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Vehicle exhaust exposure in an incident case-control study of adult asthma

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Abstract

The objective of this case-control study was to evaluate whether traffic-related air pollution exposure at home increases the risk of asthma in adults, and further to compare two commonly used exposure variables and differences between urban and rural living.

Incident cases of asthma and matched controls 20-60 years of age, were recruited in Luleå, Sweden. In total 203 cases and 203 controls were enrolled in the study. Exposure was estimated by traffic flow and measured levels of outdoor NO_2 around each home, respectively. The relation between measured levels of NO_2 and traffic flow was studied with linear regression.

The results indicated a non-significant tendency between living in a home close to a high traffic flow and an increased risk of asthma (OR_{all} =1.5, 95% CI 0.9-2.5; for long-standing residents $OR_{>2years}$=2.4, 95% CI 0.9-6.2). The association between asthma and measured NO_2 was weak and not significant, but skin prick test acted as effect modifier with a significant association among positive. The correlation between traffic flow and outdoor NO_2 was low (r=0.38).

The results suggest that living close to high traffic flows might increase the asthma incidence in adults, while the tendency for NO_2 was almost negligible. Traffic flow and NO_2 had a lower than expected correlation.

Background

Asthma and air pollution

Prevalence of asthma has increased during the last decades in countries all over the world, including Sweden (1,2). The incidence of asthma has been proved to be highest among children (3,4), but previous studies have also shown relatively high prevalence in adults (5,6). There are several known risk factors for developing asthma, among others a family history of asthma and allergic sensitization.

The relation between outdoor air pollution and airway problems has been investigated in studies with different designs. Several cross-sectional studies on children and adolescents have, mainly in children, shown an increased prevalence of wheeze, rhinitis and other respiratory symptoms with increased exposure to vehicle exhausts (7-9). Few studies have reported air pollution as a cause for asthma. In a 6-year follow up study among Japanese children a significant association was found between the annual average concentration of NO_2 and the incidence of asthma (10). A study in the UK showed that Birmingham children (0-5 years) admitted for asthma were more likely to live in areas with high traffic flows close to their home in comparison with children in a control group (11). Results from San Diego showed a weak association in a study among children up to 14 years of age (12), while a similar study in London found no associations (13).

Effects on adults have been less frequently investigated. A Japanese study found an increased prevalence of self-reported respiratory symptoms among adult women living close to very busy roads (14). Corresponding results were also seen for respiratory symptoms among adults in a Swiss study (15). Among adult nonsmoking men living in California, long-term exposure to ozone increased the risk of developing asthma (16).

Though it is obvious from many previous studies that air pollutants cause adverse effects in the airways, few studies have investigated the relation between air pollution from traffic and incidence of asthma in adults. The focus in this study is on traffic related air pollution and the occurrence of asthma among previously non-asthmatic adults; the incidence of asthma.

Measures of exposure

Several methods have been applied to measure exposure to traffic pollutants, e.g. participants own estimation of the flow of traffic around their homes, actual flow of traffic (8, 9), or the distance between the home and the nearest big road (17). NO_2 is a commonly used indicator of vehicle exhausts, and the connection between NO_2 and traffic has been previously demonstrated through correlations with other known traffic-related pollutants (18, 19).

The connection between traffic exposure and respiratory problems has been investigated in a number of studies with both specific pollutant indicators (such as NO_2) and different measures of traffic density (8, 9, 17, 20). One problem with this variety of exposure indicators is that their associations are not well described. Nor do we know to what extent they are relevant from a causal perspective. Nowadays NO_2 at ambient levels is not judged to be an important pollutant in itself, but rather an indicator of various toxic exhaust components (21).

Aim

The aim of this study was to investigate whether traffic-related air pollution exposure at home, as measured by official information about traffic flow and outdoor levels of NO_2, increases the risk for developing asthma in adults. Furthermore, we wanted to evaluate the comparability of these two commonly used exposure variables, and finally also study urban versus rural living as a potential determinant for asthma incidence in adults when traffic pollution simultaneously is adjusted for.

Method

Study design and population

A matched incidence-based case-control study was conducted in Luleå, a city with approximately 71 000 inhabitants in the northern part of Sweden. The whole municipality covers an area of almost 2100 km^2.

The study population consisted of all persons aged 20-60 years living in the municipality of Luleå at time of the study. From September 1995 to December 1999 suspected incident cases of asthma from the primary health care, local and county hospitals, private clinics and occupational physicians were reported to the OLIN-project (Obstructive Lung Disease In Northern Sweden). Each case was clinically examined and interviewed before inclusion in the study to verify onset of asthma within the last 12 months and bronchial variability. Furthermore at least four of the following criteria had to be fulfilled to be included as a case in the study, *attacks or shortness of breath, wheezing or whistling in the chest, no symptoms between the attacks or periods, at least two provoking factors with the exception of "common cold" and "physical exertion"* and *at least two attacks or periods since onset of symptoms*. For each included case a control from Luleå, matched by age and sex, was selected from the Swedish population register. Persons with a diagnosis of asthma, a history of asthma or any previous use of asthma medicines were excluded. Details about the study and clinical examination have recently been published (22).

Exposure variables

Measurement of nitrogen dioxide

The average levels of outdoor NO_2 were measured for a period of one week, which was the same for each pair (case and matched control). The sampler was placed 2.5 meters from the ground and 0.5 meters out from the facade on the side of the house least exposed to traffic. A Willems badge diffusion sampler was used for the measurements (23). The samplers were analyzed at Umeå University (24). Due to lack of capacity, we were not able to measure NO_2 for all pairs. There was however no geographic or other systematic selection involved in this. Since ambient NO_2 levels in this region due to emissions and dispersion vary with temperature, and measurements were conducted at different temperatures albeit the same week for pairs, all measured concentrations of NO_2 were standardized to correspond with the annual average temperature in the study area. The influence of temperature on the NO_2 levels (β) was established from a linear regression model, based on NO_2 concentrations measured at one urban site between April 1999 through March 2000, as a dependent variable and the corresponding weekly temperature averages as independent variables (β= -0.63, R^2=0.53). Subsequently every concentration of NO_2 measured outdoors over one week at each home was adjusted to represent an estimated annual average by using the difference between the weekly average and the yearly average temperature together with the regression coefficient.

Traffic flow within different distances from the homes

The participant's residence was located on a map using the official land registry of the area. The road network with the official traffic flows on the roads, measured either by the Swedish Road Administration or by the municipal technical office, was added to the map. For each home, a buffer zone with a radius of 200 meters was created. Within each zone, the mean traffic flow (vehicles/24-hour period, weekday) for every road crossing the zone was aggregated up to a total flow. Residences where a calculated flow could not be determined, due to lack of traffic counts on the roads within the 200 meters radius, were grouped in a low category assuming the flow of 100 vehicles/24 hours.

Usually several points with traffic counts within 200 meters of the same street are not available within 200 meters. Nevertheless, this was the situation in the most central parts of Luleå with several measurements from the same road in close range due to crossings, while elsewhere this was uncommon. This caused uncertainties in the summarization of traffic flow, and therefore after checking the registered traffic flows no participants were given a higher traffic flow than 30 000 vehicles/day.

ARC VIEW 3.1 was used for the placing of each estate, the creation of radiuses and the calculation of traffic flow (Environmental systems research institute, Redlands, CA).

Urbanization

During the measurement of NO_2 the visiting inspector also classified each home in terms of degree of urbanization into four classes; rural, small house area (residential area), apartment house area and city center. In the analyses, cases and controls were categorized as having a rural or urban residence where urban included all classes except "rural".

Statistical methods

The risks of developing asthma if exposed to high traffic flow or high NO_2 levels at home respectively, were estimated using odds ratios calculated in a conditional logistic regression model adjusted for each pair of cases and controls and the variables: family history of asthma, smoking habits, BMI (Body Mass Index), rural residence and positive skin prick test (25). Each variable was also tested as an effect modifier in an unmatched logistic regression model adjusted for the above-mentioned variables together with age and sex. Of the variables used in the adjustment some are previously known risk factors for asthma in the studied population and others are more general risk factors (22). Traffic flow was dichotomously grouped in the analysis of risk estimates, while NO_2 was analyzed as a continuous variable. The cut-off point for participants living at high traffic flows was chosen as the 3rd quartile (25 % highest values). The analysis was initially made including all participants and then restricted to those who had lived more then 2 years in their home. The analysis of effect modification was done only for the latter subsample. Only the temperature adjusted NO_2 values were included in the models due to the fact that temperature is an important factor for the variation in levels of NO_2.

Statistical calculations were carried out using SPSS 12.0 (SPSS for PC; SPSS Inc., Chicago, IL, USA.). Precisions in the point estimates were estimated by calculating 95% confidence intervals (CI).

A linear regression model was used to study the relation between NO_2 and traffic flow. The model included only cases and controls with measured traffic flow within 200 meters and an adjusted NO_2 level above the background level (2.5 $\mu g/m^3$).

Results

In total 203 cases and controls, respectively, were included in the study. The mean age was 36 years. Among the cases and controls 123 were women and 80 men. At the time for the study 125 cases (~60%) and 139 controls (~70%) had lived more then two years in their present home. The prevalence of current smoking was 25% among the cases and 23% among the controls.

Exposure variables

NO_2 levels outdoors at home were obtained for 138 cases and 136 controls. The median levels of NO_2 outdoors are presented for cases and controls in table 1. The measured levels of NO_2 were low in a European perspective. Estimated annual mean values, adjusted for temperature, were in the range of 0-27µg/m^3.

Table 1. Traffic flow (vehicles/day) and outdoor NO_2 levels in cases and controls in the entire study population, among those who had lived more then two years in their present home and in the non-rural population. Number of subjects (N), median, range and 3rd quartile.

Traffic indicator		Entire study population		Lived more then 2 years in the present home		Non-rural population	
		Cases	Controls	Cases	Controls	Cases	Controls
Traffic flow (vehicles/day)	N	199	196	124	135	160	168
	Median	100	350	100	100	3000	1950
	Range	100-30,000	100-30,000	100-30,000	100-30,000	100-30,000	100-30,000
	3rd-quartile	9845	7800	7800	5700	11387	9700
Outdoor NO_2 ($\mu g/m^3$)	N	138	136	92	97	108	116
Unadjusted [1]	Median	6.5	6.0	6.0	6.0	8.0	7.0
	Range	0.0-27.0	1.0-23.0	0.0-21.2	1.0-23.0	1.0-27.0	1.0-23.0
	3rd-quartile	11.0	11.0	10.8	10.5	11.8	12.0
Adjusted [2]	Median	5.6	6.0	5.6	5.4	6.3	6.3
	Range	2.5-29.9	2.5-23.1	2.5-21.2	2.5-23.1	2.5-29.9	2.5-23.1
	3rd-quartile	9.5	9.9	9.3	9.1	10.2	10.0

[1] Measured levels
[2]Measured levels adjusted for temperature

Approximately 95% of the study population had geocodable addresses, which was a requirement for summarizing traffic flow around the home. However, 47% of the controls and 51% of the cases lived in areas with roads for which there where no available traffic counts, and thus received the traffic flow 100 vehicle/24 hours.

A classification of degree of urbanization was possible for 197 cases and 193 controls. All but 11 cases and 15 controls had a home address possible to retrospectively geocode, but among these urbanization classification was missing for 5 cases and 9 controls. For the 12 participants with homes classified by degree of urbanization but without geocode, the classification was used to estimate their traffic flow around home. Since none of the 12 participants homes were classified as city center they were all given an estimated traffic flow of 100 vehicle/day. In addition, a sensitivity analysis showed that removing cases and controls without geocodable home address from the analysis did not change the risk estimates.

Among cases and controls classified as having rural homes approximately 90% received the flow 100 vehicles/day, while the corresponding proportion in those classified as having a home in the city center was only 5%.

Altogether, 15 cases and 17 controls got their summarized flow reduced to the maximum traffic flow of 30 000 vehicles/24 h.

The distribution (%) of cases and controls within the categorical variables used in the analysis are shown in table 2. The distributions are given for the whole material and for those who have lived more then 2 years in there present home, separately.

Table 2. Percentages of cases and controls within each of the categorical variables included in the conditional logistic regression model. The distributions are given for all participants and those who have lived more then two years in their home, separately.

Variables	Cases (%)		Controls (%)	
	All	Lived more then 2 years in the present home	All	Lived more then 2 years in the present home
Traffic flow				
Low	71.9	76.6	77.0	83.7
High	28.1	23.4	23.0	16.3
Positive skin-prick test	47.8	45.5	27.9	30.4
Family history of asthma	42.4	44.0	20.7	20.1
Smoking				
Non-smoker	49.8	51.2	53.5	47.8
Ex-smoker	25.6	24.0	23.8	29.0
Smoker	24.6	24.8	22.8	23.2
BMI				
<25	49.8	48.8	63.7	63.0
>25	50.2	51.2	36.3	37.0
Degree of urbanisation				
Rural	18.8	20.3	13.0	15.0
Urban	81.2	79.7	87.0	85.0

Relation between NO_2 and traffic flow

NO_2 was expected to increase with an increased flow of traffic. The relation between outdoor NO_2 and traffic flow is shown in figure 1. The correlation between traffic flow around home and measured levels of NO_2 was quite low (r=0.38). [Figure 1].

Vehicle exhaust exposure and asthma

Traffic flow increased the risk of developing asthma, however not significantly. This was seen both when including all participants and when the analysis was restricted to those who had lived more then 2 years in their present home (table 2).

The analysis of asthma in relation to measured levels of NO_2 showed no association to suggest high NO_2-levels to be a risk for developing asthma (OR=1.0 per µg/m^3, 95% CI 0.9-1.1). A similar result was found also when restricting the analysis to those who had lived for more then 2 years in their present home (OR=1.1 per µg/m^3, 95% CI 0.9-1.2). In the logistic regression analysis of potential effect modification, skin prick test (SPT) was a significant effect modifier in the analysis with NO_2, which is the reason that the analysis was made separately for those with and without positive SPT. A borderline significant effect of NO_2 on the risk of developing asthma was seen among participants with positive SPT (OR= 1.2 per µg/m^3, 95% CI 1.0-1.3).

Our results also indicate an increased risk of developing asthma in rural areas, though not significant, also with adjustment for our covariates including NO_2-levels or traffic flow (table 3).

Table 3. Associations from a conditional logistic regression analysis of the impact of traffic flow, outdoor NO_2 (μg/m^3) and urban versus rural living on the risk for developing asthma. The table also shows results for an unconditional analysis of NO_2 made among those with positive and negative SPT, separately. Results are shown for analyses including all participants and those restricted to persons who lived more the 2 years in their present home separately. Odds ratios (OR) and 95% confidence intervals (CI).

	Conditional logistic regression					
	All Participants			Lived more then 2 years in the present home		
Exposure variables	N	OR[1]	95% CI	N	OR[1]	95% CI
Traffic flow						
High	379	1		208	1	
Low		1.5	0.9-2.5		2.4	0.9-6.2
Outdoor NO_2 (μg/m^3)	261	1.0	0.9-1.1	156	1.1	0.9-1.2
Degree of urbanisation		OR[2]				
Urban	379	1		208	1	
Rural		1.6	0.9-3.1		2.1	0.8-5.6
		OR[3]				
Urban	261	1		156	1	
Rural		1.5	0.7-3.3		2.0	0.6-6.3
	Logistic regression					
Outdoor NO_2 (μg/m^3)					OR[4]	95% CI
Negative SPT				184	1.0	0.9-1.1
Positive SPT					1.2	1.0-1.3

[1] Adjusted for rural residence, skin prick test, family history of asthma, BMI and smoking
[2] Adjusted for traffic flow, skin prick test, family history of asthma, BMI and smoking
[3] Adjusted for NO_2, skin prick test, family history of asthma, BMI and smoking
[4] Adjusted for age, sex, rural residence, skin prick test, family history of asthma, BMI and smoking

Discussion

The results from this study showed that vehicle exhausts indicated by traffic flow around the home had a non-significant tendency to increase the risk of developing asthma. For NO_2 there was no indication of a relation when the entire data set was used as a whole. However, one third had lived less than two years at the studied address. Among participants who had lived more then 2 years in their home and had positive SPT, elevated levels of NO_2 outside home were significantly associated with incident asthma.

Associations with asthma

Studies of environmental risk factors for incident asthma among adults are rare, and only few studies have considered air pollutants. McDonnell et al found long-term exposure to ozone to be a risk factor for asthma among men aged 27-87 years, but not for woman (16). A newly published US study showed significant associations between doctor's diagnosed asthma among children and the traffic volume within 150 meters around the home (26). Our study gives some support for an effect of traffic pollutants by suggesting a non-significant increased risk for incident asthma with exposure to high traffic flow around the home.

The geographical information used for the exposure assessment was home address when entering the study. Consequently, there is likely to be exposure misclassification for participants that recently moved to their present home if the relevant exposure window is several years. We therefore focused on those who had lived more then 2 years at their present home. This eliminated 36% of the cases and 30% of the controls, but increased the risk estimate for high traffic flow to an odds ratio of 2.4, still non-significant. Approximately 50% of the participants received the traffic flow 100 vehicles/day due to missing traffic counts, which contributes to the uncertainties in the effect estimates.

The effect estimate calculated for NO_2 was low also when restricting the analysis to those who had lived for more then 2 years in their present home. When we studied those who had lived more then 2 years in their present home and had a positive SPT, levels of NO_2 outside the home were associated with an increased risk (p=0.04) of developing asthma. Living close to highly trafficked roads (27) and NO_2 outside the home (28) has in some studies proven to increase the risk for a positive SPT, and a positive SPT is a well-known risk factor for developing asthma. Adjusting for a positive SPT in stable residents may thus partly hide an association between asthma risk and previous exposure to traffic pollutants. The findings on traffic pollution and atopy as well as asthma are however not consistent, and therefore further incidence based studies are needed to confirm the strong effect seen in this small study. Rural living showed a tendency to increase the risk of developing asthma when traffic pollution is adjusted for. Rural living could be seen as an indicator of a certain lifestyle and different exposure patterns. Previously published studies have shown rural living to be protective against several different respiratory symptoms, especially when rural includes living on or close to a farm (29, 30). However, there are other studies in line with our findings showing higher prevalence of asthma among adults living in rural areas in comparison with urban areas (31).

Calculation of traffic flow

GIS has been used to describe exposure in several different types of epidemiological studies (12, 32). A problem with the geographical location of residences in our study is that this was based on official information which link addresses to the center point of the estate and not the actual building. There is consequently a risk that the zones have not been correctly created around the residences, but around another point within the estate, which could result in an over- or underestimation of the traffic flow. The problem is smaller in cities than in rural areas, owing to the fact that estates are normally quite small in densely populated areas. In practice for this study the mentioned risk for under- or overestimation is of less importance due to the low traffic flows in the rural areas.

Residences for which traffic flow could not be calculated were placed in the lower exposure category in the analyses. For the majority of these residences (93%) the absence of traffic flow information was due to lack of traffic counts for the roads within a 200 meters radius around the home, while only 7% were missing in the official land registry and not possible to geocode.

Of those residences where actual flows could not be determined, 76 % were classified as situated in rural or small house areas by the visiting environmental health officer and of those given the maximum traffic flow (30000 vehicles/day), 94% were classified as found in a city center or apartment areas. This indicates that the largest number of the participants where traffic flow could not be determined lived outside the city center, while those exposed to the highest flow lived in the most central areas of the city. The main traffic in this area is focused to the city and a few big roads while rural and small house areas are generally spared from high traffic flows. Our judgement is that the risk of misclassification by assigning these participants the traffic flow 100 vehicle/day is very small and a better option than excluding them from the analysis. An analysis made including only participants with available traffic counts would not only dramatically reduce the number of cases and controls, the regrouping into new quartiles would also reduce the differences in traffic flow (exposure) between the exposed and unexposed group.

The summarization of traffic flow was made unweighted, which means that flows were added up independently of where or how much of the roads that crossed through the 200 meter radius. The distance to the included roads was not calculated since our focus was on the flow within the radius, but also because the coordinates for the center point of the radius showed the center of the estate and not the participant's home which could be a problem especially in the more central parts of the city with many roads relatively close to the buildings.

Measurements and adjustment of NO_2

We placed the NO_2 samplers on the least trafficked side of the house since most Swedish block houses in cities have their air intake on this side of the house or on the roof. Swedes also tend to avoid traffic noise, so aired bedrooms are often situated on the quieter side of the house. For the comparison with summarized levels of traffic flow this placement of samplers could of course be questioned, but the fact that traffic flow were summarized unweighted for distance to road makes the two measures more comparable.

As a sensitivity analysis of the adjustment of measured NO_2 values based on temperature, a second type of standardization was carried out based on 29 weekly measured averages of NO_2 from one site in the center of Luleå. The ratio between weekly concentrations and the annual average at this measurement site was calculated and used to adjust the measured values at each participant's home during the same week. The results from the two methods were highly correlated (r=0.91). The adjustment based on continuous measurements from a central measuring station could seem more appropriate, but lack of weekly measurements throughout the study period made this impossible.

NO_2 indicated by traffic flow

Incomplete traffic counts on minor roads and few bigger roads resulting in NO_2-levels close to background levels most likely explain the low correlation between the estimated yearly outdoor NO_2 concentration and traffic flow within a 200-meter-radius. Surrounding buildings and topography are also important factors in the more trafficked areas.

The majority of traffic-related NO_2 is secondarily formed by the oxidation of NO, which suggests that NO_x ($NO+NO_2$) would have been a better indicator of exhaust fumes. However, at the time of these measurements, NO_2 was, and still is, the primary indicator for vehicle exhausts.

The explained variation between traffic flow and NO_2 together with the results from the analysis shows that classification of traffic pollution on the basis of one method does not guarantee the same result as would data collected with another method. Probably the difference between the exposure variables would decrease if the same comparison was made in a larger city. In this area traffic is the major source of NO_2, and several different studies confirm rising outdoor levels of NO_2 with increased density of traffic and decreased distance from high traffic flow (33, 34). However, the use of geographical exposure indicators (such as the location of the residences in relation to the source) has been discussed in previous papers and the need for complementary measurements to follow up and confirm exposure estimates has been stressed (35). These results further substantiate this discussion and highlight the difficulties of using exposure indicators.

References

1. Woolcock AJ, Peat JK. Evidence for the increase in asthma worldwide. Ciba Found Symp 1997;206:122-34.

2. Lundbäck B. Epidemiology of rhinitis and asthma. Clin Exp Allergy 1998;28:3-10.

3. Strachan DP, Butland BK, Anderson HR. Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort. BMJ 1996;312:1195-9.

4. Rönmark E, Perzanowski MS, Platts-Mills T, Lundbäck B. Incidence rates and risk factors for asthma among school children: a 2-year follow-up report from the obstructive lung disease in Northern Sweden (OLIN) studies. Respir Med 2002;96:1006-13.

5. Rönmark E, Lundbäck B, Jönsson E, Jonsson A-C, Lindström M, Sandström T. Incidence of asthma in adults - report from the Obstructive Lung Disease in Northern Sweden study. Allergy 1997;52:1071-8.

6. Lundbäck B, Rönmark E, Jönsson E, Larsson K, Sandström T. Incidence of physician-diagnosed asthma in adults – a real incidence or a result of increased awareness? Report from the Obstructive Lung Disease in Northern Sweden Studies. Respir Med 2001;95:685-92.

7. Montnémery P, Popovic M, Andersson M, Greiff L, Nyberg P, Löfdahl CG, Svensson C, Persson CGA. Influence of heavy traffic, city dwelling and socio-economic status on nasal symptoms assessed in a postal population survey. Respir Med 2003;97:970-7.

8. Duhme H, Weiland S, Keil U, Kraemer B, Schmid M, Stender M, Chambless L. The association between self-reported symptoms of asthma and allergic rhinitis and self-reported traffic density on street of residence in adolescents. Epidemiology 1996;7:578-82.

9. Ciccone G, Forastiere F, Agabiti N, Biggeri A, Bisanti L, Chellini E, Corbo G, Dell´Orco V, Dalmasso P, Volante TF, Galassi C, Piffer S, Renzoni E, Rusconi F, Sestini P, Viegi G. Road traffic and adverse respiratory effects in children. Occup Environ Med 1998;55:771-8.

10. Shima M, Nitta Y, Ando M, Adachi M. Effects of air pollution on the prevalence and incidence of asthma in children. Arch Environ Health 2002;57:529-35.

11. Edwards J, Walters S, Griffiths RK. Hospital admissions for asthma in preschool children: relationship to major roads in Birmingham, United Kingdom. Arch Environ Health 1994;49:223-7.

12. English P, Neutra R, Scalf R, Sullivan M, Waller L, Zhu L. Examining associations between childhood asthma and traffic flow using a geographic information system. Environ Health Perspect 1999;107:761-7.

13. Wilkinsson P, Elliott P, Grundy C, Shaddick G, Thakrar B, Walls P, Falconer S. Case-control study of hospital admission with asthma in children aged 5-14 years: relation with road traffic in north west London. Thorax 1999;54:1070-74.

14. Nitta H, Sato T, Nakai S, Maeda K, Aoki S, Ono M. Respiratory health associated with exposure to automobile exhaust. I. Results of cross-sectional studies in 1979, 1982 and 1983. Arch Environ Health 1993;48:53-8.

15. Zemp E, Elsasser S, Schindler C, Künzli N, Perruchoud P, Domenighetti G, Medici T, Ackermann-Liebrich U, Leuenberger P, Monn C, Bolognini G, Bongard JP, Brändli O, Karrer W, Keller R, Schöni M.H, Tschopp JM, Villiger B, Zellweger JP. Long-term ambient air pollution and respiratory symptoms in adults. Am J Respit Crit Care Med 1999;159:1257-66.

16. McDonnell WF, Abbey DE, Nishino N, Lebowitz MD. Long term ambient ozone concentration and the incidence of asthma in non-smoking adults: the AHSMOG Study. Environ Res 1999;80(2 Pt 1):110-21.

17. Vliet P, Knape M, Hartog J, Janssen N, Harssema H, Brunekreef B. Motor vehicle exhaust and chronic respiratory symptoms in children living near freeways. Environ Res 1997;74:122-32.

18. Pekkanen J, Timonen KL, Ruuskanen J, Reponen A, Mirme A. Effects of ultrafine and fine particles in urban air on peak expiratory flow among children with asthmatic symptoms. Environ Res 1997;74:24-33.

19. Modig L, Sunesson A-L, Levin J, Sundgren M, Hagenbjörk-Gusafsson A, Forsberg B. Can NO_2 be used to indicate ambient and personal levels of benzene and 1,3-butadiene in air? J. Environ Monit 2004; 6:957-62.

20. Forsberg B, Stjernberg N, Wall S. Prevalence of respiratory and hyperreactivity symptoms in relation to levels of criteria air pollutants in Sweden. Eur J Public Health 1997;7:291-6.

21. World Health Organization (WHO). Health aspects of air pollution with particulate matter, ozone and nitrogen dioxide. Report on a WHO working group. Bonn: WHO, 2003.

22. Rönnmark E, Andersson C, Nyström L, Forsberg B, Järvholm B, Lundbäck B. Obesity increases the risk for incident asthma among both men and women - Report from the Obstructive Lung Disease in Northern Sweden Studies. Eur Respir J 2005;25:282-8.

23. Willems JJH, Hofscreuder P, Eds. In field intercomparison exercise on ammonia and ammonium measurement. Commission of the European Communities, Brussels, Belgium, 1991 Air pollution Research Report 37, CNR.

24. Hagenbjörk-Gustafsson A, Forsberg B, Hestvik G, Karlsson D, Wahlberg S, Sandström T. Measurements of indoor and outdoor nitrogen dioxide concentrations using a diffusive Sampler. Analyst 1996;121:1261-4.

25. Kleinbaum DG, Klein M. Logistic regression, a self learning text, second edition. New York: Springer Verlag 1994.

26. Gauderman JW, Avol E, Lurmann F, Kuenzli N, Gilliland F, Peters J, McConnell R. Childhood asthma and exposure to traffic and nitrogen dioxide. Epidemiology 2005;16:737-43.

27. Janssen N, Brunekreef B, Vliet P, Aarts F, Meliefste K, Harssema H, Fischer P. The relationship between air pollution from heavy traffic and allergic sensitization, bronchial hyperresponsiveness, and respiratory symptoms in dutch schoolchildren. Environ Health Perspect 2003;111:1512-18.
28. Krämer U, Koch T, Ranft U, Ring J, Behrendt H. Traffic-related air pollution is associated with atopy in children living in urban areas. Epidemiology 2000;11:64-70.
29. Filipiak B, Heinrich J, Schäfer T, Ring J, Wichmann HE. Farming, rural lifestyle and atopy in adults from southern Germany- results from the MONICA/KORA study Augsburg. Clin Exp Allergy 2001;31:1829-38.
30. Leynaert B, Neukirch C, Jarvis D, Chinn S, Burney P, Neukirch F. Does living on a farm during childhood protect against asthma, allergic rhinitis, and atopy in adulthood. Am J Respir Crit Care Med 2001;164:1829-34.
31. Turkeltaub PC, Gergen PJ. Prevalence of upper and lower respiratory conditions in the US population by social and environmental factors: data from the second National Health and Nutrition Examination Survey, 1976 to 1980 (NHANES II). Ann Allergy 1991;67:147-54.
32. Bellander T, Berglind N, Gustavsson P, Jonsson T, Nyberg F, Pershagen G, Järup L. Using geographic information systems to asses individual historical exposure to air pollution from traffic and house heating in Stockholm. Environ Health Perspect 2001;109:633-9.
33. Raaschou-Nielsen O, Olsen JO, Hertel O, Berkowicz R, Skov H, Hansen ÅM, Lohse C. Exposure of Danish children to traffic exhaust fumes. Sci Total Environ 1996;189/190:51-5.
34. Nakai S, Nitta H, Maeda K. Respiratory health associated with exposure to automobile exhaust II. Personal NO_2 exposure levels according to distance from the roadside. J Expo Anal Environ Epidemiol 1995;5:125-36.
35. Huang YL, Batterman S. Residence location as a measure of environmental exposure: a review of air pollution epidemiology studies. J Expo Anal Environ Epidemiol 2000;10:66-85.

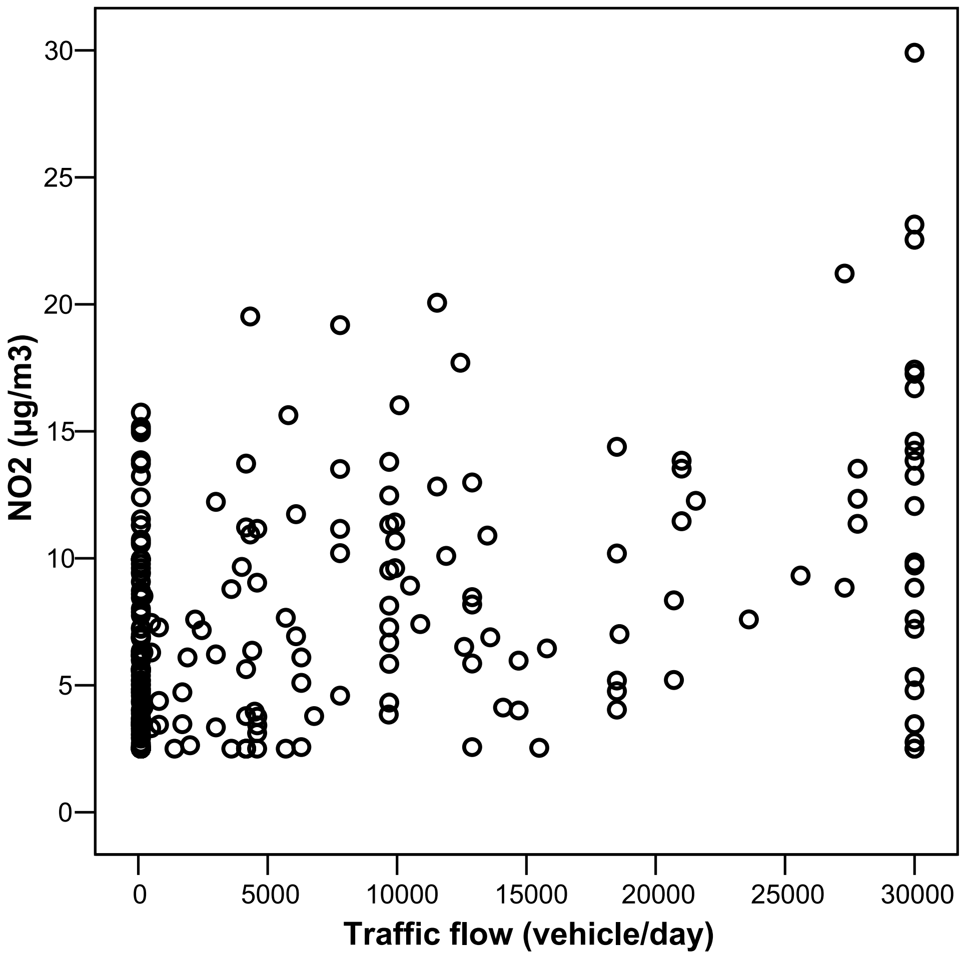

Figure 1. Scatterplot of NO_2 levels outdoors by traffic flow within 200 meters of each case and control’s home. Cases and control´s without a calculated traffic flow received the flow 100 vehicle/day, and no participants received a flow above 30000 vehicles/day.