Title: Age-specific associations of ozone and $PM_{2.5}$ with respiratory emergency department visits in the US

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Author Contributions: M.J.S. and H.M.S conceived of and designed the study; H.M.S. and A.V. acquired and processed all data; H.M.S. conducted analysis and drafted the manuscript; H.H.C. provided statistical expertise; M.J.S, H.M.S., H.H.C, L.A.D, Y.L, and A.V. interpreted the results and provided critical input into the manuscript; All authors reviewed and approved the final manuscript.

Funding: This research was supported by Centers for Disease Control and Prevention (CDC), National Center for Environmental Health, Division of Environmental Hazards and Health Effects, Environmental Health Tracking Branch. CDC supported the staff responsible for the design and conduct of the study; in the collection, analysis, and interpretation of the data; in the preparation, review, and approval of the manuscript; and in the decision to submit the manuscript for publication. This work of Y. Liu was partially supported by the NASA Applied Sciences Program (grant no. NNX16AQ28G).

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

Running Head: Ambient air pollution and respiratory morbidity

Subject Category List: 6.1

Manuscript Word Count: 3500 (not including title, abstract, acknowledgment, references, tables, and figure legends)

At a Glance Commentary:
Scientific Knowledge on the Subject: Short-term exposure to ambient ozone and fine particulate matter ($PM_{2.5}$) is associated with increases in mortality and morbidity. In the United States, robust evidence from multi-city studies exists for mortality and for hospitalizations among adults 65 and older. These studies have contributed to the establishment of National Ambient Air Quality Standards. The evidence for morbidity outcomes in people under 65, however, is limited to single-city studies. Such studies have limitations with respect to nationwide generalizability due to between-city differences in air pollution composition and population characteristics as well as differences in study methodology.

What This Study Adds to the Field: Our analysis of 894 counties is the largest US multi-city study of air pollution and respiratory emergency department visits among all ages. We observed associations between ozone and respiratory ED visits among all age groups with the highest magnitude association among adults <65. Fine particulate matter was associated with respiratory ED visits among children <19 and adults <65 but not among adults 65 and older. The associations also varied by age group for specific respiratory outcomes. Reliance on associations from a single age group or outcome to evaluate air pollution standards may over or under estimate the health benefits.

This article has an online data supplement, which is accessible from this issue's table of content online at *www.atsjournals.org*.

Abstract

Rationale: While associations between air pollution and respiratory morbidity for adults 65 and older are well-documented in the United States, the evidence for people under 65 is less extensive. To address this gap, the Centers for Disease Control and Prevention's National Environmental Public Health Tracking Program collected respiratory emergency department (ED) data from 17 states.

Objectives: Estimate age-specific acute effects of ozone and fine particulate matter ($PM_{2.5}$) on respiratory ED visits.

Methods: We conducted time-series analyses in 894 counties by linking daily respiratory ED visits with estimated ozone and $PM_{2.5}$ concentrations during the week before the date of the visit. Overall effect estimates were obtained using a Bayesian hierarchical model to combine county estimates for each pollutant by age group (children 0-18, adults 19-64, adults ≥65, and all ages) and by outcome group (acute respiratory infection, asthma, chronic obstructive pulmonary disease, pneumonia, and all respiratory ED visits).

Measurements and Main Results: Rate ratios (95% credible interval) per 10 $\mu g/m^3$ increase in $PM_{2.5}$ and all respiratory ED visits were 1.024 (1.018, 1.029) among children, 1.008 (1.004, 1.012) among adults <65, and 1.002 (0.996, 1.007) among adults 65 and older. Per 20 ppb increase in ozone, rate ratios were 1.017 (1.011, 1.023) among children, 1.051 (1.046, 1.056) among adults <65, and 1.033 (1.026, 1.040) among adults 65 and older. Associations varied in magnitude by age group for each outcome group.

Conclusions: These results address a gap in the evidence used to ensure adequate public health protection under national air pollution policies.

Abstract Word Count: 250

Key Words: particulate matter, ozone, asthma, chronic obstructive pulmonary disease, respiratory infection

Introduction

Substantial and consistent evidence supports the conclusion that short-term exposure to ambient ozone and fine particulate matter ($PM_{2.5}$) is associated with increases in mortality and morbidity (1, 2). Robust evidence exists for mortality and for hospitalizations among adults 65 and older due to the availability of national vital statistics data and Medicare data. These data have enabled many multi-city analyses, which have been instrumental in setting National Ambient Air Quality Standards (NAAQS) for the Clean Air Act (3-9). Estimates from multi-city studies provide strong evidence for determining causality between air pollution and health, for evaluating potential health benefits of proposed policies across the United States (US), and for establishing ambient air quality standards that provide adequate protection for the US population.

Because national datasets are lacking, the evidence for morbidity outcomes for US populations not covered by Medicare (i.e., individuals <65 years) often come from single-city studies (10-13). This is a particularly important issue for respiratory emergency department (ED) visits, since the vast majority of these visits occur in people under age 65 (14). Collectively, the evidence from single-city studies indicates positive associations between air pollution and ED visits for all respiratory diseases combined, and for asthma, chronic obstructive pulmonary disease (COPD), and respiratory infections (7, 15-21). While informative, these studies have limitations with respect to nationwide generalizability due to between-city differences in air pollution composition and population characteristics as well as differences in study methodology. For the current ozone and particulate matter (PM) standards (22, 23), the Environmental Protection Agency (EPA) conducted national-scale mortality risk assessments

using results from multi-city studies. For morbidity outcomes, EPA conducted similar risk assessments for hospital admissions among all ages in only 12 cities for ozone and 15 cities for PM where epidemiologic study results and necessary data were available. For respiratory related ED visits among all ages, their assessment was only conducted in Atlanta and New York City, indicating a strong need for a multi-city study.

In response to a Pew Commission report (24), the Centers for Disease Control and Prevention's (CDC) National Environmental Public Health Tracking Program (Tracking Program) was launched to integrate health, exposure, and environmental hazard data to inform environmental health programs and policies. The National Environmental Public Health Tracking Network (Tracking Network) is a web-based system with components at national, state, and local levels (ephtracking.cdc.gov). It is used to collect, integrate, analyze, and disseminate health and environmental data that drive actions to improve the health of communities. We invited 30 states known to have ED data centralized within their state to participate in the project. Using the Tracking Network, we collected daily, county respiratory ED data for all ages from 17 states representing 45% of the US population (138.5 million individuals). We used these data to perform the first nationally relevant study to estimate associations between ozone and $PM_{2.5}$ and respiratory ED visits among all ages in the US. Partial results have been previously reported in the form of an abstract (25).

Methods

We requested daily number of ED visits with a primary diagnosis of respiratory disease (International Classification of Diseases, 9th Revision (ICD-9) codes 460 – 519) aggregated by county, age group, and outcome group to minimize confidentiality concerns and increase state participation. Seventeen states (California, Colorado, Florida, Illinois, Iowa, Louisiana, Maine, Massachusetts, Minnesota, Missouri, New Hampshire, New Mexico, New York, North Carolina, South Carolina, Utah, and Vermont) provided data for 2000 through 2014 with 3 to 13 years per state (data availability varied by state) (eTable). We created 19 age-specific outcomes by grouping the data into four age groups by five outcome groups, excluding COPD among children. The age groups included all ages combined, children 0 to less than 19 years (subsequently referred to as "children"), adults 19 to less than 65 years ("adults"), and adults 65 years and older ("older adults"). The outcome groups included all respiratory outcomes combined (460 – 519), acute respiratory infection (ARI) including upper respiratory infections, bronchitis, and bronchiolitis (460 – 466.0), asthma (493), chronic obstructive pulmonary disease (COPD) (491, 492, or 496), and pneumonia (480 – 486).

For ambient air pollution concentrations, we used data from the Bayesian space-time downscaling (DS) fusion modeling approach, developed by the U.S. Environmental Protection Agency (EPA) and its partners (26). The DS modeling approach uses a Bayesian framework and spatially-varying coefficients to regress monitoring measurements from Air Quality System on the gridded output from the Community Multi-scale Air Quality (CMAQ) model. The process yields gridded, daily predictions of ozone and $PM_{2.5}$ concentrations that are more accurate and

precise than previously used modeling approaches (26-28). Predictions of daily maximum 8-hr average ozone concentrations in parts per billion ozone and daily 24-hr average $PM_{2.5}$ from the DS model were generated at census-tract centroids for the contiguous US as part of an interagency agreement between CDC and EPA. For this study, we generated daily, population-weighted county-level estimates of ozone and $PM_{2.5}$, for years 2001 through 2012. Population-weighted, county-level estimates correlate well with county-specific air monitors, which are used in the regulatory process (29, 30). Daily, county-level estimates of maximum temperature and dew point temperature in degrees Fahrenheit (°F) were generated from the North American Land Data Assimilation System (NLDAS) model (31). We converted predictions from NLDAS model from a grid resolution of 14-km X 14-km to county using a previously cited geo-imputation approach (32). We used SAS v9.3, Python v3.3.2 and ArcGIS 9.3 for preparing the environmental datasets.

We used a two-stage model to obtain nationally relevant estimates of short-term associations between ozone and $PM_{2.5}$ and respiratory ED visits. In the first stage, we fit time-series models (n = 16986) for each combination of county (n = 894) and age-specific outcome (n = 19). To minimize issues with model convergence, we excluded those county and age-specific outcome combinations where more than 90% of days had zero ED visits (n = 4681). In these counties, the population is low resulting in too few ED visits for the time-series model to fit. We modeled an unconstrained distributed lag for lag days 0 through 6 to capture the cumulative association of exposures over the past week using a Poisson log-linear model that accounted for overdispersion. We fit single-pollutant models for ozone and $PM_{2.5}$ and two-pollutant models with both. Models included: (1) non-linear functions of same day maximum temperature, same day maximum dew

point temperature, and previous six-day average maximum temperature as natural cubic splines with 3 degrees of freedom; (2) a non-linear function of calendar date as a natural cubic spline with 12 degrees of freedom per year of county data; and (3) indicator variables for day of week and for holidays. For the second stage, two-level Bayesian hierarchical models with non-informative priors were fit to combine county-specific effect estimates for each age-specific outcome to obtain nationally relevant effect estimates for ozone and $PM_{2.5}$ (33). We report the rate ratio (RR) and 95% Credible Interval (CI), which we generated using the posterior probability distribution. Given our assumptions, the 95% CI has the property that there is a 95% probability that the true RR falls within the interval. We evaluated the sensitivity of our results by running the models with various degrees of freedom on calendar date (6, 8, 10, and 12 per year) and with three combinations of weather variables: 1) temperature, 2) temperature and dew point temperature, and 3) temperature, dew point temperature, and previous six-day average temperature. We also ran the models with lag day –1 (pollution on the following day) as a negative control exposure to estimate the association with ozone and $PM_{2.5}$ on the day after the ED visit (34). All models were implemented using R statistical software (version 3.3.2; R Foundation for Statistical Computing) on CDC's high performance computing Linux cluster. Models were implemented using the glm function and purrr, broom, and TLNise packages.

Results

Our analysis included 38.4 million respiratory ED visits from 869 counties representing 45% of the U.S. population (Table 1). Children and adults had approximately 16 million visits each while older adults had about 6 million visits. The mean daily rates of respiratory ED visits per

10,000 people was 1.20 for all ages combined, 1.94 for children, 0.91 for adults, and 1.37 for older adults. Rates of ARI and asthma were highest among children, while the rates for COPD and pneumonia were highest among older adults (Figure 1). We calculated the interquartile range (IQR) of each pollutant for each county for the specific years of data used in that county's time-series analysis. The 869 county-specific IQR for daily 8-hour maximum ozone varied from 8.0 parts per billion (ppb) to 34.0 ppb with a mean IQR of 16.54 ppb (Figure 2). For 24-hour average $PM_{2.5}$ levels, the mean county IQR was 5.3 micrograms per cubic meter ($\mu g/m^3$) and ranged from 1.9 to 9.8 $\mu g/m^3$.

We observed statistically significant positive associations between ozone and all respiratory ED visits combined in both single and two-pollutant models for all age groups (Figure 3). For all ages combined, the RR per 20 ppb increase in ozone on lag days 0 through 6 for all respiratory ED visits was 1.039 (CI: 1.036, 1.042). In the two-pollutant models, the association between all respiratory ED visits and ozone was strongest among adults followed by older adults. In contrast, $PM_{2.5}$ was associated with all respiratory ED visits in both single and two-pollutant models for all age groups, except in the two-pollutant model where the association was consistent with the null among older adults (Figure 4). For all ages combined, the RR per 10 $\mu g/m^3$ increase in $PM_{2.5}$ in ozone on lag days 0 through 6 for all respiratory ED visits was 1.020 (CI: 1.017, 1.023). The RRs between all respiratory ED visits combined and $PM_{2.5}$ was higher among children than adults.

For both pollutants, the RR varied in magnitude by outcome and age group. For ozone, we observed significant and positive associations with asthma, ARI, COPD, and pneumonia among

all ages combined in both single-pollutant and two-pollutant models (Figure 3). We also observed significant, positive associations between ozone and each outcome for all age groups except for asthma among older adults. The highest magnitude RR for ozone was asthma among adults (RR: 1.064; 95% CI: 1.053, 1.076). RRs were generally highest among the adult group except for ARI where the RRs for adults and older adults were similar. The RR for the association between ozone and ARI among children was elevated and significant but lower than the RRs for adults and older adults. The RRs for pneumonia exhibit less variation than the RRs for the other outcomes. For $PM_{2.5}$ and all ages combined, we observed positive, significant associations for asthma and ARI in single and two-pollutant models and pneumonia in single-pollutant models (Figure 4). We also observed positive, significant associations for asthma and ARI among each age group. In contrast to our ozone results, we observed less variation in the RR by age group for asthma and ARI and the association for pneumonia was only significant among adults. We found little evidence of an association between $PM_{2.5}$ and COPD among any age groups in either single or two-pollutant models.

In our sensitivity analyses, the RR decreased slightly as the number of degrees of freedom decreased for ozone; association estimates for $PM_{2.5}$ changed little (eFigure 1). It is notable that, for children, many RRs for ozone decreased in magnitude from a positive association to a negative or null association as we decreased temporal control. The RR for ozone and ARI among children was consistent with the null when using either 6 or 8 degrees of freedom, but was significant and positive with either 10 or 12 degrees of freedom (eFigure 1). It is plausible that the most valid degree of temporal control may vary by outcome in relation to the degree of seasonality. For the three combinations of weather variables we evaluated, our results fluctuated

slightly for ozone but were robust for $PM_{2.5}$ with overlapping 95% credible intervals (eFigure 2). The associations observed between ozone or $PM_{2.5}$ concentrations on lag day -1 (pollution on the following day) and ED visits for asthma, COPD, and pneumonia were consistent with the null supporting our model specifications (eFigure 3).

Discussion

Our nationally relevant study, based on nearly 40 million respiratory ED visits representing all ages, addresses an important gap in air pollution epidemiology and is a valuable reference for future national air pollution standards. Our results support the EPA's determination of a likely causal relationship between $PM_{2.5}$ and respiratory effects and a causal relationship between ozone and respiratory effects (1, 2). However, our results highlight important variation in magnitude across age groups, outcomes, and pollutants. $PM_{2.5}$ and all respiratory ED visits were strongly associated among children, moderately associated among adults, and not associated among older adults. While the associations with $PM_{2.5}$ were elevated and similar among all age groups for asthma, they varied by age group for ARI and pneumonia. Conversely, the association between ozone and all respiratory ED visits was higher in magnitude among both adult groups than the association among children. The association between ozone and asthma varied by age group with the highest magnitude among adults. Associations varied by age group for ARI and COPD but were similar across age groups for pneumonia. These findings indicate that multi-city studies of populations over 65 may not be a good proxy of acute respiratory impacts on populations under 65, and that reliance on such studies could underestimate population

respiratory health impacts of $PM_{2.5}$ or ozone that were stronger in our study for younger age groups.

Few single-city studies have estimated associations of ozone or $PM_{2.5}$ across different age groups for ED visits or hospitalizations. Those that have looked specifically at asthma and generally found a greater impact on children (10, 15, 35). We observed similar associations between $PM_{2.5}$ and asthma across age groups and a stronger association for ozone on asthma among adults younger than 65, an age group previously not included in other multi-city studies of morbidity. Differences in results could be due to differences in age group specification. For example, we included all children under 19 in one age group while other studies separate children under 5 and children 5 to 19. The diagnosis of asthma in children under 5 is difficult and could result in more outcome measurement error when included in the analysis (36).

For ozone, EPA found consistent evidence of positive associations for asthma and COPD based on the few studies evaluating hospital admissions and ED visits for respiratory outcomes (2). While EPA found strong toxicological evidence supporting an association between ozone and respiratory infections and pneumonia, the epidemiologic evidence was inconsistent. We observed positive associations between ozone and ARI, asthma, COPD, and pneumonia for all age groups, with the only exception asthma among older adults while adjusting for $PM_{2.5}$. This supports EPA's conclusions and adds to epidemiological evidence for ARI and pneumonia. For $PM_{2.5}$, EPA's review of available studies produced stronger and more consistent evidence for COPD and respiratory infections effects than for asthma effects, including both ED visits and hospitalizations. In contrast, we observed significant, positive associations between $PM_{2.5}$ and

asthma and acute respiratory infections across all age groups. Pneumonia was associated with $PM_{2.5}$ among adults only while COPD was not associated with $PM_{2.5}$ in any age group analyzed. These disparate results could be due to our evaluation of ED visits among all ages versus hospitalization among adults 65 and older used in most previous studies.

The differences in magnitude across associations of outcomes, age groups, and pollutants are consistent with differences in disease pathology, respiratory tract physiology, pollutant chemistry, exposure patterns, or a combination thereof. The specific respiratory diseases leading to ED visits varies by age group with ARI, asthma, and pneumonia prominent in children; asthma and COPD in adults; and COPD and pneumonia in older adults (14). The pathology of these diseases and their impact on the respiratory tract also varies by age. Small airway obstruction related to COPD is often observed in the smallest airways, where gas exchange occurs, compared to a more proximal location among individuals with asthma (37). Similarly, among those with asthma, hyperresponsiveness tends to be more proximally located in younger individuals versus more peripherally located in older individuals (37). Age also influences respiratory tract morphology, breathing patterns, physiochemical properties of the extracellular lining fluid, immunologic responses, and mechanical properties of the lung (1, 2, 37). These differences can influence not only disease pathology but also pollutant uptake, dose, and effect on the respiratory tract. The impact of these differences on our results is further complicated by the differing physiochemical properties of ozone and $PM_{2.5}$ (1, 2). For example, ozone is a gas that can penetrate deep into the lower respiratory tract with more distal penetration in larger lungs. Conversely, evidence suggests that children may receive a larger dose of particulate

matter in the lower respiratory tract compared to adults. Together, these differences lend biological plausibility to our results.

Limitations

Although our statistical model is well established and has been evaluated extensively (33, 38-41), model misspecification is nevertheless a concern. Our county time-series analyses could be biased by an unmeasured or inadequately modeled predictor or confounder if that confounder fluctuates over time in a manner similar to ozone or $PM_{2.5}$. Our sensitivity analyses, which include modeling time trend and meteorology in various ways and estimating associations with a negative control exposure, suggest that such a bias is unlikely (34). However, our results for ozone and ARI and asthma among children were sensitive to the number of degrees of freedom included in the time control. Our main results are presented using 12 degrees of freedom per year, which is more control than was used in many previous multi-city studies. Respiratory ED visits exhibit strong seasonal patterns with sharp within-season spikes due to infectious disease, especially among children (42), which may differ from the outcomes of mortality and respiratory hospitalizations among populations over 65 covered by previous multi-city studies. As such, time-series analysis of respiratory ED visits may require more temporal control as evidenced by the amount of control used in many single city studies of respiratory ED visits (11, 20, 43, 44). As can be seen from the sensitivity analyses, which use fewer degrees of freedom, most RRs are similar but some are substantially lower, highlighting the importance of selecting a smoother that adequately captures the spikes in outcome rates.

Defining respiratory diseases based on primary diagnosis and ICD-9 codes could potentially lead to misclassification; however, such misclassification would not affect the results for all respiratory diseases combined. While county air pollution metrics are not measures of personal exposure, they are relevant metrics for air pollution policy and can produce robust and unbiased results for ambient ozone and $PM_{2.5}$ that tend to be more spatially homogenous than other air pollutants (45). Modeled air pollution data may introduce measurement error into our analyses. Wintertime DS estimates of ozone may rely more on CMAQ predictions and less on air pollutant measurements, as ozone monitoring predominantly occurs during the warmer months of the year, and year-round monitoring may not be available for colder areas of the US. As a result model predictions may have more error in colder months or areas with sparse ozone monitoring. Evaluation of the DS model has shown it to be a reasonable solution to the temporal and spatial gaps in available air pollution data (27, 28). While our study provides estimates to inform national environmental health policy by combining the local estimates, we average across the local variation in the short-term associations between air pollution and respiratory ED visits that exists, masking any between-county heterogeneity in effect estimates that may exist. Generalizability to the most rural and sparsely populated areas may be limited, as counties with 90% of days without a respiratory ED visit were excluded. Lastly, while these 17 states analyzed represent 45% of the US population, the northwest and mid-Atlantic states are under-represented. The national generalizability of our results could be impacted by regional or state differences in factors that alter the association between air pollutants and respiratory ED visits such as air pollution composition, chronic morbidity prevalence, or population behaviors.

Conclusions

Both ozone and $PM_{2.5}$ were associated with respiratory ED visits among all ages combined, and we observed variation in the magnitude of these associations across age, respiratory outcome, and pollutant. Our results provide the first nationally comprehensive risk estimates for ARI, asthma, COPD, pneumonia, and all respiratory outcomes combined for children, adults younger than 65, older adults, and all ages combined. Prior to our study, US multi-city estimates were only available for mortality or for morbidity among older adults due to limitations in nationally standardized and accessible health data. Such gaps in available data, and consequently our gaps in understanding of the relationship between health and environmental hazards, were the primary motivation for the creation of CDC's Tracking Network. By examining associations with ozone and $PM_{2.5}$ for people of all ages across hundreds of counties in the US, we address a key gap in the evidence used to inform national ambient air pollution policy.

Acknowledgements

Madhusudan Chaganthi (Waltair Technical Services (WTS), Inc) for assistance in data management; Barbara Anderson (CDC/Agency of Toxic Substances and Disease Registry) for creation of manuscript figures; Judith Qualters (CDC) and Fuyuen Yip (CDC) for support and guidance; CDC staff who maintain the high performance computing Linux cluster; Environmental Protection Agency and National Aeronautics and Space Administration staff who compiled the air pollution and meteorology data; and all the staff from the state health departments, tracking programs, and data organizations that provided the emergency department data.

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Figure Legends

Figure 1: Distribution of county level means for daily rate of respiratory emergency department visits per 10,000 population

Figure 2: Distribution of county level interquartile ranges for daily 8-hour maximum ozone and 24-hour average $PM_{2.5}$

Figure 3: Rate ratio & 95% credible interval for a 20 parts per billion increase in daily 8-hour maximum ozone from an unconstrained, distributed lag model (lags 0 – 6) (unadjusted and $PM_{2.5}$ adjusted)

Figure 4: Rate ratio & 95% credible interval for a 10 microgram per cubic meter increase in 24-hour average $PM_{2.5}$ from an unconstrained, distributed lag model (lags 0 – 6) (unadjusted and ozone adjusted)

Table 1: Overall mean and variance of county level mean daily counts and rates per 10,000 population of respiratory emergency department visits for counties analyzed by outcome and age group

Outcome	Age Group	ED Visits	Counties	Mean Daily Count	Variance Daily Count	Mean Daily Rate	Variance Daily Rate
All	All	39,975,411	869	17.26	2383.55	1.20	0.313
All	0-<19	16,096,443	836	7.34	523.19	1.94	0.914
All	19-<65	16,398,438	836	7.50	400.90	0.91	0.206
All	65+	5,884,333	789	2.78	51.35	1.37	0.296
ARI	All	18,169,816	836	8.13	498.03	0.57	0.090
ARI	0-<19	9,534,546	812	4.48	189.91	1.22	0.400
ARI	19-<65	7,176,147	774	3.49	68.61	0.42	0.058
ARI	65+	701,212	419	0.61	1.16	0.21	0.014
Asthma	All	5,761,712	691	3.10	100.70	0.14	0.005
Asthma	0-<19	2,265,810	517	1.64	22.15	0.23	0.014
Asthma	19-<65	2,717,781	594	1.76	30.87	0.13	0.004
Asthma	65+	379,423	206	0.68	1.65	0.09	0.002
COPD	All	2,385,148	678	1.32	7.19	0.10	0.003
COPD	0-<19	NA	NA	NA	NA	NA	NA
COPD	19-<65	896,808	506	0.69	1.43	0.08	0.002
COPD	65+	1,342,479	571	0.88	2.96	0.38	0.027
Pneumonia	All	4,659,863	749	2.31	35.25	0.16	0.004
Pneumonia	0-<19	1,294,844	467	1.04	6.02	0.16	0.005
Pneumonia	19-<65	1,425,621	566	0.97	4.55	0.09	0.001
Pneumonia	65+	1,660,353	589	1.04	5.27	0.46	0.036

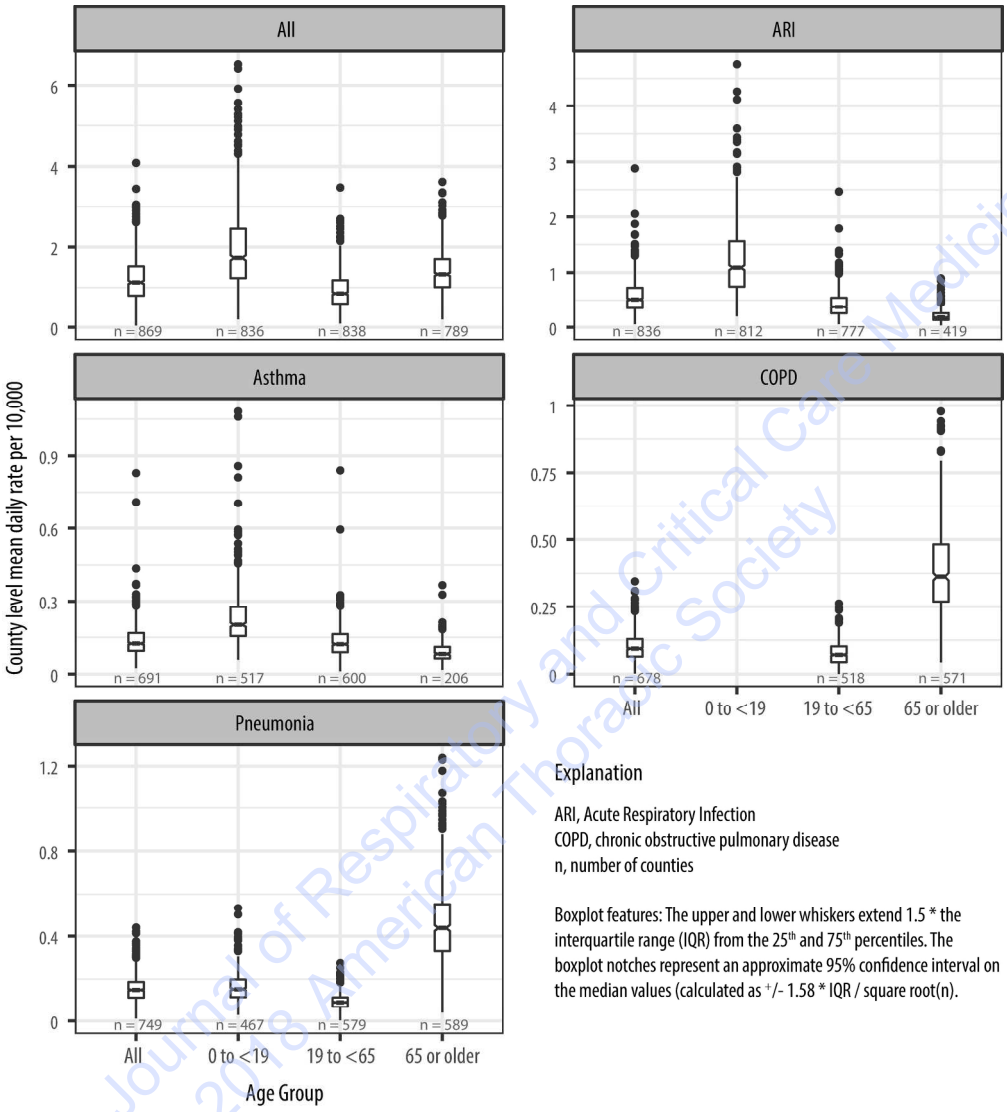

Figure 1

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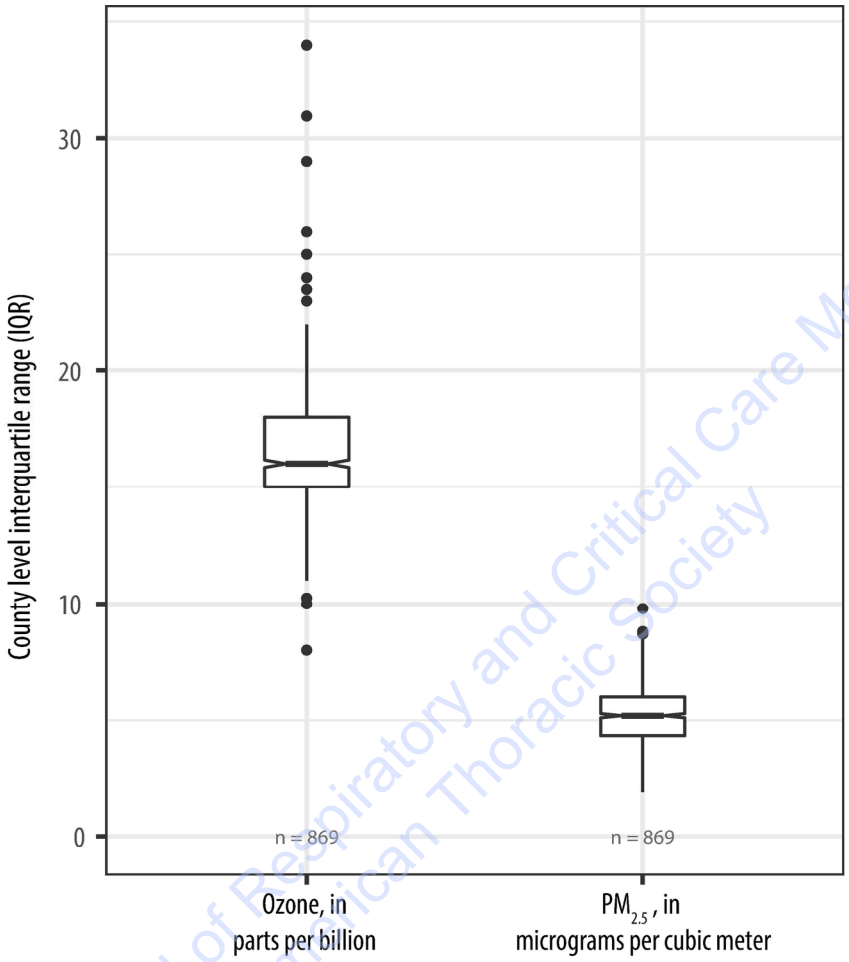

Explanation

n, Number of counties

$PM_{2.5}$, Fine particulate matter (2.5 micrometers in diameter or less)

Boxplot features: The upper and lower whiskers extend 1.5 * the interquartile range (IQR) from the 25th and 75th percentiles. The boxplot notches represent an approximate 95% confidence interval on the median values [calculated as +/- 1.58 * IQR / square root(n)].

Figure 2

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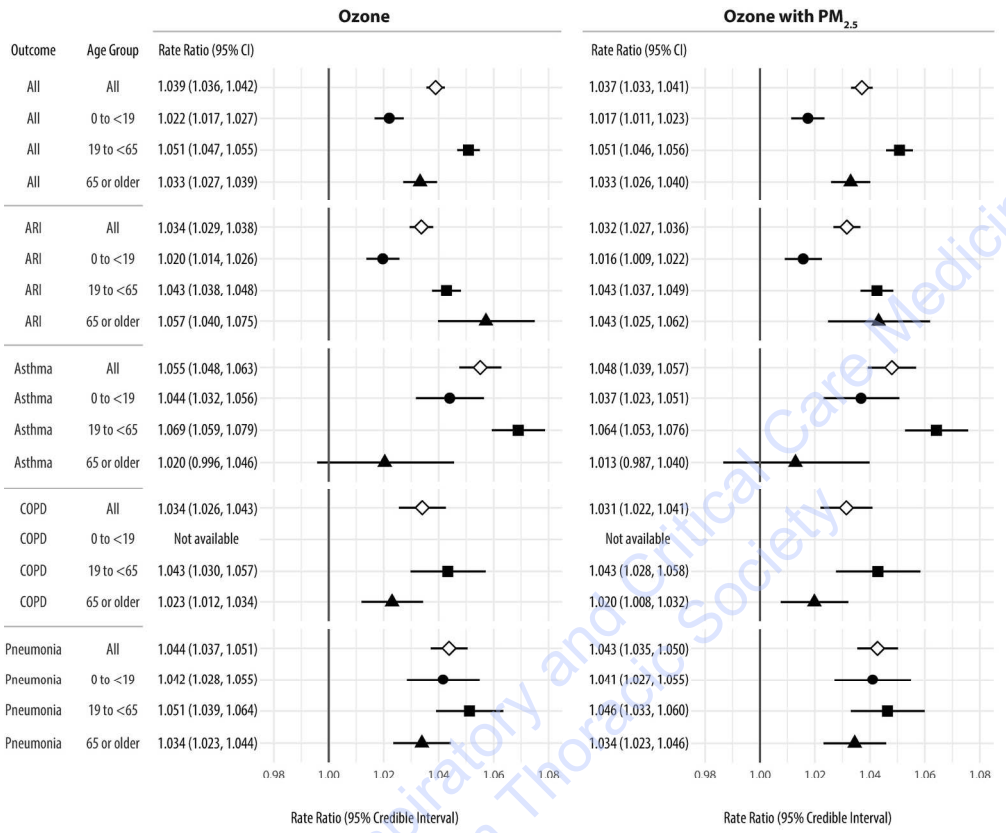
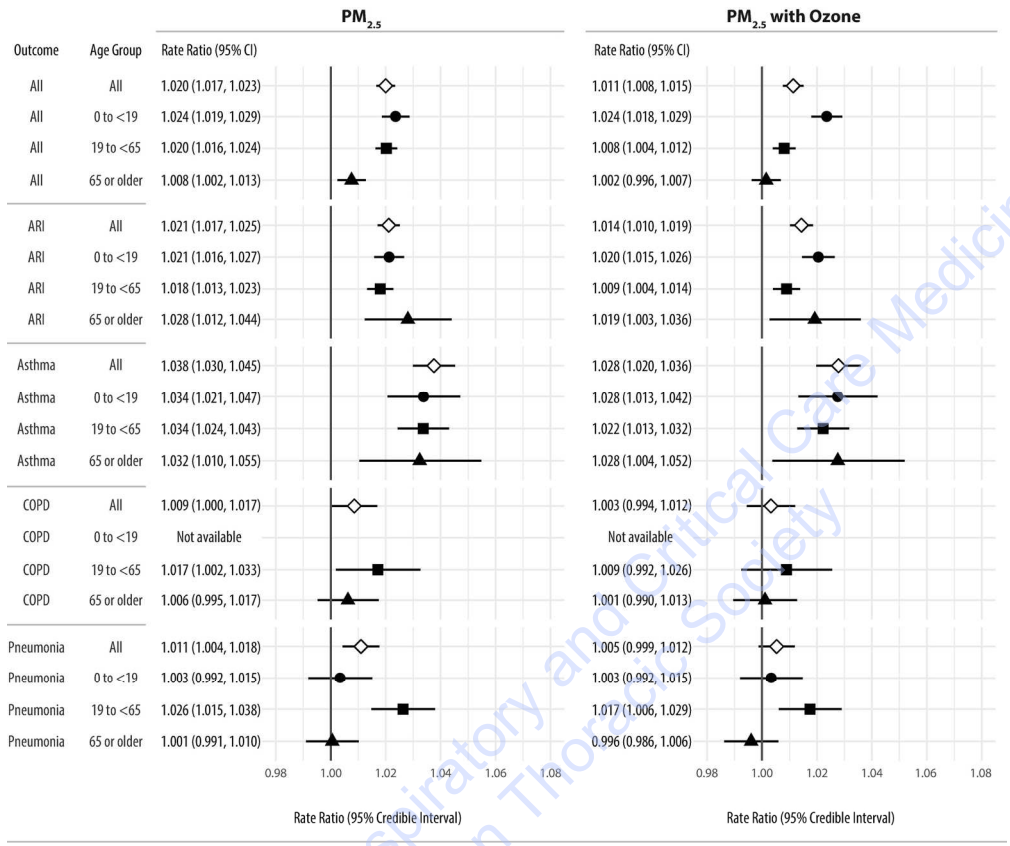


Abbreviations: $PM_{2.5}$, Fine Particulate Matter (2.5 micrometers in diameter or less); 95% CI, 95% Credible Interval; ARI, Acute Respiratory Infection; COPD, Chronic Obstructive Pulmonary Disease

Figure 3

170x146mm (300 x 300 DPI)



Abbreviations: $PM_{2.5}$, Fine Particulate Matter (2.5 micrometers in diameter or less); 95% CI, 95% Credible Interval; ARI, Acute Respiratory Infection; COPD, Chronic Obstructive Pulmonary Disease

Figure 4

170x146mm (300 x 300 DPI)

Supplemental Table and Figures: Age-specific associations of ozone and PM2.5 with respiratory emergency department visits in the US

eTable: States which provided daily respiratory emergency department data

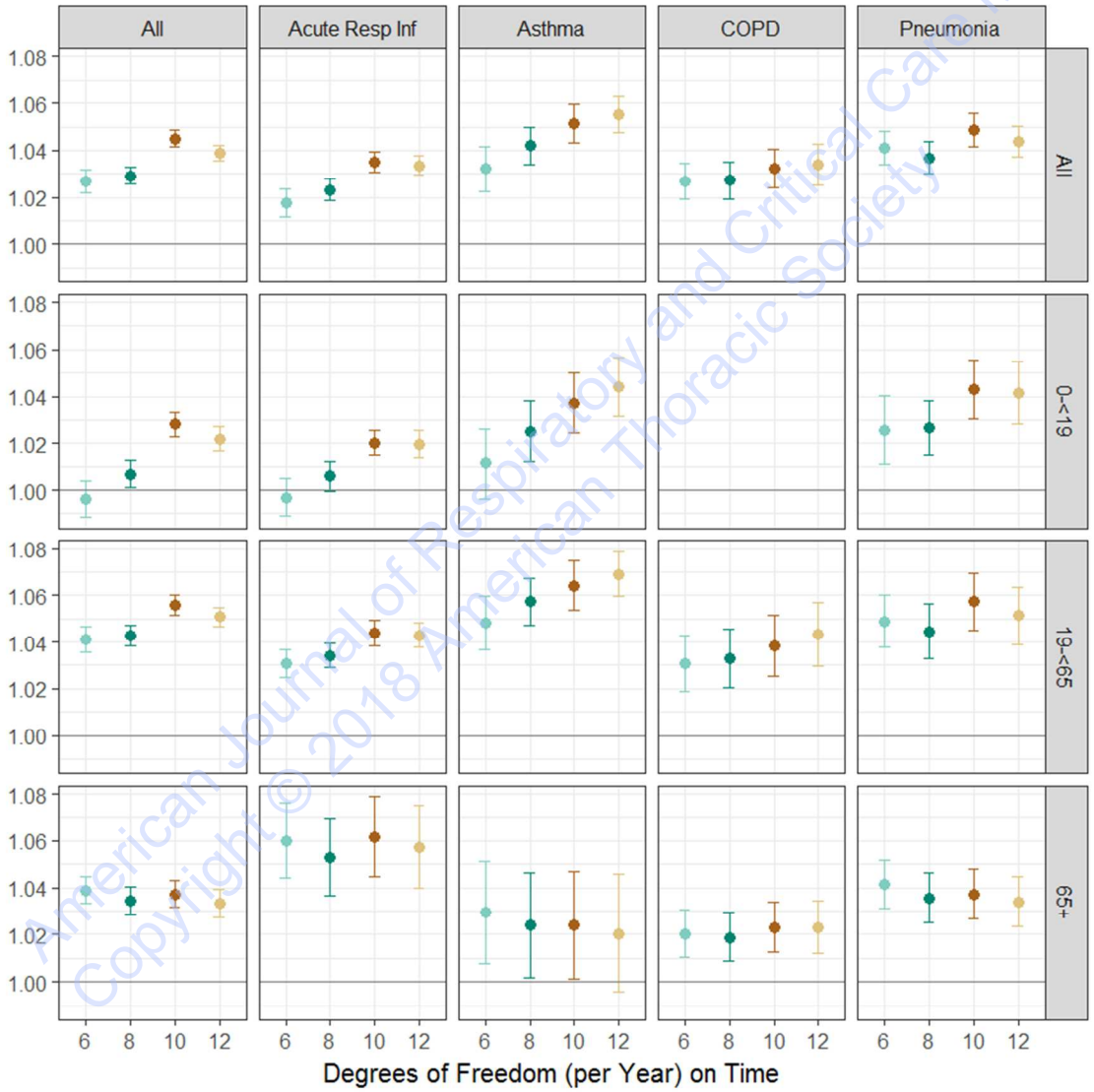
State	Counties	Years Covered
California	58	2006 - 2013
Colorado	64	2012 - 2013
Florida	67	2005 - 2014
Illinois	102	2009 - 2014
Iowa	13	2005 - 2012
Louisiana	64	2010 - 2012
Maine	16	2001 - 2011
Massachusetts	14	2002 - 2012
Minnesota	87	2007 - 2013
Missouri	115	2001 - 2012
New Hampshire	10	2000 - 2009
New Mexico	33	2010 - 2013
New York	62	2005 - 2013
North Carolina	100	2008 - 2014
South Carolina	46	2000 - 2013
Utah	29	2001 - 2013
Vermont	14	2003 - 2012

Sensitivity Analysis: Age-specific associations between ambient air pollution concentrations and respiratory emergency department visits in the United States

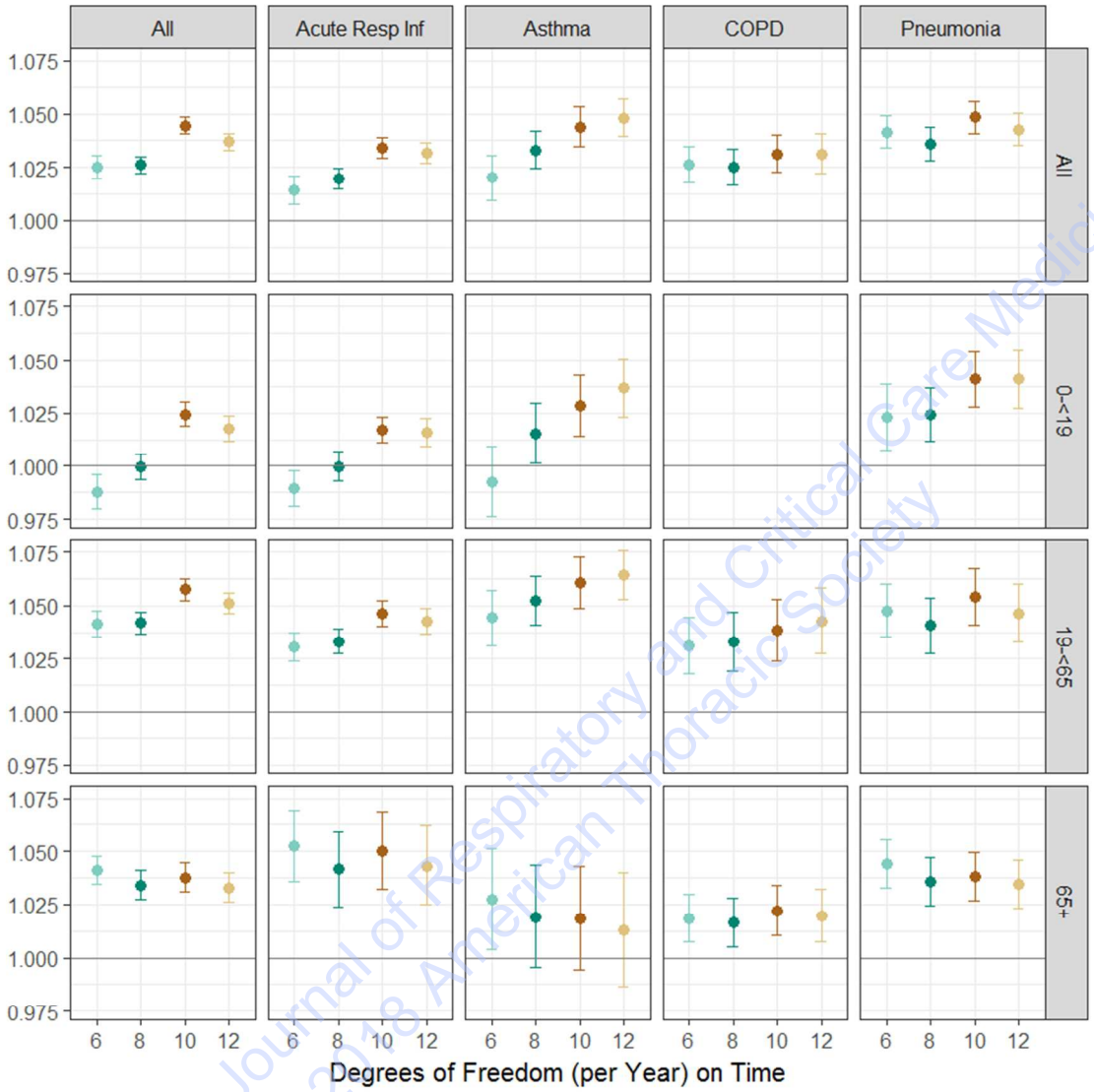
eFigure 1: Evaluation of different degrees of freedom per year as alternative specifications for control of temporal trend

(Results using 12 degrees of freedom per year were reported for the primary analysis.)

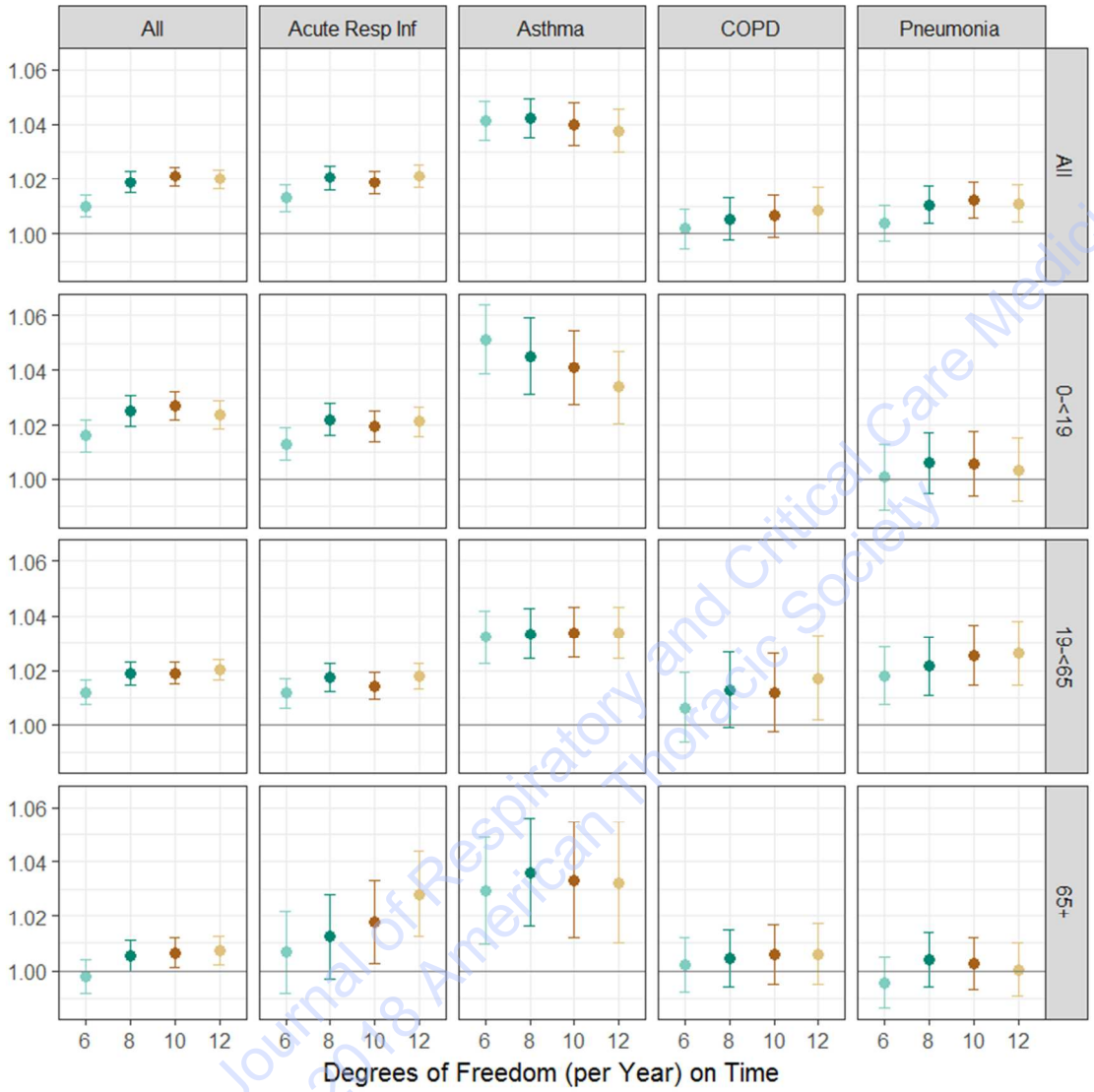
A: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 20 ppb increase in 8-hour ozone



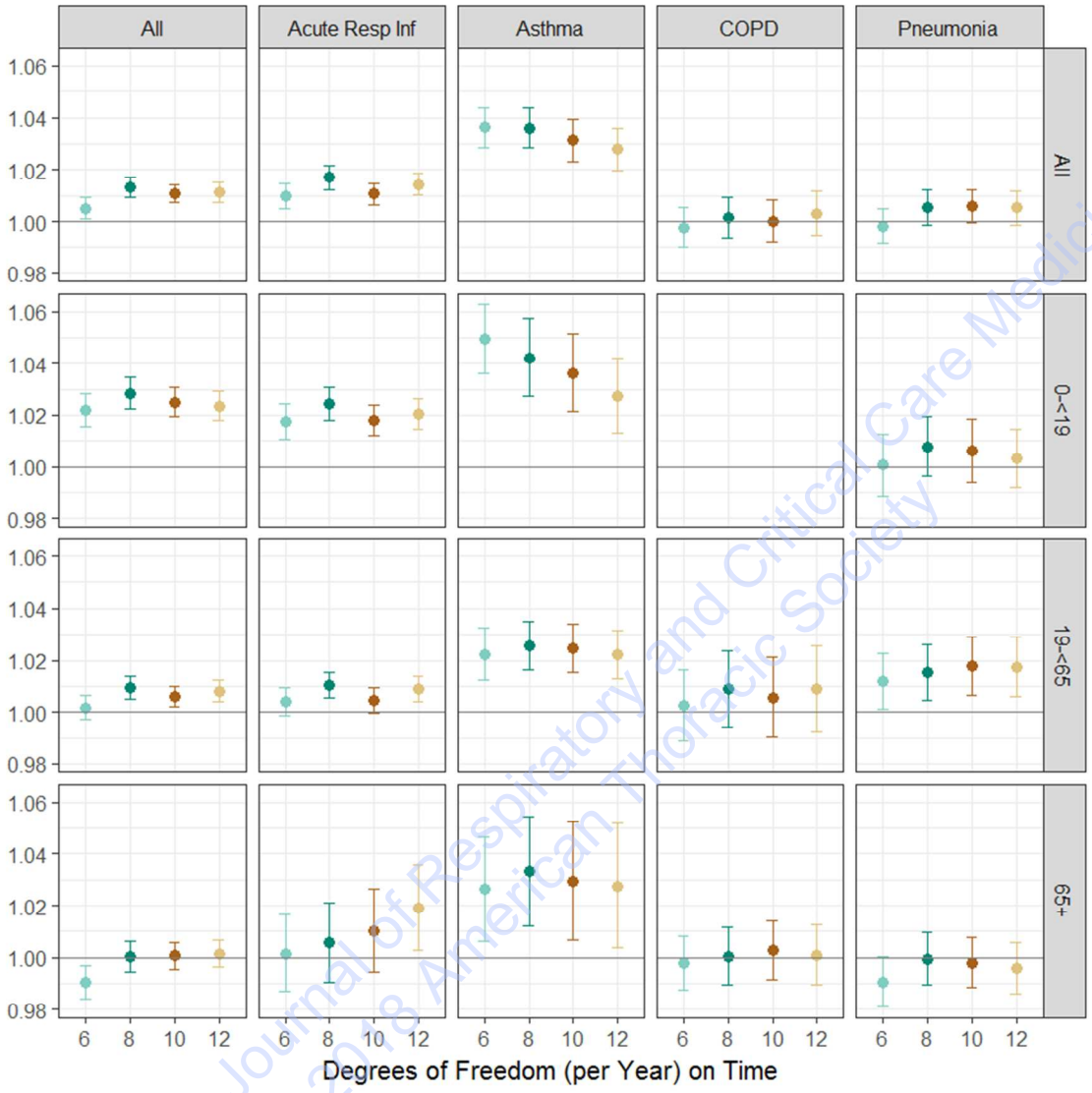
B: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 20 ppb increase in 8-hour ozone, adjusted for PM2.5



C: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 10 µg/m3 increase in 24 hour PM2.5



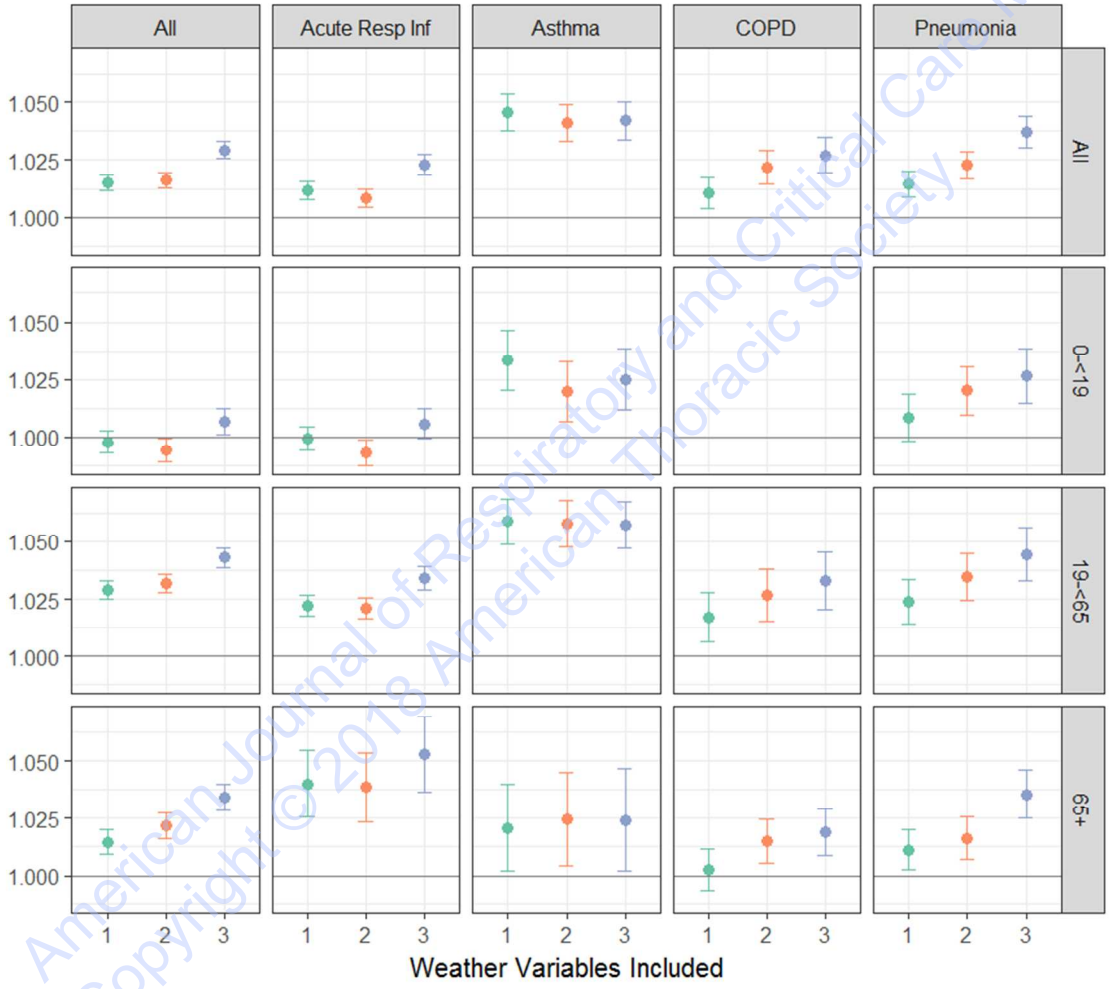
D: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 10 µg/m3 increase in 24 hour PM2.5, adjusted for ozone



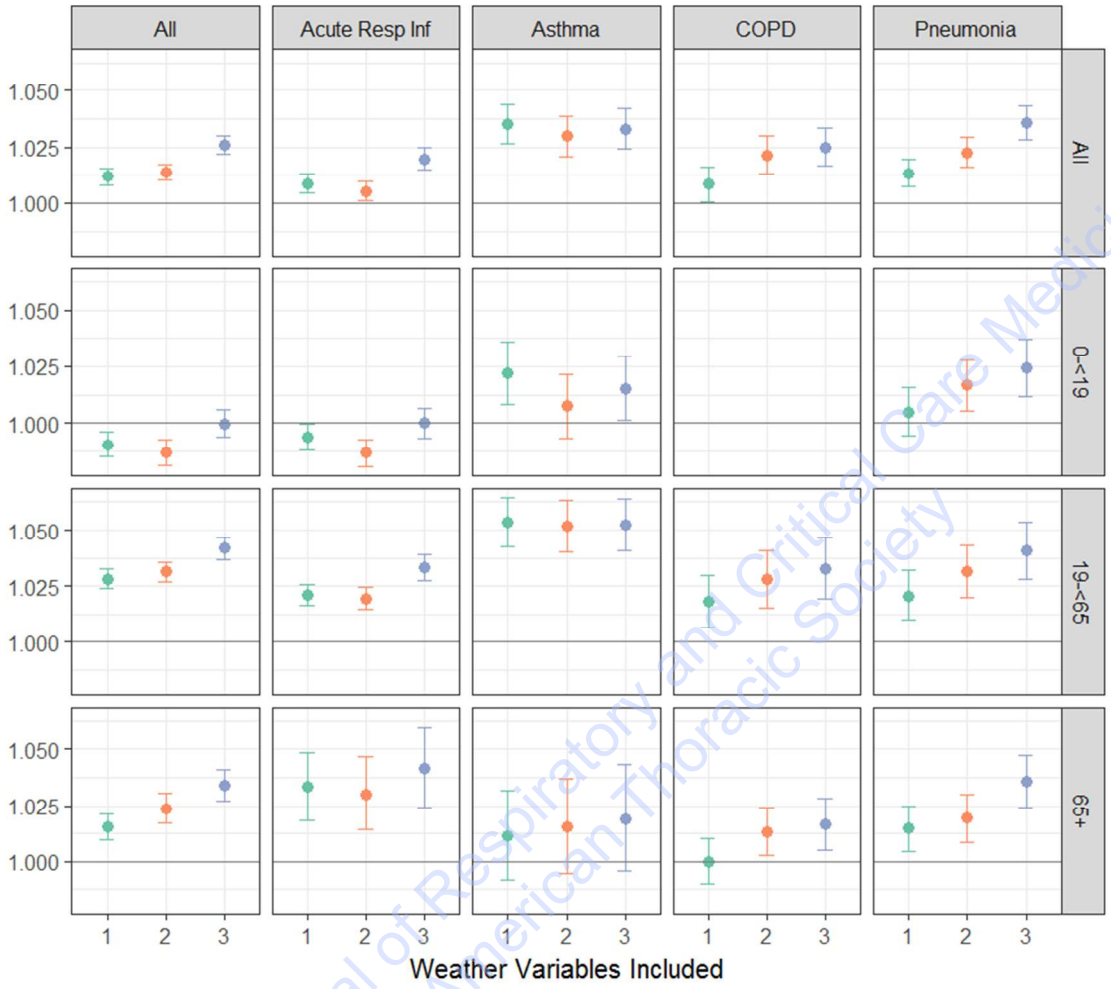
eFigure 2: Evaluation of the effect of different variables to control for weather

Three combinations of weather variables analyzed: 1) same day maximum temperature, 2) same day maximum temperature and same day maximum dew point temperature, and 3) same day maximum temperature, same day maximum dew point temperature, and previous six-day average temperature. Combination 3 was used in the primary analysis.

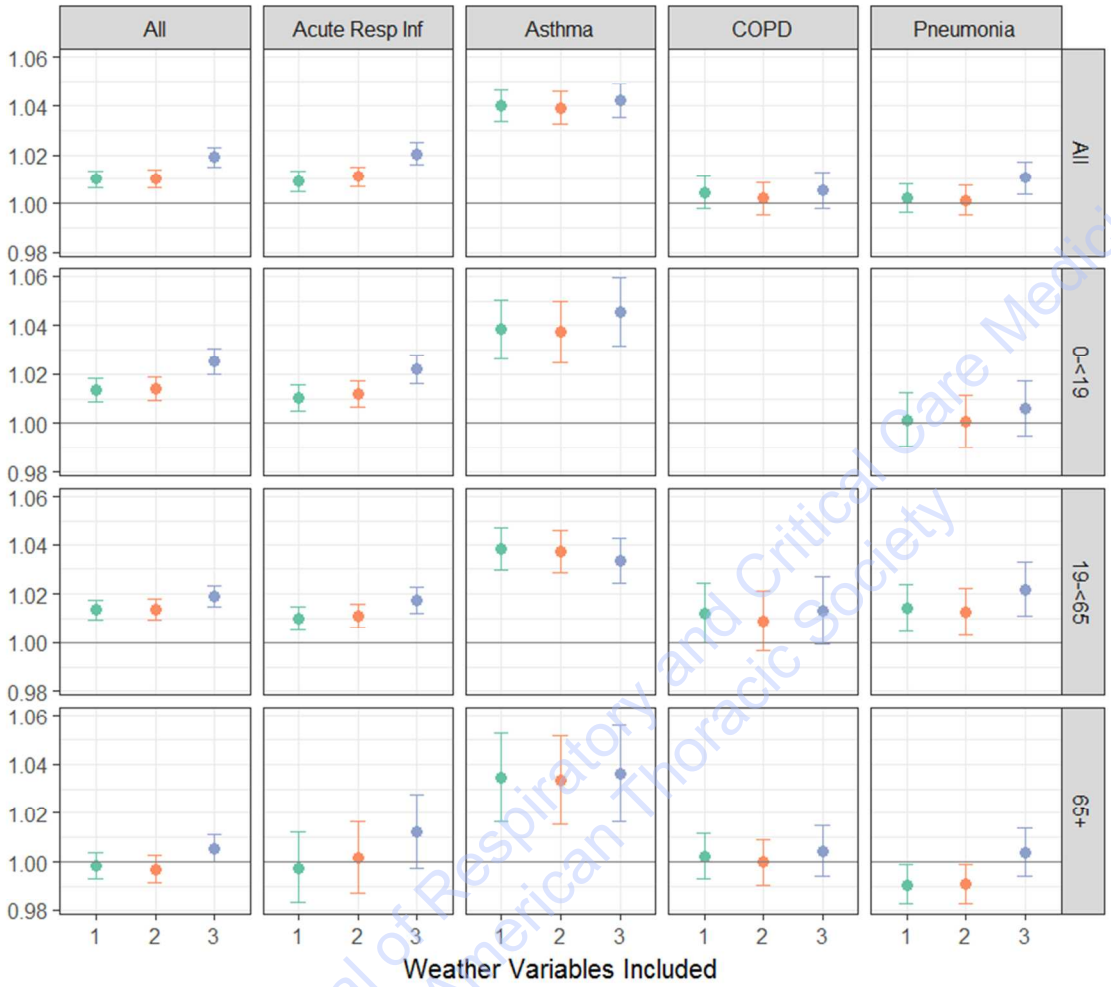
A: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 20 ppb increase in 8-hour ozone



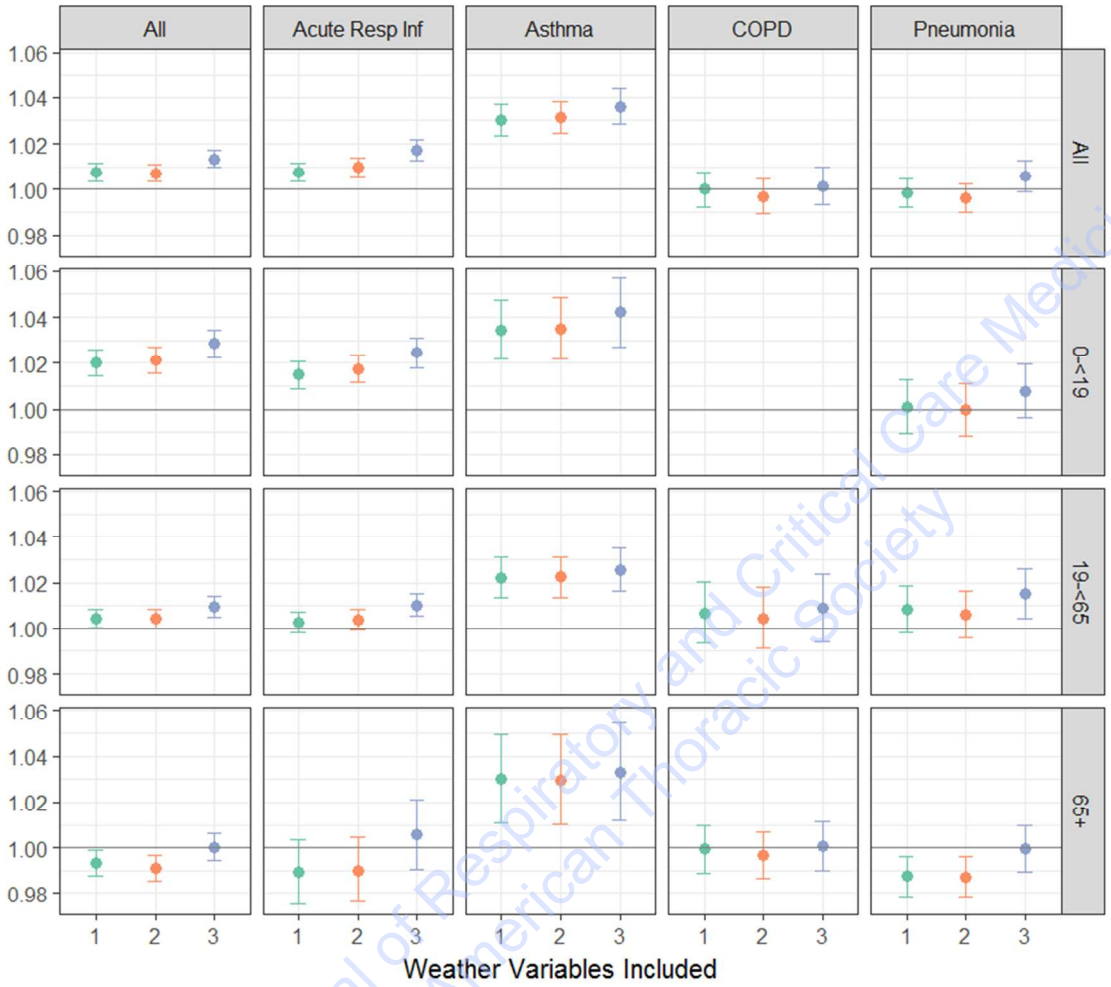
B: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 20 ppb increase in 8-hour ozone, adjusted for PM2.5



C: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 10 µg/m3 increase in 24 hour PM2.5

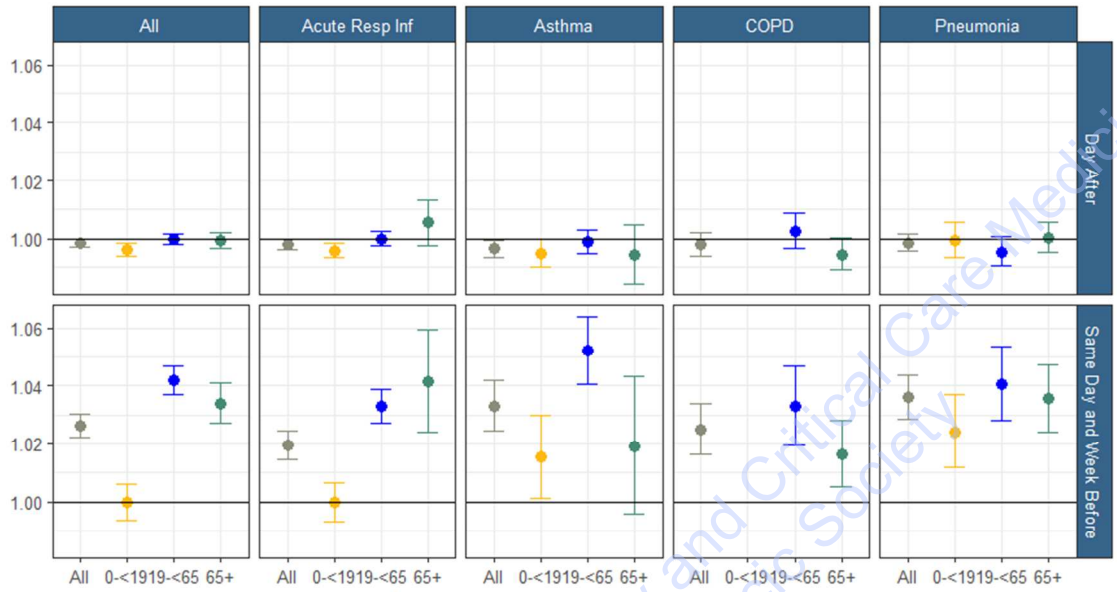


D: RR & 95% CI from an unconstrained, distributed lag model (lags 0 – 6) for a 10 µg/m3 increase in 24 hour PM2.5, adjusted for ozone



eFigure 3: Evaluation of associations between respiratory ED visits and air pollution the day after the ED visit as a negative control exposure

A: RR & 95% CI for a 20 ppb increase in 8-hour Ozone the day after an ED visit and the same day plus week before an ED visit (adjusted for PM2.5)



B: RR & 95% CI for a 10 µg/m3 increase in 24 hour PM2.5 the day after an ED visit and the same day plus week before (adjusted for ozone)