Original Investigation

Association of Changes in Air Quality With Bronchitic Symptoms in Children in California, 1993-2012

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IMPORTANCE Childhood bronchitic symptoms are significant public and clinical health problems that produce a substantial burden of disease. Ambient air pollutants are important determinants of bronchitis occurrence.

OBJECTIVE To determine whether improvements in ambient air quality in Southern California were associated with reductions in bronchitic symptoms in children.

DESIGN, SETTING, AND PARTICIPANTS A longitudinal study involving 4602 children (age range, 5-18 years) from 3 cohorts was conducted during the 1993-2001, 1996-2004, and 2003-2012 years in 8 Southern California communities. A multilevel logistic model was used to estimate the association of changes in pollution levels with bronchitic symptoms.

EXPOSURES Average concentrations of nitrogen dioxide, ozone, particulate matter with an aerodynamic diameter of less than 10 μm (PM_{10}) and less than 2.5 μm ($PM_{2.5}$).

MAIN OUTCOMES AND MEASURES Annual age-specific prevalence of bronchitic symptoms during the previous 12 months based on the parent's or child's report of a daily cough for 3 months in a row, congestion or phlegm other than when accompanied by a cold, or bronchitis.

RESULTS The 3 cohorts included a total of 4602 children (mean age at baseline, 8.0 years; 2268 girls [49.3%]; 2081 Hispanic white [45.2%]) who had data from 2 or more annual questionnaires. Among these children, 892 (19.4%) had asthma at age 10 years. For nitrogen dioxide, the odds ratio (OR) for bronchitic symptoms among children with asthma at age 10 years was 0.79 (95% CI, 0.67-0.94) for a median reduction of 4.9 ppb, with absolute decrease in prevalence of 10.1%. For ozone, the OR was 0.66 (95% CI, 0.50-0.86) for a median reduction of 3.6 ppb, with an absolute decrease in prevalence of 16.3%. For PM_{10}, the OR was 0.61 (95% CI, 0.48-0.78) for a median reduction of 5.8 $\mu g/m^3$, with an absolute decrease in prevalence of 18.7%. For $PM_{2.5}$, the OR was 0.68 (95% CI, 0.53-0.86) for a median reduction of 6.8 $\mu g/m^3$, with absolute decrease in prevalence of 15.4%. Among children without asthma (n = 3710), the ORs were 0.84 (95% CI, 0.76-0.92) for nitrogen dioxide, 0.85 (95% CI, 0.74-0.97) for ozone, 0.80 (95% CI, 0.70-0.92) for PM_{10}, and 0.79 (95% CI, 0.69-0.91) for $PM_{2.5}$; with absolute decrease in prevalence of 1.8% for nitrogen dioxide, 1.7% for ozone, 2.2% for PM_{10}, and 2.3% for $PM_{2.5}$. The associations were similar or slightly stronger at age 15 years.

CONCLUSIONS AND RELEVANCE Decreases in ambient pollution levels were associated with statistically significant decreases in bronchitic symptoms in children. Although the study design does not establish causality, the findings support potential benefit of air pollution reduction on asthma control.

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Bronchitis and chronic bronchitic symptoms in children are common yet underappreciated health issues associated with clinically important morbidity.[1-8] Several studies indicate that exposure to elevated concentrations of ambient air pollution, often at levels below regulatory standards, is associated with large increases in the prevalence of bronchitic symptoms among children with asthma,[1,5,9,10] potentially resulting in a heavy burden of disease in exposed children with substantial economic cost.[11,12]

Historically, Southern California has reported high levels of ambient air pollution due to emissions from vehicular traffic, industrial sources, 2 very large ports, and complex atmospheric photochemical reactions. Since 1992, significant improvements in air quality have been observed across Southern California due to a broad spectrum of air pollution reduction policies and strategies.[13] We hypothesized that the reductions in particulate matter with an aerodynamic diameter less than 10 µm (PM_{10}) or less than 2.5 µm ($PM_{2.5}$), nitrogen dioxide, and ozone concentrations observed across Southern California were associated with improvements in respiratory symptoms in children with or without asthma. We examined data from the Southern California Children's Health Study that include 20 years of continuous air quality monitoring data and respiratory outcome information from successive cohorts of children participating during the 1993-2012 years.

Methods

Study Population

Twelve Southern California communities were originally selected to represent a historically diverse pollution profile of regional levels of nitrogen dioxide, PM_{10}, ozone, and acid vapor.[14] Three successively recruited cohorts were used in the current study. In 1993, 1800 fourth graders, aged 9 and 10 years, were recruited from schools across 12 communities and followed up through high school graduation in 2001. In 1996, another cohort of approximately 2080 fourth graders from the same communities was recruited and followed up through high school graduation in 2004. In 2003, a new cohort of 5600 either kindergarten or first graders, aged 5 through 7 years, was recruited from 13 Southern California communities. Eight communities (Alpine, Lake Elsinore, Long Beach, Mira Loma, Riverside, San Dimas, Santa Maria, and Upland) had participants in all 3 cohorts (hereafter referred to as the 1993-2001, 1996-2004, and 2003-2012 cohorts) with air pollution data collected with consistent methods over the period of study. Two other 1993-1995 and 1993-1998 cohorts involved in the California Children's Health Study were not included in the current analysis because they had relatively shorter follow-up.[14,15] All parents or guardians of participating children provided written informed consent. The study protocol was approved by the Institutional Review Board of the University of Southern California.

Data Collection

Bronchitic Outcomes and Asthma

Bronchitic symptoms were assessed using an annual follow-up questionnaire, as previously described.[1,9] A child was considered to have had bronchitic symptoms during the previous 12 months, based on the parent's or child's report of a daily cough for 3 months in a row, congestion or phlegm other than when accompanied by a cold, or bronchitis. For the 1993-2001 and 1996-2004 cohorts, children were considered to have a history of asthma before the age of 10 years, if there was a yes answer to the question on the baseline questionnaire, "Has a doctor ever diagnosed this child as having asthma?" For the 2003-2012 cohort, a child was considered to have a history of asthma before age 10 years if an asthma diagnosis was made before age 10 years based on annual assessment starting from age 5 through 7 years. In the models, participants were classified according to whether they had asthma before age 10 years (asthma group) or did not have asthma before age 10 years and during the follow-up period (nonasthma group).

Air Pollution Measurements and Metrics

Air pollution monitoring stations were established in each of the 8 communities. For each year of follow-up, measurements were made for ozone, nitrogen dioxide, and $PM_{2.5}$, as described previously[14,16] and in the eMethods in the Supplement). Community-specific annual averages of the 24-hour PM_{10}, $PM_{2.5}$, and nitrogen dioxide and of the 10 AM to 6 PM averages of ozone were used to compute the cohort-specific mean levels for the relevant period of follow-up (9-year 1992-2000 average; 9-year 1995-2003 average; and 10-year 2002-2011 average for the 3 successive cohorts, respectively) in each community. Exposure values were lagged by 1 year for better alignment with bronchitic outcomes data that assessed symptoms during the prior 12 months.

Additional Covariates From Questionnaires

From the baseline and follow-up questionnaires, we evaluated potential confounders or modifiers of the associations with air pollution, including annual information on exposure to secondhand tobacco smoke in the home and baseline information on the ownership of a dog, cat, or any pet (including dogs and cats), sex, race/ethnicity, and housing conditions. Race/ethnicity was based on self-identified information from questionnaire responses to investigator-designed fixed-category questions on race and Hispanic ethnicity. The inclusion of race/ethnicity in the models was important in order to control for any confounding effect within and across the 3 cohorts.

Data Analysis

To assess the associations between improvements in air quality and bronchitic symptoms in children during 1993-2012, we used a multilevel logistic model[1,9,17] to examine the association between cohort- and community-specific pollution levels and longitudinal data on bronchitic symptoms. Random effects were included to account for serial dependency within children and clustering effects of children by cohort and community. Effect estimates were scaled to the corresponding median of the 8 community-level average changes in each pollutant from the 1993-2001 to the 2003-2012 study periods. Time-dependent covariates included exposure to

secondhand smoke, season or month of data collection, and a cubic spline function of age with knots at 10 and 15 to account for any nonlinear association of age with bronchitic symptoms. All results presented were obtained from asthma-specific models, which were fitted due to significant differences in prevalence of bronchitic symptoms by asthma status. Also, we examined potential effect modification by sex, race/ethnicity (limiting to Hispanic and non-Hispanic white groups), dog ownership, cat ownership, parental level of education, and exposure to secondhand smoke.[9] In all models, missing data were assumed to be missing at random. Because missing information in the adjustment variables was very modest, we used a missing indicator method as needed for any adjustment variable in order to avoid loss of sample size.[18] All of the final models were adjusted for age, sex, race/ethnicity, and exposure to secondhand smoke during the follow-up period. In addition, the models for nitrogen dioxide were also adjusted for exposure to cockroaches at home. These models also included a fixed effect for community and hence were used to make inferences on associations with community-specific secular changes in air pollution levels during the 1992-2011 periods. Two-pollutant models were fitted whenever the correlations between covariates were found to be sufficiently low in order to avoid multicollinearity. Robustness of the main study findings were tested via sensitivity analyses by limiting the analysis to those participants (1) without secondhand smoke or in utero tobacco smoke exposure, (2) with pets, (3) stratified by obesity status (ie, limiting to nonobese participants and to normal-weight participants based on age- and sex-specific <95th and <85th cutoffs, respectively, based on Centers for Disease Control and Prevention percentiles[19]), (4) with parents who completed English-language questionnaire only, (5) stratified by ethnicity (limiting to Hispanic whites only or to non-Hispanic whites only), (6) with parents completing English-language questionnaire only, (7) without any asthma medication use, or (8) with complete data during follow-up. Additional sensitivity analyses were conducted stratified by cat ownership or parental level of education. Post hoc sensitivity analyses were conducted to check if areas with increased concentrations of regulated regional air pollution levels generally had increased prevalence of bronchitic symptoms within any given cohort. Graphical displays of unprocessed data were also examined to assess if the main findings were supported by general patterns in the data.

All analyses assumed a 2-sided alternative hypothesis at .05 level of significance. All models were fitted using the R version i386 3.0.2 (R Foundation for Statistical Computing) or SAS version 9.3 (SAS Institute Inc) software packages.

Results

The study included 4602 participants (1008 from the 1993-2001, 1067 from the 1996-2004, and 2527 from the 2003-2012 cohorts) who had data from 2 or more annual follow-up questionnaires and after excluding 297 participants who were newly diagnosed with asthma during the follow-up period. The study included 49.3% girls and 51.7% boys, a similar number overall and across all cohorts (**Table 1**). The proportion of Hispanic children increased from 29.4% for the 1993-2001 cohort to 35.3% for the 1996-2004 cohort and to 55.7% for the 2003-2012 cohort. The 2003-2012 cohort had a significantly lower proportion of exposure to secondhand smoke or history of in utero exposure to maternal smoking and had a lower prevalence of ownership of any pets including cats and dogs as well as a higher prevalence of asthma at age 10 years than the mean of the 2 earlier cohorts (22.9% vs 15.1%). Additionally, the 2003-2012 cohort had larger proportions of children with health insurance, living in homes with gas stoves, and being either obese or overweight at age 10 years and had a lower proportion of children living in a carpeted home with parents who had a high school diploma. A higher proportion of the 2003-2012 cohort participants completed a Spanish-language questionnaire. The prevalence of bronchitic symptoms decreased across the 1993-2012 study period, but the reduction was larger between the 1996-2004 and the 2003-2012 cohorts than that between the 2 earlier cohorts, which showed modest change or even a slight increase at times. Levels were slightly higher at age 15 years than at age 10 years within each cohort. Children with asthma had a significantly higher overall prevalence of bronchitic symptoms (Table 1; eTable 1 and eFigure 1 in the Supplement).[20]

Overall, air pollution levels declined (especially after 2001) across the 3 cohorts as can be seen in **Figure 1**.[21] Nitrogen dioxide and ozone pollution levels in all 8 communities declined with the lowest average levels observed for the 2003-2012 cohort, with the exception of Long Beach and Santa Maria where ozone levels were higher in the 2003-2012 cohort (eTable 2 and eFigure 2 in Supplement). The decreases were larger in communities with the highest levels of pollutants. Similar declines were observed for $PM_{2.5}$, with the exception of Alpine. Changes in levels of PM_{10} were relatively smaller in most communities with modestly increased levels in some communities (eTable 2 and eFigure 2 in the Supplement).

Decreases in ambient air pollutant levels of nitrogen dioxide, ozone, PM_{10}, and $PM_{2.5}$ were associated with reductions in bronchitic symptoms at ages 10 and 15 years among children with and without asthma (**Table 2**). Among children with asthma, bronchitic symptoms at age 10 years were significantly associated with nitrogen dioxide (odds ratio [OR], 0.79; 95% CI, 0.67-0.94) for a median reduction of 4.9 ppb with a corresponding absolute decrease in prevalence of 10.1% (95% CI, 15.8%-2.9%). For ozone, the OR was 0.66 (95% CI, 0.50-0.86) for a median reduction of 3.6 ppb with corresponding absolute decrease in prevalence of 16.3% (95% CI, 24.0%-6.7%). For PM_{10}, the OR was 0.61 (95% CI, 0.48-0.78) for a median reduction of 5.8 $\mu g/m^3$ with corresponding absolute decrease in prevalence of 18.7% (95% CI, 25.0%-10.6%). For $PM_{2.5}$, the OR was 0.68 (95% CI, 0.53-0.86) for a median reduction of 6.8 $\mu g/m^3$ with corresponding absolute decrease in prevalence of 15.4% (95% CI, 22.6%-6.7%). In the above calculations, the median reductions were based on the 8 community-level changes in

Table 1. Distribution of Demographic and Other Baseline Characteristics of Participants in 3 California Children's Health Study Cohorts

Characteristic	All Participants, No. (%) (n = 4602)	Cohort Follow-up Period, No. (%)[a]			P Value[b]
		1993-2001 (n = 1008)	1996-2004 (n = 1067)	2003-2012 (n = 2527)	
Age at baseline, mean (SD), y	8.0 (1.7)	9.9 (0.6)	9.7 (.6)	6.6 (.7)	<.001
Sex					
Girls	2268 (49.3)	493 (48.9)	530 (49.7)	1245 (49.3)	.94
Boys	2334 (50.7)	515 (51.1)	537 (5.3)	1282 (5.7)	
Race/ethnicity					
Asian	198 (4.3)	56 (5.6)	59 (5.5)	83 (3.3)	<.001
Black	172 (3.7)	48 (4.8)	53 (5.0)	71 (2.8)	
Hispanic white	2081 (45.2)	296 (29.4)	377 (35.3)	1408 (55.7)	
Non-Hispanic white	1883 (40.9)	550 (54.6)	518 (48.5)	815 (32.3)	
Other	268 (5.8)	58 (5.8)	60 (5.6)	150 (5.9)	
Dog ownership					
No	2676 (59.2)	479 (47.5)	481 (45.1)	1716 (7.1)	<.001
Yes	1847 (40.8)	529 (52.5)	586 (54.9)	732 (29.9)	
Cat ownership					
No	3318 (73.4)	640 (63.5)	684 (64.1)	1994 (81.5)	<.001
Yes	1205 (26.6)	368 (36.5)	383 (35.9)	454 (18.5)	
Any pets at home					
No	1631 (36.1)	262 (26.0)	236 (22.1)	1133 (46.3)	<.001
Yes	2892 (63.9)	746 (74.0)	831 (77.9)	1315 (53.7)	
Spanish questionnaire					
No	3870 (84.1)	931 (92.4)	930 (87.2)	2009 (79.5)	<.001
Yes	732 (15.9)	77 (7.6)	137 (12.8)	518 (2.5)	
Parental high school graduation					
No	754 (17.1)	144 (14.6)	136 (13.4)	474 (19.6)	<.001
Yes	3663 (82.9)	842 (85.4)	880 (86.6)	1941 (8.4)	
Health insurance					
No	599 (13.3)	163 (16.6)	162 (15.4)	274 (11.1)	<.001
Yes	3909 (86.7)	821 (83.4)	889 (84.6)	2199 (88.9)	
Exposure to smoke in utero					
No	3963 (88.7)	807 (82.1)	890 (85.3)	2266 (92.9)	<.001
Yes	503 (11.3)	176 (17.9)	153 (14.7)	174 (7.1)	
Exposure to secondhand smoke					
No	3831 (85.1)	738 (74.5)	803 (76.4)	2290 (93)	<.001
Yes	672 (14.9)	252 (25.5)	248 (23.6)	172 (7)	
Any pests at home					
No	1145 (27.2)	194 (20.9)	189 (19.6)	762 (32.9)	<.001
Yes	3070 (72.8)	736 (79.1)	777 (8.4)	1557 (67.1)	
Cockroaches at home					
No	3709 (88)	769 (82.7)	817 (84.6)	2123 (91.5)	<.001
Yes	506 (12)	161 (17.3)	149 (15.4)	196 (8.5)	
Carpet at home					
No	216 (4.8)	32 (3.2)	43 (4.1)	141 (5.8)	.003
Yes	4261 (95.2)	959 (96.8)	1004 (95.9)	2298 (94.2)	
Mildew at home					
No	3294 (76.4)	714 (73.8)	789 (76.8)	1791 (77.4)	.08
Yes	1016 (23.6)	254 (26.2)	238 (23.2)	524 (22.6)	
Water damage at home					
No	3813 (85.7)	828 (84.1)	920 (87.4)	2065 (85.6)	.11
Yes	636 (14.3)	156 (15.9)	133 (12.6)	347 (14.4)	

(continued)

Table 1. Distribution of Demographic and Other Baseline Characteristics of Participants in 3 California Children's Health Study Cohorts (continued)

Characteristic	All Participants, No. (%) (n = 4602)	Cohort Follow-up Period, No. (%)[a] 1993-2001 (n = 1008)	1996-2004 (n = 1067)	2003-2012 (n = 2527)	*P* Value[b]
Gas stove at home					
No	916 (20.6)	252 (25.6)	282 (27)	382 (15.7)	<.001
Yes	3539 (79.4)	733 (74.4)	762 (73)	2044 (84.3)	
Asthma medication use					
No	3671 (79.8)	865 (85.8)	918 (86.0)	1888 (74.7)	<.001
Yes	931 (20.2)	143 (14.2)	149 (14.0)	639 (25.3)	
Categorized BMI at age 10 y					
BMI percentile <85	2356 (67.4)	669 (73.1)	684 (72.1)	1003 (61.4)	<.001
85≤BMI percentile <95	534 (15.2)	132 (14.4)	131 (13.8)	271 (16.6)	
≥95 BMI percentile	608 (17.4)	114 (12.5)	134 (14.1)	360 (22.0)	
BMI at age 10 y, mean (SD)	18.7 (3.7)	18.4 (3.3)	18.2 (3.5)	19.1 (3.9)	<.001
Asthma status at age 10 y					
Yes	892 (19.4)	150 (14.9)	164 (15.4)	578 (22.9)	<.001
No	3710 (80.6)	858 (85.1)	903 (84.6)	1949 (77.1)	
BCP					
Age 10 y					
Asthma group					
No	400 (60.4)	68 (47.2)	78 (51.3)	254 (69.4)	<.001
Yes	262 (39.6)	76 (52.8)	74 (48.7)	112 (3.6)	
Nonasthma group					
No	2519 (88.8)	714 (86.2)	719 (85.4)	1086 (93.0)	<.001
Yes	319 (11.2)	114 (13.8)	123 (14.6)	82 (7.0)	
Age 15 y					
Asthma group					
No	313 (67.6)	69 (61.6)	81 (67.5)	163 (7.6)	.25
Yes	150 (32.4)	43 (38.4)	39 (32.5)	68 (29.4)	
Nonasthma group					
No	1535 (81.9)	456 (79.7)	495 (78.9)	584 (86.4)	<.001
Yes	340 (18.1)	116 (20.3)	132 (21.1)	92 (13.6)	

Abbreviations: BCP, bronchitis, cough, or phlegm; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared.

[a] Numbers may not always add up to overall total of 4602 participants due to missing data.

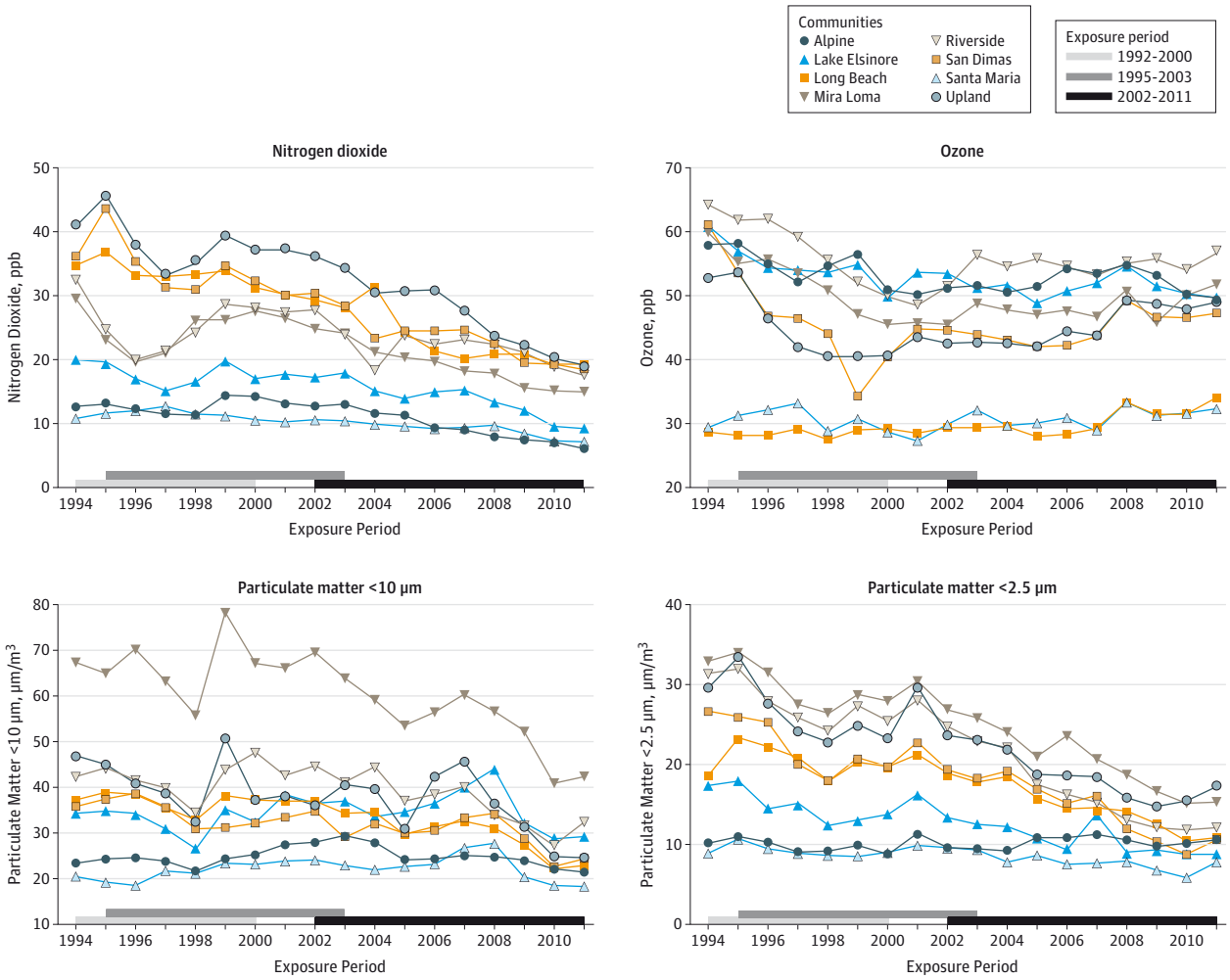
[b] Examining differences between cohorts based on χ^2 test (for categorical variables) and *F* test (for the continuous variables).

mean pollution levels during the 1992-2000, 1995-2003, and 2002-2011 calendar years, averaging periods for the 3 cohorts. The absolute differences in prevalence were calculated relative to the adjusted baseline prevalence of 48% for the 1993-2001 cohort.

Among children without asthma, the corresponding ORs for the associations with prevalence of bronchitic symptoms were relatively smaller: 0.84 (95% CI, 0.76-0.92) for nitrogen oxide with a corresponding absolute decrease in prevalence of 1.8% (95% CI, 2.7%-0.9%); 0.85 (95% CI, 0.74-0.97) for ozone, with a corresponding absolute decrease in prevalence of 1.7% (95% CI, 2.9%-0.3%); 0.80 (95% CI, 0.70-0.92) for PM_{10}, with a corresponding absolute decrease in prevalence of 2.2% (95% CI, 3.3%-0.9%), and 0.79 (95% CI, 0.69-0.91) for $PM_{2.5}$, with a corresponding absolute decrease in prevalence of 2.3% (95% CI, 3.4%-1.0%) (Table 2). The absolute differences in prevalence were calculated relative to adjusted baseline prevalence of 11.1% for the 1993-2001 cohort. Corresponding results at age 15 years were either similar or slightly larger (Table 2). In post hoc analyses, areas with increased concentrations of regulated regional air pollution levels generally had increased prevalence of bronchitis within any given cohort (eFigure 3 in the Supplement). Similar associations were seen in graphs of unprocessed data, focusing on prevalences at age 10 years (eFigure 4 in the Supplement). Due to high multicollinearity between nitrogen dioxide, PM_{10}, and $PM_{2.5}$ (eTable 3 in the Supplement), 2-pollutant models were only possible with ozone. Based on these 2-pollutant models, the associations with ozone became nonsignificant (except for the ozone + nitrogen dioxide model in the asthma group) while the estimates for each of the other pollutants remained significant (eTable 4 in the Supplement).

Based on models with random effects for the air pollution estimates, there was no heterogeneity of model estimates by community of residence. Plots of the predicted changes in prevalence of bronchitic symptoms by changes in air pollution levels across the study period showed that relatively larger changes in prevalence of bronchitic symptoms were observed in communities with larger changes in air pollutant levels (**Figure 2**), indicating that decreases in symptoms were not an artifact of temporal confounding acting

Figure 1. Annual Mean Air Pollutant Levels During the Follow-up Period of the California Children's Health Study by Community, 1994-2001



Plots depict data for 1994-2011, even though the models use 1992-2011 exposure data to examine associations with 1993-2012 data on bronchitic symptoms. This is because data for 1992 and 1993 were not complete and had to be substituted with 1994 data in some cases. For particulate matter less than 10 µm, mean pollutant concentrations from 1994 were used for Alpine, Riverside, and Upland for 1992 and 1993 due to missing data. Similarly, particulate matter less than 2.5 µm mean pollutant concentrations from 1994 were used for 1992 and 1993, for all 8 communities, due to missing data. The light gray bar represents the 1992-2000 exposure years; dark gray, 1995-2003; and black, 2002-2011.

across communities. For example, in the asthma group, a 12-µg/m^3 decline in $PM_{2.5}$ for children in Riverside was associated with a 20% reduction in bronchitic symptom prevalence, whereas in Alpine, a decline of 0.5 µg/m^3 was associated with a negligible change in the prevalence of bronchitic symptoms.

Sensitivity analyses were conducted to test the robustness of study findings by limiting the analysis to important subgroups (eMethods in the Supplement). The estimated reductions in bronchitic symptoms were robust to any of these restrictions (eTable 5 in the Supplement) and remained similar when examined at ages 10, 13, and 15 years (Table 2; eTable 6 in the Supplement). Results from models limited to data with overlapping ages for all 3 cohorts (ie, between ages of 10 and 15 years) were similar to those based on the whole age range (Table 2; eTable 7 in the Supplement). The results presented in eTable 7 were based on exposure averaging periods that were relevant to the overlapping age periods. Specifically, we used 1992-1997, 1995-2000, and 2006-2011 years, respectively, for the 3 successive cohorts.

In the asthma group, the associations with nitrogen dioxide and $PM_{2.5}$ were significantly larger in boys and among children with a family dog (**Table 3**). Reductions in bronchitic symptoms as a function of improvement in air quality were qualitatively similar for ages 10 and 15 years or were slightly larger for age 15 years in some cases. None of the other interaction tests by parental level of education, race/ethnicity, cat ownership, or exposure to secondhand smoke were found to be statistically significant. Models that tested for effect modification by cat or dog ownership used data from 4523 children, due to missing relevant questionnaire data.

Table 2. Relative Changes in Bronchitic Symptoms Associated With Reductions in Air Pollution by Asthma Status, 1993-2012

Asthma Status	Nitrogen Dioxide			Ozone			Particulate Matter					
							<10 µm			<2.5 µm		
	OR (95% CI)[a]	Absolute Prevalence Differences (95% CI), %[b]	P Value	OR (95% CI)[a]	Absolute Prevalence Differences (95% CI), %[b]	P Value	OR (95% CI)[a]	Absolute Prevalence Differences (95% CI), %[b]	P Value	OR (95% CI)[a]	Absolute Prevalence Differences (95% CI), %[b]	P Value
10-Year-Olds												
Asthma	0.79 (0.67 to 0.94)	−10.1 (−15.8 to −2.9)	.007	0.66 (0.50 to 0.86)	−16.3 (−24.0 to −6.7)	.002	0.61 (0.48 to 0.78)	−18.7 (−25.0 to −10.6)	<.001	0.68 (0.53 to 0.86)	−15.4 (−22.6 to −6.7)	.002
Nonasthma	0.84 (0.76 to 0.92)	−1.8 (−2.7 to −0.9)	<.001	0.85 (0.74 to 0.97)	−1.7 (−2.9 to −0.3)	.02	0.80 (0.70 to 0.92)	−2.2 (−3.3 to −0.9)	.001	0.79 (0.69 to 0.91)	−2.3 (−3.4 to −1.0)	<.001
15-Year-Olds												
Asthma	0.76 (0.64 to 0.89)	−8.3 (−12.4 to −3.8)	<.001	0.66 (0.50 to 0.86)	−11.7 (−17.2 to −4.8)	.002	0.61 (0.48 to 0.77)	−13.4 (−17.9 to −7.9)	<.001	0.64 (0.50 to 0.82)	−12.4 (−17.2 to −6.2)	<.001
Nonasthma	0.78 (0.71 to 0.86)	−3.3 (−4.3 to −2.1)	<.001	0.85 (0.75 to 0.98)	−2.2 (−3.7 to −0.3)	.02	0.78 (0.68 to 0.89)	−3.3 (−4.7 to −1.6)	<.001	0.71 (0.61 to 0.81)	−4.3 (−5.8 to −2.8)	<.001

Abbreviation: OR, odds ratio.

[a] Odds ratios are per median decreases in pollution levels based on the 8 community-level average changes during the period between the 1993-2001 and the 2003-2012 cohorts (4.9 ppb and 3.6 ppb for nitrogen dioxide and ozone, respectively, and 5.8 µg/m^3 and 6.8 µg/m^3 for PM_{10}, and $PM_{2.5}$, respectively). For example, nitrogen dioxide (see first data column in eTable 2), the decreases from the 1992-2000 to the 2002-2011 averaging periods, for the 1993-2001 to the 2003-2012 cohorts respectively, were as follows (in ascending order): 2.0 ppb, Santa Maria; 3.6 ppb, Alpine; 3.8 ppb, Riverside; 4.3 ppb, Lake Elsinore; 5.4 ppb, Miraloma, 11.0 ppb, Long Beach; 11.5 ppb, Upland; and 11.9 ppb, San Dimas. This leads to a median of 4.9 (average of the 2 middle-ranked communities: Long Beach and Miraloma). Odds ratios are by asthma status, adjusted for age, sex, race/ethnicity, and longitudinal exposure to secondhand tobacco smoke.

[b] The absolute differences in prevalence were calculated relative to the adjusted baseline prevalence for the 1993-2001 cohort (48% for the asthma group and 11.1% for the nonasthma group).

Discussion

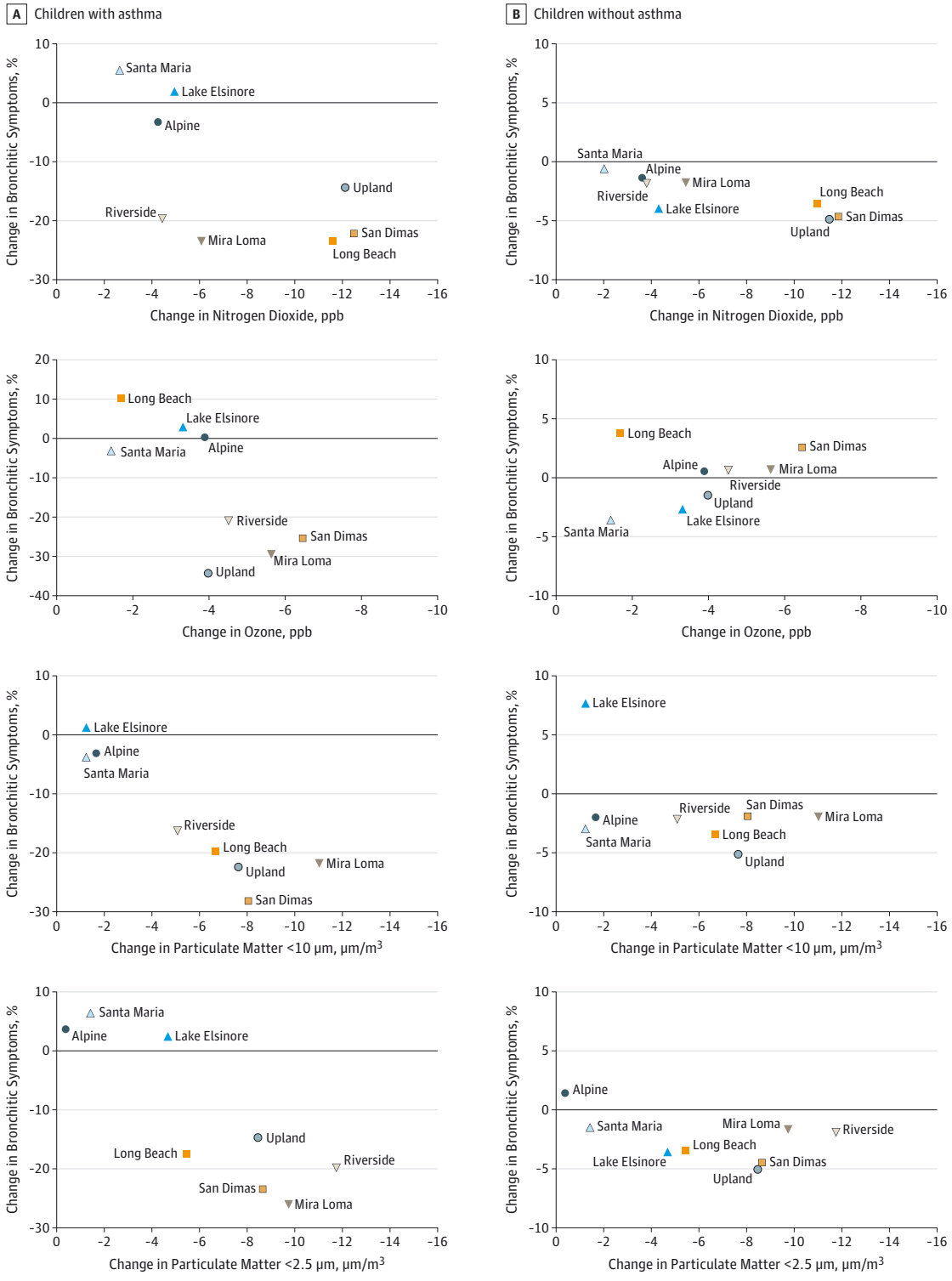
The findings from this study demonstrate that reductions in levels of ambient air pollution over the past 20 years in Southern California were associated with significant reductions in bronchitic symptoms in children with and without asthma. The reductions were proportionally larger in children with asthma and remained similar when examined at 10, 13, and 15 years of age during the follow-up period (Table 2; eTable 6 in the Supplement). Among patients with asthma, the reductions in bronchitic symptoms tended to be larger in boys and among children from households with dogs.[9]

The reductions in bronchitic symptoms were larger in communities that showed higher improvements in air quality levels (Figure 2), indicating that the findings were robust to temporal confounding.[22] The findings remained robust during subgroup analysis by several factors that could contribute to differential biases or potential overestimation or underestimation of the study findings (eTable 5 in the Supplement). Any temporal trends in asthma diagnosis, prevalence, severity, or medication use are unlikely to account for these findings because our models also included spline terms for age to account for any secular trends in bronchitic symptoms. The linear relationship between change in air quality and changes in prevalence across all communities is consistent with an effect of air pollution reduction and also suggests that the results are not explained by a secular temporal trend (Figure 2).

These results are consistent with findings from a large multicommunity Swiss study involving 9591 children. The study showed that moderate improvements in air quality were associated with significant reductions in respiratory symptoms, based on cross-sectional health assessments between 1992 and 2001.[23]

Several studies have shown that areas with increased concentrations of regulated regional air pollution levels have increased prevalence of bronchitis,[4,5,7] a finding that has also been confirmed in this study (eFigure 3 in the Supplement). Some studies have shown that yearly variations in pollutant concentrations are positively associated with bronchitis prevalence, especially among children with asthma.[1,9] Few previous studies have evaluated whether trends in reductions in air pollution levels over decades have led to reductions in bronchitic symptoms. Results from 2 repeated surveys in former East Germany showed that within-community reductions in total suspended particulates and sulfur dioxide levels following reunification were associated with substantial reductions in total bronchitis prevalence and other nonallergic respiratory symptoms.[3,24] It is possible that confounding by other temporal community characteristics or trends in respiratory outcomes across cohorts could explain these results. However, the consistency of associations in diverse populations and study designs and the biological patterns of susceptibility observed in studies of air pollution and bronchitis suggest that the associations and the benefits observed in our study are causally related to air pollution reductions.

Figure 2. Predicted Change in Bronchitic Symptom Prevalence at Age 10 Years vs the Change in Mean Air Pollutants Over the Study Period by Community[a]



[a] Plots depict the predicted changes from the longitudinal model in prevalence of bronchitic symptoms at age 10 years (across the 1993-2001 and 2003-2012 cohorts) as functions of the changes in mean exposures levels, comparing high to low mean pollution levels for the 1992-2000, 1995-2003, and the 2002-2011 averaging periods. The estimates used in the plots are based on longitudinal models with adjustments for sex, race/ethnicity, and a spline function of age with knots (break points) at 10 and 15 years of age.

Table 3. Relative Changes in Bronchitic Symptoms Associated With Reductions in Air Pollution by Age, Sex, Dog Ownership, and Asthma Status, 1993-2012

Effect Modifier	Nitrogen Dioxide[a]			Ozone[b]			Particulate Matter					
							<10 μm[b]			<2.5 μm[b]		
	OR (95% CI)[c]	*P* Value	*P* Value for Interaction[d]	OR (95% CI)[c]	*P* Value	*P* Value for Interaction[d]	OR (95% CI)[c]	*P* Value	*P* Value for Interaction[d]	OR (95% CI)[c]	*P* Value	*P* Value for Interaction[d]
10-Year-Olds												
Asthma												
Boys	0.72 (0.60-0.86)	<.001	.01	0.66 (0.50-0.86)	.002	.61	0.59 (0.46-0.76)	<.001	.27	0.55 (0.42-0.72)	<.001	.02
Girls	0.86 (0.71-1.03)	.09		0.64 (0.49-0.85)	.002		0.64 (0.50-0.82)	<.001		0.82 (0.62-1.09)	.16	
Dog												
Yes	0.71 (0.6-0.85)	<.001	.01	0.70 (0.54-0.91)	.009	.18	0.60 (0.47-0.77)	<.001	.06	0.57 (0.43-0.74)	<.001	.03
No	0.85 (0.7-1.02)	.08		0.65 (0.49-0.86)	.002		0.67 (0.51-0.88)	.003		0.79 (0.59-1.06)	.12	
Nonasthma												
Boys	0.82 (0.74-0.91)	<.001	.18	0.85 (0.74-0.98)	.02	1.00	0.80 (0.70-0.92)	.002	.71	0.78 (0.67-0.92)	.002	.20
Girls	0.84 (0.76-0.93)	.001		0.83 (0.73-0.96)	.01		0.81 (0.71-0.93)	.002		0.79 (0.68-0.92)	.002	
Dog												
Yes	0.83 (0.74-0.92)	<.001	.20	0.84 (0.74-0.97)	.01	.28	0.83 (0.72-0.95)	.006	.34	0.79 (0.67-0.92)	.002	.44
No	0.85 (0.77-0.95)	.003		0.88 (0.77-1.02)	.09		0.80 (0.70-0.94)	.006		0.81 (0.69-0.96)	.01	
15-Year-Olds												
Asthma												
Boys	0.70 (0.59-0.84)	<.001	.02	0.69 (0.53-0.91)	.008	.16	0.59 (0.46-0.76)	<.001	.14	0.56 (0.43-0.73)	<.001	.03
Girls	0.83 (0.69-1.00)	.048		0.67 (0.50-0.88)	.005		0.63 (0.49-0.81)	<.001		0.75 (0.56-0.99)	.04	
Dog												
Yes	0.70 (0.59-0.84)	<.001	.03	0.68 (0.52-0.88)	.004	.15	0.60 (0.47-0.76)	<.001	.06	0.54 (0.41-0.71)	<.001	.03
No	0.82 (0.68-0.99)	.04		0.65 (0.49-0.85)	.002		0.67 (0.51-0.88)	.004		0.72 (0.54-0.96)	.03	
Nonasthma												
Boys	0.78 (0.71-0.87)	<.001	.99	0.85 (0.74-0.98)	.02	.99	0.77 (0.68-0.89)	<.001	.49	0.72 (0.61-0.84)	<.001	.34
Girls	0.78 (0.71-0.87)	<.001		0.84 (0.73-0.96)	.01		0.78 (0.68-0.90)	<.001		0.69 (0.60-0.81)	<.001	
Dog												
Yes	0.80 (0.72-0.89)	<.001	.58	0.85 (0.74-0.97)	.02	.99	0.80 (0.70-0.92)	.001	.38	0.74 (0.63-0.86)	<.001	.68
No	0.80 (0.72-0.89)	<.001		0.87 (0.75-1.00)	.048		0.78 (0.68-0.91)	.002		0.73 (0.62-0.86)	<.001	

Abbreviation: OR, odds ratio.

[a] Odds ratios are adjusted for age, sex, race/ethnicity, longitudinal, secondhand smoke, and cockroaches at baseline.

[b] Odds ratios are adjusted for age, sex, race/ethnicity, and longitudinal secondhand smoke.

[c] Odds ratios are per median decreases in pollution levels based on the 8 community-level average changes during the period between the 1993-2001 and the 2003-2012 cohorts (4.9 ppb and 3.6 ppb for nitrogen dioxide and ozone, respectively, and 5.8 μg/m^3 and 6.8 μg/m^3 for particulate matter less than 10 and less than 2.5, respectively).

[d] *P* values for tests of interaction effects between air pollutants and effect modifiers.

Larger reductions in prevalence of bronchitic symptoms in children with asthma and with dogs as pets have been observed in previous analyses of the within-cohort variability in pollution concentrations across years in the California Children's Health Study.[1,9] These differences were predicted based on the known susceptibility of children with asthma to the pollutants studied and the higher levels of endotoxin, which has been shown to potentiate pollutant exposures, in the homes of children with dogs.

This study has several strengths, including the prospective study design enabling evaluation of associations related to temporal trends in air pollution across several large ethnically diverse cohorts of children from the same communities on trends in bronchitic symptoms, substantial range in exposures to the spectrum of complex multipollutant mixtures available in Southern California representing the full national range in the United States, and the opportunity to test whether the associations varied by patterns in susceptibility

factors. A major strength of the study was the consistency of protocols in collecting bronchitic symptoms, covariate information, and air pollution monitoring throughout the long study period.

The findings should also be interpreted in light of some limitations. The outcome measure is based on relatively imprecise assessment of health outcomes defined using questionnaire-based reporting of symptoms. However, these outcomes have been widely used in previous epidemiological studies and have shown robust associations with regional pollutants.[1,3-5,7,9] The components of the bronchitic symptom outcomes used in this study are suggestive of chronic, indolent symptoms that may follow an illness, acute exacerbation of asthma, or chronic inflammation that would likely be remembered well. Questionnaire-based report of respiratory symptoms might also reflect repeated acute exacerbation, but acute bronchitis has been reported to have a marked influence on quality of life, in adults and in children, and to persist for several weeks, so such episodes also would be likely to be remembered well.[11,25]

It is possible that false-positive misclassification of asthma might have resulted in an underestimation of the true effect of air pollution in children with asthma, given that children with asthma were more sensitive than children who did not have asthma. The misclassification of personal exposure based on community monitors may also have resulted in some underestimation of the magnitude of associations. However, because concentrations of $PM_{2.5}$ and PM_{10} vary gradually with geographic distance in Southern California, exposure misclassification for children who attend school in their communities is unlikely to produce a large attenuation of associations. Ozone showed limited gradient across these communities but has large indoor-outdoor concentration differences that depend on housing characteristics and operation. The resulting exposure misclassification would likely result in artificially low model estimates for ozone. Reporting bias is an unlikely explanation for the observed within-community between-cohorts associations because any awareness of long-term trends in air pollution within any community is unlikely to have been a determinant of reporting of bronchitis. The shift in ethnic composition across the 3 cohorts with a growing Hispanic population and lower socioeconomic status is a potential source of bias. However, bias in the estimates from this change in ethnic distribution is not likely to have a major effect because sensitivity analyses based on models that only considered Hispanic children gave results that were similar to those that included all children. These findings should be interpreted in the context of the observational design of the study and limitations associated with the use of ecologic community-level ambient (and personal level) exposure estimates in investigating the statistical associations. However, the study design with individual-level longitudinal data on bronchitic outcomes and adjustment factors may help to reduce some of the limitations that occur in studies with a purely ecologic design, such as aggregation bias, ecologic bias, or both.[17,26]

Conclusions

Decreases in ambient concentrations of nitrogen dioxide, ozone, PM_{10}, and $PM_{2.5}$ were associated with statistically significant decreases in bronchitic symptoms in children with and without asthma. While the study design does not establish causality, the findings support potential benefit of air pollution reduction on asthma control.

ARTICLE INFORMATION

Author Contributions: Drs Berhane and Gilliland had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Berhane, Gauderman, Avol, Gilliland.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Berhane, Chang, Avol, Lurmann, Gilliland.
Critical revision of the manuscript for important intellectual content: Chang, McConnell, Gauderman, Avol, Rapapport, Urman, Gilliland.
Statistical analysis: Berhane, Chang, Gauderman, Rapapport, Urman, Gilliland.
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