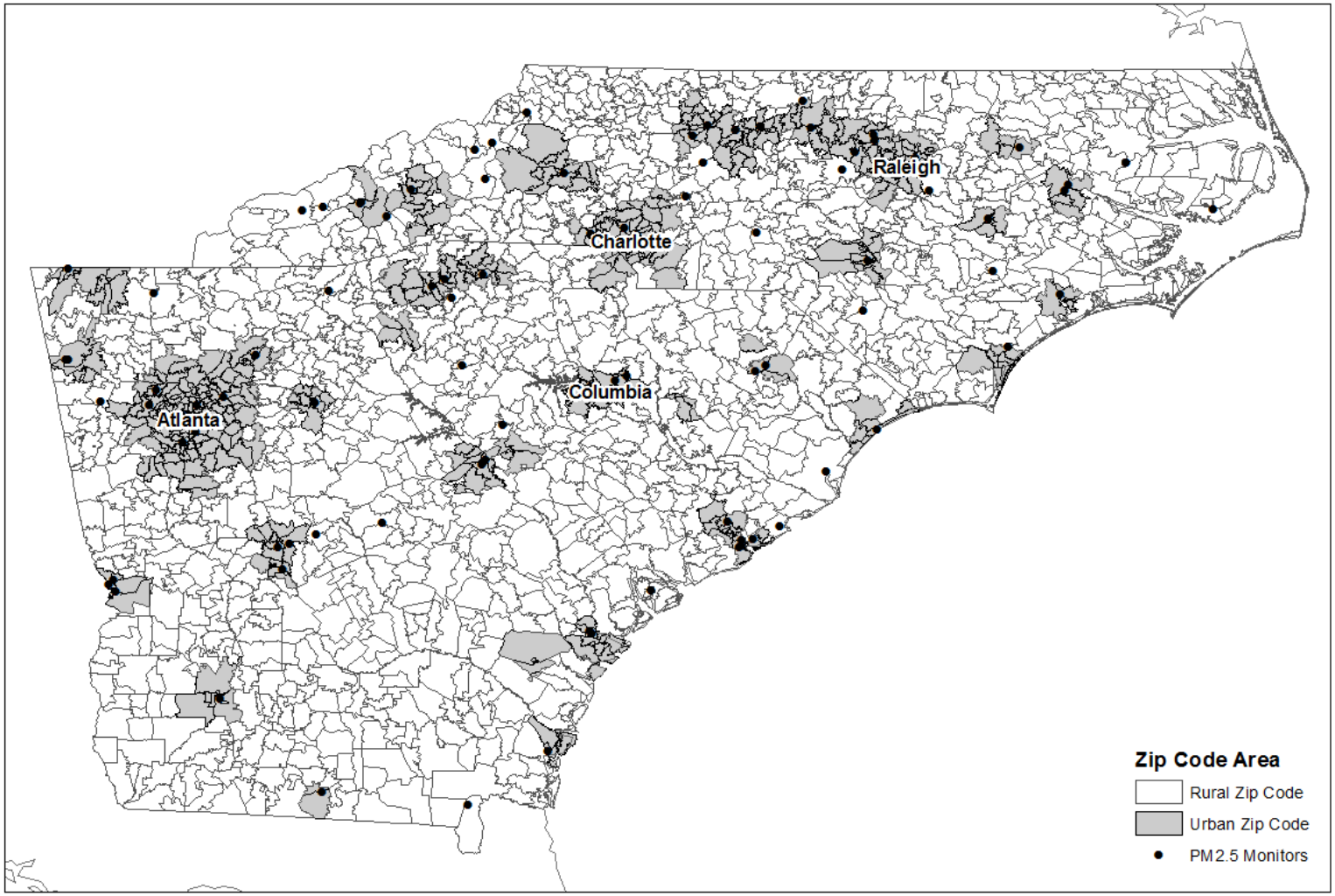

Figure III-1. Map of study area

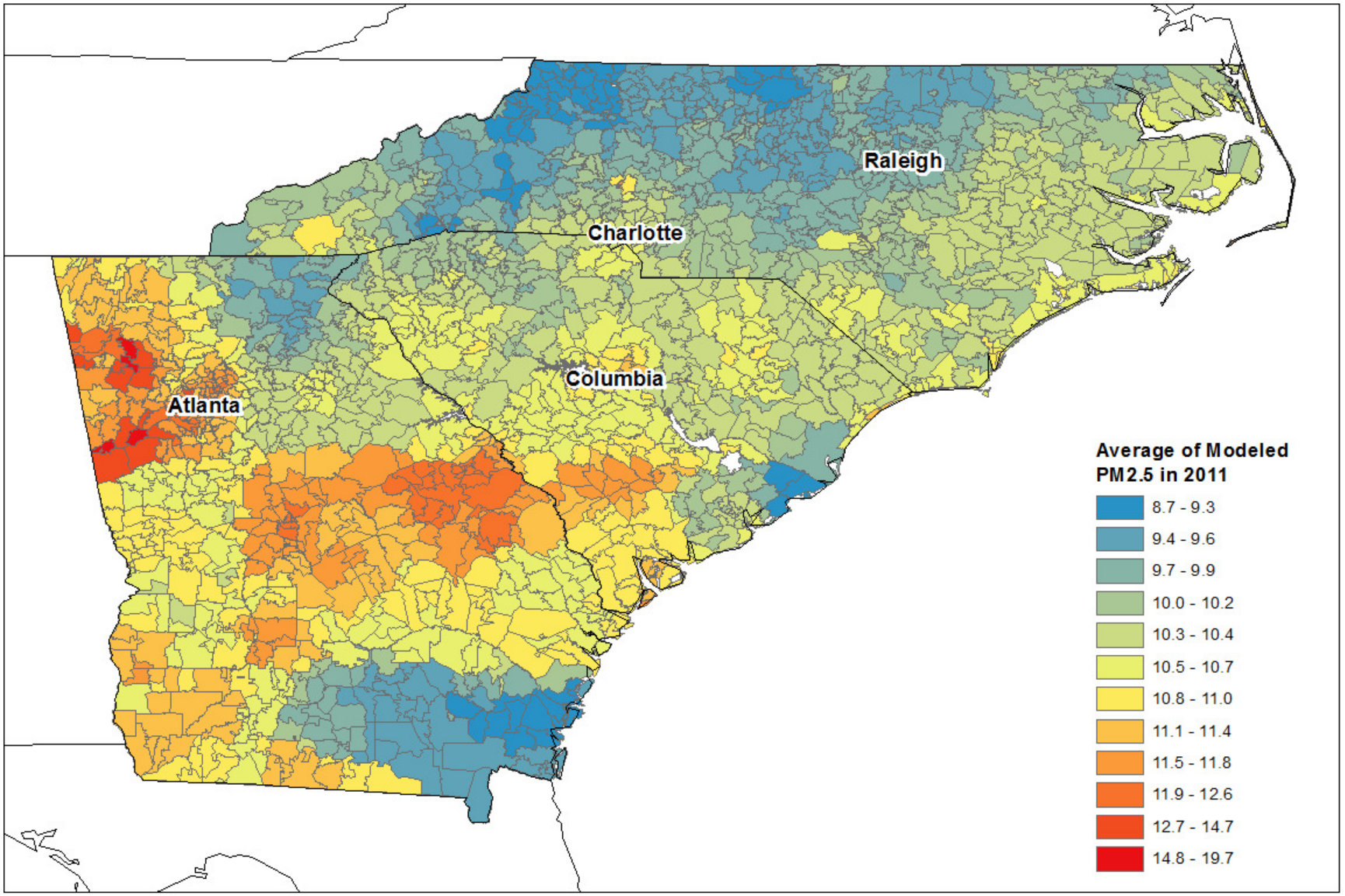

Figure III-2. Average of predicted $PM_{2.5}$ by zip code in 3 States in 2011

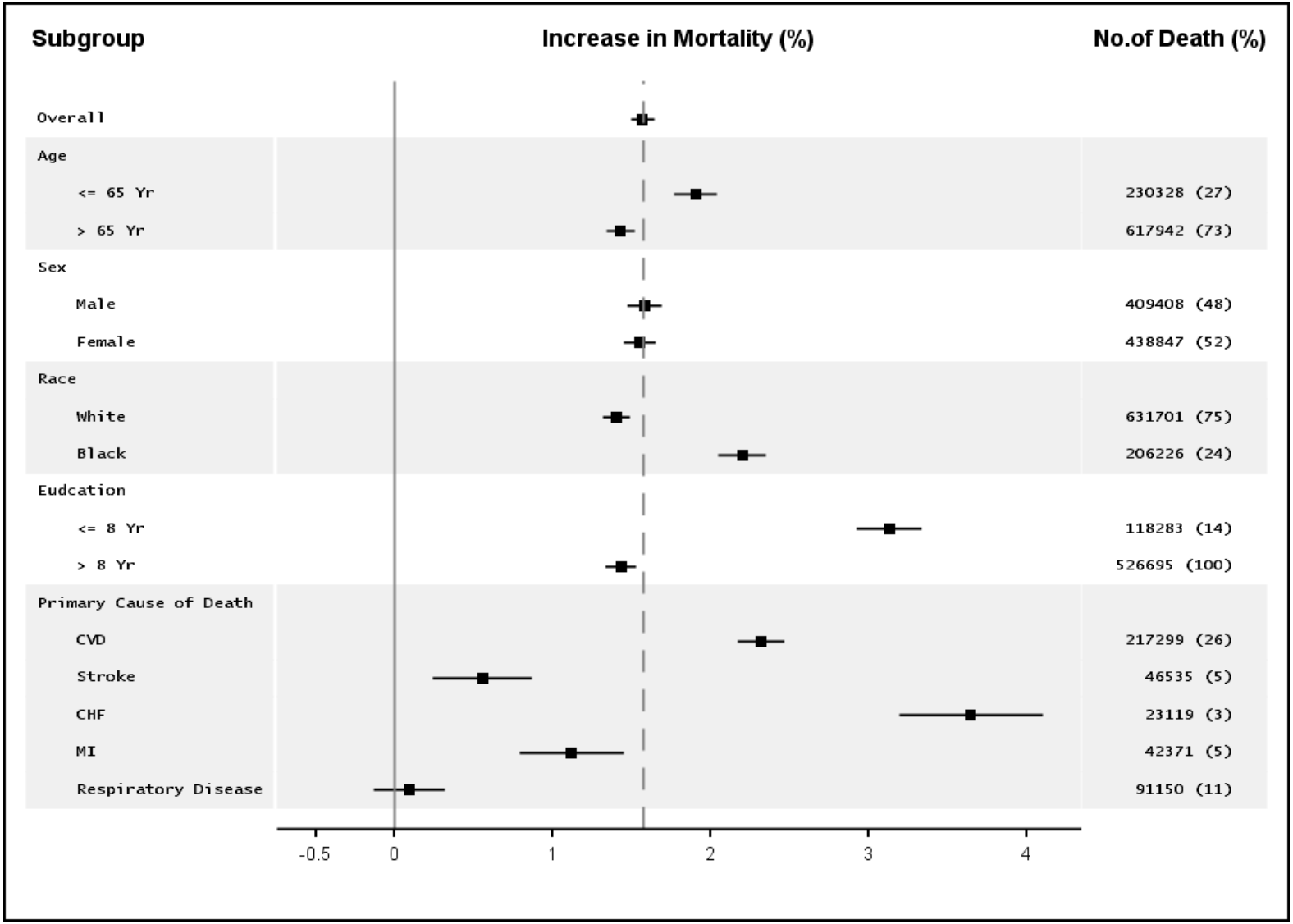

Figure III-3. Stratified analyses

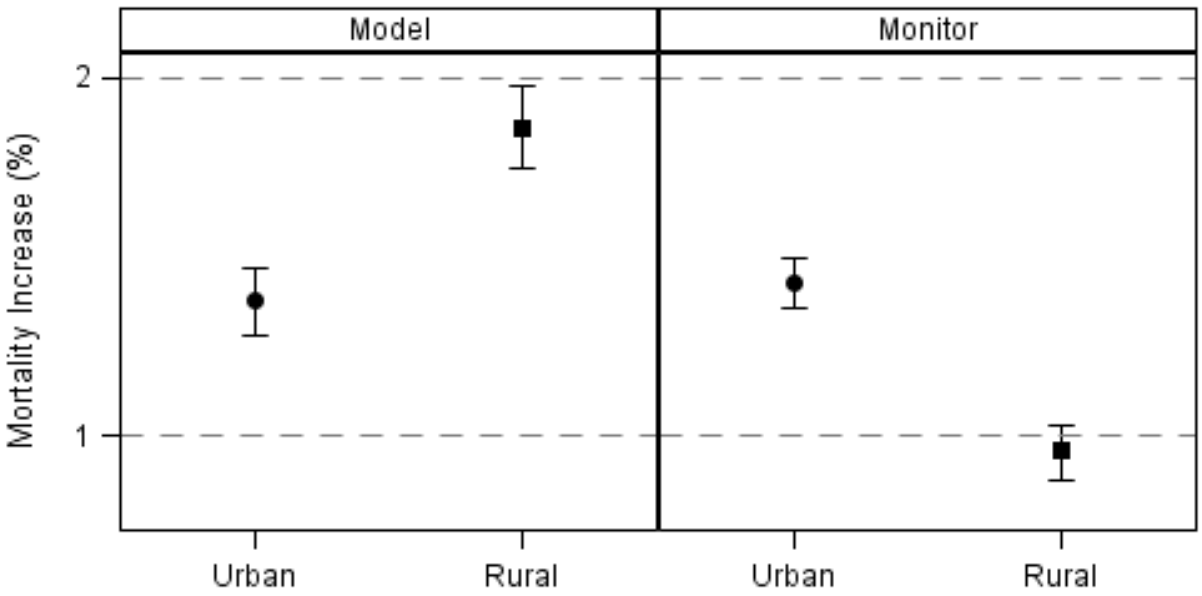

Figure III-4. Difference in the effect of $PM_{2.5}$ by residence and exposure metric

CONCLUSION

In our first paper, we found that the effects of a given temperature on mortality vary spatially and temporally based on how unusual it is for that time and location. This suggests changes in variability of temperature may be more important for health as climate changes than changes of mean temperature. More emphasis should be placed on warnings targeted to early heat/cold temperature for the season or month rather than focusing only on the extremes.

In our second topic, we have demonstrated that the use satellite imagery and other land use variables with a mixed-effect model produces reliable predictions of daily $PM_{2.5}$ for the extensive area of the southeastern United States. By incorporating land use terms and spatial smoothing, our models perform much better than previous studies. Therefore, our model results can be used in various epidemiological studies investigating the effects of $PM_{2.5}$ allowing one to assess both acute and chronic exposures with the implication of a new application. Our model results will extend the existing studies on $PM_{2.5}$ mainly targeted only for urban areas tied to the lack of monitors into new areas which used not to be studied such as rural areas.

In our third topic, our findings indicate that increased mortality especially for CVD and CHF were associated with $PM_{2.5}$ exposures. In addition, we have demonstrated that our AOD-based exposure models can be successfully applied to epidemiologic studies investigating the acute effects of $PM_{2.5}$. This will add a new study population in rural area, and by doing this, the result from those analyses will be given more generalizability of the conclusion.