



Indoor particulate matter and lung function in children

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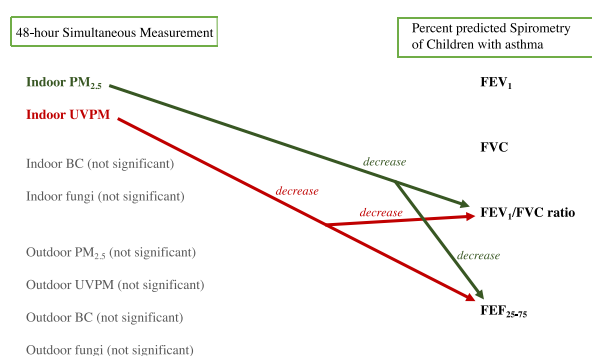
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HIGHLIGHTS

- Reduced lung function (FEV₁/FVC ratio and FEV_{25–75}) is more strongly associated with indoor particles than outdoor particles.
- Lung function is more strongly associated with UVP than PM_{2.5} or black carbon.
- Low levels of black carbon indoors (0.6 µg/m³) may not be associated with lung function.

GRAPHICAL ABSTRACT



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ABSTRACT

People generally spend more time indoors than outdoors resulting in a higher proportion of exposure to particulate matter (PM) occurring indoors. Consequently, indoor PM levels, in contrast to outdoor PM levels, may have a stronger relationship with lung function.

To test this hypothesis, indoor and outdoor PM_{2.5} and fungal spore data were simultaneously collected from the homes of forty-four asthmatic children aged 10–16 years. An optical absorption technique was utilized on the collected PM_{2.5} mass to obtain concentrations of black carbon (BC) and ultraviolet light absorbing particulate matter (UVP; a marker of light absorbing PM_{2.5} emitted from smoldering organics). Enrolled children completed spirometry after environmental measurements were made. Given the high correlation between PM_{2.5}, BC, and UVP, principal component analysis was used to obtain uncorrelated summaries of the measured PM. Separate linear mixed-effect models were developed to estimate the association between principal components of the PM variables and spirometry values, as well as the uncorrelated original PM variables and spirometry values.

A one-unit increase in the first principal component variable representing indoor PM (predominantly composed of UVP and PM_{2.5}) was associated with 4.1% decrease (99% CI = −6.9, −1.4) in FEV₁/FVC ratio. 11.3 µg/m³ increase in indoor UVP was associated with 6.4% and 14.7% decrease (99% CI = −10.4, −2.4 and 99% CI = −26.3, −2.9, respectively) in percent predicted FEV₁/FVC ratio and FEV_{25–75} respectively. Additionally, 17.7 µg/m³ increase in indoor PM_{2.5} was associated with 6.1% and 12.9% decrease (99% CI = −10.2, −1.9 and 99% CI = −24.9, −1.0, respectively) in percent predicted FEV₁/FVC ratio and FEV_{25–75}, respectively. Outdoor PM, indoor BC, and indoor fungal spores were not significantly associated with lung function.

The results indicate that indoor PM is more strongly associated with lung function in children with asthma as compared with outdoor PM.

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1. Introduction

While ambient air pollutants including particulate matter with aerodynamic diameter $<2.5\ \mu\text{m}$ ($\text{PM}_{2.5}$) have generally declined in the United States over the past decade (Chen et al., 2015), exposure to traffic-related air particles continue to be linked with respiratory health problems including reduced lung function, an indicator of respiratory health (Chen et al., 2015; Rice et al., 2013; Cotes et al., 2009). Elevated outdoor particulate matter (PM) levels are directly linked to a decrease in lung function in children (Gehring et al., 2013). Similarly, exposure to outdoor fungal spores is associated with an increased risk of hospital admissions and emergency department visits for asthma-related events in children (Atkinson et al., 2006). Approximately 28% of indoor $\text{PM}_{2.5}$ originate from outdoor sources (Habre et al., 2014a). This estimate can be 53–73% during low indoor activity (Kopperud et al., 2004), and is modified by particle penetration efficiency (Abt et al., 2000) and geographical location (Meng et al., 2005). Because indoor PM is composed of PM with indoor and outdoor origin, and people spend about 90% of their time indoors (Klepeis et al., 2001), a substantial proportion of exposure to PM may occur indoors. Consequently, indoor PM is likely to have a stronger association with lung function than outdoor PM.

The elemental components of $\text{PM}_{2.5}$ produced from indoor sources may differ from $\text{PM}_{2.5}$ of outdoor origin (Habre et al., 2014a). Analysis performed by Habre et al. suggests that the elemental carbon (EC) components of $\text{PM}_{2.5}$ from many indoor sources originate from smoldering combustion (Habre et al., 2014a), as found during cigarette smoking and using fireplaces. On the other hand, the EC components of $\text{PM}_{2.5}$ from outdoor sources originate mainly from internal-combustion engine exhaust soot (Habre et al., 2014a). Given that light absorbing particles are emitted both from smoldering combustion and internal-combustion engine exhaust, distinguishing between the associated health effects from exposure to these different $\text{PM}_{2.5}$ types is complex when light absorbance is measured with optical methods using a single wavelength. Many studies of light absorbing components of $\text{PM}_{2.5}$ have been based on concentrations of light absorbing particles measured with a single wavelength (Pan et al., 2018; Dons et al., 2012).

To obtain distinct measurements of airborne soot particles (black carbon, BC) and light absorbing $\text{PM}_{2.5}$ emitted from smoldering organics such as burning cigarettes, light absorbance measured continuously from 350 nm to 1000 nm have been used to distinguish between BC and cigarette smoke, respectively (Yan et al., 2011). We hypothesize that this technique can be utilized to obtain specific measurements of BC and cigarette smoke, and distinguish between the association of these PM types on lung function. Studying the association between UVP, BC, $\text{PM}_{2.5}$ and lung function will facilitate the understanding of safe indoor PM levels. Moreover, additional studies are needed to distinguish between the association of different combustion-related PM and respiratory health (World Health Organization, 2012). The objective of this study was two folds:

- (1) To differentiate between the association of BC and lung function, and ultraviolet light absorbing particulate matter, UVP and lung function.
- (2) To compare the magnitude of association between outdoor PM and lung function, and indoor PM and lung function.

2. Methods

2.1. Study overview

Between September 2015 to August 2017, 44 asthmatic children of 10–16 years old residing in 43 homes were recruited from an ongoing randomized intervention study conducted in the Cincinnati-Kentucky-Indiana tristate area (Cox et al., 2018). Subjects were recruited from

the Cincinnati Children's Hospital Medical Center Asthma Clinic and the Cincinnati Childhood Allergy and Air Pollution Study (LeMasters et al., 2006). A cross-over study design was used in the intervention study to test the efficiency of a portable high efficiency particulate air (HEPA) cleaner in reducing indoor particle concentrations (Fig. S1) (Cox et al., 2018). In the current study, since we are studying the association between indoor $\text{PM}_{2.5}$ mass (and its light-absorbing proportion) and lung function, only measurements conducted at the baseline (i.e., before the use of HEPA or placebo HEPA air cleaners) were used (Supplemental material 1.0).

The inclusion criteria in the intervention study were physician diagnosis of asthma and residing in a dwelling with an estimated outdoor level of $\geq 0.33\ \mu\text{g}/\text{m}^3$ elemental carbon attributable to traffic, as determined from an earlier study (Ryan et al., 2008). Spirometry tests were conducted on subjects, and indoor measurements of $\text{PM}_{2.5}$ mass and its light-absorbing proportion were made in the homes of subjects. Other factors including fungal spores (Atkinson et al., 2006), pet dander (Lowe et al., 2004), breathing/nasal medication use and socioeconomic status (Blanc et al., 2006; Demissie et al., 1996) that may potentially affect lung function were also quantified. The study received ethical approval from the University of Cincinnati Institutional Review Board.

2.2. Assessment of subject characteristics

Housing characteristics and occupant activities that could potentially modify the lung function of study participants were documented with a questionnaire administered to the parent (mother or father). The questions included the presence of pets (cats and dogs), the presence of at least one smoker residing in the home, breathing/nasal medication use within the last 72 h of spirometry, and annual household income as a surrogate for socioeconomic status. All responses were documented as categorical variables. Information on the frequency of subjects experiencing asthma symptoms were also collected via a questionnaire. A geographical information system (ArcGIS 9.0, Environmental Systems Research Institute, Inc., Redlands, CA) was used to calculate the distance of the study homes to the nearest highway or interstate (Ryan et al., 2008).

2.3. Assessment of environmental exposures

Two 48-h measurements of $\text{PM}_{2.5}$ and fungal spores were conducted outdoors and in the bedrooms (indoors) of 43 homes resided by the 44 study participants. The two measurements were spaced approximately 1-month apart from each other. $\text{PM}_{2.5}$ samples were collected on 37-mm Teflon filters with a single-stage Personal Modular Impactor (SKC, Inc., PA) that had an aerodynamic particle cut-off of $2.5\ \mu\text{m}$ at 3 L/min. For quality assurance, blank filter samples were deployed in parallel in 10% of $\text{PM}_{2.5}$ samples. Filter samples were analyzed gravimetrically and blank corrected (Zhang et al., 2017). Using an integrating sphere with absorption measured continuously from 350 nm to 1000 nm, reflectance analysis was carried out on the collected $\text{PM}_{2.5}$ mass to obtain concentrations of black carbon (BC) and ultraviolet light absorbing particulate matter, (UVP, second-hand cigarette smoke) (Yan et al., 2011). The limit of detection (LOD) for BC was $1.4\ \text{ng}/\text{mm}^2$ of the filter (Yan et al., 2011); equivalent to an air concentration of $0.12\ \mu\text{g}/\text{m}^3$ in this study. Furthermore, the LOD for UVP was $0.7\ \text{ng}/\text{mm}^2$ of the filter (Yan et al., 2011); equivalent to $0.18\ \mu\text{g}/\text{m}^3$ in this study (Yan et al., 2011). Non-detectable measurements of indoor and outdoor BC and UVP were replaced with LOD/2 as suggested by Hornung and Reed (Hornung and Reed, 1990).

Fungal spores were collected on 25-mm Teflon filters with 1- μm pore size (Merck Millipore, Billerica, MA) using a Button Inhalable Aerosol Sampler (SKC, Inc., PA) at 4 L/min. Utilizing mold specific quantitative PCR (MSQPCR) assays, 36 species were reported as spore equivalents (SE) per filter as described previously (Haugland and Vesper, 2002; Vesper et al., 2007; Haugland et al., 2002). Results for

each of the 36 species were summed per filter and then divided by the volume of air per sample yielding a concentration of summed MSQPCR-fungi in spore equivalents per cubic meter (SE/m³).

2.4. Assessment of lung function

Spirometry was conducted at the end of each 48-h PM measurement using a commercially available spirometer (KoKo Sx 1000, nSpire Health, Longmont, CO) following the American Thoracic Society Standards (ATS) (Crapo et al., 1995). Calibration check for the spirometer was performed with a 3 L syringe prior to each spirometry test. Volume verification was performed by discharging the 3 L syringe at three different flow rates varying between 0.5 and 12 L/s (analogous to the flow rate anticipated during subject testing). The observed volume at each flow rate was within the accuracy requirement of $\pm 3.5\%$ as recommended by ATS (Crapo et al., 1995). Because age, height, gender, and race explain >65% of the variability in lung function (Hankinson et al., 1999), percent predicted spirometry values were used ($100 \times \text{observed value/predicted value}$). Since study participants were 10–16 years old, spirometry predictive values were based on Wang et al. (1993) (standards for 6–18-year olds) versus Hankinson et al. (1999) (8–80-year olds). Height of subjects was measured by subject standing against the wall with socks on. Gender and racial data were obtained by parent report. Data on percent predicted forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), FEV₁/FVC ratio and forced expiratory flow between 25 and 75% of forced vital capacity (FEF_{25–75}) were collected as these are commonly used in clinical and research settings to monitor obstructive lung disease, such as asthma. The spirometer was programmed to interpret spirometer readings based on an algorithm provided by McKay and Lockey (1991).

2.5. Statistical analysis

Statistical analyses were performed with R statistical software (RStudio, 2016). To investigate the association between exposure to PM and percent predicted spirometry results, a linear mixed-effect model was utilized. Each subject and each home were assigned unique identifying numbers, and repeated measures were controlled for by having a unique intercept for each home and each subject, and the fixed effects of PM concentrations and other covariates on lung function were assessed. Because BC, and UVP are produced from incomplete combustion and contribute to PM_{2.5}, concentrations of these PM may be highly correlated.

To address collinearity in our exposure metrics, principal components of the PM variables were calculated after the investigation of high correlation between the PM variables. Because fungal spores were measured in spore equivalents per cubic meter (SE/m³) and other PM in $\mu\text{g}/\text{m}^3$, the variables were normalized in order to have measurements on the same scale before applying principal component analysis (PCA). The principal components of the normalized PM variables (fungal spores, PM_{2.5}, BC, and UVP) were calculated with the “stats” package in R statistical software, then used in the linear mixed-effect model (Eq. (S2)). Separate linear mixed-effect models for indoor and outdoor measurements were developed with the “lmerTest” package in R statistical software. The presence of pets in the home, breathing/nasal medication use and annual household income were added as covariates. Eq. (S2) shows the model for analyzing the association between the principal components of indoor PM and percent predicted spirometry results.

In addition to PCA, we also explored the independent association of PM_{2.5}, UVP, BC, fungal spores and lung function using the normalized PM variables in linear mixed models. The normalized PM variables were used so that the regression estimates obtained can be comparable to the regression estimates from the models containing principal components. In cases where the normalized PM variables were highly correlated (Spearman $r \geq 0.7$), only one of the correlated PM variables were

included in the same model. Different models for studying the same percent predicted spirometry value were developed. The regression model containing all the PM variables is given in Eq. (S3). For each spirometry variable there were 4 models developed using the PM variables as predictors of spirometry results. Therefore a Bonferroni correction was applied, and p values < 0.0125 ($0.05/4$) were considered statistically significant (equivalent to 99% CI).

Group comparisons of UVP and PM_{2.5} concentrations in the homes of smokers and non-smokers were performed with analysis of variance (ANOVA), followed by a Tukey's honestly significant difference (HSD) test to adjust for repeated measures with the “multcomp” package in R statistical software. Similarly, group comparisons of percent predicted spirometry results of subjects living in homes with and without smokers was performed. The Tukey's HSD test was used to determine the significant difference between each group.

3. Results

We had a total of 44 subjects in 43 homes. Fourteen PM samples were lost due to pump failures and sample contamination. Furthermore, one spirometry observation was invalid because it did not meet the ATS acceptability criteria for spirometry. Thus, repeat measurements were obtained from 28 homes and single observations from 15 homes, making a total of 71 paired observations of lung function and PM concentrations. Of these, two observations on breathing/nasal medication use (Yes/No) within the last 72 h were missing.

3.1. Study participants

Table 1 shows the characteristics of the study participants. All 44 participants were reported being non-smokers with a mean age of 12.3 years (Table 1). Study participants included 33.3% females. The majority of the subjects (78.7%) resided in non-smoking homes and 21.3% in homes that had at least one smoker present. Over half of the study participants had parents with annual incomes $> \$50,000$. Over 40% of the subjects reported experiencing asthma symptoms at most once per month within the last 12 months. The median distance of a study home to a highway or interstate was 374 m (Table 1). In 38.9% of the 69 visits that had observations on breathing/nasal medication use, subjects took at least one medication within the last 72 h. There were a variety of breathing/nasal medications taken; the most common was Albuterol (26%) (Fig. S2).

3.2. Summary of indoor and outdoor PM

The mean concentrations of indoor BC, indoor UVP, indoor PM_{2.5}, and indoor fungal spores were $0.6 \mu\text{g}/\text{m}^3$, $5.8 \mu\text{g}/\text{m}^3$, $14.6 \mu\text{g}/\text{m}^3$ and 420 spore equivalents per cubic meter (SE/m³), respectively (Table 2). There was a strong correlation between indoor UVP and indoor BC ($r = 0.72$) (Fig. 1A). Similarly, indoor PM_{2.5} and indoor BC ($r = 0.70$) as well as indoor UVP and indoor PM_{2.5} ($r = 0.80$) were strongly correlated (Fig. 1B and C). In contrast, indoor fungal spores were not correlated with PM_{2.5}, BC, and UVP (Fig. 1D–F).

The mean concentrations of outdoor BC, outdoor UVP, outdoor PM_{2.5}, and outdoor fungal spores were $0.9 \mu\text{g}/\text{m}^3$, $2.0 \mu\text{g}/\text{m}^3$, $13.0 \mu\text{g}/\text{m}^3$, and 3965 SE/m³, respectively (Table S1). Outdoor UVP and outdoor BC were weakly correlated ($r = 0.39$) (Fig. S3A). Conversely, outdoor PM_{2.5} and outdoor BC were strongly correlated ($r = 0.74$) (Fig. S3B). Without one influential observation, outdoor UVP and outdoor PM_{2.5} were also strongly correlated ($r = 0.80$) (Fig. S3C). Outdoor fungal spores were weakly correlated with PM_{2.5}, BC, and UVP (Fig. S3D–F).

Indoor and outdoor PM were not strongly correlated (Fig. S4) with the highest correlation observed between indoor and outdoor BC ($r = 0.49$). Fig. S5 shows the indoor/outdoor ratio of the measured PM from the 71 sampling periods. The median indoor/outdoor ratios for

Table 1
Subject Characteristics (n = 44).

	Mean (SD) or %
Age (years)	12.3 (2)
Sex (male)	66.7%
Smoking (No)	100.0%
Height (cm)	164.1 (38.1)
Weight (kg)	57.8 (16.8)
Caucasian	48.9%
African-American	36.2%
Hispanic	14.9%
Smoking parents or other home occupants	21.3%
Living with at least one dog/cat (Yes)	68.0%
>\$50,000 household income	51.1%
>\$40,000–\$50,000 household income	2.1%
>\$30,000–\$40,000 household income	10.6%
>\$20,000–\$30,000 household income	10.6%
>\$10,000–\$20,000 household income	12.8%
<\$10,000 household income	12.8%
Subject experience of asthma symptoms/hospitalization due to asthma	
Never within the last 12 months	6.5%
Rarely (less than once a month)	34.8%
Sometimes (1–4 times a month)	47.8%
Often (more than once a week but not daily)	10.9%
Proximity of homes to road (highway or interstate)	Distance (m)
Minimum	26
First quartile (Q1)	135
Median	374
Mean	520
Third quartile (Q3)	504
Maximum	3867
SD	683

BC, UVPM, PM_{2.5} and fungal spores were 0.6, 0.9, 0.8 and 0.1, respectively. However, the indoor/outdoor ratios of UVPM and PM_{2.5} in the homes where a smoker resided were significantly higher than the levels in non-smoking homes (Fig. 2). In the homes where smokers resided, median indoor/outdoor ratio for UVPM, and PM_{2.5} were 6.9 and 3.5, respectively (Fig. 2). In contrast, in non-smoking homes, median indoor/outdoor ratio for UVPM and PM_{2.5} were 0.9 and 0.7, respectively.

The fractions of light absorbing PM (UVPM and BC) in the sampled PM_{2.5} mass were relatively low. The median BC and UVPM fractions of indoor PM_{2.5} mass were 0.04 and 0.23, respectively (Fig. S6A and B), and the non-light absorbing fraction was 0.73 (Fig. S6C). In the sampled outdoor PM_{2.5} mass, the median fractions of BC and UVPM were 0.10 and 0.23, respectively (Fig. S6D and E).

3.3. Principal components

The first three principal components (PC1–PC3) of indoor PM from the study homes explained 98% of the variation in the data (BC,

UVPM, PM_{2.5}, and fungal spores). PC1–PC3 were subsequently included as independent variables in the analysis of indoor PM and lung function. Similarly, the first three principal components of outdoor PM explained 86.2% of the variation in the data and were used in the regression models developed for the analysis of outdoor PM and lung function.

For the principal components derived for indoor PM, PC1 was predominantly made up of UVPM and PM_{2.5}; the linear weights of UVPM and PM_{2.5} were the highest in comparison to the weights of BC and fungal spores (Table S2). Table S3 shows the linear weights for the principal components of outdoor PM. The first principal component of outdoor PM was predominantly composed of PM_{2.5}, UVPM and BC (Table S3).

3.4. Spirometry results

Fig. 3 shows the variation in percent predicted spirometry results. The percent predicted FEV₁ ranged from 48%–163%, with a median of 100%. Percent predicted FVC values were less varied, ranging from 71%–184%, with a median of 108%. Percent predicted FEV₁/FVC ratio had a median of 92% (range = 54–115%), and percent predicted FEF_{25–75} had a median of 80% (range = 24–160%). Other summary statistics of subjects' percent predicted spirometry results are given in Table S4. There was no significant difference between spirometry results from subjects residing in homes with occupants that smoked and subjects residing in non-smoking homes (Fig. S7). Over 50% of the subjects had normal spirometry values (Table 3).

3.5. Change in lung function associated with exposure to PM

Tables S5 and S6 show the intercepts of the developed regression models, which represents the mean percent predicted spirometry results of the subjects in the absence of the independent variables. In addition, the percent change in FEV₁, FVC, and the visualized estimates in Figs. 4 and 5 (i.e., percent change in percent predicted FEV₁/FVC ratio and FEF_{25–75}) are given.

None of the outdoor PM variables were significantly associated with lung function. Furthermore, there were no significant associations between indoor and outdoor PM variables (BC, UVPM, PM_{2.5}, fungal spores) and percent predicted FEV₁ and percent predicted FVC (Tables S5 and S6). In contrast, indoor PM_{2.5} and indoor UVPM were significantly associated with percent predicted FEV₁/FVC ratio and FEF_{25–75}.

Figs. 4 and 5 show that indoor PM was significantly associated with reduced percent predicted FEV₁/FVC ratio. Principal component 1 (Table S3), predominantly composed of indoor UVPM and indoor PM_{2.5}, was significantly associated with reduced percent predicted FEV₁/FVC ratio (Fig. 4A, $\beta = -4.1$, 99% CI = $-6.9, -1.4$). A one standard deviation increase in indoor UVPM (11.3 $\mu\text{g}/\text{m}^3$) was significantly associated with reduced percent predicted FEV₁/FVC ratio (Fig. 4C, $\beta = -6.4$, 99% CI = $-10.4, -2.4$). Similarly, one standard deviation increase in indoor PM_{2.5} (17.7 $\mu\text{g}/\text{m}^3$) was also associated with significant decrease in percent predicted FEV₁/FVC ratio (Fig. 4C, $\beta = -6.1$, 99% CI = $-10.2, -1.9$). In contrast, indoor BC was not significantly associated with percent predicted FEV₁/FVC ratio (Fig. 4G).

Indoor PM was significantly associated with reduced percent predicted FEF_{25–75}. Principal component 1 (Table S3), predominantly composed of indoor UVPM and indoor PM_{2.5}, was significantly associated with reduced percent predicted FEF_{25–75} (Fig. 5A, $\beta = -9.5$, 99% CI = $-17.7, -1.3$). A one standard deviation increase in indoor UVPM (11.3 $\mu\text{g}/\text{m}^3$) was significantly associated with reduced percent predicted FEF_{25–75} (Fig. 5C, $\beta = -14.7$, 99% CI = $-26.3, -2.9$). Similarly, one standard deviation (17.7 $\mu\text{g}/\text{m}^3$) increase in indoor PM_{2.5} was significantly associated with reduced percent predicted FEF_{25–75} (Fig. 4C, $\beta = -12.9$, 99% CI = $-24.9, -1.0$). Indoor BC was not significantly associated with percent predicted FEF_{25–75} (Fig. 4G).

Among the covariates, the association between family income and lung function was not significant, but having pets (dogs/cats) were

Table 2
Measured levels of indoor particulate matter in study homes (repeated measures, n = 71).

	BC ($\mu\text{g}/\text{m}^3$)	UVPM ($\mu\text{g}/\text{m}^3$)	PM _{2.5} ($\mu\text{g}/\text{m}^3$)	Fungi (SE/ m^3)
Minimum	<LOD	<LOD	<LOD	1
Q1	0.2	0.8	5.3	84
Median	0.5	1.6	8.7	198
Mean	0.6	5.8	14.6	420
Q3	0.8	4.8	14.5	599
Maximum	3.0	60.2	81.4	2346
SD	0.5	11.3	17.7	502

BC = black carbon, UVPM = ultraviolet absorbing particulate matter (light absorbing PM_{2.5} emitted from smoldering organics such as smoking cigarettes and burning fireplace wood), Fungi = fungal spore equivalents per cubic meter (SE/ m^3), Q1 = 25th percentile, Q3 = 75th percentile, LOD for BC = 0.12 $\mu\text{g}/\text{m}^3$, LOD for UVPM = 0.18 $\mu\text{g}/\text{m}^3$, LOD for PM_{2.5} = 0.3 $\mu\text{g}/\text{m}^3$.

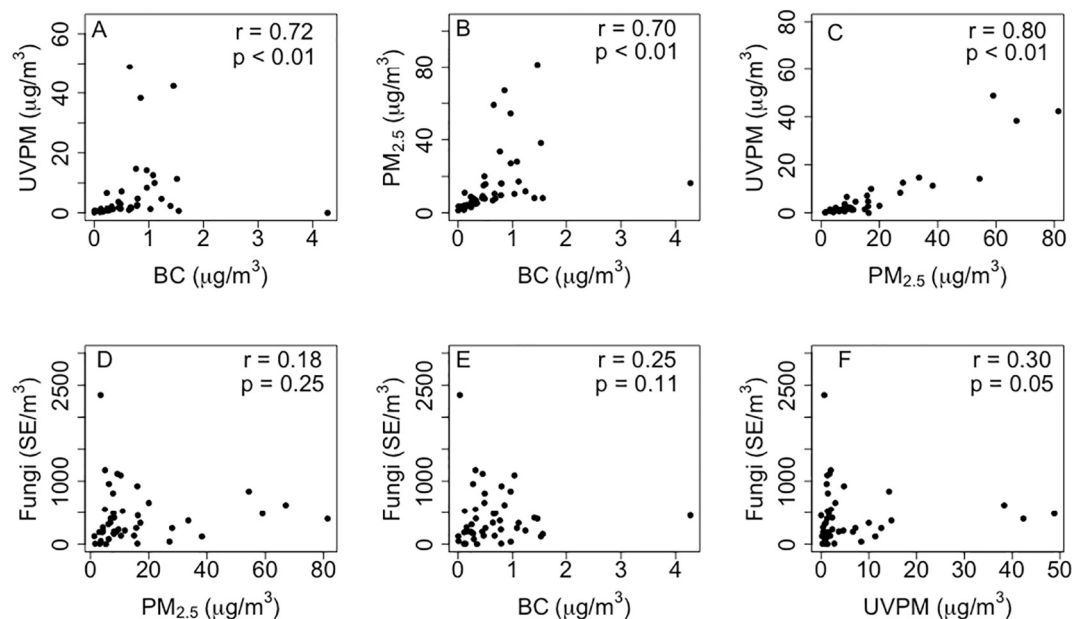


Fig. 1. Correlation plots of the mean concentrations of measured indoor particulate matter in each home ($n = 43$). r = Spearman correlation coefficient, UVPM = ultraviolet light absorbing particulate matter (light absorbing $PM_{2.5}$ emitted from smoldering organics such as smoking cigarettes and burning fireplace wood), BC = black carbon, $PM_{2.5}$ = particulate matter with aerodynamic diameter $\leq 2.5 \mu m$, Fungi = fungal spore equivalents per cubic meter (SE/m^3).

significantly associated with a decrease in percent predicted FEV_1/FVC ratio and percent predicted FEF_{25-75} , when compared to not having pets. In a sensitivity analysis on the 69 observations of breathing/nasal medications use within the last 72 h of spirometry (Yes/No), lung function measurements, PM concentrations and other covariates, breathing/nasal medications use was not significant (results not shown).

4. Discussion

Our results show that 48-h average concentration of indoor PM, but not outdoor PM were associated with reduced lung function in children

with asthma. Increase in indoor UVPM and indoor $PM_{2.5}$, but not indoor BC and indoor fungal spores were associated with reduced percent predicted FEV_1/FVC ratio and percent predicted FEF_{25-75} . Of all the measured combustion-related PM, UVPM had the strongest inverse relationship (highest β) with percent predicted FEV_1/FVC ratio and percent predicted FEF_{25-75} . The association between exposure to light absorbing $PM_{2.5}$ emitted from smoldering organics such as burning cigarettes (UVPM) and adverse respiratory outcome may be stronger in contrast to exposure to BC and adverse respiratory outcome.

4.1. Interpretation of results

The results indicate that indoor PM level is a better metric for PM exposure assessment than outdoor PM levels. However, the relationship between outdoor PM and respiratory health must not be

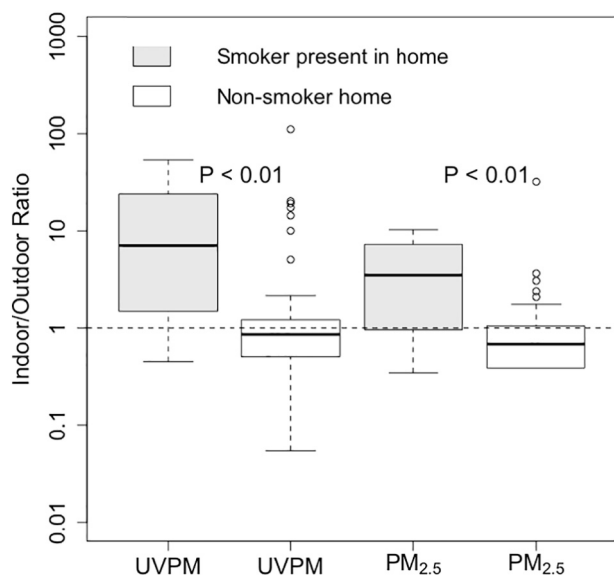


Fig. 2. Indoor/outdoor ratios of UVPM and $PM_{2.5}$ stratified by presence of smoker in the residence. P -values obtained from Tukey's HSD test (controlling for repeated measures). From below, horizontal line in boxplot represents minimum (excluding outliers), 25th, 50th, 75th percentiles and maximum (excluding outliers); Circles = outliers. Smoker home ($n = 12$) = a home where at least one occupant smokes at least one cigarette per day, non-smoker home ($n = 59$) = a home where no occupant smoked.

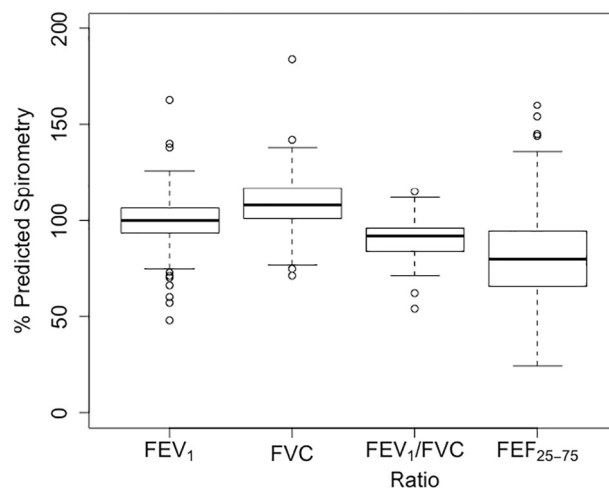


Fig. 3. Boxplots of the spirometry results from the 71 observations. FEV_1 = Forced expiratory volume in 1 s, FVC = Forced vital capacity, FEV_1/FVC ratio is the value obtained from dividing FEV_1 by FVC and multiplying by 100, FEF_{25-75} = Forced expiratory flow at 25–75% of the FVC . From below, horizontal line in boxplot represents minimum (excluding outliers), 25th, 50th, 75th percentiles and maximum (excluding outliers); Circles = outliers.

Table 3
Subject spirometry interpretations.

Interpretations	Percentage of subjects
Normal spirometry values indicating absence of any significant degree of pulmonary impairment	58.3%
FVC and FEV ₁ normal, and normal reduction in FEV ₁ /FVC ratio that may occur in healthy individuals	13.8%
Early obstructive pattern	2.8%
Mild obstructive pattern	16.7%
Moderate obstructive pattern	1.4%
Moderately severe obstructive pattern	1.4%
Mixed obstructive/restrictive pattern	4.2%
Mild restrictive pattern	1.4%

Spirometry interpretations were obtained from the spirometer (KoKo Sx 1000, nSpire Health, Longmont, CO) automatically after a test was conducted. Manufacturers of the spirometer designed it to give interpretations of spirometry values based on McKay and Lockey (1991)

underemphasized, given the weighty evidence of the association between outdoor PM and respiratory health (Chen et al., 2015; Rice et al., 2013; Gehring et al., 2013). Our results suggest that greater statistical power is needed to identify a significant association with outdoor PM and lung function, than with indoor PM and lung function. Sample size calculations using the regression estimates of outdoor PM and equations for calculating sample size for longitudinal studies with correlated repeated measures (Liu and Liang, 1997; Diggle et al., 2002) revealed that a required sample size of >20 per subject is needed. Some cross-sectional and longitudinal studies on the relationship between outdoor PM and lung function were based on the exposure of 5921 children to annual averages of outdoor PM (Gehring et al., 2013), 11,000 children followed up for 8 years (Chen et al., 2015; Urman et al., 2014), daily averages of PM collected over three months and daily assessments of respiratory health (Lee et al., 2007). In other studies with smaller sample size, PM_{2.5} in addition to traffic-related gaseous pollutants were measured and included in their models (Rice et al., 2013; Lee et al., 2007; Cakmak et al., 2011; Korrick et al., 1998; Son et al., 2010; Alexeeff et al., 2007; Chang et al., 2012; Schindler et al., 2001; Lagorio et al., 2006). In our study, despite a short monitoring time (48 h) and relatively small sample size (71), we demonstrated an association between indoor PM and reduced lung function.

Unlike other studies, we did not observe a significant association between indoor BC and lung function. In comparison to indoor UVP and indoor PM_{2.5}, the variation of BC was low, making an association difficult to detect with our sample size. It is also possible that optical methods used to assess exposure to BC in previous studies may be confounded by other particles such as UVP if only a single wavelength was used. Consequently, outcomes made about exposure to BC in such studies, may also be associated with UVP. The lack of a significant association between fungal spores and respiratory health in the current study is consistent with results from another cohort of Cincinnati children, as reported by Lierl and Hornung (Lierl and Hornung, 2003). Conversely, Atkinson et al. demonstrated a positive relationship between thirty different taxa of fungal spores outdoors and asthma-related hospital visits in London (Atkinson et al., 2006). The fungal species analyzed in the current study and those analyzed by Atkinson et al. are different. Further research into fungal spore exposure and lung function may aid in understanding the differences in the studies.

4.2. How do our results compare with prior knowledge?

The finding of an association between indoor PM_{2.5} and respiratory health is consistent with results from previous studies. McCormack et al. showed an association between PM_{2.5} and asthma symptoms such as wheezing (McCormack et al., 2008), and Delfino et al. demonstrated a relationship between increased indoor PM_{2.5} and reduced

FEV₁ among children with asthma (Delfino et al., 2004). Airway obstruction results in decreased airflow and decreases in FEV₁ and FEF_{25–75}. Therefore, the FEV₁/FVC ratio and FEF_{25–75} are used as markers for airway obstruction (Barreiro and Perillo, 2004). We observed a reduction in FEV₁/FVC ratio that was associated with increased PM_{2.5} and UVP levels. Values of FEF_{25–75} give suggestions on the state of the bronchus and therefore asthma status (Boutin et al., 2015; Simon et al., 2010). Our data suggest that increase in PM_{2.5} and UVP was associated with bronchial constriction and airway obstruction in the subjects studied. Previous studies suggest that this relationship may not exist in non-asthmatic children (Neas et al., 1994; Trenga et al., 2006), indicating a stronger correlation of PM_{2.5} and lung function in children with asthma (Guarnieri and Balmes, 2014). While UVP and PM_{2.5} may be associated with airway obstruction, the data suggest that the level of obstruction may not be clinically severe, given that the relationships between FEV₁ (value used to measure severity of obstructive diseases) (Jakeways et al., 2003; Johnson and Theurer, 2014) and all the PM variables were not significant.

Analysis performed by Habre et al. shows that during the winter, the odds of wheezing and coughing among children with asthma exposed to indoor PM_{2.5} of outdoor origin is greater when compared to the odds of wheezing and coughing from exposure to outdoor PM_{2.5} (Habre et al., 2014b). In the same population during fall and spring, the odds of wheezing and coughing from exposure to indoor PM_{2.5} emitted from indoor sources was greater when compared to the odds of wheezing and coughing from exposure to outdoor PM_{2.5} (Habre et al., 2014b). Results in the current study are similar to that of Habre et al. showing a stronger association between indoor PM_{2.5} and lung function in contrast to outdoor PM_{2.5} and lung function.

The spirometry values of the subjects in the current study are comparable to spirometry values of other children with asthma (Trenga et al., 2006). Using percent predicted FEV₁/FVC of ≤70% as the threshold for airway obstruction (Anthonisen et al., 1994), majority of the subjects in the current study had relatively good spirometry results. Only 2.8% of subjects had percent predicted FEV₁/FVC of ≤70%. Similarly, average indoor levels of PM_{2.5} (median indoor = 8.7 µg/m³) and BC (median indoor = 0.5 µg/m³) in the current study are comparable to levels reported in other studies (Karotki et al., 2014; Coombs et al., 2016; Baxter et al., 2007). On the other hand, measured outdoor PM_{2.5} and BC in the current study (mean = 13.0 µg/m³ and 0.9 µg/m³, respectively) are higher than the levels reported in some earlier studies (Rice et al., 2013; Gehring et al., 2013).

4.3. Secondary results

In the current study, the covariates accounted for in the regression estimates for the PM variables were the presence/absence of pets and family income. Presence of pets was associated with reduced percent predicted FEV₁/FVC ratio and percent predicted FEF_{25–75}, but the association between socioeconomic status (as determined from family income) and lung function was not significant. Exposure to pet dander may reduce lung function in children sensitized to pet or food allergens (Lowe et al., 2004). Furthermore, sensitization to mite dust is associated with reduced lung function (ULRIK and Backer, 1999). As the prevalence of sensitization in children with asthma is relatively high (ULRIK and Backer, 1999), there may be an increased chance of finding significant associations between pets and lung function in children with asthma.

The median indoor/outdoor ratio of BC in the current study (0.6) indicate that on the average, infiltration was a major source of indoor BC in the studied homes. The substantial difference in indoor/outdoor ratio of UVP and PM_{2.5} in the homes of smokers (6.9 and 3.5, respectively) when compared to non-smoking homes (0.9 and 0.7, respectively) suggests that tobacco smoke was a major source of indoor UVP and indoor PM_{2.5} in the study homes. In the current study, parents of the subjects were asked about the smoking status of people residing in the home, and second-hand cigarette smoke was assessed

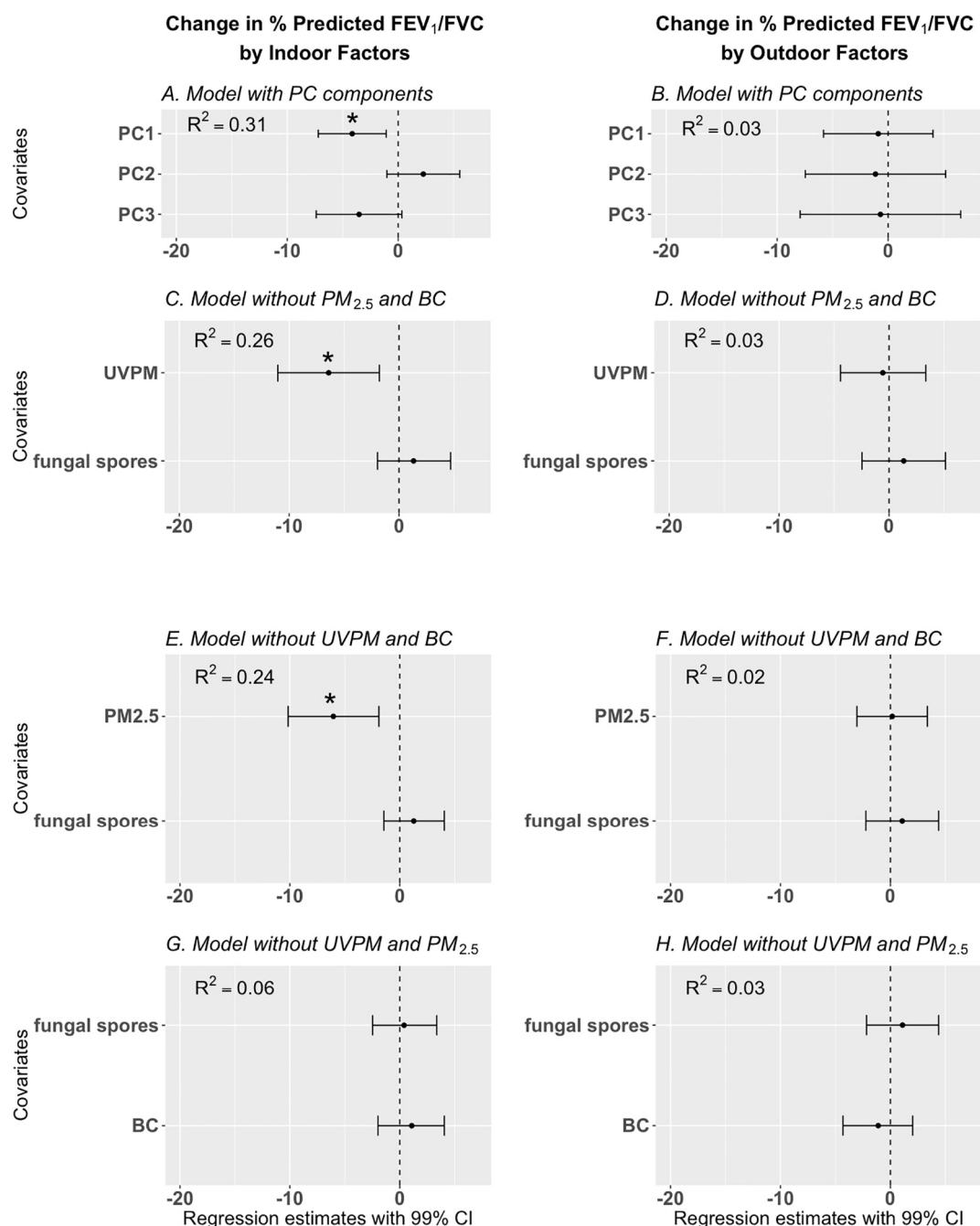


Fig. 4. Results of regression models developed to explore the association between 48-h measurements of particulate matter (indoor and outdoor simultaneously) and percent predicted FEV₁/FVC ratio (adjusted for age, height, gender, and race). Dots = regression estimates; error bars = 99% CI = 99% confidence interval of regression estimate (adjusted for presence/absence of pets and family income). * indicates statistically significant finding, BC = black carbon, UVPM = ultraviolet light absorbing particulate matter, PC components = principal components of BC, UVPM, PM_{2.5} and fungal spores. In Fig. 4C–H, one standard deviation increase in BC, UVPM, PM_{2.5}, and fungal spores are associated with the corresponding regression estimates in the Figures. Four different models are presented to avoid multicollinearity of UVPM, BC, and PM_{2.5}.

using UVPM as a surrogate. The results indicate that some parents may have misclassified the smoking status of home occupants. Ultraviolet light absorbing PM (UVPM) is an objective assessment of second-hand cigarette smoke, and PM_{2.5} is also emitted from smoking cigarettes. Expectedly, measurements of UVPM and PM_{2.5} were significantly higher in the homes where at least one smoker resided. Furthermore, indoor PM_{2.5} and UVPM were inversely associated with percent predicted FEV₁/FVC ratio and FEF_{25–75}. However, the difference in percent predicted FEV₁/FVC and FEF_{25–75} was not significant among children in the homes of smokers versus non-smokers. To solve the potential

problem of subject recall bias, direct measures of tobacco smoke exposure such as cotinine levels in hair (Brunst et al., 2012) and UVPM should be used to assess exposure, but our study was not specifically designed to answer this question.

5. Limitations

Since reduced lung function can be potentially affected by unstudied pollutants, such as NO₂ and O₃, results of our investigation should be taken with caution. This study can be improved upon by examining

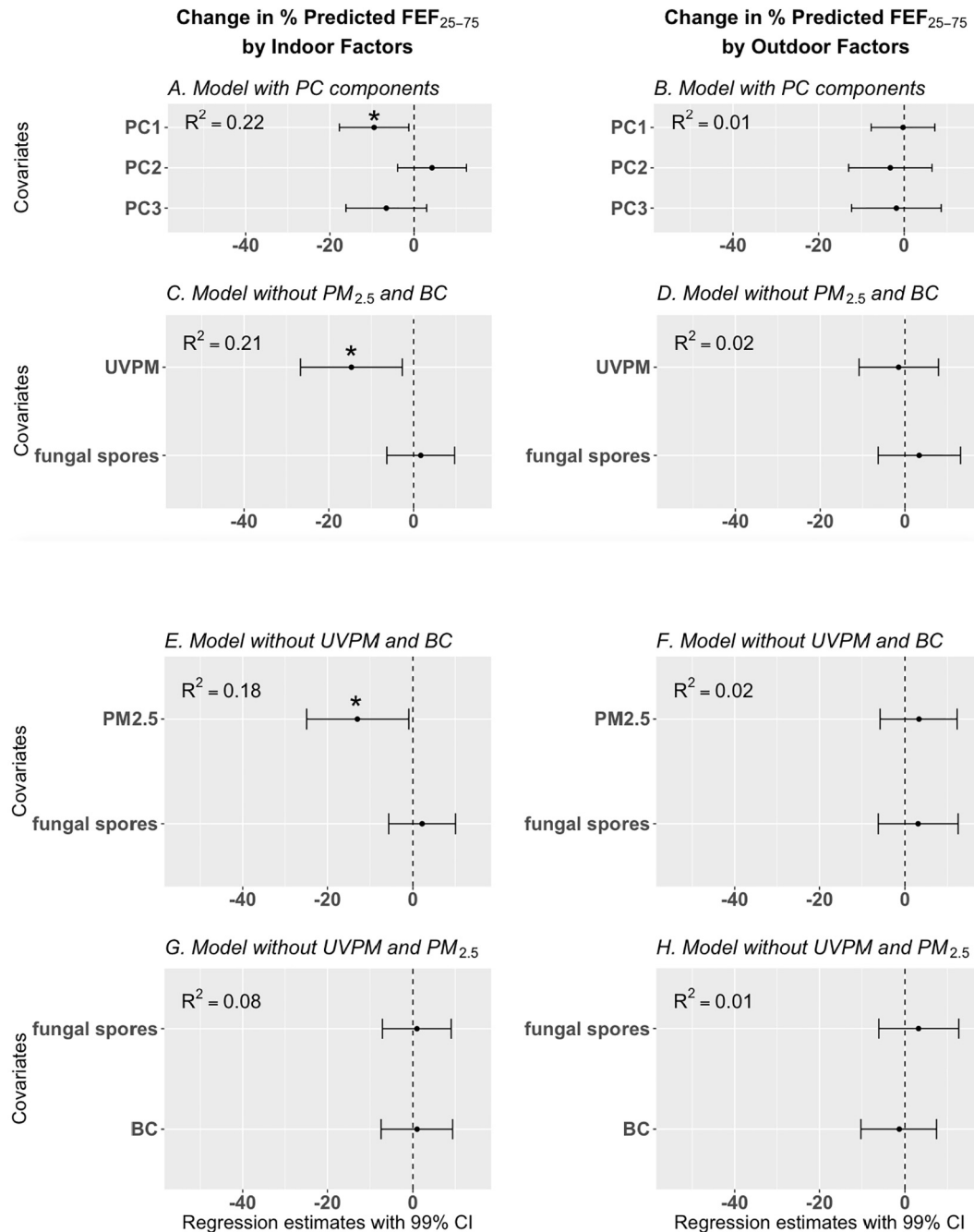


Fig. 5. Results of regression models developed to explore the association between 48-h measurements of particulate matter (indoor and outdoor) and percent predicted forced expiratory flow between 25 and 75% of the forced vital capacity (FEF₂₅₋₇₅) [adjusted for age, height, gender, and race], regression estimates are adjusted for presence/absence of pets and family income. In Figs. 5C–H, one standard deviation increase in BC, UVPM, PM_{2.5}, and fungal spores are associated with the corresponding regression estimates in the Figures. See Fig. 4 footnotes for additional figure descriptions.

the association between PM concentrations and lung function in a larger set of subjects for longer periods. Furthermore, adjusting for seasonal differences of particulate matter concentrations will improve upon our study. Nevertheless, we were able to show significant associations between 48-h averages of indoor PM concentrations and lung function in 44 subjects.

6. Conclusions and implications

Indoor PM is a better predictor of lung function in comparison to outdoor PM. Both indoor UVPM (a surrogate of light absorbing

PM_{2.5} from smoldering organics such as burning cigarettes) and indoor PM_{2.5} significantly reduce FEV₁/FVC ratio and FEF₂₅₋₇₅. The association between exposure to UVPM and reduced lung function may be stronger than that of PM_{2.5}, BC and reduced lung function. Exposure to low levels of BC indoors (mean = 0.6 µg/m³) may not significantly reduce lung function. Our results suggest that indoor PM (in comparison to outdoor PM) is associated with decreased lung function in children with asthma. We recommend that children with asthma avoid indoor environments with PM emitted from smoldering organics such as burning cigarettes, wood or incense.

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Notice

The U.S. Environmental Protection Agency (EPA) through its Office of Research and Development collaborated in the research described here. It has been subjected to the Agency's peer review and has been approved as an EPA publication. Mention of trade names or commercial products does not constitute endorsement or recommendation by the EPA for use. The findings and the conclusions in this report are those of the authors and do not necessarily represent the views of the US EPA.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2019.01.309>.

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