
Introduction: What is PM_{2.5}?

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Fine Particulate Matter, or PM_{2.5} is fine inhalable particles, with diameters that are generally 2.5 micrometers or smaller.¹ The average human hair is about 70 micrometers in diameter, thus the largest PM_{2.5} is 30 times smaller than human hair. PM_{2.5} is a complex mixture whose constituents vary in size, shape, density, surface area, and chemical composition. The major components of PM_{2.5} are; a) ammonium sulfate, b) ammonium nitrate, c) organic carbonaceous mass, d) elemental carbon, and e) crustal material.² PM_{2.5} often also includes many constituents that can be harmful to human health when breathed. These can include lead, arsenic, elemental carbon soot, and sulfuric acid. The nitrogen oxide compounds (NO_x) come from vehicular emissions and coal-based power plants. Ammonium and sulfur oxide compounds (SO_x) come from burning coal in power plants and application of nitrogen fertilizers in agriculture. Carbon compounds including volatile organic carbon mass come from vehicular emissions and waste burning.³ The proportion of the constituents of PM_{2.5} depends upon the sources. So, there are spatial and temporal variations of the constituents of PM_{2.5}. Because of small size, PM_{2.5} can remain suspended in the air for several days to weeks and they can be transported by winds over large distances, and thus PM_{2.5} is subject to atmospheric transboundary transport in the continent.⁴ Therefore, the impacts of PM_{2.5} do not remain confine to the sources, rather spread to distant locations.

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Documented PM_{2.5} Adverse Health Effects

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The human health impacts due to exposure to outdoor fine particulate matter air pollution, or PM_{2.5} are staggering. According to the Global Burden of Disease Study, in 2015, exposure to PM_{2.5} was deemed to be the 5th leading risk factor for mortality worldwide accounting for approximately 4.2 million deaths and 103.1 million disability adjusted life years.¹ While the United States has lower levels of air pollution than many countries, the health impacts from PM_{2.5} are still substantial. Recent estimates from the Global Burden of Disease Project indicate that there are more than 100,000 deaths annually in the United States due to PM_{2.5}.

Exposure to ambient PM_{2.5} causes many adverse human health outcomes. Substantial health impacts occur from both daily increases, and longer-term exposures that come from living in highly polluted areas for several years or decades.

Daily increases in PM_{2.5} increase the risk of asthma attacks, and hospitalizations for other respiratory diseases, heart disease, and stroke. They increase the risk of death. Children, the elderly, and those with pre-existing health conditions (like diabetes) are most vulnerable to these health impacts.

Many studies have consistently have shown that long term exposure to PM_{2.5} exposure increased the mortality from all-cause mortality, with stronger effects for respiratory and cardiovascular disease. Some of these findings were nearly 30 years ago, such as those from the Harvard Six Cities Studies,² and the American Cancer Prevention II Study.³

In 2013, the International Agency for Research on Cancer has classified PM_{2.5} as a human carcinogen based on findings from both experimental studies, and human studies of lung cancer.⁴ It has since been linked to increased risks for a number of other cancer sites, including female breast cancer,⁵ and leukemia.⁶ Exposure to ambient air pollution has also been recently linked to a number of neurodegenerative diseases, including dementia.^{7, 8}

Long term exposure to PM_{2.5} does not only impact the risk of chronic disease in older individuals, but also impacts infants and children. Exposure to PM_{2.5} during pregnancy has been linked to increased risk of pre-term birth and low birthweight babies. A systematic review of epidemiological studies with study population in the US found that exposure to PM_{2.5} was associated with increased risk of preterm birth in 19 of 24 studies (79%) and low birth weight in 25 of 29 studies (86%).⁹ The authors noted that the subpopulations at highest risk were persons with asthma and minority groups, especially black mothers.

In summary, exposure to PM_{2.5} is a human health hazard. The associated economic costs for treatment, lost wages, and has been estimate to cost the U.S. roughly 5 percent of its yearly gross domestic product (GDP) in damages (\$790 billion in 2014).¹⁰

Thank you for your attention.

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Biological plausibility PM_{2.5} on health effects

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As my colleagues have mentioned, PM_{2.5}, which is short for particulate matter at or below 2.5 µm in aerodynamic diameter, is small enough to reach the deepest parts of human lungs. In fact, PM_{2.5} irritates and corrode the walls of the alveoli, the tiny air sacs where gas exchange in the human body takes place¹.

While some have questioned how public exposures to small particles could cause such severe adverse health effects, the EPA's most recent PM_{2.5} Integrated Science Assessment from December 2019 provided the evidence of the biological plausibility of PM_{2.5} health effects. Its executive summary cited both animal toxicological and controlled human exposure studies showing the biological plausibility of respiratory, cardiovascular, and overall mortality effects observed in epidemiologic studies investigating the effects of short- and long-term PM_{2.5} exposure. Experimental exposure studies that used concentrated ambient particle exposures provided evidence of a direct effect of PM_{2.5} on adverse outcomes including increased reactive oxygen species leading to oxidation of lung cells, damage to genetic material impairing DNA repair, imbalance in calcium homeostasis hindering intracellular messaging, and increased local and systemic inflammation through overexpression of inflammatory transcription factors and cytokines. Together, these effects on the cellular level compound and lead to dysfunction in the human respiratory and cardiovascular systems.

In experimental settings, negative health effects of PM_{2.5} were observed in the range of PM_{2.5} concentrations found in the United States. In animal exposure studies, mice that breathed outdoor air with an average PM_{2.5} concentrations of 16.8 µg/m³ had lower lung function than mice in the same location that breathed filtered air². A similar mouse model study comparing

effects of city air at $22.1 \mu\text{g}/\text{m}^3$ versus its filtered-air counterpart reported increased lung inflammation and narrowing of the pulmonary arteries due to arterial wall thickening³. This finding was confirmed by other researchers, who additionally found that coronary arteries, those surrounding the heart, become thickened with $\text{PM}_{2.5}$ inhalation⁴.

In summary, evidence from experimental exposure studies support that there is biological plausibility for $\text{PM}_{2.5}$'s observed negative health effects among humans. The conclusions outlined in the EPA's Integrated Science Assessment on biological plausibility echo those reached by the National Academy of Sciences⁵, the World Health Organization⁶, the American Heart Association⁷, and the Royal College of Physicians⁸. Since $\text{PM}_{2.5}$'s effects can be explained on the biological and cellular levels, the case for $\text{PM}_{2.5}$'s causal effects on human health is strong.

Evidence for Causal Inference of $\text{PM}_{2.5}$ Health Effects

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There is consistent evidence that both short- and long-term exposures to fine particles cause adverse health outcomes, including death, cardiorespiratory morbidity, and others. Denial of this causality by pollution has happened in the past. In the '60s, when people were doubting the causality between cigarette smoking and lung cancer, Sir Bradford Hill—an English statistician—proposed a set of criteria necessary for epidemiologic evidence of a causal relationship (instead of merely a statistical association) between an exposure and an outcome. The Bradford Hill criteria have since been widely used in public health research to establish epidemiologic evidence of causal relationships. These criteria also hold in the relationship between short- and long-term exposure to fine particles and adverse health outcomes. One criterion, for example, is that of **biological plausibility**. As Dr. Fong just discussed, there is strong biological plausibility—accompanied by numerous **experimental studies**—on $\text{PM}_{2.5}$'s observed negative health effects among humans. Another criterion is that of an **exposure – response relationship**, i.e., that greater exposure leads to greater incidence of the outcome. Indeed, $\text{PM}_{2.5}$ health studies have characterized the shape of the exposure – response curve between short- and long-term exposure to fine particles and different adverse health outcomes, and all report findings in agreement with the Bradford Hill criterion. A third criterion is that of **temporality**, in that the exposure needs to precede the observed effect. Indeed, all studies have assigned $\text{PM}_{2.5}$ exposures to study participants at times (days if studying short-term effects or year(s) if studying long-term effects) before the observed health outcomes. Some recent studies, furthermore, have explicitly additionally examined exposures after the outcome (an epidemiologic approach called 'negative control exposure') and have reported associations only with those exposures before the outcome but not with exposures following the outcome, as required by the Bradford Hill criterion. Finally, one of the Bradford Hill criteria is that of **consistency or reproducibility** across studies. Indeed, health studies of $\text{PM}_{2.5}$ have consistently reported harmful associations in humans across studies, geographic regions, and populations.

Moreover, there have been recent developments in methods for epidemiologic analyses that are more robust to potential sources of bias compared to conventionally used methods, called '**causal inference methods**'. Many recent air pollution studies have used such methods and have consistently reached the exact same conclusions as studies using conventional (or not causal inference) modeling approaches. For example, in the largest long-term PM_{2.5} – mortality study to date, leveraging information on more than 68.5 million Medicare enrollees (Wu et al. 2020), we compared estimated effects using two conventional and three causal inference modeling approaches. All methods yielded near-identical effect estimates. Secondly, we restricted analyses to participants always living in locations with PM_{2.5} concentrations below 12 µg/m³ and also estimated very consistent causal effects across methods. Furthermore, we estimated that lowering the annual PM_{2.5} national standard from 12 to 10 µg/m³ would save around 15 thousand lives per year. Our study provided the most comprehensive evidence to date of the link between long-term PM_{2.5} exposure and mortality, even at levels below current standards.

In summary, there is undisputable robust evidence that both short- and long-term exposures to fine particles cause adverse health outcomes, including—but by no means limited to—death.

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PM_{2.5} Effects at Levels Below the Prevailing Standards

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Thank you for the opportunity to address the OMB today. The presentations made by my colleagues so far set the stage for us to visit and address a critical part of why we are here today—to express our strong opposition to the EPA’s decision to retain the current PM_{2.5} NAAQS standard.

Our call rests on several important body of scientific literature enumerating the many ways in which PM_{2.5} is harmful to human health at levels below the current NAAQS standard. This body of scientific literature includes the EPA’s own most recent Integrated Science Assessment (ISA) for Particulate Matter.

The ISA Executive Summary stated that “evidence continues to support a linear, no-threshold concentration – response relationship, but with less certainty in the shape of the curve at lower concentrations (i.e., below about 8 µg/m³).”¹

Our organization concurs with the opinion expressed in the ISA as representing the state of the science. Therefore, for the purposes of today’s call regarding the evidence for serious health effects below the current NAAQS standard, I highlight three selected studies below. These studies are a few among many more studies that have essentially come to similar conclusions as the ones found here:

1. The first study is the Canadian Community Health Survey cohort that studied 300,000 people across Canada. The mean annual PM_{2.5} concentration in the participants was only 6.3 µg/m³ and the 95th percentile was 11.3 µg/m³. They reported a strong association between PM_{2.5} in that range and mortality rates. Moreover, the authors specifically examined whether there was a threshold concentration below which no effects were seen in their study and found none.²
2. Another study of US Medicare beneficiaries examined the association of PM_{2.5} concentrations below the EPA standard (12 µg/m³) and mortality rates in 32.8 million members over 13 years. The study had a little less than 248 million person-years of follow-up and about 12 million deaths among the participants with annual PM_{2.5} concentration below 12 µg/m³. The authors reported a strong association between PM_{2.5} in that range and mortality.³

3. More recently, in a study just published this year, a study evaluated the relationship of ambient PM_{2.5} exposure with cause-specific cardiovascular disease (CVD) mortality in over 565 thousand US men and women, aged 50 to 71 years. They found that when compared with participants with PM_{2.5} exposure < 8 µg/m³ (referent concentration), risks for CVD mortality were statistically significantly increased among participants with PM_{2.5} exposures in the range of 8–12 µg/m³, documenting that significant adverse health effects are occurring in the US below the current standard (12 µg/m³) that the EPA wants to retain.⁴

Again, these three studies were selected out of a continually growing and expanding body of scientific evidence that enumerates the significant effects of exposure to low levels of PM_{2.5} on human health.

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PM_{2.5} Standard Setting Process Problems and ISEE Recommendations

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The North American Chapter of the ISEE remains concerned about the litany of unwarranted changes the EPA has made to the Clean Air Scientific Advisory Committee (CASAC) and the NAAQS review process. The current CASAC is unqualified to interpret epidemiologic studies, given that it lacks adequate depth and diversity of epidemiologic expertise. The myriad of changes to the NAAQS review process are collectively harmful to the quality, credibility, and integrity of the scientific review process and to the CASAC as an advisory body.

In particular, CASAC's PM Committee was inappropriately disbanded without notice on October 10, 2018. It comprised a set of appropriate experts from diverse scientific disciplines, including epidemiology, toxicology, and human clinical studies, and found substantial evidence in favor of lowering the PM_{2.5} standards. Despite being disbanded, this independent former CASAC committee reviewed the EPA's Integrated Science Assessment (ISA), and concluded "the current suite of primary fine particle (PM_{2.5}) annual and 24-hour standards are not protective of public health." They suggested that the annual standard should be revised to a range of 8 to 10 µg/m³, and the 24-hour standard should be revised to a range of 25 to 30 µg/m³. This

conclusion was based on consistent epidemiological evidence from multiple multi-city studies, augmented with evidence from single-city studies, at policy-relevant ambient concentrations, and are supported by research from experimental models in animals and humans, and by accountability studies. These data provide clear and compelling scientific evidence that the current PM_{2.5} standards are not adequate to protect human health, and that EPA has ignored the “best available science”.

While past implementation of the current PM_{2.5} NAAQS undoubtedly has reduced the burden of disease associated with air pollution exposures, there is still significant need for improvement. The Global Burden of Disease Study has estimated that some 100,000 Americans die each year from PM_{2.5} air pollution exposure at current levels. Lowering the annual standard from 12 µg/m³ to 8 µg/m³ (the lower end of the proposed range, and close to the Canadian 2020 standard) would substantially lower PM_{2.5} pollution in the US and would, upon achieving compliance, avoid tens of thousands of needless deaths each year. Clearly, the longer the EPA delays taking action on lowering this PM_{2.5} standard, the more American lives will be needlessly lost.

We strongly oppose the EPA decision to retain the current PM_{2.5} NAAQS standards. This decision is clearly contrary to the state of the science, which demonstrates that deaths and heart attacks are produced by PM_{2.5} at concentrations between 8 and 12 µg/m³ and, hence, that the Administrators’ decision violates the Clean Air Act requirement to use the “best available science” and to set standards “to protect public health with an adequate margin of safety.” The EPA proposal does neither. ISEE recommends the lower standards that would be consistent with the current state of the science and the Clean Air Act: 25 µg/m³ for the 24-hr standard, and 8 µg/m³ for the annual standard.

Thank you. I hope you take our comments to heart.