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Do Coarse Mass Particles Increase Daily Mortality? New Findings from a Multi-Country, Multi-City Study

The thousands of liters of air inhaled daily contain myriad particles that are diverse in size, origin, composition, and potential toxicity. For regulatory and air pollution control purposes, airborne particulate matter (PM) is classified by aerodynamic diameter (1, 2). At present, air pollution control is focused on reducing PM ⩽ 2.5 μm in aerodynamic diameter ($PM_{2.5}$), a size range encompassing combustion-generated particles that reach the smaller airways and alveoli. For $PM_{2.5}$, the U.S. Environmental Protection Agency (EPA) first promulgated an annual National Ambient Air Quality Standard (NAAQS) in 1997 at 15.0 μg/m^3, which was tightened to 12.0 in 2012. The recently revised World Health Organization (WHO) Air Quality Guidelines propose an $PM_{2.5}$ level at 5.0 μg/m^3, lower than levels in most urban areas. There is also a NAAQS for PM ⩽10 μm in aerodynamic diameter (PM_{10}), which includes both $PM_{2.5}$ and larger particles in the size range from $PM_{2.5}$ up to PM_{10}.

In the United States, the increasingly stringent NAAQS for PM have driven improvements in air quality (3). However, PM in the 2.5 to 10 μm band is not specifically regulated and the potential toxicity of particles in this size range has not received the attention directed at smaller particles. The larger particles are primarily crustal in origin, and include road and desert dust and some bioaerosols, e.g., pollens (1). These larger particles are deposited in the upper airway and the larger airways of the lung, where they can cause injury through inflammation and other mechanisms. The most common indicator for particles in this size range, generally referred to as coarse mass PM, is the mass difference between PM_{10} and $PM_{2.5}$, i.e., $PM_{10-2.5}$. Given their differing sources, strategies to address $PM_{2.5}$ may have little impact on $PM_{10-2.5}$.

To date, the evidence on $PM_{10-2.5}$ has not been considered as sufficient to warrant regulation. The most recent EPA Integrated Science Assessment (ISA) for PM found the evidence for adverse health effects of $PM_{10-2.5}$ to be unconvincing and the WHO Guidelines, while covering PM_{10}, did not consider $PM_{10-2.5}$ (1).

In this issue of the *Journal* (pp. 999–1007), Liu and colleagues, a large international collaborative team, report the findings of a pooled daily time-series analysis that assesses associations of $PM_{10-2.5}$ with daily counts for all deaths, respiratory deaths, and cardiovascular deaths in 205 cities in 20 countries (4). The investigators find significant positive associations with each of the three outcomes and the associations are robust to consideration of other pollutants. Additionally, as found with $PM_{2.5}$ in other studies, the modeled exposure-response relationships showed an association down to the lowest concentrations, weighing against thresholds that might anchor regulations and guidelines (5). The 20 countries span a range of environments, although most are high- or middle-income. There was significant but explained variation across the three WHO regions considered. For the 20 countries included, desert dust was not a major source of $PM_{10-2.5}$ so that new insights were not gained on this problematic contributor to coarse mass PM.

The Multi-City Multi-Country (MCC) Collaborative Research Network performed this study (6). The group has used a large pooled data set to carry out multiple analyses directed at air pollution and temperature and health. The Network's analyses

Originally Published in Press as DOI: 10.1164/rccm.202206-1178ED on June 23, 2022

reflect the evolution of time-series studies over the last three decades, from studies based in single cities to large, multi-country, multi-city studies made possible by methods for handling large data bases and pooling across cities. The investigators used a common analytical approach, eliminating one nagging source of heterogeneity in pooling published estimates of association. The incorporation of multiple locations allows for exploration of meaningful spatial variation and the large sample size obviates the limitation of inadequate power.

What are the implications of the findings? Time-series studies have previously linked $PM_{10-2.5}$ to adverse health effects. For example, a daily time-series study in 272 cities in China linked $PM_{10-2.5}$ to mortality from nonaccidental and cardiopulmonary causes (7). Potential confounding of the association of coarse mass PM by smaller particles has been a consideration in interpreting the findings of time-series studies of $PM_{10-2.5}$ (8). For example, Peng and colleagues reported that daily admissions for cardiovascular and respiratory diseases of Medicare participants were positively associated with $PM_{10-2.5}$ but the associations were attenuated by control for $PM_{2.5}$ (9). In the new study by Liu and colleagues, control for $PM_{2.5}$ attenuated the associations, but they remained statistically significant (4).

The authors propose that the results suggest " … the need to establish a unique guideline or regulatory limit for daily concentrations of $PM_{2.5-10}$. The evidence has been found wanting by the EPA in the most recent PM ISA. This new study adds robust epidemiological evidence on $PM_{10-2.5}$ and daily mortality, but—by itself—it does not shift the weight of evidence towards causation of adverse effects by coarse mass PM. Certainty as to the causation of adverse health effects by coarse mass PM would be bolstered by advancing understanding of toxicity to complement the epidemiological findings. Additionally, evidence on long-term effects from cohort studies is limited (8) and recent reports from the very large, national-level investigations supported by the Health Effects Institute have not addressed coarse mass PM (10).

For some parts of the world, e.g., the Middle East, high levels of coarse mass PM from sand and dust storms are of particular concern (2). The problem reaches regionally and globally via transport and there is concern that it will be amplified by desertification brought on by drought from climate change. Based on a broad review of the toxicological evidence, Fussell and Kelly conclude there is biological plausibility supporting epidemiological findings on exposures to airborne PM coming from sand and dust storms (11). Daily time-series studies in regions where such exposures take place would be a useful complement to the findings of Liu and colleagues. This new study offers a template for filling this gap. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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