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Global Effect Factors for Exposure to Fine Particulate Matter

Peter Fantke\textsuperscript{1,*}, Thomas E. McKone\textsuperscript{2,3}, Marko Tainio\textsuperscript{4,5}, Olivier Jolliet\textsuperscript{6}, Joshua S. Apte\textsuperscript{7}, Katerina S. Stylianou\textsuperscript{6}, Nicole Illner\textsuperscript{1}, Julian D. Marshall\textsuperscript{8}, Ernani F. Choma\textsuperscript{9}, John S. Evans\textsuperscript{9}

\textsuperscript{1} Quantitative Sustainability Assessment, Department of Technology, Management and Economics, Technical University of Denmark, Produktionstorvet 424, 2800 Kgs. Lyngby, Denmark
\textsuperscript{2} School of Public Health, University of California, Berkeley, CA 94720, United States
\textsuperscript{3} Lawrence Berkeley National Laboratory, Berkeley, CA 94720, United States
\textsuperscript{4} UKCRC Centre for Diet and Activity Research, University of Cambridge, Cambridge, UK
\textsuperscript{5} Systems Research Institute, Polish Academy of Sciences, Warsaw, Poland
\textsuperscript{6} School of Public Health, University of Michigan, Ann Arbor, MI 48109, United States
\textsuperscript{7} Department of Civil, Architectural and Environmental Engineering, University of Texas at Austin, Austin, TX 78712, United States
\textsuperscript{8} Department of Civil and Environmental Engineering, University of Washington, Seattle, WA 98122, United States
\textsuperscript{9} Department of Environmental Health, Harvard Chan School of Public Health, Boston, MA 02115, United States

*Corresponding author: Tel.: +45 45254452, fax: +45 45933435. E-mail: pefan@dtu.dk
Abstract

We evaluate fine particulate matter (PM$_{2.5}$) exposure-response models to propose a consistent set of global effect factors for product and policy assessments across regions and spatial scales. Relationships among exposure concentrations and PM$_{2.5}$-attributable health effects largely depend on location, population density, and mortality rates. Existing effect factors build mostly on an essentially linear exposure-response function with coefficients from the American Cancer Society study. In contrast, the Global Burden of Disease analysis offers a non-linear Integrated Exposure-Response (IER) model with coefficients derived from numerous epidemiological studies covering a wide range of exposure concentrations. We explore the IER, additionally provide a simplified regression as function of PM$_{2.5}$ level, mortality rates and severity, and compare results with effect factors derived from the recently published Global Exposure Mortality Model (GEMM). Uncertainty in effect factors is dominated by the exposure-response shape, background mortality, and geographic variability. Our central IER-based effect factor estimates for different regions do not differ substantially from previous estimates. However, IER estimates exhibit significant variability by location, driven primarily by PM$_{2.5}$ concentrations and mortality rates variations. Using the IER as basis for effect factors presents a consistent picture of global PM$_{2.5}$-related effects for use in product and policy assessment frameworks.

Keywords: PM$_{2.5}$, effect factors, air pollution, life cycle impact assessment, health impact assessment
1 Introduction

1.1 History of epidemiology-based effect factors

We evaluate fine particulate matter (PM$_{2.5}$) exposure-response models to propose a consistent set of global effect factors across spatial scales for use in product and policy assessments, such as life cycle impact assessment (LCIA). Exposure to PM$_{2.5}$ is the leading environmental contributor to human disease burden, with more than seven million deaths globally attributed to ambient and household PM$_{2.5}$ exposure in 2015.\(^1\) The influence of exposure to PM$_{2.5}$ on mortality rates became clear with the ‘Harvard Six Cities’ study in 1993.\(^2\) The effect seen was so large that a second, larger, study was conducted involving more than 500,000 subjects from 151 communities within the United States (US). This ‘American Cancer Society’ (ACS) study,\(^3\) published in 1995, confirmed the relationship between exposure to PM$_{2.5}$ and mortality rates for concentrations and composition of PM$_{2.5}$ in the US, with an effect size roughly one third as large as that found in the Six Cities study.

At about the same time, Hofstetter\(^4\) began working on methods for comparing environmental impacts from pollutant emissions along product and service life cycles. As part of this effort, he developed the first approach to address exposure to PM$_{2.5}$ in large-scale emission-based comparisons. In such comparisons, the most common measure of the relationship between population exposure and health effects is the ‘effect factor’, typically expressed in terms of years of life lost (YLL) or disability-adjusted life years (DALY) for a given population per kg intake (e.g., via inhalation) of a pollutant. To be suitable for evaluating different emission situations, such effect factors are combined with human intake fractions relating PM$_{2.5}$ emissions to population intake.\(^5\)-\(^7\) Hofstetter\(^4\) applied for his effect factor estimates the PM$_{2.5}$ risk coefficient from the ACS study (0.4% increase in mortality among adults \(\geq 30\) years of age) per \(\mu g/m^3\) to cardiopulmonary mortality rates for European adults of 1400 death per 100,000 person-years. He assumed that the entire effect seen in the ACS study was due to PM$_{2.5}$ exposure and used a severity factor of 6.6 YLL/death, deriving effect factors for Europe of 41 YLL per kg PM$_{2.5}$ or sulfate inhaled.

Over the past 25 years, the Six Cities and ACS studies have been frequently extended and reanalyzed,\(^8\)-\(^11\) and several new cohorts have been evaluated.\(^12\)-\(^20\) These studies have repeatedly confirmed that mortality rates are higher at higher levels of PM$_{2.5}$ exposure—even
after accounting (at the individual level) for differences in behavior, socioeconomic status and
other factors known to affect mortality rates. A recent meta-analysis of these studies
associated a 1.1% increase in cardiovascular mortality per µg/m³ increase in PM$_{2.5}$, with
study-to-study results variability thought to be attributable to difference in particle
composition, building air exchange rates, demographic factors, and meteorology.\textsuperscript{21}

In parallel, several research groups have published new PM-related effect factors,
including estimates yielding 58 YLL per kg PM$_{10}$ inhaled in Europe,\textsuperscript{22} and 64 YLL (78
DALY) per kg PM$_{2.5}$ inhaled in the US.\textsuperscript{23} More recent estimates are more variable and in part
substantially larger than previous estimates,\textsuperscript{24,25} with estimates for example ranging for
Europe from 192 YLL (France) to 622 YLL (Bulgaria) per kg PM$_{2.5}$ inhaled, and for North
America from 151 YLL (Mexico) to 395 YLL (Canada), with the US at 287 YLL, per kg
PM$_{2.5}$ inhaled.\textsuperscript{24}

All described estimates have relied on risk coefficients from the original ACS study or
one of its follow-up studies. Van Zelm et al. (2008)\textsuperscript{22} used a risk coefficient of 0.43%
(0.26–0.91%) per µg/m³ PM$_{10}$ based on Künzli’s synthesis of results from the Six Cities and
ACS studies.\textsuperscript{26} We note that because the ACS study is much larger than the Six Cities study,
Künzli’s pooled risk coefficient is quite similar to the coefficient from the ACS study.
Further, although the original coefficients were applied to PM$_{2.5}$, in an attempt to be
conservative, Künzli et al.\textsuperscript{26} presented these as if they applied to all inhalable particles (PM$_{10}$).
Gronlund et al.\textsuperscript{23} used risk coefficients of 0.6% (0.2–1%) and 0.8% (0.1–1.6%) per µg/m³
PM$_{2.5}$ for, respectively, cardiopulmonary mortality and lung cancer, taken from the 2002
extension of the ACS study.\textsuperscript{8} These were applied to disease-specific background mortality
rates in the US in 1982–88 (640 deaths per 100,000 persons and year for cardiopulmonary
disease, and 82 deaths per 100,000 persons and year for lung cancer), combined with severity
factors of 13 YLL (17 DALY) per death for cardiopulmonary disease, and 27 YLL (28
DALY) per death for lung cancer. Recent studies\textsuperscript{24,25} used 1.3% (1.0–1.6%) and 1.4%
(0.6–2.3%) per µg/m³ PM$_{2.5}$ for, respectively, cardiopulmonary mortality and lung cancer
from the 2009 reanalysis of the ACS study, adjusted for ecological covariates.\textsuperscript{9} (Table 6) The
underlying risk coefficients are approximately three times larger than those used to support
Hofstetter’s original estimate of 41 YLL/kg PM$_{2.5}$ inhaled.\textsuperscript{4}
These studies have attempted to characterize the uncertainty inherent in their results by relying on estimates of the parameter uncertainty in risk coefficients from the underlying epidemiological studies. None of these analyses considered the epistemic uncertainty introduced by using a study conducted in the US to estimate health impacts from exposure to PM$_{2.5}$ in other regions.\textsuperscript{25}

The original ACS study cohort was exposed to annual average PM$_{2.5}$ concentrations varying from 9 to 34 $\mu$g/m$^3$ while worldwide PM$_{2.5}$ levels vary from <5 $\mu$g/m$^3$ to >300 $\mu$g/m$^3$.\textsuperscript{27} If the true relationship between PM$_{2.5}$ concentration and mortality is strictly proportional, risk estimates derived using a proportional exposure-response model would be appropriate. However, if the true exposure-response relationship is non-linear, this approach (i.e., extrapolating globally from US results) is not satisfactory. Furthermore, the ACS study cohort was exposed to PM$_{2.5}$ with a composition resulting from a specific source mixture and US atmospheric conditions, while worldwide PM$_{2.5}$ compositions may differ significantly from those in the US.\textsuperscript{28} However, while assessing and comparing emission scenarios aims at evaluating all possible source types, consistently differentiating various anthropogenic and non-anthropogenic PM$_{2.5}$ sources would require globally spatialized data that are currently lacking. Finally, the ACS study cohort includes residents with an ethnic mix, health-relevant behaviors (e.g., smoking, diet), socioeconomic status, and access to health care all specific to the US. However, if the influence of these co-exposures or behavioral factors is not multiplicative, then the use of an exposure-response model based on relative risk does not provide a satisfactory approach for decomposing observed mortality into components attributable to exposure to ambient PM$_{2.5}$ and components attributable to other causal factors.

These issues of synthesizing evidence, shape of exposure-response, potential differential toxicity, and extrapolation of epidemiological results from the US and Western Europe to the rest of the world are relevant to various assessment communities, but also to regulatory authorities around the world. All of them face the question of how best to synthesize and interpret this large and growing body of evidence on the mortality effects from PM exposure. One synthesis effort of particular interest underlies the Global Burden of Disease (GBD) studies. Since 2010, the GBD has relied on an ‘Integrated Exposure-Response’ (IER) model to characterize risks from exposure to PM$_{2.5}$.\textsuperscript{1,29-31} In this effort, (i) a
variety of exposure-response functions was explored instead of assuming proportionality; (ii) a counterfactual level of pollution was explicitly accounted for, below which no effect would be seen; (iii) evidence from all major cohort studies of ambient PM$_{2.5}$ and mortality was synthesized; and (iv) it was assumed that all fine particles were equivalently toxic (per unit mass inhaled), incorporating evidence from studies involving exposure to active and passive cigarette smoke, and indoor smoke from cooking and heating using dung and other dirty fuels.\textsuperscript{32,33} The IER approach has been well received and provided the basis for a number of prominent estimates of the global impact of exposure to PM$_{2.5}$\textsuperscript{29,34-36}

1.2 Towards appropriate global effect factors estimates

At the 2016 Pellston expert workshop on ‘Global Guidance for Life Cycle Impact Assessment Indicators and Methods’,\textsuperscript{37,38} an international group of researchers focused on understanding the applicability of the IER for developing globally applicable PM$_{2.5}$ effect factors linking change in mortality to change in exposure. Main goal was to provide PM$_{2.5}$ effect factors appropriate for different emission situations (unknown location, known continent or subcontinent, known country or subnational region, and urban area emissions with known city. For each situation, we apply the IER from the 2015 GBD study to (i) understand the factors responsible for variation in derived effect factors; (ii) compare these results with previous estimates and with estimates derived using an alternative exposure-response model; and (iii) promote discussion of the importance of approaches for synthesizing evidence and characterizing effect factor uncertainty. Combining our effect factors with intake fractions will allow for a spatialized evaluation of different PM$_{2.5}$ emission situations suitable for use in LCIA, comparative risk and impact assessments, and analyses of emission reduction policies.

2 Materials and Methods

2.1 General approach followed

Our approach for deriving effect factors for exposure to PM$_{2.5}$ involves the following steps: (1) A synthesis of epidemiological literature is used to provide a risk coefficient, $\beta$ (% increase in mortality rate per $\mu$g PM$_{2.5}$/m$^3$), or a set of $d$ disease-specific (and, for certain
diseases, age-specific) risk coefficients, $\beta_{d1}, \beta_{d2}, \ldots, \beta_{dn}$, reflecting the selected synthesis of exposure-response functions of some arbitrary shape. (2) Estimates of the annual mean PM$_{2.5}$ exposure concentrations (µg/m$^3$) and data on overall mortality rates, $M$ (deaths per person-year), in the regions of interest are obtained. (3) Exposure estimates are combined with mortality rates to compute, in each region of interest, the relative risk, $RR$ (dimensionless), corresponding to the ambient PM$_{2.5}$ exposure concentration level, $C$ (µg/m$^3$), the attributable risk fraction, $ARF$ (dimensionless), as the fraction of mortality attributable to exposure to PM$_{2.5}$, and the related PM$_{2.5}$-attributable mortality, $M_{PM_{2.5}}$ (deaths/year). (4) Estimates of severity, $SF$ (YLL/death or DALY/death), appropriate for each cause of death or disability and region of interest are obtained. (5) Above factors are used to compute the health effects (YLL or DALY) from exposure to PM$_{2.5}$ in each region of interest as exposure-response factor, $ERF = dM_{PM_{2.5}}/dC \times SF$. (6) To link health burden to human intake, the change in intake is computed as product of the change in annual PM$_{2.5}$ concentration, $\Delta C$ (µg/m$^3$), a nominal breathing rate, $BR$ (m$^3$/person/d), and the population count in each region of interest, $N_{pop}$ (persons). After converting µg to kg and days to year, we yield a dose-response factor, $DRF = \frac{ERF}{(N_{pop} \times BR \times 10^9 \text{kg} \times 365 \text{days/year})}$. (7) Effect factors, $EF$ (YLL or DALY per kg PM$_{2.5}$ inhaled), are finally calculated and defined as the slope of the relationship between effects and inhalation exposure. This process provides additional health burden attributable to PM$_{2.5}$ exposure, $\Delta M_{PM_{2.5}}$ (deaths/year), per increment of increased intake of PM$_{2.5}$, $\Delta I$ (kg inhaled/year), by the exposed population in each region of interest.

Following this approach, our analysis relies on the IER model from the 2015 GBD study, and uses data for PM$_{2.5}$ exposure concentration, mortality, severity, population count, and breathing rates as detailed in the following.

### 2.2 Synthesis of epidemiological evidence

There have been several attempts to synthesize evidence from existing epidemiological studies, but none as ambitious as the GBD’s IER. On the assumption of equitoxicity of PM$_{2.5}$ (i.e. assuming particles are equivalently toxic per unit mass inhaled), the IER considers evidence not only from epidemiological studies of ambient PM$_{2.5}$, but also...
from epidemiological studies examining the impact of exposure to indoor smoke, and from
exposure to both active and passive cigarette smoke.\textsuperscript{32,33} The general form of the GBD’s IER
relative risk ($RR$) models is:

$$RR(C) = \begin{cases} 1 + \alpha \times (1 - e^{-\beta \times (C - C_0)^\delta}) & \text{for } C \geq C_0 \\ 1 & \text{for } C < C_0 \end{cases}$$

(1)

with $C$ as the PM$_{2.5}$ exposure concentration, $C_0$ as the theoretical minimum risk exposure level
(TMREL; also referred to as ‘counterfactual’), $1 + \alpha$ as the maximum relative risk, $\beta$ as the
ratio of relative risk at low-to-high PM$_{2.5}$ exposure, and $\delta$ as the power of PM$_{2.5}$ exposure
concentration.

The 2010 GBD study was the first major application of the IER model.\textsuperscript{29} This model is
well known, has been widely used, and has been refitted twice, incorporating additional
demographic studies and using somewhat different statistical methods. The 2013
coefficients\textsuperscript{32} have been used extensively.\textsuperscript{34,35} The most recent update produced the 2015
coefficients that provided the basis for a study reviewing 25 years of mortality attributable to
PM$_{2.5}$ exposure.\textsuperscript{36} The IER model is applied separately to each of five causes of death:
ischemic heart disease (IHD), stroke, chronic obstructive pulmonary disease (COPD), and
lung cancer in adults, as well as acute lower respiratory infections (ALRI) in children. For
IHD and stroke, the IER model is applied separately to each of 12 age groups: 25-29 years,
…, 75-79 years, and $\geq$ 80 years. For COPD and lung cancer, IER model parameters are
estimated only once, and they apply to all individuals over 25 years of age. For ALRI, the
model is applied to children below 5 years of age.

The IER model used in the GBD study\textsuperscript{32} accounts for uncertainty by providing 1000
equally likely sets of values for the model coefficients $\alpha$, $\beta$, $\delta$, and $C_0$ for each disease and
age group of interest. These sets of coefficients are generated by creating 1000 equally likely
datasets and then determining the values of $\alpha$, $\beta$, $\delta$, and $C_0$, with a mean $C_0 = 4.2$ $\mu g/m^3$.
Individual datasets are generated by drawing one set of values of relative risk and PM$_{2.5}$
exposure concentration for each cohort study under consideration from a pool of relative risk
and PM$_{2.5}$ exposure concentration values thought to represent the study.

Strengths of the GBD’s IER model include:\textsuperscript{36} (i) It reflects virtually all available
published cohort studies of mortality attributable to PM$_{2.5}$ exposure. (ii) It begins with a
highly flexible set of exposure-response functions and objective criteria to select among them. (iii) It uses sophisticated statistical methods to account for between-study heterogeneity. (iv) It provides users with an approach for characterizing parameter uncertainty. (v) It includes input from a large group of leading experts in the field of PM$_{2.5}$ epidemiology. (vi) It is published in the peer-reviewed literature, widely used, and updated frequently. (vii) It covers the entire range of PM$_{2.5}$ exposure concentrations of interest, by incorporating evidence from studies of ambient PM$_{2.5}$, indoor PM$_{2.5}$ from cook stoves and passive smoking, along with data on PM$_{2.5}$ exposures and risks among active smokers.

Potential limitations of the GBD’s IER model include: (i) The effect of including epidemiological evidence from studies of direct smoking is to flatten the exposure-response function at high concentrations, which is especially relevant for populations exposed to highly polluted ambient air (e.g., urban China, India). (ii) A secondary effect of including evidence from direct smoking is that reported uncertainty in estimates of the slope decreases as the concentration increases, with the result that for regions with highly polluted ambient air the IER suggests that the slope is known quite precisely, whereas in fact there is the least direct evidence. (iii) The IER model provides no information about model uncertainty introduced by fundamental lack of scientific understanding of issues necessary to interpret the results as causal, or to apply risk estimates to populations that have not been studied epidemiologically, or which are exposed to PM with different composition or particle size than those seen in the considered epidemiological studies. (iv) The validity of the IER model, hence, depends on two strong assumptions. The first assumption is that PM$_{2.5}$ toxicity does not depend on source or chemical composition, since despite substantial efforts, neither epidemiological nor toxicological research has conclusively identified particular sources or components that uniquely determine the toxicity of PM$_{2.5}$. When used to evaluate emissions, the second assumption is that the exposure concentration needed for the IER model can be obtained from the total inhaled PM$_{2.5}$ mass per unit emission provided by the intake fraction.
2.3 Model input data

2.3.1 Spatial resolution of the analysis

Our analysis considers 175 countries, 18 of which were further divided into sub-national regions. The US was divided into 51 regions (50 states and American Samoa). India was divided into 64 regions (32 urban and 32 rural). China was divided into its 34 provinces; Mexico into 32 states; Brazil into 26 states; Saudi Arabia into 13 provinces; and the UK into 13 counties. In addition, several countries (including Australia, Canada, Gabon, Indonesia, Kenya, Norway, Somalia, Spain, and Uganda) were divided into two and Russia into three regions located in different sub-continents. This yields 419 regions studied. When aggregating regional and national results to the level of 8 continents and 16 sub-continents, we grouped Africa and the Middle East as one continent, Latin America and the Caribbean as one continent, and which identify the northern regions of North America, Europe and Central Asia as a distinct continental region. In addition, we considered 3448 cities (i.e. urbanized areas with more than 100,000 inhabitants). Following these spatial resolutions renders our resulting effect factors consistent with related intake fraction estimates.

2.3.2 Fine particulate matter exposure levels

We obtained consistent estimates of the 2016 annual average concentrations of PM$_{2.5}$ prevalent in each of the 419 regions and 3448 cities considered in our analysis from the World Health Organization. PM$_{2.5}$ exposure levels used in support of national (or subnational) effect factors reflect population-weighted averages of outdoor PM$_{2.5}$ concentrations across rural and urbanized areas within each region. PM$_{2.5}$ exposure levels used in support of city-specific effect factors reflect population-weighted averages of outdoor PM$_{2.5}$ concentrations in each respective urban area. For comparing cities or regions, the provided resolution in PM$_{2.5}$ concentrations is sufficient, while higher resolutions would be required for evaluating sources within a given city. Effect factors for ambient environments include both exposures indoors and outdoors (i.e. without signification contribution from indoor sources). We derive additional effect factors intended for application to situations, where indoor sources constitute a substantial contribution to PM$_{2.5}$ exposure. We use archetypal levels to characterize environments with significant indoor emissions, for example related to cook stoves, applying
an average indoor PM$_{2.5}$ concentration of 250 µg/m$^3$ as representative of such environments.$^{43,44}$ Since indoor emissions can vary among countries and households as function of sources and renewal rates, additional scenarios can be evaluated following our general approach for deriving effect factors.

2.3.3 Mortality data

Estimates of age- and disease-specific mortality, $M$ (deaths/year), for each of the five target health outcomes included in the IER (i.e. IHD, stroke, COPD, lung cancer, and ALRI) in each of the 419 regions of interest for the year 2015 were obtained from the GBD Collaborative Network.$^{45}$ For IHD and stroke, we obtained specific data for each of 12 age groups (25-29, …, 75-79, and $\geq$ 80 years). For COPD and lung cancer, we obtained data for adult mortality (age $\geq$ 25 years). For ALRI, we used data on mortality of infants and very young children (age $\leq$ 5 years). Mortality data are available for countries or sub-national regions, and are applied additionally to all cities in their respective regions.

2.3.4 Attributable risk fraction and deaths attributable to PM$_{2.5}$ exposure

Multiplying the attributable risk fraction, $ARF$ (dimensionless), by the current overall mortality, $M$ (death/year), in any given region, provided us the mortality (i.e. number of deaths) attributable to PM$_{2.5}$ exposure, $M_{PM2.5}$ (deaths/year), in that region, i.e. $M_{PM2.5} = ARF \times M$. For the case of ambient air pollution, in which the entire population is exposed, the attributable risk fraction is a simple function of the relative risk, i.e. $ARF = (RR - 1)/RR$.

2.3.5 Severity factors

Estimates of disease- and region-specific severity factors for mortality, $SF_{YLL}$ (YLL/death), and for morbidity and mortality combined, $SF_{DALY}$ (DALY/death), for the year 2015 were obtained from the GBD Collaborative Network.$^{45}$ Severity varies up to a factor of five, mainly due to regional differences in life expectancy.$^{46}$ In the calculation of YLL, the GBD has relied since 2015 on a reference life table constructed using the lowest age-specific mortality rates seen in 2013 in any population larger than 5 million capita.$^{46}$
2.3.6 Exposed population and breathing rate

To compare emission scenarios, we relate emission mass to exposure in order to apply effect factors, using available intake fraction methods as well as population and breathing rate data.\textsuperscript{39} We obtained population counts across all ages, \(N_{\text{pop}}\) (capita), for 3448 cities\textsuperscript{41} and for 419 regions of interest for the year 2015.\textsuperscript{45} Population counts were summed to city and region definitions. To assess intake, we used a nominal population-average breathing rate of \(BR = 11.68 \text{ m}^3/\text{d/person},\textsuperscript{39,44}\) accounting for time fractions spent and activity indoors and outdoors,\textsuperscript{44,47} and the equilibrium fraction of ambient particles penetrating indoors.\textsuperscript{39} Due to missing global spatialized data, we assumed an equal distribution of time spent indoors/outdoors across cities and regions. This approach leads to a value lower than the breathing rates typically used in the intake fraction literature. However, to facilitate combining effect factors with intake fractions, which also include information on time spent indoors/outdoors and on breathing rates, the same values for these aspects should be used in both and finally cancel out.

2.4 Approaches for deriving the effect factor slope

As effect factors reflect health impacts attributable to a unit change in \(\text{PM}_{2.5}\) intake, they are obtained as the slope of the relationship between mortality and mass of \(\text{PM}_{2.5}\) inhaled. When studying the environmental performance of product or service systems, different slopes are relevant for addressing different perspectives. Consequential studies assess environmental impacts expected in consequence of choosing one studied system over another. This perspective requires ‘marginal’ effect factor slopes. In contrast, attributional studies assess environmental impacts along one life cycle of a given system and require using ‘average’ effect factor slopes. For a linear exposure-response function, marginal and average slopes are identical. However, for non-linear functions, such as GBD’s IER, marginal and average slopes differ. Different effect factors are therefore needed for consequential and attributional studies. Hence, we provide marginal effect factors \(EF_{\text{marginal}}\) at a given region or city exposure working point \((C, \mu\text{g/m}^3)\), and average effect factors \(EF_{\text{average}}\) between a given region or city exposure working point \((C, \mu\text{g/m}^3)\) and the theoretical minimum risk exposure.
level \((C_0, \mu g/m^3)\). Both types of effect factors are calculated as a function of the difference in mortality attributable to PM\(_{2.5}\) exposure, \(M_{\text{PM2.5}}\) (deaths/year), divided by the difference in intake, \(I\) (kg/year):

\[
EF^{\text{marginal}}(C_j) = \frac{dM_{\text{PM2.5},j}}{dl_j} \times SF_{ir} = \frac{\sum_{i,j} \left( RR_i(C_j + \Delta C_j) - RR_i(C_j) \right) \times \frac{M_{i,r}}{RR_i(C_r) \times N_{\text{pop},r}} \times SF_{ir}}{\Delta C_j \times BR \times f_{\text{d to yr}} \times f_{\text{kg to } \mu g}} 
\]

\[
EF^{\text{average}}(C_j) = \frac{M_{\text{PM2.5}}(C_j) - M_{\text{PM2.5}}(C_0)}{I(C_j) - I(C_0)} \times SF_{ir} \times \frac{M_{ir}}{RR_i(C_r) \times N_{\text{pop},r}} \times SF_{ir}
\]

Equations 2a and 2b are derived from substituting the relative risk in the relation of PM\(_{2.5}\) attributable mortality (see Section 2.3.4) and PM\(_{2.5}\) exposure levels as described in Section 2.1. More specifically, \(RR_i(C_j)\) is the relative risk obtained from eq 1 for disease \(i\) at the PM\(_{2.5}\) exposure level \(C_j\) in \(j\)th city (for urban effect factors) or in region \(j = r\) (for regional effect factors). \(M_{ir}\) is the overall mortality in region \(r\) for disease \(i\), which contains the city of interest and all other cities and rural areas in a given region. \(SF_{ir}\) is the corresponding region- and disease-specific severity factor. \(N_{\text{pop}}\) is the exposed population and \(BR\) the individual breathing rate. Units are corrected via factors \(f_{\text{d to yr}} = 365\) days/year and \(f_{\text{kg to } \mu g} = 10^9\) \(\mu g/kg\). Ratio \((M_{ir})/(RR_i(C_r) \times N_{\text{pop},r})\) is the regional background mortality rate without the influence of PM\(_{2.5}\) exposure, calculated based on the corresponding PM\(_{2.5}\) concentration of that region (i.e. \(C_r\)). If this ratio is multiplied by \((RR_i(C_r) - 1)\) in eq 2b, we get the attributable mortality rate due to PM\(_{2.5}\) exposure. We finally divide by inhaled PM\(_{2.5}\) mass per person (deaths/kg inhaled) and multiply by the severity (DALY/death) to yield the effect factor (DALY/kg inhaled).

2.5 Implementation and model evaluation

We implemented both the marginal and average approaches in Analytica Release 4.6 and in Microsoft Excel 2016 to derive effect factors for the considered 419 regions and 3448 cities. Results from the two implementations were compared as a quality control measure. All
Simulations were run using the full set of 1000 equally likely realizations of relative risk model parameters, and uncertainty ranges around effect factors are based on Monte Carlo simulations performed in Analytica.

To evaluate our effect factor estimates, we followed two distinct approaches. First, we simplified the effect factor model in a regression, focusing on understanding the most relevant aspects influencing variability in effect factors. This yields additional insight in aspects contributing to linking health effects to human intake, and provides a simple tool for practitioners to estimate effect factors based on only knowing the most relevant key inputs, namely PM$_{2.5}$ concentration, mortality rates and disease severity. Second, we compare our effect factors against recent spatialized factors, and against factors obtained following our proposed approach but using another exposure-response relationship, namely the recently published Global Exposure Mortality Model (GEMM), synthesizing epidemiological evidence from cohorts in 16 countries. Unlike GBD’s IER, GEMM exclusively considers studies on ambient PM$_{2.5}$ exposure.

### 3 Results

#### 3.1 Effect factors for total mortality for different levels of spatial aggregation

We summarize our results starting with the most general case in which the location of the PM$_{2.5}$ emission source is unknown (Table 1). In this case, our central effect factor estimates, $EF$ (DALY/kg PM$_{2.5}$ inhaled), reflect the population-weighted (as surrogate for emission-weighted) average of the marginal and average slopes for morbidity and mortality attributable to PM$_{2.5}$ exposure. When there is no information about emission location, geographic variability contributes significantly to overall effect factor uncertainty. We characterize uncertainty by providing confidence intervals, as well as expected values obtained from the distributions of possible values.

<table>
<thead>
<tr>
<th>Region</th>
<th>Marginal slope</th>
<th>Average slope</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regions</td>
<td>Cities</td>
</tr>
<tr>
<td>Global average</td>
<td>44 (17−127)</td>
<td>54 (35−124)</td>
</tr>
</tbody>
</table>
Table showing continental and sub-continental regions with associated values for DALY/kg PM$_{2.5}$ inhaled.

<table>
<thead>
<tr>
<th>Continent Regions</th>
<th>Value (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>115 (91–141)</td>
</tr>
<tr>
<td>Latin America</td>
<td>44 (18–80)</td>
</tr>
<tr>
<td>Europe</td>
<td>74 (23–141)</td>
</tr>
<tr>
<td>Africa &amp; Middle East</td>
<td>43 (4–106)</td>
</tr>
<tr>
<td>Central Asia</td>
<td>49 (17–129)</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>33 (21–77)</td>
</tr>
<tr>
<td>Northern regions</td>
<td>123 (84–165)</td>
</tr>
<tr>
<td>Oceania</td>
<td>178 (116–297)</td>
</tr>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sub-continental Regions</th>
<th>Value (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Asia</td>
<td>49 (17–127)</td>
</tr>
<tr>
<td>Indochina</td>
<td>48 (29–79)</td>
</tr>
<tr>
<td>Northern Australia</td>
<td>177 (115–293)</td>
</tr>
<tr>
<td>Southern Australia &amp; New Zealand</td>
<td>176 (115–293)</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>56 (27–94)</td>
</tr>
<tr>
<td>North, East &amp; Central Africa</td>
<td>37 (3–133)</td>
</tr>
<tr>
<td>Argentina+</td>
<td>48 (23–120)</td>
</tr>
<tr>
<td>Brazil+</td>
<td>60 (18–81)</td>
</tr>
<tr>
<td>Central America+ &amp; Caribbean</td>
<td>30 (17–75)</td>
</tr>
<tr>
<td>USA &amp; Southern Canada</td>
<td>115 (92–139)</td>
</tr>
<tr>
<td>Northern Europe &amp; Northern Canada</td>
<td>125 (88–164)</td>
</tr>
<tr>
<td>Europe</td>
<td>75 (24–141)</td>
</tr>
<tr>
<td>East Indies &amp; Pacific</td>
<td>85 (68–193)</td>
</tr>
<tr>
<td>India+</td>
<td>28 (20–41)</td>
</tr>
<tr>
<td>Eastern China</td>
<td>26 (21–32)</td>
</tr>
<tr>
<td>Japan &amp; Korean peninsula</td>
<td>57 (25–79)</td>
</tr>
</tbody>
</table>

Effect factors based on the average slope of the exposure-response function between the exposure working point and the theoretical minimum risk exposure level tend to be ~2.5 times larger than effect factors based on the marginal slope of the exposure-response function evaluated at the exposure working point. The mean marginal slope effect factor averaged over the 419 considered regions is 44 DALY/kg PM$_{2.5}$ inhaled, with 95% of region-specific values falling in the range from 17 to 127 DALY/kg PM$_{2.5}$ inhaled. In contrast, the mean average slope effect factor averaged over the same 419 regions is 115 DALY/kg PM$_{2.5}$ inhaled, with 95% of region-specific values falling in the range from 49 to 355 DALY/kg PM$_{2.5}$ inhaled. The mean marginal slope effect factor averaged over the 3448 considered cities is 54 DALY/kg PM$_{2.5}$ inhaled, with 95% of city-specific values falling in the range from 35 to 124
DALY/kg PM$_{2.5}$ inhaled. In contrast, the mean average slope effect factor averaged over these same 3448 cities is 137 DALY/kg PM$_{2.5}$ inhaled, with 95% of region-specific values in the range from 55 to >1000 DALY/kg PM$_{2.5}$ inhaled. Typical city effect factors appear to be slightly (20 to 30%) larger than effect factors for regions with a wider variability across cities.

We next consider the case in which the location of PM$_{2.5}$ emissions is relatively well known, where we can identify either the city or the country (or subnational region) in which a PM$_{2.5}$ source of interest is located. Marginal and average slope effect factors for all 419 regions and 3448 cities are provided in the Supplementary Information (SI).

To provide factors for an intermediate level of spatial detail, between unknown source location and rather precise source specification, we developed and summarize in Figure 1 the average effect factors for regions and cities, aggregated at the level of continents. We estimated the continental weighted median effect factors by pooling the effect factors for each region or city, using weights representing the fraction of the population of the continent contributed by each region or city. The continental median as well as the 2.5% and 97.5% cumulative probability values come from the distribution

\[
(p_1 \times EF_1 + p_2 \times EF_2 + ... + p_m \times EF_m),
\]

where $p_1, p_2, ..., p_m$ are probabilistic weights (Bernoulli variables) taking the value 1 with probability $p$ and 0 with probability $1 - p$, and $EF_1, EF_2, ..., EF_m$ are probabilistic characterizations of the effect factors from each region or city within a given continent. Marginal and average slope effect factors for (sub-)continents are provided in Table 1.

Figure 1 shows average effect factor estimates across regions and urban areas per continent, respectively. In addition, Figure 1 shows the distribution of the average effect factor for the indoor environment archetype with substantial indoor emission sources. For indoor environments, the effect factor based on the average slope between the exposure working point and the theoretical minimum risk exposure level is recommended, since indoor exposure reduction efforts will usually lead to substantial (non-marginal) change in indoor PM$_{2.5}$ concentrations.$^{49}$
Figure 1. Population-weighted distribution of average effect factors due to PM$_{2.5}$ exposure across cities (urbanized areas) and regions (including all rural and urban areas within a region) per continent, with a comparison to the average effect factor appropriate for scenarios with substantial emissions from indoor sources. Boxes represent median and inter-quartile ranges, and whiskers represent ranges containing 95% of continent-specific effect factors. Continents are arranged from left-to-right in order of mean effect factors. Bars represent total population count (capita) in each continental region and across cities per region.

Effect factors tend to be higher for exposure levels in North America, Oceania and Northern Regions than for exposure levels in Southeast Asia, Africa and the Middle East, Latin America and Central Asia. Effect factors in Europe tend to fall between these. While there are differences in the typical effect factor by continent, the within-continent variation tends to be larger than differences between values typical for various continents.

Indoor effect factors are lower than outdoor effect factors primarily due to the high working point exposures indoors (due to cooking) that push the non-linear model into a region of lower slopes.

Figure 2 illustrates the variability and uncertainty in median average effect factor estimates for PM$_{2.5}$ exposure in each of the 3448 considered cities. Of the 3618 cities initially
considered, 170 were excluded from our analysis because their mean ambient annual PM$_{2.5}$ concentration was below the theoretical minimum risk exposure level, yielding an effect factor that is either zero or almost infinite. The vertical axis in Figure 2 reflects the range of city-specific effect factor estimates, which vary from less than 10 to 1900 DALY/kg PM$_{2.5}$ inhaled. The horizontal axis shows z-score indicating how many standard deviations the median effect factor for a specific city is from the mean across cities, calculated as $z$-score $= (X - \mu)/\sigma$, with $X$ as median effect factor for a given city, $\mu$ as mean effect factor across cities, and $\sigma$ as standard deviation. The fact that the 3448 city-specific median effect factor estimates lie, approximately, on a straight line suggests that median average urban effect factor estimates are approximately log-normally distributed, with a median of 133 DALY/kg PM$_{2.5}$ inhaled and a geometric standard deviation of 1.95 (summarized in the box plot on the right side of Figure 2).
Figure 2. Median effect factor estimates for PM$_{2.5}$ exposure in 3448 cities (top) and in 419 regions (bottom) with 95% confidence intervals for each city and region, and with the distribution across all cities (top) and across all regions (bottom) indicated as right-side box plots. Z-scores indicate how many standard deviations city-/region-specific median effect factors are from the respective mean across all considered cities/regions. Median effect factors based on GEMM$^{48}$ are indicated as white dashes for comparison. Light color bars around median values indicate confidence interval ranges.

To illustrate the dependence of effect factors on PM$_{2.5}$ exposure concentration levels, we have color-coded the data shown in Figure 2. Blue data points correspond to cities with PM$_{2.5}$ concentrations between 5.8 and 15 µg/m$^3$; yellow data points correspond to cities with
PM$_{2.5}$ concentrations between 15 and 25 µg/m$^3$; and red data points correspond to cities with PM$_{2.5}$ concentrations above 25 µg/m$^3$. Finally, grey data points indicate cities with mean PM$_{2.5}$ concentrations at or below the upper confidence interval limit of the theoretical minimum risk exposure level of 5.8 µg/m$^3$. Increasing PM$_{2.5}$ exposure concentrations yield lower effect factors for both cities and regions. This reflects the influence of the underlying non-linear exposure-response model, suggesting modest reductions in health burden in highly polluted areas unless PM$_{2.5}$ levels markedly decline.$^{36}$

Uncertainty in each of our effect factor estimates is reflected in the error bars shown for each city- and region-specific value. Because the GBD’s IER model is highly non-linear with a slope that approaches infinity as PM$_{2.5}$ concentration levels approach the theoretical minimum risk exposure levels (which are themselves uncertain), effect factors become increasingly uncertain at levels of PM$_{2.5}$ near this exposure level, usually reaching magnitudes beyond 500 DALY/kg inhaled. For comparison, effect factors based on GEMM (see Figure 2) generally deviate from results based on GBD’s IER within a factor of two, but also suggest a less extreme trend at both ends of the PM$_{2.5}$ concentration range. In fact, very high effect factors are rather an artefact in the underlying exposure-response driven by studies on active smokers rather than ambient PM$_{2.5}$ exposure, while very low effect factors are an artefact for forcing the curve to meet the minimum risk exposure level.

To relate effect factors in cities to those of their respective regions, we plot in Figure 3 the relationship of average effect factors between the various cities in each of the 175 considered countries (sub-national regions were aggregated to national estimates), and the average slope effect factor for the respective country (considering all rural and urban areas in that country). Only 147 out of the 175 considered countries contain cities with more than 100,000 inhabitants. For these countries, the number of cities ranges from a single city in e.g. Iceland to 337 cities in India and 827 cities in China. In several countries, city-specific effect factors vary considerably, indicating that it is important to distinguish urban and rural factors and individual cities whenever related emission information is available. City-specific effect factors being higher than the related country averages across cities indicates that the overall country average is driven by (usually large) cities with higher PM$_{2.5}$ levels and related lower effect factors.
3.2 Determinants of effect factors: Simplified regression

In an effort to understand the determinants of effect factors related to PM$_{2.5}$ exposure, we analyzed our results statistically. We found that for urban areas, marginal and average effect factors are well approximated with simple regression models of the following form:

$$EF = \frac{(k_1 + k_2 \times M_{\text{adult}}) \times SF}{C - k_3}$$

(3)

where $M_{\text{adult}}$ is the total adult mortality (deaths/person-year) from the four related diseases considered by GBD’s IER model for age groups $\geq 25$ years, $SF$ is the average severity factor.
(over all age groups) for the same four diseases, $C$ is the annual average ambient PM$_{2.5}$
exposure concentration ($\mu$g/m$^3$) in the area of interest, and $k_1$, $k_2$, and $k_3$ are fitting
parameters.

First, we compared effect factors with their respective PM$_{2.5}$ exposure levels (Figure
4a). Using $1/C$ as regression model explained 18% of the variance when taking average slope
effect factors across our 419 considered regions. In a second model for the same dataset, we
estimated effect factors from $1/(C - k_3)$, which explained 22% of effect factors variance.
Including mortality into the regression of the form $(k_2 \times M^{\text{adult}})/(C - k_3)$ already explained
77% of our effect factor variance. Finally, we introduced severity factors into the model,
which then takes the form as in eq 3 and explains 94% of the variance of average slope effect
factors across regions as shown in Figure 4b.

For the 419 regions in our analysis, optimal values of model parameters for marginal
slope effect factors, $EF^{\text{marginal}}_{\text{region}}$, are $k_1 = 8$ deaths/person-year, $k_2 = 15,028$, and $k_3 = 0
\mu$g/m$^3$; yielding an $R^2 = 0.95$. For average slope effect factors, $EF^{\text{average}}_{\text{region}}$, in the 419 regions,
the optimal parameter values are $k_1 = 0$ deaths/person-year, $k_2 = 28,100$, and $k_3 = 3.9
\mu$g/m$^3$; yielding an $R^2 = 0.94$. It can be shown that for an average slope effect factor, the
constant $k_2$ is an estimate of the average adjusted relative risk value of $10^9 \frac{\mu g}{kg} \times$
$\left[\frac{(RR(C) - 1)/RR(C)}{(BR \times 365 \text{ days/year})}\right]$. With the value of the nominal per-capita daily
breathing rate of 11.68 m$^3$/person/d used in our analysis, an estimate of $k_2$ of 28,100 is
consistent with an average attributable risk fraction of 0.12, corresponding to a relative risk of
$RR = 1.136$. The constant $k_3$ of 3.9 $\mu$g/m$^3$ is an estimate of the theoretical minimum risk
exposure level of PM$_{2.5}$.

For the 3448 cities considered in our analysis, the optimal values of model parameters
for marginal slope effect factors, $EF^{\text{marginal}}_{\text{city}}$, are $k_1 = 11$ deaths/person-year, $k_2 = 13,800,$
and $k_3 = 0.3 \mu$g/m$^3$; giving $R^2 = 0.96$. For average slope effect factors in cities, $EF^{\text{average}}_{\text{city}}$, the
optimal parameter values are $k_1 = 11$ deaths/person-year; $k_2 = 36,311$, and $k_3 = 1.7 \mu$g/m$^3$;
giving $R^2 = 0.89$. It can be shown that for a marginal slope effect factor, the constant $k_2$ is
again an estimate of the average adjusted relative risk value, which is consistent with an
average attributable risk fraction of 0.154, corresponding to a relative risk of $RR = 1.182$. 
The constant $k_3$ of 1.7 µg/m$^3$ is again an estimate of the theoretical minimum risk exposure level of PM$_{2.5}$. Overall, our simplified regression model predicts effect factors very well, using only information on PM$_{2.5}$ exposure concentration, total adult mortality and severity for any given region or city, which is readily available from the GBD study and global PM$_{2.5}$ monitoring data.

Figure 4. Effect factors estimated in the present study derived from the GBD IER (Integrated Exposure-Response) model\textsuperscript{36} for 419 regions compared against (a) their respective PM$_{2.5}$ exposure levels, (b) our simplified regression model, (c) effect factors provided by van Zelm et al. (2016),\textsuperscript{24} and (d) effect factors derived from the Global Exposure Mortality Model (GEMM).\textsuperscript{48} Regression coefficients in (b) are for effect factors ($EF$, DALY/kg inhaled) in regions (including urban and rural areas). $M^{\text{adult}}$ (deaths/person-year), $SF$ (DALY/death), and $C$ (µg/m$^3$), respectively denote total adult mortality (considering IHD, stroke, COPD and lung
cancer, for age groups \( \geq 25 \) years), average severity factor over all age groups for the same diseases, and annual average PM\(_{2.5}\) exposure concentration per region. Plotted effect factor ranges are restricted to 800 DALY/kg inhaled.

### 4 Discussion

#### 4.1 Applicability of our effect factors

We proposed a consistent set of global effect factors that can be combined with human intake fractions\(^{39}\) in support of comparative assessments that are relevant to a broad range of emission and related exposure situations; applicable to a diverse number of populations, cities, and countries; and applicable for different levels of spatial aggregation. While we can currently not differentiate between anthropogenic and non-anthropogenic PM\(_{2.5}\) sources (i.e. our approach is equally applicable to both), future efforts should focus on providing effect factors that are differentiated by source type. We found that estimating PM\(_{2.5}\) effect factors requires information for five underlying aspects, namely (i) shape and parameters of the epidemiology-based exposure-response function; (ii) levels of PM\(_{2.5}\) exposure in the considered population; (iii) mortality rates for PM\(_{2.5}\) exposure-related diseases; (iv) severity factors reflecting loss of life expectancy and duration and severity of disease-related disability preceding death; and (v) amount of air inhaled by the exposed population. Of these, the most critical and uncertain information is that related to the exposure-response function.

Comparing 4.2 with 8.9 million deaths globally estimated for 2015 using respectively GBD’s IER model\(^ {36}\) and the GEMM\(^ {48}\) (using all cohorts) indicates uncertainty of the exposure-response of at least a factor of two. This is dominating as compared to other contributors to uncertainty (breathing rates, exposure concentrations, and indoor/outdoor time patterns), which generally vary much less than a factor of two.\(^ {41,44}\) In the mid-1990’s, evidence about the exposure-response relating chronic exposure to mortality was limited to the results from two cohort studies—the Six Cities study\(^ {2}\) and the ACS study\(^ {3}\)—these gave central effect estimates, which differed by a factor of three. More than twenty years later, results from a dozen relatively large cohort studies and an equal number of smaller cohorts contribute to our understanding of this issue.
A number of effect factors estimates for PM$_{2.5}$ exposure has been proposed. All estimates have relied, almost exclusively, on evidence from one cohort, i.e. the ACS study$^3$ (and its extensions and re-analyses). Although it is one of the largest and best-studied cohorts and used by regulatory authorities in the US and Europe, we have identified concerns about ACS. Particularly, because of its use of ambient air exposures and health data for the US, it may be unable to provide the best possible synthesis of evidence on mortality effects of chronic exposure to PM$_{2.5}$ for use in the development of globally applicable effect factors.

The IER model provides an alternative synthesis,$^{32}$ has been used to support estimates of the Global Burden of Disease since 2010, and has provided the basis for a number of independent studies of the mortality impacts of chronic exposure to ambient PM$_{2.5}$.\textsuperscript{1,29,30,33-36} GBD’s IER model relies on evidence from all major cohort studies of mortality related to chronic exposure to PM$_{2.5}$ and supplements this with information from studies of mortality impacts from exposure to smoke in households, which rely on dirty fuels for indoor cooking and heating, and from studies of exposure to both active and passive cigarette smoke. Using this model in our approach to develop global effect factors constitutes a more consistent picture than relying on evidence from a single region, thereby accounting for spatial variability in important underlying aspects including PM$_{2.5}$ exposure levels, mortality and disease severity.

4.2 Evaluation against other factors and models

We have explored the implications of using the synthesis provided by GBD’s IER model for deriving effect factors and have observed the following: First, our central estimates of global population-weighted marginal region and city effect factors are 44 and 54 DALY/kg PM$_{2.5}$ inhaled, respectively. The variability in marginal slope effect factors across regions is substantial. If the location of a PM$_{2.5}$ emissions source is unknown, the marginal slope effect factor could be between 17 and 127 (with 95% confidence). Similar variability is found for emissions across cities. Second, our central estimates of the global population-weighted average slope region and city effect factors are 2 to 3 times as large as the corresponding marginal slope effect factors. The variability in average slope effect factors is also substantial. If the location of an emissions source is unknown, the average slope effect factor could be
between 49 and 355 (with 95% confidence). Similar variability is again found for emissions across cities. We recommend applying the average effect factors rather than the marginal effect factors in cases where substantial variations in background PM$_{2.5}$ exposure concentrations are expected over the lifetime of a considered system under analysis. This is for example the case in China, where substantial reduction in concentrations have been observed in the last years and are expected in the coming decade, or for analyzing indoor PM mitigation scenarios, for which cooking alternatives can strongly reduce PM exposure levels. Third, although effect factors tend to be somewhat higher for some continents (North America, Oceania, Northern Regions) than for others (Southeast Asia, Central Asia, Latin America, Africa & the Middle East), most of the variability in effect factors is within-continent and is determined largely by variation in the average annual mean PM$_{2.5}$ exposure concentrations from place-to-place. This occurs because of the non-linearity of the IER exposure-response, which exhibits low slopes at high PM$_{2.5}$ exposure concentrations and increasingly large slopes as PM$_{2.5}$ exposure concentrations decrease toward the theoretical minimum risk exposure level of PM$_{2.5}$. Fourth, our estimates of the population-weighted marginal and average slope effect factors for Europe are respectively ~70 and ~150 DALY/kg PM$_{2.5}$ inhaled, and for North America respectively ~110 and ~290 DALY/kg PM$_{2.5}$ inhaled. Differences between Europe and US are mainly driven by lower PM$_{2.5}$ levels in the US (leading to higher exposure-response slopes), and our estimates are only slightly larger than previous estimates of 58 YLL per kg PM$_{2.5}$ inhaled (Europe)$^{22}$ and 78 DALY per kg PM$_{2.5}$ inhaled (US).$^{23}$ Fifth, similar to recent studies,$^{24,25}$ we provide estimates of effect factors appropriate for various countries and regions worldwide. Our estimates of population-weighted marginal slope effect factors are both variable and uncertain, with typical values varying from 27 DALY/kg PM$_{2.5}$ inhaled (95% confidence interval: 17 to 120) in Central Asia to 168 DALY/kg PM$_{2.5}$ inhaled (95% confidence interval: 78 to 306) in Northern Regions. Previous estimates are also variable and uncertain, varying from 87 YLL/kg PM$_{2.5}$ inhaled in Thailand to 857 YLL/kg PM$_{2.5}$ inhaled in Kazakhstan.$^{24}$ However, as Figure 4c shows, the different sets of estimates present quite distinct pictures of both the patterns and sources of variability and the nature and extent of uncertainty in effect factor estimates. These
differences are primarily due to the non-linearity in GBD’s IER model being the major source of variability in our estimates, a feature not present in earlier estimates.\textsuperscript{24,25}

In conducting this analysis, we are not proposing that effect factors based on GBD’s IER model are more reliable than estimates based on other syntheses of the epidemiological evidence for mortality effects of PM\textsubscript{2.5}. Instead, the goal of our analysis is to illustrate the importance of the approach used to synthesize exposure-response evidence for compiling a globally consistent set of effect factors that allow for evaluating emission and emission reduction situations at different spatial levels. We note that uncertainty about how to synthesize epidemiological evidence is arguably the largest, often unacknowledged source of uncertainty in PM\textsubscript{2.5} effect factor estimates. To evaluate this aspect, we finally developed effect factors following our general approach but using the recently published Global Exposure Mortality Model (GEMM),\textsuperscript{48} and compared results against our factors based on GBD’s IER model (see Figure 2). Comparing both sets of effect factors for the 419 considered regions, we find that GEMM-based factors overall agree well with IER-based factors (Figure 4d); however, despite some deviations especially at very high and very low PM\textsubscript{2.5} exposure levels, where the GEMM is less non-linear than the IER model. This suggests that the relative risk estimates underlying our analysis could be potentially limited at both extremes of the considered PM\textsubscript{2.5} range to yield effect factors that are better aligned with GEMM and less influenced by artefacts related to the IER shape. An advantage of using GEMM as underlying exposure-response model could be that each included cohort can be fitted separately for a given region. However, additional research is required to select for example the appropriate cohorts in GEMM for regions where no epidemiological evidence is currently available.

Based on the current state-of-the-science synthesis used by the GBD study,\textsuperscript{36} our effect factor estimates can be consistently coupled with indoor and outdoor region and city specific intake fractions\textsuperscript{39} for use in LCIA, comparative risk and health impact assessments, and emission reduction policy analyses. Our continental, country- and region-level, and city-specific effect factors thereby capture important variability in mortality from exposure to PM\textsubscript{2.5}, which is not possible with currently available spatialized models. As science advances and new syntheses of the epidemiological evidence on mortality attributable to PM\textsubscript{2.5}
exposure becomes available, our approach can easily accommodate this new information to produce updated global effect factors for exposure to PM$_{2.5}$.

4.3 Recommendations for policy and practitioners

Effect factors for exposure to PM$_{2.5}$, combined with intake fractions,$^{39}$ provide important insight when evaluating different emission and emission reduction situations. Effect factors vary considerably across cities and regions (Figure 1, Figure 3), with lower effect factors in areas with higher PM$_{2.5}$ exposure and highest effect factors in areas with PM$_{2.5}$ exposure close to the minimum risk exposure level (Figure 2, Figure 4a). Current spatial models are unable to capture the most important related variabilities in effect factors (see Figure 4c). Our consistent set of global effect factors addresses this spatial variability by covering different spatial scales through parameterized cities and countries (or sub-national regions), continents and global averages that can be applied as function of information available about emission location. We recommend using as underlying exposure-response model GBD’s IER covering a wide range of PM$_{2.5}$ exposure concentrations based on a large set of epidemiological studies from different regions,$^{36}$ while further exploring other models, such as GEMM.$^{48}$ GEMM is generally in good agreement with the IER, but also exhibits important differences, such as a more linear behavior at high PM$_{2.5}$ exposures (see Figure 4d).

However, important questions still need to be addressed before GEMM can be applied in a global context, for example the selection of appropriate cohorts in areas without available epidemiological evidence. We generally recommend applying effect factors derived from an average slope, where substantial variations in background PM$_{2.5}$ exposure are expected over the lifetime of an assessed product system or as consequence of emission or exposure reduction efforts. Finally, when only limited information is available regarding PM$_{2.5}$ exposure, mortality and disease severity, we recommend applying our simplified regression model (eq 3, Figure 4b) with different fitting coefficients for regions, cities, and marginal versus average slopes. Further research should focus on providing globally spatialized data on time spent indoors/outdoors, breathing rates, additional health outcomes associated with PM$_{2.5}$ exposure, epidemiological evidence in regions currently not covered, and effect factors differentiated by source type.


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Supporting Information

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

The operational PM$_{2.5}$ effect factor model and all numerical effect factor results are provided as Microsoft® Excel® workbook (XLSX).

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Population-weighted distribution of average effect factors due to PM2.5 exposure across cities (urbanized areas) and regions (including all rural and urban areas within a region) per continent, with a comparison to the average effect factor appropriate for scenarios with substantial emissions from indoor sources. Boxes represent median and inter-quartile ranges, and whiskers represent ranges containing 95% of continent-specific effect factors. Continents are arranged from left-to-right in order of mean effect factors. Bars represent total population count (capita) in each continental region and across cities per region.
Median effect factor estimates for PM2.5 exposure in 3448 cities (top) and in 419 regions (bottom) with 95% confidence intervals for each city and region, and with the distribution across all cities (top) and across all regions (bottom) indicated as right-side box plots. Z-scores indicate how many standard deviations city-/region-specific median effect factors are from the respective mean across all considered cities/regions. Median effect factors based on GEMM are indicated as white dashes for comparison. Light color bars around median values indicate confidence interval ranges.
Distribution of average slope median effect factors across cities per country ranked according to increasing country-specific average effect factors that include all rural and urban areas for 147 countries with at least one city with more than 100,000 inhabitants.
Effect factors estimated in the present study derived from the GBD IER (Integrated Exposure-Response) model\textsuperscript{35} for 419 regions compared against (a) their respective PM\textsubscript{2.5} exposure levels, (b) our simplified regression model, (c) effect factors provided by van Zelm et al. (2016),\textsuperscript{24} and (d) effect factors derived from the Global Exposure Mortality Model (GEMM).\textsuperscript{47} Regression coefficients in (b) are for effect factors (EF, DALY/kg inhaled) in regions (including urban and rural areas). $M_{\text{adult}}$ (deaths/person-year), $SF$ (DALY/death), and $C$ ($\mu$g/m$^3$), respectively denote total adult mortality (considering IHD, stroke, COPD and lung cancer, for age groups $\geq 25$ years), average severity factor over all age groups for the same diseases, and annual average PM2.5 exposure concentration per region. Plotted effect factor ranges are restricted to 800 DALY/kg inhaled.

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TOCart

69x44mm (300 x 300 DPI)