Are All Air Pollution Particles Equal? – How Constituents and Sources of Fine Air Pollution Particles ($PM_{2.5}$) Affect Health

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PMEH
POLLUTION MANAGEMENT & ENVIRONMENTAL HEALTH

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Abbreviations

Al	aluminum
ACS	American Cancer Society
BC	black carbon
Br	bromine
Ca	calcium
Cl	chlorine
Cu	copper
CVD	cardiovascular disease
EC	elemental carbon
EDV	emergency department visit
Fe	iron
IHD	ischemic heart disease
K	potassium
LMICs	low- and middle-income countries
LUR	land use regression
Mg	magnesium
Mn	manganese
$\mu g/m^3$	micrograms per cubic meter
Na	sodium
NH_4^+	ammonium
Ni	nickel
NO_2	nitrogen dioxide
NO_3^-	nitrate
OC	organic carbon
Pb	lead
PM	Particulate Matter—A mixture of solid particles and liquid droplets found In the air
$PM_{2.5}$	Particulate Matter equal to or less than 2.5 microns in diameter
PM_{10}	Particulate Matter equal to or less than 10 microns in diameter
RSD	respiratory disease
S	sulfur
Se	selenium
Si	silicon
SO_4^{2-}	sulfate
Ti	titanium
V	vanadium
Zn	zinc

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Preface

Improving the air we breathe is quite literally an endeavor of global proportions, importance, and urgency. Across the world, outdoor air pollution kills an estimated 4.2 million people a year and harms millions more, makes cities less livable, hampers economic competitiveness, harms ecosystems, and disproportionally affects the most vulnerable.

Decades of global studies have shown that air pollution made of inhalable, microscopic particles known as fine particulate matter, or $PM_{2.5}$, is especially harmful to humans. Most studies on the health impacts of the particles have focused on their mass, with the assumption that particles of the same mass are equally harmful, regardless of their source.

Yet $PM_{2.5}$ can come from a variety of sources - such as vehicle exhaust, road dust, industrial smokestacks, and biomass burning - and can be made of different chemical constituents. Evolving evidence shows that the danger to humans can actually vary depending on the source and chemical composition of $PM_{2.5}$. Furthermore, particles in low- and middle-income countries usually have very different sources and compositions from particles in high-income countries. Therefore, health effects per unit mass of $PM_{2.5}$ are likely different in low- and middle-income countries than those in high-income countries, which form the basis of present global and regional assessments of health impacts. This report offers a comprehensive review of the health effects of short- and long-term exposure to the different sources and constituents of outdoor $PM_{2.5}$ air pollution.

The report finds that $PM_{2.5}$ mass and chemical constituents from fossil fuel combustion are some of the most toxic and damaging to health. The health risk is particularly great from coal combustion- and traffic-related $PM_{2.5}$ particles, which are most consistently associated with cardiovascular mortality, especially from heart attacks. These findings are supported by links between hospitalizations and mortality and chemical constituents, notably sulfate and elemental carbon, that are important markers of coal burning and diesel-fueled traffic respectively.

It is envisaged that these important findings will bring a new focus to the fight against air pollution in developing countries. Because reducing $PM_{2.5}$ emissions from fossil fuel combustion, such as sulfur-emitting coal-fired power plants and diesel vehicles, can produce the most significant health benefits, countries' air pollution control efforts should prioritize these sources. Such efforts could also help to mitigate climate change, as these same fossil fuel combustion sources contribute significantly to global climate pollution.

About This Work

The pioneering analytical work in this report builds on a growing body of evidence that the World Bank is building to inform more effective and efficient pollution management interventions and harness the transition to a circular economy in low- and middle-income countries. This growing body of evidence focuses on strengthening the knowledge base that will prompt dedicated action to tackle the forms of pollution that cause the most significant health and social costs in low-and middle-income countries. It also advances inter-disciplinary approaches to assess the linkages between pollution management and circular economy and the World Bank's dual goals of eradicating poverty and promoting shared prosperity. Recent contributions from this body of work include: (i) the monetary valuation of the global cost of mortality and morbidity caused by exposure to ambient fine particulate matter air pollution; (ii) bolstering the case for establishment and strengthening of ground-level air quality monitoring networks in low- and middle-income countries; (iii) the development of a systematic framework to support analysis of health impacts from land-based pollution; and (iv) economic and financial instruments to support the transition to circular economy.

Acknowledgments

This report was prepared by a team led by **Yewande Awe**, with the core team consisting of **George Thurston** (New York University School of Medicine), **Bart Ostro** (University of California, Davis), and **Ernesto Sánchez-Triana** (World Bank). **Dr. Thurston** and **Dr. Ostro** prepared the background report.

The contribution of **Dr. Chris Lim** (Yale University) to the preparation of this report is appreciated. The team would like to acknowledge, with thanks, the valuable advice and inputs of the peer reviewers: **Jiang Ru, Martin Ochoa, Tamer Rabie**, and **Stephen Dorey.** This report also benefitted from comments and other inputs provided by the following colleagues: **Fernando Loayza**, **Marcelo Bortman**, **Momoe Kanada**, and **Hocine Chalal** The contributions of **Phil Dickerson** (US Environmental Protection Agency AirNow program) and **Joanne Green** (Ricardo Energy, formerly of The Clean Air Institute) are also appreciated.

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About the Authors

George Thurston's research has focused on the human health effects of air pollution, especially regarding fine particulate matter ($PM_{2.5}$). It has involved studies of air pollution exposure and their health effects in panels of individual human subjects, as well as large cohorts. In 1987, he published the first research documenting the association between $PM_{2.5}$ mass and its components with mortality. Recent awards include the 2012 "Haagen Smit Prize" from Atmospheric Environment.

Dr. Thurston has also been a leader in bringing scientists and physicians together to reach consensus on key issues. He led the recent American Thoracic Society (ATS) and European Respiratory Society (ERS) Statement on "What Constitutes an Adverse Effect of Air Pollution" (2017), and received the 2017 American Thoracic Society's Public Service Award. He has also been a pioneer researching the human health co-benefits of climate change mitigation, first publishing in Science on the issue in 2001.

Yewande Awe is a Senior Environmental Engineer at the World Bank where she also holds a leadership position in the Bank's Air Quality Management Community of Practice. She has led and been team member, in the preparation and supervision of policy-based programs, investment projects, technical assistance operations, and analytical activities in several countries. She has worked on projects in Antigua and Barbuda, Argentina, Bolivia, Bosnia and Herzegovina, Kosovo and North Macedonia, Colombia, Dominica, El Salvador, Grenada, Guatemala, Jamaica, Mexico, Nigeria, Peru, Poland, St. Kitts and Nevis, St. Lucia, St. Vincent and the Grenadines, and Yemen. She has authored several publications, in peer reviewed scientific journals, on environmental engineering, environmental health and emerging strategies for environmental quality monitoring in low- and middle-income countries.

She was Scientific Adviser for the First Global Conference on Air Pollution and Health, and a member of the Report Steering Committee for the Lancet Commission on Pollution and Health. She sits on the Board of Directors for Pearson College UWC in Canada, a pre-university school in a movement of 18 global schools dedicated to uniting cultures and countries around the world through education. Awe is involved with Women in Technology International, a global organization dedicated to empowering innovators and building inclusive cultures. Nominated by her colleagues, she serves as Respectful Workplace Advisor at the World Bank. Awe holds a PhD in Environmental Engineering from Imperial College London, United Kingdom.

Bart Ostro was the Chief of the Air Pollution Epidemiology Section, California Environmental Protection Agency (CalEPA) for almost 25 years and is now a Research Professor at the University of California at Davis. His primary responsibilities at CalEPA included formulating the Agency's recommendations for state air pollution standards and investigating the health effects of air pollution and climate change. Dr. Ostro was a co-author of the U.S. EPA Regulatory Impact Analysis that was a basis for the federal ban of lead in gasoline. He chaired the U.S. EPA's Science Advisory Board Clean Air Council, and served

on the National Academy of Sciences' Committee on Estimating the Benefits of Proposed Air Pollution Regulations. He has published over 100 scientific papers and has consulted for several federal and international institutions and governments. He was honored with Special Achievement Awards from the U.S. EPA and the California Air Resources Board. In 2005 he was given the American Lung Association of California's Clean Air Award, presented to the individual who "has made the most significant contribution to the cause of cleaner air in California."

Ernesto Sánchez-Triana is the Global Lead for Pollution Management and Circular Economy for the World Bank. He has worked on projects in numerous countries, including, among others, Afghanistan, Argentina, Bangladesh, Bhutan, Bolivia, Brazil, Ecuador, India, the Lao People's Democratic Republic, Mexico, Pakistan, Panama, Paraguay, and Peru. Before joining the World Bank, he taught at Colombia's National University and worked for the Inter-American Development Bank. He also served as Director of Environmental Policy at Colombia's National Department of Planning and as President of the Board of Directors of the Cundinamarca Environmental Protection Agency.

Dr. Sánchez-Triana has led the preparation of numerous policy-based programs, investment projects, technical assistance operations, and analytical works. He holds an engineer degree from Universidad de Los Andes (Colombia), and two master of science degrees and a PhD from Stanford University. He has authored numerous publications on air quality management, air quality monitoring, circular economy, cleaner production, climate change, country environmental analyses, energy efficiency, energy policy, environmental economics, environmental sustainability, environmental health, environmental impact assessment, environmental management, industrial sustainable growth, green growth, land-based pollution, organizational learning, policy strategic environmental assessments, sustainable development, and water resources management.

I. Executive Summary

- Global studies of the health impacts of fine particulate matter ($PM_{2.5}$) have been based on particle mass, but there is evolving evidence indicating that adverse health effects can vary depending on the source and composition of $PM_{2.5}$. This complicates the equitoxicity assumption commonly made regarding particle air pollution while raising the question as to which types of $PM_{2.5}$ are most toxic.
- This report provides a comprehensive review of health effects of short- and long-term exposures to source-related components and trace constituents (specific markers of the individual sources) of fine particulate matter ($PM_{2.5}$) in outdoor air pollution. The analysis evaluates the data and methods used, as well as the uncertainties in the underlying epidemiological studies, based on the relevant published literature.[1]
- Most deaths attributed to outdoor $PM_{2.5}$ air pollution (for example, by the Global Burden of Disease study) are caused by cardiovascular disease (CVD). The current evidence summarized in this report indicates that trace constituents from $PM_{2.5}$ and $PM_{2.5}$ mass from fossil-fuel combustion are among the greatest contributors to $PM_{2.5}$ toxicity. Notably, $PM_{2.5}$ from fossil-fuel combustion poses a larger cardiovascular disease risk per unit mass of $PM_{2.5}$ than soil or biomass particles.
- Of the fossil-fuel combustion particles, coal- and traffic-related $PM_{2.5}$ were found to be most consistently associated with cardiovascular mortality, especially due to ischemic heart disease (heart attacks) in both the short- and long-term exposure studies that were reviewed.
- The importance of coal combustion and traffic-emission sources to the overall associations of $PM_{2.5}$ mass with mortality and hospital admissions is supported by the health risk associations that are also observed with their source-specific trace constituents. For example, particulate selenium and sulfur are important markers for coal combustion. Particulate sulfur compounds in the environment are usually present as ammonium sulfate, ammonium bisulfate, or sulfuric acid. Similarly, elemental carbon (EC) is a strong marker for traffic, especially for diesel-fueled vehicle emissions. Based on the results of several recent epidemiological and toxicological studies, some researchers reported results indicating that particulate sulfur is among the most, if not the most, important constituent of $PM_{2.5}$ associated with adverse health effects such as additional hospital admissions and mortality.
- The long-term studies reviewed in this report indicate that the cardiovascular disease risks of sulfate, EC, and $PM_{2.5}$ from coal combustion are larger than that from $PM_{2.5}$ mass, in general. Furthermore, a fairly consistent association between sulfate and cardiovascular mortality is indicated.

1 This report covers literature published through October 2018.

- The apparently central role of particulate sulfur in these $PM_{2.5}$-health associations may not be due to the direct adverse effects of sulfur but more likely to its usual occurrence in intimate mixtures with other compounds concentrated in fossil-fuel combustion particles, including transition metals that can cause systemic oxidative stress in the human body. Oxidative stress is a known predictor of cardiovascular disease. The acidic nature of particulate sulfur compounds in the environment (for example, sulfuric acid) has been shown to make such transition metals more bioavailable, enhancing the potential of sulfur-containing particles to cause oxidative stress and serious adverse health effects throughout the human body.

- However, it is possible that since particulate sulfur is more homogeneous spatially (that is, more equally dispersed over a wider area) than constituents of primary $PM_{2.5}$, such as EC, measurement of exposure to particulate sulfur might be more accurately obtained by a limited set of monitors (or a single monitor) in a metropolitan area than more spatially variable constituents of $PM_{2.5}$. Such greater accuracy of measurement would lead, in general, to a greater likelihood of observing an association.

- $PM_{2.5}$ mass, its source-specific mass components, and its elemental constituents are less consistently associated with respiratory disease (RSD) outcomes than with cardiovascular disease outcomes in general, except for short-term exposures to $PM_{2.5}$ from biomass combustion.

- In general, weaker associations were found between mortality and concentrations of $PM_{2.5}$ from biomass combustion or crustal sources (for example, windblown soil). These two sources are extremely varied spatially and temporally, especially for estimating long-term exposure. A resulting population exposure misclassification could contribute to the lack of detection of their health associations. In addition, there are fewer US metropolitan areas studied that have significant concentrations of biomass and soil sources, which may limit the ability of national-scale studies to identify risks of these two sources of $PM_{2.5}$. On the other hand, emissions from traffic and their markers (for example, EC) are also quite spatially variable within a metropolitan area (for example, near versus far from roadways), causing exposure misclassification, but still show consistent associations with adverse health effects across studies.

- Particles in low- and middle-income countries (LMICs) usually have very different sources and compositions from particles in high-income countries. Therefore, health effects per unit mass of $PM_{2.5}$ are likely different in LMICs than those in high-income countries, which form the basis of present global and regional assessments of health impacts.

- Overall, this report's key finding from the review of currently available acute (or short-term) and long-term studies suggest that reductions in the emissions of $PM_{2.5}$ from fossil-fuel combustion, such as sulfur-emitting coal-fired power plants and diesel vehicles, can produce the most significant health benefits per microgram per cubic meter ($\mu g/m^3$) of $PM_{2.5}$ reduced. In addition, these $PM_{2.5}$ emissions reductions would provide additional climate mitigation benefits, since these same fossil-fuel combustion sources contribute significantly to global climate pollution, most notably in the form of CO_2 and elemental carbon emissions.

- The relative lack of studies of the health effects of $PM_{2.5}$ constituents in the published literature for LMICs supports the need for these countries to begin measuring the

concentrations of the source-marker constituents of their particulate mixes (for example, arsenic for coal combustion and vanadium for oil combustion). Particulate sulfur and EC, which can be measured continuously, are especially important combustion markers to monitor more widely than at present. Such efforts will help determine the contribution of specific sources to $PM_{2.5}$ mass and help prioritize subsequent pollution-control efforts.

- There is also a great need to conduct short- and long-term epidemiological studies of mortality and hospitalization in LMICs, where biomass burning for cooking and heating is a significant source of $PM_{2.5}$ but a less-well quantified human health risk relative to fossil-fuel-combustion $PM_{2.5}$. In order to develop economically efficient abatement strategies that maximize human health benefits per ton of $PM_{2.5}$ emissions reduced, it is essential to (i) measure the concentration of $PM_{2.5}$ from the specific source (in this case, biomass burning), or of a marker of the source (for example levoglucosan), and (ii) determine the specific toxicities of the various $PM_{2.5}$ contributions from specific sources in LMICs.
- Ambient air pollution–control efforts in LMICs need to account for both the contributing sources of $PM_{2.5}$ and the toxicity of the $PM_{2.5}$ from each source category. The strongest evidence to date of increased risk of cardiovascular disease health effects per unit mass of $PM_{2.5}$ is found from coal combustion and diesel-fueled traffic. Therefore, future mitigation efforts that focus on monitoring and regulating the constituents of $PM_{2.5}$ from these sources should be prioritized. Reducing pollution from these sources can be expected to return greater cardiovascular health benefits per unit mass of $PM_{2.5}$ reduced than if $PM_{2.5}$ mass continues to be addressed equally, irrespective of source and composition.

“The strongest evidence to date of increased risk of cardiovascular disease health effects per unit mass of $PM_{2.5}$ is found from coal combustion and diesel-fueled traffic. Therefore, future mitigation efforts that focus on monitoring and regulating the constituents of $PM_{2.5}$ from these sources should be prioritized.”

II. Contextual Background and Objective

This report was produced as part of a program of analytical work conducted under the framework of the World Bank's multi-donor funded Pollution Management and Environmental Health (PMEH) Program. The overall aim of the work is to develop knowledge and guidance for the improvement of air quality monitoring and the estimation of health risks and effects of ambient air pollution in LMICs. One component of the analytical work focuses on improving the estimation of health impacts of ambient air pollution in LMICs. In this context, the analytical work aims to accumulate new evidence related to health impact estimation, particularly in LMICs. While exposure to fine particulate matter mass ($PM_{2.5}$) has been associated with a wide range of adverse human health effects at multiple locations around the globe, the absolute size of the effect has varied from place to place and over time, presumably because the source and nature of the particles is known to also vary over time and place. This report therefore aims to enhance the understanding of the health effects associated with specific constituents and sources of fine particles ($PM_{2.5}$).

III. Introduction

Over the past few decades, epidemiological studies have reported consistent associations[2] between both short- and long-term exposures to fine particulate matter air pollution—that is, the mass concentration of particles ≤ 2.5 micrometers in diameter ($PM_{2.5}$)—and mortality. In the air pollution studies, short-term refers to exposures of a day or multiple days while long-term refers to exposures of a year or more. Studies of short-term $PM_{2.5}$ exposures to constituents and mortality have been reported for the European Union, North America, South America, the West Pacific, and Asia (Achilleos et al. 2017; Chen et al. 2017) while long-term exposure and mortality studies have been published mostly in North America and Western Europe (Atkinson et al. 2014; Brook et al. 2010; Chen et al. 2017; US EPA 2009).

It is important to recognize, however, that ambient $PM_{2.5}$ mass consists of a heterogeneous mixture of solid and liquid particles generated by many sources (for example, cars and trucks, fossil-fuel combustion, industrial emissions, biomass, windblown dust), and, until recently, there has been only limited evidence as to which trace constituents or sources of $PM_{2.5}$ mass are associated with the greatest risks. In this context, the term "constituents" refers to specific elements and compounds that are contained in $PM_{2.5}$, while "components" are groupings of $PM_{2.5}$ constituents that are of the same origin, especially "source-related components" which are groupings of constituents that comprise the $PM_{2.5}$ from a specific source category, such as coal combustion. Constituents that are fairly unique to a source component (for example, vanadium for residual oil combustion and arsenic for coal combustion particles) are termed "tracers" for those source categories, as their presence indicates a $PM_{2.5}$ mass contribution from the source in which they are enriched, relative to $PM_{2.5}$ mass from other sources.

The fact that the mix of $PM_{2.5}$ mass source components and their respective constituent contributions to the mass vary over time and space also likely means that the toxicity of $PM_{2.5}$ mass varies from place to place and over time as well. But this aspect of $PM_{2.5}$ has been largely unaddressed by past $PM_{2.5}$ mass studies that have most often treated all $PM_{2.5}$ as the same, irrespective of the wide $PM_{2.5}$ mass composition and source variations across places and time.

The US National Research Council has highlighted the importance of investigating characteristics and constituents of particulate matter (PM) that contribute to its toxicity (National Research Council 2004). Indeed, information regarding the relative toxicity of $PM_{2.5}$ constituents and/or source components would have important implications for establishing ambient air quality standards, targeting pollution-control strategies to

2 Here, the term "association" is defined as a statistical relationship between two or more events, characteristics, or other variables—for example, an association between exposure to X and a health effect, Y. A constituent X may be the toxic agent but is more likely serving as a marker for toxic pollution from a source and is not itself the specific causal agent. In this case, the constituent is referred to as being health-associated. Association, per se, does not imply causality but is a key element in the assessment of causality (Hill 1965)

ensure improved cost efficiency, and enhancing the accuracy of health impact assessments by focusing efforts on the most toxic constituents/components. Routine collection of speciated $PM_{2.5}$ data (that is, when the mass sample is analyzed for its compositional constituents, such as metals and ions; for example, see Spengler and Thurston [1983]) in the US and some other countries now provides opportunities to examine relationships between specific PM constituents and both morbidity and mortality. In addition, several of the constituents are known to be tracers for specific $PM_{2.5}$ sources, which enables an indication of their relative source-specific $PM_{2.5}$ health impacts. Moreover, the constituents can be grouped together to quantitatively estimate source-specific $PM_{2.5}$-component contributions to $PM_{2.5}$ mass using source apportionment methods, providing an even more direct assessment of source-specific health impacts (Thurston et al. 2005).[3]

Below, the available epidemiological studies using the above-noted $PM_{2.5}$-air-pollution source and constituent exposure metrics have been reviewed to determine these various metrics' respective impacts on adverse health outcomes. In this discussion, these $PM_{2.5}$ health studies are broken into two categories: (1) short-term acute studies (for example, considering risks of daily exposures to air pollution), and (2) long-term chronic studies (for example, considering risks of annual average exposures). The focus of the review is on the most severe adverse health effects that have been associated with $PM_{2.5}$ mass: mortality and hospital admissions. These evaluations will allow insight into which source-specific $PM_{2.5}$ components (or their trace constituent markers) may be driving the associations found in studies of long- and short-term $PM_{2.5}$ exposure. These source components, therefore, are those that should become priorities for pollution-control strategies.

"The fact that the mix of $PM_{2.5}$ mass source components and their respective constituent contributions to the mass vary over time and space also likely means that the toxicity of $PM_{2.5}$ mass varies from place to place and over time as well."

3 Source apportionment is a statistical process by which the total $PM_{2.5}$ mass is separated into components that are associated with a specific source or source class based on the intrinsic characteristics of PM from that source or source class. For example, before lead was removed from gasoline, it was a very reliable tracer of automobile combustion $PM_{2.5}$ (Cooper and Watson 1980; US EPA 1984). This then allows these estimates of source-specific $PM_{2.5}$ mass to also be considered in $PM_{2.5}$ health effects analyses.

IV. Challenges and Uncertainties

There are many challenges that contribute to the difficulty of determining the relative harmfulness of the various constituents and sources of $PM_{2.5}$. First, the risk associated with an individual constituent or source may be confounded by correlated (measured or unmeasured) co-pollutants[4] or other $PM_{2.5}$ sources. There are often strong correlations among the particle constituents and co-pollutants emitted from the same sources, complicating the separation of their respective roles in associations with health impacts.

Strong statistical intercorrelations can reflect (1) a consistent chemical signature of multiple pollutants associated with PM emitted from individual major source categories, and/or (2) the similarity of certain pollutant constituents derived from different sources, such as gasoline and diesel vehicles. For example, a high correlation (of between r = 0.5 and 0.8) among elemental constituents was reported for study participants located within 10 kilometers of a monitor in California (Ostro et al. 2010). Importantly, this concern can be addressed by the consideration of $PM_{2.5}$ source components (comprising their respective source-specific groups of constituents) versus considering individual elemental constituents (that is, ignoring their multiple sources).

Second, there may be significant constituent- and source-specific $PM_{2.5}$ differences in the ultimate population exposures, making it difficult to determine the underlying differences in toxicity. Specifically, different $PM_{2.5}$ constituents and source components will likely vary in terms of the amount of time a person is exposed to each of them, since some are more spatially homogenous than others. In addition, other aspects of exposure (for example, indoor versus outdoor, exercising versus resting, proximity to source) will impact the risks associated with a given source in any given study. Thus, even if two components were equally harmful on a per-unit basis, epidemiological studies might still indicate differences in harm, due to their exposure differences (for example, in spatial variability).

Third, comparing the health effects of $PM_{2.5}$ source-related components over multiple cities may be difficult since the constituents that make up the source can differ by location across studies. However, in practice, this has not been found to be a major issue, as the source-specific characteristics are relatively stable even though their contributions to the total mass can vary greatly (Thurston et al. 2011).

4 Co-pollutants are defined here as other, usually gaseous, air pollutants (for example, nitrogen oxides, NOx) that may be emitted by the same sources (for example, motor vehicles) as specific $PM_{2.5}$ constituents (for example, elemental black carbon from diesel vehicles). As a result, separating their individual health effects can be difficult. Similarly, co-exposure to other $PM_{2.5}$ sources can complicate the attribution of effects to a single source. Thus, many studies are needed to discern their respective associations, as considered in this report.

Fourth, the extent of association of a given tracer constituent or source-related component with a health effect outcome (for example, daily hospital admission counts) could be due to differences in the amount of their respective monitoring (for example, the number of stations, relative to their individual variability over time and space). Thus, differential misclassification of exposure among the source-component contributions (and/or their tracer constituent levels) can impact the subsequent risk estimates.

Finally, for some sources, such as windblown soil and dust, the health effects may be more associated with particles larger than 2.5 micrometers in aerodynamic diameter. These health effects can include effects on the upper airways, such as the exacerbation of asthma, chronic bronchitis, or emphysema.

However, despite these concerns, it has been found that the overall uncertainty contributed by variability in the method of source apportionment of $PM_{2.5}$ mass is small compared to the overall $PM_{2.5}$-health-association uncertainty (Thurston et al. 2005). As a result of this consistency, certain clear patterns are discernible, and some reasonable conclusions can be made by reviewing the available studies. Below, a summary and review of the epidemiological studies of health effects associations of both short- and long-term exposure to $PM_{2.5}$ source-specific components (or their constituent tracers) is provided. The review is followed by the Summary and Conclusions section that discusses the overarching issues in these $PM_{2.5}$ source and constituent associations, caveats, and overall findings.

V. Methods

The various studies of short-term exposure considered in this analysis are summarized in tables 1 and 2. In order to give an indication of the strength of the health risk found with the various $PM_{2.5}$ constituents or source-specific components, the following designations were used in the tables: 0 if they were considered but were not statistically significant even at the p (or p-value) = 0.10 level; 0.5 if they were significant at the p = 0.10 level; and 1.0 if they were significant at the p = 0.05 level. The p-value indicates the likelihood of incorrectly rejecting the hypothesis of no observed association. If, over all studies in a category, a strength of association was found to be present 50 percent of the time or more (for example, ≥ 5 significance index in 10 cases), then the constituent/source was considered to be sufficiently consistent in its association with that health outcome. This provided a normalized index, allowing direct comparisons of the strength of associations across the various health outcomes and $PM_{2.5}$ components. Tables 3 and 4 summarize the studies of associations of long-term exposure to $PM_{2.5}$ constituents and/or source-specific $PM_{2.5}$ with mortality only. There were too few long-term exposure studies published to date of morbidity outcomes with trace constituents or source-specific $PM_{2.5}$ to provide the power to make meaningful health risk comparisons. The overall findings of each study considered are summarized below. Based on these review findings, as well as the overall semiquantitative evaluations of the studies in tables 1 through 4, conclusions are drawn regarding the sources and constituents most related to mortality and morbidity.

VI. Short-Term Exposure

A. Associations of Short-Term Exposure to $PM_{2.5}$ Source-Related Components, and/or Their Constituent Tracers, with Daily Mortality

The first study identified that evaluated the acute (day-to-day) risks of $PM_{2.5}$ constituents or source-specific $PM_{2.5}$ with mortality used the Harvard Six Cities Study's cohort data to evaluate the source-specific $PM_{2.5}$ using a single trace element as a marker (or "target") of that source across six US cities (Laden et al. 2000). The $PM_{2.5}$ sources and their elemental tracers identified in all six cities were: crustal (silicon, Si, as tracer), mobile sources (traffic) emissions (lead, Pb, as tracer), and coal combustion (selenium, Se, as tracer). Of these, mobile sources and coal were statistically significant overall, while the crustal component (primarily from windblown soil) was consistently not associated overall with daily mortality or in any of the individual six cities considered. Overall, the authors concluded that combustion particles in the fine fraction from mobile and coal combustion sources, but not fine crustal particles, were associated with increased mortality.

As part of a US Environmental Protection Agency (EPA) Workshop on Source Apportionment of PM Health Effects (Thurston et al. 2005), Mar et al. (2006) and Ito et al. (2006) published multianalyses of the impacts on daily mortality from exposure to $PM_{2.5}$ sources in Phoenix, Arizona, and Washington, DC, respectively. In Phoenix, the sources with the largest cardiovascular disease (CVD) mortality risk size across analyses were secondary particulate matter[5] (resulting from sulfate, SO_4^{2-}) and traffic. For total mortality, the associations were weaker. Sea salt was also found to be associated with both total and cardiovascular mortality, but at a less biologically plausible five-day lag after exposure. Fine particle soil and biomass burning factors were not associated with increased risks in Phoenix. For Washington, DC, Ito et al. (2006) reported that the largest (and most significant) percent excess deaths per increment of $PM_{2.5}$ sources for total mortality was for SO_4^{2-}. Primary coal-related $PM_{2.5}$ (identified by three workshop teams) was similarly significantly associated with total mortality with the same three-day lag as sulfate. Risk estimates for traffic-related $PM_{2.5}$, while significant in some cases, were more variable. Soil-related PM showed smaller risks. Overall, these two cities both gave support for associations of daily mortality with the SO_4^{2-} constituent, which is a result of fossil-fuel combustion. Of the sources considered by the various analyses, coal burning was most consistently associated with daily mortality.

Ostro et al. (2007) and Ostro et al. (2008) published studies addressing daily data from 2000 to 2003 on mortality (all-cause, cardiovascular, respiratory, and mortality age > 65 years) and $PM_{2.5}$ mass and its constituents in California. The constituents considered

5 Secondary particulate matter is defined here as particles not directly emitted from a pollution source (for example, a power plant stack) as particles but instead formed in the atmosphere from gaseous air pollutants, such as sulfates, which are formed from sulfur dioxide gas. Sulfate and nitrate are often considered sources since they are not directly emitted, but they also could be considered constituents.

included elemental and organic carbon (EC and OC), nitrates, sulfates, and various metals. $PM_{2.5}$ mass and several constituents were found to be associated with multiple mortality categories, especially CVD deaths. For example, for a three-day lag, CVD deaths increased by 1.6 percent, 2.1 percent, 1.6 percent, and 1.5 percent for $PM_{2.5}$, EC, OC, and nitrates, respectively. The authors concluded that their findings supported the hypothesis that combustion-associated pollutants are particularly important to $PM_{2.5}$-associated mortality. Separate models were run after stratification by gender, race/ethnicity (White, Hispanic, Black), and education (high school graduation or not). After stratification, daily counts of cardiovascular mortality were associated with $PM_{2.5}$ and several of its species including EC, OC, nitrates, sulfates, potassium, copper, and iron. For many of these species, there were significantly higher risk estimates among those with lower educational attainment and Hispanic individuals.

Cakmak et al. (2009) evaluated the association between several elements of $PM_{2.5}$ and mortality in the general population of Santiago, Chile, during the period 1998 to 2006. The strongest individual constituent mortality association was seen with elemental carbon. Using factor analysis, a group of elements consistent with a mobile combustion source (carbon monoxide, nitrogen dioxide, and elemental and organic carbon) was significantly associated with total mortality. Soil-sourced particles had a weaker but statistically significant association with mortality. Of the many sources examined, the authors concluded that particulate air pollution from motor vehicle exhaust had the greatest observed risk on mortality in this Chilean city.

Zhou et al. (2010) used time-series analyses to determine the associations between daily fine-$PM_{2.5}$ mass and its constituents with daily all-cause, CVD, and RSD mortality in two US cities: Seattle, Washington, and Detroit, Michigan. Total and CVD mortality in Detroit were most positively associated with warm-season $PM_{2.5}$ secondary aerosols and traffic markers but negatively with soil $PM_{2.5}$. In Seattle, total and CVD mortality were most closely associated with $PM_{2.5}$ from traffic and other combustion sources, including residual oil and wood burning, during the cold season.

Ito et al. (2011) examined the role of $PM_{2.5}$ and its key chemical constituents on both CVD hospitalizations and mortality in New York City for the years 2000–2006. Coal combustion–related trace constituents (for example, selenium) were associated with CVD mortality in summer and CVD hospitalizations in winter, whereas elemental carbon and NO_2 showed associations with these outcomes in both seasons.

Ostro et al. (2011) examined the risks of various source-specific $PM_{2.5}$ components and/or their tracer constituents on daily mortality for years 2003 through 2007 in Barcelona, Spain. Source apportionment for $PM_{2.5}$ and PM_{10} identified eight different sources. Case-crossover regression analysis[6] was used to estimate the risks of each source - specific component. There were significant associations found between road dust, minerals, fuel oil combustion, vehicle exhaust, and traffic with all-cause mortality and $PM_{2.5}$. For cardiovascular mortality, associations were also observed for the sulfate/organics $PM_{2.5}$ constituents. In some cases, relative risks were higher for specific sources than for total $PM_{2.5}$ mass.

6 Case-crossover analysis is an alternative to time-series analyses in which a case's (individual's) exposure immediately prior to or during the case-defining event (for example, a hospital admission) are compared with that same person's exposure at other "reference" times.

Son et al. (2012) investigated the daily association between daily mortality and $PM_{2.5}$ mass and its constituents in Seoul, Republic of Korea, from August 2008 through October 2009. Magnesium (Mg) concentration was associated with total mortality on the following day. Several constituents that were among the largest contributors to $PM_{2.5}$ total mass—nitrate (NO_3^-), SO_4^{2-}, and ammonium (NH_4^+)—were moderately associated with same-day cardiovascular mortality. Other constituents having smaller mass contributions (Mg and chlorine [Cl]) exhibited moderate associations with respiratory mortality on the following day.

Cao et al. (2012) examined the short-term association between $PM_{2.5}$ constituents and daily mortality in Xi'an, a heavily polluted Chinese city, from 2004 to 2008. After adjustment for $PM_{2.5}$ mass, they found significant positive associations of total, cardiovascular, or respiratory mortality with OC, EC, ammonium, nitrate, chlorine, and nickel for at least one of the multiple lag days that were examined. Nitrate demonstrated stronger associations with total and cardiovascular mortality than $PM_{2.5}$ mass. The authors concluded that their findings added support to previously reported evidence of $PM_{2.5}$-related health risks in China, suggesting that combustion-associated air pollutants are particularly important.

Huang et al. (2012) also evaluated the association of daily $PM_{2.5}$ and constituents with all-cause and cause-specific mortality data (2004–2008) in inland Xi'an, China. Secondary pollutants (sulfate and ammonium), combustion-related constituents (elemental carbon, sulfur, chlorine), and transition metals (chromium, lead, nickel, and zinc) appeared most responsible for increased risk from $PM_{2.5}$ exposure, particularly in the cold months. In Xi'an, water-soluble and carbonaceous aerosols from coal combustion and vehicle emissions were found to be the dominant species in $PM_{2.5}$ in the cold months, when health risk associations were the strongest in this study. The authors concluded that they observed a significant mortality association with exposure to $PM_{2.5}$ and species originating from fossil-fuel combustion, vehicle emission, and industry process sources.

Sacks et al. (2012) applied various regression models developed in previous multicity time-series studies of air pollution and mortality to data from Philadelphia, Pennsylvania (May 1992–September 1995). Single-pollutant analyses examined daily cardiovascular mortality associations with $PM_{2.5}$ mass and constituents and gaseous pollutant data. Principal component analysis yielded source-related components for species associated with traffic, crustal material, residual oil, and coal. The traffic and crustal (that is, soil) source-specific components showed consistently positive associations with mortality) in the warm season, while the coal combustion factor showed consistently positive associations with variations in daily mortality in the cold season.

Krall et al. (2013) estimated short-term associations between daily mortality and $PM_{2.5}$ constituents across 72 urban US communities from 2000 to 2005. Using US Environmental Protection Agency (EPA) Chemical Speciation Network data, they analyzed seven constituents that together composed 79–85 percent of $PM_{2.5}$ mass: organic carbon matter (OCM), elemental carbon (EC), silicon, sodium ion, nitrate, ammonium, and sulfate. Results indicated that OCM, EC, silicon, and sodium ion were associated with estimated increases in mortality. Unlike $PM_{2.5}$ mass associations with mortality in past studies, the

authors did not find evidence that chemical constituent mortality risks varied by season or region across the nation, indicating that health risk associations with constituents are more stable than with $PM_{2.5}$ mass. This result is consistent with the hypothesis that $PM_{2.5}$ composition drives its toxicity, rather than mass, per se.

Dai et al. (2014) estimated the risks of $PM_{2.5}$ species on mortality and how air infiltration rates into buildings may modify the association. $PM_{2.5}$ data for 75 mostly eastern and midwestern US cities from 2000 to 2006. These results were used in an analysis to determine which $PM_{2.5}$ source-specific constituents contributed the most to the association of $PM_{2.5}$ mass with mortality. Silicon (predominantly from windblown soil) and sulfur (predominantly from fossil-fuel combustion) were associated with both all-cause and CVD mortality, whereas only sulfur was related to respiratory deaths. Indeed, the authors observed that the risk of $PM_{2.5}$ mass on all-cause and respiratory mortality was increased by an increased presence of sulfur in the $PM_{2.5}$. Coal combustion emissions are a major contributor to sulfur in the US, which suggests that species derived from coal combustion might have greater toxicity, especially due to respiratory diseases (RSDs).

Heo et al. (2014) evaluated the association of daily mortality counts in Seoul, Korea, with $PM_{2.5}$ chemical speciation data collected every three days as well as nine sources of $PM_{2.5}$ mass resolved through source apportionment using data from March 2003 through November 2007. Organic carbon, elemental carbon, and lead were associated with mortality outcomes when using multipollutant models adjusted for other chemical species levels. Source-specific $PM_{2.5}$, including gasoline- and diesel-powered vehicles, as well as biomass burning, were associated with respiratory mortality and cardiovascular mortality, respectively. There were moderate associations of industry and roadway emissions with cardiovascular mortality.

Li et al. (2015) investigated the association of both daily mortality and morbidity with particulate matter and its constituents in data collected in Beijing, China, from January 2005 through December 2009. Non-accident mortality was associated with potassium (K), sulfate (SO_4^{2-}), calcium (Ca), and nitrates (NO_3^-). Similar findings were found for respiratory mortality, and sulfate was significantly associated with cardiovascular disease mortality. The authors concluded that combustion-related products, traffic sources, vegetative burning, and crustal component and resuspended road dust may play a key role in the associations between air pollution and public health in Beijing.

Basagana et al. (2015) considered five cities in southern Europe: three cities in Spain, namely Barcelona (2003–2010), Madrid (2007–2008), and Huelva (2003–2010); and two cities in Italy, namely Rome (2005–2007) and Bologna (2011–2013). A case-crossover design was used to link (i) cardiovascular and respiratory hospital admissions; (ii) total mortality, cardiovascular mortality and respiratory mortality, with (iii) 16 $PM_{2.5}$ constituents. Most of the elemental constituents studied—namely EC (elemental carbon), SO_4^{2-} (sulfate), Si (silicon), Ca (calcium), Fe (iron), Zn (zinc), Cu (copper), Ti (titanium), Mn (manganese), V (vanadium), and Ni (nickel)—were associated with increased changes in cardiovascular and/or respiratory hospitalizations. For mortality, although positive associations were identified (between both Fe and Ti and total mortality; between EC,

Mn, and Mg (magnesium) and cardiovascular mortality; and between NO_3^- and respiratory mortality), the patterns across outcomes were less clear. Given the noted variations in health associations for the different $PM_{2.5}$ constituents, the authors recommended that more studies should include a focus on PM speciation associations with health.

Kim et al. (2012) analyzed daily concentrations of $PM_{2.5}$ constituents measured over five years in order to investigate associations with daily mortality. The mortality relative risks (RRs) estimated for EC and OC were larger than those for sulfate and nitrate. They generally did not observe associations between constituents and cardiovascular or respiratory mortality but did find associations with ischemic heart disease mortality. In addition, there were $PM_{2.5}$ constituent associations with cancer mortality, particularly by EC and OC. The authors concluded that $PM_{2.5}$ constituents originating from combustion-related sources were more strongly associated with daily mortality than were secondary inorganic aerosols.

B. Short-Term Exposure to $PM_{2.5}$ Sources and Constituents and Their Associations with Daily Morbidity

Sarnat et al. (2008) analyzed the association of emergency department (ED) visits (in Atlanta, Georgia, from November 1998 to December 2002) for combined CVD and respiratory causes with speciated $PM_{2.5}$ data. Source-specific $PM_{2.5}$ components were estimated using several $PM_{2.5}$ source apportionment approaches. All the methods indicated that $PM_{2.5}$ from mobile sources showed the most consistent associations with both cardiovascular and respiratory EDVs. The same observation was true for $PM_{2.5}$ from biomass burning. In addition, there were consistent associations between sulfate-rich secondary $PM_{2.5}$ and respiratory visits. Despite differences between the source apportionment methods, the consistent findings across methods confirmed that modeled source-apportioned data produce robust estimates of acute health risk, consistent with the findings by Thurston et al. (2005) and Thurston et al. (2011).

Bell et al. (2009) linked two national datasets: (1) A US EPA database used to form long-term average concentrations of $PM_{2.5}$ chemical constituents across the US for 2000–2005, and (2) daily cardiovascular and respiratory Medicare hospitalizations for persons 65 years or older in 106 US counties from 1999 through 2005. It was found that communities with a generally higher $PM_{2.5}$ content of nickel, vanadium, and elemental carbon yielded a higher risk of hospitalizations associated with short-term exposure to $PM_{2.5}$.

Ito et al. (2011), as discussed above, examined the role of $PM_{2.5}$ and its key chemical constituents on CVD hospitalizations and mortality in New York City for the years 2000–2006. Coal combustion–related constituents (for example, selenium) were associated with CVD hospitalizations in winter, whereas elemental carbon and NO_2 (both major products of traffic-related emissions in urban areas) showed associations with CVD hospitalizations in both seasons. The authors noted that the $PM_{2.5}$ constituents associated

with the regional transported pollutants from coal combustion (Se and SO_4^{2-}) exhibited the season-specific association pattern most similar to that of $PM_{2.5}$ mass, suggesting that they are major contributors to the risks associated with $PM_{2.5}$ mass.

Kim et al. (2012) explored the associations of hospital admissions with daily $PM_{2.5}$ chemical constituents for five years in the Denver Aerosol Sources and Health (DASH) study. Daily sulfate and nitrate constituents were more highly correlated with $PM_{2.5}$ mass over time than were EC and OC. Estimated short-term associations of $PM_{2.5}$ chemical constituents, especially EC and OC, were immediate (that is, same day) for cardiovascular admissions. By contrast, estimated short-term associations of sulfate and nitrate were delayed in time for cardiac and respiratory admissions. Of all the subcategories of cardiovascular disease admissions, ischemic heart disease admissions showed immediate risks for EC and OC that paralleled the pattern observed for total cardiovascular disease admissions.

Levy et al. (2012) performed a literature review and conducted a multisite time-series analysis of hospital admissions and exposure to $PM_{2.5}$ constituents (elemental carbon, organic carbon matter, sulfate, and nitrate) in a population of 12 million US Medicare enrollees for the period 2000–2008. The analysis found statistically significant associations between short-term changes in elemental carbon and cardiovascular hospital admissions. However, the analyses were limited to those constituents that dominate $PM_{2.5}$ mass and are significantly correlated with $PM_{2.5}$ (that is, EC, nitrate, sulfate, and OCM), limiting the usefulness of this study for evaluating source- or constituent-specific impacts.

Mostofsky et al. (2012) analyzed data on 18 $PM_{2.5}$ constituents and data from 1,060 patients admitted to a Boston, Massachusetts, medical center with ischemic stroke in 2003–2008. The authors utilized several options for modeling the association between constituents and health outcomes that account for the impact of $PM_{2.5}$. The different methods yielded relative rankings of the association between constituents and ischemic stroke that were fairly consistent across models. Although many trace constituents (such as Se, Ni, Br, Pb) represent negligible contributions to total $PM_{2.5}$, Mostofsky et al. detected associations between several elemental constituents and stroke risk. This was thought to be because constituents with a small mass may nonetheless have high toxicity on their own, or (more likely) they are correlated with (that is, markers of) other co-occurring $PM_{2.5}$ constituents or source-specific mixtures. Models considering constituent concentrations, after adjusting the model for the risks of $PM_{2.5}$ mass (for example, simultaneously including $PM_{2.5}$ mass as a model variable), indicated that higher levels of black carbon (BC), Ni, and V were associated with higher stroke risk. However, the authors noted that it was unclear whether adjustment for $PM_{2.5}$ mass correctly accounts for confounding, or whether it inadvertently overadjusts for (that is, confounds the risks of) constituents that are highly correlated with $PM_{2.5}$ mass, but that are also inherently toxic. In models in which the overall association of $PM_{2.5}$ mass was not adjusted for in the model, the strongest associations with stroke risk were seen for black carbon (BC), nickel (Ni), and sulfur (S).

Bell et al. (2013) examined pollutant sources for associations with risk of hospital admissions for cardiovascular and respiratory causes. The data included over 330,000 Medicare participants in four counties in Connecticut and Massachusetts from August 2000 to

February 2004. Source apportionment was used to estimate daily $PM_{2.5}$ contributions from sources (traffic, road dust, oil combustion, and sea salt, as well as a regional source representing coal combustion and other sources). Associations of daily $PM_{2.5}$ constituents and sources with cardiovascular and respiratory hospitalizations were estimated with time-series analyses. $PM_{2.5}$ and $PM_{2.5}$ road dust were associated with cardiovascular hospitalizations, as were several $PM_{2.5}$ constituents: calcium, black carbon (BC), vanadium, and zinc. $PM_{2.5}$ from road dust and sea salt was associated with respiratory hospitalizations, as were the constituents aluminum, calcium, chlorine, black carbon, nickel, silicon, titanium, and vanadium. In the study area, motor vehicle emissions were a main contributor to ambient Zn and BC, road dust to Si and Al, oil combustion to V and Ni, sea salt to Cl, and regional sources to S. The authors concluded that, in the studied counties, the most harmful particles, based on their estimated risks, included: black carbon, calcium, and $PM_{2.5}$ from the road dust source.

As discussed above, Li et al. (2015) investigated the association of both daily mortality and morbidity with particulate matter and/or its constituents in Beijing, China, from 2005 through 2009. For morbidity, sulfate was associated with respiratory diseases, especially during the warm season.

Jones et al. (2015) conducted a case-crossover analysis using daily average ambient $PM_{2.5}$ total mass and species estimates derived from the Community Multiscale Air Quality (CMAQ) model and available ambient observations. They examined the association between the chemical constituents of PM (including elemental and organic carbon, sulfate, nitrate, ammonium, and other remaining mass) and respiratory hospitalizations in New York State. Modification of the $PM_{2.5}$-hospitalization association was assessed via models stratified by mass fractions of both primary and secondary PM constituents. The authors concluded that ambient concentrations of $PM_{2.5}$ and secondary aerosols (including sulfate, ammonium, and nitrate) were positively associated with respiratory hospitalizations in New York State.

Ostro et al. (2016) used city-specific $PM_{2.5}$ mass source apportionment in eight major metropolitan areas in California from 2005 to 2009 to examine the associations of source-specific $PM_{2.5}$ exposures from vehicular emissions, biomass burning, soil, and secondary nitrate and sulfate sources with emergency department visits (EDVs) for cardiovascular and respiratory diseases. Using a case-crossover analysis, they observed associations of vehicular emissions with all cardiovascular EDVs. Vehicular emissions, biomass burning, and soil sources were associated with all respiratory EDVs and with EDVs for asthma. The soil source, which includes resuspended road dust, generated the highest risk estimate for asthma. Overall, the authors concluded that their results provide additional evidence of the public health consequences of exposure to specific sources of $PM_{2.5}$ and indicate that some source-specific components of $PM_{2.5}$ may pose higher risks (per $\mu g/m^3$) than the overall $PM_{2.5}$ mass.

C. Summary of Short-Term Studies

Tables 1 and 2 summarize the findings reviewed above regarding the associations between health outcomes and short-term exposures to $PM_{2.5}$ constituents and source-specific components. From these tables, it is observed that traffic-related $PM_{2.5}$ is among the most consistently associated source components. Acute exposure to traffic $PM_{2.5}$ shows consistent associations with CVD mortality (significance scoring of 4 in six studies), as well as with CVD hospital admissions (significance score of 5 in six CVD hospital admissions studies). Similarly, looking at the traffic-related $PM_{2.5}$ constituent associations with acute health outcomes, elemental carbon (EC, a marker for traffic-based combustion) is consistently associated with CVD mortality and morbidity (significance score of 8 in 12 studies, and significance score of 6 in seven CVD hospital admissions studies). However, copper (Cu), which is often cited as a tracer for traffic emissions from metal brake wear, is not found to be consistently associated with CVD mortality or hospital admissions (though it is moderately associated with respiratory hospital admissions). Roadway-related $PM_{2.5}$ also appears to be generally associated with CVD mortality and more moderately with respiratory disease (RSD) hospital admissions. This observation lends further support to the importance of the traffic source as reported for $PM_{2.5}$ mass associations with mortality and morbidity. Especially revealing is the fact that traffic $PM_{2.5}$ and EC (primarily emitted by diesel vehicles in urban areas) are both related to CVD mortality and hospital admissions, but Cu is not. This suggests that it is the diesel-powered vehicles that are driving these traffic-related adverse risk associations, not the gasoline-powered vehicle emissions (which also cause Cu emissions from brake wear but not nearly as much EC as diesel vehicles). These findings about EC are supported by the recent meta-analysis by Achilleos et al. (2017), which found EC strongly associated with all-cause and cardiovascular mortality. Its correlate, black carbon, was reported to be associated with respiratory mortality.

Acute exposure to $PM_{2.5}$ from coal combustion is also especially associated with CVD mortality (significance score of 2 in three studies considering that exposure and outcome). In addition, the associations of trace element constituents of coal combustion (that is, Se and S) with these health outcomes are reasonably consistent with the conclusion about the importance of coal combustion-related $PM_{2.5}$. Both Se and S, which are significantly generated from coal burning are also often correlated with CVD mortality. Thus, coal-burning $PM_{2.5}$, when present, appears to be an important driver of the acute CVD toxicity of $PM_{2.5}$ mass. The meta-analysis of Achilleos et al. (2017) reported associations between sulfate and all-cause mortality and more modest associations with cardiovascular mortality. Some of their sulfate measures used by the authors were converted from sulfur, which could have added some uncertainty to the estimates.

Acute exposures to residual oil combustion-derived $PM_{2.5}$ were also found to be consistently associated with CVD mortality (significance score of 3 for four studies) and hospital admissions (2 for four), across the available studies where it was considered. In support of these findings, vanadium, a known oil combustion tracer, was also associated with total mortality (2 of four), CVD hospital admissions (2 of four), and RSD admissions

(3 of three). There is also evidence of a vanadium effect report in Achilleos et al. (2017).

Acute exposure to $PM_{2.5}$ derived from biomass combustion is also identified as associated with CVD mortality (score of 3 for three studies available for review). However, potassium (K), a common marker for biomass burning (for example, wood burning), was not consistently associated with any outcome in those studies. However, K can come from various sources, including windblown dust, and the lack of findings may be due in part to total K being a less-specific marker of biomass than water-soluble K or levoglucosan. In contrast, the meta-analysis by Achilleos et al. (2017) reports evidence of risk from K exposure with all-cause, cardiovascular, and respiratory mortality. Organic carbon (OCM) was found to be consistently associated with total mortality and with CVD hospital admissions, and OCM is a contributor in the source apportionment analysis to the biomass source, but it is but one source of many for OCM. The overall results suggest that the estimated effect of biomass is not robust across various data and methods used in studies that examine this source, and the biomass $PM_{2.5}$ source association with acute mortality and morbidity is only moderately supported by constituent and source-specific analyses from developed countries to date. However, given the abundant and consistent use of biomass for heating and cooking in LMICs, it constitutes a major area of future research.

Source-specific PM identified as "industrial" (for example, from steel mills) was also found to be moderately associated with CVD mortality (2.5 significance score for five studies) and hospital admissions (2 for three studies). However, it was difficult to discern supportive associations with constituents commonly associated with industrial emissions. For example, lead (Pb), emitted by lead-smelting operations, was not found to be consistently associated with CVD outcomes. However, manganese (Mn), which is emitted by the steel industry, was associated with acute CVD mortality and RSD admissions. Thus, the results for industry sources and constituents were mixed, and not as compelling as combustion categories, except for the steel industry.

Soil $PM_{2.5}$ source impacts were associated with CVD mortality (4 for six studies) but not RSD mortality. However, soil was not associated with CV or RSD hospital admissions. Similarly, Si (a key constituent of soil) was also significantly associated with CVD mortality but not RSD mortality or any hospital admissions category. In contrast, the meta-analysis by Achilleos et al. (2017) reports associations between markers of soil (silicon and calcium) with both all-cause and cardiovascular mortality. This indicates a lack of risk-estimate robustness of soil-related $PM_{2.5}$ mass associations across the various study data and methods.

Neither CVD nor RSD mortality was found to be associated with acute exposure to salt $PM_{2.5}$ (for example, resulting from ocean sea spray) or with salt's key tracers, sodium (Na) or Cl. However, an association was found with RSD hospital admissions, while its key constituents, Na and Cl were also found to be associated with increased RSD morbidity.

Overall, the collective evidence from tables 1 and 2, consistent with the above discussions of the individual studies, indicates that the particles from combustion, and especially fossil-fuel combustion, are the most consistent major driving factors in the acute $PM_{2.5}$

exposure associations found with mortality and morbidity. Of the fossil-fuel sources, coal combustion and its secondary $PM_{2.5}$ products (for example, sulfates), when present, were an important driver of the $PM_{2.5}$-CVD association. Acute exposures to residual oil combustion–derived $PM_{2.5}$ was also found to be consistently associated with CVD mortality and hospital admissions. Of the traffic sources, acute exposure to diesel-combustion $PM_{2.5}$ were suggested as the traffic component most associated with adverse health risks. Biomass and soil $PM_{2.5}$ were also found to be associated, but less consistently, with both mortality and morbidity. However, there are fewer studies that include these two sources, and their results were less robust across study design and methods than most of the other sources.

"Particles from combustion, and especially fossil-fuel combustion, are the most consistent major driving factors in the acute $PM_{2.5}$ exposure associations found with mortality and morbidity."

VII. Long-Term Exposure to $PM_{2.5}$ Sources and Constituents and Their Associations with Mortality

For long-term exposure studies, search terms from the bibliographic source PubMed including "long-term exposure" or "chronic exposure" with "species," "components," or "constituents" were used in the development of table 3. The first published efforts to examine the associations of long-term exposure to $PM_{2.5}$ mass, constituents and sources with mortality was an ecological cross-sectional study[7] of 1980 mortality rates in 98 US metropolitan areas (Ozkaynak and Thurston 1987). Data on $PM_{2.5}$, its trace element constituents, and sulfates were obtained from the US EPA Inhalable Particle Monitoring Network (IPMN) that operated from 1979 to 1982. Multiple regression was used to control for metropolitan area-wide population characteristics, such as median age, percent above 65 years of age or older, population density, percent in poverty, and percent with a college degree. Although this was an ecological population study, it gave similar $PM_{2.5}$ mass-mortality associations as later cohort studies with individual-level characteristics data (for example, Pope et al. [2002]). In addition to fine particles, sulfate (the only constituent individually studied in this analysis) was associated with mortality rates (0.7 percent increase per $\mu g/m^3$, $PM_{2.5}$, 95 percent confidence interval (CI) = 0.2–1.2[8]; and 2.2 percent per $\mu g/m^3$ SO_4^{2-}, 95 percent CI = 1.2–3.0). An additional analysis was conducted of the association of mortality with source-specific $PM_{2.5}$ components, as derived from the trace element constituents (Thurston et al. 1984), including soil (associated with Si, Fe), auto emissions (Pb and Br), residual oil combustion (V and Ni), metals (Zn, Mn, Fe), and coal combustion (Se, S). Of these source-specific $PM_{2.5}$ components, coal combustion had the most significant impact on mortality (Thurston et al. 1987), which was also later confirmed by the subsequent source-specific $PM_{2.5}$ analysis of the American Cancer Society (ACS) cohort (Thurston et al. 2016).

7 Unlike a cohort study that considers individual-level deaths and characteristics over time, an ecological cross-sectional mortality study is one that considers mortality rates of entire populations (for example, of cities), as well as their population characteristics (for example, percent > 65 years old in a city), and compares them cross-sectionally (that is, across populations in different locations).

8 A "95 percent CI" refers to the 95th-percentile confidence interval of the estimate provided.

Dockery et al. (1993) used the cohort of the Harvard Six Cities Study to examine the risks of $PM_{2.5}$, PM_{10}, and sulfate on mortality. The data included a 14- to 16-year-long follow-up of approximately 8,100 adults from cities in the eastern and midwestern US. A Cox proportional hazards regression model was applied. Among the results, the analysis indicated statistically significant associations between mortality and both $PM_{2.5}$ and sulfate (the only constituent examined). Converting the results indicated a 2.9 percent (95 percent CI = 1.0, 4.6) change in all-cause mortality per $\mu g/m^3$ of sulfate. This compared to a 1.2 percent (95 percent CI = 0.4, 2.1) change in all-cause mortality per $\mu g/m^3$ of $PM_{2.5}$. These cohort results were confirmatory to the previously published cross-sectional results (for example, Ozkaynak and Thurston 1987). However, in these studies, sulfates were highly correlated with $PM_{2.5}$, so it is difficult to disentangle the two risk estimates. A subsequent reanalysis of the Harvard Six Cities Study data included examination of cardiopulmonary mortality with a risk increase of 3.5 percent (95 percent CI = 0.7, 6.1) per $\mu g/m^3$ of sulfates (Krewski et al. 2000).

Pope et al. (1995), Krewski et al. (2000), and Pope et al. (2002) examined survival among 550,000 nationwide participants from the American Cancer Society Prevention Study II cohort. The risks of long-term exposure to sulfates were based on the IPMN and other EPA monitoring data. The study examined individuals that were followed from 1982 to 1998. For all-cause mortality, the change in mortality per $\mu g/m^3$ of sulfates was 1.3 percent (95 percent CI = 1.1, 1.5), versus risks for $PM_{2.5}$ of 0.6 percent (95 percent CI = 0.4, 0.9). Sulfate risks on cardiopulmonary mortality were estimated to be 1.8 percent increase in mortality per $\mu g/m^3$ (95 percent CI = 1.2, 2.4). The authors concluded that long-term exposure to combustion-related fine particulate air pollution is an important environmental risk factor for cardiopulmonary and lung cancer mortality (Pope et al. 2002).

More recently, several studies have evaluated the possible associations of long-term exposures to $PM_{2.5}$ constituents and/or sources with mortality. Smith et al. (2009) used data from the American Cancer Society Prevention Study II cohort to analyze the risks of long-term exposures to $PM_{2.5}$, sulfate, and black carbon. Sulfate data were similar to that used by Krewski et al. (2000) and a three-year average (2003–2005) of elemental carbon data was developed from data made available by research funded by the Health Effects Institute (Thurston et al. 2011). In this work, there was a subcohort of 350,000 participants from 66 metropolitan areas followed from 1982 to 2000 for which complete data were available. Mortality risks were estimated with models for independent pollutants and various combinations of co-pollutants. The researchers tested two-way linear interactions between all pollutants. A Cox proportional hazards model was used to assess the all-cause and cardiopulmonary mortality risk estimates. For all-cause mortality, the risk estimates per $\mu g/m^3$ were 0.6 percent (95 percent CI = 0.2, 1.0) for $PM_{2.5}$, 1.1 percent (95 percent CI = 0.8, 1.4) for sulfate and 5.5 percent (95 percent CI = 0.74, 10.51) for EC. The respective constituent risks for cardiopulmonary mortality were 1.3 percent (95 percent CI = 0.8, 1.8), 1.6 percent (95 percent CI = 1.03 to 2.08) and 10.6 percent (95 percent CI = 2.9, 18.9). The large and significant risk estimates for both sulfate and elemental carbon in this analysis again pointed toward fossil-fuel combustion products as a major contributor to the $PM_{2.5}$ associations with mortality.

Ostro et al. (2010) examined long-term exposure among 102,000 California women teachers and administrators from the California Teachers Study (CTS) who were followed from 2001 through 2007. To reduce exposure misclassification[9], the sample was restricted to those living within 30 kilometers of a fixed-site monitor in the US Environmental Protection Agency's Species Trend Network. This resulted in a study population of just under 45,000 women. $PM_{2.5}$ constituents examined included EC, OC, sulfate, nitrate, iron, potassium, silicon, and zinc. A Cox proportional hazards model was used to derive the risk estimates. For cardiopulmonary mortality, among the major constituents of $PM_{2.5}$, statistically significant risk estimates were observed with sulfate and silicon, along with $PM_{2.5}$ mass. For IHD, the largest risks were observed for EC and sulfate, consistent with the ACS study results, although estimates were fairly similar among the constituents, except for silicon and OC which had somewhat lower estimates.

For comparative purposes, the CTS IHD results were converted into risks per one μg/m^3. For cardiopulmonary mortality, the risk of one μg/m^3 of sulfates was 3.4 times that of $PM_{2.5}$, while EC was 6.1 times that of $PM_{2.5}$. For IHD, the ratio of risks relative to $PM_{2.5}$ was 4.0 and 13.2 for sulfates and EC, respectively (Ostro et al. 2010).

The same data set (CTS) was examined using exposure data at the residential level provided by a chemical transport model that computed pollutant concentrations from over 900 sources in California (Ostro et al. 2015). Besides particle mass, monthly concentrations of 11 species and eight sources of primary particles were generated at 4-kilometer grids throughout the state. Both chemical constituents and sources of $PM_{2.5}$ were examined, and the focus was on cardiovascular and IHD-related mortality. Specifically, the following $PM_{2.5}$ constituents were examined: copper, iron, manganese, nitrate, elemental carbon (EC), organic carbon, "other" species (that is, mineral dusts and constituents not measured), "other" metals (those besides Cu, Fe, and Mn that were explicitly resolved), and secondary organic aerosols. Sulfates were not measured. The sources of primary aerosols were not estimated via $PM_{2.5}$ source apportionment methods but instead by the University of California, Davis/California Institute of Technology (UCD/CIT) chemical transport model from calculated meteorological fields and emissions estimates for different sources to predict source-specific airborne particulate matter concentrations. These $PM_{2.5}$ sources included on- and off-road gasoline, on- and off-road diesel, wood smoke, meat cooking, high-sulfur fuel combustion (including distillate oil, marine vessel fuel, aircraft jet fuel, and liquid and solid waste fuels), and "other anthropogenic." It is important to note that most electricity in California is produced from natural gas, with little or no use of coal or oil.

There were many statistically significant associations between the constituents and IHD mortality in the CTS cohort, the outcome of interest in the study. The highest mortality risk was associated with EC, considered to be a tracer for diesel exhaust. Among the sources, there were statistically significant associations between IHD and all four of the vehicle sources, meat cooking, and high-sulfur-content fuel combustion in California. High-sulfur-content fuel combustion includes emissions from distillate oil from industrial boilers, marine vessel fuel, aircraft jet fuel, and liquid and solid waste fuels. Thus, overall, this study indicates that exposures to traffic (EC) and sulfur combustion are among the

9 Exposure misclassification occurs when the exposure assigned to an individual or population is over- or under-estimated.

most important sources of mortality. To obtain an approximation of the relative toxicity, the risks of $PM_{2.5}$, EC, and sulfur combustion were converted to a common denominator of one $\mu g/m^3$. The percent increase in mortality is 1.7 percent (95 percent CI = 0.8, 2.7) for $PM_{2.5}$, 16.4 percent (95 percent CI = 6.1, 26.9) for EC, and 19.2 percent (95 percent CI = 5.0, 30.6) for sulfur combustion. Thus, on a per $\mu g/m^3$ basis, the results are suggestive of greater toxicity for motor vehicle and sulfur-emitting sources than for overall $PM_{2.5}$ in general. Note that some caution should be exercised in interpreting these figures, given the inherent uncertainty in measuring the PM constituents and estimating $PM_{2.5}$ source contributions.

Gan et al. (2011) examined the risk of coronary heart disease mortality in a cohort of 450,000 individuals in Vancouver, Canada, during the period of 1999 through 2002. Five-year averages of both black carbon (subsequently converted to EC) and $PM_{2.5}$ developed from land use regressions were used as exposures. The risk estimate for a one $\mu g/m^3$ change in EC was 7.7 percent (95 percent CI = 3.9, 6.5) versus, for $PM_{2.5}$, 0.6 percent (95 percent CI = -1.3, 3.1).

Vedal et al. (2013) used data from the Women's Health Initiative–Observational Study (WHI-OS), a cohort of about 90,000 women from 45 US cities across the country, to investigate the risks of constituents on total cardiovascular mortality and several subclasses. Also, first events of cardiovascular disease were examined. Besides $PM_{2.5}$, data on EC, OC, sulfur, and silicon were obtained from the US speciation dataset and the Interagency Monitoring of Protected Visual Environments (IMPROVE) network. The authors' source apportionment analysis indicated that these constituents were, respectively, markers of local combustion including traffic, primary gasoline and biomass combustion and secondary OC formation, secondary sulfate formation, and crustal/soil. The cohort was followed from 1995 to 2005, while the pollution measurements were for 2009. In the basic analysis across metropolitan areas, OC was most consistently associated ($P < 0.05$) with cardiovascular death and many of its subclasses including atherosclerotic and cerebrovascular deaths. $PM_{2.5}$, EC, and sulfur were more modestly associated ($P < 0.06$) with atherosclerotic deaths and silicon was associated ($P < 0.05$) with deaths from possible coronary heart disease. The risk estimates suggest much larger risks per $\mu g/m^3$ for these constituents than for $PM_{2.5}$ mass as a whole. Regarding cardiovascular events, sulfur was associated with total cardiovascular events (MI, coronary revascularization, stroke, atherosclerotic cardiac disease death, possible CVD death, and cerebrovascular death), stroke and stroke death, and myocardial infarction. Of the other constituents, OC was associated with stroke and stroke death. The Health Effects Institute review committee noted the difficulties in measuring EC at a small spatial scale.

Wang et al. (2014) conducted an analysis of 320,000 individuals from 19 European cohorts in 12 countries as part of the ESCAPE study. The cohorts began from 1985 to 2000 and were followed for approximately 11 years. Estimates of $PM_{2.5}$ constituents were developed using land use regression (LUR) models that provided modest fits of the data: for sulfur and silicon, the average correlation between the LUR estimates and air monitor measurements across the cohorts was 0.37 and 0.49, respectively. Eight constituents

representing major sources in Europe were examined including copper, iron, potassium, nickel, sulfur, silicon, vanadium, and zinc. Four models with increasing control for confounders were run. Basically, no associations with cardiovascular mortality were observed for any of the constituents, but sulfur and silicon exhibited the highest risk estimates.

Chung et al. (2015) examined 12.5 million Medicare enrollees residing in the eastern United States. A seven-year average from 2000 to 2006 pollution exposures was developed for six major constituents of $PM_{2.5}$ taken from the US EPA chemical speciation network. The constituents included elemental carbon (EC), organic carbon matter (OCM), sulfate (SO_4^{2-}), silicon (Si), nitrate (NO_3^-), and sodium (Na). Rather than using a traditional Cox regression, the authors used a novel Bayesian hierarchical regression model to determine whether changes in monthly mortality rates were associated with monthly changes in the concentrations of the $PM_{2.5}$ constituent. The regression model for a given constituent controlled for other constituents by including a term for the annual average of $PM_{2.5}$. The authors also examined whether the risk of the seven-year average of $PM_{2.5}$ on mortality was modified by the concentrations of the constituents. In their basic model, they found that EC, Si, and nitrates were associated with mortality. They also found that $PM_{2.5}$ mass that contained more sulfates demonstrated significantly greater risk estimates.

Kioumourtzoglou et al. (2015) attempted to determine whether PM composition modified the risks on mortality. Their sample included 19 million Medicare enrollees from 81 US cities from around the country for the years 2000 to 2010. Source clusters were developed using EPA monitoring data for 24 species. Most metropolitan areas relied on a single monitor to measure species concentrations. After controlling for long-term trends and factors varying across cities, the authors examined whether within-city year-to-year changes in the constituent concentrations were associated with corresponding changes in mortality. Overall, the authors concluded that the strongest positive modifications of the association between $PM_{2.5}$ and mortality were from (i) sulfates in the Southeast, (ii) metals associated with ship emissions in harbor cities, and (iii) industrial emissions and elemental carbon in several parts of the country.

Another recent study examined the risk of $PM_{2.5}$ source-related components and their tracer constituents using a subset of the national American Cancer Society's Cancer Prevention Study II cohort (Thurston et al. 2016). A total of 446,000 adults in 100 US metropolitan areas were followed from 1982 to 2004. In this case, the average of concentrations from the available US EPA speciation monitors in each city were used as a measure of metropolitan area-wide concentrations of the pollutants. Sixteen constituents and eight sources were examined. Four different Cox regression models focusing on IHD mortality were employed, where additional controls for possible confounding factors were progressively introduced. Among the constituents that contributed significantly to $PM_{2.5}$ mass, EC (a tracer for traffic) and sulfur (a tracer for combustion from coal and residual oil) were statistically significant in most models, while organic carbon and silicon were not. Of note, the risks relating to the coal-related mass component were not altered when other sources were controlled for in models with two sources. $PM_{2.5}$ from both wind-blown soil and biomass combustion was not associated with IHD mortality. Based

on the model including random effects but no population-based contextual variables, mortality risk estimates for $PM_{2.5}$ mass, coal combustion, and EC were 1.6 percent (95 percent CI = 0.6, 2.5), 4.6 percent (95 percent CI = 1.5, 9.1), and 11.5 percent (95 percent CI = 0, 22.6), respectively, on a $\mu g/m^3$ basis.

In a prior analysis of sources of $PM_{2.5}$ and other health endpoints using these same data, Thurston et al. (2013) also reported associations between all-cause mortality and both traffic and coal sources, between respiratory mortality and both traffic and soil, and between lung cancer and coal.

Using these studies of long-term exposure (table 3), it is possible to more appropriately assess the source risk estimates on a comparable "per $\mu g/m^3$ of $PM_{2.5}$ mass" basis. Each of the constituents (for example, EC and SO_4^{2-}) is a general indicator of $PM_{2.5}$ source contributions (for example, diesel traffic and fossil-fuel combustion, respectively). However, these associated source-specific $PM_{2.5}$ constituents actually include more $PM_{2.5}$ mass than the single constituent alone. Fortunately, there are estimates of the mass associated with these key source tracers for the US (Thurston et al. 2011). Based on that research, EC represents 15.3 percent of the total $PM_{2.5}$ mass associated with traffic sources. Therefore, multiplying the EC concentration by 1/.153 (= 6.54) yields an estimate of the associated $PM_{2.5}$ mass in $\mu g/m^3$. Thus, the reported risk per $\mu g/m^3$ of EC needs to be divided by 6.54 to give an estimate of the impact per $\mu g/m^3$ on a $PM_{2.5}$ mass basis that is comparable to the overall $PM_{2.5}$ mass risk per $\mu g/m^3$. Based on the studies of Gan et al. (2011), Ostro et al. (2015), and Thurston et al. (2016), the EC risk estimates are estimated as 13, 10, and 6.9 times that of overall $PM_{2.5}$ mass, respectively. Using the mean of these ratios (10) and adjusting for the actual $PM_{2.5}$ mass associated with EC, the EC associated mass risk is estimated at approximately 1.5 times that of $PM_{2.5}$ mass, in general.

In order to determine the sulfate-specific mortality risks, similar associated mass calculations were conducted to take into account the ammonium ion that is also associated with measured sulfate mass. As summarized in table 4, the available studies report a mean sulfate risk of 2.7 times that of $PM_{2.5}$ mass. Based on the ratio of ammonium sulfate to sulfate molecular weights (132/96 = 0.73), sulfate makes up about 73 percent of the total sulfate-associated $PM_{2.5}$ mass. Therefore, after adjustment for total mass, the sulfate-associated $PM_{2.5}$ risk estimate (that is, per $\mu g/m^3$ $PM_{2.5}$ mass of sulfate) is about 2.7 * 0.73 = 2.0 times the mortality risk of overall $PM_{2.5}$ per $\mu g/m^3$ mass. When similarly considering the source-specific mass impacts, the highest ischemic heart disease mortality risks per $\mu g/m^3$ found by Thurston et al. (2016) was for coal-combustion-specific $PM_{2.5}$, which was approximately five times the risk per $\mu g/m^3$ as found for ambient $PM_{2.5}$ mass, in general.

VIII. Summary and Conclusions

Taken together, the available short- and long-term exposure studies suggest the following:

- This is the first $PM_{2.5}$-health-effects review that, to the authors' knowledge, collectively examines both short- and long-term exposures to fine particle constituents and sources, taking into account the data and methods used as well as the uncertainties in the underlying epidemiological studies.
- The current evidence summarized in this report indicates that trace constituents from $PM_{2.5}$ and $PM_{2.5}$ mass from fossil-fuel combustion are among the greatest contributors to $PM_{2.5}$ toxicity. The results of both the short- and long-term exposure studies strongly suggest that the $PM_{2.5}$ mass component derived from fossil-fuel combustion is of particular concern for public health. The health risk is particularly great from coal combustion- and traffic-related $PM_{2.5}$. For the latter, the many associations with elemental carbon (EC) from soot exposure indicate that, of traffic-related sources, diesel-fueled vehicles are particularly associated with adverse human health impacts. These two sources, coal- and traffic-related $PM_{2.5}$, are most consistently associated with cardiovascular mortality, especially ischemic heart disease (heart attacks) in both the short- and long-term exposure studies.
- The importance of coal-combustion and traffic-emission sources to the overall $PM_{2.5}$ mass associations with mortality and hospital admissions is supported by the health-risk associations that are also observed with their source-specific trace constituent markers. For example, particulate selenium and sulfur are important markers for coal and fossil-fuel combustion, while elemental carbon is a strong marker for traffic, and especially for diesel-fueled vehicle, emissions. Based on prior epidemiological and toxicological studies, Lippmann at al. (2013) attempted to draw conclusions about the importance of the different $PM_{2.5}$ constituents, finding that sulfate (a marker primarily of coal and residual-fuel-oil combustion) was clearly among the most, if not the most, important adverse health-associated constituents of $PM_{2.5}$.
- As summarized in tables 3 and 4, after adjusting for per $\mu g/m^3$ mass equivalence, the long-term studies indicate that the cardiovascular disease risks of sulfate, EC, and $PM_{2.5}$ mass from coal combustion are larger than that of $PM_{2.5}$ mass, in general.
- This review of the studies indicates a fairly consistent association between sulfate and cardiovascular mortality. This may well be because sulfates do not occur as pure chemicals in the air but in intimate mixtures with other compounds, including transition

metals. Thus, the acidic nature of sulfur compounds in the environment (for example, as ammonium sulfate, ammonium bisulfate, or sulfuric acid) can make transition metals more bioavailable, increasing those particles' potential to cause oxidative stress and serious adverse health effects in the human body (for example, see COMEAP [2009] and Fang et al. [2017]).

- However, there is a caveat concerning the potential confounding effects of exposure characteristics on the reported sulfate associations. Specifically, it is possible that since sulfate is more homogeneous spatially (that is, more equally dispersed over a wider area) than many other $PM_{2.5}$ constituents and source-related components, exposures to sulfate might well be measured more accurately by a small set of monitors (or a single monitor) in a metropolitan area than some of the other, more spatially variable, constituents or source-related components. Such superior measurement of exposures leads, in general, to a greater likelihood of observing an association.

- In contrast, $PM_{2.5}$ mass, its constituents, and its source-related components are less consistently associated with respiratory disease mortality, except for short-term exposures to $PM_{2.5}$ from biomass burning.

- In general, weaker associations were most often found between mortality and concentrations of $PM_{2.5}$ from biomass combustion or crustal sources. However, several short-term exposure studies report associations between biomass and mortality. These two sources are extremely varied spatially and temporally, especially for estimating long-term exposure. This could contribute to the lack of detection of their health associations. In addition, there are fewer US metropolitan areas studied that have significant concentrations of biomass and soil sources, which may limit the ability of national-scale studies to identify risks of these two sources of $PM_{2.5}$. On the other hand, traffic emissions and their markers (for example, EC), which are often associated with mortality, are also quite variable spatially within a metropolitan area, but they still show consistent associations with adverse health.

- Overall, this report's key findings from the review of currently available acute (or short-term) and long-term studies suggest that reductions in the emissions of $PM_{2.5}$ from fossil-fuel combustion, such as sulfur-emitting coal-fired power plants and diesel vehicles, can produce the most significant health benefits per $\mu g/m^3$ of $PM_{2.5}$ reduced. In addition, these $PM_{2.5}$ emissions reductions would provide additional climate-mitigation benefits, since these same fossil-fuel combustion sources contribute significantly to climate change, most notably in the form of CO_2 and elemental carbon emissions.

- The relative dearth of $PM_{2.5}$-constituent health effects studies found for LMICs in this review supports the need for LMICs in particular to begin measuring the concentrations of the constituents of their particulate mixes. Particulate S and EC, which can be measured continuously (McMurry 2000), are especially important combustion markers to monitor more widely. This will help determine the contribution of specific sources to $PM_{2.5}$ mass and would help prioritize subsequent pollution-control efforts. To date, results indicate a need to focus on reducing $PM_{2.5}$ pollution from fossil-fuel combustion, especially coal-burning and diesel-vehicle emissions.

- There is an especially great need to conduct short- and long-term cohort epidemiological studies of mortality and hospitalization in LMICs, where biomass burning for cooking and heating is a significant source of $PM_{2.5}$ but of uncertain human health risk

relative to fossil-fuel combustion particulate matter. In order to develop economically efficient abatement strategies that maximize human health benefits per ton of $PM_{2.5}$ emissions reduced, it is essential to (i) measure the concentration of $PM_{2.5}$ from the specific source (in this case biomass burning), or of a marker of the source (for example levoglucosan), and (ii) determine the specific toxicities of source-specific contributions to $PM_{2.5}$ in LMICs.

- Efforts to control ambient air pollution in LMICs need to account for both the contributing sources of $PM_{2.5}$ and the toxicity of the $PM_{2.5}$ from each source category. The strongest evidence to date of increased risk of CVD health effects per unit mass of $PM_{2.5}$ is found from coal combustion and diesel-fueled traffic. Therefore, future mitigation efforts that focus on monitoring and regulating the constituents of $PM_{2.5}$ from these sources should be prioritized. Reducing pollution from these sources can be expected to return greater cardiovascular health benefits per unit mass of $PM_{2.5}$ reduced than if $PM_{2.5}$ mass continues to be addressed equally, irrespective of source and composition.

"The current evidence summarized in this report indicates that trace constituents from $PM_{2.5}$ and $PM_{2.5}$ mass from fossil-fuel combustion are among the greatest contributors to $PM_{2.5}$ toxicity. The results of both the short and long-term exposure studies strongly suggest that the $PM_{2.5}$ mass component derived from fossil-fuel combustion is of particular concern for public health. The health risk is particularly great from coal combustion and traffic-related $PM_{2.5}$."

Appendix

TABLE 1 Associations of Adverse Health Effects with Acute Exposures to $PM_{2.5}$ Constituents

MORTALITY															
	Authors	Year	Location	City	Outcomes	PM	OCM	EC	BC	TC	Nitrate	Nitrite	Sulfate	Sulfite	NH_4^+	AI
1	Laden	2000	US	6 cities	All											0
2	Ostro	2007	US	6 California counties	All	1	0.5	0.5			0.5		1			0
					CVD	1	0.5	1			0.5		1			0
					RSD	1	0	0			0		0			0
3	Ostro	2008	US	6 California counties	CVD	1	0	1			0.5		1			
4	Cakmak	2009	Chile	Santiago	All	1	1	1								0
					CVD	1	1	1								0
					RSD	1	1	1								0
5	Zhou	2010	US	Detroit and Seattle	All	1		1								1
					CVD	1		1								0
					RSD	0		0								0
6	Ito	2011	US	New York City	CVD	1	1	1			1		1			
7	Son	2012	Korea	Seoul	All	0	0	0			0		0		0	
					CVD	0	0	0			0.5		0.5		1	
					RSD	0	0	0			0		0		0	
8	Cao	2012	China	Xi'an	All	1	1	1			1		1		1	
					CVD	1	1	1			1		1		1	
					RSD	1	1	1			1		1		1	
9	Huang	2012	China	Xi'an	All	1	0	1			0		0		0	
					CVD	1	0	1			0		0		0	
					RSD	1	0	0			0		0		0	
10	Sacks	2012	US	Philadelphia	CVD	0										
11	Krall	2013	US	72 cities	All	1	1	1			0		0		0	
12	Dai	2014	US	75 cities	All	0	0	0								0
					CVD	0	0	0								0
					RSD	1	0	0								0
13	Heo	2014	Korea	Seoul	All	0	1	0			0		0			
					CVD	1	1	0			0		0			
					RSD	0	0	1			0		0			
14	Li	2014	China	Beijing	All	1					1	0	1		0	
					CVD	1					1	0	1		0	
					RSD	1					1	0	1		0	
15	Basagana	2015	Europe	5 cities	CVD	1	0	1		0	0		1			
					RSD	1	0.5	1		0.5	0		0.5			
16	Kim	2015	US	Denver	All	0	1	1			0		0			
					CVD	0	0	0			0		0			
					RSD	0	0	0			0		0			
	Fraction ALL cause sig					7.0/11	5.5/9	6.5/10			2.5/8		3.0/8		1.0/5	1.0/5
	Fraction CVD sig					9.0/13	4.5/11	8.0/12			4.5/10		6.5/10		2.0/4	0.0/4
	Fraction RSD sig					7.0/11	2.5/9	4.0/10			2.0/8		2.5/8		1.0/4	0.0/4
	Fraction any category significant					10./13	7./12	10./13			5./11		6.5./11		2./5	1./5

As	Br	Ca	Cl	Cr	Co	Cu	F	Fe	K	Mg	Mn	Na	Ni	Pb	S	Se	Si	Ti	V	Zn
0	0	0	0			0		1	0		0		1	1	1	0	0		1	0
	0	1	1			1		1	1		1		0	1	1		1	1	1	1
	0	0	1			1		1	1		1		0	0	0.5		0	1	1	1
	0	0	0			1		0	0		0		0	0	0		0	1	0.5	0.5
		0	0			0		1	0.5						0.5			0.5		1
	1	0	0	0		0		0	0		0	0	0	0	0	0	0			0
	0	0	0	0		0		0	0		0	0	0	0	0	0	0			0
	0	0	0	0		0		0	0		0	0	0	0	0	0	0			0
								0	1			0	0		1		1		0	1
								0	1			0	0		1		1		0	1
								0	0			0	0		0		0		0	0
	1											1	0			1	1		0	1
		0	0						0	1		0								
		0	0						0	0		0								
		0	0.5						0	0.5		0								
1			1						1	0		0	1		1					
0			1						1	1		0	1		1					
0			1						1	1		1	1		0					
	0		1	1					0				1	0	1					0
	0		1	1					0				1	0	1					0
	0		1	0					1				0	1	1					0
						0		0.5	0				0		1	1	0.5		0	0
												1					1			
		1				0		0	0			0	0		0.5		1		0	0
		0				0		0	0			0	0		0		0		0	0
		0				0		0	0			0	0		0.5		0		0	0
	0					0								0						0
	0					1								1						1
	1					0								1						0
		1	0				0		1	0		0								
		0	0				0		1	0		0								
		0	0				0		1	0		0								
		0				0		0	0	0	1		0				0	0	0	0
		0				0		1	0	0	0		1				0	0	1	1
	1.0/5	3.0/6	3.0/7			1.0/5		2.0/5	4.0/9	1.0/3	1.0/3	1.0/6	3.0/7	2.0/5	5.5/7		4.0/6	1.0/1	2.0/4	2.0/7
	1.0/5	0.0/7	3.0/7			2.0/7		2.5/7	4.5/11	1.0/4	2.0/3	1.0/7	2.0/9	1.0/4	4.0/8	2.0/3	2.5/7	1.5/3	1.0/6	5.0/10
	1.0/4	0.0/6	2.5/6			1.0/5		1.0/5	3.0/9	1.5/4	0.0/3	1.0/6	2.0/7	2.0/4	1.5/6		0.0/5	1.0/2	1.5/4	1.5/7
	3./6	3./8	4./8			2./8		4.5/8	5.5/12	2./4	2./3	3./8	3./8	3./4	6.5/8	2./4	4.5/8	1.5/3	2./6	5./11

TABLE 1 (CONTINUED) Associations of Adverse Health Effects with Acute Exposures to $PM_{2.5}$ Constituents

HOSPITALIZATIONS															
	Authors	Year	Location	City	Outcomes	PM	OCM	EC	BC	TC	Nitrate	Nitrite	Sulfate	Sulfite	NH_4^+	Al
1	Sarnat	2008	US	Atlanta	CVD	1	1	1			0		0			
					RSD	0	0	0			0		1			
2	Bell	2009	US	106 counties	CVD		0	1			0		0		0	0
					RSD		0	1			0		0		0	0
3	Ito	2011	US	New York City	CVD	1	1	1			1		1			
4	Lall	2011	US	New York City	CVD			0								
					RSD			0								
5	Kim	2012	US	Denver	CVD	0.5	1	1			0		0			
					RSD	0	0	0			0		0			
6	Levy	2012	US		CVD		0	1			0		0			
					RSD		0	0			0		0			
7	Mostof-sky	2012	US	Boston	Ischemic	1			1							
8	Bell	2013	US	4 counties	CVD	1			1							0
					RSD	0			1							1
9	Li	2014	China	Beijing	CVD	1					0	0	0		0	
					RSD	1					0	0	1		0	
10	Jones	2015	US	New York State	RSD	1	1	0			1		1		1	
11	Ostro	2016	US	8 metros	CVD	0	0	1			0		0			
					RSD	1	1	1			1		0			
	Fraction CVD sig					4.5/6	3.0/6	6.0/7			1.0/7		1.0/7		0.0/2	
	Fraction RSD sig					3.0/7	1.0/6	2.0/7			2.0/7		3.0/7		1.0/3	
	Fraction any category significant					7.5/9	5./7	6./8			3./8		4./8		1./3	

Source: Compiled by the authors of this report based on the works of the authors indicated in the table.
Note: CVD = cardiovascular disease, OCM = organic carbon matter, PM = particulate matter, RSD = respiratory disease, sig = statistically significant, TC = total carbon.

As	Br	Ca	Cl	Cr	Co	Cu	F	Fe	K	Mg	Mn	Na	Ni	Pb	S	Se	Si	Ti	V	Zn
									1							0	0			1
									0							0	0			0
0		0	0			0		0	0	0		0	1	0			0	0	1	0
0		0	0			0		0	0	0		0	1	0			0	0	1	0
	1											1	1			1	1		0	1
											0		0		0		0			
											1		0		0		0			
0	0	0		0		0		0	0		0	0	0.5	0	0.5	0	0	0	0	0
	0.5	1	0						0						0		0	0	1	0
	0	1	1						0						0		1	1	1	0
		0	0				0		0	1		1								
		0	1				1		0	1		1								
						0		0	1		0		0		0		0	0	0	1
						1		1	1		1		0		0		1	0	1	1
	1.5/2	1.0/3	0.0/3			0.0/2		0.0/2	2.0/5		0.0/2	2./4	2.5/4		0.0/3		1.0/6	0.0/3	2.0/4	3.0/5
	0.0/1	1.0/3	2.0/3			1.0/2		1.0/2	1.0/5		2.0/2	1./2	1.0/3		0.0/3		2.0/5	1.0/3	3.0/3	1.0/4
	1.5/3	1./4	2./3			1./3		1./3	2./6		2./3	2./4	2.5/5		0.5/4		3./7	1./4	3./5	3./6

TABLE 2 Associations of Adverse Health Effects with Acute Exposures to $PM_{2.5}$ Source Components

MORTALITY														
	Authors	Year	Location	City	Outcomes	Residual Oil	Coal	Traffic	Biomass	Soil	Roadway	Salt	Industry	2nd Nitrate	2nd Sulfate
1	Laden	2000	US	6 cities	All	0	1	1		0		0	0		
2	Mar	2006	US	Phoenix	All			0	0	0		1	1		0
					CVD			1	1	0		1	1		1
3	Ito	2006	US	Washington, DC	All	0	1	1	0	1		0	0	0	1
					CVD	1	1	1	1	1		0	0	1	1
4	Cakmak	2009	Chile	Santiago	All	1		1		1			1		
					CVD	1		1		1			1		
					RSD	1		1		1			1		
5	Ostro	2011	Spain	Barcelona	All	1		1		0	1	0	0	0	0
					CVD	1		1		1	1	0	0	1	1
6	Sacks	2012	US	Philadelphia	CVD	0	1	0		1	0				
7	Heo	2014	Korea	Seoul	All		0	0	0	0	0	0	0		0
					CVD		0	0	1	0	0.5	0	0.5		0
					RSD		0	1	0	0.5	0	0	0		0
	Fraction ALL cause sig					2./4	2./3	4./6	0/3	2.0/6	2./3	0/5	2.0/6		1./4
	Fraction CVD sig					3./4	2./3	4./6	3./3	4.0/6	1.5/3	1./4	2.5/5		3./4
	Fraction RSD sig						0/1	1./1	0/1	0.5/1	0/1	0/1	0/1		0/1
	Fraction ANY sig					3./5	3./4	6./7	3./3	4.5/7	2.5/3	1./5	2.5/6		3./4

Source: Compiled by the authors of this report based on the works of the authors indicated in the table.
Note: CVD = cardiovascular disease, RSD = respiratory disease, sig = statistically significant.

TABLE 2 (CONTINUED) Associations of Adverse Health Effects with Acute Exposures to $PM_{2.5}$ Source Components

HOSPITALIZATIONS														
	Authors	Year	Location	City	Outcomes	Residual Oil	Coal	Traffic	Biomass	Soil	Roadway	Salt	Industry	2nd Nitrate	2nd Sulfate
1	Sarnat	2008	US	Atlanta	CVD			1	1	0	0		1	0	0
					RSD			0	0	0	0		0	0	1
2	Lall	2011	US	New York City	CVD	0		1		0			0		0
					RSD	0		0		0			1		0
3	Bell	2013	US	4 counties	CVD	0		0			1	0			0
					RSD	0		0			1	1			0
4	Kioumourtzoglou	2014	US	Boston	CVD	1		1		0	0	0			1
5	Ostro	2016	US	8 metros	CVD			1	0	0.5				0	0
					RSD			1	1	0.5				1	0
6	Krall et al.	2017	US	63 counties	CVD	1		1		0		1	1		1
	Fraction CVD sig					2./4		5./6		0.5/5	1./3	1./3	2./3		2./6
	Fraction RSD sig					0/2		1./4		0.5/4	1./2	1./1	1./2		1./4
	Fraction ANY sig					2./4		5./6		0.5/5	1./3	2./3	3./3		3./6

Source: Compiled by the authors of this report based on the works of the authors indicated in the table.
Note: CVD = cardiovascular disease, RSD = respiratory disease, sig = statistically significant.

TABLE 3 Associations of Long-Term Exposure to $PM_{2.5}$ Constituents with Mortality

First Author (year)	Years	Population	Exposures	Statistical Method	Significant Species and Sources	Comment	Mortality Outcomes
Ozkaynak (1987)	1980	US	IPMN	Multiple regression	Sulfate	Sulfate effect on all-cause about 3x $PM_{2.5}$	All
Dockery (1993), Krewski	1977–1991	Six eastern and midwestern cities	Six-City Data	Cox PH	Sulfate	Sulfate effect on all-cause is 2.4x $PM_{2.5}$	All CP LC
Pope (1995), Krewski (2000)	1982–1989	American Cancer Society	EPA and IPMN	Cox PH	Sulfate	Sulfate effect on all-cause is about 2x $PM_{2.5}$	All CP CV RD LC
Smith (2009)	1982–2000	American Cancer Society	EPA and IPMN	Cox PH	Sulfate, EC	Sulfate effect on all-cause 2x $PM_{2.5}$, EC effect 9x $PM_{2.5}$.; sulfate effect on CP 1.2x $PM_{2.5}$, EC 10x $PM_{2.5}$	All CP
Ostro (2011)	2001–2007	California Teachers Cohort	EPA Speciation Network	Cox PH	EC, silicon, sulfate	EC effect on CP 6x $PM_{2.5}$; sulfate effect CP 3.4x $PM._{2.5}$	All CP IHD RD
Gan (2011)	1999–2002	Vancouver, Canada	Land use regression	Cox PH	EC (converted from BC)	Only component examined; EC effect on coronary heart disease about 13x $PM_{2.5}$	CV
Vedal (2013)	1995–2005	Women's Health Initiative	EPA Speciation Network	Cox PH	OC, EC, sulfur	OC strongest association with CV mortality; sulfur with first CV event	CV STR ART PCHD FCE
Wang (2014)	1985–2012?	Europe	Land use regression	Cox PH	No associations	Sulfur and silicon produce highest risk estimates	CVD
Ostro (2015)	2001–2007	California Teachers Cohort	Chemical transport model	Cox PH	EC, nitrate, SOA; gas and diesel engines, sulfur fuel combustion	EC highest risk or IHD among components about 10x $PM_{2.5}$; no major sulfate sources in California	All CV IHD RD
Chung (2015)	2000–2006	1.25 Medicare enrollees, eastern US	EPA Speciation Network	Bayesian hierarchical	EC, nitrate, silicon, sulfate	Basic model examined monthly changes in exposure; sulfate and Na significantly modified effect of $PM_{2.5}$	All
Kioumourtzoglou (2015)	2000–2010	US	EPA Speciation Network	Extended Cox PH	Sulfate, EC vanadium, nickel	Clusters of fuel oil combustion, power plant emissions, EC, and metals have significant regional impacts	All
Thurston (2016)	1982–2004	American Cancer Society	EPA Speciation Network	Cox PH	EC (traffic tracer) and sulfur (coal and oil combustion tracer)	For IHD, effect of EC and coal is 11.5% and 4.6% per ug/m3 versus 1.6% for $PM_{2.5}$ (10x and 2.8x $PM_{2.5}$)	IHD
						Fraction all sig	
						Fraction CVD or CP or STR Sig	
						Fraction RSD sig	
						Fraction IHD sig	
						Fraction any category significant	

Source: Compiled by the authors of this report based on the works of the authors indicated in the table.
Note: ART = atherosclerotic, BC = black carbon, CP = cardiopulmonary, CV = cardiovascular, CVD = cardiovascular disease, EC = elemental carbon, EPA = United States Environmental Protection Agency, FCE = first cardiac event, IHD = ischemic heart disease, IPMN = United States Environmental Protection Agency's Inhalable Particle Monitoring Network, LC = lung cancer, OC = organic carbon, OCM = organic carbon matter, PCHD = possible coronary heart disease, PH = proportional hazards, RD = respiratory, RSD = respiratory disease, Sec Org = secondary organics, sig = statistically significant, SOA = secondary organic aerosol, STR = stroke.

$PM_{2.5}$	OCM	EC	Nitrate	Sulfate	Sec Org	As, Cl, Se	Ca	Cu	Fe	K	Mg	Mn	Na	Ni	Pb	S	Si	V	Zn
1				1								1							
1 1 0				1 1 0															
1 1 1 0 0				1 1 1 0 1															
		1 1		1 1															
0 1 1 0	0 0 1 0	0 0 1 0	0 1 1 0	0 1 1 0					0 0 1 0	0 0 1 0							0 1 1 0		0 0.5 1 0
0		1																	
0 0 0 0 1	1 1 1 0 0	0 0 0.5 0 0														0 0 0.5 0 1	0 0 0 0 1		
0								0	0	0				0	0		0	0	0
0 0.5 1 0	0 0 0.5 0	0 0 1 0	0 1 1 0		0 0.5 1 0			0 0 1 0	0 0 0 0			0 0 0 0								
1	0	1	1	1									1						
1		1		1							1			1	1			1	1
1	0	1				1	0		1	0		0	0	0	1	1	0	1	0
5/7	0/4	8/8		6/7					0/2	0/1					1/1		0/1	1/2	2/2
4.5/8	1/2	3/5		4/4					0/2	0/2					1/1		1/2	1/3	0.5/2
0/2	**0/2**	**0/2**		**0/2**					**0/2**	**0/1**					**0/0**		**0/1**	**0/1**	**0/1**
3/3	**3/3**	**3.5/4**		**2/2**					**2/3**	**1/2**					**1/1**		**1/2**	**2/2**	**1/2**
9/11	**3/5**	**8/8**		**8/8**					**2/4**	**1/3**					**2/3**		**2/4**	**2/3**	**2/4**

TABLE 4 Associations of Long-Term Exposure to $PM_{2.5}$ Sources with Mortality

First Author (year)	Years	Population	Exposures	Statistical Method	Significant Species and Sources	Comment	Mortality Outcomes
Ozkaynak (1987)	1980	US	IPMN	Multiple regression	Sulfate	Sulfate effect on all-cause about 3x $PM_{2.5}$	All
Dockery (1993), Krewski (2000)	1977–1991	Six eastern and midwestern cities	Six-City Data	Cox PH	Sulfate	Sulfate effect on all-cause is 2.4x $PM_{2.5}$	All CP LC
Pope (1995), Krewski (2000)	1982–1989	American Cancer Society	EPA and IPMN	Cox PH	Sulfate	Sulfate effect on all-cause is about 2x $PM_{2.5}$	All CP CV RD LC
Smith (2009)	1982–2000	American Cancer Society	EPA and IPMN	Cox PH	Sulfate, EC	Sulfate effect on all-cause 2x $PM_{2.5}$, EC effect 9x $PM_{2.5}$.; sulfate effect on CP 1.2x $PM_{2.5}$, EC 10x $PM_{2.5}$	All CP
Ostro (2011)	2001–2007	California Teachers Cohort	EPA Speciation Network	Cox PH	EC, silicon, sulfate	EC effect on CP 6x $PM_{2.5}$; sulfate effect CP 3.4x $PM._{2.5}$	All CP IHD RD
Gan (2011)	1999–2002	Vancouver, Canada	Land use regression	Cox PH	EC (converted from BC)	Only component examined; EC effect on coronary heart disease about 13x $PM_{2.5}$	CV
Vedal (2013)	1995–2005	Women's Health Initiative	EPA Speciation Network	Cox PH	OC, EC, sulfur	OC strongest association with CV mortality; sulfur with first CV event	CV STR ART PCHD FCE
Wang (2014)	1985–2012	Europe	Land use regression	Cox PH	No associations	sulfur and silicon produce highest risk estimates	CVD
Ostro (2015)	2001–2007	California Teachers Cohort	Chemical transport model	Cox PH	EC, nitrate, SOA; gas and diesel engines, sulfur fuel combustion	EC highest risk or IHD among components about 10x $PM_{2.5}$; no major sulfate sources in California	All CV IHD RD
Chung (2015)	2000–2006	1.25 Medicare enrollees, eastern US	EPA Speciation Network	Bayesian hierarchical	EC, nitrate, silicon, sulfate	Basic model examined monthly changes in exposure; sulfate and Na significantly modified effect of $PM_{2.5}$	All
Kioumourtzoglou (2015)	2000–2010	US	EPA Speciation Network	Extended Cox PH	Sulfate, EC vanadium, nickel	Clusters of fuel oil combustion, power plant emissions, EC, and metals have significant regional impacts	All
Thurston (2016)	1982–2004	American Cancer Society	EPA Speciation Network	Cox PH	EC (traffic tracer) and sulfur (coal and oil combustion tracer)	For IHD, effect of EC and coal is 11.5% and 4.6% per $\mu g/m^3$ versus 1.6% for $PM_{2.5}$ (10x and 2.8x $PM_{2.5}$)	IHD
						Fraction all sign	
						Fraction CVD or CP sig	
						Fraction RSD sig	
						Fraction IHD sig	
						Fraction any category significant	

Source: Compiled by the authors of this report based on the works of the authors indicated in the table.

Note: ART = atherosclerotic, BC = black carbon, CP = cardiopulmonary, CV = cardiovascular, CVD = cardiovascular disease, EC = elemental carbon, EPA = United States Environmental Protection Agency, FCE = first cardiac event, IHD = ischemic heart disease, IPMN = United States Environmental Protection Agency's Inhalable Particle Monitoring Network, LC = lung cancer, OC = organic carbon, PCHD = possible coronary heart disease PH = proportional hazards RD = respiratory, RSD = respiratory disease, sig = statistically significant, SOA = secondary organic aerosol, STR = stroke.

Traffic	Powerplant /coal	Biomass	Crustal	Industrial Process	Fuel oil combustion
0 0 1 0		0 0 0 0			1 1 1 0
	1	0	0	1	1
0	1	0	0	1	0

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