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Addressing Global Mortality from Ambient $PM_{2.5}$

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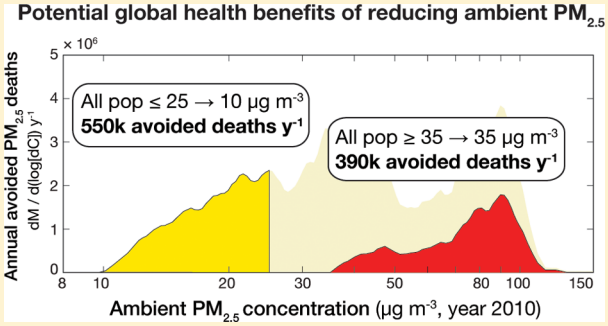
Supporting Information

ABSTRACT: Ambient fine particulate matter ($PM_{2.5}$) has a large and well-documented global burden of disease. Our analysis uses high-resolution (10 km, global-coverage) concentration data and cause-specific integrated exposure-response (IER) functions developed for the Global Burden of Disease 2010 to assess how regional and global improvements in ambient air quality could reduce attributable mortality from $PM_{2.5}$. Overall, an aggressive global program of $PM_{2.5}$ mitigation in line with WHO interim guidelines could avoid 750 000 (23%) of the 3.2 million deaths per year currently (ca. 2010) attributable to ambient $PM_{2.5}$. Modest improvements in $PM_{2.5}$ in relatively clean regions (North America, Europe) would result in surprisingly large avoided mortality, owing to demographic factors and the nonlinear concentration-response relationship that describes the risk of particulate matter in relation to several important causes of death. In contrast, major improvements in air quality would be required to substantially reduce mortality from $PM_{2.5}$ in more polluted regions, such as China and India. Moreover, forecasted demographic and epidemiological transitions in India and China imply that to keep $PM_{2.5}$-attributable mortality rates (deaths per 100 000 people per year) constant, average $PM_{2.5}$ levels would need to decline by ~20−30% over the next 15 years merely to offset increases in $PM_{2.5}$-attributable mortality from aging populations. An effective program to deliver clean air to the world's most polluted regions could avoid several hundred thousand premature deaths each year.



1. INTRODUCTION

Ambient fine particulate matter air pollution ($PM_{2.5}$) is a major risk factor for ill health and death.[1−6] Epidemiological studies have established robust causal associations between long-term exposure to $PM_{2.5}$ and premature mortality from endpoints such as heart disease, stroke, respiratory diseases, and lung cancer, thereby substantially reducing life expectancy.[1−8] In the Global Burden of Disease 2010 comparative risk assessment (GBD),[9] ~3.2 million worldwide year-2010 deaths were attributed to ambient air pollution from $PM_{2.5}$, ranking as the sixth largest overall risk factor for global premature mortality. For comparison, the burden of disease from ambient $PM_{2.5}$ is larger than other well-recognized global health threats, such as malaria and HIV-AIDS combined (year-2010 deaths: 1.2 million and 1.5 million, respectively).[9,10]

Here we explore the magnitude of ambient concentration reductions that would be required to substantially decrease mortality from $PM_{2.5}$. By analyzing high-resolution (~10 km) estimates of mortality attributable to ambient $PM_{2.5}$, we address the following questions that define the overall scale of the $PM_{2.5}$ mitigation challenge: How many people die from $PM_{2.5}$ exposure, where, and under what conditions? How many premature deaths could be avoided by achieving concentration X in region Y? By how much would ambient $PM_{2.5}$ concentrations need to be reduced in order to cut attributable mortality by a given amount? To address these questions, we employ methods and data developed for the GBD study that enable consistent assessment of risks from $PM_{2.5}$ in all regions of the world.

2. MATERIALS AND METHODS

We develop spatially resolved analyses at 0.1° grid resolution (~10 km at midlatitudes) for (i) premature mortality attributable to ambient $PM_{2.5}$ exposures and (ii) reductions in attributable mortality that could be achieved with reductions in ambient $PM_{2.5}$ concentration. We selected the year 2010 as the most recent period of analysis that was publicly available in the

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Global Burden of Disease 2010 data set. We consider premature mortality attributable to ambient $PM_{2.5}$ for five major disease endpoints for which particulate matter was considered a risk factor in the GBD. For adults (age ≥25), these endpoints are ischemic heart disease (IHD), cerebrovascular disease (stroke), chronic obstructive pulmonary disease (COPD) and lung cancer (LC), and for children under 5, acute respiratory lung infection (ALRI). In 2010, these five major diseases together accounted for 20.1 million deaths (~290 deaths per 10^5 population, ~38% of all-cause mortality).[10] A subset of this cause-specific mortality is attributable to $PM_{2.5}$, accounting for ~6% of global all-cause deaths.[9]

2.1. Input Data. *2.1.1. Global $PM_{2.5}$ and Population Surfaces.* We obtained global spatially resolved estimates of year-2010 annual-average ambient $PM_{2.5}$ concentrations at 0.1° grid resolution.[11] This $PM_{2.5}$ surface (Brauer et al. 2012) uses a global data set of ambient measurements to calibrate (i) estimates of ground-level $PM_{2.5}$ from a combination of satellite aerosol optical depth retrievals and the GEOS-Chem chemical transport model, and (ii) estimates from chemical transport model simulations (TM5 model). We use the same global gridded population data set (GPWv3)[12] as Brauer et al. (2012) to apportion regional year-2010 estimates of population[13] to individual grid pixels in our mortality model.

2.1.2. Concentration-Response Functions. Any global assessment of the mortality risks associated with ambient $PM_{2.5}$ is contingent on assumptions about the shape of concentration-response (C-R) relationships for the full range of conditions experienced by the global population. However, evidence on C-R relationships for long-term mortality from $PM_{2.5}$ is predominantly based on cohort studies from North America and Europe, where concentrations are comparatively low. To address this data gap, previous assessments have developed extrapolations for high concentrations.[14,15] Extrapolations based on linear or log-linear C-R models yield implausibly high estimates of relative risk (e.g., RR ≫ 2) for high concentrations.[16−18] Instead, Burnett et al. (2014),[16] building on Pope et al. (2009, 2011),[17,18] developed integrated exposure-response functions (IERs) that constrain the shape of the C-R relationship using mortality data for even higher exposure concentrations (e.g., household air pollution from the use of solid fuels, secondhand tobacco smoke, active tobacco smoking).[16] Following the GBD2010, we employ those IERs to estimate relative risks attributable to $PM_{2.5}$ exposure for the five end points (for adults: stroke, IHD, COPD and LC; for under-5 children: ALRI). Sensitivity cases described in online Supporting Information (SI) consider alternative C-R functions with sharply divergent assumptions about the shape of the concentration-response relationship at higher concentrations (>30 $\mu g\ m^{-3}$).

The IER framework parametrizes the dependence of relative risk, *RR*, on concentration, *C*, based on meta-analysis of observed data:[16]

$$RR(C) = 1 + \alpha[1 - \exp(-\gamma(C - C_0)^{\delta})] \quad \text{for } C > C_0$$
$$RR = 1 \quad \text{for } C \le C_0 \qquad (1)$$

For each endpoint, C_0 represents a theoretical minimum-risk concentration above which there is evidence indicating health benefits of $PM_{2.5}$ exposure reductions (range: 5.8−8.0 $\mu g\ m^{-3}$), and parameters α, γ, and δ determine the overall shape of the concentration-response relationship as the result of a stochastic fitting process.[16] For each endpoint, Burnett et al. provide a distribution of 1000 point estimates of C_0, α, γ, and δ, with age-specific modification factors for IHD and stroke mortality.[19] For computational tractability, we develop here a lookup table for each endpoint that reports the mean value of the RR sampling distribution for $PM_{2.5}$ concentrations in the range of 0−410 $\mu g\ m^{-3}$ in 0.1 $\mu g\ m^{-3}$ steps (see SI).

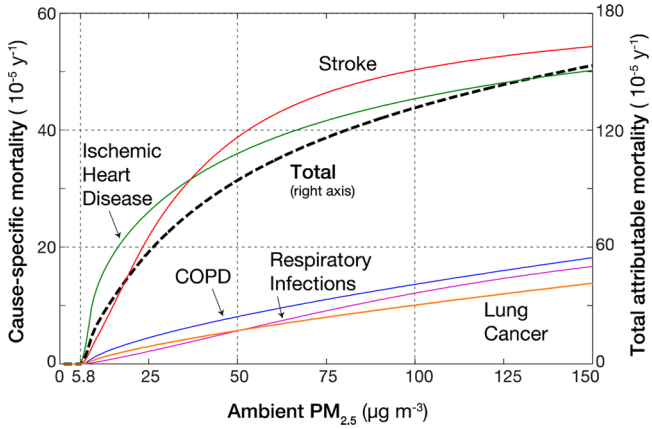

Figure 1. Global concentration-mortality relationships for ambient $PM_{2.5}$ for five individual endpoints (solid lines, left axis) and total of five causes (dashed line, right axis) based on integrated exposure response curves developed for the GBD studies (Burnett et al, 2014). Vertical axes indicate per-capita mortality rates attributable to $PM_{2.5}$ for a hypothetical global population uniformly exposed to a given level of $PM_{2.5}$. Plotted data illustrate the relative contribution of individual disease endpoints to total mortality for a typical population exposed at a given concentration by incorporating concentration-response curves and global disease incidence data (see SI for method). Note that adult ischemic heart disease (IHD) and stroke account for ~70% of combined $PM_{2.5}$-attributable mortality for all five causes. Other causes are chronic obstructive pulmonary disease (COPD) and lung cancer (LC) in adults, and acute lower respiratory infections (ALRI) in children.

Figure 1 illustrates cause-specific concentration-response relationships with each endpoint weighted by its global background disease rate (see SI for details of derivation). IER relationships for stroke and IHD dominate total mortality (combined, accounting for ~70% of total mortality, on average) and are supralinear, increasing most sharply at low concentrations. For COPD, ALRI, and LC, the C-R is more nearly linear; on average, those three endpoints in combination account for ~30% of attributable mortality.

2.1.3. Mortality and Demographic Data. Year-2010 age-specific mortality data and population age structures were obtained from the Institute for Health Metrics and Evaluation (Seattle, WA) for 21 international regions.[10] This dataset provides age- and cause-specific mortality data for the five endpoints (IHD, stroke, COPD, LC, ALRI). For sensitivity analyses, we considered how future changes in demographics and disease rates would affect mortality attributable to $PM_{2.5}$ using year-2030 World Health Organization (WHO) projections of population and cause- and age-specific mortality for 10 global regions (see SI).[20,21]

2.2. Modeling Framework. We adapted a calculation approach developed for the GBD to estimate mortality impacts of $PM_{2.5}$ in each grid cell. We estimate the premature mortality *M* for population age stratum *z* and disease endpoint *j* attributable to ambient $PM_{2.5}$ for grid cell *i* located in region *k*

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using the attributable-fraction type relationship presented in eq 2, below. For compactness of notation, the age stratum subscript z is omitted in the presentation here.

$$M_{i,j} = P_i \times \hat{I}_{j,k} \times (RR_j(C_i) - 1), \text{ where } \hat{I}_{j,k} = \frac{I_{j,k}}{\overline{RR}_{j,k}} \quad (2)$$

Here, P_i is the population of grid cell i, $I_{j,k}$ is the reported regional average annual disease incidence (mortality) rate for endpoint j in region k, C_i represents the annual-average $PM_{2.5}$ concentration in cell i, $RR_j(C_i)$ is the relative risk for end point j at concentration C_i, and $\overline{RR}_{j,k}$, as defined below, represents the average population-weighted relative risk for end point j within region k:

$$\overline{RR}_{j,k} = \frac{\sum_{i=1}^{N} P_i \times RR_j(C_i)}{\sum_{i=1}^{N} P_i} \quad (3)$$

The parameter grouping introduced in eq 2, $\hat{I}_{j,k} = I_{j,k}/\overline{RR}_{j,k}$, represents the hypothetical "underlying incidence" (i.e., cause-specific mortality rate) that would remain for region k if $PM_{2.5}$ concentrations were reduced to the theoretical minimum risk concentration throughout that region.

To estimate the change in mortality, $\Delta M_{i,j}$, in grid cell i under a scenario where concentrations are changed from C_i to some arbitrary alternative concentration C_i^* without altering the underlying incidence, we use the following relationship:

$$\Delta M_{i,j} = P_i \times \hat{I}_{j,k} \times (RR_j(C_i^*) - RR_j(C_i)) \quad (4)$$

Finally, estimates of year-2010 attributable mortality M (and potential changes of this mortality ΔM) are developed by summing over all j disease endpoints for all i grid cells within a defined region.

Several key assumptions accompany the estimation of changes in attributable mortality that result from changes in $PM_{2.5}$: (1) the underlying demographic, age, and non-$PM_{2.5}$ exposure/disease structure of a population remains fixed as concentrations change, as would be the case if the reductions in $PM_{2.5}$ occurred instantaneously and in the absence of changes in other pollutant levels; (2) changes in ambient $PM_{2.5}$ occur jointly in all modeled grid cells, with those changes uniformly distributed across the entire population within each grid cell;[22] (3) lag effects are negligible; and (4) the C-R relationship is assumed to be a valid representation of the relationship between *changes* in population exposure and population risk. Owing to these assumptions, inferences are more robust for comparisons among estimates than for individual point estimates. Because multiple risk factors typically exist for any disease (and moreover, avoiding death from one cause does not prevent ultimate mortality), strictly speaking, reductions in attributable mortality should not be construed as "lives saved." However, $PM_{2.5}$ exposure substantially reduces life expectancy.[23,24] An approximate scale of this lost life expectancy is reflected in GBD2010 data. The global ratio of $PM_{2.5}$-attributable years of life lost (YLL) to all-cause mortality (global totals for 2010: 72.4 million attributable YLL,[9] 52.8 million all-cause deaths[10]) implies that exposure to $PM_{2.5}$ air pollution reduces average global life expectancy by ~1.4 years. This value is consistent with other estimates (e.g., ~0.5−1 years in the U.S.,[17,23] ~1.6 years for a city at 25 μg m^{-3},[25] and ~3−5 years in polluted regions of China[24]).

2.3. Modeled Scenarios. We estimate potential reductions in premature mortality for several scenarios in which $PM_{2.5}$ levels reach a fixed target. First, we consider a set of four scenarios in which $PM_{2.5}$ concentrations in all grid cells that exceed a specific target concentration are reduced to that target level. Specifically, we consider four guideline concentrations specified by the World Health Organization: 35 μg m^{-3} (interim target 1, IT-1), 25 μg m^{-3} (IT-2), 15 μg m^{-3} (IT-1), or the global air quality guideline of 10 μg m^{-3} (AQG). For each of those four scenarios, we assign a global target concentration C^* to all grid cells in which the local concentration C_i exceeds C^* and then employ eq 4 to estimate the resulting global change in attributable mortality. Second, we consider a "meet next target" scenario in which all areas with concentrations above 10 μg m^{-3} achieve the corresponding next-lowest WHO concentration target: either the global AQG or level IT-3, IT-2, or IT-1 (i.e., concentrations above 35 μg m^{-3} are reduced to 35 μg m^{-3}, concentrations between 25 and 35 μg m^{-3} are reduced to 25 μg m^{-3}, and so on). Third, we consider the fractional reductions in $PM_{2.5}$ concentrations that would be required to achieve a given percentage reduction in attributable mortality (e.g., 25% or 50% mortality reduction) within a defined region. Here, we use eq 4 to iteratively solve for the percentage concentration reduction P that yields a desired mortality target for a region when each grid cell in that region i is assigned the concentration $C_i^* = C_i\,(1 - P)$. Finally, we employ a similar iterative solution approach to examine how future concentrations would need to change in order to hold per-capita attributable mortality constant at circa-2010 levels after accounting for projected future changes in age structure and the patterns of underlying disease incidence (see section 2.1.1 and SI).

3. RESULTS AND DISCUSSION

3.1. Global and Regional Patterns in Mortality from $PM_{2.5}$. Using publicly available data and similar methods to those employed by the GBD2010 assessment, our spatially resolved model estimates that 3.24 million worldwide premature deaths were attributable to $PM_{2.5}$ in year 2010. That estimate agrees to within 0.5% of the published GBD2010 estimate for premature mortality attributable to ambient $PM_{2.5}$.[9]

Mortality from ambient $PM_{2.5}$ varies substantially among world regions. For the five causes of death considered here, Figures 2a-c display estimated year-2010 premature mortality surfaces for $PM_{2.5}$ (attributable deaths km^{-2} y^{-1}) in (a) the northern Americas, (b) Europe and northern Africa, and (c) Asia. Those three domains of similar spatial extent encompass 3.1 million premature deaths attributable to $PM_{2.5}$ (97% of global total) and a population of 5.9 billion people (86% of global total). Population-weighted mean ambient $PM_{2.5}$ concentrations are higher in the Asian domain (38 μg m^{-3}) than in the northern Americas (12 μg m^{-3}) and Europe and northern Africa (19 μg^{-3}). Accordingly, per-capita and total mortality attributable to $PM_{2.5}$ are highest in the Asian domain (63 deaths per 10^5 population; 2.3 million total deaths) and lowest in the northern Americas domain (25 deaths per 10^5 population, 150 000 total deaths; see Figure 2). Overall, the Asian domain alone accounts for 53% of the total global population and 72% of total mortality attributable to $PM_{2.5}$. The spatial concentration of premature mortality attributable to $PM_{2.5}$ ("$PM_{2.5}$ mortality density," attributable deaths km^{-2} y^{-1}) is highest in Asia, owing to the interaction of high population density, high disease prevalence, and high levels of $PM_{2.5}$ in these areas. Regions of high $PM_{2.5}$ mortality density in Asia include rural as well as urban areas. For example, in Figure 2,

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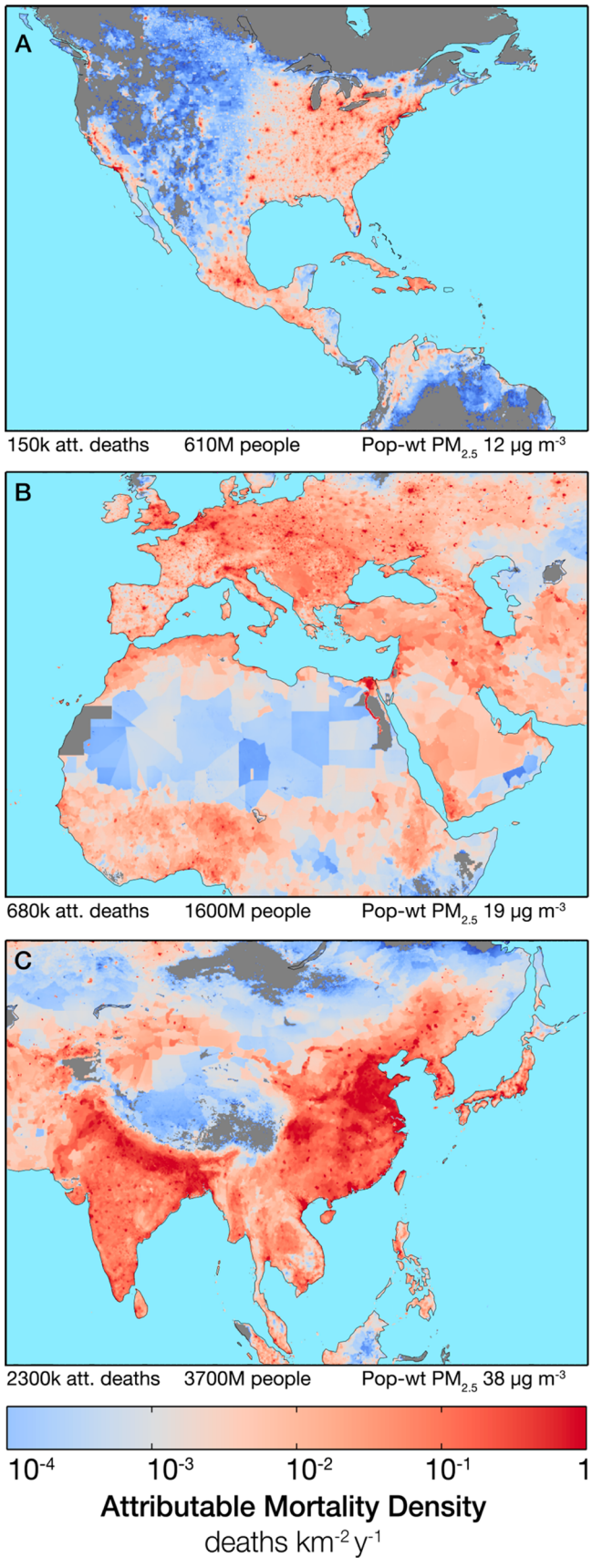

Figure 2. Attributable premature mortality surfaces for $PM_{2.5}$ at 10 km resolution for (A) the northern Americas, (B) Europe and northern Africa, and (C) Asia; units for logarithmic color scale: premature deaths km^{-2} y^{-1}. Dark gray regions indicate areas without attributable mortality, owing to ambient $PM_{2.5}$ below the theoretical minimum-risk concentration level or to unavailable input data. Spatial patterns reflect the multiplicative effect of (i) local variations in $PM_{2.5}$ mortality risk and population density and (ii) regional variation in per-capita cause-specific disease rates. See SI for population-normalized maps.

$PM_{2.5}$ mortality density in *rural* north India and eastern China is comparable to *urban* levels in Europe and North America (~1 attributable death km^{-2} y^{-1}).

In addition to regional variation in ambient $PM_{2.5}$, patterns of attributable mortality depend on the size and density of the exposed population, baseline disease incidence rates, and the age structure of the population. SI Figure SI.2 maps spatial patterns of mortality attributable to $PM_{2.5}$ on a per-capita basis. Per-capita mortality is notably high in urban and rural areas of eastern China; those levels substantially exceed the highest rates in India (found across the Gangetic basin). Urban areas stand out as per-capita mortality hotspots in many high-income countries owing to elevated $PM_{2.5}$. Regions with older-than-average populations and/or high underlying rates of cardiovascular disease (e.g., the former Soviet Union) tend to have higher per-capita rates of attributable mortality than might be expected based on $PM_{2.5}$ concentrations alone. Likewise, the comparatively young populations currently partially offset the burden of disease from $PM_{2.5}$ in polluted countries such as India and China. Overall, national average per-capita mortality rates attributable to $PM_{2.5}$ vary by more than order of magnitude, with example per-capita rates of ~92 (China), ~58 (Russia), ~47 (India), ~40 (Germany), ~33 (United States), and ~6 (Australia) (units: year-2010 deaths per 10^5 people).

3.2. Population-Concentration-Mortality Distribution.

Mortality attributable to $PM_{2.5}$ occurs across the entire spectrum of conditions, from clean to polluted. To visualize how the regional impacts of $PM_{2.5}$ are distributed across this concentration range, we plot the distribution of global population (Figure 3a) and premature mortality (Figure 3b) as a function of ambient $PM_{2.5}$ by (i) dividing the distribution of global concentrations into 400 logarithmically spaced bins (range: 0.1–410 μg m^{-3}) and then (ii) computing the bin-width-normalized sum of these parameters for the grid cells in each concentration bin.

The global population-$PM_{2.5}$ distribution (Figure 3a) is approximately log-normal (GM: 20 μg m^{-3}, GSD: 2.1), with a broad peak between ~15–25 μg m^{-3} and a long tail that exceeds 100 μg m^{-3}. Global population-weighted mean, median, and interquartile range (IQR) $PM_{2.5}$ concentrations are respectively 27, 19, and 12–34 μg m^{-3}. Population-weighted concentrations in China (mean 59 μg m^{-3}, IQR: 38–81 μg m^{-3}) substantially exceed levels in India (28; 20–35 μg m^{-3}), which are in turn elevated above those in Western Europe (13; 11–15 μg m^{-3}) and the U.S. (12; 10–14 μg m^{-3}).

Since mortality risks increase with concentration, the global mortality-concentration distribution (Figure 3b) is skewed to the right of the population-concentration distribution (Figure 3a). Using the mortality distribution, we segment the total global mortality attributable to $PM_{2.5}$ into five equal-mortality groupings ("mortality quintiles" Q1–Q5, ~650 000 year-2010 deaths per quintile) with increasing concentration (Table 1, Figure 3b). Per-capita mortality attributable to $PM_{2.5}$ is 5× higher for the top mortality quintile (~120 deaths per 100 000)

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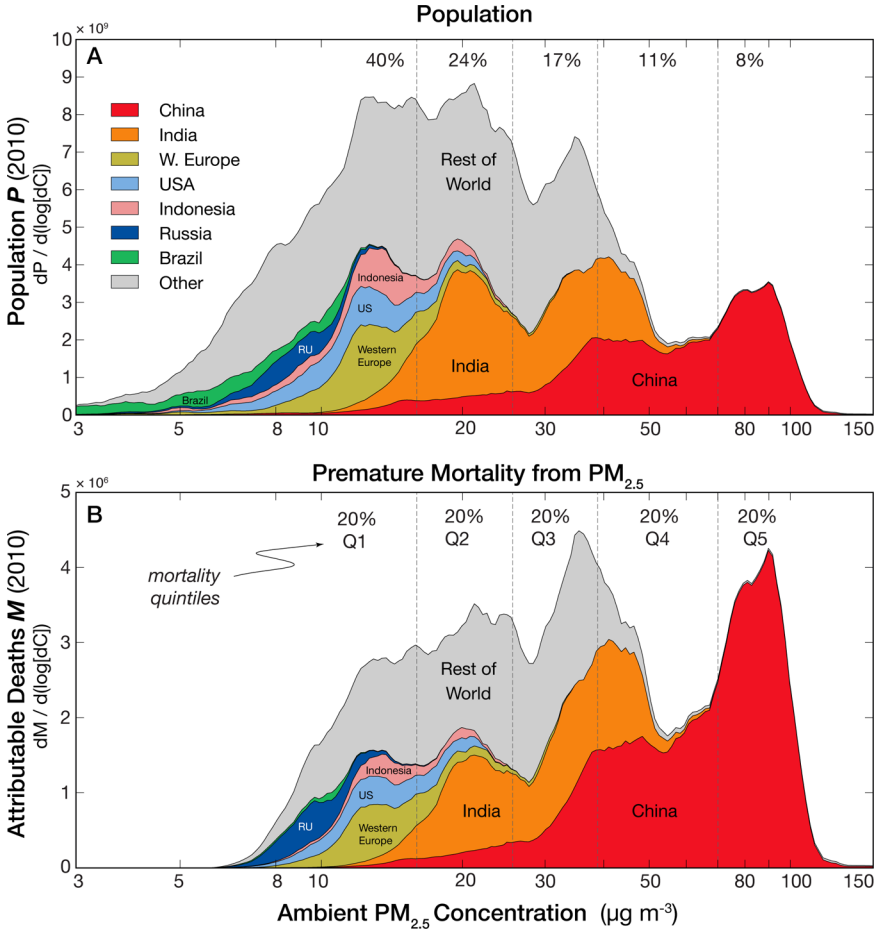

Figure 3. Global and regional distributions of population (A) and premature mortality attributable to year-2010 $PM_{2.5}$ (B) as a function of ambient $PM_{2.5}$ concentration. Plotted data reflect local smoothing of bin-width normalized distributions computed over 400 logarithmically spaced bins; equal-sized plotted areas would reflect equal populations (A) or equal mortality (B). Dashed vertical lines (in both plots) demarcate boundaries of mortality quintiles (Q1−Q5, Table 1) that apportion the $PM_{2.5}$ concentration distribution into 5 bins with equal number of premature deaths.

Table 1. Concentration-Based Quintiles[a] of Attributable Mortality from Year-2010 Ambient $PM_{2.5}$ in Global Population

	$PM_{2.5}$ concentration ($\mu g\ m^{-3}$)		population		attributable mortality rate[b]		
	range	mean[d]	billions	% of total	total, × 10^3	per 10^5 pop	top 3[c] countries
Q1[a]	0−16.0	10.5	2.74	40%	650	24	RU, US, UA
Q2	16.0−25.6	20.3	1.66	24%	650	39	IN, CN, JP
Q3	25.6−38.8	31.9	1.17	17%	650	55	IN, CN, PK
Q4	38.8−70.0	49.7	0.78	11%	650	84	CN, IN, VN
Q5	70.0−410	87.3	0.54	8%	640	120	CN, SA, TM

[a]Mortality quintiles Q1-Q5 are each concentration-ordered groupings of 10km grid cells. Each quintile represents ~20% of global attributable mortality from $PM_{2.5}$. [b]Year-2010 mortality rate (deaths y^{-1}) attributable to ambient $PM_{2.5}$ exposure. [c]Countries with highest attributable mortality in each bin. RU-Russia, US-United States, UA-Ukraine, IN-India, CN-China, JP-Japan, PK-Pakistan, VN-Vietnam, SA-Saudi Arabia, TM-Turkmenistan. [d]Population weighted mean.

than for the bottom quintile (~24 deaths per 100 000; see Table 1). At the high [low] end of the concentration range, 20% [20%] of all premature deaths from $PM_{2.5}$ are experienced by the ~8% [40%] of the world population who live in areas with levels higher than 70 $\mu g\ m^{-3}$ [lower than 16 $\mu g\ m^{-3}$].

Regions with concentration below ~20 $\mu g\ m^{-3}$ account for about half of the global population and ~30% of all global mortality attributable to $PM_{2.5}$. The substantial burden of disease from $PM_{2.5}$ in these cleaner regions is partly attributable to the relatively steep rise in risks for ischemic heart disease and stroke mortality at low concentrations (Figure 1) and partially attributable to many regions in cleaner locales (U.S., Russia, Western Europe) having older populations with high background rates of cardiovascular disease.

3.3. Mortality Benefits of Reducing Ambient $PM_{2.5}$. Table 2 presents potential reductions in premature mortality that could be achieved through scenarios with sharply reduced global $PM_{2.5}$ levels. The supralinear IER yields counterintuitive results: (1) for a given reduction in concentration, reductions in per-capita mortality are higher in cleaner locales. (2) Mortality benefits of reductions in $PM_{2.5}$ have increasing returns to scale: doubling the size of a concentration reduction would reduce attributable mortality by more than a factor of 2. For example, limiting global maximum $PM_{2.5}$ concentrations to the WHO

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Table 2. Potential for Reductions in $PM_{2.5}$ to Reduce Attributable Mortality

	meet AQG[a]			next target[a]			mortality −50%[a]		mortality −25%[a]	
	ΔC[b]	mortality reduction		ΔC[b]	mortality reduction		ΔC[b]		ΔC[b]	
	$\mu g\ m^{-3}$	$\times 10^3$	%	$\mu g\ m^{-3}$	$\times 10^3$	%	$\mu g\ m^{-3}$	%	$\mu g\ m^{-3}$	%
Q1[c]	1.7	160	24%	1.3	120	19%	2.6	25%	1.3	13%
Q2	10	390	60%	4.9	170	26%	8.7	43%	4.7	23%
Q3	22	480	74%	4.3	73	11%	16	51%	9.1	28%
Q4	40	530	82%	15	132	20%	29	58%	17	34%
Q5	77	550	87%	53	250	40%	59	68%	38	44%

[a]We consider the following scenarios, described in greater detail in methods: "Meet AQG" − maximum global concentration is 10 $\mu g\ m^{-3}$; "Next Target" − all regions reduce $PM_{2.5}$ concentration to next lowest WHO air quality guideline or interim target level; "Mortality −50%; −25%" − $PM_{2.5}$ concentrations reduced by a constant percentage in each mortality quintile that is sufficient to reduce total mortality in quintile by 50 or 25%. For these latter two scenarios, equal 50% or 25% mortality reductions occur in each quintile. [b]Reduction in population weighted $PM_{2.5}$ within a mortality quintile required to reach target level for each scenario. [c]Quintiles defined in Table 1 and Figure 3.

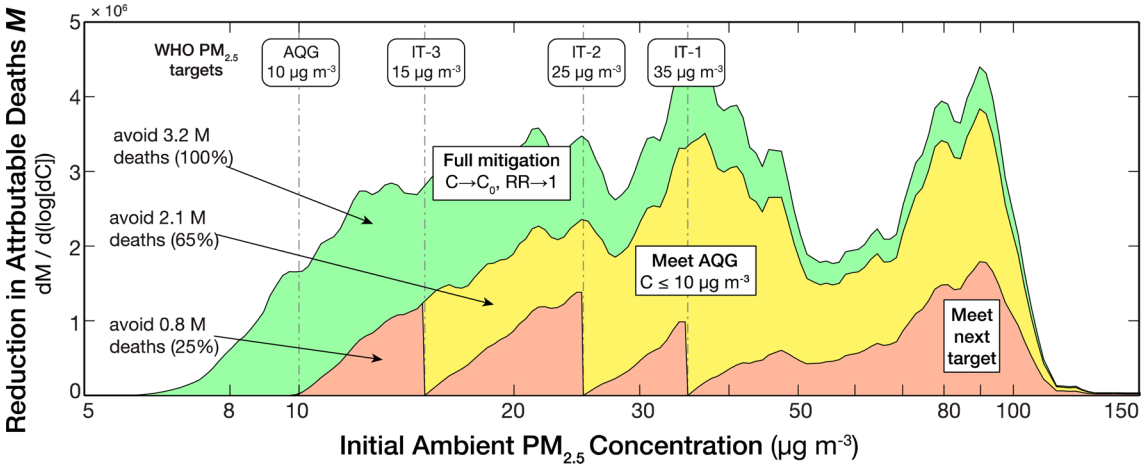

Figure 4. Potential to avoid premature mortality attributable to $PM_{2.5}$ for the year-2010 global ambient concentration distribution. Plots indicate reduction in attributable mortality (vertical axis) for three alternative scenarios with lower $PM_{2.5}$, displayed as a function of initial ambient $PM_{2.5}$ concentration (horizontal axis). For "meet next target" scenario, initial concentrations are reduced globally to the next available WHO $PM_{2.5}$ air quality target (see vertical dashed lines). For "meet AQG" scenario, all regions with concentrations above the WHO air quality guideline target attain 10 $\mu g\ m^{-3}$. In "full mitigation" scenario, global $PM_{2.5}$ levels are set to the counterfactual concentration $C_0 = 5.8\ \mu g\ m^{-3}$. The integral of a single curve between two concentration end points reflects the mortality reduction potential for a particular scenario applied to all areas with $PM_{2.5}$ in that concentration range.

interim target levels of 35 $\mu g\ m^{-3}$, 25 $\mu g\ m^{-3}$ and 15 $\mu g\ m^{-3}$ $PM_{2.5}$ would avoid respectively 0.39, 0.73, and 1.4 million annual premature deaths. Attaining the $PM_{2.5}$ air quality guideline of 10 $\mu g\ m^{-3}$ globally would avert ∼2.1 million attributable deaths, ∼65% of all premature mortality attributable to $PM_{2.5}$. (Preventing the remaining ∼35% of $PM_{2.5}$-attributable mortality would require further reducing concentrations from 10 $\mu g\ m^{-3}$ to the theoretical minimum-risk concentration, 5.8 $\mu g\ m^{-3}$.) Note that ∼50% more deaths are avoided at the AQG target of 10 $\mu g\ m^{-3}$ as at 15 $\mu g\ m^{-3}$, and roughly twice as many deaths are avoided at 15 $\mu g\ m^{-3}$ as at 25 $\mu g\ m^{-3}$.

Figure 4 and Table 2 describe the relationship between avoided mortality and concentration targets for three scenarios where all grid cells achieve either (i) the next available WHO concentration target ("next target"), (ii) the WHO air quality guideline (10 $\mu g\ m^{-3}$), or (iii) full abatement of $PM_{2.5}$ to the theoretical minimum-risk concentration. The incremental approach embodied in the "next target" scenario would avoid ∼750 000 annual deaths, of which ∼390 000 avoided deaths would result from limiting concentrations in the most polluted locales to 35 $\mu g\ m^{-3}$. Achieving the 10 $\mu g\ m^{-3}$ WHO AQG globally would avoid ∼3× as many deaths as the "next target" scenario, with substantial benefits for attaining 10 $\mu g\ m^{-3}$ even for populations that already live at low and intermediate concentrations.

Three key findings stand out. First, there is large potential to reduce high rates of per-capita mortality from $PM_{2.5}$ in the more polluted regions; however very large changes in ambient $PM_{2.5}$ may be necessary. Table 2 reports the reduction in $PM_{2.5}$ levels required to achieve a 25% and 50% attributable mortality reduction in each mortality quintile. For example, in the quintile with the highest concentrations (Q5), halving attributable mortality would require a ∼68% reduction in ambient $PM_{2.5}$ levels (pop-wt mean reduction: 59 $\mu g\ m^{-3}$). Second, for the less-polluted regions, substantial health benefits remain from further cleanup. For example, for the cleanest quintile (Q1), attributable mortality could be halved with a ∼25% reduction in ambient $PM_{2.5}$ concentrations (pop-wt mean reduction: 2.6 $\mu g\ m^{-3}$). Achieving 10 $\mu g\ m^{-3}$ in Q1 and Q2 would avoid ∼550 000 attributable deaths with a mean concentration reduction of 4.9 $\mu g\ m^{-3}$.

Third, substantial health benefits could accrue from achieving global $PM_{2.5}$ levels even lower than the WHO AQG targets. For example, consider an especially ambitious hypothetical $PM_{2.5}$ target of 8 $\mu g\ m^{-3}$. For the ∼2.7 billion people in the lowest-

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concentration mortality quintile (Q1, 40% of global population, $C \leq 16$ $\mu g\ m^{-3}$), attaining this target would require reducing population-weighted mean concentrations by ~3 $\mu g\ m^{-3}$ (~30%). Reaching this hypothetical 8 $\mu g\ m^{-3}$ target in Q1 would avoid ~60% of the attributable deaths in this region (~400 000 annual deaths), roughly 2.5 times as many premature deaths as could be avoided under the 10 $\mu g\ m^{-3}$ AQG.

3.4. Sensitivity Analyses and Limitations. *3.4.1. Demographic and Epidemiological Drivers.* Our core estimates of potential reductions in mortality attributable to changes in ambient $PM_{2.5}$ assume that other drivers of mortality are held constant. Of course, large-scale future changes in ambient $PM_{2.5}$ levels are likely to require time to be realized and therefore to be accompanied by ongoing epidemiological and demographic transitions that are forecasted to alter mortality and life expectancy.[9,10,26] For example, as the world population "ages" and undergoes the epidemiologic transition to a higher burden of non-communicable diseases (that is, comparatively young individuals reach ages and lifestyles where heart disease, stroke and other diseases are major causes of death), per-capita mortality attributable to air pollution may increase. We used year-2030 demographic and disease projections from WHO[20] (see SI) to assess the sensitivity of our conclusions to these trends.

Overall, our key qualitative and comparative conclusions are not strongly affected by future demographic and mortality projections. Regardless of projected trends, substantial reductions in attributable mortality in the most polluted regions will require comparatively large improvements in ambient $PM_{2.5}$ levels relative to less polluted locales. However, point estimates of attributable mortality for individual regions are somewhat sensitive to assumptions about future demographics and disease structure. For example, if circa-2010 $PM_{2.5}$ levels were to remain constant, year-2030 projections suggest that per-capita mortality attributable to $PM_{2.5}$ would increase in India (+21%) and China (+23%). This result is chiefly driven by projections of a dramatic increase in the age >50 populations in India and China, which more than offsets a projection of slight improvement in age-specific cardiovascular disease mortality rates (see SI). A crucial corollary of this point is that $PM_{2.5}$ levels in 2030 would have to decline by 20% (India) and 29% (China) merely to hold per-capita mortality attributable to $PM_{2.5}$ constant at year-2010 levels.

Because mortality data were available at comparatively coarse spatial resolution, an implicit assumption in our approach is that the underlying disease incidence (i.e., the portion not related to air pollution) is spatially invariant within each region. This assumption is a simplification. Underlying disease incidence varies within each region owing to differences in urbanization, income, demographics, employment, age distribution, and health care access. To investigate the sensitivity of results to spatially invariant input data, we conducted a parametric exploration that reapportioned underlying per-capita mortality rates within each region from urban to rural areas while maintaining a constant regional average. Overall, our qualitative conclusions and quantitative results change only slightly (<5−10%) for a large-scale reapportionment of underlying disease from urban to rural areas (see SI). However, the addition of fine-scale data on subregional variation in mortality rates would likely improve the spatial accuracy of our model predictions and may slightly alter the attributable mortality patterns observed in Figure 2.

3.4.2. Shape of C-R Relationship. Many of our qualitative conclusions are tightly linked to the supralinear shape of the integrated exposure-response (IER) functions used in the core assessment, which were developed for use over the full range of global $PM_{2.5}$ conditions. As a sensitivity analysis, we estimated global cardiopulmonary disease (CPD) mortality for log-linear and power-law C-R relationships that were developed for the US population in the American Cancer Society Cohort.[3] As described in the SI, these widely used C-R functions are extrapolated from a large U.S. cohort ($C < 25$ $\mu g\ m^{-3}$) to global PM conditions. Overall, estimates of total global cardiopulmonary mortality for the alternative C-R functions are of similar magnitude to our core mortality results, in line with recent findings elsewhere.[27] For the power-law and log-linear C-R relationships, we estimated respectively ~3.6 and ~4.1 million year-2010 deaths attributable to $PM_{2.5}$. However, the mortality-concentration distribution is sharply different for the log-linear scenario than for the power-law and core analyses (SI Figure SI.3). Risk estimates of the extrapolated log-linear model appear implausible at high concentrations (SI Figure SI.1). However, although global totals are approximately equal for the log-linear as for the IER, the number of deaths at the low [high] end of the concentration range is approximately half [double] for the log-linear as for the IER (SI Figure SI.3). Instead, recent epidemiological evidence suggests that the C-R relationship for $PM_{2.5}$ cardiovascular endpoints may be supralinear (concave) − i.e., similar in shape to the IER relationship we assume here, and with a convexity opposite of the log-linear model.[16,17,28−30] The IER relationships produce risk estimates that align broadly with emerging evidence at extreme ends of the ambient $PM_{2.5}$ concentration distribution.[16,30−32] However, long-term cohort studies are needed to more precisely constrain the shape of the $PM_{2.5}$ C-R relationship under the cleanest and most polluted conditions.

3.4.3. Concentration Data. Additional uncertainties relate to possible biases in the input $PM_{2.5}$ distribution. The modeled $PM_{2.5}$ surface of Brauer et al.[11] appears to underestimate monitored annual-average $PM_{2.5}$ levels for large cities in some areas of the world (e.g., India, Brazil, Indonesia); agreement is stronger in low-concentration, high-income regions. Overall, this possible bias suggests that the contribution of high-concentration regions to total population and attributable mortality may be underestimated. Larger overall benefits may accrue from mitigating $PM_{2.5}$ in those areas. Local $PM_{2.5}$ concentrations in excess of background levels (e.g., near primary $PM_{2.5}$ sources such as traffic, cooking, and biomass burning) are likewise not accounted for here. Finally, our results are contingent on the assumed theoretical minimum-risk concentration distribution C_0 (range: 5.8−8.0 $\mu g\ m^{-3}$). Alternative assumptions of C_0 based on a hypothetical, regionally variable "natural background" $PM_{2.5}$ concentration would affect regional attributable mortality estimates.

3.5. Implications for Policy and Future Research. The mortality impacts of ambient $PM_{2.5}$ are very large globally, accounting for ~3.2 million premature deaths in 2010. Premature mortality from $PM_{2.5}$ is not restricted to the world's most polluted regions (Figure 3b); accordingly, there is substantial potential to avert premature mortality from $PM_{2.5}$ across the entire global concentration distribution (Figure 4). However, the required scale of intervention to achieve a given mortality reduction differs significantly between clean and polluted locales.

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For countries that are now beginning to address high levels of ambient $PM_{2.5}$, the supralinear concentration-response relationship implies that initial improvements in ambient $PM_{2.5}$ need to be considered as part of a longer-term strategy for clean air.[33] For example, China and India have recently adopted annual average $PM_{2.5}$ standards of respectively 35 and 40 $\mu g\ m^{-3}$ (compare to the U.S. EPA's recently adopted standard of 12 $\mu g\ m^{-3}$). Achieving this level of pollution control (to 35−40 $\mu g\ m^{-3}$) will present major engineering and policy challenges in these areas, yet result in only partial (∼20−30%) mitigation of the overall burden of disease. However, there are many compelling reasons for polluted regions to pursue initial steps toward a longer-term plan to aggressively reduce ambient $PM_{2.5}$. First, for a supralinear C-R relationship, initial mitigation efforts "open the door" to the mortality benefits of future controls, since the marginal benefit of reducing concentrations increases with each subsequent $PM_{2.5}$ reduction. Economic theory suggests that initial control efforts may be achieved at comparatively low unit cost, and thus with a favorable benefit-cost ratio.[33] Moreover, if marginal mortality benefits increase in parallel with marginal control costs, then it may ultimately prove cost-effective to pursue aggressive emissions reductions.[33,34] Second, initial control efforts offer the opportunity to develop the regulatory capacity that is likely a prerequisite for more ambitious controls. Third, there are other cobenefits of controlling $PM_{2.5}$, which can include directly and indirectly linked health and climate change mitigation benefits of controlling other pollutants that are coemitted from major $PM_{2.5}$ sources.[35,36] Moreover, the population exposure benefit per unit emission control may be especially high in densely populated regions of India and China.[37] Finally, and most crucially, we note that there are potentially substantial aggregate mortality benefits of pursuing clean air in populous countries with high $PM_{2.5}$. For example, nearly ∼70% of the total averted mortality that would result from attaining 10 $\mu g\ m^{-3}$ globally would occur in India and China alone (∼1.4 million fewer deaths). As mentioned above, ambient concentrations in India and other polluted areas may be underestimated here; if so, the benefits of improved air quality for those areas may be larger than this estimate.

Our results also suggest that there is substantial potential to reduce $PM_{2.5}$-attributable mortality in less polluted regions. Because of the steep concentration-response relationship at lower concentrations, comparatively small absolute reductions in $PM_{2.5}$ (e.g., for Q1: 1−3 $\mu g\ m^{-3}$, 10−25% of baseline) for these regions could avert hundreds of thousands of premature deaths globally. Thus, continued improvement in ambient $PM_{2.5}$ levels in already-clean locales[38] may have large health benefits. Costs of control might increase sharply as very low concentrations are approached. For locales with significant long-range transport of $PM_{2.5}$ from upwind areas, it may be difficult to achieve such aggressive mitigation targets even with near-complete mitigation of local sources.

Our analysis highlights a need for further research in the following areas. First, any assessment of the potential health benefits of $PM_{2.5}$ mitigation is contingent on assumptions about the shape of the concentration-response relationship. Priorities for epidemiological research include (a) constraining the shape of the $PM_{2.5}$ concentration-response relationship through cohort studies of mortality in high-concentration regions (especially for populous developing countries such as China and India) and for populations in very clean areas (e.g., $C < 8$ $\mu g\ m^{-3}$); and (b) rigorous assessments of the relationship between *changes in* $PM_{2.5}$ and *changes in* life expectancy.[7] Second, the economics of policies to aggressively reduce global $PM_{2.5}$ mortality are poorly understood. Economically optimal policies require information on options and costs for emissions control through, for example, global and local "$PM_{2.5}$ mitigation supply curves" analogous to the cost-of-carbon curves used in climate policy analysis. Third, more precise characterization of personal- and urban-scale contributions to $PM_{2.5}$ exposure could reduce uncertainties about the global distribution of exposure to and premature mortality from $PM_{2.5}$.

■ ASSOCIATED CONTENT

Supporting Information

Online Supporting Information (SI) files provide further information on data for the discretized C-R relationship and results for sensitivity analyses. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.5b01236.

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