HEI STATEMENT

Synopsis of Research Report 238

Ambient Air Pollution and COVID-19 in Southern California

BACKGROUND

Exposure to air pollution has been linked with increased risks of influenza, respiratory syncytial virus, and other types of respiratory infection. Some epidemiological studies conducted early in the COVID-19 pandemic reported that rates of COVID-19 death were higher in areas with greater levels of air pollution, suggesting a possible association between air pollution and risk of death or poor health outcomes due to COVID-19. The early studies, however, had notable methodological shortcomings (e.g., a lack of high-resolution estimates of exposure or detailed information on individuals, such as socioeconomic status) and thus had a high potential for biased results. To investigate the potential associations between air pollution, COVID-19, and human health further, HEI funded five studies in various countries in the fall of 2020. This Statement highlights a study conducted by Dr Michael Kleeman and colleagues at the University of California, Davis.

APPROACH

The investigators used two sources of health data, one from the California Department of Public Health (CDPH) and the other from the Kaiser Permanente Southern California (KPSC) healthcare system, from June 2020 through January 2021. The CDPH data included information on about 773,000 COVID-19 cases and 14,000 deaths due to COVID-19 across 308 ZIP codes in Los Angeles County. The KPSC cohort consisted of more than 20,000 adult patients in Southern California who were diagnosed with COVID-19 and hospitalized within 21 days of a positive COVID-19 diagnosis or test, and this dataset contained detailed information on patient characteristics and all aspects of patient care.

Two different approaches were used to estimate outdoor air pollutant concentrations. The investigators used both an advanced chemical transport model and a land use regression sta-

What This Study Adds

- This study evaluated associations between estimated outdoor air pollution concentrations and risk of COVID-19 disease, COVID-19 disease progression or recovery, deaths due to COVID-19, and long COVID-19 conditions among a study population in Southern California.
- The study used administrative data from the state of California and a cohort of hospitalized patients with COVID-19 from a large healthcare system, combined with high-resolution estimates of outdoor air pollution concentrations calculated using chemical transport and statistical land use regression models.
- Kleeman and colleagues found that increased risk of COVID-19 death was associated with estimated annual average exposures to ultrafine particulate matter, fine particulate matter, and several specific components of fine particulate matter; however, their findings on associations between ozone exposure and COVID-19 death in the administrative and healthcare system datasets were inconsistent.
- Exposures to several pollutants were also associated with progression from hospitalization to more severe COVID-19 illness and with several long COVID-19 outcomes.
- The findings from this study provide useful insights into how air pollution might contribute to adverse COVID-19 health outcomes, and these insights might apply to future respiratory infectious disease pandemics. However, the findings reported here likely only apply to individuals who become severely ill, requiring hospitalization.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Michael Kleeman at the University of California, Davis, and colleagues. Research Report 238 contains the detailed Investigators' Report and a Commentary on the study prepared by the HEI Review Committee.

tistical model to produce highly refined estimates of daily outdoor concentrations of ultrafine particulate matter, fine particulate matter, fine particulate matter components, nitrogen dioxide, and ozone at multiple spatial resolutions for 2016, 2019, and 2020. Average long-term (annual) and short-term (30-day) exposure estimates were linked to ZIP codes for the CDPH data and patients' residential addresses in the KPSC cohort.

Kleeman and colleagues used various regression modeling approaches to evaluate associations between both single- and multipollutant air pollution exposures and COVID-19 outcomes. To analyze outcomes regarding COVID-19 cases and deaths in the CDPH data, the investigators used negative binomial models with adjustment for ZIP code-level demographic and socioeconomic factors. For the KPSC cohort, they used Cox proportional hazards models to analyze outcomes of patient deaths and multistate survival modeling to analyze outcomes related to patients transitioning to recovery or more severe states of illness (i.e., admission to intensive care, needing ventilation, or death). The investigators also evaluated whether weather (temperature and relative humidity) influenced the effect of long-term outdoor air pollution exposures on the risk of COVID-19 death. Additionally, they used logistic regression to analyze long COVID-19 outcomes 3 months and 12 months after discharge from the hospital in the KPSC cohort.

KEY RESULTS

Air Pollution Exposure Estimated outdoor air pollution exposures varied across the different types of analyses and statistical methods used in the study. The range of estimated average long-term (annual) air pollutant exposures in Southern California was around 9–13 μg/m^3 for fine particulate matter, 13–22 parts per billion for nitrogen dioxide, and 55–66 parts per billion for ozone. In general, the statistical model produced higher estimates of nitrogen dioxide exposure around Los Angeles than did the chemical transport model; these models also produced different estimates of where exposures to fine particulate matter were highest in southern California. For most of the analyses in this study, the investigators used outdoor air pollution concentrations estimated using the chemical transport model.

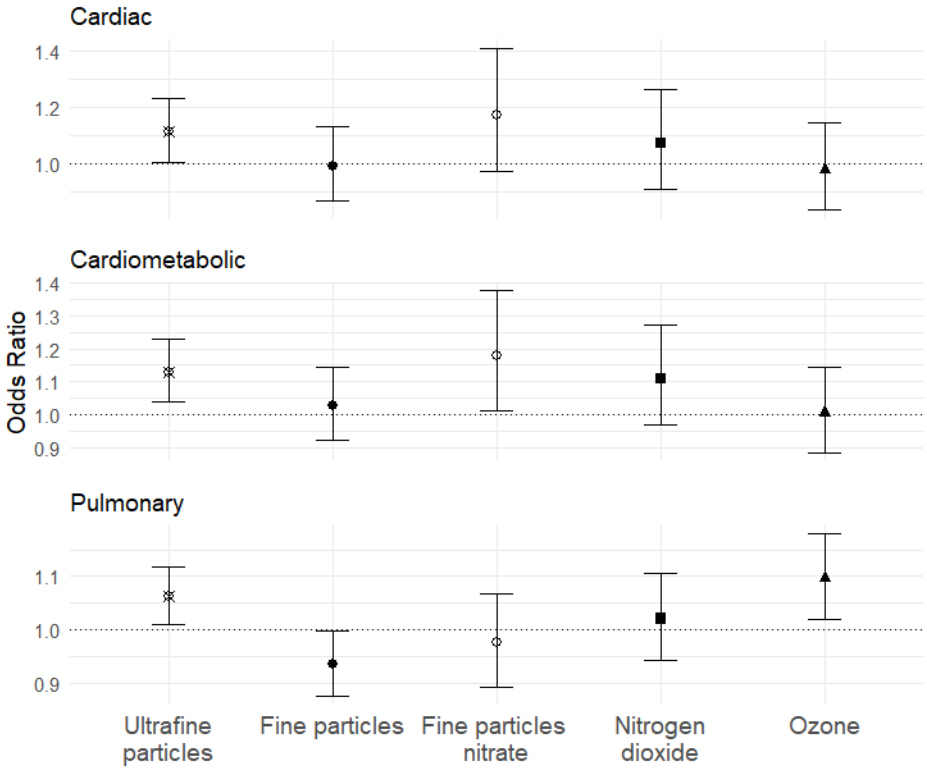
COVID-19 Cases and Deaths In the CDPH dataset, Kleeman and colleagues observed that higher estimated exposures to ultrafine particulate matter, fine particulate matter, and some of its components, and ozone were associated with elevated risks of COVID-19 incidence and death, with the strongest risks being associated with ozone concentrations. The two-pollutant models showed slightly elevated risks of both COVID-19 incidence and death associated with most combinations of these pollutants. In the KPSC cohort, the investigators observed that elevated risks of COVID-19 death were associated with exposures to most particulate matter pollutants and nitrogen dioxide but not with ozone; the risk estimates for fine particulate matter and nitrogen dioxide generally remained elevated in two-pollutant models. The investigators found that higher temperatures and higher relative humidity levels weakened the associations between long-term air pollutant exposures and risk of COVID-19 death.

Transition to More Severe COVID-19 States Greater estimated long-term exposures to fine particulate matter, nitrogen dioxide, and ozone were associated with higher risks of progressing to more severe COVID-19 illness. Greater estimated long-term exposures to fine particulate matter were also associated with higher risks of progressing from more severe COVID-19 illness to death. Across these three pollutants, the risk of deterioration (defined as a patient progressing from hospitalization to needing ventilation or intensive care) associated with the highest (versus the lowest) level of exposure increased by as much as 16% to 21%, depending on the pollutant. Among the analyzed associations between pollutant exposures and risk of transition to adverse COVID-19 outcomes, the strongest risk estimate was observed for the association between ozone exposure and transitioning from recovery after COVID-19 hospitalization to death. The two-pollutant models also demonstrated that exposures to fine particulate matter, nitrogen dioxide, and ozone were generally associated with elevated risks of transitioning from COVID-19 hospitalization to deterioration.

Long COVID-19 Higher estimated short-term exposures to ultrafine particulate matter, fine particulate matter nitrate, and ozone were associated with increased risks for long COVID-19 outcomes in the 3 months following discharge from the hospital (**Statement Figure**), including pulmonary, cardiometabolic, and cardiac outcomes, but not neurological outcomes. The strongest risk estimate per unit increase in estimated pollutant exposure was observed for the association between short-term particulate matter nitrate exposure and cardiometabolic long COVID-19. In two- or three-pollutant models, risk estimates for short-term ultrafine particulate matter exposures and long COVID-19 outcomes remained elevated (as did the risk estimate for short-term ozone exposure and pulmonary long COVID-19). Fewer positive associations were observed between short-term air pollution exposures and long COVID-19 outcomes in the 12 months following discharge from the hospital.

INTERPRETATION AND CONCLUSIONS

In its independent evaluation of the Investigators' Report on this study, the HEI Review Committee concluded that the study improved the level of understanding about associations between exposures to outdoor air pollution and adverse health outcomes of COVID-19. Specifically, the study demonstrated



Statement Figure. Associations between short-term air pollutant exposures and long COVID-19 outcomes occurring within 3 months after hospital discharge in the Kaiser Permanente Southern California cohort. These results from single-pollutant models show odds ratios and 95% confidence intervals estimated per interquartile range increases in pollutant exposure (estimated from the chemical transport model). Source: Adapted from Investigators' Report Figure 18.

that multiple air pollutants were associated with increased risks of COVID-19 incidence, death due to COVID-19, progression to more severe illness after a COVID-19 diagnosis, and long COVID-19 outcomes. The Committee especially appreciated that Kleeman and colleagues explored factors that had not previously been investigated in earlier studies, such as COVID-19 health outcomes specific to multiple different health states and long COVID-19 conditions, as well as the effect of weather on the outcomes of interest. The Committee also valued the use of individual-level health information obtained from a large healthcare system and the calculation of highly refined estimates of long-term and short-term exposures to multiple outdoor air pollutants, including specific components of fine particulate matter.

This study provided further evidence of an association between fine particulate matter, as well as nitrogen dioxide (only in the KPSC cohort), and an increased risk of death due to COVID-19. The findings contributed new information indicating that long-term exposures to fine particulate matter, nitrogen dioxide, and ozone each were associated with transitioning from COVID-19 hospitalization to deterioration to more severe illness, whereas short-term exposures to ultrafine particulate matter, fine particulate matter nitrate, and ozone were associated with several long COVID-19 outcomes. However, the ability to generalize the findings of this study to the broader population may be limited because the current population has now gained some form of natural or vaccine-induced immunity to COVID-19.

Overall, this study offers both additional evidence and new contributions that enable a better understanding of the relationship between outdoor air pollution and adverse health outcomes of COVID-19, thus providing valuable insights that might be relevant to future outbreaks of other infectious respiratory diseases. Importantly, although air pollution is an important modifiable environmental risk factor, efforts to improve air quality as a means of reducing health risks should be viewed as part of a broader collection of public health and prevention measures aimed at reducing the adverse health effects of future outbreaks.