SUPPLEMENTAL MATERIAL

Associations of Children's Lung Function With Ambient Air Pollution: Joint Effects Of Regional And Near-Roadway Pollutants

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METHODS

Study Subjects

The current analysis is from a Children's Health Study (CHS) cohort established in 2002-2003 in 13 Southern California communities when participants were 5-7 years of age.[1] Eight communities with an original enrollment of 3618 contributed to the current analysis. (Due to resource limitations, lung function was not measured in five). These eight communities represent a broad range of regional exposure, including Santa Barbara, a clean coastal community; Long Beach, a coastal city with high PM and NO_2 levels but low ozone levels; and inland communities with high PM and relatively high ozone levels. The communities were selected based in addition on the presence of large gradients in near-roadway exposure. During the 2007-2008 school year lung function was measured on 1,523 cohort participants (82% of the active cohort). In addition, in schools with participants with high residential NRAP exposure, a supplementary cohort of 352 children was recruited from classrooms of participants already undergoing follow-up and parents provided informed consent for lung function testing prior to field testing. Of these more recently enrolled children, 288 (82%) were available and completed testing. In total, 1811 children from eight Southern Californian communities (Anaheim, Glendora, Long Beach, Mira Loma, Riverside, Santa Barbara, San Dimas, and Upland) participated in lung function testing.

The study was approved by the University of Southern California Institutional Review Board, and written informed consent was obtained from a parent or guardian of each participant.

Distance-based Exposure Measurements

Participant residence and school addresses were standardized and their locations were geo-coded to 13 m perpendicular to the side of the adjacent road, using the Tele Atlas database and software (Tele Atlas, Inc., Boston, CA, www.na.teleatlas.com). Distance to the nearest major road was estimated using ESRI ArcGIS Version 9.2 (ESRI, Redlands, CA, www.esri.com). A major road was defined based on functional classification by the California Department of Transportation as a freeway (with limited access) or other highway (typically with heavy traffic volume), or a major or minor arterial thoroughfare. Each direction of travel was represented as a separate roadway, and the shortest distance was estimated from the residence to the middle of the nearest side of the freeway or major road. We included in the analysis only children with addresses that could be geo-coded accurately. Specifically, only residential addresses for which the Tele Atlas geo-coding software assigned its highest quality match code were included. These addresses were located on the correct side of the street with their relative position between cross streets determined by linear interpolation of residence number between the nearest intersections.

Residential and school address distance to a freeway were categorized as <500 m, 500-999 m, 1,000-1,499 m, and >1,500 m, based on the distribution of the residences of participants, recent evidence for extended increased concentration of fresh traffic pollutants on this scale, and results from a previous CHS cohort that have shown respiratory health associations on this spatial scale.[2-6] Distance to the nearest major road (including freeways) was categorized as <75 m, 75 to 150 m, >150 m to 300 m, and >300 m, based on the markedly increased exposure and risk of asthma within 75 m of major roadways in previous studies (including this cohort at study entry), which decreased to background levels by 150 to 300 m [1 7-10].

Land-use Regression Modeling of NO, NO_2, and NO_x

For a detailed description of sample collection and model selection, see Franklin, 2012.[11] Land-use regression (LUR) models of NO, NO_2, and NO_x, were developed based on 942 collected samples across 12 communities in southern California. In 2005-2006, concentrations of pollutants were collected using Ogawa samplers that were deployed for 2 weeks in the winter and 2 weeks in the summer. NO, NO_2, and NO_x were chosen as surrogates of the near roadway air pollution because of the existence of inexpensive monitors that can readily be deployed across multiple locations. A natural log transformation of these pollutants was performed prior to modeling. Because the main focus during the development of the models was to understand the within-community or local distribution of these pollutants, the measured concentrations of these pollutants and each of the predictors were subtracted (deviated) from the community-specific town means. The final LUR models included both a freeway and a non-freeway component of CALINE4-modeled NRAP (a Gaussian line-source dispersion model),[12] distance to the nearest freeway and its squared value, distance to the nearest non-freeway major road, non-freeway traffic volume and population within a 300m buffer, and elevation. To assess the performance of the models, 10-fold cross validation was performed in which the data was split into 10 parts, and nine of the parts were used for training the model, while one part was held out for validation purposes. This was repeated 10 times so that each part had an opportunity to be validated by the rest of the data. The 10-fold cross validation R^2-values for predicting local variation in traffic exposures based on these predictors were 63% for NO, 71% for NO_2, and 71% for NO_x.

These models were used to predict local annual average concentrations of NO, NO_2, and NO_x at the residence and school of each child in the lung function study. Predicted concentrations from the LUR model were on a log-deviated scale. To make these predictions more interpretable, we added back a natural log transformed community mean (calculated from the original sampling) to each predicted value, which was then exponentiated to get the predictions on a part per billion scale. These predictions were then deviated again from the community mean (unlogged) of a given pollutant in order to examine the local effects of these pollutants.

Regional Exposures

Since the beginning of this study, regional pollutant levels have been measured continuously at a central monitoring location in the study communities. Measures of regional pollutants included hourly concentrations of NO_2 (determined from NO_x-NO measured by chemiluminescence), 24-hour $PM_{2.5}$ concentrations (measured by the Federal Reference Method (FRM)) or hourly $PM_{2.5}$ concentrations (measured by Beta Attenuation Monitor (BAM)), 24-hour PM_{10} concentrations (measured by the FRM) or hourly PM_{10} concentrations (measured by BAM or Tapered Element Oscillation Microbalance (TEOM)), and hourly O_3 concentrations (measured on ultraviolet photometers). PM data collected from BAM and TEOM monitors were adjusted, based on comparison with collocated FRM data, to represent FRM equivalence, while the 8-hour average concentration of O_3 from 10am to 6pm in each community was used in assessment of O_3 effects. For statistical modeling, the regional level of each pollutant was computed as the mean of the six years of measurements from cohort recruitment (2002) to the recording of lung function tests (2007).

Statistical Methods

We fitted multiple linear regression models to investigate associations of FVC and FEV_1 with each of the above indicators of NRAP exposure. A base model was first developed using variables that are known predictors of lung function or were suspected to influence lung function measurements. This base model included age at time of lung function testing, sex, an interaction term between age and sex, race, an indicator for Hispanic ethnicity, log of height (measured at time of lung function testing) and its squared value, body-mass index (BMI) and its squared value, presence of acute respiratory illness during lung function testing, indicator variables for which field technician administered the test, and indicator variables for study community. A log transformation of each pulmonary function measure was used to satisfy the assumptions of linear regression.

The NRAP exposure values for each child from the spatial land-use regression model were deviated from their respective community-specific mean. These community-specific centered NRAP exposure values are constructed by design to be orthogonal (uncorrelated) to cross-community regional exposures, which allows for the simultaneous modeling of near-roadway and regional exposures. Each deviated exposure metric was entered into the base model one at a time to test its association with lung function. Health effect estimates are reported as the percent change in lung function per increase of two standard deviations in the corresponding exposure. Distance-based exposures were categorized, and health effect estimates are reported as the percent change in lung function compared to the reference category.

Effects of regional air pollution on FVC and FEV_1, either individually or in combination with NRAP, were assessed with a mixed model that included a random intercept for each study community. With the exception of indicator variables for study community, the same set of adjustment variables were included as above. The health effect estimate for each regional pollutant was scaled to the corresponding range of that pollutant across study communities. Potential effect modification of NRAP by regional air pollutants was assessed by formal testing using appropriate interaction terms between the two pollutants.

For school level analyses, a mixed model that included a random intercept for each school and a fixed effect for community was used. To model the joint effects of NRAP at each child's residence and school attended, the residential assigned exposure was deviated from the school assigned exposure and both were included in the same mixed model.

To examine the robustness of findings, additional sensitivity analyses were performed, including adjustment for potential confounders and stratification by sex and asthma status. Covariates considered in statistical analyses included race, Hispanic ethnicity, history of doctor-confirmed diagnosis of asthma, parental income and education, health insurance coverage, *in utero* exposure to maternal smoking, secondhand tobacco smoke (SHS) exposure and presence in the home of pets, mold, or a gas stove. Variables selected for further adjustments were chosen based on prior literature. Complete covariate information for sex, race, and Hispanic ethnicity was obtained, while most of the rest of the data had less than 10% missing, although 18% of responses for income was missing, Missing indicators were included in models for incomplete covariate information in order to maintain sample size when comparing across models. Differences between subgroups were examined by testing for effect modification as described above.

In all analyses, we assumed a two-sided alternative hypothesis and 0.05 significance level. All analyses were performed using Statistical Analysis System (SAS version 9.2; SAS Institute Inc., Cary, NC).

RESULTS

A substantial proportion of participants' households had incomes less than $30,000 (27%) or less than a high school education (21%). (See Table 1). Eleven percent reported no health insurance coverage for the child. Most homes had a gas stove (87%) and almost half of families had at least a dog (36%) and/or a cat (19%). A small proportion of subjects reported secondhand tobacco smoke exposure (4%) and household mold problems (11%).

We examined the relationship of lung function participation rate of cohort members with key sociodemographic and other characteristics. After adjusting for community (to correspond to the analytic approach for assessment of NRAP effects), non-participants were more likely to be boys and to have asthma (Table S-4). Otherwise, participants and non-participants were generally similar across a broad range of demographic, social and housing characteristics.

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Supplemental Material, Table S-1. Distribution of residential distances to freeways and other major roads for CHS participants in 8 study communities

	Total	Freeway (m) †				Large road (m) †			
		<500	500-1,000	1,000-1,500	>1,500‡	<75	75-150	150-300	>300‡
	N	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Anaheim	190	115 (62.2)	35 (18.9)	13 (7.0)	22 (11.9)	37 (20.0)	44 (23.8)	83 (44.9)	21 (11.4)
Glendora	310	41 (13.3)	23 (7.4)	46 (14.9)	199 (64.4)	31 (10.0)	41 (13.3)	77 (24.9)	160 (51.8)
Long Beach	131	16 (12.6)	37 (29.1)	18 (14.2)	56 (44.1)	20 (15.7)	29 (22.8)	49 (38.6)	29 (22.8)
Mira Loma	273	41 (15.4)	39 (14.7)	24 (9.0)	162 (60.9)	36 (13.5)	38 (14.3)	55 (20.7)	137 (51.5)
Riverside	167	36 (21.8)	42 (25.5)	23 (13.9)	64 (38.8)	17 (10.3)	26 (15.8)	38 (23.0)	84 (50.9)
San Dimas	249	80 (32.5)	80 (32.5)	62 (25.2)	24 (9.8)	26 (10.6)	42 (17.1)	73 (29.7)	105 (42.7)
Santa Barbara	265	110 (44.0)	50 (20.0)	32 (12.8)	58 (23.2)	52 (20.8)	56 (22.4)	72 (28.8)	70 (28.0)
Upland	226	39 (17.3)	46 (20.4)	54 (24.0)	86 (38.2)	35 (15.6)	33 (14.7)	51 (22.7)	106 (47.1)
Total	1811	478 (27.0)	352 (19.9)	272 (15.3)	671 (37.8)	254 (14.3)	309 (17.4)	498 (28.1)	712 (40.2)

† Do not sum up to total population due to missing values.
‡ Reference group for distance-related analyses.

Supplemental Material, Table S-2. Correlation of regional pollutants from central sites. Each pollutant represents the 24-hour average concentration over the study period from 2002 until 2007 with the exception of O_3, which represents the 8-hour average from 10am to 6pm.

Pollutant	$PM_{2.5}$	PM_{10}	NO_2
O_3 (10am-6pm)	0.66	0.63	0.12
$PM_{2.5}$		0.80*	0.60
PM_{10}			0.06

* $p<0.05$

Supplemental Material, Table S-3. Correlation of near-roadway predicted exposures.

Pollutant	NO_2	NO_x
NO	0.92	0.98
NO_2		0.98

Supplemental Material, Table S-4: Characteristics of participants and non-participants in lung function testing

	Participants		**Non-participants**		
	N (total=1811)	**%**†	**N (total=402)**	**%**†	**p-value**‡
Male	871	48.1	232	57.7	<0.01
Race					
Asian	86	4.8	19	4.7	0.13
Black	39	2.2	16	4.0	
Don't Know	239	13.2	71	17.7	
Mixed	229	12.6	51	12.7	
Other	486	26.8	90	22.4	
White	732	40.4	155	38.6	
Hispanic ethnicity					
Don't Know	92	5.1	34	8.5	0.12
Hispanic	1028	56.8	214	53.2	
Not Hispanic	691	38.2	154	38.3	
SES					
Income					
<$30,000	402	27.1	112	34.6	0.10
$30,000 or more	1084	73.0	212	65.4	
Parental education					
Did not finish high school	345	20.6	79	21.6	0.22
High school diploma or some college	854	51.0	201	55.1	
College diploma or greater	477	28.5	85	23.3	
Insurance*	1508	89.3	321	88.9	0.58
Home characteristics/Potential exposures					
Gas stove	1462	86.5	311	86.4	0.53
Dog	599	35.8	127	37.7	0.41
Cat	312	18.8	60	18.0	0.98
Mold past 12 months	172	10.5	36	10.2	0.71
Secondhand smoke exposure	67	3.8	17	4.5	0.64
In-utero exposure to maternal smoking	99	5.8	26	7.2	0.25
Health conditions					
Acute respiratory illness§	164	9.4	-	-	-
Medical diagnosis of asthma	334	19.5	94	24.3	0.08

† Due to missing values, denominators (n) for each percentage may differ.
‡ P-value, adjusted for community, comparing the characteristic distribution of non-participating subjects to subjects with lung function measurements.
§Respiratory illness information collected only on subjects undergoing PFT.