COVID-19 Pandemic: A Wake-Up Call for Clean Air

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Since its identification in Wuhan, China, coronavirus disease (COVID-19) has infected more than 104 million people and killed over 2.2 million people worldwide (1). Recent studies of air pollution and COVID-19 cases and mortality in diverse international settings add convinc ingly to a large body of evidence showing that exposure to air pollution exacerbates viral respiratory infections and consequently widens health disparities. Meanwhile, the global lockdown response through a near global economic standstill resulted in a temporary improvement in short-term air quality, likely reducing non–COVID-19 deaths. A large proportion of the global population, including those in Europe and the United States, still live in areas where ambient air pollution levels exceed World Health Organization guidelines, with racial minorities being disproportionally affected. In this commentary, we review studies linking air pollution to worse COVID-19 outcomes and discuss several ways in which the COVID-19 pandemic highlights the urgent need to address the global problem of air pollution through sustainable local and national policies to improve respiratory health and equity worldwide.

Proposed Mechanisms for Air Pollution and Worsened Viral Respiratory Infection

Air pollution exposure is associated with higher rates of hospitalizations and deaths from respiratory tract infections (2–5). Multiple studies have shown that elevated levels of air pollutants such as particulate matter (PM) and nitrogen dioxide (NO_2) impair the innate immune response and lead to both increased susceptibility to viruses and more severe viral infections (4, 6, 7). Experimental studies conducted in humans indicate that air pollution damages cilia in the respiratory tract, the first line of defense against respiratory infections, and causes oxidative stress that may increase epithelial permeability (4, 6, 8, 9). Air pollution exposure also impairs the ability of macrophages to phagocytose, thereby reducing viral clearance and promoting infectivity (4, 6). Consistent with this mechanistic evidence, human mortality has been higher in more polluted areas during prior respiratory viral pandemics such as severe acute respiratory syndrome and the influenza pandemic of 1918 (10, 11).

In the case of COVID-19, several additional mechanisms have been proposed for how short-term air pollution exposure may augment severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission or severity of infection. PM and NO_2 exposures lead to *in vitro* overexpression of respiratory ACE-2 (angiotensin-converting enzyme 2), the cellular target for SARS-CoV-2, which could, in theory, promote viral entry and infection (12, 13). Speculation has been offered that airborne particles may act as platforms for SARS-CoV-2, allowing viral aerosols to remain suspended in the air for longer distances than in the case of droplets, thereby enhancing transmission between individuals (14, 15). The evidence to support this hypothesis comes from a study identifying SARS-CoV-2 RNA on outdoor PM in Bergamo, Italy, and a similar study finding higher levels of influenza RNA in air samples collected during Asian dust storms (16, 17). However, a more recent study in Italy concluded that outdoor airborne transmission is unlikely to play a significant role in the spread of SARS-CoV-2 after identifying only minimal atmospheric concentrations of the virus (18). Although evidence in China suggests that short-term (e.g., daily) PM exposure is associated with higher COVID-19 infection rates, this may be explained by greater viral entry and replication by mechanisms described above rather than via PM (19, 20). No controlled exposure

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Table 1. Studies evaluating long-term air pollution exposure and COVID-19 incidence or mortality

Study	Country	Exposure	COVID-19 Outcome	Principal Findings
Wu *et al.* (April 2020)	United States	$PM_{2.5}$ Average between 2000 and 2016	Mortality rate	Increase of 1 $\mu g/m^3$ in $PM_{2.5}$ associated with an 8% increase in mortality rate
Cole *et al.* (June 2020)	The Netherlands	$PM_{2.5}$, NO_2, and SO_2 Average between 2015 and 2019	Cases Hospital admissions Deaths	1 $\mu g/m^3$ increase in $PM_{2.5}$ associated with 9.4 more cases, 3.0 more hospital admissions, and 2.3 more deaths NO_2 (but not SO_2) associated with cases and deaths
Hendryx *et al.* (June 2020)	United States	$PM_{2.5}$*, diesel PM† and O_3*	Cases Deaths	$PM_{2.5}$ and diesel PM associated with higher prevalence and mortality Diesel PM appeared to be the primary driver for associations with $PM_{2.5}$
Travaglio *et al.* (June 2020)	England	$PM_{2.5}$, PM_{10}, SO_2, NO_2, NO, and O_3 Average between 2018 and 2019	Cases Deaths Infectivity rate	NO and NO_2 significant predictors of cases independent of population density 1 $\mu g/m^3$ increase in SO_2 and NO associated with 17% and 2% higher mortality, respectively O_3 negatively associated with cases and deaths $PM_{2.5}$, PM_{10}, and SO_2 associated with SARS-CoV-2 infectivity (OR, 1.12, 1.07, and 1.32, respectively) but not cases or deaths
Konstantinoudis *et al.* (August 2020)	England	$PM_{2.5}$ and NO_2 Average between 2014 and 2018	Mortality rate	1 μ/m^3 increase in $PM_{2.5}$ and NO_2 associated with 1.4% and 0.5% higher mortality rate, respectively
Liang *et al.* (October 2020)	United States	$PM_{2.5}$, NO_2, and O_3 Annual mean between 2010 and 2016	CFR Mortality rate	NO_2 associated with 11.3% and 16.2% higher CFR and mortality rate, respectively, per IQR $PM_{2.5}$ associated with 14.9% higher mortality rate per IQR, but not with CFR No association between O_3 and CFR or mortality rate

Definition of abbreviations: CFR = case fatality rate; COVID-19 = coronavirus disease; IQR = interquartile range; NO = nitric oxide; NO_2 = nitric dioxide; O_3 = ozone; OR = odds ratio; PM = particulate matter; $PM_{2.5}$ = particulate matter <2.5 μm in diameter; PM_{10} = particulate matter <10 μm in diameter; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SO_2 = sulfur dioxide.
*Average for 2016.
†Average for 2014.

studies have confirmed that ambient PM concentrations increase transmission of SARS-CoV-2 or other respiratory viruses, and a recent expert workshop on SARS-CoV-2 transmission did not identify ambient pollution as a factor promoting disease transmission but instead recommended that it be examined further (21).

Exposure to ambient air pollution in the decades preceding the pandemic may worsen the severity of illness among those who are infected with COVID-19. Long-term air pollution exposure increases the risk of chronic cardiovascular, metabolic, and pulmonary conditions that are consistently linked to worse outcomes in those infected with respiratory viruses, especially COVID-19 (3, 22). In addition, long-term air pollution exposure increases the risk of developing acute respiratory distress syndrome (ARDS), the primary cause of death among those with respiratory failure from COVID-19 (23–25).

Associations between Air Pollution and COVID-19 Infection Rates and Mortality

A growing body of evidence suggests that higher long-term exposure to outdoor pollutants, mostly to PM and NO_2, increases the risk of infection and death from COVID-19 (26–31). One study estimates that particulate air pollution has contributed 15% to COVID-19 mortality worldwide, including 17% in

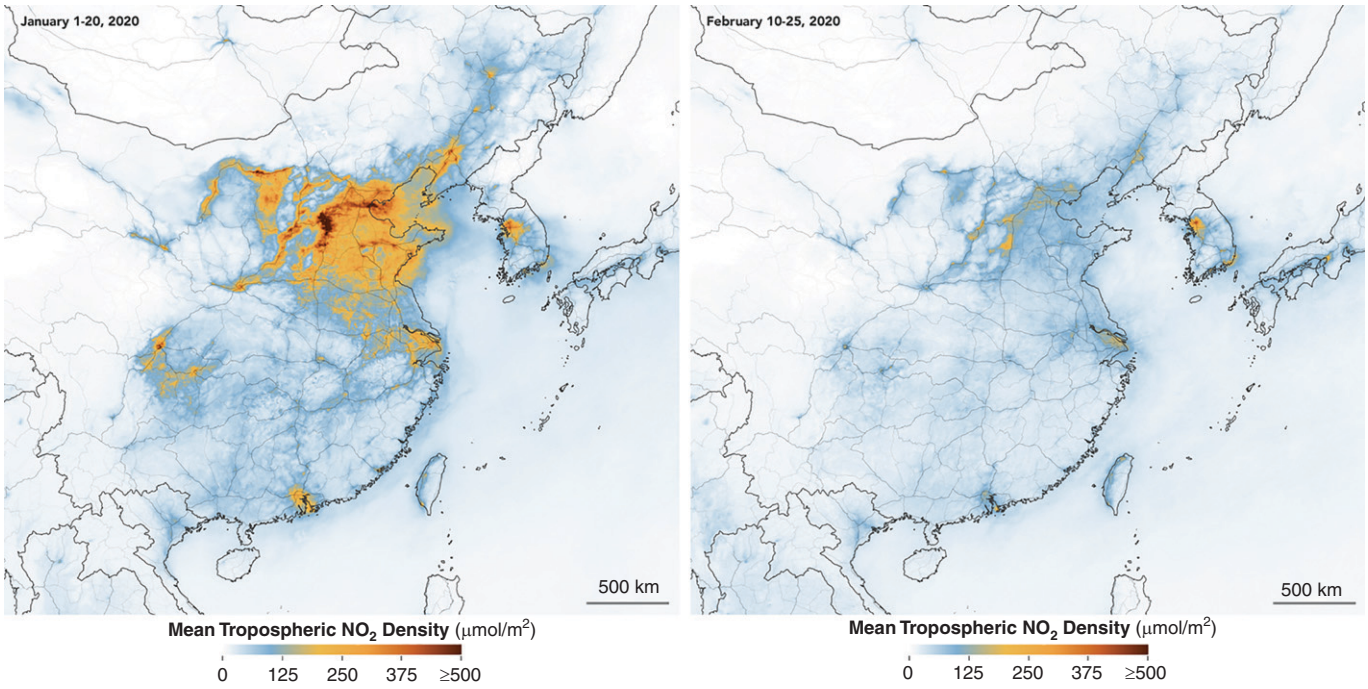

Figure 1. Decrease in nitrogen dioxide levels over China between January and February 2020 after economic lockdown. Reprinted by permission from Reference 47.

North America and 19% in Europe (32). Table 1 includes studies published to date that used models to evaluate associations of long-term air pollution exposures and COVID-19 cases and deaths, controlling for many potential confounders such as timing of outbreak, population density, socioeconomic status, and comorbidities. Notably, current studies remain restricted to county- or municipal-level exposure and outcome data and are unable to adjust for individual-level risk factors given the limited publicly available data (33).

COVID-19 has disproportionately affected racial/ethnic minorities and low-income communities who have suffered higher rates of hospitalizations and mortality (34, 35). Ambient air pollution may contribute to these severe disparities. In the United States, racial minorities on average have higher exposure to PM $<$2.5 μm in diameter ($PM_{2.5}$) and NO_2 compared with Caucasians, an inequality that has worsened despite improving air quality (36). Racial minorities are more likely to live in areas closer to industrial pollution and to work in business sectors with higher exposure to pollution. These inequalities in residential and occupational air pollution exposure may be a cause of the stark disparities of the COVID-19 pandemic along racial and ethnic lines.

COVID-19 Pandemic Highlights Scale of Pollution-related Mortality

In an effort to control the spread of COVID-19, government policies dramatically decreased industrial activity and transportation, causing rapid improvements in air quality. Studies spanning multiple continents show NO_2 concentrations decreased by 50%, $PM_{2.5}$ concentrations by 40%, and PM $<$10 μm in diameter concentrations by 60% during global lockdowns (Figures 1 and 2) (37, 38). The decline in air pollution levels likely improved mortality from noncommunicable diseases and thus may have softened the blow from COVID-19. $PM_{2.5}$ reductions during initial lockdowns are estimated to have avoided approximately 24,000 and 2,100 premature deaths in China and Europe, respectively, with similar health benefits attributed to NO_2 reductions (39, 40). Although there are historical examples of short-term air quality improvements leading to declines in admissions for respiratory conditions, similar studies have not yet been conducted for the COVID-19 lockdowns, and such studies would likely be confounded by overall reduced health care use during the lockdowns (41).

More than 91% of the world lives in areas that exceed the World Health Organization's air quality guidelines, and more people are impacted by worsening air quality each year (42, 43). In the United States, approximately 45% of the population or 150 million Americans live in counties marked by ozone or $PM_{2.5}$ levels that exceed standards by 10 or more days per year, an increase compared with the previous 3 years, according to the American Lung Association's 2020 State of the Air Report (43). Despite these growing numbers, government authorities, including the U.S. Environmental Protection Agency, weakened air quality management by suspending the requirement to report PM emissions during the COVID-19 outbreak in an effort to stimulate the economy (44). On December 7, 2020, the Environmental Protection Agency opted to retain current national standards for fine PM against the advice of experts in the field, who cited extensive evidence that current standards are responsible for thousands of premature deaths each year (45, 46).

The COVID-19 pandemic has highlighted the widespread health consequences of ambient air pollution, including acute effects on respiratory immune defenses and chronic effects that

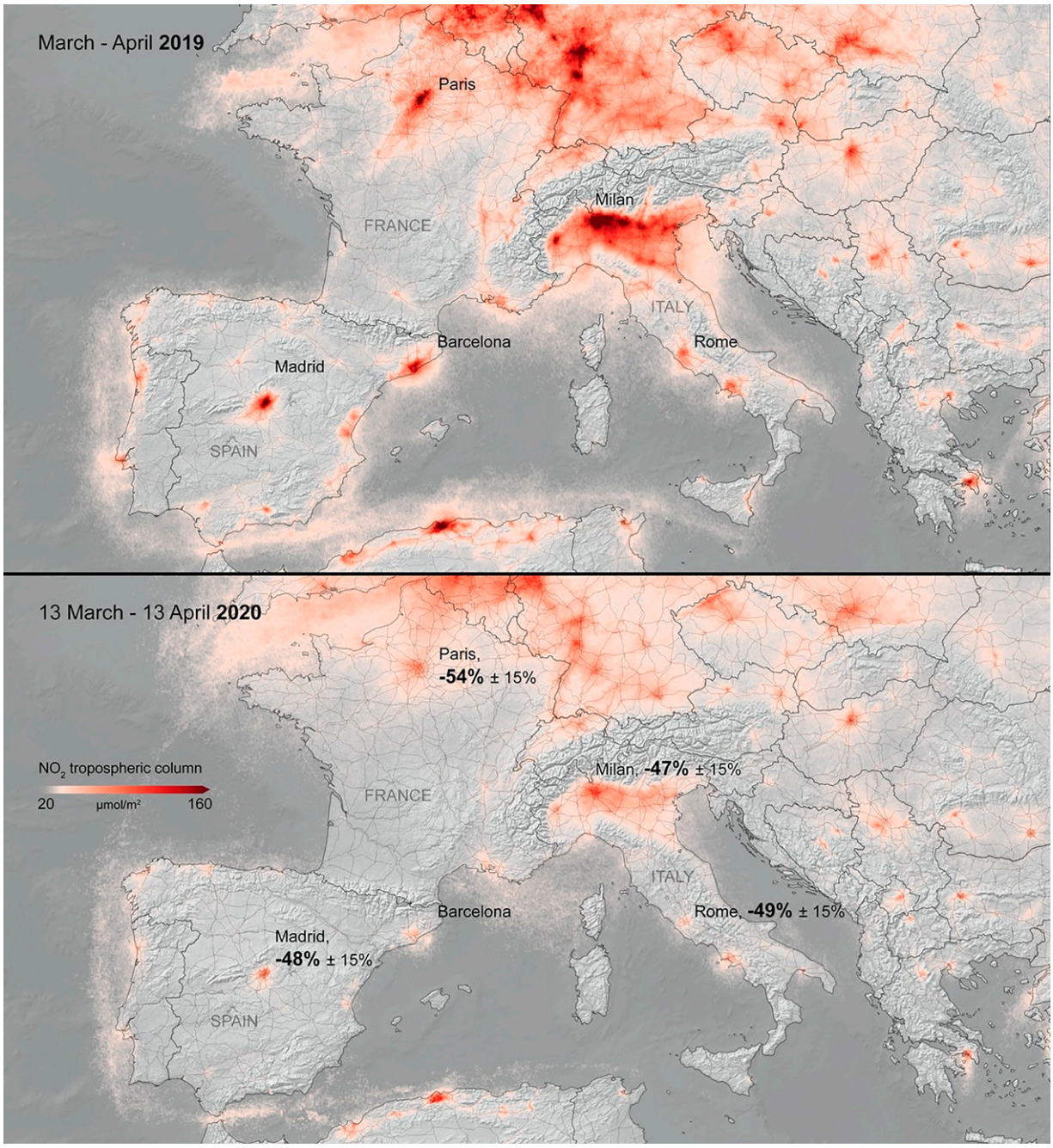

Figure 2. Decrease in nitric dioxide levels over Europe during economic lockdown in spring 2020 compared with spring 2019. Reprinted by permission from Reference 48.

lead to higher risk of chronic cardiopulmonary disease and ARDS. These chronic health effects likely explain the higher COVID-19 mortality among those exposed to more air pollution. The pandemic has also provided a glimpse into the health benefits of cleaner air. As we emerge from this devastating public health crisis, COVID-19 is a wake-up call for the need to adopt stricter air quality standards and end our tolerance for pollution in disadvantaged neighborhoods. As part of our post–COVID-19 recovery, we must clean up the air to improve respiratory health and equality worldwide. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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