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Ambient PM$_{2.5}$ exposure and rapid spread of COVID-19 in the United States

Rajan K. Chakrabarty$^{a,b,*}$, Payton Beeler$^{a,1}$, Pai Liu$^{a,1}$, Spondita Goswami$^c$, Richard D. Harvey$^c$, Shamsh Pervez$^d$, Aaron van Donkelaar$^{a,c}$, Randall V. Martin$^a$

$^a$ Center for Aerosol Science and Engineering, Department of Energy, Environmental and Chemical Engineering, Washington University in St. Louis, St. Louis, MO 63130, USA

$^b$ Institute for Public Health, Washington University in St. Louis, St. Louis, MO 63130, USA

$^c$ Experimental Psychology Program, Department of Psychology, Saint Louis University, St. Louis, MO 63108, USA

$^d$ School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh 492010, India

$^e$ Department of Physics and Atmospheric Science, Dalhousie University, Halifax, NS B3H 4R2, Canada

HIGHLIGHTS

• Long-term air pollution renders a population more susceptible to COVID-19.
• Exposure to PM$_{2.5}$ associates with COVID-19 basic reproduction ratio ($R_0$) in the US.
• $R_0$ and PM$_{2.5}$ association is prominent for PM$_{2.5}$ concentrations below NAAQS standard.
• Secondary inorganic composition in PM$_{2.5}$ impacts $R_0$ significantly.
• Black carbon (soot) moderates the relation between secondary inorganic composition and $R_0$.

GRAPHICAL ABSTRACT

ABSTRACT

It has been posited that populations being exposed to long-term air pollution are more susceptible to COVID-19. Evidence is emerging that long-term exposure to ambient PM$_{2.5}$ (particulate matter with aerodynamic diameter 2.5 μm or less) associates with higher COVID-19 mortality rates, but whether it also associates with the speed at which the disease is capable of spreading in a population is unknown. Here, we establish the association between long-term exposure to ambient PM$_{2.5}$ in the United States (US) and COVID-19 basic reproduction ratio ($R_0$), a dimensionless epidemic measure of the rapidity of disease spread through a population. We inferred state-level $R_0$ values using a state-of-the-art susceptible, exposed, infected, and recovered (SEIR) model initialized with COVID-19 epidemiological data corresponding to the period March 2–April 30. This period was characterized by a rapid surge in COVID-19 cases across the US states, implementation of strict social distancing measures, and a significant drop in outdoor air pollution. We find that an increase of 1 μg/m$^3$ in PM$_{2.5}$ levels below current national ambient air quality standards associates with an increase of 0.25 in $R_0$ (95% CI: 0.048–0.447). A 10% increase in secondary inorganic composition, sulfate-nitrate-ammonium, in PM$_{2.5}$ associates with ≈10% increase in $R_0$ by 0.22 (95% CI: 0.083–0.352), and presence of black carbon (soot) in the ambient environment moderates this relationship. We considered several potential confounding factors in our analysis, including gaseous air pollutants.

* Corresponding author at: Center for Aerosol Science and Engineering, Department of Energy, Environmental and Chemical Engineering, Washington University in St. Louis, St. Louis, MO 63130, USA.

E-mail address: chakrabarty@wustl.edu (R.K. Chakrabarty).

1 These authors contributed equally.
1. Introduction

In December 2019, a new strain of coronavirus, SARS-CoV-2, began infecting residents of Wuhan Province, China (Chinazzi et al., 2020; Li et al., 2020b; Wu et al., 2020a; Xu et al., 2020). In the following months, the disease caused by SARS-CoV-2 – coronavirus disease 2019 (COVID-19) – has spread to nearly every country around the globe, and the situation had rapidly evolved into a global pandemic (Chinazzi et al., 2020; Gilbert et al., 2020). The viral entry of SARS-CoV-2 has been shown to use Angiotensin-converting enzyme 2 (ACE2) as its co-host receptor (Wan et al., 2020). ACE2 plays a crucial role in lung protection by cleaving and converting angiotensin II (Ang II) to the cardioprotective angiotensin 1–7 (Ang 1–7) (Tikellis and Thomas, 2012). Clinical observations of COVID-19 patients (Guan et al., 2020) suggest a mechanism involving viral loads of SARS-CoV-2 depleting residual ACE2 activity and impairing host defenses. This causes an imbalance between Ang II and Ang 1–7, resulting in high circulating levels of Ang II, which induces pulmonary vasoconstriction, inflammation, and oxidative stress (Deroiuch, 2020). Consequently, depleted lungs, typically in the form of acute lung injury or its most serious form, acute respiratory distress syndrome, manifest in patients with COVID-19 (Li et al., 2020a).

A recent study by Italian medical researchers posited a causal link between SARS-CoV-2 infection rate and long-term air pollution exposure in a population (Frontera et al., 2020). They postulated a “double-hit phenomenon”: patients chronically exposed to high levels of fine particulate matter (PM$_{2.5}$; particulate matter with aerodynamic diameter 2.5 μm or less) present themselves with an overexpression of ACE2 (Lin et al., 2018), which readily facilitates penetration of the viral infection. This in turn depletes ACE2 receptors and gives rise to more severe forms of the disease. Subsequently, the spread of the disease accelerates among the population. Exposure to PM$_{2.5}$ has a well-established association with increased risks and severe outcomes during infectious disease outbreaks, including COVID-19, the 2009 H1N1, and the 1918 Spanish influenza pandemics (Clay et al., 2018; Clay et al., 2019; Morales et al., 2017; Wu et al., 2020b). Exposure to PM$_{2.5}$ has been causally linked to occurrences of chronic respiratory disease, infectious respiratory disease, asthma, inflammation, and decreased lung function (Zhou et al., 2020). Recent studies have have strongly associated COVID-19 mortality with long-term air pollution exposure in the US (Wu et al., 2020b), as well as identifying that long-term meteorological and climatic variables play a minor role in comparison to the amount of susceptible population for confounding factors in our analysis including gaseous air pollutants, meteorological variables, race, population density, age distribution, hospital and ICU beds, median household size and income, and time delay in state’s issuance of stay-at-home orders (Wu et al., 2020b).

2. Methods

2.1. Inference of the COVID-19 basic reproduction ratio

We inferred state-wise $R_0$ values by fitting the prediction of a susceptible-exposed-infected–infected–recovered (SEIR) model (Li et al., 2020c; Liu et al., 2020a) to confirmed COVID-19 cases (Dong et al., 2020). Our epidemic model accounts for the age-stratified disease transmissibility (Wallinga et al., 2006), and possible large-scale undocumented transmission (Li et al., 2020c) of COVID-19 in the US. The detailed model structure and parameterization follow that outlined in recent publications (Li et al., 2020c; Liu et al., 2020a), except that here we neglected the influence of interstate mobility of COVID-19 carriers on long-term disease progression, considering the rapid decline in domestic traffic after the nationwide implementation of stay-at-home orders. The inference timespan was set between March 02 and April 30 (coinciding the nationwide social distancing period), so as to minimize the influences of other human behaviors and social activities on epidemic dynamics. The daily number of confirmed COVID-19 cases was acquired from a real-time epidemic tracking dashboard published by Johns Hopkins University (Dong et al., 2020).

The fitting procedure can be described as such: First, the daily number of state-wise confirmed-and-active COVID-19 cases (Dong et al., 2020) was tracked and recorded, which can be written as a time-series $S_n(t)$ (subscript $n$ denotes each US state, superscript $t$ indicates “reported”, and $t$ is time incrementing with a unit of days between March 02 and April 30). Next, the SEIR prediction was fitted with the ground truth using twenty consecutive days of epidemic size data. Specifically, we took twenty consecutive elements from the $S_n(t)$ time series and used an established epidemiological parameter $R_0$, the basic reproduction ratio, to estimate the transmission dynamics. This in turn depletes ACE2 receptors and gives rise to more severe forms of the disease. Subsequently, the spread of the disease accelerates among the population. Exposure to PM$_{2.5}$ has a well-established association with increased risks and severe outcomes during infectious disease outbreaks, including COVID-19, the 2009 H1N1, and the 1918 Spanish influenza pandemics (Clay et al., 2018; Clay et al., 2019; Morales et al., 2017; Wu et al., 2020b). Exposure to PM$_{2.5}$ has been causally linked to occurrences of chronic respiratory disease, infectious respiratory disease, asthma, inflammation, and decreased lung function (Zhou et al., 2020). Recent studies have have strongly associated COVID-19 mortality with long-term air pollution exposure in the US (Wu et al., 2020b), as well as identifying that long-term meteorological and climatic variables play a minor role in comparison to the amount of susceptible population for confounding factors in our analysis including gaseous air pollutants, meteorological variables, race, population density, age distribution, hospital and ICU beds, median household size and income, and time delay in state’s issuance of stay-at-home orders (Wu et al., 2020b).
series, generating a “minibatch” written as $\hat{x}_i^j(t_i)$. Here, $t_i$ is defined as an initial date. A total of 41 minibatches can be generated, where $i$ increments between 1 and 41. For each minibatch $\hat{x}_i^j(t_i) : t_i + 19$, we initialize the SEIR model with $\hat{x}_i^j(t_i)$, and then the model guessed a value for $R_0$ and predicted the epidemic trends on the following nineteen days, written as $\hat{f}_i^j(t_i) : t_i + 19$. The values of $R_0$ were inferred in a trial-and-error manner, by minimizing the root-mean-square-error between $\hat{f}_i^j(t_i) : t_i + 19$ and $\hat{x}_i^j(t_i) : t_i + 19$. This process can be formally written as:

$$\arg\min_{R_0, n, t} \| \hat{f}_i^j(t_i) : t_i + 19 | R_0, n, t, \eta, \xi, \epsilon \|_2^2 .$$

(1)

Here, $R_0, n, t$ represents the basic reproduction ratio values inferred for state $n$ within the timespan between $t_i$ and $t_i + 19$, respectively. $\eta, \xi, \epsilon$ denotes the unknown documentation ratio and exposure ratio, which were simultaneously inferred along with $R_0, n, t$. Finally, for each state $n$, we calculated a time-averaged reproduction ratio $R_{0,n}$ by taking the arithmetic mean values of the $R_0, n, t$, series.

2.2. Acquisition of PM2.5 exposure profiles

We calculated the state-level long-term (averaged between 2012 and 2017) PM2.5 exposure profiles using recently published datasets (Van Donkelaar et al., 2019). The PM2.5 exposure levels were estimated monthly across the entire continental United States by combining observations from ground-based monitors, GEOS-Chem model outputs, and satellite observations. The original dataset provides annually-resolved PM2.5 mass concentration, along with the fraction of constituent species, as functions of geographic coordinates at a grid resolution of 0.01° x 0.01° (Van Donkelaar et al., 2019). This spatiotemporal distribution can be written as $\hat{x}_n,k,year(x, latitude, longitude, year)$, where $x$ generically denotes PM2.5 concentration or composition. Next, we labelled each data point $x_p$ per the state $n$ wherein $x$ resides, such as $x_n,k,year \approx \hat{x}_n,k,year(x_p)$, where $k$ denotes the kth point residing within state $n$. Then we aggregated and averaged PM2.5 exposure profile within each $n$, and obtained the state-level yearly-resolved dataset, $X_n,year = K^{-1} \sum_{k=1}^{K} x_n,k,year$, where $K$ is the total number of data points residing in state $n$.

We examine association between long-term state-level PM2.5 exposure $x$ and the state-wise COVID-19 transmissibility $R_0$. The correlation between $x$ and $R_0$ was quantified with the widely-adopted GAM model (Wood, 2001; Zhang et al., 2019). The core function used in the GAM can be expressed as:

$$R_0 = b + s(x, df = 4) + \epsilon,$$

(2)

where $b$ denotes a constant intercept; $s(\cdot)$ denotes a thin-plate basis smooth function; $\epsilon$ denotes a zero centered Gaussian noise; $df$ stands for degrees of freedom, and $df = 4$ was chosen because no high-level of nonlinearity was observed in the data trends. The restricted maximum likelihood method was adopted in the optimization to prevent overfitting. The GAM fitting and analysis were conducted using R software and the “mgcv-1.8-31” package.

2.4. Moderation analysis

We used the Johnson-Neyman technique to investigate two-way interactions between PM2.5 composition and their effect on $R_0$. The Johnson-Neyman technique allows one to investigate the size of effect that an independent “predictor” variable has on the dependent “response” variable (in this case $R_0$), given the value of a second “moderating” variable (Carden et al., 2017). Details on the Johnson-Neyman technique can be found in the work by Carden et al. (Carden et al., 2017) When the moderating variable has a statistically significant effect on the relationship between the predictor and the response variable, there is said to be a two-way interaction between the predictor and moderating variable (Carden et al., 2017).
PM$_{2.5}$ as a whole, that is, SNA denotes the summation of the fraction of each individual species.

We next quantitatively establish the link between $R_0$ and the composition-specific PM$_{2.5}$ exposure by fitting the GAM (Wood, 2001; Zhang et al., 2019). Fig. 2 shows the output of GAM with PM$_{2.5}$ concentration and SNA fraction as the input. Panel (a) again shows that the relationship between $R_0$ and PM$_{2.5}$ concentration demonstrates a "two-regime" behavior: First, when PM$_{2.5}$ concentration is below 6 μg/m$^3$, a rapid increase in $R_0$ can be observed along with increasing PM$_{2.5}$ concentration; This increasing trend slows down upon reaching its plateau (at PM$_{2.5}$ concentration ≈ 6 μg/m$^3$). A spline analysis shows that a 1.0 μg/m$^3$ increase in PM$_{2.5}$ concentration was associated with increase in $R_0$ by 0.310 (95% CI: 0.088–0.532) and 0.190 (95% CI: 0.062–0.317), when PM$_{2.5}$ concentration ∈ (2, 4) μg/m$^3$ and ∈ (4, 6) μg/m$^3$, respectively. When PM$_{2.5}$ concentration > 6 μg/m$^3$, the increasing trend starts to reach its plateau, and the correlation becomes statistically insignificant. Panel (b) shows that the positive relationship between $R_0$ and SNA fraction takes up a near linear functionality. Throughout the entire range of SNA fraction, a 10% increase in SNA fraction associates with an increase in $R_0$ by 0.218 (95% CI: 0.083–0.352). The GAM analysis on the $R_0$-BC fraction and $R_0$-OM fraction correlation can be found in the Supplementary materials (Fig. S1).

Fig. 3 shows the results of Johnson-Neyman analysis (Carden et al., 2017), where SNA fraction is the predictor variable and BC fraction is the moderating variable. These results indicate that the direct relationship between SNA fraction and $R_0$ is dependent on BC fraction. Fig. 3(a) shows the value of $R_0$ as a function of SNA fraction and BC fraction. Fig. 3 shows that in areas where a large portion of PM$_{2.5}$ is made up of SNA, an increase in BC fraction leads to an increase in $R_0$. However, if SNA makes up a smaller portion of PM$_{2.5}$, an increase in BC fraction leads to a decrease in $R_0$. Alternatively, as BC fraction increases, the positive relationship between $R_0$ and SNA fraction becomes more prominent. Fig. 3(b) elaborates on this phenomenon by plotting the $R_0$ gradient value along the direction of changing BC fraction. This result shows that for SNA fraction greater than 38.8%, a 1% increase in BC fraction leads to an increase in $R_0$ (upper and lower 95% CI are given by grey shaded region). State-wise population density also weakly moderated the association between $R_0$ – PM$_{2.5}$ and $R_0$ – SNA fraction, respectively (see Fig. S2 in Supplementary information).

Given that we find both population density and SNA fraction to be highly correlated with $R_0$, a logical argument might arise regarding the relation of $R_0$ with SNA simply being a compositional surrogate for population density. Especially since SNA aerosol precursors are closely linked to urbanization, one might argue that it is difficult to delineate the effect of SNA fraction and population density on $R_0$. We aim to address this concern and strengthen our argument by citing specific examples wherein confounding relationship of $R_0$ with population density and SNA with population density do not hold valid. A justified comparison would be between Alabama and Louisiana, two states that are similar climatically, socioeconomically, and demographically (see Table S11). In comparing these states, we find that their population densities differ by only 1.04%, but Louisiana has 5% higher fraction of SNA. Despite their similarity in population density, $R_0$ in Louisiana is 20.7% higher than Alabama. This example shows that when comparing two states that differ only in SNA fraction, the positive association between SNA fraction and $R_0$ still holds.

4. Discussion

To the best of our knowledge, this is the first nationwide study to estimate the relationship between long-term exposure to PM$_{2.5}$ and the
rapidity of COVID-19 spread in the US. Up to 6 μg/m³ PM2.5 ambient concentrations, which is below current regulatory standards (EPA, 2019), we find that a 1.0 μg/m³ increment in long-term exposure associates with a 0.25 increase in \( R_0 \). Short-term exposure due to outdoor air pollution dropped significantly during the months of March and April in the US (Tanzer-Gruener et al., 2020), yet our findings suggest that long-term exposure to pollutants had rendered the nationwide population susceptible to the virus spread. Although our study design cannot provide insights into potential biological mechanisms, the results indicate that long-term exposure to fine particulate matter air pollution increases COVID-19 spread plausibly via the “double hit phenomenon” (Frontera et al., 2020).

Our observation of a high degree of association between long-term exposure to low ambient PM2.5 and \( R_0 \) has major policy implications.
The 2019 policy assessment review for the PM2.5 National Ambient Air Quality Standards (NAAQS) in the US recommended a revision to the annual PM2.5 concentration standards from 12 μg/m³ to 9 μg/m³ (EPA, 2019). This recommendation was primarily guided by general observations of positive and statistically significant health effect associations for PM2.5 air quality distributions characterized by overall mean (or median) concentrations at or above 9.6 μg/m³ (EPA, 2019). It is noteworthy to recognize the limitations of these approaches—epidemiologic studies evaluate associations between distributions of ambient PM2.5 and health outcomes and do not necessarily identify the specific exposures that caused reported effects. In reality, associated health effects and risk factors could occur over the entire distribution of ambient PM2.5 concentrations evaluated, and past studies have not necessarily identified a population level threshold below which PM-associated health effects cease to occur. Thus, our findings contribute to the growing body of evidence of PM2.5 concentration-response relationships near the lower end of the PM2.5 air quality distribution by providing new evidence of a relationship of PM2.5 with \( R_0 \) at levels below the current NAAQS (Dirgawati et al., 2019; Makar et al., 2017; Pinault et al., 2016).

With respect to PM2.5 composition, we find a 10% increase in sulfate-nitrate-ammonium (SNA) ionic fractions to be associated with a 0.218 (≈10%) increase in \( R_0 \) (95% CI: 0.083–0.352). This strong association of \( R_0 \) with secondary inorganic fraction in PM2.5, which could be modulated in the presence of BC aerosol, highlight the long-term health risks associated with combustion emissions by fossil fuels (EPA, 2019). The formation pathways of secondary inorganic aerosol in the atmosphere involve the photochemical oxidation of gaseous sulfur dioxide (SO₂) and nitrogen dioxide (NO₂), both of which are predominantly emitted from coal-fired power plants and vehicles. While the oxidation chemistry of NO₂ to form nitric acid (HNO₃) is relatively straightforward, partitioning of nitrate to sol phase depends on a number of factors including temperature (Kroll et al., 2020). NO₂ has also been shown to accelerate the oxidation of SO₂ to form sulfates (Wang et al., 2020). Not surprisingly, this study finds a positive correlation between \( R_0 \) and NO₂ emissions and annual temperature variations, respectively (see Supplementary material Table S10). Although decades of strict air quality regulations in the US have resulted in significant reductions of NO₂ levels (Kroll et al., 2020), recent reversal of environmental regulations which weaken limits on gaseous emissions from power plants and vehicles threaten the country’s future air quality scenario (Pulido et al., 2019).

We consider it important to acknowledge the limitations of this study. First, the robustness of our model prediction could be limited by the coarse-grain spatial representation of model variables, such as the PM2.5 exposure profile and \( R_0 \). County-level distribution of PM2.5 composition and \( R_0 \) values are readily washed away upon averaging the data points residing within the state boundaries. Based on past findings (Crouse et al., 2020), we anticipate a county-level analysis will not alter the nature of the relationship established between the variables in this study, although the strength of their associations might vary. The inherent ability to accurately quantify the number of COVID-19 cases due to limited testing capacity during the March–April timeframe presents another potential limitation. The large uncertainty represented by the shaded area in Fig. 3 suggests that the variation in \( R_0 \) is not fully accounted for by the PM2.5 exposure profile. Caution must be taken when extrapolating results from this study to generalize the virus spread in other countries and drive public health responses. The basic reproduction ratio is a complex property of an epidemic and is highly sensitive to the underlying model used to estimate it, the specific population demographic, and time period of study (Ridenhour et al., 2018).

Future analysis should include COVID-19 epidemic parameters and PM2.5 exposure data at finer-grain levels, e.g. county-level (Wu et al., 2020b). Research on disproportionate impacts of air pollution on at-risk populations, including minority populations and populations with lower socioeconomic status, during the epidemic is another understudied area. Synergistic analysis of air quality and population demographic information suggest that the highest PM2.5 concentrations in a given area tended to be measured at locations where populations lived or were more likely to be below the poverty line and constituted larger percentages of racial and ethnic minorities. Last but not least, the design limitations of this study calls for detailed research on biological mechanisms responsible for the observed associations.

Data availability

The epidemiological COVID-19 data used in this study can be accessed at https://github.com/pliu1991/COVID19PM25_supporting_data_and_files. The historical PM2.5 exposure data (V4.NA.02.MAPLE) can be accessed at: https://sites.wustl.edu/acag/datasets/surface-pm2-5/. The data was produced as part of the following paper: van Donkelaar, A., R. V. Martin, C. Li, R. T. Burnett, (2019) Regional Estimates of Chemical Composition of Fine Particulate Matter using a Combined Geosciences-Statistical Method with Information from Satellites, Models, and Monitors, Environ. Sci. Technol., 53, 5, 2595–2611. Gaseous air pollutant and annual meteorological datasets were obtained from the Environmental Protection Agency at: https://aqis.epa.gov/aqsweb/airdata/download_files.html.

Code availability

The epidemic dynamic model and statistical analysis codes can be accessed at https://github.com/pliu1991/COVID19PM25_supporting_data_and_files.

CRediT authorship contribution statement

Rajan K. Chakrabarty: Conceptualization, Methodology, Writing - original draft. Payton Beeler: Writing - original draft, Software, Methodology, Data curation. Pai Liu: Writing - original draft, Software, Methodology, Data curation. Spondita Goswami: Software, Methodology. Richard D. Harvey: Supervision. Aaron van Donkelaar: Writing – review & editing. Randall V. Martin: Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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