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Invited Perspective: Forward Progress in Characterizing the Mortality Burden of $PM_{2.5}$ for India

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Home to nearly 1.4 billion people (World Bank 2022), India is one of the most populated countries in the world. India also has some of the highest levels of air pollution, with an estimated population-weighted mean fine ambient particulate matter [PM $\leq$2.5 µm in aerodynamic diameter ($PM_{2.5}$)] concentration of $91.7\ \mu g/m^3$ in 2019 and virtually all people living at levels above the World Health Organization's (WHO) Air Quality Guidelines (India State-Level Disease Burden Initiative Air Pollution Collaborators 2021). Given these high exposures, it has been estimated that nearly 1 million deaths and 31 million years of healthy life were lost in 2019 due to ambient $PM_{2.5}$.

These burden estimates clearly suggest a public health problem requiring intervention. However, these estimates (and other global and regional estimates) rely on evidence generated from elsewhere in the world—largely in North America and Europe, and only more recently from Asia and the Middle East. Although experts have argued that relying on estimates from other nations should produce reliable estimates for India in the absence of area-specific information (GBD MAPS Working Group 2018; Ministry of Health and Family Welfare, Government of India 2015), why has local evidence not been available? The answer lies with a historic lack of data in India. Reporting by the Civil Registration System Division in India indicates steady improvement in the capture of deaths by administrative records over time but the data completeness did not exceed 70% until after 2018 (ORGI 2020). For many states and region territories, the capture is closer to 50% and, nationally, <20% of deaths are medically certified with an underlying cause. In addition, local and national air pollution data and modeled estimates have only become widely available in the last 5–10 y.

Brown et al. (2022) address this knowledge gap by leveraging data from the Million Death Study and satellite-derived estimates of ambient $PM_{2.5}$ concentrations for India. Specifically, they linked ambient $PM_{2.5}$ (0.1° resolution) to cause-specific mortality rates for nearly 7,500 urban postal codes and rural villages throughout India. In these communities, nearly 7 million individuals were actively surveilled for mortality using a validated instrument. For every $10\text{-}\mu g/m^3$ increase in estimated $PM_{2.5}$, they documented a 9% higher rate for stroke mortality (95% confidence interval: 1.04, 1.14) after adjustments for age, sex, time, area-level urbanicity, area-level socioeconomic characteristics, and place. More modest associations were observed with nonaccidental and chronic respiratory disease mortality, and null associations were found with heart attack mortality. Notably, given the interquartile range in India ($\sim 20\ \mu g/m^3$), these associations appear even larger (up to 1.17) when expressed as contrasts between high- and low-exposed individuals.

Overall, these findings confirm that air pollution likely results in premature mortality in India, mostly via stroke. Many of the associations, however, were weaker than what may have been expected given the current global evidence on the association between air pollution and respiratory and cardiovascular diseases. This may be important because burden estimates, including those by the Global Burden of Disease project and WHO assume that air pollution–mortality relationships are supralinear (India State-Level Disease Burden Initiative Air Pollution Collaborators 2021) even though relatively few studies have assessed the concentration–response function at high $PM_{2.5}$ levels. In fact, the concentration–response function used before 2019 relied on extrapolations from tobacco smoking (Burnett et al. 2014), although newer estimates use data from five studies in China, Hong Kong, and 21 nations of the Prospective Urban Rural Epidemiology study (India State-Level Disease Burden Initiative Air Pollution Collaborators 2021; GBD 2019 Risk Factors Collaborators 2020).

There are several possible explanations for the weaker associations observed in this study. One simple explanation is that any sample has normal variation and that the confidence intervals for this study include values consistent with previous estimates. Another possibility relates to differential toxicity of local sources. In India, $PM_{2.5}$ has a larger fraction from biomass burning as compared with North America and Europe (McDuffie et al. 2021; GBD Maps Working Group 2018), which could be less toxic than other sources. Evidence supporting this hypothesis comes from China, where associations with daily mortality were weaker in rural areas (where more biomass burning occurs) than in urban areas (where fossil fuel combustion dominates) (Chen et al. 2017). Yet the same rural–urban trends did not seem to hold in India. A second causal hypothesis relates to India's lower life expectancy than other nations (World Bank 2022) that inform the air-pollution mortality relationship. This could result in weaker associations if $PM_{2.5}$ is less toxic at younger ages or in the context of more competing risks. However, Brown et al. (2022) did not observe consistent effect modification by age.

It is also possible, as with all epidemiological studies, that residual bias influenced the results. Although deaths were recorded for individuals, the data were analyzed as rates per geographic area with age and sex as the only individual-level covariates. This could

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imply that residual confounding may remain. Although adjustment for place may capture some variation in individual and community risk factors that correlate with air pollution, knowing how granular of an adjustment to include can be quite challenging and the results of Brown et al. (2022) did show strong sensitivity to adjustment for place. It may also be that the definitions for cause-specific mortality, such as from heart attacks, differed from other studies and may have impacted the magnitude of their findings. Similarly, it is possible that the use of verbal autopsies may have introduced some differential error by place.

Despite these potential issues, this study is important as the first to evaluate long-term $PM_{2.5}$ exposure and mortality across all of India. Together with other recent studies (Hadley et al. 2022; Hystad et al. 2019, 2020), it begins to resolve a critical research gap on the adverse health effects of air pollution in low- and middle-income countries and regions with high levels of ambient air pollution. Somewhat curiously, results from this study differ significantly from the global body of evidence, especially on cardiovascular outcomes. This warrants attention and the work should be extended with confirmation of these findings in other data sets with individual-level data, evaluations of household air pollution–mortality relationships, and use of personal exposure estimates in future analyses. Fortunately, there is a rapid growth of research in India, including studies such as the Longitudinal Aging Study of India (Bloom et al. 2021), Tamil Nadu Air Pollution and Health Effects (Balakrishnan et al. 2015), Global Environmental and Occupational Health–India (Walia et al. 2020), and Cardiovascular Health Effects of Air Pollution in Andhra Pradesh, India (Tonne et al. 2017). There are also ongoing efforts to strengthen collaborations and technical expertise on air pollution epidemiology through the Collaborative for Air Pollution and Health Effects Research–India. Therefore, we expect to see a rapid expansion in the research building upon this work in the future. Better characterization of the health effects of $PM_{2.5}$ in India will ultimately be useful in informing future strategies to improve public health in India as well as our understanding of health effects of air pollution globally.

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