Low-Level Air Pollution Associated With Death
Policy and Clinical Implications
Junfeng Zhang, PhD

Globally, an estimated 3.3 million annual premature deaths (5.86% of global mortality) are attributable to outdoor air pollution, although ambient air pollution has been regulated under national laws in many countries. In the United States under the Clean Air Act, the primary National Ambient Air Quality Standards (NAAQS) are intended to protect human health, with an adequate margin of safety, including sensitive populations such as children, older adults, and individuals with respiratory diseases. Under the Clean Air Act, the standards are reviewed every 5 years to account for new scientific evidence regarding their appropriateness and adequacy for protecting public health.

Historically, this science-based review process has resulted in continued evolution of the NAAQS. For example, an annual and 24-hour standard for fine particulate matter (PM$_{2.5}$) and an 8-hour standard for ozone were added in 1997. The 24-hour PM$_{2.5}$ standard was lowered from 65 μg/m$^3$ in 1997 to 50 μg/m$^3$ in 2006. The 8-hour ozone standard was lowered from 0.08 parts per million (ppm) in 1997 to 0.075 ppm in 2008 and then to 0.070 ppm in 2015. At the next review of NAAQS for PM$_{2.5}$ and ozone, new scientific evidence will be evaluated in recommending whether the current standards should be revised.

In this issue of JAMA, Di et al report findings that day-to-day changes in PM$_{2.5}$ and ozone ambient concentrations were significantly associated with higher risk of all-cause mortality at levels well below the current daily NAAQS. Using a case-crossover design and conditional logistic regression analysis in a data set involving 22 million deaths among US Medicare participants during 2000-2012, the authors estimated that a 10-μg/m$^3$ increase in PM$_{2.5}$ and a 10-parts-per-billion increase in warm-season (ie, between April 1 and September 30) ozone in the 2 days prior to death were, respectively, associated with a 1.05% (95% CI, 0.95%-1.15%) and 0.51% (95% CI, 0.41%-0.61%) increase in daily mortality rate. The authors also identified susceptible subgroups, reporting that nonwhite individuals, Medicaid-eligible individuals, women, and adults 85 years and older had significantly higher mortality risk associated with PM$_{2.5}$ levels and that individuals aged from 75 to 84 years and 85 years and older had higher mortality risk associated with increased ozone levels. Importantly, the authors did not find evidence of a threshold in the exposure-response relationship for either pollutant, suggesting that there is no “absolute” safe level of exposure to PM$_{2.5}$ or ozone.

The findings of Di et al may have implications for forecasting and personal monitoring of exposure to PM$_{2.5}$ and ozone, which could allow individuals at increased risk to reduce or mitigate their exposure. The study showed that when PM$_{2.5}$ or ozone concentration was higher on a particular day, more deaths occurred 2 days later. Predictions of pollutant concentrations for the next few days, such as weather forecasting, can be made readily available to the public. (For example, this has already occurred2 days later. Predictions of pollutant concentrations for the next few days, such as weather forecasting, can be made readily available to the public. (For example, this has already

The Medicare cohort used in this study includes individuals residing in rural areas without nearby air pollution monitors, but the authors were able to estimate exposure to PM$_{2.5}$ and ozone using predictive models of data from remote air monitors, satellite-based measurements, and other data sets. Pollutant concentrations in rural areas are generally lower than in urban areas. The findings from this study add unique evidence, applicable to both rural residents and more vulnerable groups, to raise public awareness concerning health risks associated with low-level PM$_{2.5}$ and ozone pollution. The findings suggest that the current NAAQS for these pollutants should be reevaluated.

The findings from this epidemiological investigation by Di et al are supported by mechanistic insights from recent studies of pathophysiological responses to PM$_{2.5}$ and ozone exposure. It is now well accepted that short-term exposure to PM$_{2.5}$ has cardiorespiratory effects through increased pulmonary and systemic inflammation, increased oxidative stress, enhanced thrombogenesis, and autonomic dysfunction. At relatively high concentrations, ozone impairs lung function and increases the incidence of asthma attacks. As a highly reactive oxidant, ozone has long been considered to mainly affect the respiratory system. However, a recent study showed that at levels below those capable of causing lung function changes, ozone is associated with increases in pulmonary inflammation, blood pressure, and platelet activation (a risk factor for thrombosis). Rodent studies show that ozone compromises immune function against bacterial infection. Not only do these mechanistic studies support the biological plausibility of exposure-mortality associations, such as those found by Di et al, but they also provide insights for potential “therapeutic” interventions. For instance, a limited number of studies suggested that antioxidant supplementation may reduce the effects of PM$_{2.5}$ or ozone. More intervention trials should be conducted to examine the efficacy of using dietary supplementation, medications, or personal protective equipment in alleviating the adverse health effects of air pollution in the general population and particularly in more susceptible populations.

The findings of Di et al may have implications for forecasting and personal monitoring of exposure to PM$_{2.5}$ and ozone, which could allow individuals at increased risk to reduce or mitigate their exposure. The study showed that when PM$_{2.5}$ or ozone concentration was higher on a particular day, more deaths occurred 2 days later. Predictions of pollutant concentrations for the next few days, such as weather forecasting, can be made readily available to the public. (For example, this has already
been done in China.) Individuals can be advised to minimize their outdoor activities when outdoor pollutant levels are projected to be higher. However, staying indoors may be more helpful in avoiding exposure to ozone than to PM$_{2.5}$ because less than 30% of ambient ozone penetrates indoor spaces when windows and doors are closed, whereas more than 80% of PM$_{2.5}$ enters the indoor space in the absence of an air cleaning device such as central or room filtration.

In the study by Di et al., several subgroups of Medicare recipients, including nonwhite individuals, women, Medicaid-eligible individuals, and older adults (>70 years) were found to have increased susceptibility to PM$_{2.5}$ and ozone. These susceptibility factors should be considered in developing personalized protection strategies, such as staying indoors on heavy pollution days and during exacerbations of underlying respiratory conditions, and wearing personal protective equipment, such as N95 face masks and respirators when outdoors. Individuals at increased risk may also wish to avoid places such as heavily polluted city streets. Furthermore, with rapid technological advancements, it becomes increasingly feasible to use low-cost, light-weight pollutant monitors in residences and workplaces or to be worn by individuals. Such exposure data can be integrated into a mobile health platform as part of an overall health management plan to achieve maximal risk reductions.

Such individual-level protections, however, are only a complement to the ultimate solution of emission controls. In 2015, 107 million and 23 million people lived in US counties where air quality did not meet the standards for ozone and PM$_{2.5}$, respectively. While efforts are needed to bring these nonabatement counties into compliance with the current NAAQS, regulators should continue to consider emerging scientific evidence such as that reported by Di et al. and should further lower the standards to minimize health risks. Some may argue that it would be too costly to make further improvements in air quality when pollution levels are relatively low. However, pollution controls required by the Clean Air Act have been associated with preventing an estimated hundreds of thousands of premature deaths and with estimated economic benefits exceeding the costs. It can be assumed that even greater health benefits could result from further emission reductions, which can be achieved through cleaner energy production (eg, by renewable, nonpolluting sources such as wind and solar power) and a cleaner transportation fleet (eg, with electric and hybrid vehicles and low-emission mass transportation).

**REFERENCES**


