

Supplementary Online Content

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eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Data Analysis

Modeling Approach

The multilevel modeling approach used in this study has been previously described.¹⁻³ In this study a multilevel Poisson regression with a random effect was specifically used for the main analysis of associations between air pollution exposure and incident asthma. The model was fitted to ungrouped person-time data.⁴ In “Poisson regression analysis of ungrouped data” by Loomis *et al.* each observation represented one person-year, thus all observations contributed equal weight and an offset term did not need to be specified. In contrast, in the current analysis all person-time for a given participant were combined into a single observation and an offset term for follow-up time was used to represent time at risk. In this two-level Poisson model t , c , and i denote community, cohort, and participant, respectively. In the first level we modeled participant-specific rate of asthma incidence (μ_{tci}) as a function of participant-specific covariates Z_{tci} (e.g., baseline age, sex, race, ethnicity, etc.) and an offset for participant-specific follow-up time F_{tci} [Eq. 1]. Here, A_{tc} represents community and cohort-specific rates of asthma, which were used in the second-level model.

$$\text{Log } \mu_{tci} = \log F_{tci} + A_{tc} + \gamma_1 Z_{tci} \quad [\text{Equation 1}]$$

In the second level, community and cohort-specific adjusted rates of asthma (A_{tc}) from level 1 were regressed as functions of community and cohort-specific mean annual air pollution concentration (X_{tc}) and community-cohort level error (e_{tc}), [Eq. 2]. Community indicators (*Community*) were also included in the second-level model as adjustments to focus health point estimates on secular changes in air pollutions within-community rather than across communities.

$$A_{tc} = \alpha + \beta_1 X_{tc} + \gamma_2 \text{Community} + e_{tc} \quad [\text{Equation 2}]$$

These two regression models were combined to yield a more efficient mixed-effects model [Eq. 3].

$$\text{Log } \mu_{tci} = \log F_{tci} + \alpha + \beta_1 X_{tc} + \gamma_1 Z_{tci} + \gamma_2 \text{Community} + e_{tc} \quad [\text{Equation 3}]$$

The main parameter of interest in the above Poisson model is the within-community across-cohorts parameter coefficient of improvements in air pollution on asthma incidence rates, β_1 . Models were fitted using SAS procedure GLIMMIX, specifying “dist=poisson” for Poisson distribution and including an offset for person-time (natural log-transformed).

eTable 1. Distribution of Selected Characteristics Among Participants Included and Excluded From the Current Study of the Children's Health Study, 1993-2014

Characteristic	All Participants, N (%)			Cohort Follow-up Period, N (%)						
				1993-2001		1996-2004		2006-2014		
	Included	Excluded due to missing baseline asthma status	Excluded due to missing years 3 and 4 questionnaires	Included	Excluded due to missing baseline asthma status	Included	Excluded due to missing baseline asthma status	Included	Excluded due to missing baseline asthma status	Excluded due to missing years 3 and 4 questionnaires
Participants	4140	143	268	1093	29	1170	39	1877	75	268
Person-years of follow-up	24254	664	-	6201	132	6842	188	11211	343	-
Age at baseline, mean (SD), years	9.5 (0.6)	9.5 (0.7)	-	9.9 (0.5)	10.1 (0.6)	9.5 (0.4)	9.6 (0.4)	9.3 (0.7)	9.2 (0.8)	-
Sex										
<i>Female</i>	2179 (52.6)	75 (52.5)	109 (40.7)	569 (52.1)	16 (55.2)	606 (51.8)	22 (56.4)	1004 (53.5)	37 (49.3)	109 (40.7)
<i>Male</i>	1961 (47.4)	68 (47.5)	159 (59.3)	524 (47.9)	13 (44.8)	564 (48.2)	17 (43.6)	873 (46.5)	38 (50.7)	159 (59.3)
Ethnicity										
<i>Hispanic</i>	1686 (40.7)	53 (37.1)	159 (59.3)	307 (28.1)	12 (41.4)	413 (35.3)	16 (41.0)	966 (51.5)	25 (33.3)	159 (59.3)
<i>Non-Hispanic</i>	2310 (55.8)	75 (52.4)	85 (31.7)	776 (71.0)	14 (48.3)	750 (64.1)	19 (48.7)	784 (41.8)	42 (56.0)	85 (31.7)
<i>Missing</i>	144 (3.5)	15 (10.5)	24 (9.0)	10 (0.9)	3 (10.3)	7 (0.6)	4 (10.3)	127 (6.8)	8 (10.7)	24 (9.0)
Race										
<i>Asian/Pacific Islander</i>	178 (4.3)	11 (7.7)	8 (3.0)	60 (5.5)	3 (10.3)	56 (4.8)	3 (7.7)	62 (3.3)	5 (6.7)	8 (3.0)
<i>Black</i>	145 (3.5)	7 (4.9)	11 (4.1)	50 (4.6)	3 (10.3)	54 (4.7)	2 (5.1)	41 (2.2)	2 (2.7)	11 (4.1)
<i>Native American Indian/Other</i>	890 (21.5)	30 (20.1)	67 (25.0)	182 (16.7)	7 (24.1)	249 (21.3)	9 (23.1)	459 (24.5)	14 (18.7)	67 (25.0)
<i>White</i>	2273 (54.9)	58 (40.6)	92 (34.3)	704 (64.4)	9 (31.0)	692 (59.2)	15 (38.5)	877 (46.7)	34 (45.3)	92 (34.3)
<i>Mixed</i>	392 (9.5)	20 (14.0)	27 (10.1)	76 (7.0)	1 (3.5)	106 (9.1)	7 (18.0)	210 (11.2)	12 (16.0)	27 (10.1)
<i>Missing</i>	262 (6.3)	17 (11.9)	63 (23.5)	21 (1.9)	6 (20.7)	13 (1.1)	3 (7.7)	228 (12.2)	8 (10.7)	63 (23.5)
Parental education										
<i>High school graduate or below</i>	1424 (34.4)	51 (35.7)	114 (42.5)	379 (34.7)	8 (27.6)	385 (32.9)	14 (35.9)	660 (35.2)	29 (38.7)	114 (42.5)
<i>Some college or above</i>	2476 (59.8)	52 (36.4)	118 (44.0)	689 (63.0)	8 (27.6)	728 (62.2)	9 (23.1)	1059 (56.4)	35 (46.7)	118 (44.0)
<i>Missing</i>	240 (5.8)	40 (28.0)	36 (13.4)	25 (2.3)	13 (44.8)	57 (4.9)	16 (41.0)	158 (8.4)	11 (14.7)	36 (13.4)

Table continues on next page

eTable 1 (continued). Distribution of Selected Characteristics Among Participants Included and Excluded From the Current Study of the Children's Health Study, 1993-2014

Characteristic	All Participants, N (%)			Cohort Follow-up Period, N (%)						
	Included	Excluded due to missing baseline asthma status	Excluded due to missing years 3 and 4 questionnaires	1993-2001		1996-2004		2006-2014		
				Included	Excluded due to missing baseline asthma status	Included	Excluded due to missing baseline asthma status	Included	Excluded due to missing baseline asthma status	Excluded due to missing years 3 and 4 questionnaires
Gas stove in home										
<i>No</i>	784 (18.9)	17 (11.9)	42 (15.7)	243 (22.2)	2 (6.9)	287 (24.5)	5 (12.8)	254 (13.5)	10 (13.3)	42 (15.7)
<i>Yes</i>	3153 (76.2)	92 (64.3)	194 (72.4)	824 (75.4)	14 (48.3)	860 (73.5)	20 (51.3)	1469 (78.3)	58 (77.3)	194 (72.4)
<i>Missing</i>	203 (4.9)	34 (23.8)	32 (11.9)	26 (2.4)	13 (44.8)	23 (2.0)	14 (35.9)	154 (8.2)	7 (9.3)	32 (11.9)
Play team sport										
<i>No</i>	1938 (46.8)	56 (39.2)	-	532 (48.7)	7 (24.1)	539 (46.1)	16 (41.0)	867 (46.2)	33 (44.0)	-
<i>Yes</i>	2104 (50.8)	56 (39.2)	-	542 (49.6)	9 (31.0)	597 (51.0)	9 (23.1)	965 (51.4)	38 (50.7)	-
<i>Missing</i>	98 (2.3)	31 (21.7)	-	19 (1.7)	13 (44.8)	34 (2.9)	14 (35.9)	45 (2.4)	4 (5.3)	-
In utero exposure to smoking										
<i>No</i>	3455 (83.5)	87 (60.8)	215 (80.2)	876 (80.2)	11 (37.9)	966 (82.6)	20 (51.3)	1613 (85.9)	56 (74.7)	215 (80.2)
<i>Yes</i>	484 (11.7)	15 (10.5)	23 (8.6)	187 (17.1)	5 (17.2)	177 (15.1)	4 (10.3)	120 (6.4)	6 (8.0)	23 (8.6)
<i>Missing</i>	201 (4.9)	41 (28.7)	30 (11.2)	30 (2.7)	13 (44.8)	27 (2.3)	15 (38.5)	144 (7.7)	13 (17.3)	30 (11.2)
Secondhand smoke exposure										
<i>No</i>	3006 (72.6)	74 (51.7)	181 (67.5)	757 (69.3)	8 (27.6)	808 (69.1)	16 (41.0)	1441 (76.8)	50 (66.7)	181 (67.5)
<i>Yes</i>	874 (21.1)	29 (20.3)	54 (20.2)	302 (27.6)	9 (31.0)	308 (26.3)	6 (15.4)	264 (14.1)	14 (18.7)	54 (20.2)
<i>Missing</i>	260 (6.3)	40 (28.0)	33 (12.3)	34 (3.1)	12 (41.4)	54 (4.6)	17 (43.6)	172 (9.2)	11 (14.7)	33 (12.3)
Parental history of asthma										
<i>No</i>	3235 (78.2)	87 (60.8)	159 (59.3)	852 (78.0)	10 (34.5)	912 (78.0)	19 (48.7)	1471 (78.4)	58 (77.3)	159 (59.3)
<i>Yes</i>	687 (16.6)	14 (9.8)	53 (19.8)	175 (16.0)	2 (6.9)	172 (14.7)	1 (2.6)	340 (18.1)	11 (14.7)	53 (19.8)
<i>Missing</i>	218 (5.3)	42 (29.4)	56 (20.9)	66 (6.0)	17 (58.6)	86 (7.3)	19 (48.7)	66 (3.5)	6 (8.0)	56 (20.9)
Spanish questionnaire										
<i>No</i>	3486 (84.2)	107 (74.8)	197 (73.5)	1014 (92.8)	19 (65.5)	1012 (86.5)	29 (74.4)	1460 (77.8)	59 (78.7)	197 (73.5)
<i>Yes</i>	654 (15.8)	36 (25.2)	71 (26.5)	79 (7.2)	10 (34.5)	158 (13.5)	10 (25.6)	417 (22.2)	16 (21.3)	71 (26.5)

eTable 2. P Values for Evidence of Effect Modification of the Asthma Incidence and Air Pollution Association Based on Partial Likelihood Ratio Tests for Interaction Terms With Pollutant and Potential Effect Modifier in the Children's Health Study, 1993-2014

Potential Effect Modifier	Pollutant	
	NO ₂	PM _{2.5}
Sex	0.53	0.20
Ethnicity	0.41	0.82
Race	0.46	0.22
In utero exposure to smoking	0.13	0.74
Secondhand smoke exposure	0.62	0.13
Parental education	0.60	0.87
Parental history of asthma	0.86	0.78
Native American ancestry (above/below 50%)	0.53	0.65
High/low 1993 air pollution level	0.80	0.07

eTable 3. Results of Sensitivity Analyses for Incidence Rate Ratios (IRR) Associated With Reduction in Nitrogen Dioxide (NO₂) and Particulate Matter <2.5 μm (PM_{2.5}) in the Children's Health Study, 1993-2014. Main analysis based on 4140 children, including 525 incident asthma cases

Sensitivity Analysis	N	N cases	NO ₂		PM _{2.5}	
			IRR (95% CI)	P value	IRR (95% CI)	P value
Excluded one town						
<i>Alpine</i>	3665	471	0.80 (0.71, 0.90)	<0.001	0.80 (0.65, 0.99)	0.04
<i>Lake Elsinore</i>	3724	468	0.77 (0.68, 0.87)	<0.001	0.73 (0.59, 0.90)	0.004
<i>Lake Gregory</i>	3651	466	0.80 (0.71, 0.91)	<0.001	0.84 (0.69, 1.02)	0.07
<i>Long Beach</i>	3731	466	0.86 (0.75, 0.98)	0.03	0.87 (0.71, 1.06)	0.16
<i>Mira Loma</i>	3645	477	0.80 (0.71, 0.90)	<0.001	0.80 (0.65, 1.00)	0.05
<i>Riverside</i>	3679	464	0.80 (0.70, 0.90)	<0.001	0.71 (0.56, 0.89)	0.003
<i>San Dimas</i>	3715	467	0.77 (0.67, 0.89)	<0.001	0.84 (0.67, 1.04)	0.12
<i>Santa Maria</i>	3650	471	0.81 (0.72, 0.91)	<0.001	0.82 (0.67, 0.99)	0.04
<i>Upland</i>	3660	450	0.80 (0.70, 0.91)	0.001	0.84 (0.67, 1.05)	0.13
Excluded participants reporting wheeze in prior 12 months at baseline	3835	439	0.82 (0.72, 0.93)	0.002	0.80 (0.65, 0.98)	0.03
Excluded participants reporting 3+ months of cough in prior 12 months at baseline	3987	481	0.78 (0.69, 0.88)	<0.001	0.80 (0.63, 1.00)	0.05
Excluded participants reporting either wheeze or 3+ months of cough in prior 12 months at baseline	3723	411	0.81 (0.71, 0.92)	0.002	0.79 (0.62, 0.99)	0.04
Excluded first year of follow-up	3712	444	0.77 (0.68, 0.88)	<0.001	0.81 (0.65, 1.01)	0.07
Excluded cohort E participants where year 3 survey used as baseline	3942	501	0.81 (0.72, 0.92)	<0.001	0.83 (0.67, 1.01)	0.07
Re-included participants with missing baseline asthma status	4283	574	0.85 (0.76, 0.95)	0.004	0.88 (0.73, 1.05)	0.15
Imputed asthma diagnosis date to 6 months after prior questionnaire	4140	525	0.80 (0.71, 0.90)	<0.001	0.82 (0.67, 0.99)	0.04
Restricted to longer follow-up						
<i>Followed until event or year 7 or later</i>	2864	525	0.82 (0.72, 0.92)	<0.001	0.81 (0.66, 0.98)	0.03
<i>Followed until event or year 5 or later</i>	3439	525	0.80 (0.71, 0.90)	<0.001	0.80 (0.66, 0.98)	0.03
Adjusted for:						
<i>Income, education, and insurance</i>	4140	525	0.79 (0.70, 0.89)	<0.001	0.80 (0.65, 0.98)	0.03
<i>Exposure to smoking in utero, and secondhand smoke exposure</i>	4140	525	0.80 (0.71, 0.90)	<0.001	0.81 (0.66, 0.98)	0.03
<i>Pests in home, pets in home, and carpet in child's bedroom</i>	4140	525	0.81 (0.71, 0.91)	<0.001	0.82 (0.68, 1.00)	0.05
<i>Ozone</i>	4140	525	0.80 (0.70, 0.92)	0.001	-	
<i>PM₁₀</i>	4140	525	0.79 (0.69, 0.90)	<0.001	0.81 (0.64, 1.01)	0.07
Omitted random effect for cohort nested within community	4140	525	0.80 (0.71, 0.90)	<0.001	0.81 (0.67, 0.98)	0.03
Bootstrap at community level instead of random effect	4140	525	0.80 (0.71, 0.90)	<0.001	0.81 (0.66, 0.98)	0.03
Included a fixed effect for cohort	4140	525	0.82 (0.69, 0.97)	0.02	1.39 (0.95, 2.02)	0.09
Incidence rate ratios (IRR) are per median changes in air pollution concentrations observed among the nine communities between 1993 and 2006 (-4.3 ppb for NO ₂ and -8.1 μg/m ³ for PM _{2.5}).						
Models adjusted for community as a fixed effect, age at baseline, sex, ethnicity, race, gas stove in home, participation in sports, and community-level average temperature for baseline year.						
Model for PM _{2.5} adjusting for PM ₁₀ was not included because Pearson partial correlation coefficient, controlling for community, was 0.83.						

eTable 4. Results of Sensitivity Analyses Using Cox Proportional Hazards Models for Ozone (O₃), Nitrogen Dioxide (NO₂), Particulate Matter <10 μm (PM₁₀) and <2.5 μm (PM_{2.5}) in the Children's Health Study, 1993-2014

Model	O ₃		NO ₂		PM ₁₀		PM _{2.5}	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Main Cox PH model	0.85 (0.71, 1.01)	0.07	0.80 (0.71, 0.90)	<0.001	0.94 (0.83, 1.06)	0.29	0.81 (0.66, 0.98)	0.03
Main model with spline for calendar year	1.00 (0.78, 1.28)	0.99	0.82 (0.69, 0.97)	0.02	1.02 (0.89, 1.17)	0.78	1.28 (0.90, 1.83)	0.17
Main model with time-varying exposure	0.92 (0.75, 1.12)	0.41	0.87 (0.80, 0.94)	<0.001	0.97 (0.90, 1.03)	0.33	0.83 (0.70, 0.99)	0.04
Hazards rate ratios (HR) are per -8.9 ppb for O ₃ ; -4.3 ppb for NO ₂ ; -4.0 μg/m ³ for PM ₁₀ ; and -8.1 μg/m ³ for PM _{2.5} (median changes in air pollution concentrations observed among the nine communities between 1993 and 2006).								
Models adjusted for community as a fixed effect, age at baseline, sex, ethnicity, race, gas stove in home, participation in sports, and community-level average temperature for baseline year. Random effect for cohort nested within community not included.								
Time-varying exposure were 1-year lagged annual mean air pollutant concentration								

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