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Eczema, respiratory allergies, and traffic-related air pollution in birth cohorts from small-town areas

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ABSTRACT

Background: Traffic-related air pollution (TAP) impairs respiratory health and could influence the development of allergies, as was demonstrated in urban areas with relatively high pollution. Whether eczema is affected by TAP was rarely investigated.

Objective: To investigate whether exposure to TAP affects eczema and respiratory allergies also in small-town areas with lower concentrations of pollution.

Methods: Between 1995 and 1999, we recruited 3390 newborns from small-town areas. Diagnoses and symptoms of eczema and respiratory allergies were recorded by annual questionnaires. Seventy-seven percent of families participated until the child's 6th birthday, when a clinical test for eczema and IgE-sensitization was performed. Individual exposure to traffic-related soot and NO₂ at the children's home addresses was determined by land-use-regression. We used Cox-regression/log-binomial-regression to determine its confounder-adjusted association with incidence and prevalence of eczema and respiratory allergies.

Results: The prevalence of eczema at age 6 was significantly higher in children who resided in areas where TAP was higher. The adjusted relative risk for doctor diagnosed eczema for instance was 1.69 (95% confidence interval 1.04–2.75) per 90%-range of soot concentration. Current eczema at the 6 year clinical investigation was likewise associated, children with parental allergies showed significantly stronger effects ($p < 0.05$). Incidence of eczema was not affected. No associations between TAP and asthma, hay fever, or allergic sensitization emerged.

Conclusion: Eczema was sensitive to TAP, effects emerged even in lower polluted small-town areas of Germany. They could be seen for prevalence but not incidence of eczema. This is equivalent to a longer duration of eczema in exposed children.

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1. Introduction

In affluent industrialized countries, traffic-related air pollution (TAP) constitutes an increasing fraction of anthropogenic air pollution. Numerous studies have investigated the effects of exposure to TAP on children's respiratory health and allergies. [1–

24]. Most studies done so far demonstrated the effects of TAP on asthma or related symptoms; most found positive associations although not all were significant. Nine studies of those mentioned above specifically investigated hay fever or related symptoms, and all but one [1] found a positive association. Eight studies investigated allergic sensitization and one-half found a positive association with TAP. The association between eczema and exposure to TAP has not been well investigated. Eight studies have addressed this association [3,7,8,10,12,13,21,24], and four showed a significant positive one. We therefore specifically focused on eczema.

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Most of the studies were conducted in urban areas with relatively high levels of pollution. Thus we lately demonstrated for children from the urban portion of the GINIplus and LISApplus birth cohorts [25,26] (Munich, South Germany), that asthma, hay fever, eczema and allergic sensitization against outdoor allergens were associated with TAP. [24] It is unknown, whether effects also emerge in rural, small town areas, where pollution is lower. To clarify this question we used the rural portion of the GINIplus and LISApplus birth cohorts (Wesel, North/West Germany).

2. Material and methods

2.1. Study area

The study was conducted in the North-Western part of North-Rhine Westphalia (Germany), which comprises 37 adjacent communities up to 100 km north of the Ruhr area that are inhabited by 8000–80,000 people each. The landscape is flat, ranging from 25 to 50 m above sea level and farm houses lay singly between small central towns. Only a few highways and major roads cross the area, connecting the Ruhr area with the Netherlands and northern Germany and interconnecting the towns. The study area covers approximately 3300 km² and is referred to as the “Wesel” area.

2.2. Study subjects

Subjects were participants in two ongoing birth cohort studies: the “German Infant study on the influence of Nutrition Intervention plus air pollution and genetics on allergy development” study (GINIplus) and the “Life style Immune System Allergy plus air pollution and genetics” study (LISApplus). Detailed descriptions of recruitment are provided elsewhere. [27,28] Briefly, in GINIplus, 5991 newborns were recruited between September 1995 and June 1998 from 16 maternity wards in Munich and “Wesel”. Families with a history of allergies ($n = 2252$) agreed to participate in the nutrition intervention arm of GINIplus, all others participated in the non-intervention arm. Children from both groups were followed up with identical instruments at the ages of 1, 2, 3, 4, and 6 years. In LISApplus, 3097 neonates from Munich, Leipzig, Bad Honnef, and “Wesel” were recruited between December 1997 and January 1999. They were followed up at the ages of 0.5, 1, 1.5, 2, 4, and 6 years.

In our analysis, inclusion was restricted to the 3390 children recruited from the “Wesel” area, 3042 from GINIplus and 348 from LISApplus. The study protocol was approved by the local ethics committee and written informed consent was obtained from all participating families.

2.3. Exposure assessment

Exposure assessment procedures were identical to those in the “Traffic Related Air Pollution and Childhood Asthma” (TRAPCA) study [29], which was done in the Munich metropolitan area as well as in the Netherlands and in Stockholm and based on one measurement campaign in 1999/2000. Details of the exposure assessment for the small town “Wesel” area have been described elsewhere. [30] In short, the models were based on a 1-year measurement program conducted in 2002, concentrations of NO₂, fine particulate mass (PM_{2.5}), and filter absorbance of PM_{2.5} as a marker for soot concentration, were measured at 30 points and 14-day samples were taken for each season and site. The NO₂ concentration and PM_{2.5} absorbance as a marker of soot, but not PM_{2.5} mass, could be described by a linear combination of daily traffic and the distance to a highway. These land-use regression-models for NO₂ and PM_{2.5} absorbance (“soot”) were applied to the

home addresses of the cohort members to describe individual levels of long-term exposure. Additionally, exposure was characterized by the distance from the domicile to the next major road: living near (<50 m using Geographic Information System (GIS)) a major road traversed by more than 10,000 cars per day. If the child moved between birth and 6 years of age the mean of the values calculated for the different addresses was used to characterize lifelong exposure.

2.4. Determination of outcomes and covariates by questionnaires

At each follow-up, the subjects' parents completed questionnaires about health outcomes and covariates.

2.4.1. Outcomes

At each follow up, parents were asked whether a physician had diagnosed asthma, asthmoid/spastic/obstructive bronchitis, hay fever, or atopic eczema in the child since the last follow-up. If the last follow up was 2 years ago, then the prevalence of the diagnosis was asked separately for the 2 individual years. Additionally, parents were asked whether the child had experienced the following: wheezing, sneezing/running stuffed nose without a cold, or an intermittent, itchy skin rash that lasted at least two weeks. In the 6th year questionnaire, the ISAAC (International Study on Asthma and Allergies in Childhood [31]) core questions for 6- and 7-year olds were included (different definition of eczema symptoms: intermittent itchy rash lasting at least 6 months).

2.4.2. Covariates

Covariates were parental allergy (asthma, hay fever, or eczema in the father or mother, determined at the birth of child); gender; education of parents (maximum education of either parent categorized as <10 years = 10 years, and >10 years); maternal smoking during pregnancy; smoking in the child's home; contact with dog, cat, or other furry animal in the 1st year of life; elder siblings; use of gas for cooking; home dampness, indoor moulds; and living on a farm. The list of covariates was the same as in the Munich portion of this cohort with the exception of “living on a farm”, which was not relevant for the urban Munich children.

2.5. Determination of specific IgE and eczema

Upon the child's 6th birthday, a clinical examination was offered to all families. Current eczema was determined following the ISAAC II protocol. [32] Specific IgE against common food allergens and inhalant allergens were determined by standardized methods with CAP-RAST FEIA (Pharmacia Diagnostics, Freiburg, Germany). A screening test for atopy was used to detect specific IgE antibodies against inhalant allergens (SX1: timothy grass, rye, birch, mugwort, house-dust mites, cats, dogs and moulds) in the serum. The children who had positive results for SX1 were tested for single specific allergens. Sensitisation to pollen allergens (outdoor) included timothy grass, rye, birch, and mugwort and sensitisation to indoor allergens included house-dust mites, cats, dogs and moulds. Inhalant sensitisation and specific allergen sensitisation were defined as any specific IgE-antibody value ≥ 0.35 kU/l.

2.6. Statistical analysis

We used Cox-regression analysis to evaluate the risk for allergy diagnosis and symptoms associated with TAP exposure at birth. The development of eczema, itchy skin rash, and sneezing between the birth and the age of 6 years was analyzed. For asthma/spastic/obstructive bronchitis, wheezing and hay fever the analysis was restricted to the 3- to 6-years age range because asthma and hay

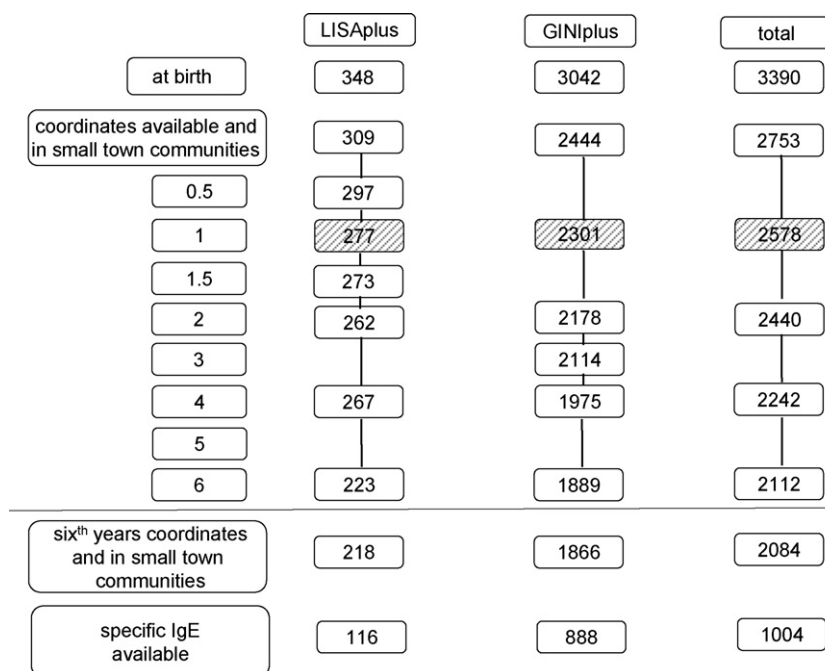


Fig. 1. Participation in the cohort study based on the first year when all parents filled out a common questionnaire about their children's health for the first time. All participants were from the "Wesel" area.

fever cannot be diagnosed with certainty before the third birthday. We tested the proportionality assumption of the Cox model by creating interactions of all covariates with time. These interactions were incorporated into the model when significant ($p < 0.05$). [33] All covariates were considered as potential confounders. Additionally, the design variables "study" (GINIplus or LISAplus), "intervention" (yes or no), and "study formula" (four different randomly assigned formulas applied in the intervention study [25]) were implemented. The SAS procedure PHREG (SAS 9.3) was applied for Cox regression and its exact method was used.

In addition, we analyzed the association between exposure and allergy prevalence for children in the 6th year of life by applying log-binomial models using a previously published procedure, [34,35,36] this procedure was applied because several prevalences were greater than 0.1 and odds ratios estimated by logistic regression are not good approximations for prevalence ratios in these cases. The same covariates as identified in the Cox regression were used in these models.

3. Results

3.1. Participation

At birth, 3390 children from small towns ("Wesel" area) were recruited for participation in this study. Nineteen percent ($n = 637$) were excluded from the analysis because no birth address was available, or they lived in the adjacent, more polluted Ruhr Area. Seventy-seven percent participated between the first and 6th year (Fig. 1). In general, participation depended on parental education, eighteen percent of non-participants, but only 13% of participants, had parents with fewer than 10 years of education. Non-participants were more likely to have a mother who smoked, to have contact with furry pets, and be non-breast-fed. Participation did not depend on the allergies present in the family or the child.

Questionnaire response was better than response in the clinical examination, about 50% of the children, who gave a questionnaire at the age of 6 years, also participated in the clinical examination at the age of 6 ($n = 1004$). The average prevalence of allergies or

symptoms was 1.7-times higher in participants of the examination than in non-participants, having sent a questionnaire only. However, participation in the clinical examination did not depend on exposure.

3.2. Exposure

Table 1 characterizes exposures to TAP for the cohorts. At their birth addresses, the PM 2.5 absorbance (soot) ranged from $0.8 \times 10^{-5} \text{ m}^{-1}$ to $2.3 \times 10^{-5} \text{ m}^{-1}$ and NO_2 concentrations ranged from $13.9 \mu\text{g}/\text{m}^3$ to $41.4 \mu\text{g}/\text{m}^3$. Exposure at the birth address was highly correlated with exposure at the 6-years address, but children were less likely to live near a busy road at the age of 6 years than at birth. The relative risks describing the association between exposure and respiratory allergies and eczema were based on the inner 90% range: $0.5 \times 10^{-5} \text{ m}^{-1}$ $\text{PM}_{2.5}$ absorbance and $9 \mu\text{g}/\text{m}^3$ NO_2 .

3.3. Covariates

All covariates considered as potential confounders are described in Table 2. Both cohorts were similar with regard to the prevalence of these covariates; however, minor differences did occur. Children from the later-born LISAplus cohort had better educated parents and mothers more likely to have smoked during pregnancy, illustrating known trends. Other differences reflected differences in study design: 40% of the members of GINIplus were enrolled in the intervention arm and about 20% received one of four special intervention formulas. [25]

3.4. Cumulative incidence and prevalence of eczema and respiratory allergies

The cumulative incidence up to age 6 and the prevalence at the age of 6 are presented in Table 3. Doctors diagnosed eczema in more than 20% of the children between birth and age 6. Eight percent still had doctor-diagnosed eczema in the 6th year of life. The point prevalence of manifest eczema at the clinical investiga-

Table 1

Characteristics of traffic-related pollution exposure estimated for the home addresses of the cohort members at birth and 6 years of age.

	Min	5th percentile	25th percentile	50th percentile	Mean	75th percentile	95th percentile	Max
At birth (N=2753)								
PM 2.5 absorbance (soot) (10^{-5} m^{-1})	0.8	1.3	1.5	1.6	1.6	1.7	1.9	2.3
NO ₂ ($\mu\text{g}/\text{m}^3$)	13.6	19.5	22.3	23.9	24.0	25.4	29.1	41.4
Distance to major road	$\leq 50 \text{ m}$ 17.2%		$\leq 250 \text{ m}$ 62.0%		$\leq 1000 \text{ m}$ 98.1%		$> 1000 \text{ m}$ 1.9%	
At age 6 years (N=2084)								
PM2.5 absorbance (soot) (10^{-5} m^{-1})	0.8	1.2	1.5	1.6	1.6	1.7	1.8	2.3
NO ₂ ($\mu\text{g}/\text{m}^3$)	13.6	19.2	22.2	23.7	23.7	24.9	27.7	42.1
Distance to major road	$\leq 50 \text{ m}$ 12.9%		$\leq 250 \text{ m}$ 59.7%		$\leq 1000 \text{ m}$ 97.6%		$> 1000 \text{ m}$ 2.4%	

tion was 4%. The cumulative incidence of doctor-diagnosed asthma/obstructive/spastic bronchitis was 20% and 10%, respectively. Hay fever and related symptoms were reported with similar frequencies but were still uncommon in these 6-year olds. Twenty-six percent of the children who gave blood during the clinical examination were sensitized against inhalant allergens.

The prevalence of outcome variables in the “Wesel” area was different from the prevalence in Munich [24]. Whereas the prevalence of asthmatic/spastic/obstructive bronchitis/asthma was higher in “Wesel” (10.4%) than in Munich (6.6%), the prevalence of eczema was comparable (7.9% in “Wesel” and 9.1% in Munich), and the prevalence of hay fever, related symptoms and sensitization against inhalant allergens finally was lower in “Wesel” (4.8%, 13.5%, 26.0%) than in Munich (5.8%, 15.8%, 31.5%).

3.5. Association of eczema and respiratory allergies with traffic-related exposure

3.5.1. Incidence

The incidences of diagnoses and symptoms were not associated with TAP exposure at birth; none of the adjusted relative risks were significantly greater than one (Table 4).

3.5.2. Prevalence

In contrast to incidence, the prevalence of doctor-diagnosed eczema in the 6th year of life was associated with exposure (Table 5); specifically, the prevalence was significantly higher if soot concentration was higher (1.69-times, 95% confidence interval [CI], 1.04–2.75). The relative risk for current eczema at

the day of the investigation was even higher (2.13) but not significant because of the smaller numbers of children having participated in the clinical examination. The risk for current eczema was 2.2 for children living less than 50 m from streets with heavy traffic and this was nearly significant ($p = 0.068$). The difference between cumulative incidence and prevalence can be explained by differences in duration of eczema, which was longer in children with greater exposure to TAP. The adjusted (same covariates as above) geometric mean duration of doctor diagnosed eczema during the first 6 years of life was 2.7 years (95% CI, 2.4–3.1) for children with a birth address less than 50 m from a main road ($> 10,000$ cars/day) as compared to 2.2 years (95% CI, 2.0–2.3) for children living farther away. This difference was statistically significant ($p < 0.05$).

Effects on other outcomes than eczema could not be detected.

The effects of TAP on eczema were higher for children with parental allergy. This interaction between predisposition and exposure was highly significant for current eczema. In children with parental allergy the relative risk for current eczema, when soot concentration was higher, was 23. Because of small numbers however the confidence interval is very large: 95% CI: 2.3–230.

4. Discussion

In this small-town portion of the birth cohort studies GINIplus and LISApplus, we found a positive association between individually estimated TAP exposure and the prevalence of eczema at age 6, but not with asthma, hay fever or atopy. The effect on eczema was due to a longer duration of eczema in children exposed to higher levels of TAP.

Table 2

Description of covariates for the two cohorts LISApplus and GINIplus.

	LISApplus		GINIplus		All	
	N	%	N	%	N	%
Gender, male	277	53.4	2301	51.2	2578	51.5
Parents' years of schooling < 10	272	11.8	2296	14.3	2568	14.1
Parents' years of schooling = 10	272	36.8	2296	41.3	2568	40.8
Parents' years of schooling > 10	272	51.5	2296	44.3	2568	45.1
Smoking of mother during pregnancy	263	20.5	2258	16.4	2521	16.9
Smoking in home	273	31.5	2247	29.3	2520	29.6
Use of gas for cooking	273	2.6	2224	4.4	2497	4.2
Contact with dog (1 year)	275	17.1	2272	12.1	2547	12.6
Contact with cat (1 year)	275	10.2	2272	6.7	2547	7.1
Contact with other furry pet (1 year)	275	2.9	2272	2.6	2547	2.6
Moulds in home	276	19.9	2252	19.4	2528	19.5
Dampness in home	277	4.0	2254	3.9	2531	3.9
Biological siblings at birth of child	275	51.6	2296	54.2	2571	53.9
Participant of intervention study	277	0.0	2301	35.3	2578	31.5
Living on a farm	243 ^a	8.2	1768 ^b	10.2	2011	9.9
Parental Allergies	257	44.0	2278	40.8	2535	41.1

^a 4th year questionnaire.^b 6th year questionnaire.

Table 3

Description of allergic manifestations in children: cumulative incidence up to the age of 6, prevalence in the 6th year, and point prevalence of flexural eczema and specific IgE-sensitization at 6th birthday.

	Cumulative incidence ^a up to age 6		Prevalence in 6th year of life	
	N	%	N	%
Doctor- diagnosed eczema	2553 ^b	23.1 ^b	1971	7.9
Symptom for eczema	2522 ^b	30.7 ^b	2060	5.7
Current eczema at day of investigation			1004	4.4
Doctor-diagnosed asthmatic/spastic/obstructive bronchitis/asthma	2200 ^c	19.7 ^c	1974	10.4
Symptom for asthmatic/spastic/obstructive bronchitis/asthma	2217 ^c	15.1 ^b	2046	9.0
Doctor-diagnosed hay fever	2210 ^c	6.5 ^c	1976	4.8
Symptom for hay fever	2574 ^b	27.9 ^b	2075	13.5
Sensitization ^d against				
Inhalant allergens (SX1)	–	966	26.0	
Outdoor allergens	–	964	18.8	
Indoor allergens	–	964	17.6	

^a Estimated by life table methods.

^b N at age 1 year and cumulative incidence 1st–6th year of life.

^c N at age 4 year and cumulative incidence 4th–6th year of life.

^d Specific IgE > 0.35 kU.

This study has several strengths, one of which is the individual-based exposure assessment. Exposure assessments were performed according to procedures previously applied in the metropolitan Munich area, in Stockholm, and the Netherlands. [29] Measurements from small-town areas are rare; we have demonstrated that even in such areas, considerable variations in traffic-related NO₂ and filter absorbance (“soot”) do occur. Exposure characteristics in “Wesel” differed from those in Munich and in the adjacent Netherlands: PM_{2.5} mass concentrations in “Wesel” were fairly high [30] yet they were unrelated to traffic, in contrast to the two other study regions. It is likely that agricultural sources of PM_{2.5} mass and/or long range transportation from the Ruhr area predominate in the “Wesel” area. However, filter absorbance was related to traffic and the ranges and means of the values were only slightly lower than in the other areas. Mean NO₂ concentrations were considerably lower in “Wesel” than in Munich (mean: 34.0 µg/m³ versus 23.8 µg/m³) [19], demonstrating lower overall pollution.

Associations between TAP, eczema and respiratory allergies in the metropolitan Munich area differ from the results gained in the lower polluted “Wesel” area; even though identical outcome determinations and types of individual exposure assessment were used. [24] In Munich, a significant and positive association

between TAP exposure and asthma, hay fever, eczema and allergic sensitization emerged whereas in “Wesel” only eczema was affected. The existence of an effect of TAP on eczema even in moderately polluted areas indicates that eczema is sensitive to TAP. The results from the questionnaires were confirmed by the results of the clinical examination performed once the children reached the age of 6 years. Eczema has not been examined often in studies concerning the effects of TAP; so far positive associations have been found in studies conducted in urban areas. [3,13,19,24]

The higher overall pollution in Munich than in “Wesel” might also be the reason for higher prevalence of hay fever and inhalant sensitization in Munich than in “Wesel”. Asthma related outcomes however occurred more often in “Wesel” than in Munich. This must be due to other causes than TAP and might eventually be related to the high overall particle pollution, which was not related to traffic, or to climatic factors.

Another strength of this study is the use of a cohort with outcome assessments at several points in time. To date, no study has used the design of a cohort study to disentangle the effects on eczema incidence from those on prevalence. For the small-town area of “Wesel”, we demonstrated that the effect of TAP on eczema was due to prolongation of the duration of eczema and not to the incidence of new cases.

Table 4

Association between traffic-related pollution exposure at birth-address and eczema, asthma and hay fever between birth and the 6th year of life: results of COX regression.

	N	Soot ^b	NO ₂ ^c	<50 m ^d
		Adjusted ^a RR (95% CI) p	Adjusted ^a RR (95% CI) p	Adjusted ^a RR (95% CI) p
Doctor-diagnosed eczema ^e	2380	1.13 (0.88–1.44) 0.336	1.11 (0.85–1.44) 0.447	1.01 (0.81–1.27) 0.925
Symptom for eczema ^e	2364	1.03 (0.83–1.28) 0.783	1.05 (0.83–1.33) 0.661	1.14 (0.94–1.39) 0.187
Doctor-diagnosed asthmatic/spastic/ob-structive bronchitis/asthma ^f	2059	1.16 (0.87–1.54) 0.301	1.17 (0.86–1.58) 0.319	0.86 (0.66–1.14) 0.305
Symptom for asthmatic/spastic/ob-structive bronchitis/asthma ^f	2067	0.84 (0.61–1.17) 0.303	0.76 (0.53–1.09) 0.131	0.78 (0.57–1.08) 0.138
Doctor-diagnosed hay fever ^f	2066	1.28 (0.78–2.11) 0.331	1.22 (0.72–2.06) 0.462	1.09 (0.69–1.72) 0.704
Symptom for hay fever ^e	2399	1.05 (0.84–1.32) 0.648	1.01 (0.79–1.28) 0.943	1.00 (0.81–1.23) 0.981

^a Adjusted for study (LISApplus, GINIplus), gender, years of parental schooling, maternal smoking in pregnancy, environmental tobacco smoke, use of gas for cooking, contact with dog, cat, other furry pet, moulds in home, dampness in home, biological siblings at birth of child, participant of intervention, intervention formulas, living on a farm, parental disease atopy, hay fever or eczema, year × gender (eczema, symptom of eczema), year × contact with dog (eczema), year × maternal smoking (symptoms of hay fever).

^b Soot: absorbance of particles less than 2.5 µm diameter ($0.5 \times 10^{-5} \text{ m}^{-1}$).

^c NO₂: nitrogen dioxide (9 µg/m³).

^d <50 m: distance between child's address and the nearest major road less than 50 m.

^e 1st–6th year of life.

^f 4th–6th year of life.

Table 5

Association between traffic-related pollution exposure, combined from addresses at birth and at 6th year, and prevalence of eczema, asthma and hay fever in the 6th year of life and the point prevalence of eczema and allergic sensitization (results of log binomial regression).

	N	Soot ^b	NO ₂ ^c	<50 m ^d
		Adjusted ^a RR (95% CI) p	Adjusted ^a RR (95% CI) p	Adjusted ^a RR (95% CI) p
Doctor-diagnosed eczema	1741	1.69 (1.04–2.75) 0.035	1.55 (0.95–2.52) 0.079	1.42 (0.91–2.22) 0.121
Symptom for eczema	1823	1.03 (0.57–1.86) 0.911	0.94 (0.49–1.77) 0.838	1.54 (0.92–2.57) 0.097
Current eczema at day of investigation	890	2.13 (0.67–6.81) 0.201	1.70 (0.50–5.82) 0.399	2.22 (0.94–5.23) 0.068
Doctor-diagnosed asthmatic/spastic/ob-structive bronchitis/asthma	1745	1.03 (0.67–1.59) 0.894	0.95 (0.59–1.52) 0.814	0.82 (0.51–1.32) 0.413
Symptom for asthmatic/spastic/ob-structive bronchitis/asthma	1808	0.75 (0.49–1.14) 0.172	0.64 (0.40–1.03) 0.654	0.76 (0.45–1.28) 0.298
Doctor-diagnosed hay fever	1744	1.40 (0.73–2.70) 0.309	1.25 (0.62–2.52) 0.531	0.78 (0.38–1.62) 0.507
Symptom for hay fever	1831	1.06 (0.75–1.51) 0.730	1.05 (0.72–1.54) 0.787	0.80 (0.54–1.20) 0.280
Sensitization against Indoor allergens	865	0.89 (0.50–1.59) 0.705	0.84 (0.45–1.60) 0.559	0.89 (0.52–1.55) 0.689
Sensitization against Outdoor allergens	865	0.73 (0.42–1.26) 0.257	0.85 (0.46–1.57) 0.604	0.87 (0.51–1.48) 0.612

^a Adjusted for study (LISApplus, GINIplus), gender, years of parental schooling, maternal smoking in pregnancy, environmental tobacco smoke, use of gas for cooking, contact with dog, cat, other furry pet, moulds in home, dampness in home, biological siblings at birth of child, participant of intervention, intervention formulas, living on a farm, parental asthma, hay fever or eczema.

^b Soot: absorbance of particles less than 2.5 µm diameter ($0.5 \times 10^{-5} \text{ m}^{-1}$).

^c NO₂: nitrogen dioxide (9 µg/m³).

^d <50 m: distance between child's address and the nearest major road less than 50 m at no address, at one address or at both addresses.

A genetically impaired skin barrier function is a hall mark of eczema. [37] This defect of function enhances the penetration of environmental allergens into the skin, resulting in inflammatory reactions. [38] The inflammatory potential of small particles is well known [39] and has been demonstrated in epidermal keratinocytes. [40] The penetration of particles might also be enhanced in eczematous skin and lead to a longer duration of inflammatory symptoms. This could be an explanation for our result of a TAP related prolongation of the duration of eczema.

The association between doctor diagnosed eczema and the chosen indicators of exposure to TAP was strongest for soot; however in Munich the strongest association with eczema was seen for NO₂. Therefore from the results of our study we cannot attribute the effects to a single pollutant. We even cannot rule out the possibility that other traffic-related exposures, such as exposure to noise, could also be involved in the effects observed.

We explored whether selective participation might have biased the results of our cohort study. Participation in the yearly questionnaires was dependent on exposure, more highly exposed children participated less often, but participation was unrelated to diagnosis or symptoms; therefore, bias in our parameter estimates is unlikely. Participation in the clinical examination depended on a positive allergy diagnosis but did not depend on exposure, therefore bias in the estimates gained for allergic sensitization, or for current eczema, also seems unlikely.

In conclusion, in small-town areas on the Dutch-German border an association of TAP exposure with eczema, but not with asthma, hay fever or allergic sensitization was detected. Eczema, with its known impact on quality of life, lasted longer in children with greater exposure to TAP even in these areas with generally lower pollution than the areas included in previous studies addressing this topic.

Conflict of interest statement

None declared.

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