## Title

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## Publication Date

2014-02-01

## DOI

10.1016/j.envres.2013.12.007

Peer reviewed

Published in final edited form as:
*Environ Res*. 2014 February ; 129: 1–10. doi:10.1016/j.envres.2013.12.007.

# Annual Average Ambient Particulate Matter Exposure Estimates, Measured Home Particulate Matter, and Hair Nicotine are Associated with Respiratory Outcomes in Adults with Asthma

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## Abstract

**Background—**While exposure to outdoor particulate matter (PM) has been associated with poor asthma outcomes, few studies have investigated the combined effects of outdoor and indoor PM (including secondhand tobacco smoke).

**Objective—**To examine the associations between PM and asthma outcomes.

**Methods—**We analyzed data from a cohort of adults with asthma and rhinitis (n=302; 82% both conditions; 13% asthma only; 5% rhinitis alone) including measures of home PM, tobacco smoke exposure (hair nicotine and self-report), ambient PM from regional monitoring, distance to roadway, and season (wet or dry). The outcomes of interest were frequent respiratory symptoms and forced expiratory volume in 1 second ($FEV_1$) below the lower limit of normal (NHANES reference values). Multivariable regression analyses examined the associations (Odds Ratio [OR] and 95% Confidence Interval [95%CI]) between exposures and these outcomes, adjusted by sociodemographic characteristics.

**Results—**In adjusted analyses of each exposure, the highest tertile of home PM and season of interview were associated with increased odds for more frequent respiratory symptoms (OR=1.64 95%CI: [1.00, 2.69] and OR = 1.66 95%CI: [1.09, 2.51]). The highest tertile of hair nicotine was significantly associated with $FEV_1$ below the lower limit of normal (OR=1.80 95%CI: [1.00, 3.25]). In a model including home PM, ambient PM, and hair nicotine, and season, only two associations remained strong: hair nicotine with $FEV_1$ below the lower limit of normal and season



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**Conflict of interest statement:** The authors have no competing financial interests to declare.

of measurement (dry, April-October) with increased respiratory symptoms (OR=1.85 95%CI: [1.00, 3.41] and OR = 1.54 95%CI: [1.0, 2.37]). When that model was stratified by sex, the highest tertiles of ambient PM and hair nicotine were associated with $FEV_1$ below the lower limit of normal among women (OR=2.23 95%CI: [1.08, 4.61] and OR=2.90 95% CI: [1.32, 6.38]), but not men. The highest tertile of hair nicotine was also associated with increased respiratory symptoms in women but not men (OR=2.38 95% CI: [1.26, 4.49]). When stratified by age, the middle quartile of ambient PM and the highest hair nicotine tertile were associated with increased respiratory symptoms (OR=2.07 95%CI: [1.01, 4.24] and OR=2.55 95%CI: [1.21,5.36]) in those under 55 but not in the older stratum.

**Conclusions—**Exposure to PM from both home and ambient sources is associated with increased symptoms and lower lung function in adults with asthma, although these associations vary by type of PM, the respiratory outcome studied, sex and age.

### Keywords

Particulate matter; indoor air quality; outdoor air quality; hair nicotine; asthma; respiratory symptoms; lung function

## Introduction

Exposure to outdoor particulate matter (PM) has been associated in multiple epidemiological studies with increased risk of various asthma outcomes, including symptoms (McConnell et al. 2003), short-term decreases in lung function (Delfino et al. 2004), and clinical exacerbations leading to health care utilization (Barnett et al. 2005). The evidence for such effects, however, is more robust for children than for adults with asthma (Patel and Miller 2009).

The health impacts of outdoor fine PM ($PM_{2.5}$), largely from combustion sources, are generally considered to be greater than those of coarse fraction PM ($PM_{10–2.5}$) (Brunekreef and Forsberg 2005). $PM_{10–2.5}$ can also be partly anthropogenic (Gent et al. 2009), but these larger particles tend to be of crustal or biological origin. Relatively few studies have specifically focused on $PM_{10–2.5}$ and asthma outcomes (Lin et al. 2002; Mann et al. 2010; Balmes et al. 2009)..

Moreover, most studies of asthma and PM (whether fine or coarse) have relied on measurements at regional air quality monitoring stations to classify individual-level exposure. These stations are usually at a considerable distance from where the individuals being studied live and investigators typically do not integrate time away from the home into the exposure estimates derived from such monitoring data, thus leading to inherent exposure misclassification. Although individual-level exposure assessment with personal monitoring may be more precise, this is not feasible to implement widely and even when possible, such monitoring may not distinguish among various sources of PM, both indoor and outdoor.

Given such challenges, it is not surprising that few studies have investigated the effects on asthma of both outdoor and indoor PM. Of note, a study of subjects with asthma or chronic obstructive pulmonary disease in four European cities reported no consistent associations

between lung function and 24-hour average particle number or particle mass concentrations measured at central site monitoring stations, nor did the results change when home outdoor or home indoor concentrations of PM were substituted for the central site measurements (de Hartog et al. 2010).

To address this knowledge gap, we analyzed cross-sectional data from a cohort of adults with asthma for whom we have performed home visits yielding outdoor and indoor PM measurements as well as hair nicotine measurements as a biomarker for tobacco smoke exposure, an important source of indoor PM. In addition, we have geocoded residential addresses for the cohort, allowing estimates of exposure to regional ambient PM and distance to roadway as a surrogate for traffic. These multi-factorial PM exposure data provided the opportunity to take a more integrated approach to assessing the potential associations between various sources of PM exposure and asthma outcomes in adults. We hypothesized that both outdoor and indoor PM exposures would be associated with increased asthma symptoms and decreased lung function.

## Methods

### Study Cohort and Subject Recruitment

We used data from an established cohort of adults with asthma and rhinitis collected by both structured interviews and, in a subset of the cohort, home visits assessing lung function, measuring indoor and outdoor PM exposure, and collecting a biomarker of secondhand tobacco smoke exposure. Geocoded residential addresses allowed linkage to ambient air quality monitoring data and calculation of distances to roadways of various sizes. This asthma cohort was established through the merger of two different study groups that were recruited separately and studied independently, but following an identical study protocol. The details of the recruitment, selection, and retention for the merged asthma and rhinitis cohort have been published previously (Chen et al. 2011; Trupin et al. 2013).

The flow of subject recruitment, retention, and integration into the single cohort is illustrated in Figure 1. In the first of the two parent study groups, the Asthma Rhinitis Cohort, recruitment of adults with asthma, rhinitis (including allergic rhinitis, chronic sinusitis, hay fever, or chronic postnasal drip), or both conditions occurred through community-based sampling of physicians or random digit dial identification of adults with report of a physician’s diagnosis of these conditions. Subjects were between age 18 and 50 at the time of enrollment, and those with concomitant diagnoses of chronic bronchitis, chronic obstructive pulmonary disease, or emphysema were ineligible. In the second study group, labeled in the figure as the Severe Asthma Cohort, the subjects were originally recruited from adult members of Northern California Kaiser Permanente. This health care maintenance organization provides health care to 25% to 30% of the region’s population and has demographic characteristics representative of the general population except for at the extremes of income distribution. Recruitment for that group was based on hospitalization for asthma (International Classification of Diseases 9th revision [ICD-9] code 493.xx as the primary discharge diagnosis or as a secondary code linked to an acute asthma-related respiratory condition). Potential subjects with a primary or secondary discharge diagnosis of chronic bronchitis, emphysema, or chronic obstructive pulmonary disease were excluded.

Both groups were recruited within the same northern California geographical region and for the integration were limited to baseline age of 18 to 60 at original recruitment. The merged cohort will be referred to here as the Asthma and Rhinitis Cohort. The study protocol was approved by the University of California San Francisco Committee on Human Research. Telephone interviews took place with verbal consent by agreement to participate; home visits included a written consent document.

## Subject Interviews

All participants underwent a single baseline structured telephone interview administered by trained personnel using computer-assisted interviewing software. The interviews were approximately 45 minutes in duration and were conducted in English, although Spanish language assistance was available when needed (only two of 549 interviews). The interviews elicited data on demographics, occupation, smoking, clinical symptoms, asthma and rhinitis medication usage, and activity limitations. As shown in Figure 1, of 711 possible participants in the study, 549 (77%) completed the baseline interview. Follow-up interview status differed significantly between the two study groups from which subjects were recruited: 85% vs. 68%. Overall, those interviewed were approximately 4 years older and less likely to be current or former smokers compared with those not interviewed.

## Home Visits

A home study team conducted a one-time comprehensive survey of the home environment, at which spirometry was performed and hair collected for nicotine assay. Environmental data gathered during the home visit included measures of PM inside and outside the home. The study geographic range extended throughout northern California from Fresno to the Oregon and Nevada borders, including urban, suburban, and rural dwellers. Excluding those who had moved out of this range since their original study recruitment (n=53), 496 subjects were eligible for home visits. A total of 302 visits were ultimately completed, 61% of those eligible (see Figure 1). The median time elapsed between interview and home visit was 6.1 weeks.

The home interviews took place from April 2008 through September 2009. The average time elapsed between the telephone interview (at which symptoms were ascertained) and the home visit (at which lung function was measured) was 66±68 days (median=43 days). In terms of seasonality (defined as wet [November-March] or dry [April –October] season consistent with northern California climactic conditions), 60% of the interviews and 63% of the home visits, respectively, took place during the dry season.

## Exposure Variables

**Particulate Matter at the Home—**We obtained a “snapshot” of indoor and outdoor exposures by measuring PM concentrations at the home in real time during the home visit using a nephelometer (DustTrak-8520, TSI, Inc., Shoreview, MN). Three 3-minute measurements were performed at three separate home locations: just outside the front door, in the main living area, and in the kitchen. The nephelometer measurements should be considered to represent relative concentrations of PM because the instrument was not

calibrated against a known concentration of a specific aerosol. The particles measured by the nephelometer are considered to approximate $PM_{2.5}$.

**Tobacco Smoke Exposure—**We studied hair nicotine as a biomarker of secondhand tobacco smoke exposure, which we considered a potential source of PM exposure. Overall, 288 hair samples were analyzed for nicotine (12 declined analysis or were bald and two other samples did not have sufficient hair weight collected for analysis). Concentrations of nicotine in hair were determined using liquid chromatography-tandem mass spectrometry. Deuterium-labeled nicotine (nicotine-d9) was used as an internal standard. The limit of detection was variable, depending on weight of hair obtained; 116 (38%) of study subjects had undetectable hair nicotine, which was treated as a measurement value of 0. All of these 0 value observations were included in the lowest tertile of exposure. In addition, potential tobacco smoke exposure was also assessed by interview and was categorized for this analysis as none, secondhand, or from active smoking.

**Ambient Air Quality Estimates—**We estimated ambient PM exposure by geo-coding the subjects' residences and linking these data to regional fixed site air pollution monitoring data. Geo-coding, the process of assigning latitude and longitude coordinates to subjects' addresses, was carried out by Sonoma Technology (Petaluma, CA, USA) using the TeleAtlasMultiNet™ USA roadway database (Tele Atlas, Lebanon, NH, USA), which contains detailed roadway and address information and high positional accuracy. TeleAtlas Eagle Geocoding Technology was used to locate addresses in the TAMN database, yielding a corresponding latitude and longitude coordinate pair. When necessary, addresses were verified using data sources, such as aerial photography from the US Geological Survey and online address location services such as Yahoo!® and MapQuest®. Analyses were performed using ArcGIS software (version 9.3; ESRI, Redlands, CA).

The geo-coded addresses were linked to 2008 US Environmental Protection Agency (EPA) air quality data for PM exposure estimates. Annual average ambient PM with a mass median aerodynamic diameter <2.5 μm ($PM_{2.5}$) and annual average PM with a mass median aerodynamic diameter <10 μm ($PM_{10}$) exposures were estimated using ambient measurements interpolated (inverse distance weighted) from up to four air quality monitoring stations within 50 km of the geo-coded residences. The coarse fraction of ambient PM ($PM_{10–2.5}$) was calculated by subtracting $PM_{2.5}$ from $PM_{10}$ estimates. To avoid potential confounding by season, annual average estimates of PM were used.

**Traffic Exposure (Distance to Roadway)—**As a surrogate of potential PM exposures from vehicular sources, we used distance of the subjects' homes from roadways of differing sizes (Liu et al. 2003). We used two distance-to-roadway metrics in the analyses: distance to nearest larger roadway (primary interstate highway, primary state highway, or secondary state/county arterial roads) and, separately, distance to nearest major roadway (interstate and state highways only). Straight-line distances were calculated from the geo-coded residential locations to nearest roadways of the three types: interstate highways (road class 1), state highways (road class 2), and arterial roads (road class 3), with minimum distance set to 10 meters for all roadways.

### Asthma Outcome Measures

We analyzed two dependent variables in this study: more highly symptomatic asthma (ordinal) and impaired lung function (dichotomous). Respiratory symptom assessment was based on structured questionnaire items that were administered at the time of the telephone interviews. These occurred prior to the home visits, as noted above. Respiratory symptoms for the 2 weeks preceding the interview were scored ordinally based on self-rated “asthma bother” on a 0–4 scale (0=none, 1=hardly any days or nights, 2=occasionally but not most days or nights, 3=most but not all days or nights, 4=every day or every night, whichever [day or night] ranked higher). Impaired lung function was based on spirometry obtained during the home visit. Spirometry was performed using an EasyOne Spirometer (ndd Medical Technologies, Chelmsford, MA). The EasyOne meets American Thoracic Society 1994 diagnostic standards for spirometry. Spirometric measurements, including forced expiratory volume in 1 second ($FEV_1$), were taken using a standard protocol conforming to American Thoracic Society guidelines (Society 1995). Predicted $FEV_1$ was based on equations from NHANES III that generate separate reference values for male and female non-Hispanic whites, Hispanics, and blacks (Hankinson et al. 1999). We defined an $FEV_1$ below the lower limit of normal based on NHANES reference values as impaired lung function consistent with poorer asthma control relative to higher $FEV_1$ values.

### Missing Data and Statistical Analysis

Complete data were not available for all study subjects. Among the 302 subjects who completed home visits, a total of 47 (16%) were missing values for one or more of the exposure or outcome variables. To avoid possible bias associated with listwise deletion of these variables from analysis, we conducted multiple imputation, which imputes values using statistical models that include covariates relating to each variable’s “missingness” and creates M datasets. These datasets produce M point estimates and variance estimates, which are then combined (Allison 2002). We used SAS PROC MI [SAS 9.2, Cary, NC] to create five imputed datasets as that was sufficient to provide robust estimates given the amount of missing data in our dataset (i.e., the relative efficiencies of all imputed variables after imputation were >0.98) (Rubin 1987). Because the missing data pattern was not monotone, we used the Monte Carlo method for imputation. The multiple imputation model included all variables subsequently analyzed in regression models (nine exposure variables, two outcome variables, age, gender, non-Hispanic white race/ethnicity), in addition to other variables we hypothesized would explain “missingness” (income, Black, Asian, or Latin race/ethnicity, smoking status, and second-hand smoke exposure). The nine exposure variables were particulate matter outside the home, in the kitchen, and living area; ambient PM based on air monitoring ($PM_{2.5}$ and $PM_{10–2.5}$); distance to roadway (distance to all roads class 1–3 and distance to class 1 and 2 only); and tobacco smoke exposure (hair nicotine and reported smoking exposure). The self-reported smoking variable was categorized into three inherently ordinal groups: active smoking (highest), regular secondhand smoke exposure (intermediate), or neither. We ordinally categorized the remaining exposure variables using tertiles based on their measured continuous values. We did not include in the imputation the two seasonal variables (season of interview and season of home visit) due to their correlation with each other. All regressions were run on all five imputation datasets and then combined using SAS PROC MIANALYZE.

We hypothesized that the different types of PM exposures would each be associated variably with one or both outcomes and used a hierarchical approach to the analysis. Our first step was to select exposures for further analysis with a critical value of $p<0.1$ in univariate regressions with either outcome. We used binary logistic regression to predict $FEV_1$ below the lower limit of normal. Because respiratory symptoms were assessed on an ordinal scale, we used ordinal logistic regression (i.e., the proportional odds model) for this outcome (Scott et al. 1997). The odds ratio for these regressions can be interpreted as a summary of the binary odds ratios for each of four possible ordinal binary cutpoints (e.g., 0 vs. 1 through 4; 0 and 1 vs. 2 through 4, etc.). The proportional odds test for all univariate regressions on symptoms demonstrated that the assumption of heterogeneity of the odds was not violated.

We then went on to build a series of multivariable regression models. The multivariable models included the following sociodemographic status covariates that are known to be associated with lung function: age in years, sex, race/ethnicity (non-Hispanic whites vs. all others), and education (up to high school diploma vs. additional education). The multivariable analysis was done in three phases. In the first phase, each of the selected exposure variables was included as an independent variable along with all the sociodemographic covariates in its own model. In the second phase, all selected exposure variables were included, along with the sociodemographic status covariates, in models predicting each outcome. Finally, because we hypothesized possible effect modification by sex and age in the regressions, we stratified the models in the second analytic phase, first by sex, and then by age ($<55$ vs. $\geq 55$).

## Results

### Subject Characteristics

Of the 302 subjects with home visits included in this analysis, 82% reported either a physician diagnosis or symptoms of both asthma and rhinitis, 13% asthma only, and 5% rhinitis only. There were only minor differences between interviewed subjects who did and did not complete home visits (Table 1). Overall, subjects were predominantly female and white, non-Hispanic and reported occasional respiratory symptoms in the 2 weeks preceding the interview.

Table 2 shows the distributions of all the exposure variables and the lung function outcome. Because the study cohort members completing home visits reside in Northern California, most of the annual ambient average $PM_{2.5}$ estimates are below the current US EPA standard of 15 $\mu g/m^3$, but the nephelometer measurements indicated the presence of some relatively high concentrations of particles. Few of our subjects were active cigarette smokers (8%) and selfreported regular exposure to secondhand tobacco smoke >1 hour per week was also relatively infrequent. Most subjects did not live in close proximity (≤100 m) to either interstate highways or other major roadways. Sixty percent of the interviews and 63% of the home visits were conducted during the dry season in Northern California. Slightly over half (51%) had $FEV_1$ less than the lower limit of normal.

### Univariate Analyses

In univariate logistic regression models of the associations of exposure variables with the dependent variables (Table 3), the highest tertiles of annual average ambient $PM_{2.5}$ (≥11.11 μg/m$^3$), nephelometer-measured PM in the kitchen (≥21 μg/m$^3$), and hair nicotine concentration (≥0.14 ng/mg) were associated with increased odds ratio (OR) of more frequent respiratory symptoms (OR=1.61 95%CI: [0.98, 2.63]; OR=1.75 95%CI: [1.07, 2.87]; and OR=1.72 95%CI: [1.07, 2.78]; respectively). In addition, interviews conducted during the dry season were associated with increased odds of frequent respiratory symptoms (OR=1.68 95%CI; [1.11, 2.54]). For $FEV_1$, the middle tertile of annual average ambient $PM_{2.5}$ (9.5-<11.11 μg/m$^3$) and the highest tertile of hair nicotine were associated with increased likelihood of values below the lower limit of normal based on NHANES reference equations (OR=1.69 95%CI: [0.95, 2.99] and OR=1.99 95%CI: [1.12, 3.53], respectively).

### Multivariable Analyses

The first four models of Table 4 display the results of the multivariable logistic regression analyses for the four selected exposure variables (annual average ambient $PM_{2.5}$, kitchen PM, hair nicotine, and dry season), adjusted for education, race-ethnicity, age, sex, and season of interview or home visit. The highest tertiles of annual average ambient $PM_{2.5}$, kitchen PM, and dry season remained associated with increased odds of frequent respiratory symptoms (OR=1.55 95%CI: [0.94, 2.55]; OR=1.64 95%CI; [1.00, 2.69]; and OR=1.66 95%CI; [1.09, 2.59]; respectively) with little change in the point estimates from the previous models. For lung function, the middle tertile of ambient $PM_{2.5}$ and the highest tertile of hair nicotine remained associated with $FEV_1$ below the lower limit of normal (OR=1.69 95%CI: [0.94, 3.03] and OR=1.80 95%CI: [1.00, 3.25], respectively). In Model 5, in which all exposure variables were included, the point estimates decreased, except that the highest tertile of hair nicotine remained associated with reduced lung function (OR=1.85 95% CI: [1.00, 3.41]) and dry season remained associated with increased respiratory symptoms (OR=1.54 95%CI:[1.00, 2.37]).

To assess whether these associations differed by sex and age, we carried out stratified analyses (Table 5). Among females (n=222), the point estimates for annual average ambient $PM_{2.5}$ exposure were higher than in the non-stratified analysis in both the middle and highest tertiles for $FEV_1$ below the lower limit of normal (OR=1.93 95%CI: [0.94, 3.95] and OR=2.23 95%CI: [1.08, 4.61], respectively), and for the highest tertile of hair nicotine for both outcomes (ORs >2). In males (n=80), only the highest tertile of kitchen PM was associated with frequent respiratory symptoms (OR=2.52 95%CI: [0.88, 7.24]). In the participants younger than 55, the middle tertile of ambient $PM_{2.5}$ (9.5-<11.11 μg/m$^3$) and the highest tertile of hair nicotine were associated with increased respiratory symptom frequency (OR=2.07 95%CI: [1.01, 4.24] and OR=2.55 95%CI: [1.21, 5.36], respectively). The highest tertile of hair nicotine was also associated with $FEV_1$ below than the lower limit of normal (OR=2.23 95%CI: [0.92, 5.43]) in the younger group. In participants 55 or older, only dry season was associated with frequent respiratory symptoms (OR=1.95 95%CI; [0.99, 3.85]) and none of the exposures tested was associated with decreased $FEV_1$.

We also repeated the multivariable analyses after excluding the small number of current smokers and there were no substantive changes in the results, including those related to hair nicotine (data not shown).

## Discussion

The results of our analysis indicate that exposures to more than one type of PM can be relevant to respiratory symptoms and lung function among adults with asthma. Ambient $PM_{2.5}$ was associated with frequent respiratory symptoms in the entire cohort and decreased lung function in women, but not men. Coarse fraction PM was not associated with either outcome. Home PM measured in kitchens was associated with respiratory symptoms, but not with decreased lung function. Hair nicotine was associated with decreased lung function, even in a multi-exposure model that included both ambient $PM_{2.5}$ and kitchen PM.

The results of our stratified analyses underscore that, in addition to taking multiple PM-related exposure measures into account, it is also important to consider effect modification by sex and age. As noted above, the ambient $PM_{2.5}$ association with lung function was observed among women but not men. Hair nicotine was associated with both frequent respiratory symptoms and decreased lung function among women, but not men. Somewhat surprisingly, kitchen PM was associated with frequent respiratory symptoms among men, but not women. In participants 55 or older, there was little evidence of effect of any of the exposures of interest on respiratory symptoms or lung function. Because of sample size limitations, we had insufficient power to study more age strata. Similarly, we did not have study power to stratify among different subsets of subjects based on clinical asthma categorizations or original sampling frame, although the potential heterogeneity of the cohort is a study strength insofar as it subsumes a wider spectrum of disease and thus may allow for more general inferences than from more narrowly defined groups (e.g., from a tertiary referral center).

A limited number of population- or community-based studies of adults with asthma have taken an integrated approach to the potential health effects of multiple types of PM exposure. Nonetheless, our findings are consistent with and build upon what has been reported previously about effects of type-specific PM. Ambient $PM_{2.5}$ has previously been associated with exacerbation of asthma in multiple studies (Peden and Reed 2010). On the other hand, fine PM measured at subject homes rarely has been studied. An early effort to measure outdoor $PM_{2.5}$ at homes was conducted by a group in Seattle (Liu et al. 2003). These investigators measured outdoor and indoor $PM_{2.5}$ at 108 homes as well as personal PM and also obtained central-site monitoring data. In two subsequent studies using a repeated measures design, they reported that $PM_{2.5}$ measured outside of homes was associated with increased exhaled nitric oxide (FeNO) in a small number of elderly subjects (n=7) with asthma (Jansen et al. 2005) and with decreased $FEF_{25–75}$ in a small number of children (n=13) with asthma (Trenga et al. 2006). Another study from Italy by Maestrelli and colleagues followed adult subjects (n=32) with asthma periodically over 2 years and showed that measured personal exposure to $PM_{10}$ during the 24 hours prior to assessment was associated with respiratory symptoms, but not FeNO or $FEV_1$ (Maestrelli et al. 2011). In contrast, a study of panels of adults with asthma from four major European cities by de

Hartog and colleagues (total n=93) showed no effect of home outdoor $PM_{2.5}$ on $FEV_1$ (de Hartog et al. 2010). While our study was cross-sectional, our sample size is larger than any of the above investigations. Our results support an effect of home outdoor PM on asthma symptoms, but not on $FEV_1$.

Only limited data are available relating indoor $PM_{2.5}$ concentrations and asthma outcomes, and these are primarily from small studies of children. Koenig and colleagues from the Seattle group reported indoor $PM_{2.5}$ exposure was associated with decreased $FEV_1$ in a subgroup of 10 children not using inhaled corticosteroids (Koenig et al. 2005). A study of 19 children with asthma in southern California found significant decrements in $FEV_1$ associated with indoor $PM_{2.5}$ (Delfino et al. 2004). That study found a stronger association between indoor $PM_{2.5}$ and $FEV_1$ than for central-site $PM_{2.5}$ and $FEV_1$. A longitudinal study of 150 inner city preschool children with asthma, conducted in Baltimore investigated the impact of indoor $PM_{2.5}$ and $PM_{2.5–10}$ on asthma outcomes (Breysse et al. 2010). Indoor coarse PM was associated with substantial increases in asthma symptoms, while indoor fine PM was associated with both asthma symptoms and rescue medication use. In the study by Trenga and colleagues, noted above, indoor $PM_{2.5}$ was associated with lower $FEF_{25–75}$ in children with asthma not on anti-inflammatory medications (Trenga et al. 2006).

While several studies of adults with asthma have used questionnaire data to assess exposure to indoor sources of combustion other than tobacco use, these studies have produced conflicting results (Eisner et al. 2002; Hersoug et al. 2010; Ostro et al. 1994; Qian et al. 2007; Eisner and Blanc 2003). One previous study from the Po Valley in Italy that actually measured indoor $PM_{2.5}$ concentrations in the homes of 383 adult subjects, including 72 with asthma, showed an association between those concentrations and respiratory symptoms in the winter, but not in the summer (Simoni et al. 2002). In addition, the study by Jansen and coworkers noted above showed that measured indoor black carbon, but not indoor $PM_{2.5}$, was associated with higher FeNO in a small number of elderly subjects with asthma (Jansen et al. 2005). The results from our study with measured indoor concentrations suggest that exposure to indoor fine PM indeed does impact asthma negatively.

Secondhand tobacco smoke (SHS) is a major remediable source of fine PM in homes in the developed world. The effects of exposure to SHS on asthma outcomes are well documented, including in work from earlier waves of participation by the cohort we analyze here (Eisner et al. 2002; Eisner et al. 2005; Eisner 2008). Nonetheless, exposure assessments in epidemiological studies of the relationship between SHS and asthma outcomes are typically based on questionnaire data (Eisner et al. 2002; Grassi et al. 2006; Hersoug et al. ; Jaakkola et al. 2003; Janson et al. 2001; Jayet et al. 2005; Jindal et al. 1994). Because over 90% of our subjects were not current smokers, our study is one of the first to assess exposure to SHS in adult asthma with a measured biomarker, hair nicotine. Nicotine is the principal identifying constituent of tobacco, and epidemiological studies of the health effects of SHS exposure have sought to measure nicotine or one of its metabolites. Level of nicotine in hair has been suggested as a possible marker of long-term tobacco smoke exposure, with each cm of hair representing approximately 1 month of exposure (Al-Delaimy 2002). For the analysis reported here, we reasoned that measured nicotine in hair might be a better marker of SHS exposure than self-reported questionnaire data. However, since 25% of our subjects

had no detectable nicotine in their hair samples and 8% are active smokers, we included self-reported tobacco smoke exposure in the data analysis. Interestingly, hair nicotine, but not self-reported exposure, was significantly associated with decreased $FEV_1$ in univariate analyses. In fact, the hair nicotine association with decreased $FEV_1$ emerged as the strongest one in our analysis. Not only did this association persist when adjusted for sociodemographic covariates, it was the only exposure-outcomeassociation that remained in a multi-exposure model. We plan to further evaluate the utility of hair nicotine as a biomarker of SHS in future analyses.

Exposure to traffic-related pollution has been well documented to be associated with asthma outcomes. Traffic emissions are a mixture of pollutants, including fine and ultrafine PM. In this analysis, we used distance to roadway as the metric of exposure to traffic emissions, and unlike a previous study that involved some of the same subjects with asthma (Balmes et al. 2009), we did not find that living near a highway had a negative effect on either respiratory symptoms or lung function. In that analysis, however, we used distance to roadway of any size as our surrogate exposure measure. Distance to roadway is a relatively crude metric of exposure to traffic emissions and some exposure misclassification in our data is likely. With a mixed urban, suburban, and rural cohort such as ours, it may be that land-use factors linked to socioeconomic status and distance to roadway lead to confounding that we were unable to account for in our analyses. Another approach to traffic exposure assessment is the use of traffic density within radial buffers around a residential address. In a recent study from Australia, Cook and colleagues found an association between asthma health care utilization and traffic density within a 150-meter buffer around a residence, but not within a 50-meter buffer (Cook et al. 2011). We did not use traffic density due to lack of data for a substantial proportion of our participants. In particular, heavy-duty vehicle density might be better correlated with exposure to diesel exhaust particles that may be of particular relevance in asthma.

We found that the dry season (April-October) in Northern California was associated with more frequent respiratory symptoms in our cohort. While it is not clear why such a seasonal pattern of symptoms should be observed among asthmatic adults, the dry season is also the warmest time of the year in Northern California when the highest concentrations of ozone and coarse PM, as well as the highest pollen counts, occur.

There are other potential limitations to our analysis as well in addition to those already mentioned. The structured interview from which the symptom frequency data were obtained preceded by ~6 weeks the home visit at which kitchen PM was measured by nephelometer such that this exposure was assessed after that outcome (although simultaneous with lung function measurement). The regional air quality monitoring data that we analyzed were annual average concentrations, thereby representing more chronic exposures, while the nephelometer measurements were one-time “snapshot” assessments. Although these differences introduce greater heterogeneity in the exposures we included in our modeling, this is consistent with the concept that exposure assessment for epidemiological studies of air pollution health effects should take into account time spent in different microenvironments. Although the sample size of the cohort included in the analysis is reasonably large, the number of males is relatively small, which limits the power and

generalizability of our gender-stratified sub-analysis. In addition, because the participants interviewed were somewhat older and less likely to be current or former smokers, some selection bias may have been introduced. Although we included educational attainment among the sociodemographic variables studied and this does correlate with economic status, we did not include income in our modeling, since this in itself can be an outcome rather than a cause of increased symptoms or poorer lung function (e.g., through disability). While our cohort has a wide distribution of symptom frequency and lung function, the number of persons with severe asthma (who may be the most responsive) was relatively limited. Also, although we had fairly few study participants with rhinitis alone, these might have blunted associations between PM and respiratory symptoms or lung function. While we did include a biomarker of tobacco smoke exposure, hair nicotine, this is more likely to have reflected exposure in recent days to weeks, not solely exposure in the hours preceding spirometry for which urine cotinine measurement would have been preferable. In addition, hair nicotine was undetectable in approximately one third of participants.

Despite these limitations, our study of adults with asthma has several strengths. In terms of exposure assessment, it is one of the very few that have obtained actual measurements of PM concentrations within and outside of subjects' homes. In addition, it is the first study of adults with asthma to assess exposure to SHS by measurement of hair nicotine. Although the analysis was cross-sectional, the cohort has been followed longitudinally and is well characterized. That the results of the multivariable models were reasonably consistent with those of the univariate analyses is reassuring, especially with regard to the primary finding that home PM is associated with increased risk of frequent asthma symptoms.

### Conclusions

Our results suggest that exposure to particulate matter both within and outside the home can increase odds of respiratory symptoms in adults with asthma. Exposure to ambient particulate matter based on regional air quality monitoring data was associated with decreased $FEV_1$ among women, adding support from a study in adults to the evidence in children that chronic exposure to this pollutant can negatively impact lung function. Hair nicotine was associated with both frequent respiratory symptoms and decreased $FEV_1$, demonstrating that exposure to secondhand tobacco smoke remains an important contributor to the health status of people with asthma.

## Acknowledgments

**Grant support:** NIH R01 ES010906

## Abbreviations

| | |
|---|---|
| **EPA** | US Environmental Protection Agency |
| **$FEV_1$** | forced expiratory volume in 1 second |
| **ICD-9** | International Classification of Diseases, 9th revision |
| **NHANES III** | Third National Health and Nutrition Examination Survey |

| | |
|---|---|
| **95%CI** | 95 percent confidence interval |
| **OR** | odds ratio |
| **PM** | particulate matter |
| **$PM_{2.5}$** | fine particulate matter with a mass median aerodynamic diameter <2.5 μm |
| **$PM_{10}$** | particulate matter with a mass median aerodynamic diameter <10 μm |
| **$PM_{10–25}$** | coarse particulate matter |

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## Highlights

- Environmental exposures were associated with asthma outcomes in adults.
- Kitchen PM was associated with respiratory symptoms in both sexes.
- Ambient PM was associated with lower lung function in women.
- Hair nicotine was also associated with symptoms and lower lung function in women.

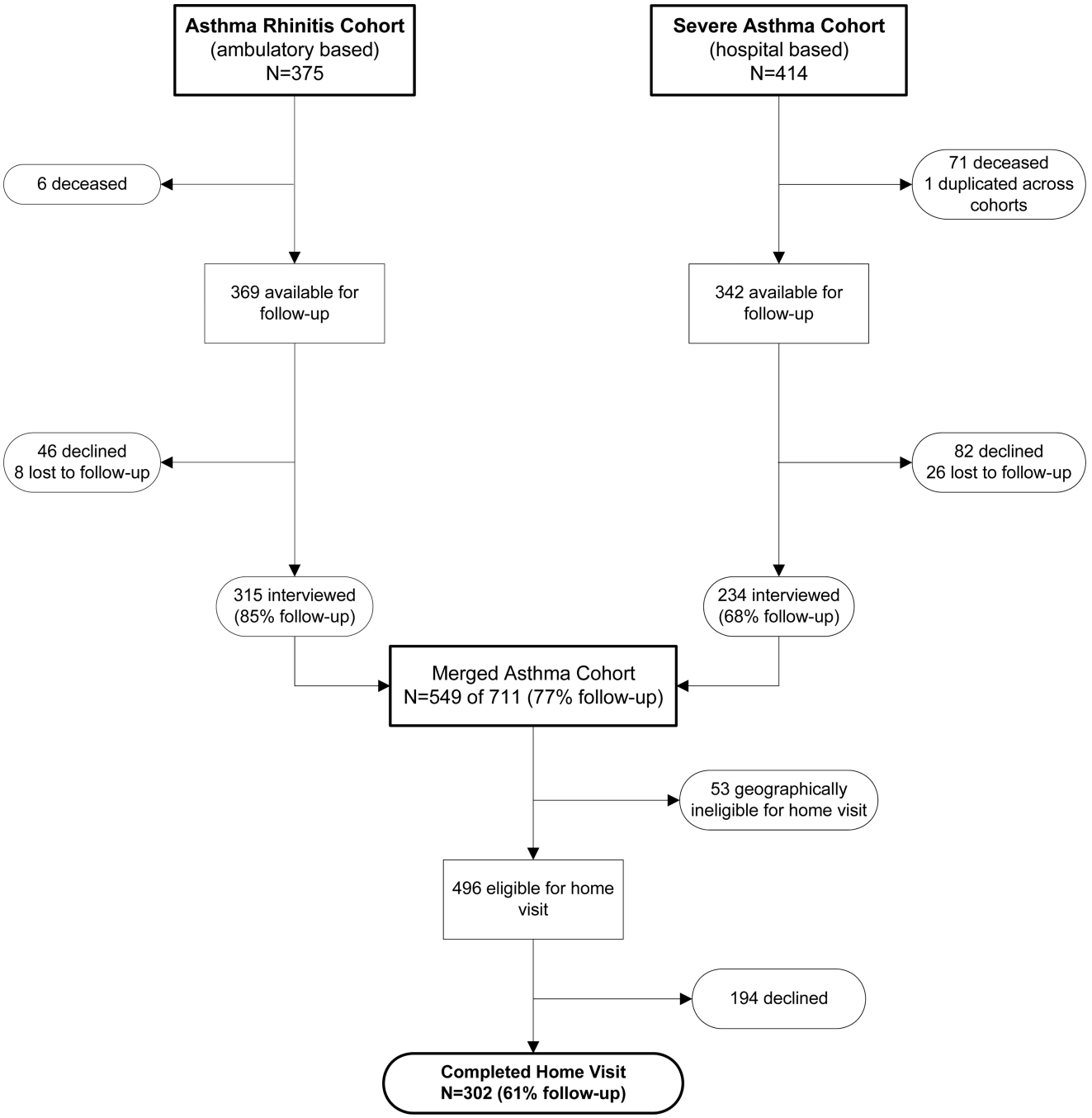


**Figure 1.**
Subject Recruitment and Participation

**Table 1**

Demographic and Clinical Characteristics of 549 Subjects by Home Visit Status

| Characteristic[a] | Home Visit (N=302) | | | No Home Visit[b] (N=247) | | |
|---|---|---|---|---|---|---|
| | n | % | (95% CI) | n | % | (95% CI) |
| Parent asthma study group | | | | | | |
| Asthma-rhinitis cohort | 177 | 58.6 | (53.1, 64.2) | 138 | 55.9 | (49.7, 62.1) |
| Severe asthma cohort | 125 | 41.4 | (35.8, 46.9) | 109 | 44.1 | (37.9, 50.3) |
| Female | 222 | 73.5 | (68.5, 78.5) | 185 | 74.9 | (69.5, 80.3) |
| Non-Hispanic white | 178 | 58.9 | (53.4, 64.5) | 149 | 60.3 | (54.2, 66.4) |
| High school education or less | 49 | 16.2 | (12.1, 20.4) | 55 | 22.3 | (17.1, 27.5) |
| Smoking status | | | | | | |
| Current | 24 | 7.9 | (4.9 ,11) | 29 | 11.7 | (7.7, 15.8) |
| Former | 110 | 36.4 | (31, 41.9) | 76 | 30.8 | (25, 36.5) |
| Never | 168 | 55.6 | (50, 61.2) | 142 | 57.5 | (51.3, 63.7) |
| Current smoke exposure | | | | | | |
| None | 217 | 71.9 | (66.8, 76.9) | 171 | 69.2 | (63.5, 75.0) |
| Indirect | 61 | 20.2 | (15.7, 24.7) | 47 | 19.0 | (14.1, 23.9) |
| Current smoker | 24 | 7.9 | (4.9, 11) | 29 | 11.7 | (7.7, 15.8) |
| Respiratory symptom frequency[d] | | | | | | |
| None | 85 | 28.1 | (23.1, 33.2) | 69 | 27.9 | (22.3, 33.5) |
| Hardly any | 51 | 16.9 | (12.7, 21.1) | 44 | 17.8 | (13.0, 22.6) |
| Occasionally | 73 | 24.2 | (19.3, 29) | 56 | 22.7 | (17.5, 27.9) |
| Most days or nights | 44 | 14.6 | (10.6, 18.5) | 37 | 15.0 | (10.5, 19.4) |
| Every day or night | 49 | 16.2 | (12.1, 20.4) | 41 | 16.6 | (12.0, 21.2) |
| | | Mean | (95% CI) | | Mean | (95% CI) |
| Age in years | | 52.2 | (51.2 ,53.2) | | 52.7 | (51.5,53.8) |
| Severity of asthma score[c] | | 9.7 | (8.9 ,10.4) | | 9.7 | (8.9 ,10.5) |

CI: confidence interval

[a] All characteristics measured at time of telephone interview prior to home visit.

[b] Of those without a home visit, 53 were not geographically eligible and 194 declined.

[c] From a previously validated measure that incorporates current symptoms and medications as well as longer term indicators of severity, e.g., hospitalization, intubation, and past and chronic corticosteroid administration; maximum score = 28.

[d] Symptom frequency is included within the severity of asthma score as the maximum of daytime and nighttime frequency in the past two weeks.

**Table 2**

Particulate Matter Exposures and Lung Function in the Analysis Subset (N=302)

| Characteristic | Min | Q1 | Median | Q3 | Max | Mean ± SD |
|---|---|---|---|---|---|---|
| Ambient particulate matter, 24-hour average annual concentration (μg/m$^3$) | | | | | | |
| $PM_{2.5}$ | 6.4 | 9.4 | 9.9 | 11.9 | 19.9 | 10.8 ± 2.6 |
| $PM_{10-2.5}$ (coarse fraction) | 5.0 | 9.8 | 11.5 | 14.1 | 31.9 | 12.1 ± 3.9 |
| Particulate matter at residence (μg/m$^3$) | | | | | | |
| Outside | 1.0 | 8.0 | 14.0 | 27.0 | 578.0 | 26.3 ± 49.1 |
| Kitchen | 1.0 | 8.0 | 14.0 | 28.0 | 1130.0 | 39.1 ± 107.3 |
| Living area | 1.0 | 9.0 | 14.0 | 27.0 | 1100.0 | 40.5 ± 111.2 |
| Cigarette smoking status | | | | | | |
| Hair nicotine (ng/mg) | 0.00 | 0.00 | 0.05 | 0.35 | 184.52 | 2.97 ± 14.99 |
| Smoke exposure[a] | 0.0 | 0.0 | 0.0 | 1.0 | 2.0 | 0.4 ± 0.6 |
| Traffic exposure at residence, distance to nearest roadway | | | | | | |
| Nearest highway[b] (m) | 10.0 | 106.1 | 217.6 | 421.1 | 3847.0 | 351.3 ± 461.0 |
| Nearest primary highway[c] (km) | 0.03 | 0.64 | 1.37 | 2.61 | 23.23 | 2.25 ± 2.90 |
| Season of outcome measurement | | | | | | |
| | | **n** | **(%)** | | | |
| Dry season[d] at telephone interview | | 182 | (60.3) | | | |
| Dry season[d] at home visit | | 189 | (62.6) | | | |
| Dry season[d] at both | | 145 | (48.0) | | | |
| FEV1 <lower limit of normal | | 155 | (51.0) | | | |

Q1: lower quartile; Q3: upper quartile; SD: standard deviation; PM: particulate matter.

[a]Smoke exposure defined as none (0), secondhand (1), active smoker (2).

[b] Highway defined as any of the following: primary interstate highway (road class 1), primary state highway (road class 2), or secondary state/county highway (road class 3).

[c] Primary highway defined as either primary interstate highway (road class 1) or primary state highway (road class 2).

[d] Respiratory symptoms measured at time of telephone interview; lung function measured at subsequent home visit. Average time elapsed between interview and home visit was 66 ± 68 days.

**Table 3**

Exposures to Particulate Matter as Univariate Predictors of Respiratory Outcomes (N=302)

| | | Respiratory symptoms (ordinal logistic regression) | | | $FEV_1$ <lower limit of normal (binary logistic regression) | | |
|---|---|---|---|---|---|---|---|
| **Exposure** | **Exposure level** | **OR** | **(95% CI)** | ***P*** | **Estimate** | **(95% CI)** | ***P*** |
| Ambient particulate matter, 24-hour average annual concentration (μg/m$^3$) | | | | | | | |
| $PM_{2.5}$ | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (9.5– <11.11 μg/m$^3$) | 1.44 | (0.88,2.37) | 0.15 | 1.69 | (0.95,2.99) | 0.07 |
| | Highest (≥11.11 μg/m$^3$) | 1.61 | (0.98,2.63) | 0.06 | 1.28 | (0.72,2.25) | 0.40 |
| $PM_{10–2.5}$ (coarse fraction) | Lowest (<10.68 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (10.68–12.68 μg/m$^3$) | 0.86 | (0.53,1.41) | 0.55 | 1.24 | (0.71,2.99) | 0.45 |
| | Highest (≥12.71 μg/m$^3$) | 1.07 | (0.66,1.75) | 0.78 | 1.45 | (0.82,2.25) | 0.20 |
| Particulate matter at residence (μg/m$^3$) | | | | | | | |
| Outside | Lowest (≤9 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (10– 20 μg/m$^3$) | 1.16 | (0.70,1.93) | 0.57 | 0.97 | (0.55,1.72) | 0.93 |
| | Highest (>20 μg/m$^3$) | 1.44 | (0.85,2.41) | 0.17 | 1.10 | (0.59,2.05) | 0.77 |
| Kitchen | Lowest (≤10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (11– 21 μg/m$^3$) | 1.56 | (0.95,2.58) | 0.08 | 1.01 | (0.57,1.77) | 0.98 |
| | Highest (≥21 μg/m$^3$) | 1.75 | (1.07,2.87) | 0.03 | 1.04 | (0.58,1.85) | 0.90 |
| Living area | Lowest (≤10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (10– 22 μg/m$^3$) | 1.17 | (0.72,1.91) | 0.53 | 1.08 | (0.62,1.88) | 0.78 |
| | Highest (>22 μg/m$^3$) | 1.41 | (0.85,2.33) | 0.18 | 1.07 | (0.58,1.96) | 0.83 |
| Cigarette smoking status | | | | | | | |
| Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (>0.0–<0.14 ng/mg) | 1.34 | (0.81,2.2) | 0.25 | 0.70 | (0.39,1.24) | 0.22 |
| | Highest (≥0.14 ng/mg) | 1.72 | (1.07,2.78) | 0.03 | 1.99 | (1.12,3.53) | 0.02 |

| Exposure | Exposure level | Respiratory symptoms (ordinal logistic regression) OR | (95% CI) | *P* | $FEV_1$ <lower limit of normal (binary logistic regression) Estimate | (95% CI) | *P* |
|---|---|---|---|---|---|---|---|
| Smoke exposure | none *(ref)* | 1.00 | — | | 1.00 | — | |
| | Indirect | 1.49 | (0.90,2.47) | 0.12 | 0.82 | (0.46,1.47) | 0.51 |
| | current smoker | 1.21 | (0.57,2.55) | 0.62 | 0.87 | (0.37,2.03) | 0.75 |
| Traffic exposure at residence, distance to nearest roadway | | | | | | | |
| Proximity nearest highway[a] | Lowest (>334 m) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (131 – 334 m) | 1.26 | (0.77,2.06) | 0.35 | 0.97 | (0.54,1.73) | 0.92 |
| | Highest (≤131 m) | 0.77 | (0.47,1.26) | 0.30 | 0.98 | (0.55,1.75) | 0.95 |
| Proximity to primary highway[b] | Lowest (≥ 1.98 km) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Middle (0.82–1.97 km) | 0.71 | (0.43),1.16 | 0.17 | 0.95 | (0.53,1.68) | 0.85 |
| | Highest (≤8.17 km) | 0.80 | (0.49),1.30 | 0.37 | 1.02 | (0.58,1.80) | 0.94 |
| Season of outcome measurement[c] | | | | | | | |
| Season | Wet (November-March) *(ref)* | 1.00 | — | | 1.00 | — | |
| | Dry (April-October) | 1.68 | (1.11,2.54) | 0.01 | 1.33 | (0.83,2.13) | 0.24 |

$FEV_1$: forced expiratory volume in one second; PM: particulate matter; OR: odds ratio; CI: confidence interval.

[a] Highway defined as any of the following: primary interstate highway (road class 1), primary state highway (road class 2), or secondary state/county highway (road class 3).

[b] Primary highway defined as either primary interstate highway (road class 1) or primary state highway (road class 2).

[c] Respiratory symptoms measured at time of telephone interview; $FEV_1$ measured at subsequent home visit.

**Table 4**

Exposures to Particulate Matter as Predictors of Respiratory Outcomes in Multivariable Analyses (N=302)

| | | | Respiratory symptoms (ordinal logistic regression) | | | $FEV_1$ <lower limit of normal (binary logistic regression) | | |
|---|---|---|---|---|---|---|---|---|
| **Model**[a] | **Exposure** | **Exposure level** | **OR** | **(95% CI)** | ***P*** | **OR** | **(95% CI)** | ***P*** |
| 1 | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 1.38 | (0.84, 2.27) | 0.21 | 1.69 | (0.94, 3.03) | 0.08 |
| | | Highest (≥11.11 μg/m$^3$) | 1.55 | (0.94, 2.55) | 0.09 | 1.30 | (0.73, 2.32) | 0.37 |
| 2 | Home PM -- kitchen | Lowest (≤ 10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 1.49 | (0.90, 2.46) | 0.12 | 1.00 | (0.56, 1.77) | 1.00 |
| | | Highest (≥21 μg/m$^3$) | 1.64 | (1.00, 2.69) | 0.05 | 0.97 | (0.54, 1.74) | 0.92 |
| 3 | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0 - <0.14 ng/mg) | 1.24 | (0.75, 2.05) | 0.41 | 0.65 | (0.36, 1.16) | 0.14 |
| | | Highest (≥0.14 ng/mg) | 1.47 | (0.89, 2.4) | 0.13 | 1.80 | (1.00, 3.25) | 0.05 |
| 4 | Season of outcome measurement[b] | Wet (November-March) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Dry (April-October) | 1.66 | (1.09, 2.51) | 0.02 | 1.39 | (0.85, 2.25) | 0.19 |
| 5 | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 1.33 | (0.80, 2.20) | 0.27 | 1.48 | (0.81, 2.70) | 0.21 |
| | | Highest (≥11.11 μg/m$^3$) | 1.39 | (0.83, 2.31) | 0.21 | 1.33 | (0.73, 2.42) | 0.35 |
| | Home PM — kitchen | Lowest (≤ 10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 1.43 | (0.86, 2.38) | 0.16 | 0.99 | (0.55, 1.78) | 0.98 |
| | | Highest (≥21 μg/m$^3$) | 1.40 | (0.84, 2.34) | 0.20 | 0.93 | (0.50, 1.72) | 0.81 |
| | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0-<0.14 ng/mg) | 1.20 | (0.72, 2.01) | 0.48 | 0.69 | (0.38, 1.26) | 0.22 |
| | | Highest (≥0.14 ng/mg) | 1.47 | (0.88, 2.45) | 0.14 | 1.85 | (1.00, 3.41) | 0.05 |
| | Season of outcome measurement[b] | Wet (November-March) *(ref)* | 1.00 | — | | 1.00 | — | |

| Model[a] | Exposure | Exposure level | Respiratory symptoms (ordinal logistic regression) OR | (95% CI) | P | $FEV_1$ <lower limit of normal (binary logistic regression) OR | (95% CI) | P |
|---|---|---|---|---|---|---|---|---|
| | | Dry (April-October) | 1.54 | (1.00, 2.37) | 0.05 | 1.33 | (0.80, 2.2) | 0.27 |

$FEV_1$: Forced expiratory volume in one second; OR: odds ratio; CI: confidence interval; PM: particulate matter.

[a]Models 1 – 4 include the exposure and education, race-ethnicity, age in years, sex, and season of outcome measurement (dry vs. wet); Model 5 includes all exposures as well as education, race-ethnicity, age in years, sex, and season of outcome measurement (dry vs. wet).

[b]Respiratory symptoms measured at time of telephone interview; $FEV_1$ measured at subsequent home visit.

**Table 5**

Exposures to Particulate Matter as Predictors of Respiratory Outcomes in Multivariable Analyses, Stratified by Sex and Age

| | | | Respiratory symptoms (ordinal logistic regression) | | | $FEV_1$ <lower limit of normal (binary logistic regression) | | |
|---|---|---|---|---|---|---|---|---|
| **Subgroup** | **Exposure** | **Exposure level** | **OR** | **(95% CI)** | ***P*** | **OR** | **(95% CI)** | ***P*** |
| Females (n=222)[a] | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 1.33 | (0.74, 2.41) | 0.34 | 1.93 | (0.94, 3.95) | 0.07 |
| | | Highest (≥11.11 μg/m$^3$) | 1.68 | (0.91, 3.11) | 0.10 | 2.23 | (1.08, 4.61) | 0.03 |
| | Home PM -- kitchen | Lowest (≤10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 1.39 | (0.78, 2.48) | 0.27 | 0.92 | (0.46, 1.81) | 0.80 |
| | | Highest (≥21 μg/m$^3$) | 1.09 | (0.59, 2.00) | 0.78 | 0.76 | (0.36, 1.58) | 0.46 |
| | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0-<0.14 ng/mg) | 1.35 | (0.75, 2.43) | 0.32 | 0.85 | (0.43, 1.69) | 0.64 |
| | | Highest (≥0.14 ng/mg) | 2.38 | (1.26, 4.49) | 0.01 | 2.90 | (1.32, 6.38) | 0.01 |
| | Season[b] | Wet (November-March) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Dry (April-October) | 1.59 | (0.95, 2.65) | 0.08 | 1.25 | (0.68, 2.29) | 0.48 |
| Males (n=80)[a] | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 1.07 | (0.36, 3.15) | 0.91 | 0.58 | (0.15, 2.16) | 0.42 |
| | | Highest (≥11.11 μg/m$^3$) | 0.96 | (0.36, 2.58) | 0.94 | 0.34 | (0.10, 1.14) | 0.08 |
| | Home PM -- kitchen | Lowest (≤10 μg/m$^3$) *(ref* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 2.23 | (0.72, 6.97) | 0.17 | 2.11 | (0.56, 7.98) | 0.27 |
| | | Highest (≥21 μg/m$^3$) | 2.52 | (0.88, 7.24) | 0.09 | 1.93 | (0.54, 6.96) | 0.31 |
| | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0-<0.14 ng/mg) | 0.74 | (0.23, 2.40) | 0.62 | 0.32 | (0.07, 1.37) | 0.13 |
| | | Highest (≥0.14 ng/mg) | 0.57 | (0.21, 1.50) | 0.25 | 0.77 | (0.24, 2.47) | 0.67 |
| | Season[b] | Wet (November-March) *(ref)* | 1.00 | — | | 0.38 | (0.08, 1.72) | 0.21 |

| Subgroup | Exposure | Exposure level | Respiratory symptoms (ordinal logistic regression) OR | (95% CI) | *P* | $FEV_1$ <lower limit of normal (binary logistic regression) OR | (95% CI) | *P* |
|---|---|---|---|---|---|---|---|---|
| | | Dry (April-October) | 1.33 | (0.55, 3.22) | 0.53 | 1.60 | (0.54, 4.72) | 0.40 |
| Age ≥55 (n=164)[c] | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 2.07 | (1.01, 4.24) | 0.05 | 1.95 | (0.83, 4.59) | 0.12 |
| | | Highest (≥11.11 μg/m$^3$) | 1.60 | (0.78, 3.26) | 0.20 | 1.33 | (0.57, 3.10) | 0.51 |
| | Home PM -- kitchen | Lowest (≤10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 1.71 | (0.85, 3.41) | 0.13 | 1.06 | (0.46, 2.45) | 0.89 |
| | | Highest (≥21 μg/m$^3$) | 1.41 | (0.67, 2.95) | 0.36 | 0.87 | (0.35, 2.20) | 0.78 |
| | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0-<0.14 ng/mg) | 1.48 | (0.73, 3.00) | 0.27 | 0.89 | (0.38, 2.05) | 0.78 |
| | | Highest (≥0.14 ng/mg) | 2.55 | (1.21, 5.36) | 0.01 | 2.23 | (0.92, 5.43) | 0.08 |
| | Season[b] | Wet (November-March) *(ref)* | 1.00 | — | | 0.38 | (0.08, 1.72) | 0.21 |
| | | Dry (April-October) | 1.25 | (0.70, 2.22) | 0.45 | 1.74 | (0.85, 3.58) | 0.13 |
| Age ≥55 (n=138)[c] | $PM_{2.5}$ -- average annual concentration | Lowest (≤9.49 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (9.5-<11.11 μg/m$^3$) | 0.83 | (0.39, 1.74) | 0.62 | 0.99 | (0.41, 2.39) | 0.97 |
| | | Highest (≥11.11 μg/m$^3$) | 1.33 | (0.62, 2.81) | 0.46 | 1.28 | (0.53, 3.12) | 0.58 |
| | Home PM -- kitchen | Lowest (≤10 μg/m$^3$) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (11–21 μg/m$^3$) | 1.21 | (0.55, 2.67) | 0.63 | 0.87 | (0.35, 2.18) | 0.77 |
| | | Highest (≥21 μg/m$^3$) | 1.36 | (0.61, 3.03) | 0.46 | 1.00 | (0.39, 2.57) | 0.99 |
| | Hair nicotine | Lowest (0 ng/mg) *(ref)* | 1.00 | — | | 1.00 | — | |
| | | Middle (>0.0-<0.14 ng/mg) | 1.04 | (0.47, 2.31) | 0.92 | 0.43 | (0.17, 1.11) | 0.08 |
| | | Highest (≥0.14 ng/mg) | 0.99 | (0.47, 2.09) | 0.98 | 1.47 | (0.62, 3.50) | 0.39 |
| | Season[b] | Wet (November-March) *(ref)* | 1.00 | — | | 0.38 | (0.08, 1.72) | 0.21 |
| | | Dry (April-October) | 1.95 | (0.99, 3.85) | 0.05 | 1.00 | (0.47, 2.14) | 0.99 |

FEV1: Forced expiratory volume in one second; OR: odds ratio; CI: confidence interval; PM: particulate matter.

[a] Model adjusted for all four exposures, education, race-ethnicity, and age (defined dichotomously as <55 vs. ≥55).

[b] Season of outcome measurement (dry vs. wet); symptoms measured at telephone interview; FEV1 at subsequent home visit.

[c] Model adjusted for all four exposures, education, race-ethnicity, and sex.