Ambient Metals, Elemental Carbon, and Wheeze and Cough in New York City Children through 24 Months of Age

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Rationale: **The effects of exposure to specific components of ambient fine particulate matter ($PM_{2.5}$), including metals and elemental carbon (EC), have not been fully characterized in young children.**

Objectives: **To compare temporal associations among $PM_{2.5}$; individual metal constituents of ambient $PM_{2.5}$, including nickel (Ni), vanadium (V), and zinc (Zn); and EC and longitudinal reports of respiratory symptoms through 24 months of age.**

Methods: **Study participants were selected from the Columbia Center for Children's Environmental Health birth cohort recruited in New York City between 1998 and 2006. Respiratory symptom data were collected by questionnaire every 3 months through 24 months of age. Ambient pollutant data were obtained from state-operated stationary monitoring sites located within the study area. For each subject, 3-month average inverse-distance weighted concentrations of Ni, V, Zn, EC, and $PM_{2.5}$ were calculated for each symptom-reporting period based on the questionnaire date and the preceding 3 months. Associations between pollutants and symptoms were characterized using generalized additive mixed effects models, adjusting for sex, ethnicity, environmental tobacco smoke exposure, and calendar time.**

Measurements and Main Results: **Increases in ambient Ni and V concentrations were associated significantly with increased probability of wheeze. Increases in EC were associated significantly with cough during the cold/flu season. Total $PM_{2.5}$ was not associated with wheeze or cough.**

Conclusions: **These results suggest that exposure to ambient metals and EC from heating oil and/or traffic at levels characteristic of urban environments may be associated with respiratory symptoms among very young children.**

Keywords: traffic; heating oil combustion; metals; asthma

Epidemiologic evidence links increases in ambient levels of fine particulate matter ($PM_{2.5}$) to asthma exacerbations, lung function decrements, and greater use of medical services for asthma (1–3). Because of geographic and seasonal differences in $PM_{2.5}$ composition and $PM_{2.5}$–associated health effects (4–7), current mass-based standards for ambient $PM_{2.5}$ may not adequately target specific components that are causally associated with adverse health effects. Diesel exhaust particles are a significant driver of local urban $PM_{2.5}$ levels and are a dominant source of atmospheric elemental carbon (EC) (8). Traffic is an important source of ambient metals from tailpipe emissions, brake and tire abrasion, and resuspended roadway dust (9, 10). In New York City (NYC), residual oil combustion for heating contributes to ambient nickel (Ni) and vanadium (V) concentrations that exceed levels in most other cities in the United States (6, 11). Given the large contributions of traffic and heating oil combustion to urban ambient $PM_{2.5}$ levels, there is a need to characterize the contributions of specific components, such as metals and EC, to adverse health effects.

Studies have demonstrated that communities with higher EC concentrations have higher a prevalence of asthma and chronic respiratory symptoms (12, 13). More recently, proximity to major roadways has been associated with chronic respiratory symptoms, asthma, and allergic sensitization (14, 15). One key longitudinal study in Southern California observed that long-term exposure to EC, $PM_{2.5}$, nitrogen dioxide, and acid vapors, derived primarily from motor vehicle emissions, were associated with deficits in lung function growth between 10 and 18 years of age (16).

Relatively fewer studies have examined respiratory health effects associated with ambient metals exposures. In a national-

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Associations between ambient fine particulate matter ($PM_{2.5}$) and asthma development and acute asthma exacerbations are well documented. However, health effects of exposure to specific airborne components from traffic and heating oil combustion, including metals and elemental carbon, have not been fully characterized.

What This Study Adds to the Field

We present evidence that implicates exposures to ambient nickel, vanadium, and elemental carbon as possible risk factors for respiratory symptoms in a young inner-city cohort. The report provides evidence that exposures to $PM_{2.5}$–associated metals and elemental carbon from sources such as heating oil combustion and traffic may be important health-relevant $PM_{2.5}$ fractions associated with asthma morbidity in urban children as young as 2 years of age.

(*Received in original form January 22, 2009; accepted in final form September 9, 2009*)

Supported by the National Institute of Environmental Health Sciences (grants R01 ES013163, P50ES015905, P01 ES009600, P30 ES 009089, and R01 ES008977), US Environmental Protection Agency (grants R827027, RD-832141), Irving General Clinical Research Center (grant RR00645), Educational Foundation of America, Gladys & Roland Harriman Foundation, The New York Community Trust, and Trustees of the Blanchette Hooker Rockefeller Fund.

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

Am J Respir Crit Care Med Vol 180. pp 1107–1113, 2009
Originally Published in Press as DOI: 10.1164/rccm.200901-0122OC on September 10, 2009
Internet address: www.atsjournals.org

scale study, $PM_{2.5}$–associated risks of respiratory and cardiovascular hospital admissions were higher in communities with higher levels of $PM_{2.5}$–related Ni, V, and EC (5). Recently, increases in ambient zinc (Zn) were associated with increases in asthma emergency department visits and hospital admissions among children living in Baltimore, Maryland (17). Mechanistic support is provided by observations of greater release of proinflammatory cytokines from airway cells in response to metals exposure (18, 19). Studies are needed that elucidate the potential health effects of ambient metal exposures in young children living in urban communities with high asthma morbidity (20) and that examine the differential health effects associated with exposures to ambient metals, EC, and $PM_{2.5}$.

We hypothesized that exposure to ambient metals and EC would be associated with wheeze and cough among young urban children. In a longitudinal design, associations between local measurements of ambient metals, EC, and $PM_{2.5}$ and concurrent respiratory symptoms among children through 24 months of age were characterized. The findings provide evidence of a link between the disproportionately high burden of ambient metals and diesel emission sources and disproportionately high asthma morbidity among young residents of NYC and possibly other cities. Some results have previously been reported in the form of abstracts (21, 22).

METHODS

Study Cohort Data

Detailed methods are provided in the online supplement. Children living in Northern Manhattan and the South Bronx were enrolled between 1998 and 2006 into a prospective birth cohort study conducted by the Columbia Center for Children's Environmental Health (23–25). Briefly, 725 fully enrolled pregnant women, recruited from prenatal clinics associated with New York Presbyterian Medical Center or Harlem Hospital, were followed throughout pregnancy and provided maternal and/or cord blood at delivery. Informed consent was obtained in accordance with the Columbia University Institutional Review Board. Data on subject characteristics, residence, environmental tobacco smoke (ETS) exposure, and respiratory symptoms were collected by questionnaires administered to mothers in person or by telephone every 3 months when their children were between 3 and 24 months of age.

Stationary Site Monitoring

Twenty-four–hour average ambient concentrations of $PM_{2.5}$ and $PM_{2.5}$ fractions of Ni, V, Zn, and EC were measured every third day by the New York State Department of Environmental Conservation between 1999 and 2007. Datasets were downloaded (http://www.dec.ny.gov/) for two sites in the Bronx that were located in the study area: New York Botanical Gardens (NYBG) and Intermediate School 52 (IS52). Data were aggregated by week and site as described (26).

Statistical Analysis

Associations between metals, EC, and $PM_{2.5}$ and the presence of wheeze and cough were analyzed using generalized additive mixed effects models using the mgcv library in R version 2.9.0 (R Foundation for Statistical Computing, Vienna, Austria). Nitrogen dioxide (NO_2) was evaluated as a gaseous indicator of traffic emissions. Single pollutant models were constructed in which each pollutant was analyzed as a parametric continuous variable. For each subject, 3-month moving average concentrations of Ni, V, Zn, EC, and $PM_{2.5}$ were calculated for each symptom-reporting period based on the follow-up questionnaire date and the preceding 3 months. Exposures were assigned to subjects by calculating inverse-distance weighted concentrations using pollutant measurements from IS52 and NYBG. Address data were collected only at prenatal, 6-, 12-, and 24-month questionnaires, and addresses at interim time points were assigned using data on moves since last questionnaire and previous addresses. A first-order autoregressive correlation structure was specified to account for correlation among the repeated observations collected over a 2-year period from each subject. Other covariates included parametric terms for sex, ethnicity, postnatal ETS exposure, and a nonparametric smoothed term for calendar time using natural cubic splines (4.7 degrees of freedom per calendar year).

The robustness of results was evaluated using the following methods: models that included gaseous and particulate copollutants related to traffic, models that excluded the highest 5% of pollutant concentrations, and analyses stratified by season. For stratified analyses, season was defined as a dichotomous variable: "cold/flu season" (September 1–March 31) or "noncold/flu season" (April 1–August 31).

In descriptive summaries of symptom prevalence and pollutant levels, season was defined by calendar year as follows: winter = December 21 to March 20, spring = March 21 to June 20, summer = June 21 to September 20, and fall = September 21 to December 20. Except for generalized additive mixed effects models, statistical tests and modeling were performed using SAS 9.1.3 (Cary, NC, release 2005), and results with $P < 0.05$ were considered statistically significant.

RESULTS

Cohort Characteristics

Among 687 subjects who reached their second birthday by October 31, 2007, 653 (90% of the fully enrolled) provided follow-up data and were included in this study. Seventy-five percent of participants completed at least five of the eight follow-up questionnaires, and 20% completed all eight questionnaires. Thirty-four subjects (5%) were lost to follow-up between 3 and 24 months of age. Characteristics of the study population are shown in Table 1. Approximately 64% of mothers identified themselves as Dominican, and 36% identified themselves as African American. A majority of mothers had at least a 12-grade education, and greater than 90% reported receiving Medicaid at enrollment. At 24 months of age, 30% of children were told by a doctor that they have or may have asthma. There were no significant differences in any of the displayed demographics between the full cohort at 24 months of age and the subgroup that had completed one or more follow-up questionnaires.

TABLE 1. SELECTED COHORT CHARACTERISTICS

	Cohort at 24 Mo of Age, % (*n = 687*)	Children with Follow-up Data, % (*n = 653*)
Child's sex		
Male	48	49
Female	52	51
Mother's ethnicity		
Dominican	65	64
African American	35	36
Mother with at least 12th grade education	64	64
Maternal history of smoking		
Child age 6 mo	13	13
Child age 12 mo	12	12
Child age 24 mo	11	11
Any time, child age 0–24 mo	11	12
Smoker in household		
Child age 6 mo	25	25
Child age 12 mo	23	23
Child age 24 mo	19	19
Any time, child age 0–24 mo	25	27
Maternal history of asthma	23	22
Mother receiving Medicaid at enrollment	91	90
Child with asthma/possible asthma*	30	30

* Doctor says child has or might have asthma at time of 24-month questionnaire.

Spatial and Temporal Trends in Ambient Metals, EC, and $PM_{2.5}$

Across all time points, 72 to 78% of subjects lived closer to IS52, and 22 to 28% of subjects lived closer to NYBG. The range of mean distance was 3.9 to 4.2 km for IS52 and 5.8 to 5.9 km for NYBG. Between 2000 and 2007, mean concentrations of Ni, EC, and NO_2 varied significantly between IS52 and NYBG (*see* Tables E1–E4 in the online supplement). Mean concentrations of pollutants also varied significantly by season (Table E5). Concentrations of metals in fall and winter often were double the levels in spring and summer, whereas EC concentrations were higher in winter and fall by approximately 27%. $PM_{2.5}$ concentrations were significantly higher in winter and summer by 24%. NO_2 concentrations were significantly higher in winter and spring but by less than 10%.

Prevalence of Wheeze and Cough

Forty-seven percent of subjects reported wheeze during at least one follow-up period through 24 months of age, whereas 89% reported cough. The overall prevalence of wheeze and cough did not change over the study period between 1998 and 2007 but did display consistent seasonal patterns, with maxima in winter and fall months and minima in spring and summer months (Figure 1). The proportions of subjects reporting wheeze in the fall and winter were similar and averaged approximately 20 and 19%, respectively. The proportions of subjects reporting wheeze in the spring and summer were similar and averaged approximately 14% each. The proportion of subjects reporting cough was highest in the fall at 56.2%. The proportions of subjects reporting cough in the winter, summer, and spring and summer were 53.3, 40.3, and 37.0%, respectively.

Association between Ambient Metals, EC, $PM_{2.5}$, and Wheeze and Cough

Significant positive associations were observed between metals and wheeze but not cough. Among all pollutants evaluated, the largest effect estimates were observed in association with Ni exposure. In models that adjusted for sex, ethnicity, postnatal ETS exposure, and calendar time, an increase in interquartile range (IQR) concentration of ambient Ni (0.014 $\mu g/m^3$) was associated significantly with a 28% increased probability of wheeze (P = 0.0006) (Table 2). These findings were robust to the inclusion of the copollutants EC, NO_2, copper (Cu), and iron (Fe), with an 11% decrease in the magnitude of effect.

Vanadium and wheeze were not significantly associated in the single-pollutant model (Table 2). An IQR (0.003 $\mu g/m^3$) increase in 3-month average concentrations of V was associated with a 10% increased probability of wheeze (P = 0.13). However, after adjusting for EC, NO_2, Cu, and Fe, there was suggestion of an association between V and wheeze (β = 0.14 per IQR increase in V; P = 0.08). Zinc was not associated with wheeze in single- or multipollutant models.

EC was not significantly associated with wheeze or cough in single- or multipollutant models that included NO_2 and Ni (Table 2). Total $PM_{2.5}$ was not associated significantly with wheeze or cough in single-pollutant models. $PM_{2.5}$ was negatively associated with wheeze in a multipollutant model that included NO_2 and Ni ($\beta = -0.13$ per IQR increase in $PM_{2.5}$; P = 0.03). Adjustment for Ni but not NO_2 resulted in the change of the $PM_{2.5}$ effect estimate from positive and nonsignificant to negative and significant. Ni was strongly and positively associated with wheeze and was more positively correlated with $PM_{2.5}$ in the cold/flu season (r = 0.41) than in the noncold/flu season ($r = -0.21$), which may explain the apparent protective effects of $PM_{2.5}$ on wheeze. An IQR (0.004 ppm) increase in NO_2 was significantly associated with a 26% increased probability of wheeze (P = 0.002) (Table 2). However, in the multipollutant model that included EC and Ni, the effect estimate decreased to 0.13 per IQR increase in NO_2, and the association became nonsignificant (P = 0.27). The association between NO_2 and cough was not significant in the single-pollutant model, but there was suggestion of an association in a model that adjusted for EC and Ni (β = 0.14 per IQR increase in NO_2; P = 0.08).

Effects of the Cold/Flu Season

To examine differences in effects by season, multipollutant analyses were performed after stratifying by cold/flu season. Despite the 50% smaller sample sizes in these models, significant relationships were observed between several pollutants and symptoms, mostly during the cold/flu season (Table 3). For example, Ni and V remained significantly associated with wheeze in the model that included only observations during the cold/flu season, and the effect estimates were larger than those estimated in the all-season models. EC was significantly associated with cough in analyses restricted to observations during the cold/flu

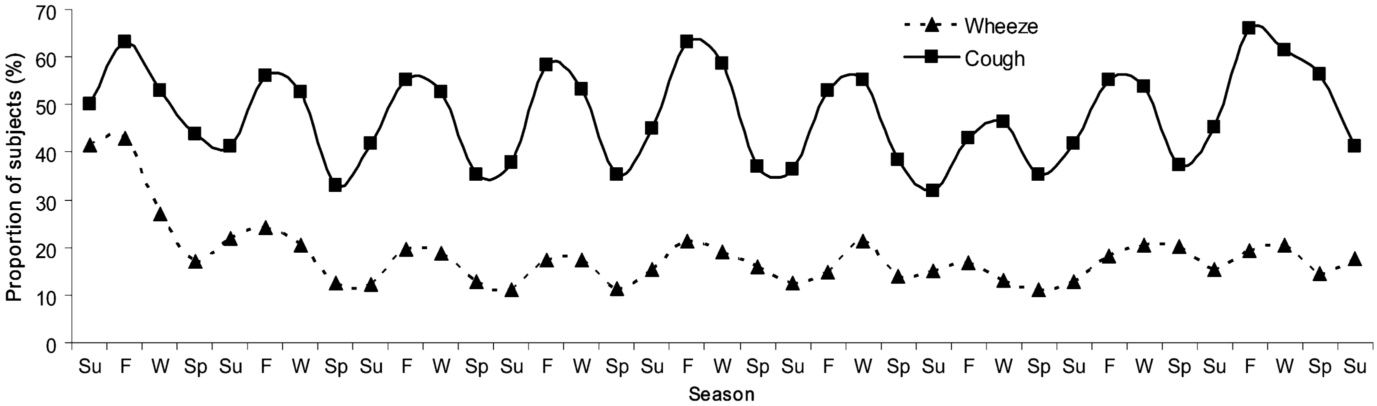

Figure 1. Seasonal trends in wheeze and cough. Prevalence calculated as the proportion of subjects reporting the presence of wheeze or cough each season. Wheeze prevalence was higher in the fall (September 21–December 20) and winter (December 21–March 20) ($P < 0.0001$) compared with spring (March 21–June 20). Similar proportions of subjects reported wheeze in the spring and summer (June 21–September 20). The prevalence of cough was higher in fall, winter, and summer ($P < 0.0001$ for all three seasons) compared with spring. F = fall; Sp = spring; Su = summer; W = winter.

TABLE 2. EFFECT ESTIMATES OF THE PRESENCE OF WHEEZE OR COUGH ASSOCIATED WITH THE 3-MONTH AVERAGE AMBIENT POLLUTANT CONCENTRATIONS

		Single Pollutant Model		Multipollutant Model	
Pollutant (IQR)	Symptom	β-coefficient*	*P* Value	β-coefficient	*P* Value
Ni[†] (0.014 μg/m^3)	n[‡]	636 (3,085)		636 (3,075)	
	Wheeze	0.28[§]	0.0006	0.25[§]	0.0006
	Cough	−0.05	0.51	−0.14	0.10
V[†] (0.003 μg/m^3)	n	636 (3,085)		636 (3,075)	
	Wheeze	0.10	0.13	0.14	0.08
	Cough	0.04	0.49	−0.04	0.59
Zn[†] (0.018 μg/m^3)	n	636 (3,085)		636 (3,075)	
	Wheeze	0.04	0.66	0.01	0.94
	Cough	0.03	0.75	−0.17	0.15
EC[¶] (0.29 μg/m^3)	n	636 (3,075)		636 (3,075)	
	Wheeze	0.04	0.43	0.02	0.66
	Cough	0.04	0.34	0.05	0.25
$PM_{2.5}$[¶] (2.1 μg/m^3)	n	638 (3,131)		636 (3,075)	
	Wheeze	−0.0009	0.89	−0.13[§]	0.03
	Cough	−0.03	0.62	−0.06	0.36
NO_2[‖] (0.004 ppm)	n	650 (3,553)		636 (3,075)	
	Wheeze	0.26[§]	0.002	0.13	0.27
	Cough	0.05	0.44	0.14	0.08

Definition of abbreviations: EC = elemental carbon; IQR = interquartile range.

* Beta coefficient estimates change in probability of outcome per IQR increase in pollutant concentration adjusted for sex, ethnicity, smoking by mother or other smoker in the home, or calendar week (df = 4.72).

[†] Copollutants include EC, NO_2, copper, and iron.

[‡] Total number of subjects included in model (number of subjects × number of observations per subject).

[§] Statistically significant ($P < 0.05$).

[¶] Copollutants include NO_2 and Ni.

[‖] Copollutants include EC and Ni.

season, and the association between NO_2 and cough was borderline significant ($P = 0.05$). In analyses restricted to the noncold/flu season (April 1 to August 31), NO_2 was significantly associated with wheeze (Table 3). Significant negative associations were observed during the cold/flu season between Zn and cough and $PM_{2.5}$ and wheeze in multipollutant models. For $PM_{2.5}$ and wheeze, adjustment for Ni resulted in a negative effect estimate for $PM_{2.5}$. For Zn and cough, adjustment for Fe produced a negative effect estimate for Zn. Fe was significantly associated with cough in the multipollutant model and was more highly

TABLE 3. EFFECTS ESTIMATES OF PRESENCE OF WHEEZE OR COUGH ASSOCIATED WITH 3-MONTH AVERAGE AMBIENT POLLUTANT CONCENTRATIONS STRATIFIED BY SEASON

		Cold/Flu Season* (*n = 580; N =1,661*)[†]		Noncold/Flu Season[‡] (*n = 606; N = 1,414*)	
Pollutant	Symptom	β-coefficient[§]	*P* Value	β-coefficient	*P* Value
Ni	IQR	0.012 μg/m^3		0.009 μg/m^3	
	Wheeze	0.31[¶]	0.003	0.46	0.07
	Cough	−0.14 (0.10)		−0.20	0.30
V	IQR	0.0033 μg/m^3		0.0029 μg/m^3	
	Wheeze	0.31[¶]	0.0003	0.17	0.39
	Cough	−0.15	0.13	0.12	0.46
Zn	IQR	0.011 μg/m^3		0.007 μg/m^3	
	Wheeze	−0.13	0.46	0.34	0.25
	Cough	−0.31[¶]	0.04	0.20	0.44
EC	IQR	0.319 μg/m^3		0.232 μg/m^3	
	Wheeze	0.07	0.32	−0.02	0.80
	Cough	0.11[¶]	0.04	−0.001	0.99
$PM_{2.5}$	IQR	2.1 μg/m^3		1.9 μg/m^3	
	Wheeze	−0.30[¶]	0.008	0.02	0.85
	Cough	−0.06	0.36	−0.13	0.18
	IQR	0.0040 ppm		0.0038 ppm	
NO_2	Wheeze	−0.08	0.47	0.38[¶]	0.02
	Cough	0.22[¶]	0.05	0.12	0.33

Definition of abbreviations: EC = elemental carbon; IQR = interquartile range.

* Number of observations per subject. Includes observations between September 1 and March 31.

[†] n = total number of subjects included in model. N = number of subjects × number of observations per subject.

[‡] Includes observations between April 1 and August 31.

[§] Beta coefficient estimates change in probability of outcome per increase in IQR of pollutant concentration adjusted for sex, ethnicity, smoking by mother or other smoker in the home, calendar week, and copollutants as described in Table 2.

[¶] Statistically significant ($P < 0.05$).

correlated with Zn during the cold/flu season ($r = 0.52$) than during the noncold/flu season ($r = 0.29$), which may provide explanation for the apparent protective effect of Zn on cough in the cold/flu season.

Sensitivity and Exploratory Analyses

To examine whether the observed findings were driven by extreme pollutant measurements, relationships with symptoms were examined after excluding the highest 5% pollutant concentrations. Extreme measurements were clustered by season and year. Timing of peak measurements also varied among pollutants. For example, peak concentrations of Ni and V were measured between December 2000 and February 2001. High concentrations of EC and Zn were measured between January and February 2006. Peak NO_2 concentrations were predominantly clustered between February and May 2000. After excluding peak Ni measurements, associations with wheeze remained significant in single and multipollutant models (Table E6). After excluding extreme V concentrations, associations with wheeze were no longer significant in the multipollutant model. There was a suggestion of negative association between Zn and cough, and the association between $PM_{2.5}$ and wheeze was significantly negative only in multipollutant models. Similar to the full model, NO_2 was significantly associated with wheeze after excluding the highest 5% concentrations; however, the association was not robust to the inclusion of the copollutants Ni and EC.

Exploratory cross-sectional analyses were conducted to examine the effects of prenatal pollutant exposures, implicated in asthma pathogenesis (24, 27), on wheeze and cough at later ages (data not shown). Ambient metals, EC, and $PM_{2.5}$ concentrations from the 3 months before birth were not associated with symptoms at 9 months of age, and exposures between 3 and 6 months before birth were not associated with symptoms at 12 months of age. Models that included prenatal ETS as a covariate did not produce results that differed from models that included postnatal ETS as a covariate (Table E7).

DISCUSSION

Our objective was to characterize the differential relationships between exposure to ambient $PM_{2.5}$ and its specific components, including metals and EC, and respiratory symptoms in a cohort of very young children living in high-density NYC neighborhoods. We found that Ni and V were associated significantly with wheeze in this cohort during the first 24 months of life after adjusting for sex, ethnicity, ETS, seasonal trends, and copollutants. EC was associated significantly with cough only during the cold/flu season. This study provides new evidence using an individual-level longitudinal study design that specific components of $PM_{2.5}$ related to residual oil combustion and/or traffic are associated with adverse respiratory health effects in children during the first 2 years of life. $PM_{2.5}$, a heterogeneous mix of particles of various chemical constituents from multiple sources, was not associated significantly with wheeze or cough. This latter result suggests that mass-based standards for total $PM_{2.5}$ may not adequately protect against adverse health effects from exposures to the individual toxic metals and EC components, which are believed to represent approximately only 4 and 3% of the mass, respectively (28).

Children participating in this study reside in NYC communities that have very high pediatric asthma prevalence and hospitalization rates (20) and that contain major trucking thoroughfares, bus depots, and waste transfer stations that emit multiple air pollutants (29). Traffic emissions, particularly from diesel vehicles, are a dominant source of EC in the atmosphere. Traffic also contributes to ambient metals from direct tailpipe emissions, brake and tire abrasion, and resuspension of roadway dust (9, 10). Residual oil fuel, which is the major source of ambient Ni and V in NYC, continues to be used for space heating in older residential and commercial buildings that are common in the study area (11). Concentrations of EC, Ni, V, and Zn are higher at the Bronx monitoring sites in our study area, compared with an average of 87 counties in the United States (7), and Ni concentrations at the Bronx sites are higher than those at other NYC monitoring sites (11). These results suggest that metals and EC from heating oil combustion and diesel traffic may be important ambient pollutants that contribute to asthma-related symptoms in these communities.

The largest effect size and most consistent associations were observed between Ni and wheeze. The effects of Ni on wheeze were robust to the inclusion of indicators of traffic emissions such as EC and NO_2. Although NO_2 was significantly associated with wheeze in a single-pollutant model, associations became nonsignificant when Ni and EC were included in the model. Therefore, residual oil combustion, an important nontraffic source of ambient Ni in the study area, could be responsible for many asthma-related symptoms among young residents of these communities. Recent studies support a role for Ni in increasing risk of asthma-related outcomes. In a national-scale study, county- and season-specific $PM_{2.5}$ risk estimates for respiratory and cardiovascular admissions were higher in counties and seasons with a $PM_{2.5}$–Ni fraction in the 75th compared with the 25th percentile (5). Additionally, in reanalyses of the National Mortality and Morbidity Air Pollution Study data, PM_{10} mortality risk estimates were higher for communities with higher long-term averages of ambient Ni and V (4, 6), and this effect modification was driven by strong associations observed in NYC (4). Although these previous studies included adult populations, their findings support the premise that Ni and V may be important airborne pollutants that contribute to adverse respiratory health effects in NYC.

In analyses stratified by the cold/flu season, larger effect estimates for Ni and V on wheeze and significant effects of EC on cough were observed in models containing observations from only the cold/flu season (September 1 to March 31) (Table 3). Concentrations of metals and EC are higher in the winter due to emissions from heating sources such as roof-top furnaces and due to lower mixing height in the atmosphere, resulting in diminished dispersion of emitted pollutants (7, 11). Respiratory symptoms and asthma exacerbations show peaks in the fall and winter and are related to viral infections (30). In models that excluded the highest 5% of pollutant concentrations, V and EC were no longer associated with wheeze and cough, respectively, suggesting that extreme concentrations occurring primarily during winter may be highly influential in terms of their effects on respiratory symptoms. Nickel remained significantly associated with wheeze after removing the highest 5% measurements. In a study of human airway cells, coexposure to human rhinovirus and nitrogen dioxide (NO_2) or ozone stimulated greater production of the proinflammatory cytokine IL-8 than did exposure to rhinovirus or either pollutant alone (31). Therefore, significant associations between Ni and V and wheeze and EC and cough during the cold/flu season may occur as a consequence of synergistic effects on airway inflammation induced by exposures to viral infections and airborne Ni. NO_2 was significantly associated with wheeze during the noncold/flu season after adjusting for Ni and EC. NO_2 concentrations did not display strong seasonal variation (Table E5). Hence, the effects of NO_2 on wheeze may have been masked by the larger effects of Ni and/or viral infections exposures during the cold/flu season and became apparent in the absence of exposures to high Ni concentrations and/or viral infections during the noncold/flu season. Unexpected significant negative associations were observed between $PM_{2.5}$ and wheeze and between Zn and cough that were driven by effects in the cold/flu season. Because these apparent protective effects were observed only in multipollutant models, they are likely explained by the inclusion of copollutants, such as Ni and Fe, that were found to have strong positive effects on symptoms and by higher correlations between pollutants observed in the cold/flu season.

Ambient levels of Ni, V, or EC may serve as surrogates of pollutant mixtures or other individual components from residual oil combustion and/or traffic that are causally associated with respiratory symptoms. Many $PM_{2.5}$ species evaluated in our models displayed high correlation between sites (Tables E1 and E4) and were highly correlated with other trace elements within sites (Tables E2 and E3), making it difficult to distinguish among the effects of pollutants from common sources. For example, due to the high correlation among Ni and V, we did not include them in the same model to evaluate as potential confounders. Copper (Cu) and iron (Fe) were moderately correlated with Ni, V, and Zn and have been associated with increased mortality (32, 33) and stimulation of airway inflammation (34) in the literature. In the current study, however, neither Cu nor Fe was associated with wheeze or cough in single-pollutant models (data not shown), and neither altered the observed associations between Ni or V and wheeze. EC and NO_2, both indicators of traffic tailpipe emissions, were moderately correlated at NYBG but not significantly correlated at IS52. EC was significantly associated with cough during the cold/flu season after adjusting for NO_2 and Ni, and NO_2 was significantly associated with wheeze during the noncold/flu season after adjusting for Ni and EC. Thus, although traffic emissions appear to contribute to respiratory morbidity, it is difficult to distinguish between the effects of particulate and gaseous pollutants.

We acknowledge several limitations to this study. The study population was comprised of only Dominican and African American children living in Northern Manhattan and the South Bronx, and populations that differ in ethnic composition may differ with respect to the relative strength of association between particular outcomes and exposures. Furthermore, this cohort may differ from the overall population in several other factors, including asthma prevalence, the distribution of traffic- and oil combustion-related pollutants, genetic polymorphisms, and cultural differences that may influence symptom reporting and behaviors relevant to the dose of environmental exposures.

To characterize associations between EC, metals, and $PM_{2.5}$ and respiratory symptoms, exposures were assigned using data from two monitoring sites located in the study area: IS52 and NYBG. Previously, personal exposures of NYC adolescents to $PM_{2.5}$–associated Ni, Zn, and BC were observed to display the greatest spatial variability, whereas exposures to V showed the least spatial variability (35). In the current study, significant differences were observed in mean concentrations of Ni and EC between sites, and EC was weakly correlated between sites. Small-scale differences in EC, occurring mostly in the winter and spring periods, have been attributed to local stack emissions of EC that cause random spikes in ambient concentrations (Dr. Oliver Rattigan, NYSDEC, personal communication). Using data from existing monitoring stations to represent individual exposures to pollutants with high spatial variability may not represent true exposure as accurately as personal or residential measurements. To incorporate spatial heterogeneity in ambient concentrations of $PM_{2.5}$ components, exposure estimates were assigned to subjects using inverse-distance weighted pollution measurements from the two stationary monitoring sites. In these longitudinal analyses, relationships between pollutants and symptoms were examined within subjects over time, and previous studies have shown that central site measurements of $PM_{2.5}$, EC, and metals are correlated temporally with personal exposures within subjects. Thus, in the current analyses, central site measurements may provide reasonable estimates of exposure (36). Given the significant spatial differences observed in ambient Ni and EC concentrations, exposure misclassification may be higher for these pollutants. However, such measurement error is likely to be random and would tend to underestimate the effects of Ni and EC on respiratory symptoms.

Symptom data covered a 3-month period and were compared with concurrent 3-month averages of metals, EC, and $PM_{2.5}$. Much of the previous evidence regarding the effects of particulate matter or its components pertains to acute (daily) exposures to metals or EC in time-series analyses or to long-term exposures (yearly or multiyear) in cohort studies. For example, deficits in lung function growth have been observed in children in association with community-level pollution exposures between 10 and 18 years of age (16). In a recent population-level time series study of children 0 to 17 years of age living in Baltimore, Maryland, high ambient Zn levels, measured at a central monitoring site, were associated with increases in asthma emergency department visits and hospitalizations on the following day (17). From its onset, the Columbia Center for Children's Environmental Health chose the 3-month time interval as the shortest duration in which structured, high-quality questionnaires could be administered to hundreds of women as part of the parent cohort design. The intent was to capture recent chronic (i.e., subacute) exposures and related symptoms. For the purpose of this study, our hypothesis testing was based on determining the effects of subacute environmental exposures on respiratory symptoms, in part to ascertain a signal that goes beyond those related to hourly or daily changes in activities. Given the longitudinal design of our study, collecting data about symptoms on shorter lags (e.g., the previous 7 days) may have improved our characterization of the associations between metals and EC exposures and respiratory symptoms. However, our findings provide evidence that subacute (i.e., 3 months) exposures of very young urban children may be associated with increased probability of respiratory symptoms in addition to acute and long-term exposures to metals and BC or EC that are documented in the literature.

In conclusion, the associations between increases in ambient concentrations of Ni, V, and EC (but not total $PM_{2.5}$) and increased probability of respiratory symptoms, after adjusting for copollutants, suggest that specific $PM_{2.5}$ components related to residual oil combustion and/or traffic may be health-relevant $PM_{2.5}$ fractions associated with increased respiratory morbidity in children through 24 months of age. Although it has been previously demonstrated that exposures to traffic-related air pollution early in life may be important risk factors for later development of asthma (24, 37), the current results improve our understanding of the potential deleterious consequences of exposure to specific metals for children in inner cities. Given that metal and EC components of ambient $PM_{2.5}$ are only indirectly regulated as part of the $PM_{2.5}$ mass-based standard, improved regulatory action directed at specific sources, such as traffic and residential boilers, or at ambient concentrations of individual components, such as EC and metals, may be needed to help protect young children living in urban areas.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

Acknowledgment: The authors thank Oliver Rattigan, David Wheeler, Paul Sierzenga, Dirk Felton, and Patrick Lavin from the Bureau of Air Quality Surveillance of the New York State Department of Environmental Conservation; Dr. Shuang Wang for statistical consultation; and the women and children who participated in the study.

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