HEI

STATEMENT

Synopsis of Research Report 212, Phase 2

HEALTH EFFECTS INSTITUTE

Mortality–Air Pollution Associations in Low-Exposure Environments (MAPLE): Phase 2

BACKGROUND

Growing scientific evidence indicates that effects of air pollution on health are observed at concentrations below current air quality standards. Combined with the large burden of disease attributed to air pollution exposure, this is resulting in consideration of more stringent air quality standards and guidelines. To improve our understanding of exposure–response functions for mortality and morbidity at low concentrations of fine particulate matter ($PM_{2.5}$), nitrogen dioxide, ozone, and other ambient air pollutants, HEI issued RFA 14-3, *Assessing Health Effects of Long-Term Exposure to Low Levels of Ambient Air Pollution*. Three studies based in the United States, Canada, and Europe were funded. The studies used state-of-the-art exposure assessment methods with large cohorts in high-income countries where ambient concentrations are generally lower than current air quality guidelines and standards for Europe and the United States. HEI convened an independent Low-Exposure Epidemiology Studies Review Panel to evaluate the studies' strengths and weaknesses. This Statement highlights results from the study in Canada.

What This Study Adds

- The MAPLE study evaluated whether exposure to fine particulate matter ($PM_{2.5}$) at concentrations below current air quality standards was associated with an increased risk of nonaccidental death among 7.1 million Canadian adults.
- Combining satellite data, air monitor sampling, and atmospheric modeling, the investigators estimated outdoor $PM_{2.5}$ exposures across Canada from 1981 to 2016.
- They applied comprehensive epidemiological analyses in a large representative sample of Canadian adults to evaluate the risk of death at different $PM_{2.5}$ exposure ranges and to identify the lowest concentration at which associations with health effects could be detected.
- Long-term outdoor $PM_{2.5}$ exposures as low as 2.5 μg /m^3 were associated with increased risk of death, with variation across different geographical regions and with smaller effects when adjusted for ozone concentrations.
- This study identified associations with health effects at $PM_{2.5}$ concentrations below the current U.S. ambient air quality standard of 12 μg/m^3, suggesting that lowering the standard could yield further health benefits.

APPROACH

The Mortality–Air Pollution Associations in Low-Exposure Environments (MAPLE) study by Brauer and colleagues aimed to characterize the association between long-term exposure to outdoor $PM_{2.5}$ and death in a nationally representative sample of Canadian adults, with a focus on $PM_{2.5}$ concentrations below current air quality standards. They created $PM_{2.5}$ exposure estimates across North America from 1981 to 2016 that incorporated satellite, ground monitor, and atmospheric modeling data. The study had the following objectives:

1. To evaluate the association between long-term outdoor $PM_{2.5}$ exposure and total and cause-specific nonaccidental death, including assessments among people with exposures below the current U.S. air quality standard
2. To evaluate these associations across regions of Canada with different atmospheric conditions while accounting for exposure to the co-occurring pollutant ozone
3. To examine whether the association between $PM_{2.5}$ exposure and death changed over different exposure ranges
4. To identify the $PM_{2.5}$ concentration below which there was no association with increased risk of death.

This Statement, prepared by the Health Effects Institute, summarizes a research project funded by HEI and conducted by Dr. Michael Brauer at The University of British Columbia, School of Population and Public Health, Vancouver, BC, Canada, and colleagues. The complete report, *Mortality–Air Pollution Associations in Low Exposure Environments (MAPLE): Phase 2*, © 2022 Health Effects Institute, can be obtained from HEI or our website (see last page).

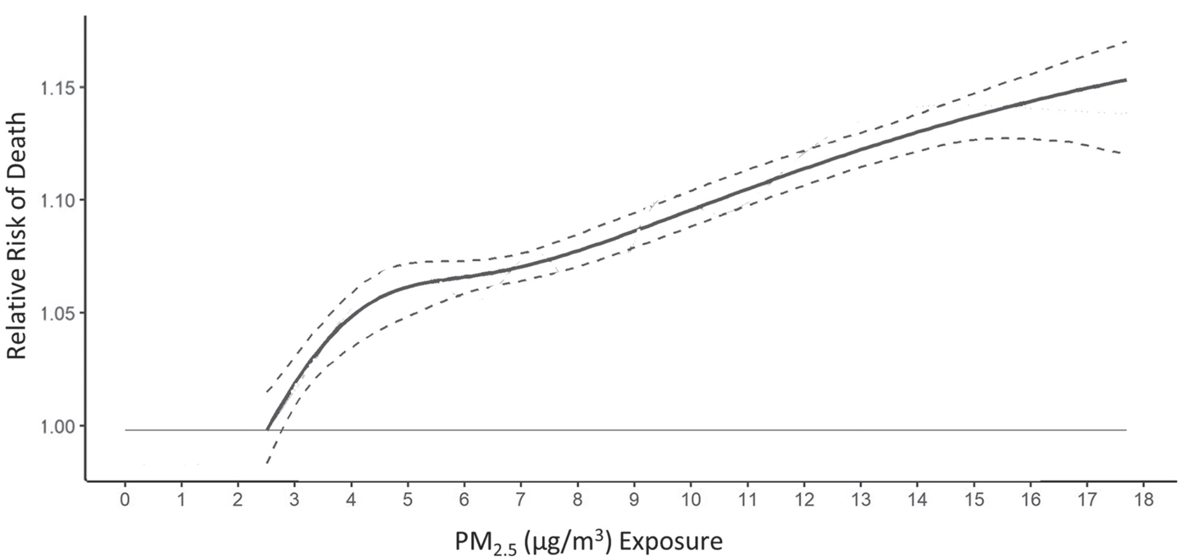
The investigators assembled a census-based cohort that combined three cycles of the Canadian Census Health and Environment Cohort. It comprised 7.1 million people and recorded 1.3 million deaths over the 25-year study period (1991–2016). They estimated outdoor $PM_{2.5}$ concentrations averaged over 10 years at a 1×1 km resolution and then assigned exposure for each participant based on home postal codes and accounted for address changes. They used Cox hazards regression to assess the overall average association of the assigned $PM_{2.5}$ exposure with death. In addition, they used the Shape Constrained Health Impact Function model to examine the shape of the association over the full range of exposures as well as whether the association changed over different exposure ranges. The analyses were adjusted for the region of Canada, census year, and many individual- and community-level sociodemographic factors. The specific causes of death evaluated were death from cardiovascular disease, cerebrovascular disease, ischemic heart disease, heart failure, diabetes, nonmalignant respiratory disease, chronic obstructive pulmonary disease (COPD), pneumonia, lung cancer, and kidney failure.

KEY RESULTS

Long-term outdoor $PM_{2.5}$ exposure was associated with increased total nonaccidental death (hazard ratio per 4.16 μg/m^3 = 1.034; 95% confidence interval = 1.030–1.039). In other words, an interquartile range increase in $PM_{2.5}$ exposure from the 25th to 75th percentile was associated with 32 more deaths for every 100,000 people each year when compared with the average annual death rate over the 25-year study period. Given Canada's population in 2016, this rate equates to 7,848 more deaths every year. In cause-specific analyses, higher $PM_{2.5}$ exposure was also associated with increased risk of death due to cardiovascular disease, ischemic heart disease, cerebrovascular disease, diabetes, pneumonia, respiratory disease, and COPD.

The shape of the association between $PM_{2.5}$ and death was nonlinear; this means that the association varied for different concentrations of $PM_{2.5}$ exposure (Statement Figure). The relative risk of death increased rapidly from the minimum $PM_{2.5}$ concentrations of 2.5 μg/m^3. At $PM_{2.5}$ concentrations of 5 μg/m^3 and above, the relative risk of death increased linearly at a shallower slope. The investigators did not detect a definitive $PM_{2.5}$ concentration below which no health effects were observed; they observed positive associations with risk of death near the lowest $PM_{2.5}$ exposure in this study, 2.5 μg/m^3.

Results were similar when limiting the analysis to people with $PM_{2.5}$ exposure below 12 μg/m^3, the current U.S. air quality standard. In contrast, there was no association when limiting the analysis to people with $PM_{2.5}$ exposure below the former Canadian standard of 10 μg/m^3. Brauer and colleagues suggested that higher exposures were influential in deriving the statistical estimates of the association between $PM_{2.5}$ and death. However, they noted that limiting the exposure concentration to 10 μg/m^3 resulted in a sample group of people



Statement Figure. Shape of the association between outdoor $PM_{2.5}$ exposure and nonaccidental death. This plot shows how the risk of death changes over different $PM_{2.5}$ exposure concentrations. The relative risk of death compares the lowest observed $PM_{2.5}$ concentration (2.5 μg/m^3) to all higher concentrations. (Adapted from Investigators' Report Figure 29.)

who were demographically different from the original nationally representative sample. Therefore, the results from the restricted sample might not apply to the population of Canada as a whole. Furthermore, the association was smaller when adjusting for co-occurring pollutant ozone, and different results were observed for the different regions of Canada. The results were similar after adjusting for lifestyle factors and for regional differences in population characteristics and healthcare access. That suggests that co-occurring pollutants and atmospheric conditions are important determinants of the association between $PM_{2.5}$ and death.

INTERPRETATION AND CONCLUSIONS

This study found that low-level $PM_{2.5}$ exposure was associated with increased risk of total and cause-specific deaths. The results also found that the risk of death is not the same across all $PM_{2.5}$ concentrations. The largest change in the increased risk of death occurred among people with the lowest $PM_{2.5}$ exposure concentrations. The results were largely in agreement with prior studies that have shown increased risk of death for total, respiratory, and cardiovascular-related mortality. This study adds to the growing number of studies that suggest the shape of the association is steepest at lower $PM_{2.5}$ concentrations.

In its independent review of the study, HEI's Low-Exposure Epidemiology Studies Review Panel commended the investigators for assembling such comprehensive data, creating state-of-the-art $PM_{2.5}$ exposure estimates and thorough statistical analyses. However, the Panel noted that some results were difficult to interpret. For example, the Shape Constrained Health Impact Function showed that the shape of the association was largest at lower $PM_{2.5}$ concentrations but limiting the Cox hazards analysis to people with $PM_{2.5}$ exposures below 10 μg/m^3 showed no association. There were also different results for specific regions of Canada that could not be attributed to measured demographic differences but which might reflect differences in the mixture of air pollutants. Because the study had a large sample size and good statistical power, the Panel concluded that the effects of bias more so than random error could have influenced the results. Sources of bias might include confounding factors that the investigators were unable to control for, such as other copollutants. Exposure measurement error could have also differed across the urban versus rural regions of Canada.

In conclusion, the Panel agreed that this study found evidence of associations between $PM_{2.5}$ and health effects at concentrations well below 12 μg/m^3, the current U.S. ambient air quality standard. Future work is needed to investigate the influence of other copollutants and atmospheric conditions.

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