Environmental Science & Technology

Policy Analysis

pubs.acs.org/est

Blue Skies Bluer?

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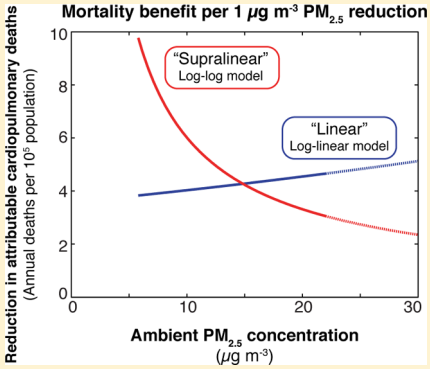
Supporting Information

ABSTRACT: The largest U.S. environmental health risk is cardiopulmonary mortality from ambient $PM_{2.5}$. The concentration−response (C−R) for ambient $PM_{2.5}$ in the U.S. is generally assumed to be linear: from any initial baseline, a given concentration reduction would yield the same improvement in health risk. Recent evidence points to the perplexing possibility that the $PM_{2.5}$ C−R for cardiopulmonary mortality and some other major endpoints might be supralinear: a given concentration reduction would yield greater improvements in health risk as the initial baseline becomes cleaner. We explore the implications of supralinearity for air policy, emphasizing U.S. conditions. If C−R is supralinear, an economically efficient $PM_{2.5}$ target may be substantially more stringent than under current standards. Also, if a goal of air policy is to achieve the greatest health improvement per unit of $PM_{2.5}$ reduction, the optimal policy might call for greater emission reductions in already-clean locales—making "blue skies bluer"—which may be at odds with environmental equity goals. Regardless of whether the C−R is linear or supralinear, the health benefits of attaining U.S. $PM_{2.5}$ levels well below the current standard would be large. For the supralinear C−R considered here, attaining the current U.S. EPA standard, 12 $\mu g\ m^{-3}$, would avert only ~17% (if C−R is linear: ~ 25%) of the total annual cardiopulmonary mortality attributable to $PM_{2.5}$.



1. INTRODUCTION

Air pollution poses a serious threat to human health. Globally, outdoor air pollution kills ~3 million people per year, a number that exceeds deaths attributable to HIV-AIDS and malaria combined.[1] In the U.S. alone, more than 100 000 deaths are attributable to outdoor air pollution each year.[1−3] Fine-particle air pollution ($PM_{2.5}$) accounts for the vast majority of the burden of disease from outdoor air pollution, primarily though elevated risks for heart attacks, strokes, and other cardiovascular and pulmonary diseases that lead to premature death.

Policy-driven reductions in $PM_{2.5}$ concentrations in the U.S. have saved thousands of lives annually.[4] The associated annual monetized benefits are estimated at between $19 billion and $167 billion, against annual abatement costs of ~ $7 billion in 2001 dollars.[5] By a wide margin, regulations that control fine particles are the most economically beneficial of all federal regulations.[5]

The purpose of the present paper is to highlight and examine the implications of a crucial but perhaps underappreciated aspect of the science of particulate pollution: the shape of the concentration−response (C−R) function, which describes the relationship between $PM_{2.5}$ concentrations and health outcomes, emphasizing premature mortality due to cardiopulmonary disease.[6−8] Our focus is on ambient air pollution in the U.S., since this topic has not been explored for that environment, but results here may inform conditions in other clean air locations.

The usual understanding for $PM_{2.5}$ in relatively clean environments is that there is no threshold below which $PM_{2.5}$ exposure is not harmful, and also that the C−R is approximately linear: each unit change in concentration produces approximately the same incremental change in health risk regardless of the baseline concentration. According to this understanding, the first unit of exposure is just as damaging as an incremental increase at any other level of exposure. Recent epidemiological evidence for $PM_{2.5}$, however, suggests that C−R might be supralinear: a given incremental change in concentration would yield a greater reduction in health risk as the initial baseline becomes cleaner.[6,7,9,10] Supralinearity implies that the first units of exposure are the most damaging, with incremental increases growing progressively less so.

Nonlinearities and "low-dose effects" (i.e., effects at low doses that are poorly predicted by effects at high doses) are well documented for several toxicants,[11−17] with evidence of sigmoidal or other nonlinear C−Rs appearing at least as far back as the early 1900s.[18−21] Risk management has long highlighted the importance of the shape of the C−R relationship.[22−24] As others have reported, for $PM_{2.5}$, good evidence exists for a supralinear C−R if one considers a very

Received: June 29, 2015
Revised: November 3, 2015
Accepted: November 4, 2015

DOI: 10.1021/acs.est.5b03154
Environ. Sci. Technol. XXXX, XXX, XXX−XXX

wide range of concentrations, ranging from clean ambient conditions, to high indoor exposures (e.g., secondhand smoke), and up to active tobacco smoking.[6−8] The recent Global Burden of Disease 2010 assessment employed a family of novel supralinear "Integrated Exposure Response" (IER) functions for five major health endpoints over that broad range of $PM_{2.5}$ exposures.[1,9]

The implications of supralinearity, for our understanding of environmental policy and for the directions of future research in environmental health, are significant. These questions have begun to receive attention for pollution globally.[25,26] The present analysis contains a complementary message. We focus here on ambient conditions in the U.S., where $PM_{2.5}$ concentrations are relatively low. Although the scientific evidence for supralinearity in this case is not yet conclusive,[10,27] we argue that the implications of supralinearity for air-quality management, policy, economics, and environmental health in the U.S. are sufficiently profound that the issue merits careful consideration. Our mathematical derivation of, and comparison between, the linear and supralinear C−R functions illustrate the dramatic difference in cardiopulmonary mortality attributable to $PM_{2.5}$ depending on the C−R function. Below, we demonstrate that the following are policy implications if the C−R relationship for cardiopulmonary mortality from $PM_{2.5}$ were supralinear, rather than linear: (i) the overall cardiopulmonary mortality impact of $PM_{2.5}$ would be substantially higher, (ii) the number of premature deaths that could be avoided by achieving stringent $PM_{2.5}$ standards would be correspondingly higher, and (iii) the greatest marginal improvements in the per-capita health impact of $PM_{2.5}$ might arise by further improving air quality in already-clean locations ("making blue skies bluer").

2. MATERIALS AND METHODS

2.1. Analysis Framework. In this section we develop an analytical framework that illuminates the policy implications of a potentially supralinear C−R for ambient $PM_{2.5}$. The framework is based on core results from a major long-term study, the American Cancer Society (ACS) cohort.[27] The ACS C−R derives exclusively from exposures to ambient $PM_{2.5}$ in the U.S., in contrast to the much broader range of concentrations considered in the IER function of Burnett et al. (2014).[9] The ACS study has substantially influenced U.S. $PM_{2.5}$ policy; it underpins several major cost-benefit calculations by the U.S. EPA, including for the most recent National Ambient Air Quality Standard (NAAQS) for $PM_{2.5}$, the Cross-State Air Pollution Rule, and the Mercury and Air Toxics Standards. We focus on cardiopulmonary disease (CPD) mortality, which accounts for ∼90% of attributable U.S. deaths from $PM_{2.5}$,[28] and includes mortality from heart disease, stroke, and chronic obstructive pulmonary disease (COPD).

Krewski et al. (2009) report two potential C−R relationships for CPD mortality, both derived from Cox proportional hazards models.[27] First, a log−linear C−R: the logarithm of survival is proportional to concentration. They and we refer to this model as "linear." As shown in Figure 1(a), for the concentration range considered here (∼5 to ∼25 $\mu g\ m^{-3}$), it is approximately, though not precisely, linear. Second, a log−log C−R: the logarithm of survival is proportional to the logarithm of concentration. They refer to this model as "logarithmic"; we refer to it as "supralinear". Krewski et al. report (p. 27) that while the linear and supralinear models had comparable

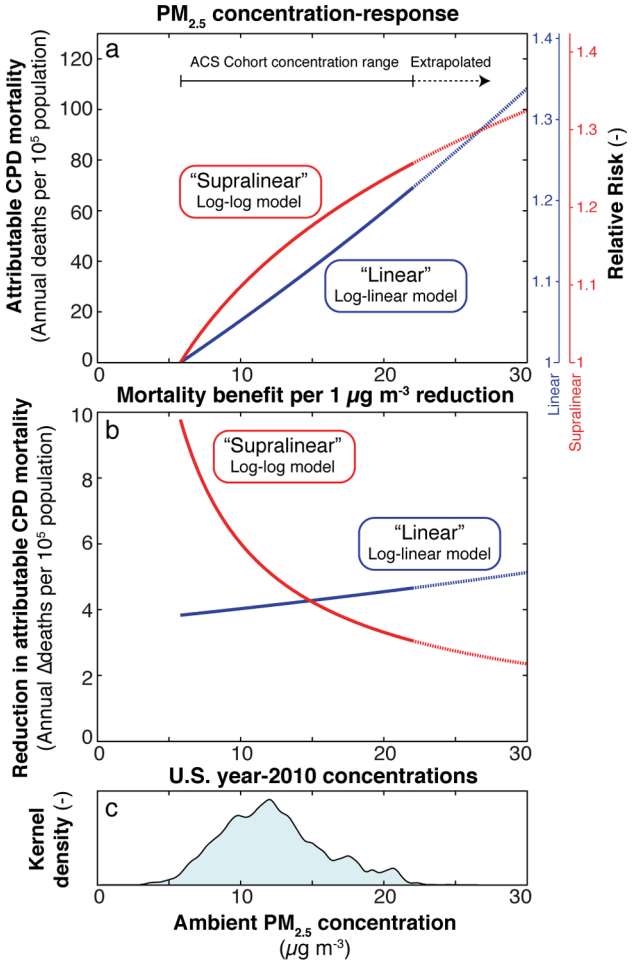


Figure 1. (a) Concentration−response (C−R) relationship for cardiopulmonary mortality from ambient fine particle exposure, derived from Krewski et al. (2009), reproduced here in Table 1. The blue line reflects a commonly used, log−linear C−R. (Krewski et al.[27] and we refer to it as "linear" because it is nearly linear for the concentration range investigated here.) The red curve reflects the supralinear (log−log) C−R. Dashed lines represent extrapolation beyond the observed year-2000 $PM_{2.5}$ concentration range in Krewski et al. (5.8−22 $\mu g\ m^{-3}$). Attributable premature mortality (left axis) is estimated from relative risk (RR, plotted separately for each function on right axes) and assumes a baseline year-2010 rate of 345 adult cardiopulmonary deaths per 100 000 population. (b) Estimates of marginal benefit from an incremental air pollution improvement (1 $\mu g\ m^{-3}$, corresponding to ∼5−15% improvement from typical clean urban conditions). For the supralinear curve, marginal benefits increase sharply with decreasing concentration. Mortality benefits per unit concentration change are approximately equal to the local slope of attributable mortality, plotted in Figure 1(a). (c) Population-weighted distribution of year-2010 ambient $PM_{2.5}$ concentrations for the U.S.[30]

predictive power, the latter "was a slightly better predictor of the variation in survival" among study regions (MSA variance; see Table 1 below).

We first derive continuous linear and supralinear C−R relationships (see Table 1) using the relative risk (RR) point estimates reported in Table 11 of Krewski et al. (2009). The algebraic steps required in deriving the relevant C−R functions are important but straightforward. Because they are lengthy, we include them in the Supporting Information (SI). In these functions, risks are expressed relative to a theoretical minimum-

DOI: 10.1021/acs.est.5b03154
Environ. Sci. Technol. XXXX, XXX, XXX−XXX

Table 1. Linear and Supralinear $PM_{2.5}$ Concentration−Response (C−R) Models for Cardiopulmonary Mortality (Extended Analysis of American Cancer Society Cohort Study)[a]

	linear C−R	supralinear C−R
relative risk[a]	1.128 (any 10 $\mu g\ m^{-3}$ increment)	1.208 (5→15 $\mu g\ m^{-3}$)
		1.127 (10 → 20 $\mu g\ m^{-3}$)
concentration dependence[b,c]	$\ln(\text{survival}) \sim \beta C$	$\ln(\text{survival}) \sim \gamma \ln(C)$
implied C−R function[c]	$RR = \exp[\beta(C - C_{min})]$	$RR = (C/C_{min})^{\gamma}$
parameter estimate[b]	$\beta = 0.012045$	$\gamma = 0.17225$
MSA variance[d]	1.86×10^{-3}	1.66×10^{-3}

[a]Adapted from cardiopulmonary disease mortality entry in Table 11 of the Health Effects Institute extended analysis of the American Cancer Society (ACS) CPS-II cohort study, Krewski et al. (2009). Continuous supralinear C−R function derived from two relative-risk point estimates from 5 to 15 $\mu g\ m^{-3}$ and from 10 to 20 $\mu g\ m^{-3}$ in Krewski et al. [b]See Supporting Information (SI) for derivations. [c]Here, C represents the ambient concentration at which the relative risk RR is evaluated, and C_{min} represents the theoretical minimum-risk concentration for which RR = 1. We assume C_{min} = 5.8 $\mu g\ m^{-3}$ $PM_{2.5}$, consistent with the minimum annual-average concentration assigned to subjects in the ACS Cohort Study. [d]Refers to variance of predicted mortality for model clustered at the metropolitan statistical area (MSA) level.

risk concentration, C_{min}. For this theoretical minimum-risk concentration, we use 5.8 $\mu g\ m^{-3}$, the lowest concentration in the ACS data set. For this family of linear and supralinear C−R functions, *changes* in mortality attributed to $PM_{2.5}$ that result from changes in concentration are independent of the assumed value of C_{min}. This interesting property of the C−R functions is illustrated via mathematical derivation in the SI.

We stress that the true shape of the C−R relationship remains an open question at low concentrations, such as those typical of U.S. conditions. Our usage of the Krewski et al. C−R functions is thus *illustrative* in exploring the implications of what might follow if a supralinear C−R were true for the U.S. However, other lines of evidence bear quantitative or qualitative resemblance to the supralinear C−R we employ here. In recent work,[26] we found that the U.S.-specific supralinear cardiopulmonary C−R of Krewski et al. (2009) closely reproduces the shape of the cardiovascular and pulmonary IER functions of Burnett et al. (2014). We consider the IER in sensitivity analyses in the SI. Other recent studies and reviews also point to the plausibility of a supralinear C−R at lower concentrations.[10,29]

We employ the following population attributable fraction relationship[26] to calculate per-capita mortality rates attributable to $PM_{2.5}$:

$$AM(C^*) = M_{obs} \times \frac{RR(C^*) - 1}{\overline{RR}(C_{obs})} \quad (1)$$

In eq 1, $AM(C^*)$ represents the modeled attributable CPD mortality rate at an arbitrary $PM_{2.5}$ concentration C^*, M_{obs} is the observed CPD mortality rate for a given population exposed to an average ambient concentration of C_{obs} (here, the CPD mortality rate is total, not attributable), $RR(C^*)$ is the CPD mortality relative risk at the arbitrary $PM_{2.5}$ concentration C^* compared to the risk at C_{min}, and $\overline{RR}(C_{obs})$ is the U.S. population-weighted mean relative risk for CPD mortality for the observed concentration distribution. Specifically, this population-weighted relative risk $\overline{RR}(C_{obs})$ is defined as

$$\overline{RR}(C_{obs}) = \frac{\sum_i^N P_i \times RR(C_{obs,i})}{\sum_i^N P_i} \quad (2)$$

We employ a gridded population data set (described below) to derive the ambient $PM_{2.5}$ exposure distribution of the U.S. population. The population-weighted relative risk $\overline{RR}(C_{obs})$ is the mean relative risk evaluated over all $i = 1...N$ grid cells with population P_i and annual average $PM_{2.5}$ concentration $C_{obs,i}$.

Next, as described below, we relate marginal *changes* in concentration (ΔC) and marginal *changes* in attributable CPD mortality rate (ΔAM) by computing the reduction in AM for a 1 $\mu g\ m^{-3}$ $PM_{2.5}$ reduction from an initial baseline concentration, over the range of ~5 to ~30 $\mu g\ m^{-3}$.

2.2. Input Data. *2.2.1. Mortality Data.* The year-2010 adult cardiopulmonary mortality, M_{obs}, is ~345 deaths (age >30) per 100 000 all-age population, which is ~40% of the year-2010 all-cause mortality for adults. This value reflects cause-specific mortality data from the 2010 Global Burden of Disease (GBD) assessment for the "high-income North America" region, which is dominated by U.S. adults.[28] Krewski et al. (2009) classified as cardiopulmonary mortality all subject deaths with ICD-9 codes in the ranges 409−440 and 460−519.[27] Examples of major causes of death within these codes include ischemic and hypertensive heart diseases, cerebrovascular disease, acute respiratory infections, COPD, pneumonia, and influenza. To reconstruct the cardiopulmonary disease category from GBD data, we used the GBD causes of death indicated in SI Table S1.

2.2.2. $PM_{2.5}$ Concentrations. We obtained estimates of U.S. year-2010 ambient $PM_{2.5}$ concentrations and population from the 10-km gridded surface of Brauer et al. (2012) that was developed for the GBD 2010 assessment.[30] This data set reports a fitted annual-average $PM_{2.5}$ concentration based on surface observations, satellite aerosol optical depth retrievals, and estimates from a chemical transport model.[30] The U.S. population-weighted annual-average year-2010 ambient $PM_{2.5}$ concentration for this data set is 12.2 $\mu g\ m^{-3}$, with 10th and 90th percentile values of 7.8 and 17.5 $\mu g\ m^{-3}$, respectively.

2.3. Mortality Estimates. At and below the theoretical minimum-risk concentration (here, 5.8 $\mu g\ m^{-3}$), relative risk values are by definition equivalent to 1.0, and thus no excess mortality can be attributed to $PM_{2.5}$ exposure. At concentrations above C_{min}, attributable CPD mortality rate increases along with relative risks. To develop the AM curves for each function, an estimate of the baseline population-weighted relative risk $\overline{RR}(C_{obs})$ is required. Using eq 2 and the gridded population and $PM_{2.5}$ data sets described above, we estimate year-2010 population-weighted relative risks for CPD mortality of 1.08 and 1.12 for the linear and supralinear C−R functions, respectively compared to the baseline risk at C_{min}. In other words, estimated excess mortality risks attributable to year-2010 ambient $PM_{2.5}$ would be approximately 50% higher if the supralinear C−R were true, rather than the linear C−R.

Figure 1a displays cardiopulmonary disease mortality relative risks (RR, right axes) and AM (left axis) for the linear and supralinear C−R functions at arbitrary ambient concentrations values (C^*). For any given C−R function, a constant linear proportionality exists between AM and RR that allows both curves to be plotted simultaneously on separate y-axes. This proportionality factor, which appears as the term M_{obs}/

DOI: 10.1021/acs.est.5b03154
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$\overline{RR}(C_{obs})$ in eq 1, can be intuitively understood as the "underlying" cardiopulmonary mortality that would remain if $PM_{2.5}$ levels were reduced to a level where there were no excess mortality risks from $PM_{2.5}$ (i.e., at or below the theoretical minimum-risk concentration C_{min}). This derived value, which we shall define here as $M_{min} = M_{obs}/\overline{RR}(C_{obs})$, is unique for each C−R relationship. In plotting Figure 1a, we maintain a common left axis for AM, but apply a separate right axis to quantify the relative risks for the supralinear and linear C−R functions.

To estimate the change in attributable mortality ΔAM for a given change in concentration from an arbitrary starting concentration C_1 to an arbitrary ending concentration C_2, we apply eq 1 sequentially to derive the following relationship:

$$\Delta AM = AM(C_1) - AM(C_2) = M_{min} \times [RR(C_1) - RR(C_2)] \quad (3)$$

To illustrate the shape of the *marginal per-capita* mortality benefits that would result from a reduction in $PM_{2.5}$ levels, we compute ΔAM for a fixed 1 $\mu g\ m^{-3}$ reduction in $PM_{2.5}$, starting at any arbitrary initial concentration C_1 (Figure 1(b)) for both the linear and supralinear C−R relationships considered in Figure 1(a). Marginal per-capita mortality benefits are expressed in units of (annual Δdeaths per 10^5 population) per ($\mu g\ m^{-3}$ concentration change).

Finally, to characterize the *aggregate* U.S. mortality benefits ΔAB that could be achieved by limiting nationwide $PM_{2.5}$ levels to a given maximum value C_{max}, we apply eq 1 to each area in the U.S., separated into 10 km × 10 km grids. Here, we apply a hypothetical national ambient concentration distribution $\hat{C}$, in which the concentration in any grid cell i is subject to the following minimization criterion: $\hat{C}_i = \min(C_{obs}, C_{max})$. In other words, the concentration $\hat{C}_i$ in each grid cell i is assigned the minimum of either a hypothetical concentration target, or the year-2010 observed ambient concentration. The aggregate mortality benefit from this concentration reduction is then estimated as

$$\Delta AB = M_{min} \times \sum_{i=1}^{N} P_i \times [RR(C_{obs}) - RR(\hat{C}_i)] \quad (4)$$

Here, ΔAB represents the cardiopulmonary mortality (deaths y^{-1}) that could be avoided by limiting U.S. year-2010 $PM_{2.5}$ concentrations to a maximum concentration C_{max} over all $i = 1. . .N$ U.S. grid cells with population P_i. This broadly illustrative calculation is contingent on several assumptions, which are described in detail in Apte et al. (2015).[26] Briefly, these assumptions include that (i) concentrations change rapidly relative to other demographic and epidemiological factors that underlie mortality from $PM_{2.5}$ such that baseline mortality rates are assumed to be constant; (ii) the lag effects between the time of a concentration change and health effects are negligible, (iii) the C−R relationship is a valid representation of *changes* in concentration and *changes* in risk, and (iv) the C−R function is an unbiased representation of a causal relationship between air quality and adverse health outcomes.[26]

3. RESULTS

Figure 1(a) illustrates relative risks and per-capita attributable mortality rates for the linear and supralinear C−Rs. Both functions indicate broadly comparable levels of attributable mortality risk (~15−75 CPD deaths from $PM_{2.5}$ per 100 000 population) over the U.S. ambient $PM_{2.5}$ concentration range (~5−25 $\mu g\ m^{-3}$; see Figure 1(c)). At year-2010 U.S. concentrations, attributable cardiopulmonary mortality is higher for the supralinear C−R than for the linear C−R: ~120 000 and ~80 000 deaths y^{-1}, respectively. (Those two values bracket the U.S. year-2010 $PM_{2.5}$-attributable mortality estimate from the current Global Burden of Disease study: ~ 103 000 deaths.) Table 2 indicates that for any concentration limit below the current 12 $\mu g\ m^{-3}$ NAAQS, the estimated benefit to human health (reduction in attributable premature mortality) is greater with the supralinear C−R than with the linear C−R. This finding is reproduced for a sensitivity case that considers the supralinear IER from Burnett et al.[9] (see SI). Figure 1(a) illustrates an important aspect of this finding: to reach a given attributable mortality rate in most U.S. locales, lower concentrations would have to be achieved if the C−R is supralinear than if it is linear. (See SI for further details.) At concentrations above 25 $\mu g\ m^{-3}$, in the extrapolated region of the curves in Figure 1(a), the attributable CPD mortality for a linear C−R is greater than for the supralinear C−R.

Table 2. Potential Reductions in $PM_{2.5}$-Attributable Cardiopulmonary Mortality by Limiting Maximum $PM_{2.5}$ Levels in the U.S

	linear C−R		supralinear C−R	
	deaths y^{-1}	%[a]	deaths y^{-1}	%
year-2010 attributable mortality	80 100		122 000	
mortality reduction for achieving $C \le C_{max}$ throughout the U.S.				
C_{max} = 15 $\mu g\ m^{-3}$[b]	7600	9%	6400	5%
C_{max} = 12 $\mu g\ m^{-3}$[c]	20 400	25%	20 400	17%
C_{max} = 10 $\mu g\ m^{-3}$[d]	35 600	44%	40 400	33%
C_{max} = 8 $\mu g\ m^{-3}$	55 300	69%	71 800	59%

[a]Percentage reduction in annual $PM_{2.5}$ attributable mortality relative to year-2010 levels for a hypothetical standard that immediately limited annual $PM_{2.5}$ levels to the target concentration C_{max}. [b]Previous U.S. EPA $PM_{2.5}$ National Ambient Air Quality Standard (NAAQS) was 15 $\mu g\ m^{-3}$ annual average. [c]Current U.S. EPA $PM_{2.5}$ NAAQS is 12 $\mu g\ m^{-3}$ annual average. By happenstance, values in this row (to three significant digits: 20 400) are equal for linear and supralinear C−R. [d]Current World Health Organization $PM_{2.5}$ air quality guideline is 10 $\mu g\ m^{-3}$ annual average.

The slopes of the two C−Rs in Figure 1(a) differ substantially. That difference is reflected in Figure 1(b), which displays the marginal change in CPD mortality per 1 $\mu g\ m^{-3}$ change in $PM_{2.5}$, as a function of initial concentration. For the linear C−R, the marginal benefit per 1 $\mu g\ m^{-3}$ $PM_{2.5}$ reduction is slightly larger at high concentrations than at low concentrations, but with relatively little variation over the typical U.S. concentration range (~4 avoided CPD deaths per 100 000 population for a 1 $\mu g\ m^{-3}$ concentration reduction). In contrast, the marginal mortality benefit for the supralinear C−R increases steeply with declining concentration: a 1 $\mu g\ m^{-3}$ reduction in $PM_{2.5}$ at 10 $\mu g\ m^{-3}$ would avoid roughly twice as many CPD deaths as the same concentration reduction at 25 $\mu g\ m^{-3}$ (Figure 1(b), ~ 6 vs ~3 avoided CPD deaths per 100 000 population, for a 1 $\mu g\ m^{-3}$ reduction). A crucial corollary of this finding is that for a supralinear C−R, the CPD mortality benefits of $PM_{2.5}$ abatement would be disproportionately higher for large than for small concentration reductions

DOI: 10.1021/acs.est.5b03154
Environ. Sci. Technol. XXXX, XXX, XXX−XXX

(e.g., the health benefit from a 3 μg m^{-3} reduction is more than three times the benefit of a 1 μg m^{-3} reduction).

Table 2 illustrates the approximate CPD mortality reductions that could be achieved by limiting the year-2010 ambient $PM_{2.5}$ concentration distribution to concentrations no higher than a given target concentration C_{max}. For either C−R function, linear or supralinear, attaining the current EPA NAAQS (12 μg m^{-3}) nationwide would avoid ∼20 000 annual premature CPD deaths from $PM_{2.5}$, equivalent to respectively 17% and 25% of the year-2010 baseline CPD deaths from $PM_{2.5}$. The similarity of this result for both C−R functions (both values are 20 400; see Table 2) is happenstance: as is evident in Figure 1, both functions have similar slopes near the NAAQS. The *aggregate* mortality benefits of achieving further concentration reductions are a joint function of the shape of the C−R relationship and the current distribution of $PM_{2.5}$ exposures among the U.S. population. Approximately 50% of the U.S. population lives in areas that meet the NAAQS (C < 12 μg m^{-3}). The mortality-reduction benefits of meeting increasingly stringent $PM_{2.5}$ limits (i.e., levels below the NAAQS) would be greater for the supralinear C−R than for the linear C−R (Table 2). This result arises owing to the increasing marginal benefits for the supralinear C−R as even lower concentrations are reached (Figure 1a,b). For either the linear or supra-linear C−R, attaining dramatic (e.g., > 50%) reductions in $PM_{2.5}$-attributable mortality in the U.S. would likely require attaining ambient concentrations even lower than the World Health Organization $PM_{2.5}$ air quality guideline of 10 μg m^{-3}.

4. DISCUSSION

Our analyses represent a thought experiment: *What if* the C−R for fine particles is supralinear for the range of concentrations experienced in the U.S.? (If one instead considers the entire range of concentrations experienced around the world (from under 5 to over 100 μg m^{-3}) − which is not what we did here− then there is nothing hypothetical about this question. For that broad concentration-range, C−R seemingly must be supra-linear.)[9,31]

The quantity of evidence in support of supralinearity is less decisive for the range of concentrations experienced in the U.S. and other relatively clean places. But even here, the implications of supralinearity are so stark, so striking, that even the more moderate support for supralinearity still suggests that exploring what it would mean for our understanding of the relationship between fine particles and human health is crucially important.

In this section we next touch on what supralinearity could mean for researchers in specific domains: policy, environmental economics, engineering, and epidemiology.

The policy implications of a supralinear C−R are rather troubling. Section 109 of the Clean Air Act directs the EPA to set air-quality standards so as to "protect the public health," while providing "an adequate margin of safety."[32] Even if the C−R is linear, that admonition is somewhat a fiction: within the range of concentrations considered, the scientific consensus is that no safe threshold exists. Strictly speaking, the Section 109 language cannot be obeyed at any observed level of urban pollution (or, perhaps, any observed level of pollution above the theoretical minimum-risk level C_{min}). Lower concentrations are associated with lower health risk all the way down (until the theoretical minimum-risk level C_{min}). Based on current evidence, there seems to be little or no doubt that potentially large health benefits could be achieved even for reductions that take us well below the NAAQS. (See, for example, Shi et al., who observed short- and long-term mortality impacts from $PM_{2.5}$ even at concentrations cleaner than 12 μg m^{-3}).[33]

Supralinearity of the C−R brings this same issue into still sharper relief. It means that the marginal health benefits conferred upon people living in the cleanest places are even greater than those conferred upon people living in dirty places. Given this fact, the NAAQS level justified by the health science is more stringent than would otherwise be the case. Suppose, for argument's sake, that the C−R function is linear and also that EPA's recently enacted annual-average $PM_{2.5}$ standard of 12 μg m^{-3} actually does provide the "correct" level of health protection according to Section 109. This choice delivers a particular level of absolute health risk (i.e., attributable deaths per capita) for those living with 12 μg m^{-3}.

Now imagine that we discover incontrovertible evidence that the correct C−R is actually Krewski et al.'s (2009) supralinear C−R. In that case, how might EPA respond to the new understanding? For this thought experiment, let us say that the EPA decides that they wish to achieve the same level of cardiopulmonary mortality risk as before. In that case, the NAAQS should be shifted to 9.2 μg m^{-3}. This consideration is one of the policy implications of a supralinear C−R, and it is evident in Figure 1. The point here is not to argue whether a certain level of risk is the "correct" level, but instead that in choosing the standard of 12 μg m^{-3} while using the linear result from Krewski et al. (2009), EPA is in effect establishing "acceptable risk"; if the supralinear C−R turns out to be true, then the same risk level would correspond to a much cleaner concentration (here, 9.2 rather than 12 μg m^{-3}).

Even calculating the health impact of a given policy change becomes a delicate matter if the C−R is supralinear. In the case of a linear C−R, one can compute the health impact of any individual pollution source without concern for the emissions of nearby sources. For a supralinear C−R, though, the health impact of any individual pollution source depends inextricably upon the emissions of other sources.[34−36] Of the many implications of this challenge, we highlight one: different health impact assessment methods may be necessary for questions that are attributional (e.g., "how many deaths per year are attributable to economic sector X?") than for those that are consequential (e.g., "how many deaths per year could be avoided by implementing policy Y?"). If C−R is supralinear, the health impact of any individual action or policy cannot be assessed in isolation because any policy that lowers the baseline $PM_{2.5}$ concentration therefore also increases the health benefits of further reductions.

Supralinearity has implications for environmental economics as well. A first consideration is spatial. Emission reductions in one place can have a very different health impact than reductions elsewhere. Deciding where reductions should be achieved, and how large they should be, means assessing the marginal health benefits per unit of exposure change as well as the relationship between exposure changes and emissions changes. These in turn depend on population density, urban form, meteorology, and atmospheric chemistry,[37,38] as well as abatement costs. How to compute the benefits and compare them meaningfully across the landscape? A supralinear C−R would suggest that the marginal benefits per person of reducing $PM_{2.5}$ concentrations are greatest where the air is already cleanest. However, concentrations tend to be highest in urban areas where population density is high, which implies that reductions in those areas benefit a greater number of people. Balancing those competing forces can be quite difficult: The

DOI: 10.1021/acs.est.5b03154
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marginal benefit per person is greatest in cleaner locations, but aggregate marginal benefit might will be greatest in more-populated locations, which on average have higher pollution.

The implication of supralinearity can be expressed in another way: it means that marginal benefits are increasing in abatement. This possibility runs contrary to a nearly universal assumption in environmental economics, that marginal benefits decline or remain constant as abatement increases.[39] The textbook economic treatment of environmental policy is usually based upon the assumption that marginal abatement costs are increasing in abatement.[39] From this, one might imagine that cleanup costs are low where the air is dirty. This is not at all clear, however. Indeed, abatement costs may well be higher in the most polluted U.S. locations, where inexpensive abatement options have already been implemented, than in cleaner U.S. locations, for which inexpensive abatement options may still exist.[40]

The possibility of a supralinear C−R suggests a number of promising research areas for air-quality engineering as well. For example, it would call for greater emphasis on developing and implementing technologies that reduce concentrations specifically in comparatively clean locations. Designing abatement strategies becomes more complicated with a supralinear C−R because of spatial interdependencies among sources. Emission reductions at one source, which improve downwind air quality, make subsequent reductions from downwind sources even more valuable. Spatially targeted emission reductions that make one region especially clean could yield larger health benefits than more diffuse reductions that lead to small improvements in many dirty locations.

The possibility of a supralinear C−R is, fundamentally, an epidemiological question. We suggest that the question should be the target of substantial research effort. There is a high potential payoff to research into the curvature of C−R, especially at low concentrations. Some framings for epidemiological results—for example, investigating only the overall-average added risk per $\mu g\ m^{-3}$ − enforce a linear approach and therefore are suboptimal for uncovering curvature in the C−R. If risks are assumed to be unchanging below the theoretical minimum-risk concentration, then selection of that theoretical minimum-risk concentration may be crucial to the policy implications of an investigation. Research relating *changes in* concentration with *changes in* health[41,42] is especially relevant to policy decisions. If emerging evidence of a supralinear C−R[43] at lower concentrations is confirmed, a number of possibilities arise. Because the burden of disease attributable to $PM_{2.5}$ is higher under a supralinear C−R, it follows that many more premature deaths from air pollution than previously thought could be averted if society invests in cleaner air.

Perhaps the most vexing aspect is that as a society we might achieve the greatest marginal improvements in per capita premature mortality by cleaning further those places that are already relatively clean—that is, by making blue skies bluer. For a supralinear C−R, upholding the Clean Air Act's goal of protecting human health may entail a dramatic tightening of national air-quality standards. In addition, making the "blue skies bluer" might involve a complementary health-focused regulatory approach, separate from the NAAQS, to improve air quality in locations that already meet the NAAQS. New challenges for environmental justice may arise, if one prioritizes clean-air locations over dirty-air locations; relative to the overall population, low-income and nonwhite individuals tend to have greater exposure to air pollution[44,45] and to be more susceptible to air pollution.[46−49] Ethical aspects are important and must play a critical role in the issues raised here.

We finish by returning where we began, with our title and its suggestion that, if supralinearity is true in the U.S., blue skies should be bluer. (The literal meaning of the phrase "blue skies bluer" turns out to be scientifically consistent with supralinearity: visibility impairment has a supralinear dependence on $PM_{2.5}$.[50−52]) Our emphasis is on the health effects of pollution and the perplexing implications of supralinearity for clean-air policy and human health. Our analysis is aimed at a single pollutant ($PM_{2.5}$) and a single health endpoint (cardiopulmonary mortality). Whether the C−R is supralinear for other pollutants and other health endpoints is worthy of concerted research effort.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.5b03154.

Derivations, input data, calculations and sensitivity analyses (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Michael Brauer, Aaron Cohen, Maureen Cropper, Bill Nazaroff, Jennifer Peel, C. Arden Pope III, and Kirk Smith for fruitful comments and discussions.

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