Traffic-related Air Pollution and Lung Function in Children at 8 Years of Age

A Birth Cohort Study

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***Rationale*: Long-term exposure to air pollution has been related to lung function decrements in children, but the role of timing of exposure remains unknown.**

***Objectives*: To assess the role of long-term exposure to air pollution on lung function in school-age children.**

***Methods*: More than 1,900 children in the Swedish birth cohort BAMSE were followed with repeated questionnaires, dynamic spirometry, and IgE measurements until 8 years of age. Outdoor concentrations of particulate matter with an aerodynamic diameter less than 10 μm (PM_{10}) from road traffic were estimated for residential, day care, and school addresses from birth and onward using dispersion modeling. The relationship between time-weighted average exposure during different time windows and FEV at 8 years was analyzed by linear regression, adjusting for potential confounding factors, including short-term exposure to air pollution.**

***Measurements and Main Results*: A 5th to 95th percentile difference in time-weighted average particulate matter less than 10 μm in aerodynamic diameter exposure during the first year of life was associated with a reduced FEV_1 of −59.3 ml (95% confidence interval, −113 to −5.6) at 8 years of age. The negative association was particularly pronounced in children concomitantly sensitized to common inhalant or food allergens (−136.9 ml; 95% confidence interval, −224.1 to −49.7). Exposure after the first year of life seemed to have less impact on lung function at 8 years.**

***Conclusions*: Our results indicate that exposure to traffic-related air pollution during infancy affects lung function in children up to 8 years of age and particularly in those sensitized to common inhalant or food allergens.**

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Long-term exposure to ambient air pollution has been associated with reduced lung function in children. However, the role of timing of exposure remains unclear, as does possible effect modification by allergic status and other factors.

What This Study Adds to the Field

In this prospective birth cohort study, we found an association between traffic-related air pollution exposure during infancy and decreased lung function in children up to 8 years of age. Our results suggest stronger effects in children sensitized to common allergens. Early life exposure to traffic-related air pollution seems to have long-term respiratory consequences in susceptible groups, such as children with atopy.

Keywords: spirometry; forced expiratory volume; sensitization; dispersion modeling; particulate matter

A considerable body of research has shown adverse effects of long-term exposure to ambient air pollution on children's respiratory health (1–7). However, the evidence on lung function effects seems inconsistent because some of the larger studies reported no associations (8, 9). Heterogeneity in study designs, exposure assessment, and spirometric measures used across the studies may have contributed to the different results (10). Furthermore, the impact of air pollution on lung function development in the context of concomitant respiratory symptoms and sensitization has attained only limited consideration in prospective studies. The Children's Health Study from California showed associations between community-average pollutant concentrations and diminished lung function development in children aged 10–18 years (11). The observed effect remained statistically significant in the subgroup of children without asthma, but the children with asthma were too few for precise risk estimation. A birth cohort study from Oslo indicated stronger air pollution effects in children with asthma compared with those without asthma. However, because of wide confidence intervals (CIs) the findings have to be interpreted with caution (1). Studies have demonstrated associations between traffic-related air pollution and sensitization (12–16), but to our knowledge, no prospective study has evaluated effect modification by sensitization status on lung function effects related to air pollution exposure.

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Author Contributions: E.S.S. was responsible for the practical conduct of the project including planning, coordination, and analyzing of the data, which was supervised by E.M. and G.P. E.S.S. and O.G. wrote a first version of the manuscript. O.G. was responsible for the long-term exposure assessment after consultancy from T.B. M.B. contributed with statistical consultancy in general. J.H. and M.S. provided consultancy regarding lung physiology and had overall responsibility for the lung function measurements. I.K., E.M., and G.P. designed the study. I.K. and G.P. planned the initial cohort and supervised the collection of data. All authors contributed to the interpretation of the data, revised the manuscript, and approved the final manuscript.

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Early exposure to ambient air pollution seems to be important for respiratory effects in later life (6, 17–19). However, only one prospective study has investigated different aspects of timing of traffic-related air pollution exposure in relation to lung function (1). Recent data show that alveoli are formed not only during early postnatal period, but also throughout childhood and adolescence (20), which may contribute to age-related vulnerability. In addition, effects of long- and short-term air pollution exposure have generally not been considered in the same study. In the two cohort studies that included short- and long-term exposure simultaneously, only the long-term effect remained significant after adjustments (1, 11). There is a need for additional epidemiologic evidence on vulnerable time periods for air pollution exposure, particularly during childhood, and on effect modification by short-term exposure.

We have previously reported an association between exposure to traffic-related air pollution during the first year of life and lower peak expiratory flow at age 4 years in a Swedish birth cohort, BAMSE (12). In the present study from the same cohort, lung function data from extended follow-up to 8 years are analyzed together with effect modification by sex, allergic sensitization, and asthma. Furthermore, assessment of several time windows enabled evaluation of critical time periods of increased susceptibility to the adverse effects of air pollution exposure. Some of the results from this study have been previously reported in the form of an abstract (21).

METHODS

More details are provided in the online supplement.

Study Subjects and Measurements

During 1994–1996, 4,089 new-born infants were recruited to the prospective cohort study BAMSE (Children, Allergy, Milieu, Stockholm, Epidemiological Survey) from four municipalities in Stockholm County. A detailed description of the study design, enrolment criteria, and procedures for data collection is provided elsewhere (22). Briefly, data on background characteristics were requested in a questionnaire at baseline (median child age, 2 mo). Questionnaires focusing on the children's respiratory health and allergic diseases, and on various exposure factors, were completed at 1, 2, 4, and 8 years of age. The response rates were from 96% and 84%, for the 1- and 8-year questionnaires, respectively. In addition, 2,630 children (64% of the original cohort) attended a clinical examination at age 8 years including maximum expiratory flow volume tests and blood sampling. Moving out of the study area and unwillingness to participate were the main reasons for drop out from the clinical follow-up. The maximal values of FVC, FEV_1, and $FEV_{0.5}$ were used for analysis. In addition, we computed FEV below 80% and 85% of the predicted value based on the present study population and using age, sex, height, and weight as predictors. Also, standard deviation scores for FEV_1 were calculated taking age, sex, height, and ethnicity into consideration (23). The Ethics Committee of Karolinska Institute, Stockholm, Sweden, approved the study.

The methodology for calculating individual long-term exposure to local traffic-related particulate matter less than 10 μm in aerodynamic diameter (PM_{10}) and NO_x has been described in detail elsewhere (13). In short, the lifetime residential, day care, and school addresses were geocoded, and time-weighted average outdoor levels for the different time windows were calculated using emission inventories and a gaussian air dispersion model. Short-term exposure was estimated using daily air quality measurements and meteorologic data from urban background and rural monitoring stations.

Statistical Analyses

Associations between air pollution and lung function were analyzed using linear regression and results are presented as β values and 95% CIs. Air pollution concentrations were entered as continuous variables without transformation and the results are provided as change in lung function per 7 $\mu g/m^3$ increase in PM_{10} concentration (corresponding to the 5th to 95th percentile difference in time-weighted average concentration). The final models were adjusted for covariates based on study design or on earlier literature if they were shown to lead to more than 10% change in the β coefficient. Only municipality, sex, age, height, and heredity for asthma or allergy fulfilled these criteria. To account for possible influence by short-term effects of air pollution, we fitted a model that adjusted for the average ozone and PM_{10} levels, temperature, and relative humidity for lags of 1–3 and 1–7 days before each child's lung function test.

Long-term exposure time windows were defined as the first year of life, 1–4 years, and 4–8 years. We explored the inclusion of several exposure time windows simultaneously into the model, but because of substantial collinearity the main analyses shown use models unadjusted for the other time windows.

A total of 1,924 subjects (47%) were included in the analyses with information on exposure, confounders, and lung function measurements. All analyses were performed with STATA 11 software package (StataCorp LP, College Station, TX).

RESULTS

Table 1 illustrates some main characteristics of the study population. The distribution of covariates was comparable among all children in the cohort and those with lung function measurements included in the present analyses. Furthermore, estimated exposure levels were similar in children included in the study and in those of the whole cohort. A description of lung function and anthropometry data obtained at the 8-year clinical examination is given in Table 2. A total of 6.8% and 10.5% of subjects with spirometric measurements had less than 85% predicted FEV_1 and $FEV_{0.5}$ levels, respectively, and approximately half of these had less than 80% predicted levels.

Exposure to traffic-PM_{10} during the first year of life was associated with FEV deficit of 59.3 ml (−113 to −5.6) in FEV_1 and −62.4 ml (−113.7 to −11.1) in $FEV_{0.5}$ for a 5th to 95th percentile difference in time-weighted exposure. Similar effects were seen for FVC, but not statistically significant. However, no clear effects on lung function were seen in relation to air pollution exposure after infancy (Figure 1). A sensitivity analysis using FEV_1 expressed as standard deviation scores confirmed the negative effect of traffic-PM_{10} exposure on lung function ($P = 0.04$). Further analyses suggested stronger effects in boys, in those sensitized against any common inhalant or food allergens, and in those with asthma, with deficits in FEV_1 of −79.6 ml (−155.7 to −3.5), −136.9 ml (−224.1 to −49.7), and −90.6 ml (−293.4 to 112.3), respectively (Table 3). However, the apparent effect modification was not statistically significant ($P = 0.35$, 0.13, and 0.69, respectively). No association was seen between sensitization *per se* and the lung function measurements (data not shown).

We also analyzed effects at less than 80% and 85% of predicted FEV_1 and $FEV_{0.5}$ to determine whether exposure to air pollution was associated with clinically important lung function deficits. Strong associations were indicated between exposure to traffic-PM_{10} during the first year of life and FEV less than 80% and 85% of predicted. Corresponding odds ratios of 4.1 (95% CI, 0.8–20.3) and 6.1 (95% CI, 2.3–16.5) and 4.0 (95% CI, 1.2–13.1) and 2.5 (95% CI, 1.0–6.3) were seen for FEV_1 and $FEV_{0.5}$, respectively (Figure 2). First year exposure remained significant after adjusting for the other exposure time periods (data not shown).

Additional adjustment for temperature, relative humidity, ozone, and PM_{10} levels during 3–7 days before each child's pulmonary function test showed little effect on the estimates of the long-term effects of air pollution (*see* Table E1 in the online supplement).

TABLE 1. DESCRIPTIVE DATA FOR THE BAMSE COHORT AND OF THOSE WITH DATA ON LUNG FUNCTION AT 8 YEARS OF AGE

Covariates*	Full Cohort (*n = 4,089*)	Study Population at 8 Years (*n = 1,924*)†
Girls, n (%)	2,024 (49.5)	937 (48.7)
Birth weight, g; mean (SD)	3,530 (558)	3,538 (548)
Birth length, cm; mean (SD)	50.2 (2.6)	50.2 (2.5)
Length of pregnancy, wk; mean (SD)	39.8 (2)	39.8 (1.8)
Mother's smoking during pregnancy or at birth of child, n (%)	563 (13.8)	252 (13.1)
Socioeconomic status of parents, n (%)		
Unskilled blue-collar workers	260 (6.4)	103 (5.4)
Skilled blue-collar workers	435 (10.7)	180 (9.4)
Low level white collar workers	605 (14.9)	264 (13.8)
Intermediate level white collar workers	1,179 (29)	588 (30.6)
High level white collar workers	1,539 (37.8)	769 (40.1)
Others (students, unemployed)	54 (1.3)	16 (0.8)
Heredity, n (%)		
No parental allergy or asthma	2,841 (70.5)	1,308 (68)
One parent with allergy or asthma	1,066 (26.4)	551 (28.6)
Both parents with allergy or asthma	125 (3.1)	65 (3.4)
Traffic-PM_{10}, mean/median (5th–95th percentile)‡		
Exposure during first year of life	4.2/3.7 (0.9–8.1)§	4.2/3.8 (0.9–7.9)
Exposure between 1–4 yr of life	3.7/3.4 (0.8–7.6)‖	3.7/3.5 (0.9–7.6)
Exposure between 4–8 yr of life	3.5/3.1 (0.7–7.5)¶	3.5/3.2 (0.8–7.4)

Definition of abbreviations: BAMSE = Children, Allergy, Milieu, Stockholm, Epidemiological Survey; PM_{10} = particulate matter less than 10 μm in aerodynamic diameter.

* Covariates relate to the first year of child's life.

† Includes subjects with data on lung function measurements, municipality, heredity, sex, age, length at 8-year examination, and exposure information for all time periods.

‡ Source-specific contribution to residential outdoor levels estimated from local traffic with dispersion models. Presented in $\mu g/m^3$.

§ Data for 4,017 children who had complete exposure information for the first year of life.

‖ Data for 3,515 children who had complete exposure information for 1–4 years of life period.

¶ Data for 3,103 children who had complete exposure information for 4–8 years of life period.

Results using traffic-NO_x as exposure indicator were consistent with those using traffic-PM_{10}, although the level of statistical significance varied. For example, exposure during the first year of life was associated with a deficit of −34.9 ml (−80.1 to 10.4) in FEV_1 for a 5th to 95th percentile difference in time-weighted exposure to traffic-NO_x (47 $\mu g/m^3$), whereas the corresponding deficit was −98.9 ml (−169.4 to −28.4) among those sensitized at 8 years. The odds ratios associated with 80% and 85% of predicted FEV_1 were 2.1 (95% CI, 0.6–8.1) and 3.4 (95% CI, 1.6–7.4), respectively, for first year exposure to traffic-NO_x.

DISCUSSION

In this prospective birth cohort study, exposure to traffic-related air pollution during infancy was associated with a decreased lung function in children at 8 years of age. There was a tendency toward stronger effects in boys, in those with asthma, and particularly in those sensitized to allergens. No significant impact of short-term air pollution exposure on the estimates of the long-term effects of air pollution was found. Our results are in general concordance with the findings from the Children's Health Study in Southern California (3, 11) and from the Oslo Birth Cohort (1), which indicated that exposure to pollution from traffic has adverse effects on children's lung function development. Several studies did not find any effect of air pollution on the pulmonary function, which might in part be attributable to their cross-sectional design and less refined exposure assessment (8, 9).

It has been shown that children are particularly susceptible to the adverse effects of air pollution and environmental tobacco smoke and that timing of exposure plays a critical role (1, 6, 12, 13, 19, 24, 25). Prenatal exposure and during infancy seems particularly harmful. Children may also be more exposed to many air pollutants compared with adults because of their higher ventilation per minute in relation to body size and often higher physical activity. In addition, the development of mature systemic immune responses during early childhood could be of importance (26). Our findings provide further support that early life exposure has long-lasting impact on lung function development.

We mainly found effects on FEV_1 and $FEV_{0.5}$, which reflect the mechanical properties of the airways and not as much on FVC, representing lung size. This is in line with the California health study (3, 11) and the Oslo cohort findings (1), even though the California study found the largest effect on midexpiratory flow, possibly more representing the bronchioles. Differences in effects on lung function variables from air pollution

TABLE 2. LUNG FUNCTION AND ANTHROPOMETRY DATA FROM 8-YEAR EXAMINATION IN THE BAMSE COHORT

Variable	N	Mean	SD	%
Length, m	1,924	1.32	0.06	
Age, yr	1,924	8.3	0.5	
FEV_1, ml	1,851	1,781	269	
$FEV_{0.5}$, ml	1,670	1,326	213	
FVC, ml	1,879	2,068	327	
FEV_1/FVC, %	1,812	86.2	5.7	
$FEV_{0.5}$/FVC, %	1,633	64.3	7.4	
FEV_1, <85% pred	125			6.8
$FEV_{0.5}$, <85% pred	176			10.5
FVC, <85% pred	116			6.2
FEV_1, <80% pred	50			2.7
$FEV_{0.5}$, <80% pred	90			5.4
FVC, <80% pred	56			3.0

Definition of abbreviations: % pred = % of predicted based on age, sex, height, and weight and interactions of sex with age, height, and weight; BAMSE = Children, Allergy, Milieu, Stockholm, Epidemiological Survey.

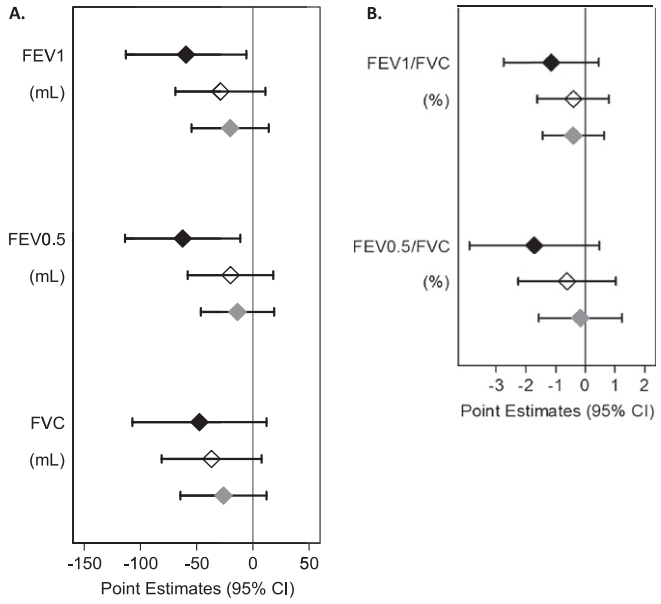

Figure 1. Lung function measurements in relation to traffic particulate matter less than 10 μm in aerodynamic diameter (PM_{10}) exposure during different time periods of life (*black*, first year of life exposure; *white*, first to fourth year exposure; *gray*, fourth to eighth year exposure). CI = confidence interval. Adjusted for municipality, sex, age, height, and heredity. Results are presented in milliliters (*A*) and percentages (*B*) for a difference in PM_{10} level from 5th to 95th percentile, corresponding to 7 μg/m^3.

might partly be explained by the mixture of components in traffic-related emission. We have in our study focused on PM_{10} as exposure estimate, which in Stockholm is primarily influenced by coarse particles (>2.5 μm), although it also contains fine and ultrafine particles. Our results are in general agreement with the other studies considering that levels of smaller particles, such as $PM_{2.5}$, correlate to PM_{10} and are also supported by our findings for traffic-NO_x, which correlate with fine particulate emissions from motor vehicles.

From an individual perspective the estimated effect on lung function seen in our study is rather small (−3.3% for FEV_1 and −4.7% for $FEV_{0.5}$), but even a slight shift in the population distribution of lung function can substantially increase the prevalence of subjects exhibiting respiratory function below clinical thresholds. In our study this is indicated by the sharply increased risks of having a lung function below 80% and 85% of predicted. The cut point 80% of predicted was chosen because it is generally used in clinical settings to identify persons who are at increased risk for adverse respiratory effects. However, few children were identified with this lung function reduction and 85% of predicted was also used, but the results remained similar. Our analyses were internally adjusted for age, height, and sex but results were consistent also when the lung function analyses were based on external reference data using standard deviation scores (23).

We also investigated the effect modification by including interaction terms with sex, current asthma, and allergic sensitization. Although the interactions were not statistically significant, there was a tendency for a stronger effect on lung function in subjects sensitized to common allergens. We have earlier shown in this cohort that air pollution exposure during the first year of life is associated with sensitization at 4 years of age (12, 13), but not at 8 years of age; however, no association was found between sensitization *per se* and FEV_1. Thus, the effects from PM_{10} on lung function do not seem to be explained by sensitization affecting lung function. Data regarding the role of allergic sensitization as a risk factor for lung function loss in relation to air pollution exposure in children are limited. Several cross-sectional studies have reported larger effects of air pollution exposure on lung function in children with a diagnosis of asthma, allergies, eczema, or any combination (i.e., in children with a predisposing bronchial sensitivity) (27, 28). Although the exact mechanisms are unclear, it has been suggested that air pollution and sensitization might be independently involved in the induction of Th2 immune response. For instance, it has been shown that diesel exhaust particles stimulate an unfavorable Th2-skewed immune response to allergens and that allergic children experience subclinical asthma-like changes in their lung function (29, 30). Thus, air pollution exposure in allergic children may exert a synergistic effect on the allergic inflammation response to specific allergens or an irritative effect on the airways.

Several studies have shown an association between short-term exposure to outdoor air pollution and lung function impairment in children (31); however, simultaneous effects of long- and short-term exposures on lung function have rarely been investigated within the same study. We included short- and long-term air pollution exposures in the models to exclude possible confounding or decreased precision of the long-term exposure estimates by short-term exposure. The sensitivity analysis with adjustment for temperature, relative humidity, and short-term exposures (previous days' concentrations of O_3 and PM_{10}) showed,

TABLE 3. ASSOCIATION BETWEEN EXPOSURE TO TRAFFIC PM_{10} DURING THE FIRST YEAR OF LIFE AND FEV_1 AT 8 YEARS OF AGE (N = 1,851)

	N	Traffic PM_{10} Point Estimates in Milliliters (95% CI)*	*P* Value
All subjects	1,851	−59.3 (−113 to −5.6)	0.03
Girls	902	−37.1 (−112.7 to 38.4)	0.34
Boys	949	−79.6 (−155.7 to −3.5)	0.04
Sensitized at 8 yrs†	606	−136.9 (−224.1 to −49.7)	<0.01
Not sensitized at 8 yrs	1,119	−44.8 (−116.6 to 26.9)	0.22
Asthma at 8 yrs‡	144	−90.6 (−293.4 to 112.3)	0.38
No asthma at 8 yrs	1,696	−55.4 (−111.2 to 0.3)	0.05

Definition of abbreviations: CI = confidence interval; PM_{10} = particulate matter less than 10 μm in aerodynamic diameter.

*Results are presented in milliliters for a difference in PM_{10} level from 5th to 95th percentile, corresponding to 7 μg/m^3. Adjusted for municipality, sex, age, height, and heredity.

† Defined as IgE values for phadiatop greater than or equal to 0.35 kU/L or IgE value for food-mix greater than or equal to 0.35 kU/L.

‡ Defined as at least four episodes of wheeze in the last 12 months or at least one episode in combination with prescription of inhaled corticosteroids.

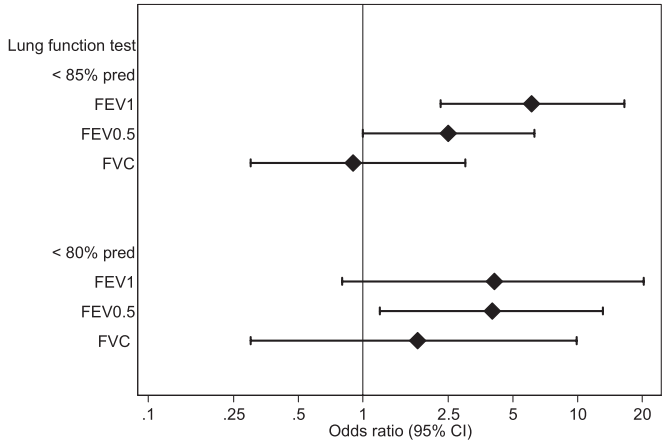

Figure 2. Association between first year of life exposure to traffic. PM_{10} and FEV less than 80% and 85% of predicted. % pred = % of predicted based on age, sex, height, and weight and interactions of sex with age, height, and weight; CI = confidence interval; PM_{10} = particulate matter less than 10 μm in aerodynamic diameter. Odds ratios are calculated for a 7 $\mu g/m^3$ difference in PM_{10} level corresponding to a 5th to 95th percentile difference. Adjusted for municipality and heredity.

however, little influence of short-term exposure on the effect estimates for long-term exposure on lung function. Similar findings were reported from the California health study and Oslo cohort (1, 11). Our study has several advantages, including its combination of a prospective design; large number of participants; individual long-term exposure to air pollutants (incorporating their time-activity patterns); objective measurement of lung function; evaluation of effect modification by sex, asthma, or increased IgE levels to common allergens; and influence of the short-term variation in air pollution exposure. In particular, the exposure estimates for each study subject were obtained from a time- and space-resolved dispersion model enhanced by addition of street canyon contribution for addresses in the most polluted street segments, and by including not only residential addresses but also addresses of day care and schools.

Some potential weaknesses of this study should be recognized. One is that model calculations of PM_{10} concentrations were only done for 2004 and extrapolated to the other years of follow-up. The most important local source of PM_{10} in many urban areas in Sweden is coarse particles resulting from road surface erosion by cars with studded tires and sanding or salting of roads in the winter (32). Because of the stable use of studded tires in the Stockholm area during the study period, and traffic load in the inner city, the emissions of PM_{10} have not changed substantially (33). Road moisture has a crucial impact on the yearly variations of PM_{10} concentrations. Unfortunately, this could not be taken into consideration because of lack of relevant data (32). However, several validation studies have shown good agreement between modeled and measured air pollution concentrations (34, 35). Results were supported by analyses using traffic-NO_x as indicator, where the exposure assessment was based on dispersion modeling at repeated occasions during the observation period (13). This is expected because of the high correlation between the two exposure measures.

Some misclassification of true individual exposure levels has probably affected the results, especially because no indoor environments were characterized and no individual time-activity data were used. However, the errors in the assessments of exposure and disease are most likely to be independent and making such misclassification would thus be expected to weaken any true associations. Imprecision in the lung function measurements primarily results from its dependence on the children's cooperation. However, because one trained team examined all the children using the same equipment and method of measuring, masked to the exposure, such bias is likely unimportant. Selective participation is probably of limited concern because subjects in air pollution studies are generally unaware of their precise level of exposure, and lung function is objectively evaluated (36). We tested a comprehensive set of known risk factors for childhood respiratory disorders with regard to possible confounding effects, including socioeconomic status, home environment characteristics, maternal smoking, and so forth, but none except those included in the models showed clear confounding effect. Still, the possibility of residual confounding cannot be ruled out.

To conclude, our results indicate that exposure to ambient air pollution from traffic during the first year of life is associated with lung function deficits in children up to 8 years, particularly in those sensitized to common allergens.

Author disclosures are available with the text of this article at www.atsjournals.org.

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