Respiratory hospitalizations in association with fine PM and its components in New York State

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Abbreviations: EPA - US Environmental Protection Agency; NYS – New York State; CMAQ - Community Multiscale Air Quality

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ABSTRACT

Background: Despite observed geographic and temporal variation in PM-related health morbidities, only a small number of epidemiologic studies have evaluated the relation between $PM_{2.5}$ chemical constituents and respiratory disease. Most assessments are limited by inadequate spatial and temporal resolution of ambient PM measurements and/or by their approaches to examine the role of specific PM components on health outcomes.

Methods: In a case-crossover analysis using daily average ambient $PM_{2.5}$ total mass and species estimates derived from the Community Multiscale Air Quality (CMAQ) model and available observations, we examined the association between the chemical components of PM (including elemental and organic carbon, sulfate, nitrate, ammonium, and other remaining) and respiratory hospitalizations in New York State. We evaluated relationships between levels (low, medium, high) of PM constituent mass fractions, and assessed modification of the $PM_{2.5}$- hospitalization association via models stratified by mass fractions of both primary and secondary PM components.

Results: Average daily $PM_{2.5}$ concentrations in New York State were generally lower than the National Ambient Air Quality (NAAQS) 24-hour average concentration standard. Year-round analyses showed statistically significant positive associations between respiratory hospitalizations and $PM_{2.5}$ total mass, sulfate, nitrate, and ammonium concentrations at multiple exposure lags (0.5-2% per IQR increase). Primarily in the summer months, the greatest risks of respiratory hospitalizations were observed per IQR increase in the secondary species sulfate and ammonium concentrations at lags of 1-4 days (1.0-2.0%). Although there were subtle differences in associations observed between mass fraction tertiles, there was no strong evidence to support modification of the $PM_{2.5}$-respiratory disease association by a particular constituent.

Conclusions: Ambient concentrations of $PM_{2.5}$ and secondary aerosols including sulfate, ammonium, and nitrate were positively associated with respiratory hospitalizations, although patterns varied by season. Exposure to specific fine PM constituents is a plausible risk factor for respiratory hospitalization in New York State.

INTRODUCTION

Fine particles less than 2.5 microns in diameter ($PM_{2.5}$) are emitted directly from sources or are formed in the atmosphere through gas and/or aqueous phase reactions of primary pollutants such as NOx and SO_2. A substantial body of epidemiologic evidence exists in support of the association between short-term exposure to ambient fine particles and respiratory morbidity, including hospitalizations and emergency department (ED) visits, increased medication use, symptoms, and infections (Dominici et al. 2006, Host et al. 2008, Karakatsani et al. 2003, Tecer et al. 2008, von et al. 2002). Most of these studies have quantified health burdens in relation to $PM_{2.5}$ total mass only, although examination of relationships with the components of $PM_{2.5}$ could potentially explain observed geographic variation in PM-related health risk (Atkinson et al. 2014). A better understanding of the potential toxicity of other PM components may inform source-related regulatory controls for particulates, which are currently focused on reductions in total particle mass rather than constituent species.

Several more recent epidemiological investigations have identified associations between short-term exposure to the constituents of fine PM ($PM_{2.5}$) and respiratory morbidity (Bell et al. 2009, Ostro et al. 2009, Peng et al. 2009). These studies identified significant species-related respiratory health risks, but were limited to examination of either children or older adult populations and lacked daily exposure estimates. The U.S. Environmental Protection Agency's (EPA) Chemical Speciation Network (CSN) collection of PM component data remains limited in spatial coverage and by a 1 in 3 or 1 in 6 day sampling scheme, posing a challenge to valid estimation of acute health risks. The availability of air quality models such as the Community Multiscale Air Quality (CMAQ) model to estimate daily PM mass and species data is an alternate approach to estimate human exposure to ambient outdoor PM at a finer temporal scale, but predictions from such models are subject to biases and errors. Integrating available observations with air quality model predictions provides a promising approach for enhancing time- and space-resolved PM concentrations fields (Garcia et al. 2010). Few existing studies have examined PM constituents using a case-crossover design, although this method is increasingly common in the epidemiological air quality literature and provides advantages for confounding adjustment over traditional time-series analysis.

This study investigated the association between daily ambient $PM_{2.5}$ species concentrations and respiratory hospitalizations in New York State (NYS) using 24-hour average PM constituent concentrations estimated by combining CMAQ outputs with available observations. Our objective was to characterize the relationship between ambient PM species and respiratory hospitalization in a large,

age and racially/ethnically diverse population using a case-crossover approach. A secondary objective was to determine whether certain fine PM constituents modify the $PM_{2.5}$-respiratory disease association.

METHODS

Design and population

A case-crossover approach was used to assess the short-term association between ambient $PM_{2.5}$ species and risk of respiratory hospitalization among the entire residential population of NYS, 2000-2005. The hazard period for the case-crossover analysis was defined as the day of admission. A time-stratified control selection was employed, with control days sampled from the same month and day of the week as the case date in seven-day intervals. This method of control sampling is thought to be the least prone to bias (Janes, Sheppard, and Lumley 2005), particularly for studies of air pollution (Carracedo-Martinez et al. 2010),because each case acts as its own control, accounting for many individual-level confounders (e.g., smoking). Statewide hospital discharge data was obtained from the NYS Department of Health State Planning and Research Cooperative System (SPARCS), representing data from 95% of NYS hospitals. Mandated under Title 10 NYS Public health law, the SPARCS database includes data from all facilities certified for inpatient care or providing ambulatory surgery services, excluding psychiatric and veterans hospitals (NYSDOH 2014). Patient information obtained for analyses included principal diagnosis, a unique personal identifier, date of birth, gender, race, ethnicity, residential address, and date of admission. Respiratory admissions were extracted based on principal diagnosis from International Classification of Disease (Version 9) (ICD-9) codes, including asthma (ICD-9 code 493), chronic bronchitis (491), chronic airway obstruction (496), and emphysema (492).

Non-varying individual-level factors such as age, gender, race/ethnicity, land use characteristics, and other features of residence which may be relevant to both outdoor air pollution exposures and respiratory disease hospitalization were addressed as confounders by the case-crossover design. These factors were therefore examined only as effect modifiers via stratified analyses. Daily, day-of-the-week, and secular trends in health and exposure data were also largely addressed by design. Seasons were defined as winter: (December, January, February); spring (March, April, May); summer (June, July, August); and fall (September, October, November), and trends were evaluated via stratified analysis.

Pollutant and meteorological data

The daily average total $PM_{2.5}$ mass and species concentrations in $\mu g/m^3$ used in this study were developed following the approach described in Hogrefe et al. (2009) from the CMAQ model, a three-dimensional Eulerian (i.e., gridded) atmospheric chemistry and transport modeling system that simulates particulate matter and other airborne pollutants. Specifically, these data were estimated by bias-correcting CMAQ concentrations provided on a 12km by 12 km modeling grid with available CSN measurements, assuming seasonally varying species-specific biases (Hogrefe et al. 2009). The chemical species of interest included components which make up the largest fractions of $PM_{2.5}$ total mass: secondary aerosols sulfate (SO_4), ammonium (NH_4), nitrate (NO_3), elemental carbon (EC), the carbon-only portion of the organic carbon aerosol (OC), and crustal/other $PM_{2.5}$, including the non-carbon organic matter (OTH). Daily eight-hour maximum ozone (O_3) concentrations in ppb were available at the same 12km spatial resolution for adjustment as a co-pollutant. Meteorological variables including daily mean ambient temperature, universal apparent temperature (UAT) in °F, humidity, wind, and barometric pressure were obtained from the National Climactic Data Center for 14 climate regions across NYS.

After restriction to NYS residences, hospital admissions data were geocoded using an automated process in Mapmarker Plus® (v. 10). The patient's geocoded address was then joined to a 12-km CMAQ exposure grid surface in a Geographic Information System (GIS), and 24-hour average concentrations for total and speciated $PM_{2.5}$ masses from the CMAQ dataset were assigned to individuals based on their street-level geocodes falling within the assigned exposure grid. Admissions were further assigned to meteorological variables by linkage of their residential address to the NYS climate regions, as was done in another NYS analysis (Fletcher et al. 2012).

Statistical analysis

Univariate and bivariate analyses were used to generate descriptive statistics for health and PM data, year round and by season. The mass fractions of each chemical constituent (i.e., the proportion of bias-corrected CMAQ $PM_{2.5}$ total mass that is comprised of each species) were estimated as the bias-corrected CMAQ species concentration divided by the $PM_{2.5}$ concentration, and were ranked into tertiles (low, medium, high) for analysis. Spearman rank correlations between $PM_{2.5}$ total mass, species, ozone, and UAT were also computed.

We assessed the association between PM species and total respiratory hospitalizations using single-pollutant conditional logistic regression models for each species mass concentration, both across

the entire study period and in season-stratified models. The interquartile range (IQR) of$PM_{2.5}$ total mass and its species were used as the unit of exposure for analyses. Final models further adjusted only for daily UAT, as ozone did not remain a significant predictor. To provide context for associations with PM components in light of their relationship with $PM_{2.5}$ mass, we further explored concomitant relationships between PM mass fractions using a similar approach to that of Rich et al. in their analysis of CMAQ data in New Jersey (Rich et al. 2013). We also evaluated whether mutual adjustment of models for $PM_{2.5}$ mass influenced any estimated risks.

We used the PHREG procedure in SAS® (version 9.2) to tabulate hazard ratios (HRs) along with 95% confidence intervals (95%CI) from regression models. We assessed effect modification by stratifying analyses by sociodemographic and regional characteristics (e.g., age, race/ethnicity, gender, New York City vs. upstate) and PM species mass fractions (e.g., low, medium, high), and assessed the statistical significance of these interactions via cross-product terms included in models. The criterion for statistical significance in all analyses was $p<0.05$.

RESULTS

Pollutant concentrations and relationships

A total of 469,095 respiratory hospitalizations occurred during the study period. After removing non-geocodable records or those missing covariate information, the case-crossover dataset for analysis included 419,938 case days and 1,363,625 control days (up to 4 control days per case). Asthma admissions comprised the largest proportion (51%) of respiratory hospitalizations, followed by chronic bronchitis (34%) and the remaining diagnoses 15% (data not shown).

Table 1 summarizes the statewide average distributions of fine PM and the percent contributions of each species to total $PM_{2.5}$ mass. The median concentration of $PM_{2.5}$ total mass during the study period was 6.64 $\mu g/m^3$. Extremely high daily concentrations were infrequent occurrences and consequently the IQR value (7.48 $\mu g/m^3$) was close to the median concentration. Exceedance of the National Ambient Air Quality (NAAQS) 24-hour standard for $PM_{2.5}$ (35 $\mu g/m^3$) occurred on roughly nine percent of days across the 6-year study period; 60% of these exceedances occurred in New York City (NYC) (data not shown). Overall, SO_4 dominated the composition of $PM_{2.5}$ total mass (49.9%), with the ammonium (16.2%) and OC (11.3%) each contributing the next largest mass fractions. These mass fractions varied with season (data not shown), as expected due to seasonally-varying source emissions.

Seasonal variation in outdoor $PM_{2.5}$ total mass and species concentrations was evident (Figure 1). Sulfate and ammonium concentrations peaked during the summer months, reflective of the temperature- and humidity-driven secondary formations from oxidation of sulfur dioxide emissions in the presence of ammonia. Concentrations of NO_3, OC aerosols, and other species followed an inverse pattern, peaking during the cooler months. While the mass fractions changed by season, SO_4 was the predominant species in each (25-68%). Consistent with seasonally stable mobile source contributions, EC concentrations were the least varied by season, and ranged from 1.6 to 4.3% of total mass. With the exception of NH_4 (r= 0.94 to 0.98), the Spearman correlations between species and total mass concentrations reflect the observed seasonal variation in $PM_{2.5}$ composition (Table 2). $PM_{2.5}$ total mass was correlated strongly with both EC and OC species in the winter (r>0.85), but was only weakly correlated (r=0.33 to 0.54) with OC during the summer. In contrast, SO_4 and total $PM_{2.5}$ mass were moderate-to-strongly correlated regardless of season.. Patterns in correlations between the carbon species were predictably high. Notably, O_3 and $PM_{2.5}$ concentrations were generally only weakly correlated, although more so (r=0.59) during the summer months, when levels of both tend to be higher.

Epidemiological relationships

Single-pollutant models adjusting for UAT yielded modest positive associations between most PM species and respiratory hospitalization, although not all achieved statistical significance (Figure 2). Year-round models adjusted for season showed significant associations with total $PM_{2.5}$ mass for all exposure lags, and for SO_4, NO_3, and NH_4 species. In the summer months, $PM_{2.5}$ remained significantly associated with up to a 2.5% increase in hospitalization per IQR change in mass, at lags of 1 to 4 days and a trend toward increasing effect with lagged exposure. Associations with SO_4 and NH_4 concentrations during the summer months mirrored those for $PM_{2.5}$ mass. Smaller effects were observed for these species in the winter and spring months (up to 2% increase per IQR) with hospitalizations more strongly associated with same-day and 3- and 4-day lagged exposures. Associations with NO_3 were more substantial in the cooler months. The EC component was not associated with respiratory admissions when assessed in single-pollutant models, and OC only very modestly in the summer months (~1% increase in admissions per IQR of summertime OC for lags 1-4; Figure 2). Mutually adjusting single-pollutant species models for $PM_{2.5}$ mass did not appreciably change any of these associations (data not shown).

In analyses of mass fraction, the highest average concentrations of the secondary species SO_4 and NH_4, and lowest for NO_3, were evident when $PM_{2.5}$ was most depleted of both of the carbon species

(Figure 3a). Correspondingly, when $PM_{2.5}$ was comprised of the greatest proportions of EC and OC, both SO_4 and NH_4 concentrations were low (Figure 3b). The crustal/other $PM_{2.5}$ category tracked well with levels of OC. The complexity of these relationships as driven by temporal and spatial heterogeneity in emissions of both primary PM and $PM_{2.5}$ precursors is further illustrated upon stratification by season and region (Supplemental Figure 1). The lowest SO_4 levels in the summertime coincided with nearly two-fold greater levels of EC than are observed in the winter months. Whereas, an opposite trend was observed for NO_3, when lower temperatures yield higher emissions and ground level concentrations of nitrates from nitrogen sources. Moreover, the EC contribution during periods of low SO_4 concentrations is twice as great in NYC compared to the rest of NYS, likely reflecting its greater volume of traffic-related emissions and resultant elevated EC levels.

Models of $PM_{2.5}$ –associated respiratory hospitalizations within tertiles of each of the PM species mass fractions did not yield noticeable patterns in year-round analyses (Figure 4). Generally, although many point estimates were significant or borderline significant, confidence intervals overlapped between the tertiles, indicating no consistent evidence of modification of the exposure-disease relationship by specific PM mass fractions. Stratification of these models by season (Supplemental Table 1) identified associations that better corresponded with the general patterns evident in mass fraction tertile relationships (Figure 3), but there were no statistically significant interactions.

Analyses stratified by age, diagnosis subgroup and sociodemographic characteristics that adjusted for UAT and season showed no modification of risk by these factors (data not shown). Similarly, we did not identify noteworthy differences in PM-respiratory disease associations between NYC and the rest of the state.

DISCUSSION

This analysis of short-term PM exposures and hospitalizations demonstrated that fine PM and several of its constituents may play a role in triggering respiratory health endpoints. Short-term IQR changes in $PM_{2.5}$ concentration were associated with up to nearly a 3% increased risk of respiratory hospitalizations in single-pollutant models, with the strongest significant effects observed per IQR increase in $PM_{2.5}$, SO_4 and NH_4 species concentrations during the summer months. We also observed small but statistically significant associations between respiratory admissions and small increases in secondary species concentrations during the winter. Associations in models stratified by species mass fractions found no compelling evidence that observed $PM_{2.5}$ associations were modified by varying levels of its components.

The small increases in respiratory hospitalization risk associated with $PM_{2.5}$ in these analyses (e.g., 0.5-2.5%), including for SO_4, NH_4, and NO_3 species are generally consistent with other studies examining fine PM and respiratory morbidity (Atkinson et al. 2014). In their nationwide time-series analysis of Medicare recipients, Peng et al. (2009) found 0.82% to 1.07% increases in respiratory ED visits among U.S. Medicare recipients per a 10-ug/m^3 increase in EC and organic matter (OM) species in a nation-wide time series analysis (Peng et al. 2009). Similarly, Bell et al. (2009) found significant associations with same day EC, OM, and nitrate concentrations and respiratory hospitalizations in their analysis of the same population. A case-crossover study of Medicare enrollees (≥ 65 years) in Boston, Massachusetts found a16.3 µg/m^3 $PM_{2.5}$ total mass associated with a 6.5% increase in risk of ED visits for pneumonia and 1.7 µg/m^3 black carbon associated with an 11.7% increased risk (Zanobetti and Schwartz 2006). Although we did not examine pneumonia-related hospitalizations specifically, the IQR value in the present study was also substantially lower than in that analysis. Moreover, the IQR for total $PM_{2.5}$ mass observed in our data was only slightly higher than one-half the NAAQS standard for 24-hour average $PM_{2.5}$, and effect estimates were correspondingly small. Findings from a study in a pediatric population support the elevated risks we observed for secondary species (1-3% increases per 1.5 and 5.7 µg/m^3 of SO_4 and NO_3, respectively)(Ostro et al. 2009). Direct comparisons to other studies are further complicated given the small number of studies which have examined PM components in relation to respiratory outcomes, differences in study design, location and populations, choice of statistical models and exposure units, and the respiratory health endpoints examined. However, the fact that we observed increased hospitalizations even at these low ambient $PM_{2.5}$ levels underscores the public health significance of these results.

We found that SO_4 was most strongly related to respiratory hospitalization, particularly in the summer months, when $PM_{2.5}$ was composed predominantly of this species. One study of respiratory ED visits in children found significant associations with SO_4 concentrations during the warm season (Strickland et al. 2010). The National Particle Component Toxicity (NPACT) initiative's analysis of data from 158 U.S. cities found excess risks of similar magnitude to our study (0.5-1%) for respiratory hospitalizations in association with $PM_{2.5.}$ Significant or nearly significant excesses were identified in association with nitrogen dioxide, sulfur dioxide, OC, and SO_4 during the warm season (Lippmann et al. 2013). Two studies in Chile also found associations with the sulfur content of $PM_{2.5}$, including with respiratory-related ED visits (Cakmak et al. 2009) and respiratory mortality (Valdes et al. 2012) . The SOPHIA study in Atlanta, GA reported a 1% increase in respiratory-related ED visits per 3.8 ug/m^3 of SO_4 during non-winter months, a result very comparable to those observed from our data (Tolbert et al.

2009). There is also biologic plausibility to support observed relationships between fine particle species and respiratory admissions, given the respirable fraction and a fairly well-characterized pathway leading to airway inflammation. Sulfates, nitrates, and carbon species in particular are all known respiratory irritants (IOM 2000). Our observation of associations with SO_4 during the summer months is further supported by the fact that respiratory hospitalizations in NYS tend to peak during the fall (NYSDOH 2009), along with the seasonal increase in infectious triggers.

The seasonal behavior of PM species concentrations was quite evident in our data. The secondary aerosols resulting from atmospheric photochemical transformation were, as expected, elevated in warmer periods. Abundant summertime levels of ambient SO_4 and NH_4 coincided with low levels of EC, OC, other PM species, and NO_3(concentrations peak in wintertime when lower temperatures favor the increase of nitrate particulates over gaseous forms (Pitchford et al. 2009)). Others have described the complexity of the heterogeneous OC species including variation in volatility based on temperature, humidity, and other characteristics (EPA 2004, Hallquist et al. 2009, Turpin, Saxena, and Andrews 2000). However, at the extremes of our data, the OC fractions tracked well with EC. We note that it is not just temperature and sunlight driving the formation of secondary PM, but also the availability of atmospheric precursors, such as NH_3 and NO_x. Therefore, we expected that mass fraction tertiles would reflect differences in the composition of $PM_{2.5}$ under different conditions, such as season or by region.

Our finding of an association with the sulfate constituent of fine PM could indicate poor control of confounding in single-pollutant models by total $PM_{2.5,}$ other PM species, or gaseous pollutants.. Several studies have identified increased respiratory risks associated with SO_4in a single-pollutant context (Burnett et al. 1997, Ostro et al. 2009, Peng et al. 2009), but findings from multi-pollutant settings are equivocal. Peng et al. (2009) found no change in the association between sulfate-related respiratory ED visits in single and multi-pollutant models (Peng et al. 2009). An Atlanta-based study observed significant associations between SO_4 concentrations and pediatric respiratory ED visits that attenuated and became non-statistically significant when adjusted for other pollutants (Strickland et al. 2010). Similarly, Bell et al. (2009) report substantially attenuated risk estimates for PM species when models were adjusted for covarying species, although they did not examine multi-pollutant models with SO_4 specifically (Bell et al. 2009). In the current analysis, mutual adjustment for $PM_{2.5}$ in species-specific models did not materially change our results.

This challenging task of identifying health risks in multi-pollutant exposure scenarios, such as simultaneous exposure to the components of PM, has been previously addressed in several ways. Single-

pollutant models favored by some researchers to examine independent effects of PM species on health risks are limited by poor control of confounding by covarying exposures, including $PM_{2.5}$ total mass. However, when correlations between $PM_{2.5}$ and several of its components are high, attempts to compare results from both single- and multi-pollutant models as done by others, may violate common statistical independence assumptions. However, the utility of either approach depends on both pollutant relationships and the research question of interest (Tolbert et al. 2009). Mostofsky et al. (2012) demonstrate several approaches to address the impacts of $PM_{2.5}$ on PM species-associated risks, including modeling constituents adjusted for $PM_{2.5}$ mass, as proportions of $PM_{2.5}$ mass, as residuals from constituent regression on $PM_{2.5}$ mass, and as interactions between constituent concentrations or proportions and $PM_{2.5}$ mass (Mostofsky et al. 2012). In analyses of cerebrovascular endpoints, they concluded that each approach yields similar interpretations in regard to the relative ranking of PM-species associations on risk. We employed several of these approaches and also found general consistency in our results. By examining the excess in hospitalizations associated with $PM_{2.5}$ and its constituents both individually and mutually-adjusted, for total $PM_{2.5}$ concentrations by tertiles of the constituent mass fractions, and by describing mass fraction relationships, we were able to comprehensively address the question of the influence of PM composition on $PM_{2.5}$-associated respiratory admissions risk. The combination of approaches points to the importance of the summertime-dominant secondary species, SO_4 and NO_3 occurring with NH_4, as influencing the $PM_{2.5}$-associated respiratory hospitalization risk in our data. These findings correspond with those for at least one cardiovascular endpoint, where greater relative odds of transmural myocardial infarctions were observed when outdoor $PM_{2.5}$ concentrations were richer in secondary aerosols (Rich et al. 2013).

The variation in risk observed at lags of 0 to 4 days in this study for $PM_{2.5}$ and several species is consistent with those observed by other studies examining PM species with hospitalizations as an endpoint (Bell 2012, Dominici et al. 2006). An analysis of 187 U.S. counties during the same study period as our analysis indicated a stronger risk gradient in the Northeastern U.S., with respiratory hospitalization risk most elevated 2 days post-exposure (Bell 2012). In a time-series analysis, the NPACT study similarly identified lag effects of 1 to 3 days (Lippmann et al. 2013). In contrast, other studies of PM species have identified either no such lagged response for hospitalization (Bell et al. 2009). Lagged effects in our data varied by both species and season. Whether they are an artifact of a clinical process, such as a delay between an ED visit to a hospitalization or reflective of a true etiologic process is unknown, but was not measurable with our data.

This study remains among the small number of epidemiological investigations of component-specific respiratory health effects of fine PM. As PM sources and atmospheric conditions differ between the Northeastern U.S. and other regions, both the composition of fine PM and the burden of PM-associated health risks would be expected to differ geographically. The large and ethnically diverse population geographic heterogeneity across NYS enabled examination of species-specific effects across strata of space, time, and other relevant characteristics. Only a few studies have had adequate PM data to assess species-specific health effects across such a large geographic area at fine spatial and temporal scales, and no studies have examined PM species estimates from a combination of observations and CMAQ data in relation to respiratory health endpoints in NYS. Our use of a case-crossover design was beneficial in that it effectively controlled for many individual-level confounding factors, which the commonly applied time series approaches cannot, in an otherwise ecologic data setting.

Exposure misclassification arising from the ecologic scale of the exposure data is the primary threat to this study's validity, and potentially e resulted in attenuation of the PM-respiratory hospitalization association. Our estimated exposures offer improvements over those drawn from the CSN for similar analyses of PM-associated morbidity and mortality. although one concern is whether the combined CMAQ/observation approach accurately reflect outdoor species concentrations, particularly for SO_4 concentrations during the summer and fall, when they tend to be overestimated (Hogrefe et al. 2009). However, as noted above, the simulated data used for these analyses have already been subject to a partial validity assessment and are corrected to address known over/ underestimation of particular species by season (Hogrefe et al. 2009). We also identified small but significant associations with SO_4 during the winter months, when CMAQ generally underestimates these concentrations. A sensitivity analysis using year-specific seasonal adjustment factors applied to CMAQ instead of applying multi-year adjustment factors (Hogrefe et al. 2009) found no appreciable differences in the magnitude or direction of our season-stratified effect estimates, suggesting that at least assumptions made in combining the CMAQ data with observations had minimal impact on our results. However, we acknowledge that differential error in the CMAQ prediction of PM species may have impacted this analysis. For instance, CMAQ as configured in this study has limited ability to capture small-scale variation in concentrations at resolutions finer than 12km (Hogrefe et al. 2009) and the CSN monitoring network is not dense enough to introduce additional spatial texture at finer scales.. This may in part reflect the known poorer correlation between central site monitors for aerosols with comparatively localized combustion sources (Lippmann et al. 2013). Moreover, the degree of measurement or estimation error may also differ by pollutant (Mostofsky et al. 2012, Dionisio et al. 2013), and

concentration gradients of pollutants with greater heterogeneity over short distances will likely not be resolved by the 12km-grid combined CMAQ / observation fields used in this study. Sulfate, NO_3, and NH_4 are more homogeneous and regionally dispersed as a result of photochemical transformation from primary sources (EPA 2004);ammonium is mostly present as ammonium sulfate (peaking in summer) and/or ammonium nitrate (peaking in winter), and is not easily interpreted as an independent constituent. Poorer representation and therefore greater exposure misclassification/risk attenuation is therefore expected for near-roadway pollutants, such as EC and crustal/other constituents, and most of these were not associated with hospitalization in our analysis. Fine-scale (<1km) modeling or more advanced bias correction techniques, such as demonstrated recently by Crooks and Özkaynak (Crooks and Özkaynak 2014), could be applied for $PM_{2.5}$ to conduct a more robust analysis of this rich health dataset. Additionally, the combined CMAQ/observed ambient exposure estimates used in this study may not represent total exposures to $PM_{2.5}$ from all other sources, such as occupational or indoor generated PM sources. These may differ in their composition and toxicity, and also vary differently from outdoor particles. To the extent that these exposures relate to inter-individual characteristics or socio-demographics, our study design and stratified analyses likely addressed these concerns.

The combined modeled-observed data approach used in this study was designed specifically to overcome spatial and temporal gaps in ambient monitoring networks (Hogrefe et al. 2009). Despite its limitations, some factors which might additionally affect outdoor pollutant concentrations and subsequently human exposures over very short time periods, such as wind speed, direction, and other aspects of meteorology are already accounted for in the CMAQ simulations. The number of stations in NYS that actually measured $PM_{2.5}$ species during the study period was small, and alternative choices for epidemiologic analysis such as restricting to individuals who lived in close proximity to a monitor, or classifying exposures based on the nearest monitor regardless of distance an individual's residence, would impair study power and introduce substantial exposure misclassification. Moreover, our time-stratified case-crossover design should address any expected short-term temporal variation in the combined CMAQ/observed fields, such as commuting patterns, as well as spatial aspects of CMAQ prediction error, since cases and controls (days) are representative of the same spatial location. Irrespective of the limits of PM fields used in this study, any resulting exposure misclassification should be non-differential with respect to respiratory hospitalization, and the CMAQ/observed data offer an improvement upon previous approaches. Measurement error could be further reduced by use of refined exposure indicators, such as those that incorporate outdoor-indoor infiltration, or by developing and applying location-specific population $PM_{2.5}$ and species exposure predictions as in the EPA's

Stochastic Human Exposure and Dose Simulation (SHEDS) model (Baxter et al. 2013, Burke, Zufall, and Ozkaynak 2001, Dionisio et al. 2013).

Although O_3 has been previously associated with increases in NYS respiratory hospitalizations (Lin et al. 2008), this co-exposure was only weakly correlated with $PM_{2.5}$ levels and therefore we did not adjust analyses for this pollutant. Our evaluation was limited to the particulate species comprising the largest fractions of fine PM in our data; other constituents with suspected toxicity, such as metals or aeroallergens, were not examined. The low PM concentrations and small effect estimates observed in our analysis may have been limited in our ability to discern meaningful differences in associations between strata of clinical diagnoses, sociodemographics, or regional characteristics.

Our findings of an association between chemical species of fine PM and respiratory hospitalizations in New York State are biologically plausible and consistent with existing studies indicating that PM composition may be an important explanatory factor for PM-associated respiratory health risk. Overall, results corroborate previously observed associations between particulate-sulfate and respiratory endpoints and generally identified the strongest and most consistent health responses in association with secondary PM. The only such study in New York thus far, our data also reflect the complexity of assessing the health impacts of exposure to PM species, and indicate that a finer exposure resolution may be necessary for studying health effects of locally generated PM, especially primary aerosols. We suggest that the combination of refined ambient exposure metrics that take into account location-specific data and indoor-outdoor infiltration rates or methods that otherwise correct for differential model prediction errors may further improve epidemiologic assessments of PM species and respiratory health.

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List of Figure Captions:

Figure 1. Seasonal trends in average daily $PM_{2.5}$ total mass and species concentrations, New York State, 2000-2005.

Figure 2. Year-round and season-stratified hazard ratios^{+} (HRs) of respiratory hospitalization for 0-4 day lags per IQR change in $PM_{2.5}$ total mass and species, 2000-2005. (a) Year-round data; (b) winter; (c) summer; (d) fall; (e) spring.

Figure 3. Mean composition of $PM_{2.5}$ mass, by species mass fraction tertile. (a) High sulfate, ammonium and low EC, OC, nitrate and other. (b) Low sulfate, ammonium and high EC, OC, nitrate and other.

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Table 1. Distributions of pollutant concentrations and percent contribution of each $PM_{2.5}$ component to $PM_{2.5}$ total mass, New York State, 2000-2005.

	Min	25th	Mean	Median	75th	Max	IQR	$PM_{2.5}$ Mass Fraction[+]
$PM_{2.5}$	<.01	3.63	8.03	6.64	11.11	69.46	7.48	-
EC	-	0.08	0.23	0.16	0.28	9.16	0.20	2.9
OC	-	0.41	0.91	0.71	1.15	23.54	0.74	11.3
SO_4	-	1.18	4.01	2.33	5.45	40.62	4.27	49.9
NH_4	-	0.55	1.30	1.06	1.82	10.93	0.27	16.2
NO_3	-	0.04	0.87	0.27	1.09	24.63	1.05	10.8
Other	-	0.33	0.71	0.56	0.91	14.99	0.58	8.8
O_3	2.75	28.30	36.89	35.14	44.00	123.39	15.69	-
UAT	-22.96	24.23	40.68	42.57	59.49	85.11	35.26	-

Abbreviations: $PM_{2.5}$=particulate matter <2.5µm (ug/m^3); EC=elemental carbon; OC=organic carbon; NH_4= ammonium; NO_3=nitrate; SO_4=sulfate; Other=including non-carbon organic matter; O_3=ozone (ppb); UAT: average universal apparent temperature (°F).

[+] The proportion across the study period, calculated based on mean concentrations.

Table 2. Correlations between ambient outdoor $PM_{2.5}$, ozone, and temperature, by season.

	Winter									**Summer**								
	PM_{25}	EC	OC	SO_4	NH_4	NO_3	OTH	O_3	UAT	PM_{25}	EC	OC	SO_4	NH_4	NO_3	OTH	O_3	UAT
PM_{25}	1.00									1.00								
EC	0.86	1.00								0.54	1.00							
OC	0.85	0.96	1.00							0.33	0.75	1.00						
SO_4	0.81	0.50	0.48	1.00						0.97	0.40	0.16	1.00					
NH_4	0.96	0.73	0.71	0.86	1.00					0.94	0.61	0.38	0.89	1.00				
NO_3	0.87	0.77	0.75	0.58	0.87	1.00				0.51	0.61	0.54	0.13	0.43	1.00			
OTH	0.88	0.95	0.98	0.76	0.77	0.54	1.00			0.45	0.82	0.96	0.49	0.55	0.28	1.00		
O_3	-0.34	-0.30	-0.23	-0.35	-0.32	-0.30	-0.25	1.00		0.59	0.42	0.31	0.42	0.13	0.41	0.37	1.00	
UAT	0.40	0.24	0.20	0.42	0.21	0.56	0.22	-0.42	1.00	0.55	0.29	0.10	0.50	-0.10	0.56	0.16	0.52	1.00
	Spring									**Fall**								
PM_{25}	1.00									1.00								
EC	0.68	1.00								0.69	1.00							
OC	0.65	0.90	1.00							0.67	0.88	1.00						
SO_4	0.90	0.40	0.37	1.00						0.91	0.41	0.40	1.00					
NH_4	0.98	0.63	0.58	0.90	1.00					0.97	0.66	0.62	0.89	1.00				
NO_3	0.51	0.69	0.63	0.19	0.54	1.00				0.42	0.66	0.52	0.12	0.49	1.00			
OTH	0.69	0.91	0.98	0.63	0.65	0.42	1.00			0.72	0.90	0.97	0.68	0.55	0.46	1.00		
O_3	0.26	0.08	0.18	0.25	-0.07	0.31	0.18	1.00		0.28	0.06	0.17	0.26	-0.23	0.38	0.17	1.00	
UAT	0.39	0.07	0.10	0.36	-0.33	0.57	0.10	0.42	1.00	0.44	0.17	0.28	0.37	-0.33	0.56	0.26	0.57	1.00

Abbreviations: $PM_{2.5}$=particulate matter <2.5µm (ug/m^3); EC=elemental carbon; OC=organic carbon; NH_4= ammonium; NO_3=nitrate; SO_4=sulfate; OTH=including non-carbon organic matter; O_3=ozone (ppb); UAT: average universal apparent temperature (°F).

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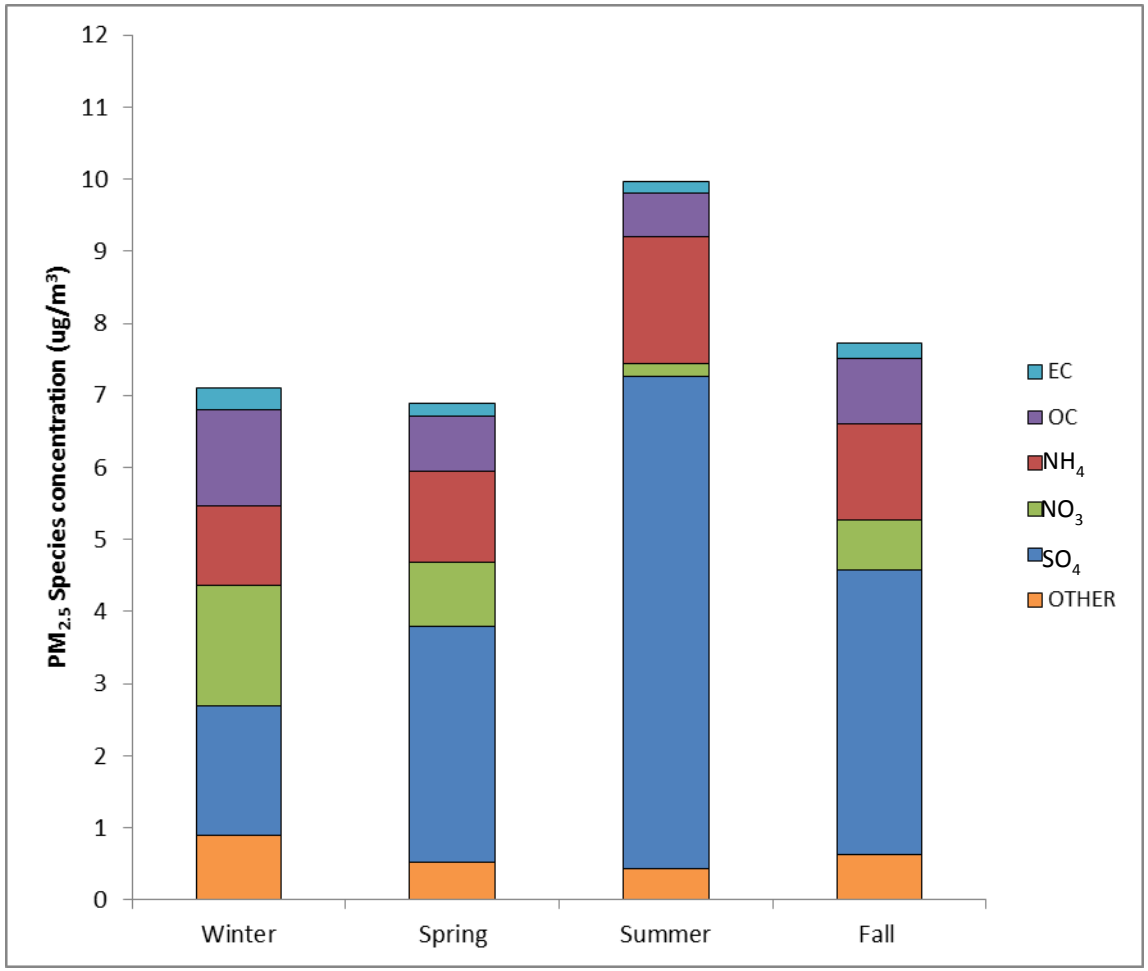

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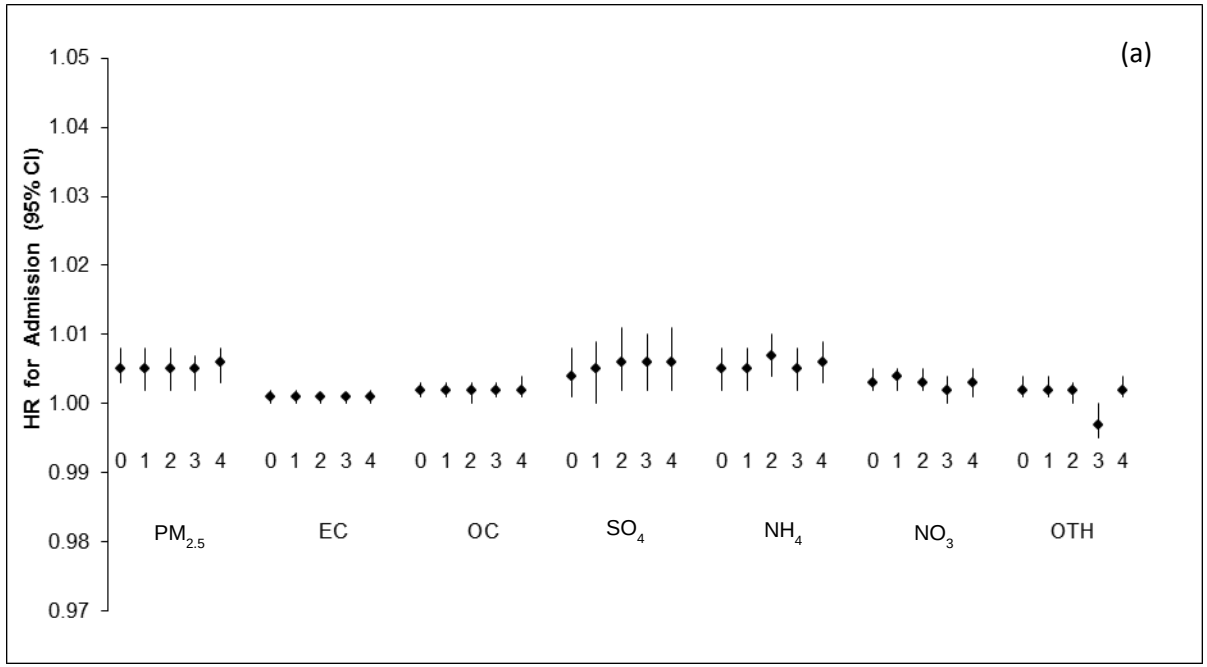

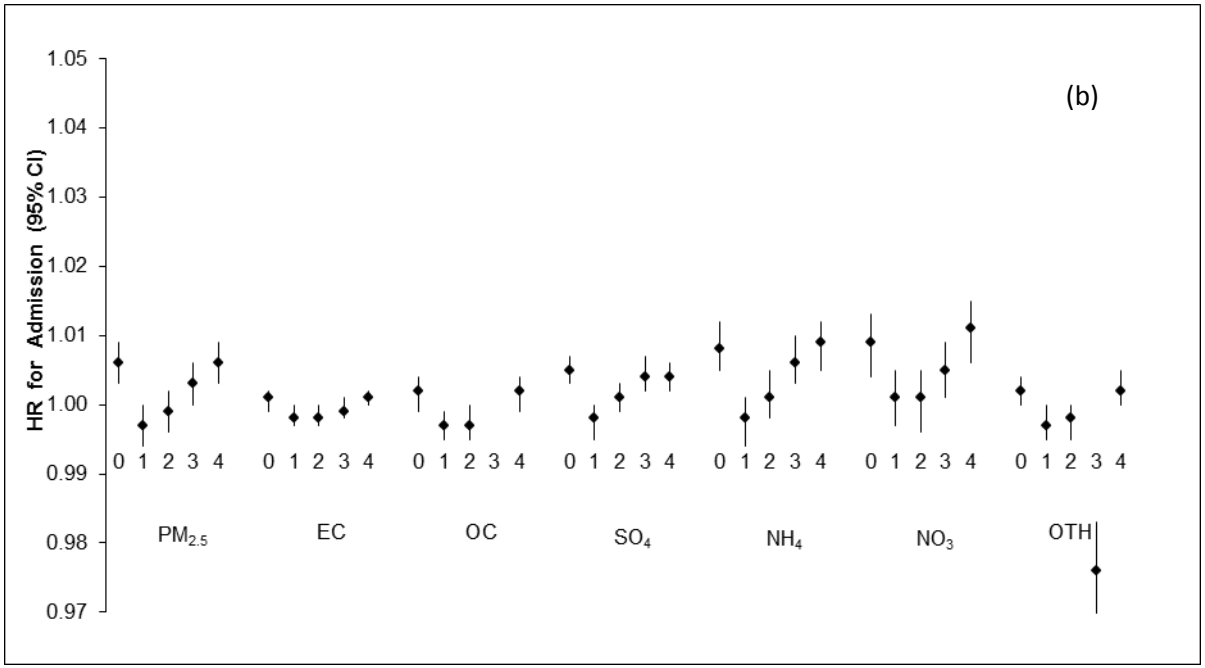
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HR for Admission (95% CI)
1.05
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1.03
1.02
1.01
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0.97
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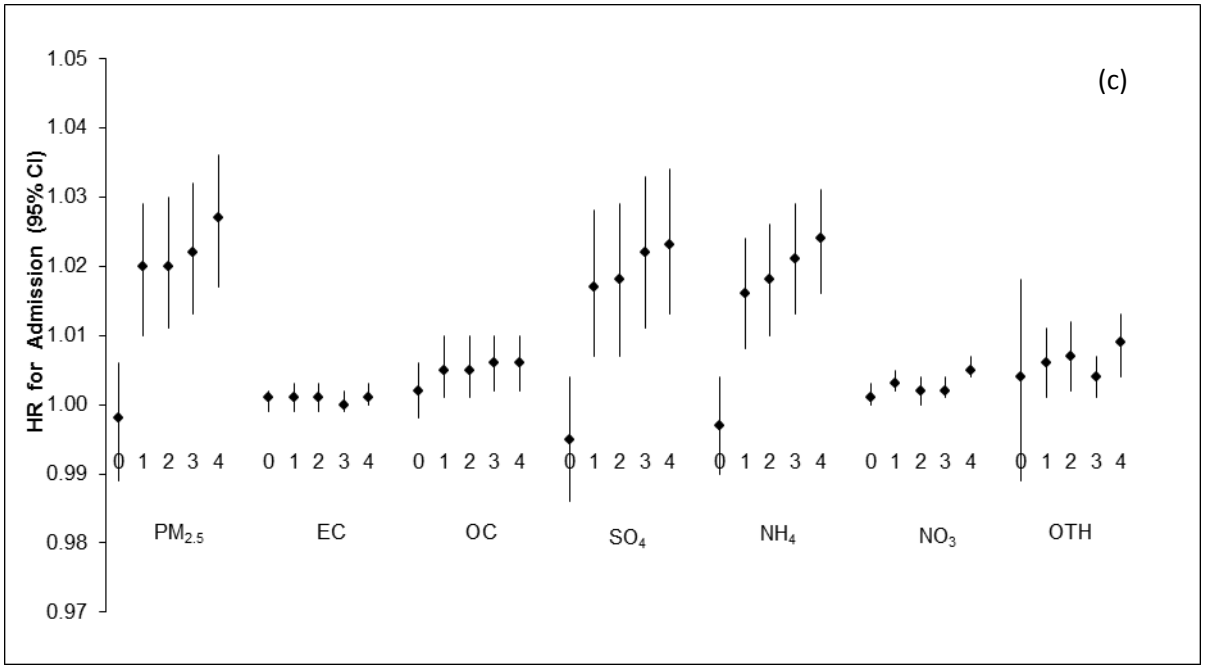
PM2.5
EC
OC
SO4
NH4
NO3
OTH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EC
OC
SO4
NH4
NO3
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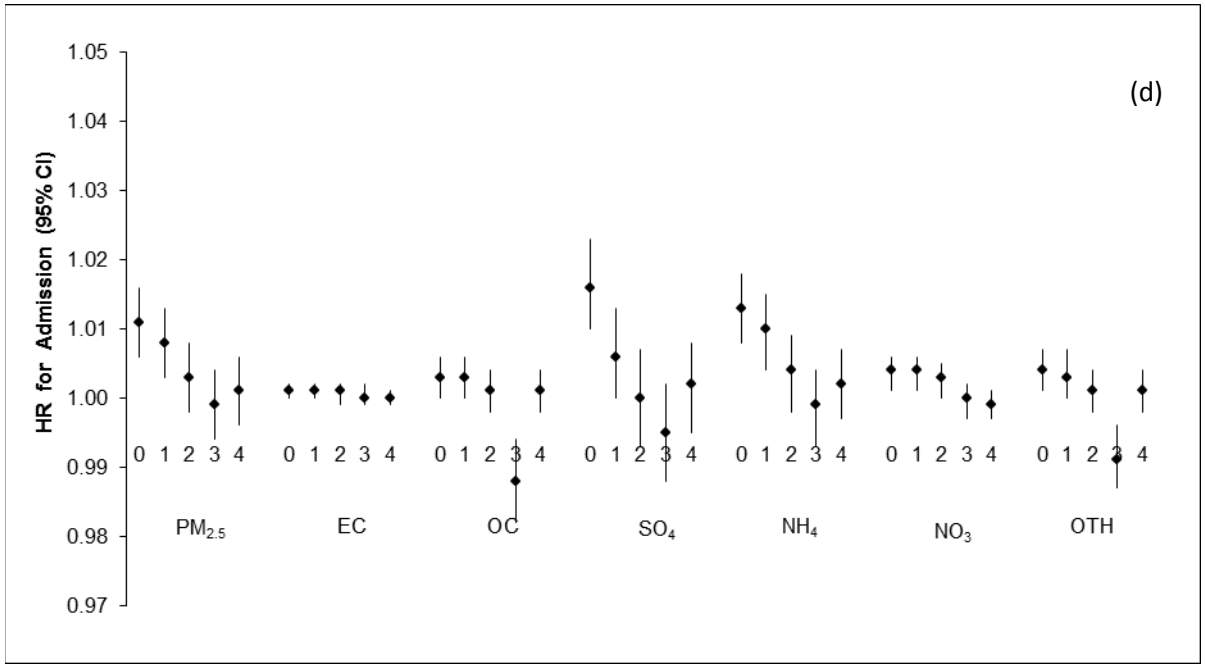
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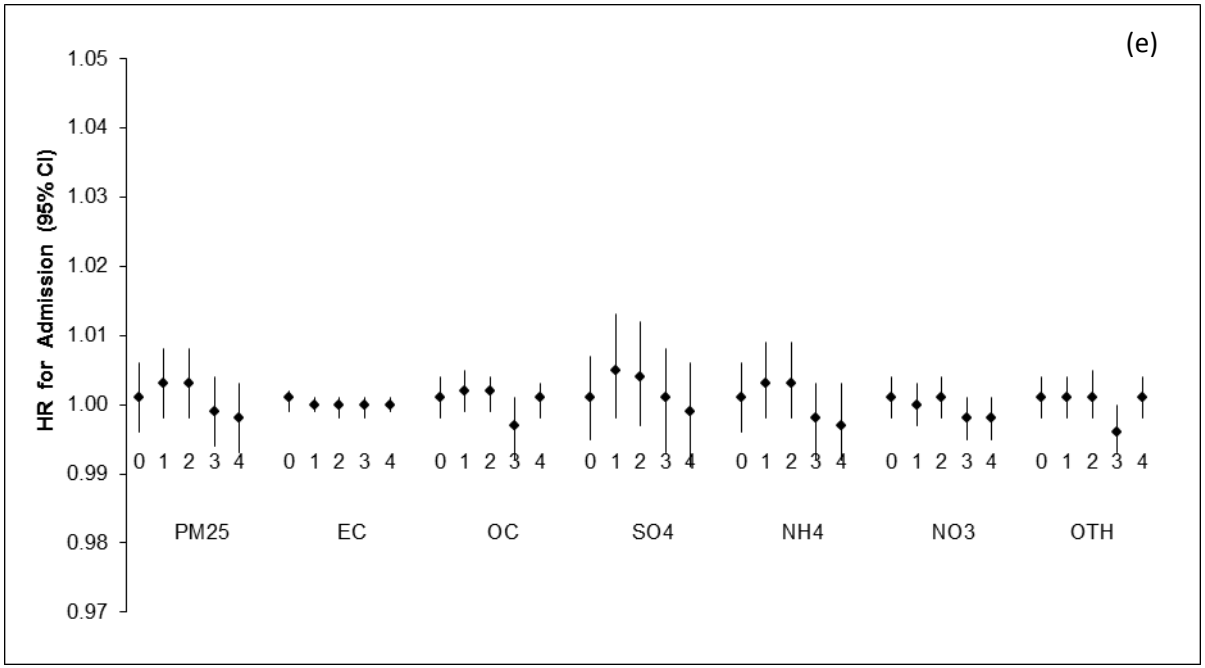
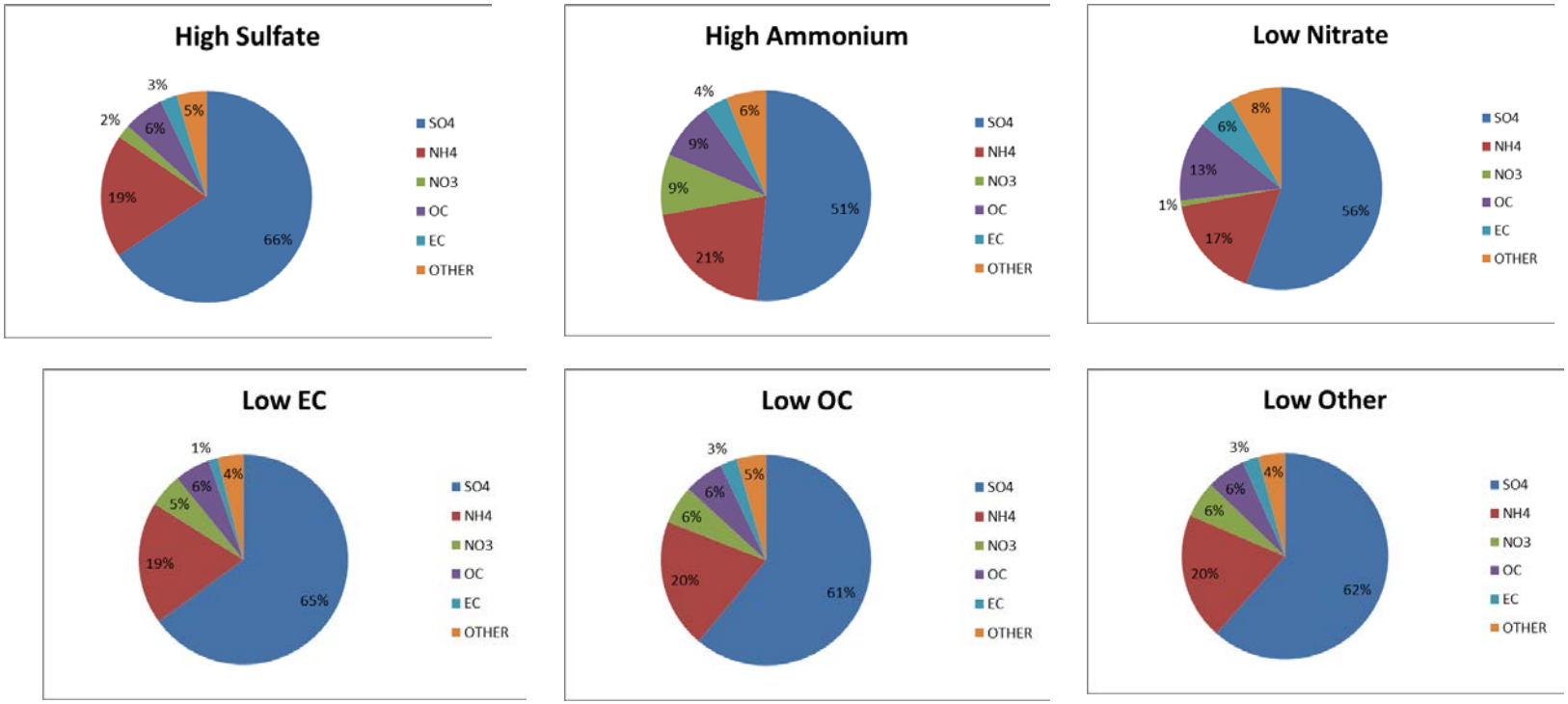


[+]Models adjusted for universal apparent temperature.

Figure 3. Mean composition of $PM_{2.5}$ mass, by species mass fraction tertile. (a) High sulfate, ammonium and low EC, OC, nitrate and other. (b) Low sulfate, ammonium and high EC, OC, nitrate and other.

(a)



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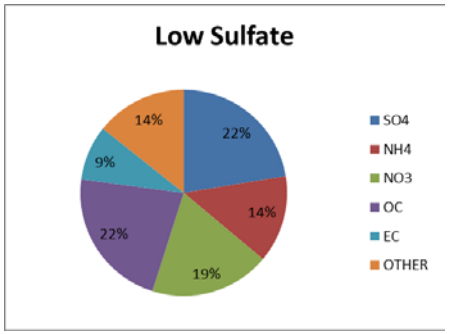
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OC
EC
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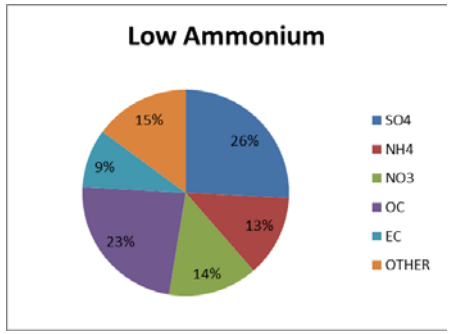
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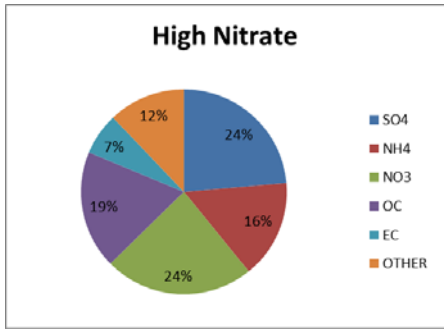
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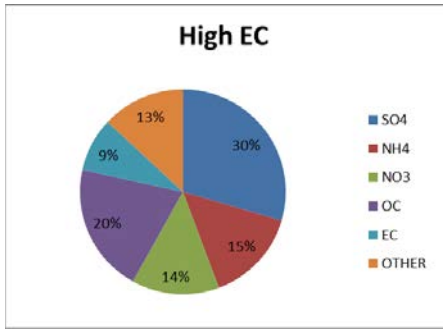
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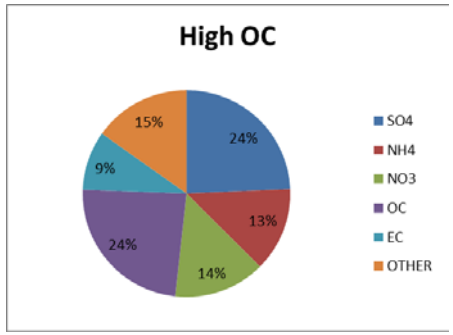
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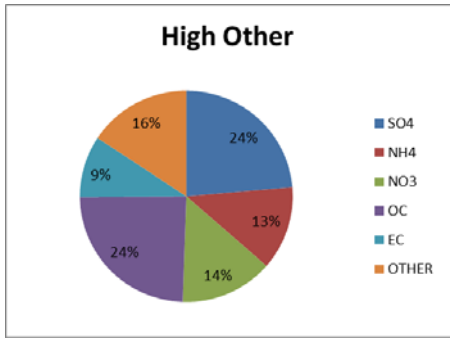
High Other
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SO4
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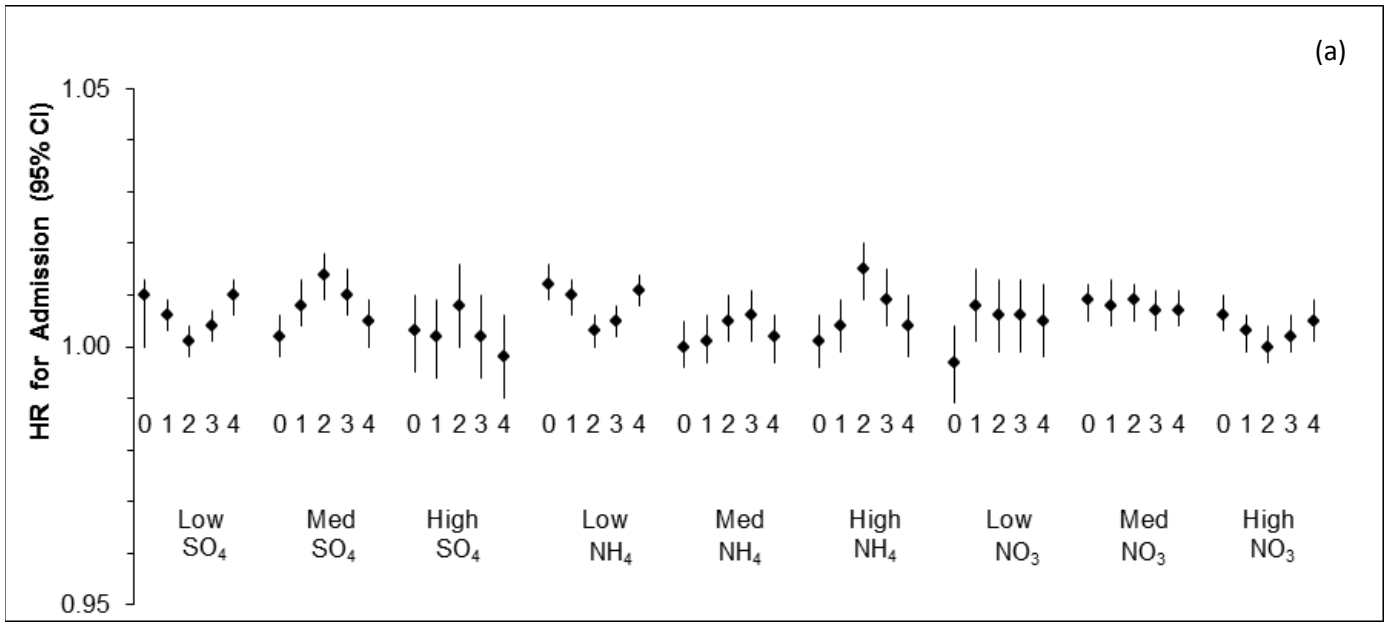
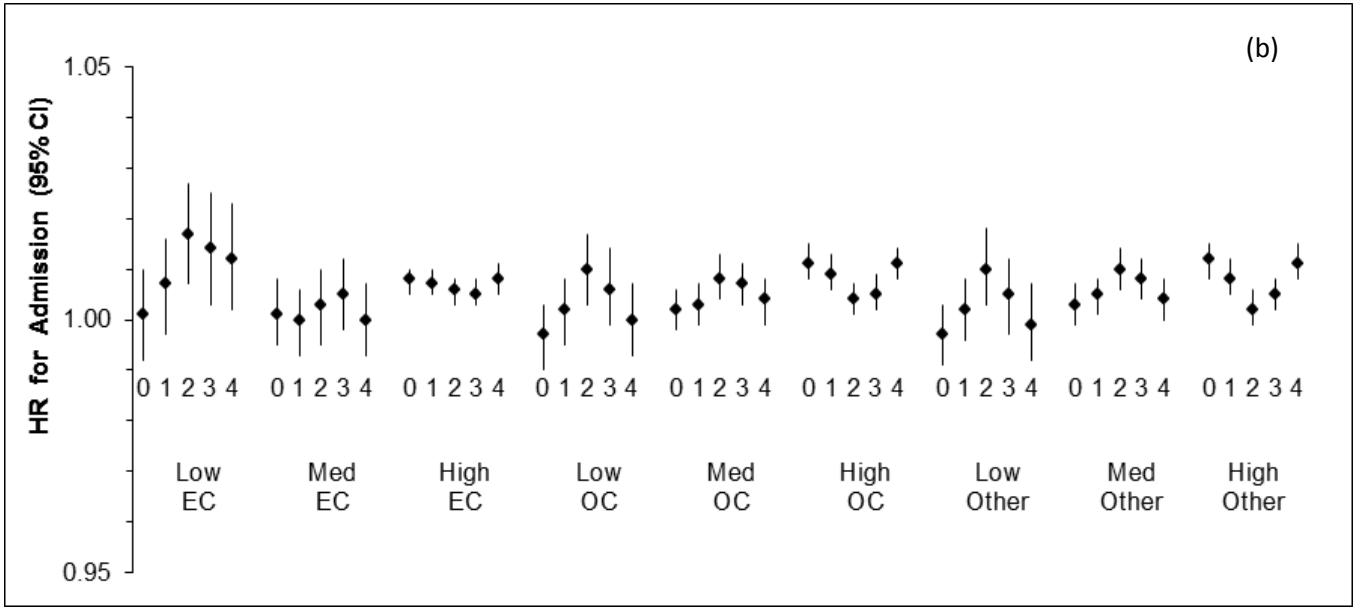
Figure 4. Hazard ratios[+] (HRs) of respiratory hospitalization for 0-4 day lags per IQR change in $PM_{2.5}$ total mass, 2000-2005, by tertiles of species mass fraction. (a) secondary $PM_{2.5}$ species, (b) carbon components and other $PM_{2.5}$.



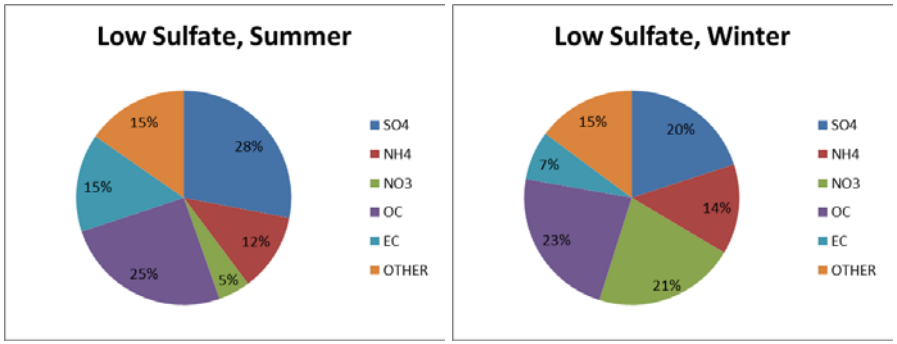


[+]Models adjusted for universal apparent temperature.

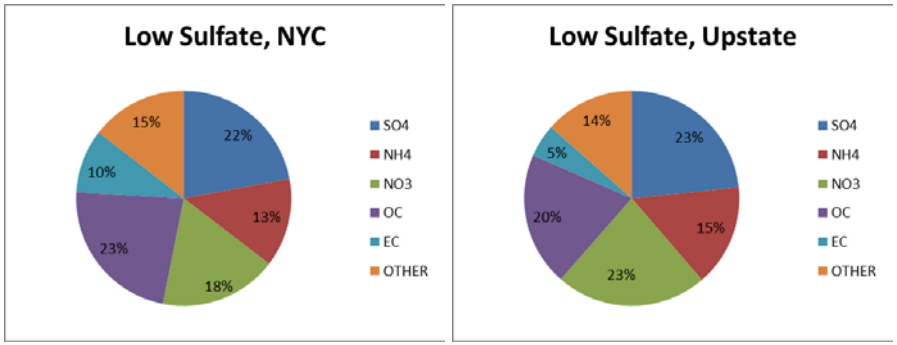
SUPPLEMENTAL MATERIALS

Supplemental Figure 1. Mean composition of $PM_{2.5}$ mass, by species mass fraction tertile. (a) Comparison of low sulfate tertiles in summer and winter; (b) Comparison of New York City and the rest of New York State.

(a)



(b)



Supplemental Table 1. Season-stratified hazard ratios (HRs) of respiratory hospitalization per IQR change in $PM_{2.5}$ total mass, 2000-2005, by tertiles of species mass fraction.

SUMMER

	Lag Day	HR	95%CI LL	95%CI UL		Lag Day	HR	95%CI LL	95%CI UL
Low SO_4	**0**	0.998	0.987	1.009	Low NO_3	**0**	1.019	0.984	1.054
	1	1.029	1.017	1.042		**1**	1.033	0.996	1.071
	2	1.026	1.014	1.040		**2**	1.017	0.980	1.056
	3	1.026	1.014	1.037		**3**	1.014	0.977	1.054
	4	1.032	1.021	1.044		**4**	1.058	1.017	1.101
Medium SO_4	**0**	0.997	0.981	1.014	Medium NO_3	**0**	0.988	0.972	1.003
	1	1.002	0.986	1.018		**1**	1.014	0.998	1.031
	2	1.012	0.995	1.029		**2**	1.009	0.993	1.026
	3	1.012	0.995	1.030		**3**	1.025	1.008	1.043
	4	1.006	0.989	1.024		**4**	1.028	1.011	1.046
High SO_4	**0**	1.004	0.983	1.027	High NO_3	**0**	0.999	0.989	1.010
	1	1.024	1.001	1.048		**1**	1.021	1.010	1.032
	2	1.009	0.984	1.035		**2**	1.025	1.014	1.036
	3	1.022	0.996	1.049		**3**	1.022	1.011	1.033
	4	1.038	1.011	1.066		**4**	1.025	1.014	1.036
Low NH_4	**0**	1.002	0.984	1.020	Low EC	**0**	0.999	0.971	1.028
	1	1.032	1.014	1.051		**1**	1.024	0.993	1.055
	2	1.014	0.998	1.031		**2**	1.009	0.976	1.043
	3	1.026	1.009	1.042		**3**	1.018	0.985	1.053

	4	1.046	1.029	1.063		**4**	1.043	1.008	1.079
Medium NH_4	**0**	0.993	0.979	1.007	Medium EC	**0**	1.006	0.983	1.030
	1	1.016	1.002	1.031		**1**	1.020	0.998	1.043
	2	1.017	1.002	1.032		**2**	1.029	1.005	1.053
	3	1.012	0.997	1.027		**3**	1.039	1.014	1.064
	4	1.015	1.001	1.030		**4**	1.036	1.012	1.061
High NH_4	**0**	1.004	0.991	1.018	High EC	**0**	0.995	0.985	1.005
	1	1.021	1.006	1.035		**1**	1.019	1.008	1.029
	2	1.028	1.014	1.043		**2**	1.020	1.009	1.030
	3	1.029	1.014	1.045		**3**	1.020	1.010	1.031
	4	1.023	1.009	1.038		**4**	1.024	1.014	1.035
Low other	**0**	1.002	0.980	1.024	Low OC	**0**	1.004	0.983	1.026
	1	1.020	0.998	1.043		**1**	1.018	0.996	1.040
	2	1.002	0.979	1.026		**2**	1.013	0.989	1.037
	3	1.022	0.997	1.047		**3**	1.028	1.003	1.054
	4	1.033	1.008	1.059		**4**	1.041	1.015	1.066
Med other	**0**	1.003	0.990	1.016	Medium OC	**0**	0.995	0.982	1.008
	1	1.017	1.003	1.031		**1**	1.012	0.998	1.026
	2	1.026	1.011	1.040		**2**	1.021	1.006	1.036
	3	1.014	0.999	1.028		**3**	1.018	1.003	1.033
	4	1.014	1.000	1.029		**4**	1.017	1.002	1.032
High other	**0**	0.994	0.978	1.010	High OC	**0**	1.003	0.989	1.017
	1	1.027	1.013	1.041		**1**	1.032	1.018	1.046
	2	1.020	1.007	1.033		**2**	1.021	1.008	1.034
	3	1.028	1.016	1.041		**3**	1.023	1.011	1.036
	4	1.034	1.021	1.047		**4**	1.030	1.017	1.042

WINTER

	Lag Day	HR	95%CI LL	95%CI UL		Lag Day	HR	95%CI LL	95%CI UL
Low SO_4	**0**	1.008	1.003	1.013	Low NO_3	**0**	1.003	0.998	1.008
	1	0.997	0.993	1.002		**1**	0.992	0.985	0.998
	2	0.993	0.989	0.998		**2**	1.002	0.997	1.007
	3	1.000	0.996	1.004		**3**	1.007	1.002	1.013
	4	1.005	1.000	1.009		**4**	1.007	1.002	1.012
Medium SO_4	**0**	1.019	1.012	1.026	Medium NO_3	**0**	1.006	1.002	1.010
	1	1.000	0.994	1.005		**1**	0.999	0.995	1.003
	2	1.005	1.000	1.011		**2**	1.000	0.995	1.004
	3	1.009	1.003	1.015		**3**	1.003	0.999	1.007
	4	1.021	1.015	1.028		**4**	1.011	1.005	1.016
High SO_4	**0**	1.001	0.996	1.005	High NO_3	**0**	1.012	1.005	1.020
	1	0.994	0.988	1.000		**1**	0.996	0.990	1.002
	2	1.009	1.002	1.016		**2**	0.992	0.986	0.999
	3	1.008	1.001	1.015		**3**	0.999	0.992	1.006
	4	0.999	0.993	1.005		**4**	0.999	0.993	1.006
Low NH_4	**0**	1.010	1.005	1.014	Low EC	**0**	1.005	0.987	1.023
	1	0.999	0.994	1.004		**1**	0.999	0.981	1.018
	2	0.999	0.995	1.003		**2**	1.027	1.007	1.046
	3	1.004	1.000	1.008		**3**	1.023	1.004	1.041
	4	1.011	1.007	1.016		**4**	0.986	0.968	1.005
Medium NH_4	**0**	1.007	1.002	1.013	Medium EC	**0**	1.005	0.998	1.012

	1	0.997	0.992	1.002		**1**	0.991	0.984	0.999
	2	0.998	0.993	1.004		**2**	0.998	0.989	1.007
	3	1.003	0.998	1.009		**3**	1.009	1.001	1.018
	4	1.006	1.001	1.012		**4**	1.001	0.993	1.009
High NH_4	**0**	1.001	0.995	1.007	High EC	**0**	1.008	1.005	1.012
	1	0.993	0.986	0.999		**1**	0.999	0.996	1.003
	2	1.009	1.001	1.017		**2**	1.001	0.997	1.004
	3	1.010	1.002	1.017		**3**	1.004	1.001	1.008
	4	1.001	0.994	1.008		**4**	1.010	1.007	1.014
Low other	**0**	1.000	0.994	1.005	Low OC	**0**	1.000	0.994	1.006
	1	0.991	0.985	0.998		**1**	0.992	0.985	0.999
	2	1.008	1.000	1.015		**2**	1.005	0.997	1.012
	3	1.012	1.004	1.019		**3**	1.012	1.004	1.019
	4	1.000	0.994	1.006		**4**	1.001	0.994	1.007
Medium other	**0**	1.005	0.999	1.011	Medium OC	**0**	1.003	0.998	1.008
	1	0.998	0.993	1.003		**1**	0.995	0.991	1.000
	2	0.997	0.991	1.003		**2**	0.997	0.992	1.002
	3	1.003	0.996	1.009		**3**	1.002	0.997	1.008
	4	1.009	1.003	1.015		**4**	1.005	0.999	1.010
High other	**0**	1.011	1.007	1.016	High OC	**0**	1.012	1.008	1.017
	1	0.999	0.995	1.004		**1**	1.001	0.996	1.006
	2	1.000	0.995	1.004		**2**	1.001	0.997	1.005
	3	1.004	1.000	1.008		**3**	1.004	0.999	1.008
	4	1.011	1.001	1.015		**4**	1.013	1.008	1.017

FALL

	Lag	**HR**	**95%CI LL**	**95%CI UL**		**Lag**	**HR**	**95%CI LL**	**95%CI UL**

	Day					Day			
Low SO_4	**0**	1.010	1.004	1.016	Low NO_3	**0**	1.080	0.993	1.024
	1	1.005	0.999	1.011		**1**	1.002	0.989	1.015
	2	0.996	0.989	1.002		**2**	1.009	0.995	1.022
	3	0.993	0.987	1.000		**3**	1.008	0.994	1.023
	4	0.999	0.994	1.005		**4**	1.006	0.991	1.021
Medium SO_4	**0**	1.017	1.006	1.027	Medium NO_3	**0**	1.018	1.008	1.029
	1	1.015	1.005	1.025		**1**	1.016	1.007	1.026
	2	1.011	1.002	1.020		**2**	1.003	0.995	1.011
	3	1.011	1.002	1.021		**3**	1.003	0.996	1.011
	4	1.009	0.998	1.019		**4**	1.006	0.998	1.013
High SO_4	**0**	1.010	0.997	1.024	High NO_3	**0**	1.006	1.000	1.013
	1	1.006	0.993	1.019		**1**	1.001	0.994	1.008
	2	1.021	1.006	1.036		**2**	1.000	0.992	1.007
	3	1.012	0.995	1.029		**3**	0.990	0.983	0.998
	4	1.004	0.988	1.021		**4**	0.994	0.987	1.001
Low NH_4	**0**	1.016	1.009	1.023	Low EC	**0**	1.012	1.006	1.017
	1	1.010	1.002	1.018		**1**	1.008	1.003	1.014
	2	0.997	0.990	1.005		**2**	1.002	0.997	1.007
	3	0.997	0.991	1.004		**3**	0.999	0.994	1.004
	4	1.002	0.996	1.009		**4**	1.001	0.996	1.006
Medium NH_4	**0**	1.006	0.998	1.015	Medium EC	**0**	1.019	1.000	1.039
	1	1.004	0.996	1.013		**1**	1.015	0.998	1.033
	2	1.002	0.994	1.011		**2**	1.022	1.001	1.042

	3	0.996	0.987	1.006		**3**	0.997	0.975	1.019
	4	0.993	0.983	1.002		**4**	1.007	0.986	1.029
High NH_4	**0**	1.004	0.994	1.014	High EC	**0**	0.998	0.980	1.016
	1	1.003	0.994	1.013		**1**	0.990	0.972	1.009
	2	1.014	1.004	1.025		**2**	1.010	0.989	1.031
	3	1.012	1.000	1.024		**3**	1.010	0.989	1.032
	4	1.017	1.005	1.030		**4**	1.012	0.991	1.034
Low other	**0**	1.002	0.991	1.012	Low OC	**0**	1.004	0.992	1.017
	1	1.008	0.998	1.018		**1**	1.000	0.988	1.012
	2	1.022	1.010	1.035		**2**	1.013	0.999	1.028
	3	1.016	1.002	1.030		**3**	1.009	0.992	1.026
	4	1.014	1.000	1.027		**4**	1.007	0.991	1.023
Medium other	**0**	1.005	0.997	1.013	Medium OC	**0**	1.004	0.997	1.012
	1	1.003	0.994	1.011		**1**	1.006	0.998	1.014
	2	1.006	0.998	1.014		**2**	1.010	1.001	1.018
	3	1.002	0.993	1.011		**3**	1.004	0.995	1.013
	4	0.999	0.989	1.009		**4**	1.004	0.994	1.013
High other	**0**	1.018	1.011	1.025	High OC	**0**	1.017	1.010	1.024
	1	1.008	1.000	1.015		**1**	1.009	1.002	1.017
	2	0.993	0.986	1.000		**2**	0.996	0.989	1.003
	3	0.995	0.988	1.001		**3**	0.996	0.990	1.002
	4	1.001	0.995	1.007		**4**	1.001	0.995	1.007

SPRING

	Lag Day	**HR**	**95%CI LL**	**95%CI UL**		**Lag Day**	**HR**	**95%CI LL**	**95%CI UL**

Low SO_4	**0**	1.007	1.000	1.013	Low NO_3	**0**	1.001	0.988	1.014
	1	0.999	0.992	1.007		**1**	1.003	0.991	1.016
	2	0.999	0.992	1.006		**2**	0.996	0.984	1.007
	3	0.995	0.988	1.002		**3**	1.001	0.991	1.012
	4	1.001	0.994	1.008		**4**	1.002	0.993	1.012
Medium SO_4	**0**	0.995	0.987	1.004	Medium NO_3	**0**	1.004	0.995	1.012
	1	1.010	1.002	1.018		**1**	1.014	1.006	1.022
	2	1.014	1.005	1.022		**2**	1.015	1.007	1.022
	3	1.009	1.000	1.018		**3**	1.007	0.999	1.015
	4	1.002	0.993	1.010		**4**	0.999	0.992	1.008
High SO_4	**0**	0.997	0.983	1.01	High NO_3	**0**	1.003	0.997	1.010
	1	0.999	0.986	1.013		**1**	1.001	0.993	1.009
	2	0.999	0.985	1.014		**2**	0.994	0.985	1.003
	3	0.996	0.983	1.010		**3**	0.993	0.985	1.001
	4	0.986	0.974	0.999		**4**	0.995	0.987	1.004
Low NH_4	**0**	1.010	1.002	1.018	Low EC	**0**	0.998	0.980	1.016
	1	1.003	0.995	1.012		**1**	1.014	0.995	1.032
	2	1.000	0.993	1.007		**2**	1.024	1.003	1.045
	3	0.993	0.986	1.000		**3**	1.013	0.992	1.034
	4	1.000	0.993	1.008		**4**	1.001	0.981	1.021
Medium NH_4	**0**	0.994	0.986	1.001	Medium EC	**0**	0.999	0.983	1.014
	1	1.001	0.993	1.009		**1**	0.995	0.979	1.012
	2	1.005	0.996	1.014		**2**	0.980	0.962	0.998
	3	1.005	0.996	1.013		**3**	0.991	0.974	1.008
	4	0.997	0.988	1.005		**4**	0.994	0.977	1.011

High NH_4	**0**	0.998	0.988	1.008	High EC	**0**	1.002	0.997	1.007
	1	1.005	0.994	1.015		**1**	1.003	0.997	1.009
	2	1.009	0.997	1.021		**2**	1.004	0.998	1.010
	3	1.006	0.994	1.019		**3**	0.999	0.993	1.005
	4	0.997	0.985	1.009		**4**	0.999	0.993	1.004
Low other	**0**	0.989	0.977	1.000	Low OC	**0**	0.990	0.978	1.002
	1	1.000	0.988	1.012		**1**	0.999	0.986	1.011
	2	1.005	0.991	1.020		**2**	1.005	0.990	1.019
	3	1.002	0.988	1.015		**3**	1.003	0.989	1.017
	4	0.995	0.982	1.008		**4**	0.995	0.982	1.009
Medium other	**0**	0.999	0.991	1.006	Medium OC	**0**	0.997	0.990	1.004
	1	1.001	0.993	1.009		**1**	0.999	0.992	1.006
	2	1.005	0.996	1.014		**2**	1.002	0.994	1.011
	3	1.004	0.996	1.012		**3**	1.004	0.996	1.012
	4	0.997	0.988	1.005		**4**	0.998	0.990	1.006
High other	**0**	1.008	1.000	1.016	High OC	**0**	1.012	1.003	1.020
	1	1.005	0.997	1.013		**1**	1.009	1.000	1.018
	2	1.002	0.995	1.009		**2**	1.004	0.997	1.011
	3	0.996	0.989	1.003		**3**	0.995	0.988	1.002
	4	1.001	0.994	1.009		**4**	1.000	0.993	1.008