Traffic-related air pollution and respiratory health during the first 2 yrs of life

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ABSTRACT: As part of an international collaborative study on the impact of Traffic-Related Air Pollution on Childhood Asthma (TRAPCA), the health effects associated with long-term exposure to particles with a 50% cut-off aerodynamic diameter of 2.5 µm (PM2.5), PM2.5 absorbance, and nitrogen dioxide (NO$_2$) were analysed.

The German part of the TRAPCA study used data from subpopulations of two ongoing birth cohort studies (German Infant Nutrition Intervention Programme (GINI) and Influences of Lifestyle Related Factors on the Human Immune System and Development of Allergies in Children (LISA)) based in the city of Munich. Geographic information systems (GIS)-based exposure modelling was used to estimate traffic-related air pollutants at the birth addresses of 1,756 infants. Logistic regression was used to analyse possible health effects and potential confounding factors were adjusted for.

The ranges in estimated exposures to PM2.5, PM2.5 absorbance, and NO$_2$ were 11.9–21.9 µg·m^{-3}, 1.38–4.39×10^{-5} m^{-1}, and 19.5–66.9 µg·m^3, respectively. Significant associations between these pollutants and cough without infection (odds ratio (OR) (95% confidence interval (CI)): 1.34 (1.11–1.61), 1.32 (1.10–1.59), and 1.40 (1.12–1.75), respectively) and dry cough at night (OR (95% CI): 1.31 (1.07–1.60), 1.27 (1.04–1.55), and 1.36 (1.07–1.74), respectively) in the first year of life were found. In the second year of life, these effects were attenuated.

There was some indication of an association between traffic-related air pollution and symptoms of cough. Due to the very young age of the infants, it was too early to draw definitive conclusions from this for the development of asthma.
Eur Respir J 2002; 19: 690–698.

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Motor traffic is a major source of air pollutants such as nitrogen dioxide (NO$_2$) and suspended particulate matter. Recent research has focused on the impact of traffic-related air pollution on morbidity and mortality [1]. Whereas most epidemiological studies deal with short-term effects, only a few studies have reported long-term effects [2]. Therefore, there is a need for more studies assessing the long-term effects of outdoor air pollution.

In recent years, several studies have indicated that exposure to NO$_2$ [3–5], and particulate matter [6], proximity of homes to roadsides [7] and motorways [8] as well as exposure to high rates of road traffic [9] and in particular to truck traffic [8, 10–13] increases the risk of respiratory symptoms. The associations between traffic-related air pollution and asthma and lung function are less clear. A positive association between hospital admission for asthma and traffic density among children was reported by one case-control study [14], whereas another case-control study failed to show such an association [15]. In two studies lung function was found to be decreased with increasing traffic density [8], whereas no associations with pulmonary function measures were found in others [9, 16].

A major deficiency in many of these studies involves the estimation of exposure. Proximity to road traffic [3, 7, 8, 15], census data on car traffic and/or truck traffic [8, 9, 14, 17], and self-reported traffic intensities [10–13] were used as proxies for exposure to traffic

exhaust. One study used modelled NO_2 concentrations [3]. Only a few studies relied on exposure measurements [8, 17, 18]. Since it is not feasible to measure personal exposure for large study populations, exposure modelling based on either pollution dispersion models or measurement data seems to be a useful approach. BRIGGS and co-workers [19, 20] presented a regression-based approach for mapping long-term exposure to NO_2 using Geographic information systems (GIS), which can be easily applied to large study populations.

As part of an international collaborative study on the impact of Traffic-Related Air Pollution on Childhood Asthma (TRAPCA), the health effects associated with long-term exposure to NO_2, particles with a 50% cut-off aerodynamic diameter of 2.5 μm (PM2.5) and PM2.5 absorbance in Sweden, the Netherlands, and Germany were analysed. The results of the German part of the TRAPCA study using data for the first 2 yrs of life from two ongoing birth cohort studies (German Infant Nutrition Intervention Programme (GINI) and Influences of Lifestyle Related Factors on the Immune System and Development of Allergies in Children (LISA)) carried out in the city of Munich are described. A GIS-based exposure modelling similar to that used by BRIGGS and co-workers [19, 20] was used.

Materials and methods

Study area

The study was conducted in the city of Munich, the capital of Bavaria, situated in the South of Germany. In 1999 Munich had a population of ~1.32 million inhabitants in an area of 3,104,400 m^2 and there were 703,231 cars registered [21].

Study population

The German part of the TRAPCA study used data from two ongoing birth cohorts, GINI and LISA. There was no overlap between the two studies, as the children were either participants of the GINI study or participants of the LISA study, but not of both studies.

For the GINI cohort, parents who attended one of 16 maternity hospitals in the two study regions of Munich and Wesel were invited to participate in the study. From September 1995–June 1998, a total of 5,991 healthy, term newborns, whose parents had a sufficient knowledge of the German language, were recruited. A subgroup of 2,252 infants with at least one atopic parent or sibling took part in the intervention program (GINI intervention study) and were randomly assigned to one of four study formulas. The remaining infants took part in the GINI observation study. Both the intervention and observation studies, are referred to as GINI study in the remainder of this paper.

The participants of the LISA study were recruited from the two large German cities, Munich and Leipzig. Parents were recruited during pregnancy. From December 1997–January 1999, newborns from parents who were born in Germany and had German nationality from six obstetrical clinics in Munich and four obstetrical clinics in Leipzig were defined as the target population for the study. Neonates fulfilling at least one of the following criteria were excluded from the study: premature birth (maturity <37 gestational weeks), low birth weight (<2,500 g), congenital malformation, symptomatic neonatal infection, antibiotic medication, hospitalization or intensive medical care during neonatal period, immune-related diseases of the mother (autoimmune disorders, diabetes, hepatitis B), long-term medication or abuse of drugs and alcohol. The final study population consisted of 2,443 neonates.

For the TRAPCA cohort, all infants with birth addresses in Munich (without surrounding communities, postal code 80000–81999), of whom questionnaire data was available for the first year of life, and who did not move away from Munich within the first year of life (fig. 1) were selected. A total of 1,757 infants, 1,084 form the GINI cohort and 673 from the LISA cohort, fulfilled these criteria. For one infant, no GIS data was available. Thus, the final cohort consisted of 1,756 infants.

The studies were approved by the medical association of the state of Bavaria (Landesaerztekammer Bavaria) and were carried out in accordance with the institutional guidelines for the protection of human subjects. Informed consent was obtained from all parents of the participating children.
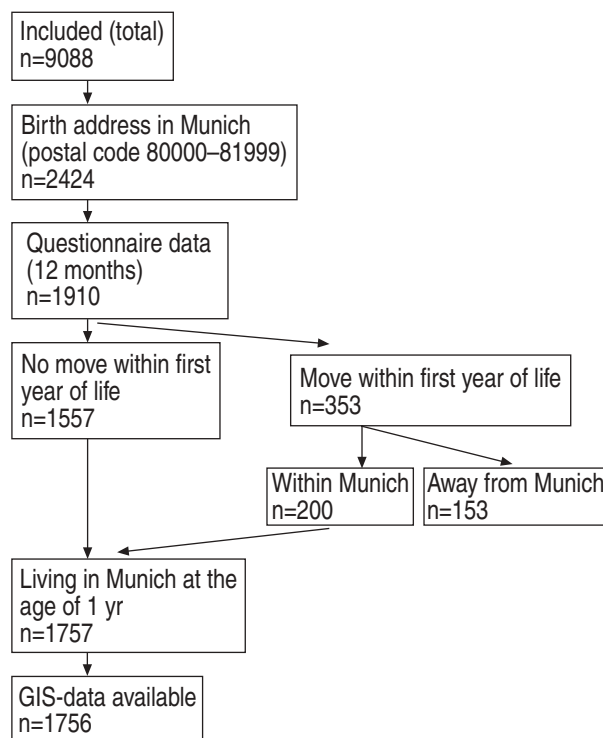

Fig. 1.–Description of the study population.

Respiratory symptoms

Respiratory symptoms were assessed by parental completed questionnaires. Parents of the GINI cohort received a questionnaire at birth, and then every 12 months; parents of the LISA cohort received a questionnaire at birth, and then every 6 months. Data derived from these questionnaires was used for the definition of the primary outcomes. The questionnaire requested information regarding wheezing, symptoms of cough, sneezing, running and/or stuffed nose without a cold, bronchial asthma, bronchitis, and respiratory infections. The wording of the questions used for the definition of these outcome variables was identical in the two cohorts.

Confounding variables

Information on potential confounding variables was also assessed by parental completed questionnaires. Data from these questionnaires included information on sex, parental history of atopy (asthma and/or hayfever and/or eczema), parental education, siblings, environmental tobacco smoke (ETS) at home, use of gas, home dampness, visible indoor moulds, and the keeping of pets.

Estimation of ambient air pollution exposure for the cohort

Since it is not feasible to measure personal exposure to air pollution (NO_2, $PM_{2.5}$, and $PM_{2.5}$ absorbance) for all study subjects, exposure modelling was used. $PM_{2.5}$ absorbance was used as a marker for diesel "soot" in order to distinguish potential health effects of emissions from all motorized vehicles from those of heavy vehicles only. Regression models were developed based upon measurements and simple predictor variables from a GIS that was available for the measurement sites and for each subject. In total, 40 measurement sites were selected. These sites were divided among urban background and street sites. To capture all of the variation in air pollution concentrations that might be experienced by the study subjects, street sites that were located both at main roads and at side roads were selected. The background sites were spread over the whole city from the inner city to the suburb.

At each site, four 14-day measurements were conducted, such that each site was measured in each season once. For $PM_{2.5}$ sampling the Harvard impactor (Air diagnostics Inc., Naples, Maine, USA) [22] was operated according to a standard operating procedure. Following sample collection, the same $PM_{2.5}$ filters were transported to laboratories for weighing and reflectance measurements. $PM_{2.5}$ absorbance (the reflectance of the filters) was measured according to procedures described previously [23]. NO_2 was measured with Palmes tubes, according to a standardized operating procedure [24]. For all pollutants annual averages were calculated. In brief, measurements at the 40 sites were not performed simultaneously. Therefore differences among the sites may have occurred due to temporal variation. As the measurements were intended to incorporate spatial variability only, the annual averages were adjusted for the impact of temporal variability using data from one site where continuous measurements were made over the entire study period.

The annual average concentrations were related to a set of predictor variables obtained from a GIS, using regression modelling. The following GIS variables were collected using GIS ARC VIEW version 3.2. (ESRI, Redlands, CA, USA): traffic density, heavy vehicle intensity, household density, population density. All these variables were determined for three different circular buffers around the sites. A detailed description of the GIS variables and the regression models will be provided in separate papers. In brief, a substantial fraction of the variability in annual concentrations at the measurement sites could be explained by the GIS variables. A larger percentage of the absorbance of $PM_{2.5}$ and NO_2 was explained than for $PM_{2.5}$. The most influential variables were traffic intensities in the 50 and 250 m buffers and address density in the 300 m buffer (for NO_2). The percentage of variability explained by the model (R^2) was 0.56, 0.67, and 0.62 for $PM_{2.5}$, $PM_{2.5}$ absorbance, and NO_2, respectively.

For 1,756 study subjects birth addresses could be converted into geographical coordinates. Using these coordinates the values for all the potential predictors were obtained for all study subjects. A quantitative estimate of air pollution exposure was obtained for each child by means of the regression model.

Statistical methods

Multiple logistic regression analyses were performed to analyse the relationship between respiratory symptoms and disease on the one hand and estimated air pollution exposure on the other hand. Potential confounding factors such as sex, parental atopy, maternal education, siblings, ETS at home, use of gas for cooking, home dampness, indoor moulds, and keeping of dogs and cats were adjusted for. Concentrations of $PM_{2.5}$, $PM_{2.5}$ absorbance, and NO_2 were all divided by their respective interquartile ranges, in order to create exposure variables that would yield mutually comparable coefficients in the statistical analyses. Results are presented as adjusted odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was defined by a two-sided alpha level of 5%.

Results

Description of the study population

A description of the study population is given in table 1. Lifetime prevalence of the selected outcomes are given for the age of 1 and 2 yrs, respectively.

Table 1. – Description of the study cohort

Variable	Frequency n/N	Prevalence %
Age of 1 yr		
Wheezing	258/1722	15.0
Cough w/o infection	151/1655	9.1
Dry cough at night	123/1737	7.1
Doctor diagnosed bronchial asthma	6/1731	0.4
Doctor diagnosed asthmoid/ spast./obstr. bronchitis	196/1735	11.3
Doctor diagnosed respiratory infections	1212/1728	70.1
Sneezing, running/stuffed nose w/o a cold	254/1743	14.6
Age of 2 yrs[#]		
Wheezing	416/1627	25.6
Dry cough at night	228/1614	14.1
Doctor diagnosed bronchial asthma	16/1600	1.0
Doctor diagnosed asthmoid/ spast./obstr. bronchitis	303/1616	8.8
Doctor diagnosed respiratory infections	1528/1695	90.2
Sneezing, running/stuffed nose w/o a cold	354/1638	21.6
Confounding variables		
Female sex	832/1756	47.4
Parental atopy	935/1756	53.3
ETS at home	398/1704	23.4
Maternal education		
<12 grades	633/1751	36.1
≥12 grades	1118/1751	63.9
Siblings	700/1712	40.9
Use of gas for cooking	221/1731	12.8
Home dampness	115/1731	6.6
Indoor moulds	534/1735	30.8
Keeping of pets	318/1739	18.3
Cat	159/1735	9.2
Dog	70/1735	4.0

n/N: number of subjects/total number of subjects; ETS: environmental tobacco smoke; obstr.: obstructive; spast.: spastic; w/o: without. [#]: lifetime prevalence.

All prevalence, except the prevalence of asthma, were sufficiently high to analyse the association with exposure to air pollution. Data on cough without a cold was available for the first year of life only. Pets were kept in 18% of homes and cats were more common than dogs. More than 50% of children had a positive parental history of atopy. Maternal education was high (64% of mothers had ≥12 grades).

Exposure to ambient air pollutants

The distribution of the estimated exposures to $PM_{2.5}$, $PM_{2.5}$ absorbance, and NO_2 are presented in table 2. There is a substantial variability in exposure to all three pollutants. Estimated exposures to $PM_{2.5}$, $PM_{2.5}$ absorbance, and NO_2 ranged from 11.9–21.9 $\mu g \cdot m^3$, from 1.38–4.39×10^{-5} m^{-1}, and from 19.5–66.9 $\mu g \cdot m^3$, respectively. The range in exposure

Table 2. – Distribution of estimated annual averages in the cohort

	$PM_{2.5}$ $\mu g \cdot m^{-3}$	$PM_{2.5}$ absorbance 10^{-5} m^{-1}	NO_2 $\mu g \cdot m^{-3}$
Minimum	11.9	1.38	19.5
10th percentile	12.2	1.47	21.6
25th percentile	12.5	1.54	23.0
50th percentile	13.1	1.70	26.4
Mean	13.4	1.77	27.8
75th percentile	14.0	1.88	31.5
90th percentile	14.9	2.13	35.2
Maximum	21.9	4.39	66.9

$PM_{2.5}$: particles with a cut-off aerodynamic diameter of 2.5 μm; NO_2: nitrogen dioxide.

was smallest for $PM_{2.5}$, where the difference between the 10th and 90th percentile was relatively small (12.2–14.9 $\mu g \cdot m^{-3}$). The exposure estimates for the different pollutants were very highly correlated. The correlations of $PM_{2.5}$ with $PM_{2.5}$ absorbance and NO_2 were 0.96 and 0.99 respectively; the correlation of $PM_{2.5}$ absorbance and NO_2 was 0.95.

Relationship between ambient air pollutant exposure and symptoms

Results of the multiple logistic regression analyses are presented in table 3. The associations between $PM_{2.5}$, $PM_{2.5}$ absorbance, and NO_2 on the one hand and cough without infection (OR (95% CI): 1.34 (1.11–1.61), 1.32 (1.10–1.59), and 1.40 (1.12–1.75), respectively) and dry cough at night in the first year of life (OR (95% CI): 1.31 (1.07–1.60), 1.27 (1.04–1.55), and 1.36 (1.07–1.74), respectively) on the other hand were found to be statistically significant. The effects on dry cough at night were attenuated for the second year of life. All other ORs were close to unity. Results of the multiple logistic regression analysis stratified for sex showed stronger effects in males compared to females (tables 4 and 5).

In addition, multiple logistic regression analyses stratified for parental atopy were conducted. The effects on dry cough at night were found to be somewhat higher in the group of children without parental atopy compared to children with parental atopy (data not shown). But differences between children with and without parental atopy were less pronounced than differences between males and females.

Discussion

In this study, reports of cough without infection and dry cough at night in the first year of life were found to be associated with exposure to traffic-related air pollution. The associations were attenuated for the second year of life. Stratified analyses showed stronger associations for males compared to females.

Exposure to traffic-related air pollution was assessed in a more sophisticated way than in many

Table 3. – Multiple logistic regression analysis of associations between symptoms in the first and second year of life and exposure to traffic-related air pollution

Exposure variable	Symptom variable					
	Wheeze	Cough without infection	Dry cough at night	Obstr./spast./ asthmoid bronchitis	Respiratory infections	Sneezing, runny/ stuffed nose
Age of 1 yr						
Subjects n	1597	1528	1607	1606	1600	1614
$PM_{2.5}$	0.91 (0.76–1.09)	1.34 (1.11–1.61)	1.31 (1.07–1.60)	0.98 (0.80–1.20)	1.04 (0.91–1.19)	1.01 (0.85–1.20)
$PM_{2.5}$ abs	0.93 (0.78–1.12)	1.32 (1.10–1.59)	1.27 (1.04–1.55)	0.99 (0.81–1.22)	1.03 (0.90–1.18)	0.95 (0.79–1.14)
NO_2	0.87 (0.70–1.08)	1.40 (1.12–1.75)	1.36 (1.07–1.74)	0.97 (0.77–1.23)	1.06 (0.91–1.24)	0.99 (0.81–1.22)
Age of 2 yrs						
Subjects n	1517		1507	1510	1577	1523
$PM_{2.5}$	0.96 (0.83–1.12)	NA	1.20 (1.02–1.42)	0.92 (0.78–1.09)	0.98 (0.80–1.20)	0.96 (0.82–1.12)
$PM_{2.5}$ abs	0.98 (0.84–1.14)	NA	1.16 (0.98–1.37)	0.94 (0.79–1.12)	0.99 (0.80–1.22)	0.92 (0.78–1.09)
NO_2	0.94 (0.79–1.12)	NA	1.24 (1.02–1.51)	0.90 (0.74–1.10)	0.98 (0.78–1.25)	0.93 (0.78–1.12)

Data are presented as [#] adjusted odds ratio of symptoms (95% confidence interval) associated with a change in concentration of 1.5 μg·m^{-3} for $PM_{2.5}$, 0.4×10^{-5}·m^{-1} for $PM_{2.5}$ abs and 8.5 μg·m^{-3} for NO_2. $PM_{2.5}$: particles with a 50% aerodynamic cut-off diameter of 2.5 μm; NO_2: nitrogen dioxide; obstr.: obstructive; spast.: spastic; NA: not available. [#]: Adjusted for sex, parental atopy (yes/no), maternal education, siblings (y/n), environmental tobacco smoke at home (y/n), use of gas for cooking (y/n), home dampness (y/n), indoor moulds (y/n), keeping of dogs (y/n) and cats (y/n) study (German Infant Nutrition Intervention Programme (GINI)-intervention, GINI-observation, Lifestyle Related Factors on the Human Immune System and Development of Allergies in children (LISA)).

other studies relying on proximity to road traffic [3, 7, 8, 15], census data on car traffic and/or truck traffic [8, 9, 14, 17], and self-reported traffic intensities [10–13] as proxies for exposure to traffic exhaust. These results show that the variance of measured, traffic-related air pollutants could be readily explained by a small number of variables present in available GIS databases [24]. It has been shown that the incorporation of additional variables besides distance to roadsides and immediate traffic intensity provided further additional explanatory power.

In the present study, rather unspecific respiratory symptoms were found to be associated with estimated exposure to traffic-related air pollution. No other cohort studies on the association between exposure to traffic-related air pollutants and respiratory health in infancy have been published to date. Most studies on the effects of traffic-related air pollution on asthma in children are cross-sectional studies dealing with school children. These studies have suggested that exposure to air pollution is associated with increased reporting of respiratory and allergic symptoms and illnesses

Table 4. – Multiple logistic regression analysis of associations between symptoms in the first and second year of life and exposure to traffic-related air pollution in males

Exposure variable	Symptom variable					
	Wheeze	Cough without infection	Dry cough at night	Obstr./spast./ asthmoid bronchitis	Respiratory infections	Sneezing, runny/ stuffed nose
Age of 1 yr						
Subjects n	844	811	50	845	846	853
$PM_{2.5}$	0.91 (0.72–1.16)	1.43 (1.14–1.80)	1.39 (1.08–1.78)	0.97 (0.76–1.25)	1.04 (0.87–1.25)	0.97 (0.77–1.24)
$PM_{2.5}$ abs	0.91 (0.71–1.15)	1.38 (1.11–1.71)	1.31 (1.04–1.67)	1.00 (0.78–1.27)	1.03 (0.86–1.23)	0.90 (0.70–1.16)
NO_2	0.86 (0.65–1.14)	1.52 (1.16–2.00)	1.45 (1.07–1.98)	0.96 (0.72–1.28)	1.05 (0.85–1.31)	0.94 (0.71–1.25)
Age of 2 yrs						
Subjects n	801		797	791	832	801
$PM_{2.5}$	0.93 (0.76–1.14)	NA	1.25 (1.01–1.55)	0.92 (0.74–1.14)	0.99 (0.74–1.31)	0.91 (0.73–1.12)
$PM_{2.5}$ abs	0.92 (0.75–1.13)	NA	1.17 (0.95–1.44)	0.91 (0.72–1.13)	0.96 (0.73–1.26)	0.83 (0.66–1.05)
NO_2	0.88 (0.69–1.12)	NA	1.28 (0.99–1.66)	0.89 (0.69–1.14)	0.99 (0.71–1.37)	0.86 (0.66–1.11)

Data are presented as adjusted [#] odds ratio of symptoms (95% confidence intervals) associated with a change in concentration of 1.5 μg·m^{-3} for $PM_{2.5}$, 0.4×10^{-5}·m^{-1} for $PM_{2.5}$ abs and 8.5 μg·m^{-3} for NO_2. $PM_{2.5}$: particles with a 50% cut-off aerodynamic diameter of 2.5 μm; NO_2: nitrogen dioxide; obstr.: obstructive; spast.: spastic; NA: not available. [#]: Adjusted for parental atopy (yes/no), maternal education, siblings (y/n), environmental tobacco smoke at home (y/n), use of gas for cooking (y/n), home dampness (y/n), indoor moulds (y/n), keeping of dogs (y/n) and cats (y/n) study (German Infant Nutrition Intervention Programme (GINI)-intervention, GINI-observation, Lifestyle Related Factors on the Human Immune System and Development of Allergies in Asthma (LISA)).

Table 5. – Multiple logistic regression analysis of associations between symptoms in the first and second year of life and exposure to traffic-related air pollution in females

Exposure variable	Symptom variable					
	Wheeze	Cough without infection	Dry cough at night	Obstr./spast./ asthmoid bronchitis	Respiratory infections	Sneezing, runny/ stuffed nose
Age of 1 yr						
Subjects n	753	717	757	761	754	63
$PM_{2.5}$	0.94 (0.70–1.27)	1.19 (0.84–1.70)	1.17 (0.81–1.68)	0.98 (0.68–1.41)	1.06 (0.87–1.31)	1.08(0.84–1.41)
$PM_{2.5}$ abs	1.01 (0.74–1.37)	1.25 (0.87–1.78)	1.16 (0.79–1.71)	0.94 (0.63–1.39)	1.05 (0.85–1.30)	1.06(0.80–1.39)
NO_2	0.90 (0.64–1.28)	1.22 (0.81–1.85)	1.20 (0.78–1.84)	0.97 (0.63–1.48)	1.09 (0.86–1.38)	1.09(0.80–1.47)
Age of 2 yrs						
Subjects n	716		710	719	745	722
$PM_{2.5}$	1.04 (0.83–1.30)	NA	1.13 (0.86–1.48)	0.91 (0.68–1.21)	0.98 (0.73–1.31)	1.04(0.83–1.31)
$PM_{2.5}$ abs	1.07 (0.85–1.36)	NA	1.12 (0.84–1.48)	0.95 (0.71–1.28)	1.04 (0.75–1.43)	1.06(0.83–1.34)
NO_2	1.03 (0.80–1.34)	NA	1.17 (0.86–1.60)	0.90 (0.65–1.25)	0.98 (0.70–1.39)	1.04(0.79–1.35)

Data are presented as [#] adjusted odds ratio of symptoms (95% confidence intervals) associated with a change in concentration of 1.5 $\mu g \cdot m^{-3}$ for $PM_{2.5}$, $0.4 \times 10^{-5} \cdot m^{-1}$ for $PM_{2.5}$ abs and 8.5 $\mu g \cdot m^{-3}$ for NO_2. $PM_{2.5}$: particles with a 50% aerodynamic diameter of 2.5 μm; NO_2: nitrogen dioxide; obstr.: obstructive; spast.: spastic; NA: not available. [#]: Adjusted for parental atopy (yes/no), maternal education, siblings (y/n), environmental tobacco smoke at home (y/n), use of gas for cooking (y/n), home dampness (y/n), indoor moulds (y/n), keeping of dogs (y/n) and cats (y/n) study (German Infant Nutrition Intervention Programme (GINI)-intervention, GINI-observation, Lifestyle Related Factors on the Human Immune System and Development of Allergies in Asthma (LISA)).

such as upper respiratory symptoms [18], cough symptoms [4, 8, 16, 25, 26], wheeze [3, 6, 8, 9, 11, 12, 25], bronchitic symptoms [12], bronchitis [4, 16, 26], asthma [8, 10, 25, 27], runny nose [8], and allergic rhinitis [11, 13], medical care visits for asthma [14] and decreased lung function [6, 9, 17, 28]. Only a few studies, assessing the relationship between NO_2 and particle concentrations and respiratory symptoms and illnesses in infants, were found in literature. These studies did not provide unequivocal evidence of air pollution effects. BRAUN-FAHRLANDER and co-workers [5, 29] analysed associations between outdoor NO_2 concentrations and respiratory symptoms in Swiss children aged 0–5 yrs. They found the frequency of respiratory symptoms per child per day [27] as well as the duration of respiratory symptoms [5] increased with increasing levels of NO_2. Furthermore, they found an association between particle concentrations and incidence and duration of respiratory symptoms [5]. PERSHAGEN et al. [30] found NO_2 concentrations estimated from validated dispersion models related to incidence rates of wheezing bronchitis in females aged 4 months–4 yrs (90% of the children were <2 yrs). In another study conducted by MAGNUS et al. [31], an association between bronchial obstruction in children aged 0–5 yrs and NO_2 levels measured inside and outside the childrens' homes as well as the distance of the child's home to the nearest street, could not be shown. SAMET et al. [32] analysed the relationship between indoor NO_2 and incidence rate of upper and lower respiratory illness in infants aged 0–18 months and no association could be shown. The same was true for FARROW et al. [33] who failed to show an association between symptoms and concentrations of NO_2 measured inside the bedrooms and outside the homes of infants aged 3–12 months. In these indoor studies, however, NO_2 represents emissions from unvented gas stoves, which may have a very different composition than traffic exhaust.

Results for cough were not presented separately for the studies dealing with infants, but they were for some of the studies dealing with schoolchildren. Five studies showed a significant association between symptoms of cough and traffic-related air pollution [4, 8, 16, 25, 26]. The effects for wheeze reported for several other studies, as well as the effects for bronchitis, could not be confirmed by the present study, but reports of wheeze in children aged 1 or 2 yrs probably represent different disease patterns than reports of wheeze in school children. The prevalence of asthma was not sufficient to allow an analysis of the relationship with traffic-related air pollution.

Associations between exposure to traffic-related air pollutants and parameters of respiratory health for the Dutch and the Swedish centres will be published in separate papers. Analyses of the respiratory symptom data of the Dutch part of the TRAPCA study have shown an association between exposure to traffic-related air pollution and wheeze and asthma in the first 2 yrs of life. The significant association between cough and air pollution in the German cohort could not be confirmed. In Sweden there was a nonsignificant positive association between asthma at the age of 2 yrs (the only end point analysed) and air pollution. Since the diagnosis of specific respiratory illnesses during the first years of life is difficult, a more definitive conclusion about the risk of traffic-related air pollution on respiratory health and in particular on asthma requires further studies when the children are older.

Only a few studies have reported stratified analyses by sex. VAN VLIET et al. [8], BRUNEKREEF et al. [17], and PERSHAGEN et al. [30] found stronger effects for

females compared to males. This disagrees with the results in this study of stronger effects in males compared to females. PERSHAGEN et al. [30] argued that air pollution effects might be more difficult to detect in cases where very young males have a higher incidence of symptoms than females. In accordance with PERSHAGEN et al. [30], higher incidences of respiratory symptoms in males compared to females were also found in the present study (data not shown). This is also consistent with a retrospective analysis of the data of the European Respiratory Health Survey [34] which showed that males aged 0–5 yrs have a significantly higher risk of developing asthma than females. It has been shown that females aged 0–2 yrs have larger airways in relation to lung size than males [35], and that specific airway resistance is lower at any given height in female then in male infants of this age group [36]. These differences in lung growth and development between males and females might be responsible for the higher incidences of symptoms and the greater susceptibility of males, resulting in higher effects of air pollution in males compared to females. However, separate analyses for males and femalea are available for a very limited number of studies and the differences are still not completely understood.

There was a high correlation found between estimated concentrations of PM2.5, PM2.5 absorbance, and NO$_2$ and therefore similar associations with health outcomes for the three pollutants. Thus, it was impossible to distinguish potential health effects of emissions from all motorized vehicles from those of heavy vehicles only.

The effects of traffic-related air pollutants on symptoms of cough were attenuated for the second year of life. The meaning of this finding is not quite clear. It could be due to the fact that 454 infants moved within the second year of life hence introducing some "noise". But results of additional analyses without those children (for whom estimated exposures at their birth address does not represent lifetime exposure) differed only marginally from those presented in table 3 (data not shown). Furthermore, one might speculate that the associations between traffic-related air pollution at birth addresses and symptoms of cough were attenuated as a result of an increased mobility of the children in the second year of life e.g. due to day-care attendance. Further analyses when the children are older will have to show whether the effects observed in the present study are transient or whether traffic-related air pollutants have nontransient effects on the development of inhalant allergy, asthma and other chronic respiratory conditions in children.

The aim of the present study was to analyse the health effects associated with long-term exposure to traffic-related air pollutants. It is generally agreed to refer to studies designed as the TRAPCA study, as studies on long-term exposure of air pollution. In fact, the study was not designed in a way that allowed for the disentanglement long-term effects from short-term effects. The observed effects of annual average concentrations of traffic-related air pollutants on life time prevalence of symptoms of cough might also result from short-term exposure, that is exposure just before onset of symptoms, given that a location with a higher annual average concentration is also more likely to have higher peaks in daily average concentrations in the course of the 1-yr period of interest. Since both, exposure and health data, were collected on an annual basis and not on a daily basis, it is impossible, by the design of the study, to distinguish between long-term and short-term effects. However, study designs, like that of the present study, are referred to as long-term study designs, although they include both, long-term and short-term effects. In contrast to this, studies on short-term effects relating day-to-day variation in air pollution concentration to day-to-day variation in health outcomes have a completely different study design.

Reporting bias is possible when there is increased awareness of exposure in parents of symptomatic children. However, the underlying cohort studies have been primarily designed to analyse the effects of nutrition and lifestyle-related factors on the development of atopic disease and the immune system. Thus, the parents were not aware of the hypothesis of the present study. Furthermore, parents were unaware of the estimated exposures to air pollutants. Therefore, it seems unlikely that the relationship between traffic-related air pollution and symptoms of cough may have been caused by over-reporting of symptoms by parents exposed to high levels of air pollution.

A large set of confounding variables was taken into account in this study, and all results presented were adjusted for these variables. After adjustment for sex parental atopy, maternal education, siblings, ETS at home, use of gas for cooking, home dampness, indoor moulds and the keeping of dogs and cats the associations of symptoms of cough with traffic-related air pollution remained.

To conclude, there is some indication of an association between exposure to traffic-related air pollution and symptoms of cough. Associations were stronger in males than in females. Due to the very young age of the children, it is too early to draw definitive conclusions from this for the development of asthma. Thus, the association between long-term exposure to traffic-related air pollution and respiratory symptoms needs further study when the children are older.

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