Validation of traffic-related air pollution exposure estimates for long-term studies

Sofie Van Roosbroeck

Van Roosbroeck, S. / Validation of traffic-related air pollution exposure estimates for long-term studie.
PhD thesis, 2007, Institute for Risk Assessment Sciences (IRAS), Utrecht University, the Netherlands

ISBN 978-90-393-4547-4

Printed by Ridderprint Offsetdrukkerij BV, Ridderkerk, the Netherlands
Cover by M. de Vaal and M. Brouwer, Multimedia Centre Veterinary Medicine, Utrecht University
Lay-out by H. Otter, Multimedia Centre Veterinary Medicine, Utrecht University

Validation of traffic-related air pollution exposure estimates for long-term studies

Validatie van blootstellingsindicatoren van verkeersgerelateerde luchtverontreiniging voor lange termijn studies
(met een samenvatting in het nederlands)

Proefschrift ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de rector magnificus, prof. dr. W.H. Gispen, ingevolge het besluit van het college voor promoties in het openbaar te verdedigen op maandag 4 juni 2007 des middags te 2.30 uur

door

Sofie Van Roosbroeck

geboren op 28 september 1978
te Wilrijk, België

Promotor: Prof. dr. ir. B. Brunekreef

Co-promotoren: Dr. ir. G. Hoek
Dr. ir. N. A. H. Janssen

The studies described in this thesis were financially supported by the National Institute for Public Health and the Environment (RIVM) in The Netherlands.

"Un secret des progrès de tout homme dans la vie est précisement de s'appliquer toujours à faire le mieux possible et en toute conscience ce que l'on entreprend, même les plus petites choses." -*Charton*-

"The finish line is only the beginning of a whole new race." –*Edward Bright Ebersol*-

"Als je doet wat je leuk vindt, hoef je nooit te werken." –*Mahatma Gandhi*-

Voor Jos en Sigrid,
mijn vrienden,
mijn allereerste mentors,
mijn lieve lieve ouders.

Chapter one

General Introduction

Air pollution, an ongoing concern

Worldwide health effects of outdoor air pollution exposure have been gaining more and more interest during the last decades. Outdoor levels of some pollutants such as particulates, sulfur oxides and carbon monoxide have been declining in Western Europe and North America because of emission-control strategies for motor vehicles, heating, power generation and industry. Nevertheless outdoor air quality problems still exist partly due to increasing use of motor vehicles.[1] Current levels of airborne fine particles may shorten life expectancy of European citizens on average by nine months.[2] Air pollution is estimated to cause about 800 000 annual premature deaths worldwide,[3] more than 40 000 early deaths per year in some West European countries,[4] and consequently, causes increasing medical expenses.

Also, the improving air quality does not seem to be reflected in reduced exposure for the whole population. Currently, EU limit values for annual average concentrations are set to 40 $\mu g/m^3$ for nitrogen dioxide (NO_2) and particulate matter (PM_{10}).[5] However, in 2002, standards for NO_2 were exceeded along busy roads, and standards for PM_{10} were exceeded in a limited number of urban areas in the Netherlands.[6] This draws the attention to variation of air pollution on a local scale.

Health effects related to air pollution

Air pollution consists of both gaseous and particulate pollutants. Gaseous pollutants include nitrogen oxides (NO_2 and NO), ozone (O_3), and sulfur dioxide (SO_2). Particulate matter refers to a mixture of solid and/or liquid particles suspended in the air with a complex chemical composition (including metals, elemental and organic carbon and polycyclic aromatic hydrocarbons (PAHs). Particulate matter is often classified into size categories based on the aerodynamic diameter. A common distinction is particles with a diameter less than 10 µm (PM_{10}), less than 2.5 µm ($PM_{2.5}$) or, less than 0.1 µm ($PM_{0.1}$). $PM_{2.5}$ and $PM_{0.1}$ are often referred to as fine particles and ultrafine particles, respectively. The difference between PM_{10} and $PM_{2.5}$ particles is described as coarse particles.

Pollutants of current interest in western countries include especially particulate matter, ozone and nitrogen dioxide.[7, 8] Epidemiological studies, conducted mostly in Europe and North America, have shown both short- and long-term health effects of outdoor ambient air pollution.

The short-term effects of exposure to air pollution have been well documented. In the USA, the National Mortality, Morbidity and Air Pollution Studies (NMMAPS) covered 90 cities and showed

associations between the level of PM and cardiovascular and respiratory mortality.[9] A similar study in Europe, the Air Pollution and Health, a European Approach (APHEA2) found that short-term changes in particulate air pollution were associated with cardiovascular and respiratory mortality in 29 European cities.[10]

From a public health point of view, effects related to long-term average exposure to air pollution are of the greatest interest, since adverse health effects were found at relatively low concentrations of particulate matter, suggesting that large parts of the world are at risk. Results of three prospective cohort studies have suggested that long-term exposure to particulate matter air pollution is associated with increased mortality from respiratory and cardiovascular disease and from lung cancer.[11-13] The largest study to date showed mortality associations with $PM_{2.5}$ indicating a 6% increase in the risk of death from all causes, and a 12% and 14% increase for death from cardiovascular illness and lung cancer respectively, all expressed per 10 $\mu g/m^3$-increment in $PM_{2.5}$ concentration.[13] Other studies found associations between long-term exposure to air pollution and lower respiratory symptoms, chronic obstructive pulmonary disease, reduction in lung function and atherosclerosis.[13, 14]
Most previous studies have compared large study areas with different ambient air pollution concentrations, assuming that exposure was uniform within each study area. However, the Small Area Variation in Air quality and Health (SAVIAH) study found important differences in NO_2 concentrations within the same city partly related to differences between busy and quiet streets.[15,16] They concluded that a substantial fraction of the variation in average pollutant concentration could be explained by traffic-related variables.[17] Another study on the local scale related proximity to a major road to increased concentrations of NO_2 and black smoke.[18]

Traffic and health

Some more recent health studies have specifically focused on exposure to traffic-related air pollution of subjects living near busy roads and related health problems. Elderly adults living within 50 m of a major road or within 100 m of a freeway were found to have significantly increased risk of death due to cardiopulmonary causes in two European studies,[19,20] increased risk for all-cause mortality and increased risk of symptoms of chronic respiratory disease in a Canadian study,[21] and increased risk of respiratory disease, like persistent wheeze or chronic phlegm in a US veteran study.[22] More recently, traffic density was associated with increased

mortality in a cohort of male US military veterans.[23] Other studies have focused more on children's exposure to traffic-related air pollution. Two Dutch studies have been conducted to assess the effects of emissions from major freeways on respiratory health of school children.[24-28] In these studies, ambient and indoor exposure to freeway emissions at the school was found to be associated with adverse health effects. A similar survey from Germany showed associations in children between living close to busy roads and respiratory symptoms such as asthma, wheeze, and cough.[29]

Traffic-related air pollutants

In Western Europe the transport sector contributes to about 25% of emissions of particulate matter and about 40% of the emissions of nitrogen oxides.[30, 31] Other contributors of air pollution emissions are industry (building, mining, manufacturing activities), power stations, refineries, heating, farming and combustion in households. Traffic emissions include a wide variety of pollutants, such as particles, nitrogen oxides, volatile organic components such as benzene and carbon monoxide. Particle emissions can be distinguished into exhaust emissions and emissions due to brake or tire wear. Exhaust emissions are typically ultrafine particles. A substantial fraction consists of elemental and organic carbon. The term soot is often used to refer to particles generated by incomplete combustion of fuel. Brake or tire wear result in coarse particles that can be resuspended into the air by movement of traffic.

Validity of traffic-related characteristics in health studies

Studies linking traffic-related air pollution and health have generally used traffic-related characteristics on the street of residence, such as distance to busy roads, traffic intensity on the street of residence, or estimated outdoor concentrations based on such characteristics as a measure of exposure. Very little information is available about the validity of these indicators of exposure as an estimate of personal exposure to traffic-related air pollution. Given recent reports of significant within-city variations of air pollution exposures and associated health effects, the fact that subjects spend generally up to 80% of their time indoors and can spend a substantial amount of time away from their home address, validation with personal exposure measurements is especially important.

The lack of validation data for long-term exposure studies contrasts sharply with the information that has recently become available for assessing the validity of ambient monitoring for short-term exposure studies. There now is a range of studies conducted in the USA, Canada and Europe that have documented that the temporal variation in ambient fine particulate air pollution is reflected in temporal variation of personal exposure.[32-36] Overall, personal and ambient concentrations were moderately to highly correlated for both $PM_{2.5}$ and soot. High correlations over time cannot as such be translated as high correlations on a spatial level. Therefore, these studies do not allow a conclusion about the validity of ambient air concentrations for long-term exposure studies since we use spatial contrasts in the outdoor air.

There are some earlier studies that assessed the link between traffic variables and long-term personal exposure of PM_{10} or soot. In a Dutch panel study on the acute effects of air pollution, personal PM_{10} measurements were assessed in an adult population.[37] Higher personal levels of PM_{10} were found in subjects living along a busy road when compared to subjects living away from busy roads, suggesting an important role for the home location in personal exposure to traffic-related air pollution. Within the framework of the previous study, a re-analysis of the collected PM_{10} filters was performed.[38] Personal levels of PM_{10} absorption coefficients, as a proxy for soot (elemental carbon), were measured for subjects living along busy and quiet roads in Amsterdam. Living at a busy road contributed significantly to the personal PM_{10} absorption coefficient measurements. Similar, the ULTRA study, a European Union funded study on exposure and risk assessment for fine and ultrafine particles in the ambient air, conducted among elderly adults living in Amsterdam and Helsinki, showed that having a major street within 100 meter of the home location was found to be a major determinant of personal levels of $PM_{2.5}$ absorption coefficients.[39] These studies had limitations as they were set up as validation studies for time series studies. Limitations include limited variability of traffic related characteristics.

A Dutch study assessed repeated personal NO_2 measurements in children from three schools near freeways with a range of traffic intensities from 45,000 to 150,000 vehicles per day and demonstrated significant differences in average personal NO_2 exposure of school children.[26] This study was specifically designed to assess the validity of long-term average exposure at the school. Studies using repeated personal exposure measurements and being designed to provide a meaningful contrast in average ambient air pollution do not exist for the probably more relevant

$PM_{2.5}$ and particulate matter components such as soot. This lack of data hampers the interpretation of studies on long-term air pollution exposures.

Study aim and outline of the thesis

The objective of this thesis is to investigate the validity of using outdoor concentrations and/or traffic-related indicator exposure variables as a measure for exposure assessment in epidemiological studies on the long-term effect of traffic-related air pollution. Therefore, concurrently outdoor and personal exposure to the traffic-related air pollutants $PM_{2.5}$, soot and NO_x was repeatedly monitored in locations with varying degree of traffic intensity in populations of both children and elderly adults.

In Chapter 2 we investigate whether differences in outdoor levels of air pollutants are reflected in differences in personal exposure in a group of children that all attend the same school located at an urban background location, but vary in traffic intensity at the residential address.

In Chapter 3 we further investigate on the role of the school location in the personal exposure of schoolchildren. Schools with different proximities to traffic are included in the study.

Chapter 4 describes the personal exposure to traffic-related air pollutants assessed in a group of older adults, living at busy roads or at background locations. In this chapter we also study the contribution of participating in traffic and spending time outdoors to the personal exposure to traffic-related air pollutants.

In Chapter 5 the impact of using outdoor concentrations as an estimate for the personal level of air pollutants is further worked out. Here we apply a measurement error adjustment approach to describe what the effect is on the previously estimated health risks.

Finally, in Chapter 6 we discuss the main results, argue on the strengths and limitations of this study, provide comparisons between chapters and relate to previous research.

References

[1]Curtis L, Rea W, Smith-Willis P, Fenyves E, Pan Y. Adverse health effects of outdoor air pollutants. Environ Int 2006; 32(6):815-30.

[2]Amann M, Bertok I, Cofala J, Gyarfas F, Heyes C, Klimont Z, et al. Baseline scenarios for the Clean Air for Europe (CAFE) programme. Final report to the European Commission for the study on 'Development of the baseline and policy scenarios and integrated assessment modelling framework for the Clean Air for Europe (CAFE) programme -Lot 1'. Laxenburg, Austria: International Institute for Applied Systems Analysis (IIASA); 2004.

[3]Cohen AJ, Ross Anderson H, Ostro B, Pandey KD, Krzyzanowski M, Kunzli N, et al. The global burden of disease due to outdoor air pollution. J Toxicol Environ Health A 2005; 68(13-14):1301-7.

[4]Kunzli N, Kaiser R, Medina S, Studnicka M, Chanel O, Filliger P, et al. Public-health impact of outdoor and traffic-related air pollution: a European assessment. Lancet 2000; 356(9232):795-801.

[5]EU. Guideline 1999/30/EG van de raad van 22 april 1999 betreffende de grenswaarden voor zwaveldioxide en stikstofdioxiden, zwevende deeltjes en lood in de lucht. Publicatieblad van de Europese Gemeenschappen; 1999. Report No.: No L 163/41.

[6]Buijsman E. Year Overview Air Quality (Jaaroverzicht luchtkwaliteit 2002). Bilthoven: National Institute for Public health and the Environment (RIVM); 2004 april 2004. Report No.: 500037004.

[7]WHO. Health Aspects of Air Pollution: a Systematic Review of Health Aspects of Air Pollution in Europe. Copenhagen: World Health Organization Regional Office for Europe; 2004 June 2004. Report No.: E83080.

[8]Brunekreef B, Holgate ST. Air pollution and health. Lancet 2002; 360(9341):1233-42.

[9]HEI. Revised Analyses of Time-Series Studies of Air Pollution and health. Special Report. Boston MA: Health Effects Institute; 2003 May 2003.

[10]Katsouyanni K, Touloumi G, Samoli E, Gryparis A, Le Tertre A, Monopolis Y, et al. Confounding and effect modification in the short-term effects of ambient particles on total mortality: results from 29 European cities within the APHEA2 project. Epidemiology 2001; 12(5):521-31.

[11]Dockery DW, Pope CA, 3rd, Xu X, Spengler JD, Ware JH, Fay ME, et al. An association between air pollution and mortality in six U.S. cities. N Engl J Med 1993; 329(24):1753-9.

[12]Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knutsen SF, Lawrence Beeson W, et al. Long-term inhalable particles and other air pollutants related to mortality in nonsmokers. Am J Respir Crit Care Med 1999; 159(2):373-82.

[13]Pope CA, 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. Jama 2002; 287(9):1132-41.

[14]Goss CH, Newsom SA, Schildcrout JS, Sheppard L, Kaufman JD. Effect of ambient air pollution on pulmonary exacerbations and lung function in cystic fibrosis. Am J Respir Crit Care Med 2004; 169(7):816-21.

[15]Fischer P, Hoek G, Reeuwijk Hv, DJ B, Lebret E, Wijnen Jv, et al. Traffic-related differences in outdoor and indoor concentrations of particles and volatile organic compounds in Amsterdam. Atmos Environ 2000; 34:3713-3722.

[16]Briggs D, Collins S, Elliot P, Fischer P, Kingham S, Lebret E, et al. Mapping urban air pollution using GIS: a regression-based approach. Int J Geographical Information Science 1997; 11(7):699-718.

[17]Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U, et al. Estimating long-term average particulate air pollution concentrations: application of traffic indicators and geographic information systems. Epidemiology 2003; 14(2):228-39.

[18]Roorda-Knape M, Janssen N, Hartog Jd, Vliet Pv, Harssema H, Brunekreef B. Air pollution from traffic in city districts near major motorways. Atmos Environ 1998; 32(11):1921-1930.

[19]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 2002; 360(9341):1203-9.

[20]Gehring U, Heinrich J, Kramer U, Grote V, Hochadel M, Sugiri D, et al. Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. Epidemiology 2006; 17(5):545-51.

[21]Finkelstein MM, Jerrett M, Sears MR. Traffic air pollution and mortality rate advancement periods. Am J Epidemiol 2004; 160(2):173-7.

[22]Garshick E, Laden F, Hart JE, Caron A. Residence near a major road and respiratory symptoms in U.S. Veterans. Epidemiology 2003; 14(6):728-36.

[23]Lipfert FW, Baty JD, Miller JP, Wyzga RE. PM2.5 constituents and related air quality variables as predictors of survival in a cohort of U.S. military veterans. Inhal Toxicol 2006; 18(9):645-57.

[24]Brunekreef B, Janssen NA, de Hartog J, Harssema H, Knape M, van Vliet P. Air pollution from truck traffic and lung function in children living near motorways. Epidemiology 1997; 8(3):298-303.

[25]Vliet Pv, Knape M, Hartog Jd, Janssen N, Harssema H, Brunekreef B. Motor vehicle exhaust and chronic respiratory symptoms in children living near freeways. Environ Res 1997; 74:122-132.

[26]Rijnders E, Janssen NA, van Vliet PH, Brunekreef B. Personal and outdoor nitrogen dioxide concentrations in relation to degree of urbanization and traffic density. Environ Health Perspect 2001; 109 Suppl 3:411-417.

[27]Janssen N, Vliet PHNv, Aarts F, Harssema H, Brunekreef B. Assessment of exposure to traffic related air pollution of children attending schools near motorways. Atmos Environ 2001; 35:3875-3884.

[28]Janssen N, Brunekreef B, van Vliet P, Aarts F, Meliefste K, Harssema H, et al. The relationship between air pollution from heavy traffic and allergic sensitization, bronchial hyperresponsiveness, and respiratory symptoms in Dutch schoolchildren. Environ Health Perspect 2003; 111(12):1512-8.

[29]Nicolai T, Carr D, Weiland SK, Duhme H, von Ehrenstein O, Wagner C, et al. Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. Eur Respir J 2003; 21(6):956-63.

[30]Janssen NAH, Brunekreef B, Hoek G, Keuken MP. Traffic-related air pollution and health (Verkeersgerelateerde luchtverontreiniging en gezondheid; een kennisoverzicht). TNO report. Apeldoorn: Institute for Risk Assessment Sciences (IRAS) and TNO Environment, Energy and Proces Innovation(TNO); 2002 september 2002.

[31]Kibble A, Harrison R. Point sources of air pollution. Occup Med (Lond) 2005; 55(6):425-31.

[32]Janssen NAH, Hoek G, Harssema H, Brunekreef B. Personal exposure to fine particles in children correlates closely with ambient fine particles. Arch Environ Health 1999; 54:95-101.

[33]Ebelt ST, Petkau AJ, Vedal S, Fisher TV, Brauer M. Exposure of chronic obstructive pulmonary disease patients to particulate matter: relationships between personal and ambient air concentrations. J Air Waste Manag Assoc 2000; 50(7):1081-94.

[34]Janssen N, de Hartog JJ, Hoek G, Brunekreef B, Lanki T, Timonen KL, et al. Personal exposure to fine particulate matter in elderly subjects: relation between personal, indoor, and outdoor concentrations. J Air Waste Manag Assoc 2000; 50(7):1133-43.

[35]Sarnat JA, Koutrakis P, Suh HH. Assessing the relationship between personal particulate and gaseous exposures of senior citizens living in Baltimore, MD. J Air Waste Manag Assoc 2000; 50(7):1184-98.

[36]Williams R, Suggs J, Creason J, Rodes C, Lawless P, Kwok R, et al. The 1998 Baltimore Particulate Matter Epidemiology-Exposure Study: part 2. Personal exposure assessment associated with an elderly study population. J Expo Anal Environ Epidemiol 2000; 10(6 Pt 1):533-43.

[37]Janssen NA, Hoek G, Brunekreef B, Harssema H, Mensink I, Zuidhof A. Personal sampling of particles in adults: relation among personal, indoor, and outdoor air concentrations. Am J Epidemiol 1998; 147(6):537-47.

[38]Wichmann J, Janssen NAH, van der Zee S, Brunekreef B. Traffic-related differences in indoor and personal absorption coefficients measurements in Amsterdam, The Netherlands. Atmos Environ 2005; 39:7384-7392.

[39]Lanki T, Ahokas A, Alm S, Janssen NA, Hoek G, De Hartog JJ, et al. Determinants of personal and indoor PM(2.5) and absorbance among elderly subjects with coronary heart disease. J Expo Sci Environ Epidemiol 2006. (doi:10.1038/sj.jes.7500470)

Chapter two

Long-term personal exposure to traffic-related air pollution among school children, a validation study

Sofie Van Roosbroeck
Janine Wichmann
Nicole A.H. Janssen
Gerard Hoek
Joop H. van Wijnen
Erik Lebret
Bert Brunekreef

(Published in Science of the Total Environment 2006; 368: 565-573)

Abstract

Several recent studies suggest an association between long-term exposure to traffic-related air pollution and health. Most studies use indicators of exposure such as outdoor air pollution or traffic density on the street of residence. Little information is available about the validity of these measurements as an estimate of long-term personal exposure to traffic-related air pollution. In this pilot study, we assessed outdoor and personal exposure to traffic-related air pollution in children living in homes on streets with different degree of traffic intensity.

The personal exposure of 14 children aged 9-12 years to 'soot', NO_x (NO and NO_2) was assessed in Amsterdam between March and June 2003. Each child's personal exposure was monitored during four repeated 48-h periods. Concurrently, in- and outdoor NO_x measurements were carried out at the school and at the home of each participating child. Measurements were supplemented by a questionnaire on time activity patterns and possible indoor sources. Flow-controlled battery operated pumps in a made-to-fit backpack were used to sample personal exposure to 'soot', determined from the reflectance of $PM_{2.5}$ filters. Exposure to NO_x was assessed using Ogawa passive samplers. Children living near busy roads were found to have a 35% higher personal exposure to 'soot' than children living at an urban background location, despite that all children attended the same school that was located away from busy roads. Smaller contrasts in personal exposure were found for NO (14%), NO_2 (15%) and NO_x (14%). This finding supports the use of 'living near a busy road' as a measure of exposure in epidemiological studies on the effects of traffic-related air pollution in children.

Introduction

Several recent studies show associations between air pollution and health.[1] Results of three prospective cohort studies have suggested that long-term exposure to particulate matter (PM) air pollution is associated with increased mortality from respiratory and cardiovascular disease and lung cancer.[2-4] These studies have compared several large study regions with different ambient air pollution concentrations, on the assumption that exposure was uniform within each region.

Due to recent reports of a significant variation of outdoor traffic related air pollution within cities, a Dutch cohort study assessed exposure to air pollution on a smaller spatial scale by taking the

proximity to major roads into account using a geographic information system (GIS).[5] Participants who lived closer to major roads had a significantly increased risk of death resulting from cardio respiratory causes.[5]

Several cross-sectional studies have also shown associations between traffic-related air pollution and adverse health effects.[6] These studies used indicators of exposure, such as traffic density on the street of residence, distance between the home and busy roads and/or estimated outdoor concentrations based on such characteristics. Little information, however, is available about the validity of these measurements as an estimate of long-term personal exposure to traffic-related air pollution.

The availability of validation data for short-term exposure studies is far more than that available for long-term monitoring. Several studies have documented that the temporal variation in outdoor particulate matter air pollution is reflected in temporal variation of personal exposure.[7, 8] However, these studies do not provide information on the validity of outdoor air pollution concentrations for long-term exposure studies, which require spatial contrast in average outdoor air pollution.

A study conducted in the Netherlands at three schools near freeways with a range of traffic intensities from 45 000 to 150 000 vehicles per day showed significant differences in the long-term average personal nitrogen dioxide (NO_2) exposure of school children.[9] Rijnders et al.[9] found an estimated difference of 8.2 $\mu g/m^3$ (SE 1.8) between personal NO_2 exposure of the children attending the school with the highest and lowest traffic intensity; a difference of 46%. The increase in school outdoor NO_2 for these children was 41%, whereas the difference in home outdoor NO_2 concentration was 28%.[9] A study by Monn[10] also focused on long-term exposure and showed highly significant correlations (R^2>0.9) on a city-level between outdoor and personal annual mean estimates of exposure to NO_2. However, no long-term studies have involved personal sampling of the probably more relevant particulate matter, with a 50% cut off of 2.5 µm in aerodynamic particle size ($PM_{2.5}$), and particulate components such as 'soot'. This lack of data hinders the interpretation of epidemiological studies on long-term air pollution exposures. In this pilot study we therefore aimed to evaluate the feasibility of personal monitoring for PM, since these procedures are known to be high demanding for the participants. Since epidemiological studies on long-term effects of traffic-related air pollution identify children as a sensitive group, we selected school children as participants in this study. We assessed personal exposure to traffic-related air pollutants, $PM_{2.5}$, 'soot', and NO_x in locations with varying degrees of traffic

intensity. The overall objective of this study was to test the validity of traffic-related characteristics as an estimate for the personal long-term exposure to traffic-related air pollution, including $PM_{2.5}$, 'soot' and NO_x.

Methods

Participant selection

We conducted a pilot study in an urban background school in Amsterdam. With the cooperation of the school board, 40 children from grades 7 and 8 (9 to 12 years of age) were asked to participate in the study. These children received an invitation with a cover letter explaining the purpose of the study. Candidates were asked to return a participation form and parents had to sign an informed consent form.

Study design

Personal exposure to traffic-related air pollution was monitored four times per child in March, April, May and June of 2003. Children carried a personal $PM_{2.5}$ sampler (figure 1) and an Ogawa passive sampler (figure 2), to provide personal NO_x measurements, continuously for 48 hours. Concurrently, home indoor and outdoor measurements of NO_x, and school indoor and outdoor NOx, and $PM_{2.5}$ concentrations were collected using identical sampling equipment. Light absorbance was measured from all $PM_{2.5}$ filters as a proxy for 'soot' or elemental carbon. Absorption coefficients of $PM_{2.5}$ filters have been shown to be highly correlated with measurements of Elemental carbon (EC) or 'soot'.[8, 11-13] Elemental carbon or 'soot' is a product of incomplete combustion and has been found to correlate with diesel exhaust.[14-16] In this paper, absorption of the $PM_{2.5}$ filters will be referred to as 'soot'.

Measurements took place from Monday to Wednesday or from Wednesday to Friday. In total, this study comprehended 8 measurement periods of 48 hours. During each measurement period five to nine personal measurements, their matching in- and outdoor home measurements, and the in- and outdoor measurement at the school were conducted. Children lived in streets with varying traffic intensity. We ensured that samples for children living in streets with low and high traffic intensity were attained simultaneously.

Figure 1. BGI-400 battery operated pump with flow rate of 4 l/min.

Figure 2. Ogawa passive sampler.

Sampling methods

Personal $PM_{2.5}$ measurements were conducted with $PM_{2.5}$ GK2.05 cyclones (BGI Inc., Waltham, MA) that were designed and constructed for the EXPOLIS study and flow-controlled battery operated pumps (BGI-400) at a flow rate of 4 l/min.[17] Batteries suitable for 48-h sampling were used. Children could wear the sampler in a custom-made backpack that contained an internal sound isolation covering (figure 3). We provided and distributed insulated boxes (figure 4) in which the backpack with the sampler could be placed in order to further reduce pump noise levels so that the noise would not disturb the participants over night. To assess personal NO, NO_2 and NO_x, we used Ogawa passive samplers (Ogawa & Company USA, Inc.) with pre-coated NO_2 and NO_x collection pads.

The personal measurements were started at the school, in order to motivate the group of children as a whole and to give detailed instructions on how to wear the sampling equipment. Children could wear the badge attached to their clothing using an alligator clip. Children were instructed to wear and keep the backpack and badge as close as possible. However, they were allowed to place the backpack with sampler nearby during indoor sedentary activities (watching TV, reading) or activities during which wearing the sampler would be too inconvenient or impossible (such as sleeping or swimming). Parents recorded the kind and duration of such activities, as well as the position of the backpack with sampler in a time activity questionnaire, which also collected data

on housing conditions, daily activity patterns, school travel mode and possible indoor sources of $PM_{2.5}$ and NO_x.

Figure 3. Backpack with internal sound isolation covering to carry personal PM sampler.

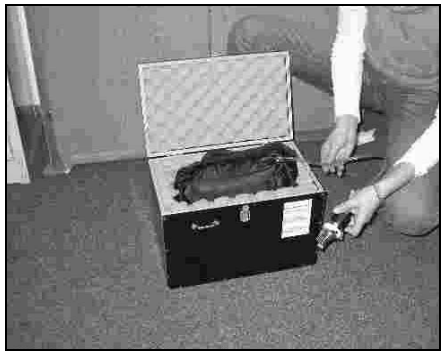

Figure 4. Insinulated box.

Outdoor $PM_{2.5}$ concentrations and 'soot' were measured using the same sampling equipment as used for the personal sampling measurements. For all $PM_{2.5}$ measurements the same filters (Anderson Teflon 37 mm) were used. Indoor and outdoor NO_x measurements were also carried out with the same sampler used for the personal sampling, however, for the outdoor measurements, a shelter was used to protect the badge from the weather (figure 5). For all pollutants, at least one outdoor field blank per 48-h measurement period was collected.

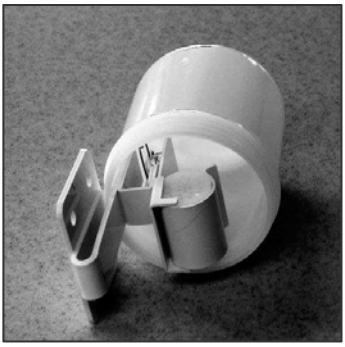

Figure 5. Ogawa passive sampler with shelter.

Analytical procedures

The $PM_{2.5}$ mass was determined by weighing a filter before and after sampling using a Mettler MT5 micro-balance (Mettler-Toledo, Greifensee, Switzerland) with 1µg reading precision. Filters were stored at 4°C and were weighed after equilibrating for 24 hours in a temperature (20 to 23°C) and humidity (30 to 40%) controlled room. Details on the analytical procedures can be found elsewhere.[8,18]

To assess light absorption of the $PM_{2.5}$ mass, first reflectance was measured using an EEL 43 reflectometer, according to Standard Operating Procedures (SOP) developed for the ULTRA study (SOP ULTRA/KTL-L1.0) on the same filters used to determine $PM_{2.5}$ mass.[19] Each filter was measured at five standard spots and the average reflectance was calculated. Next, the reflectance of the $PM_{2.5}$ filters was transformed into absorption coefficients (a) according to the following formula (ISO 9835 (1993))[20]:

$$a = (A/2V) * \ln (R_0/R_s)$$

where A = loaded filter area (m^2), V = sampled volume (m^3), R_0 = average reflectance of field blank filters, and R_s = reflectance of the sampled filter. Absorption coefficients were expressed in $m^{-1} \times 10^{-5}$.

NO_2 and NO_x were collected using precoated NO_2 or NO_x 14.5-mm pads (p/Ns PS-114 and PS-124, Ogawa & Co Inc.) deployed in personal sampler bodies (p/N P-100, Ogawa & Co.). For the details on the sampling and analysis of the Ogawa passive samplers, we refer to the manufacturer's instructions (Ogawa USA, Inc., Pompano Beach, Florida, ogawausa.com).[21]

Pads were loaded into samplers and stored in airtight cups for transport to or from sampling sites. Following collection, samplers were refrigerated until analysed. Using a sulfanilamide solution and N-(1-Naphthyl)-ethylenediamine dihydrochloride (NEDA) as colour producing reagent, the NO_x and NO_2 concentrations were determined by an analysis based upon the Saltzman method, with a spectrometer at a wavelength of 545 nm. NO concentrations were obtained by taking the difference of NO_x and NO_2 concentrations.

Traffic counts and meteorological data

Data on traffic intensity were obtained from the department of Infrastructure, Transport and Traffic, Amsterdam in The Netherlands. Data on wind direction per hour were obtained from the Royal Dutch Meteorological Institute (KNMI). The measurements were taken at the nearest measurement site, Amsterdam Schiphol airport, which is located south west of, and at about 10 km distance from the background school in the city centre of Amsterdam. A home was considered downwind if the wind was directing within 60º from the perpendicular line to the road in the direction of the home. For the measurements near a busy road, the percentage of time that the home was downwind from the road during the measurement was calculated. Next, these measurements were divided into two groups; one with downwind for more than 50% of the exposure time (i.e. longer than 24 hours) and one with less than 50% of the exposure time. Hence, the influence of wind direction on air pollution concentration for these two groups was assessed using multiple regression analysis.

Statistical analysis

The statistical analysis of the data was carried out using the statistical software program SAS (version 8e).

First, the distribution of personal, indoor and outdoor concentrations were obtained for the 'busy road' and 'background' groups separately. Definitions for the busy road group and the background group were designed taking the distribution of the proximity to busy roads of the participants into account. Accordingly, 'Living near a busy road' was defined as living closer than 75 m to a road with traffic density of at least 10 000 cars per 24 h. 'Living at a background location' was defined as living further away than 75 m from a road with traffic density of at least 10 000 cars per 24 h. In urban settings, roads affect air pollution only at short distances, typically 50 m to 100 m from a road. Ratios of the geometric means were calculated and differences between the groups were tested using a t-test. Next, the personal, indoor and outdoor concentrations of 'soot', NO, NO_2 and NO_X were logarithmically transformed to obtain normal distribution. Mixed effect model repeated measures analysis (proc mixed) was applied to perform a multiple regression model that included subject as a random factor that adjusted for repeated measurements of the same child.

Furthermore, results can be confounded by possible indoor sources, and different distribution of measurements over the sampling days. Therefore, adjustment for these variables was included in

the regression model. As a result, the regression analysis used the logarithm of a pollutant concentration as a dependent variable and 'living near a busy road', exposure to environmental tobacco smoke (ETS) and cooking as independent binary variables.
To study the effect of possible outliers, Cook's d values were calculated, and regression models were conducted again with the exception of main outliers of Cook's D.

Results

Fourteen children responded and enrolled into the study. All fourteen children completed the four 48-h measurements. In total we collected 55 valid personal measurements for 'soot' and 41 for NO_x, 6 in- and outdoor measurements at the school location, and 42 in- and outdoor measurements at the homes of the participants. The variation in proximity of busy roads to the residential addresses and the traffic intensity of these busy roads is shown in table 1. Five children lived near a busy road, of which one (ID10) actually lived on a busy road (14 400 cars per 24 h). The others lived at a background location.
No $PM_{2.5}$ mass data are reported as we found unrealistically high concentrations in this study, likely due to cyclone malfunctioning. Visible coarse particles could be detected on some filters. The cyclone may not have been hooked tight enough to the backpack, therefore light physical activity of the participant could make the cyclone spin around and make the inlet of the pump point towards the participant's clothing instead of forward for short periods of time. In a further experiment we prevented the cyclone from spinning and normal $PM_{2.5}$ mass date were reported. This interpretation is also supported by the results of school outdoor sampling, where the whole sampling set-up was firmly attached to an exterior school wall. The average school outdoor concentrations for $PM_{2.5}$ mass and 'soot' were 10.8 $\mu g/m^3$ and 0.95 m^{-1} 10^{-5} respectively, which can both be considered as regular background levels. When comparing this outdoor level to the average personal 'soot' concentration, we find an increase of only 30%, (of which a part can be allocated to exposure to ETS) whereas the personal exposure to $PM_{2.5}$ mass increases with an unrealistic factor 5 compared to the outdoor exposure.

Table 1. Detailed information on the proximity to busy roads near the residential address.

ID	Distance to busy roads	Traffic intensity of busy road (cars/24h)	Floor
1	10 m	2003	2
	150 m	15 800	
2	45 m	24 500	1
	135 m	49 000	
3	60 m	25 300	3
4	165 m	35 500	4
5	120 m	10 200	0
6	271 m	15 000	0
7	120 m	25 300	2
	128 m	13 700	
	180 m	21 700	
8	301 m	15 000	1
9	23 m	14 400	0
10	6 m	14 400	2
11	377 m	35 500	2
12	241 m	13 100	0
	437 m	14 400	
	512 m	14 400	
13	60 m	13 700	1
	75 m	25 300	
14	128 m	21 700	2

Participants living near a busy road are highlighted in grey. The distance to major roads was reflected as the distance from the door of the house to the middle of the road.

In general, children spent little time in traffic and little time outdoors. Median time spent in a car during 48 h was zero (with a 25%–75% interquartile range of 0-0.75). The median time spent cycling was a little higher, 0.75 h (Q25-Q75= 0-1.50). The median time spent outdoors, other then cycling, was 3.5 h (Q25-Q75=1.67-5.0). Of the 55 completed questionnaires, 18 reported an exposure to ETS, 37 reported an exposure to cooking, 8 reported an exposure to vacuum cleaning and 7 to dusting off. None of the participants reported having used a gas stove, heater nor fireplace.

Further, higher personal 'soot' concentrations were found on days with elevated 'soot' levels in the outdoor air (we found a correlation coefficient of 0.98 between the personal 'soot' concentrations of the background group and the school outdoor 'soot' concentrations). This supports the reliability of the absorbance measurements.

The average reflectance of the field blank filter was 100.5 (n=8, S.D. 0.86). The limit of detection (LOD), calculated as three times the standard deviation of the blanks, was 0.087 m^{-1} 10^{-5} for absorption; all absorption coefficients were above this LOD. The average field blank for NO_x was 6.91 ppb (n=15, S.D. 2.64), after exclusion of one very high field blank (28.65 ppb). For NO_2 and NO the averages were 2.86 ppb (n=16, S.D. 2.23) and 4.05 ppb (n=15, S.D. 2.47), respectively. The LOD was 7.93, 6.68 and 7.40 ppb for NO_x, NO_2 and NO, respectively. All values for NO_2 and NOx were above the LOD. With NO, 57% of the values were below the LOD. Therefore, we retained most values and only substituted the negative values (0.03%) by zero.

Figure 6 shows the distribution of the personal measurements of 'soot', NO, NO_2 and NO_x for the 'busy road' and 'background' group. In general, mean personal exposure to 'soot', NO, NO_2 and NO_x for children living near a busy road was higher than for the children living at a background location.

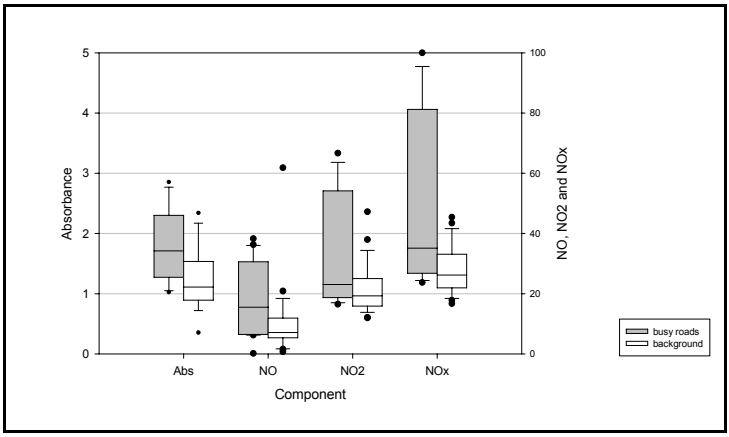

Figure 6. Distribution of personal exposure of 'soot' ($10^{-5}m^{-1}$), NO, NO_2 and NO_X (ppb) of children living near a busy road and children living at a background location. The scale of the figure was reduced to 100 ppb for NO, NO_2 and NO_x for clarity reasons. Accordingly, three observations (NO_x concentration of 185 ppb and 109 ppb and one NO concentration of 145 ppb) were not included in the figure.

Table 2. Home outdoor, home indoor and personal pollutant concentrations for children living near a busy road and for children living at an urban background location.

	Geometric Mean (min – max)						
	N	Busy road group		N	Background group		
Home Outdoor							
NO (ppb)	15	7.69	(3.19 – 29.37)	26	4.31	(1.41 – 21.12)	1.78*
NO_2 (ppb)	15	19.69	(14.44 – 26.84)	27	17.81	(13.20 – 26.58)	1.11
NO_x (ppb)	15	28.22	(20.70 – 50.40)	27	22.20	(12.31 – 39.65)	1.27*
Home Indoor							
NO (ppb)	15	10.18	(1.03 – 43.82)	24	8.50	(0.19 – 109.95)	1.20
NO_2 (ppb)	15	24.53	(13.87 – 79.84)	27	20.09	(11.25 – 69.41)	1.22
NO_x (ppb)	15	36.97	(18.36 – 123.97)	27	30.88	(14.01 – 179.47)	1.20
Personal							
'soot' ($m^{-1}.10^{-5}$)	20	1.70	(1.02 – 2.86)	35	1.23	(0.44 – 2.56)	1.38*
NO (ppb)	15	9.21	(0.19 – 38.09)	25	7.69	(0.71 – 145.47)	1.20
NO_2 (ppb)	15	24.29	(16.61 – 62.18)	26	20.91	(11.94 – 46.99)	1.16
NO_x (ppb)	15	36.97	(23.81 - 100.48)	26	30.88	(16.61 – 184.93)	1.20

Ratio of geometric means is the ratio of the overall geometric mean of the 'busy road' group versus the overall geometric mean of the 'background' group. N is the number of 48-h sampling periods. *t-test with $p<0.01$; for testing the difference of the distributions between the two groups.

A summary of the crude data is presented in table 2. We found a significant increase in NO and NO_x in the outdoor air for the busy road group compared to the background group. Elevated ratios were found for all home indoor pollutants, however they were not statistically significant. Table 2 further shows the results for the difference in exposure to the pollutants on the personal level. Comparable elevated ratios were found for NO, NO_2 and NO_x; and a significant increase in personal 'soot' was found. The children from the busy road group had a 38% higher personal

exposure to 'soot' compared to the children from the background group. Contrasts in the outdoor pollutant concentrations of the busy road group versus the background group were stronger for NO than for NO_2.

Mean outdoor 'soot' measured at the school location was 0.95 (S.D. 0.20) m^{-1} 10^{-5}. Mean NO_x concentration was 23.63 (S.D. 5.91) ppb outdoors, and 19.37 (S.D. 4.53) ppb indoors.

Table 3. Percentage increase in personal, home indoor and home outdoor 'soot', NO, NO_2 and NO_x exposure (95% Confidence Interval), when living near a busy road for adjusted and unadjusted model.

		Home outdoor	Home indoor	Personal
'soot'	Unadjusted	/	/	38 (12, 72)*
	Adjusted	/	/	35 (9, 68)*
NO	Unadjusted	77 (16, 169)*	20 (-51, 194)	21 (-46, 161)
	Adjusted	75 (12, 175)*	21 (-65, 314)	14 (-49, 156)
NO_2	Unadjusted	10 (-2, 25)	23 (-11, 70)	17 (-10, 51)
	Adjusted	10 (-6, 28)	26 (-28, 120)	15 (-28, 82)
NO_x	Unadjusted	27 (8, 44)*	20 (-21, 82)	19 (-14, 67)
	Adjusted	27 (4, 55)*	22 (-41, 153)	14 (-35, 97)

Multiple Regression analysis; * $p<0.05$. Regression results were adjusted for ETS, cooking, repeated measurements and different distribution of measurements over the sampling days.

After adjustment for possible indoor combustion sources and day of measurement, the multiple regression model in table 3 shows that the percentage increase in personal 'soot' of busy road children versus background children slightly decreases (35% vs. 38%), but it remained significant (table 3). The percentage increase in outdoor NO slightly decreased (77% vs. 75%) and the percentage increase in outdoor NO_x remained the same (27%); both also remained statistically significant. Children exposed to ETS on a sampling day had a higher exposure to 'soot'; ETS had only little effect on personal NO_x, and cooking had no effect on any of the measured pollutants. Taking ETS into account however, did not change the estimates for living on a busy road.

'Soot' was sampled during 8 different sampling days, resulting in 55 measurements, whereas NO_x was sampled during 6 sampling days, due to delayed assembling of the NO_x badges and therefore resulting in less NO_x measurements (41). After excluding all 'soot' measurements on days that no NO_x concentrations were sampled, the percentage increase in personal 'soot' of busy road children versus background children decreased from 35 to 28% and it remained significant.

An outlier analysis using Cook's d values showed that outliers did not influence the results; neither had sampling day an effect on the effect estimates.

Table 4 shows the increase in 'soot', NO_2, NO and NO_x concentrations for the measurements during which the home is down wind for more and less then 50% of the sampling time. Both were compared to the measurements of children living at background locations that were sampled simultaneously. Out of the 55 personal measurements, 7 were sampled during sampling periods with more than 50% down wind, 13 with less than 50% down wind and 35 measurements were sampled in children living at background locations, all spread out over 8 sampling periods of 48 hours. On days with more than 50% down wind, children living at a busy road had a 54% higher personal exposure to 'soot' compared to background children. On days with less than 50% down wind the increase in personal exposure to 'soot' remains 31% for the busy road children. All increases in outdoor concentrations of NO, NO_2 and NO_x were statistically significant on days with more than 50% down wind. The increases for personal and home indoor concentrations were rather small and not statistically significant.

Table 4. Percentages increase (95% Confidence Interval) in exposure to 'soot', NO, NO_2 and NO_x for high and low percentage of time that the home is downwind from a major road.

	'soot'	NO	NO_2	NO_x
Home Outdoor				
>50% down wind	/	202 (75, 421)*	23 (2, 48)*	62 (31, 101)*
<50% down wind	/	36 (-9, 103)	4 (-10, 20)	12 (-5, 32)
Home Indoor				
>50% down wind	/	14 (-76, 432)	14 (-37, 105)	18 (-45, 153)
<50% down wind	/	20 (-67, 331)	27 (-28, 125)	21 (-40, 146)
Personal				
>50% down wind	54 (11, 114)*	73 (-47, 467)	4 (-35, 65)	21 (-34, 120)
<50% down wind	31 (1, 72)*	1 (-59, 148)	15 (-23, 86)	15 (-32, 93)

Multiple Regression analysis; * $p<0.05$

Discussion

A significant difference in personal exposure to 'soot' between children living near busy roads and children living at background locations in Amsterdam was found. This significant contrast could not be demonstrated for the indoor and personal concentrations of NO, NO_2 and NO_x, in spite of significant differences in outdoor NO and NO_x concentrations.

The modest increase in personal exposure of children living near a busy road to 'soot' and especially NO_2 and NO is partially related to the modest difference in traffic exposure. The children in the high exposed group of the current study lived within 75m of a busy road with a traffic intensity of 10 000 cars per 24h. There was a 10% increase in outdoor NO_2 and 75% in outdoor NO for children living near busy roads compared to those who were not. No outdoor 'soot' measurements were available. Rijnders et al.[9] found an increase of 46% in personal exposure to NO_2 for the children from the school located near the busiest highway (169 637 cars per 24 h) compared to the children attending the school located near the relatively non busy highway (45 129 cars per 24 h). The school outdoor NO_2 was increased by 41% and the home outdoor NO_2 concentration was increased by 28%. A study by Roorda-Knape et al.[22] selected residential districts within 300 m from a major motorway with traffic intensities varying from 80

000 to 152 000 cars per 24 h. They found differences of 56% and 40% in exposure to outdoor NO_2 when comparing measurements in two different city districts at different distances (15 to 305 m and 32 to 260 m respectively) from the roadside. The differences in outdoor 'soot' were 100% in one city district and 40% in the other. A study by Fischer et al.[23], also conducted in the centre of Amsterdam, performed measurements at 'low' and 'high' traffic homes, where 'high traffic home' was defined as a home right on a main street with average traffic intensity of 16 800 vehicles per 24 h. Differences in outdoor NO_2 and 'soot' were about 25% and 75% respectively. Several other traffic-related air pollution studies performed measurements at school sites near roads with even higher traffic intensities.[12,24] Kim et al.[24] measured among other pollutants, NO and NO_2 at 10 schools during several seasons. They found differences in concentrations between schools distant and nearby freeways with average traffic intensity of 170 000 cars per 24 h. Outdoor concentrations of NO_2 varied from 20.5 ppb for the schools without a major traffic source to 25.2 for the schools near the freeways. For NO measurements were 17.3 and 31.0 ppb respectively. This results in outdoor differences of 23% for NO_2, 80% for NO and 22% for 'soot'. When compared to our findings, these differences for the outdoor measurements were overall higher for NO_2 and comparable for NO.

Recently, two French studies concurrently assessed personal exposure to $PM_{2.5}$ while monitoring outdoor levels of the same or similar pollutants.[25,26] In the framework of the VESTA study, personal exposure to $PM_{2.5}$ of children in French urban environments and outdoor PM_{10} levels were assessed simultaneously.[25] They evaluated the relative contribution of outdoor and indoor sources to personal exposure and concluded that proximity of the home to urban traffic emissions was a main determinant.[25] The significant differences in personal exposure to 'soot' between children living near busy roads or not from the recent study are in agreement with these findings. Difference in personal 'soot' was significant, while the personal NO_2 and NO concentrations were not. Fischer et al.[23] had documented that the outdoor contrast for pollutants like 'soot' in the city of Amsterdam was substantially larger than for NO_2 (about 75% versus 25%), which is a secondary pollutant, and therefore it has a more homogeneous spatial distribution. Indeed, in the current study the contrast in outdoor NO_2 was only 10%. The differences for NO were larger than for NO_2 in the outdoor air. This is as expected since NO is a primary pollutant and more reactive and NO_2 a secondary one. NO_x emitted from motorized traffic is largely emitted as NO and therefore, contrasts in exposure, related to living near a busy road, are expected to be larger for NO than for NO_2. The small indoor and personal difference in NO is probably due to indoor

sources and the reactivity of NO. Indoor and personal NO_x concentrations exceed outdoor NO_x concentrations. The 95% confidence intervals found for home indoor and personal NO and NO_x concentrations were much larger than those for the outdoor concentrations, indicating a role for indoor sources. Götschi et al.[27] demonstrated little impact of indoor sources on 'soot'.

Reasons for the differences in significance between outdoor on the one hand and indoor and personal exposures on the other include the impact of indoor sources. Additionally, an outdoor sampler was either exclusively exposed to low or high levels, whereas a child living near a busy road was probably exposed to both high levels at home and low levels at school.

One of the limitations of this study is that we did not succeed in collecting reliable $PM_{2.5}$ mass. However, in the recent study, 'soot' and NO_x were used as specific markers for traffic-related air pollution. Particle mass ($PM_{2.5}$ mass) however, was only aimed to be included in order to allow comparisons with previous studies on traffic-related air pollution, as it is not considered to be a very specific indicator for traffic-related air pollution[23], and has also been reported to underestimate spatial variation of traffic-related air pollution.[28] Furthermore, the sampling of coarse particles has not affected 'soot' concentrations, since there's only a minor difference in assessing absorbance on PM_{10} collected filters then on $PM_{2.5}$ collected filters.[11,23]

Although wind data came from the nearest measurement site possible, the KNMI describes the scenery of the measurement site as predominantly grass and farmland mixed with infrastructure and buildings. The wind data of this site do not necessarily reflect the wind data for individual streets, as the architectural situation is more complex. Thus, the results of the wind direction analysis should be carefully considered.

Another point for discussion is to what extent the 4-month monitoring design is suitable for long-term exposure assessment. Obtaining long-term average personal exposures is complicated because of the demanding nature of personal monitoring for PM, the number of repeated measurements needs to be limited to a number that is realistic and feasible for the participants. Thus, the absolute concentrations of pollutants may not be representative for long-term averages. However, the focus of the comparison is the spatial contrast of exposure. Therefore, the design was accurately carried out to make sure that concurrently five to nine 48-h measurements were performed on the same day in participants from both exposure groups.

Conclusion

Measuring long-term average personal exposure to traffic-related air pollution is complicated, because of the highly demanding nature of personal monitoring for particulate matter. The current design, however, succeeded in assessing whether the average personal exposure of children living near busy roads differed from those living at background locations. The results of this pilot study show that personal exposure to traffic-related particles is significantly higher for children living along busy roads, despite the fact that all participating children spent a substantial amount of time at the same school, located away from busy roads. This finding supports the use of 'living along a busy road' as a measure of exposure in epidemiological studies on the effects of traffic-related air pollution. It is still unclear, however, whether this conclusion will hold for populations other than children.

Acknowledgements

The authors like to thank all the young participants, their parents and their teachers. Wichmann J. received a Dutch Huygens Scholarship during 2002 - 2003.

References

[1]Brunekreef B, Holgate ST. Air pollution and health. Lancet 2002; 360:1233-42.

[2]Abbey DE, Nishino N, McDonnell WF, Burchette RJ, Knutsen SF, Lawrence Beeson W, Yang JX. Long-term inhalable particles and other air pollutants related to mortality in nonsmokers. Am J Respir Crit Care Med 1999; 159:373-82.

[3]Dockery DW, Pope CA, 3rd, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG, Jr., Speizer FE. An association between air pollution and mortality in six U.S. cities. N Engl J Med 1993; 329:1753-9.

[4]Pope CA, III, Thun MJ, Namboodiri MM, Dockery DW, Evans JS, Speizer FE, Heath CW, Jr. Particulate air pollution as a predictor of mortality in a prospective study of U.S. adults. Am J Respir Crit Care Med 1995; 151:669-674.

[5]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 2002; 360:1203-9.

[6]Delfino RJ. Epidemiologic evidence for asthma and exposure to air toxics: linkages between occupational, indoor, and community air pollution research. Environ Health Perspect 2002; 110 Suppl 4:573-89.

[7]Janssen NAH, Hoek G, Harssema H, Brunekreef B. Personal exposure to fine particles in children correlates closely with ambient fine particles. Arch Environ Health 1999; 54:95-101.

[8]Janssen NA, de Hartog JJ, Hoek G, Brunekreef B, Lanki T, Timonen KL, Pekkanen J. Personal exposure to fine particulate matter in elderly subjects: relation between personal, indoor, and outdoor concentrations. J Air Waste Manag Assoc 2000; 50:1133-43.

[9]Rijnders E, Janssen NA, van Vliet PH, Brunekreef B. Personal and outdoor nitrogen dioxide concentrations in relation to degree of urbanization and traffic density. Environ Health Perspect 2001; 109 Suppl 3:411-417.

[10]Monn C. Exposure assessment of air pollutants: a review on spatial heterogeneity and indoor/outdoor/personal exposure to suspended particulate matter, nitrogen dioxide and ozone. Atmos Environ 2001; 35:1-32.

[11]Cyrys J, Heinrich J, Hoek G, Meliefste K, Lewne M, Gehring U, Bellander T, Fischer P, van Vliet P, Brauer M, Wichmann HE, Brunekreef B. Comparison between different traffic-related

particle indicators: elemental carbon (EC), PM2.5 mass, and absorbance. J Expo Anal Environ Epidemiol 2003; 13:134-43.

[12]Janssen N, Vliet Pv, Aarts F, Harssema H, Brunekreef B. Assessment of exposure to traffic related air pollution of children attending schools near motorways. Atmos Environ 2001; 35:3875-3884.

[13]Kinney PL, Aggarwal M, Northridge ME, Janssen NA, Shepard P. Airborne concentrations of PM(2.5) and diesel exhaust particles on Harlem sidewalks: a community-based pilot study. Environ Health Perspect 2000; 108:213-8.

[14]Froschl B, Niessner R. Urban aerosol analysis: is determination of 1-nitropyrene equivalent to the quantification of carbon? J Aerosol Sci 1997; 28:S71-S72.

[15]Scheepers PT, Velders DD. Gas chromatogaphic-mass spectrometric determination of nitro polycyclic aromatic hydrocarbons in airborne particulate matter from workplace atmospheres contanimated with diesel exhaust. J Chromatography 1994; 677:107-121.

[16]Scheepers PT, Martens MH, Velders DD, Fijneman P, van Kerkhoven M, Noordhoek J, Bos RP. 1-Nitropyrene as a marker for the mutagenicity of diesel exhaust-derived particulate matter in workplace atmospheres. Environ Mol Mutagen 1995; 25:134-47.

[17]Koistinen KJ, Kouse A, Tenhola V, Hänninen O, Jantunen MJ, Oglesby L, Kuenzli N, Georgoulis L. Fine Particle (PM2.5) Measurement methodology, Quality Assurance Procedures, and Pilot Results of the EXPOLIS Study. J Air Waste Manage Assoc 1999; 49:1212-1220.

[18]Brunekreef B, Janssen NA, de Hartog JJ, Oldenwening M, Meliefste K, Hoek G, Lanki T, Timonen KL, Vallius M, Pekkanen J, Van Grieken R. Personal, indoor, and outdoor exposures to PM2.5 and its components for groups of cardiovascular patients in Amsterdam and Helsinki. Res Rep Health Eff Inst 2005; 127:1-70; discussion 71-9.

[19]Pekkanen J, Timonen KL, Tiittanen P, Vallius M, Lanki T, Sinkko H, Ruuskanen J, Mirme A, Kulmala M, Vanninen E, Bernard A, Ibald-Mulli A, et al. ULTRA: Exposure and risk assessment for fine and ultrafine particles in ambient air. Study manual and data book. B9/2000. Kuopio: KTL, National Public Health Institute.

[20]ISO. Ambient air-determination of a black smoke Index (ISO 9835): International Organization for Standardization, 1993.

[21]Ogawa C. NO, NO_2, NO_x and SO_2 sampling protocol using the ogawa sampler. 1998. Accessed at www.agawausa.com in 2002.

[22]Roorda-Knape M, Janssen N, Hartog Jd, Vliet Pv, Harssema H, Brunekreef B. Air pollution from traffic in city districts near major motorways. Atmos Environ 1998; 32:1921-1930.

[23]Fischer P, Hoek G, Reeuwijk Hv, DJ B, Lebret E, Wijnen Jv, Kingham S, Elliot P. Traffic-related differences in outdoor and indoor concentrations of particles and volatile organic compounds in Amsterdam. Atmos Environ 2000; 34:3713-3722.

[24]Kim JJ, Smorodinsky S, Lipsett M, Singer BC, Hodgson AT, Ostro B. Traffic-related air pollution near busy roads: the East Bay Children's Respiratory Health Study. Am J Respir Crit Care Med 2004; 170:520-6.

[25]Gauvin S, Reungoat P, Cassadou S, Déchenaux J, Momas I, Just J, Zmirou D. Contribution of indoor and outdoor environments to PM2.5 personal exposure of children - VESTA study. Sci Tot Environ 2002; 297:175-181.

[26]Nerriere E, Zmirou-Navier D, Blanchard O, Momas I, Ladner J, Le Moullec Y, Personnaz MB, Lameloise P, Delmas V, Target A, Desqueyroux H. Can we use fixed ambient air monitors to estimate population long-term exposure to air pollutants? The case of spatial variability in the Genotox ER study. Environ Res 2005; 97:32-42.

[27]Götschi T, Oglesby L, Mathys P, Monn C, Manalis N, Koistinen K, Jantunen M, Hanninen O, Polanska L, Kunzli N. Comparison of black smoke and PM2.5 levels in indoor and outdoor environments of four european cities. Environ Sci Technol 2002; 36:1191-1197.

[28]Hoek G, Meliefste K, Cyrys J, Lewné M, Bellander T, Brauer M, Fischer P, Gehring U, Heinrich J, Van Vliet P, Brunekreef B. Spatial variability of fine particle concentrations in three European areas. Atmos Environ 2002; 36:4077-4088.

Chapter three

Long-term personal exposure to $PM_{2.5}$, Soot and NO_x in children attending schools located near busy roads, a validation study

Sofie Van Roosbroeck
José Jacobs
Nicole A.H. Janssen
Marieke Oldenwening
Gerard Hoek
Bert Brunekreef

(Published in Atmospheric Environment 2007; 41: 3381-3394)

Abstract

Several studies have investigated the health of children attending schools located near busy roads. In this study, we have measured personal exposure to traffic-related pollutants in children to validate exposure classification based on school location. Personal exposure to $PM_{2.5}$, soot, NO_x and NO_2 was measured during four 48-hour periods. The study involved 54 children attending four different schools, two of which were located within 100 meter of a major road (one ring road and one freeway) and the other two were located at a background location in the city of Utrecht, The Netherlands. Outdoor monitoring was conducted at all school sites, during the personal measurements. A questionnaire was administered on time activity patterns and indoor sources at home. The outdoor concentration of soot was 74% higher at the freeway school compared to its matched background school. Personal exposure to soot was 30% higher. For NO_x the outdoor concentration was 52% higher at the freeway school compared to its background school. The personal concentration of NO_x was 37% higher for children attending the freeway school. Differences were smaller and insignificant for $PM_{2.5}$ and NO_2. No elevated personal exposure to air pollutants was found for the children attending the school near the ring road. We conclude that the school 's proximity to a freeway can be used as a valid estimate of exposure in epidemiological studies on the effects of the traffic-related air pollutants soot and NO_x in children.

Introduction

Recent studies have associated living near busy roads with impaired health.[1-4] Subjects living close to freeways or major urban roads were found to have a significantly increased risk of death due to cardiorespiratory causes in a Dutch cohort study.[5] A study carried out in England and Wales showed excess risk of mortality from stroke when living near busy roads.[6] Other studies focused on children's health; Dutch children living near freeways had increased prevalence of respiratory symptoms such as cough, wheeze, runny nose, asthma and allergic sensitization.[7,8] A study by Nicolai et al.[9] showed associations in children between living within 50 meter to a high traffic street (>30 000 vehicles per 24 h) and respiratory symptoms (asthma, wheeze and cough). In all epidemiological studies indicators of exposure to traffic-related air population, like estimated outdoor concentrations based on traffic density on the street of residence and/or distance of the residence to busy roads, have been used to link exposure and health effects. Yet, the average

outdoor concentration of an air pollutant may not reflect true exposure, since people usually spend a significant amount of time indoors and indoor-outdoor relationships may vary between homes. To date, only limited personal exposure studies support validity of these indicators of long-term exposure to traffic-related air pollution. A study conducted in the Netherlands found a difference of 8.2 μg/m^3 (46%) for personal NO_2 exposure of children from a school located near a freeway with high traffic intensity (150 000 vehicles per 24 h) versus low traffic intensity (45 000 vehicles per 24 h).[10] When comparing the same group of children, the increase in school outdoor NO_2 was 41%, whereas the increase in home outdoor NO_2 concentration was 28%. Monn's study[11] found highly significant correlations (R^2>0.9) on a city-level for outdoor versus personal annual mean estimates of exposure to NO_2. However, no long-term studies have involved personal monitoring of $PM_{2.5}$ (particulate matter with a 50% cut off of 2.5 μm in aerodynamic particle size) and particulate components such as soot. This lack of data hampers the interpretation of epidemiological studies on small-scale variations of long-term air pollution exposures.

Recently, several epidemiological studies have examined respiratory health in children (lung function, respiratory symptoms, bronchial hyperresponsiveness, sensitization to common allergens) and measured outdoor air pollutant concentrations using a school-based measurement design.[4,7-9] Therefore, we selected school children as participants in this study to repeatedly monitor personal exposure to the traffic-related air pollutants $PM_{2.5}$, soot, NO_x and NO_2. The primary aim of the study was to investigate whether the personal exposure to traffic-related air pollution in children attending a school near a busy road was higher than the personal exposure in children attending a school at a background location. The secondary aim was to assess differences in personal exposure associated with living near busy roads. This study focuses on the use of outdoor traffic-related air pollution and characteristics such as traffic intensity of busy roads as a suitable estimate for personal exposure in epidemiological studies on the long-term effects of traffic-related air pollution.

Materials and Methods

Participant and school selection

Personal exposure to traffic-related air pollution was monitored in children (10-12 year), attending four schools with varying proximity to traffic in Utrecht, The Netherlands. Utrecht is a

city of about 230 000 inhabitants and a number of freeways surrounding the city. We sought to compare exposures of children attending schools within 100 m of a major freeway or ring road (>45 000 vehicles per 24 h) with those at schools at urban background locations. Seven schools were approached with a letterrequesting an introductory meeting before four schools were found that were willing toparticipate in the study. Two schools were within 100 meter of a major freeway or ring road (>45 000 vehicles per 24 h) and two schools were at an urban background close to one of the busy road schools (table 1).

Table 1. Characterization of the schools' proximity to busy roads.

school	distance to nearest busy road	traffic intensity (vehicles/24 h)	type of road	orientation down wind[a]	% time down wind[b]
school 1	>250	n.a.[c]	/	/	/
school 2	88	45 200	Ring road	36º	40
school 3	75	97 800	Freeway	267º	64
school 4	>300	n.a.[c]	/	/	/

[a]Angle from which wind is directing to be considered *'downwind'* for the school. [b] Percentage time that the school was downwind from the road during the measurements. [c] Not applicable.

The school boards that decided not to participate declined because of the demanding nature of the study and previous time-consuming participation in other studies. Next, with the cooperation of the school board, children from these four schools were asked to participate in the study during an oral presentation with an accompanying movie in their classroom. The children received an invitation with a cover letter explaining the purpose of the study. Candidates were asked to return a participation form and parents had to sign an informed consent form.

Air pollution measurements

The personal monitoring of traffic-related air pollution was performed in 48-hour periods, and repeated four times for each participant, spread out over nine months. During each sampling period, children from a school at an urban background location and from a school near a busy road were measured simultaneously (paired school design) to limit bias of the comparison due to weather-driven temporal variations. Measurements took place from Monday to Wednesday or from Wednesday to Friday. On average 7 personal measurements were conducted

simultaneously, spread out over 31 sampling periods. Outdoor measurements as well as indoor measurements at the school location were performed concurrently to the personal measurements. Components that were measured were $PM_{2.5}$ mass, the absorbance of $PM_{2.5}$ (soot), NO_x and NO_2. Absorbance of $PM_{2.5}$ filters has been shown to be highly correlated with measurements of elemental carbon (EC) or 'soot'.[12-15] In this work, we will therefore refer to absorbance of the $PM_{2.5}$ filters as 'soot'. Elemental carbon or soot is a product of incomplete combustion and is currently mainly due to diesel exhaust in the absence of significant wood combustion.[16-18]

Personal $PM_{2.5}$ measurements were conducted with $PM_{2.5}$ GK2.05 cyclones (BGI Inc., Waltham, MA) that were designed and constructed for the EXPOLIS study and flow-controlled battery operated pumps (BGI-400) at a flow rate of 4 l/min.[19] Batteries suitable for 48-hour sampling were used. Children could wear the sampler in a custom-made backpack that contained an internal sound isolation covering. We provided and distributed insulated boxes in which the backpack, with the sampler, could be placed, in order to further reduce pump noise levels so that the sampler could be placed near the bed of the participant over night. To assess personal NO_2 and NO_x, we used Ogawa passive samplers (Ogawa & Company USA, Inc.) with pre-coated NO_2 and NO_x collection pads. These Ogawa samplers could be attached as a badge to the children's clothing.

The personal measurements were started up at the school, in order to motivate the group of children as a whole and to give detailed instructions on how to wear the sampling equipment. Participants were instructed that the badge and inlet of the sampler always needed to be attached near the breathing zone, to the collar of the child's clothing or the shoulder strap of the bag, using an alligator clip. Participants were instructed to wear and keep the backpack and badge as close as possible. However, they were allowed to place the backpack nearby during indoor sedentary activities (such as watching TV or reading) or activities during which wearing the sampler would be too inconvenient or impossible (such as sleeping or swimming). Children had to record the kind and duration of those activities, as well as the position of the backpack in a time activity questionnaire.

Outdoor $PM_{2.5}$, soot, NO_2 and NO_x concentrations were measured using the same sampling equipment as used for personal sampling. However, for the outdoor measurements a shelter was used to protect the equipment from sun and rainfall. For all $PM_{2.5}$ measurements the same filters (Anderson Teflon 37 mm) were used.

To test the accuracy of the measurements of NO_x and NO_2, Ogawa samples were co-located within 1 m of a fixed ambient air monitoring station (site 363) operated by National Institute for Public Health and the Environment (RIVM). This station is located along a busy road (27 616 vehicles per 24 h). In this monitoring network, chemiluminescence monitors are used for measurements of NO and NO_2. To test the precision of outdoor and personal measurements, we further assessed duplicate samples of $PM_{2.5}$, soot, NO, NO_2 and NO_x. For the personal duplicates, adult volunteers were asked to simultaneously carry two personal samplers during 48 h. Outdoor duplicates were measured at the freeway school and at an urban background location. All duplicates were collected throughout the study period.

Questionnaire

A questionnaire collected data on housing conditions, daily activity patterns, school travel mode and possible indoor sources. We used questions on environmental tobacco smoke (ETS) (Has anybody smoked in your home during the measurement? Has your child been in a room, other than your own home, where people smoked?), cooking on gas (Has your child been in a room where there was a warm meal prepared using a gas cookery?) and burning candles (Were there any candles or incense burnt in the house during the measurement?).

Gravimetric analysis

The $PM_{2.5}$ mass was determined by weighing a filter before and after sampling using a Mettler MT5 micro-balance (Mettler-Toledo, Greifensee, Switserland) with 1 µg reading precision. Filters were stored at 4°C and weighed after equilibrating for 24 h in a temperature (20°C to 23°C) and humidity (30% to 40%) controlled room. Details on the analytical procedures can be found elsewhere.[13, 20]

Reflectance analysis

To assess light absorption of the $PM_{2.5}$ mass, first reflectance was measured using an EEL 43 reflectometer, according to Standard Operating Procedures (SOP) developed for the ULTRA study (SOP ULTRA/KTL-L1.0) on the same filters used to determine $PM_{2.5}$ mass.[21] Each filter was measured at five standard spots and the average reflectance was calculated. Next, the reflectance of the $PM_{2.5}$ filters was transformed into absorption coefficients (a). According to ISO 9835 (1993)[22]

$$a = (A/2V) \times \ln(R_0/R_s)$$

where A = loaded filter area (m^2), V = sampled volume (m^3), R_0 = average reflectance of field blank filters, and R_s = reflectance of the sampled filter. Absorption coefficients were expressed in $m^{-1} \times 10^{-5}$. The regression equation of Roorda-Knape et al.,[23]

$$\textit{black smoke}\ (\mu g/m^3) = -3.663 + 9.897 \times \textit{soot absorbance}\ (m^{-1}10^{-5})$$

with R^2=0.94 and n=40, was used to provide soot concentrations in $\mu g/m^3$ for comparison with other studies.

NO_x analysis

NO, NO_2 and NO_x were collected using precoated NO_2 or NO_x 14.5-mm pads (p/Ns PS-114 and PS-124, Ogawa & Co.) deployed in personal sampler bodies (p/N P-100, Ogawa & Co.). Sampling and analysis was performed according to manufacturer protocols (Ogawa USA, Inc., Pompano Beach, Florida, ogawausa.com).[24]

Pads were loaded into samplers and stored in airtight cups for transport to or from sampling sites. Following collection, samplers were refrigerated until analysed. Using a sulfanilamide solution and N-(1-Naphthyl)-ethylenediamine dihydrochloride (NEDA) as a color producing reagent, the NO_x and NO_2 absorbances were determined by an analysis based upon the Saltzman method, with a photospectrometer at a wavelength of 545 nm. Absorbances were converted into weights (ng) using the absorbance of the blanks and the slope of the standard NO_2 solution curve. The NO weight was then obtained by taking the difference between the NO_x weight and the NO_2 weight. Next, weights were transformed into concentrations (ppb) by multiplying the collected weights with the concentration coefficients for NO and NO_2 and dividing by sampling time.

Traffic counts

Only limited information on recent traffic intensities, like traffic intensities on freeways around Utrecht, was available from the municipal administration from Utrecht. Therefore, we performed traffic counts on all streets where the schools and homes of the participants were located and on all main streets within 100 meter between 9.00 am and 3.00 pm. For 15 minutes traffic, driving in

both directions, was counted using a stopwatch and counter. Rush hour was excluded and attention was paid to document specific situations e.g. school children collection at lunchtime. Traffic counts of 15 minutes were converted to traffic intensities during day hours (7.00 am to 7.00 pm) by multiplying by 48 (=4*12). The percentage of the total traffic that occurs during day hours on municipal roads in The Netherlands amounts to 78%.[25] We assumed that this percentage did not change over time and that it is independent of the traffic intensity on a road. As a result, traffic intensities during day hours were therefore multiplied by 1.29 (=1/0.78) to calculate traffic intensities per 24 h. To test the reliability of these traffic counts, we performed repeated counting in 13 streets and compared our traffic intensities with municipal data where available, both resulting in very high correlation coefficients (0.98 and 0.96 respectively). The absolute levels of our traffic counts and the municipal data were also comparable (absolute mean difference of 10%). Distances from schools or residences to busy roads were measured using maps at 1:10 000 or 1:5 000 scale. As a result, an addition to the general aim of the study could be made, i.e. investigating whether the personal exposure to traffic-related air pollution in children living near busy roads was higher than in children living at a background location.

Wind direction data

For the measurements performed at schools near busy roads, the percentage of time that the school was downwind from the main road during the measurement was calculated. A school was considered downwind if the wind was directing within 60º from the perpendicular line to the road in the direction of the school. Data on wind direction per hour were obtained from the site de Bilt from Royal Dutch Meteorological Institute. De Bilt is located less than 5 km from Utrecht.

Statistical analysis

The statistical analysis was carried out using the statistical software program SAS (version 8e).

First, the distribution of personal, indoor and outdoor concentrations was obtained for the four schools separately. Ratios of the median concentrations of pollutants were calculated per matched school comparison. Next, concentrations of pollutants were logarithmically transformed to obtain normal distribution and analyses were done by multiple linear regression. Differences between schools can be confounded by sources in the homes of the children. Therefore, adjustment for these possible indoor sources was included in the regression model. In the final regression analysis the logarithm of a pollutant concentration was used as a dependent variable and 'attending the school near the ring road', 'attending the school near the freeway', 'living near

a busy road', exposure to 'ETS', 'cooking on gas' and 'burning candles' as independent binary variables and 'the outdoor concentration at a background site' as a continuous variable. The latter variable was included to account for temporal variation in background air pollution between sampling days. Mixed effect model repeated measures analysis (proc mixed) was applied to perform a multiple regression model that included subject as a random factor to adjust for repeated measurements. The estimated parameters of the regression models are expressed as ratios for the group for who the concerning variable was present versus absent. We tested the effect of percentage time that the school was downwind from the busy road by adding a downwind-variable and interaction term (composed of the downwind variable and a variable indicating whether the school is located near a busy road or at a background location) to the multiple regression model. The downwind variable was binary, with a zero value when there was downwind during less than 50% of the exposure time (i.e. shorter than 24 h) and value one when there was downwind for more than 50% of the exposure time. To study the effect of possible outliers, Cook's *d* values were calculated, and regression models were conducted again with the exception of main outliers of Cook's *d*.

Results

School and participant profile

Invitation letters were distributed to 102 school children, 54 of them were enrolled in the study (response rate 53%). Of these, 15 attended a school near a freeway (97 800 vehicles/24 h), 11 attended a school near a ring road (45 200 vehicles/24 h), and 28 attended an urban background school (table 1). We will refer to schools 1 and 4 as the background schools, to school 2 as the school near the ring road, and to school 3 as the school near the freeway. Due to restrictions on the number of samples that could be attained at one time, each school near a busy road was paired with one background school (school 1 and 2; school 3 and 4). Therefore, comparison will only be made between schools that were paired during the study.

We defined 'living near a busy road' as living within 75 meter of a road with traffic intensity of 10 000 vehicles per 24 h or more, or living within 100 meter of a road with traffic intensity of 45 000 vehicles per 24 h or more. Of the 54 participants, ten lived near a busy road (table 3), of these, four children were attending the school near a ring road (school 2), four were attending the school located near a freeway (school 3), and two were attending the background school which

was paired with the freeway school (school 4). Most children (about 60%) lived near a street with traffic intensity below 1000 vehicles per 24 h and about 20% of the participants lived near a street with traffic intensity between 1000 and 10 000 vehicles per 24 h. About 20% of the participants lived near a street with high traffic intensity (>10 000 vehicles/24h). No children were living on a street with high traffic intensity, however, for two children the backside of the house bordered with a busy road (>25 000 vehicles/24 h).

Table 2. Characterization of the homes' proximity to busy roads for the ten children living near busy roads.

ID	Traffic intensity at street of residence (vehicles/24 h)	Distance to nearest busy road (m)	Traffic intensity of nearby busy road (vehicles/24 h)	Intermediate infrastructure	Type of intermediate infrastructure	Floor	School
14	991	55	11 455	Yes	Houses	1	2
17	0	100	45 264	Yes	Houses. Trees and plants.	0	2
20	62	100	45 264	Yes	One line of houses. Trees and plants.	0	2
22	124	32	45 264	No	Trees and plants. Backside house borders with busy road.	0	2
30	124	63	45 264	Yes	One line of houses. Trees and plants.	0	3
31	124	63	45 264	Yes	One line of houses. Trees and plants.	0	3
32	124	88	97 800	No	Trees.	0	3
36	248	100	97 800	No	Trees.	0	3
41	62	25	27 616	No	None, backside house borders with busy road.	0	4
44	0	100	106 200	Yes	One house.	0	4

Participants living near a busy road, according to a more strict definition from a study by Hoek et al. (2002. The Lancet, vol. 360) investigating long-term exposure to traffic-related air pollution, are highlighted in gray.

Quality Control and Quality Assurance

The average reflectance of the field blank filter (n=42) was 99.2 (S.D. 1.42). The limit of detection (LOD), calculated as three times the standard deviation of the blanks divided by the sampled volume, was 0.089 m^{-1} 10^{-5} for soot; all sample soot measurements were above the LOD. The average weight of the field blank filter was 5.6 µg (S.D. 0.0088) and the matching LOD was 2.26 µg/m^3. None of the sample filter weights were below this limit. The average field blank for NO_x and NO was 21.15 (S.D. 3.05) and 19.42 (S.D. 2.75) respectively, after exclusion of one very high field blank (42.16 ppb) and one very low field blank (8.12 ppb). For NO_2 the average was 1.65 (S.D. 1.19), after exclusion of one very high field blank (6.26 ppb). The LOD were 3.58 ppb, 9.15 ppb and 8.25 ppb for NO_2, NO_x and NO respectively.

Table 3. Median pollutant concentrations and ratio of the medians for the two busy road schools versus their matched background schools.

		School near ring road versus background school					School near freeway versus background school				
		N	Background	N	Busy	Ratio	N	Background	N	Busy	Ratio
$PM_{2.5}$	Outdoor	10	19	10	19	0.97	13	17	13	17	1.01
	Personal	46	27	38	40	1.48	53	20	55	23	1.15
Soot	Outdoor	10	1.63	10	1.74	1.07	13	1.64	13	2.85	1.74
	Personal	46	1.87	38	2.13	1.14	53	1.67	55	2.25	1.35
NO_2	Outdoor	12	24	12	19	0.80	13	21	13	30	1.43
	Indoor	14	8	14	9	1.09	16	19	16	16	0.86
	Personal	47	12	39	13	1.10	51	17	56	15	0.90
NO_x	Outdoor	12	36	12	27	1.01	13	30	13	54	1.52
	Indoor	13	26	13	19	0.72	16	26	16	39	1.46
	Personal	43	34	38	44	1.30	51	36	56	44	1.21

Abbreviations: $PM_{2.5}$, particulate matter with a 50% cut off of 2.5 um in aerodynamic diameter particle size; NO_2, nitrogendioxide; NO_x, total nitrogenoxides. Units for $PM_{2.5}$ and soot are ug/m^3 and m^{-1} 10^{-5} respectively, and for NO_2 and NO_x, the unit is ppb.

Most values for NO_2 and NO_x were above the LOD (99.9% and 99.2%). Values below the LOD were retained and negative values of NO_x (0.3%) were substituted by zero. There were no negative values for NO_2. For NO, 75% of all values were above the LOD. For the outdoor measurements of NO, 60% of the values were above the LOD. For the LOD determination of NO, first the NO weights of all the individual field blank samples were obtained by taking the difference between NO_x and NO_2 weights of all individual field blanks, then weights were transformed into concentrations and finally the LOD was calculated as mentioned previously. As NO concentrations were not determined directly, and neither was the LOD for NO, but derived from NO_x and NO_2, we decided not to report NO results.

We found very comparable levels (absolute mean difference of 12% for NO and 3% for NO_2) and high correlation coefficients between the NO (0.93) and NO_2 (0.96) concentrations from the co-located measurements with the Ogawa badge and the fixed ambient air monitoring network. Coefficients of variation (CV) and median absolute differences between the duplicate measurements were calculated and good repeatability (CV below 5%) was seen for all pollutants. The median absolute difference between $PM_{2.5}$ duplicates was below 1 $\mu g/m^3$ for personal and outdoor measurements.

Personal exposure related to school location

Due to pump failure and sickness of some participants, 34 measurements were lost, leaving 182 (84%) complete personal measurements. Figure 1 shows the distribution of the personal and school outdoor measurements of $PM_{2.5}$ and soot (figure 1a) and NO_2 and NO_x (figure 1b) for the four schools separately. Table 3 provides the quantitative summary. In the paired school design, differences in outdoor and personal concentration of soot and NO_x were seen between the freeway school and the background school (school 3 and 4), for NO_2 and $PM_{2.5}$ the levels were comparable between the two schools. In the comparison of the ring road school with its matched background school (school 1 and 2), minimal contrasts in outdoor pollution were seen. However, for $PM_{2.5}$ and NO_x contrasts in personal concentration in the absence of an outdoor contrast were seen. For some pollutants (NO_2 and NO_x) indoor levels were assessed as well as shown in the table. School indoor concentrations of NO_2 and NO_x were not different between exposed and background schools, except for indoor NO_x at the freeway school.

During 40% of the personal measurements the child had been exposed for some time to cooking on gas and during 35% of the measurements, candles had been burnt in the house. These indoor source exposures were distributed equally in the children of the four schools. During 27% of the

measurements children were exposed to ETS; school 3 and school 4 had comparable numbers, school 1 on the other hand had a significantly lower number of children exposed to ETS (1% vs. 14%) when compared to school 2.

Children from the ring road school (school 2) lived more often in apartments (46%), compared to children from other schools (18%, 0% and 0% for school 1, 3 and 4 respectively). In general, children spent little time in traffic; median time spent in traffic was 1.0 h with a 25 – 75 % interquartile range (Q25-Q75) of 0.5-1.5 h during 48 h. Children spent, more specifically, about 5 minutes (Q25-Q75= 0-1.0 h) in a car and about 30 minutes (Q25-Q75= 0.2-1.0 h) cycling.

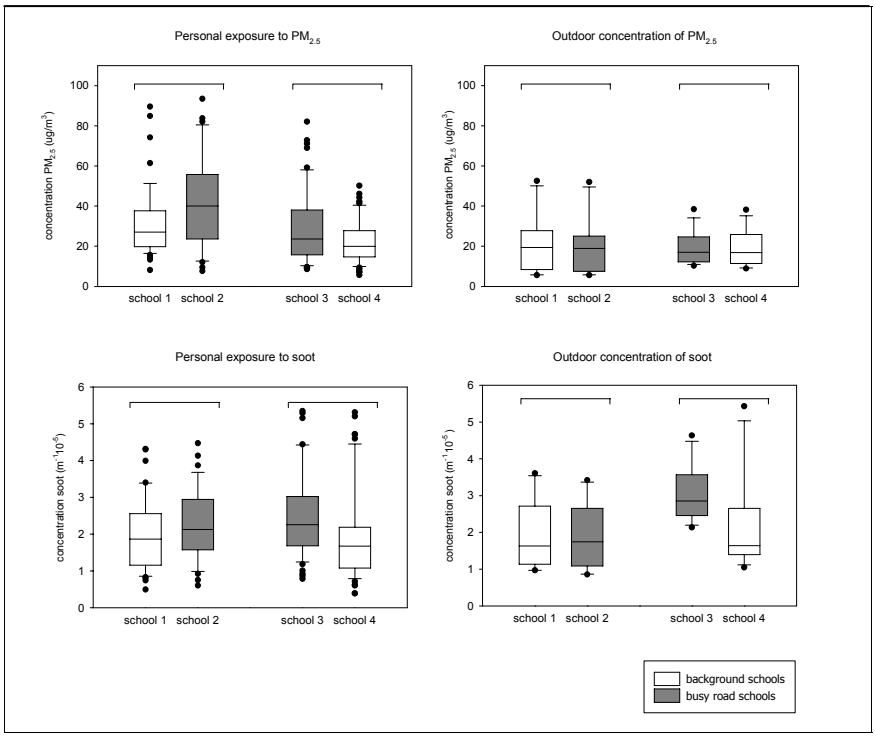

Figure 1a. Box plots of personal and outdoor concentrations of $PM_{2.5}$ (µg/m^3) and soot (m^{-1} 10^{-5}) for the four schools. School 1 + 2 (ring road) and school 3 + 4 (freeway) were measured simultaneously. (Soot concentrations of 1, 2 and 3 m^{-1}10^{-5} correspond to 6.23, 16.13 and 26.03 µg/m^3, respectively.)

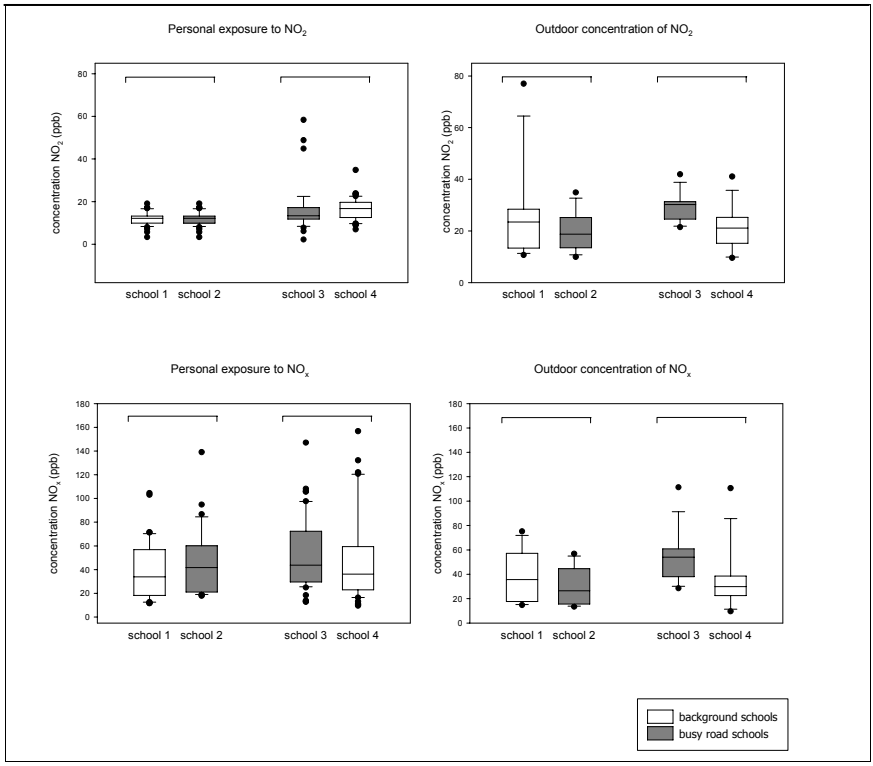

Figure 1b. Box plots of personal and outdoor concentrations NO_2 (ppb) and NO_x (ppb) for the four schools. For reasons of presentation, the scale of the figure was reduced. Three personal observations of NO_x, two from school 1 and one from school 2 were therefore were not included in the figure (NO_x concentrations of 348.2; 238.2; 200.8). School 1 + 2 (ring road) and school 3 + 4 (freeway) were measured simultaneously.

Table 4 and 5 present the ratios derived from the parameter estimates from the multiple regression analysis for $PM_{2.5}$, soot, NO_2 and NO_x respectively. Most of these ratios for ring road school and freeway school correspond well with the ratios from table 3. The variation of personal exposure to soot was significantly explained by attending the school near the freeway, the outdoor soot concentration at a background site, exposure to ETS and burning candles (table 4).

Table 4. Relationship between personal exposure to $PM_{2.5}$ and soot, and proximity to traffic and indoor sources.

	$PM_{2.5}$		Soot	
	Ratio[a]	[CI][b]	Ratio[a]	[CI][b]
Crude Model				
Intercept	24.08*	[20.44-28.36]	1.75*	[1.56-1.95]
School near ring road	1.69*	[1.23-2.30]	1.22#	[0.99-1.51]
School near freeway	1.13	[0.86-1.48]	1.34*	[1.12-1.60]
Home near busy road	0.74*	[0.55-1.00]	0.86	[0.71-1.05]
Adjusted Model [c]				
Intercept	13.95	[11.46-16.97]	0.79	[0.70-0.90]
School near ring road	1.32#	[0.99-1.76]	1.16	[0.96-1.40]
School near freeway	1.09	[0.88-1.36]	1.30*	[1.12-1.51]
Home near busy road	0.84	[0.66-1.07]	0.92	[0.78-1.08]
Outdoor concentration at background site	1.21*	[1.15-1.28]	1.35*	[1.31-1.40]
ETS	1.36*	[1.10-1.69]	1.24*	[1.07-1.42]
Cooking on gas	0.95	[0.81-1.12]	0.95	[0.85-1.06]
Burning candles	1.14	[0.97-1.34]	1.23*	[1.11-1.38]

[a]Ratio for group for who the concerning variable was present versus absent calculated from multiple regression analysis with the logarithm of the pollutant as a dependent variable; for the intercept the ratio was reported as the exponential value of the parameter estimate; for $PM_{2.5}$ the ratio for outdoor concentration at background site is expressed for a 10-ug/m^3 increment, and for soot for a 1-m^{-1}10^{-5} increment. [b]95% Confidence Interval. [c]Multiple regression analysis with exclusion for those observations during which a child was away from home for more than eight hours per 48 h (school time not included). *Statistically significant with *p*-value < 0.05. #Statistically significant with *p*-value < 0.10. Units for $PM_{2.5}$ and soot are ug/m^3 and m^{-1} 10^{-5} respectively. Abbreviations: ETS, environmental tobacco smoke.

Table 5. Relationship between personal exposure to NO_2 and NO_x, and proximity to traffic and indoor sources.

	NO_2		NO_x	
	Ratio[a]	[CI][b]	Ratio[a]	[CI][b]
Crude Model				
Intercept	13.85*	[12.35-15.55]	36.58*	[31.98-41.85]
School near ring road	1.04	[0.83-1.29]	1.26#	[0.98-1.62]
School near freeway	1.06	[0.88-1.28]	1.33*	[1.08-1.63]
Home near busy road	0.98	[0.80-1.21]	0.86	[0.68-1.09]
Adjusted Model [c]				
Intercept	12.33	[10.37-14.67]	8.89*	[13.69-20.35]
School near ring road	1.00	[0.76-1.32]	1.40*	[1.00-1.96]
School near freeway	1.06	[0.85-1.32]	1.37*	[1.05-1.80]
Home near busy road	0.99	[0.77-1.26]	0.82	[0.61-1.11]
Outdoor concentration at background site	1.07*	[1.03-1.12]	1.20*	[1.17-1.23]
ETS	0.89	[0.75-1.06]	0.87	[0.71-1.08]
Cooking on gas	1.01	[0.90-1.15]	1.09	[0.94-1.26]
Burning candles	1.01	[0.89-1.15]	1.18*	[1.01-1.37]

[a]Ratio for group for who the concerning variable was present versus absent calculated from multiple regression analysis with the logarithm of the pollutant as a dependent variable; for the intercept the ratio was reported as the exponential value of the parameter estimate; ratios for the outdoor concentrations at background site are expressed for a 10-ppb increment. [b]95% Confidence Interval. [c]Multiple regression analysis with exclusion for those observations during which a child was away from home for more than eight hours per 48 h (school time not included). *Statistically significant with p-value < 0.05. #Statistically significant with p-value < 0.10. The unit for NO_2 and NO_x is ppb. Abbreviations: ETS, environmental tobacco smoke.

Children attending the school near the freeway had a 30% higher personal exposure to soot than children attending a school at a background location. The variation of personal exposure to $PM_{2.5}$ was significantly explained by exposure to ETS and outdoor $PM_{2.5}$ concentration at a background site and the attribution of attending a school near a ring road was marginally significant. For NO_2

the variation was only meaningfully described by the outdoor NO_2 concentration at the background site (table 5). With NO_x, the variation in personal exposure was significantly explained by attending a school near a ring road, attending a school near a freeway, the outdoor NO_x concentration at a background site and burning candles. When comparing the group of children attending the freeway school versus the background school, we observed that they had a 37% higher personal exposure to NO_x. Living near busy roads was not associated with increased personal exposure of any of the pollutants.

Sensitivity analysis

The multiple regression analysis was repeated restricted to observations without the most important known sources of $PM_{2.5}$ and NO_x. The ratio of personal exposure to $PM_{2.5}$ when comparing a group of children attending a school near a busy road versus a background school was elevated (1.32) and marginally significant. After restriction to days without exposure to ETS, the ratio remained elevated (1.29) but lost significance. The ratio of personal exposure to $PM_{2.5}$ when comparing a group of children attending a freeway school versus a background school did not change. Neither did the ratios when looking at personal exposure to soot. After excluding measurements during which a child was exposed to cooking on gas, the ratio of personal exposure to NO_x when comparing children from the ring road school versus the background school changed from 1.40 to 1.03 and lost significance, suggesting residual confounding. The results for the freeway comparison showed hardly any differences after excluding measurements during which a

child was exposed to cooking on gas, 1.37 vs. 1.33 respectively, the latter remaining significant.

The results for NO_2 and NO_x were not strongly influenced by outliers. After excluding the most influential outliers, established with Cook's *d* values, parameter estimates hardly changed. Ratios for exposure to NO_2 for both school comparisons remained unchanged after similar restrictions.

When applying a more strict definition for living near a busy road, only 5 out of 54 children remained in the category living near busy roads (table 3).[5] However, with this selection, the ratios for comparing children living near busy roads versus children living at a background location hardly changed.

Adding time spent in traffic to the multiple regression model did not change the ratios for living near busy roads compared to living at a background location for soot (0.92; 95% CI 0.78-1.10) nor for NO_x (0.82; 95% CI 0.61-1.08). Time spent in traffic was itself not associated with personal exposure.

Wind direction

To evaluate the impact of wind direction on the personal exposure to $PM_{2.5}$, soot, NO_2 and NO_x, we added the percentage of time that the school had been downwind from the ring road or freeway during the measurements with an interaction term to the model. The school near the freeway had relatively more measurement periods during downwind conditions than the ring road school. None of the interactions with downwind were significant. Likely, this model is lacking power to show significant interaction. As an illustration, the difference in personal exposure to NO_x nearly doubled (1.46 versus 1.23) for the freeway school on days with downwind compared with days without downwind.

Discussion

Attending a school near a freeway was reflected in increased personal exposure to soot and NO_x, whereas attending a school near a ring road was not associated with increased personal exposure of any of the traffic-related pollutants.

Some other traffic-related air pollution exposure studies have used a similar measurement design using school locations near busy roads.[4,14] Kim et al.[4] found differences in outdoor levels of $PM_{2.5}$, soot, NO_2 and NO_x between schools more distant versus nearby freeways (with average traffic intensity of 170 000 vehicles per 24 h) of 8%, 22%, 23% and 45% respectively. The differences in outdoor pollutants we found in our study were comparable. Fischer et al.[26] found about 20% higher outdoor $PM_{2.5}$ concentrations at homes on main streets in Amsterdam, and for soot the difference was even higher, about 80%. Unlike our study, the sampling equipment for the outdoor measurements were attached to the façade of the house, located on a busy street. Therefore differences might be larger than in our study where the school was located at some distance from a busy road. Also, in Amsterdam, more often street canyons occur, whereas the two selected schools in our study were located in more open terrain. Hochadel et al.[27] found differences in outdoor levels of soot, NO_2 and $PM_{2.5}$ between traffic and background sites of 22%, 28% and 2% respectively. In our study, pronounced differences between the freeway school and its matching urban background school were seen in outdoor levels of soot and NO_x, compared to rather minor contrasts in outdoor $PM_{2.5}$ and these findings are in line with other studies.[26-28]

In contrast with available information on outdoor levels, only a few studies have looked at personal levels of traffic-related air pollution. A Dutch study conducted personal and outdoor

measurements at schools near freeways with different traffic intensity (45 000 to 150 000 vehicles per 24 h) and found an increase of 46% in personal NO_2 and 41% in outdoor NO_2 when comparing schools near the busiest freeways with schools near the relatively less busy freeway.[10]
In general, difference in exposure to traffic-related pollutants was seen for the comparison of the freeway school with its matched background school. The distance of school 2 to the ring road (88 m) and its traffic intensity (45 200 vehicles per 24 h) may partly explain the smaller increases in exposure found when comparing school 2 with school 1. The traffic intensity of the freeway (97 800 vehicles per 24 h) in the proximity of school 3 is more than double the traffic intensity of the ring road close to school 2. A study by Janssen et al.[14] illustrated that it was truck traffic intensity in particular that showed associations with air pollution concentrations. The truck traffic intensity of the freeway in our study was about 11 000 trucks per 24 h, which is in line with Janssen's study (5000 to 22 000 trucks per 24 hr). The truck traffic intensity of the ring road however was less than half of the lower limit of Janssen's study (about 2500 trucks per 24 h). This might be an additional clarification why hardly any contrast in exposure to air pollution concentrations was found for the school located near a ring road and its matched background school. Furthermore, a row of houses was located between school 2 and the ring road, whereas no buildings were located between school 3 and the freeway. A study by Bloemen et al.[29] investigated the exposure of an urban population in the Netherlands to traffic-related air pollution by measuring benzene levels at various places and different periods. Among other findings, they noticed that the level of benzene dropped back significantly (about 40%) when measuring at the rear side (7.5 $\mu g/m^3$) compared to the façade (12.5 $\mu g/m^3$) of houses located at busy roads. This suggests that the effect of a barrier between the road and the sampling point on measured concentrations may be sizable.
Although no contrast in outdoor $PM_{2.5}$ for the ring road school was seen, an elevated ratio in personal exposure was found, even after restriction for exposure to ETS. The ring road school had a significantly higher number of children exposed to ETS when compared with its matched background school (14% vs. 1%). Therefore, the comparison with the ring road school may have been disturbed when restricting to days without exposure to ETS. Possibly inaccurate reporting of parental smoking may have led to misclassification here. A similar point for discussion is the increase in personal exposure to NO_x for the ring road school when no difference in outdoor levels of NO_x could be shown between the ring road school and the background school. After excluding days during which children were exposed to cooking on gas, the elevated ratio for NO_x for the ring road school (1.40) dropped considerably (1.03) and lost significance, suggesting

residual confounding. This, combined with the lack in outdoor contrast, indicates that there was no demonstrable increase in personal exposure due to the traffic-related air pollutant NO_x for the ring road school. In contrast, the significantly increased personal exposure to NO_x (1.37) for the freeway school remained (1.33) after restricting to days without exposure to gas cooking, which corresponds well with the differences in outdoor levels of NO_x between freeway school and it's matched background school.

No differences in personal exposure between children living near busy roads and children living at an urban background location were seen. Whereas we did find significant differences in exposure to traffic-related pollutants when comparing the group of children based on the proximity of the school they attend to busy roads. Comparing the relevance of the school location versus the home location however should be considered with caution, as this design was more suitable for the school comparison (matching sampling periods equally between busy road school and background school). This is unlike a previous study, assessed in one urban background school in Amsterdam, where sampling days were matched simultaneously between children living in streets with low and high traffic intensity.[30] Concurrently, in the latter study, small differences in personal exposure to NO and NO_2 and a significant difference for soot (35%) were found when comparing a group of children living near busy roads versus living at an urban background location.

In the current study, the two busy road schools were also on average located closer to much busier roads than the homes that were selected as 'close to busy roads'. Further, children were mostly present at home during less busy traffic hours, as children are often at school for periods of rush hour traffic. Other findings may be seen when studying personal exposure to traffic-related pollutants in an adult, non-working or retired population, who generally spend more time at their residence. Wichmann et al.[31] investigated personal levels of PM_{10} absorption coefficients in an adult population living along busy and quiet roads in Amsterdam (The Netherlands). They reported a statistically significant 29% increase in personal absorption coefficients of PM_{10} for adults living along busy roads versus quiet streets. No such increase in personal exposure to soot was found in the present study when comparing children living near, instead of on, busy roads and children living at an urban background location.

The results for the homes and the ring road school illustrate that the impact of a busy road may be very local. In the compact Dutch cities, other buildings may easily diminish the impact of a busy road to non-significant. In epidemiological studies therefore short distances should be evaluated.

Although not significant, wind direction clearly seemed to have a notable effect on personal exposure to traffic-related air pollution, and this was in line with the expectations. The differences in exposure to pollutants were slightly increased on days with more than 24 h of downwind conditions. Stronger effects of wind direction were found in other studies.[14, 23] Possibly the effect of downwind is influenced by wind speed, as there were more downwind days with moderate wind speed (over 3.4 m/s) compared to no downwind days with moderate wind speed (35% vs. 13%). Another reason why only slight increases were seen in the present study might be the orientation of the freeway school compared to the freeway. School 3 is situated at the east side of the road, implying that on downwind days the wind is predominantly coming from the west and on upwind days from the east. School 2 is located southwest from the ring road. Apart from road traffic, air pollution episodes in the Netherlands are associated with wind directions from south to east. Easterly winds, coming from Central and Eastern Europe, lead to higher air pollution concentrations.[32] In our study, the average outdoor soot concentration at the background school, matched to the freeway school, was 2.12 m^{-1} 10^{-5} (17.32 $\mu g/m^3$) on upwind days, whereas the concentration was somewhat lower (2.06 m^{-1} 10^{-5} or 16.73 $\mu g/m^3$) on downwind days. Accordingly, a predominantly eastern wind direction can lead to minimal differences in busy versus background locations.

Conclusion

Increased personal exposure to the traffic-related air pollutants soot and NO_x was seen for children attending a school within 100 meter of a freeway. No increased personal exposure in any of the studied air pollutants was found for children attending a school located within 100 meter of a ring road. The larger distance, lower traffic intensity and presence of obstacles probably contribute to this lack of contrast.

This study shows that the schools' proximity to a freeway can be used as a valid estimate of exposure in epidemiological studies in children on the effects of the traffic-related air pollutants soot and NO_x.

Acknowledgements

The authors like to thank all the young participants and their parents and teachers.

References

[1]Delfino RJ. Epidemiologic evidence for asthma and exposure to air toxics: linkages between occupational, indoor, and community air pollution research. Environ Health Perspect 2002; 110 Suppl 4:573-89.

[2]Garshick E, Laden F, Hart JE, Caron A. Residence near a major road and respiratory symptoms in U.S. Veterans. Epidemiology 2003; 14:728-36.

[3]Heinrich J, Topp R, Gehring U, Thefeld W. Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. Environ Res 2005; 98:240-249.

[4]Kim JJ, Smorodinsky S, Lipsett M, Singer BC, Hodgson AT, Ostro B. Traffic-related air pollution near busy roads: the East Bay Children's Respiratory Health Study. Am J Respir Crit Care Med 2004; 170:520-6.

[5]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA. Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 2002; 360:1203-9.

[6]Maheswaran R, Elliott P. Stroke mortality associated with living near main roads in England and Wales. Stroke 2003; 34:2776-2780.

[7]Janssen N, Brunekreef B, van 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; 111:1512-8.

[8]Vliet Pv, Knape M, Hartog Jd, Janssen N, Harssema H, Brunekreef B. Motor vehicle exhaust and chronic respiratory symptoms in children living near freeways. Environ Res 1997; 74:122-132.

[9]Nicolai T, Carr D, Weiland SK, Duhme H, von Ehrenstein O, Wagner C, von Mutius E. Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. Eur Respir J 2003; 21:956-63.

[10]Rijnders E, Janssen NA, van Vliet PH, Brunekreef B. Personal and outdoor nitrogen dioxide concentrations in relation to degree of urbanization and traffic density. Environ Health Perspect 2001; 109 Suppl 3:411-417.

[11]Monn C. Exposure assessment of air pollutants: a review on spatial heterogeneity and indoor/outdoor/personal exposure to suspended particulate matter, nitrogen dioxide and ozone. Atmos Environ 2001; 35:1-32.

[12]Cyrys J, Heinrich J, Hoek G, Meliefste K, Lewne M, Gehring U, Bellander T, Fischer P, van Vliet P, Brauer M, Wichmann HE, Brunekreef B. Comparison between different traffic-related particle indicators: elemental carbon (EC), PM2.5 mass, and absorbance. J Expo Anal Environ Epidemiol 2003; 13:134-43.

[13]Janssen N, de Hartog JJ, Hoek G, Brunekreef B, Lanki T, Timonen KL, Pekkanen J. Personal exposure to fine particulate matter in elderly subjects: relation between personal, indoor, and outdoor concentrations. J Air Waste Manag Assoc 2000; 50:1133-43.

[14]Janssen N, Vliet PHNv, Aarts F, Harssema H, Brunekreef B. Assessment of exposure to traffic related air pollution of children attending schools near motorways. Atmos Environ 2001; 35:3875-3884.

[15]Kinney PL, Aggarwal M, Northridge ME, Janssen NA, Shepard P. Airborne concentrations of PM(2.5) and diesel exhaust particles on Harlem sidewalks: a community-based pilot study. Environ Health Perspect 2000; 108:213-8.

[16]Froschl B, Niessner R. Urban aerosol analysis: is determination of 1-nitropyrene equivalent to the quantification of carbon? J Aerosol Sci 1997; 28:S71-S72.

[17]Scheepers PT, Martens MH, Velders DD, Fijneman P, van Kerkhoven M, Noordhoek J, Bos RP. 1-Nitropyrene as a marker for the mutagenicity of diesel exhaust-derived particulate matter in workplace atmospheres. Environ Mol Mutagen 1995; 25:134-47.

[18]Scheepers PT, Velders DD. Gas chromatogaphic-mass spectrometric determination of nitro polycyclic aromatic hydrocarbons in airborne particulate matter from workplace atmospheres contanimated with diesel exhaust. J Chromatography 1994; 677:107-121.

[19]Koistinen KJ, Kouse A, Tenhola V, Hänninen O, Jantunen MJ, Oglesby L, Kuenzli N, Georgoulis L. Fine Particle (PM2.5) Measurement methodology, Quality Assurance Procedures, and Pilot Results of the EXPOLIS Study. J Air Waste Manage Assoc 1999; 49:1212-1220.

[20]Brunekreef B, Janssen NA, de Hartog JJ, Oldenwening M, Meliefste K, Hoek G, Lanki T, Timonen KL, Vallius M, Pekkanen J, Van Grieken R. Personal, indoor, and outdoor exposures to PM2.5 and its components for groups of cardiovascular patients in Amsterdam and Helsinki. Res Rep Health Eff Inst 2005; 127:1-70; discussion 71-9.

[21]Pekkanen J, Timonen KL, Tiittanen P, Vallius M, Lanki T, Sinkko H, Ruuskanen J, Mirme A, Kulmala M, Vanninen E, Bernard A, Ibald-Mulli A, et al. ULTRA: Exposure and risk assessment for fine and ultrafine particles in ambient air. Study manual and data book. B9/2000. Kuopio: KTL, National Public Health Institute.

[22]ISO. Ambient air-determination of a black smoke Index (ISO 9835): International Organization for Standardization, 1993.

[23]Roorda-Knape M, Janssen N, Hartog Jd, Vliet Pv, Harssema H, Brunekreef B. Air pollution from traffic in city districts near major motorways. Atmos Environ 1998; 32:1921-1930.

[24]Ogawa C. NO, NO_2, NO_x and SO_2 sampling protocol using the ogawa sampler. 1998. Accessed at www.agawausa.com in 2002.

[25]Dassen AGM, Dolmans JHJ, Jabben J, Hamminga NAR, Hoffmans WH, Nijland HA. Noise in the 5th Environmental Assessment (Geluid in de vijfde Milieuverkenning) 408129 009. Bilthoven: National Institute of Public Health and the Environment (RIVM), 2000.

[26]Fischer P, Hoek G, Reeuwijk Hv, DJ B, Lebret E, Wijnen Jv, Kingham S, Elliot P. Traffic-related differences in outdoor and indoor concentrations of particles and volatile organic compounds in Amsterdam. Atmos Environ 2000; 34:3713-3722.

[27]Hochadel M, Heinrich J, Gehring U, Morgenstern V, Kuhlbusch T, Link E, Wichmann HE, Krämer U. Predicting long-term average concentrations of traffic-related air pollutants using GIS-based information. Atmos Environ 2006; 40:542-553.

[28]Lena TS, Ochieng V, Carter M, Holguin-Veras J, Kinney PL. Elemental carbon and PM(2.5)levels in an urban community heavily impacted by truck traffic. Environ Health Perspect 2002; 110:1009-15.

[29]Bloemen HJT, Balvers TTM, van Scheindelen HJ, Lebret E, Oosterlee A, Drijver M. The Bezene Research in South of Kennemerland, The Netherlands (Het Benzeen Onderzoek Zuid-Kennemerland). Bilthoven: National Institute of Public Health and the Environment (RIVM) and Municipal Health Service Haarlem (GGD), 1993.

[30]Van Roosbroeck S, Wichmann J, Janssen NA, Hoek G, van Wijnen JH, Lebret E, Brunekreef B. Long-term personal exposure to traffic-related air pollution among school children, a validation study. Sci Total Environ 2006; 368: 565-573.

[31]Wichmann J, Janssen NAH, van der Zee S, Brunekreef B. Traffic-related differences in indoor and personal absorption coefficients measurements in Amsterdam, The Netherlands. Atmos Environ 2005; 39:7384-7392.

[32]van der Zee S, Hoek G, Harssema H, Brunekreef B. Characterization of particulate air pollution in urban and non-urban areas in the Netherlands. Atmos Environ 1998; 32:3717-3729.

Chapter four

Validity of residential traffic intensity as an estimate of long-term personal exposure to traffic-related air pollution among adults

Sofie Van Roosbroeck
Gerard Hoek
Kees Meliefste
Nicole A.H. Janssen
Bert Brunekreef

(Submitted)

Abstract

The validity of traffic intensity near the home as an estimate for the personal long-term exposure to traffic-related air pollution in an adult population was tested. Personal and near-home outdoor exposure to $PM_{2.5}$, soot, NO, NO_2 and NO_x was monitored four to five times during 48 h periods in older adults. Twenty-three participants lived at busy roads (> 10 000 vehicles/24 h) and 22 lived at urban background locations. The relation between average personal exposure and traffic intensity at the residential address was explored taking indoor sources into account.

Large differences in home outdoor concentrations were found for soot (68%), NO (127%) and NO_x (35%) comparing busy road locations with urban background. For $PM_{2.5}$ (14%) and NO_2 (22%) the difference was smaller. Slightly elevated ratios were found for personal exposure to soot (1.18, 95% confidence interval (CI): 1.04, 1.35) when comparing adults living at busy roads with adults living at quiet roads. For NO, increased personal exposure (1.31) was seen for the same comparison, but this difference failed to reach statistical significance (CI: 0.92, 1.87). Traffic intensity on the street of residence predicted personal exposure to soot but not to $PM_{2.5}$ or nitrogenoxides. Participation in traffic and spending time outdoors were associated with increased personal exposure of soot and $PM_{2.5}$, but not with NO_x.

Introduction

There is substantial evidence linking long-term exposure to traffic-related air pollution with serious health effects. Effects related to long-term exposure include increases in lower respiratory symptoms, chronic obstructive pulmonary disease and atherosclerosis, reduction in lung function, and reduction in life expectancy due to cardiopulmonary mortality and lung cancer.[1] In none of these studies personal exposure to air pollution was measured. Instead, surrogates of exposure such as the concentration in outdoor air measured at a central site or measures of traffic intensity near the home or school were used.

Some recent studies have specifically focused on the health of adults living near busy roads. Adults living at (self-reported) busy roads showed increased non-allergic respiratory symptoms and to a lesser degree increased hay fever and allergic sensitization.[2] In a Swiss cohort, associations between living within 20 m of a main street and attacks of breathlessness, wheezing with breathing problems, and regular phlegm were demonstrated.[3] Older adults living within 50 m

of a major road or within 100 m of a freeway were found to have significantly increased risk of death due to cardiopulmonary causes in two European studies,[4,5] increased all-cause mortality in a Canadian study,[6] and increased risk of respiratory disease, like persistent wheeze or chronic phlegm in a US veteran study.[7] Maheswaran and Elliott showed associations between living within 200 m of a main road and mortality from stroke.[8]

Several studies in different parts of the world have documented that outdoor concentrations of traffic-related air pollutants in proximity to busy roads are clearly elevated above background air pollution levels.[9-15] However, there is currently only one study that has documented that personal exposure to soot is increased in adults living at major roads.[16] We therefore conducted a study of the validity of residential traffic intensity as an estimate for the personal long-term exposure to traffic-related air pollution in older adults. The results of this study will enable us to better interpret epidemiological studies of subjects living close to busy roads.

Methods

Study design

From November 2004 to July 2005, personal exposure of 47 older adults to traffic-related air pollution was monitored five times per participant. We selected non-smoking adults aged over 50 years and living in the city of Utrecht, the Netherlands. Approximately half of the population was selected from residents living at high traffic intensity roads, the other half from locations nearby quiet roads. The traffic-related air pollutants of interest were $PM_{2.5}$ (particles smaller than 2.5 µm in aerodynamic diameter), soot, nitric oxide (NO), nitrogen dioxide (NO_2) and NO + NO_2 (NO_x). We evaluated the difference in average personal exposure related to traffic intensity at the residential address, taking indoor sources into account.

Population

Based on the traffic data report of the Province of Utrecht, December 2001, we selected high and low traffic intensity locations, with an attempt to maximize the contrast in expected ambient concentrations. 'High traffic intensity' residential addresses were defined as homes located on a street with a traffic intensity higher than 10 000 vehicles/24 h. 'Low traffic intensity' residential addresses were defined as homes located on a street with traffic intensity less than 5000 vehicles/24 h and more than 50 m away from a road with traffic intensity higher than 10 000

vehicles/24 h and more than 400 m away from a freeway with traffic intensity higher than 70 000 vehicles/24 h. Further inclusion criteria were: non-smoking household, subject working less than 30 h/week and aged over 50 years.

An invitation to participate in the study and a cover letter explaining the purpose of the study was posted to all subjects living on the selected streets. Candidates were asked to return their participation form and returned forms were followed up with regard to their exact address and the proximity to busy or major roads. Each participant was asked to sign an informed consent form.

Sampling schedule

Personal exposure to traffic-related air pollution was monitored five times per participant. Sampling duration was 48 hours per measurement. Measurements took place from Monday to Wednesday or from Wednesday to Friday, and were started during a home visit. In total, the study consisted of 38 measurement periods of 48 h. During each sampling period, participants from low traffic and high traffic roads were sampled simultaneously to prevent that temporal variation could bias the comparison between high and low traffic intensity locations. Concurrently, outdoor measurements at a central urban background site in Utrecht and outdoor measurements at the homes (façade) located on busy roads were conducted. For logistic reasons we could not perform measurements at the low traffic homes. We assumed that the air pollutant levels at the low-traffic homes could be adequately assessed by the levels at the central urban background site.

Sampling methods

Personal $PM_{2.5}$ measurements were conducted with $PM_{2.5}$ cyclones and flow-controlled battery operated BGI-400 pumps (4 l/min). Samplers were carried in a custom-made backpack. Outdoor $PM_{2.5}$ concentrations were measured using the same equipment. To assess NO_x levels, Ogawa passive samplers (Ogawa & Company USA, Inc.) were used with pre-coated NO_2 and NO_x collection pads. The samplers were attached as a badge to the participant's clothing, or for the outdoor measurements a shelter was used to protect the badge from sun and rainfall. $PM_{2.5}$ was determined by weighing the Teflon filter before and after sampling; soot was determined by measuring reflectance of the $PM_{2.5}$ filters; NO_2 and NO_x were measured with spectrophotometric methods.[17] NO was calculated as the difference of NO_x and NO_2. Details on the analysis methods of $PM_{2.5}$ mass, $PM_{2.5}$ absorption and NO_x can be found elsewhere.[17-21]

Quality assurance and quality control

The limit of detection (LOD), calculated as three times the standard deviation of the blanks (n=42) divided by the sampled volume, was 0.21 m^{-1} 10^{-5} for soot and 1.39 μg/m^3 for $PM_{2.5}$. We retained all original values below the LOD in the data analysis. We replaced negative values by zero. All sample soot measurements were above the LOD. For $PM_{2.5}$, one sample filter weight was under the LOD and negative. For NO_x, NO_2 and NO (n=21) the LOD was 3.75 ppb, 4.41 ppb and 5.26 ppb respectively. All sample values for NO_2 and NO_x were above the LOD. For NO, 72% of all values were above the LOD. Coefficients of variation (CV) between field duplicate measurements were calculated and good repeatability (no more than 5% deviation) was seen for $PM_{2.5}$, soot, NO, NO_2 and NO_x, i.e. all variables measured.

Questionnaire and additional data

After each 48 h measurement period, participants were asked to complete a questionnaire on daily activity patterns, participation in traffic, time spent outdoors and possible indoor sources, like occurrence of smoking in the home during the measurements, using a gas stove, burning of candles, etc. Data on weather conditions were obtained from the Royal Dutch Meteorological Institute. Traffic counts were performed once on all streets where the participants lived between 9.00 am and 3.00 pm. For 15 minutes traffic, driving in both directions, was counted using a stopwatch and counter. Traffic counts of 15 minutes were converted to traffic intensities during day hours (7.00 am to 7.00 pm) by multiplying by 48 (=4*12). The percentage of the total traffic that occurs during day hours on municipal roads in The Netherlands amounts to 78%.[22] We assumed that this percentage did not change over time and that it is independent of the traffic intensity on a road. As a result, traffic intensities during day hours were therefore multiplied by 1.29 (=1/0.78) to calculate traffic intensities per 24 h. To test the reliability of these traffic counts, we performed repeated counting in 13 streets and compared our traffic intensities with municipal data where available, both resulting in very high correlation coefficients (0.98 and 0.96 respectively). The absolute levels of our traffic counts and the municipal data were also comparable (absolute mean difference of 10%). Distances from residences to busy roads were measured using maps at 1:10 000 or 1:5 000 scale.

Statistical analysis

In all analyses, we used the outdoor and personal concentrations averaged over the five observation periods for each participant. The distribution of personal and outdoor levels of all

pollutants was evaluated for the busy road group and for the background group. Differences in personal exposure between busy road- and background subjects might be confounded by indoor sources. We used multiple linear regression analyses (SAS PROC MIXED) to adjust for potential confounders with the logarithm of the personal exposure as the dependent variable. Independent variables were 'home at a busy road' (model 1) or 'total traffic intensity on street of residence' (model 2), and 'concentration at background site', 'exposure to environmental tobacco smoke (ETS)', 'exposure to burning candles' and 'exposure to gas cooking'. The last four independent variables were also averaged over the 5 observation periods. The continuous variable 'concentration at a central background site' was added to account for temporal variation in background air pollution between sampling days. The estimated parameter of the regression model 1 for the traffic characteristic variable was expressed as the ratio of average personal exposure for the group living at a busy road versus the group living at background locations. For model 2 the ratio was expressed for a 10 000 vehicles/24h increment. All statistical analyses were carried out using the statistical software program SAS (version 8e) (SAS Institute Inc., Cary, NC, USA).

Residual scatter plots for the adjusted relations between $PM_{2.5}$, soot, NO, NO_2 and NO_x, and the traffic intensity on street of residence (adjusted for ETS, gas cooking and burning candles) were added.

Results

Study population

Seventy-one adults agreed to participate, and of these, 47 fulfilled the criteria and were enrolled into the study. Forty-five participants completed four to five 48 h measurements. Of these 45, 23 lived at a busy road; the other 22 lived at a quiet street. The average traffic density on the street of residence was 345 vehicles/24 h (interquartile range (IQR): 155-495) and 16 910 vehicles/24 h (IQR: 11 703-22 059) in the background group and busy road group respectively (figure 1). Participants were 68 years of age on average. There were about as many males as females enrolled, the greater part of females to the background group (table 1).

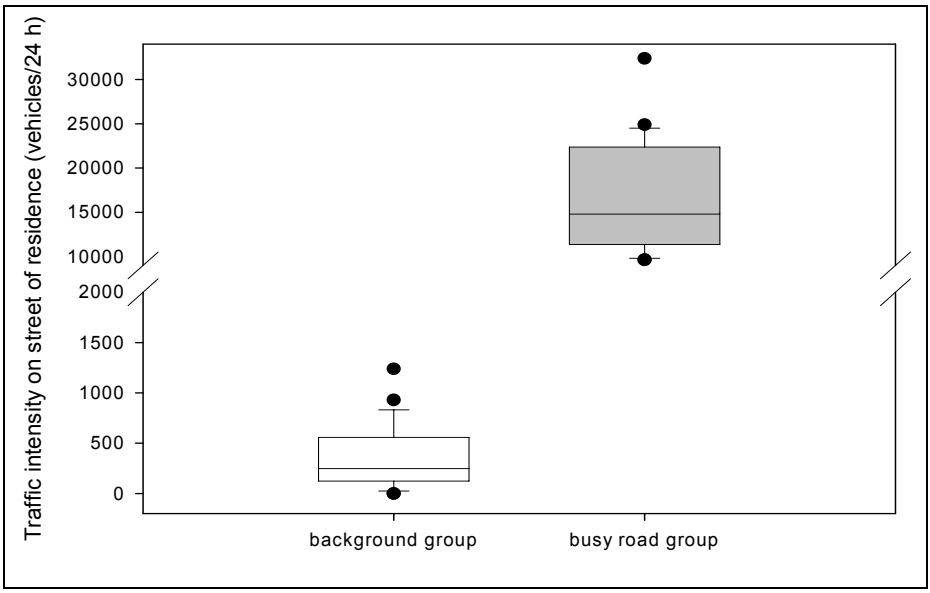

Figure 1. Traffic intensity on street of residence for the participants living at a background location and for the participants living at a busy road.

Personal exposure related to home location

Due to pump failure 9 measurements were lost, leaving 216 complete personal measurements. Figure 2 shows the distribution of the average personal and home outdoor measurements of $PM_{2.5}$, soot, NO, NO_2 and NO_x for the two groups of participants separately. Large differences in home outdoor air concentrations were found for soot (68%), NO (127%) and NO_x (35%) when comparing the busy road locations with the central urban background site. For $PM_{2.5}$ (14%) and NO_2 (22%) the difference in outdoor concentrations was smaller.

The difference in personal exposure was much smaller for all pollutants. This was confirmed in the statistical analysis in which we adjusted for indoor sources of the measured pollutants (table 2). Adults living on a busy road had an 18% higher personal exposure to soot than adults living at background locations (table 2). The increase in personal exposure to soot was 10% with a 10 000 vehicles/24 h-increment.

Table 1. Distribution of general characteristics of participants and their daily activities.

	Busy road group n=23	**Background group n=22**
Participants characteristics (n=45)		
Age *(average (SD))*	69 (10)	68 (9)
Male *(n (%))*	13 (27)	8 (36)
Pet ownership *(n (%))*	5 (22)	6 (27)
Living in		
Apartment *(n (%))*	2 (9)	4 (18)
House *(n (%))*	21 (91)	18 (82)
Living room on		
Ground level *(n (%))*	21 (91)	21 (95)
First floor *(n (%))*	2 (9)	1 (5)
Bedroom on		
Ground level *(n (%))*	3 (13)	2 (9)
First floor *(n (%))*	18 (78)	20 (91)
Second floor *(n (%))*	2 (9)	0 (0)
Employed *(n (%))*	4 (17)	4 (18)
with average working time *(average (SD))*	22 (11)	15 (4)
Open kitchen *(n (%))*	8 (35)	10 (45)
Unvented water heater in kitchen *(n (%))*	2 (9)	2 (9)
Gas cooking stove		
without fume hood *(n (%))*	0 (0)	1 (5)
with fume hood and external vent *(n (%))*	5 (23)	8 (36)
with fume hood and recirculation *(n (%))*	15 (68)	8 (36)
Participants' activities during 48 hr measurements periods (n=216)		
Time spent in traffic in hrs *(average (SD))*	0.5 (0.9)	0.4 (0.8)
Time spent outdoor in hrs *(average (SD))*	2.6 (3.9)	3.6 (3.4)
Time spent at home in hrs *(average (SD))*	43.0 (5.6)	40.8 (5.8)
Exposed to ETS *(n (%))*	13 (12)	23 (22)
Exposed to burning candles *(n (%))*	17 (16)	17 (16)
Exposed to gas cooking *(n (%))*	54 (51)	57 (63)
Living room window (street side) open *(n (%))*	10 (9)	16 (15)

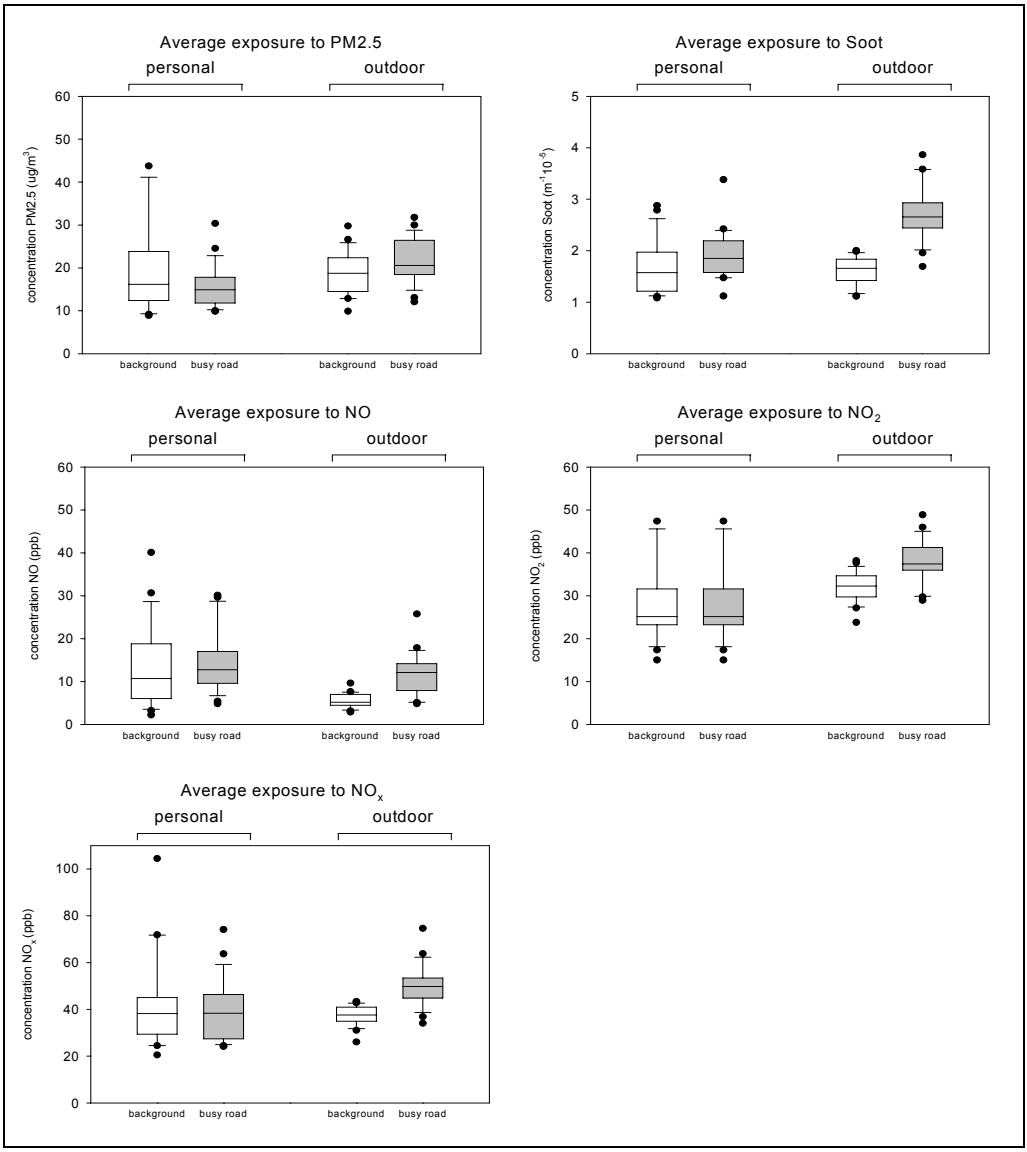

Figure 2. Distribution of individual average personal and outdoor exposure to $PM_{2.5}$, Soot, NO, NO_2 and NO_x for adults living at a background location or at a busy road.

Personal exposure to NO was 31% higher in subjects living at busy roads but this difference failed to achieve statistical significance. For $PM_{2.5}$, NO_2 and NO_x no differences were seen in personal exposure between adults living at busy roads compared to adults living on an urban background location. Model 1 explained 44%, 40%, 35%, 16% and 19% of the variance in personal exposure between subjects for soot, $PM_{2.5}$, NO, NO_2 and NO_x respectively. For model 2, the explained variance was comparable (51%, 42%, 32%, 16% and 18%). Figure 3 further illustrates the weak association between traffic intensity at the home address and personal exposure. In contrast, the relationship between traffic intensity at the home address and outdoor concentrations appeared to be solid. Traffic intensity explained between 5% and 50% of the variation of the outdoor pollutant levels, whereas it only explained 0% to 7% of the personal exposure to these pollutants. Similarly, living at a busy road explained between 10% and 63% of the variation of the outdoor pollutant levels, and 0% to 7% of the variation of the personal exposure.

Table 2. Ratio of average personal exposure to $PM_{2.5}$, Soot, NO, NO_2 and NO_x and proximity of traffic, calculated with multivariate regression analysis.

	Model 1 with home at busy road				Model 2 with total traffic intensity at street of residence			
	Crude		Adjusted		Crude		Adjusted	
	Ratio*	95% CI	Ratio*	95% CI	Ratio*	95% CI	Ratio*	95% CI
$PM_{2.5}$	0.85	0.68, 1.07	0.92	0.76, 1.12	0.95	0.83, 1.08	0.99	0.89, 1.10
Soot	1.14	0.98, 1.33	1.18	1.04, 1.35	1.08	0.99, 1.17	1.10	1.03, 1.18
NO	1.42	0.97, 2.08	1.31	0.92, 1.87	1.19	0.96, 1.46	1.17	0.96, 1.42
NO_2	0.87	0.72, 1.05	0.91	0.74, 1.12	0.96	0.86, 1.07	0.98	0.87, 1.10
NO_x	0.97	0.79, 1.20	0.96	0.77, 1.19	1.00	0.88, 1.12	0.90	0.25, 3.11

*Ratio of average personal exposure for group living at busy road vs. background location, using multiple regression analysis with the logarithm of the pollutant as a dependent variable and with *'home on a busy road'* (model 1) or *'total traffic intensity on street of residence (per 10 000 vehicles/24 h)'* (model 2), and *'concentration at background site'*, *'exposure to ETS'*, *'exposure to burning candles'* and *'exposure to gas cooking'* as independent variables.

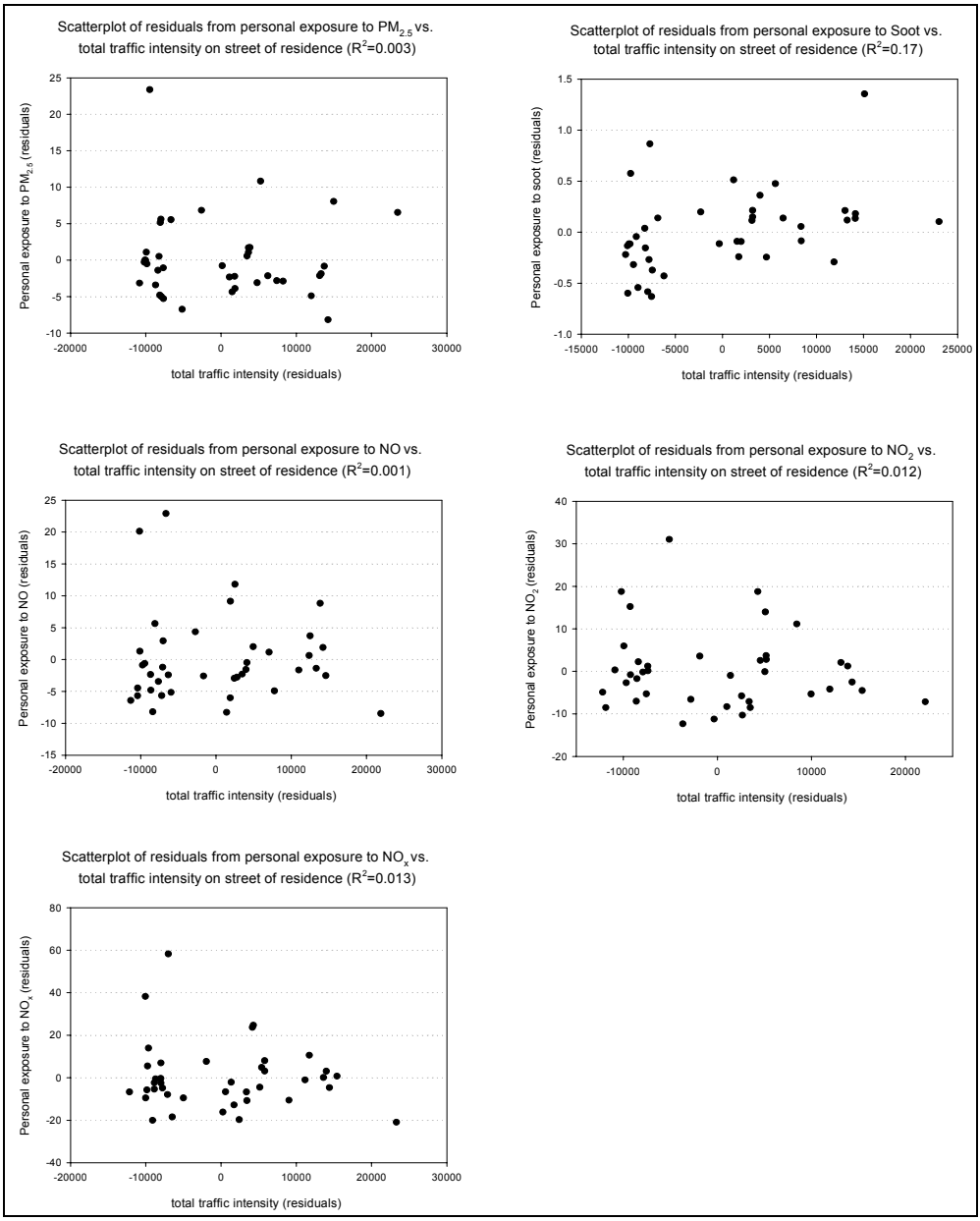

Figure 3. Partial residual plots from average personal exposure versus traffic intensity on the street of residence, for all pollutants.

Sensitivity analysis

To test for potential residual confounding by indoor sources, we also specified models for observation periods without the major indoor source for the specific pollutant. After excluding measurements during which participants were exposed to ETS, the ratio of personal exposure to soot increased from 1.18 to 1.20 (95% confidence interval (CI): 1.01, 1.44) for model 1, and from 1.10 to 1.14 (CI: 1.04, 1.25) for model 2. The ratio for personal exposure to $PM_{2.5}$ hardly changed after applying the same restriction, 1.00 (CI: 0.83, 1.20) and 0.99 (CI: 0.89, 1.11) for model 1 and 2 respectively. When excluding days during which participants were exposed to gas cooking, the ratio of average personal exposure to NO comparing participants living at a busy road with participants living at a background location, increased strongly to 2.06 for model 1, and 1.57 for model 2. However, none of these increased ratios were significant. For NO_2 and NO_x the ratios were 0.78 (CI: 0.36, 1.68) and 0.83 (CI: 0.33, 2.12) for model 1 and, 0.91 (CI: 0.56, 1.47) and 0.95 (CI: 0.55, 1.64) for model 2.

Overall, the distance from the front door to the kerbside of the street varied between 2 and 30 m. Adding distance to the street into the regression model did not change the ratios for either of the traffic characteristic variables, and distance itself was not associated with personal exposure.

Expanding the regression model with more lifestyle or residence-related characteristics (time spent indoor, sex, living in an apartment, having a window on the street side open during the measurement and having an open kitchen) did not change the effect estimates for any of the pollutants; for soot the ratios were 1.22 (CI: 1.08, 1.39) and 1.10 (CI: 1.03, 1.18) for model 1 and 2 respectively. Having an open kitchen contributed significant to the explained variance of the personal exposure.

Effect of time activity patterns

The difference in personal exposure to soot between the group living at a busy road vs. background location was larger when participants spent more time at home. For subjects spending more than 43 h at home out of the 48-hour measurement period, the ratio for living on a busy road was 1.28 (CI: 1.06, 1.54) vs. 1.07 (CI: 0.85, 1.35) for subjects spending less than 43 h at home.

To evaluate the impact of spending time in traffic (car) and spending time outdoors, we specified a model in which we, next to the previous variables, added 'time spent in traffic' and 'time spent outside'. The results of this extended model are shown in table 3. Elevated ratios were seen for

time spent in traffic for $PM_{2.5}$ and soot. The increase in personal exposure to $PM_{2.5}$ when spending 1 h in traffic was 28% (table 3). For soot, the increase was 12%. Increases in personal exposure to $PM_{2.5}$ and soot when spending 1 h outdoors were only slighted elevated (4% and 3% respectively). For NO, NO_2 and NO_x no increases in personal exposure were seen in relation to spending time in traffic or outdoors.

Table 3. Relationship between personal exposure to different air pollutants and time spent in traffic and outdoors.

	Time spent in traffic		Time spent outdoors	
	Ratio*	95% CI	Ratio*	95% CI
$PM_{2.5}$	1.28	1.08, 1.51	1.04	1.00, 1.09
Soot	1.12	1.00, 1.27	1.03	1.00, 1.06
NO	0.99	0.71, 1.40	0.95	0.87, 1.04
NO_2	0.94	0.78, 1.15	0.97	0.92, 1.01
NO_x	0.97	0.79, 1.20	0.96	0.91, 1.01

*Ratio of average personal exposure is expressed for a 1 h-increment, using multiple regression analysis with the logarithm of the pollutant as a dependent variable and with *'home on a busy road', 'concentration at background site', 'exposure to ETS', 'exposure to burning candles', 'exposure to gas cooking'*, and with *'time spent in traffic' (first column) or 'time spent outdoors' (second column)* as independent variables.

Discussion

Living at a busy road was reflected in a small increase in personal exposure to soot and NO for a population of older adults living in Utrecht. The difference in personal exposure was much smaller than the difference of outdoor concentrations measured directly outside the home. No increase in personal exposure was found for $PM_{2.5}$, NO_2 and NO_x, despite demonstrable differences in outdoor air concentrations between participants living at busy roads and quiet streets. However, time spent in traffic and time spent outdoor was related to significantly increased personal exposure to soot and $PM_{2.5}$.

Few studies have been published that we can compare our results to. Two studies found comparable differences in personal exposure to soot for adults (1.29) and for children (1.38) living at busy and quiet streets in Amsterdam, the Netherlands.[16,17]

The small difference in personal exposure related to living at a major road was not related to a lack of relevant contrast in traffic. The contrast in traffic intensity on the street of residence was very distinct (345 vs. 16 910 vehicles/24 h) with no overlap between the two groups. The selected homes were located between 2 and 30 meter from the road, a typical situation for urban areas. The current results cannot be generalized to roads with a higher traffic intensity and typically larger distance of homes to the road, such as freeways.

The differences in outdoor pollutant concentrations in our study were comparable to the findings in a number of previous studies. Similar strong contrasts in outdoor air were reported in a study conducted in three European areas: differences in $PM_{2.5}$ and soot between traffic and urban background sites of 17% and 55% respectively were reported.[10] In the framework of the SAVIAH study, outdoor measurements at 'low' and 'high' (16 800 vehicles/24 h on average) traffic homes in Amsterdam, the Netherlands, were performed.[9] A difference of 75% for soot, and 25% for NO_2 was found. A recent study by Van Roosbroeck et al. (accepted for publication by Atm. Env. 2007) looked at exposure in school children but also included measurements at their home address. Similar differences were found for NO (78%), NO_2 (11%) and NO_x (27%) when comparing homes near busy roads (> 14 000 vehicles/24 h) to homes at a background location.[17]

It is likely that three factors explain the smaller difference in personal exposure compared to the difference in outdoor concentrations: time activity patterns, non-quantitative penetration of outdoor air pollution in homes and indoor sources of the measured air pollutants. Relevant time activity variables in the current study were time spent in the own home, time spent in traffic and time spent outdoors. The small difference in personal exposure, as opposed to the strong difference in outdoor concentrations, was found in a study population that spent a large fraction of its time in the home. Various studies have investigated indoor/outdoor relationships and found that in the absence of indoor sources, indoor particle concentrations are lower than outdoor concentrations, depending on the particle size. In Amsterdam, it was found that the I/O ratio for soot was larger than for $PM_{2.5}$ which suggests that the small soot particles more readily penetrate.[18] It is well known that the reactivity of NO and NO_2 results in a substantial reduction of concentrations upon infiltration in the home.

The percentage explained variance in the model used is sufficient considering the fact that we are modelling personal exposure, nevertheless there is room for improvement. The wide 95%

confidence intervals for personal exposure may suggest the presence of indoor sources that we were unable to account for. Götschi et al.[23] demonstrated little impact of indoor sources on personal soot concentrations. Subjects were sampled on 4-5 times for 48 hours. Inevitably, the accuracy and precision of the calculated averages for estimating true long-term average personal exposure are limited. We have paired observations, and we have adjusted for temporal variation measured at a background location, but such adjustments have inevitable limitations for pollutants that exhibit strong spatial contrasts. Keeping these limitations in mind, our results do suggest that substantial misclassification of exposure may occur by using traffic intensity at the residential address as an exposure estimate.

In conclusion, personal soot exposure of older adults living at major roads was increased compared to adults living at quiet roads. No significant difference was found for $PM_{2.5}$ or nitrogenoxides. Participation in traffic and spending time outdoors both significantly contributed to personal exposure to soot and $PM_{2.5}$, and should therefore be considered important covariates in future studies.

Acknowledgements

The authors like to thank Hans Jongsma for his assistance with the sampling/fieldwork and especially, the participants for their loyal contribution to the research.

References

[1]Pope CA, 3rd, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. Jama 2002; 287:1132-41.

[2]Heinrich J, Topp R, Gehring U, Thefeld W Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. Environ Res 2005; 98:240-249.

[3]Bayer-Oglesby L, Schindler C, Hazenkamp-von Arx ME, Braun-Fahrlander C, Keidel D, Rapp R, Kunzli N, Braendli O, Burdet L, Sally Liu LJ, Leuenberger P, Ackermann-Liebrich U Living near Main Streets and Respiratory Symptoms in Adults: The Swiss Cohort Study on Air Pollution and Lung Diseases in Adults. Am J Epidemiol 2006; 164:1190-8.

[4]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 2002; 360:1203-9.

[5]Gehring U, Heinrich J, Kramer U, Grote V, Hochadel M, Sugiri D, Kraft M, Rauchfuss K, Eberwein HG, Wichmann HE Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. Epidemiology 2006; 17:545-51.

[6]Finkelstein MM, Jerrett M, Sears MR Traffic air pollution and mortality rate advancement periods. Am J Epidemiol 2004; 160:173-7.

[7]Garshick E, Laden F, Hart JE, Caron A Residence near a major road and respiratory symptoms in U.S. Veterans. Epidemiology 2003; 14:728-36.

[8]Maheswaran R, Elliott P Stroke mortality associated with living near main roads in England and Wales. Stroke 2003; 34:2776-2780.

[9]Fischer P, Hoek G, Reeuwijk Hv, DJ B, Lebret E, Wijnen Jv, Kingham S, Elliot P Traffic-related differences in outdoor and indoor concentrations of particles and volatile organic compounds in Amsterdam. Atmos Environ 2000; 34:3713-3722.

[10]Hoek G, Meliefste K, Cyrys J, Lewné M, Bellander T, Brauer M, Fischer P, Gehring U, Heinrich J, Van Vliet P, Brunekreef B Spatial variability of fine particle concentrations in three European areas. Atmos Environ 2002; 36:4077-4088.

[11]Janssen N, van Mansom D, van der Jagt K, Harssema H, Hoek G Mass concentration and elemental composition of airborne particulate matter at street and background locations. Atmos Environ 1997; 31:1185-1193.

[12]Namdeo A, Bell MC Characteristics and health implications of fine and coarse particulates at roadside, urban background and rural sites in UK. Environ Int 2005; 31:565-73.

[13]Gilbert NL, Woodhouse S, Stieb DM, Brook JR Ambient nitrogen dioxide and distance from a major highway. Sci Total Environ 2003; 312:43-6.

[14]Roorda-Knape M, Janssen N, Hartog Jd, Vliet Pv, Harssema H, Brunekreef B Air pollution from traffic in city districts near major motorways. Atmos Environ 1998; 32:1921-1930.

[15]Smargiassi A, Baldwin M, Pilger C, Dugandzic R, Brauer M Small-scale spatial variability of particle concentrations and traffic levels in Montreal: a pilot study. Sci Total Environ 2005; 338:243-51.

[16]Wichmann J, Janssen NAH, van der Zee S, Brunekreef B Traffic-related differences in indoor and personal absorption coefficients measurements in Amsterdam, The Netherlands. Atmos Environ 2005; 39:7384-7392.

[17]Van Roosbroeck S, Wichmann J, Janssen NA, Hoek G, van Wijnen JH, Lebret E, Brunekreef B Long-term personal exposure to traffic-related air pollution among school children, a validation study. Sci Total Environ 2006; 368:565-573.

[18]Brunekreef B, Janssen NA, de Hartog JJ, Oldenwening M, Meliefste K, Hoek G, Lanki T, Timonen KL, Vallius M, Pekkanen J, Van Grieken R Personal, indoor, and outdoor exposures to PM2.5 and its components for groups of cardiovascular patients in Amsterdam and Helsinki. Res Rep Health Eff Inst 2005; 127:1-70; discussion 71-9.

[19]Janssen, de Hartog JJ, Hoek G, Brunekreef B, Lanki T, Timonen KL, Pekkanen J Personal exposure to fine particulate matter in elderly subjects: relation between personal, indoor, and outdoor concentrations. J Air Waste Manag Assoc 2000; 50:1133-43.

[20]Pekkanen J, Timonen KL, Tiittanen P, Vallius M, Lanki T, Sinkko H, Ruuskanen J, Mirme A, Kulmala M, Vanninen E, Bernard A, Ibald-Mulli A, al e ULTRA: Exposure and risk assessment for fine and ultrafine particles in ambient air. Study manual and data book. B9/2000. Kuopio: KTL, National Public Health Institute. 2000.

[21]Ogawa C NO, NO_2, NO_x and SO_2 sampling protocol using the ogawa sampler. Accessed at www.agawausa.com in 2002. 1998.

[22]Dassen AGM, Dolmans JHJ, Jabben J, Hamminga NAR, Hoffmans WH, Nijland HA. Noise in the 5th Environmental Assessment (Geluid in de vijfde Milieuverkenning) 408129 009. Bilthoven: National Institute of Public Health and the Environment (RIVM), 2000.

[23]Götschi T, Oglesby L, Mathys P, Monn C, Manalis N, Koistinen K, Jantunen M, Hanninen O, Polanska L, Kunzli N Comparison of black smoke and PM2.5 levels in indoor and outdoor environments of four european cities. Environ Sci Technol 2002; 36:1191-1197.

Chapter five

The impact of adjustment for exposure measurement error on the relationship between traffic-related outdoor air pollution and respiratory symptoms in children

Sofie Van Roosbroeck
Ruifeng Li
Gerard Hoek
Erik Lebret
Bert Brunekreef
Donna Spiegelman

(Submitted)

Abstract

Respiratory and eye symptoms were found to be associated with outdoor concentrations of soot and NO_2 outside of childrens' schools in a previous study. We assessed the impact of measurement error adjustment on the estimated health effects related to traffic-related outdoor air pollution. Concentrations of air pollutants outside childrens' schools were validated by personal measurements of exposure to traffic-related air pollution. The prevalence ratio of four health outcomes (current wheeze, conjunctivitis, phlegm and elevated total serum immunoglobulin E (IgE)) was estimated using school outdoor measurements, and then adjusted for measurement error using the personal exposure data by applying a regression calibration method. The measurement error adjustment analysis was carried out for a main study/external validation design. The measurement error-adjusted analysis showed effect estimates related to soot and NO_2 that were two to three times higher than estimated in the original study. The adjusted prevalence ratio for current phlegm was 5.3 (95% CI, 1.2-22.6), compared to 2.2 (95% CI, 1.3-3.9) before measurement error adjustment, for a 9.3 ug/m^3 increase in soot, and 3.8 (95% CI, 1.0-14.2), compared to 1.8 (95% CI, 1.1-2.8), for a 17.6 µg/m^3 increase in NO_2. Corrections of similar magnitude for the prevalence of current wheeze, current conjunctivitis and total elevated total IgE were observed.

The estimates of the effect of exposure to outdoor air pollution on respiratory and other health effects may be substantially attenuated when exposure measurement used outdoor concentrations in childrens' schools instead of personal exposure.

Introduction

During the last decades, the adverse effects of air pollution on cardio-respiratory health have become well established.[1] Pollutants of current interest in Western countries include especially particulate matter, ozone and nitrogen dioxide.[1,2] From a public health point of view, effects related to long-term average exposure to air pollution are of the greatest interest. In the last decade, a number of epidemiological studies have shown associations between small-scale variations in exposure to traffic-related air pollution and prevalence of respiratory symptoms such as cough and wheeze in both children[3,4] and adults.[5,6] Other studies found increased cardiopulmonary mortality rates related to small-scale variations in traffic-related air pollution.[7-9]

Measuring long-term average personal exposure to traffic-related air pollution is difficult, because of the highly demanding nature of personal monitoring, especially for particulate matter. Therefore, most studies have used surrogates of exposure such as the concentration in outdoor air measured at relevant sites (e.g. the school) or modeled using dispersion models or land-use regression models.[10] Surrogates of outdoor air concentrations such as distance to major roads or the traffic intensity on the residential road have been used as well.[10] However, people spend a large percentage of their time indoors, live at locations with varying traffic intensity, live in homes that differ in indoor sources and air exchange rate, affecting penetration of outdoor air into the home, and have different activity patterns. All these factors contribute to differences between outdoor air concentrations and personal exposure. An obvious question, therefore, is how representative these outdoor concentrations are for the 'true' personal exposure. Other researchers have raised concerns about the use of ambient concentrations of $PM_{2.5}$, elemental carbon and NO_2 as surrogates for personal exposure, since they do not always seem to reflect personal exposure.[11-14]

In the present paper, we explore the effect of adjusting for exposure measurement error in a study that associated school outdoor levels of air pollutants with chronic respiratory symptoms and other health outcomes in school children living close to freeways.[3] We reported associations between annual average outdoor air pollution concentrations measured at the school and prevalence of wheeze, conjunctivitis, phlegm and elevated total serum immunoglobulin E (IgE) in school children attending schools near major freeways of varying traffic intensity. Validation studies were performed nested in the main study[15] and externally.[16] We used statistical methods to adjust for exposure measurement error, according to the regression calibration method.[17-19]

Materials and methods

Study overview

In the measurement error analysis, we considered the school outdoor concentrations of an air pollutant to be the *surrogate* exposure and the personal exposure as the *true* exposure. A regression calibration method for correcting the original ORs and corresponding CI estimates from the epidemiological study for systematic and random error using a regression model was developed previously.[17,18] This method was later generalized to estimate risk ratios and prevalence ratios.[19] The method requires a main study in which health outcome, surrogate

exposure and confounding covariates are available and a validation study in which true exposure, surrogate exposure and confounding covariates are assessed. This paper describes the application of two external validation studies, i.e. one validation study using soot measurements and one validation study using NO_2 measurements. The main study consists of epidemiological data from Janssen et al.,[3] the NO_2 validation study consists of data including personal NO_2 measurements from Rijnders et al.[15] and, the soot validation study consists of data including personal soot measurements from Van Roosbroeck et al.[16]

Background of the studies

The main study is an epidemiological study that examined respiratory health of 2083 children from 24 schools located within 400 m of freeways in the Netherlands.[3] Respiratory symptoms were collected by the questionnaire designed by the International Study of Asthma and Allergies in Childhood (ISAAC II). Details on how the health outcomes were defined are described elsewhere.[20] Data on traffic-related characteristics, such as traffic intensities and distance to a major road, were collected. Measurements of soot and NO_2 were conducted at all 24 schools between April, 1997 and July, 1998. Annual average concentrations of soot and NO_2 outside all schools were calculated as described in detail by Janssen et al.[21]

The first validation study was nested in the main study. In that study, personal and school outdoor NO_2 concentrations were measured in 110 schoolchildren from three of these 24 schools.[15] The average personal NO_2 concentration was based on one to four 1-week measurements in four different seasons. The average school outdoor concentrations were measured in the same weeks. All measurements were performed using Palmes diffusion tubes that could whether be attached to the back side of a home using a specially designed device for the outdoor measurement or be attached to a badge and worn between breast and head for the personal measurement. Details on the sampling methods are described elsewhere.[15] Since the participants were recruited from the main study, the same health outcome and confounder information was available.

The second validation study was conducted six years after the main study. In this study, we collected personal soot measurements in Dutch school children using flow-controlled battery operated pumps in a made-to-fit backpack.[16] From March to June 2003, personal monitoring of soot was performed during four 48-hour periods in 54 school children aged 10 to 12 years. The children were recruited from four schools in Utrecht with different proximity to busy roads. Outdoor measurements at the school location were performed concurrently to the personal

measurements using the same sampling device. All pollutant concentrations from the original exposure study were averaged per child and then standardised for background concentrations according to Janssen's method.[21] Further details on the sampling methods are described elsewhere.[22]

Both validation studies reported absolute differences in personal exposure between children classified as high and low exposed according to outdoor characteristics. For the purpose of this paper, we calculated the correlation between individual average personal and outdoor exposures.

Data analysis

In the main study, the sample sizes vary by health outcome. Information on respiratory symptoms was collected by a parent-completed questionnaire among 2083 schoolchildren and total IgE was determined in a subgroup of 881 school children. Some information on covariates and/or health outcomes were missing and could therefore not be included in the measurement error analysis, again resulting in a smaller population study than the original epidemiological study. Sample sizes for current wheeze, current conjunctivitis and current phlegm were 1862, 1871 and 1843 respectively. Sample size was 774 for total IgE.

In the validation studies, only those children with three or four repeated measurements and no missing data on the confounding covariate information were included in the analysis, leaving 67 participants in the NO_2 validation study and 45 in the soot validation study. Since the group of children selected for the personal NO_2 measurements was drawn from the group of 2083 children and not from the 881 selection, some information on covariates and/or health outcomes were missing in the validation dataset and thus sample size was smaller when looking at total elevated IgE in the NO_2 validation study (n = 43).

Rosner et al.'s regression calibration method for adjustment of point and interval estimates for bias due to exposure measurement error is a three-step procedure.[18] First, the unadjusted point estimates and their variances are obtained by fitting the standard regression model in the main study, here, a log-binomial model. Then, in the validation study, the measurement error model parameters are estimated by regressing the true exposure on the surrogate exposure and all other covariates included in the primary regression model. Finally, the estimates are adjusted for measurement error by combining these two sets of estimates and their variance-covariances. In order for this method to be valid, we need to verify that the assumptions associated with it are applicable to the data at hand. These assumptions include[18,23]: 1) the measurement error model is linear and homoscedastic; 2) the main study model is linear on the assumed scale, here, on the

log scale; 3) measurement error is not severe; and 4) the surrogate exposure contains no further information about the distribution of disease once data on the true exposure is available.

To assess the validity of the first assumption, concerning the linearity of measurement error model, here, the linear relationship between personal exposure to soot and NO_2, with their corresponding surrogates, we fit stepwise restricted cubic splines[24] using a SAS macro (http://www.hsph.harvard.edu/faculty/spiegelman/blinplus.html) developed for this purpose, to compare the linear measurement error models to models with a step-wise 17-knot restricted cubic spline function to flexibly assess any non-linearity in the relationship. There was no evidence for any non-linearity in either measurement error model.[25]

Homoscedasticity of the measurement error models was assessed by computing the correlation between the predicted values and the absolute values of residuals of the linear measurement error models. For soot, the Pearson correlation coefficient was 0.09, indicating no violation of this assumption. For NO_2, the correlation was 0.34, which suggested some heteroscedasticity. However, there is quite a bit of evidence indicating that the standard linear regression calibration gives a good approximation, nevertheless. For example, Schmid and Rosner[26] used a mixture model to treat misclassification of the 0's in alcohol intake separately from measurement error in the non-zero values in the Nurses' Health Study, where the correlation between the absolute value of the residuals and the predicted values from the measurement error model was 0.44, quite a bit higher than what was observed here.[26] In an analysis of breast cancer incidence in relation to alcohol intake, the results from this more complex method of correction for measurement error in alcohol intake from the food frequency questionnaire compared to multiple diet records was not materially different from the results that used standard linear regression calibration as given by Rosner et al.[18] The mixture model gave a relative risk (95% CI) of 1.52 (1.23-1.87) compared to 1.62 (1.23-2.12) from the standard linear regression calibration. In addition, we have engaged in further investigation and development of methods to accommodate heteroscedasticity in the measurement error model. In an unpublished manuscript by Spiegelman and colleagues (http://www.hsph.harvard.edu/faculty/spiegelman/manuscripts/beta_RCH.pdf), an extended regression calibration estimator was developed that uses a second order Taylor series expansion to obtain an estimator that allows for heteroscedasticity. In an extensive simulation study which allowed for correlations of the residual variance with the predicted values of the measurement error model to be as large as 0.6, the extended estimator offered little improvement over the standard regression calibration estimator used in this paper, which exhibited little bias and nominal coverage probability (table 5 of the above-referenced report).

Similarly, in two examples, including one from the Nurses' Health Study looking at alcohol intake in relation to breast cancer incidence as in Schmid et al.[26], the results given by the standard regression calibration estimator were similar to those when the extended estimator was applied (table 4 of the above-referenced report). Both gave results very close to those given by the maximum likelihood estimator for misclassification of alcohol intake[27] where no parametric assumptions are made at all. We therefore conclude that although some heteroscedasticity of the measurement error model for NO_2 was evident here, it is unlikely to appreciably detract from the validity of the measurement error adjusted results.

To assess the validity of the second assumption, concerning the linearity of the relationship between the exposures, soot and NO_2, with the four outcomes on the natural log scale, we again fit large stepwise restriction cubic spline models, and none of the eight models showed any non-linearity. The third assumption can be satisfied by a small measurement error approximation, that is, if $\beta^2\sigma^2$ is small, where β is the log relative risk for exposure obtained from the primary regression model in the main study and σ^2 is the residual variance of the measurement error model fit in the validation study. For all the health outcomes, $\hat{\beta}^2\hat{\sigma}^2$ was very small (ranging from 0.000005 to 0.0002), so this assumption was taken to hold. The last assumption can be empirically verified only when the validation study includes outcome data with a sufficient number of cases. Here, there was some outcome data in the NO_2 validation study only, but the case counts were too low, so we were unable to verify the assumption. We note, however, that this assumption is biologically plausible in the sense that ambient exposure as measured by area monitoring would not be expected to have any health effect, once personal exposure is fully accounted for.

Diagnostics and statistical analyses were performed using Splus (MathSoft, Inc.) and SAS (Version 9e, SAS Institute Inc., Cary, NC). The SAS macro for adjusting for measurement error used in this paper is publicly available and can be downloaded at the URL (http://www.hsph.harvard.edu/faculty/spiegelman/blinplus.html).

Results

Table 1 presents the traffic characteristics, air pollution concentrations of soot and NO_2, the prevalence of current wheeze, current conjunctivitis, current phlegm, and elevated total IgE, and

other characteristics for main and validation study participants. The prevalences of the four health outcomes were very similar between the NO_2 validation and main study participants. Traffic characteristics and covariate information were also comparable. The levels of school outdoor NO_2 were similar between the main and validation studies. The levels of soot, however, were higher in the validation study. Spiegelman et al.[21] show that the only compatibility assumption needed for validity of the regression calibration method is that the measurement error model estimate can reasonably be assured to be the one that would have been observed in the main study, had true exposure measurements been available.

Figure 1 shows the scatterplot of the personal level of soot versus the school outdoor concentration in the validation study. The correlation coefficient between the true and the surrogate exposure was 0.53. After including all confounding covariates used in the main study regression model, exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age and current pet possession, to the measurement error model, the multiple correlation coefficient increased to 0.71 (measurement error model shown in table 2). This suggests that a reasonably accurate estimate of personal exposure of a school child to soot from the school outdoor concentration along with covariate information on life style and possible indoor sources was obtained. The correlation coefficient of the true versus surrogate exposure was considerably lower for NO_2 (0.35) (figure 2). However, including the main study model covariates to the measurement error model increased the multiple correlation coefficient to 0.77 (measurement error model shown in table 3). This indicates the important contribution of indoor sources in the home to the total personal NO_2 exposure.

Prevalence ratios for the association between exposure to soot and different health outcomes are shown before and after adjustment for measurement error (table 4). The unadjusted estimate of the prevalence ratio (PR) for current wheeze was 1.45 (95% CI, 0.80-2.61), and after adjusting for measurement error, the estimate was 2.15 (95% CI, 0.59-7.74). Effects of measurement error adjustment for current conjunctivitis, current phlegm and elevated total IgE were somewhat larger (table 4). The larger confidence intervals reflect the small sample size of the validation study, as well as the increased estimate of uncertainty due to the magnitude of the measurement error observed.

Table 5 presents the results of the regression calibration approach applied to NO_2 exposure. The adjusted prevalence ratios, expressed for a difference in NO_2 of 17.6 $\mu g/m^3$, were about double the unadjusted PR for current wheeze, current phlegm and total elevated IgE (table 5). For

current conjunctivitis, the prevalence increased 3-fold for a 17.6 μg/m^3-increment compared to the unadjusted PR.

Table 1. Basic characteristics of the main and validation study participants.

	Soot validation study (N = 45)	NO_2 validation study (N = 67)	Main study (N = 1871)
Traffic characteristics [mean (SD)]			
Car traffic intensity near school (cars/24hr)	47 016 (26 598)	76 623 (38 065)	90 406 (34 457)
Truck traffic intensity near school (trucks/24hr)	3948 (4438)	12 852 (7605)	12 806 (4618)
Total traffic intensity near school (vehicles/24hr)	50 067 (30 936)	89 474 (45 387)	103 212 (35 995)
Distance from school to busy road (m)	193 (113)	202 (139)	221 (103)
Air pollution concentrations [a] [mean (SD)]			
Average School Outdoor soot (ug/m^3)	20.8 (6.1)	/	10.2 (2.1)
Average Personal soot (ug/m^3)	17.8 (5.7)	/	/
Average School Outdoor NO2 (ug/m^3)	/	37.4 (7.0)	34.5 (5.1)
Average Personal NO2 (ug/m^3)	/	23.7 (9.3)	/
Health outcomes [n (%)]			
Current wheeze	/	6 (9.2)	176 (9.5)
Current conjunctivitis	/	9 (13.9)	133 (7.1)
Current phlegm, no cold	/	5 (7.8)	175 (9.5)
Elevated total IgE[b]	/	12 (27.9)	315 (40.7)
Other characteristics [n (%)]			
Parental smoking in the home (% yes)	16 (36)	39 (58)	1080 (58)
Gas cooking (% yes)	25 (56)	52 (78)	1574 (84)
Unvented water heater in kitchen (% yes)	1 (2)	5 (7)	165 (9)
Gender (% male)	21 (47)	35 (52)	914 (49)
Age (mean (SD))	11 (0.8)	10 (0.9)	9 (1.6)
Current pet possession (% yes)	26 (58)	41 (61)	1113 (59)

[a]Air pollution concentrations were standardised for background concentrations (following Janssen et al. 2001). The average school outdoor concentrations for the main study are the average of 24 annual average school concentrations. [b]Sample size for NO_2 validation and main study are 43 and 774, respectively, when looking at elevated total IgE as a health outcome.

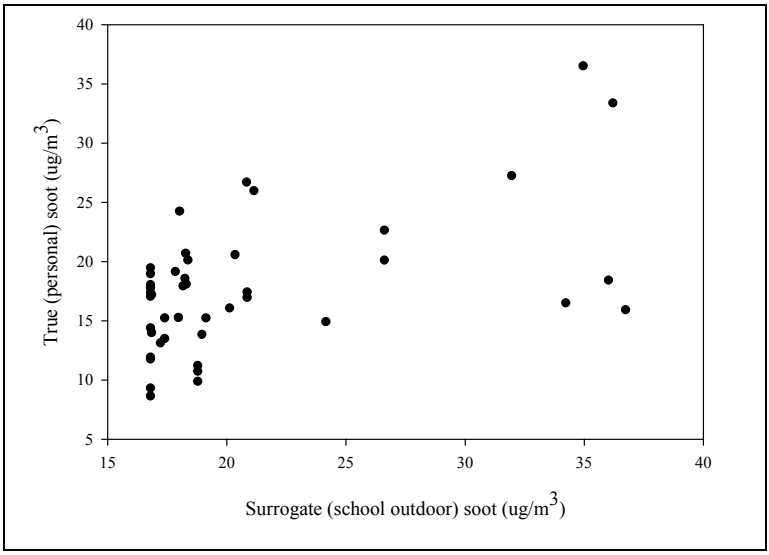

Figure 1. Scatterplot of outdoor school soot versus personal soot in the validation study (n=45); r=0.53.

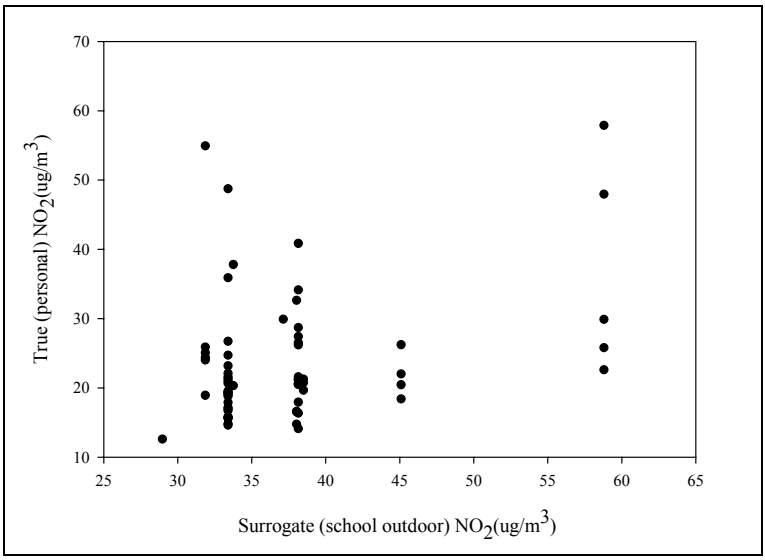

Figure 2. Scatterplot of outdoor school NO_2 versus personal NO_2 in the validation study (n=67); r=0.35.

Table 2. Measurement error model for average personal exposure to soot (μg/m^3) (n = 45).

Variable name	$\hat{\gamma}$	$S\hat{E}(\hat{\gamma})$	p-value
Intercept	13.16	12.48	0.30
School outdoor soot (μg/m^3)	0.48	0.13	< 0.001
Exposure to ETS (yes /no)	5.72	1.80	< 0.01
Exposure to gas cooking (yes /no)	2.55	1.76	0.16
Presence of unvented water heater in the kitchen (yes /no)	-1.84	4.81	0.70
Sex (boy/girl)	0.19	1.42	0.89
Age (yr)	-0.80	1.01	0.43
Current pet possession (yes /no)	1.62	1.37	0.25

$\hat{\gamma}$ = regression slope; $S\hat{E}(\hat{\gamma})$ = standard error. For all categorical variables yes is coded as '1' and no as '0'.

It was not possible for us to adjust for the same possible confounders in this analysis, as has been done in the original analysis. First, not all covariates were available in the validation studies. Secondly, because the number of observations is much smaller in both validation studies, not as many variables can be included in regression models. However, the ORs, adjusted for the more limited set of confounders given in the footnotes to tables 4 and 5, corresponded well with the ORs from the original analysis.[3] For soot, the new versus original ORs (95% CI) were 1.49 (0.77-2.88) vs. 1.43 (0.66-3.07), 2.35 (1.14-4.85) vs. 2.54 (1.15-5.60), 2.47 (1.30-4.68) vs. 2.41 (0.96-6.04) and 2.39 (1.29-4.44) vs. 2.67 (1.16-6.12) for current wheeze, current conjunctivitis, current phlegm and elevated total IgE, respectively. For NO_2, the new versus original ORs (95% CI) were 1.66 (0.99-2.78) vs. 1.74 (0.99-3.05) for current wheeze, 2.37 (1.33-4.25) vs. 2.60 (1.38-4.90) for current conjunctivitis, 1.80 (1.09-2.98) vs. 1.72 (0.82-3.62) for current phlegm and 2.57 (1.58-4.18) vs. 3.12 (1.81-5.38) for elevated total IgE.

Since the NO_2 validation study was nested in the original validation study, health outcome date on the validation study participants was available and, as a result, these data could be employed in an internal validation study, following methods developed by Spiegelman et al. (2001)[28]. However, the sample size of the validation study was too low, and therefore also the number of cases (table 1), to reliably estimate prevalence ratios of the four health outcomes. In view of the

technical complexities of obtaining long-term personal exposure measurements, the possibilities for sufficiently powered internal validation studies of this kind likely will remain small.

Table 3. Measurement error model for personal exposure to NO_2 (μg/m^3) (n = 67).

Variable name	$\hat{\gamma}$	$S\hat{E}(\hat{\gamma})$	p-value
Intercept	6.67	8.95	0.46
School outdoor NO_2 (μg/m^3)	0.42	0.11	< 0.001
Exposure to ETS (yes/no)	1.94	1.69	0.26
Exposure to gas cooking (yes/no)	2.53	1.85	0.18
Presence of unvented water heater in the kitchen (yes/no)	24.89	3.17	< 0.0001
Sex (boy/girl)	-2.41	1.60	0.14
Age (yr)	-0.13	0.86	0.88
Current pet possession (yes/no)	-1.92	1.63	0.24

$\hat{\gamma}$ = regression slope; $S\hat{E}(\hat{\gamma})$ = standard error. For all categorical variables yes is coded as '1' and no as '0'.

Table 4. Association between exposure to soot (ug/m^3) and selected health outcomes

	Current Wheeze	Current Conjunctivitis	Current phlegm	Elevated total IgE
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Unadjusted analysis	1.45 (0.80-2.61)	2.18* (1.13-4.21)	2.24* (1.27-3.93)	1.69* (1.21-2.36)
Adjusted analysis	2.15 (0.59-7.74)	5.06* (1.02-24.96)	5.29* (1.24-22.62)	2.98* (1.22-7.26)

Prevalence ratios are calculated for the main study/external validation study design and expressed for a 9.3 ug/m^{3}difference. Adjusted for exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age and current pet possession.* p < 0.05; # p < 0.10.

Table 5. Association between exposure to NO_2 (ug/m^3) and selected health outcomes

	Current Wheeze	Current Conjunctivitis	Current Phlegm	Elevated total IgE
	PR (95% CI)	PR (95% CI)	PR (95% CI)	PR (95% CI)
Unadjusted analysis	1.58$^{\#}$ (0.99-2.51)	2.22* (1.31-3.76)	1.76* (1.10-2.81)	1.83* (1.39-2.42)
Adjusted analysis	2.94$^{\#}$ (0.85-10.18)	6.60* (1.33-32.77)	3.82* (1.03-14.21)	4.20* (1.54-11.48)

Prevalence ratios are calculated for the main study/external validation study design and expressed for a 17.6 ug/m^3 difference. Adjusted for exposure to parental smoking, gas cooking, presence of an unvented water heater in the kitchen, sex, age and current pet possession. $p < 0.05$; $^{\#}$ $p < 0.10$.

Discussion

The regression calibration method allowed us to explore what the effect of adjustment for exposure measurement error correction was on the estimated health risks, when using school outdoor measurements of air pollutants as a surrogate for personal exposure. The effect estimates adjusted for measurement error were substantially higher than the ones previously reported, indicating attenuation of risk when using school outdoor concentrations instead of personal exposure measurements.

The strength of this analysis is that it uses the health outcome data from over 2000 children from the main study in which personal exposure was not directly measured, to obtain a single quantitative estimate of the effect of personal exposure to soot and NO_2 on health outcomes. An important limitation is, however, the loss in power of the analysis, as evident in the broader confidence intervals. From a statistical point of view, these confidence intervals reflect the true power in the study for an approximately unbiased result, in contrast to the original adjusted analysis, which gives a biased confidence interval around a biased point estimate.

Information on potential confounders was not the same in the full study and in the external validation study. However, recalculation of ORs in the main study with the more limited set of confounders available in the external validation study produced nearly identical results. In our

tables in this paper, comparisons are always between effect estimates calculated using exactly the same set of potential confounders.

This is the first time such a measurement error adjusted analysis has been conducted in a study on the health effects of soot or NO_2 including measurements of personal exposure. Li et al.[29] presented a measurement error corrected estimate for the effect of indoor NO_2 exposure on respiratory symptoms in subjects where exposure was not directly measured but information on NO_2 sources and residential characteristics were available. The measurement error corrected estimate (OR, 1.60; 95% CI, 1.10-2.32) compared well with the estimate found in the validation study (OR, 1.41; 95% CI, 1.13-1.75), where direct indoor NO_2 measurements and health outcome information were available. Horick et al.[19] applied the same measurement error adjustment method to airborne and house dust endotoxin measurements, and demonstrated a very large impact on the point estimate of effect (measurement error corrected estimate (RR, 5.56; 95% CI, 1.19-26.03) compared to the uncorrected estimate (RR, 1.45; 95% CI, 1.20-1.76). Confidence intervals increased substantially, as in the current study. Correlations between personal exposure and outdoor air pollutant concentrations in the present study were higher than correlations between living-room airborne and living-room floor dust endotoxin in the Horick study, so in our case correction for measurement error produced smaller differences.

The impact of adjustment for measurement error was approximately the same for NO_2 and soot. For the interpretation of the impact of the measurement error correction, a critical assumption is that personal exposure measurements reflect the true biologically relevant exposure. This is probably less true for NO_2 than for soot. First, NO_2 is generally not considered to be the only or most important causal agent from traffic-related air pollution, but rather a convenient indicator of the mixture of traffic pollutants. In contrast, there is evidence that soot does represent a causal agent in the mixture from controlled exposure studies of diesel soot.[30-32] Second, indoor sources are important in addition to outdoor air pollution in determining personal NO_2 exposure. Although we adjusted for indoor sources in the measurement error model, without personal measurements of exposure which separate indoor sources from outdoor, it is not possible to apply the measurement error methods which would estimate these separate effects in an unbiased manner.[18] However, indoor sources are less important for soot, as evidenced by the smaller change in the multiple correlation after adding indoor source indicators to the surrogate exposure in the measurement error model. Third, the personal NO_2 concentrations were considerably lower than ambient concentrations in the NO_2 validation study. This is because NO_2 is reactive, and indoor concentrations are lower because the NO_2 reacts away even when indoor sources are

present. Soot penetrates well into indoor environments and has only limited sinks, resulting in indoor concentrations that are typically 60-70% of the outdoor concentration in the absence of indoor sources. We do argue that the unadjusted risk estimates were underestimated, however it is likely that adjustment for NO_2 measurement error would be less sizable than presented.

In contrast to the endotoxin study reported by Horick et al.[19] and the NO_2 study reported by Li et al.[29], the exposure estimation in the current study is likely to be subject to both Berkson and classical measurement error. In the endotoxin and NO_2 studies, as well as in the current analysis, error of the classical type was introduced because the measured exposure, repeated or not, was likely to vary around the true exposure. In addition, in the current analysis, a school's average was assigned to each participating child attending that school and, accordingly, error of the Berkson type was introduced. Berkson creates little bias in risk estimates compared to the classical error, that was found to have more serious consequences.[33] The regression method used in the current work handles both types of error or a combination.

In conclusion, estimated effects of soot and NO_2 in school children increased after adjusting for exposure measurement error, suggesting that bias had occurred when school outdoor levels of air pollutants were used as indicators of the personal exposure to air pollutants of children.

References

[1]Brunekreef B, Holgate ST Air pollution and health. Lancet 2002; 360:1233-42.

[2]WHO. Health Aspects of Air Pollution: a Systematic Review of Health Aspects of Air Pollution in Europe E83080. Copenhagen: World Health Organization Regional Office for Europe, 2004.

[3]Janssen N, Brunekreef B, van 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; 111:1512-8.

[4]Nicolai T, Carr D, Weiland SK, Duhme H, von Ehrenstein O, Wagner C, von Mutius E Urban traffic and pollutant exposure related to respiratory outcomes and atopy in a large sample of children. Eur Respir J 2003; 21:956-63.

[5]Heinrich J, Topp R, Gehring U, Thefeld W Traffic at residential address, respiratory health, and atopy in adults: the National German Health Survey 1998. Environ Res 2005; 98:240-249.

[6]Garshick E, Laden F, Hart JE, Caron A Residence near a major road and respiratory symptoms in U.S. Veterans. Epidemiology 2003; 14:728-36.

[7]Gehring U, Heinrich J, Kramer U, Grote V, Hochadel M, Sugiri D, Kraft M, Rauchfuss K, Eberwein HG, Wichmann HE Long-term exposure to ambient air pollution and cardiopulmonary mortality in women. Epidemiology 2006; 17:545-51.

[8]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 2002; 360:1203-9.

[9]Finkelstein MM, Jerrett M, Sears MR Traffic air pollution and mortality rate advancement periods. Am J Epidemiol 2004; 160:173-7.

[10]Jerrett M, Arain A, Kanaroglou P, Beckerman B, Potoglou D, Sahsuvaroglu T, Morrison J, Giovis C A review and evaluation of intraurban air pollution exposure models. J Expo Anal Environ Epidemiol 2005; 15:185-204.

[11]Nerriere E, Zmirou-Navier D, Blanchard O, Momas I, Ladner J, Le Moullec Y, Personnaz MB, Lameloise P, Delmas V, Target A, Desqueyroux H Can we use fixed ambient air monitors to estimate population long-term exposure to air pollutants? The case of spatial variability in the Genotox ER study. Environ Res 2005; 97:32-42.

[12]Sarnat SE, Coull BA, Schwartz J, Gold DR, Suh HH Factors affecting the association between ambient concentrations and personal exposures to particles and gases. Environ Health Perspect 2006; 114:649-54.

[13]Sorensen M, Loft S, Andersen HV, Raaschou-Nielsen O, Skovgaard LT, Knudsen LE, Nielsen IV, Hertel O Personal exposure to PM2.5, black smoke and NO2 in Copenhagen: relationship to bedroom and outdoor concentrations covering seasonal variation. J Expos Anal Environ Epidemiol 2005:1-10.

[14]Oglesby L, Kunzli N, Roosli M, Braun-Fahrlander C, Mathys P, Stern W, Jantunen M, Kousa A Validity of ambient levels of fine particles as surrogate for personal exposure to outdoor air pollution--results of the European EXPOLIS-EAS Study (Swiss Center Basel). J Air Waste Manag Assoc 2000; 50:1251-61.

[15]Rijnders E, Janssen NA, van Vliet PH, Brunekreef B Personal and outdoor nitrogen dioxide concentrations in relation to degree of urbanization and traffic density. Environ Health Perspect 2001; 109 Suppl 3:411-417.

[16]Van Roosbroeck S, Jacobs J, Janssen N, Oldenwening M, Hoek G, Brunekreef B Long-term personal exposure to PM2.5, Soot and NOx in children attending schools located near busy roads, a validation study. Accepted for publication by Atmospheric Environment 2006.

[17]Rosner B, Willett WC, Spiegelman D Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. Stat Med 1989; 8:1051-69; discussion 1071-3.

[18]Rosner B, Spiegelman D, Willett WC Correction of logistic regression relative risk estimates and confidence intervals for measurement error: the case of multiple covariates measured with error. Am J Epidemiol 1990; 132:734-45.

[19]Horick N, Weller E, Milton DK, Gold DR, Li R, Spiegelman D Home endotoxin exposure and wheeze in infants: correction for bias due to exposure measurement error. Environ Health Perspect 2006; 114:135-40.

[20]ISAAC. Phase II Modules of the International Study of Asthma and Allergies in Childhood (ISAAC). Münster, Germany: University of Münster, 1998.

[21]Janssen N, Vliet PHNv, Aarts F, Harssema H, Brunekreef B Assessment of exposure to traffic related air pollution of children attending schools near motorways. Atmos Environ 2001; 35:3875-3884.

[22]Van Roosbroeck S, Wichmann J, Janssen NA, Hoek G, van Wijnen JH, Lebret E, Brunekreef B Long-term personal exposure to traffic-related air pollution among school children, a validation study. Sci Total Environ 2006; 368:565-573.

[23]Kuha J Corrections for exposure measurement error in logistic regression models with an application to nutritional data. Stat Med 1994; 13:1135-48.

[24]Durrleman S, Simon R Flexible regression models with cubic splines. Statistics in Medicine 1989; 8:551-561.

[25]Govindarajulu US, Spiegelman D, Thurston SW, Eisen EA Comparing smoothing techniques for modeling exposure-response curves in Cox models. Statistics in Medicine 2007; In Press.

[26]Schmid CH, Rosner B A Bayesian approach to logistic regression models having measurement error following a mixture distribution. Stat Med 1993; 12:1141-53.

[27]Spiegelman D, Rosner B, Logan R Estimation and inference for logistic regression with covariate misclassification and measurement error in main study/validation study designs. Journal of the American Statistical Association 2000; 95:51-61.

[28]Spiegelman D, Carroll RJ, Kipnis V Efficient regression calibration for logistic regression in main study/internal validation study designs with an imperfect reference instrument. Stat Med 2001; 20:139-160.

[29]Li R, Weller E, Dockery DW, Neas LM, Spiegelman D Association of indoor nitrogen dioxide with respiratory symptoms in children: application of measurement error correction techniques to utilize data from multiple surrogates. J Expo Sci Environ Epidemiol 2006; 16:342-50.

[30]Mills NL, Tornqvist H, Robinson SD, Gonzalez M, Darnley K, MacNee W, Boon NA, Donaldson K, Blomberg A, Sandstrom T, Newby DE Diesel exhaust inhalation causes vascular dysfunction and impaired endogenous fibrinolysis. Circulation 2005; 112:3930-6.

[31]Nordenhall C, Pourazar J, Ledin MC, Levin JO, Sandstrom T, Adelroth E Diesel exhaust enhances airway responsiveness in asthmatic subjects. Eur Respir J 2001; 17:909-15.

[32]Salvi S, Blomberg A, Rudell B, Kelly F, Sandstrom T, Holgate ST, Frew A Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers. Am J Respir Crit Care Med 1999; 159:702-9.

[33]Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, Cohen A Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environ Health Perspect 2000; 108:419-26.

Chapter six

General Discussion

Main findings

In the past decade a large number of epidemiological studies have evaluated associations between long-term average air pollution concentrations related to motorized traffic and morbidity and mortality. These studies used indicators of exposure such as residential traffic intensity, distance to major roads, or modeled or measured outdoor air pollution concentrations near the home or school. At the beginning of the current study, the validity of these exposure indicators was largely unknown.

We therefore performed an extensive monitoring program of personal exposure to traffic-related air pollutants to evaluate the validity of exposure indicators commonly used in epidemiological studies on the long-term effect of traffic-related air pollution. We selected children and older adults as population groups, as health effects related to traffic-related air pollution have been reported for these population groups. Different population groups were included because due to differences in time activity patterns, relationships between outdoor exposure indicators and personal exposure may differ. Concurrent 48-hour outdoor and personal exposure to $PM_{2.5}$, soot and NO_x was repeatedly monitored in participants who were living in homes, or attending schools exposed to different levels of traffic-related air pollution.

First we documented that personal 48-hour monitoring of particulate matter with four repeated measurements using an active PM and a passive NO_x sampling device was feasible in a population of 9 to 12 year old school children. Next, we showed that personal exposure to soot, was significantly higher for children living within 75 m of busy roads (10 000 vehicles per 24 h or more), despite the fact that all participating children spent a substantial amount of time at the same school, located away from busy roads. This finding supports the use of 'living near a busy road' as a measure of exposure in epidemiological studies on the effects of the traffic-related air pollutant soot. Indoor and personal exposure to NO, NO_2 and NO_x was not increased for children living near a busy road, in spite of significant differences in outdoor NO and NO_x concentrations measured in front of homes located near and away from busy roads.

In a second field study, personal exposure to soot and NO_x was increased for children attending a school within 100 meter of a freeway with a traffic intensity of 97 800 vehicles per 24 h compared to children attending a nearby urban background school. Children attending a school within 100 meter of a ring road with a traffic intensity of 45 200 vehicles per 24 h did not show increased personal exposure compared to children attending the urban background school. The larger

distance of the school to the road, lower traffic intensity and presence of obstacles between the school and the road probably contributed to this lack of contrast. The study showed that the 'school's proximity to a freeway' can be used as a valid estimate of exposure in epidemiological studies in children on the effects of the traffic-related air pollutants soot and NO_x but only for freeways with high enough density of traffic.

A third study was conducted among older adults. Personal soot exposure of older adults living at major roads (10 000 vehicles per 24 h or more) was increased compared to adults living at quiet roads. No contrast was found for NO_2, NO_x and $PM_{2.5}$. Participation in traffic and spending time outdoors both significantly contributed to personal exposure to soot and $PM_{2.5}$ but not NO_x.

Applying a measurement error adjustment using data on personal and outdoor soot concentrations from the second study and data on personal and outdoor NO_2 from previous research, we found two to three times stronger associations between respiratory symptoms and exposure to soot and NO_2 in school children. This finding suggests that considerable bias may occur when using school outdoor levels of the air pollutants used as indicators for the personal exposure of children to these air pollutants.

Effect of measurement error in exposure

Epidemiological studies linking environmental exposure with impaired health have generally used surrogates of exposure like a single measurement instead of the average of several repeated measurements, a measurement in the environment instead of a personal measurement, an individual's affiliation to a group instead of its individual observation, etc. Valid measurements of exposure are essential to epidemiological research. The extent to which these surrogate exposures differ from the 'true' level of exposure is called exposure measurement error.[1,2] When exposure is assessed inaccurately and/or imprecisely, estimates of the association between exposure and health effect can be biased. The type of measurement error has major implications for the effects of the error. Errors can be differential or non-differential; random or systematic; classical or Berkson type.[1,2] Classical measurement error occurs when exposure is measured and repeated measurements vary around the 'true' value. This usually results in bias towards the null, that is effect estimates underestimate the true effect estimate.[1,2] The Berkson type error arises when all individuals belonging to a group are assigned the group's average. Berkson error usually causes little to no bias of the exposure response slope, but it does decrease precision.[1,2] In practice, exposure measurement often has both classical and Berkson components, as we believe

is the case in the current analysis, although one usually predominates.[2] We discuss non-differential misclassification in the three performed exposure studies, as this is the main problem in epidemiological studies of traffic-related air pollution using objective exposure indicators. There is a series of studies that have evaluated the association between self-reported traffic intensity at the street of residence and respiratory symptoms from the same questionnaire.[3,4] In these studies differential misclassification of exposure may occur, since subjects with asthma may more readily report their home as being highly exposed to traffic than healthy subjects. All three field studies contain classical error, using traffic intensity and distance to road of every participant's residence as surrogates. The current work also focused on the effect of exposure measurement error that had occurred in a previously conducted study that associated annual average outdoor air pollution concentrations measured at the school with health in school children living close to freeways.[5] The exposure estimation in this study is likely to be subject to both Berkson and classical measurement error. Error of the classical type was introduced because the measured school outdoor level was likely to vary around the true outdoor school level, and in addition, error of the Berkson type was introduced because a school's average level was assigned to each participating child attending that school.

Recently, correction strategies for measurement error of both classical- and Berkson-type have been introduced[6-8] and some applications of measurement error correction on studies linking air pollution with health have been published.[9-11] Zeger[11] has argued that for time series studies of outdoor air pollution, the error of using measured outdoor air pollution at a fixed site as a proxy for individual personal exposure, can be divided into the error in measuring the true outdoor concentration; the error of using the true outdoor concentration for the group average personal exposure and finally the difference between the individual exposure and the group-average personal exposure. He shows that especially the second component is important in determining attenuation of concentration – response functions. The third component is mostly Berkson error. In occupational epidemiology, there is a systematic discussion of the effect of grouped versus individual exposure assignment.[12-14] In that field, the standard is to perform personal exposure measurements as stationary measurements generally do not reflect true exposures well.

The strategy used to correct for exposure measurement error on the current data was a calibration regression.[7,8,15] Using school outdoor measurements of air pollutants as a surrogate for personal measurements resulted in strongly reduced effect estimates, as expected from the relatively low correlation between personal and school ambient pollutant concentrations. This calls for more awareness for these and other aspects of errors in exposure characterization in

studies on long-term effects of traffic-related air pollution. In the next sections, the errors in exposure indicators evaluated in the current study are discussed in more detail.

Residential address traffic intensity

Living near or at a busy road was shown to be significantly associated with personal exposure to the traffic-related pollutant soot in the first and third study. Comparing children living within 75 meter of a busy road, with traffic intensity of 10 000 vehicles per 24 h or more, with children living away from busy roads in Amsterdam, resulted in a 35% (95% CI, 9-68%) difference in personal exposure to soot. Adults living at busy roads in Utrecht were found to have an 18% (95% CI, 4-35%) higher personal exposure to soot when compared to adults living away from busy roads. In the second study, however, no increased personal soot exposure of children was found for children living near high-traffic residential addresses: estimate -8% (95% CI, -22-8%).
The differences between the studies may be due to the study design and the studied population. Only the third study was specifically designed to assess residential traffic intensity as the main indicator, resulting in e.g. simultaneous measurements at busy and quiet roads and a nearly balanced number of subjects living at busy and quiet roads. In the first and second study only a small number of children lived near busy streets (5 of 14 children in the first study; 10 of 54 children in the second study). Most of these children did not live *in* busy streets but *near* busy streets. A further difference between the first and second study is that the population was more homogenous in the first study as they all attended one school, whereas they attended four schools in the larger Utrecht area in the second study. Finally, the larger amount of time adults spent at home than the children may have contributed.
Janssen et al.[16] presented results of personal monitoring of PM_{10} in non-smoking adults living in Amsterdam. They showed higher personal levels of PM_{10} in adults living along a busy road when compared to subjects living away from busy roads. Within the framework of the previous study, a re-analysis of the collected PM_{10} filters was performed.[17] We believe that it is suitable to compare these results to our personal soot results, since determining absorption coefficients based on PM_{10} or $PM_{2.5}$ filters is more or less equivalent, as the blackness of the filter is mainly due to the smaller fraction of particles.[18,19] The variation of personal PM_{10} absorption coefficients (or soot) was significantly explained by the outdoor soot level, the type of road at which the participants lived, the time spent in traffic and time spent outdoors.[17] They concluded that living near a busy road and the ambient background levels were the dominant predictors of the personal

exposure.[17] An increase in personal soot of 29% was found when comparing the group of adults living near busy roads with the group living away busy roads. Similarly, the ULTRA study showed that having a major street within 100 meter of the home location was found to be a major determinant of personal levels of soot (here measured as $PM_{2.5}$ absorption coefficients).[20] Adults living near a busy street in Amsterdam and Helsinki had a 22% and 37%, respectively, increased personal exposure to soot. In the current study, adults living at busy roads in Utrecht were found to have an 18% higher personal exposure to soot when compared to adults living away from busy roads and also, a significant contribution to the variation in personal exposure to soot and $PM_{2.5}$ from time spent in traffic and outdoors was seen. Comparing children living within 75 m of a busy road with traffic intensity of 10 000 vehicles per 24 h with children living away from busy roads in Amsterdam, resulted in a 35% difference in personal exposure to soot. These increases in personal exposure to soot were in line with previous studies. Previous studies, however, were set up as validation studies for time series studies, and therefore include limited variability of traffic related characteristics and non-simultaneous measurements at busy and quiet roads.

Traffic intensity at home may fail to represent the true exposure because:

a. It does not predict outdoor air pollution at the home adequately
b. Outdoor air pollution near the home is not well related to indoor air pollution
c. People spend a certain fraction of time elsewhere

In general, clear differences in outdoor air pollutant concentrations were seen between locations with different proximity to traffic. For NO_x the outdoor contrast ranged from 27% between homes near and away from busy roads in Amsterdam, 35% between homes at or away from busy roads in Utrecht, to 52% between a school near a freeway compared to a school at a background location. For NO_2 the contrast was less distinct (11% to 43%) and for NO more distinct (75% to 127%). The differences in outdoor soot were about 70%, but differences were negligible for outdoor $PM_{2.5}$ (1% to 14%).

Assessing the variability of ambient pollutant concentrations within one city is receiving more and more interest[21-25] and differences in outdoor levels of traffic-related air pollutants on a city district scale or between busy and quiet roads have been demonstrated repeatedly.[18,21,26-28] Moreover, two exposure studies have shown that variation of traffic-related pollutants within cities measured close to busy roads may exceed the variation between cities.[29,30] In two Dutch cities outdoor $PM_{2.5}$ and PM_{10} were found to be significantly higher (30%) near busy roads as compared to

background locations, and for outdoor soot the difference was 160%.[28] Other studies have shown comparable contrasts in PM up to about 30% and even stronger contrasts for soot and NO_2 when comparing heavily trafficked locations with background locations.[18,19,31] In the framework of the multicenter study relating traffic related air pollution with childhood asthma (TRAPCA), measurements of PM_{10}, $PM_{2.5}$ and the reflectance of $PM_{2.5}$ filters in outdoor air at 40 representative sites in each study area (Munich, Stockholm and Amsterdam) were performed.[19] Clear differences between more and less heavily trafficked sites within one city were found. Concentrations of elemental carbon at the heavily trafficked urban sites were on average 43%-84% higher than those at urban background sites; for soot the difference varied between 26%-76%; and for $PM_{2.5}$ mass the difference was smaller (8%-35%).[19] In Amsterdam, outdoor concentrations of PM_{10} and $PM_{2.5}$ mass were 15 to 20% higher at homes located at heavily trafficked streets compared to those in low traffic areas, while soot concentrations were about 100% higher.[18] A very recent study by Naess et al.[32] estimated air pollutant concentrations in 470 neighbourhoods within one city (Oslo) and provided detailed exposure contrasts in NO_2 (range 2-73 ug/m^3), PM_{10} (range 7-30 ug/m^3) and $PM_{2.5}$ (range 7-22 ug/m^3). The rather smaller contrasts within one city in outdoor $PM_{2.5}$ in comparison with contrasts in soot or NO_x found in our study are thus in line with other studies.[18,19,28,31-34]

Outdoor levels of $PM_{2.5}$ and the other pollutants measured at the ring road school in the second monitoring study were not increased compared to the background school, even though the ring road school was located within 88 m of a road with 45 200 vehicles per 24 h. This is likely due to the lower traffic intensity (compared to the freeway school that was studied), and in particular the lower truck traffic intensity, and the presence of buildings between sampling point and pollutant source. A clear suggestion for GIS based studies is thus to include small distances and as much on-site information as possible in order to assess exposure as accurately as possible.

Personal monitoring takes into account complex dynamics involved in the timeframe and location of the exposures, like diurnal patterns in traffic emissions, home and school location, penetration rates of outdoor to indoor environment, architectural situation of the accommodation and surroundings, time-activity patterns and commuting activities. In spite of the fact that these complexities are not captured fully by any of the indicator variables, the increased personal exposures to soot in the first and third study for subjects living near a busy road do suggest that these indicator variables predict differences in personal exposure to some extent.

School outdoor air pollution concentrations

The differences in outdoor air concentrations for NO_2, NO, soot, and to a lesser extent $PM_{2.5}$ between locations with different proximity to traffic that were generally found, were not reflected to the same extent in differences in personal exposure in the current study. Reduced contrasts in personal exposure were seen for soot and NO_x, and no contrast was seen for the other pollutants, suggesting that outdoor concentrations for these other pollutants were no proper surrogates for personal concentrations in the contexts that we studied. A first point we need to address here is to what extent the outdoor levels are representative for the indoor levels. As most people spend approximately 85% to 90% of their time indoors, it is generally accepted that a large proportion of the personal exposure to outdoor air occurs in the indoor environment. In the current study only limited indoor sampling was performed. In the Amsterdam children's study, the slightly elevated indoor levels of NO, NO_2 and NO_x (no indoor $PM_{2.5}$ or soot measurements were assessed) correspond to the small increases in personal exposure. In the Utrecht children's study school indoor NO_2 and NO was measured. No elevated indoor levels were found in the ring road school, which corresponds to the lack in outdoor contrast. For the freeway school only the NO_x levels were elevated in the indoor environment. The penetration rate of outdoor particles to the indoor environment and the effect of indoor sources are important issues here. Best known indoor sources of particulate air pollution are smoking, cooking, candle burning, woodstoves, dusting, vacuum cleaning.[35,36] In consequence, participants in the current research were asked about these sources in a questionnaire that accompanied every 48 h measurement. Next, we need to examine how valid these indoor concentrations are for the personal level. Indoor pollutants measured at school or home over long periods may to some extent capture time-dynamics in components of long-term exposure to the traffic-related exposure, however a major lack remains that the effect of time-activity patterns on the individual personal level is not taken into account.

We are aware of only one other study that was specifically designed to assess the validity of long-term average exposure to NO_2 at the school and included repeated personal exposure measurements and schools located in areas near freeways with different traffic intensities were included in order to be able to study a meaningful contrast in average ambient air pollution.[37] Repeated personal NO_2 measurements were conducted in children from three schools near freeways and the childrens' average personal NO_2 exposure were found to be significantly different between children attending schools near freeways with varying traffic intensities.[37] The

difference was 8.2 ug/m^3 (46% increase) in personal exposure to NO_2 between children from the school with the highest traffic intensity (349 m from freeway with traffic intensity of 169 637 vehicles per 24 h) and children from the school with the lowest traffic intensity (62 m from freeway with traffic intensity of 45 129 vehicles per 24 h).

In our study personal exposure to NO_2 was elevated in both study designs involving children as participants, yet only slightly, and the differences never achieved statistical significance. The comparison with the Rijnders study should be made with caution however. The larger sample size (n=110) and duration of the monitoring time (one-week measurements) used in the Rijnders study increased the power of the study as compared to the current study. Next, the study locations were selected according to different criteria compared to our school design study. All schools were located within 400 m from a freeway with traffic intensities varying from 169 637 vehicles per 24 h, classified as very busy school location, to 45 129 vehicles per 24 h, classified as not busy school location.[37] In contrast, in our study the schools categorized as a busy road schools were located within 100 m of a major freeway or ring road with much lower traffic intensity of 45 000 or 97 800 vehicles per 24 h, respectively, and the schools categorized as 'not busy' or background schools were located further away than 250 m from any type of major urban road.

Time spent in traffic

In the current study a significant contribution to the variation in personal exposure to soot and $PM_{2.5}$ from time spent in traffic and outdoors was seen. The average time spent in traffic and outdoors in the current study on adults living in Utrecht was 0.5 h per 48 h and 2.8 h per 48 h, respectively. Spending time in traffic was equivalent to spending time in a car in this context. When spending 1 hour in traffic or outdoors, the personal exposure to $PM_{2.5}$ was increased with 28% and 4% respectively. The increases in personal exposure to soot were 12% when spending 1 hour in traffic, and 3% when spending one hour outdoors. The increased personal exposure to soot (10%) with a 10 000 vehicles per 24 h-increment we found in our study is thus more or less equivalent to spending 1 hour in traffic (12%).

The effects of spending time in traffic and spending time outdoors we found in our study confirm results from the ULTRA study, where average time spent in traffic and outdoors was 0.2 h and 1.3 h per day, respectively, in Amsterdam and 0.4 h and 1.1 h per day, respectively, in Helsinki.[38] Time spent in traffic was in both cities strongly associated with personal soot concentrations.

Time spent outdoors was also positively associated, yet only borderline significant.[38] In a different study, personal PM_{10} exposure was collected among adult participants living near and away from busy roads in Amsterdam.[17] The variation of personal soot (PM_{10} light absorption coefficients) was significantly explained by the time spent in traffic and time spent outdoors, next to the outdoor soot and the type of road at which the participants lived.[17]

Time spent in traffic was reflected in the personal exposure in the current study, despite that it is such a small percentage of the 48 h measurement period. Since transport micro environments are relatively more heavily polluted than others and the fact that most journeys are made during rush hours, when the increased volume of traffic results in high ambient pollution levels, these short exposures can contribute disproportionately to the total exposure. The importance of taking into account time-activity patterns including commuting, apart from both local spatial and temporal variability, in exposure assessment has been highlighted before.[39-41] Gulliver and Briggs[39] have developed GIS-based systems to model human journey-time exposures to traffic-related air pollution (PM_{10}).

It should be emphasized, however, that the current study was not designed to look at the effect of time spent in traffic. The health effects of spending time in traffic have rarely been studied,[42,43] and more research on this would be of great value, given the impact of it on the personal exposure to traffic-related air pollution.

Limitations

An assumption in all studies is that the monitored personal exposure is "the golden standard" and reflects the true exposure. This assumption may be more valid for soot than for NO_2. First, NO_2 is generally not considered to be the main causal agent from traffic-related air pollution, but probably more a convenient indicator of the mixture of traffic pollutants. To the extent that dispersion / chemical reactions from source to receptor locations differ for NO_2 and the causal agent(s), measured concentrations may not be an improvement compared to the simple traffic indicators. There is more evidence suggesting that soot is related to health effects due to soot exposure alone.[44-46] Secondly, we are actually interested in personal exposure to ambient-generated air pollution. We measured personal exposure that may be affected by indoor sources as well. Indoor sources (such as gas cooking) are probably more important in determining personal NO_2 exposure than personal soot exposure. While we adjusted for indoor sources in the measurement error model, residual impacts cannot be excluded. Indoor sources are less

important for soot, as evidenced by the smaller change in the multiple correlations after adding indoor source indicators to the surrogate exposure in the measurement error model.

Obtaining long-term personal exposure to traffic-related air pollution is demanding. Especially the active monitoring of particulate matter with relatively heavy and noisy pumps is labour-intensive for participants and research staff has to deal with time-consuming sampling setup and analysis. The passive sampling for NO_x using small badges with precoated pads is a more workable strategy. Large-scale studies are usually forced to use relatively easily obtained surrogates of exposure like outdoor monitors with the eye on the logistics of the field work and the financial burden. Personal monitoring, however, better reflects the dynamics of time-activity patterns and penetration rates of outdoor to indoor environment. To provide more accurate and precise health effect estimates the large-scale studies should be combined with personal monitoring to include information on the association between personal and surrogate exposure so that the exposure response relationship between long-term exposure and health can be re-evaluated and adjusted for exposure measurement error.

Another point for discussion is the relatively small number of repeated measurements, and to what extent the average is representative for the long-term average. In consideration of the feasibility of sampling for the participant, the number of repeated measurements needs to be limited. However, some repetition of the personal exposure measurement over time is desirable to cover the variability due to changes in source intensities, life style factors and meteorological conditions. Also, we argue that perhaps not the absolute level of average personal exposure, but merely the contrast in personal exposure between groups with different proximity to traffic is the relevant measure here.

The conclusions from our studies cannot readily be applied in other population groups or settings, if important determinants such as time activity patterns, housing stock and air exchange rates (affecting penetration of outdoor air pollution) differ substantially from our validation studies. The current study showed for example consistent effects of traffic participation for adults, but not for children. In the adults study, the contrast for soot exposure was larger for those spending more time in their own home.

Conclusions and Recommendations

Differences in outdoor levels of soot and differences in proximity to traffic were reflected in differences in personal soot concentrations. We therefore conclude that outdoor concentrations of soot and living near a busy road or attending a school near a busy road, are valid proxy measures for personal exposure to soot. Time spent in traffic, time spent outdoors, burning candles and exposure to Environmental Tobacco Smoke were found to be important determinants of personal soot concentrations.

Our study was conducted in a small number of specific Dutch settings, and results cannot be easily extrapolated to other populations or settings. Repetition of this work in such other settings is recommended as for example composition of traffic can be different, topography and/or meteorology may be different, and time-activity patterns may be different. It is therefore important to validate the use of outdoor pollutants and exposure indicators like distance to road and traffic intensity in different populations.

References

[1]Armstrong BK, White E, Saracci R. Principles of Exposure Measurement in Epidemiology. Oxford:Oxford University Press, 1992.

[2]Armstrong BG.1998 Effect of measurement error on epidemiological studies of environmental and occupational exposures. Occup.Environ Med. 55:651-656.

[3]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.1998 Road traffic and adverse respiratory effects in children. SIDRIA Collaborative Group. Occup Environ Med 55:771-8.

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

[5]Janssen N, Brunekreef B, van Vliet P, Aarts F, Meliefste K, Harssema H, Fischer P.2003 The relationship between air pollution from heavy traffic and allergic sensitization, bronchial hyperresponsiveness, and respiratory symptoms in Dutch schoolchildren. Environ Health Perspect 111:1512-8.

[6]Heid IM, Kuchenhoff H, Miles J, Kreienbrock L, Wichmann HE.2004 Two dimensions of measurement error: classical and Berkson error in residential radon exposure assessment. J Expo Anal Environ Epidemiol 14:365-77.

[7]Spiegelman D, Carroll RJ, Kipnis V.2001 Efficient regression calibration for logistic regression in main study/internal validation study designs with an imperfect reference instrument. Stat Med 20:139-160.

[8]Weller EA, Milton DK, Eisen EA, Spiegelman D.2005 Regression calibration for logistic regression with multiple surrogates for one exposure (submitted for publication).

[9]Dominici F, Zeger SL, Samet JM.2000 A measurement error model for time-series studies of air pollution and mortality. Biostatistics 1:157-75.

[10]Li R, Weller E, Dockery DW, Neas LM, Spiegelman D.2006 Association of indoor nitrogen dioxide with respiratory symptoms in children: application of measurement error correction techniques to utilize data from multiple surrogates. J Expo Sci Environ Epidemiol 16:342-50.

[11]Zeger SL, Thomas D, Dominici F, Samet JM, Schwartz J, Dockery D, Cohen A.2000 Exposure measurement error in time-series studies of air pollution: concepts and consequences. Environ Health Perspect 108:419-26.

[12]Seixas NS, Sheppard L.1996 Maximizing accuracy and precision using individual and grouped exposure assessments. Scand J Work Environ Health 22:94-101.

[13]Preller L, Kromhout H, Heederik D, Tielen MJ.1995 Modeling long-term average exposure in occupational exposure-response analysis. Scand J Work Environ Health 21:504-12.

[14]Tielemans E, Kupper LL, Kromhout H, Heederik D, Houba R.1998 Individual-based and group-based occupational exposure assessment: some equations to evaluate different strategies. Ann Occup Hyg 42:115-9.

[15]Rosner B, Willett WC, Spiegelman D.1989 Correction of logistic regression relative risk estimates and confidence intervals for systematic within-person measurement error. Stat Med 8:1051-69; discussion 1071-3.

[16]Janssen NA, Hoek G, Brunekreef B, Harssema H, Mensink I, Zuidhof A.1998 Personal sampling of particles in adults: relation among personal, indoor, and outdoor air concentrations. Am J Epidemiol 147:537-47.

[17]Wichmann J, Janssen NAH, van der Zee S, Brunekreef B.2005 Traffic-related differences in indoor and personal absorption coefficients measurements in Amsterdam, The Netherlands. Atmos Environ 39:7384-7392.

[18]Fischer P, Hoek G, Reeuwijk Hv, DJ B, Lebret E, Wijnen Jv, Kingham S, Elliot P.2000 Traffic-related differences in outdoor and indoor concentrations of particles and volatile organic compounds in Amsterdam. Atmos Environ 34:3713-3722.

[19]Cyrys J, Heinrich J, Hoek G, Meliefste K, Lewne M, Gehring U, Bellander T, Fischer P, van Vliet P, Brauer M, Wichmann HE, Brunekreef B.2003 Comparison between different traffic-related particle indicators: elemental carbon (EC), PM2.5 mass, and absorbance. J Expo Anal Environ Epidemiol 13:134-43.

[20]Lanki T, Ahokas A, Alm S, Janssen NA, Hoek G, De Hartog JJ, Brunekreef B, Pekkanen J.2006 Determinants of personal and indoor PM(2.5) and absorbance among elderly subjects with coronary heart disease. J Expo Sci Environ Epidemiol. (doi: 10.1038/sj.jes.7500470)

[21]Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U, Heinrich J, Cyrys J, Bellander T, Lewne M, Brunekreef B.2003 Estimating long-term average particulate air pollution concentrations: application of traffic indicators and geographic information systems. Epidemiology 14:228-39.

[22]Brunekreef B, Holgate ST.2002 Air pollution and health. Lancet 360:1233-42.

[23]McConnell R, Berhane K, Yao L, Jerrett M, Lurmann F, Gilliland F, Kunzli N, Gauderman J, Avol E, Thomas D, Peters J.2006 Traffic, susceptibility, and childhood asthma. Environ Health Perspect 114:766-72.

[24]Gauderman WJ, Vora H, McConnell R, Berhane K, Gilliland F, Thomas D, Lurmann F, Avol E, Kunzli N, Jerrett M, Peters J.2007 Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. The Lancet DOI:10.1016/S0140-6736(07)60037-3.

[25]Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD.2007 Long-term exposure to air pollution and incidence of cardiovascular events in women. N Engl J Med 356:447-58.

[26]Hoek G, Brunekreef B, Goldbohm S, Fischer P, van den Brandt PA.2002 Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study. Lancet 360:1203-9.

[27]Roorda-Knape M, Janssen N, Hartog Jd, Vliet Pv, Harssema H, Brunekreef B.1998 Air pollution from traffic in city districts near major motorways. Atmos Environ 32:1921-1930.

[28]Janssen N, van Mansom D, van der Jagt K, Harssema H, Hoek G.1997 Mass concentration and elemental composition of airborne particulate matter at street and background locations. Atmos Environ 31:1185-1193.

[29]Briggs DJ, de Hoogh C, Gulliver J, Wills J, Elliott P, Kingham S, Smallbone K.2000 A regression-based method for mapping traffic-related air pollution: application and testing in four contrasting urban environments. The Science of The Total Environment 253:151-167.

[30]Zhu Y, Hinds WC, Kim S, Shen S, Sioutas C.2002 Study of ultrafine particles near a major highway with heavy-duty diesel traffic. Atmospheric Environment 36:4323-4335.

[31]Hoek G, Meliefste K, Cyrys J, Lewné M, Bellander T, Brauer M, Fischer P, Gehring U, Heinrich J, Van Vliet P, Brunekreef B.2002 Spatial variability of fine particle concentrations in three European areas. Atmos Environ 36:4077-4088.

[32]Naess O, Nafstad P, Aamodt G, Claussen B, Rosland P.2006 Relation between Concentration of Air Pollution and Cause-Specific Mortality: Four-Year Exposures to Nitrogen Dioxide and Particulate Matter Pollutants in 470 Neighborhoods in Oslo, Norway. Am J Epidemiol.

[33]Hochadel M, Heinrich J, Gehring U, Morgenstern V, Kuhlbusch T, Link E, Wichmann HE, Krämer U.2006 Predicting long-term average concentrations of traffic-related air pollutants using GIS-based information. Atmos Environ 40:542-553.

[34]Lena TS, Ochieng V, Carter M, Holguin-Veras J, Kinney PL.2002 Elemental carbon and PM(2.5)levels in an urban community heavily impacted by truck traffic. Environ Health Perspect 110:1009-15.

[35]Ozkaynak H, Xue J, Spengler J, Wallace L, Pellizzari E, Jenkins P.1996 Personal exposure to airborne particles and metals: results from the Particle TEAM study in Riverside, California. J Expo Anal Environ Epidemiol 6:57-78.

[36]Wallace L.1996 Indoor particles: a review. J Air Waste Manag Assoc 46:98-126.

[37]Rijnders E, Janssen NA, van Vliet PH, Brunekreef B.2001 Personal and outdoor nitrogen dioxide concentrations in relation to degree of urbanization and traffic density. Environ Health Perspect 109 Suppl 3:411-417.

[38]Brunekreef B, Janssen NA, de Hartog JJ, Oldenwening M, Meliefste K, Hoek G, Lanki T, Timonen KL, Vallius M, Pekkanen J, Van Grieken R.2005 Personal, indoor, and outdoor exposures to PM2.5 and its components for groups of cardiovascular patients in Amsterdam and Helsinki. Res Rep Health Eff Inst:1-70; discussion 71-9.

[39]Gulliver J, Briggs DJ.2005 Time-space modeling of journey-time exposure to traffic-related air pollution using GIS. Environ Res 97:10-25.

[40]Oglesby L, Kunzli N, Roosli M, Braun-Fahrlander C, Mathys P, Stern W, Jantunen M, Kousa A.2000 Validity of ambient levels of fine particles as surrogate for personal exposure to outdoor air pollution--results of the European EXPOLIS-EAS Study (Swiss Center Basel). J Air Waste Manag Assoc 50:1251-61.

[41]Kunzli N, Tager IB.2000 Long-term health effects of particulate and other ambient air pollution: research can progress faster if we want it to. Environ Health Perspect 108:915-8.

[42]Peters A, von Klot S, Heier M, Trentinaglia I, Hormann A, Wichmann HE, Lowel H.2004 Exposure to traffic and the onset of myocardial infarction. N Engl J Med 351:1721-30.

[43]Adar SD, Gold DR, Coull BA, Schwartz J, Stone PH, Suh H.2007 Focused exposures to airborne traffic particles and heart rate variability in the elderly. Epidemiology 18:95-103.

[44]Mills NL, Tornqvist H, Robinson SD, Gonzalez M, Darnley K, MacNee W, Boon NA, Donaldson K, Blomberg A, Sandstrom T, Newby DE.2005 Diesel exhaust inhalation causes vascular dysfunction and impaired endogenous fibrinolysis. Circulation 112:3930-6.

[45]Nordenhall C, Pourazar J, Ledin MC, Levin JO, Sandstrom T, Adelroth E.2001 Diesel exhaust enhances airway responsiveness in asthmatic subjects. Eur Respir J 17:909-15.

[46]Salvi S, Blomberg A, Rudell B, Kelly F, Sandstrom T, Holgate ST, Frew A.1999 Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers. Am J Respir Crit Care Med 159:702-9.

Chapter seven

Summary

Several recent studies have suggested associations between long-term exposure to traffic-related air pollution and cardiorespiratory health. In general, most of these studies used indicators, such as traffic density on the street of residence, distance of the home address to busy roads, or estimated outdoor concentrations of traffic-related air pollutants, as a measure of exposure. Very little information is available about the validity of these indicators of exposure as an estimate of personal exposure to traffic-related air pollution. The objective of this thesis was to investigate the validity of using outdoor concentrations and/or traffic-related indicator exposure variables as a measure for exposure assessment in epidemiological studies on the long-term effect of traffic-related air pollution. Therefore, outdoor concentrations of and personal exposures to the traffic-related air pollutants $PM_{2.5}$, soot and NO_x were concurrently and repeatedly monitored in locations with varying degree of traffic intensity in populations of both children and elderly adults.

The feasibility of monitoring personal particulate matter was tested (**Chapter 2**), and we observed that repeating the number of measurements up to four times was workable in a population of 14 school children aged 9 to 12 year, since the compliance rate was 100%. Further, we investigated whether differences in outdoor levels of air pollutants were reflected in differences in personal exposure in a group of children who all attended the same school located at an urban background location in Amsterdam, The Netherlands, but lived at streets that varied in traffic intensity. In this context, an 'urban background' location is defined as a location away from the immediate influence of road traffic or other local sources, in practice at distances of at least 75 m away from these. We conducted concurrent personal and school 48-hour soot and NO_x measurements, and in addition, 48-hour indoor and outdoor NO_x measurements were performed at the home. We showed that personal exposure to soot was significantly higher (35%) for children living within 75 m of busy roads (10 000 vehicles per 24 h or more), despite the fact that all participating children spent a substantial amount of time at the same school, located away from busy roads. This finding supports the use of 'living near a busy road' as a measure of exposure in epidemiological studies on the effects of the traffic-related air pollutant soot. Indoor and personal exposure to NO, NO_2 and NO_x was not increased for children living near a busy road, in spite of significant differences in outdoor NO (78% increase) and NO_x (27% increase) concentrations measured in front of the home.

In **Chapter 3** we described our investigation into the role of the school location in the personal exposure of schoolchildren. Four schools in Utrecht, The Netherlands, with different proximities to

roads with varying traffic densities were included in the study. Two schools were located within 100 meter of a major road, one ring road with a traffic intensity of 45 200 vehicles per 24 h and one freeway with a traffic intensity of 97 800 vehicles per 24 h. The other two schools were located at background locations in the city of Utrecht. In total 54 children were enrolled in the study. Simultaneously, personal exposure to and school outdoor levels of soot and NO_x were monitored during four repeated 48h measurement periods. The outdoor concentration of soot and NO_x were respectively 74% and 52% higher at the freeway school compared to its matched background school. No increased outdoor levels were seen for the ring road school compared to its matched urban background school. The personal exposure to soot and NO_x was increased (30% and 37% respectively) for children attending the school near the freeway compared to children attending the matched urban background school. Children attending the school near the ring road did not show increased personal exposure compared to the matched urban background school. A clear effect of wind direction on personal exposure to traffic-related air pollution was seen. The differences in exposure to pollutants were slightly increased on days with more than 24 h out of 48 h of downwind conditions; e.g. the increase in personal exposure to NO_x for children attending the freeway school on 'downwind' days was 46% compared to 23% on 'non-downwind' days.

In general, difference in exposure to traffic-related pollutants was seen for the comparison of the freeway school with its matched background school, and no differences were seen for the ring road comparison. The larger distance to the road (88 m vs. 75 m), the lower traffic intensity on the ring road compared to the freeway, and the presence of obstacles between the ring road school and the ring road probably contributed to this lack of contrast. These results illustrate that the impact of a busy road may be very local. The study showed that the 'school 's proximity to a freeway' can be used as a valid estimate of exposure in epidemiological studies in children on the effects of the traffic-related air pollutants soot and NO_x, provided traffic density is high enough, and the school is located at close distance.

In **Chapter 4** we compared the average personal exposure to traffic-related air pollution of 23 older adults living in homes located at high traffic-intensity streets with 22 older adults living in homes located at low traffic-intensity streets, in the city of Utrecht, the Netherlands. For each subject, five 48-hour measurements were conducted during a one-year period. Components that were measured were $PM_{2.5}$ mass, the absorbance of $PM_{2.5}$ mass ('soot'), NO_2 and NO_x. During each sampling period, subjects from both high and low traffic intensity streets were measured to

prevent that temporal variation would bias the comparison between high and low traffic intensity locations.

Personal soot exposure of older adults living at major roads (10 000 vehicles per 24 h or more) was increased (18%) compared to adults living at quiet roads. Correspondingly, we found a 10% increase in personal exposure to soot with a 10 000 vehicles per 24 h–increment. Increased personal exposure (31%) was seen for NO when comparing adults living at busy roads with adults living at quiet roads but this difference failed to reach statistical significance. No contrast was found for NO_2, NO_x and $PM_{2.5}$. Strong contrasts in home outdoor concentrations were found for soot (68%), NO (127%) and NO_x (35%) comparing busy road locations with urban background. For $PM_{2.5}$ (14%) and NO_2 (22%) the contrast was smaller. Participation in traffic and spending time outdoors both significantly contributed to personal exposure to soot and $PM_{2.5}$. In this population, traffic intensity of the street of residence predicted personal exposure to 'soot' but not $PM_{2.5}$ or nitrogen oxides. In future studies, participation in traffic and time spent outdoors are important covariates to consider.

Inaccurate exposure assessment causes measurement error and, accordingly, can bias the relationship between exposure and health. Therefore, the impact of using outdoor concentrations as an estimate for the personal level of air pollutants on the previously estimated health risks is further addressed in **Chapter 5**. Here, a measurement error adjustment was applied, using data on personal and outdoor soot concentrations from the second field study and data on personal and outdoor NO_2 concentrations from previous research. In the measurement error analysis, we considered the school outdoor concentrations of an air pollutant to be the surrogate exposure and the personal exposure as the true exposure. We used a regression calibration method for correcting the original effect estimates and corresponding CI estimates from the epidemiological study for systematic and random error using a logistic regression model. The unadjusted estimate of the prevalence ratio (PR) for current phlegm was 2.24 (CI, 1.27-3.93), and after adjusting for measurement error, the estimate was 5.29 (CI, 1.24-22.62), expressed for a 9.3 ug/m^3-increment in soot. The unadjusted estimate of the prevalence ratio, expressed for a 17.6 ug/m^3-increment in NO_2, for current phlegm was 1.76 (CI, 1.10-2.81), and after adjusting for measurement error, the estimate was 3.82 (CI, 1.03-14.21). These increments reflect the difference between the highest and the lowest outdoor levels of air pollutants measured at the exposed schools in the previous epidemiological study. Effects of measurement error adjustment for current wheeze, current conjunctivitis and elevated total IgE were comparable. Overall, we found two to three times

stronger associations between respiratory symptoms and exposure to soot and NO_2 in schoolchildren. This finding suggests that considerable bias may occur when using school outdoor levels of the air pollutants as indicators for the personal exposure to these air pollutants of children.

In conclusion, differences in outdoor levels of soot and differences in proximity to traffic were reflected in differences in personal soot concentrations. We therefore conclude that outdoor concentrations of soot and living near a busy road or attending a school near a busy road, are valid proxy measures for personal exposure to soot. Time spent in traffic, time spent outdoors, burning candles and exposure to Environmental Tobacco Smoke were found to be important determinants of personal soot concentrations as well.
Our study was conducted in a small number of specific Dutch settings, and results cannot be easily extrapolated to other populations or settings. Repetition of this work in such other settings is recommended as for example composition of traffic can be different, topography and/or meteorology may be different, and time-activity patterns may be different. It is therefore important to validate the use of outdoor pollutants and exposure indicators like distance to road and traffic intensity in different populations.

Samenvatting

Uit talrijke studies blijkt dat blootstelling aan luchtverontreiniging veroorzaakt door verkeer leidt tot schade aan de gezondheid van hart, bloedvaten en luchtwegen. In de meeste van deze studies wordt de blootstelling aan verkeersgerelateerde luchtverontreiniging geschat met behulp van concentraties in de buitenlucht, de afstand van de woning tot drukke wegen of de verkeersintensiteit op het thuisadres. Dit proefschrift gaat na hoe valide het gebruik van deze schatters is als maat voor de lange-termijn blootstelling aan verkeersgerelateerde luchtverontreiniging in epidemiologische studies. De meetstrategie bestond uit het systematisch meten van persoonlijke blootstelling van kinderen en volwassenen aan verkeersgerelateerde luchtverontreiniging (fijn stof ($PM_{2.5}$), roetdeeltjes en stikstofoxiden (NO_x)) op plaatsen met verschillende verkeersintensiteiten en tegelijkertijd ook het meten van de concentraties van deze stoffen in de buitenlucht.

In **hoofdstuk 2** gaan we nader in op de voorstudie, waarbij het de bedoeling was vooraf de uitvoerbaarheid van het meten van persoonlijke blootstelling na te gaan. Om persoonlijke concentratieniveaus van verkeersgerelateerde luchtverontreiniging te verkrijgen, lieten we vrijwilligers een badge, om NO_x te meten, en een rugzakje met de nodige meetapparatuur, om fijn stof en roetdeeltjes te verzamelen, dragen gedurende 48 uren. Aan de voorstudie namen veertien kinderen tussen 9 en 12 jaar deel, die allemaal op dezelfde school zaten, gelegen op een achtergrondlocatie in Amsterdam. Het tot vier keer toe herhalen van een 48-uurs meting bleek haalbaar voor deze populatie, aangezien de uitval 0% bedroeg. De verschillen in roetconcentraties in de buitenlucht tussen kinderen die nabij drukke wegen wonen (binnen 75 m van een weg met 10.000 voertuigen per 24 u of meer) versus kinderen die op een achtergrondlocatie in de stad wonen, konden ook teruggevonden worden in contrasten in persoonlijke blootstelling aan roet. Achtergrondlocatie werd gedefinieerd als een locatie op minstens 75 m van direct verkeer of andere lokale bronnen. Kinderen die nabij drukke wegen woonden, kwamen in aanraking met 35% meer roetdeeltjes dan kinderen die op een achtergrondlocatie in de stad woonden. Dit ondanks het feit dat alle kinderen naar dezelfde school gaan. Deze bevindingen suggereren dat 'het wonen nabij een drukke weg' een goede indicatie geeft van de persoonlijke blootstelling aan roet. De persoonlijke en binnenhuis metingen van NO, NO_2 and NO_x waren niet hoger bij kinderen die nabij drukke wegen woonden. De buitenmetingen uitgevoerd aan de voorzijde van de woning waren dit wel; 78% hoger voor NO en 27% hoger voor NO_x.

Hoofdstuk 3 beschrijft iets uitgebreider de rol van de schoollocatie in de persoonlijke blootstelling aan verkeersgerelateerde luchtverontreiniging. Aan deze studie namen vier scholen in Utrecht deel. De scholen varieerden in nabijheid van verkeer. Twee scholen waren gelegen binnen een straal van 100 m van een drukke weg, een ringweg met verkeersintensiteit van 45.200 voertuigen per 24 u en een snelweg met verkeersintensiteit van 97.800 voertuigen per 24 u. De andere twee scholen lagen op een achtergrondlocatie in de stad Utrecht. Vierenvijftig kinderen in totaal namen deel aan de studie. De meting van roetdeeltjes, fijn stof en NO_x in de buitenlucht werd gelijktijdig uitgevoerd met de persoonlijke metingen. Elke meting duurde 48 u. De buitenlucht concentratie van roetdeeltjes en NO_x waren 74% en 52% hoger op de school nabij de snelweg in vergelijking met de school op de achtergrondlocatie. Bij de school nabij de ringweg konden we geen verhoogde buitenluchtconcentraties vaststellen ten opzichte van de school op de achtergrondlocatie. De persoonlijke meting van roetdeeltjes en NO_x was hoger (30% en 37%) bij kinderen die nabij de snelweg naar school gingen in vergelijking met de school op de achtergrondlocatie. Kinderen die bij de ringweg naar school gingen vertoonden geen verhoogde blootstelling.
Doorgaans vonden we dus verschillen in blootstelling aan verkeersgerelateerde luchtverontreiniging terug tussen de school nabij de snelweg en de gerelateerde school op de achtergrondlocatie en zagen we bij de andere schoolvergelijking deze verschillen niet. De grotere afstand van de school tot de ringweg (88 m vs. 75 m), de lagere verkeersintensiteit van de ringweg in vergelijking met de snelweg en de aanwezigheid van barrières tussen de ringweg en de school aan de ringweg, dragen mogelijk bij tot het gebrek aan contrast. Deze resultaten wijzen erop dat de invloed van een drukke weg op de concentraties van luchtverontreiniging erg lokaal kan zijn. We besluiten dat 'het al dan niet naar school gaan bij een drukke weg' een goede indicatie kan geven van de persoonlijke blootstelling aan roet en NO_x, gegeven dat de verkeersintensiteit van de drukke weg hoog genoeg is en de afstand tussen de school en de drukke weg niet te groot is.

In **hoofdstuk 4** hebben we de gemiddelde persoonlijke blootstelling aan verkeersgerelateerde luchtverontreiniging van 23 oudere volwassenen, wonend aan een drukke weg (10.000 voertuigen per 24 u), vergeleken met die van 22 volwassenen, wonend aan een rustige weg in Utrecht. De vrijwilligers droegen 5 keer, verspreid over een jaar, 48 uur lang een persoonlijke monitor om $PM_{2.5}$, NO_x en roetdeeltjes te meten. Om te voorkomen dat de dag-tot-dag variatie de vergelijking tussen drukke en rustige locaties zou kunnen verstoren, werd er tijdens elke

meetperiode zowel gemeten bij mensen die aan drukke wegen woonden als bij mensen die aan rustige wegen woonden. Bij volwassenen die wonen aan een drukke weg in de stad werden 18% meer roetdeeltjes gemeten dan bij volwassenen die wonen op een achtergrondlocatie in de stad. Analoog, vonden we een verhoging van 10% in de persoonlijke blootstelling aan roetdeeltjes per verhoging van 10.000 voertuigen per 24 u. Ook werd een verhoogde persoonlijke blootstelling (31%) aan NO vastgesteld bij het vergelijken van volwassenen die aan een drukke weg wonen met volwassenen die aan een rustige weg wonen, maar dit verschil was niet statistisch significant. De persoonlijke blootstelling aan NO_2, NO_x en $PM_{2.5}$ vertoonde geen verschil tussen deze twee groepen. De contrasten van roet, NO en NO_x in de buitenlucht aan de woning waren respectievelijk 68%, 127% en 35% bij het vergelijken van woningen aan drukke wegen versus rustige wegen. Voor $PM_{2.5}$ (14%) en NO_2 (22%) waren de contrasten kleiner. Deelname aan het verkeer, en tijd doorbrengen in de buitenlucht bleken significant bij te dragen tot de persoonlijke blootstelling aan roet en $PM_{2.5}$. In deze groep van oudere volwassenen bleek dat de verkeersintensiteit aan het thuisadres een belangrijke schatter is van de persoonlijke blootstelling aan roet, maar niet aan $PM_{2.5}$ of NO_x. Deelname aan het verkeer en tijd doorgebracht in de buitenlucht zijn belangrijke parameters om mee te nemen in verder onderzoek.

Het onnauwkeurig bepalen van de blootstelling introduceert meetfouten, die vervolgens de relatie tussen blootstelling en gezondheid kunnen vertekenen. Daarom wordt in **hoofdstuk 5** de invloed van het gebruik van buitenluchtconcentraties, in plaats van persoonlijke concentraties, van verkeersgerelateerde luchtverontreiniging op de in eerder onderzoek geschatte gezondheidsrisico's bestudeerd. Een correctiemethode voor de meetfout werd toegepast met gebruik van gegevens over persoonlijke en buitenluchtconcentraties van roetdeeltjes uit onze tweede studie en gegevens over persoonlijke en buitenluchtconcentraties van NO_2 uit eerder onderzoek. Bij deze correctiemethode beschouwen we de buitenluchtconcentraties van luchtvervuiling op de school als een surrogaat blootstelling en de persoonlijke meting van luchtverontreiniging als de echte blootstelling. We gebruikten een regressiecalibratie-methode om de origineel geschatte effectparameters en bijbehorende betrouwbaarheidsparameters uit eerder uitgevoerde epidemiologische studies te corrigeren voor systematische en toevallige meetfouten. De ongecorrigeerde effectparameter (prevalentie ratio (PR)) voor huidig fluim was 2.24 (95% CI, 1.27-3.93), en na correctie 5.29 (95% CI, 1.24-22.62), uitgedrukt per volumestijging van 9.3 ug/m^3 roetdeeltjes. De ongecorrigeerde effect parameter (PR) uitgedrukt per volumestijging van 17.6 ug/m^3 NO_2 voor huidig fluim was 1.76 (95% CI, 1.10-2.81), en na correctie 3.82 (95% CI,

1.03-14.21). De stijgingen reflecteren telkens het verschil tussen de hoogste en de laagste gemeten buitenluchtmetingen op de scholen uit eerder onderzoek. Het effect van de correctiemethode was vergelijkbaar voor een aantal andere symptomen; huidig piepen, huidig conjunctivitis en totaal verhoogd IgE. In het algemeen vonden we twee tot drie keer sterkere associaties tussen respiratoire symptomen en blootstelling aan roetdeeltjes en NO_2 bij schoolkinderen. De resultaten van deze correctiemethode suggereren dat bij schoolkinderen vertekening van het gezondheidseffect kan optreden wanneer de buitenluchtconcentraties bij de school gebruikt worden als schatter van de persoonlijke blootstelling aan roetdeeltjes en NO_2.

Concluderend kan gesteld worden dat waar er verschillen in roetconcentraties in de buitenlucht en contrasten in verkeersintensiteit waren, we ook contrasten in persoonlijke blootstelling aan roet terug konden vinden. We besluiten dan ook dat 'buitenluchtmetingen van roet', 'wonen aan een drukke weg' of 'naar school gaan nabij een drukke weg' allen valide schatters zijn van de persoonlijke blootstelling aan roet. Ook de tijd doorgebracht in het verkeer, de tijd die buiten wordt doorgebracht, het branden van kaarsen en passief roken bleken bij te dragen tot de persoonlijke blootstelling aan roet. Enige voorzichtigheid is geboden bij de interpretatie van de resultaten. Dit onderzoek werd uitgevoerd bij Nederlandse vrijwilligers in Nederlandse steden. De bevindingen kunnen daardoor niet zomaar veralgemeend worden voor andere landen en bevolkingsgroepen, aangezien de verkeerssamenstelling, topografie, meteorologie per stad of land en de tijdsbestedingen van de deelnemers erg kan verschillen. Herhaling van soortgelijke metingen in andere steden of met andere bevolkingsgroepen is daarom noodzakelijk.

Affiliation of contributors

Bert Brunekreef

Environmental Epidemiology Group, Institute for Risk Assessment Sciences (IRAS), Utrecht University and Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands

Gerard Hoek, José Jacobs, Kees Meliefste and Marieke Oldenwening

Environmental Epidemiology Group, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands

Nicole A.H. Janssen and Erik Lebret

Centre for Environmental Health Research, National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands

Ruifeng Li

Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

Donna Spiegelman

Department of Biostatistics and Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA

Janine Wichmann

School of Health Systems and Public Health, University of Pretoria, South Africa

Joop H. van Wijnen

Department of Environmental Medicine, Municipal Health Service Amsterdam (GG&GD), The Netherlands

List of Publications

Sofie Van Roosbroeck, Ruifeng Li, Gerard Hoek, Erik Lebret, Bert Brunekreef and Donna Spiegelman. The impact of adjustment for exposure measurement error on the relationship between traffic-related outdoor air pollution and respiratory symptoms in children. (submitted for publication)

Sofie Van Roosbroeck, Gerard Hoek, Kees Meliefste, Nicole A. H. Janssen and Bert Brunekreef. Validity of residential traffic intensity as an estimate of long-term personal exposure to traffic-related air pollution among adults. (submitted for publication)

Haitske Graveland, Sofie Van Roosbroeck, Willeke Rensen and Bert Brunekreef. Traffic-Related Air Pollution, Health and Exhaled Nitric Oxide in Dutch Schoolchildren. *European Respiratory Journal* (submitted for publication).

Sofie Van Roosbroeck, José Jacobs, Nicole A. H. Janssen, Marieke Oldenwening, Gerard Hoek and Bert Brunekreef. Long-term personal exposure to $PM_{2.5}$, Soot and NO_x in children attending schools located near busy roads, a validation study. *Atmospheric Environment* (2007) 41:3381-3394.

Sofie Van Roosbroeck, Janine Wichmann, Nicole A. H. Janssen, Gerard Hoek, Joop H. van Wijnen, Erik Lebret and Bert Brunekreef. Long-term personal exposure to traffic-related air pollution among school children, a validation study. *Science of the Total Environment* (2006) 368:565-573.

Gina L. Ambrosini, Sofie Van Roosbroeck, Dorothy Mackerras, Lin Fritschi, Nicholas H. de Klerk, William Musk. The reliability of ten-year dietary recall: implications for cancer research. *The Journal of Nutrition* (2003) 133:2663-2668.

Curriculum Vitae

Sofie Anna Hilda Van Roosbroeck was born in Wilrijk (Antwerp, Belgium) on September 28th 1978. She graduated from secondary school in sciences-mathematics in 1996 at the Onze-Lieve-Vrouw-van-Lourdes College in Edegem (Antwerp, Belgium). Next, she studied Nutrition and Dietetics at the Catholic University of Leuven in Belgium and received her degree cum laude in 2000. As a part of her thesis she got acquainted with the Wageningen University (The Netherlands) and attended some lectures there. She returned to Wageningen University from September 2000 untill March 2002 to complete a MSc degree in Nutrition and Health with a specialization in Epidemiology. In addition to this MSc degree she enrolled for an occupational traineeship in nutritional epidemiology at the Department of Public Health of The University of Western Australia in Perth (Australia), where she worked on the reliability of food frequency questionnaires in cancer research and epidemiology. From September 2002 she started working for the Institute for Risk Assessment Sciences (IRAS) at Utrecht University (The Netherlands) on a PhD project in environmental epidemiology, described in this manuscript. Since September 2006 she is temporarily employed as a scientific researcher at IRAS in the framework of a European project INTARESE (Integrated Assessment of health Risks of Environmental Stressors in Europe) to contribute to risk assessment of environmental exposures. In July 2007 she will join the Epidemiology and Social Medicine Unit from the University of Antwerp in their research on Cancer Prevention.

Dankwoord

Geachte lezers, wat volgt, is een dankwoord in het *schoon Vlaams!* Bert, Gerard en Nicole, om het met een koninklijk meervoud te zeggen, dit is "ons" proefschrift en ik ben er ongeloofelijk content mee. Mijn eerste woord van dankbaarheid gaat uit naar mijn promotor. Bert, duizend maal dank dat u me deze kans hebt gegeven en dat u gedurende het hele onderzoeksproject vertrouwen in me hebt gehad en me bijgestuurd hebt waar nodig. Ik heb énorm graag bij het IRAS gewerkt. Gerard, de-beste-co-promotor-in-de-wereld-award gaat naar u, vast en zeker, zeker en vast! Duidend maal dank voor uw enthousiasme tijdens onze overleggen. Als geen ander wist je me keer op keer gerust te stellen en belangrijker nog, te inspireren! Ik heb zo veel geleerd van u! Bedankt! Nicole, ik zal niet snel vergeten dat je zelfs Dick aanspoorde (onder druk zette?) om me tijdelijk onderdak te bezorgen. Hartelijk dank voor die warme ontvangst tijdens mijn allereerste werkdagen in Utrecht en voor je bereidheid om het project verder te willen opvolgen ook al werd dat logistiek gezien iets moeilijker. Joop van Wijnen, Erik Lebret en Janine Wichmann wil ik danken voor hun sympathieke betrokkenheid. Dear Donna and Ruifeng (Department of Epidemiology, Harvard University, Boston, USA), thank you so much for welcoming me to Boston and making time for me. I have learned so much of you in so little time. I have really enjoyed my stay with you. Alle vrijwilligers, die hebben deel genomen aan de luchtmetingen, wil ik van harte danken. Zonder jullie was er niet veel geweest om over te schrijven. Ik wil graag ook alle collega's bij het IRAS bedanken voor de warme gezelligheid die er heerst op de jenalaan. Suzanne en Saskia, bedankt dat jullie mijn paranimfen willen zijn! Suzanne, je bent écht een schat-van-een-mens, weet je dat? Saskia, een wijntje bij de presentatievoorbereiding? En dat de kloefkappers thuisblijven, hé? Rob, vaak waren we elkaars luisterend oor en gaven we elkaar raad, vaak over het werk, maar ook vaak daarbuiten over koetjes en kalfjes, ge zijt altijd aangenaam gezelschap! Colin, Anjoeka en Jeroen, mijn feestcommissie-handlangers, feestjes organiseren met jullie was zo leuk, tenminste als de slager ons niet vergat op de dag van de jaarlijkse IRAS-BBQ. Ulrike, je bent echt een super collega, altijd bereid te helpen, én mét de glimlach! Bedankt! Dank aan mijn thesisstudenten, José en Haitske in het bijzonder, ik ben fier op jullie, dames, knap gedaan! Chère Ingrid, le cinéma français à Utrecht, ça va me certainement manquer. A la prochaine, j'espère, peut-être à Anvers ou à Bruxelles? Marieke, Kees en Hans bedankt voor jullie deskundige begeleiding in het complexe veldwerk. Mijn kamergenoten Lidwien, Daisy en Saskia zijn medeverantwoordelijk voor de creatie van een super cosy kantoor. Sommige collega's dachten dat onze kamer een reisbureau was, en dat komt niet alleen door de prachtige planten en foto's en posters van verre landen, maar ook doordat er telkens een paar

zonnetjes aan het werk waren daar! Ik ga jullie oprecht missen. Lieve IRAS collega's allemaal, we zien elkaar vast wel weer, misschien allemaal wel een paar kilootjes lichter, aangezien nu jullie vaste chocolade- en bierleverancier aan een nieuwe ronde begint. Maar als we elkaar weer treffen op een Belgian Beer Night, dan weet ik nog héél goed wie wat prefereert … Bert alias West Malle tripel, Gerard alias Kasteelbier blond, Wouter alias Leffe blond, Lidwien alias La Chouffe, Saskia alias Kersenbier of Ne Kastaar, Jeroen alias Hoegaarden Grand Cru, … u vraagt, wij tappen met de glimlach!

Pieter-Jan, bedankt dat je mij altijd kan laten lachen en dansen, ge zijt mijnen held. Charlotte en Boris, Sofie, Joke, Laura, Barbara, Tom, Heather, Matt, Dianne en zovele anderen…, bedankt voor telkens weer mijn vrienden te zijn, omringd door jullie voel ik me rijk, héél rijk. Bedankt dat jullie me graag zien ook al weten jullie niet altijd heel precies waar mijn werk over gaat. Laat ik het nog eenmaal op papier zetten; ee-pie-dee-mie-ooh-loo-gie is de leer die de oorzaken van ziekten identificeert door hun voorkomen in de populatie te bestuderen. En voor wie nog twijfelt … Ja! Epidemiologie is plezant!!

Adik, hartelijk bedankt dat ge mijn lieve peter, mon cher parrain, zijt, ik kan altijd bij u terecht voor wijze woorden en gezelligheid.

Tot slot, hoeveel talent en geluk er ook mee gemoeid moge zijn, niets heeft me meer geholpen dan de steun van mijn ouders. Merçi mama, merçi papa.