

Exposure to Air Pollution and Severe COVID-19 Outcomes in Catalonia, Spain

BACKGROUND

Research from toxicological, clinical, and population health studies has linked air pollution exposure with a risk of respiratory infections, influenza, and respiratory syncytial virus. Some early epidemiological studies reported that rates of COVID-19 deaths were higher in areas with higher levels of air pollution, raising the possibility of a link between air pollution and risk of COVID-19 infection or poor outcomes. These early studies had pronounced methodological limitations (e.g., lacking detailed information on individual- and community-level socioeconomic status or challenges to identifying COVID-19 diagnoses accurately) such that the potential for biased results was high. In May 2020, only two months after the World Health Organization declared the COVID-19 outbreak *a global pandemic*, HEI issued Request for Applications 20-1B, soliciting proposals for studies to investigate the potential links between air pollution, COVID-19, and human health. Five studies in various countries were selected, and this Statement highlights a study by Dr. Cathryn Tonne and colleagues at the Barcelona Institute for Global Health (ISGlobal).

APPROACH

Tonne and colleagues aimed to evaluate whether long- and short-term exposure to outdoor air pollution was associated with COVID-19-related hospital admissions or mortality in Catalonia, Spain, and to identify subgroups of the population at greater risk to the effects of exposure. Briefly, the investigators linked records from medical and population registries to create a population-based cohort that included nearly the full adult population of Catalonia (a total of 4.6 million people), with follow-up from January 1, 2015, to December 31, 2020. Levels of various air pollutants at residential addresses were estimated using newly developed spatiotemporal models for nitrogen dioxide, fine particles (particulate matter <2.5 $\mu\text{g}/\text{m}^3$ in aerodynamic diameter), coarse particles (particulate matter <10 $\mu\text{g}/\text{m}^3$ in aerodynamic diameter), and ozone at a spatial resolution of 250 meters. They considered several health outcomes, including COVID-19-related hospital admissions, deaths, and other outcomes indicating disease severity.

What This Study Adds

- This study evaluated associations between exposure to outdoor air pollution and risk of hospital admissions, disease severity, and death related to coronavirus disease 2019 (COVID-19) among 4.6 million adults in Catalonia, Spain.
- Tonne and colleagues reported higher risk of these COVID-19-related outcomes associated with higher short- and long-term exposures to nitrogen dioxide and to fine and coarse atmospheric particles.
- They reported that people who experienced long-term exposures to relatively high concentrations of outdoor air pollution and are characterized as having a lower socioeconomic status had a higher risk of COVID-19-related hospitalization than did others.
- Important strengths of the study include the high quality of the datasets, namely a population-based cohort that included many individual and area characteristics, and exposure models for several pollutants with high spatiotemporal resolution.
- This study provides evidence that both short- and long-term exposures to outdoor air pollution could increase the risk of severe COVID-19 outcomes.

In their main analyses, Tonne and colleagues used Cox proportional hazards models to estimate associations between the air pollution exposure estimates and the selected health outcomes. Their main statistical models adjusted for age, sex, tobacco smoking status, individual income, health risk group, and many area-level variables; some models were also adjusted for daily temperature and wave of the pandemic. They evaluated whether the association between long-term exposures to air pollution and COVID-19-related hospital admissions varied among subgroups defined by age, sex, hypertension, diabetes mellitus, chronic obstructive lung disease, individual income, and neighborhood socioeconomic status. They also explored many additional models to evaluate the sensitivity of their results by adjusting for additional covariates (e.g., comorbidities, other indicators of socioeconomic status, and tobacco smoking status).

KEY RESULTS

The exposure models for nitrogen dioxide and ozone developed for this study were able to describe the patterns of these pollutants across the study area and for all years relatively well. Those for coarse and fine particles, however, were somewhat less accurate in describing pollutant patterns.

The investigators reported elevated risks of COVID-19-related outcomes associated with exposures to higher annual mean levels of all pollutants except ozone, with which they reported lower risks (**Statement Figure**). Estimates of risk from models with annual mean exposures to nitrogen dioxide were greater than those from models with annual mean exposures to the other pollutants considered. Results from two-pollutant models were generally similar to those from single-pollutant models.

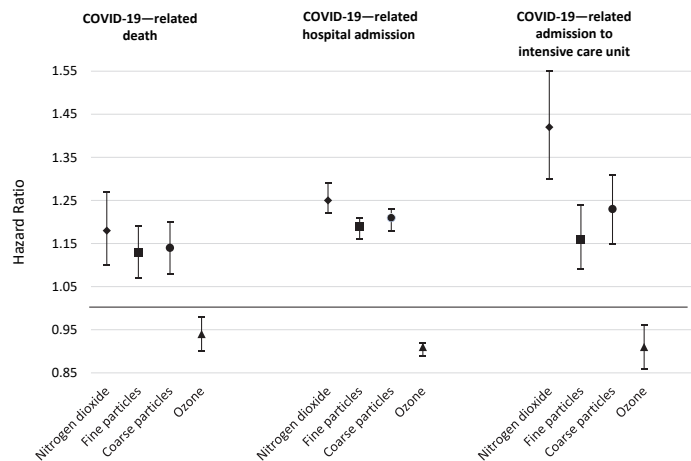
The investigators also reported that higher short-term exposures (i.e., over the previous few days) to nitrogen dioxide and both fine and coarse particles were associated with an elevated risk of COVID-19-related hospital admissions during the second wave of the pandemic. Specifically, they reported that risk of hospital admissions was associated with cumulative exposures measured up to seven days preceding an event. Short-term variations in ozone concentrations, however, were associated with lower risk of hospital admission.

The investigators also examined whether the combined effects of exposures to air pollution and selected characteristics of the population (e.g., age, sex, socioeconomic status, pre-existing health conditions) were associated with increased risk of COVID-19-related hospital admission. Here, they reported evidence that those characterised by lower socioeconomic status (according to several indicators at the individual and area levels) and who had long-term exposures to relatively high concentrations of nitrogen dioxide or fine particles were at increased risk of hospital admission for COVID-19 as compared to others. They also reported that the risk of hospitalization did not vary appreciably among subgroups defined by the presence of chronic comorbid conditions (i.e., diabetes, hypertension, and chronic obstructive lung disease).

INTERPRETATION AND CONCLUSIONS

In its independent evaluation of the Investigators' Report, the HEI Review Committee concluded that this study represents an important contribution to the scientific knowledge about potential associations between exposures to outdoor air pollution and the risk of severe cases of COVID-19.

The Committee was impressed that the investigators were careful to exclude air pollution data from 2020 from their analyses of longer-term, annual exposures



Statement Figure. Associations between estimated annual average air pollution concentrations and COVID-19-related outcomes among cohort participants. Data shown are hazard ratios and 95% confidence intervals estimated per interquartile range increases in 1-year mean exposure. (Source: Investigators' Report Table 6.)

when pandemic-related restrictions on mobility led to decreased emissions from traffic and other sources. The study demonstrated elevated risks for severe COVID-19 outcomes associated with daily and annual exposures to nitrogen dioxide and fine and coarse particles (and opposite results with ozone) in this population-based cohort of 4.6 million adults. Most other studies typically have had access to data on only short- or long-term exposures, not both, and many do not have access to such high-quality exposure models for multiple pollutants. The study also provides evidence suggesting that individuals with lower individual- and area-level socioeconomic status might have been more susceptible than others to the effects of long-term exposures to nitrogen dioxide and fine particles on COVID-19-related hospitalization. This susceptibility among those of lower socioeconomic status could be due to many factors, including more frequent or more intense exposures to pollutants, higher levels of psychosocial stress, or higher incidence of pre-existing health conditions or genetic traits that increase susceptibility to effects of exposure.

The many sensitivity analyses generally demonstrated findings consistent with the main analyses and thus supported the robustness of the results. Some results, however, were difficult to interpret and understand. For example, the associations reported between ozone and the risk of severe COVID-19 outcomes were unexpected and difficult to explain. Some of the challenges to interpreting those results are because the long-term exposures to ozone were negatively correlated with those to nitrogen dioxide and because the range of spatial variation captured by the ozone model was relatively small.

Ultimately, this study has provided important additional evidence that short- and long-term exposures to outdoor air pollution do appear to be associated with severe COVID-19 outcomes.