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Effect of Particulate Air Pollution on Lung Function in Adult and Pediatric Subjects in a Seattle Panel Study*

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Study objective: **To determine whether increased exposure to particulate matter air pollution (PM), measured with personal, residential, or central site monitoring, was associated with pulmonary function decrements in either adults with COPD or children with asthma.**

Participants: **We studied 57 adults with or without COPD and 17 children aged 6 to 13 years with physician-diagnosed asthma in Seattle during a 3-year panel study.**

Study design and measurements: **Indoor and outdoor PM measurements were made at subjects' homes. The subjects wore personal exposure monitors for 10 consecutive 24-h periods, and PM was also measured at a central outdoor location. We assessed the within-subject effect of particulate exposure on FEV_1 and peak expiratory flow (PEF) in adults, and maximal midexpiratory flow (MMEF), PEF, FEV_1, and symptoms in children.**

Results: **FEV_1 decrements were associated with 1-day lagged central site PM $\leq$ 2.5 μm in diameter ($PM_{2.5}$) in adult subjects with COPD. In children not receiving antiinflammatory medication, same day indoor, outdoor, and central site exposures to $PM_{2.5}$ were associated with decrements in MMEF, PEF, and FEV_1. Associations with $PM_{2.5}$ and lung function decrements were also observed for 1-day lagged indoor (MMEF, PEF, FEV_1) and personal (PEF only) exposures. Antiinflammatory medication use in children significantly attenuated the PM effect on airflow rates and volumes.**

Conclusions: **This study found consistent decrements in MMEF in children with asthma who were not receiving medications. It is notable that effects were observed even though PM exposures were low for an urban area. These findings suggest the need for future larger studies of PM effects in this susceptible population that repeatedly measure spirometry to include MMEF and potentially more sensitive markers of airway inflammation such as exhaled breath condensate and exhaled nitric oxide.** ***(CHEST 2006; 129:1614–1622)***

Key words: adults; asthma; children; COPD; lung function; particulate air pollution

Abbreviations: BMI = body mass index; CI = confidence interval; eNO = exhaled nitric oxide; EPA = Environmental Protection Agency; MMEF = maximal midexpiratory flow; PEF = peak expiratory flow; PM = particulate matter air pollution; $PM_{2.5}$ = particulate matter air pollution ≤ 2.5 μm in diameter; PM_{10} = particulate matter air pollution ≤ 10 μm in diameter

Lung function has been one of the most important assessment tools available to investigators of the health effects of air pollution. Although some measurements of lung function require sophisticated equipment, basic lung function parameters can be measured with spirometers. Whereas there is no question that lung function in children is decreased on exposure to particulate matter air pollution (PM),[1–5] the situation in adults in not quite as clear. Nevertheless, there are some studies that document such a relationship. Both FEV_1 and peak expiratory flow (PEF) have been used to assess the effects on lung mechanics from exposure to PM. For instance, Grievink and associates[6] studied a panel of adults in Europe with chronic respiratory disease and reported decrements in PEF. Van der Zee and coworkers[7] studied a large cohort of adult subjects aged 50 to 70 years both with and without chronic respi-

ratory disease over a period of three winters. Fairly large decrements were reported per 100 $\mu g/m^3$ PM ≤ 10 μm in diameter (PM_{10}) in morning PEF measured on the same day lag as outdoor air pollutants. Brauer and colleagues[8] reported an association between lung function and personal exposure to PM in a panel study of subjects with COPD in Vancouver, BC. Although not significant, decrements of 3% and 1% in FEV_1 were associated with PM_{10} or PM ≤ 2.5 μm in diameter ($PM_{2.5}$), respectively. In a study from Finland, Penttinen et al[9] reported that both the number concentration and the size of particles (0.1 to 1 μm) were determinants of associations between PM and decreased lung function. However these associations were mainly nonsignificant. The number of accumulation mode particles was consistently inversely associated with PEF in a group of 78 adult subjects with asthma. We have reported associations between $PM_{2.5}$ and decrements in lung function (1.8-mL decrement in FEV_1 per 1 $\mu g/m^3$ $PM_{2.5}$)[10] and symptom exacerbation[11] in children with asthma in Seattle.

Current research is focused on understanding better the identification of susceptible populations and differentiating personal, indoor, and outdoor exposure from central site exposures. There is some concern that pollutants measured at central sites do not represent individual or residential community exposures. In this article, we present data on relationships between lung function changes in both adults and children over 5- to 10-day monitoring periods during which daily PM was measured outside, inside, and on the person in Seattle.

Materials and Methods

We performed a 3-year panel study (from 1999 to 2002) in Seattle that evaluated cardiac and respiratory effects of personal, indoor, and outdoor measures of air pollution in 57 elderly subjects who were either healthy or had respiratory or cardiac disease. We also studied 17 children with asthma. The experimental design and exposure monitoring methods are described below. A detailed discussion of the exposure assessment methods and results has been published previously.[12]

Subjects were recruited through distribution of advertisements at clinics, senior centers, and retirement homes. All but one of the adult subjects was > 65 years of age; 85% were between 71 years and 90 years of age. The children were 6 to 13 years of age. Many of the subjects (55%) enrolled for more than one monitoring period (session). The inclusion criteria for the adult subjects with respiratory disease were physician-diagnosed COPD and FEV_1 between 30% and 70% of predicted. Because of the high incidence of hypertension in normal elderly subjects, those with hypertension were not excluded from the adult group, which also included subjects with a history of myocardial infarction or angina. All subjects were nonsmokers and lived with nonsmokers. The children all had physician-diagnosed asthma and were recruited from a large asthma and allergy clinic. Since children with asthma experience small airway inflammation in response to extrinsic triggers,[13,14] maximal midexpiratory flow (MMEF) was added as a potentially more sensitive (than FEV_1 or PEF) indicator of small airway function.

Personal, indoor, and outdoor monitoring was conducted for all subjects. $PM_{2.5}$ and PM_{10} gravimetric 24-h measurements were obtained inside and outside subjects' residences with single-stage inertial Harvard impactors operated at a flow rate of 4 L/min (Air Diagnostics and Engineering; Naples, ME).[15] Each subject also carried a personal monitor (Harvard Personal Environmental Monitor for $PM_{2.5}$; Harvard School of Public Health; Boston, MA) for 24 h each day, which was worn or placed close to the person. These integrated fixed-site and personal measurements were collected over 24 h for 5 to10 consecutive session days. Exposure monitoring began 1 day prior to health measurements to provide 24-h exposure data to help compensate for lag structure. Subjects were monitored during 26 exposure sessions: 13 in year 1 (October 1999 through August 2000) and 13 in year 2 (October 2000 through May 2001). Twelve of the subjects completed one monitoring session each in year 3 (October 2001 through February 2002).

Lung function measurements in adults were collected using portable spirometers (VM Plus; Clement Clarke; Columbus, OH) that record both FEV_1 and PEF, consisting of a modified Mini-Wright peak flowmeter and standard mouthpiece. The spirometers were calibrated with a 3-L syringe at the beginning of each 10-day session. Lung function measurements in the children (FEV_1, PEF, MMEF) were also collected using spirometers (MicroDL; Micro Direct; Lewiston, ME). Lung function maneuvers were collected according to American Thoracic Society guidelines.[16] Lung function data not conforming to American Thoracic Society within-test reproducibility criteria were excluded. Subjects were instructed to withhold use of bronchodilator medications within 4 h of the scheduled technician visit. Technicians coached the subjects in spirometric maneuvers once a day during the daily visit to subjects' residences. All subjects completed daily symptom and medication-use diaries.

Mixed-effects random intercept longitudinal regression models were applied to test for decreases in lung function associated with a 10 $\mu g/m^3$ increase in exposure. Nested random intercepts were included to accommodate variation in susceptibility among subjects (a subject-specific random intercept) as well among sessions within subjects (a subject-session specific random intercept). Pulmonary function and exposure measurements were analyzed using SAS software (Proc Mixed; SAS Institute; Cary, NC). Seasonal confounding is a major concern when subjects are observed during different times of the year. In addition to

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controlling for climatologic covariates, we controlled for seasonal confounding by decomposing daily $PM_{2.5}$ concentrations into three components: let X*isd* be a $PM_{2.5}$ exposure measure for subject *i* on day *d* of session *s*. Then X*isd* = X*i* + (X*is* – X*i*) + (X*isd* – X*is*). X*i* is subject *i*'s average exposure during the time he or she was observed, X*is* – X*i* is the difference between his or her average during session *s* and his or her overall average exposure, and X*isd* – X*is* is the difference between his or her daily exposure on day *d* of session *s* and his or her average exposure during session *s*. When modeling, we included all three components as separate covariates; however, we believe that the first two are confounded by season, and we do not interpret parameters associated with them. We believe X*isd* − X*is* is less confounded by season, and the parameter associated with it is our estimation target. We interpret the parameter estimate as the expected response change (in lung function) for short-term changes in $PM_{2.5}$ concentrations. Additional control was made for temperature, relative humidity, age, gender, and body mass index (BMI) for children. COPD status and its interaction term were included for the adults, and antiinflammatory medication status and its interaction term were included for children. A sensitivity analysis including daily co-pollutants (carbon monoxide and nitrogen dioxide) was evaluated. The central site CO and NO_2 concentrations were decomposed in the same way to adequately control for their potentially confounding effects. We used SAS software (Proc MI; SAS Institute) to construct five imputation samples. Multiple imputation samples were constructed for the four central site covariates with missing data (CO [1 day], NO_2 [42 days], temperature [2 days], relative humidity [2 days]) plus central site $PM_{2.5}$, which was measured on all study days. Parameter estimates corresponding to PM covariates were combined using standard procedures.[17,18]

Results

Adult Subjects

A total of 57 subjects (24 with COPD and 33 without COPD) were included in this analysis. The COPD subjects ranged in age from 65 to 89 years; non-COPD subjects were 56 to 88 years old. The median age for both groups was 76 years. Many of the subjects (33%) enrolled for more than one session (10-day monitoring period). The median percentage of predicted FEV_1 at screening for the subjects was 56% for COPD subjects and 100% for non-COPD subjects. The percentage of predicted FEV_1 value for two subjects with COPD at screening was $> 75\%$ and for one COPD subject was $< 30\%$. Subjects were stratified into those with and without COPD. Subject characteristics and outcome variables are shown in Table 1.

Median 24-h $PM_{2.5}$ values from three central sites in Seattle representative of the residential area in this study were 10.3 $\mu g/m^3$ (207 days). Median 24-h $PM_{2.5}$ values outside subjects' residences were 8.6

Table 1—*Demographics and Outcome Summary of Study Participants*

	Adults			Children		
Variables	COPD	No COPD	Overall	Medication	No Antiinflammatory Medication*	Overall
Subjects, No.	24	33	57	11	6	17
Subject sessions, No.†	36	49	85	20	11	29
Subject days, No.	287	405	692	194	97	268
Female subjects, No. (%)	15 (63)	16 (48)	31 (54)	1 (9)	4 (50)	4 (24)
Median age (range), yr	75.5 (65–89)	76 (56–88)	76 (56–89)	9 (6–11)	8.5 (6–12)	9 (6–12)
Median height (range), m	1.7 (1.5–1.9)	1.7 (1.5–1.9)	1.7 (1.5–1.9)	1.5 (1.3–1.6)	1.5 (1.2–1.7)	1.5 (1.2–1.7)
Median weight (range), kg	77 (43–105)	71 (50–120)	75 (43–120)	39 (28–63)	47 (30–61)	42 (28–63)
BMI (range), kg/m^2	26 (19–36)	25 (19–42)	25 (19–42)	19 (14–27)	22 (17–25)	20 (14–27)
Median daily β-agonist use (range), No.	0 (0–4)	0 (0–0)	0 (0–4)			
Median baseline FEV_1 % predicted (range), %	55.7 (24.1–83.8)	100.5 (75.4–146.8)	84.6 (24.1–146.8)	96 (67–112)	105 (81–119)	98 (67–119)
Median baseline PEF % predicted (range), %	39 (15–119)	99 (37–211)	84 (15–211)	79 (69–113)	80 (79–94)	80 (69–113)
Median baseline FEV_1/FVC (range), %	61 (37–86)	79 (66–87)	74 (37–87)	83 (66–93)	86 (73–96)	84 (66–96)
FEV_1 during sessions (range), L	1.1 (0.3–2.3)	1.9 (1–3.8)	1.6 (0.3–3.8)	1.9 (0.7–2.5)	1.8 (0.5–3.4)	1.9 (0.5, 3.4)
PEF during sessions (range), L/min	238 (51–467)	471 (200–758)	383 (51–758)	260 (56–392)	233 (39–506)	254 (39–506)
MMEF during sessions (range), L/min				110 (24–203)	92 (21–320)	107 (21–320)
Mean daily as-needed rescue inhaler puffs (SD), No.				0.13 (0.51)	0.16 (0.53)	0.15 (0.52)

*This group was not prescribed antiinflammatory medications; bronchodilator medications were prescribed.

†One male subject, classified in the antiinflammatory medication group, was not prescribed a leukotriene inhibitor medication during one study session, so was analyzed in the No-Antiinflammatory Medication category for that session.

$\mu g/m^3$ (646 subject days). Median indoor 24-h $PM_{2.5}$ values were 7.6 $\mu g/m^3$ (649 subject days). Median personal 24-h $PM_{2.5}$ values were 8.5 $\mu g/m^3$ (596 subject days). In this study, we observed strong correlations ($r = 0.70$) between home outdoor and central site $PM_{2.5}$ measurements, similar to those previously reported for the larger panel study.[12,19] Exposure distributions of outdoor $PM_{2.5}$ by subject session (10-day monitoring period) are given in Table 2.

Our primary analyses assessed associations between change in lung function (FEV_1 or PEF) and personal, indoor, outdoor, and central site $PM_{2.5}$ and outdoor coarse fraction of PM. In the initial analysis, there were not any associations among these variables, with the one exception of a positive association with coarse fraction in subjects without COPD (data not shown). We also performed a sensitivity analysis that added two outdoor gaseous air pollutants to the model, CO and NO_2. In this analysis, associations between decreases in FEV_1 and central site $PM_{2.5}$ were observed overall for same-day and 1-day lagged ($-$ 35.5 mL; 95% confidence interval [CI], $-$ 70.0 to $-$ 1.0; and $-$ 40.4 mL; 95% CI, $-$ 71.1 to $-$ 9.6, respectively) and in the COPD group ($-$ 70.8 mL; 95% CI, $-$ 118.4 to $-$ 23.1) for 1-day lagged exposure. The 1-day lagged outdoor $PM_{2.5}$ associations with FEV_1, although not statistically significant, showed the strongest COPD interaction effect. No associations between PEF and PM exposure were observed for adult subjects (Table 3).

Pediatric Subjects With Asthma

Demographic and descriptive data for the 17 study subjects are listed in Table 1. Median age of subjects was 9 years (range, 6 to 12 years), with 13 male and 4 female subjects participating. Ages were comparable in medication groups, although a larger percentage of male subjects were in the antiinflammatory medication-use group. Eleven subjects were prescribed antiinflammatory medication that included inhaled corticosteroids (n = 7), leukotriene inhibitors (n = 3), and a combination of inhaled corticosteroids and leukotriene inhibitors (n = 1). Of the six subjects not prescribed antiinflammatory medications, one reported use of extended bronchodilators and the remainder used bronchodilators regularly or as needed. Most study subjects had mild persistent asthma as indicated by the use of daily antiinflammatory control medication and normal baseline FEV_1.

Daily air pollution and meteorologic measurements are presented in Table 2. Median 24-h $PM_{2.5}$ values from three central sites in the Seattle area were 11.2 $\mu g/m^3$ (98 days). Median 24-h $PM_{2.5}$ values outside subjects' residences were 9.6 $\mu g/m^3$ (291 subject days). Median indoor 24-h $PM_{2.5}$ values were 7.5 $\mu g/m^3$ (296 subject days). Median personal 24-h $PM_{2.5}$ values were 11.3 $\mu g/m^3$ (263 subject days). Session-specific outdoor PM levels are presented in Figure 1. In this study, we observed strong correlations ($r = 0.77$) between home outdoor and central site $PM_{2.5}$ measurements.[12,19]

Results of tests for associations between pediatric spirometric measures (MMEF, PEF, FEV_1) and PM metrics are presented in Table 4. These analyses included adjustment for CO and NO_2. Same-day $PM_{2.5}$ measured at indoor, outdoor, and central sites was significantly associated with declines in MMEF among pediatric subjects with asthma who were not

Table 2—*Daily Air Pollution and Meteorologic Measurements

Variables	No.	Minimum	25th Percentile	50th Percentile	75th Percentile	Maximum
Subject-specific exposure, $\mu g/m^3$ (319 subject-days for children, 692 for adults)						
Personal $PM_{2.5}$	263/596	1.0/1.3	8.1/5.9	11.3/8.5	16.3/12.4	49.4/66.6
Indoor $PM_{2.5}$	296/649	2.2/1.6	5.7/5.1	7.5/7.6	10.2/10.8	36.3/65.3
Local outdoor $PM_{2.5}$	291/646	2.8/0.0	6.4/6	9.6/8.6	14.8/13.1	40.4/41.5
Coarse outdoor ($PM_{10} - PM_{2.5}$)	280/617	0.0/0.0	3.3/3.3	4.7/5.0	6.9/7.1	25.3/25.7
Central site exposure† (98 study days for children, 207 for adults)						
$PM_{2.5}$, $\mu g/m^3$ (average of Kent, Lake Forest Park, Lynwood)	98/207	4.3/3.1	8.2/7.6	11.2/10.3	16.9/15.7	40.3/40.3
NO_2, parts per billion	98/207	8.0/8	18.9/17.2	22.6/20.9	26.4/25.4	36.2/36.2
CO, parts per 10,000,000	98/207	7.6/6.3	10.0/9.6	12.5/11.6	15.8/14.6	25.0/25.0
Temperature, °F	98/207	33.0/33.5	40.3/41.3	44.3/47.7	49.5/53.6	68.7/69.3
Relative humidity, %	98/207	55.3/45.1	71.0/71.1	78.5/80	84.7/85.3	98.1/98.1

*Data are presented as values for children/adults.

†For central site exposures, we used multiple imputations with five samples to construct a complete central site exposure dataset. There were missing data on 1 day for CO, 22 days for NO_2 (42 for adults), 2 days for temperature, and 2 days for relative humidity. The values reported are based on the mean daily value from the five imputation samples.

Table 3—*Change in Adult Lung Function per 10 μg/m^3 Change in PM**

Exposure	Lag	FEV_1, mL				PEF, L/min			
		Overall	No COPD	COPD	p Value†	Overall	No COPD	COPD	p Value†
Personal $PM_{2.5}$	0	− 6.0 (− 29.1–17.2)/596	− 4.6 (− 31.0–21.9)/353	− 10.2 (− 55.8–35.4)/243	0.832	1.5 (− 2.2–5.2)/589	3.4 (− 0.9–7.6)/350	− 4.3 (− 11.5–3.0)/239	0.072
	1	12.0 (− 12.9–36.9)/529	19.3 (− 8.2–46.7)/314	− 19.0 (− 74.1–36.2)/215	0.218	2.1 (− 1.9–6.1)/524	1.9 (− 2.5–6.3)/312	2.6 (− 6.3–11.5)/212	0.886
Indoor $PM_{2.5}$	0	− 12.8 (− 44.5–19.0)/649	− 15.8 (− 50.0–18.4)/387	2.6 (− 71.7–76.8)/262	0.651	− 0.5 (− 5.6–4.6)/641	0.1 (− 5.4–5.6)/383	− 3.2 (− 15.1–8.7)/258	0.615
	1	19.4 (− 11.3–50.1)/588	28.4 (− 4.6–61.3)/346	− 29.7 (− 102.9–43.5)/242	0.146	2.3 (− 3.3–7.8)/580	2.5 (− 3.5–8.4)/343	1.1 (− 12.0–14.3)/237	0.853
Outdoor $PM_{2.5}$	0	− 1.4 (−35.6, 32.7)/646	1.5 (− 36.1, 39.2)/383	− 8.9 (−62.2, 44.4)/263	0.718	2.3 (−3.3, 7.9)/296	4.0 (−2.2, 10.1)/37	− 1.8 (− 10.6–6.9)/259	0.222
	1	− 2.4 (− 37.6–32.7)/583	10.7 (− 26.9–48.4)/344	− 45.2 (− 102.6–12.1)/239	0.064	0.4 (− 5.6–6.4)/575	2.0 (− 4.4–8.4)/341	− 4.8 (− 14.6–4.9)/234	0.184
Coarse outdoor	0	− 27.9 (− 87.5–31.8)/617	− 49.2 (− 22.3–23.9)/369	7.3 (− 84.7–99.4)/248	0.322	5.3 (− 5.1–15.7)/609	5.1 (− 7.7–17.8)/365	5.7 (− 10.3–21.6)/244	0.95
	1	47.1 (− 5.1–99.4)/555	74.3 (6.8–141.8)/330	11.5 (− 65.4–88.3)/225	0.212	− 2.5 (− 11.6–6.5)/549	− 5.8 (− 17.5–5.9)/327	1.7 (− 11.5–14.9)/222	0.389
Central $PM_{2.5}$	0	− 35.5 (− 70.0– − 1.0)/692	− 32.6 (− 69.5–4.3)/405	− 43.6 (− 95.0–7.8)/287	0.671	1.5 (− 4.2–7.1)/683	2.5 (− 3.5–8.6)/401	− 1.5 (− 9.9–6.9)/282	0.339
	1	− 40.4 (− 71.1– − 9.6)/692	− 29.0 (− 62.5–4.5)/405	− 70.8 (− 118.4– − 23.1)/287	0.101	− 2.3 (− 7.4–2.9)/683	− 0.5 (− 6.1–5.0)/401	− 7.1 (− 15.0–0.9)/282	0.122

*Data are presented as mean (95% CI)/No. of subject days. $PM_{2.5}$ exposure was decomposed into three components: (1) each subject's overall mean, (2) the difference between each subject's session-specific mean and his or her overall mean, and (3) the difference between subjects' daily values and the session-specific mean. All three were modeled though coefficients reported correspond to the parameter associated with (3). We controlled for gender, age, central site temperature and relative humidity, CO, and NO_2. CO and NO_2 were decomposed into three components as was done with $PM_{2.5}$.

†$PM_{2.5}$ measure by COPD status interaction.

prescribed antiinflammatory medications (97 observations from 11 subject sessions, n = 6). Same-day indoor $PM_{2.5}$ was associated with a 45.9-mL decrease in FEV_1 overall, with a stronger association in the no-antiinflammatory medications group (− 75.9 mL). PEF decrements were significantly associated with indoor $PM_{2.5}$ (same day and lagged) both overall and in the no-antiinflammatory medications group. Personal 1-day lagged $PM_{2.5}$ was associated with a 10.5 L/min decrement in PEF, which contributed to a significant interaction between personal $PM_{2.5}$ and medication group (p = 0.02). Indoor results for MMEF in the no-antiinflammatory medications group are consistent with those for PEF, while same-day outdoor and central site $PM_{2.5}$ decrements for MMEF are stronger than those for PEF. The medication group and $PM_{2.5}$ interactions are greater for MMEF than PEF.

In the analysis that did not control for CO and NO_2 (data not shown), same-day indoor $PM_{2.5}$ was associated with a 69.3-mL decrease in FEV_1 (95% CI, − 137.0 to − 1.82) among subjects in the no-antiinflammatory medications group; there were comparable decrements in FEV_1 associated with 1-day lagged indoor $PM_{2.5}$ for all groups. Decrements in PEF were observed in the non-antiinflammatory medication group for same day and 1-day lagged indoor (− 12.3 L/min; 95% CI, − 24.6 to − 0.1; and − 15.6 L/min; 95% CI, − 28.2 to − 3.1, respectively), and 1-day lagged personal (− 9.9 L/min; 95% CI, − 18.0 to − 1.8) $PM_{2.5}$ exposure. These associations were not observed for subjects prescribed antiinflammatory medications. Significant declines in MMEF were observed overall (− 10.5 L/min; 95% CI, − 15.4 to −5.7) and in both medication categories for 1-day lagged indoor $PM_{2.5}$ measurements. The largest decrement (− 13.7 L/min; 95% CI, − 21.4 to − 5.9) was in the group not prescribed antiinflammatory medications.

For both MMEF (indoor, outdoor, central site) and PEF (personal), there was a significant interaction by antiinflammatory medication category, which was not significant for FEV_1. That is, the estimated negative effects of PM on MMEF and PEF were significantly stronger in the group without antiinflammatory medication than in the group with such medication. There were no significant associations for derived outdoor coarse fraction and lung function changes (with or without controlling for CO and NO_2). Some stronger associations were observed in the analysis controlling for centrally measured CO and NO_2. These included a significant overall effect between PEF, FEV_1, and same-day indoor $PM_{2.5}$ measurements, as well as between PEF and 1-day lagged indoor $PM_{2.5}$. However, controlling for gases weakened the overall association for MMEF and the

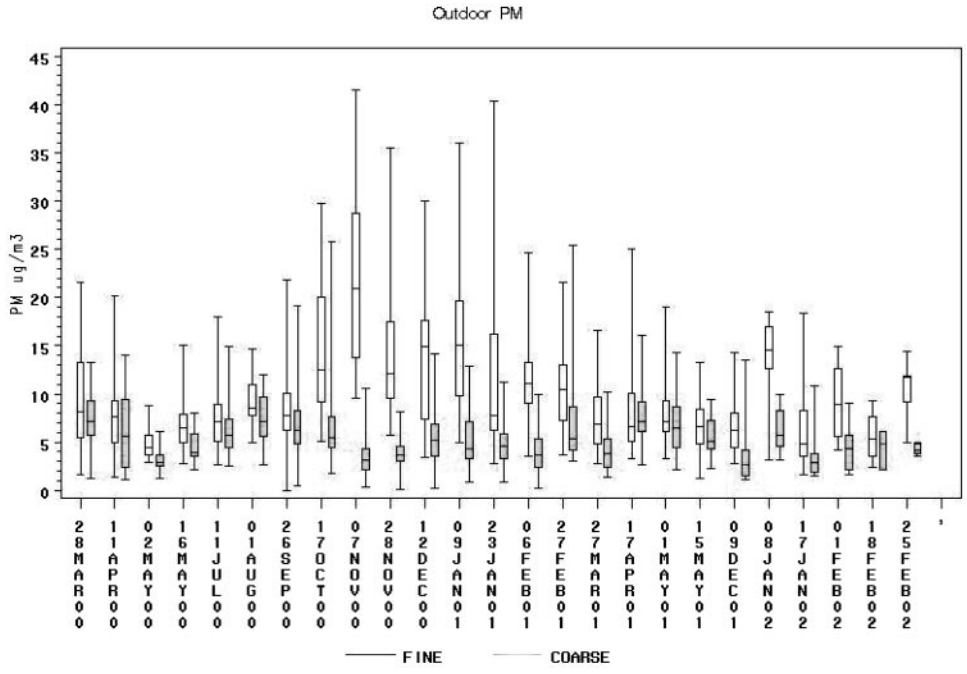

FIGURE 1. Outdoor fine (white) and coarse (shaded) particulate measurements by session for adult and pediatric subjects.

medication group associations for 1-day lagged indoor $PM_{2.5}$, although the overall association remained significant for FEV_1.

DISCUSSION

This study found decrements in lung function associated with PM exposure in both elderly adults with COPD and children with asthma. Associations were strongest for central site $PM_{2.5}$ and FEV_1 in adults with COPD. PEF results in this group are consistent with those for FEV_1, but the association is weaker. Unfortunately, the association between PM and MMEF could not be tested in the adults since the lung function instrument used by those subjects measured only FEV_1 and PEF. The absence of a significant association between PM and PEF in COPD subjects may be a function of disease process, *ie*, subjects with moderate COPD may have difficulty with this effort-dependent maneuver. In these subjects, FEV_1 appears to be a more robust measure of effect than PEF. Antiinflammatory medications were prescribed for COPD subjects, which may also weaken the association between PM and lung function decrements in this group. And, in contrast to the pediatric study subjects, the adults not receiving antiinflammatory medications did not have pulmonary disease, so they are less likely to experience lung function changes as a result of PM exposure.

Decrements in MMEF were associated with increased $PM_{2.5}$ in the children with asthma. We noted consistent decrements in all spirometric measures (FEV_1, MMEF, and PEF) only in children not prescribed antiinflammatory medications. Some children with asthma have small airway inflammation in response to extrinsic triggers.[13,14] Therefore, we selected MMEF as a potentially more sensitive indicator of small airway function. Although our study found a statistically significant change in MMEF for outdoor and central site $PM_{2.5}$ that was not present for FEV_1, our result may not be clinically meaningful due to the low ambient $PM_{2.5}$ levels experienced in this study.

MMEF and FEV_1 results supported our *a priori* hypothesis that asthmatic children who were receiving daily antiinflammatory medication would be less sensitive to $PM_{2.5}$ effects than asthmatic children who were not receiving such medication. The strongest interaction effect of antiinflammatory medication was observed for indoor, central site, and outdoor $PM_{2.5}$ associations with MMEF and 1-day lagged personal $PM_{2.5}$ and PEF. This finding is consistent with prior epidemiologic and controlled exposure studies of air pollution[20–22] and a proinflammatory mechanism of air pollutant health effects.[23] Our earlier report[24] of an association between increase in exhaled nitric oxide (eNO) and outdoor, indoor, personal, and central site $PM_{2.5}$ in these same chil-

Table 4—*Change in Pediatric Lung Function per 10 μg/m³ Change in PM

		FEV_1, mL				PEF, L/min				MMEF, L/min			
Exposure	Lag	Overall	No Antiinflammatory Medication†	Medication	p Value‡	Overall	No Antiinflammatory Medication†	Medication	p Value‡	Overall	No Antiinflammatory Medication†	Medication	p Value‡
Personal $PM_{2.5}$	0	−13.08 (−38.26 to 12.10)/222	−41.73 (−94.31 to 10.84)/60	−4.61 (−34.49 to 25.28)/162	0.224	0.31 (−4.02 to 4.64)/222	0.22 (−8.85 to 9.29)/60	0.34 (−4.67 to 5.35)/162	0.982	−0.99 (−3.96 to 1.98)/222	−3.32 (−9.52 to 2.88)/60	−0.31 (−3.77 to 3.16)/162	0.403
	1	−16.12 (−42.61 to 10.37)/197	−30.99 (−82.17 to 20.19)/53	−10.87 (−45.01 to 23.27)/144	0.506	−2.19 (−6.49 to 2.12)/197	−10.48 (−18.68 to −2.28)/53	0.74 (−4.21 to 5.69)/144	0.02	−1.08 (−4.05 to 1.88)/197	−2.49 (−8.23 to 3.25)/53	−0.59 (−4.06 to 2.89)/144	0.575
Indoor $PM_{2.5}$	0	−45.90 (−89.92 to −1.88)/249	−75.92 (−145.16 to −6.67)/69	−28.50 (−94.72 to 37.71)/180	0.272	−8.68 (−16.64 to −0.72)/249	−13.34 (−25.90 to −0.79)/69	−5.98 (−15.85 to 3.89)/180	0.346	−3.29 (−8.52 to 1.94)/249	−12.65 (−20.74 to −4.56)/69	2.14 (−4.17 to 8.45)/180	0.003
	1	−64.78 (−111.27 to −18.28)/222	−65.08 (−136.98 to 6.82)/61	−64.60 (−147.23 to 18.04)/161	0.991	−9.22 (−17.51 to −0.93)/222	−17.13 (−29.86 to −4.41/61	−4.19 (−14.59 to 6.20)/161	0.109	−11.08 (−16.26 to 5.90)/222	−13.84 (−21.82 to −5.85)/61	−9.33 (−15.89 to −2.78)/161	0.372
Outdoor $PM_{2.5}$	0	−13.11 (−57.41 to 31.19)/244	−24.42 (−81.22 to 32.38)/65	−3.59 (−75.88 to 68.70)/179	0.536	−6.27 (−14.07 to 1.53)/244	−7.52 (−17.56 to 2.51)/65	−5.22 (−14.77 to 4.34)/179	0.701	−4.13 (−9.28 to 1.01)/244	−8.23 (−14.77 to −1.69)/65	−0.68 (−6.87 to 5.50)/179	0.051
	1	−9.37 (−54.73 to 36.00)/217	16.52 (−45.76 to 78.80)/57	−26.76 (−89.53 to 36.01)/160	0.232	−5.64 (−13.73 to 2.44)/217	−6.92 (−18.03 to 4.19)/57	−4.78 (−14.42 to 4.86)/160	0.742	−0.73 (−6.02 to 4.56)/217	−1.19 (−8.45 to 6.07)/57	−0.42 (−6.72 to 5.87)/160	0.855
Coarse outdoor	0	−7.43 (−69.41 to 54.55)/233	−63.87 (−199.58 to 71.84)/64	6.57 (−96.90 to 110.04)/169	0.359	4.53 (−6.60 to 15.67)/233	2.05 (−22.36 to 26.45)/64	5.15 (−7.90 to 18.19)/169	0.823	−0.01 (−7.29 to 7.28)/233	−7.14 (−23.16 to 8.87)/64	1.76 (−6.78 to 10.30)/169	0.326
	1	−25.61 (−88.16 to 36.94)/206	−96.48 (−232.48 to 39.52)/45	−8.63 (−217.39 to 200.14)/150	0.255	−3.35 (−14.31 to 7.62)/206	−6.56 (−30.90 to 17.78)/45	−2.58 (−15.35 to 10.19)/150	0.773	−2.07 (−9.25 to 5.12)/206	−14.39 (−30.11 to 1.32)/45	0.89 (−7.56 to 9.33)/150	0.086
Central Site $PM_{2.5}$	0	−12.32 (−53.21 to 28.56)/268	−33.59 (−89.99 to 22.82)/70	−2.13 (−71.99 to 67.73)/198	0.283	−5.62 (−12.86 to 1.62)/268	−6.32 (−16.31 to 3.68)/70	−5.29 (−13.42 to 2.85)/198	0.843	−2.10 (−6.99 to 2.79)/268	−8.21 (−14.79 to −1.62)/70	0.82 (−4.48 to 6.12)/198	0.008
	1	5.75 (−33.27 to 44.76)/268	31.30 (−29.91 to 92.51)/70	−3.53 (−67.32 to 60.27)/198	0.278	−2.45 (−9.34 to 4.43)/268	−0.83 (−11.60 to 9.95)/70	−3.04 (−10.76 to 4.67)/198	0.697	−0.12 (−4.67 to 4.42)/268	−0.22 (−7.34 to 6.90)/70	−0.09 (−5.19 to 5.01)/198	0.973

*Data are presented as mean (95% CI)/No. of subject days. $PM_{2.5}$ exposure was decomposed into three components: (1) each subject's overall mean, (2) the difference between each subject's session-specific mean and his or her overall mean, and (3) the difference between subjects' daily values and the session-specific mean. All three were modeled though coefficients reported correspond to the parameter associated with (3). We controlled for gender, age, BMI, central site temperature and relative humidity, CO, and NO_2. CO and NO_2 were decomposed into three components as was done with $PM_{2.5}$.

†This group was not prescribed antiinflammatory medications; bronchodilator medications were prescribed.

‡$PM_{2.5}$ measure by medication status interaction.

dren supports a direct effect on pulmonary inflammation as a potential source of asthma exacerbation. Bronchodilator use was comparable between the two medication groups (Table 1) and was not associated with $PM_{2.5}$ exposure in either group (data not shown). It was beyond the scope of this study to evaluate whether antiinflammatory medication was clinically indicated for some of the subjects in the no-antiinflammatory medication group. Thus, the possibility that the prescribed medications were not always adequate to control asthma exacerbations cannot be ruled out.

It is important to note that these effects were seen in an air shed, where $PM_{2.5}$ values are considerably below the Environmental Protection Agency (EPA) 24-h standard of 65 $\mu g/m^3$ and slightly below the annual standard of 15 $\mu g/m^3$ (Fig 1). The finding of associations despite low PM mass concentrations suggests that particle number, specifically the contribution of ultrafine particles, is of consequence. This question is of considerable interest and is currently the subject of numerous studies. For example, a Helsinki, Finland study[9] reported high correlations between particle mass concentrations for $PM_{2.5}$ and particle number concentrations in the accumulation mode range (0.01 to 1 μm; $r = 0.85$) but weaker correlations between $PM_{2.5}$ and particle number concentrations in the ultrafine range (0.01 to 0.1 μm; $r = 0.26$). This study[9] reported consistent associations between accumulation mode particles and decrements in PEF among adult asthmatic subjects; while inverse associations with ultrafine particles and PEF were observed, they were not significant. The correlation between $PM_{2.5}$ and ultrafine particles is dependent in part on the proximity to the source of ultrafine particles. Measurements of ultrafine particles were not available for our study.

Concentrations of gaseous pollutants are highly correlated with PM.[4] In this study, for example, the correlation coefficients with local outdoor $PM_{2.5}$ were $r = 0.51$ for NO_2 and $r = 0.70$ for CO and with central site $PM_{2.5}$ were $r = 0.56$ for NO_2 and $r = 0.77$ for CO. These gases may be better surrogates than PM for exposure to certain air pollution sources such as traffic.[25] However, PM, NO_2, and CO all come from mobile sources and wood smoke. Both CO and NO_2 were significantly ($p < 0.05$) but inconsistently associated with decrements in lung function in our study populations (data not shown). For example, gases were significantly associated at 1-day lags with decreased FEV_1 in non-COPD adults, and also associated with decrements in FEV_1 (NO_2, CO) and MMEF (NO_2) in pediatric subjects. So, we cannot rule out that associations between the gases and lung function may be part of the PM effect.[26]

Moreover, the within-subject variation of PM (daily PM exposure relative to that subject's session mean) was < 5 $\mu g/m^3$, which limits our ability to determine whether larger changes in PM may lead to more consistent or clinically meaningful decrements in lung function. Another exposure factor is temporal variation of PM among the years of study. The adult subjects with COPD were studied mainly from March to October 2000, and their average outdoor exposure was 9.2 ± 5.1 $\mu g/m^3$. Whereas the children with asthma were all studied from November 2000 to May 2001, their average outdoor exposure was 11.3 ± 6.4. Wintertime PM concentrations in year 1 in Seattle were below average due to relatively warm, wet, and windy weather. The daily average hours of stagnation were 8.8 in year 1 and 11.6 in year 2.[12]

The absence of consistent associations between spirometric measures or lower respiratory symptoms (data not shown) and particulate exposure in this study, especially in adults, may be partially explained by the use of 24-h average $PM_{2.5}$ exposures rather than short-term or peak exposures. In a published study[22] in which an association with symptoms was observed for peak exposures (PM_{10}), increased odds ratios for both 8-h maximum and 24-h mean particulate exposures were also noted for subjects not receiving antiinflammatory medications. Our results contrast with earlier findings in Seattle that reported a robust association between both lung function[10] and symptoms and $PM_{2.5}$[11,27] in children with asthma in Seattle. Symptoms reported frequently do not correlate with FEV_1[28] or other markers of pulmonary effects such as eNO.[29] A study[30] that describes reporting of asthma symptoms by young (7- to 10-year-old) children indicates they may not have accurate perceptions of their asthma status.

In this study, the most consistent effects across all lung function end points were observed for indoor exposures. The composition of indoor PM may include allergens from both indoor and outdoor sources, endotoxin, and fine particles of outdoor origin that penetrate indoors, as well as particles that are generated indoors from cooking, vacuuming, and personal activities. Outdoor-generated particles accounted for an average of 81% (range, 54 to 100%) of indoor particles measured in the homes of eight children in this study.[31] In a recent article,[32] we described the lack of associations of eNO in these children with particles of indoor origin.

Our study has a number of strengths that add to the validity of our findings. These include residential level PM exposures, repeated measures on the same individual, and inclusion of medication and asthma history of the participants. Despite these strengths, our study had limitations. These include the small range and absolute level of PM exposure, the small number of participants

in the study, the 24-h averaging time of PM, and the absence of aeroallergen measurements.

This study found consistent decrements in MMEF in children with asthma who were not receiving antiinflammatory medications. These findings suggest the need for future larger studies of PM effects in this susceptible population that repeatedly measure spirometry to include MMEF and potentially more sensitive markers of airway inflammation (*eg*, biomarkers of effect in exhaled breath condensate, and eNO). These future studies should also better assess the interaction of allergens on these PM-induced airway effects.

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Effect of Particulate Air Pollution on Lung Function in Adult and Pediatric Subjects in a Seattle Panel Study

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