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## Title: What we breathe impacts our health: improving understanding of the link between air pollution and health

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#### Abstract

Air pollution contributes to the premature deaths of millions of people each year around the world, and air quality problems are growing in many developing nations. While past policy efforts have succeeded in reducing particulate matter and trace gases in North America and Europe, adverse health effects are found at even these lower levels of air pollution. Future policy actions will benefit from improved understanding of the interactions and health effects of different chemical species and source categories. Achieving this new understanding requires air pollution scientists and engineers to work increasingly closely with health scientists. In particular, research is needed to better understand the chemical and physical properties of complex air pollutant mixtures, and to use new observations provided by satellites, advanced in-situ measurement techniques, and distributed micro monitoring networks, coupled with models, to better characterize air pollution exposure for epidemiological and toxicological research, and to better quantify the effects of specific source sectors and mitigation strategies.

### Introduction

What we breathe impacts our health. Over the past 20 years, evidence for adverse health effects of ambient air pollution has grown dramatically.<sup>1,2</sup> It is now widely recognized that exposure to outdoor air pollution contributes to a broad array of acute and chronic health effects, ranging from minor physiological impacts to death from respiratory and cardiovascular disease.<sup>3,4</sup> It is also recognized that the effects on human health are large and widespread. The Global Burden of Disease (GBD) study<sup>5</sup> ranked exposure to ambient fine particulate matter ( $PM_{2.5}$ ) as the ninth most important risk factor contributing to the global burden of disease, responsible for 3.2 (95% uncertainty interval: 2.8-3.6) million premature deaths in 2010; in East Asia, it was the fourth largest contributor. Household air pollution from solid fuel combustion ranked fourth globally (first in South Asia), responsible for 3.5 (2.7-4.5) million deaths. These two risk factors are the most important environmental exposures for health globally, comparable in impact to other risk factors that are more widely appreciated, such as tobacco smoking, alcohol use, and high body-mass index. It is estimated that in 2005, 89% of the global population lived in areas exceeding the WHO's air quality guideline for annual average PM<sub>2.5</sub> (10 µg m<sup>-</sup> <sup>3</sup>).<sup>6</sup> The most highly polluted areas are often megacities that also have high population, particularly in South and East Asia,<sup>7,8</sup> and while highly populated regions of Asia have a large burden of disease from air pollution, health effects of air pollution occur globally (Figure 1) and include rural populations. Future increases in global urbanization, particularly in rapidly developing countries, and aging of global populations will likely increase the size of the population vulnerable to air pollution. These trends suggest that reductions in emissions will be required to prevent increases in health effects.<sup>9</sup>

In recent decades, governments have adopted standards for specific air pollutants that are measured widely, including ozone and indicators of particulate matter such as PM<sub>2.5</sub>. These standards, along with emission controls and technological changes, have been remarkably effective at driving air quality improvements in North America<sup>10</sup> and Western Europe, though ozone, NO<sub>2</sub>, PM<sub>2.5</sub>, and PM<sub>10</sub> standards are still violated in some regions. The improvements in PM<sub>2.5</sub> air quality have brought demonstrable increases in life expectancy in the US.<sup>11</sup>

Despite this progress in understanding air pollution and its health effects, and in controlling air pollution in some parts of the world, scientific understanding of air pollution and its health effects is incomplete in ways that are important for air pollution management and public health. In particular, both gaseous and particulate air pollution consist of complex mixtures with chemical and physical characteristics that vary over space and time. These pollutants result from sources with different emission characteristics, and from photochemical reactions that transform air pollutants while they are transported and mix with pollutants from other sources. As indicators of this mixture, individual pollutants such as PM<sub>2.5</sub> and ozone have demonstrated associations with human health. Still the effects

of the complex mixtures themselves are far less understood.<sup>12</sup> Therefore several motivating scientific questions currently exist that are also important for policy:

- What specific characteristics and components of air pollution, or specific mixtures of air pollutants, are responsible for specific health effects?
- How important are certain source sectors and source regions for air pollution health effects in a particular location, region, or globally?
- Would other indicators of complex air pollution mixtures and their interactions with human health be more effective for future air quality management?
- What are the human health implications of alternative future strategies for emissions controls and energy use?

In this paper, we discuss recent changes in global air pollution, and in our understanding of air pollution and its health effects, and consider how research in this area can best provide useful information to inform policy decisions in the coming decades. We suggest that addressing the motivating questions above, and moving the field forward in the coming decades, requires stronger interactions between health scientists – including researchers in toxicology, exposure science, epidemiology, and clinical medicine – and air pollution scientists from the perspectives of atmospheric science, chemistry, physics, and engineering. We focus on research in these two communities that aims to better understand the health effects of ambient air pollution. We summarize recent progress in each of these communities, and in research through which these communities have interacted, that we believe capture the most important scientific advances in recent years. Finally, we offer suggestions for future research that builds on these results.

#### The changing nature of global air pollution

Air pollutant concentrations around the world continue to change due to demographic, societal, economic, and technological development, along with the implementation of air quality regulations in large parts of the world. Broadly, concentrations of key air pollutants are generally decreasing in North America and Europe while they are increasing in China, India, and many less industrialized regions. In North America and Europe, decreases of roughly 1.5 to 4% yr<sup>-1</sup> have been observed for PM<sub>2.5</sub>, PM<sub>10</sub> and sulfate, from 1990 to 2009; decreases in carbonaceous PM of 2.5-7.5 % yr<sup>-1</sup> have also been observed in North America.<sup>13</sup> Trends in global estimates of PM<sub>2.5</sub> since the late 1990s show decreases over the eastern US, but increases over the Middle East, eastern and southern Asia, Latin America, and Africa (Figure 2).<sup>14</sup> High PM concentrations are particularly pronounced in China and India, exemplified by the extremely high pollution episodes of January 2013 in northeast China, where measured PM<sub>2.5</sub> daily average concentrations exceeded 500 µg m<sup>-3</sup>,<sup>15</sup> twenty times the 24-hour World Health Organization (WHO) air quality guideline.

Tropospheric ozone in the Northern Hemisphere is observed to show a rise in the baseline levels (concentrations unaffected by local pollution), with decreases and increases in peak values depending on region. Ozone concentrations have decreased since the 1990s in the eastern US,<sup>16</sup> while over North America and Europe there are indications of rising baseline and declining peak ozone levels,<sup>17,18</sup> reflecting the changing roles of regional and remote ozone sources. Over Asia, ozone increases of about 0.5-1 % yr<sup>-1</sup> have been observed since the 1990s.<sup>16</sup> Satellite observations of NO<sub>2</sub>, an important ozone precursor, indicate increases of more than a factor of two in Asia, and decreases in Europe and North America (30-50%) over the last two decades.<sup>19,20</sup>

In addition to these broad trends, the mixture of air pollution from different sources within each world region is changing. For example, while anthropogenic SO<sub>2</sub> emissions have decreased substantially between 1990 and 2011 in Western Europe (-77%) and North America (-65%), they have increased rapidly in Asia (+63%).<sup>21</sup> Air pollution is already severe in some large African cities, and is poised to quickly intensify due to the rapid growth in urban population and relative lack of emission controls.<sup>22</sup>

Looking to the future, climate change may have significant effects on ozone, PM<sub>2.5</sub>, and other pollutants,<sup>23</sup> and fire emissions may be significantly influenced by both changes in climate and fire management practices.<sup>24,25</sup>

## Progress in characterizing air pollution

Over recent decades, knowledge of atmospheric composition and its chemistry and physics has grown tremendously, even though air pollutants are not currently monitored in many cities around the world. New and improved instruments, including aerosol mass spectrometers and proton transfer reaction mass spectrometers<sup>26</sup>, have led revolutionary progress in measuring atmospheric chemical components in ambient environments with high time resolution, especially components in PM and volatile organic compounds (VOCs).<sup>27</sup> Novel analysis methods also more directly investigate the characteristics of aerosol components that may lead to health effects, such as the formation of reactive oxygen species in aerosol that may cause oxidative stress.<sup>28,29</sup> This improved chemical analysis has supported investigation of the importance of specific chemical species for health. In some cases, motivation for understanding the health effects of chemical species has come from the atmospheric science community, such as for isocyanic acid from wood smoke.<sup>30</sup>

Instruments have also been made increasingly mobile to better characterize concentrations and human exposure<sup>31</sup> through mobile and wearable monitors<sup>32,33</sup> deployed in a variety of microenvironments including near roadways.<sup>34</sup> Low-cost instruments are being developed and deployed in micro-networks to characterize fine-scale variations in air pollutant concentrations and human exposure, and to extend monitoring to new locations.<sup>35</sup> But as these low-cost and portable monitors have not demonstrated the same accuracy as more established methods, they are best used in conjunction with other methods, for example to provide understanding of spatial variation while more established methods may correct for bias. Finally, satellite observations of many air pollutants, such as PM<sub>2.5</sub>, NO<sub>2</sub>, O<sub>3</sub>, CO, and formaldehyde, now offer global coverage with remarkable spatial and temporal resolution (Figure 3). Satellite-derived PM<sub>2.5</sub> estimates exhibit a high degree of consistency with ground-based observations globally,<sup>36</sup> in long-term trends,<sup>14</sup> and at the regional scale.<sup>37,38</sup> Observations from satellites, together with ground-based observations, have been critical in constraining the magnitude and trends in global emissions and and air pollutant concentrations, and in quantifying the intercontinental transport of pollutants.<sup>39</sup>

The improved understanding of chemical and other atmospheric processes has been successfully incorporated into models that simulate the transport and transformation of air pollutants at local, regional, and global scales. In addition to improving model processes, global atmospheric models can now simulate global atmospheric chemistry at horizontal resolutions below 1°x1°, and regional models can simulate air quality over a continent at resolutions below 10x10 km. Modeling at finer scale is important as concentrations can vary strongly within urban regions, where population density is high, to avoid spatial misalignment and biases.<sup>40</sup> Models continue to face challenges such as limitations of existing emission inventories, in representing explicit chemical process such as those forming secondary organic aerosols,<sup>41</sup> and in correctly simulating multi-decadal changes in air pollution. Nonetheless these models provide the potential to estimate human exposures to ambient pollutant concentrations at fine temporal and spatial scales and by emission source sector. New modeling systems are aiming to better estimate the concentrations to which individuals are exposed by combining coarse-resolution model estimates or satellite observations with land use regression modeling.<sup>42</sup>

Despite this progress, substantial challenges remain to better characterize the mixtures of gases and particles that make up air pollution, and to improve this understanding throughout the world. The measurement techniques used for routine monitoring are also imperfect. For example, it is widely recognized that the U.S. Federal Reference method for NO<sub>2</sub>, and several international methods that are based on it, measures more than just NO<sub>2</sub>, capturing more oxidized nitrogen compounds.<sup>43,44</sup>

#### Progress in understanding air pollution health effects

Our understanding of air pollution health effects has a strong foundation in toxicological and short-term epidemiological studies focusing on individual pollutants. Long-term epidemiological studies provide evidence for relatively large health effects of chronic, long-term exposure to PM (e.g., as measured by PM<sub>2.5</sub>) and ozone.<sup>4,45,46</sup> Associations between exposure to pollution and health have been observed in North America, Europe, and Asia, despite large differences in source composition, pollutant concentrations, and population health characteristics.<sup>47</sup> However, some studies have identified differences in health estimates for particles by region and by season, which may relate to differences in source composition.<sup>48-52</sup>

While past studies have focused on individual pollutants, often while controlling for variations in other pollutants, the epidemiology community recognizes that health effects may relate to the body's response to complex mixtures of air pollution.<sup>53</sup> Unravelling the contributions and interactions of individual components or sources in a multi-pollutant mixture is a growing research focus, but also prone to fundamental difficulties, as epidemiological studies must account for complex correlations between different pollutants and between the contributions of multiple sources, and both toxicological and epidemiological studies suggest that pollutants in combination may have synergistic or non-linear impacts.<sup>54,55</sup>

Nevertheless, some recent research that investigates the health impacts of particular sources suggests that specific sources, especially combustion sources, produce pollutant mixtures that may be more harmful than others. Such differences in toxicity would not be apparent in analyses of total PM<sub>2.5</sub> mass.<sup>55</sup> For example, recent studies have shown that sources like fuel oil combustion, coal combustion, traffic, and traffic-related particle pollution may have greater health risks than total PM<sub>2.5</sub> mass, or than regional sources and associated components such as sulfates and nitrates.<sup>50,52,55-57</sup> Likewise, a meta-analysis of studies focused on black carbon (BC) as an indicator for combustion PM, finding that the increase in life expectancy of a hypothetical traffic abatement policy was 4 to 9 times greater when evaluated for the BC reduction than for an equivalent reduction of PM<sub>2.5</sub> mass.<sup>58</sup> Another study found greater toxicological effects for particles from incomplete combustion sources resulting from two-wheel vehicles and domestic fires than from diesel vehicles.<sup>59</sup> Although this literature is growing, the evidence to date is not entirely consistent in identifying the most harmful sources or chemical components, and has not excluded any specific PM source, component, or size fraction from being a contributor to PM toxicity.<sup>60,61</sup>

Analyses of relationships between sources and health outcomes depend on imperfect indicators of the specific sources (like NO<sub>2</sub> or BC for traffic) or imperfect source estimates based on modeled approaches (e.g., source factorization methods), and these relationships are difficult to extrapolate to other regions or time periods that have different sources, chemistry, meteorology, and exposure and population characteristics. For example, the BC emissions from traffic in the US are markedly different than those in Europe, which has more diesel vehicles.

Past epidemiological studies have largely used measured pollutant concentrations at fixed monitors to represent the exposure of large populations. The relationship between air pollutant concentrations at finer scales and at these fixed monitors has become a subject of increased interest, as have efforts to attempt to characterize personal exposure through micro networks and wearable monitors, as well as using land use regression to estimate fine-scale variations.<sup>62</sup> In particular, there is a demand for information regarding near-road exposures and residential combustion, in different settings around the world, as both occur near where people live and work.

Finally, as most epidemiological evidence derives from studies in North America and Europe, there is a critical need for more research to be conducted in other regions, capturing effects over a wider range of concentrations, pollutant mixtures, and population, exposure, and health characteristics.

### **Policy context**

Where air pollution has been reduced, such as in North America and Europe, improvements have been forced by regulations and related public policies, and enabled by the development of improved emission control technologies, such as scrubbers on power plants and catalytic converters on motor vehicles, or by changes in energy sources and use. While initiatives of individual national governments have driven air pollution control in North America, international actions have always been important in Europe, including those undertaken through the Convention on Long-Range Transboundary Air Pollution.<sup>63</sup> As the importance of air pollution for global health, and of intercontinental air pollution transport, has increasingly been recognized, international initiatives are now playing an increasing role in addressing global air pollution, including recent resolutions by the United Nations Environment Assembly<sup>64</sup> and the World Health Assembly<sup>65</sup>, and the creation of the Climate and Clean Air Coalition<sup>66</sup>. In this global framework, the air quality management experiences in North America and Europe may be useful as other nations design regulations that adapt to their social, economic, and political circumstances, including the importance of different emissions sources, such as the need to better address emissions from open biomass burning in developing countries. There is clearly a need to improve understanding of local air pollution problems in cities throughout the world, starting with ambient measurements and the creation of emission inventories,<sup>8</sup> with the aim to constrain the relative contributions of different sources to pollutant concentrations and health effects. Likewise, there is a need to develop efficient and affordable energy sources and transportation options, providing alternatives to current practices, especially in developing nations.

There is also increasing interest in the relationships between actions to improve air quality and actions to address climate change. Actions to reduce greenhouse gas (GHG) emissions often reduce coemitted air pollutants from the same sources, and studies of the co-benefits of GHG reductions have found that the monetized benefits of air quality and health improvements are comparable to, or may exceed, the direct costs of GHG reductions.<sup>67-69</sup> Similarly, actions that focus on reductions in short-lived climate pollutants (SLCPs), including black carbon and ozone precursors, have been shown to bring substantial air quality and health improvements in addition to slowing the rate of climate change.<sup>70</sup> Given these strong links between air pollution and climate change, policies can be better coordinated to address both problems simultaneously.

### **Research directions**

In atmospheric science, fundamental research is needed on the chemical and physical properties of air pollutant mixtures as emissions from a variety of sources mix and age photochemically.<sup>71,72</sup> This research includes improving our mechanistic understanding of chemical interactions at the atmospherebiosphere interface, including the effects of biological particles.<sup>73,74</sup> Epidemiologic studies, which are currently limited by the availability of exposure estimates and rely heavily on pollutants that are measured widely and routinely, should consider other air pollutants suspected to be important for health, such as polycyclic aromatic hydrocarbons (PAHs), metals, reactive oxygen species, and other chemical components of PM. Particle size is likely also important for health, suggesting the importance of measures such as ultrafine PM and particle number concentrations.<sup>75,76</sup> Atmospheric science can contribute by developing low-cost methods of measuring these pollutants, as well as making monitors for other pollutants more accurate and less expensive.<sup>31,35</sup> Adoption of new instrumentation on a wider scale should be encouraged,<sup>77</sup> including in routine networks, and information on measurement uncertainty should be provided for incorporation into health studies. Likewise, there is a need to improve atmospheric models through improvements in the descriptions of fundamental processes and optimal assimilation of atmospheric observations, to better constrain emission estimates and quantify source-receptor relationships.

Atmospheric science is now entering an era of data proliferation provided by satellite observations and comparatively affordable and easily deployed sensors, including wearable monitors.<sup>31</sup>

An important challenge is to extract more information from these observations, and to combine these data with more accurate monitoring techniques to better represent human exposure, using high resolution air quality models and advanced data assimilation methods. For example, active research is now improving methods of inferring aerosol composition or near-ground ozone from satellite observations.<sup>78,79</sup> Recent work has statistically combined the available surface measurements with global atmospheric modeling and satellite observations to yield estimates of global PM<sub>2.5</sub> surface concentrations at fine resolution,<sup>6</sup> and other studies have applied comparable methods for similar purposes.<sup>80-82</sup> The recent availability of global estimates have been influential in catalyzing consideration of air pollution as an important determinant of population health and as an important sustainable development metric.<sup>83</sup> While North America and Europe have a longer history of air pollution monitoring and a more detailed characterization of ambient concentrations, substantial challenges exist in better characterizing pollutant mixtures at fine spatial and temporal scales. Even greater challenges exist across much of Asia, Africa, the Middle East, and Latin America, where available measurements are severely limited.

More work is needed to improve these approaches and to expand them to additional key pollutants, through improved measurement technology, more widespread surface observations, improvements to satellite retrievals, and advancements in models. It is critically important that the quality and coverage of surface monitoring networks and satellite observations be not only maintained but expanded. Similar observational needs from the climate community regarding SLCPs suggest that investments can be leveraged to benefit both communities. Likewise, increased attention is needed to better understand how ambient concentration relates to the actual exposure of individuals as they move through indoor and outdoor environments in their daily activities.

Improved estimates of air pollutant concentrations at fine spatial and temporal resolution could then be used to estimate exposure for air pollution epidemiology, as more spatially-resolved concentration estimates can improve quantification of exposure-health relationships.<sup>84</sup> Especially needed would be source apportionment of PM and modeling to identify exposure due to emissions from particular sources. And by estimating exposures for larger populations globally, epidemiological research can address a wider range of conditions. While North America and Europe have successfully reduced air pollution, it is important to continue to research the further benefits to human health of achieving lower concentrations, as current evidence suggests that health effects occur at concentrations below current standards.<sup>1,2</sup> Meanwhile, the very high concentrations found in the most polluted regions strongly impact human health. Examination of a wide range of exposures, pollutant mixtures, and population health status is therefore important for epidemiology. In this context, better relating research on the health effects of exposure from indoor cookstoves with that from ambient air pollution will prove fruitful. Similarly, relationships between air pollutants, meteorological parameters (temperature, humidity), and other parameters like allergens should be investigated and will be important for anticipating the effects of future climate change. Finally, intervention studies following rapid changes in air pollutant concentrations have proven very useful in understanding health effects,<sup>85</sup> and opportunities to research such interventions should be identified and pursued. To support epidemiological studies under a wider range of conditions, epidemiologists need to engage with health authorities to improve the collection of high-quality and relevant health data. Ideally, health data would be collected with spatial and temporal resolution that approaches that of the available concentration data.

Health effects science can also be improved by aiming for a better understanding of the biological mechanisms by which specific pollutants impact neurological, cardiovascular, respiratory, and other aspects of human health. Research that combines advanced experimental techniques that characterize atmospheric composition properties, and biological markers in 'real life' situations, could contribute to understanding of specific biological mechanisms. One promising approach to investigating

biological mechanisms would involve heavily-instrumented urban supersites where detailed measurements of air pollutants and modeling are coordinated with intensive toxicological and population health research aimed at particular hypotheses. Such work can explore relevant chemical pathways by better combining detailed atmospheric chemistry with detailed biochemical and medical information. For example, new air quality measurements including online detection of short-lived hazardous compounds, such as organic radicals and reactive oxygen intermediates in particles, could be combined with toxicological experiments including the determination of oxidative stress in cell cultures exposed to ambient air and epidemiological investigations on airway, cardiovascular, and inflammatory diseases.

### A path forward

Research on air pollution and health is at an important cross-road. Tremendous progress has been made in reducing air pollution and improving public health in North America and Europe through regulation and related public policy actions targeting PM<sub>2.5</sub>, ozone, and other individual pollutant species. For areas that are developing rapidly, such as India and China, development decisions, for example concerning energy use, in upcoming decades will have enormous implications for air quality and health. In the future, air pollution control efforts would benefit from a more specific understanding of the chemical species and source categories that have the greatest influences on human health, including developing risk functions separately for different sources (e.g., coal combustion and traffic), allowing control actions to be better prioritized. Achieving this new understanding requires progress in individual disciplines, as well as greater interdisciplinary interactions. This new understanding of air pollution health effects can yield improved policies and regulations that more specifically and effectively target particular chemical components and/or sources of air pollution, bringing greater public health benefits at potentially lower cost. While there is ample evidence of the health effects of air pollution to drive decision-making in polluted regions, better understanding can more effectively prioritize control actions among many sources of air pollution, where resources are lacking. In North America and Europe, continued improvements may come at a higher cost, and understanding the differential effects of sources can better prioritize decisions. Further work is needed to incorporate this emerging understanding of health effects into improved model simulations and assessments of human health outcomes, providing better quantification of the health benefits of different actions to mitigate emissions. For example, recent research has identified the importance of different emission sectors for global air quality and health.<sup>86-88</sup> Such tools can then better inform choices of new energy technologies globally over the next century, as we confront the overlapping challenges posed by energy security, air pollution, and climate change, while meeting the energy needs of a growing global population and economy.

The research communities of air pollution science and air pollution health have been traditionally somewhat segregated, as its practitioners often have different disciplinary backgrounds, use different techniques and language, and attend separate meetings. Moving the field forward in the coming decades requires more effective interactions, so that each community can better understand the new findings, and capabilities, limitations, and priorities for research of the other. Interdisciplinary collaborations need to be supported and rewarded through increased funding for interdisciplinary research and by valuing such collaborations in promotion decisions. Through better educational opportunities, junior air pollution scientists should be exposed to the challenges of understanding human health, and vice-versa. Meetings should better encourage interdisciplinary dialogue and break down disciplinary boundaries. Since air pollution is important globally, it is important that these improvements should take place internationally.

Acquired knowledge regarding air pollution health effects, coupled with the increased capacity to measure air pollutants via expanded ground-level monitoring networks, satellite-based estimates,

and low cost specialized sensors, and with better atmospheric models linking emissions to ambient air pollution and personal exposures, can inform more effective strategies to reduce pollution and population exposure in the regions with the most considerable air pollution problems, especially those that currently lack the capacity to address them. Such developments are on the critical path to reducing the substantial burden of disease due to air pollution.

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Image to accompany Abstract.

Ambient particulate matter pollution Both sexes, All ages, 2010 DALYs per 100,000

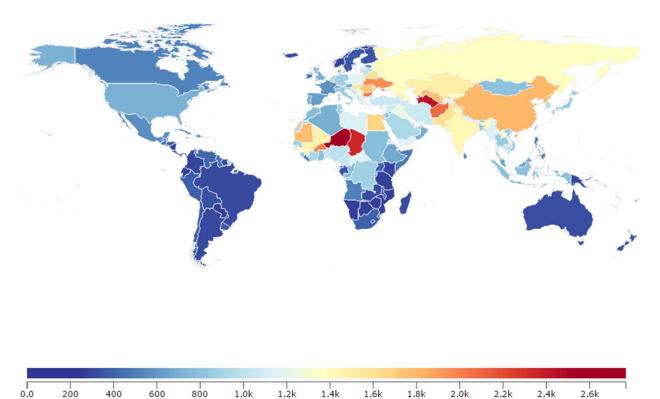


Figure 1 – Total rate of health burden in 2010 due to exposure to ambient PM<sub>2.5</sub> pollution (disabilityadjusted life-years per year per 100,000 population), from the Global Burden of Disease 2010 (Institute of Health Metrics and Evaluation, University of Washington).

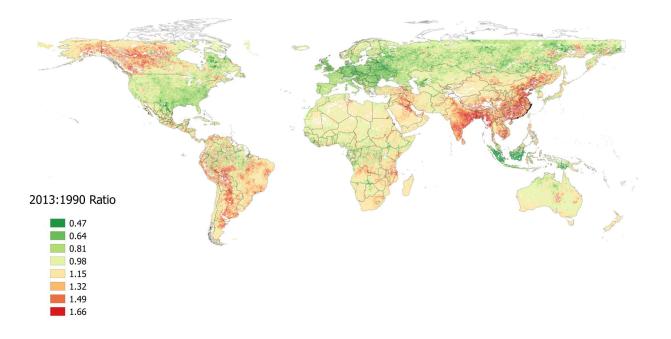


Figure 2 – Ratio of estimated annual average  $PM_{2.5}$  concentrations in 2013 to 1990, at 0.1° x 0.1° resolution, following methods of Brauer et al. (2012). Red indicates a large relative increase during this period; green indicates decreases.

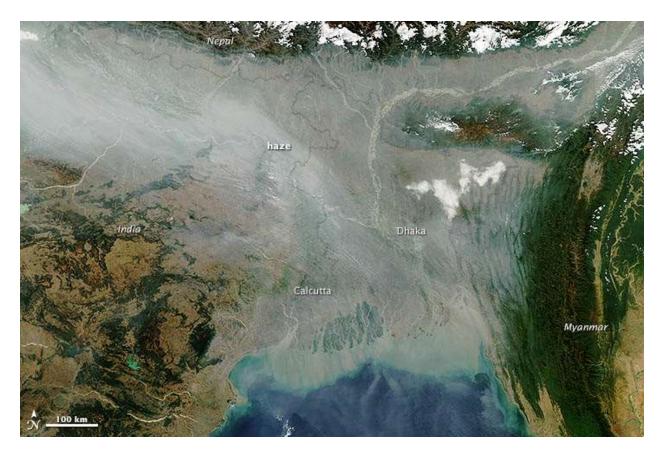


Figure 3 – Satellite image showing a thick river of haze over the Indo-Gangetic Plain on January 10, 2013, as captured by the Moderate Resolution Imaging Spectroradiometer (MODIS) on NASA's Aqua satellite. Image courtesy of NASA Earth Observatory.

(http://earthobservatory.nasa.gov/IOTD/view.php?id=80148)