Association between Air Pollution and Lung Function Growth in Southern California Children

Results from a Second Cohort

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A cohort of 1,678 Southern California children, enrolled as fourth graders in 1996, was followed for 4 years to determine whether the growth in lung function of the children was associated with their exposure to ambient air pollutants. These subjects comprised the second cohort of fourth grade children participating in the Children's Health Study. Significant deficits in lung function growth rate were associated with exposure to acid vapor, NO_2, particles with aerodynamic diameter less than 2.5 μm ($PM_{2.5}$), and elemental carbon. For example, the average annual growth rates of maximal midexpiratory flow and forced expiratory volume in 1 second were reduced by approximately 11% ($p = 0.005$) and 5% ($p = 0.03$), respectively, across the observed range of acid exposure. Exposure to acid vapor was also associated with reductions in the ratio of maximal midexpiratory flow to forced vital capacity ($p = 0.02$), whereas exposure to ozone was correlated with reduced growth in peak flow rate ($p = 0.006$). Larger deficits in lung function growth rate were observed in children who reported spending more time outdoors. These findings provide important replication of our previous findings of an effect of air pollution on lung function growth that were based on the first fourth-grade cohort from the Children's Health Study (*Am J Respir Crit Care Med* 2000;162:1383–1390).

Keywords: lung function growth; children; air pollution

In a recent report, we described an association in children between long-term exposure to outdoor air pollutants and reductions in the growth of lung function (1). The data were obtained from the Children's Health Study (CHS), a 10-year investigation of children's respiratory health in 12 Southern California communities. On the basis of data on 1,498 children who entered the CHS as fourth graders in 1993 and who were followed for 4 years until 1997 (Cohort 1), we found a nearly 10% reduction in the growth rate per year of FEV_1 and maximal midexpiratory flow (MMEF) in the most polluted communities compared with that in the least polluted communities. The pollutants linked to these reductions were particles with aerodynamic diameter less than 10 μm (PM_{10}), $PM_{2.5}$, NO_2, and inorganic acid vapor. We were unable to disentangle the independent effects of these pollutants due to their high degree of correlation across communities. No significant associations were observed between lung function growth and ozone. Two other studies, one conducted in Austria (2) and the other in Poland (3), have also reported associations between ambient air pollutants and lung function growth in children. Collectively, these studies strengthen earlier evidence (4–7) that long-term exposure to air pollution can produce chronic health effects.

The design of the CHS has provided us the opportunity to attempt replication of our earlier findings. In 1996, we enrolled a second cohort of 2,081 fourth grade children (Cohort 2) from the same 12 study communities. Data collection protocols were the same as those used for Cohort 1. This report focuses on the relationship between air pollution and lung function development of the children in Cohort 2 over the 4-year period from 1996 to 2000. Side-by-side comparisons of pollutant-effect estimates from Cohorts 1 and 2 will also be provided.

METHODS

Study Subjects

Details of the CHS community selection, subject recruitment, and study design have been published previously (7, 8). Cohort 2 consisted of 2,081 fourth grade children (average age, 9.9 years) enrolled in 1996 from 12 Southern California communities. Baseline information for each child, including medical history and housing characteristics, was obtained via questionnaires filled out by a parent or guardian. In the spring of 1996, and every spring thereafter, a team of CHS field technicians traveled to study schools to measure participants' lung function. A rolling-seal spirometer (Spiroflow; P.K. Morgan Ltd., Gillingham, UK) was used to obtain up to seven maximal forced expiratory maneuvers on each child. A more detailed description of the pulmonary function testing protocol has been reported previously (7). A total of 1,678 children had at least two pulmonary function tests (PFT) from 1996 to 2000 and had complete data on all adjustment variables (described below). Outcome measures analyzed in this report include FVC, FEV_1, MMEF (also known as $FEF_{25-75\%}$), the ratio MMEF/FVC, and peak expiratory flow rate (PEFR). The study protocol was approved by the institutional review board for human studies at the University of Southern California, and consent was provided by parents for all study subjects.

Air Pollution Data

Air pollution monitoring stations were in place in each of the 12 study communities for the duration of subject follow-up, and pollution levels were monitored continuously throughout each study year. Stations measured hourly concentrations of ozone (O_3), PM_{10}, and NO_2 and obtained filter-based 2-week integrated samples for measuring $PM_{2.5}$ and acid vapor. The latter included both inorganic (nitric, hydrochloric) and organic (formic, acetic) acids. For statistical analysis, we created an acid vapor metric as the sum of nitric, formic, and acetic acid concentrations. Hydrochloric acid was excluded from this sum because the concentrations over a 2-week period were very low and close to the detection limit. In addition to measuring $PM_{2.5}$ mass, we determined concentrations of elemental carbon (EC) and organic carbon (OC) using the NIOSH 5040 method (9). The $PM_{2.5}$ filter was also analyzed for concentrations of nitrate, sulfate, and ammonium, but

(*Received in original form November 13, 2001; accepted in final form April 1, 2002*)

Supported in part by the California Air Resources Board (contract A033-186), the National Institute of Environmental Health Sciences (grant SP30ES07048-06), the Environmental Protection Agency (cooperative agreement CR822685), and the Hastings Foundation.

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This article has an online data supplement, which is accessible from this issue's table of contents online at www.atsjournals.org

Am J Respir Crit Care Med Vol 166. pp 76–84, 2002
DOI: 10.1164/rccm.2111021
Internet address: www.atsjournals.org

these levels were so highly correlated with $PM_{2.5}$ mass across communities that we chose not to include them in this report. We computed the annual average of the 24-hour (O_3, PM_{10}, NO_2) or 2-week ($PM_{2.5}$, EC, OC, acid) average concentrations. For O_3, we also computed the annual average of the 10:00 A.M. to 6:00 P.M. average. Analogous hour-specific averages for PM_{10} and NO_2 were not used, as they were highly correlated with their corresponding 24-hour averages. We computed the mean over 4 years (1996–1999) of the annual average concentrations in each community and used these in the statistical analysis of lung function growth.

Statistical Analysis

To investigate the relationship between lung function growth and air pollution, we applied the same analytic approach as that previously applied to Cohort 1 (1). The data consisted of 7,106 PFT obtained over the 4-year period on 1,678 study subjects. We used a 3-level regression modeling approach to investigate variation in lung function growth across the 12 communities in relation to variation in average air quality, with adjustment for individual and time-varying covariates. Details of each regression model are given below.

The first model was a linear regression of 7,106 log-transformed lung function measures on age, to estimate each subject's intercept and growth slope. This model included adjustment for time-varying covariates, including height, body mass index, subject report of doctor-diagnosed asthma and cigarette smoking in the previous year, report of respiratory illness and exercise on the day of the test, and interactions of each of these variables with sex to allow for male–female differences. The models also included barometric pressure, temperature at test time, and sets of indicator variables for field technician and spirometer.

The second model was a linear regression of the 1,678 person-specific adjusted growth slopes from the first model on a set of community indicators, to obtain the mean growth slope for children in each of the 12 communities. Adjustments were made for person-specific covariates, including sex, race/ethnicity, and baseline report of asthma. Residuals from both the first and second linear regression models satisfied the model assumptions of normality and homoscedasticity.

The final model was a linear regression of the 12 community-average lung function growth rates on 4-year community-average pollution level. The parameter of interest was the slope from this third regression, which was reported as the difference in estimated percent growth rate per year between the most and the least polluted communities. Negative pollutant-effect estimates indicate reduced lung function growth with increased exposure. The pollutant-specific range from the least to the most polluted community was used for scaling to facilitate comparison of effect estimates among different pollutants. Each pollutant was analyzed separately for its relationship to lung function growth, and scatterplots were used to display the relationships graphically. We also estimated the effect of each pollutant after adjustment for each of the other pollutants, by regressing the community-average growth rates on pairs of pollutants.

A single mixed model that combined all three of the aforementioned regression models was used to estimate pollutant effects and to test hypotheses. The MIXED procedure in SAS (10) was used to fit the models. A two-sided alternative hypothesis and a 0.05 significance level were assumed in all testing. The primary analyses used all study subjects. However, we also conducted separate analyses in strata defined by time spent outdoors, as this factor was believed *a priori* to be important in determining a given child's exposure to the ambient pollutants under study. Children were asked how much time they spent outdoors between 3:00 P.M. and 6:00 P.M. on each of five weekday afternoons. We classified each child as "more outdoors" or "less outdoors" on the basis of whether the average time spent outdoors over the 5-day period was above or below the median time for all children. We also considered sex, baseline asthma status, and race/ethnicity as possible pollutant-effect modifiers, and we added appropriate interaction terms to the mixed model to test these hypotheses.

In addition to our analysis of Cohort 2, we show pollutant-effect estimates for Cohort 1 for comparison. The lung function and air pollutant data used for Cohort 1 were based on the first 4 years of follow-up of that cohort (1993–1997), as described in our previous report (1). However, that report did not include analysis of EC, as data on EC concentrations have only recently become available. To facilitate direct comparison across cohorts, we scaled pollutant effects for Cohort 1 to the same range as that used for Cohort 2 (i.e., to the difference from the least to the most polluted community over the Cohort 2 study period).

RESULTS

Annual average pollutant levels for each community during the Cohort 2 study period are shown in Figure E1 (*see* online data supplement). Compared with the variation between communities, there was relatively little variation within communities over the 4-year observation period. Table 1 shows pairwise correlations between community average air pollution levels over the study period. Ozone concentrations (both 24-hour and 10 A.M.–6 P.M. average) were not significantly correlated with any other pollutant, with the exception of a negative correlation between 24-hour ozone and NO_2 ($r = -0.60$). However, the remaining pollutants were correlated with one another, with coefficients ranging from $r = 0.58$ (OC with NO_2) to $r = 0.97$ (OC with PM_{10}).

The Cohort 2 sample consisted of roughly equal numbers of males and females and included 52% white non-Hispanics, 32% Hispanics, and approximately 5% each of black, Asian, and other ethnic groups (Table 2). Overall, 14% of subjects reported doctor diagnosis of asthma at baseline, ranging from 8% (Riverside) to 19% (San Dimas). Between the weekday hours of 3:00 P.M. and 6:00 P.M., children spent an average of 1.3 hours outdoors, with most children spending between 0.5 and 2.3 hours outdoors during this time. An average of 4.3 PFT (of a possible 5) was recorded on each study subject.

TABLE 1. CORRELATIONS AMONG COMMUNITY MEAN POLLUTION LEVELS

Pollutant†	O_3	NO_2	Acid Vapor	PM_{10}	$PM_{2.5}$	PM_{10}–$PM_{2.5}$	Elemental Carbon	Organic Carbon
O_3, 10 A.M.–6 P.M.	0.77**	−0.23	0.30	0.13	0.14	0.10	−0.05	0.11
O_3		−0.60*	−0.22	−0.37	−0.39	−0.31	−0.48	−0.34
NO_2			0.83***	0.64*	0.77**	0.46	0.93***	0.58*
Acid vapor‡				0.79**	0.87***	0.63*	0.90***	0.74*
PM_{10}					0.95***	0.95***	0.86***	0.97***
$PM_{2.5}$						0.81**	0.93***	0.89***
PM_{10}–$PM_{2.5}$							0.71*	0.96***
Elemental carbon								0.81**

Definition of abbreviation: PM_{10} = particles with aerodynamic diameter less than 10 μm.
* $p < 0.05$.
** $p < 0.005$.
*** $p < 0.0005$.
† 24-hour average (unless otherwise noted) pollution level from 1996 to 1999.
‡ Acid vapor is the sum of nitric, formic, and acetic acid vapor concentrations.

TABLE 2. CHARACTERISTICS OF THE STUDY POPULATION

	No. of Subjects*	Mean No. of PFTs	Female Sex (%)	Race Distribution, %					Ever Asthma† (%)	No. of Hours Outdoors‡	
				White	Hispanic	Asian	Black	Other		Median	10th, 90th
Alpine	157	4.2	50	76	19	1	0	3	14	1.7	(0.8, 2.6)
Alascadero	144	4.3	44	74	17	1	1	8	18	1.4	(0.7, 2.4)
Lake Elsinore	139	4.2	53	55	32	4	1	6	13	1.4	(0.6, 2.4)
Lake Arrowhead	145	4.3	52	71	22	0	1	6	14	1.1	(0.4, 1.8)
Lancaster	159	3.8	52	51	30	3	10	6	16	1.4	(0.6, 2.3)
Lompoc	147	4.3	47	46	37	9	5	3	10	1.1	(0.3, 2.1)
Long Beach	133	4.2	44	33	22	14	23	8	15	1.2	(0.5, 2.3)
Mira Loma	125	4.3	51	40	54	2	1	2	15	1.2	(0.6, 2.1)
Riverside	126	4.3	55	41	39	1	11	8	8	1.4	(0.6, 2.6)
San Dimas	141	4.5	52	48	36	10	1	5	19	1.1	(0.3, 2.3)
Santa Maria	133	4.0	51	20	62	9	2	7	13	1.1	(0.5, 2.4)
Upland	129	4.4	50	66	18	9	5	3	12	1.2	(0.3, 2.0)
All	1,678	4.3	50	52	32	5	5	6	14	1.3	(0.5, 2.3)

Definition of abbreviation: PFT = pulmonary function test.
* Number of subjects with at least two PFTs from 1996 to 2000.
† Doctor-diagnosed asthma at baseline.
‡ Number of hours spent outdoors on weekdays between 3:00 P.M. and 6:00 P.M.; values are the median and the 10th and 90th percentiles.

Over the 4-year study period, FEV_1 increased at an average rate of 11.8% per year in the cohort, with equivalent growth rates in males and females. However, the average FEV_1 growth rates varied across the 12 communities, from 11.0 to 12.4%. Figure 1 shows a plot of the community-specific growth rates versus the corresponding 4-year average pollutant concentrations. There was a significant negative correlation between FEV_1 growth rates and acid vapor ($r = -0.55$, $p = 0.03$). The predicted growth rates, depicted by the plotted regression line, decreased from 12.1 to 11.5% across the range of observed acid concentrations. This absolute difference of 0.6% corresponds to a relative reduction of 5% in average FEV_1 growth rate for those exposed to the highest compared with those exposed to the lowest observed acid concentration (i.e., 0.6%/12.1%). Negative correlations were also observed between FEV_1 growth rates and the other pollutants, but none achieved statistical significance. Analogous plots are shown for MMEF growth in Figure 2. MMEF growth rates were negatively correlated with concentrations of acid vapor ($p = 0.005$), NO_2 ($p = 0.02$), $PM_{2.5}$ ($p = 0.05$), and EC ($p = 0.04$). The predicted MMEF growth rates declined from approximately 11.6 to 10.3% across the range of observed acid concentrations, with this absolute difference of 1.3% corresponding to a relative reduction of 11%.

Table 3 shows the estimated absolute differences in growth rates from the most to the least polluted community for the five PFT measures and for all pollutants. Although most pollutant-effect estimates were negative for FVC, none achieve statistical significance. The associations of FEV_1 and MMEF with acid vapor shown in Figures 1 and 2, respectively, also held for nitric and formic acids separately and to a smaller extent for acetic acid. The ratio MMEF/FVC was correlated with NO_2 ($p = 0.04$), acid vapor ($p = 0.02$), and nitric ($p = 0.01$) and formic acids ($p = 0.02$). Each pollutant-effect estimate for MMEF/FVC (e.g., −0.96% for acid vapor) was approximately equal to the difference between the corresponding pollutant-effect estimates for MMEF (e.g., −1.28%) and FVC (e.g., −0.33%). The predicted PEFR growth declined by 1.2% across the range of 10 A.M.–6 P.M. O_3 ($p = 0.006$). None of the PFT measures was significantly associated with 24-hour O_3, PM_{10}, PM_{10}–$PM_{2.5}$, or OC. Adjustment for indoor sources of air pollution, including a gas stove, any pet, a cat, a dog, or a tobacco-smoking parent in the home, did not alter any pollutant-effect estimate by more than 10% of its unadjusted values (data not shown). We therefore concluded that any differences among communities in the prevalence of these indoor sources of air pollution did not confound the ambient pollutant-effect estimates. Additionally, there was no significant evidence of pollutant-effect modification by sex, ethnicity, or asthma status. As an example of the similarity in pollutant-effect estimates by asthma status, the decline in FEV_1 growth rate across the observed range of acid vapor was 0.50% in individuals with asthma and 0.63% in individuals without asthma, a difference that was not statistically significant ($p = 0.75$).

In two-pollutant models for FEV_1, effect estimates for acid vapor remained negative after adjustment for any other pollutant (Table 4, third row). On the other hand, adjustment for acid (Table 4, third column) substantially changed the univariate estimates (Table 4, main diagonal) of all other pollutants except for O_3. Table 5 shows similar two-pollutant analysis of MMEF. Here again, estimates of the acid vapor–effect remained negative with adjustment for any other pollutant, whereas adjustment for acid altered the effect estimate of every other pollutant. For example, the estimated univariate NO_2 effect (−1.10%) dropped in magnitude (0.03%) and became nonsignificant with adjustment for acid. For both FEV_1 and MMEF, the only two-pollutant model in which both pollutants were statistically significant predictors of growth included 10 A.M.–6 P.M. O_3 and NO_2, indicating that these pollutants might each contribute independently to reduced lung function growth. For example, the estimated effects on MMEF from this two-pollutant model were −1.11% ($p = 0.02$) for O_3 (Table 5, row 1, column 2) and −1.31% ($p = 0.003$) for NO_2 (Table 5, row 2, column 1). In additional models, inclusion of an O_3-by-NO_2 interaction did not significantly improve model fit for either FEV_1 or MMEF.

The directions and magnitudes of pollutant effects observed in Cohort 2 were generally comparable to those observed in Cohort 1 (Table 6). As an example, for FEV_1, the acid-effect estimates in Cohorts 1 and 2 were −0.82% ($p = 0.01$) and −0.63% ($p = 0.03$), respectively, and the corresponding acid-effect estimates for MMEF were −1.16% ($p = 0.02$) and −1.28% ($p = 0.005$), respectively. For all combinations of PFT and pollutant shown in Table 6, we formally tested whether the pollutant-effect estimates were different between the two cohorts; no significant differences were detected.

In each cohort, the strength of the pollutant effects was greater in children who reported spending more time out-

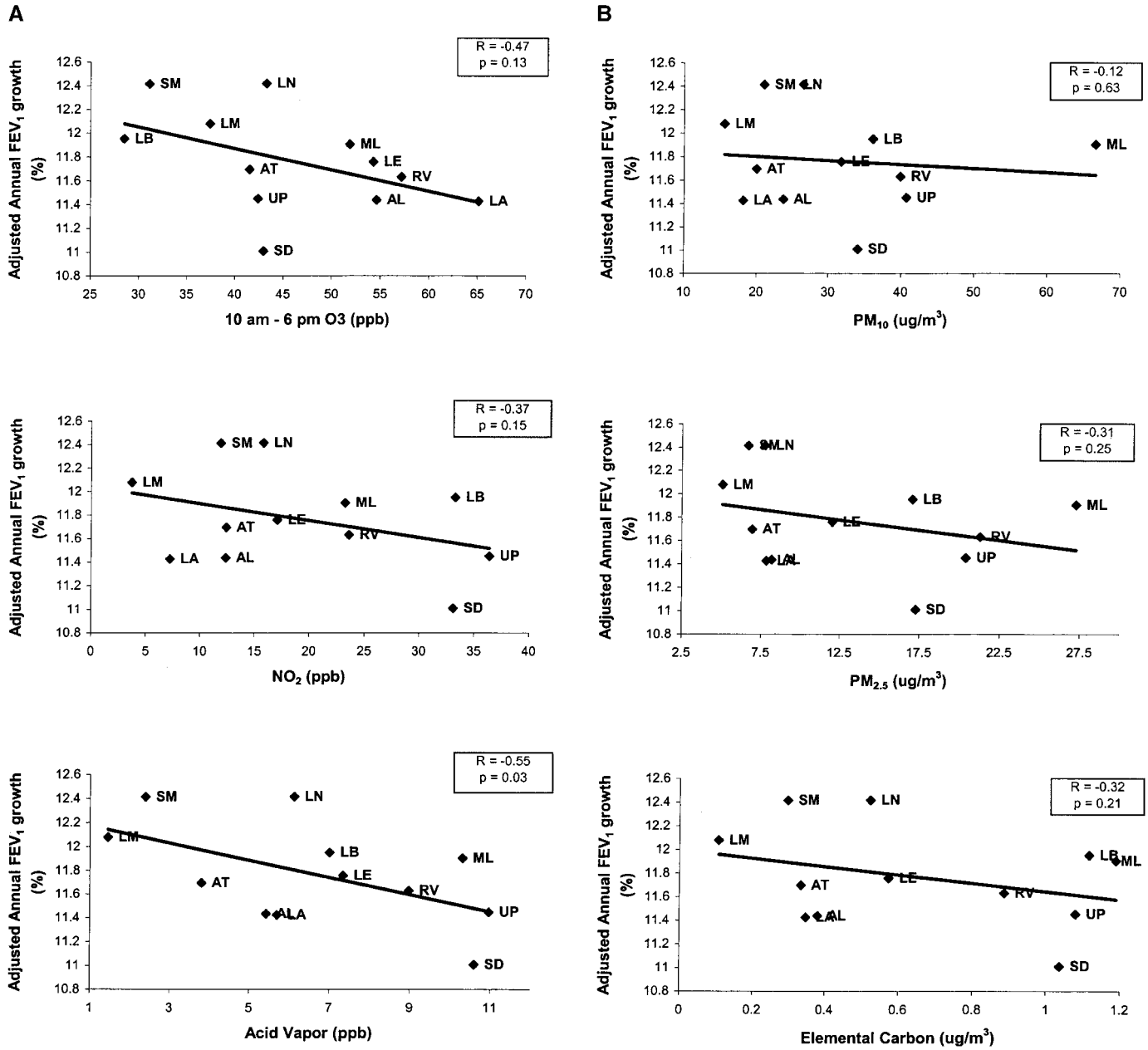

Figure 1. Adjusted average annual FEV_1 growth rates in the 12 communities versus the mean pollutant concentrations over the study period. AL = Alpine; AT = Atascadero; LE = Lake Elsinore; LA = Lake Arrowhead; LN = Lancaster; LM = Lompoc; LB = Long Beach; ML = Mira Loma; RV = Riverside; SD = San Dimas; SM = Santa Maria; UP = Upland.

doors (Table 7). For example, across the range of acid vapor, FEV_1 growth rates in the more-outdoors children declined by 1.1% in Cohort 1 ($p = 0.02$) and by 1.0% in Cohort 2 ($p = 0.002$). The corresponding declines in growth rate in the less-outdoors children were only 0.4% in Cohort 1 ($p = 0.18$) and 0.3% in Cohort 2 ($p = 0.45$). Several other statistically significant associations between PFT growth and pollutants were observed in the more-outdoors children, whereas no significant associations were observed in the more-indoors children.

DISCUSSION

The results, based on the second fourth-grade cohort from the CHS, provide further evidence that ambient levels of air pollution in southern California have a detrimental effect on lung function growth in children. These findings are in general agreement with the results that were based on the first fourth-grade cohort (1). Also replicated from the Cohort 1 analysis is the finding of larger pollutant effects in children who reported spending more time outdoors. The replication of a previous result and the observation of a larger health effect in those who were more exposed are results that support a causal association. Additional studies in other populations are needed to further assess causal relationships.

Across cohorts and lung function measures, we observed significant associations with several of the pollutants, including both particles and gases. Although the correlations among pollutants were generally high, some trends emerged from the analysis of the two cohorts. For example, fine particles ($PM_{2.5}$) and the EC portion of $PM_{2.5}$ generally showed stronger associations

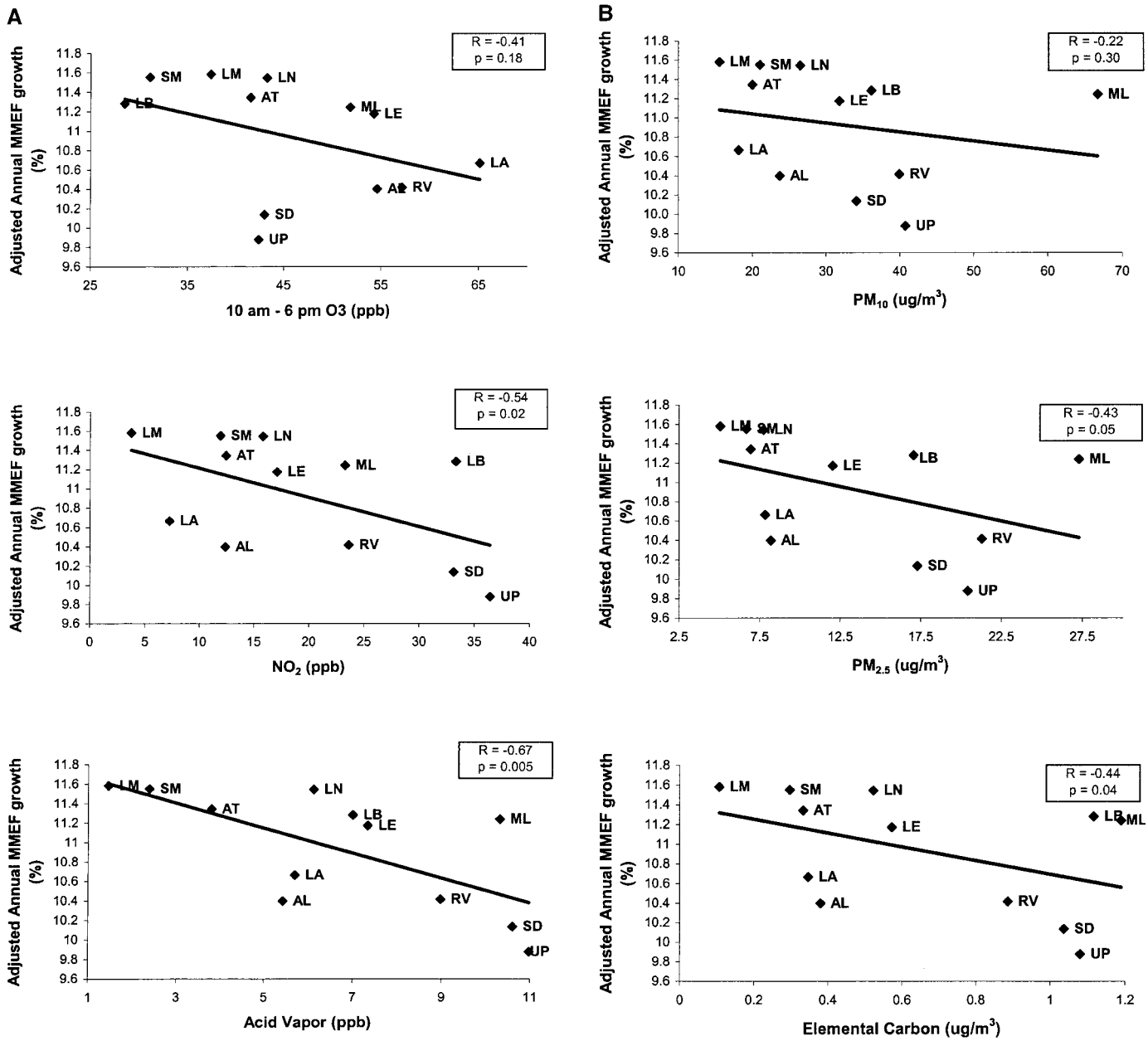

Figure 2. Adjusted average annual MMEF growth rates in the 12 communities versus the mean pollutant concentrations over the study period. AL = Alpine; AT = Atascadero; LE = Lake Elsinore; LA = Lake Arrowhead; LN = Lancaster; LM = Lompoc; LB = Long Beach; ML = Mira Loma; RV = Riverside; SD = San Dimas; SM = Santa Maria; UP = Upland.

with lung function growth than did PM_{10}, PM_{10}–$PM_{2.5}$, and OC. Associations with PM_{10} observed in Cohort 1 were not replicated in Cohort 2. For PM_{10}, as well as for PM_{10}–$PM_{2.5}$ and OC, Mira Loma had very high levels relative to the other communities (Figures 1 and 2). As an example of how this one community influenced the Cohort 2 results, elimination of Mira Loma from the analysis of MMEF changed the PM_{10}-effect estimate from −0.67% ($p = 0.30$, Table 3) to −2.32% ($p = 0.01$). However, we had no *a priori* reason to exclude Mira Loma from the analysis, and we therefore relied on the full 12-community analysis for our inferences. Of the gaseous pollutants, associations with acid vapor and NO_2 observed in Cohort 1 were replicated in Cohort 2. However, the associations observed with ozone in Cohort 2 were not previously observed in Cohort 1.

A major source of ambient EC in Southern California is the combustion of diesel fuel (11, 12). The observed associations with EC may therefore indicate a more general association between lung function and exposure to diesel exhaust particles. A previous study of children in the Netherlands also provided evidence of a relationship between diesel exhaust particles and reduced lung function. Specifically, reductions in FEV_1, MMEF, and PEFR were associated with exposure to two proxies for diesel emissions, including truck-traffic on nearby roads and levels of black smoke (13). Given that EC largely resides in the fine particle fraction of PM and thus is transported much like a gas, concentrations of EC in any given location will depend on a combination of both local and upwind sources of diesel exhaust particles.

Our finding of an association in Cohort 2 between ozone and PEFR, and between ozone and other lung function measures in children spending more time outdoors, also has some support from prior studies. In a study of Swiss children, expo-

TABLE 3. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY

	Differences in Growth Rate†				
Pollutant§	FVC % (*95% CI*)	FEV_1 % (*95% CI*)	MMEF % (*95% CI*)	MMEF/FVC % (*95% CI*)	PEFR % (*95% CI*)
O_3, 10 A.M.–6 P.M.	−0.33 (−0.90, 0.24)	−0.55 (−1.27, 0.16)	−0.80 (−1.94, 0.36)	−0.44 (−1.39, 0.52)	−1.21 (−2.06, −0.36)†
O_3	−0.10 (−0.73, 0.54)	−0.17 (−1.00, 0.67)	−0.09 (−1.41, 1.24)	0.02 (−0.99, 1.04)	−0.65 (−1.77, 0.49)
NO_2	−0.23 (−0.76, 0.29)	−0.48 (−1.12, 0.17)	−1.10 (−2.00, −0.20)*	−0.88 (−1.71, −0.04)*	−0.17 (−1.18, 0.84)
Acid vapor	−0.33 (−0.82, 0.17)	−0.63 (−1.21, −0.05)*	−1.28 (−2.16, −0.40)‡	−0.96 (−1.77, −0.14)*	−0.74 (−1.62, 0.14)
Nitric	−0.36 (−0.84, 0.13)	−0.71 (−1.25, −0.17)†	−1.41 (−2.29, −0.53)‡	−1.06 (−1.87, −0.24)*	−0.76 (−1.62, 0.12)
Formic	−0.39 (−0.89, 0.11)	−0.70 (−1.28, −0.12)*	−1.41 (−2.32, −0.49)‡	−1.03 (−1.88, −0.18)*	−0.62 (−1.58, 0.35)
Acetic	−0.28 (−0.84, 0.28)	−0.56 (−1.24, 0.13)	−1.17 (−2.14, −0.20)*	−0.89 (−1.78, 0.02)	−0.80 (−1.77, 0.17)
PM_{10}	−0.03 (−0.68, 0.62)	−0.21 (−1.04, 0.64)	−0.67 (−1.92, 0.59)	−0.63 (−1.63, 0.38)	−0.42 (−1.60, 0.77)
$PM_{2.5}$	−0.14 (−0.67, 0.40)	−0.39 (−1.06, 0.28)	−0.94 (−1.87, 0.00)*	−0.78 (−1.62, 0.06)	−0.44 (−1.41, 0.55)
PM_{10}–$PM_{2.5}$	0.11 (−0.58, 0.80)	0.07 (−0.83, 0.98)	−0.19 (−1.60, 1.24)	−0.29 (−1.36, 0.08)	−0.30 (−1.57, 0.99)
EC	−0.17 (−0.67, 0.33)	−0.40 (−1.02, 0.23)	−0.92 (−1.78, −0.05)*	−0.74 (−1.53, 0.05)	−0.20 (−1.15, 0.76)
OC	0.01 (−0.67, 0.70)	−0.15 (−1.04, 0.75)	−0.55 (−1.90, 0.83)	−0.55 (−1.61, 0.52)	−0.36 (−1.62, 0.91)

Definition of abbreviations: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; OC = organic carbon; PEFR = peak expiratory flow rate.
* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.005$.
§ All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of O_3 (10 A.M.–6 P.M.), 39.8 ppb of O_3, 32.7 of NO_2, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 $\mu g/m^3$ of PM_{10}, 22.2 $\mu g/m^3$ of $PM_{2.5}$, 29.1 $\mu g/m^3$ of PM_{10}–$PM_{2.5}$, 1.1 $\mu g/m^3$ of EC, and 10.2 $\mu g/m^3$ of OC.

sure to outdoor ozone was associated with significant reduction in peak flow after 10 minutes of heavy exercise (14). A similar study of children in the Netherlands observed a negative correlation between post-training peak flow and ozone on the day before the experiment, but it found no association with ozone concentration during exercise (15, 16). In a study of children with mild asthma in Mexico City, decreases in evening peak flow were associated with both same-day and previous-day concentrations of 1-hour maximum ozone (17). A number of summer camp studies, performed in different geographic locations by several research teams, have reported acute decrements in PEFR or FEV_1 associated with exposure to ambient O_3 (18–24). The longer-term effect of exposure to ambient ozone on children's lung function was investigated by Austrian researchers (2). They obtained repeated PFT over a 3-year period from children in nine Austrian cities and reported associations between ozone and reduced growth in FEV_1 and FVC. Collectively, these studies indicate that ozone might have both short- and long-term effects on children's lung function.

Of all the pollutants studied, acid vapor showed the most consistent effect on lung function growth in Cohort 2 and across both cohorts. There are some prior reports on the relationship between acid air pollutants and lung function, although the results are, in general, equivocal. Koenig and coworkers demonstrated reductions in pulmonary function after exposure to high concentrations of nitric acid (25) and with exposure to nitric or sulfuric acid in combination with oxidants (26). However, similarly conducted studies were unable to replicate these results (27, 28). A study of Dutch schoolchildren reported associations between pulmonary function in children and same-day concentrations of nitrous acid that exists in equilibrium with nitric acid (29). In a cross-sectional study of children in 24 North American cities, Raizenne and coworkers (30) showed decrements in FVC and FEV_1 with increased exposure to acid sulfate aerosol. No prior studies, though, have investigated the longitudinal effects of acid exposure on the developing lungs of children.

Acid vapor in our study was defined as the sum of nitric, formic, and acetic acids concentrations, each of which was individually associated with decreased lung function growth. The two-pollutant models in Cohort 2 indicated that adjustment for any other pollutant did not qualitatively change the estimated acid effect. Thus, it does not appear that the observed acid effect is simply due to its being correlated with another of the observed pollutants. In fact, the reverse is indicated, specifically that the univariate associations of other pollutants (e.g., NO_2, $PM_{2.5}$) with FEV_1 and MMEF may be

TABLE 4. DIFFERENCE IN ANNUAL FEV_1 PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY, TWO-POLLUTANT MODELS

	Adjustment Pollutant					
Main Pollutant‡	O_3 (10 A.M.–6 P.M.)	NO_2	Acid Vapor	PM_{10}	$PM_{2.5}$	EC
O_3, 10 A.M.–6 P.M	**−0.55**	−0.71*	−0.38	−0.54	−0.50	−0.57
NO_2	−0.62*	**−0.48**	0.21	−0.64	−0.44	−0.64
Acid vapor	−0.53	−0.80	**−0.63***	−1.34†	−1.27*	−1.43*
PM_{10}	−0.13*	0.29	1.10	**−0.21**	2.40*	0.91
$PM_{2.5}$	−0.33	−0.05	0.76	−2.26*	**−0.39**	0.01
EC	−0.42	0.16	0.86	−1.01	−0.41	**−0.40**

Definition of abbreviations: EC = elemental carbon; PM_{10} = particles with aerodynamic diameter less than 10 μm.
* $p < 0.05$.
† $p < 0.01$.
‡ Each row gives effect estimates for the indicated pollutant after adjustment for the pollutant listed at the top of the column. Boldface estimates are from the single-pollutant models shown in Table 3. *See* Table 3 footnote for the description of units.

TABLE 5. DIFFERENCE IN ANNUAL MMEF PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY, TWO-POLLUTANT MODELS

Main Pollutant§	Adjustment Pollutant					
	O_3 (10 A.M.–6 P.M.)	NO_2	Acid Vapor	PM_{10}	$PM_{2.5}$	EC
O_3, 10 A.M.–6 P.M	**−0.80**	−1.11*	−0.40	−0.73	−0.65	−0.83
NO_2	−1.31†	**−1.10***	0.03	−1.30*	−0.96	−1.45*
Acid vapor	−1.18*	−1.31	**−1.28**‡	−2.33†	−2.14*	−2.44*
PM_{10}	−0.57	0.36	1.63	**−0.67**	3.98*	1.38
$PM_{2.5}$	−0.86†	−0.18	1.02	−3.97	**−0.94***	−0.20
EC	−0.94*	0.36	1.25	−1.85*	−0.74†	**−0.92***

Definition of abbreviations: EC = elemental carbon; MMEF = maximal midexpiratory flow.
* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.005$.
§ Each row gives effect estimates for the indicated pollutant after adjustment for the pollutant listed at the top of the column. Boldface estimates are from the single-pollutant models shown in Table 3. *See* Table 3 footnote for the description of units.

due to the correlation of these pollutants with acid vapor. However, we cannot rule out the possibility that some pollutant(s) we did not measure is responsible for the observed health effects and that acid vapor is simply our best marker of that pollutant or pollutant mixture. More specifically, acid vapor concentration may be our best indicator of downwind transport coupled with atmospheric chemical processes. This conjecture is supported by the observation that acid vapor is the pollutant we studied that most clearly distinguishes the four communities downwind of the greater Los Angeles area (Mira Loma, Riverside, San Dimas, Upland) from the remaining eight communities (*see* Figure E1 or Figure 1). Whether acid vapor is causally related to reduced lung function development or whether it is simply our best marker for another causative substance or mixture, this pollutant deserves further study.

TABLE 6. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY: COMPARISON OF COHORTS 1 AND 2

PFT	Pollutant†	Cohort 1 (*n = 1,457*‡, *%, 95% CI*)	Cohort 2 (*n = 1,678*‡, *%, 95% CI*)
FVC	O_3, 10 A.M.–6 P.M.	−0.22 (−0.77, 0.33)	−0.33 (−0.90, 0.24)
	NO_2	−0.46 (−0.92, 0.00)	−0.23 (−0.76, 0.29)
	Total acid	−0.55 (−0.97, −0.11)*	−0.33 (−0.82, 0.17)
	PM_{10}	−0.60 (−1.18, −0.01)*	−0.03 (−0.68, 0.62)
	$PM_{2.5}$	−0.42 (−0.86, 0.03)	−0.14 (−0.67, 0.40)
	EC	−0.49 (−0.88, −0.09)*	−0.17 (−0.67, 0.33)
FEV_1	O_3, 10 A.M.–6 P.M.	−0.32 (−1.14, 0.50)	−0.55 (−1.27, 0.16)
	NO_2	−0.66 (−1.34, 0.02)	−0.48 (−1.12, 0.17)
	Total acid	−0.82 (−1.44, −0.19)*	−0.63 (−1.21, −0.05)*
	PM_{10}	−0.94 (−1.78, −0.10)*	−0.21 (−1.04, 0.64)
	$PM_{2.5}$	−0.63 (−1.28, 0.02)	−0.39 (−1.06, 0.28)
	EC	−0.71 (−1.30, −0.12)*	−0.40 (−1.02, 0.23)
MMEF	O_3, 10 A.M.–6 P.M	−0.43 (−1.64, 0.80)	−0.80 (−1.94, 0.36)
	NO_2	−0.92 (−1.95, 0.12)	−1.10 (−2.00, −0.20)*
	Total acid	−1.16 (−2.12, −0.19)*	−1.28 (−2.16, −0.40)***
	PM_{10}	−1.41 (−2.61, −0.21)*	−0.67 (−1.92, 0.59)
	$PM_{2.5}$	−0.94 (−1.88, 0.01)	−0.94 (−1.87, 0.00)*
	EC	−1.07 (−1.94, −0.19)*	−0.92 (−1.78, −0.05)*
PEFR	O_3, 10 A.M.–6 P.M	−0.36 (−1.34, 0.63)	−1.21 (−2.06, −0.36)**
	NO_2	−0.82 (−1.62, −0.02)*	−0.17 (−1.18, 0.84)
	Total acid	−1.00 (−1.75, −0.25)**	−0.74 (−1.62, 0.14)
	PM_{10}	−1.27 (−2.15, −0.37)**	−0.42 (−1.60, 0.77)
	$PM_{2.5}$	−0.82 (−1.55, −0.09)*	−0.44 (−1.41, 0.55)
	EC	−0.89 (−1.57, −0.20)*	−0.20 (−1.15, 0.76)

Definition of abbreviations: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; PEFR = peak expiratory flow rate; PFT = pulmonary function test.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.005$.
† All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of O_3 (10 A.M.–6 P.M.), 39.8 ppb of O_3, 32.7 of NO_2, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 $\mu g/m^3$ of PM_{10}, 22.2 $\mu g/m^3$ of $PM_{2.5}$, 29.1 $\mu g/m^3$ of PM_{10}–$PM_{2.5}$, 1.1 $\mu g/m^3$ of EC, and 10.2 $\mu g/m^3$ of OC.
‡ Cohort 1 includes children enrolled in 1993 as fourth graders and followed through 1997. Cohort 2 includes children enrolled in 1996 as fourth graders and followed through 2000. The results shown for Cohort 2 are equivalent to those shown in Table 3.

Generally speaking, children in a community with high pollution will be more likely than children in a lower-pollution community to be exposed to short-term episodes of very high concentrations of pollutants. In southern California, concentrations of most of the pollutants we studied are highest in the afternoon hours, and therefore children who spend time outdoors during this time may receive a substantially higher dose to their lungs on a polluted day than children who remain indoors. At least 70% of the subjects reported having a home air conditioner in our polluted communities, a factor that can further increase the discrepancy between indoor and outdoor concentrations of ozone and some other pollutants. Prior reports, some of which have been summarized previously in this article, indicate that short-term exposure to high pollution can have acute effects on respiratory symptoms and lung function. A study of children in Poland has shown a link between repeated respiratory symptoms and reduced lung function growth (31). Our observations of reduced lung function growth with increasing annual average pollution level may thus be a consequence of repeated acute respiratory events after short-term increases in pollution levels. Our finding of larger deficits in children who reported spending more time outdoors in the afternoon adds some support to this possibility. However, additional study is needed to investigate the temporal relationship between acute respiratory events and lung function development.

In summary, the observed associations in this second fourth-grade cohort of the CHS generally replicated the findings from the first CHS fourth-grade cohort. Analysis of Cohort 2 showed the strongest associations with acid vapor. The observed pollutant-effect estimates were larger for MMEF than for the other PFT measures. This finding, in conjunction with significant associations between pollution and the volume-corrected measure, MMEF/FVC, indicates that long-term pollution exposure may affect the development of small airways in the lung. Further follow-up of CHS participants will allow determination of whether pollution-related deficits in lung function growth persist into adulthood, resulting in lower maximal attained lung function, and perhaps, leading to increased risk of respiratory illness.

TABLE 7. DIFFERENCE IN ANNUAL PERCENT GROWTH RATES FROM THE LEAST TO THE MOST POLLUTED COMMUNITY

		Cohort 1				Cohort 2			
		More Outdoors†		Less Outdoors		More Outdoors†		Less Outdoors	
		Difference in Growth‡		Difference in Growth		Difference in Growth‡		Difference in Growth	
PFT	Pollutant‡	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
FVC	O_3, 10 A.M.–6 P.M.	−0.02	(−0.70, 0.66)	−0.05	(−0.55, 0.45)	−0.69	(−1.26, −0.11)*	−0.07	(−0.93, 0.80)
	NO_2	−0.45	(−1.01, 0.12)	−0.14	(−0.63, 0.36)	−0.44	(−0.99, 0.12)	−0.15	(−0.92, 0.62)
	Acid vapor	−0.43	(−1.01, 0.15)	−0.25	(−0.75, 0.25)	−0.63	(−1.13, −0.13)*	−0.12	(−0.88, 0.64)
	PM_{10}	−0.35	(−1.10, 0.42)	−0.52	(−1.10, 0.07)	−0.44	(−1.11, 0.22)	0.32	(−0.60, 1.24)
	$PM_{2.5}$	−0.23	(−0.80, 0.35)	−0.32	(−0.76, 0.12)	−0.47	(−0.99, 0.06)	0.14	(−0.65, 0.93)
	EC	−0.43	(−0.94, 0.08)	−0.28	(−0.73, 0.16)	−0.44	(−0.94, 0.08)	0.01	(−0.73, 0.75)
FEV_1	O_3, 10 A.M.–6 P.M.	−0.31	(−1.44, 0.83)	−0.06	(−0.71, 0.60)	−0.83	(−1.66, 0.00)	−0.35	(−1.25, 0.56)
	NO_2	−0.96	(−1.83, −0.08)*	−0.36	(−0.97, 0.26)	−0.82	(−1.56, −0.08)*	−0.21	(−1.03, 0.61)
	Acid vapor	−1.10	(−1.94, −0.25)*	−0.44	(−1.07, 0.20)	−1.01	(−1.65, −0.38)***	−0.31	(−1.11, 0.49)
	PM_{10}	−1.12	(−2.24, 0.01)	−0.65	(−1.39, 0.09)	−0.63	(−1.60, 0.35)	0.20	(−0.80, 1.21)
	$PM_{2.5}$	−0.74	(−1.63, 0.14)	−0.49	(−1.05, 0.07)	−0.80	(−1.51, −0.08)*	−0.01	(−0.86, 0.84)
	EC	−0.97	(−1.72, −0.21)*	−0.40	(−0.97, 0.17)	−0.74	(−1.44, −0.03)*	−0.09	(−0.87, 0.71)
MMEF	O_3, 10 A.M.–6 P.M.	−0.67	(−2.54, 1.23)	0.28	(−1.09, 1.66)	−0.58	(−2.09, 0.95)	−0.97	(−2.52, 0.61)
	NO_2	−1.59	(−2.95, −0.20)*	−0.72	(−2.09, 0.66)	−1.48	(−2.84, −0.11)*	−0.51	(−1.92, 0.93)
	Acid vapor	−1.83	(−3.20, −0.43)*	−0.66	(−2.07, 0.76)	−1.35	(−2.65, −0.03)*	−0.99	(−2.28, 0.32)
	PM_{10}	−2.05	(−3.69, −0.37)*	−0.89	(−2.53, 0.78)	−0.54	(−2.14, 1.09)	−0.64	(−2.36, 1.12)
	$PM_{2.5}$	−1.46	(−2.70, −0.20)*	−0.71	(−1.96, 0.55)	−0.95	(−2.26, 0.39)	−0.74	(−2.16, 0.70)
	EC	−1.74	(−2.98, −0.49)**	−0.57	(−1.83, 0.70)	−1.03	(−2.29, 0.25)	−0.54	(−1.89, 0.82)
PEFR	O_3, 10 A.M.–6 P.M.	−0.94	(−2.48, 0.63)	0.31	(−0.79, 1.42)	−1.62	(−2.93, −0.29)*	−0.87	(−2.09, 0.37)
	NO_2	−1.42	(−2.52, −0.30)*	−0.36	(−1.46, 0.75)	−0.52	(−1.98, 0.96)	0.38	(−0.77, 1.55)
	Acid vapor	−1.74	(−2.82, −0.66)***	−0.32	(−1.45, 0.82)	−1.27	(−2.51, −0.01)*	−0.01	(−1.18, 1.17)
	PM_{10}	−1.81	(−3.11, −0.49)**	−0.87	(−2.19, 0.46)	−0.71	(−2.41, 1.03)	0.22	(−1.21, 1.66)
	$PM_{2.5}$	−1.33	(−2.34, −0.31)*	−0.47	(−1.47, 0.54)	−0.73	(−2.12, 0.69)	0.13	(−1.08, 1.35)
	EC	−1.36	(−2.34, −0.37)**	−0.41	(−1.42, 0.61)	−0.52	(−1.88, 0.86)	0.41	(−0.69, 1.52)

Definition of abbreviations: CI = confidence interval; EC = elemental carbon; MMEF = maximal midexpiratory flow; PEFR = peak expiratory flow rate; PFT = pulmonary function test.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.005$.

† More/less outdoors is based on reported time spent outdoors during weekday afternoons. Subjects were split into the two groups on the basis of the median of reported time outdoors with each cohort.

‡ All pollutant-effect estimates are based on single-pollutant models. Differences in average annual percent growth rates are shown per increase in annual average of 36.6 ppb of O_3 (10 A.M.–6 P.M.), 39.8 ppb of O_3, 32.7 of NO_2, 9.5 ppb of acid vapor, 3.5 ppb of nitric acid, 1.8 ppb of formic acid, 5.0 ppb of acetic acid, 51.5 $\mu g/m^3$ of PM_{10}, 22.2 $\mu g/m^3$ of $PM_{2.5}$, 29.1 $\mu g/m^3$ of PM_{10}–$PM_{2.5}$, 1.1 $\mu g/m^3$ of EC, and 10.2 $\mu g/m^3$ of OC.

Acknowledgment: The authors are very grateful for the important input from the External Advisory Committee composed of David Bates, Morton Lippmann, Jonathan Samet, Frank Speizer, John Spengler, Arthur Winer, and Scott Zeger. They acknowledge the contributions of Clint Taylor, Ken Bowers, and Cindy Stover for their role in providing high-quality air pollution data and the CHS field team for providing high-quality health data. They also acknowledge the cooperation of the school principals, teachers, students, and their parents in each of the 12 study communities.

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