Traffic-Related Air Pollution and Lung Function In Children At 8 Years Of Age - A Birth Cohort Study

Erica S. Schultz,¹ Olena Gruzieva,¹,² Tom Bellander,¹,³ Matteo Bottai,¹ Jenny Hallberg,⁴,⁵ Inger Kull,¹,⁴,⁶ Magnus Svartengren,⁷ Erik Melén,¹,⁶,⁸ Göran Pershagen¹,³

¹ Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
² Department of Social Medicine and Health Care, National O.O.Bohomolets Medical University, Kyiv, Ukraine
³ Centre for Occupational and Environmental Medicine, Stockholm County Council, Sweden
⁴ Department of Clinical Science and Education, Södersjukhuset, Karolinska Institutet, Stockholm, Sweden
⁵ Sachs Children’s Hospital, Södersjukhuset, Stockholm
⁶ Centre for Allergy Research, Karolinska Institutet, Stockholm, Sweden
⁷ Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden
⁸ Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Stockholm, Sweden

Corresponding author:
Göran Pershagen, MD, PhD, Professor
Karolinska Institutet, Institute of Environmental Medicine,
Nobels väg 13 Box 210, SE- 171 77, Stockholm, Sweden
E-mail: Goran.Pershagen@ki.se
Phone: +46-8-524 87460
Fax: +46-8-304571
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 wrote together with O.G 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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Descriptor number: 6.1 Air Pollution: Epidemiology

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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 well as possible effect modification by allergic status and other factors.

What This Study Adds to the Field

In this prospective birth cohort study we found 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 atopic children.

This article has an online data supplement, which is accessible from this issue's table of content online at www.atsjournals.org
ABSTRACT

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: Over 1900 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 <10 μm (PM\textsubscript{10}) from road traffic were estimated for residential, daycare and school addresses from birth and onwards using dispersion modelling. The relationship between time-weighted average exposure during different time windows and forced expiratory volumes at 8 years was analyzed by linear regression, adjusting for potential confounding factors, including short-term exposure to air pollution.

Results: A 5\textsuperscript{th} to 95\textsuperscript{th} percentile difference in time-weighted average PM\textsubscript{10} exposure during the first year of life was associated with a reduced forced expiratory volume in one second (FEV\textsubscript{1}) of -59.3 mL, 95% confidence interval (CI): -113.0 to -5.6 at 8 years of age. The negative association was particularly pronounced in children concomitantly sensitized to common inhalant and/or food allergens (-136.9 mL, 95% CI: -224.1 to -49.7). Exposure after the first year of life appeared 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 and/or food allergens.

Word count: 249

Key words: spirometry, forced expiratory volume, sensitization, dispersion modeling, particulate matter
INTRODUCTION

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 appears inconsistent as some of the larger studies reported no associations (8, 9). Heterogeneity in study designs, exposure assessment, as well as 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 to 18 years (11). The observed effect remained statistically significant in the subgroup of non-asthmatics, but the asthmatic children were too few for precise risk estimation. A birth cohort study from Oslo indicated stronger air pollution effects in asthmatic children compared with non-asthmatics. However, because of wide confidence intervals 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.

Early exposure to ambient air pollution appears 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 both 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 epidemiological evidence on vulnerable time periods for air pollution exposure, particularly during childhood, as well as 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 (Children, Allergy, Milieu, Stockholm, Epidemiological Survey) (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).

MATERIALS AND METHODS

More details are provided in the online data supplement.

Study Subjects and measurements
During 1994 - 1996, 4089 new-born infants were recruited to the prospective cohort study BAMSE 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 months). Questionnaires focusing on the children’s respiratory health and allergic diseases, as well as on various exposures factors were completed at 1, 2, 4 and 8 years of age. The response rates were from 96% to 84%, for the 1 and 8 year questionnaires,
respectively. In addition, 2630 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 forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV₁), and forced expiratory volume in 0.5 sec (FEV₀.₅) 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, gender, height and weight as predictors. Also, standard deviation scores for FEV₁ were calculated taking age, sex, height and ethnicity into consideration (23). The Ethics Committee of Karolinska Institutet, Stockholm, Sweden, approved the study.

The methodology for calculating individual long-term exposure to local traffic-related PM₁₀, as well as NOₓ, has been described in detail elsewhere (13). In short, the life-time 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. In addition, short-term exposure was estimated using daily air quality measurements and meteorological 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% confidence intervals (CIs). Air pollution concentrations were entered as continuous variables without transformation and the results are provided as change in lung function per 7 µg/m³ increase in PM₁₀ 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 and/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 to 3 and 1 to 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 1924 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 (College Station, TX, USA).

**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 forced expiratory volumes deficit of -59.3 mL (-113.0 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. On the other hand, no clear effects on lung function were seen in relation to air pollution exposure after infancy (Figure 1). A sensitivity analysis using FEV\textsubscript{1} expressed as standard deviation scores confirmed the negative effect of traffic-PM\textsubscript{10} exposure on lung function (p=0.04). Further analyses suggested stronger effects in boys, in those sensitized against any common inhalant and/or food allergens, and in those with asthma, with deficits in FEV\textsubscript{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%, as well as 85% of predicted FEV\textsubscript{1} and FEV\textsubscript{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\textsubscript{10} during the first year of life and forced expiratory volumes below 80% and 85% of predicted. Corresponding odds ratios of 4.1; 95% CI, 0.8-20.3, and 6.1 (2.3 –16.5) as well as 4.0 (1.2-13.1) and 2.5 (1.0-6.3) were seen for FEV\textsubscript{1} and FEV\textsubscript{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\textsubscript{10} levels during three-to-seven days before each child’s pulmonary function test showed little effect on the estimates of the long-term effects of air pollution (Table E1 in the online data supplement).

Results using traffic-NO\textsubscript{x} as exposure indicator were consistent with those using traffic-PM\textsubscript{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\textsubscript{1} for a 5\textsuperscript{th} to 95\textsuperscript{th} percentile difference in time-weighted exposure to traffic-NO\textsubscript{x} (47 µg/m\textsuperscript{3}), while 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 FEV₁ were 2.1 (95% CI 0.6-8.1), and 3.4 (1.6-7.4), respectively, for first year exposure to traffic-NOₓ.

**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 towards 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, as well as 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 appear particularly harmful. Children may also be more exposed to many air pollutants compared to 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 the lung function development.

We mainly found effects on FEV₁ and FEV₀.₅, which reflect the mechanical properties of the airways and not as much on FVC, representing lung size. This is in line with the
Californian health study (3, 11) and the Oslo cohort findings (1), even though the Californian study found the largest effect on midexpiratory flow, MMEF, possibly more representing the bronchioles. Differences in effects on lung function variables from air pollution 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 gender, 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 FEV₁. Thus, the effects from PM₁₀ on lung function does not appear 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 either 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 both 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 infavourable 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 both 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, as well as short-term exposures (previous days’ concentrations of O₃ and PM₁₀) showed, however, little influence of short-term exposure on the effect estimates for long-term exposure on lung function. Similar findings were reported from CHS 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 gender, asthma or increased IgE levels to common allergens, as well as 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, as well as 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/salting of roads in the winter (32). Due to the stable use of studded tires in the Stockholm area during the study period, as well as 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. However, this could not be taken into consideration because of lack of relevant data (32). On the other hand, 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 since no indoor environments were characterized and no individual time-activity data was used. However, the errors in the assessments of both 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, blinded to the exposure, such bias is likely unimportant. Selective participation is probably of limited concern as 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 etc, 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.

ACKNOWLEDGMENTS

We thank all BAMSE cohort participants, nurses and research team, as well as Tomas Lind for his generous help with the short-term air pollution exposure assessment.
REFERENCES


TABLE 1. Descriptive data for the BAMSE cohort and of those with data on lung function at 8 years of age

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Full cohort (N=4089)</th>
<th>Study population at 8 yrs (n=1924)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls, n/N %</td>
<td>2024</td>
<td>937</td>
</tr>
<tr>
<td>Birth weight (grams); mean (SD)</td>
<td>3530 (558)</td>
<td>3538 (548)</td>
</tr>
<tr>
<td>Birth length (cm); mean (SD)</td>
<td>50.2 (2.6)</td>
<td>50.2 (2.5)</td>
</tr>
<tr>
<td>Length of pregnancy (weeks); mean (SD)</td>
<td>39.8 (2.0)</td>
<td>39.8 (1.8)</td>
</tr>
<tr>
<td>Mother’s smoking during pregnancy or at birth of child, n/N %</td>
<td>563</td>
<td>13.8</td>
</tr>
<tr>
<td>Socioeconomic status of parents, n/N %:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unskilled blue-collar workers</td>
<td>260</td>
<td>103</td>
</tr>
<tr>
<td>Skilled blue-collar workers</td>
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<td>180</td>
</tr>
<tr>
<td>Low level white collar workers</td>
<td>605</td>
<td>264</td>
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<tr>
<td>Intermediate level white collar workers</td>
<td>1179</td>
<td>588</td>
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<tr>
<td>High level white collar workers</td>
<td>1539</td>
<td>769</td>
</tr>
<tr>
<td>Others (students, unemployed)</td>
<td>54</td>
<td>16</td>
</tr>
<tr>
<td>Heredity, n/N %</td>
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<td></td>
</tr>
<tr>
<td>No parental allergy or asthma</td>
<td>2841</td>
<td>1308</td>
</tr>
<tr>
<td>One parent with allergy or asthma</td>
<td>1066</td>
<td>551</td>
</tr>
<tr>
<td>Both parents with allergy or asthma</td>
<td>125</td>
<td>65</td>
</tr>
<tr>
<td>Traffic-PM10; mean/median (5th, 95th percentile):‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposure during first year of life:</td>
<td>4.2/3.7 (0.9-8.1)§</td>
<td>4.2/3.8 (0.9-7.9)</td>
</tr>
<tr>
<td>Exposure between 1-4 years of life:</td>
<td>3.7/3.4 (0.8-7.6)¶</td>
<td>3.7/3.5 (0.9-7.6)</td>
</tr>
<tr>
<td>Exposure between 4-8 years of life:</td>
<td>3.5/3.1 (0.7-7.5)¶*</td>
<td>3.5/3.2 (0.8-7.4)</td>
</tr>
</tbody>
</table>

* Covariates relate to the first year of child’s life
† Data include subjects with data on lung function measurements, municipality, heredity, sex, age, length at 8yr examination, as well as exposure information for all time periods
‡ Source-specific contribution to residential outdoor levels estimated from local traffic with dispersion models. Presented in µg/m³
§ Data for 4017 children who had complete exposure information for the first year of life
¶ Data for 3515 children who had complete exposure information for 1-4 years life period
¶* Data for 3103 children who had complete exposure information for 4-8 years life period
<table>
<thead>
<tr>
<th>Variable</th>
<th>No</th>
<th>Mean</th>
<th>SD</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Length (m)</td>
<td>1924</td>
<td>1.32</td>
<td>0.06</td>
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<tr>
<td>Age (yr)</td>
<td>1924</td>
<td>8.3</td>
<td>0.5</td>
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<tr>
<td>FEV\textsubscript{1} (ml)</td>
<td>1851</td>
<td>1781</td>
<td>269</td>
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<tr>
<td>FEV\textsubscript{0.5} (ml)</td>
<td>1670</td>
<td>1326</td>
<td>213</td>
<td></td>
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<tr>
<td>FVC (ml)</td>
<td>1879</td>
<td>2068</td>
<td>327</td>
<td></td>
</tr>
<tr>
<td>FEV\textsubscript{1}/FVC (%)</td>
<td>1812</td>
<td>86.2</td>
<td>5.7</td>
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<tr>
<td>FEV\textsubscript{0.5}/FVC (%)</td>
<td>1633</td>
<td>64.3</td>
<td>7.4</td>
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<tr>
<td>FEV\textsubscript{1}, &lt;85% pred</td>
<td>125</td>
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<td>6.8</td>
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<tr>
<td>FEV\textsubscript{0.5}, &lt;85% pred</td>
<td>176</td>
<td></td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td>FVC, &lt;85% pred</td>
<td>116</td>
<td></td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td>FEV\textsubscript{1}, &lt;80% pred</td>
<td>50</td>
<td></td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>FEV\textsubscript{0.5}, &lt;80% pred</td>
<td>90</td>
<td></td>
<td>5.4</td>
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<tr>
<td>FVC, &lt;80% pred</td>
<td>56</td>
<td></td>
<td>3.0</td>
<td></td>
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</tbody>
</table>

Definition of abbreviations: FEV\textsubscript{1} = forced expiratory volume during 1 second. FEV\textsubscript{0.5} = FEV during 0.5 second. FVC = forced vital capacity. % pred = % of predicted based on age, gender, height and weight and interactions of gender with age, height and weight.
### TABLE 3. Association between exposure to [Traffic-PM]_10 during the first year of life and FEV₁ at 8 years of age (n=1851)

<table>
<thead>
<tr>
<th>Traffic-PM₁₀</th>
<th>No</th>
<th>Point Estimates in ml (95% CI)*</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>1851</td>
<td>-59.3 (-113.0 to -5.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>Girls</td>
<td>902</td>
<td>-37.1 (-112.7 to 38.4)</td>
<td>0.34</td>
</tr>
<tr>
<td>Boys</td>
<td>949</td>
<td>-79.6 (-155.7 to -3.5)</td>
<td>0.04</td>
</tr>
<tr>
<td>Sensitized at 8 yrs†</td>
<td>606</td>
<td>-136.9 (-224.1 to -49.7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Not sensitized at 8 yrs</td>
<td>1119</td>
<td>-44.8 (-116.6 to 26.9)</td>
<td>0.22</td>
</tr>
<tr>
<td>Asthma at 8 yrs‡</td>
<td>144</td>
<td>-90.6 (-293.4 to 112.3)</td>
<td>0.38</td>
</tr>
<tr>
<td>No asthma at 8 yrs</td>
<td>1696</td>
<td>-55.4 (-111.2 to 0.3)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Definition of abbreviations: PM₁₀ = Particulate matter <10 µm in aerodynamic diameter. FEV₁ = forced expiratory volume during 1 second. CI = confidence interval
*Results are presented in ml for a difference in PM₁₀ level from 5th to 95th percentile, corresponding to 7 µg/m³. Adjusted for municipality, sex, age, height and heredity
†Defined as IgE values for phadiatop ≥0.35kU/l and /or IgE-value for food-mix ≥0.35kU/l
‡Defined as at least 4 episodes of wheeze in the last 12 months or at least 1 episode in combination with prescription of inhaled corticosteroids
FIGURE LEGENDS

Figure 1. Lung function measurements in relation to traffic particulate matter < 10 µm in aerodynamic diameter (PM$_{10}$) exposure during different time periods of life

(black=first year of life exposure, white=1-4$^{th}$ year exposure, gray= 4-8$^{th}$ year exposure).
Abbreviations: FEV$_1$ = forced expiratory volume during 1 second; FEV$_{0.5}$ = FEV during half a second; FVC = forced vital capacity; CI = confidence interval. Adjusted for municipality, sex, age, height and heredity. Results are presented in ml (A) and % (B) for a difference in PM$_{10}$ level from 5$^{th}$ to 95$^{th}$ percentile, corresponding to 7 µg/m$^3$.

Figure 2. Association between first year of life exposure to traffic- PM$_{10}$ and forced expiratory volumes below 80% and 85% of predicted

Definition of abbreviations: PM$_{10}$ = Particulate matter<10 µm in aerodynamic diameter. CI= confidence interval. FEV$_1$ = forced expiratory volume during 1 second. FEV$_{0.5}$ = FEV during 0.5 second. FVC = forced vital capacity. % pred = % of predicted based on age, gender, height and weight and interactions of gender with age, height and weight. *Odds ratios are calculated for a 7 µg/m$^3$ difference in PM$_{10}$ level corresponding to a 5$^{th}$ to 95$^{th}$ percentile difference. Adjusted for municipality and heredity.
Figure 1
Figure 2
Online data supplement

METHODS

Assessment of long-term exposure to PM$_{10}$ and NO$_x$

A Gaussian dispersion model and a wind model, both part of the Airviro Air Quality Management System, were used to calculate the temporal and spatial distribution of PM$_{10}$ and NO$_x$ (http://airviro.smhi.se). Input data to the wind model include meteorological measurements at a height of 50 m in southern Stockholm, as well as land use variations and local topographic conditions. Historical emission databases for NOx were available for the years 1990, 1995, 2000, 2002-2004, and for PM$_{10}$ – for 2004 (Figure E1). The model calculations were interpolated to obtain concentrations for all years during the follow-up period for the children.

The calculations were performed on a 25 m resolution grid for the addresses in the more densely populated areas, such as urban areas. Outside these areas the model applied a 100 m grid or a 500 m calculation grid. To compensate for the coarse resolution of the dispersion calculations over rural areas, adjustments were made using concentration gradients near roads with more than 10 000 vehicles per day.

Levels of pollution at street level in the inner city are generally higher than at rooftop height because of the close vicinity of road traffic and the poorer ventilation of the emissions. Therefore, a street canyon contribution was calculated for addresses in the most polluted streets in the Stockholm inner city flanked by buildings on both sides and with high levels of air pollutants, using the Airviro street canyon model (http://airviro.smhi.se). To define which streets that should be considered as highly polluted we used already existing street canyon model calculations of NO$_2$ for the year 2006. Streets where the 98$^{th}$ percentile of the daily
mean value for NO\textsubscript{2} at two meters above street level was higher than 48 μg/m\textsuperscript{3} were classified as polluted street segments. For both PM\textsubscript{10} and NO\textsubscript{X} the calculated concentrations at half-height level in the street canyons were assigned to addresses situated closer than 40 meters from the polluted street segments. The NO\textsubscript{X} concentrations were also adjusted for the differences in the meteorological conditions between the years. However, no such adjustment was done for PM\textsubscript{10}, due to the lack of relevant data to adjust for road moisture, which has a major impact on PM\textsubscript{10} concentrations.

\textbf{Short-term exposure assessment}

Hourly mean values for PM\textsubscript{10} were measured on two streets in the Stockholm city center- at the rooftop of one building and at 3 meters above street level. Measurements were also performed at a rural station located 70 km southwest of Stockholm. Approximately 1 to 3 % of the observations were missing each year. Missing values for PM\textsubscript{10} at one of the city center measuring stations were imputed using predictions from a linear regression model based on PM\textsubscript{10} for the same point in time from the other two stations. If data from the rural station were lacking it was excluded from the imputation model. After imputation, less than 0.1 % of the values were missing.

Ozone was measured at a rural station situated 70 km northeast of Stockholm. To predict missing values at this station observations from another rural station located 20 km southwest of Stockholm was used. Before imputation the yearly number of missing values was up to 1.6%. After imputation no ozone observations was missing.

\textbf{Lung function measurements}
Maximum expiratory flow volume tests were performed (N=2113), using a spirometer (2200 Pulmonary Function Laboratory; Sensormedics, Anaheim, CA, USA). Each subject performed several slow and forced vital capacity expirations using nose clip. The maximal values of forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV₁), and forced expiratory volume in 0.5 sec (FEV₀.₅) were extracted and used for analysis, given that the child’s effort was coded as being high by the test leader, the curve passed visual quality inspection, and that the two highest readings were reproducible according to ATS/ERS criteria (E1).

Definition of asthma and allergic sensitization

Asthma was defined as at least 4 episodes of wheeze in the last 12 months prior to the date of answering the questionnaire at 8 years or at least 1 episode in combination with prescription of inhaled corticosteroids (E2). The blood samples taken at 8 years of age were analyzed with Phadiatop® [a mix of common inhalant allergens: birch, timothy, mugwort, cat, dog, horse, mold and house dust mite] and fx5® (a mix of common food allergens: cow’s milk, egg white, soy bean, peanut, cod fish and wheat) (ImmunoCAP System, Phadia AB, Uppsala, Sweden). Sera with an IgE value equal to or greater than 0.35 kU/L were regarded as positive.

Confounder testing

In addition to the chosen adjustment covariates (municipality, sex, age, height and heredity for asthma and/or allergy) the following potential confounders were evaluated: gestational age, birth weight, birth length, current passive smoking, maternal smoking during pregnancy or at birth of child, socioeconomic status of parents, possession of furred pets at birth and current, ethnicity, mold and moist in house during first year of life, year the house was built, but none of these were found to have any influence on the effect of air pollution. Further, we
evaluated sex, asthma status and sensitization status as potential effect modifiers for the relationship between lung function and air pollution through stratified analyses and introducing the appropriate interaction term in the model.

**References**


TABLE E1. Exposure to traffic-PM$_{10}$ during the first year of life and FEV1 at 8 years of age, adjusted for subsequent exposure time windows or short-term exposure (n=1851)

<table>
<thead>
<tr>
<th>Traffic-PM$_{10}$</th>
<th>All Children</th>
<th>In Boys</th>
<th>In Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main model†</td>
<td>-59.3 (-113.0 to -5.6)</td>
<td>-79.6 (-155.7 to -3.5)</td>
<td>-37.1 (-112.7 to 38.4)</td>
</tr>
<tr>
<td>Main model + adjustment for:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM$_{10}$ 1-4 yrs + 4-8 yrs</td>
<td>-57.3 (-124.8 to 10.2)</td>
<td>-76.3 (-170.6 to 18.0)</td>
<td>-34.0 (-130.6 to 62.5)</td>
</tr>
<tr>
<td>Rh + Temp</td>
<td>-58.0 (-111.6 to -4.4)</td>
<td>-86.1 (-162.2 to -10.1)</td>
<td>-39.1 (-114.6 to 36.5)</td>
</tr>
<tr>
<td>Rh + Temp + PM$_{10}$(1-3 day)</td>
<td>-58.2 (-111.9 to -4.5)</td>
<td>-86.4 (-162.6 to -10.3)</td>
<td>-39.0 (-114.6 to 36.5)</td>
</tr>
<tr>
<td>Rh + Temp + PM$_{10}$(1-7 day)</td>
<td>-59.2 (-112.8 to -5.6)</td>
<td>-87.1 (-163.2 to -11.0)</td>
<td>-40.1 (-115.6 to 35.4)</td>
</tr>
<tr>
<td>Rh + Temp + Ozone (1-3 day)</td>
<td>-57.8 (-111.5 to -4.2)</td>
<td>-84.7 (-160.7 to -8.7)</td>
<td>-39.2 (-114.8 to 36.4)</td>
</tr>
<tr>
<td>Rh + Temp + Ozone (1-7 day)</td>
<td>-57.6 (-111.3 to -4.0)</td>
<td>-85.2 (-161.3 to -9.2)</td>
<td>-39.0 (-114.5 to 36.6)</td>
</tr>
</tbody>
</table>

Definition of abbreviations: PM$_{10}$ = Particulate matter<10 µm in aerodynamic diameter. FEV$_1$ = forced expiratory volume during 1 second. CI = confidence interval. Rh = Relative humidity. Temp = Temperature. *Results are presented in ml 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.
Figure E1. Timing of dispersion models used for air pollution exposure assessment in the BAMSE cohort.
Figure E1