Supplementary Information for:

A Framework for Estimating the U.S. Mortality Burden of Fine Particulate Matter Exposure Attributable to Indoor and Outdoor Microenvironments

Parham Azimi, Ph.D.,[1] Brent Stephens, Ph.D.[1]
[1]Department of Civil, Architectural, and Environmental Engineering, Illinois Institute of Technology, Chicago, IL USA

Table of contents

Selecting appropriate exposure-response effect estimates for $PM_{2.5}$ of outdoor origin

Epidemiology studies that have investigated associations between premature all-cause mortality and long-term outdoor $PM_{2.5}$ concentrations in the U.S. have reported various relative risks (RR) commonly ranging from 6% per 10 μg/m^3 (95% CI: 2% to 11%) to 26% per 10 μg/m^3 (95% CI: 8% to 47%).[1–9] The differences in magnitudes of RR from each study are attributable to a combination of varying cohort population demographics, population susceptibility, outdoor $PM_{2.5}$ sources and compositions, and other factors including those that affect infiltration and persistence in residential indoor environments where people spend most of their time.[10–16] Despite this variability, it is common to assume that all outdoor $PM_{2.5}$ is equally potent in producing premature mortality regardless of geographic location or other factors for these kinds of population-level analyses.[9] Therefore, we utilize a central pooled estimate of RR for the increase in long-term all-cause mortality associated with outdoor $PM_{2.5}$ concentrations in the U.S. of 7.3% per 10 μg/m^3 (95% CI: 3.7% to 11%) as reported in a recent quantitative meta-analysis of outdoor $PM_{2.5}$ concentration-response effect estimates.[17] This estimate is similar in magnitude to, albeit somewhat higher than, another recent pooled effect estimate of 6% (95% CI: 4% to 8%) for all-cause mortality made using a meta-analysis of studies from both the U.S. and Europe.[18] We convert the pooled RR estimate of 1.073 per 10 μg/m^3 to an effect estimate (i.e., $\beta_{PM2.5}$) of 0.0070 (95% CI: 0.0036 to 0.0104), where $\beta_{PM2.5} = \ln(RR)/10$.[19] We fit a Weibull distribution to these reported values in MATLAB, resulting in a mean (±SD) value of $\beta_{PM2.5}$ = 0.0070 (±0.0016) per μg/m^3 with distribution shape factors of $\alpha = 0.765$ and $\beta = 4.95$. A Weibull distribution was used because it yields a distribution that is very close to normal in shape, but does not produce any negative values.

Modifying exposure-response function effect estimates for $PM_{2.5}$ of outdoor origin

Average times spent in each microenvironment were taken directly from the 1992-1994 National Human Activity Pattern Survey (NHAPS),[20] as described in the main text. Average outdoor $PM_{2.5}$ infiltration factors for each microenvironment (i.e., F_j) were culled from the existing literature as follows. We assumed the average ambient $PM_{2.5}$ infiltration factor inside U.S. residences was 0.59 according to the mean value reported in a recent review of 17 studies spanning over 1000 U.S. homes.[21] We assumed the average $PM_{2.5}$ infiltration factor in all other indoor locations other than residences was 0.49 based on the average modeled indoor concentrations of outdoor origin from a simulation study of small and medium commercial buildings that were designed to reasonably represent the U.S. office building stock.[22] Briefly, we used MATLAB to fit Weibull and lognormal distributions to their reported percentiles of indoor and outdoor $PM_{2.5}$ concentrations, then used Monte Carlo simulations with 20,000 iterations to build a distribution of infiltration factors based on these two distributions (i.e., $F_{inf} = C_{in}/C_{out}$ in the absence of indoor sources). Here we use the mean value of the resulting distribution. While this analysis ignored other non-residential buildings, we are not aware of other robust data sets on infiltration factors in non-office non-residential buildings in the U.S. However, an infiltration factor of 0.49 is reasonably in range with those reported in other non-residential buildings in Europe, including workplaces in Finland[23] and schools in Germany[24] and Spain.[25] For vehicles, we assumed an average ambient $PM_{2.5}$ infiltration factor of 0.43, assuming personal vehicles operate 50% of the time in recirculated air mode and 50% of the time in outdoor air ventilation mode with infiltration factors of 0.25 and 0.61, respectively.[26] Finally, we assumed that people are exposed to 100% of $PM_{2.5}$ of outdoor origin when they spend time outdoors (i.e., $F_{outdoor} = 1$).

Scenario 1: Nationwide estimate based primarily on prior field studies

Here we describe all relevant model inputs and data sources that were used for the nationwide $PM_{2.5}$ mortality estimate made in Scenario 1. To characterize what we assume to be nationally representative time-activity patterns, Table S1 shows stair-step distribution characteristics for the amount of time spent in each of the four microenvironments considered herein, which we transcribed from Figure 3 in Klepeis et al. (2001).[20] Values for the fraction of time spent in residences, vehicles, and outdoors were all sampled directly from the stair-step distributions in Table S1, while the time spent in other indoor locations was estimated by subtracting the sum of times spent in these three microenvironments from a total of 1440 minutes (i.e., 24 hours).

To characterize indoor $PM_{2.5}$ concentrations of indoor origin in all non-residential indoor microenvironments, we assumed an arithmetic mean (± SD) of 4.18 ± 4.98 μg/m^3, which was suggested for the range of indoor $PM_{2.5}$ concentrations resulting from general office work environments in Finland.[23] We constructed a lognormal distribution that resulted in the same arithmetic mean ± SD to avoid negative values while matching the same summary statistics (GM = 2.69 μg/m^3 and GSD = 2.56). Although this approach is limited to office buildings in Finland, we are not aware of other studies that have similarly quantified the indoor and ambient contributions to indoor concentrations in non-residential buildings in the U.S. We also consider it reasonable to assume the same values for all non-residential indoor microenvironments regardless of building function based on the close similarities in indoor $PM_{2.5}$ concentrations reported in a recent study of a wide variety of small and medium sized commercial environments in California.[27]

To characterize indoor $PM_{2.5}$ concentrations of outdoor origin in non-residential indoor environments, we sampled from the same beta distribution of infiltration factors in small and medium U.S. commercial buildings that we constructed previously from Ben-David et al. (2017).[22] Shape factors for the infiltration factor beta distribution in MATLAB were: $\alpha = 1.82$ and $\beta = 1.91$ (Figure S1). Similarly, to characterize $PM_{2.5}$ concentrations of outdoor origin inside vehicles, we sampled equally from two beta distributions fit to reported summary statistics of infiltration factors measured in vehicles operating half the time in recirculated air mode and half the time in outdoor air ventilation mode, with mean ± SD infiltration factors of 0.25±0.12 and 0.61±0.17, respectively.[26] Shape factors for the assumed beta distributions were $\alpha = 2.98$ and $\beta = 8.72$ for recirculating systems and $\alpha = 4.32$ and $\beta = 2.73$ for outdoor air ventilation (Figure S1). We also introduced an in-vehicle exposure modification factor to Equation 3-b to account for near-road $PM_{2.5}$ concentrations that are 22% higher, on average, than central site monitor or background levels.[28] This factor is not incorporated directly into the model framework but is applied uniformly to each model iteration during application. We assumed there are no indoor sources of $PM_{2.5}$ inside vehicles because the focus is on non-smoking microenvironments and it is reasonable to assume there are minimal other $PM_{2.5}$ sources inside most vehicles.

To characterize indoor $PM_{2.5}$ concentrations from both indoor and outdoor sources in residences, we rely on two of the largest data sources for field measurements of which we are aware: the Relationship of Indoor, Outdoor and Personal Air (RIOPA) study[29] and the Multi-Ethnic Study of the Atherosclerosis and Air Pollution (MESA Air).[30,31] The RIOPA study sampled indoor and outdoor $PM_{2.5}$ concentrations concurrently for 48 hours in 212 non-smoking residences in three U.S. cities.[32] Similarly, MESA Air measured indoor and outdoor $PM_{2.5}$ concentrations concurrently over a 2-week period in 208 homes in warm seasons and 264 homes

in cold seasons in seven U.S. cities. Both studies are unique in that they included large sample sizes of homes in multiple U.S. cities and also reported distributions of $PM_{2.5}$ infiltration factors, which can be either directly or indirectly used to estimate the relative contributions of both indoor and outdoor sources to indoor $PM_{2.5}$ concentrations in the sample residences. Because the two studies differed in their population demographics and geographic locations, we use them to conduct three versions of Scenario 1, including sampling input parameters affecting indoor concentrations of $PM_{2.5}$ of indoor and outdoor origin from: (a) RIOPA only, (b) MESA only, and (c) equally from both RIOPA and MESA. For Scenarios 1a and 1b, we assume that either RIOPA or MESA is generally representative of the entire U.S. residential building stock. Because this may not be a valid assumption for either study, Scenario 1c assumes that, when sampled together with equal weighting, the two studies are more generally representative than either study alone.

For the RIOPA-only scenario, we estimated distributions of annual average residential indoor $PM_{2.5}$ concentrations of outdoor origin for the year 2012 by sampling from distributions of infiltration factors reported in the study homes and multiplying them by samples drawn from distributions of the U.S. annual average outdoor $PM_{2.5}$ concentration for 2012, as described in the main text. Meng et al. (2005) modeled the distributions of outdoor $PM_{2.5}$ infiltration factors of a subset of 114 of the study homes that had one complete set of 48-hour measurements, resulting in a mean (±SD) of 0.54 ± 0.16.[33] We fit a beta distribution to the reported mean ± SD infiltration factors from RIOPA, resulting in shape factors of $\alpha = 4.70$ and $\beta = 4.00$ (Figure S1).

To obtain distributions of the indoor $PM_{2.5}$ concentration resulting from indoor sources alone, lognormal distributions were first fit to match the reported means and standard deviations of indoor and outdoor $PM_{2.5}$ concentrations from the RIOPA study, as shown in Table S2. Next,

distributions for the indoor $PM_{2.5}$ concentration resulting from only indoor sources in the RIOPA residences were estimated using Equation S1 combined with sampling from lognormal distributions for indoor and outdoor $PM_{2.5}$ concentrations and the beta distribution for outdoor $PM_{2.5}$ infiltration factors. Using this approach, we make the necessary assumption that $\Delta C_{PM2.5,AG,residences}$ varies over time (i.e., from year to year) because ambient concentrations vary over time, and that infiltration factors are constant over time. Similarly, we assume that indoor emission sources, and thus $\Delta C_{PM2.5,IG,residences}$, are also constant over time.

$$C_{PM2.5,IG,residence,in} = C_{PM2.5,residence} - (C_{PM2.5,out} * F_{residence}) \quad \text{(S1)}$$

where $C_{PM2.5,IG,residence}$ is the indoor $PM_{2.5}$ concentration of indoor origin estimated in the RIOPA residences ($\mu g/m^3$); $C_{PM2.5,residence}$ is a sampled value of the indoor $PM_{2.5}$ concentration in RIOPA residences based on the distributions fit to data reported in Meng et al. (2005)[32] ($\mu g/m^3$); $C_{PM2.5,out}$ is a sampled value of the simultaneous outdoor $PM_{2.5}$ concentration in the RIOPA study based on the distributions fit to data reported in Meng et al. (2005)[32] ($\mu g/m^3$); and $F_{residence}$ is a sampled value of the corresponding outdoor $PM_{2.5}$ infiltration factor for the same RIOPA residences based on the distributions fit to data reported in Meng et al. (2005)[33] (-). Using this approach, we estimate that the average contribution of indoor sources to indoor $PM_{2.5}$ concentrations in the RIOPA study was ~9.5 $\mu g/m^3$, or ~63% of the total indoor $PM_{2.5}$ concentration, with ~37% coming from outdoor sources, on average.

For the MESA Air scenario, we also created distributions of annual average residential $PM_{2.5}$ concentrations of indoor and outdoor origin for 2012 by sampling from distributions of infiltration factors and indoor $PM_{2.5}$ concentrations that were attributable to indoor sources, as both were reported directly by Allen et al. (2012).[34] Similar to RIOPA, a beta distribution was fit to the reported mean ± SD infiltration factors (0.62±0.21), with shape factors of $\alpha = 2.69$ and $\beta =$

1.65 (Figure S1). We also fit lognormal distributions to the summary statistics for indoor $PM_{2.5}$ concentrations that were attributable to indoor sources (i.e., $C_{PM2.5,residence,in}$) in Allen et al. (2012), using the average of cold and warm seasons to represent an assumed annual average (Table S2). Using this approach, the average contribution of indoor sources to indoor $PM_{2.5}$ concentrations in MESA Air was ~2.76 μg/m^3, or only ~30% of the total indoor $PM_{2.5}$ concentration, on average, with ~70% coming from outdoor sources. Clearly, the MESA and RIOPA scenarios represent very different assumptions for the relative contributions of indoor and ambient sources to residential indoor $PM_{2.5}$ concentrations. For the combined 50/50 RIOPA/MESA scenario, we sampled from each of the generated distributions equally.

In an attempt to verify our model framework, we also repeated Scenario 1 with inputs modified to match those used by Fann et al. (2017)[35] to estimate the ambient $PM_{2.5}$ mortality burden in the US in 2010. In theory, our model framework should be able to reasonably recreate mortality estimates made using only outdoor $PM_{2.5}$ concentrations as surrogates for exposure (i.e., the approach used in Fann et al. 2017) since outdoor concentrations should be appropriately re-assigned in the model as exposure estimates in various microenvironments. We re-ran the analysis using the following inputs for the US adult population 35 years and older in 2010: Pop = 162,828,035; y_0 = 1450.8 per 100,000 persons per year, $\beta_{PM2.5}$ = 0.583 mean with SD of 0.096 (and a beta distribution fit through the mean and SD), population-weighted average outdoor $PM_{2.5}$ concentration of 8.8 μg/m^3 (taken directly from Fann et al. 2017), and a threshold outdoor $PM_{2.5}$ concentration of zero. Using the model framework with these assumptions and keeping all other assumptions from the 50/50 RIOPA/MESA combined scenario the same, our best estimate (i.e., median value) of the total annual mortality burden associated with exposure to $PM_{2.5}$ of both indoor and outdoor origin across all microenvironments in 2010 was ~198,100 deaths (IQR

of ~149,600 to ~281,100). The relative microenvironmental exposure contributions were similar to those in Figure 2c in the main text, and our best estimate of the mortality burden associated with exposure to $PM_{2.5}$ of outdoor origin summed across all microenvironments was ~124,500 deaths (IQR of ~49,400 to ~169,700). The result was very similar to the central estimate of ~120,000 (95% CI of 83,000 to 160,000) annual deaths made by Fann et al. (2017),[35] which serves as a reasonable check on the validity of our modeling approach and the accuracy of our results, at least for $PM_{2.5}$ of ambient origin, even though we consider much less detail in geographical variations in population and ambient exposures than Fann et al. (2017). For comparison, the estimated mortality burden associated with indoor $PM_{2.5}$ sources in this scenario was ~73,600 deaths (IQR of ~10,700 to ~118,300).

Scenario 3: Global Burden of Disease Integrated Exposure-Response model

The Global Burden of Disease (GBD) study and others[36–40] have used the integrated exposure-response (IER) model developed by Burnett et al. (2014),[41] which estimates the relative risk (RR_i) of long-term exposure to a wide range of $PM_{2.5}$ concentrations and sources for multiple causes of mortality using Equation S2.

$$RR_i = 1 + \alpha_i \left[1 - e^{-\gamma_i (C - C_0)^{\delta_i}}\right] \quad \text{for } C > C_0 \tag{S2-a}$$

$$RR_i = 1 \quad \text{for } C \leq C_0 \tag{S2-b}$$

where C is the exposure concentration ($\mu g/m^3$), C_0 is the concentration below which there is an assumption of no additional risk ($\mu g/m^3$), i is one of five causes of mortality, and α_i, γ_i, and δ_i are statistical parameters that result from fitting the model to RR results from a large number of global epidemiological studies for each mortality endpoint. The premature mortality M for a

given population range *j* and disease endpoint *i* is estimated for a given region using Equation S3.[36]

$$M_{i,j} = Pop_j \widehat{y_0}_{i,j}(RR_{i,j}(C)) - 1) \quad \text{where } \widehat{y_0}_{i,j} = \frac{y_{0\,i,j}}{\overline{RR}_i} \tag{S3}$$

where Pop_j is the region's population for age range *j* and $y_{0_{i,j}}$ is the region's annual average disease incidence for population age range *j*, and $\overline{RR}_i$ is the average population-weighted relative risk for endpoint *i*, as shown in Equation S4.[36]

$$\overline{RR}_i = \frac{\sum_{j=1}^{N_i} Pop_j RR_{i,j}(C)}{\sum_{j=1}^{N} Pop_j} \tag{S4}$$

where N_i is the total number of age ranges for endpoint *i*.

The IER methodology was developed in part because the exposure-response function in Equation 1 in the main text is based on epidemiology cohort studies in the U.S. and Europe with outdoor $PM_{2.5}$ concentrations typically below 30 μg/m^3, which may not be representative for countries with much higher ambient air pollution levels[37] or for other, higher, $PM_{2.5}$ exposures such as secondhand- or active-smoking. Therefore, the IER methodology integrates estimates of the RR of multiple causes of mortality, including ischemic heart disease (IHD), cerebrovascular disease (stroke), chronic obstructive pulmonary disease (COPD), and lung cancer (LC) for adults over 25, as well as acute lower respiratory infection (ALRI) for children under 5, that have been associated with a wide range of $PM_{2.5}$ exposure concentrations (i.e., from 0 to ~30,000 μg/m^3) resulting from a variety of $PM_{2.5}$ sources, including ambient air pollution, secondhand smoke, active smoking, and household air pollution. RR estimates are then converted to population-wide excess mortality estimates using age-specific mortality and demographic data.

As an example application of the IER approach, Cohen et al. (2015) estimated that approximately 88,400 deaths (95% CI: 66,800-115,000) were associated with outdoor $PM_{2.5}$ exposures in the U.S. in 2015.[39] Similarly, Apte et al. (2015) estimated that approximately 103,000 deaths (CI unknown) were associated with outdoor $PM_{2.5}$ exposures in the U.S. in 2010.[36] As another example, Wang et al. (2017)[42] used the IER model – combined with look-up tables for RR values across a range of ambient $PM_{2.5}$ concentrations from 5.8 to 410 $\mu g/m^3$ provided by Apte et al. (2015)[37] – to estimate the mortality burden associated with ambient $PM_{2.5}$ exposure in high-income North America (i.e., Canada and the U.S.) to be only ~51,000 deaths in 2010. We approximate the U.S. mortality burden from this same estimate to be in the range of ~45,000 given that Canada had ~11% of the population of the U.S. in 2010. Another more recent study introduced the Global Exposure Mortality Model (GEMM), building on the IER model, for estimating global mortality associated with ambient $PM_{2.5}$ exposures. Their estimate of excess all-cause mortality attributable to ambient $PM_{2.5}$ in North America in 2015 was ~213,000 deaths, while the same estimate using the IER approach was only 95,000, suggesting that the IER model underestimates all-cause mortality.[43]

For comparison purposes, we re-ran a version of Scenario 1 using the IER model approach (i.e., substituting Equations S1-S4 for Equation 1 in the Monte Carlo analysis) to estimate the premature mortality for adults 35 years and older attributable to IHD, stroke, COPD, and LC. We excluded ALRI in young children because of its extremely low prevalence in the U.S. We considered one age range (i.e., 35 years and older) for COPD and LC, and ten age ranges for IHD and stroke (i.e., 35-40, 40-45, 45-50, 50-55, 55-60, 60-65, 65-70, 70-75, 75-80, and +80 years old). Table S3 summarizes the population and disease incidence for each of these age groups and disease conditions gathered from the CDC WONDER system.[44] We used the RR

look-up tables from Apte et al. (2015)[37] similar to Wang et al. (2017)[42] to assign a RR value for each mortality endpoint and modeled concentration. This necessitates making the assumption of a 5.8 $\mu g/m^3$ threshold concentration, below which no additional mortality is assumed.

Using the IER approach with inputs from Scenario 1, we estimate that the total mortality associated with $PM_{2.5}$ exposure from all sources and across all microenvironments is ~38,400 deaths annually (Table S4). We estimate that exposure to $PM_{2.5}$ of outdoor origin across all microenvironments accounted for ~24,000 deaths in 2012 (IQR of ~9,200 to ~32,700 deaths), and exposure to $PM_{2.5}$ of indoor origin across all microenvironments accounted for ~14,400 deaths (IQR of ~2,000 to ~22,400). Results from the IER scenario are drastically lower than results from Scenario 1 and 2 for several reasons, primarily including: (1) the use of a 5.8 $\mu g/m^3$ threshold concentration compared to the no-threshold assumption; (2) the IER model presents a different model form and parameter fits that may yield different effect estimates from the traditional exposure-response (E-R) function and effect estimates used herein; and (3) the IER model is fit through ambient air pollution studies at the low end of the concentration range, and is thus not modified for microenvironmental exposures to $PM_{2.5}$ of outdoor origin that would have occurred in the original cohort studies. Results for the total mortality associated with $PM_{2.5}$ of outdoor origin from the IER scenario are also lower than previous estimates, including: just over half of that reported by Wang et al. (2017)[42] (mostly attributed to our modification of ambient origin exposures by microenvironmental infiltration factors), and approximately one-quarter of that reported by Cohen et al. (2015)[39] and Apte et al. (2015)[36] (mostly attributed of the aforementioned underlying discrepancies that exist between Wang et al. and Cohen et al. and Apte et al., for reasons that are not immediately clear).

For these varied reasons, a comparison between the IER approach in Scenario 3 and the E-R approaches in Scenario 1 and 2 is not directly valid without some additional modification. Therefore, we re-ran Scenario 1 again using the original E-R model form (i.e., Equation 1 in the main text) with the following changes to provide a more appropriate comparison to the IER model: (1) we introduced a threshold concentration of 5.8 μg/m^3 to each model iteration, below which no excess mortality is assumed to occur; (2) we used unmodified effect estimates (i.e., assuming $\Sigma F_j \times t_j = 1$ in Equation 4 in the main text) rather than our modified effect estimates; and (3) we used both our primary all-cause mortality endpoint effect estimate (i.e., $\beta = 0.0070$ per μg/m^3)[17] and a lower effect estimate that has been used in other recent studies (i.e., $\beta = 0.0058$ per μg/m^3)[5] because we are uncertain as to which effect estimate would yield similar mortality predictions as the IER approach with RRs from Apte et al. (2015).[37]

Results from the two additional Scenario 1 case studies are shown in Table S4 below the GBD IER case studies. The median total mortality estimates using the generic E-R model (Equation 1 in the main text) with $\beta = 0.0070$ per μg/m^3 and $\beta = 0.0058$ per μg/m^3 were ~42,600 and ~36,000 deaths annually, respectively. Results from the IER model application were approximately in between these two estimates, which suggests that the application of the IER model yields mortality estimates that are approximately equivalent to applying the E-R model form with the assumption of an unmodified total all-cause mortality excess RR of ~6 to ~7% per 10 μg/m^3 with a threshold of 5.8 μg/m^3. Importantly, the similarities in both model results using the same or equivalent inputs also suggests that the vast majority of the difference in mortality estimates between Scenario 3 and Scenarios 1 and 2 is driven by the assumption of a 5.8 μg/m^3 threshold concentration in Scenario 3 compared to a zero threshold concentration in Scenarios 1 and 2. This is a critical discrepancy that the research community must address if analyses like

this and others are to be relied upon for informing high-level policy decisions. Our original assumption of a no threshold concentration is consistent with a number of studies that have demonstrated or suggested that there is no evidence of a population threshold in the relationship between long-term exposure to ambient $PM_{2.5}$ and mortality.[8,45–47] However, the majority of applications of the IER model have assumed either a threshold concentration of 5.8 $\mu g/m^3$ (e.g., [36,42]) or a distribution between 2.4 and 5.8 $\mu g/m^3$ (e.g., [39]). Since a large portion of the mortality burden estimated using these types of risk assessment functions is attributable to $PM_{2.5}$ concentrations at the lower end of the curve, these two modeling assumptions can yield vastly different mortality estimates.

References

1 Di Q, Wang Y, Zanobetti A, Wang Y, Koutrakis P, Choirat C *et al.* Air Pollution and Mortality in the Medicare Population. *New England Journal of Medicine* 2017; **376**: 2513–2522.

2 Dockery DW, Pope CA 3rd, Xu X, Spengler JD, Ware JH, Fay ME *et al.* An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993; **329**: 1753–1759.

3 Jerrett M, Burnett RT, Ma R, Pope CA, Krewski D, Newbold KB *et al.* Spatial Analysis of Air Pollution and Mortality in Los Angeles: *Epidemiology* 2005; **16**: 727–736.

4 Krewski D, Jerrett M, Rt B, R M, E H, Y S *et al.* Extended follow-up and spatial analysis of the American Cancer Society study linking particulate air pollution and mortality. *Res Rep Health Eff Inst* 2009; : 5–114; discussion 115-36.

5 Laden F, Schwartz J, Speizer FE, Dockery DW. Reduction in Fine Particulate Air Pollution and Mortality: Extended Follow-up of the Harvard Six Cities Study. *Am J Respir Crit Care Med* 2006; **173**: 667–672.

6 Pope CA, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE *et al.* Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults. *Am J Respir Crit Care Med* 1995; **151**: 669–674.

7 Pope CA, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K *et al.* Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002; **287**: 1132–1141.

8 Roman HA, Walker KD, Walsh TL, Conner L, Richmond HM, Hubbell BJ *et al.* Expert Judgment Assessment of the Mortality Impact of Changes in Ambient Fine Particulate Matter in the U.S. *Environmental Science & Technology* 2008; **42**: 2268–2274.

9 US EPA. The Benefits and Costs of the Clean Air Act from 1990 to 2020. U.S. Environmental Protection Agency Office of Air and Radiation: Washington, DC, 2011http://www.epa.gov/cleanairactbenefits/feb11/fullreport_rev_a.pdf.

10 Eftim SE, Samet JM, Janes H, McDermott A, Dominici F. Fine particulate matter and mortality: a comparison of the six cities and American Cancer Society cohorts with a medicare cohort. *Epidemiology* 2008; **19**: 209–216.

11 Hodas N, Meng Q, Lunden MM, Rich DQ, Özkaynak H, Baxter LK *et al.* Variability in the fraction of ambient fine particulate matter found indoors and observed heterogeneity in health effect estimates. *Journal of Exposure Science and Environmental Epidemiology* 2012; **22**: 448–454.

12 Puett RC, Schwartz J, Hart JE, Yanosky JD, Speizer FE, Suh H *et al.* Chronic particulate exposure, mortality, and coronary heart disease in the nurses' health study. *Am J Epidemiol* 2008; **168**: 1161–1168.

13 Zeger SL, Dominici F, McDermott A, Samet JM. Mortality in the Medicare population and chronic exposure to fine particulate air pollution in urban centers (2000-2005). *Environ Health Perspect* 2008; **116**: 1614–1619.

14 Chen C, Zhao B, Weschler CJ. Indoor exposure to "outdoor PM10". *Epidemiology* 2012; **23**: 870–878.

15 Ji W, Zhao B. Estimating mortality derived from indoor exposure to particles of outdoor origin. *PLOS ONE* 2015; **10**: e0124238.

16 Bell ML, Ebisu K, Peng RD, Dominici F. Adverse Health Effects of Particulate Air Pollution: Modification by Air Conditioning. *Epidemiology* 2009; **20**: 682–686.

17 Fann N, Gilmore EA, Walker K. Characterizing the Long-Term PM $_{2.5}$ Concentration-Response Function: Comparing the Strengths and Weaknesses of Research Synthesis Approaches: Characterizing Long-Term PM $_{2.5}$ Concentration-Response Function. *Risk Analysis* 2016; **36**: 1693–1707.

18 Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B *et al.* Long-term air pollution exposure and cardio- respiratory mortality: a review. *Environmental Health* 2013; **12**. doi:10.1186/1476-069X-12-43.

19 Rackes A, Ben-David T, Waring MS. Outcome-based ventilation: A framework for assessing performance, health, and energy impacts to inform office building ventilation decisions. *Indoor Air* 2018. doi:10.1111/ina.12466.

20 Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P *et al.* The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. *J Expo Anal Environ Epidemiol* 2001; **11**: 231–252.

21 Chen C, Zhao B. Review of relationship between indoor and outdoor particles: I/O ratio, infiltration factor and penetration factor. *Atmos Environ* 2011; **45**: 275–288.

22 Ben-David T, Rackes A, Waring MS. Alternative ventilation strategies in U.S. offices: Saving energy while enhancing work performance, reducing absenteeism, and considering outdoor pollutant exposure tradeoffs. *Building and Environment* 2017; **116**: 140–157.

23 Hänninen OO, Palonen J, Tuomisto JT, Yli-Tuomi T, Seppanen O, Jantunen MJ. Reduction potential of urban PM2.5 mortality risk using modern ventilation systems in buildings. *Indoor Air* 2005; **15**: 246–256.

24 Fromme H, Diemer J, Dietrich S, Cyrys J, Heinrich J, Lang W *et al.* Chemical and morphological properties of particulate matter (PM10, PM2.5) in school classrooms and outdoor air. *Atmospheric Environment* 2008; **42**: 6597–6605.

25 Rivas I, Viana M, Moreno T, Bouso L, Pandolfi M, Alvarez-Pedrerol M *et al.* Outdoor infiltration and indoor contribution of UFP and BC, OC, secondary inorganic ions and metals in PM 2.5 in schools. *Atmospheric Environment* 2015; **106**: 129–138.

26 Hudda N, Fruin SA. Models for Predicting the Ratio of Particulate Pollutant Concentrations Inside Vehicles to Roadways. *Environmental Science & Technology* 2013; **47**: 11048–11055.

27 Wu X, Apte MG, Bennett DH. Indoor Particle Levels in Small- and Medium-Sized Commercial Buildings in California. *Environmental Science & Technology* 2012; **46**: 12355–12363.

28 Karner AA, Eisinger DS, Niemeier DA. Near-Roadway Air Quality: Synthesizing the Findings from Real-World Data. *Environmental Science & Technology* 2010; **44**: 5334–5344.

29 Weisel CP, Zhang J, Turpin BJ, Morandi MT, Colome S, Stock TH *et al.* Relationship of Indoor, Outdoor and Personal Air (RIOPA) study: study design, methods and quality assurance/control results. *Journal of Exposure Analysis and Environmental Epidemiology* 2004; **15**: 123–137.

30 Cohen MA, Adar SD, Allen RW, Avol E, Curl CL, Gould T *et al.* Approach to Estimating Participant Pollutant Exposures in the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *Environ Sci Technol* 2009; **43**: 4687–4693.

31 Kaufman JD, Adar SD, Allen RW, Barr RG, Budoff MJ, Burke GL *et al.* Prospective Study of Particulate Air Pollution Exposures, Subclinical Atherosclerosis, and Clinical Cardiovascular Disease: The Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air). *American Journal of Epidemiology* 2012; **176**: 825–837.

386 32 Meng QY, Turpin BJ, Korn L, Weisel CP, Morandi M, Colome S *et al.* Influence of ambient
387 (outdoor) sources on residential indoor and personal PM2.5 concentrations: Analyses of
388 RIOPA data. *J Expo Anal Environ Epidemiol* 2005; **15**: 17–28.

389 33 Meng QY, Turpin BJ, Polidori A, Lee JH, Weisel C, Morandi M *et al.* PM2.5 of ambient
390 origin: estimates and exposure errors relevant to PM epidemiology. *Environmental Science*
391 *& Technology* 2005; **39**: 5105–5112.

392 34 Allen RW, Adar SD, Avol E, Cohen M, Curl CL, Larson T *et al.* Modeling the residential
393 infiltration of outdoor PM2.5 in the Multi-Ethnic Study of Atherosclerosis and Air Pollution
394 (MESA Air). *Environmental Health Perspectives* 2012; **120**: 824–830.

395 35 Fann N, Kim S-Y, Olives C, Sheppard L. Estimated Changes in Life Expectancy and Adult
396 Mortality Resulting from Declining PM2.5 Exposures in the Contiguous United States:
397 1980–2010. *Environmental Health Perspectives* 2017; **125**. doi:10.1289/EHP507.

398 36 Apte JS, Marshall JD, Cohen AJ, Brauer M. Addressing Global Mortality from Ambient
399 $PM_{2.5}$. *Environmental Science & Technology* 2015; **49**: 8057–8066.

400 37 Lelieveld J, Evans JS, Fnais M, Giannadaki D, Pozzer A. The contribution of outdoor air
401 pollution sources to premature mortality on a global scale. *Nature* 2015; **525**: 367–371.

402 38 Rohde RA, Muller RA. Air Pollution in China: Mapping of Concentrations and Sources.
403 *PLOS ONE* 2015; **10**: e0135749.

404 39 Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K *et al.* Estimates and 25-
405 year trends of the global burden of disease attributable to ambient air pollution: an analysis
406 of data from the Global Burden of Diseases Study 2015. *The Lancet* 2017; **389**: 1907–1918.

407 40 Chowdhury S, Dey S, Smith KR. Ambient PM2.5 exposure and expected premature
408 mortality to 2100 in India under climate change scenarios. *Nature Communications* 2018; **9**.
409 doi:10.1038/s41467-017-02755-y.

410 41 Burnett RT, Pope CA III, Ezzati M, Olives C, Lim SS, Mehta S *et al.* An Integrated Risk
411 Function for Estimating the Global Burden of Disease Attributable to Ambient Fine
412 Particulate Matter Exposure. *Environmental Health Perspectives* 2014.
413 doi:10.1289/ehp.1307049.

414 42 Wang J, Xing J, Mathur R, Pleim JE, Wang S, Hogrefe C *et al.* Historical Trends in PM2.5-
415 Related Premature Mortality during 1990–2010 across the Northern Hemisphere.
416 *Environmental Health Perspectives* 2016; **125**. doi:10.1289/EHP298.

417 43 Burnett R, Chen H, Szyszkowicz M, Fann N, Hubbell B, Pope CA *et al.* Global estimates of
418 mortality associated with long-term exposure to outdoor fine particulate matter. *PNAS* 2018;
419 : 201803222.

420 44 CDC. National Center for Health Statistics WONDER Online Database: Compressed
421 Mortality File 1999-2016 Series 20, No. 2V. CDC WONDER.
422 2017.https://wonder.cdc.gov/cmf-icd10.htm (accessed 22 May2018).

423 45 Crouse DL, Peters PA, van Donkelaar A, Goldberg MS, Villeneuve PJ, Brion O *et al.* Risk
424 of Nonaccidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low
425 Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort Study.
426 *Environmental Health Perspectives* 2012; **120**: 708–714.

427 46 Schwartz J, Coull B, Laden F, Ryan L. The Effect of Dose and Timing of Dose on the
428 Association between Airborne Particles and Survival. *Environmental Health Perspectives*
429 2007; **116**: 64–69.

430 47 Pinault L, Tjepkema M, Crouse DL, Weichenthal S, van Donkelaar A, Martin RV *et al.*
431 Risk estimates of mortality attributed to low concentrations of ambient fine particulate
432 matter in the Canadian community health survey cohort. *Environmental Health* 2016; **15**.
433 doi:10.1186/s12940-016-0111-6.

434
435

Figures

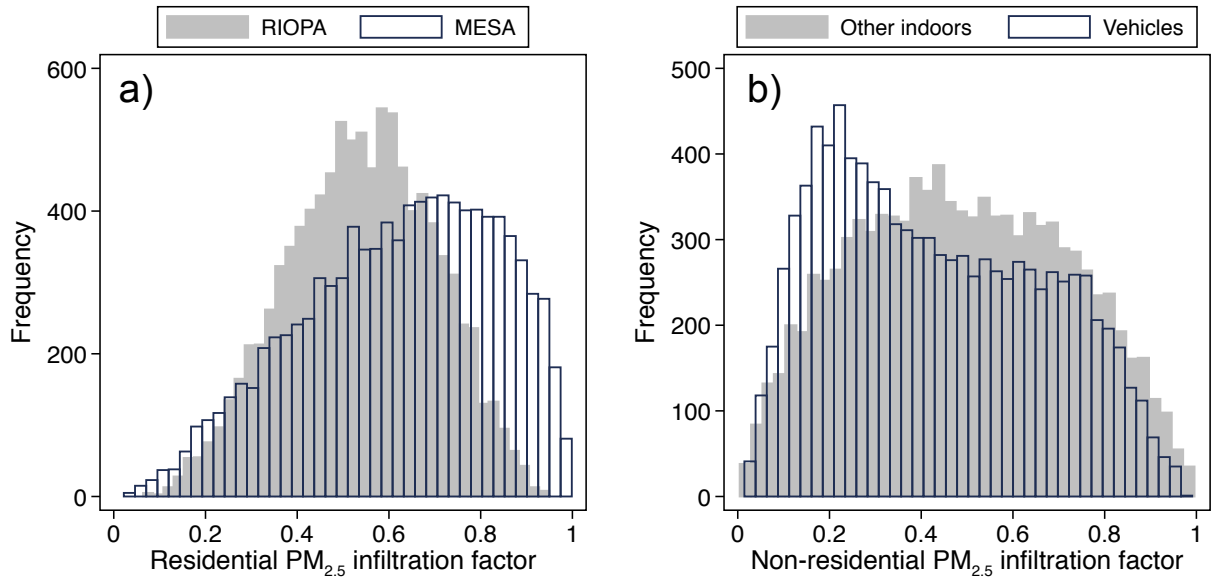

Figure S1. Beta distributions of $PM_{2.5}$ infiltration factors used in Scenario 1: a) two residential distributions (RIOPA and MESA) and b) other indoor environments and vehicles (which were also used in Scenario 2). Distribution shape factors are described in the SI text.

Tables

Table S1. Summary of stair-step distribution characteristics for the amount of time spent in various microenvironments based on Figure 3 in Klepeis et al. (2001), used in all model scenarios

	Residences		Vehicles		Outdoors		Other indoor locations	
	Reported	Modeled	Reported	Modeled	Reported	Modeled	Reported	Modeled
Average (min)	990	978	79	59	109	98	262	305
Bin #	Range (min)	Prob.	Range (min)	Prob.	Range (min)	Prob.	Range (min)	Prob.
1	0-50	0.0085	0-60	0.6475	0-60	0.5564	Back-calculated	Back-calculated
2	50-100	0.0028	60-120	0.0965	60-120	0.2700		
3	100-150	0.0028	120-180	0.0727	120-180	0.1080		
4	150-200	0.0038	180-240	0.0441	180-240	0.0240		
5	200-250	0.0038	240-300	0.0330	240-300	0.0120		
6	250-300	0.0038	300-360	0.0240	300-360	0.0090		
7	300-350	0.0038	360-420	0.0240	360-420	0.0054		
8	350-400	0.0058	420-480	0.0120	420-480	0.0054		
9	400-450	0.0068	480-540	0.0120	480-540	0.0025		
10	450-500	0.0125	540-600	0.0120	540-600	0.0025		
11	500-550	0.0125	600-660	0.0090	600-660	0.0025		
12	550-600	0.0200	660-720	0.0048	660-720	0.0025		
13	600-650	0.0300	720-780	0.0030	720-780	0.0000		
14	650-700	0.0400	780-840	0.0018	780-840	0.0000		
15	700-750	0.0500	840-900	0.0018	840-900	0.0000		
16	750-800	0.0655	900-960	0.0018	900-960	0.0000		
17	800-850	0.0655	960-1020	0.0000	960-1020	0.0000		
18	850-900	0.0675	1020-1080	0.0000	1020-1080	0.0000		
19	900-950	0.0615	1080-1140	0.0000	1080-1140	0.0000		
20	950-1000	0.0500	1140-1200	0.0000	1140-1200	0.0000		
21	1000-1050	0.0450	1200-1260	0.0000	1200-1260	0.0000		
22	1050-1100	0.0496	1260-1320	0.0000	1260-1320	0.0000		
23	1100-1150	0.0450	1320-1380	0.0000	1320-1380	0.0000		
24	1150-1200	0.0475	1380-1440	0.0000	1380-1440	0.0000		
25	1200-1250	0.0447						
26	1250-1300	0.0466						
27	1300-1350	0.0418						
28	1350-1400	0.0428						
29	1400-1440	0.1205						

Table S2. Summary of distributions of residential indoor and outdoor $PM_{2.5}$ concentrations, $PM_{2.5}$ infiltration factors, and indoor $PM_{2.5}$ concentrations attributable to outdoor sources in the RIOPA and MESA Air studies that were used to fit distributions to the indoor $PM_{2.5}$ concentrations that result from indoor sources in Scenario 1

Study	Reference	Model Parameter	Distribution Type	Mean ± SD ($\mu g/m^3$)*
RIOPA	Meng et al. (2005)[32]	Indoor $PM_{2.5}$ concentration	Lognormal	GM: 15.6 GSD: 1.7
		Outdoor $PM_{2.5}$ concentration	Lognormal	GM: 14.3 GSD: 1.9
	Meng et al. (2005)[33]	$PM_{2.5}$ infiltration factor	Beta	0.54 ± 0.16
	Calculated	Indoor $PM_{2.5}$ concentration attributable to indoor sources	n/a	8.7 ± 11.8
MESA Air	Allen et al. (2012)[34]	Indoor $PM_{2.5}$ concentration (cold season)	n/a	10.4 ± 7.0
		Indoor $PM_{2.5}$ concentration (warm season)	n/a	12.8 ± 5.6
		Outdoor $PM_{2.5}$ concentration (cold season)	n/a	13.5 ± 5.8
		Outdoor $PM_{2.5}$ concentration (warm season)	n/a	15.8 ± 3.9
		Indoor $PM_{2.5}$ concentration attributable to indoor sources (cold season)	n/a	2.8 ± 4.8
		Indoor $PM_{2.5}$ concentration attributable to indoor sources (warm season)	n/a	2.7 ± 4.0
		$PM_{2.5}$ infiltration factor	Beta	0.62 ± 0.21
	Calculated	Indoor $PM_{2.5}$ concentration attributable to indoor sources (combined seasons)	Lognormal	GM: 1.5 GSD: 3.1

*For lognormal distributions, GM = geometric mean and GSD = geometric standard deviation.
n/a = values reported in the cited references but not used directly in the model application.

Table S3. Summary of the IER model input parameters used herein for adults 35 years and older. Data taken from the CDC WONDER system.[43]

Cause of Mortality	Age ranges	Population in 2012	Average disease incidence (y_0)
COPD	+ 35	166,516,716	0.000840
Lung Cancer	+ 35	166,516,716	0.000948
IHD	35 - 39	19,488,199	0.000082
	40 - 44	21,028,221	0.000171
	45 - 49	21,689,479	0.000354
	50 - 54	22,579,259	0.000631
	55 - 59	20,772,517	0.000996
	60 - 64	17,813,685	0.001517
	65 - 69	13,977,353	0.002159
	70 - 74	10,008,039	0.003260
	75 - 79	7,489,583	0.005340
	+ 80	11,670,381	0.016506
Stroke	35 – 39	19,488,199	0.000029
	40 – 44	21,028,221	0.000053
	45 – 49	21,689,479	0.000097
	50 – 54	22,579,259	0.000146
	55 – 59	20,772,517	0.000219
	60 – 64	17,813,685	0.000334
	65 – 69	13,977,353	0.000523
	70 – 74	10,008,039	0.000961
	75 – 79	7,489,583	0.001789
	+ 80	11,670,381	0.005845

Table S4. Mean, standard deviation (SD), and interquartile range (IQR: 25th to 75th percentiles) of the estimated contributions to total $PM_{2.5}$ exposures resulting from IER and E-R models with unmodified effect estimates and a threshold concentration of 5.8 µg/m³ for the U.S. population 35 years and older in 2012.

Applied Model	Outdoor or Indoor Sources	Microenvironment	Mean fraction of total $PM_{2.5}$ exposure ± SD	IQR of fraction of total $PM_{2.5}$ exposure	Mean estimate of annual deaths attributed to total $PM_{2.5}$ exposure ± SD	IQR of estimate of annual deaths attributed to total $PM_{2.5}$ exposure
Unmodified IER model	Due to $PM_{2.5}$ of outdoor origin	Residences	41.9% ± 24.1%	21.9% - 58.7%	16,089 ± 9,244	8,410 - 22,545
		Other indoor locations	10.8% ± 12.8%	0.0% - 16.8%	4,144 ± 4,928	0 - 6,460
		Vehicles	2.4% ± 4.0%	0.3% - 2.7%	916 ± 1,524	120 - 1,023
		Outdoor	7.4% ± 11.3%	1.7% - 6.9%	2,840 ± 4,355	667 - 2,649
	Total outdoor contribution		62.5% ± 25.4%		23,989 ± 9,756	9,196 - 32,677
	Due to $PM_{2.5}$ of indoor origin	Residences	28.2% ± 26.5%	5.2% - 47.9%	10,838 ± 10,159	2,011 - 18,397
		Other indoor locations	9.3% ± 13.0%	0.0% - 13.0%	3,554 ± 4,991	0 - 5,002
	Total indoor contribution		37.5% ± 25.4%		14,393 ± 9,756	2,011 - 23,398
	Total contribution		100%		38,382*	11,208 - 56,075
Unmodified E-R model (β = 0.0070 per µg/m³)	Due to $PM_{2.5}$ of outdoor origin	Residences	42.0% ± 24.0%	22.3% - 58.8%	17,903 ± 10,231	9,526 - 25,049
		Other indoor locations	10.9% ± 13.0%	0.0% - 16.8%	4,648 ± 5,534	0 - 7,144
		Vehicles	2.4% ± 4.0%	0.3% - 2.7%	1,029 ± 1,710	130 - 1,164
		Outdoor	7.2% ± 11.2%	1.7% - 6.4%	3,052 ± 4,762	745 - 2,738
	Total outdoor contribution		62.5% ± 25.3%		26,632 ± 10,766	10,401 - 36,096
	Due to $PM_{2.5}$ of indoor origin	Residences	28.3% ± 26.5%	5.1% - 48.2%	12,054 ± 11,290	2,193 - 20,546
		Other indoor locations	9.2% ± 13.0%	0.0% - 12.7%	3,937 ± 5,532	0 - 5,395
	Total indoor contribution		37.5% ± 25.3%		15,991 ± 10,766	2,193 - 25,940

	Total contribution		100%		42,623*	12,594 - 62,036
Unmodified E-R model (β = 0.0058 per µg/m³)	Due to $PM_{2.5}$ of outdoor origin	Residences	41.9% ± 23.8%	22.6% - 58.6%	15,097 ± 8,590	8,155 - 21,118
		Other indoor locations	10.9% ± 12.9%	0.1% - 17.0%	3,921 ± 4,644	22 - 6,131
		Vehicles	2.3% ± 3.7%	0.3% - 2.7%	844 ± 1,346	126 - 979
		Outdoor	7.5% ± 11.5%	1.8% - 7.0%	2,688 ± 4,128	640 - 2,535
	Total outdoor contribution		62.6% ± 25.2%		22,550 ± 9,079	8,942 - 30,763
	Due to $PM_{2.5}$ of indoor origin	Residences	28.1% ± 26.3%	5.2% - 48.2%	10,108 ± 9,479	1,860 - 17,359
		Other indoor locations	9.4% ± 13.0%	0.0% - 13.2%	3,371 ± 4,669	13 - 4,755
	Total indoor contribution		37.4% ± 25.2%		13,478 ± 9,079	1,873 - 22,114
	Total contribution		100%		36,028*	10,815 - 52,877

* The estimates of total contributions are based on the median values.