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Data sheet

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Abstract: The objective of this pilot study is to investigate the relation between asthma and wheeze debut and individually estimated exposure to traffic-related air pollutants with a validated exposure system (AirGIS). A non-smoking cohort with recently acquired asthma or wheeze as well as matched controls was identified from a large cross-sectional study. All residential and working addresses with corresponding time periods for a 10 year period were successfully identified for all study participants (N=33) and exposure estimated for both urban background and street level. Individual levels of air pollutants in the years preceding debut of asthma or wheeze were analyzed using survival analysis. No significant correlations between exposure levels and onset of disease or symptom were demonstrated. A tendency towards higher levels of nitrogen oxides exposure during the year prior to debut was seen in wheeze cases. Substantial problems in determining time of onset were encountered. It is recommended that the analytic methods developed in this pilot study are used in a larger prospective cohort to investigate individual traffic-related air pollutants as a risk factor for the development of new asthma and wheeze.

Keywords: Asthma, AirGIS, new onset asthma, traffic, air pollution, adult

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Contents

Summary in English

The background for the project is that traffic-related air pollution may provoke the onset of asthma. The objective of this pilot study is to investigate the relation between asthma and wheeze debut and individually estimated exposure to traffic-related air pollutants with a validated exposure system (AirGIS).

The project applied the following methodology. A non-smoking cohort with recently acquired asthma or wheeze as well as matched controls were identified from a large cross-sectional study. All residential and working addresses with corresponding time periods for a 10 year period were successfully identified for all study participants (N=33). Using AirGIS traffic-related air pollutant levels from both urban background and street level were estimated for the 10 year study period on an hourly basis. Individual levels of air pollutants in the years preceding debut of asthma or wheeze were analyzed using survival analysis.

The project showed that accumulated individual median NO_2 exposure (mg/m^3 x hour) for the 10 year study period was 1,145 (asthma cases), 1,268 (wheeze cases) and 1,005 (controls). No significant correlations between exposure levels and onset of disease or symptom were demonstrated. A tendency towards higher levels of nitrogen oxides exposure during the year prior to debut was seen in wheeze cases. Substantial problems in determining time of onset were encountered.

This pilot study successfully demonstrated the feasibility of using AirGIS to study correlations between individual traffic-related air pollution exposure and new onset asthma and wheeze.

It is recommended that the analytic methods developed in this pilot study are used in a larger prospective cohort to investigate individual traffic-related air pollutants as a risk factor for the development of new asthma and wheeze.

Summary in Danish

Baggrunden for projektet er, at luftforurening fra trafik kan fremprovokere udvikling af astma. Formålet med dette pilot projekt er at undersøge sammenhængen mellem udsættelse for trafikforurening og nye tilfælde af astma samt hvæsende vejrtrækning hos voksne. Projektet indgår som et led af projektet "Risikofaktorer for astma i voksenalderen", også kaldet RAV-projektet.

Metodemæssigt tager vi udgangspunkt i en kohorte af ikke-rygere med nyligt konstateret astma eller hvæsen og en matchende kontrolgruppe identificeret fra et større tværsnitsstudie. Alle bopæls- og arbejdsadresser blev identificeret for de 33 deltagere i studiet samt de tidsperioder, hvor personerne havde opholdt sig på disse adresser over en tiårsperiode.

Eksponering for trafikrelateret luftforurening på adresseniveau blev modelleret med luftkvalitets- og eksponeringssystemet AirGIS udviklet af Danmarks Miljøundersøgelser. Luftforureningsniveauet for både gade- og bybaggrundsniveau blev beregnet for de relevante tidsperioder inden for den tiårige periode. Individuel eksponering i årene forud for debut af astma eller hvæsende vejrtrækning blev analyseret med overlevelses statistik.

Projektet viste, at den akkumuleret individuelle medianværdi af NO_2 eksponeringer (mg/m^3 x hour) for den tiårige periode var 1,145 (astma tilfælde), 1,268 (tilfælde med hvæsen) og 1,005 (kontrolgruppe). Der var ingen signifikant sammenhæng mellem eksponering og udvikling af sygdom eller symptomer. En tendens til højere eksponeringsniveauer i året forud for debut blev set for tilfælde med hvæsende vejrtrækning. Der var substantielle problemer forbundet med at tidsbestemme, hvornår sygdomsfrembruddet opstod.

Dette projekt har succesfuldt demonstreret anvendeligheden af AirGIS til at studere sammenhængen mellem individuel eksponering fra luftforurening fra trafik og udvikling af astma og hvæsende vejrtrækning.

Det anbefales, at de udviklede metoder i dette pilot projekt anvendes i et større prospektivt kohorte studie til at undersøge individuel eksponering for trafikrelateret luftforurening som en risikofaktor for udvikling af nye astma og hvæsende vejrtrækning tilfælde.

1 Introduction

The incidence and prevalence of asthma has been increasing in developed countries over the past few decades. This higher prevalence suggests that urbanization and air pollution may be relevant risk factors (Wong et al, 2004; Byrd et al, 2006; D'Amato et al, 2005).

1.1 Air pollution as risk factor for asthma

Several studies have established air pollution as a significant factor associated with increased morbidity in asthmatics. Traffic exhaust is one of the main sources of air pollution, especially in urban areas where populations are exposed to the highest air pollution levels. Recent epidemiologic studies have investigated the influence of meteorological factors and traffic-related air pollution on asthma hospitalization. Positive correlations between seasonal variations in hospitalization and traffic-related air pollutants such as nitrogen oxides, carbon monoxide and fine fraction particles have been reported (Chen et al, 2006; Migliaretti et al. 2005). Low ambient levels of traffic-related NO_2 have been identified as a consistent risk factor for hospital admission rates from asthma in addition to other covariant risk factors, e.g. socioeconomic, health control, tobacco smoke and family history (Ramos et al., 2006; Magas et al., 2007).

In experimental studies, nitrogen dioxide exposure has been shown to elicit inflammatory reactions and muscle tone changes in the airway of animals (Hussain et al., 2004) and inflammatory reactions in humans (Blomberg et al., 1999).

Epidemiological studies have attempted to evaluate the effects of air pollution from traffic sources on the prevalence and incidence of asthma. The results have been inconclusive partially due to difficulties in exposure estimation. Most studies have been performed in children (Nicolai et al., 2003; Shima et al., 2003; Gauderman et al., 2005; Brauer et al., 2002) and only a few in adults (de Marco et al., 2002; Modig et al 2006). Focus has been on fine fraction particles ($PM_{2.5}$ or PM_{10}), diesel exhaust products, O_3, NO_2 and NO_x.

1.2 Exposure assessment

Different methods have been used to estimate airway pollutant exposures. These methods range from subjectively experienced traffic load to partly quantitative studies using distance from main roads as a proxy for air pollution exposure. Models that interpolate air pollutant monitoring data and spatial distribution measurements to estimate individual exposure over time have also been applied (Brauer et al., 2002). Recently models based on Geographic Information Systems (GIS) where residential addresses are linked to information on road distribution and traffic counts have emerged (Bellander et al., 2001). In a comparative study GIS-based models produced more reliable exposure estimates than subjective assessment when validated with measured air pollution data (Heinrich et al., 2005).

1.3 Objectives of pilot study

The aim of this pilot study was to test a model for investigating traffic-related air pollution as a risk factor for the development of new onset asthma in young adults. A pilot study approach was believed to be necessary to evaluate the bases for a time consuming full-scale prospective study.

The study used an advanced and validated GIS-based model for estimating individual air pollution and exposure at address levels based on deterministic air quality modelling (Jensen et al. 2001). Hypothesizing an immediate effect of exposure on the development of asthma or wheeze, levels of exposure preceding symptom debut were defined and correlated with disease onset in model testing.

2 Material and methods

The study subjects had participated in a clinical investigation as part of a Danish population-based study of risk factors for asthma in adults, RAV 2002-04 (Skadhauge et al 2005).

2.1 Study subject selection and investigation

The European Community Respiratory Health Survey (ECRHS) screening questionnaire was sent to an age and sex stratified random sample of 10,000 persons between 20 and 44 years of age in five counties in West-Denmark. In this pilot study respondents living in four selected municipalities with a total of 114,502 inhabitants in the selected age groups (2002 Danish Statistical Agency) were included. The population of these four municipalities accounts for approximately 6 % of the initial study population. Never-smoking responders answering affirmatively to the question "Have you ever had asthma?" were selected. Focusing on new onset asthma only those with asthma debut in the preceding five years (debut year 1997 to 2002) were selected. As only seven cases of asthma were found the inclusion criteria was extended to include never-smoking individuals who answered yes to the question "Have you experienced wheezing in the last 12 months?" identifying 11 additional subjects (wheeze cases). From the basic population in the four municipalities 29 never-smoking controls without respiratory symptoms were randomly selected stratified by gender, age and municipality. This extension of the case population was chosen regarding the primary study aim to establish a model to analyze air pollution effects on new onset asthma. Wheezing was regarded as a symptom of possible mild asthma. Analyses of asthma and wheeze cases were done separately.

From this cohort, 33 persons agreed to participate and were interviewed by telephone regarding debut of asthma or wheeze as well as all residences, work places and working hours in the period January 1, 1993 to December 31, 2002. From these data for each person and for every hour in the period 1993 to 2002 the location of all home and work addresses were registered. Transportation times between work and home as well as leisure time (time out of work) was calculated as time at home address.

Three controls had stayed abroad for shorter periods. These individuals were assigned exposure levels believed to be representative for conditions abroad. In the case of alternating shifts a working period was defined as a period containing half of both shifts. For one person working outdoors in alternating locations in his hometown the residential address for the actual period was used to estimate workplace exposure.

For each individual, the study period was subdivided into new periods for every change in residence or workplace. Exposure estimates were generated by multiplying the average concentration of the pollutant per hour with the number of hours spent at each location for each period. This was done for two exposure indicators: urban background and street concentrations at each specified address. In this pilot study summations of exposure per calendar year were used as exposure periods in model testing.

2.2 Modelling of exposure to traffic air pollution

AirGIS was used to model air pollution from traffic exhaust. AirGIS is a location-based human exposure model system used to support air pollution epidemiology as well as air quality assessment and management in Denmark (Jensen et al. 2001). The system is based on the Danish Operational Street Pollution Model (OSPM) (Berkowicz 2000a), digital maps on roads with traffic data, buildings with building height data and geo-coded addresses of study subjects. It applies a Geographic Information System (GIS). AirGIS estimates ambient air pollution levels at high temporal (hourly) and spatial (address) resolutions. The model system enables estimation of air quality levels and human exposures at a large number of addresses in an automatic way provided required input data is available. One of the features of AirGIS is that it is possible to automatically generate street configuration data for the OSPM. Street configuration data includes street orientation, street width, building heights in wind sectors, etc. The OSPM requires input data on traffic for the individual street in question, street configuration data, emission factors, urban background concentration data and meteorological data. The OSPM has an internal vehicle emission module.

Exposure indicators in the present study were street concentrations and urban background concentrations at residential and workplace addresses of each study subject taking into account the time spent at each location. Traffic emission factors were available for PM_{10}, $PM_{2.5}$ and ultra-fine particles but lack of regional background monitoring data for the study period prohibited calculation of urban background and hence street concentration for these particles.

Traffic data is not only required for streets where the exposure addresses are located but also for all other roads since they contribute to the urban background levels at the address in question. Traffic data include Average Daily Traffic (ADT) and vehicle composition (passenger cars, vans, lorries and buses). A national traffic database only exists for state and county roads managed by the Danish Road Directorate in co-operation with the 14 counties and goes back to 1990. However, almost all exposure addresses were located on municipal roads and the municipalities maintain limited traffic databases, if any. Therefore, traffic data for the residential and workplace addresses in this project were obtained through telephone and email contact to the relevant municipalities.

The OSPM also requires urban background concentration data that represents the contribution from vehicle emissions within a larger area. Urban background levels represent conditions at roof top level in a city, in a backyard or in a park. Urban background data were modelled with the Urban Background Model (UBM) - an area source based dispersion model (Berkowicz 2000b). Traffic data for the UBM model was based on the aforementioned national traffic database and for remaining road links on a digital road network where traffic was assigned to all remaining road links based on a statistical top-down approach that distributed known kilometres travelled at county level to individual road links based on a number of criteria like road type and population density on a 1x1 km^2 grid. Emission data was also established on a 1x1 km^2 grid based on kilometres travelled and OSPM emission factors. Regional background concentrations were taken from a regional background station close to the border of the model domain.

Meteorological data from one year (1999) were used for all exposure years since the variation in climate is limited in Denmark. The variation usually affects annual concentration levels with less than about 10%. The OSPM and UBM include routines for describing photo-chemical interactions between NO, NO_2 and O_3 (Palmgren et al., 1996).

The output of the model system includes street concentrations as well as urban background concentrations. For the present study traffic-related air pollution in terms of nitrogen oxides (NO_x), nitrogen dioxide (NO_2) and carbon monoxide (CO) was calculated.

2.3 Validation of modelled exposures

The OSPM has been extensively validated against kerb side air monitoring stations not only in Denmark but also in other parts of Europe and Asia (Aquilina and Micallef, 2004; Berkowicz et al., 1998; 2002, 2005, 2008; Gokhale et al., 2005; Hertel & Berkowicz, 1989; Hertel et al., 2001; Ketzel et al., 2000; Kukkonen et al., 2000, 2003; Ziv et al., 2002; Vardoulakis et al., 2002; Vardoulakis et al., 2007; Vardoulakis et al., 2003)

The OSPM has also been validated for use in epidemiological studies focusing on long-term exposure using a large set of NO_2 measurements collected in an epidemiological study concerning traffic pollution and children cancer representing 204 different locations in urban and rural conditions in the Greater Copenhagen Area (Raaschou-Nielsen et al., 2000).

For the present study the performance of the UBM was evaluated against measurement data from the only fixed urban background monitor station in the study area – the city of Odense (Figure 3.1). The annual diurnal variation is well reproduced by the UBM but the model underestimates observed NO_x levels by about 22% (only about 6% for NO_2 and O_3, not shown).

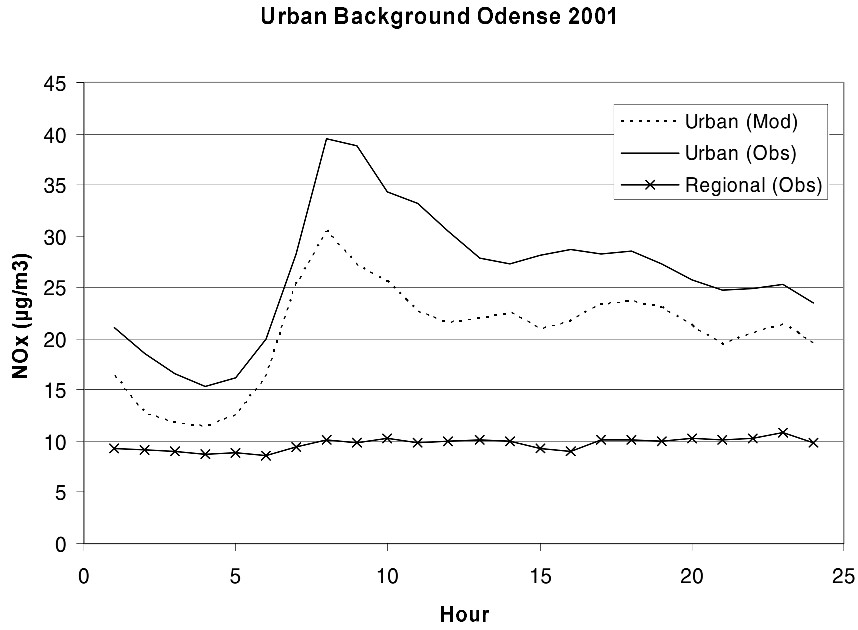

Figure 2.1 Urban Background Odense 2001. Comparison of UBM modelled annual diurnal urban background concentrations and NOx monitor data from an urban background station in the city of Odense. The regional background concentrations are also shown.

2.4 Statistical analysis

A non-parametric analysis (Kruskal-Wallis) was chosen to test the equality of the populations. Differences in annual median exposures between subgroups in the total observational period and the year prior of debut were tested. Analyses were performed on both urban background and street levels of NO_x, NO_2 and CO.

For the survival analyses of the influence of exposure in the years prior to debut logarithmic transformed values of the annual exposure for the pollutants were used and tested by a Cox regression (Breslow method for ties). All analyses were performed using STATA Statistical Software, Release 8.2. (College Station TX, USA).

3 Results

In the following the obtained results are outlined.

3.1 Demographic characteristics of participants

Five subjects with asthma, nine subjects with wheeze and 19 controls were interviewed by telephone. A total of 822 addresses (home and work) were registered mapping the whole study period for all participants. Table 3.1 lists the demographic characteristics of the participants and shows participation rates (average 70 %).

Table 3.1 Demographic characteristics of the study subjects

		Asthma cases	Wheeze cases	Controls
Number of eligible participants		7	11	29
Number of participants		5	9	19
(Percent in group)		(71 %)	(82 %)	(66 %)
Age	range	23-42	21-41	25-44
	mean	33.0	32.0	37.2
Gender	female	4	4	8
	male	1	5	11

Through the telephone interviews a status as asthma or wheezing case was confirmed but the time of asthma or symptom onset was difficult to establish.

3.2 Street and urban background concentrations

In Figure 3.1 scatter plots of the association between street and urban background levels of each pollutant are shown.

As expected urban background concentrations are lower than street concentrations as street concentrations include the emission contribution from the street in question. Urban background concentrations are a result of the emission contribution from a larger area around the street in question.

Urban background concentrations vary by a factor of about two while street concentrations vary by a factor of up to eight. The variation between urban background levels and street levels for NO_2 is less profound than for the non-reactive NO_x and CO. NO_x and NO_2 show in principle the same variation between urban and street levels although moderated for NO_2.

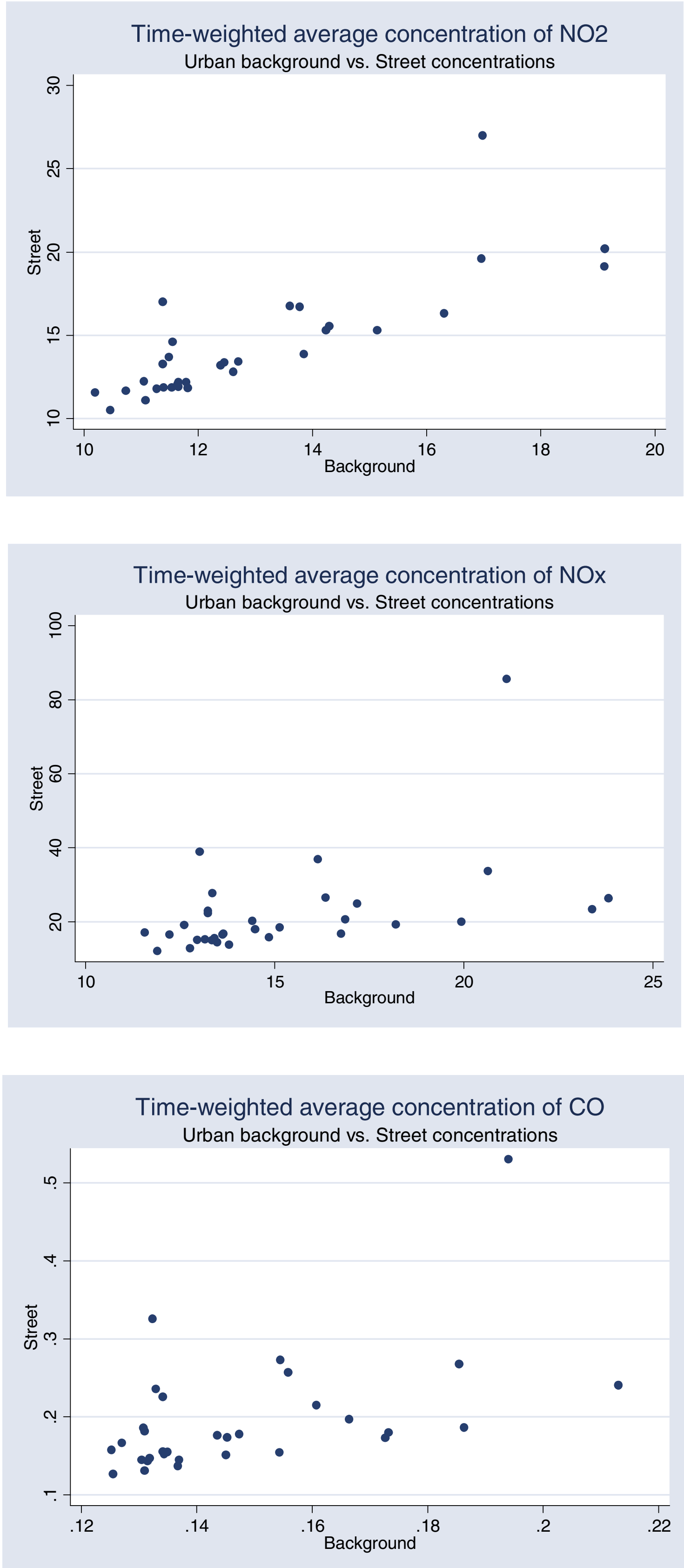

Figure 3.1 Time-weighted average concentration of air pollutants. Scatter plots of ten years average concentrations of NO_2, NO_x and CO in urban background versus street. Units: NO_2 and NOx: µg/m^3, CO: mg/m^3. Correlation factors: NO_2 =0.85, NO_x = 0.44 and CO = 0.50.

3.3 Average exposure concentrations

The time-weighted average concentrations of air pollutants per year at street and background levels of NO_x, NO_2 and CO exposures are described in Table 3.2. There were no significant differences in concentrations between the subpopulations either using street or background levels even though there was a considerable variation in inter-individual exposure levels. A tendency towards higher concentrations of NO_2 was seen in the wheeze subgroup.

Table 3.2 Time-weighted average exposure concentrations of traffic-related air pollutants

		Asthma cases	Wheeze cases	Controls
Street				
NO_2	range	12.2-16.8	11.8-20.2	10.5-27.0
µg/m^3	mean (std. dev.)	14.1 (1.90)	15.7 (3.38)	14.1 (3.93)
NO_x	range	15.7-36.8	15.0-27.8	12.1-85.6
µg/m^3	mean (std. dev.)	22.5 (8.26)	22.2 (4.58)	22.7 (16.8)
CO	range	0.15-0.27	0.15-0.24	0.13-0.53
mg/m^3	mean (std. dev.)	0.20 (0.046)	0.20 (0.046)	0.20 (0.096)
Background				
NO_2	range	11.1-14.2	11.4-19.1	10.2-17.0
µg/m^3	mean (std. dev.)	12.8 (1.22)	14.6 (3.74)	12.6 (3.74)
NO_x	range	12.6-16.9	13.2-23.8	11.6-21.1
µg/m^3	mean (std. dev.)	15.0 (1.65)	17.5 (5.11)	14.8 (5.11)
CO	range	0.13-0.17	0.13-0.24	0.12-0.21
mg/m^3	mean (std. dev.)	0.15 (0.013)	0.16 (0.036)	0.15 (0.036)

3.4 Accumulated exposures

Tables 3.3 and 3.4 describe median exposure levels in subgroups for the total study period for cases and controls as well as exposure in the year prior to debut of asthma or wheeze cases versus average annual exposure in the entire study period for controls. There were no significant differences in exposure levels between subgroups but a tendency (NO_2; $p=0.08$ and NO_x; $p=0.09$) towards higher levels of nitrogen oxides in wheeze cases in the year prior to debut was seen.

Table 3.3 Accumulated median exposure at **street level** for total period per participant and exposure in the year prior of debut of NO_2, NO_x and CO in the subgroups.

Total exposure in 1993-2003				
mg/m^3 x hour	**Asthma cases**	**Wheeze cases**	**Controls**	**Probability**
NO_2	1145	1268	1057	0.15
NO_x	1735	2031	1455	0.30
CO	16096	19584	13678	0.31
Exposure in pre-debut year.				
mg/m^3 x hour per year	**Asthma cases**	**Wheeze cases**	**Controls**	**Probability**
NO_2	104.5	143.3	105.7	0.08
NO_x	140.0	189.6	145.5	0.42
CO	1380.3	1750.6	1367.8	0.27

Table 3.4 Accumulated median exposure at **urban background** level for total period per participant and exposure in the year prior of debut of NO_2, NO_x and CO in the subgroups

Total exposure in 1993-2003				
mg/m^3 x hour	**Asthma cases**	**Wheeze cases**	**Controls**	**Probability**
NO_2	1084	1011	1024	0.43
NO_x	1290	1164	1184	0.46
CO	12600	11670	11874	0.55
Exposure in pre-debut year				
mg/m^3 x hour per year	**Asthma cases**	**Wheeze cases**	**Control**	**Probabil**
NO_2	104.5	121.4	102.4	0.08
NO_x	120.9	143.0	118.4	0.09
CO	1199.8	1339.0	1187.4	0.19

3.5 Survival analysis

Survival analysis results based on 14 events (debut of asthma or wheeze) are shown in table 3.5. No significance differences in hazard ratios related to air pollutants were demonstrated. However tendencies towards higher hazard ratios for NO_x, and NO_2 in background but not street levels were seen.

Table 3.5 Survival analysis of risk exposure for NO_2, NO_x and CO in the year prior to diagnosis.

Street level	**Hazard ratio (95 % Confidence Interval)**		**P-value for hazard ratio = 1**
NO_2	3.04	(0.41-22.7)	0.28
NO_x	1.20	(0.34-4.21)	0.78
CO	1.35	(0.29-6.20)	0.70
Background level			
NO_2	8.83	(0.78-99.8)	0.08
NO_x	7.29	(0.85-62.7)	0.07
CO	6.96	(0.46-104.8)	0.16

4 Discussion

The aim of this pilot study was to test a model for investigating possible effects of traffic-related air pollutants on provoking new onset asthma or wheeze in adults. This requires well developed tools for accurately estimating individual air pollution exposures as well as a clearly defined sizeable study population with newly developed symptoms. Although this is a small sized study we regard the population sample acceptable for model testing.

4.1 Exposure assessment

AirGIS, an advanced and previously validated model for estimating individual air pollution exposure, was applied in the study. Monitoring data from one of the participating cities in the present study was available and correlated well with data generated by the UBM element of the AirGIS system.

In this study a fixed meteorological year was used in modelling. More detailed meteorological data might have been used but with regard to the previously mentioned yearly uniform wind and weather conditions in Denmark the present procedure was considered adequate. Using debut related meteorological data requires well established time of onset of symptoms.

A basic requirement for using the present model was to identify all home and working addresses for all participants for the full study period. This was successful accomplished even though the registration was retrospective and the method was time consuming and complicated. All addresses (home and work) were registered for the 33 participants for the 10-year study period. Assumptions had to be made regarding periods where study subjects were doing shift work or were working and living abroad for just a few periods.

In spite of low exposure levels there were still adequate differences between high and low exposures to provide the necessary exposure contrasts - a necessary requirement in planning a full-scale study.

In this pilot study in-door air pollution was not considered.

4.2 Misclassification and selection bias

A potential misclassification bias regarding the self-reported asthma diagnosis may exist. The ECRHS question "Have you ever had asthma?" has been widely used and validated. This question correlates well with clinical determined asthma (Grassi et al, 2001). Asthma and wheeze cases were analyzed separately but yielded congruent results contradicting misclassification. Thus diagnostic misclassification is unlikely.

Establishing the exact date of asthma or wheeze debut using retrospective data proved to be difficult. Thus registration of debut was restricted to debut year in this model testing. More accurate identification of symptom debut would be desirable. In a planned follow-up of the basic study population a prospective determination of time of new-onset asthma may prove easier using time of medication start, doctor contacts and clinical examinations. Establishing the specific time of onset would make it possible to examine different exposure periods directly proceeding symptoms.

In this population-based study selection bias seems unlikely as all study participants were randomly selected without regarding air pollution exposure.

4.3 Statistical analyses

Testing the AirGIS system for evaluating traffic-related air pollution in provoking new onset asthma was the principle aim of this pilot study. Thus the small study population was considered acceptable. However, the small study population limited statistical analytic possibilities. Cox regression was employed in survival analyses as an example of a possible analysis method, but only 14 events (debut of asthma or wheeze) occurred in this pilot study. Thus the results should be evaluated cautiously.

No significant correlations between new onset asthma/wheeze and traffic-related air pollutants, NO_x, NO_2 and CO, were observed. However, a tendency towards higher nitrogen oxides (NO_x and NO_2) levels in wheeze cases in the year prior to debut was seen for both street and background exposure.

From the results of this pilot study an estimation of necessary sample size was performed. In comparing mean NO_2 concentrations in controls and wheeze cases (power 0.8 and alfa 0.05) a sample of 81 in each group is required. A test sample of this size is possible using cases of new onset asthma from the basic study population in a prospective study assuming annual incidence rate of asthma of one per thousand.

5 Conclusion

This pilot study has demonstrated the feasibility of using the AirGIS system to investigate correlations between individual traffic-related air pollution and new onset asthma/wheeze. The AirGIS system is useful in studying correlations between periods of individual exposure and disease development, but the model testing illustrated some logistical problems particular in determination of symptom or disease onset.

No significant associations between new onset asthma or wheeze in relation to air pollution were demonstrated, but somewhat higher exposure levels were seen in wheeze cases.

A larger prospective cohort is suggested to handle the problem determining time of onset using AirGIS to investigate the role of traffic-related air pollutants in new onset asthma/wheeze.

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The objective of this pilot study is to investigate the relation between asthma and wheeze debut and individually estimated exposure to traffic-related air pollutants with a validated exposure system (AirGIS). A non-smoking cohort with recently acquired asthma or wheeze as well as matched controls was identified from a large cross-sectional study. All residential and working addresses with corresponding time periods for a 10 year period were successfully identified for all study participants (N=33) and exposure estimated for both urban background and street level. Individual levels of air pollutants in the years preceding debut of asthma or wheeze were analyzed using survival analysis. No significant correlations between exposure levels and onset of disease or symptom were demonstrated. A tendency towards higher levels of nitrogen oxides exposure during the year prior to debut was seen in wheeze cases. Substantial problems in de-termining time of onset were encountered. It is recommended that the analytic methods devel-oped in this pilot study are used in a larger prospective cohort to investigate individual traffic-related air pollutants as a risk factor for the development of new asthma and wheeze.

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