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Exposure to air pollution and COVID-19 mortality in the United States

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Abstract

Background: United States government scientists estimate that COVID-19 may kill between 100,000 and 240,000 Americans. The majority of the pre-existing conditions that increase the risk of death for COVID-19 are the same diseases that are affected by long-term exposure to air pollution. We investigate whether long-term average exposure to fine particulate matter ($PM_{2.5}$) increases the risk of COVID-19 deaths in the United States.

Methods: Data was collected for approximately 3,000 counties in the United States (98% of the population) up to April 04, 2020. We fit zero-inflated negative binomial mixed models using county level COVID-19 deaths as the outcome and county level long-term average of $PM_{2.5}$ as the exposure. We adjust by population size, hospital beds, number of individuals tested, weather, and socioeconomic and behavioral variables including, but not limited to obesity and smoking. We include a random intercept by state to account for potential correlation in counties within the same state.

Results: We found that an increase of only 1 μg/m^3 in $PM_{2.5}$ is associated with a 15% increase in the COVID-19 death rate, 95% confidence interval (CI) (5%, 25%). Results are statistically significant and robust to secondary and sensitivity analyses.

Conclusions: A small increase in long-term exposure to $PM_{2.5}$ leads to a large increase in COVID-19 death rate, with the magnitude of increase 20 times that observed for $PM_{2.5}$ and all-cause mortality. The study results underscore the importance of continuing to enforce existing air pollution regulations to protect human health both during and after the COVID-19 crisis. The data and code are publicly available.

Introduction

The scale of the COVID-19 public health emergency is an unmatched one in our lifetime. It will have grave social and economic consequences. The suddenness and global scope of this pandemic has raised urgent questions that require coordinated and credentialed information to slow its devastation. A critically important public health objective is to identify key modifiable environmental factors, such as ambient air pollution, that could increase the severity of the health outcomes (e.g., ICU hospitalization and death) among individuals with COVID-19.

Our understanding of what causes death in COVID-19 patients is evolving. Early data from China suggests that a majority of COVID-19 deaths occurred in adults aged ≥60 years and among persons with serious underlying health conditions.[1,2] Preliminary analyses of outcomes among COVID-19 patients in the United States largely agree, reporting the highest fatality rates in persons aged ≥65. A report by last month's joint World Health Organization[3] reported that one in seven patients develops difficulty breathing and other severe complications. These patients typically suffer respiratory failure and failure of other vital systems. COVID-19 can cause viral pneumonia with additional extrapulmonary manifestations and complications including acute respiratory distress syndrome (ARDS) which has a mortality rate ranging from 27% to 45%.[4] Factors associated with mortality include sex (male), advanced age (≥65), and the presence of comorbidities including hypertension, diabetes mellitus, cardiovascular diseases, and cerebrovascular diseases. COVID-19 is also associated with a high inflammatory burden that can induce vascular inflammation, myocarditis, and cardiac arrhythmias.[5]

Although the epidemiology of COVID-19 is evolving, we have determined that there is a large overlap between causes of deaths of COVID-19 patients and the diseases that are affected by

long-term exposure to fine particulate matter ($PM_{2.5}$). The Global Burden of Disease Study identified air pollution as a risk factor for total and cardiovascular disease mortality and is believed to be responsible for 5.5 million premature deaths worldwide a year.[6] $PM_{2.5}$ contains microscopic solids or liquid droplets that are so small they can be inhaled and cause serious health problems. On Thursday, March 26, 2020 the US EPA announced a sweeping relaxation of environmental rules in response to the coronavirus pandemic, allowing power plants, factories and other facilities to determine for themselves if they are able to meet legal requirements on reporting air and water pollution.

We hypothesize that because long-term exposure to $PM_{2.5}$ adversely affects the respiratory and cardiovascular system, it can also exacerbate the severity of the COVID-19 infection symptoms and may increase the risk of death in COVID-19 patients. The association between $PM_{2.5}$ and health including pregnancy outcomes, respiratory diseases, cardiovascular diseases, neurocognitive disease in the United States and worldwide is well established.[7,8,9,10,11,12]

A recent study by our group also documented a statistically significant association between long-term exposures to $PM_{2.5}$ and ozone and risk of ARDS among older adults in the United States.[13] Numerous scientific studies reviewed by the US Environmental Protection Agency (US EPA) have linked $PM_{2.5}$ to a variety of health concerns including: premature death in people with heart or lung disease, non-fatal heart attacks, irregular heartbeats, aggravated asthma, decreased lung function, and increased respiratory symptoms such as inflammation, airway irritations, coughing, or difficulty breathing.[14]

Our study includes 3,080 counties in the United States and covering 98% of the United States population. We leverage our previous efforts that focused on estimating the long-term effects of $PM_{2.5}$ on mortality among 60 million United States' Medicare enrollees.[15,16,17] We used a well-

tested research data platform that gathers, harmonizes, and links nationwide air pollution data, census data, and other potential confounding variables with health outcome data. We augment this platform with newly collected COVID-19 data from authoritative data sources.[18] All data sources used in these analyses, along with fully reproducible code, are publicly available to facilitate continued investigation of these relationships as the COVID-19 outbreak evolves and more data become available.

Methods

Table 1 summarizes our data sources and their provenance, including links where the raw data can be extracted directly.

COVID-19 deaths: We obtain COVID-19 death counts for each county in the United States from Johns Hopkins University, Center for Systems Science and Engineering Coronavirus Resource Center.[19] This source provides the most comprehensive county level COVID-19 data to date reported by the US Centers for Disease Control and Prevention and state health departments. This includes real-time number of deaths and number of confirmed cases in each county across the United States. We collect the cumulative number of deaths for each county up to and including April 4, 2020. County level COVID-19 mortality rates are defined for our analyses as the ratio of COVID-19 deaths to county level population size.

Exposure to air pollution: We calculate county level long-term exposure to $PM_{2.5}$ (averaged for 2000 to 2016) from an established exposure prediction models.[20] The $PM_{2.5}$ exposure levels are estimated monthly at 0.01° × 0.01° grid resolution across the entire continental United States by combining satellite, modeled, and monitored $PM_{2.5}$ data in a geographically-weighted regression. These estimates have been extensively cross-validated.[21] We obtained temporally averaged $PM_{2.5}$ values (2000-2016) at the county level by averaging estimated $PM_{2.5}$ values

within a given county. We compute average 2016 PM$_{2.5}$ exposure analogously for each county to use in sensitivity analyses.

Potential Confounders: We consider the following sixteen county level variables and one state level variable as potential confounders: population density, percent of the population ≥65, percent living in poverty, median household income, percent black, percent Hispanic, percent of the adult population with less than a high school education, median house value, percent of owner-occupied housing, population mean BMI (an indicator of obesity), percent ever-smokers, number of hospital beds, and average daily temperature and relative humidity for summer (June-September) and winter (December-February) for each county, and state level number of COVID-19 tests performed. Additional detail on the creation of all variables used in the analysis is available in the Supplementary Materials.

Statistical methods

We fit zero-inflated negative binomial mixed models (ZNB).[22,23,24] using COVID-19 deaths as the outcome and PM$_{2.5}$ as the exposure of interest. The ZNB is composed of two sub-models. The first is a *count sub-model* that estimates the association between COVID-19 deaths and PM$_{2.5}$ (adjusted by covariates) among counties eligible (e.g., confirmed COVID-19 cases) to experience a COVID-19 death. The second is a *zero sub-model* that accounts for the excess of zeros that may be generated by counties not yet eligible for COVID-19 deaths (e.g., due to the absence of confirmed COVID-19 cases) and unlikely to have COVID-19 deaths as of April 4, 2020. Additional modeling details are provided in the Supplementary Materials. We include a population size offset and we adjust for all variables listed above. We also include a random intercept by state to account for potential correlation in counties within the same state, due to similar socio-cultural, behavioral, and healthcare system features and similar COVID-19 response and testing policies. We only report the result from the count sub-model. More

specifically we report exponentiated parameter estimates, the mortality rate ratios (MRR) and 95% CI from the *count sub-model*. The MRR can be interpreted as the relative increase in the COVID-19 death rate associated with a 1 μg/m^3 increase in long-term average PM$_{2.5}$ exposure among the counties eligible to experience a COVID-19 death. We do not report results from the *zero sub-model*. We carried out all analyses in R statistical software and performed model fitting using the NBZIMM package.[25]

Secondary Analysis

We conduct six secondary analyses to assess the robustness of our results to the confounder set used, potential unmeasured confounders, and outliers.

- First, because New York state has experienced the most severe COVID-19 outbreak in the United States to date and has five times higher COVID-19 deaths than the next highest state, we anticipate that it will strongly influence our analysis. As a result, we repeat the analysis excluding all counties in New York state.

- Second, existing COVID-19 testing and case count data are unable to accurately capture the size of an outbreak in a given county, and the inability to fully adjust for this factor could induce confounding in our analyses (e.g., if counties with high PM$_{2.5}$ exposure also tend to have large outbreaks relative to the population size, then their death rates per unit population could appear differentially elevated, inducing a spurious correlation with PM$_{2.5}$). To explore how this may impact our results, we conduct analyses excluding counties with less than 10 confirmed COVID-19 cases.

- Finally, we fit models omitting the following potential confounders from the model (separately):
  - Number of hospital beds
  - Number of COVID-19 tests performed
  - Population mean BMI and percent smokers (BRFSS)

○ Summer and winter temperature and relative humidity (Weather)

Sensitivity analysis

We conduct several sensitivity analyses to assess the robustness of our results to data and modeling choices.

- First, we repeat all the analyses using alternative methods to estimate exposure to PM$_{2.5}$.[26]

- Second, because our study relies on observational data, our results could be sensitive to modeling choices (e.g., distributional assumptions or assumptions of linearity). We evaluate sensitivity to such choices by conducting analyses:

  ○ Treating PM$_{2.5}$ as a categorical variable (categorized at empirical quintiles)

  ○ Adjusting for population density as a categorical variable (categorized at empirical quintiles)

  ○ Using a negative binomial model without accounting for zero-inflation.

Results for the sensitivity analyses are shown in Supplementary Materials.

Results

Our study utilized data from 3,080 counties, of which 2,395 (77.8%) have reported zero COVID-19 deaths at the time of this analysis. **Table 2** describes the data used in our analyses. All COVID-19 death counts are cumulative counts up to April 4, 2020.

Figure 1 visualizes the spatial variation of long-term average exposure to PM$_{2.5}$ and COVID-19 death rates (per 1 million population) by county. Visual inspection suggests that COVID-19 death rates are higher in the Mid-Atlantic, upper Midwest, gulf coast, and west coast regions. These spatial patterns in COVID-19 death rates generally mimic patterns in both high population density and high PM$_{2.5}$ exposure areas. In the Supplementary Materials, we provide additional visualizations and data diagnostics that justify the use of the ZNB model for our analyses. After

removal of counties with missing confounder values, our main analysis was conducted using 1,783 counties. These counties account for 90% of COVID-19 deaths up to April 4, 2020. In **Figure 2** we report the mortality rate ratios (MRR) and 95% CI for our main and secondary analyses. The results of all sensitivity analyses are shown in the Supplementary Materials. In the main analysis, the estimated MRR is 1.15 (1.05, 1.25). That is, we found that an increase of only 1 μg/m^3 in long-term average PM$_{2.5}$ is associated with a statistically significant increase of 15% in the COVID-19 death rate. This suggests that in New York County (Manhattan) if we were to lower the long-term average PM$_{2.5}$ exposure by only 1 μg/m^3, we would have expected to see 248 ($= 1905 \times (1 - 1/1.15)$) fewer COVID-19 deaths among a total of 1905 deaths up to April 04, 2020.

In secondary analyses shown in **Figure 2**, we (a) omit number of hospital beds from the adjustment set (b) omit number of tested cases in each state from the adjustment set (c) omit smoking rate and BMI from Behavioral Risk Factor Surveillance System (BRFSS) from the adjustment set (d) omit summer and winter temperature and relative humidity from the adjustment set (e) exclude data from New York state (f) exclude counties with less than 10 confirmed COVID-19 cases. The results of these analyses are consistent with the main analysis, except when the number of hospital beds is omitted from the adjustment set. In that case, the point estimate decreases, and statistical significance is attenuated. This suggests that number of hospital beds is a strong confounder.

Discussion

This is the first nationwide study in the United States that estimates the relationship between long-term exposure to PM$_{2.5}$ and COVID-19 death rates. We found statistically significant evidence that an increase of 1 μg/m^3 in long-term PM$_{2.5}$ exposure is associated with a 15% increase in the COVID-19 mortality rate. Our results are adjusted for a large set of

socioeconomic, demographic, weather, behavioral, and healthcare-related confounders and demonstrated robustness across a wide range of sensitivity analyses.

In our previous study[27] of 60 million Americans older than 65 years, we found that a of 1 mg/m3 in long-term $PM_{2.5}$ exposure is associated with a 0.73% increase in the rate of all-cause mortality. Therefore, a small increase in long-term exposure to $PM_{2.5}$ leads to a large increase in COVID-19 death rate of a magnitude that is 20 times the one estimated for all-cause mortality.

This analysis provides a timely characterization of the relationship between historical exposure to air pollution COVID-19 deaths in the United States. Research on how modifiable factors may exacerbate COVID-19 symptoms and increase mortality risk is essential to guide policies and behaviors to minimize fatality related to the outbreak. Our analysis relies on up-to-date population-level COVID-19 data and well-validated air pollution exposure measures.[27]

Strengths of this analysis include adjusting for a wide range of potential confounders and a demonstrated robustness of results to different model choices. Moreover, the analyses rely exclusively on data and code that are publicly available. This provides a platform for the scientific community to continue updating and expanding these analyses as the pandemic evolves, and data accumulate.

The inability to accurately quantify the number of COVID-19 cases due to limited testing capacity presents a potential limitation in that we are unable to fully adjust for the size of the outbreak in a given county, which could be a source of unmeasured confounding. We instead adjust by total population size. However, we anticipate that by using a zero-inflated model we provide partial adjustment for this, as we estimate the MRR accounting for the fact that some counties were not eligible to experience a COVID-19 death because they still had zero

confirmed cases. Moreover, the constantly evolving COVID-19 response measures creates a fluid scenario with regards to the availability of medical resources in a given area. The availability of these resources is likely to impact fatality rates. Because real-time, nationwide data on such measures and resources are not available, we are unable to adjust for this feature. As a result, this could represent another source of confounding.

The results of this paper suggest that long-term exposure to air pollution increases vulnerability to experiencing the most severe COVID-19 outcomes. These findings align with the known relationship between $PM_{2.5}$ exposure and many of the cardiovascular and respiratory comorbidities that dramatically increase the risk of death in COVID-19 patients. They are also consistent with findings that air pollution exposure dramatically increased the risk of death during the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003, which is caused by another type of coronavirus.[28] This study provides a motive for expanded follow-up investigations as more and higher quality COVID-19 data become available. These would include validating these results in other data sources and study types and studies of biological mechanisms, impacts of $PM_{2.5}$ exposure timing, and relationships between $PM_{2.5}$ and other COVID-19 outcomes such as hospitalization.

The results of this study also underscore the importance of continuing to enforce existing air pollution regulations during the COVID-19 crisis. Based on our result, we anticipate a failure to do so can potentially increase the COVID-19 death toll and hospitalizations, further burdening our healthcare system and drawing resources away from COVID-19 patients.

Table 1: Data Sources used in the analysis (all publicly available)

|	Source	Data
Outcome: COVID-19 Deaths	Johns Hopkins University the Center for Systems Science and Engineering (CSSE) Coronavirus Resource Center (https://coronavirus.jhu.edu/)	County level COVID-19 death count up to and including April 4, 2020
Exposure: PM$_{2.5}$ concentrations	Atmospheric Composition Analysis Group (http://fizz.phys.dal.ca/~atmos/martin)	0.01° × 0.01° grid resolution PM$_{2.5}$ prediction, averaged across the period 2000-2016 and averaged across grid cells in each county
Confounders	US Census/American Community Survey (https://www.census.gov/programs-surveys/acs/data.html)	County level socioeconomic and demographic variables for 2012-2016 American Community Survey
	US CDC BRFSS (https://www.cdc.gov/brfss/)	County level behavioral risk factor variables for 2011 (most recent year with county-level data available)
	Homeland Infrastructure Foundation-Level Data (HIFLD) (https://hifld-geoplatform.opendata.arcgis.com/datasets/hospitals)	County level number of hospital beds in 2019
	The COVID tracking project (https://covidtracking.com/)	State level number of COVID-19 tests performed up to and including April 4, 2020
	Gridmet via google earth engine https://developers.google.com/earth-engine/datasets/catalog/IDAHO_EPSCOR_GRIDMET)	4km × 4km temperature and relative humidity predictions, summer and winter averaged across the period 2000-2016 and averaged across grid cells in each county.

Table 2: Characteristics for the Study Cohort up to and including April 04, 2020

| Variable	Entire Cohort (3080 counties)	Exclude NY State (3018 counties)	Exclude County < 10 Cases (1047 counties)	With HIFLD available (2272 counties)	With BRFSS available (2214 counties)

Number of deaths	7,054	4,662	6,968	6,342	7,024
Number of hospital beds	827,799	770,716	706,051	827,799	811,070
Number of testing (State level)	1,620,460	1,336,839			
$PM_{2.5}$ ($\mu g/m^3$) (SD, standard deviation)	8.4 (2.5)	8.4 (2.5)	9.5 (2.3)	8.5 (2.5)	9.0 (2.3)
County level risk factors characteristics (SD)					
% Ever smoked	47.0 (9.2)	47.0 (9.2)	45.9 (8.0)	46.8 (8.9)	47.0 (9.2)
Mean BMI (kg/m^2)	28.1 (1.3)	28.1 (1.3)	27.9 (1.1)	28.1 (1.3)	28.1 (1.3)
% Below poverty level	10.5 (5.7)	10.6 (5.7)	9.7 (4.7)	10.3 (5.3)	10.3 (5.1)
% Below high school	21.2 (10.5)	21.3 (10.5)	19.5 (8.6)	20.6 (9.8)	21.4 (9.7)

education					
% Owner-occupied housing	74.2 (8.9)	74.2 (8.8)	70.1 (10.3)	74.1 (9.0)	73.4 (9.1)
% Hispanic	7.7 (12.3)	7.7 (12.4)	8.6 (11.3)	7.3 (11.4)	7.5 (11.5)
% Black	8.2 (14.2)	8.3 (14.3)	12.1 (15.4)	8.0 (13.6)	9.2 (13.9)
% older than 65 year-old	15.9 (4.1)	16.0 (4.1)	13.7 (3.6)	15.8 (4.0)	14.9 (3.5)
Population density (persons/mile^2)	446.0 (2121.62)	377.4 (1162.27)	1044.7 (2854.5)	514.1 (2384.8)	608.3 (2479.9)
Median household income (1000 $)	49.0 (13.1)	48.8 (13.0)	54.7 (15.6)	49.6 (12.7)	50.1 (13.6)
Median home value (1000 $)	136.6 (90.5)	135.2 (87.9)	179.8 (114.7)	134.7 (80.4)	148.8 (94.5)
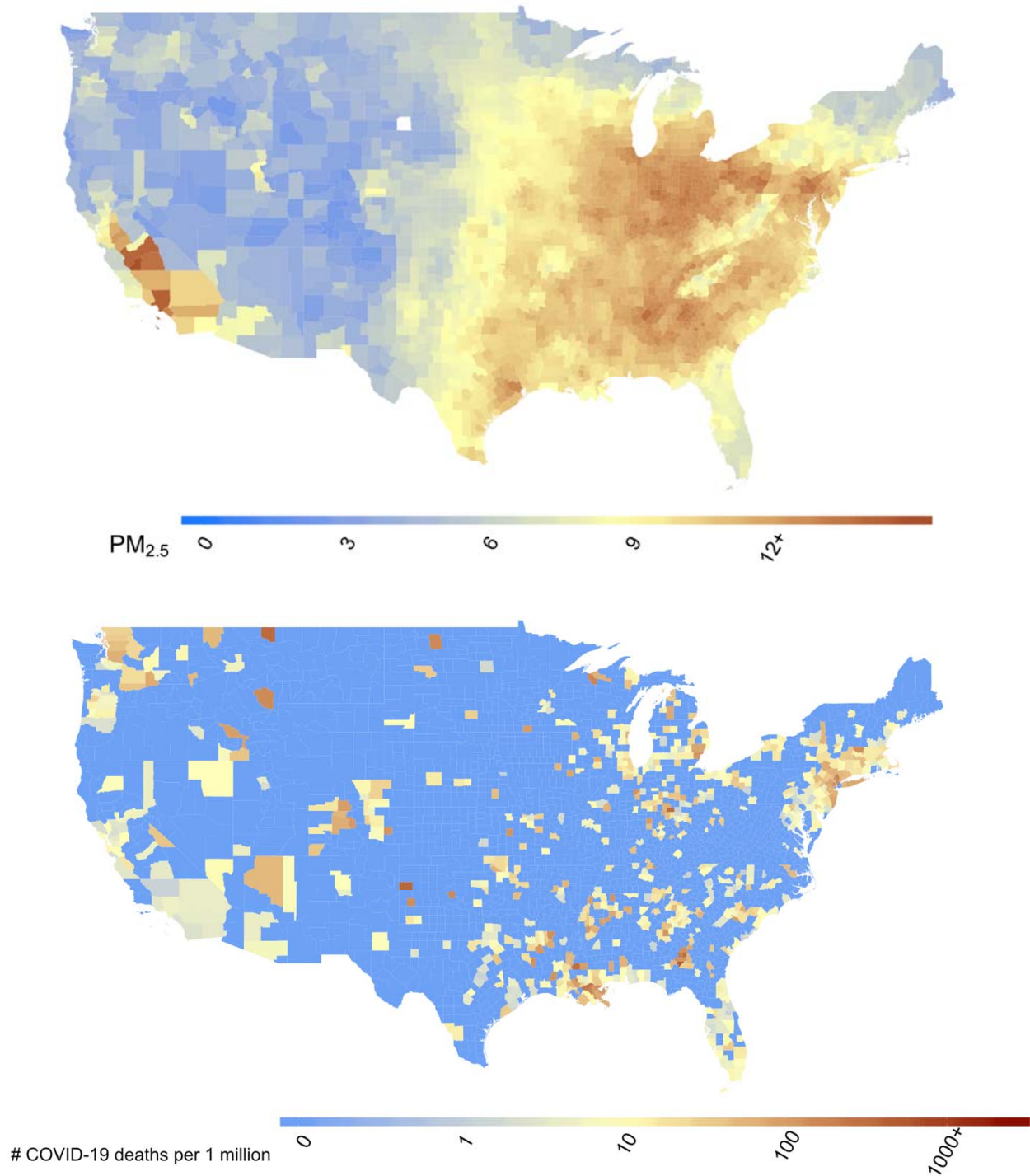
Figure 1: Maps show **(a)** county level 17-year long-term average of $PM_{2.5}$ concentrations (2000-2016) in the US in μg/m³ and **(b)** county level number of COVID-19 deaths per one million population in the US up to and including April 4, 2020.
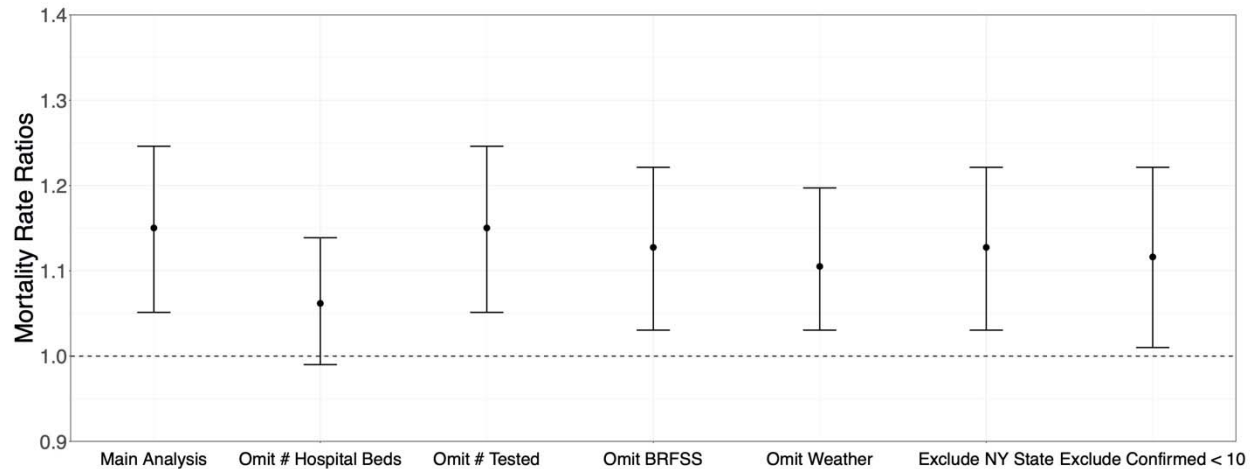
Figure 2: Mortality Risk Ratios (MRR) and 95% confidence intervals. The MRR can be interpreted as percentage increase in the COVID-19 death rate associated with a 1 μg/m^3 increase in long term average PM$_{2.5}$. The MRR from the main analysis is adjusted by seventeen potential confounders (population density, percent of the population >65, percent living in poverty, median household income, percent black, percent Hispanic, percent of the adult population with less than a high school education, median house value, percent of owner-occupied housing, population mean BMI, percent ever-smokers, summer/winter temperature/relative humidity, and number of hospital beds for each county, and number of COVID-19 tests performed for each state). In secondary analyses, we (a) omit number of hospital beds; (b) omit number of tested cases in each state; (c) omit smoking rate and BMI from BRFSS; (d) omit summer/winter temperature/relative humidity; (e) exclude data from New York state; (f) exclude data from counties with less than 10 confirmed cases. All COVID-19 death counts are cumulative counts up to and including April 04, 2020.

References

1. Wei-jie Guan, Ph.D., Zheng-yi Ni, M.D., Yu Hu, M.D., Wen-hua Liang, Ph.D., Chun-quan Ou, Ph.D., Jian-xing He, M.D., Lei Liu, M.D., Hong Shan, M.D., Chun-liang Lei, M.D., David S.C. Hui, M.D., Bin Du, M.D., Lan-juan Li, M.D., et al. for the China Medical Treatment Expert Group for Covid-19. NEJM. 2020 DOI: 10.1056/NEJMoa2002032. (https://www.nejm.org/doi/full/10.1056/NEJMoa2002032)

2. Wu, J.T., Leung, K., Bushman, M. *et al.* Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nat Med* (2020). (https://www.nature.com/articles/s41591-020-0822-7)

3. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. MMWR Morb Mortal Wkly Rep 2020;69:343-346. DOI: (http://dx.doi.org/10.15585/mmwr.mm6912e)

4. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) (https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf)

5. Diamond M, Peniston Feliciano HL, Sanghavi D, et al. Acute Respiratory Distress Syndrome (ARDS) [Updated 2020 Jan 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK436002/.

6. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 — United States, February 12–March 28, 2020. MMWR Morb Mortal Wkly Rep 2020;69:382–386. DOI: (http://dx.doi.org/10.15585/mmwr.mm6913e)

7. https://www.stateofglobalair.org/report

8. Brook RD, Franklin B, Cascio W et al. Air pollution and cardiovascular disease: a statement for healthcare professionals from the Expert Panel on Population and Prevention Science of the American Heart Association. Circulation. 2004;109(21):2655-71.

9. Di Q, Wang Y, Zanobetti A et al. Air pollution and mortality in the Medicare population. NEJM. 2017;376(26):2513-22.

10. Puett RC, Hart JE, Yanosky JD et al. Chronic fine and coarse particulate exposure, mortality, and coronary heart disease in the Nurses' Health Study. EHP. 2009;117(11):1697-701.

11. Dominici F, Peng R, Bell M et al. Fine particulate air pollution and hospital admission for cardiovascular and respiratory diseases. JAMA. 2006;295(10):1127–34.

12. Wellenius G. Ambient air pollution and the risk of acute ischemic stroke. Arch Intern Med. 2012;172(3):229–34.

13. Radim J. Šrám, Blanka Binková, Jan Dejmek, and Martin Bobak. Ambient Air Pollution and Pregnancy Outcomes: A Review of the Literature. Vol. 113, No. 1 April 2005 (https://doi.org/10.1289/ehp.6362)

14. Rhee, Jongeun et al. Impact of Long-Term Exposures to Ambient $PM_{2.5}$ and Ozone on ARDS Risk for Older Adults in the United States CHEST, Volume 156, Issue 1, 71 - 79 (https://journal.chestnet.org/article/S0012-3692(19)30711-1/abstract)

15. U.S. EPA. Integrated Science Assessment (ISA) for Particulate Matter (Final Report, 2019). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-19/188, 2019.

16. Zanobetti A, Dominici F, Wang Y, Schwartz JD. (2014). A national case-crossover analysis of the short-term effect of PM2.5 on hospitalizations and mortality in subjects with diabetes and neurological disorders. Environmental Health, 13(1):38. PMCID: PMC4064518.

17. Kioumourtzoglou MA, Schwartz J, Weisskopf M, Melly S, Wang Y, Dominici F, Zanobetti (2016) Long-term PM2.5 exposure and neurological hospital admissions in the Northeastern United States. Environmental Health Perspectives, 124(1):23-9. PMCID: PMC4710596.

18. Di Q, Wang Y, Zanobetti A, Wang Y, Koutrakis P, Dominici F, Schwartz J. (2017). Air Pollution and Mortality in the Medicare Population. New England Journal of Medicine, 376:2513-2522, June 29, 2017. PMID: 29020593 DOI: 10.1056/NEJMoa1702747 PMCID: 5766848.

19. Van Donkelaar A, Martin RV, Li C, Burnett RT. Regional estimates of chemical com-position of fine particulate matter using a combined geoscience-statistical method with information from satellites, models, and monitors. Environmental science & technology. 2019;53(5):2595–2611.

20. https://coronavirus.jhu.edu

21. Van Donkelaar A, Martin RV, Li C, Burnett RT. Regional estimates of chemical com-position of fine particulate matter using a combined geoscience-statistical method with information

from satellites, models, and monitors. Environmental science &

technology.2019;53(5):2595–2611.

22. Venables, W. N. and Ripley, B. D. (2002) "Modern Applied Statistics with S". Fourth edition.

Springer.

23. Xinyan Zhang, Himel Mallick, Xiangqin Cui, Andrew K. Benson, and Nengjun Yi (2017)

Negative Binomial Mixed Models for Analyzing Microbiome Count Data. BMC Bioinformatics

18(1):4.

24. https://rdrr.io/github/nyiuab/NBZIMM/man/glmm.zinb.html

25. Zhang, X., Mallick, H., Tang, Z., Zhang, L., Cui, X., Benson, A.K. and Yi, N., 2017. Negative

binomial mixed models for analyzing microbiome count data. BMC bioinformatics, 18(1), p.4.

26. Di Q, Amini H, Shi L, et al. An ensemble-based model of PM2.5 concentration across the

contiguous United States with high spatiotemporal resolution. Environ Int 2019; 130:

104909.

27. http://fizz.phys.dal.ca/~atmos/martin/?page_id=140