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Links between air pollution and COVID-19 in England☆

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ABSTRACT

In December 2019, a novel disease, coronavirus disease 19 (COVID-19), emerged in Wuhan, People's Republic of China. COVID-19 is caused by a novel coronavirus (SARS-CoV-2) presumed to have jumped species from another mammal to humans. This virus has caused a rapidly spreading global pandemic. To date, over 300,000 cases of COVID-19 have been reported in England and over 40,000 patients have died. While progress has been achieved in managing this disease, the factors in addition to age that affect the severity and mortality of COVID-19 have not been clearly identified. Recent studies of COVID-19 in several countries identified links between air pollution and death rates. Here, we explored potential links between major fossil fuel-related air pollutants and SARS-CoV-2 mortality in England. We compared current SARS-CoV-2 cases and deaths from public databases to both regional and subregional air pollution data monitored at multiple sites across England. After controlling for population density, age and median income, we show positive relationships between air pollutant concentrations, particularly nitrogen oxides, and COVID-19 mortality and infectivity. Using detailed UK Biobank data, we further show that $PM_{2.5}$ was a major contributor to COVID-19 cases in England, as an increase of 1 m^3 in the long-term average of $PM_{2.5}$ was associated with a 12% increase in COVID-19 cases. The relationship between air pollution and COVID-19 withstands variations in the temporal scale of assessments (single-year vs 5-year average) and remains significant after adjusting for socioeconomic, demographic and health-related variables. We conclude that a small increase in air pollution leads to a large increase in the COVID-19 infectivity and mortality rate in England. This study provides a framework to guide both health and emissions policies in countries affected by this pandemic.

1. Introduction

In December 2019, a high number of pneumonia cases with an unknown aetiology were detected in Wuhan, China. A molecular analysis of samples from affected patients revealed that their symptoms were caused by an infection with a novel coronavirus, later named severe acute respiratory syndrome (SARS) coronavirus (CoV) 2 (SARS-CoV-2), the pathogenic agent of coronavirus disease 19 (COVID-19) (Zhu et al., 2020a). Within five months, this disease had affected more than 210 countries and became a global pandemic, causing devastating consequences to public health (Wang et al., 2020a). Coronaviruses are a genus of enveloped, non-segmented, positive-sense RNA viruses belonging to the family Coronaviridae and classified within the Nidovirales order (Yi et al., 2020). Historically, illnesses caused by coronaviruses have ranged in severity, with some, including human coronaviruses-229E and -OC43, causing common cold symptoms, but SARS-CoV and Middle East respiratory syndrome coronavirus have initiated outbreaks of life-threatening pneumonia (Yi et al., 2020). While the initial symptoms of COVID-19 include fever with or without respiratory syndrome, a crescendo of pulmonary abnormalities may subsequently develop in patients (Huang et al., 2020). According to recent studies, most patients present with only a mild illness, but approximately 25% of hospital-admitted patients require intensive care because of viral pneumonia with respiratory complications (Wang et al., 2020a).

While extensive research into the pathogenesis of COVID-19 suggests that the severe disease likely stems from an excessive inflammatory response (Cao, 2020), the exact predisposing factors contributing to increased clinical severity and death in patients remain unclear. Individuals over the age of 60 years or with

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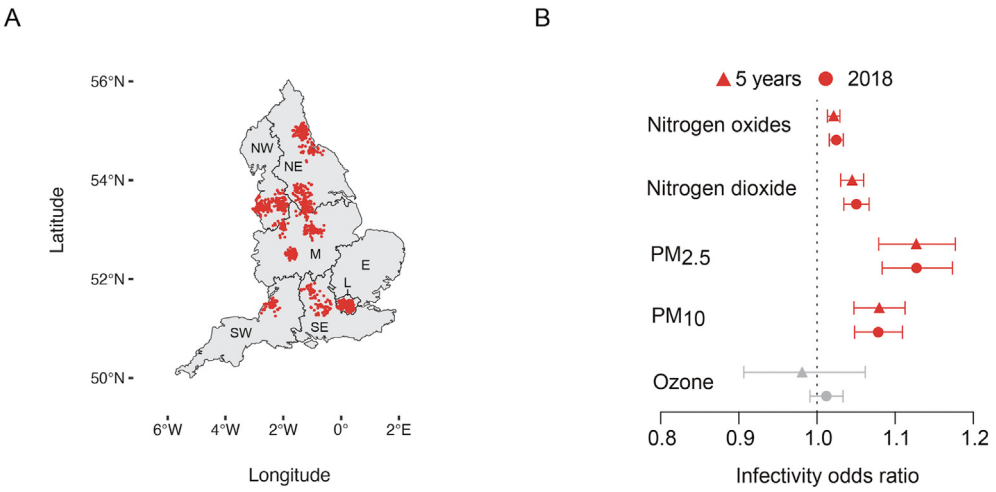

Fig. 4. Distribution and infectivity data from the UK Biobank. A) Distribution of UK Biobank subjects included in the current analysis. B) Odds ratios and respective 95% CIs for the relationship between individual exposure to several air pollutants and the number of lab-confirmed COVID-19 cases. Triangles refer to the results obtained when the long-term average (five years, 2014–2018) in the concentration of each air pollutant was taken into account and circles refer to the results obtained when the primary measure of exposure was air pollution levels in 2018. Red indicates significant associations ($p \leq 0.05$), while grey indicates a lack of significance ($p > 0.05$).

suggested to mainly depend on the resolution at which they are evaluated (Stroh et al., 2007). Therefore, we first calculated the effects of air pollution on COVID-19 mortality and spread using regional, coarse resolution data, and then high-resolution, individual-level observations obtained from the UK Biobank. By employing finer resolution grids, we found statistically significant evidence that an increase in the long-term average of $PM_{2.5}$ is associated with the largest increase in COVID-19 infectivity in England.

According to our initial findings, regional variations in nitrogen oxide and ozone concentrations in England predict the numbers of COVID-19 cases and deaths, independent of the population density. However, overall uncertainties for modelled exposure estimates at the regional scale (Stroh et al., 2007) led us to obtain increased spatial resolution. Using highly granular local authority-level measurements, we found that a 1 $\mu g/m^3$ increase in the long-term average of nitrogen oxides and dioxide levels was associated with a 1.5% and 2.5% increase in COVID-19 related mortality, respectively. Notably, these findings are consistent with studies conducted during the previous SARS outbreak, where long-term exposure to air pollutants predicted adverse outcomes in patients infected with SARS in China (Cui et al., 2003). Although nitrogen oxides are key ozone precursors, the relationship between these gases and ozone is nonlinear in ozone chemistry (Kelly and Gunst, 1990). Therefore, the negative associations between ozone levels and COVID-19 infection and mortality may be attributed to reduced nitrogen oxide conversion to ozone in urban areas, a phenomenon previously reported for areas with heavy traffic (Hagenbjork et al., 2017; Melkonyan and Kuttler, 2012). In addition, given the highly reactive nature of ozone, the inverse relationship between ozone levels and COVID-19 is consistent with increased nitric oxide scavenging close to points of emissions (Lefohn et al., 2010).

Although the molecular mechanisms underlying the relationship between pollutant exposure and COVID-19 remain to be determined experimentally, they are hypothesised to include the stimulation of chronic, background pulmonary inflammation (Ogen, 2020). Chamber studies have shown that ambient nitrogen dioxide induces infiltration of the airways by inflammatory cells in healthy volunteers (Ghio et al., 2000; Sandström et al., 1989 (Sandström et al., 1991),). In addition, exposure to these pollutants may inhibit pulmonary antimicrobial responses, reducing clearance of the virus from the lungs and promoting infectivity. Reduced phagocytic function is well documented after the exposure of macrophages to PM (Becker et al., 2003; Lundborg et al., 2006; Selley et al., 2020) and is suggested to be the mechanism that enhances viral infection in mice exposed to nitrogen dioxide (Rose et al., 1988). Acute exposure to nitrogen oxides has also been shown to decrease pulmonary function by inducing systemic oxidative stress (Guarnieri and Balmes, 2014). Both the MESA-Air and Framingham cohorts demonstrated that long-term exposure to air pollution is linked to chronic reductions in endothelial function (Krishnan et al., 2012; Wilker et al., 2014). Endothelial dysfunction may result in changes in arterial stiffness and afterload, which may translate into persistent hypertension. In this context, Faustini and colleagues (Faustini et al., 2014) reported that a 10 $\mu g/m^3$ increase in the annual concentration of two traffic-related pollutants, nitrogen dioxide and $PM_{2.5}$, is associated with large increases in both respiratory and cardiovascular mortality. As respiratory and cardiovascular diseases represent potential risk factors for COVID-19 related mortality, these studies support the hypothesis that long-term exposure to several air pollutants enhances the risk of severe COVID-19 outcomes by weakening the respiratory, cardiovascular and immune systems, thus facilitating viral invasion and severe outcomes (Conticini et al., 2020; Kulkarni et al., 2020).

Using individual-level data, our UK Biobank model indicated that exposure to $PM_{2.5}$ and PM_{10} increases the risk of COVID-19 infection, in addition to nitrogen oxides, which were previously identified as major contributors to COVID-19 infectivity in the regional and subregional analysis. The observation that exposure to $PM_{2.5}$ and PM_{10} increases the risk of COVID-19 infection conforms to the hypothesis that viruses attach to air pollutants (Reche et al., 2018), potentially explaining the propagation of SARS-CoV-2 and its infectious capacity. Nonetheless, the results of our individual-level analysis are inconsistent with our local authority models, where $PM_{2.5}$ and PM_{10} were found to be negatively associated with the infectivity rate. In this context, it must be emphasised that the ecological design of our subregional analysis likely led to some degree of exposure misclassification. Previous studies have shown that the temporal and spatial scales of exposure assessment may influence the magnitude of reported associations between air pollutant exposure and mortality (Crouse et al., 2020). For instance, Crouse and colleagues (Crouse et al., 2020) observed that the