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Modeling Individual Exposures to Ambient PM_{2.5} in the Diabetes and the Environment Panel Study (DEPS)

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Abstract

Air pollution epidemiology studies of ambient fine particulate matter (PM_{2.5}) often use outdoor concentrations as exposure surrogates, which can induce exposure error. The goal of this study was to improve ambient PM_{2.5} exposure assessments for a repeated measurements study with 22 diabetic individuals in central North Carolina called the Diabetes and Environment Panel Study (DEPS) by applying the Exposure Model for Individuals (EMI), which predicts five tiers of individual-level exposure metrics for ambient PM_{2.5} using outdoor concentrations, questionnaires, weather, and time-location information. Using EMI, we linked a mechanistic air exchange rate (AER) model to a mass-balance PM_{2.5} infiltration model to predict residential AER (Tier 1), infiltration factors ($F_{\text{inf\_home}}$, Tier 2), indoor concentrations (C_{in} , Tier 3), personal exposure factors (F_{pex} , Tier 4), and personal exposures (E , Tier 5) for ambient PM_{2.5}. We applied EMI to predict daily PM_{2.5} exposure metrics (Tiers 1–5) for 174 participant-days across the 13 months of DEPS. Individual model predictions were compared to a subset of daily measurements of F_{pex} and E (Tiers 4–5) from the DEPS participants. Model-predicted F_{pex} and E corresponded well to daily measurements with a median difference of 14% and 23%; respectively. Daily model predictions for all 174 days showed considerable temporal and house-to-house variability of AER, $F_{\text{inf\_home}}$, and C_{in} (Tiers 1–3), and person-to-person variability of F_{pex} and E (Tiers 4–5). Our study demonstrates the capability of predicting individual-level ambient PM_{2.5} exposure metrics for an epidemiological study, in support of improving risk estimation.

Keywords

air pollution; exposure modeling; particulate matter; building infiltration modeling

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Appendix A. Supplementary material
There is supplementary material for this article.

1. Introduction

Epidemiologic studies have reported associations between ambient (i.e., outdoor-generated) fine particulate matter (PM_{2.5}; particulate matter 2.5 µm in aerodynamic diameter) and various indices of acute cardiopulmonary morbidity and mortality (U.S. EPA, 2009). Due to cost and participant burden of indoor and personal air pollution monitoring, most of these studies used outdoor PM_{2.5} concentrations as exposure surrogates. However, these exposure surrogates do not account for (1) time spent indoors with ambient PM_{2.5} levels attenuated from outdoor concentrations, and (2) building-to-building and temporal variability of this attenuation. Differences between exposure surrogates, such as outdoor concentrations, and true exposures contribute to exposure measurement errors. Depending on epidemiological study design, these errors can add bias or uncertainty to health effect estimates, which was highlighted in two National Research Council reports: “Exposure Science in the 21st Century: A Vision and a Strategy” (NRC, 2012) and “Research Priorities for Airborne Particulate Matter” (NRC, 2004), and two National Academies of Sciences reports: “Health Risks of Indoor Exposure to Particulate Matter” (NAS, 2016) and “Using 21st Century Science to Improve Risk-Related Evaluations” (NAS, 2017). To help reduce measurement errors and improve PM_{2.5} health effect estimation, we developed the Exposure Model for Individuals (EMI), which addresses the recommendations of these reports (Breen et al., 2015). This study describes the application of EMI for ambient PM_{2.5} in the Diabetes and the Environment Panel Study (DEPS; Schneider et al., 2008).

The goal of DEPS is to examine ambient PM_{2.5} exposures and cardiovascular and hematologic effects in adults with type 2 diabetes living in central North Carolina (NC). Using PM_{2.5} measurements from two fixed-site air monitors, significant associations were previously found between daily ambient PM_{2.5} concentrations and various acute (maximum lag of 4 days) adverse effects: (1) altered endothelial function, (2) increased blood levels of interleukin-6 and tumor necrosis factor-α, (3) changes in indicators of cardiac repolarization, and (4) upregulated expression of receptors on circulating monocytes (Schneider et al., 2008, 2010, 2011). In this study, we applied EMI for a subsequent epidemiological analysis to address the possible limitation of using PM_{2.5} concentrations from fixed-site monitors as exposure surrogates in DEPS.

The EMI predicts individual-level exposure metrics for actual participants in epidemiological studies using outdoor concentrations, weather (e.g., temperature, wind speed), questionnaires (e.g., building characteristics), and time-location data (Breen et al., 2015). In this study, we predict five tiers of ambient PM_{2.5} exposure metrics for each health study participant in DEPS (Figure 1). We previously described the development of these five tiers of exposure metrics for ambient PM_{2.5} (Breen et al., 2015). Briefly, EMI includes three exposure metrics related to PM_{2.5} infiltration into homes (Tier 1: air exchange rate (AER), Tier 2: infiltration factors, Tier 3: indoor concentrations) and two exposure metrics that account for time spent in different indoor and outdoor locations (Tier 4: personal exposure factors, Tier 5: exposures). The importance of these five tiers of exposure metrics for epidemiological studies was highlighted in the National Academy of Sciences Report “Health Risks of Indoor Exposure to Particulate Matter” (NAS, 2016), and demonstrated in

epidemiological studies that applied population-level exposure metrics (Hodas et al., 2013; Sarnat et al., 2013; Jones et al., 2013; Mannshardt et al., 2013).

Our overall goal is to calibrate and evaluate EMI with extensive exposure data from field studies to reduce model uncertainty, and then apply EMI for epidemiological studies with limited exposure data. Therefore, we previously performed a cross-validation of EMI (Breen et al., 2010, 2015). We used measurement data from the Research Triangle Park Particulate Matter Panel Study (PM Panel Study) to evaluate the five tiers of exposure metrics for ambient PM_{2.5}. The PM Panel Study represents various residential AER and infiltration factors, outdoor and indoor concentrations, and personal exposures for 31 participants for seven consecutive days in each of four consecutive seasons for the same region of central NC as DEPS.

In this paper, we develop ambient PM_{2.5} exposure metrics for DEPS. We used housing characteristics, time-location diaries, and weather data as inputs for EMI, and measurements of ambient PM_{2.5} personal exposure factors from DEPS participants for model evaluation. We first describe the DEPS design, and then describe EMI, the method for model evaluation, and the development of daily predictions of five tiers of exposure metrics for each study participant.

2. Materials and methods

2.1 DEPS design

The DEPS was designed to examine the relationship between exposures to ambient PM_{2.5} and various indices of acute cardiovascular and hematologic effects in a cohort of adults with diabetes. Previous publications describe the study design, clinical measurements, and air pollution measurements from two fixed-site ambient PM_{2.5} monitors (Schneider et al., 2008, 2010, 2011). Briefly, the study included 22 non-smoking adult participants with type 2 diabetes living in central NC. Each participant visited the U.S. Environmental Protection Agency (EPA) Human Studies Facility (HSF) in Chapel Hill, NC at 9 am ($\pm$ 1.5 h) on 5 consecutive weekdays between November 2004 and December 2005. Various clinical measurements were collected at baseline and during four follow-up visits to yield a total of 88 participant-days of data. All volunteers signed a written consent form and the study protocol was approved by the University of North Carolina Human Studies Biomedical Institutional Review Board and the EPA.

For fixed-site air pollution monitoring, we used daily concentrations of ambient PM_{2.5} mass (24-h average, midnight - midnight) from an official network monitoring station located approximately 44 km (27 miles) east of the HSF. We also measured daily concentrations of ambient PM_{2.5} mass (24-h average, 9 am - 9 am) with a 3000K Versatile Air Pollution Sampler (URG Corp., Chapel Hill, NC, USA) (Williams et al., 2000) located on the HSF rooftop (30 m elevation).

For model evaluation of EMI, we measured daily PM_{2.5} mass concentrations (24-h average, 9 am - 9 am) with two personal exposure monitors (PEM) operating at 2 L/min (Williams et al., 2003, 2009). One PEM was worn by the participant, and another PEM was located on

the HSF rooftop. Personal monitoring was conducted with a nylon vest (Williams et al., 2003, 2009). The vest provided a means to securely and reproducibly position the air inlet in the breathing zone of the participant and allowed safe freedom of movement for normal daily activities. No restrictions were placed on participants as related to their activities. Sulfate concentrations (tracer of ambient $PM_{2.5}$ mass) for the PEM filters were determined using X-ray fluorescence (Wallace et al., 2005). These sulfate measurements were used for model evaluation, as described below.

Input data for EMI were obtained for weather, home building characteristics, and participant time-activities. Outdoor temperatures and wind speeds (10 m elevation) were obtained from local airport measurements. Daily questionnaires were used to collect occupant behavior related to building operation, including opening windows. Daily time-location diaries were used to determine duration that participants spent in seven microenvironments (indoors: home, work, other locations; outdoors: home, work, other locations; inside vehicles).

2.2 Tiers of exposure metrics

Using EMI, we modeled five tiers of daily exposure metrics for $PM_{2.5}$ for the 22 study participants and their homes (Figure 1). The five tiers, which have increasing levels of complexity and information needs, include: (Tier 1) residential air exchange rates, (Tier 2) residential infiltration factors, (Tier 3) residential indoor concentrations, (Tier 4) personal exposure factors, (Tier 5) personal exposures. For each participant, 24-h average exposure metrics were modeled on the four consecutive days with clinical measurements, and on the four days before clinical visits to yield a total of 176 participant-days. Two sets of daily 24-h averages were modeled (9 a.m. to 9 a.m., midnight to midnight), and time-matched to the daily measurements from the two fixed-site ambient $PM_{2.5}$ monitors. We also measured two tiers of exposure metrics (Tiers 4–5) based on 24-h average monitor data, which were time-matched (9 a.m. to 9 a.m.) to the equivalent modeled exposure metric. The modeling and subsequent analysis were implemented using MATLAB software (version R2015a, Mathworks, Natick, MA, USA).

2.3 Modeled exposure metrics for Tiers 1–5

For Tier 1, residential AER were predicted from questionnaires and meteorology using two different models: Lawrence Berkeley Laboratory model (LBL) and the extended LBL model (LBLX) (Breen et al., 2010). These AER models are mechanistic by accounting for the physical driving forces of the airflows (i.e., pressure differences across building envelope from indoor-outdoor temperature differences, called the stack effect, and wind). Both models include leakage airflow through unintentional openings in a building envelope (e.g., cracks around window, doors), whereas the LBLX model also includes natural ventilation through controlled openings in the building envelope (e.g., open windows). We developed separate exposure metrics using these two AER models to evaluate the potential benefit of including natural ventilation for epidemiological studies.

These AER models were previously described and evaluated for homes in the same region of central NC as DEPS (Breen et al., 2010). Briefly, the leakage airflow is defined as

$$Q_{\text{LBL}} = A_{\text{leak}} \sqrt{k_s |T_{\text{in}} - T_{\text{out}}| + k_w U^2} \quad [1]$$

where A_{leak} is the effective air leakage area, k_s is the stack coefficient, k_w is the wind coefficient, T_{in} and T_{out} are the average indoor and outdoor temperatures, respectively, and U is the average wind speed (see Supplementary Material). The AER is calculated as Q_{LBL} divided by the building volume V .

We used the LBLX model to account for natural ventilation airflow on days when participants opened windows (Breen et al., 2010). The days with open windows were determined from daily questionnaires collected on four consecutive days. If a participant reported open windows for 2–4 days, we assumed open windows for the four days before diaries were collected (lag days for the subsequent health outcome analysis).

For the LBLX model, the airflow is defined as:

$$Q_{\text{LBLX}} = \sqrt{Q_{\text{LBL}}^2 + Q_{\text{nat}}^2} \quad [2]$$

where Q_{LBL} is the leakage airflow as defined above, and Q_{nat} is the natural ventilation airflow through open windows (see Supplementary Material). The AER is calculated as Q_{LBLX} divided by V .

For Tier 2, residential $\text{PM}_{2.5}$ infiltration factors ($\hat{F}_{\text{inf\_home}}$) were predicted with a steady-state mass balance infiltration model described by

$$\hat{F}_{\text{inf\_home}} = P \text{ AER} / (\text{AER} + k_r) \quad [3]$$

where P is the penetration coefficient (dimensionless), and k_r is the indoor removal rate of $\text{PM}_{2.5}$ (h^{-1}) (Breen et al., 2010). The P and k_r were estimated by Breen et al. (2010) in the PM Panel Study from homes in the same region of NC as DEPS ($P = 0.84$, $k_r = 0.21 \text{h}^{-1}$).

For Tier 3, residential indoor concentrations of ambient $\text{PM}_{2.5}$ ($\hat{C}_{\text{in,rooftop}}$ and $\hat{C}_{\text{in,central}}$) were predicted from measured outdoor concentrations from the HSF rooftop ($C_{\text{out,rooftop}}$) and the central-site official network ($C_{\text{out,central}}$) based on the steady-state equations (Breen et al. 2015; Wallace et al., 2005)

$$\hat{C}_{\text{in,rooftop}} = \hat{F}_{\text{inf\_home}} C_{\text{out,rooftop}} \quad [4]$$

$$\hat{C}_{\text{in,central}} = \hat{F}_{\text{inf\_home}} C_{\text{out,central}} \quad [5]$$

We predicted separate residential indoor concentrations using $C_{\text{out\_rooftop}}$ and $C_{\text{out\_central}}$ to evaluate the potential benefit of applying outdoor concentrations from the HSF rooftop as compared to the central-site for a future DEPS health analysis.

For Tier 4, personal exposure factors of ambient $\text{PM}_{2.5}$ were predicted as defined by

$$\hat{F}_{\text{pex}} = f_{\text{in\_home}} \hat{F}_{\text{inf\_home}} + (f_{\text{in\_work}} + f_{\text{in\_other}}) \hat{F}_{\text{inf\_home\_bldg}} + f_{\text{in\_vehicle}} \hat{F}_{\text{inf\_vehicle}} + [6] \\ (f_{\text{out\_home}} + f_{\text{out\_work}} + f_{\text{out\_other}})$$

where f is the fraction of time spent in the seven microenvironments (indoors and outdoors at home, work, other; inside vehicles), which were determined from each participant's daily time-activity diary collected on four consecutive days. For the four days before diaries were collected (lag days), we set each participant's time spent in the seven microenvironments to the median across the four days with diaries. The $\hat{F}_{\text{inf\_home\_bldg}}$ and $\hat{F}_{\text{inf\_vehicle}}$ are the $\text{PM}_{2.5}$ infiltration factors for buildings other than homes and for vehicles, respectively. We set $\hat{F}_{\text{inf\_other\_bldg}}$ to 0.64 based on the average of three literature-reported $\text{PM}_{2.5}$ infiltration factors for offices, stores, and restaurants (Burke et al., 2001). We set $\hat{F}_{\text{inf\_vehicle}}$ to 0.44 based on the literature-reported $\text{PM}_{2.5}$ infiltration factor for cars (Ott et al., 2008).

For Tier 5, we predicted personal exposures to ambient $\text{PM}_{2.5}$ from $C_{\text{out\_rooftop}}$ and $C_{\text{out\_central}}$ as defined by (Breen et al., 2015; Wallace et al., 2005)

$$\hat{E}_{\text{rooftop}} = \hat{F}_{\text{pex}} C_{\text{out\_rooftop}} \quad [7]$$

$$\hat{E}_{\text{central}} = \hat{F}_{\text{pex}} C_{\text{out\_central}} \quad [8]$$

We predicted separate personal exposures using $C_{\text{out\_rooftop}}$ and $C_{\text{out\_central}}$ to evaluate the potential benefit of applying outdoor concentrations from the HSF rooftop as compared to the central-site for a future DEPS health analysis.

2.4 Measured exposure metrics for Tiers 4–5

For Tier 4, we determined personal exposure factors of ambient $\text{PM}_{2.5}$ as defined by (Wallace et al., 2005)

$$F_{\text{pex}} = S_{\text{personal}} / S_{\text{out\_rooftop}} \quad [9]$$

where S_{personal} and $S_{\text{out\_rooftop}}$ are the measured sulfate concentrations derived from the PEM filters worn by the participant and located on the HSF rooftop, respectively. The F_{pex} is the fraction of ambient $\text{PM}_{2.5}$ that an individual is exposed to. The F_{pex} accounts for indoor attenuation of ambient $\text{PM}_{2.5}$ and the participant's daily time within different indoor and

outdoor locations. Other studies have used personal/outdoor sulfate ratios to estimate personal exposure factors of ambient PM_{2.5} based on two assumptions: (1) no indoor sources of sulfate, and (2) physical behavior of sulfate is similar to other ambient PM_{2.5} components (Ebelt et al., 2005; Sarnat et al., 2002; Koutrakis et al., 1992). For the first assumption, studies show that few indoor sources exist (Koutrakis et al., 1992), and Wallace et al., (2005) verified this assumption for the NC homes in the PM Panel Study. In DEPS, measured F_{pex} was substantially >1 for one participant-day (1.33), which indicates a possible indoor source of sulfate (Wallace et al., 2005). Therefore, data for that participant-day was removed. For the second assumption, Sarnat et al. (2002) showed daily indoor/outdoor sulfate ratios compared closely to corresponding indoor/outdoor PM_{2.5} ratios, with no significant bias and a mean relative difference of 14%. For Tier 5, we determined personal exposures of ambient PM_{2.5} as defined by (Wallace et al., 2005)

$$E = F_{\text{pex}} C_{\text{out\_rooftop}} \quad [10]$$

2.5 Model evaluation for Tiers 4–5

To evaluate the model predictions for the Tiers 4–5, we calculated the difference ( ) and relative difference (e) as:

$$\varepsilon = 100 \left(\frac{\text{TIER}_{i,\text{pred}} - \text{TIER}_{i,\text{meas}}}{\text{TIER}_{i,\text{meas}}} \right) \quad [11]$$

$$\Delta = \text{TIER}_{i,\text{pred}} - \text{TIER}_{i,\text{meas}} \quad [12]$$

where $\text{TIER}_{i,\text{pred}}$ and $\text{TIER}_{i,\text{meas}}$ are the individual model predictions and measurements, respectively, for Tier i where $i = 4$ and 5. We also calculated the absolute values $|\varepsilon|$ and $|\Delta|$.

3. Results

For the model inputs, summary statistics are provided for the building characteristics of the homes, number of days windows were opened, weather, ambient PM_{2.5} concentrations, and time-location data (Supplementary Material, Tables S4–S7). Windows were opened on 21% of the study days. The median daily rooftop PM_{2.5} concentrations varied between 2.2 and 39.9 $\mu\text{g m}^{-3}$. The mean daily time spent by the participants was 90% indoors, 9% outdoors, and 1% inside vehicles.

3.1 Model evaluation

For the subset of days with measurements of Tier 4 and 5 exposure metrics, summary statistics are provided for measured F_{pex} and E_{rooftop} (Table 1). We had measurements for 21 participants (1 participant had missing data), which included 76 days for Tier 4 and 75 days (1 day had missing data) for Tier 5. The measured median (minimum-maximum) for F_{pex}

was 0.54 (0.33–1.05) and for E_{rooftop} was $7.1 \mu\text{g m}^{-3}$ (2.3–31.9 $\mu\text{g m}^{-3}$). These measurements are consistent with those previously reported in the PM Panel Study from participants in the same region of NC as DEPS, which measured F_{pex} from 0.16 to 1.03, and exposures from 1.7 to 35.6 $\mu\text{g m}^{-3}$. The lack of indoor sources of sulfate can be seen in the measured F_{pex} not exceeding one, except for one day close to one (1.05). Summary statistics are also provided for the modeled F_{pex} and E_{rooftop} (Table 1). Using the LBLX model, the modeled and measured F_{pex} had similar medians (25th–75th percentiles) of 0.59 (0.54–0.63) and 0.54 (0.45–0.66), respectively. The modeled and measured E_{rooftop} also had similar medians (25th–75th percentiles) of $7.4 \mu\text{g m}^{-3}$ (4.8–9.3 $\mu\text{g m}^{-3}$) and $7.1 \mu\text{g m}^{-3}$ (5.2–9.2 $\mu\text{g m}^{-3}$). Using the LBL model, the modeled F_{pex} and E_{rooftop} had slightly lower medians than using the LBLX model.

We compared daily individual modeled and measured Tier 4 and 5 (Figure 2; Supplementary Material, Tables S8–S11, Figures S1–S2). For Tier 4, F_{pex} had similar quartiles using the LBL and LBLX models with the same median $|e|$ of 14%, and same median $|b|$ of 0.08. Using the LBL and LBLX models, F_{pex} was generally overestimated with median e of 6% and 7%, respectively. For Tier 5, E_{rooftop} had similar quartiles using the LBL and LBLX models with the same median $|e|$ of 23%, and similar median $|b|$ of $1.5 \mu\text{g m}^{-3}$ and $1.6 \mu\text{g m}^{-3}$, respectively. Using the LBL and LBLX models, E_{rooftop} was generally overestimated with median e of 6% and 10%, respectively. These comparisons are consistent with those previously reported in the PM Panel Study, which showed median $|e|$ of 20% and 18% for F_{pex} , and 23% and 20% for exposures using the LBL and LBLX models, respectively.

3.2 Model predictions for DEPS

To apply EMI for DEPS, we modeled five tiers of daily exposure metrics for all 22 study participants and their homes. Model predictions for the two sets of daily 24-h averages (9 am – 9 am, midnight – midnight) are provided. Since the two sets of averages showed no substantial differences, we will describe the details of only the 9 am – 9 am averages, which are more closely time-matched to the daily health measurements. We modeled a total of 174 participant-days since the ambient $\text{PM}_{2.5}$ monitors had 2 days of missing data.

Summary statistics are provided for the overall distribution of the five tiers of model-predicted exposure metrics across the 174 days (Figures 3–4; Supplementary Material, Tables S12–S13). We first examined the exposure metrics related to the homes (Tiers 1–3). For Tier 1, the median AER (minimum–maximum) was 0.28 h^{-1} (0.06–0.64 h^{-1}) and 0.30 h^{-1} (0.06–0.72 h^{-1}) using the LBL and LBLX models, respectively. The median AER are slightly lower than those reported in the PM Panel Study, which showed median AER of 0.37 h^{-1} and 0.42 h^{-1} using the LBL and LBLX models, respectively. As compared to the PM Panel Study homes, the DEPS homes were generally newer and larger, and no households were low-income, which yield smaller leakage areas (Equation S2). Since the AER driving forces (i.e., indoor-outdoor temperature, wind speed) were similar in both studies, the lower AER in DEPS was primarily due to the tighter building envelopes.

For Tier 2, the median $F_{\text{inf\_home}}$ (minimum–maximum) was 0.48 (0.18–0.63) and 0.49 (0.18–0.65) using the LBL and LBLX models, respectively. These $F_{\text{inf\_home}}$ ranges correspond to 37–82% (LBL model) and 35–85% (LBLX model) lower indoor $\text{PM}_{2.5}$

concentrations than outdoors. The median $F_{\text{inf\_home}}$ are similar to those reported in the PM Panel Study, which showed median $F_{\text{inf\_home}}$ of 0.53 and 0.56 using the LBL and LBLX models, respectively. For Tier 3, the median $C_{\text{in,rooftop}}$ (minimum-maximum) was $5.8 \mu\text{g}/\text{m}^3$ ($1.4\text{--}16.7 \mu\text{g}/\text{m}^3$) and $5.9 \mu\text{g}/\text{m}^3$ ($1.4\text{--}17.8 \mu\text{g}/\text{m}^3$) using the LBL and LBLX models, respectively. As compared to the LBL model, the LBLX model had slightly higher median $C_{\text{in,rooftop}}$, which is consistent with the slightly higher median AER and $F_{\text{inf\_home}}$.

We then examined the overall distributions of the modeled exposure metrics related to personal exposure (Tiers 4–5). For Tier 4, the median F_{pex} (minimum-maximum) was 0.58 (0.41–0.69) for both the LBL and LBLX models, respectively. This F_{pex} range corresponds to 31–59% lower $\text{PM}_{2.5}$ exposures than outdoor concentrations. As compared to $F_{\text{inf\_home}}$, the median F_{pex} was slightly higher (i.e., lower attenuation of ambient $\text{PM}_{2.5}$) primarily due to time spent outdoors. The median F_{pex} are consistent to those reported in the PM Panel Study, which showed median F_{pex} of 0.58 and 0.60 using the LBL and LBLX models, respectively. For Tier 5, the median E_{rooftop} (minimum-maximum) was $7.0 \mu\text{g m}^3$ ($1.5\text{--}23.7 \mu\text{g}/\text{m}^3$) and $7.3 \mu\text{g m}^3$ ($1.5\text{--}25.1 \mu\text{g}/\text{m}^3$) using the LBL and LBLX models, respectively. As compared to $C_{\text{in,rooftop}}$, E_{rooftop} is slightly higher since modeled F_{pex} tends to be larger than $F_{\text{inf\_home}}$, which is consistent with the PM Panel Study.

We compared the daily variability of the modeled exposure metrics for individual homes (Tiers 1–3) and participants (Tier 4–5) (Figures 3–4). For Tier 1, the temporal AER variability (maximum-minimum) within homes was between 0.04 and 0.51 h^{-1} for both the LBL and LBLX models. This substantial temporal variability, along with the substantial house-to-house variability, was due to variations of wind speed, indoor-outdoor temperature differences, and open windows. The house-to-house variability was also due to building leakage area differences. For the six homes with open windows (3, 4, 6, 9, 11, 18), the AER median and temporal variability were larger using the LBLX model than the LBL model.

For Tier 2, the temporal $F_{\text{inf\_home}}$ variability within homes was between 0.04 and 0.31 for both the LBL and LBLX models. In plots of the homes ranked by median AER and $F_{\text{inf\_home}}$ (Figures 3–4), homes with smaller and larger median AER tend to have smaller and larger median $F_{\text{inf\_home}}$, respectively. However, the order of a few homes did not match due to the nonlinear relationship between AER and $F_{\text{inf\_home}}$ (Equation 3).

For Tier 4, the temporal F_{pex} variability within participants was smaller than $F_{\text{inf\_home}}$. This decrease in temporal variability is primarily due to time spent in microenvironments other than indoors at home, which have constant infiltration factors. In plots of the participants ranked by median F_{pex} and homes ranked by median $F_{\text{inf\_home}}$, the order of most subjects and their corresponding homes did not closely match due to variations in time spent in microenvironments with different infiltration factors.

For Tier 5, the temporal E_{rooftop} variability within subjects was larger than $C_{\text{in,rooftop}}$ for both LBL and LBLX models. When a range of outdoor concentrations are multiplied by an attenuation factor (Equations 4, 7) that can vary between 0 and 1, the resulting range of concentrations will vary between 0 and 100% of the outdoor concentration range,

respectively. Therefore, the temporal variability of $E_{\text{rooftop}} > C_{\text{in\_rooftop}}$ is primarily due to typical values of $F_{\text{pex}} > F_{\text{inf\_home}}$.

We compared the seasonal variability of the modeled exposure metrics for individual homes (Tiers 1–2) and participants (Tier 4) (Figure 5). For Tier 1, the median AER was lowest and highest in the summer and winter, respectively, for both the LBL and LBLX models. This corresponds with the median indoor-outdoor temperature difference, which was lowest and highest in the summer and winter, respectively. The median wind speeds and home leakage areas had no substantial variability between seasons. The median AER for each season was slightly higher using the LBLX model as compared to the LBL model, which is due to windows opened in each season.

For Tier 2, the median $F_{\text{inf\_home}}$ was lowest in the summer and highest in the winter, which is consistent with the median AER. For Tier 4, the median F_{pex} were similar for each season with only a small variation between 0.56 and 0.60. The seasonal increase between the median F_{pex} and $F_{\text{inf\_home}}$ was lowest in winter and highest in summer. This is primarily due to the median fraction of time spent outdoors, which was lowest in winter and second highest in summer.

4. Discussion

Our goal was to predict daily ambient $\text{PM}_{2.5}$ exposure metrics for each DEPS participant in support of improving health effect estimation for future epidemiological analysis. Using EMI, we performed an individual-level exposure assessment in DEPS that accounts for daily variations in ambient $\text{PM}_{2.5}$ exposures based on a mechanistic house-specific AER model linked to a mass-balance $\text{PM}_{2.5}$ infiltration model, infiltration factors for nonresidential buildings and vehicles, and comprehensive time-location data from each participant. We demonstrated the ability to calibrate and evaluate EMI using the PM Panel Study with extensive exposure data (Breen et al., 2015), and then apply EMI for DEPS with limited exposure data. The impact of applying EMI for an epidemiological study to improve health effect estimation will depend not only on the accuracy of the exposure assessment, but also other factors such as the health study design and the true exposure distributions (Szpiro et al., 2011, 2013). In support of optimizing the health study design, we predicted multiple tiers of exposure metrics with different levels of complexity and uncertainty, which will be used in the epidemiological analysis to help determine the benefit of more sophisticated exposure metrics.

The EMI can be applied for epidemiological studies with different size and duration. Besides DEPS, we are applying EMI for two other panel studies in central North Carolina with <30 participants across two years, a larger panel study in Detroit, Michigan with >140 children across three years (Breen et al., 2014a), and a long-term study across 10 years with >2300 participants with cardiovascular disease (Mirowsky et al., 2017). For large cohorts, daily house-specific AER and $F_{\text{inf\_home}}$ can be predicted from public property assessments and weather (Breen et al., 2014a), and time spent in different microenvironments can be determined from questionnaires (Kaufman et al., 2016) or global positioning system (GPS) data from smart phones (Breen et al., 2014b). To determine the home-specific building

characteristics needed for the AER model, a list of participant home addresses can be automatically matched to those in city or county property assessment databases.

An important and unique aspect of our exposure assessment for DEPS is the comprehensive evaluation of the exposure model predictions. We evaluated all five tiers of modeled exposure metrics with detailed measurements from an exposure substudy (PM Panel Study) in the same geographic location and housing stock as DEPS (Breen et al. 2015), and evaluated F_{pex} and E_{rooftop} with measurements from the actual DEPS participants. The uncertainty determined for the modeled exposure metrics can be used in our future epidemiological analysis to assess, and possibly reduce, any uncertainty in the health effect estimates (Spiegelman et al., 2010, Szpiro et al., 2013).

We can compare our individual-level microenvironment exposure model to those used in other panel studies. Two previous epidemiological studies predicted individual-level ambient $\text{PM}_{2.5}$ exposures based on time spent in two microenvironments (indoors and outdoors) and used regression-based infiltration models for the homes (Kaufman et al., 2016; Koenig et al., 2005). Unlike the mechanistic AER models used by our mass balance infiltration model, these regression models are empirical and do not account for the driving forces of AER (stack and wind effects). Wu et al. predicted individual-level ambient $\text{PM}_{2.5}$ exposures for a children's health study based on time-spent indoors at home, school, and in-vehicle (Wu et al., 2005). For the homes, a mass balance infiltration model was linked to an empirical AER model, which did not consider the stack and wind effects. The in-vehicle concentration was set to a constant value based on measurements from other studies. The time spent in each microenvironment was based on demographics and measured population-level distributions from other studies. In our study, we predicted daily exposures based on a mass-balance infiltration model linked to a mechanistic house-specific AER model, infiltration factors for nonresidential buildings and vehicles, and daily participant-specific time spent in seven microenvironments.

A benefit of using EMI for epidemiology studies, such as DEPS, is that modeled exposure metrics are needed for ambient $\text{PM}_{2.5}$ panel studies to account for the building-to-building and temporal variability of AER and indoor attenuation of ambient $\text{PM}_{2.5}$. Since people spend most of their time indoors, the variability of indoor attenuation can be a substantial source of variability in exposures between individuals, including studies across regions with small spatial variations in outdoor $\text{PM}_{2.5}$ concentrations. The significant variability of indoor attenuation was highlighted in the National Academy of Sciences Report "Health Risks of Indoor Exposure to Particulate Matter" (NAS, 2016). The report states that indoor attenuation of ambient $\text{PM}_{2.5}$ for homes in United States and Canada can range from less than 10% to almost 100%, depending on the home characteristics, season, and location. Furthermore, when outdoor $\text{PM}_{2.5}$ concentration is used as an exposure surrogate in panel studies, the estimated health effect parameter can be biased towards the null since it is the product of the toxicity (i.e., true health effect) and indoor attenuation of ambient $\text{PM}_{2.5}$ (Sheppard et al., 2012). Accounting for indoor attenuation (i.e., $F_{\text{inf\_home}} \cdot F_{\text{pex}}$) in epidemiological studies should yield a more accurate health effect estimate (Koenig et al., 2005). For respiratory and cardiac outcomes, a cohort study found ambient $\text{PM}_{2.5}$ exposures

had significant associations with larger effect estimates than outdoor PM_{2.5} concentrations, which were not significant (Ebelt et al., 2005).

One limitation of this study is that EMI requires detailed time-location data to determine time spent outdoors and within different indoor microenvironments. In DEPS, we used daily questionnaires, which can have uncertainty and substantial participant burden. To improve this data collection process for other studies, particularly large long-term health studies, we previously developed a model, called MicroTrac, that uses GPS data to automatically determine time spent outdoors and within different indoor locations (in-vehicle, home, work, school, other) (Breen et al. 2014b).

Another limitation of this study is the exposure metrics do not include non-ambient PM_{2.5}. Wilson et al. showed the importance of separating ambient and non-ambient pollutant exposures (Wilson et al., 2000). These include: (1) the U.S. Environmental Protection Agency regulates only ambient pollutants, and (2) PM_{2.5} from ambient and non-ambient sources has different physical and chemical properties and temporal patterns, which can induce different health effects. A previous study found stronger associations between ambient PM_{2.5} and health effects than non-ambient PM_{2.5} (Ebelt et al., 2005). When we apply EMI for health studies, we plan to separately examine factors associated with non-ambient PM_{2.5} sources (e.g., environmental tobacco smoke) as categorical variables in the health models, which can remove potential uncertainties that can be introduced by including indoor sources in the exposure predictions.

Another potential limitation of this study is that our exposure model predicts ambient PM_{2.5} exposures based on two fixed-site PM_{2.5} monitors. In the PM Panel Study, we found no substantial difference between daily ambient PM_{2.5} exposures predicted from a fixed-site PM_{2.5} monitor and those predicted from PM_{2.5} monitors outside each participant's home (Breen et al., 2015). This is consistent with data from various U.S. cities that show PM_{2.5} concentrations are spatially homogeneous within cities, and that local sources have only limited influence (U.S. EPA, 2009). Unlike PM_{2.5} components that can substantial local spatial variations from nearby sources (e.g., black carbon near major roads with high diesel traffic; U.S. EPA, 2009), this study examined total PM_{2.5} mass for participants living within 45 km (28 miles) of the PM_{2.5} monitors, and there were no major local sources. These results strengthen our confidence that using a fixed-site monitor is sufficient to estimate PM_{2.5} exposures in the same region of central NC.

5. Conclusions

This study demonstrates the ability of applying EMI to predict five tiers of individual-level exposure metrics for the homes and participants in an epidemiological study. To improve exposure assessments in DEPS, EMI accounts for (1) daily house-specific infiltration of ambient PM_{2.5} and (2) daily participant-specific time spent outdoors, in-vehicles, and indoors at home and other buildings. This capability can help provide more accurate exposure estimates for epidemiological studies, such as DEPS, in support of improving health risk estimation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Conceptual model of EMI to predict five tiers of individual-level exposure metrics for ambient $PM_{2.5}$. Tiers 1–3 are related to homes (AER – air exchange rate, F_{inf_home} – infiltration factor, C_{in} – indoor concentration), and Tiers 4–5 (F_{pex} – personal exposure factor, E – personal exposure are related to participants).

Figure 2.

Comparison of differences $|z|$ and relative differences $|z|$ between individual model predictions and measurements for Tiers 4 and 5. Results are separated by two AER models (LBL, LBLX) used for mass balance infiltration model. Shown are medians with 25th and 75th percentiles.

Figure 3.

Model predictions for Tiers 1–5 using LBL model for home AER model. Results (24-h average, 9 am - 9 am) are sorted by median values from highest to lowest. Shown are medians with 25th and 75th percentiles, and whiskers for minimum and maximum values.

Figure 4.

Model predictions for Tiers 1–5 using LBLX model for home AER model. Results (24-h average, 9 am - 9 am) are sorted by median values from highest to lowest. Shown are medians with 25th and 75th percentiles, and whiskers for minimum and maximum values.

Figure 5. Model predictions using LBLX model for home AER model across four seasons for Tiers 1, 2, 4 (A-C), time spent outdoors (D), indoor-outdoor temperature difference (E), wind speed (F), home leakage area (G), and window opening (H). Results (24-h average, 9 am - 9 am) shown are medians, 25th and 75th percentiles, and whiskers for minimum and maximum values.

Table 1.

Summary statistics for subset of days with measured Tier 4 and 5 exposure metrics, and corresponding model predictions

Tier of Exposure Metrics ^a	Measured or Modeled (AER model) ^b	Number of participants	Sample size	Measurements (24-h average) ^c								
				Mean	SD	Min	p5	p25	p50	p75	p95	Max
Tier 4: F _{pex}	Measured	21	76	0.55	0.16	0.33	0.35	0.46	0.54	0.66	0.85	1.05
	Modeled (LBL)	21	76	0.57	0.06	0.43	0.47	0.53	0.57	0.61	0.65	0.67
	Modeled (LBLX)	21	76	0.58	0.06	0.43	0.48	0.53	0.59	0.63	0.67	0.69
Tier 5: E _{rooftop} (µg/m ³)	Measured	21	75	7.6	4.1	2.3	2.7	5.2	7.1	9.2	12.2	31.9
	Modeled (LBL)	21	75	8.2	4.6	2.5	3.2	4.8	7.3	9.3	17.7	25.8
	Modeled (LBLX)	21	75	8.3	4.7	2.5	3.2	4.8	7.4	9.3	18.3	25.8

^aF_{pex}: personal exposure factor (dimensionless), E_{rooftop}: personal PM_{2.5} exposure

^bAER model corresponds to LBL or LBLX model

^cSD corresponds to standard deviation, p5–p95 correspond to percentiles