Doctoral Thesis

Measures of exposure in air pollution epidemiology and health risk assessment

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MEASURES OF EXPOSURE IN AIR POLLUTION EPIDEMIOLOGY AND HEALTH RISK ASSESSMENT

A dissertation submitted to the
SWISS FEDERAL INSTITUTE OF TECHNOLOGY ZURICH

for the degree of
DOCTOR OF NATURAL SCIENCES

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ZUSAMMENFASSUNG


Es konnte gezeigt werden, dass kurzzeitige (48 hr), personenbezogene Messungen in kleinen Stichproben (50-200 Personen) durchführbar sind. Die unterschiedlichen Messtechnologien für PEM, MEM und FSM erwiesen sich als zuverlässig und vergleichbar. Wegen expositions-relevanter Selektion der Teilnehmenden sind von EXPOLIS abgeleitete Belastungsverteilungen in Risikoabschätzungen nur bedingt einsetzbar. Die

Abstract

Epidemiological studies consistently indicate adverse health effects of ambient air pollution, though the relative health impact of the compounds of the pollution mixture has not yet been fully disentangled. There is lack of information, whether fixed site levels, often used as exposure surrogates, are associated with individual exposures to outdoor air pollutants. Since the late eighties, personal monitors have been promoted for assessment of exposures at low community air pollution levels. Within the scope of this thesis, three surrogates of human exposure to ambient air pollution and their use in health effects and risk assessment have been evaluated: i) measured short-term personal exposure to fine particle total mass and trace elements, ii) outdoor levels of fine particle total mass and trace elements and iii) questionnaire-based annoyance scores.

The implementation of the European multicentre study EXPOLIS (Air Pollution Exposure Distribution within Adult Urban Populations in Europe) has been evaluated. On the one hand, the comparability between personal (PEM), microenvironmental (MEM), and fixed site (FSM) monitors has been assessed. On the other hand, it was investigated, whether EXPOLIS suffered from exposure-relevant selection bias. To evaluate the validity of FSM-fine particle levels as exposure surrogates, four indicator groups were considered: PM$_{2.5}$ total mass; sulfur and potassium for regional air pollution; lead and bromine for traffic-related particles; and calcium for crustal particles. Using Basel data of the Elemental Analysis Study in EXPOLIS (EXPOLIS-EAS), the associations between personal exposures and home outdoor levels of the indicators were assessed. Data of the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) cross-sectional study allowed to evaluate the validity of annoyance scores to estimate long-term air pollution exposures.

It could be shown, that personal monitoring is feasible for short-term measurements (48 hr) in small population samples (50-200 subjects). The different measurement technologies, applied for PEM, MEM and FSM, proofed to yield comparable and reliable results. The observed exposure-relevant selection bias impairs the use of population exposure distributions derived from EXPOLIS in risk assessment. The validity of FSM-data was found to depend on the aspect of air pollution considered. Whereas for indicators of regional air pollution, high correlations were observed
between 48-hr personal exposures and home outdoor levels (when excluding relevant indoor sources and activities), the correlation was weaker for indicators of traffic-related and crustal particles. This is consistent with uniform spatial distribution of indicators of regional air pollutants, and higher spatial variability of traffic and crustal indicators, observed in the city of Basel. Regression of population mean annoyance scores against annual mean PM$_{10}$ and NO$_2$ concentrations, across the eight SAPALDIA areas, showed a linear relationship and strong correlations. Analysis within areas yielded consistent results. In contrast, individual scores were not associated with estimates of annual mean home outdoor NO$_2$ levels.

In conclusion, future epidemiological and risk assessment studies may rely on FSM-data to estimate human exposure to the aspect of regional, long-range air pollution. Population mean annoyance scores may serve as a simple and inexpensive tool to assess differences in long-term population exposure to the air pollution mixture. Regarding traffic-related and crustal compounds, two improving strategies could be envisaged: first, strategies capturing their spatial variability, secondly, grouping by source-specific exposures. The implementation of exposure surrogates, reflecting different aspects of the air pollution mixture, could help to identify the specific, potentially different, health effects of the different air pollution compounds and to evaluate the associated public health impact.
ABBREVIATIONS

Annoyance Scale, 11-point scale (range 0-10) for the self-assessment of study subjects of annoyance, caused by environmental stressors

BRISKA, Basel Risk Study on Ambient Air

Ca, Calcium

CO, Carbon monoxide

Diary sample, EXPOLIS-subsample for TMAD and questionnaire application without exposure or microenvironmental monitoring (indirect exposure assessment sample)

EXPOLIS, Air Pollution Exposure Distribution within Adult Urban Populations in Europe

EXPOLIS-EAS, Elemental Analysis Study in EXPOLIS

Exposure sample, EXPOLIS-subsample for exposure and microenvironmental monitoring plus TMAD and questionnaire application (direct exposure monitoring sample)

FSM, Fixed Site Monitor

GIS, Geographic Information System

K, Potassium

MEM, Microenvironmental Monitor

NO\textsubscript{2}, Nitrogen dioxide

OR, Odds Ratio

P, Penetration Factor

Pb, Lead

PEM, Personal Exposure Monitor

PM, Particulate matter

PM\textsubscript{10}, Particles with a 50% cutoff at 10 μm in aerodynamic diameter

PM\textsubscript{2.5}, Particles with a 50% cutoff at 2.5 μm in aerodynamic diameter

PM\textsubscript{2.5-10}, Particles with a 50% cutoff between 2.5 μm and 10 μm in aerodynamic diameter (coarse fraction)

S, Sulfur

SAPALDIA, Swiss Study on Air Pollution and Lung Diseases in Adults

SQ, Short Screening Questionnaire

TMAD, Time-microenvironment-activity diary

VOC, Volatile organic compound
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1 INTRODUCTION

1.1 Health Effect Assessment of Ambient Air Pollution: Open Issues

Epidemiological studies conducted in a variety of regions and populations indicate consistent associations between ambient levels of air pollutants and health outcomes. Respiratory symptoms, lung function and mortality have been observed to be related to both, short-term\textsuperscript{1-3} and long-term exposures\textsuperscript{1,2,4-6}. A large number of these studies have in common that health outcome and important covariates were measured on an individual level, whereas exposure was assigned on a group or population level, based on fixed monitoring data.\textsuperscript{7} Since the early 1980ies, personal exposure measurements have been promoted for improved exposure assessment.\textsuperscript{8-11} There is an ongoing debate whether fixed site levels are appropriate to assess the health effects of ambient air pollution.\textsuperscript{12-15} The causal association of the observed effects to the measured ambient air pollutant is only plausible, if the ambient levels, used as surrogates for population exposure, are associated with individual, personal exposures to these outdoor air pollutants.

Most studies investigating the associations between personal exposures and ambient particle levels have been limited to particle mass concentrations.\textsuperscript{9,16-19} However, total personal exposure is a combination of exposure to air pollution from outdoor sources and exposure related to indoor sources and individual activities. Hence, the particle mass of total personal exposure is a mixture of particles from a variety of indoor and outdoor sources with potentially different health relevance\textsuperscript{20,21}. The exposure of interest in a study depends on the research question to be addressed. To assess the health effects of particles either generated indoors, or of outdoor origin, or of the particle mass per se, it should be aimed at estimating personal exposure to particles either generated indoors, or of outdoor origin, or to fine particle total mass, respectively.\textsuperscript{20} The aspect of exposure most relevant to regulatory environmental policy has been recognized to be the portion of total exposure that is attributable to outdoor air.\textsuperscript{22} To reduce exposure to particles from different sources requires also different abatement strategies.\textsuperscript{20}

The strength and at the same time the limitation of the epidemiological approach for assessing health effects of ambient, outdoor air pollution is, that it investigates real
people, living in uncontrolled environments and who are exposed to the real mixture of air pollution. Some inherent limitations of evidence drawn from such observational studies have to be recognized, though: they do not assess biological mechanisms, there is only scarce information regarding the linkages between outdoor levels and personal exposures, there is a potential for confounding, on the one hand, due to risk factors associated with both, exposure and disease and, on the other hand, due to highly correlated co-pollutants. Finally, the relative health impact of different constituents of fine particles has not yet been fully disentangled. Current research in the field of health risk assessment of ambient particles aims at closing these gaps of knowledge in order to ascertain the observed health effects, in particular those of long-term, low-level exposures routinely experienced in urban areas. Several studies have found the strongest associations for fine particles (PM$_{2.5}$; particles with a 50% cutoff at 2.5 μm in aerodynamic diameter). Therefore, particular effort is given to understand the health effects of different fractions of particles and of their components. A prerequisite to do so are exposure surrogates reflecting different aspects of ambient, outdoor air pollution that may be used in epidemiological studies and for risk assessment purposes.

1.2 Goals of this Thesis

The aim of this work is to evaluate the following measures of air pollution exposure: i) measured short-term personal exposure to fine particle total mass and trace elements, ii) outdoor levels of fine particle total mass and trace elements and iii) questionnaire based annoyance scores. The validity of the three measures as exposure surrogates will be discussed, on the one hand in the context of epidemiological studies investigating long-term effects of outdoor air pollution (e.g. the Swiss studies SAPALDIA$^{5,6}$ and SCARPOL$^{34}$), where the large number of participants and the duration of the exposure of interest (lifetime) are invariable constraints. On the other hand, their validity in studies assessing the associated health risk and public health impact$^{35-38}$ will be evaluated. The relevance of improving strategies for exposure assessment in environmental epidemiology and health risk assessment will be elucidated.
In the following, the specific research questions, and the chapters where they are addressed, are introduced:

*Feasibility of personal monitoring*

Are short-term personal and microenvironmental exposure measurements of fine particles (PM$_{2.5}$) feasible in an European multicentre study?

⇒ Chapter 3 describes the PM$_{2.5}$ measurement methodology and quality assurance procedures of the EXPOLIS (Air Pollution Exposure Distributions within Adult Urban Populations in Europe) study and evaluates the comparability of the EXPOLIS microenvironmental (MEM) and personal (PEM) PM$_{2.5}$-monitors.

*Representativity of participants of a personal monitoring study*

Do participants of the full EXPOLIS exposure assessment protocol and of the less demanding time-activity-diary-only protocol represent the target population of the EXPOLIS study?

⇒ Chapter 4 describes the random population sampling process of EXPOLIS Basel and Helsinki. Using traffic volume at the home address of study subjects as exposure surrogate, it investigates whether exposure-relevant selection bias has occurred.

*Associations between ambient fine particle levels and personal exposures*

Are ambient levels of fine particles valid surrogates for human exposure to ambient particulate air pollution?

⇒ Using data of the Swiss EXPOLIS center Basel, Chapter 5 assesses the associations between ambient levels and personal exposures of fine particle mass concentrations and of trace elements for primary traffic-related particles (lead and bromine), for regional fine particle air pollution (sulfur and potassium) and for coarse mode particles (calcium).

*Annoyance scores as measure of air pollution exposure*

Can the spatial variability of the air pollution mixture be captured by questionnaire based annoyance scores?
In chapter 6 of the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) cross sectional study is used to evaluate the validity of annoyance scores as a simple tool to assess the variability of the air pollution mixture within a region.

In chapter 7 the most important findings are recapitulated and the validity of the considered exposure surrogates evaluated. The resulting implications for exposure assessment in the context of air pollution epidemiology and health risk assessment are discussed.
2 BACKGROUND

This chapter introduces the relevant theoretical background for the presented empirical work. First, the concepts of human exposure assessment (section 2.1) and related measurement error models (section 2.2) are displayed. Then, exposure assessment is put into perspective of the risk assessment framework (section 2.3). The role of exposure assessment in both, air pollution epidemiology, and health risk and impact assessment, is elucidated. Finally, the characteristics of different fractions of particulate air pollution are described (section 2.4).

2.1 Assessment of Human Exposure to Air Pollutants

The term exposure as referred to in the context of health risk assessment can be defined as the event when a person comes into contact with a pollutant of a certain concentration during a certain period of time. Thus, exposure is at the interface of the environment and the human body and is distinct from the concentration of an agent in the environment and the dose in the human body. Figure 1 illustrates the place of exposure in the continuum from emissions of a contaminant to an observable health effect.

In practice, it is hardly ever possible to actually measure the 'true' exposure of study subjects or populations. Hence, every exposure variable has to be recognized as a surrogate or a proxy for the exposure under investigation. Moreover, often the specific noxious agent of a pollutant mixture is not known or not easily measurable. Therefore, the indicator concept plays a key role in exposure characterization. A classic example are outdoor nitrogen dioxide (NO$_2$) -levels, which can be used as an indicator for traffic-related exposures. The assigned NO$_2$ level does not only represent exposure to NO$_2$ molecules per se, but rather to the complex mixture of traffic exhaust, with typical exposure patterns such as regular peak exposures in the morning and evening hours of traffic-related compounds. The adverse health effects of the NO$_2$ molecules per se can be assessed in controlled human exposure studies in the laboratory, though.
With regard to air pollutants, the challenge of human exposure assessment lays in the combination of spatio-temporal variability of the pollutants and time-microenvironment-activity patterns of populations. The interaction of these two factors result in exposure-time profiles\textsuperscript{51}, as exemplary shown in Figure 2. Based upon such profiles, different measures of exposure may be derived on the individual or population level, e.g. integrated exposure (area under the curve), average exposure, or peak exposure.\textsuperscript{51} Time-activity studies both in the United States\textsuperscript{52-54} and Europe\textsuperscript{55} have shown that people spend about 90 percent of their time indoors. Therefore, with regard to human exposure, the penetration of outdoor air pollutants into indoor environments is of particular importance. The penetration factor (P) is defined as the ability of a particle to penetrate a building envelope.\textsuperscript{56} With two different methods, one based on empirical data from the PTEAM study\textsuperscript{57} and the other on data from one instrumented house\textsuperscript{58}, P has been estimated to be close to one for fine particles. This suggests that particles less than 10\textmu m in aerodynamic diameter (PM\textsubscript{10}) penetrate building envelopes with the same efficiency as (nonreactive) gases.\textsuperscript{56} Also with data of the PTEAM study, the fraction of outdoor PM\textsubscript{2.5} and PM\textsubscript{2.5-10} (coarse fraction) found indoors at equilibrium, and at a mean air exchange rate of 0.76 hr\textsuperscript{-1}, has been estimated to be 66% and 43%, respectively.\textsuperscript{59} This suggests, that in indoor environments exposure to outdoor particles is somewhat attenuated. Particles from indoors sources may add to the fine particle concentrations stemming from outdoors.\textsuperscript{60}
In health effects assessment, fixed site monitoring (FSM) data have often been used as surrogate for human exposure to ambient, outdoor air pollution. In many cities ambient levels are routinely measured by the local authorities and thus rather easily to obtain for research purposes. Personal exposure measurement techniques, initially developed by industrial hygienists, have been adapted in the late eighties and early nineties to measure community exposures at lower levels. This allowed to envisage personal exposure measurements of fine particles in the context of air pollution health and risk assessment.

Figure 2. Exposure-time profile and derived exposure parameters (Zatarian et al.51)

Figure 3 illustrates that total personal exposure to air pollutants can be conceptualized as the sum of exposures from various sources encountered indoors, outdoors and through individual activities. Therefore, total personal exposure to fine particle mass is not a useful measure for assessing specific health effects, neither of ambient outdoor air pollutants, nor for particles generated indoors. In air pollution epidemiology and health risk assessment, the measure of interest, though, would be exposure to ambient outdoor particles.22,61
Armstrong\textsuperscript{62} points out, that the exposure variable should be specific and distinct from possible confounding exposures. With regard to exposure to fine particles, source specific indicators should allow to track personal exposure to particles generated outdoors, indoors or by individual activities. In air pollution epidemiology, particles related to indoor sources or individual activities are possible confounding exposures and should be separately recorded and evaluated in sensitivity analysis.

![Diagram](image)

\textit{Figure 3. Total personal exposure is the sum of exposures encountered in indoor and outdoor environments.}

### 2.2 Measurement Errors and Validity of Exposure Estimates

As already pointed out in the previous section, it is hardly ever possible to measure the ‘true’ exposure of study subjects or populations. As a consequence, every measure of exposure is subject to some degree of error. The precision of an exposure variable is strictly speaking a technical issue and refers to the repeatability of the measurement.\textsuperscript{45}
More important for exposure assessment is the relative precision, that is the sampling error relative to the variability of exposure in the population. The exposure measurement error for an individual can be defined as the difference between the measured exposure and the true exposure. In the context of epidemiology, validity refers to the capacity of an exposure variable to measure the true exposure in a population of interest. Poor validity of an exposure measure may lead to bias in health effect assessment, that is to a difference between the estimated association between exposure and disease and the true association.

Measurement errors can be of systematic or random nature. In the regression context of epidemiology, two error models are most relevant: the classic error model and the Berkson error model.

The classic model of measurement error in a population is

\[ X_i = T_i + b + E_i, \]

where

- \( X_i = \) observed exposure for individual \( i \)
- \( T_i = \) true exposure of individual \( i \)
- \( b = \) systematic error
- \( E_i = \) subject (or random) error (varies from subject to subject)

When exposure is measured on the individual level, mostly the classic error model applies. \( T_i \) and \( E_i \) are assumed to be independent, i.e., not to be correlated (\( \rho_{TE} = 0 \)). Random errors lead to bias, and in most cases attenuate the observable linear regression coefficient \( \beta \) of the exposure-effect association (Table 1). Systematic errors, e.g. due to poor calibration, shift the observed exposure distribution, but do not lead to bias in the exposure-response association.

The Berkson error model applies, when exposure is assigned on a group or population level. In this case, the true exposures of all individuals vary randomly about the assigned value. Formally, this can be expressed as

\[ T_i = X + E_i, \]

where

- \( T_i = \) true exposure for individual \( i \)
- \( X = \) assigned group average
- \( E_i = \) subject (random) error (varies from subject to subject)
$E_i$ is assumed to be independent of $X$ ($\rho_{XE} = 0$). In linear regression, random Berkson error in the exposure variable does not lead to biased health effect estimates\textsuperscript{63,64}, provided the assigned value represents the average exposure of the group.\textsuperscript{65} However, increasing random errors lead to larger standard errors and confidence intervals and thus to reduced power to detect an association.\textsuperscript{63} Therefore, homogeneity of the group or population exposure is a key factor for mitigation of Berkson errors. In addition, the power to detect an association depends on the exposure gradient between the groups (contrast) and the standard error of the mean exposure in a category (precision).\textsuperscript{66} The less the exposure distributions of the compared groups overlap, the smaller will be the impact of random error within the group on the study power. However, if the variance (var) of the error is not constant over the whole exposure range, in logistic regression also Berkson error may lead to biased estimates\textsuperscript{63} (Table 1).

**Table 1. Measurement errors in regression context: impact on bias of effect estimates (adapted from Steenland et al.\textsuperscript{63})**

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<th>Measurement Error Model</th>
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<td>Linear</td>
<td>Classic with normal Distribution</td>
<td>towards null (&quot;no association&quot;)</td>
</tr>
<tr>
<td>Log Linear</td>
<td>Classic, but $\sigma_{TE}^2 &gt; 0$</td>
<td>towards null</td>
</tr>
<tr>
<td></td>
<td>Classic, but $\sigma_{TE}^2 &lt; 0$</td>
<td>towards null or away null or opposite</td>
</tr>
<tr>
<td>Linear</td>
<td>Berkson</td>
<td>unbiased, but less power and less precision</td>
</tr>
<tr>
<td>Log Linear</td>
<td>Berkson and var\textsuperscript{b} ($E_i$) not constant</td>
<td>can lead away null</td>
</tr>
<tr>
<td></td>
<td>Berkson and var ($E_i$) constant</td>
<td>unbiased</td>
</tr>
</tbody>
</table>

\textsuperscript{a}$\rho_{TE}$ = correlation between true exposure and subject error

\textsuperscript{b}var = variance

The Berkson error model applies for example in the semi-individual study design.\textsuperscript{7} Fixed site air pollution levels are used as surrogate for human exposure to outdoor air pollution, whereas health outcome and covariates are assigned on the individual level. The true exposures of city dwellers are assumed to vary randomly about the assigned FSM-level. A prerequisite for unbiased effect estimates in between-cities analysis is, however, that there is no systematic error between the FSMs of the cities, i.e., that in all cities the FSM equally represents the city-average of the pollutant under consideration. In practice, though, it is difficult to evaluate the representativity of a FSM. In any case,
monitoring sites close to local sources such as high traffic density should rather not be used to obtain exposure estimates in semi-individual studies. In recent years, extensive measuring campaigns in European\textsuperscript{67-70}, American\textsuperscript{71-74} and Canadian\textsuperscript{75} cities have assessed the spatial distribution of different compounds of the air pollution mixture. For compounds with homogeneous spatial distribution, the potential for Berkson error is a priory smaller than for compounds with high spatial variability. Bias due to non-constant error variance over the whole range of exposure may occur, if the within-city variability of ambient air pollution levels is higher in cities with high levels than in cities with low levels.

A common measure of validity is the correlation between the surrogate exposure measure and the true exposure.\textsuperscript{62} In practice, since true exposure is not assessable, the correlation between the surrogate and an exposure measure, which is considered a more accurate approximation of the true exposure, can be assessed. In the context of air pollution exposure, the correlation between ambient levels and measured personal exposures to air pollutants can be used to assess the validity of ambient levels as exposure surrogates. Chapter 5 makes use of this approach. For homogeneously distributed components of ambient air pollution, with a penetration factor from outdoor to indoor close to unity, we should expect similar exposures for all inhabitants of an area, irrespective of individual itineraries. Consequently, high correlation between ambient levels and personal exposures should be expected. In contrast, short-term exposure to spatially heterogeneous components would vary more between persons due to individual time activity patterns, resulting in low personal versus ambient correlations (Figure 4).

For assessing long-term effects of outdoor air pollution, the measure of interest would be individual lifetime-exposures to air pollutants stemming from outdoor sources. Since it is not feasible to monitor lifetime personal exposures, various direct and indirect techniques have been developed, providing a variety of exposure measures for use in air pollution epidemiology and impact assessment. They range from questionnaires over environmental monitoring to personal exposure measurements or modeling techniques.\textsuperscript{76} In recent years, geographic information systems (GIS) have come into use for health effect\textsuperscript{77-80} and risk assessment\textsuperscript{36-38,81} of ambient air pollution. In practice, the choice of the measure of exposure is a trade off between the validity of the exposure estimate and the practicability to obtain this estimate, including the costs.\textsuperscript{62,82}
2.3 Exposure Assessment in a Risk Assessment Framework

Health risk assessment aims at quantifying the potential adverse health effects of human exposure to environmental pollutants. Since the early eighties, a systematic approach has been developed to provide a tool for science-based risk management decisions, generally consisting of the following four steps (Figure 5): (1) hazard identification for an agent, (2) exposure - response assessment, (3) exposure assessment on a population level and (4) risk quantification on a population level. The importance of high quality epidemiology for the first two steps has been emphasized in recent years. In contrast to animal studies, where the major drawbacks are the extrapolation across species and from high to low levels, in epidemiological studies the impact of adverse environmental factors on human health are directly assessed in the range and duration of exposure the population encounters.

Exposure assessment plays a key role in the risk assessment procedure (Figure 5). On the one hand, the exposure of participants of epidemiological studies needs to be characterized in order to establish the exposure-response relationship. This provides
effect estimates such as odds ratios (OR), relative risk estimates (RR) or linear regression slopes (β). On the other hand, a description of the exposure distribution in the population in question (e.g. the entire population of Switzerland), which is rarely identical to participants of epidemiological studies, is required before the associated risk and public health impact may be quantified. Yet, exposure assessment has inherent limitations and is often the weak point in health risk assessment of air pollution, both on the individual and on a population level. In comparison, health outcomes such as mortality or lung function may be assessed more accurately. Still, as every measure, also measures of health outcome are affected by some degree of error.

Figure 5. Risk assessment framework and role of exposure assessment.

The key requirements (and difficulties) for characterizing exposure in epidemiological studies are different from those for assessing population exposure distributions. In epidemiological studies, exposures of individual participants should be estimated as accurately as possible, whereas for risk quantification on a population level, the full range of the exposure distribution should be described, including the upper end of high
exposure groups. With regard to possible bias, in epidemiological studies, information bias due to errors in the exposure measurement is particularly relevant. In exposure assessment used for quantification of the public health impact, exposure-relevant selection bias, e.g. less participation of highly exposed population groups, may impair the results. This issue is addressed in chapter 4.

### 2.4 Characteristics of Particulate Air Pollution

Epidemiological studies investigating the health effects of ambient air pollution have found strongest and most consistent effects with indicators of fine particle air pollution, drawing the attention of the air pollution research community, risk assessors, risk managers and policy makers on particulate matter.

Particulate matter is not a well defined chemical or substance but refers to a mixture of solid and liquid particles, suspended in the air, which vary in size, composition and origin. It is convenient to classify particles by their aerodynamic properties, because these govern their transport and removal in the atmosphere, they govern their deposition in the respiratory system, they are associated with sources and they are associated with the chemical composition of particles. The aerodynamic properties may be summarized by the aerodynamic diameter, which is defined as the diameter of a sphere of unit density (1 g cm⁻³), which has the same terminal settling velocity in air as the particle under consideration:

\[ D_a = D_g \times K \times \sqrt{\frac{\rho_p}{\rho_0}} \]

where:
- \( D_a \) = Aerodynamic diameter
- \( D_g \) = Geometric diameter
- \( \rho_p \) = Density of particle
- \( \rho_0 \) = Reference density (1 g cm⁻³)
- \( K \) = Shape factor (for a sphere \( K = 1.0 \))

The aerodynamic diameter of ambient particles, usually simply called particle size, ranges from about 0.001 µm to 100 µm. Physical and chemical processes result in a trimodal size distribution of particles. Figure 6 shows these processes schematically. Table 2 in chapter 5 gives an overview of the characteristics of the three particle modes.
Coarse particles, with a size range between 1 μm and 100 μm, are mainly mechanically generated by breaking up larger solid particles. Because the amount of energy required to break the particles into smaller sizes, increases, as the size decreases, the lower limit for the production of coarse particles is at about 1 μm. Fine particles with a size range between about 0.001 μm and 1 μm are formed from gases. Within the fine particle mode, two modes can be distinguished: the nucleation mode and the accumulation mode. The nucleation mode, also called ultrafine mode, consists of particles smaller than about 0.1 μm, which are either directly emitted through combustion processes (primary particles) or generated by nucleation or condensation of gases, formed by high temperature vaporization or chemical reactions. The nucleation mode particles rapidly convert to the accumulation mode, resulting in a short half-life of minutes to hours. Consequently, they are mostly found close to sources. Accumulation mode particles (0.1-1 μm) are on the one hand formed by coagulation or condensation of nuclei mode particles. Because the efficiency of these processes rapidly decreases, as the particle size approaches 1 μm, particles normally do not grow to a diameter above approximately 1 μm. On the other hand, accumulation mode particles are generated by gas-to-particle conversion through chemical reactions. The resulting secondary sulfate and nitrate particles are the dominant component of particulate air pollution. Accumulation mode particles are eliminated mostly through rainout or washout, and have a half-life of days to weeks; thus they may travel for long distances of 100s to 1000s of km.

The three modes are closely associated with sources and the composition of particles. Coarse particles mainly stem from natural sources such as erosion, volcanic eruptions or sea spray. Furthermore, biological material such as pollen, mould spores or parts of insects, as well as coal and oil fly ash (from non-combustible material), are found in the coarse mode. Coarse particles may also be produced by abrasion of brakes or tires, and they may be re-suspended by traffic. Indoors they may be re-suspended by human activities. The source material is reflected in their elemental composition, with the minerals of the earth crust dominating (Si, Al, Ca, Fe, K, Ti, Mn, Sr). Fine particles that have been generated through combustion processes or gas-to-particle conversions contain sulfates, nitrates, elemental and organic carbon and, depending on the
composition of the combusted material (fuel or solid material), trace metals such as lead, cadmium, vanadium, nickel, copper, zinc, manganese or iron\textsuperscript{59}. Ultrafine primary particles generated by combustion of diesel-fuel have been reported to consist of about 70-95\% elemental and 5-30\% organic carbon.\textsuperscript{92}

The particle size determines also the deposition and removal of particles in the respiratory tract. Particles larger than 10\(\mu\)m are mostly retained in the nose and mouth region whereas smaller particles penetrate into the respiratory system. Particles between 1-10\(\mu\)m reach the bronchioles and are carried out on the mucociliary ladder within 24 hours.\textsuperscript{93} Particles smaller than 1 \(\mu\)m can reach the alveoli and the half time of the alveolar clearance by macrophages takes up to one year.\textsuperscript{94} Differences in the chemical composition of ultrafine, fine and coarse mode particles, reflecting their different sources and generation, suggest differences in their adverse health effects.\textsuperscript{20,21,28-30,59}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure6.png}
\caption{Schematic representation of the urban aerosol and the processes that modify it (from Hinds\textsuperscript{88}).}
\end{figure}

The specification of the cutoff for measuring particle concentrations takes account of the health relevance of the different size fractions. PM\(_{10}\) is the fraction that would be deposited in and damaging to the respiratory system. A more specific measure is PM\(_{2.5}\), separating fine from coarse mode particles with distinct profiles of sources, chemical composition and depth of penetration into the human respiratory system. Regarding the
health relevance, a size cut at 1 μm would be more appropriate; the cut at 2.5 μm is a historical artefact of sampler design available in the late 1970s. At 2.5 μm is also the minimum of the mass distribution between the accumulation and coarse mode, but fine and coarse particles may overlap in the intermodal region between 1 and 3 μm.

2.5 References (Chapters 1 and 2)


55. Boudet, C.; Zmirou, D.; Künzli, N. and Oglesby, L. "Subjects Adapt Time-Activity Patterns during Participation in a Personal Exposure Assessment


3 FINE PARTICLE (PM$_{2.5}$) MEASUREMENT METHODOLOGY, QUALITY ASSURANCE PROCEDURES AND PILOT RESULTS OF THE EXPOLIS STUDY*

3.1 Abstract

EXPOLIS is a European multicenter (Athens, Basel, Grenoble, Helsinki, Milan, and Prague) air pollution exposure study. It is the first international population-based large-scale study, where personal exposures to PM$_{2.5}$ aerosol particles (together with volatile organic compounds and carbon monoxide) are being monitored. EXPOLIS is performed in six different centers across Europe, the sampled aerosol concentrations vary greatly, and the microenvironmental samples are not collected with the same equipment as the personal samples. Therefore careful equipment selection, methods development and testing, and thorough quality assurance and quality control (QA&QC) procedures are essential for producing reliable and comparable PM$_{2.5}$ data. This paper introduces the equipment, the laboratory test results, the pilot results, the standard operating procedures, and the QA & QC procedures of EXPOLIS. Test results show good comparability and repeatability between personal and microenvironmental monitors for PM$_{2.5}$ at different concentration levels measured across Europe in EXPOLIS centers.

3.2 Introduction

Our understanding of the health effects of fine particulate matter in air has been radically changed over last decade by the results of American epidemiologists,\textsuperscript{1,2} re-analysis of the Six-Cities-Study data,\textsuperscript{3} and the European APHEA project.\textsuperscript{4} Air pollution, especially fine particulate matter (PM\textsubscript{10}, PM\textsubscript{2.5}), may be annually responsible for tens of thousands of cases of respiratory and cardiovascular mortality in Europe alone, and it can significantly shorten the life expectancy in large populations.\textsuperscript{5}

The harmful health effects of urban air pollutants may not be caused by the levels of air pollutants at those fixed monitoring sites alone, however, but instead by the personal exposures of the millions of individuals in their daily activities in indoor and outdoor urban environments and in commuting between them. These personal exposures may differ considerably from the centrally monitored ambient air level due to personal behavior, mobility, and near field sources, mostly indoors.\textsuperscript{6}

In the Total Human Environmental Exposure study (THEES), Lioy et al.\textsuperscript{7} used a Marple and Turner sharp cut 10-\textmu m personal impactor ("lollipop") together with a 4 L/min personal pump\textsuperscript{8} to evaluate personal exposures of non-smoking individuals; indoor PM\textsubscript{10} samplers\textsuperscript{8} to monitor indoor microenvironments; and outdoor PM\textsubscript{10} samplers (Harvard Impactor/IASI)\textsuperscript{9} to monitor outdoor microenvironments. Pre- and post-sampling filter mass determinations (weighing \pm 5 \mu g) were made using a microbalance. Filters were placed in a constant temperature and humidity chamber for 24 hr prior to weighing.\textsuperscript{8}

Only one large population-based study (U.S. Environmental Protection Agency [EPA] P-TEAM, Riverside, CA), in which personal PM\textsubscript{10} exposures and microenvironmental levels have been monitored has been published.\textsuperscript{6,10} In this study, exposure assessment methodology was developed to estimate the frequency distribution of human exposure to aerosol particles for a population. For this purpose the 4 L/min Casella sampling pump was modified by BGI to be carried on a belt and to draw air for 12 hr with a single set of batteries through a 2.5- or 10-\textmu m MSP inlet and filter pack.\textsuperscript{11} This personal sampler (PEM) and an AC-driven microenvironmental sampler (MEM, consisting of a Marple/Turner impactor and a 10-L/min pump) were tested both in the laboratory\textsuperscript{12} and in the field.\textsuperscript{13} The 37-mm diameter 2-\textmu m pore Teflon filters were conditioned in an
environmentally controlled weighing room for at least 24 hr prior to weighing, and they were weighed with a Cahn Mod 31 microbalance with electronic data transfer to computer. The PTEAM study protocol was tested in a nine-home pilot study in San Gabriel, CA.14

In a Dutch study on personal PM_{10} and fine particle (FP) exposures of 50-70-yr-old adults and school children,15,16 PM_{10} samples were collected by personal battery-operated Gillian pumps drawing air samples at 4 L/min through the same personal impactors as in P-TEAM8 and 37-mm diameter 3-μm pore Teflon filters. FP samples were collected by Casella respirable dust cyclones, which (when operated) at 4 L/min have a calculated cutoff size of about 3 μm. In the beginning of the study, the filters were weighed with a 10 μg (reading precision) balance requesting two repeated measurements within 50 μg. Later, all filters were weighed with a Mettler MT5 microbalance requiring two measurements within 10 μg.

The study on Air Pollution Exposure Distributions within Adult Urban Populations in Europe (EXPOLIS) focuses on the working age urban populations in Europe exposed to air pollutants (PM_{2.5}, VOCs and CO) in their homes, workplaces, and other common urban microenvironments. The population exposures are being monitored by EXPOLIS centers in Athens, Basel, Grenoble, Helsinki, Milan and Prague. In total, about 500 subjects will participate in the measurements. The overall structure of EXPOLIS study - including measured air pollutants, microenvironments, population sampling techniques, the use of questionnaires and time-activity diaries and storing and analyzing EXPOLIS data by a database - is presented elsewhere.17

This paper introduces the microenvironmental and personal PM_{2.5} sampling and filter weighing techniques and procedures, test results of the personal and microenvironmental PM_{2.5} samplers, and the quality assurance principles of PM_{2.5} used in EXPOLIS. Because different teams in six different countries have collected the samples using two different techniques for microenvironmental and personal measurements, careful testing and strict quality assurance procedures were essential to ensure data reliability and comparability both among the centers and among the indoor, outdoor and personal measurements. Because the lowest sampled PM_{2.5} masses were expected to be in the order of 10 μg, a filter weighing accuracy of ± 1 μg was the goal.
3.3 Materials and Methods

The performance criteria of the PM$_{2.5}$ sampling was to ensure quantified data for all PM$_{2.5}$ exposures and microenvironmental concentrations. The quality assurance (QA) was based on the principles that (1) all procedures should be carefully planned, tested, and performed according to standard operation procedures (SOPs) approved by the study director; (2) each unit of data must be fully traceable; and (3) any deviations or irregularities must be recorded.\textsuperscript{17}

In practice, the target detection limit of the PM$_{2.5}$ concentration is set by the low levels, down to 5 $\mu$g/m$^3$, expected in Helsinki.

3.3.1 Personal Exposure Sampling

The PM$_{2.5}$ exposure was measured by a personal exposure monitor (PEM; Figure 1). Each subject carried the sampler for a sampling period of 48 hr. It consisted of an air pump, a cyclone, and a filter holder packed together with a Langan CO monitor, a VOC sampling tube, and battery pack into a rigid aluminum briefcase filled with noise-absorbing material (total weight 5.2 kg). The modified Buck IH pump (A.P. Buck Inc., Orlando, FL) was silent, lightweight, and capable for sampling over 48 hr with six D-size alkaline batteries and therefore suitable for personal measurements. It draws air at 4 L/min using a simple volumetric flow control (i.e., keeping the pump speed constant). Small PM$_{2.5}$ cyclones (GK2.05) were designed and constructed for EXPOLIS by BGI Inc. (Waltham, MA). The design and the performance of the GK cyclones are presented in Kenny and Gussman.\textsuperscript{18} With this cyclone design the filters can be handled from pre- to post-weighing in 37-mm Millipore filter holders (Millipore Corporation, Bedford, MA), which decreases the risk of filter contamination and damage. A Gelman Teflo filter (2-$\mu$m pore size) was chosen for the sampling medium because it has a high collection efficiency, a low-pressure drop, and a low chemical background. In the laboratory, the flow rate was adjusted to 4 L/min with a bubble flow meter (e.g., Buck M-30 by A.P. Buck Inc., Orlando, FL) before and controlled after each 48-hr sampling period, with the cyclone and the actually used filter in the sampling line.

Two filter holders were provided for each subject. One 'day filter' was used for the two sampling periods beginning at leaving home for work and ending at returning home
Figure 1. The personal exposure monitor (PEM) with a PM$_{2.5}$ cyclone with a filter holder in back left corner, pump in the middle, and battery holder in the back right corner. Two spare filter holders (including filters) can be seen in the front right corner. CO monitor is in the front left corner and VOC tub is in the middle of the case.
from work (about 2 x 8-10 hr), and one 'night filter' was used for the remaining times (about 2 x 14-16 hr). The subjects were instructed on how to change the (day or night) filter holders by simply pulling the first filter holder apart from the cyclone and pressing the second filter holder in its place.

3.3.2 Microenvironmental Sampling

Microenvironmental monitors (MEMs; Figure 2) were placed at the subject's home (indoors and outdoors) and workplace for 48 hr to collect microenvironmental PM$_{2.5}$. The pumps were programmed to run at home during the expected non-working hours and in the workplace during the expected working hours for each subject. The flow rate was measured and adjusted before and controlled after each sampling with a bubble flow meter (e.g., Buck M-30).

The MEM sampler contained an EPA-WINS impactor (EPA Well Impactor Ninety-Six, BGI), a 47-mm filter holder (BGI) with a Gelman Teflo filter, and a PQ100 pump (BGI). A Graseby-Andersen PM$_{10}$ inlet was used in outdoor measurements to avoid wind and rain effects. The EPA-WINS is a single jet well impactor designed to remove particles with a 50% cut size at 2.5 μm aerodynamic particle diameter at 16.7 L/min.$^{19,20}$

The PQ100 pump was equipped with a microprocessor-controlled timing and mass flow adjustment system. The pump may be run off the household electricity supply (220/110 AC) or from a 6-V internal lead acid battery (up to 32 hr) and is enclosed in a weatherproof case. The pump is designed to pull in a sample of air at a constant mass flow controlled rate of 1.0-25 L/min (±5 %). Aluminum Y-joints for two filter holders were prepared for an option (e.g., a blank filter and an exposed one, or for two filters in rooms with heavy smoking).

3.3.3 Air Flow

Because the PEM pump has a volumetric flow control and the MEM pump a mass flow control, the airflows had to be normalized by air pressure and temperature. Normalization is particularly important in the cold Nordic winter (Helsinki) when the temperature difference between indoor and outdoor air is 20-50 °C.

In EXPOLIS all sample volumes will be normalized to 101.3 kPa (760 mmHg) air pressure at 20 °C. The PEM flow results will be normalized using the temperature data
Figure 2. The microenvironmental monitor (MEM). PM$_{2.5}$ impactor above the box, two filter holders inside the box (connected to impactor by a Y-joint), charger below the filter holders with tubing and pump outside the box. Pump was placed inside the lower part of the box connected to hoses and the doors were closed during the runs.
collected by the external temperature sensor of a Langan CO monitor (Langan Products Inc., San Francisco, CA). The MEM is programmed and calibrated to adjust the drawn air mass to the equivalent of 16.7 L/min at 20°C and 101.3 kPa.

### 3.3.4 Gravimetric Analysis

When 1-µg sensitivity is needed in the weighing, a microbalance placed on the stable stone table in a mechanically and physically stable room must be used. The Teflon Filters are electrically non-conductive and will hold the static charges collected on them. They can be deionized by an alpha radiation source (Po-210), an ionizing bar, or a piezoelectric crystal gun. If this problem is not controlled, weighing is strongly unreliable.

The filters were weighed in each EXPOLIS center by a locally available microbalance. In Helsinki, a Mettler MT5 (Mettler-Toledo AG, Greifensee, Switzerland) was used for weighing the filters. Each filter was stabilized in the weighing room for a minimum of 16 hr prior to weighing. After the sampling, the time of stabilization in the weighing room was limited to a maximum of 36 hr.

The weighing conditions were controlled by recording the temperature, relative humidity, and air pressure before and after each session. The weighing room was located on the ground floor, had no external walls or windows, and had only minimal air change rate. The indoor climate changed only slowly, with the relative humidity (R.H.) ranging from 10 to 50%, and the temperature from 18 to 30°C during the year. The standard weight was also weighed before and after each session, and each filter was deionized at both sides with a Po-210 deionizer (Staticmaster 1269 by Cahn Inc., USA) or a Multistat deionizer (Haug Biel GmbH, Germany) before each weighing. The data entry stage contained a number of checks by the database for data correctness, such as predefined sample numbers for each center and sample type and the requirement for a new pair of weighing results if the first pair of results did not agree within 1 µg. Typically one pair out of five had to be reweighed in this procedure.

When the weighed net mass (and volume) is small (less than 1/1000) compared to the filter mass (and volume), the role of air buoyancy (i.e. a filter in air looses its weight according to Archimedes’ principle), becomes a significant issue and the mass results
must be corrected for any changes in air density between the pre- and post-weighing. This is the case, for example, when weighing fine particle samples by personal or microenvironmental monitors.

Because the effect of air buoyancy depends on the air density (i.e., air pressure, temperature, and relative humidity), when weighing the filters, all masses in EXPOLIS were corrected according to eq 1:

\[ \Delta b = V_f \times (\rho_{a2} - \rho_{a1}) \times 10^9 \]  

where \( \Delta b \) is buoyancy correction (\( \mu g \)), \( V_f \) is filter volume (\( m^3 \)), \( \rho_{a2} \) is air density in the post weighing conditions (\( kg/m^3 \)), and \( \rho_{a1} \) is air density in the pre weighing conditions (\( kg/m^3 \)).

Air density was calculated according to eq 2:\n
\[ \rho_a = \frac{3.484 \times P - (0.00252 \times T - 0.02058) \times R.H.}{273.2 + T} \]  

where \( \rho_a \) is air density (\( kg/m^3 \)), \( P \) is atmospheric pressure (kPa), \( T \) is temperature (°C), and \( R.H. \) is relative humidity of air (%).

Buoyancy correction for Mettler MT5 balance was calculated according to eq 3:\n
\[ m = R \times \frac{1 - \rho_a}{\rho_a - \rho_f} \]  

where \( m \) is mass (g), \( R \) is balance display (g), \( \rho_a \) is air density (\( kg/m^3 \)), \( \rho_w \) is calibration weight density (= 8000 kg/m^3), and \( \rho_f \) is density of weighing sample (here a filter; kg/m^3).

The correction according to equation 3 for Mettler MT5 results is needed because of the difference between the filter density and the calibration weight density (8000 kg/m^3). No correction is needed for steel (\( \rho_f = 8000 \) kg/m^3). In general, the need for a buoyancy
correction depends on the balance type and how its internal design responds to the buoyancy effect.

In the weighing room climate, the most powerful factor for the buoyancy (i.e., air density) change is air pressure. The effects of room temperature and relative humidity are much weaker. An example in Table 1 highlights the magnitude of change in the observed (uncorrected) mass reading when the conditions change by +30 mm Hg, +2 °C or +20 % R.H. between pre- and post-weighing of a filter. If all of the factors work toward the same direction (e.g., increase the observed mass), the total effect of the climate change in the weighing room could be up to 10-15 µg.

Table 1. Calculated effects of the changes in the weighing room conditions to the weighted masses caused by the buoyancy effect. In this example, the assumed baseline weighing room climate is $P=740$ mmHg, $R.H.=40\%$, $T=20$ °C, the filter density is 800 kg/m$^3$, PEM and MEM filter masses are 100 mg and 120 mg, respectively.

<table>
<thead>
<tr>
<th>Cond. Change</th>
<th>$\Delta P$ (mmHg)</th>
<th>$\Delta R.H.$ (%)</th>
<th>$\Delta T$ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+30</td>
<td>+20</td>
<td>+2</td>
<td></td>
</tr>
<tr>
<td>Corresponding change in balance reading, µg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37-mm PEM filter</td>
<td>-5.9</td>
<td>+0.25</td>
<td>+1.1</td>
</tr>
<tr>
<td>47-mm MEM filter</td>
<td>-7.1</td>
<td>+0.32</td>
<td>+1.3</td>
</tr>
</tbody>
</table>

It must be underlined here that for a change in relative humidity, this correction only applies for its effect of air buoyancy. Filter mass may also need correction for relative humidity changes because of possible mass changes in hygroscopic particulate matter collected on the filter and also for the hygroscopicity of the filter itself. The need to correct the effects of hygroscopicity will be evaluated and applied as necessary after the fieldwork. Based on hygroscopicity of sulfate, the most abundant hygroscopic compound in most PM$_{2.5}$ samples, however, the hygroscopicity of the sampled mass should not produce significant effects below R.H. 65 %.22
3.3.5 Pilot

Thirteen subjects were included in a pilot study in Helsinki. All laboratory, field, and subject procedures were then performed according to preliminary standard operating procedures (SOPs). Preliminary SOPs were then revised according to these pilot experiences.

3.3.6 Duplicates and Blanks

Duplicates and field blanks were measured to assess the repeatability and detection limits of the PM$_{2.5}$ concentration measurement method (and possible filter contamination). The duplicate and field blank filters were included in the measurements throughout the whole fieldwork, and they were distributed equally between all the microenvironments (home indoor, home outdoor, and work). The number of field blank and duplicate filters was set at 5% of the number of actual sample filters - but no less than 20 filters - to assure statistical value of the results. The average field blank PM$_{2.5}$ mass increase was subtracted from all the exposed PM$_{2.5}$ mass results.

The duplicates were measured using identical monitors sampling side-by-side. The PEM samplers were either carried by the researchers, placed in one location, or included in separate microenvironmental measurements done (e.g., in transportation vehicles, nominally for 24 hr). The MEM duplicates were sampled for about 30 hr at home (indoors and outdoors) and about 15 hr at the work place, depending on the actual schedule of the subject being monitored. The method used here to analyze and report duplicate results was presented in an article by Bland and Altman.$^{23}$

The field blank filters used in EXPOLIS underwent all procedures in the laboratory and the field except that no air was drawn through them. The PEM field blanks were placed in the sampling case, in their filter holders with the protective plugs closed, for the whole sampling period of about 48 hr. The MEM field blanks were applied by using aluminum Y-joint for 48 hr, with one end connected to the EPA-WINS impactor and the other ends connected to two filter holders. Both filter holders were equipped with a filter, but air was drawn through only one.
3.3.7 Weighing

Because the flow rate of PEM was only 4 L/min and the shortest sampling periods only 16 hr, low masses (the lowest with PEM day filters, typically 30-50 µg) could be expected. For that reasons the weighing errors had to be minimized. For this purpose, three pre-field tests were carried out. The effect of static charge on the repeatability of the results was tested. In the first test, five (37-mm Gelman Teflo) filters were weighed 10 times each in a Faraday cage, which is an option in the Mettler MT5 microbalance. Using a Faraday cage eliminates the static charge effects to the weighing results. Also, a 200-mg stainless steel standard weight was measured 17 times with a Faraday cage. The second test was carried out using the small weighing pan, which is normally used in this type of balance. In this test five filters were weighed five times each, and the standard weight was weighed 25 times. The third test was also carried out with the small pan, but both sides of the filters were deionized with a Po-210 deionizer before each weighing.

3.3.8 PEM-MEM Comparison

Because two different types of PM$_{2.5}$ samplers were used in PEM (cyclone) and MEM (impactor) sampling, these two methods had to be tested side-by-side to evaluate PEM and MEM data comparability. This parallel PM$_{2.5}$ sampling test was run for 45 hr inside a laboratory in the city center of Helsinki. In this ‘Helsinki test’, five PEMs, five basic indoor MEMs, three indoor MEMs equipped with a Y-joint, and two outdoor MEMs with a Graseby-Andersen preimpactor were tested in parallel to compare the 4 L/min cyclone-based PEM sampler with a 16.7-L/min, impactor-based MEM sampler.

Additional PEM-MEM comparison tests were carried out indoors and outdoors in Helsinki and Basel. In this ‘inter-center test’. PEMs and MEMs were set side-by-side into a sampling site to test the comparability in different circumstances and different concentration levels. The sampling duration was 24 hr in all but one of these tests, where it was 46 hr.

3.3.9 SOPs

To assure the quality and comparability of the data collected in the different EXPOLIS centers, very detailed SOPs were developed and used for all laboratory, field, and subject procedures. The SOPs of the EPA National Human Exposure Assessment
Survey (NHEXAS)\textsuperscript{24} and the Good Laboratory Practice (GLP) regulations of OECD\textsuperscript{25} as applied in the KTL (National Public Health Institute of Finland) Division of Environmental Health were used as models to develop the SOPs for \textit{EXPOLIS}. The Quality Assurance Unit of KTL - Environmental Health supervised all procedures in this study.

3.4 Results

3.4.1 Pilot

Weighing repeatability for blank filters was poor in the beginning. The main reason proved to be the static charge in the filters. Getting a Po-210 deionizer and using it before each weighing solved the repeatability problem.

PEM characteristics like weight, portability, noise level, capability to run 48 hr with batteries, and overall reliability were tested and proved to be acceptable for measuring personal exposures according to procedures described in the SOPs.

In the first PEM-MEM comparison tests, PEM results were often found to be smaller than MEM results. This problem had to be solved before the field phase. In the PEM filter holder, a leakage between the parts of the plastic filter holder was found, and consequently a fraction of the airflow bypassed the filter. This was observed by sampling the filtered air with an optical particle counter. The fitting joint between the bottom and the center part of the filter holder had to be tightened by compressing the pieces together symmetrically and with force. The joint was taped to avoid any loosening during the field use, especially by the study subjects. The correct procedure, once tested and understood, was easy to learn. After the careful tightening and taping procedure, the PEM and the MEM results were comparable.

Also the timing routines in the MEM proved to be difficult to adapt to the \textit{EXPOLIS} procedure of two consecutive sampling periods in the home indoor, outdoor and workplace. The PQ100 software was then modified by BGI Inc. to meet the \textit{EXPOLIS} needs.
Because of the static charge problem in filter weighing and the PEM filter holder leakage, the mass concentration results for the pilot subjects were not reliable and were not used in any exposure analyses, but only for procedural development.

3.4.2 Duplicates, Blanks, and Detection Limit

The test results after the pilot and some early field phase duplicate results for PEMs and MEMs in Athens, Basel and Helsinki are presented in Figures 3 and 4. The average absolute difference for PEM duplicates was 2.1 μg/m³ and the standard deviation 2.0 μg/m³, and those for the MEM duplicates 0.7 μg/m³ and 0.6 μg/m³, respectively. The measurement precision as median relative standard deviation (RSD)¹⁰ were 6.7% for PEM and 2.3% for MEM.

The field blank filters showed systematic mass increase during the field measurements. The average mass increase and standard deviation in Helsinki were 5.8 μg and 5.1 μg for MEMs (n=74), and 1.8 μg and 4.1 μg for PEMs (n=66).

The detection limit was defined as three times the standard deviation in field blanks divided by the sampled volume (16 m³ for MEM and 4.3 m³ for PEM). The detection limits were 1.0 μg/m³ for MEM and 2.8 μg/m³ for PEM.

3.4.3 Weighing

The three weighing tests show that reducing the effect of static charge on the filters by the manufacturer’s Faraday cage did not produce satisfactory weighing precision, probably because of increased instability (mechanically unstable cage structure) of the whole weighing system (Table 2). When using the standard weighing pan without deionizer, the weighing precision was unacceptable for the filters due to electricity, but it was quite good for the standard weight. The wanted results were achieved when the standard weighing pan was used together with careful deionization. The standard deviation of the repeatedly measured weight of the same filters was then 1.7 μg, which is almost as good as for the standard weight with the pan. The air pressure in the weighing room changed from 729 mm Hg to 773 mm Hg during the field work period in Helsinki. A typical buoyancy correction for weighed filters in Helsinki was ±2.5 μg, with a range of −7 to 13 μg.
Table 2. The standard deviations of the 37-mm Gelman Teflo filters and the stainless steel standard weight when weighing with a Mettler MT5 Faraday cage (‘Faraday’), with a small weighing pan without deionization (‘Pan’) and with a weighing pan using Po-210 deionizer (‘Po’).

<table>
<thead>
<tr>
<th>Weighed object</th>
<th>Faraday</th>
<th>Pan</th>
<th>Pan + Po</th>
</tr>
</thead>
<tbody>
<tr>
<td>37-mm filter</td>
<td>5.9(50)</td>
<td>23(25)</td>
<td>1.7(25)</td>
</tr>
<tr>
<td>Standard weight</td>
<td>3.0(17)</td>
<td>0.9(25)</td>
<td>-</td>
</tr>
</tbody>
</table>

In the beginning of the study, weighing results were entered manually. Because of several data entry errors, the data quality was improved in Helsinki by auto loading the weighing results directly from the balance to a computer using a data transfer software (Balance Link Ver. 2.20) developed by the balance manufacturer (Mettler-Toledo AG, Switzerland).

Figure 3. PM$_{2.5}$ PEM duplicates carried by researchers in Helsinki, Basel, and Athens (n = 18). The average of two samples is set as x-axis value. Absolute average difference between main and duplicate results is 2.1 µg/m$^3$, with standard deviation of 2.0 µg/m$^3$. 
Figure 4. PM$_{2.5}$ MEM duplicates in Helsinki, Basel, and Athens (n = 27). The average of two samples is set as x-axis value. Absolute average difference between main and duplicate results is 0.7 µg/m$^3$, with standard deviation of 0.6 µg/m$^3$.

3.4.4 PEM-MEM Comparison

In the side-by-side ‘Helsinki test’ for all PEM and MEM samplers (N=15), the average observed indoor air PM$_{2.5}$ concentration was 7.1 µg/m$^3$ (RSD=3.0%). For the 5 PEMS, the result was 7.2 µg/m$^3$ (RSD=2.6 %), and for the 10 MEMs 7.0 µg/m$^3$ (RSD=3.1%). The mean difference between the mean of all the samplers and the five PEMS was 0.08 µg/m$^3$ with a standard deviation of 0.19 µg/m$^3$. For the two MEMs with Y-joints the mean was 0.03 µg/m$^3$, with a standard deviation of 0.11 µg/m$^3$, and for the three MEMs with Andersen PM$_{10}$ inlet the mean was 0.15 µg/m$^3$, with a standard deviation of 0.06 µg/m$^3$. For the five indoor MEMs, the mean and standard deviation were -0.16 µg/m$^3$ and 0.25 µg/m$^3$, respectively (Figure 5).

Results of the ‘inter-center test’ of the personal GK2.05 cyclone (PEM) and the EPA-WINS impactor (MEM) in Helsinki and Basel are presented in Figure 6. In some of the tests, there were more MEMs than PEMS side-by-side. Therefore each PEM value is presented against the mean of the MEM values in Figure 6. The mean MEM/PEM ratio
in this test was 1.04. If two outliers, the two highest concentration points, are left out from the analysis the MEM/PEM ratio was 1.02.

3.4.5 SOPs

As a result of all experiences from the laboratory tests and the field pilot, the procedures were reviewed, finalized and written into SOPs. The following SOPs were developed for PM$_{2.5}$ sampling in EXPOLIS:

- **MEM Sampler Positioning and PEM Sampler Carrying SOP** describes how the home indoor, home outdoor, and workplace MEM samplers should be located in various personal and microenvironmental settings; and how the subject should keep the PEM sampler in different circumstances; and how the subject should carry the sampler when moving.

- **PM$_{2.5}$ PEM Sampling SOP** describes the personal PM$_{2.5}$ sampler. It covers the preparation, calibration and use of the PEM sampler, and the field blank and duplicate procedures.

- **PM$_{2.5}$ MEM Sampling (Indoor and Outdoor) SOP** describes the particulate sampler for collecting PM$_{2.5}$ in indoor and outdoor microenvironments. It covers preparation, calibration, and use of the MEM sampler, collection and handling of the samples, and the field blank and duplicate procedures.

- **PM$_{2.5}$ Teflon Filter Analysis SOP** describes the handling of the Teflon filters in the laboratory before and after exposure, including coding for sampling, conditioning and weighing before and after sampling; filter holder preparation; used filter storage; data coding and filing; and quality control.

3.5 Discussion and Conclusions

The methods used in EXPOLIS to determine the human exposures to and microenvironmental concentrations of PM$_{2.5}$, and the quality assurance protocol were developed especially for this project. The methods proved to be reliable and applicable for measuring exposures down to quite low PM$_{2.5}$ concentrations in the different EXPOLIS centers.
Figure 5. PEM-MEM side-by-side comparison for PM$_{2.5}$. Five PEMs were compared to 10 MEMs, 3 (MEMY) with Y-joint and 2 with PM$_{10}$ preimpactor (MEMAnd), and five indoor MEMs (MEMIn) for 45 hr. Figure shows the mean and standard deviations of each sampler type compared to the mean of all the samplers ($n = 15$).

Figure 6. PM$_{2.5}$ concentrations measured with a personal GK cyclone (PEM) compared to a microenvironmental EPA-WINS impactor (MEM) in Basel ($n = 10$) and in Helsinki ($n = 11$). Line shows 1:1 line.
3.5.1 Pilot

The pilot phase proved to be necessary for finalizing the equipment and operating procedures for the *EXPOLIS* fieldwork. The most serious problems solved in the pilot were the portability of the PEM case and its noise prevention. The noise problem was solved by adding noise prevention material in the *EXPOLIS* PEM case, but at the same time the weight of the case increased. Optimization between these two problems was accomplished in the pilot tests. The PEM filter holder leakage was also found and solved in the pilot. After changing the procedure, the study subjects changed the filters without sample losses.

While weighing low net masses, minimizing and correcting for the weighing errors becomes critical. This was achieved by first deionising the filters carefully at both sides just before weighing, correcting the observed filter masses for the buoyancy differences due to changing air density, and ensuring that relative humidity remained below 65% in the filter conditioning and weighing room. According to air buoyancy calculations, it is obvious that better weighing accuracy can be achieved by correcting the effect of air buoyancy mathematically, using non-hygroscopic filters, and keeping the weighing room relative humidity below 65% R.H., than by using the typical climate-controlled room without air buoyancy correction. This observation can save considerable amounts of money when building and operating weighing rooms.

Buoyancy correction is hardly ever reported in the published papers. This correction becomes increasingly important in the future as more studies will be carried out for fine (PM$_{2.5}$) and ultra-fine (PM$_1$) particles with particularly low sample-to-filter mass ratios in personal exposure studies.

3.5.2 Duplicates, Blanks and Detection Limits

PEM duplicate results (Figure 3) show, as expected, larger average difference and standard deviation than MEM duplicates. This could be due to the smaller sampled masses and weaker flow control of the PEM compared with the MEM. It can also be seen that the absolute difference between the duplicate MEM samples does not depend on the concentration level, which is likely to vary between the cities and microenvironments. The same seems to be true also for the PEM samples, although the
duplicates collected at the very low concentrations of 10 μg/m³ or less show very small absolute differences.

The median PM$_{2.5}$ RSDs of EXPOLIS, 2.3% for MEM and 6.7% for PEM, agreed well with the average RSD of THEES$^8$, which was 3.3%. These values were also inside the range reported in PTEAM$^{26}$, 1.7% to 12.7%.

The field blank results show systematic blank filter mass increase, which is about 20% of the corresponding PTEAM$^{10}$ and Dutch study$^{16}$ results. The reason or contents of this increased mass are not known. The standard deviation of this mass increase remains an as yet uncorrectable source of random error, which on average distorts the MEM result by ±0.4 μg/m³ and the PEM result by ±1.0 μg/m³.

3.5.3 PEM-MEM Comparison

Side-by-side PEM-MEM method comparison in Helsinki (Figure 5) shows that the results are repeatable and that there are no systematic differences between the results obtained by the PEM and the MEM sampler with or without Y-joint or outdoor sampling inlet. PEM-MEM comparison test results in Helsinki and Basel (Figure 6) show good agreement between these two methods and thus these monitors and procedures were used in the fieldwork of EXPOLIS. In the THEES study the quality control tests of the “lollipop” method 5 tests side-by-side with the IASI sampler$^{27}$ showed agreement with a correlation coefficient of 0.99 and a regression slope of 1.06$^9$. A slightly better regression slope, 1.04, was achieved in EXPOLIS, and an even better slope, 1.01, was achieved in the Dutch study$^{16}$.

3.5.4 SOPs

Detailed SOPs are essential in all field studies where a number of staff members conduct the same repeated tasks. SOPs are even more essential in multicenter and multinational studies to ensure data quality comparability.

In general the results show that the consistent quality assurance work done at each stage of the PM$_{2.5}$ sampling and filter handling has been necessary and has paid off. Application of the equipment and procedures to EXPOLIS fieldwork is likely to yield reliable results.
3.6 References


5. WHO Working Group on "Classical" Air Pollutants and Health. Update and revision of the Air Quality Guidelines for Europe; WHO Regional Office for Europe: Copenhagen, Denmark, 1995; EUR/ICP/EAHZ 94 05/PB01.


of Toxic & Related Air Pollutants; Air Pollution Control Association: Pittsburgh, PA, 1989.


21. Weighing the Right Way with Mettler Toledo, Mettler Toledo, Greifensee, Switzerland, 1994


4 PERSONAL EXPOSURE ASSESSMENT STUDIES MAY SUFFER FROM EXPOSURE-RELEVANT SELECTION BIAS*

4.1 Abstract

We evaluated exposure-relevant selection bias within the framework of a study on personal air pollution exposure, using traffic data as exposure proxy. Based on random samples of 3000 (Basel) and 2532 (Helsinki) persons, 50 and 250 subjects, respectively, were recruited for direct monitoring and 250 (Basel, Helsinki) for indirect monitoring. In Basel, participants of direct monitoring as compared to non-participants were more likely to live at streets with low traffic volume (49% below 1st quartile vs. 27%). Adjusted for sex, age and nationality, an increase of 100 cars per hour was associated with 14 % less participation (odds ratio (OR): 0.861; 95% CI: 0.731, 1.007). Although in Helsinki, traffic volume was neither significantly related to participation in direct nor indirect monitoring, the point estimates indicate a tendency to decreased participation with increasing traffic intensity at home. We conclude that selection bias regarding exposure-relevant characteristics is likely to occur when recruiting participants for studies including demanding personal exposure assessment. Correction for factors routinely collected may not fully account for exposure-relevant bias. This is of particular importance when using exposure data for modelling population exposure distributions, whereas in epidemiological studies, a reduced range of exposure must not a priori distort the exposure-response relationship.

4.2 Introduction

Non-response and selection bias in population-based studies are well-addressed issues in epidemiological literature.\textsuperscript{1-15} The EXPOLIS (Air Pollution Exposure Distribution within Adult Urban Populations in Europe) study provides one of the first opportunities to investigate this topic within a population-based study on personal air pollution exposure. Personal exposure measurements are often considered as gold standard, since individual activities and exposures in different microenvironments (home, workplace, outdoors, traffic) are taken into account.\textsuperscript{16-20} However, assessing personal exposures is demanding for participants and, subsequently, such studies are prone to selective non-response and modified time-activity patterns during measurements ("Hawthorne effect").\textsuperscript{21-24} Such bias is of particular relevance in two fields of application: on the one hand, exposure assessment is a key element of risk assessment\textsuperscript{25}. Modelled population exposure distributions are often the bases for quantifying population health risks. If the model input (microenvironmental concentrations and time-activity patterns) and validation data (personal exposures) are collected from a biased population sample, the resulting risk estimates are probably biased. On the other hand, researchers may consider to include personal exposure measurements in new epidemiological studies, though in cohort studies, the large population sizes required are rather prohibitive. An indication whether and to what extent bias should be expected from a demanding exposure assessment protocol could facilitate the decision at the point of the study design.\textsuperscript{26}

The EXPOLIS protocol included measurements of personal exposures, home indoor and outdoor and workplace levels of fine particles (particulate matter, PM\textsubscript{2.5}), volatile organic compounds (VOCs) and carbon monoxide (CO) of a total of 500 participants, randomly selected from the adult working-age population of the urban areas Athens, Basel, Grenoble, Helsinki, Milan and Prague. Time-microenvironment-activity-diaries (TMADs) and questionnaire data on home and work environment complete the collected exposure information. The EXPOLIS design and methodology has been described in detail elsewhere.\textsuperscript{27-29}

This work evaluates whether exposure-relevant selection bias has occurred when recruiting EXPOLIS participants. For assessing such bias, some objective measure of
exposure of the target (random) population is needed, though often not available. In
the EXPOLIS centres Basel (Switzerland) and Helsinki (Finland), traffic volume at the
residential address of the random samples could be obtained from the local authorities
and was used as a proxy of traffic-related air pollution exposure. Demographic and
socioeconomic characteristics may also indicate different exposures resulting from
differing exposure-relevant activities (occupation, spare-time) across social classes
and their association with participation status was assessed.

The following questions will be addressed:

- Do EXPOLIS participants represent the target population?
- Is adjustment of exposure data collected within the framework of EXPOLIS required
  and feasible when modelling population exposure distributions of air pollutants?
- What are the major selection trends and predictors of participation in the EXPOLIS
  study?

The data will be discussed under the perspective of (i) assessing population exposure
distributions and their use in risk assessment and (ii) using personal monitoring data in
air pollution epidemiology.

4.3 Methods

4.3.1 Multistage Sampling Process

Figure 1 and 2 illustrate the multistage sampling process applied in EXPOLIS Basel and
Helsinki, respectively. Random samples of 3000 persons in Basel and of 2523 persons
in Helsinki have been drawn from the local civil register to represent the target
population (age 25-55) of EXPOLIS. In Helsinki, random sampling was additionally
restricted to Finnish-speaking residents. A SQ (SQ) on socioeconomic status, home
environment and willingness to participate has been mailed to these random samples.
Subjects indicating to work mostly outside of the area of interest were excluded. We did
not exclude subjects with undeliverable surveys from the random sample, as the targets
of those surveys may be systematically different from other non-respondents. Non-
respondents to the SQ were prompted twice in order to increase response rates and to
Figure 1. EXPOLIS Basel - Multistage sampling process. Collected information, dropouts, resulting sizes of (sub)-samples and trend status are indicated. (SQ = short screening questionnaire; TMAD = time-microenvironment-activity-diary).
Information Collected

• Civil Register
• Traffic Volume

Samples

Random Sample
n=2523 (100%)

SQ delivered
n=2476 (98%)

Responders
n=1871
Response Rate: 74%

Willing Participate
n=1428 (57%)

Contacted by phone
n=634 (25%)

Instructed for
Exposure Sample
n=190 (8%)

Diary Sample
n=234 (9%)

Exposure Sample
n=190 (8%)

Dropouts

SQ not deliverable
(n=47)

SQ not valid
(n=605)

dropped by subject
(n=443)

dropped by study
(n=794)

refusing/not able
(n=188)

diary not returned
(n=22)

Trend Status

1 Not reached

2 Non-responders

3 Not willing

4 Not selected

5 Participants

Volunteers
(n=11)

Figure 2. EXPOLIS Helsinki - Multistage sampling process. Collected information, dropouts, resulting sizes of (sub)-samples and trend status are indicated. (SQ = short screening questionnaire; TMAD = time-microenvironment-activity-diary).
achieve representative samples. From those willing to participate, two subsamples were drawn again at random: one subsample for personal exposure and microenvironmental monitoring plus diary and questionnaire application (direct exposure monitoring sample or exposure sample for short), and the second subsample for diary and questionnaire application without exposure or microenvironmental monitoring (indirect exposure assessment sample or diary sample for short). If a person selected refused or could not be reached after several trials, the subject with the next random number was contacted. In Helsinki, 11 volunteers recruited independently of the EXPOLIS random sample among participants of the ULTRA study were excluded from the current analysis. For technical reasons, recruitment of smokers had to be suspended for a few weeks at the beginning of field work. The general approach of population sampling is described in detail elsewhere.

4.3.2 Traffic Volume as Exposure Proxy

Traffic volume, which we obtained from the local authorities as a proxy of traffic-related air pollution exposure, was linked to the residential addresses of the random samples. In Basel, traffic data was extracted from the noise register, for main arteries based on traffic counts collected in 1994 by 12 continuous and 15 periodical (3 months per year) counting sites, whereas for smaller streets without counting data, standard estimates (21, 31, 41, 51 cars per hour) had been assigned. In Helsinki, traffic volumes are based on traffic counts assigned to 3165 links. Values of the closest link to the residential address were assigned in a Geographic Information System by the Helsinki Metropolitan Area Council. In both cities, several measures of traffic volume were available (Basel: cars / trucks per hour daytime and cars / trucks per hour night-time; Helsinki: vehicles / cars / trucks per hour at morning peak and vehicles / cars / trucks per hour at evening peak). These measures are highly inter-correlated (Basel: r>0.85; Helsinki: r>0.79). We decided to use as a proxy of traffic-related air pollution exposure in Basel „cars per hour daytime“ and in Helsinki „cars per hour at morning peak“. We did a sensitivity analysis and checked whether „trucks per hour daytime“ (Basel) or „trucks per hour at morning peak“ (Helsinki) would yield substantially different results. The traffic volume measures available in the two cities cannot be directly compared since peak measures as available in Helsinki should be expected to be higher than
daytime averages used in Basel. For univariate analysis, "traffic volume" was categorised into quartiles, based on the distributions in the random samples of Basel and Helsinki, respectively.

4.3.3 Representativity of Random and Monitored Samples

Distributions of basic characteristics (sex, age, nationality) of the random samples were compared to available census statistics. To evaluate the representativity of the monitored samples, distributions of demographic (Basel: sex, age, nationality; Helsinki: sex, age), socioeconomic (Basel: years of education; Helsinki: occupational class) and exposure-relevant (Basel and Helsinki: traffic volume at home, active smoking) factors of participants and non-participants were compared.

4.3.4 Impact of Traffic Volume on Participation

The association between traffic volume and completion of the exposure and diary study protocol was assessed in logistic regression models. Crude and adjusted ORs for traffic volume were calculated with adjustment for the available demographic and socioeconomic factors.

4.3.5 Selection Mechanisms

Given the sampling procedure of EXPOLIS (Figure 1 and 2), five levels of participation status could be defined, starting with those not reached at the very beginning (trend status = 1), up to those actually participating (trend status = 5). We conjectured that bias, if it has occurred, may have been enhanced at each step, as each consecutive level was more demanding for participants. We investigated patterns of trend across these participation levels for the major covariates. For continuous variables, $p$ for trend was estimated in linear regression; for categorical variables, we applied the chi-square test for trend (function mhodds in STATA, calculating a one-degree-of-freedom test for trend).

Predictors of responding, willingness to participate and actual participation were identified in logistic regression models. A first model (I) was calculated with the variables available for the random samples (Basel: sex, age, nationality, traffic volume; Helsinki: sex, age, traffic volume). In a second model (II), based on respondents to the
SQ, further potential predictors of willingness and participation were included (Basel: active smoking, educational level; Helsinki: active smoking, occupational class). The fit of the multiple logistic regression models was evaluated by Hosmer-Lemeshow χ² tests with 8 degrees of freedom36.

4.3.6 Data Analysis

Data were extracted from the EADB EXPOLIS Access Database27 and analysed using STATA Statistical Software, StataCorp 1997: Release 5.0 and 6.0 College Station, TX: Stata Corporation, on Windows 95 and Windows NT.

4.4 Results

4.4.1 Resulting Exposure and Diary Samples

Figure 1 shows the sampling steps and resulting subsamples in Basel. A total of 1862 subjects (62.1%) returned the SQ, 626 (33.6% of those answering) immediately after the first mailing, 928 (49.8%) after a first and 308 (16.5%) after a second recall by mail. 404 subjects had to be excluded (mostly empty SQ), resulting in a responders sample (valid SQ) of 1458 subjects (48.6%). Of the 302 subjects who were instructed for the diary study, 282 finally participated (diary sample). All 50 subjects who were enrolled for the exposure sample completed the EXPOLIS protocol. In Helsinki (Figure 2), all returned SQs (1871, 74%) were valid with 1040 (55.6% of those answering) received after the first mailing, 440 (23.6%) after a first recall by mail and 391 (20.9%) were prompted by phone. 234 of 256 subjects instructed for the diary study sent back valid core questionnaires and TMADs and 190 subjects of the Helsinki random sample completed the exposure assessment protocol.

4.4.2 Traffic Volume at the Residential Address

Traffic volume at home was available for 2582 (86%) subjects of the random sample in Basel and for all 2523 subjects in Helsinki, with a median distance to the link of 262 m (90th percentile 559 m, range 2-2597 m). In both cities, traffic counts showed highly skewed distributions (Figure 3). In Helsinki, a larger range (0-4167 cars per hour) and
Figure 3. Distribution of traffic volume (cars per hour) at the residential address of the random samples in Basel (top; daytime, n=2582) and Helsinki (bottom; morning peak, n=2523).
higher mean (692 cars per hour) and median (503 cars per hour) values were observed compared to Basel (0-2051, 247, 101 cars per hour respectively).

### 4.4.3 Representativity of Random and Monitored Samples

Table 1 shows that in Basel, the distributions of sex, age, nationality and city quarter in the random sample are practically identical to the underlying target population. The same is true for Helsinki regarding sex, age, civil status and housing type. In Basel, the proportion of 34% smokers in respondents to the SQ (Table 2A) corresponds to the smoking-prevalence of 33.5% observed for participants of the Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) in 1993\(^37\). The Basel random sample corresponds to 3.4% of the target population, the Helsinki sample to 0.6% of the Finnish-speaking population aged 25-55.

**Table 1. Distributions of demographic factors and city quarter in the population of Basel, the EXPOLIS target population (age 25-55) and the Basel random sample in 1996.**

<table>
<thead>
<tr>
<th>Population</th>
<th>Target Population</th>
<th>Random Sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>City of Basel (n=175,911)</td>
<td>EXPOLIS Basel (n=88,518)</td>
<td>EXPOLIS Basel (n=3000)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>83,348</td>
<td>44,683</td>
</tr>
<tr>
<td>Female</td>
<td>92,563</td>
<td>43,835</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td>na</td>
<td>33,375</td>
</tr>
<tr>
<td>35-44</td>
<td>na</td>
<td>29,187</td>
</tr>
<tr>
<td>45-55</td>
<td>na</td>
<td>25,956</td>
</tr>
<tr>
<td>Nationality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swiss</td>
<td>125,863</td>
<td>na</td>
</tr>
<tr>
<td>Non-Swiss</td>
<td>50,048</td>
<td>na</td>
</tr>
<tr>
<td>City Quarter (b)</td>
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<td></td>
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<tr>
<td>Altstadt</td>
<td>18,309</td>
<td>na</td>
</tr>
<tr>
<td>Grossbasel West</td>
<td>56,563</td>
<td>na</td>
</tr>
<tr>
<td>Grossbasel Ost</td>
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<td>na</td>
</tr>
<tr>
<td>Kleinbasel</td>
<td>52,018</td>
<td>na</td>
</tr>
</tbody>
</table>

\(a\) Data from: Statistisches Jahrbuch des Kanton Basel-Stadt, Statistisches Amt des Kantons Basel-Stadt (Editor), 1997.

\(b\) Random sample: 30 missing values.

na: Data not available.
Table 2A reveals that in Basel, participants of the demanding exposure study as compared to those not participating in direct monitoring are more likely to live at streets with low traffic volume (1st quartile: 49% vs. 27%), to be Swiss (82% vs. 68%) and have rather higher shares of females (56% vs. 49%) and of subjects older than 34 years (72% vs. 64%). The proportion of smokers in the exposure sample is clearly smaller with respect to respondents to the SQ who did not participate in direct exposure monitoring (16% vs. 35%) and the education level is rather higher (>14 years of education: 63% vs. 50%). Differences between the diary group and those not participating in the diary-only study are similar to those described for the exposure group, though traffic volume quartiles are more evenly distributed across diary-participants.

In Helsinki (Table 2B), no significant differences of the observed characteristics could be identified between the exposure sample and the target population, except maybe for occupational class. In contrast, the diary sample is biased with a clearly higher share of females compared to non-participants (62% vs. 52%) and lower traffic volume (1st quartile: 30% vs. 25%) as well as higher proportions of lower white-collar employees (43% vs. 33%) compared to respondents to the SQ not participating in the diary study.

### 4.4.4 Traffic Volume and Participation

In Basel, an increase of 100 cars per hour during daytime on the adjacent street to the residence was associated with 15% (95% CI: 0.5-28%) less participation in the exposure study (Table 3A, model I). Adjustment for sex, age and nationality did not substantially change the estimate, despite the small sample size. The impact of traffic volume on participation in the diary study is less pronounced. With respondents to the SQ as reference (model II), the association of traffic volume with participation in both, the exposure and diary study, was attenuated compared to model I, though still in the same direction. Further adjustment for education and active smoking reduced the impact of traffic volume on participation in the exposure study. No association could be seen for the diary study. In Helsinki (Table 3B), traffic volume was not significantly associated with participation in both, the exposure and diary studies. Adjustment for sex and age in model I and additionally for occupational class and smoking in model II did not substantially change the estimates for traffic volume. Replacing *cars* per hour by *trucks*
Table 2. (A) EXPOLIS Basel: Distributions of demographic, socioeconomic and exposure-relevant characteristics of subsamples compared to the random sample and responders of the short screening questionnaire (SQ).

<table>
<thead>
<tr>
<th></th>
<th>Exposure participants</th>
<th>Diary participants</th>
<th>Willing to participate</th>
<th>Responders SQ</th>
<th>Total random sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>p^a</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Demographic (n Random=3000)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
<td>44</td>
<td>0.354</td>
<td>128</td>
<td>45</td>
</tr>
<tr>
<td>Female</td>
<td>28</td>
<td>56</td>
<td>0.012</td>
<td>154</td>
<td>55</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd quartile (42-101)</td>
<td>9</td>
<td>22</td>
<td>0.015</td>
<td>60</td>
<td>25</td>
</tr>
<tr>
<td>3rd quartile (102-370)</td>
<td>7</td>
<td>17</td>
<td>0.006</td>
<td>60</td>
<td>25</td>
</tr>
<tr>
<td>4th quartile (371-2051)</td>
<td>5</td>
<td>12</td>
<td>0.005</td>
<td>51</td>
<td>21</td>
</tr>
<tr>
<td><strong>Active smoking (n Responders=1452)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>16</td>
<td>0.006</td>
<td>77</td>
<td>27</td>
</tr>
<tr>
<td>No</td>
<td>42</td>
<td>84</td>
<td>&lt;0.001</td>
<td>204</td>
<td>73</td>
</tr>
<tr>
<td><strong>Education (n Responders=1370)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10 yrs (mandatory school)</td>
<td>3</td>
<td>6</td>
<td>0.208</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>11-13 yrs (apprenticeship)</td>
<td>15</td>
<td>31</td>
<td>&lt;0.001</td>
<td>98</td>
<td>36</td>
</tr>
<tr>
<td>14-17 yrs (A-levels)</td>
<td>18</td>
<td>37</td>
<td>&lt;0.001</td>
<td>89</td>
<td>32</td>
</tr>
<tr>
<td>&gt;17 yrs (university) d</td>
<td>13</td>
<td>26</td>
<td>&lt;0.001</td>
<td>73</td>
<td>27</td>
</tr>
</tbody>
</table>

^a Chi-square-test (exposure vs. non-exposure, diary vs. non-diary, willing vs. non-willing, responders SQ vs. non-responders SQ, respectively).

^b Quartiles based on distribution in the random sample. ^c Data available from responders only.

^d Including full-time students with missing value for years of education. N/A = not applicable.
Table 2. (B) EXPOLIS Helsinki: Distributions of demographic, socioeconomic and exposure-relevant characteristics of subsamples compared to the random sample and responders of the SQ.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Exposure participants</th>
<th>Diary participants</th>
<th>Willing to participate</th>
<th>Responders SQ</th>
<th>Total random sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>p&lt;sup&gt;a&lt;/sup&gt;</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Demographic</strong></td>
<td>(n Random=2523)</td>
<td></td>
<td></td>
<td>(n Random=2523)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.577</td>
<td>0.005</td>
<td>&lt;0.001</td>
<td>0.505</td>
<td>0.575</td>
</tr>
<tr>
<td>Male</td>
<td>86</td>
<td>45</td>
<td></td>
<td>90</td>
<td>38</td>
</tr>
<tr>
<td>Female</td>
<td>104</td>
<td>55</td>
<td></td>
<td>144</td>
<td>62</td>
</tr>
<tr>
<td>Age</td>
<td>25-34</td>
<td>61</td>
<td>0.005</td>
<td>32</td>
<td>62</td>
</tr>
<tr>
<td>35-44</td>
<td>66</td>
<td>35</td>
<td></td>
<td>66</td>
<td>28</td>
</tr>
<tr>
<td>45-55</td>
<td>63</td>
<td>33</td>
<td></td>
<td>86</td>
<td>37</td>
</tr>
<tr>
<td><strong>Traffic volume</strong></td>
<td>(n Random=2523)</td>
<td></td>
<td></td>
<td>(n Random=2523)</td>
<td></td>
</tr>
<tr>
<td>Cars/h&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.901</td>
<td>0.062</td>
<td>0.001</td>
<td>0.901</td>
<td>0.062</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; quartile (&lt;247)</td>
<td>52</td>
<td>27</td>
<td></td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>2&lt;sup&gt;nd&lt;/sup&gt; quartile (248-503)</td>
<td>46</td>
<td>24</td>
<td></td>
<td>67</td>
<td>29</td>
</tr>
<tr>
<td>3&lt;sup&gt;rd&lt;/sup&gt; quartile (504-856)</td>
<td>47</td>
<td>25</td>
<td></td>
<td>46</td>
<td>20</td>
</tr>
<tr>
<td>4&lt;sup&gt;th&lt;/sup&gt; quartile (859-4167)</td>
<td>45</td>
<td>24</td>
<td></td>
<td>51</td>
<td>22</td>
</tr>
<tr>
<td><strong>Active smoking</strong></td>
<td>(n Responders=1866)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>(n Responders=1850)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>52</td>
<td>27</td>
<td>0.688</td>
<td>0.166</td>
<td>0.026</td>
</tr>
<tr>
<td>No</td>
<td>138</td>
<td>73</td>
<td></td>
<td>176</td>
<td>75</td>
</tr>
<tr>
<td><strong>Occup. class</strong></td>
<td>(n Responders=1850)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>(n Responders=1850)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Entrepreneur</td>
<td>16</td>
<td>8</td>
<td>0.042</td>
<td>0.015</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Upper white collars</td>
<td>54</td>
<td>29</td>
<td></td>
<td>61</td>
<td>26</td>
</tr>
<tr>
<td>Lower white collars</td>
<td>66</td>
<td>35</td>
<td></td>
<td>100</td>
<td>43</td>
</tr>
<tr>
<td>Blue collar/workers</td>
<td>35</td>
<td>19</td>
<td></td>
<td>37</td>
<td>16</td>
</tr>
<tr>
<td>Students</td>
<td>9</td>
<td>5</td>
<td></td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Other (including retired)</td>
<td>9</td>
<td>5</td>
<td></td>
<td>18</td>
<td>8</td>
</tr>
</tbody>
</table>

<sup>a</sup>Chi-square-test (exposure vs. non-exposure, diary vs. non-diary, willing vs. non-willing, responders SQ vs. non-responders SQ, respectively).

<sup>b</sup>Quartiles based on distribution in the random sample.

<sup>c</sup>Data available from responders only.

N/A=not applicable.
Table 3. (A) EXPOLIS Basel: Impact of traffic volume at home (crude and adjusted odds ratios), demographic characteristics, education level and smoking status on responding and participation status.

<table>
<thead>
<tr>
<th></th>
<th>Exposure participants (^a) (n=41)</th>
<th>Diary participants (^a) (n=242)</th>
<th>Willing to participate (^a) (n=471)</th>
<th>Responders SQ (^a) (n=1249)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td><strong>I Basis random sample (n=2582)(^b)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>per 100 cars/h</td>
<td>0.849 (0.725, 0.995)</td>
<td>0.968 (0.922, 1.017)</td>
<td>0.951 (0.916, 0.988)</td>
<td>0.948 (0.922, 0.974)</td>
</tr>
<tr>
<td>Multivariate model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>per 100 cars/h</td>
<td>0.861 (0.736, 1.007)</td>
<td>0.988 (0.941, 1.037)</td>
<td>0.969 (0.932, 1.006)</td>
<td>0.961 (0.934, 0.989)</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.137 (0.611, 2.116)</td>
<td>1.189 (0.907, 1.558)</td>
<td>1.097 (0.893, 1.347)</td>
<td>1.203 (1.024, 1.412)</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.169 (0.820, 1.665)</td>
<td>1.050 (0.901, 1.224)</td>
<td>0.999 (0.889, 1.124)</td>
<td>1.067 (0.973, 1.170)</td>
</tr>
<tr>
<td>Swiss nationality</td>
<td>1.844 (0.843, 4.033)</td>
<td>6.711 (4.116, 10.944)</td>
<td>4.795 (3.543, 6.490)</td>
<td>3.033 (2.543, 3.617)</td>
</tr>
<tr>
<td><strong>II Basis responders (n=1147)(^c)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude estimate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>per 100 cars/h</td>
<td>0.879 (0.746, 1.037)</td>
<td>0.985 (0.933, 1.040)</td>
<td>0.976 (0.934, 1.021)</td>
<td>N/A</td>
</tr>
<tr>
<td>Multivariate model</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>per 100 cars/h</td>
<td>0.891 (0.757, 1.048)</td>
<td>1.000 (0.946, 1.056)</td>
<td>0.991 (0.946, 1.037)</td>
<td>N/A</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.181 (0.598, 2.334)</td>
<td>1.145 (0.845, 1.551)</td>
<td>1.040 (0.808, 1.337)</td>
<td>N/A</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>1.282 (0.863, 1.903)</td>
<td>1.088 (0.912, 1.298)</td>
<td>1.047 (0.904, 1.213)</td>
<td>N/A</td>
</tr>
<tr>
<td>Swiss nationality</td>
<td>0.839 (0.359, 1.962)</td>
<td>3.184 (1.884, 5.380)</td>
<td>2.469 (1.723, 3.536)</td>
<td>N/A</td>
</tr>
<tr>
<td>per year of education(^d)</td>
<td>1.097 (1.008, 1.194)</td>
<td>1.089 (1.045, 1.135)</td>
<td>1.093 (1.056, 1.131)</td>
<td>N/A</td>
</tr>
<tr>
<td>Non-smoking</td>
<td>3.168 (1.219, 8.231)</td>
<td>1.433 (1.033, 1.987)</td>
<td>1.264 (0.971, 1.644)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

\(^a\)Overlapping samples: non-exposure=0, exposure=1; non-diary=0, diary=1; non-willing=0, willing=1; non-responders SQ=0, responders SQ=1, respectively.

\(^b\)With traffic volume available (418 missing).

\(^c\)With traffic volume, valid years of education and valid active smoking available.

\(^d\)Missing value for 24 (of 40) full time students (in responders sample).

N/A=not applicable.
Table 3. (B) EXPOLIS Helsinki: Impact of traffic volume at home (crude and adjusted odds ratios), sex, age, occupational class and smoking status on responding and participation status.

<table>
<thead>
<tr>
<th></th>
<th>Exposure participants a</th>
<th>Diary participants a</th>
<th>Willing to participate a</th>
<th>Responders SQ a</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=190)</td>
<td>(n=234)</td>
<td>(n=1428)</td>
<td>(n=1871)</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
</tbody>
</table>

I Basis random sample (n=2523)

- **Crude estimate**
  - per 100 cars/h: 0.992 (0.970, 1.014) 0.992 (0.972, 1.013) 0.978 (0.968, 0.990) 0.985 (0.973, 0.998)

- **Multivariate model**
  - per 100 cars/h: 0.992 (0.970, 1.014) 0.992 (0.972, 1.012) 0.978 (0.967, 0.989) 0.985 (0.973, 0.997)
  - Female sex: 1.090 (0.809, 1.467) 1.484 (1.126, 1.956) 1.573 (1.342, 1.844) 1.658 (1.384, 1.987)
  - Age (per 10 years): 1.007 (0.851, 1.192) 1.021 (0.876, 1.191) 1.068 (0.976, 1.170) 1.275 (1.150, 1.414)

II Basis responders (n=1871)b

- **Crude estimate**
  - per 100 cars/h: 0.996 (0.974, 1.019) 0.996 (0.976, 1.017) 0.978 (0.963, 0.993) N/A N/A N/A

- **Multivariate model**
  - per 100 cars/h: 0.998 (0.975, 1.020) 0.998 (0.978, 1.019) 0.978 (0.963, 0.993) N/A N/A N/A
  - Female sex: 0.987 (0.692, 1.323) 1.183 (0.875, 1.599) 1.184 (0.938, 1.494) N/A N/A N/A
  - Age (per 10 years): 0.960 (0.803, 1.147) 0.938 (0.798, 1.102) 0.902 (0.795, 1.023) N/A N/A N/A
  - Occupational classc
    - Upper white collars: 0.873 (0.478, 1.592) 1.237 (0.653, 2.343) 0.955 (0.577, 1.583) N/A N/A N/A
    - Lower white collars: 0.776 (0.426, 1.414) 1.448 (0.774, 2.708) 0.936 (0.568, 1.540) N/A N/A N/A
    - Blue collar/workers: 0.722 (0.383, 1.362) 0.992 (0.507, 1.943) 0.515 (0.312, 0.852) N/A N/A N/A
    - Student: 0.882 (0.358, 2.172) 0.539 (0.180, 1.611) 1.890 (0.787, 4.538) N/A N/A N/A
    - Other: 0.286 (0.121, 0.673) 0.731 (0.343, 1.559) 0.512 (0.299, 0.875) N/A N/A N/A
    - Non-smoking: 1.002 (0.708, 1.417) 1.149 (0.832, 1.588) 1.126 (0.886, 1.433) N/A N/A N/A

aOverlapping samples: non-exposure=0, exposure=1; non-diary=0, diary=1; non-willing=0, willing=1; non-responders SQ=0, Responders SQ=1, respectively.

bWith valid occupational class and active smoking available.

cReference=entrepreneur

N/A=not applicable.
per hour for sensitivity analysis in both cities did not yield substantially different results, neither in univariate comparison nor in logistic regression models.

### 4.4.5 Selection Mechanisms

Table 4 reveals consistent and significant selection trends across the five trend categories in Basel and Helsinki. Overall, in both cities, selection bias can be observed towards females, older age groups, lower traffic volume (1st quartile) and, in Basel, towards Swiss nationals. Those with undeliverable surveys have clearly the lowest share of females, lowest mean age, highest traffic volume and, in Basel, the highest share of non-Swiss nationals of all trend categories. With respondents to the SQ as reference, increasing proportions of non-smokers and subjects with higher socioeconomic status were observed from those not willing over those not selected to pooled participants.

In Basel, after adjustment for traffic volume, sex and age, Swiss nationals were about three times more likely to respond, five times more likely to be willing to participate, seven times more likely to successfully participate in the diary study and twice as likely to complete the exposure protocol (Table 3A, model I). However, the ORs probably overestimate the associations as it is well known for prevailing conditions. The more appropriate (crude) risk ratio for example of responding of a Swiss national would be 1.97. In Model II (based on respondents to the SQ), the (adjusted) estimate for Swiss nationality was reduced by about 50% for willingness to participate and participation in the diary and exposure sample, whereas the estimates for traffic volume, sex and age remained stable. Per year of education subjects were about 10% more willing to participate and actually participating in direct and indirect monitoring. Smoking status did not show a clear impact on the willingness to participate, whereas non-smokers were 1.4 times (95% CI: 1.03, 1.99) more likely to actually participate in the diary and three times (95% CI: 1.2, 8.2) more likely to participate in the exposure study. In Helsinki (Table 3B, model I) traffic volume (OR: 0.985; 95% CI: 0.973, 0.997), female sex (OR: 1.658; 95% CI: 1.384, 1.987) and age (OR: 1.275; 95% CI: 1.150, 1.414) were independent and significant predictors of responding. For willingness to participate, similar associations with traffic volume and female sex were observed. Additionally adjusted for occupational class and smoking status, traffic volume was still associated with willingness to participate (model II).
Table 4. Selection trends across the multistage sampling process in Basel and Helsinki for demographic, socioeconomic and exposure-relevant factors.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Not reached (undeliverable survey)</th>
<th>Non-responders (SQ not valid)</th>
<th>Not willing (dropped by subject)</th>
<th>Not selected (dropped by study)</th>
<th>Participants (pooled diary and exposure)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basel (n=3000)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females (%)</td>
<td>49.5</td>
<td>39.4</td>
<td>47.9</td>
<td>51.8</td>
<td>46.5</td>
<td>54.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>39.3</td>
<td>35.7</td>
<td>39.1</td>
<td>39.6</td>
<td>39.2</td>
<td>40.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Swiss nationals (%)</td>
<td>68.6</td>
<td>45.5</td>
<td>57.9</td>
<td>77.1</td>
<td>84.5</td>
<td>91.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Traffic volume</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st quartile (&lt;41 cars/h) (%)</td>
<td>27.4</td>
<td>21.5</td>
<td>23.6</td>
<td>30.9</td>
<td>37.5</td>
<td>32.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4th quartile (&gt;370 cars/h) (%)</td>
<td>24.9</td>
<td>28.1</td>
<td>27.7</td>
<td>22.7</td>
<td>19.2</td>
<td>19.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-smokers (%)</td>
<td>65.8</td>
<td>N/A</td>
<td>N/A</td>
<td>62.9</td>
<td>65.9</td>
<td>74.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean education (years)</td>
<td>14.0</td>
<td>N/A</td>
<td>N/A</td>
<td>13.5</td>
<td>14.6</td>
<td>15.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Helsinki (n=2523)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Females (%)</td>
<td>52.8</td>
<td>40.4</td>
<td>43.6</td>
<td>53.9</td>
<td>56.6</td>
<td>58.5</td>
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<tr>
<td>Mean age (years)</td>
<td>39.6</td>
<td>36.9</td>
<td>38.2</td>
<td>40.6</td>
<td>39.8</td>
<td>39.7</td>
<td>0.005</td>
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<td>Traffic volume</td>
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<tr>
<td>1st quartile (&lt;247 cars/h) (%)</td>
<td>25.2</td>
<td>12.8</td>
<td>24.0</td>
<td>23.9</td>
<td>25.9</td>
<td>28.8</td>
<td>0.018</td>
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<tr>
<td>4th quartile (&gt;859 cars/h) (%)</td>
<td>24.9</td>
<td>27.7</td>
<td>26.6</td>
<td>26.0</td>
<td>23.6</td>
<td>22.6</td>
<td>0.070</td>
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<tr>
<td>Non-smokers (%)</td>
<td>71.4</td>
<td>N/A</td>
<td>N/A</td>
<td>68.0</td>
<td>72.7</td>
<td>74.1</td>
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<td>Occupational class</td>
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<td></td>
<td></td>
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<td></td>
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<tr>
<td>Upper white collars (%)</td>
<td>24.8</td>
<td>N/A</td>
<td>N/A</td>
<td>21.5</td>
<td>26.2</td>
<td>27.2</td>
<td>0.024</td>
</tr>
<tr>
<td>Lower white collars (%)</td>
<td>34.0</td>
<td>N/A</td>
<td>N/A</td>
<td>30.5</td>
<td>34.1</td>
<td>39.2</td>
<td>0.003</td>
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<tr>
<td>Blue collar/worker (%)</td>
<td>19.0</td>
<td>N/A</td>
<td>N/A</td>
<td>24.6</td>
<td>15.4</td>
<td>17.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*aChi-square test for trend.
*bEstimated with linear regression.
*cData available from responders only.
*dMissing value for 24 (of 40) full time students.
*N/A = not applicable
The multiple logistic regression models were found satisfactory according to the Hosmer-Lemeshow \( \chi^2 \) test with 8 degrees of freedom, except for the Basel model with the outcome "participation in the exposure sample" (\( n = 37 \)) based on respondents to the SQ (\( p \chi^2 = 0.06 \)). When excluding two influential observations in this model, the OR for smoking increased from 3.2 (95 %CI 1.2-8.2) to 5.3 (1.6-17.4), whereas the other estimates remained stable and the fit of the model was improved (\( p \chi^2 = 0.31 \)).

4.5 Discussion

We have shown that in EXPOLIS, selection bias has occurred when recruiting participants for this demanding personal exposure assessment study. In Basel, selection trends towards females, older age groups, Swiss nationals, lower traffic volume, higher education level and non-smokers are reflected in biased exposure (direct exposure assessment) and diary (indirect exposure assessment) samples, though not all differences between participants and non-participants were significant, especially for the small exposure sample (\( n=50 \)). The low proportion of smokers in the exposure sample may partially be due to suspended recruiting of smokers at the beginning of field work, but this cannot explain the over-representation of non-smokers in the Basel diary sample. In Helsinki, the exposure sample does not importantly differ from the target population regarding the observed characteristics, while the diary sample shows some clear differences. Although in Helsinki, traffic volume (crude and adjusted estimates) was neither significantly related to participation in the diary nor in the exposure sample, the point estimates and selection trends across the multistage sampling process indicate, similar to Basel, a tendency to decreased participation with increasing traffic intensity at home. As in Basel, selection trends towards females, older age groups and higher socioeconomic classes could be identified.

We evaluated whether the 14% missing traffic data in Basel may have distorted the current analysis. When linking the traffic data\(^3\) to the Basel subjects of an nitrogen dioxide (NO\(_2\)) exposure study conducted in 1993\(^3\), the average NO\(_2\) level at home outdoors of 10 subjects with missing traffic volume was practically identical to the average level of the 92 subjects with traffic volume (TV) available (39 vs. 40 \( \mu \)g/m\(^3\)). The same was true for the Basel EXPOLIS exposure sample (\( N_{TV\text{missing}} = 9 \);
regarding NO\textsubscript{2} (35 vs. 37 μg/m\textsuperscript{3}) and PM\textsubscript{2.5} (18 vs. 20 μg/m\textsuperscript{3}) at home outdoors. Therefore, bias due to missing traffic data seems rather unlikely. In Helsinki, the traffic estimates are probably less valid for subjects with a large distance to the next link. However, excluding those with a distance > 1 km (n=24) and > 0.5 km (n=365) only slightly changed the estimates.

The observed bias regarding demographic and socioeconomic factors is consistent with reports on non-response and selection bias in epidemiological literature. Survey respondents have been found to be older\textsuperscript{5,6,9,11,14,15,39}, to have higher socioeconomic status\textsuperscript{6,8,11,13,14}, to have higher shares of females\textsuperscript{3,5,39}, non-smokers\textsuperscript{2,5,6,9,13} and, in surveys conducted in Switzerland, Swiss nationals\textsuperscript{10,15}. In contrast, in the large population-based SAPALDIA study, no significant differences regarding sex and smoking prevalence between participants and the target population\textsuperscript{10}, nor regarding age, sex, nationality and smoking status between respondents and non-respondents contacted by phone in one study centre\textsuperscript{8} were found.

In a study on personal exposure to NO\textsubscript{2} (measured with filter-badge monitors, PEM) in the Los Angeles Basin, Spengler et al.\textsuperscript{40} found no evidence for systematic non-participation or dropout by personal or household characteristics due to the random digital dialling process, but compared to the general population participants had lower proportions of males (49% vs. 44%) and a slight (10%) under-representation of blue-collar workers. We are not aware of evaluation of exposure-relevant bias introduced by non-respondents in an exposure assessment study similar to EXPOLIS, though the National Human Exposure Assessment Survey, NHEXAS, is planning to compare demographics of non-participants with census data to determine population sampling bias\textsuperscript{41}.

Helsinki achieved a clearly higher response rate to the SQ (74%) than Basel (49%), although in the Finnish and Swiss centres similar recruiting processes were applied. The Californian Particle Team Study, which has a number of features in common with EXPOLIS, has reported a response rate of 70% to a screening interview\textsuperscript{42}, similar to Helsinki. A review on response rates of selected exposure assessment studies carried out between 1981 and 1990 indicates screening response rates ranging from 66% to 96%.\textsuperscript{30}

In the Swiss EXPOLIS centre Basel, 57% of Swiss nationals but only 29% of non-Swiss
residents did return a valid SQ, indicating that the main selection bias has occurred at this first sampling step. This is reflected in the attenuation by about 50% of the (adjusted) estimates for nationality in model II (based on respondents to the SQ) compared to model I (based on the random sample). In Basel nationality, socioeconomic status and living conditions are closely interrelated, explaining the strong and concurrent selection towards Swiss-nationals and subjects living at streets with low traffic volume. The somewhat reduced effect of traffic volume in model II is consistent with the dropout of non-Swiss nationals between the random and responders sample. Also in Helsinki, the strongest bias seems to have been introduced at the first and easiest step of responding to the SQ. Overall, in both cities, the more demanding exposure sample seems to better represent the target population than the less tedious diary sample. A possible explanation for this paradox might be that participating in direct monitoring, though more demanding, is more attractive than just filling in a diary and questionnaires.

We have evaluated whether in EXPOLIS Basel prompted respondents to the SQ differed from early respondents regarding major characteristics. In fact, the share of non-Swiss nationals was clearly higher in those answering only after the first (22%) and second (34%) recall compared to early respondents to the SQ (11%). Those answering late with a valid SQ also more likely belonged to the lowest education category (≤10 years) than early respondents (early 10%, first recall: 22%, second recall: 24%) and the youngest age group (ages 25-34; early 32%, first recall: 37%, second recall: 35%), whereas no important differences could be observed regarding sex and distributions of traffic volume quartiles. As in particular those under-represented in the monitored samples could be motivated by prompting, the effort of two recalls seems to have been worthwhile and bias may have been somewhat reduced. The potential of recalls to increase response rates of mailed surveys is well documented in the literature. As in EXPOLIS Basel, late respondents as compared to early respondents have been reported to have lower education levels and higher shares of subjects not born in Switzerland.

We cannot rule out, that in Basel, a second recall by phone would have been more efficient than prompting by mail only. However, high expenses for translations would have been necessary to substantially increase the low response rate of non-Swiss
nationals in Basel, where 66 different nations or population groups are living with about equal groups of Italian (7% of random sample), Turkish (4%), Spanish (4%), German (3%) and former-Yugoslavian (3%) citizens. Because non-Swiss residents represent one-third of the population of Basel, we did not exclude them a priori from the random sample, although we expected that language problems may prevent some of them from participating in EXPOLIS, in accordance with a low response rate of non-native speakers in an Australian survey. In Helsinki, with a rather wealthy Swedish speaking community of 6.8%, and only 4.3% other nationals possibly living in deprived areas, potential bias due to language problems is clearly lower than in Basel. Since non-Finnish speakers - and thus persons most likely not to respond - were a priori excluded from random sampling, observable bias may have been attenuate. Thus, the generally weaker association between traffic volume and responding as well as participation in Helsinki is plausible. Moreover, high response rates in Finnish surveys are documented in literature.

A few studies have assessed the validity of traffic density data as exposure proxy and have shown significant associations between distance from trunk roads and personal and residential indoor NO$_2$ levels as well as between total traffic density and NO$_2$ levels inside schools, whereas truck traffic density was in particular a predictor of black smoke concentrations inside schools. In another study, reported traffic intensities were associated with measured front-door NO$_2$ levels at schools. Several studies using traffic density data as exposure proxy have shown consistent health effects of traffic-related air pollution. These findings suggest, that traffic volume at the residential address is a valid exposure proxy of traffic-related air pollution exposure.

We have evidence, that the exposure sample of Basel is biased towards lower traffic volume at home and thus probably lower traffic-related air pollution exposure. This is of particular importance when using exposure data of EXPOLIS for modelling population exposure distributions and, subsequently, for risk assessment. We assessed whether biased exposure data could be corrected by accounting for classic demographic and socioeconomic factors collected in all EXPOLIS centres. In Basel, adjustment for these factors did not completely correct bias regarding traffic volume at home. In contrast, demographic and socioeconomic factors, which may per se stand for differing personal exposures due to differing habits across social classes are independently related to
participation in the exposure and diary study. In particular, exposures at the high end of
the distribution, which are most likely to occur in low socioeconomic classes, may be
under-represented or even missing. This indicates an important drawback for risk
assessment purposes, where information is needed on the full distribution of exposure.25

The low share of smokers in the exposure and diary sample of Basel may also lead to
underestimating passive smoking exposure, as smokers have been reported to have
higher passive smoking exposure compared to non-smokers.58 Boudet et al.21 found
evidence that EXPOLIS participants in Grenoble spent more time at home and less time
in commuting, outdoors and other indoor microenvironments during direct exposure
measurements compared to non-monitoring days. Overall, the Hawthorn effect, the
potentially limited exposure range as well as the small fraction of the population
monitored and the limited age range restrict the generalizability of population exposure
distributions derived from EXPOLIS. Duan and Mage59 propose, in a combined
approach as applied in EXPOLIS with direct (exposure sample) and indirect (diary
sample) exposure assessment, to adjust a biased exposure sample with an unbiased diary
sample and vice versa. At least in Basel, where both, the diary and exposure samples are
biased, such correction would not fully account for distortions. Therefore, input from
external sources will be needed for correcting at least part of the bias in the EXPOLIS
simulation model.27,60

In epidemiological studies on air pollution and health, a reduced range of exposure must
not a priori distort the exposure-response relationship if the slope is constant over the
whole exposure range. The same is true for investigating associations between micro-
environmental concentrations and personal exposure levels and for assessing
determinants of air pollution exposures, though relations between determinants and
personal exposures may be modified across social classes. Still, the best protection,
though not an assurance against bias in population-based studies is a high participation
rate.26 Researchers designing studies in air pollution epidemiology should be aware that
including demanding personal exposure measurements may reduce response rates and
thus enhance bias difficult or even impossible to correct for by available factors. Besides
the described exposure-relevant bias, also unknown bias regarding health outcome
variables may be introduced.
We conclude that selection bias regarding exposure-relevant characteristics is likely to occur when recruiting participants for demanding personal exposure assessment studies. In many urban agglomerations, low socioeconomic status is related to non-response, deprived living situations and probably higher traffic-related exposures. Correction for factors routinely collected in personal exposure and epidemiological studies may not fully account for exposure-relevant bias.

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5 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)

5.1 Abstract

To evaluate the validity of fixed-site fine particle levels as exposure surrogates in air pollution epidemiology, we considered four indicator groups: (1) PM$_{2.5}$ total mass concentrations, (2) sulfur and potassium for regional air pollution, (3) lead and bromine for traffic-related and (4) calcium for crustal particles. Using data from the European EXPOLIS study, we assessed the associations between 48-hr personal exposures and home outdoor levels of the indicators. Furthermore, within-city variability of fine particle levels was evaluated. Personal exposures to PM$_{2.5}$ mass were not correlated to corresponding home outdoor levels (n=44, $r_{Spearman} =0.07$). In the group reporting neither relevant indoor sources nor relevant activities, personal exposures and home outdoor levels of sulfur were highly correlated (n=40, $r_{S}=0.85$). In contrast, the associations were weaker for traffic (Pb: n=44, $r_{S}=0.53$; Br: n=44, $r_{S}=0.21$) and crustal (Ca: n=44, $r_{S}=0.12$) indicators. This contrast is consistent with spatially homogeneous regional pollution and higher spatial variability of traffic and crustal indicators observed in Basel, Switzerland. We conclude that for regional air pollution, fixed-site fine particle levels are valid exposure surrogates. For source-specific exposures, however, fixed-site data are probably not the optimal measure. Still, in air pollution epidemiology, ambient PM$_{2.5}$ levels may be more appropriate exposure estimates than total personal PM$_{2.5}$-exposure, since the latter reflects a mixture of indoor and outdoor sources.

5.2 Introduction

Epidemiological studies conducted in a variety of regions and populations indicate consistent associations between ambient levels of air pollution and health outcomes. Respiratory symptoms, lung function, and mortality have been observed to be related to both short-term\textsuperscript{1,2} and long-term exposures\textsuperscript{2,3}. Long-term effects of ambient air pollution are often investigated in semi-individual studies\textsuperscript{4}. Whereas health outcome and important covariates are measured on the individual level, exposure is assigned on a group or population level, based on fixed-site monitoring data. The causal association of the observed health effects to the measured ambient air pollutant, however, is only plausible, if ambient levels are associated with individual, personal exposures to outdoor air pollutants.

To investigate whether personal exposures to fine particles track ambient particle levels, two designs may be applied: the cross-sectional design, assessing the spatial, between-person association; and the longitudinal design, assessing temporal, within-person associations. Recent reports\textsuperscript{5,6} have shown rather high longitudinal correlation between personal exposure and ambient PM\textsubscript{10} levels within subjects (median $r$ of 0.71 for 37 non-smoking adults with no exposure to environmental tobacco smoke and median $r$ of 0.86 for 13 children). These findings support the use of fixed monitoring data in time-series studies investigating short-term effects of ambient air pollution. In contrast, only low to moderate short-term cross-sectional associations between total personal exposure to fine particle mass and ambient levels have been observed. Pearson correlation coefficients ranged between 0.1 and 0.3\textsuperscript{7-9}. The PTEAM (Particle Total Exposure Assessment Methodology) study\textsuperscript{10} reported somewhat higher correlations for PM\textsubscript{10} when separating daytime ($r$=0.35) and nighttime exposures ($r$=0.62). Overall, these cross-sectional results suggest that ambient levels of fine particles are questionable exposure estimates in cross-sectional epidemiologic studies.

There is an ongoing debate over the most appropriate measure of exposure in air pollution epidemiology, in particular for investigating long-term health effects. The effect of ambient air pollution - the target of clean air regulations - and the effect of indoor air pollution with potentially different health relevance\textsuperscript{11} should be thoroughly
distinguished. A prerequisite to doing so is to disentangle total personal exposure into exposure to air pollution from outdoor sources and exposure related to indoor sources and individual activities. When focusing on personal exposure to particles of outdoor origin, two main determinants should be taken into account: on the one hand, the spatial distribution of the particle mixture across an urban area and across microenvironments; on the other hand, time-activity patterns of individuals, that is, time spent indoors, outdoors, or close to sources such as traffic. For spatially homogeneous components with a penetration factor from outdoor to indoor close to unity, we should expect similar exposures for all inhabitants of an area, irrespective of individual itineraries. In contrast, exposure to spatially heterogeneous components would vary more between persons due to individual time-activity patterns.

So far, research activities have focused on studying personal vs outdoor fine particle mass concentrations. The mass loaded on a filter during personal exposure measurements, however, is a mixture of exposures stemming from indoor and outdoor sources. We provide a novel approach to evaluating the validity of ambient fine particle levels as exposure surrogate in air pollution epidemiology: trace elements were used to distinguish exposures to traffic-related particles (lead and bromine), to regional long-range air pollution (sulfur and potassium), and to crustal particles (calcium).

For the current work, we used data from the Swiss center of the EXPOLIS (Air Pollution Exposure Distribution within Adult Urban Populations in Europe) study in Basel, Switzerland, where 50 participants (age 25-55, males 44%, random sample) have completed the EXPOLIS protocol. The city of Basel is located in northwest Switzerland, at 250 m above sea level, and has about 200'000 inhabitants. The EXPOLIS design and methodology have been described in detail elsewhere\textsuperscript{12-14}. Personal exposures and home outdoor levels of PM$_{2.5}$ mass and elemental concentrations, as well as time-microenvironment-activity-diaries (TMADs) and questionnaire data on home and work environment, have been used. In addition, fine particle mass concentrations (PM$_{4.0}$) of a fixed monitoring site in Basel have been obtained.

These data allowed us to address the following questions:

- Is the daily average of one ambient monitor representative for the fine particle mass concentration level prevailing in the city of Basel on this day?
• Are personal exposures to PM_{2.5} mass concentrations related to ambient fine particle levels measured at home outdoors and at the fixed monitoring site?

• Are total personal exposures to the three groups of indicator elements related to corresponding home outdoor levels of these indicators?

• Are the associations between personal exposures and home outdoor levels stronger for homogeneously distributed indicators of ambient air pollution than for indicators with higher spatial variability?

Basel is one of the study centers of the Swiss cohort study SAPALDIA\textsuperscript{15}, investigating the long-term effects of air pollution in adults. The relevance of the results for such semi-individual study designs will be discussed and the validity of ambient fine particle levels as measures of exposure evaluated.

5.3 Methods

5.3.1 Assessment of Fine Particle Levels

*Measurements of Fine Particle Mass Concentrations.* Table 1 gives a summary of the personal, microenvironmental, and fixed-site fine particle monitoring periods and applied technologies. Personal exposure to PM_{2.5} and home outdoor PM_{2.5} levels were assessed throughout 1997 within the framework of the European EXPOLIS study\textsuperscript{12}. Each participant carried the personal monitor for 48 hr, either from Monday morning to Wednesday morning or from Wednesday evening to Friday evening. The personal monitor was a rigid aluminum briefcase packed with PM_{2.5}, VOC (volatile organic compound), CO and NO\textsubscript{2} samplers. Microenvironmental monitors were placed inside and outside of the participants' homes. Only one participant was monitored at the same time. The 50 monitoring periods were equally spread over the four seasons. In quality assurance tests, the personal and microenvironmental monitors showed reliable performance.\textsuperscript{13}

Ambient PM_{4.0} levels (sampled 2.4 m above ground) of a fixed monitoring station were provided by the Swiss Monitoring Network for Air Pollutants (NABEL).\textsuperscript{16} The site is located in the suburbs of Basel (320 m above sea level, 2 km from city center) and characterized by low building density and low traffic volume. The ambient PM_{4.0} data
Table 1. Sampling periods and technologies of personal, microenvironmental and fixed-site measurements of fine particles and indicator elements.

<table>
<thead>
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<th>Environment</th>
<th>Sampling Periods a</th>
<th>Parameters</th>
<th>Technology</th>
</tr>
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<td>Personal</td>
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<td>PM2.5</td>
<td>BGI-GK2.05 Cyclone/</td>
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<tr>
<td>total</td>
<td>48-hr average b</td>
<td></td>
<td>Buck IH Pump</td>
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<td>workday</td>
<td>2 x 12 hr daytime c</td>
<td>Elements</td>
<td>ED-XRF (X-Lab 2000)</td>
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<tr>
<td>private</td>
<td>2 x 12 hr spare time/ night d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home outdoor</td>
<td>2 x 16 hr over night e</td>
<td>PM2.5</td>
<td>EPA-WINS Impactor/</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PQ 100 Pump</td>
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<td>Fixed-site monitor</td>
<td>daily averages,</td>
<td>PM4.0</td>
<td>ED-XRF (X-Lab 2000)</td>
</tr>
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<td></td>
<td>midnight to midnight</td>
<td></td>
<td>Digital High Volume</td>
</tr>
</tbody>
</table>

aStart, end and cutoff according to individual time schedules.
bFrom Monday morning to Wednesday morning or Wednesday evening to Friday evening.
cStart when subject left home for work and end when subject returned home from work, including commuting.
dStart when subject returned back home from work and end when subject left home for work, including spare time activities.
eProgrammed to start when subject normally returns back home from work and end when subject normally leaves home for work. Not identical to „personal private“.
fEnergy-dispersive X-Ray fluorescence.

From this station were available from March to December 1997 as daily averages (integrated from midnight to midnight), covering the monitoring periods of 38 out of 50 EXPOLIS participants in Basel. Time-weighted averages of the fixed-site levels were calculated to correspond to the home outdoor, personal 48-hr, personal „workday“, and personal „private“ measuring periods. The 48-hr measuring period was spread over 3 calendar days, for example starting on day 1 at about 8:00 a.m. and ending on day 3 at about 8:00 a.m. Time-weighted averages of the fixed monitor concentrations were calculated as follows:

$$\frac{h_{\text{day}1} * c_{\text{day}1} + h_{\text{day}2} * c_{\text{day}2} + h_{\text{day}3} * c_{\text{day}3}}{h_{\text{total}}}$$

where $h_{\text{day}1,2,3}$ is the number of measuring hours on day 1, 2 and 3, respectively; $c_{\text{day}1,2,3}$ is the average concentration of the fixed site monitor on day 1, 2 and 3, respectively; and $h_{\text{total}}$ is the total number of measuring hours. Time-weighted averages corresponding to the home outdoor, personal „private“, and personal „workday“ measuring periods were calculated accordingly.
Elemental Analysis of PM$_{2.5}$ Particles. The elemental composition of the PM$_{2.5}$ particles of the personal exposure and home outdoor measurements was analyzed in the framework of the Elemental Analysis Study in EXPOLIS (EXPOLIS-EAS) by energy-dispersive X-ray fluorescence spectrometry (ED-XRF)$^{17}$ on an X-Lab 2000 device (SPECTRO Analytical Instruments, 1998). Side-by-side measurements of the microenvironmental monitor indicate sufficient precision for the chosen elements with relative standard deviations ranging from 0.034 (Calcium) to 0.048 (bromine). The X-Lab 2000 software calculates for each detectable element on each sample an individual Limit of Detection (LOD). These individual LODs depend on the sample matrix, the sample load, and the elemental composition. For statistical analysis, values < LOD were replaced by one-half LOD.

Comparability of Personal, Home Outdoor and Fixed-site Monitors. Koistinen et al.$^{13}$ have shown in side-by-side tests that the EXPOLIS equipment used for microenvironmental (MEM; PQ100 pump/EPA Wins Impactor) and personal (PEM; Buck IH Pump/BGI-GK 2.05 Cyclone) measurements yield comparable PM$_{2.5}$ results (n=11; mean MEM/PEM ratio: 1.04). The same was true for the indicator sulfur (the only element with MEM and PEM values above the detection limit) in two side-by-side tests, with a mean MEM/PEM ratio of 0.99 (SD: 0.07).

To assess the comparability between fixed-site and home outdoor fine particle measurements, the EXPOLIS-microenvironmental monitor was repeatedly installed at an ambient monitoring site$^{18}$ equipped with the same model of the high-volume PM$_{4.0}$ sampler as the fixed monitoring station$^{16}$. The PM$_{4.0}$ measurements of the high-volume sampler were highly correlated with the PM$_{2.5}$ levels of the EXPOLIS-microenvironmental monitor (n=22, r=0.989, p<0.0001). The latter were, on average, 11% lower than the PM$_{4.0}$ levels of the fixed site monitor (22.3 vs 25.2 µg/m$^3$), which is plausible given the lower 50% cutoff of the EXPOLIS monitor.

In the following sections the term „fine particles“ will be used to refer to both the EXPOLIS PM$_{2.5}$ measurements and the PM$_{4.0}$ levels of the fixed site. However, since the dividing point between fine and coarse particles is between 1 and 3 µm,$^{19}$ particles between 2.5 and 4 µm are predominantly coarse mode particles. Therefore, the major part of the above mentioned mass differences of 11% is probably coarse particles.
5.3.2 Indicators of Air Pollution Exposure

For investigating the validity of ambient PM$_{2.5}$ levels as surrogates for personal exposure to outdoor particles, we distinguished three categories of air pollution: primary traffic-related particles, regional long-range air pollution, and crustal particles. The three categories are associated with the nuclei (aerodynamic diameter <0.1 μm), accumulation (<1 μm) and coarse (>1 μm) particle mode, respectively. The choice of the tracer elements was based on literature and local characteristics (emissions and earth crust). Valid calibration in ED-XRF analysis (r > 0.9) and the availability of sufficient values above the LOD (≥ 50 %) were further criteria. For the three exposure categories the following indicators were considered (Table 2):

**Regional Air Pollution: Sulfur and Potassium.** Sulfur indicates secondary long-range transport particles. Outdoor sources are combustion of coal, oil and wood. Outdoor potassium stems mostly from wood combustion in wintertime. In summer, biological material such as pollen may contribute to potassium levels, though these are rather coarse mode particles and thus less likely to be found on PM$_{2.5}$ samples. Both elements have well-defined indoor sources (S: combustion of coal or wood in fire places; K: cigarette smoke and combustion of biological material, e.g., wood in fire places). Thus, for subjects without those indoor sources or activities, sulfur and potassium may serve as indicators for regional air pollution.

**Traffic-Related Particles: Lead and Bromine.** Lead is still one of the best tracers for traffic-related particles produced by combustion of gasoline, although in Switzerland lead emissions from traffic have been substantially reduced. After the introduction of unleaded gasoline in 1985, they decreased from 1'300 (1980) to 90 tons per year (1995). Bromine is also a compound of gasoline. Primary combustion particles are predominantly found near sources, since nuclei mode particles rapidly combine to form larger accumulation mode particles. In ED-XRF analysis of brake linings commonly in use in Switzerland, lead was quantified in 10 out of 30 types of linings. The concentrations ranged up to 5 wt %. This suggests that lead-containing particles are also produced by abrasion of brakes. Such mechanically generated particles are mostly contained in the coarse fraction.
Table 2. Three categories of air pollution, associated particle mode, indicator elements and outdoor and indoor sources.

<table>
<thead>
<tr>
<th>Category of air pollution</th>
<th>Particle mode</th>
<th>Indicator elements</th>
<th>Outdoor sources</th>
<th>Indoor sources and activities</th>
<th>Excluded in stratified analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional</td>
<td>fine/accumulation</td>
<td>Sulfur (S)</td>
<td>Heating (coal, oil)</td>
<td>Combustion of coal or wood</td>
<td>Grilling &lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1 Long range Secondary</td>
<td>&lt; 1µm</td>
<td>Potassium (K)</td>
<td>Traffic</td>
<td>None</td>
<td>Using wood stove &lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wood combustion</td>
<td>Wood fires</td>
<td></td>
<td>Using fire place &lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>for heating</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traffic-combustion</td>
<td>ultrafine/nuclei</td>
<td>Lead (Pb)</td>
<td>Primary traffic</td>
<td>None</td>
<td>Smoking (sensitivity analysis)</td>
</tr>
<tr>
<td>Primary</td>
<td>&lt; 0.1 µm</td>
<td>combustion</td>
<td>Mechanical abrasion of brakes</td>
<td>None</td>
<td>Smoking (sensitivity analysis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bromine (Br)</td>
<td>Primary traffic</td>
<td>None</td>
<td>Smoking (sensitivity analysis)</td>
</tr>
<tr>
<td>Mechanical</td>
<td>coarse</td>
<td>Calcium (Ca)</td>
<td>Earth crust</td>
<td>Building materials</td>
<td>Smoking (sensitivity analysis)</td>
</tr>
<tr>
<td>3 Crustal Ubiquitous</td>
<td>&gt; 1 µm</td>
<td>Potassium (K)</td>
<td>Re-suspension by traffic</td>
<td>Re-suspension dust</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biological material</td>
<td>Wood combustion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Based on 48hr-recall questionnaire.
<sup>b</sup>Based on TMAD.
Crustal Particles: Calcium. In the region of Basel (Jurassic Plateau), the earth surface predominantly consists of limestone (CaCO₃). Also, most building materials contain calcium, for example, plaster, plaster of Paris, or concrete. Thus, calcium has both major indoor and outdoor sources. In contrast to specific outdoor tracers, outdoor calcium levels are, therefore, not expected to be associated with personal (or indoor) exposures. The crustal element calcium is mainly found in the coarse fraction. It is also related to road dust, which may be resuspended by traffic. Indoors, calcium was found to be related to cooking. Slash burn of wood has been reported to contain 1 wt % of calcium.

5.3.3 Home Outdoor Fine Particle Total Mass vs Fixed Monitoring Site Levels

For assessing the spatial variability of fine particle mass concentrations within the city of Basel, we regressed home outdoor PM₂.₅ levels of EXPOLIS participants - measured at 38 locations within the city of Basel - against the corresponding PM₄₀ levels of the fixed-site monitor. In addition, Pearson correlation coefficients were computed.

5.3.4 Personal PM₂.₅ Total Mass Exposure vs Ambient Fine Particle Levels

For investigating the association between personal exposures to PM₂.₅ mass concentrations and ambient fine particle levels, Pearson correlation coefficients were calculated between the personal „workday“ and personal „daytime“ samples and corresponding time-weighted averages of the fixed-site PM₄₀ levels. In addition, the association between average 48hr-personal exposure and home outdoor PM₂.₅ levels was assessed. This was done for all participants and stratified for particle-relevant indoor sources and activities.

5.3.5 Personal Exposure to Indicator Elements vs Home Outdoors Levels

For all indicator elements, Spearman correlation coefficients were computed for 48-hr personal exposure vs home outdoor levels. Spearman rank correlation was chosen because the estimated coefficients are robust with censored data. In a first step, all subjects with valid home outdoor and total personal exposure levels available were included (n=44). In a next step, for sulfur and potassium, subjects reporting indoor factors and/or activities with known sources for the element were excluded. For lead,
bromine and calcium, not supposed to be associated with smoking, a sensitivity analysis was done by excluding subjects reporting active and/or passive smoking (Table 2).

5.3.6 Data Analysis

Data were extracted from the EADB EXPOLIS Access Database and analyzed using STATA Statistical Software, Release 6.0; StataCorp. on Win NT 4.0, 1997.

5.4 Results

5.4.1 Home Outdoor Fine Particle Total Mass vs Fixed Monitoring Site Levels

Home outdoor PM$_{2.5}$ levels were highly correlated with corresponding, time-weighted PM$_{4.0}$ levels assessed at the fixed monitoring site (n=38, r=0.96, p<0.0001, Figure 1).

![Figure 1. Fine particle mass concentrations. Home outdoor (PM$_{2.5}$) vs time-weighted fixed-site levels (PM$_{4.0}$).](image)

Linear regression also indicates homogeneous distribution of fine particle mass concentrations within the city of Basel (cPM$_{2.5}$home out = -1.67 (95 % CI: -4.1, 0.73) + 0.99 (95 % CI: 0.89, 1.05) * cPM$_{4.0}$fixed). Home outdoor levels were, on average, 9% lower than those measured at the fixed monitoring site (20.0 vs 21.9 $\mu$g/m$^3$). This corresponds to the difference found between the EXPOLIS PM$_{2.5}$ and the fixed-site PM$_{4.0}$ monitor in the side-by-side comparison (see Methods).

5.4.2 Personal PM$_{2.5}$ Total Mass Exposure vs Ambient Fine Particle Levels

In the entire sample, PM$_{2.5}$ mass concentrations of personal „workday“ and „private“ samples were not correlated to corresponding time-weighted PM$_{4.0}$ levels at the fixed-site monitor (Figure 2, left). Excluding samples with reported active and passive
smoking as well as other particle-relevant indoor sources and activities (combustion of solid material, gas heating or cooking, air-conditioning at home or at work, home connected to garage, grilling) did not substantially improve the weak association between personal and ambient fine particle mass concentrations in the remaining small sample (n=12, r=0.21, p=0.51). The same was true for 48 hr total personal exposure vs home outdoor levels (Figure 2, right and Table 3). The median ratio of personal PM$_{2.5}$ exposure to home outdoor concentrations equaled 1.05 when all of the data were included in the analysis. This median ratio dropped to 0.77 when subjects reporting active or passive smoking were excluded from the analysis (Table 3).

5.4.3 Personal Exposure to Indicator Elements vs Home Outdoors Levels

Table 3 shows concentrations of the indicator elements measured on person and at home outdoors for all subjects and stratified by particle-relevant indoor factors and activities. Mean and median personal exposures to sulfur were, on average, lower than corresponding home outdoor concentrations. In contrast, mean and median personal exposures to bromine and calcium were higher than corresponding home outdoor levels. On average, personal lead exposures equaled the home outdoor levels. Personal potassium levels were, on average, higher than home outdoor levels, while the median levels where slightly lower. This could be explained with a few exceptionally high
personal exposures of subjects reporting smoking, grilling or indoor combustion of wood. For all indicator elements, the exclusion of indoor sources and activities did not substantially change the median ratio of personal exposures to home outdoor levels. Total personal exposure to sulfur was significantly correlated with home outdoor sulfur levels (n=44, \( r_{sp}=0.74, \ p<0.0001 \)). For those reporting neither indoor combustion nor grilling, the Spearman correlation coefficient increased to 0.85 (n=40, \( p<0.0001 \)).

![Graph 1](image1.png)

**Figure 3.** Indicators for regional air pollution. Total personal exposures vs home outdoor levels for sulfur (left) and potassium (right) in the strata of those without reporting relevant indoor sources and activities.

![Graph 2](image2.png)

**Figure 4.** Indicators for traffic-related particles. Total personal exposures vs home outdoor levels for lead (left) and bromine (right).
Table 3. Median and mean personal exposures and home outdoor levels, median and mean ratios of individual personal exposure to home outdoor levels (Ratio P48/Ho) and Spearman correlation coefficients (rsp P48 vs Ho) for PM_{2.5} mass and indicator elements.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>n&gt;LOD(^{a})</th>
<th>Total Personal Exposure</th>
<th>Home outdoors</th>
<th>Ratio P48/Ho</th>
<th>Spearman Corr.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>total n</td>
<td>Median</td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>PM_{2.5} - Mass [µg/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>18.0</td>
<td>23.7</td>
<td>17.1</td>
<td>16.7</td>
</tr>
<tr>
<td>no smoking exposure</td>
<td>20</td>
<td>15.4</td>
<td>17.5</td>
<td>13.0</td>
<td>16.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{2.5} - Sulfur [µg/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>2.2</td>
<td>2.7</td>
<td>2.4</td>
<td>3.0</td>
</tr>
<tr>
<td>no indoor/activities</td>
<td>40</td>
<td>2.2</td>
<td>2.5</td>
<td>1.4</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{2.5} - Potassium [ng/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>217.9</td>
<td>400.5</td>
<td>432.2</td>
<td>224.8</td>
</tr>
<tr>
<td>no indoor/activities</td>
<td>15</td>
<td>131.0</td>
<td>208.9</td>
<td>220.5</td>
<td>199.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{2.5} - Lead [ng/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>22.1</td>
<td>22.9</td>
<td>10.9</td>
<td>19.2</td>
</tr>
<tr>
<td>no smoking exposure</td>
<td>20</td>
<td>22.4</td>
<td>22.0</td>
<td>7.4</td>
<td>22.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{2.5} - Bromine [ng/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>7.5</td>
<td>8.1</td>
<td>4.9</td>
<td>4.7</td>
</tr>
<tr>
<td>no smoking exposure</td>
<td>20</td>
<td>6.9</td>
<td>7.0</td>
<td>4.9</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{2.5} - Calcium [ng/m³]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>all</td>
<td>44</td>
<td>193.9</td>
<td>296.5</td>
<td>579.2</td>
<td>82.1</td>
</tr>
<tr>
<td>no smoking exposure</td>
<td>20</td>
<td>218.4</td>
<td>413.3</td>
<td>839.8</td>
<td>75.0</td>
</tr>
</tbody>
</table>

\(^{a}\)Values < detection limit (LOD) replaced by \(\frac{1}{2}\) LOD; SD = Standard deviation.

\(^{b}\)Excluded: active and passive smoking according to Time-Activity-Diary.

\(^{c}\)Excluded: grilling, use of wood-stove and fire place at work and at home, according to 48h retrospective questionnaire.

\(^{d}\)Excluded: as' plus active or passive smoking, according to Time-Activity-Diary, and burning candles, according to 48hr retrospective questionnaire.
(Figure 3, left). In the entire sample, personal potassium levels were weakly correlated to home outdoor levels ($n=44$, $r_{sp}=0.33$, $p=0.03$). In the small group with no smoking exposure (active and passive) and reporting neither indoor combustion nor grilling, the correlation for potassium was rather high and significant ($n=15$, $r_{sp}=0.79$, $p<0.0001$) (Figure 3, right). For the traffic indicators, lead and bromine, personal exposures showed more variability in all strata (Figure 4). When all of the data were included in the analysis, Spearman correlation coefficient between personal exposures and home outdoor for lead and bromine equaled 0.53 ($p<0.001$) and 0.21 ($p=0.16$), respectively, indicating a weak to moderate association. Personal exposures to the ubiquitous element calcium were not associated with home outdoor levels (Figure 5). An exceptionally high personal calcium level (3'910 ng/m$^3$) was found in a subject reporting 1.5 hr of grilling. Excluding this outlier did not improve the association ($n=43$, $r_{sp}=0.16$, $p=0.31$).

5.5 Discussion and Conclusions

Our study shows that the association between short-term outdoor fine particle levels and personal exposures to particles differs, depending on what aspect of particle exposure is considered. Not only should exposure to particles of indoor and outdoor origin be distinguished, but also exposure to regional air pollution, traffic-related particles, and coarse particles. Particularly for ultrafine primary traffic particles, the spatial distribution and time spent in proximity to the source, seem to be important factors.
5.5.1 Spatial Distribution of Ambient PM$_{2.5}$ Mass Concentrations

The high correlation observed between the home outdoor PM$_{2.5}$ levels and the corresponding weighted averages of the fixed-site PM$_{4.0}$ levels suggests that the PM$_{2.5}$ level measured at home outdoors for an EXPOLIS participant represents the fine particle level prevailing in the city of Basel during the 48-hr measuring period of this participant. We conclude that, with regard to PM$_{2.5}$ mass concentrations, the home outdoor monitors may be considered as temporary fixed monitors.

The BRISKA study (Basel Risk Study on Ambient Air), investigating the spatial distribution of different fractions of particulate matter (TSP [total suspended particles], PM$_{10}$, and PM$_{4.0}$) and of their elemental composition, confirms rather homogeneous distributions of fine particle mass concentrations (PM$_{10}$ and PM$_{4.0}$) within the city of Basel. Several other studies in European and American cities have reported homogeneous PM$_{2.5}$ levels, whereas for the coarse fraction and PM$_{10}$, more within-city variability was observed. However, two recent studies reported within-city variability for both PM$_{2.5}$ and PM$_{10}$ in California and Canada.

5.5.2 Indicator Elements: Total Personal Exposure vs Outdoor levels

The contrast of high personal vs outdoor correlation for indicators of regional air pollution and lower correlations for the primary traffic indicators and calcium could at least partly be explained with homogeneous distributions of sulfur and potassium and higher spatial variability of traffic-related and crustal elements within the city of Basel. The BRISKA study could show (with elements analyzed on PM$_{10}$) that, in Basel, sulfur and potassium have in fact quite a homogeneous distribution across the city with high between-site correlation and similar levels across Basel, whereas lead and elemental carbon (another traffic indicator) show higher spatial variability, with somewhat lower between-site correlations and higher levels at high traffic-density sites. Also, calcium showed rather high spatial variability, but the levels were not related to traffic density. Thus, although the total mass of fine particles is rather homogeneous across Basel, the composition of the particles differs between locations. Studies in other European and American cities confirm that sulfates ($SO_4^{2-}$) and/or sulfur are in general the most homogeneous component. The PTEAM study has reported similar contrasts of high personal vs outdoor correlation for PM$_{10}$-sulfur and lower correlations...
for crustal and traffic-related elements (Pb and Br). Other personal exposure studies have consistently observed high personal vs outdoor correlations for SO4\textsuperscript{2-}:\textsuperscript{41,42}

Within the EXPOLIS-EAS study,\textsuperscript{17} the association between home outdoor and indoor levels also has been investigated. Indicators for fine (S) and ultrafine (Pb) mode particles were found to be highly correlated (n=45; r=0.91 and 0.90, respectively). Indoor calcium, though, was not related to outdoor levels. Similarly, Janssen et al.\textsuperscript{43} have reported for classrooms significant indoor vs outdoor correlations of PM\textsubscript{10}-sulfur, bromine, and lead, while elements related to soil (Si, Ti, and Ca), showed lower correlations. This suggests that the composition of ultrafine and fine mode particles found indoors is determined by the local outdoor particle mixture. Consistently, for fine particles, the penetration factor from outdoor to indoor has been estimated to vary between 0.7 and 1.\textsuperscript{44,45} Long et al.\textsuperscript{46} report size-dependent short-term indoor/outdoor ratios with highest values for accumulation mode particles and lower ratios for coarse and ultrafine mode particles. This difference in short-term infiltration might contribute to the observed contrast of the short-term personal vs outdoor associations of the three particle modes. Wallace \textsuperscript{33} has estimated that outdoor air is the major source of indoor particles, though indoor sources and activities add to total indoor levels\textsuperscript{47,48}. Overall, these studies suggest that we are also exposed to outdoor air indoors, where urban populations spend up to 90 percent of their time\textsuperscript{49}.

### 5.5.3 Limitations of the Study

A drawback of the present analysis is the different averaging and starting times for each of the sample types. Therefore, short-term, day-to-day variations of ambient fine particle levels (mainly determined by meteorological factors)\textsuperscript{18} are likely to have introduced some measuring error. We calculated the correlation between the home outdoor levels and the 24-hr average of calendar day 2 of the fixed-site levels, which covers only half of the 48-hr monitoring period of a participant. The correlation coefficient of 0.96 (n=39, p<0.0001) suggests that the error in correlation analysis due to not fully identical measuring periods should be minor for fine particle mass concentrations. For the elements, the possible error cannot be quantified with the available data. However, size-specific particle number measurements at six sites in the city of Basel have revealed that ultrafine particles (<0.1 \textmu m) show clearly more pronounced diurnal patterns (with peak
levels in the morning and evening hours) than accumulation mode particles in the size range between 0.1 and 0.4 μm. Therefore, the error introduced by the study design might be larger for lead and bromine than for sulfur and potassium.

For the fixed monitoring station, the elemental composition of PM$_{4.0}$ was not available; hence, we could not directly assess the between site correlation of the home outdoor locations and the fixed monitor regarding the indicator elements. Another limitation is the small study sample and the rather high shares of samples below detection limit for calcium, lead and bromine. While for such censored data estimates of mean, standard deviation, and regression parameters may be biased, median and Spearman rank correlation yield robust estimates. Furthermore, although the chosen tracers are associated with specific aspects of air pollution, they have, as all elements, multiple sources and are not exclusively found in one or the other particle mode. Finally, this work cannot give evidence about the noxious compounds of fine particles or ambient air pollution.

5.5.4 Validity of Exposure Estimates

Total personal exposure to PM$_{2.5}$ mass concentrations is the sum of community exposure to ambient particles plus individually different exposures to indoor particles and to individual particle producing activities. Therefore, ambient PM$_{2.5}$ mass concentrations may only explain part of the variability of personal PM$_{2.5}$ exposures. The low correlations between personal exposures and ambient fine particle levels observed in the current work and in U.S. personal exposure studies, as well as the phenomenon of a personal cloud of unexplained origin reported for PM$_{10}$ (though not for PM$_{2.5}$), have lead to questions of the validity of ambient air pollution levels as a measure of exposure. In the perspective of air pollution epidemiology, however, a key finding of exposure studies is that sulfur shows a high correlation between personal exposure and outdoor levels. This supports the use of ambient fine particle levels as an indicator of personal exposure to regional air pollution, one of the measures of interest when investigating health effects of ambient air. Nevertheless, our data suggest that there may be substantial measurement error regarding exposure to traffic-related compounds or crustal particles when assigning short-term fixed-site fine particle levels as exposure surrogate to a population. Alternatively, as discussed above, the
weaker associations observed for lead and bromine as compared with sulfur and potassium might be explained by differential measurement errors, resulting from the differing averaging times in EXPOLIS.

In the semi-individual study design, where the Berkson error model applies,\textsuperscript{4} in most cases, for both spatially homogeneous and heterogeneous elements, the point estimate of the observed exposure-response association would be unbiased, provided the monitor is located at a representative site. However, for compounds with high spatial variability, there would be less power to detect an association between exposure and health outcome. Wilson and Sub\textsuperscript{23} have discussed this phenomenon for the fine (PM\textsubscript{2.5}) and coarse particle fraction (PM\textsubscript{2.5-10}).

\textbf{5.5.5 Implications for Long-Term Air Pollution Studies}

We have evidence that fixed-site fine particle levels are valid proxies for population exposure to regional air pollution, predominantly consisting of secondary, long-range particles. These include accumulated traffic-generated particles. For exposures to primary traffic-related particles and to coarse particles, fixed-site data are probably not the optimal surrogate. For improved exposure assessment, one could think of a clever personal monitor that would distinguish particles of indoor and outdoor origin and identify primary traffic-related, secondary long-range and coarse particles. However, this monitor does not (yet) exist. It should also be kept in mind that assessing personal exposures to air pollutants is demanding for participants. Subsequently, such studies are prone to selective nonresponse\textsuperscript{14} and modified time-activity patterns during measurements ("Hawthorne effect")\textsuperscript{57}. Hence, alternatives are needed. Several recent cross-sectional studies have used questionnaire data on traffic exposures or traffic volume at homes\textsuperscript{58-60} and have consistently reported health effects associated with these exposure surrogates. For assessing within-city variability of the pollution mixture, population mean annoyance scores, which have been found to be associated with neighborhood NO\textsubscript{2} levels,\textsuperscript{61} could be used. Promising tools to model source specific exposures are geographic information systems (GIS)\textsuperscript{62}.

We conclude that the concept of total personal exposure as the gold standard, even if measured precisely, may not be appropriate when assessing health effects of ambient air pollution. However, in semi-individual studies, factors associated both with exposure
levels and with health outcomes may act as confounders. For example, this may be the case if low socioeconomic status is related to higher smoking prevalence and higher traffic exposure in deprived neighborhoods. Indoor exposures and individual activities should, therefore, be separately assessed and their impact thoroughly evaluated in sensitivity analysis.63

Although this work cannot give evidence of the noxious compounds of fine particles or ambient air pollution, the insights presented add plausibility to the observed long-term health effects of ambient air pollution, measured at fixed site monitors.

5.6 Implications

Accurate exposure assessment is a key step when investigating the health effects of ambient air pollution and the related public health impact. In cross-sectional analysis, we could show that 48-hr personal exposure to PM$_{2.5}$-sulfur, indicating regional air pollution, is highly correlated to corresponding outdoor PM$_{2.5}$-sulfur levels. For indicators of traffic-related and crustal particles, the associations were weaker. We conclude that epidemiologic studies on long-term effects of air pollution may rely on fixed-site fine particle mass to estimate exposures to regional air pollution. For exposures to primary traffic particles, where spatial variability and proximity to the source are important factors, estimates may be improved with data on traffic exposures.

5.7 References


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6 Validity of Annoyance Scores for Estimation of Long-term Air Pollution Exposure in Epidemiologic Studies*

6.1 Abstract

In air pollution epidemiology, estimates of long-term exposure are often based on measurements made at one fixed site monitor per area. This may lead to exposure misclassification. The present paper validates a questionnaire-based indicator of ambient air pollution levels and its applicability to assess their within-area variability. Within the framework of the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) cross-sectional study (1991), 9,651 participants reported their level of annoyance caused by air pollution on an 11-point scale. This subjective measure was compared with annual mean concentrations of particulate matter less than 10 μm in diameter (PM$_{10}$) and nitrogen dioxide. The impact of individual factors on reported scores was evaluated. Nitrogen dioxide concentrations at home outdoors (measured in 1993), smoking, workplace dust exposure, and respiratory symptoms were found to be predictors of individual annoyance scores. Regression of population mean annoyance scores against annual mean PM$_{10}$ and nitrogen dioxide concentrations (measured in 1993 and 1991, respectively) across areas showed a linear relation and strong correlations (r > 0.85). Analysis within areas yielded consistent results. The observed associations between subjective and objective air pollution exposure estimates suggest, that population mean scores, but not individual scores, may serve as a simple tool for grading air quality within areas. Reported annoyance due to air pollution should be considered an indicator for a complex environmental condition and thus might be used for evaluating the implementation of environmental policies.

6.2 Introduction

Assessment of long-term effects of air pollution on human health strongly depends on epidemiological studies. Whereas long-term health outcomes such as mortality\(^1\) or lung function\(^2\) may be accurately assessed, exposure assignment has inherent limitations in long-term air pollution studies. Exposure estimates are usually based on ambient air pollution levels, measured at fixed monitoring sites. More recent approaches, such as methods for microenvironmental and personal monitoring are feasible for assessing short-term exposure in small population samples,\(^3\) but not for monitoring individual air pollution exposure in large population samples or over longer time periods. Therefore, long-term effects of air pollution exposure are often investigated in studies where health outcome and important covariates are measured on the individual level while exposure is assigned on a group or "écologie" level.\(^4\) The resulting non-differential exposure misclassification in these studies\(^5\) might be reduced if the within-area variability of air pollution levels could be assessed. However, air pollution levels, which are normally measured by some indicator of total ambient air pollution such as particulate matter less than 10µm in diameter (PM\(_{10}\)) or nitrogen dioxide\(^6\), are mostly not available for subareas or neighborhoods, and the health effect assessment relies on an ambient air pollution gradient between study-areas\(^4\). Thus, the question arises as to whether some questionnaire-based estimate may be a useful surrogate for assessing the within-area variability of ambient air quality. The objective of this analysis was to validate an indicator for the complex mixture of air pollutants with questionnaire-based assessment of air-quality by study subjects. Apart from its impact on objective health measures\(^7\), air pollution can also be a source of annoyance. However, annoyance may also depend on individual characteristics of persons, such as their sensitivity, health status, attitude toward traffic or other sources of air pollution, or satisfaction with their living area. Furthermore, the degree of annoyance may vary with the actual context (work-leisure time; day-night). Annoyance due to environmental stressors impairs well-being and is recognized by the World Health Organization as an adverse health effect per se.

Several studies have quantified the relation between the perception of air quality and measured air pollution levels and found consistent associations between reported
annoyance due to air pollution and ambient air pollution\textsuperscript{8-12}. Data from the SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) cross-sectional study\textsuperscript{2,13} offered us the opportunity to further evaluate whether annoyance scores may serve as an indicator for long-term exposure to air pollution.

All SAPALDIA participants reported their annoyance due to air pollution at home. On the other hand, objective measures of air pollution (annual mean values) were available for each area (PM\textsubscript{10}, nitrogen dioxide), for neighborhoods within areas (nitrogen dioxide) and, for a subsample of SAPALDIA participants, for home outdoors (nitrogen dioxide). Thus, SAPALDIA allowed us to address the following questions with a large, representative population:

- Is \textit{individual} annoyance rating of ambient air pollution at home on the Annoyance Scale (described below) a valid surrogate for recent 1-year average home outdoor nitrogen dioxide levels? What is the impact of individual characteristics on the self-reported degree of annoyance?

- Is the \textit{population average} annoyance rating of ambient air pollution on the Annoyance Scale a valid surrogate for air quality in an area characterized by recent annual mean levels of nitrogen dioxide and PM\textsubscript{10}?

- Could the \textit{average} annoyance rating of ambient air pollution on the Annoyance Scale by randomly selected \textit{sub-groups} living in small areas (neighborhoods) be used to estimate differences in 1-year average air pollution levels (nitrogen dioxide) within areas?

The validity and limitations of such an indirect and simplistic but inexpensive exposure assessment tool in air pollution epidemiology will be discussed below.

\section*{6.3 Materials and Methods}

\subsection*{6.3.1 Study Population}

The SAPALDIA cross-sectional study was conducted in 1991. It included 9,651 adult participants aged 18-60 years (49 percent males) from random samples drawn in each area. The method of the SAPALDIA cross-sectional study has been described in detail elsewhere\textsuperscript{13}. The study protocol consisted of a detailed interview and extensive health
examinations. The questionnaire included the assessment of annoyance due to air pollution on an 11-point Annoyance Scale. Eight study areas in Switzerland, representing different conditions of climate, weather, and air pollution, were selected\textsuperscript{14}. They covered three major categories of areas common in Switzerland: urban and suburban areas (Geneva, Basel, Lugano and Aarau), rural areas (Payerne and Wald) and alpine areas (Davos and Montana).

### 6.3.2 Measurements of Air Pollutants

For the present investigation, three sources of air quality data were used.

**Individual-level data.** For a subsample (n = 560) of participants from the SAPALDIA diary study (1992-93), nitrogen dioxide levels had been determined with passive samplers (Palmes tubes)\textsuperscript{15} placed outside their homes in 1993\textsuperscript{16}. These subjects had been randomly selected from the eight study areas and from the neighborhoods within-areas. Based on three measurement periods of 4 weeks each (one monitor per week), annual mean levels of home outdoor nitrogen dioxide-concentrations could be estimated for 400 subjects in this subsample\textsuperscript{17}.

**Across-area variability.** Annual mean PM\textsubscript{10} and nitrogen dioxide levels were determined at one fixed monitoring site of each study area. For nitrogen dioxide, data from 1991 were used; for PM\textsubscript{10} (with no data available in 1991), 1993 data were used\textsuperscript{2-18}. PM\textsubscript{10} level was determined using sharp-cut, low-volume cascade impactors and nitrogen dioxide level was determined with chemiluminescence\textsuperscript{14}.

**Within-area variability.** Within each area, annual mean nitrogen dioxide concentrations were estimated for 6-13 subareas (neighborhoods), based on passive sampler measurements made in 1991\textsuperscript{19}. These neighborhoods, which ranged from 0.5 km to 4 km in diameter, were quite homogenous in terms of topography, type of buildings, construction density, and traffic volume.

### 6.3.3 Measurements of Annoyance

Study subjects self-assessed their degree of annoyance on an 11 point scale referred to as the Annoyance Scale. Possible scores on the scale range from 0 (no disturbance at all) to 10 (intolerable disturbance). The Annoyance Scale has previously been applied for the assessment of annoyance caused by ambient air-pollution\textsuperscript{9-11}. During the
SAPALDIA computer-assisted personal interview, a picture of the Annoyance Scale in the form of a thermometer was presented and the participant was asked, "How much are you annoyed by outdoor air pollution (from traffic and industry) at your actual home, if you keep the windows open?" The participant indicated his or her score and the interviewer directly entered it, rounded to the nearest integer.

6.3.4 Descriptive Analysis

Distribution parameters (mean, median, percentiles) for the Annoyance Scale scores were calculated for all areas. In addition, mean sub-population scores were computed for all neighborhoods. Furthermore, three annoyance categories (low = 0-3, medium = 4-7, high = 8-10) were defined, consistent with previous studies. Their distribution was determined for areas and for neighborhoods within areas. From a public health and regulatory perspective, the percentage of subjects scoring high, i.e., those who are considerably impaired in their well-being, is of particular interest.

6.3.5 Regression Analysis: Annoyance Levels versus Objective Air Pollution Measures

Annoyance Scale scores (individual scores, population mean scores) and scores indicating a high level of annoyance (scores of 8-10) were considered as dependent variables, and objective measures of air pollution exposure were considered as independent variables. The validity of the Annoyance Scale as a surrogate-measure for long-term air pollution exposure was assessed using three different approaches.

Individual perceptions. In a first approach, individual Annoyance Scale scores were regressed against estimates of individual annual mean levels of nitrogen dioxide at home outdoors, based on passive sampler measurements. This approach included 400 individuals who had all data available. For multivariate regression, the following factors were tested as potential predictors of reported levels of annoyance: demographic and socioeconomic factors (sex, age, nationality and educational level); smoking status (never, former or current smoker); the presence of respiratory symptoms and conditions (wheezing without cold, tightness in chest, attacks of shortness of breath, attacks of cough, constant phlegm (day and night), shortness of breath while walking, and asthma); low lung function (values lower than the fifth percentile of reference values for forced expiratory volume in 1 second (FEV₁), mid-expiratory flow (FEF₂₅-₇₅), and FEV₁/forced expiratory volume in 1 second (FEV₁/FEF₂₅-₇₅)).
vital capacity); and indoor exposures (environmental tobacco smoke at home and at work and workplace exposure to dust, gas, vapors, aerosol, smells, noise). In multivariate logistic regression analysis, a "high annoyance" rating (scores of 8-10 on the Annoyance Scale) was considered as an outcome measure.

Population means across areas. In a second approach, population mean scores of reported annoyance were calculated for the eight study areas and were regressed against annual mean PM$_{10}$ and nitrogen dioxide values obtained at the fixed site monitor in each area. First, all SAPALDIA participants were included. In a second step, population mean scores were recalculated based only on subjects ($N = 1,351$) living in the neighborhood where the fixed monitoring site of an area was located.

Sub-population means within areas. In a third approach, population mean scores were calculated for each neighborhood and regressed against estimated annual mean nitrogen dioxide levels (based on measurements made with passive samplers) in the respective neighborhoods.

The fit of the models was evaluated, and the underlying distributional assumptions were examined. Statistical analysis was carried out with the Stata software package$^{21}$.

6.4 Results

Table 1 shows the characteristics of the cross-sectional study population of SAPALDIA. Table 2 shows annual mean PM$_{10}$ and nitrogen dioxide values, as well as population mean annoyance scores for the eight SAPALDIA study areas. In all areas, the attributed scores ranged from 0 to 10. However, score distributions were clearly different between study areas. In the alpine and rural areas, with a median of zero, only a few subjects reported a high level of annoyance (in Montana, the 75th percentile point was 1; in Wald, it was 3; in Davos, 5), whereas in urban areas the median was 4 (Basel, Geneva) or 5 (Lugano) and 75th percentiles points were greater than 7.

6.4.1 Individual Perceptions

The correlation of the individual, subjective annoyance scores with estimates of annual mean levels of nitrogen dioxide at home outdoors ($n = 400$) was rather low ($r = 0.36$), indicating a wide range of individual perceptions at a given level of ambient air quality
Figure 1. Scatterplot of individual Annoyance Scale scores versus estimated nitrogen dioxide (NO₂) levels at home outdoors (annual means) based on passive sampler measurements, Swiss Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) subsample (n = 400).

(Figure 1). In univariate linear regression analysis, nitrogen dioxide level at home outdoors explained 12.6 percent of the Annoyance Scale score variability, with an average increase of 0.92 points per 10 µg per m³ of nitrogen dioxide (Table 3, crude estimate). The multivariate model presented in Table 3 included all further covariates found to have an impact on subjective annoyance grading. Independent of the nitrogen dioxide level, current smokers scored 1.0 points lower (p = 0.01), whereas workplace exposure to dust led to 1.1-point higher scores (p = 0.007). Respiratory health was also found to be a predictor of individual scoring: on average, subjects affected by shortness of breath scored 1.3 points higher (p = 0.013), and those suffering from constant phlegm scored 1.2 points higher (p = 0.045). Average scores of subjects with asthma were 1.3 points lower (p = 0.017). Since, in the alpine areas with low air pollution levels, the
Table 1. Characteristics (%) of the population of the SAPALDIA* cross-sectional study (sex, age, education and nationality†), 1991.

<table>
<thead>
<tr>
<th></th>
<th>Alpine areas</th>
<th>Rural areas</th>
<th>Urban / Suburban areas</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Montana (n=794)</td>
<td>Davos (n=745)</td>
<td>Wald (n=1518)</td>
<td>Payerne (n=1495)</td>
</tr>
<tr>
<td>Male sex</td>
<td>50.8</td>
<td>49.0</td>
<td>49.7</td>
<td>48.2</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>34.8</td>
<td>25.5</td>
<td>32.5</td>
<td>32.3</td>
</tr>
<tr>
<td>36-50</td>
<td>41.0</td>
<td>51.8</td>
<td>43.8</td>
<td>42.3</td>
</tr>
<tr>
<td>51-61</td>
<td>24.2</td>
<td>22.7</td>
<td>23.7</td>
<td>25.4</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>20.8</td>
<td>7.2</td>
<td>14.0</td>
<td>33.7</td>
</tr>
<tr>
<td>Medium</td>
<td>58.9</td>
<td>77.9</td>
<td>74.0</td>
<td>58.3</td>
</tr>
<tr>
<td>High</td>
<td>20.3</td>
<td>14.9</td>
<td>12.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Swiss Nationality</td>
<td>87.3</td>
<td>83.2</td>
<td>90.8</td>
<td>84.4</td>
</tr>
</tbody>
</table>

*SAPALDIA, Swiss Study on Air Pollution and Lung Diseases in Adults.
†For all four factors significant differences in frequency distribution between areas (χ² test, p < 0.02).
Table 2. Objective and subjective measures of ambient air pollution levels in SAPALDIA* study-areas.

<table>
<thead>
<tr>
<th></th>
<th>Alpine areas</th>
<th>Rural areas</th>
<th>Urban / Suburban areas</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Montana</td>
<td>Davos</td>
<td>Wald</td>
<td>Payerne</td>
</tr>
<tr>
<td></td>
<td>(n=794)</td>
<td>(n=745)</td>
<td>(n=1,518)</td>
<td>(n=1,495)</td>
</tr>
<tr>
<td>Levels of air pollutants† (µg/m³)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM₁₀ (1993)</td>
<td>10.4</td>
<td>10.1</td>
<td>16.7</td>
<td>16.9</td>
</tr>
<tr>
<td>Nitrogen dioxide (1991)</td>
<td>9.2</td>
<td>20.4</td>
<td>21.8</td>
<td>23.1</td>
</tr>
<tr>
<td>Annoyance Scale scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.1</td>
<td>2.4</td>
<td>1.9</td>
<td>3.1</td>
</tr>
<tr>
<td>Median</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Level of annoyance‡ (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slightly annoyed</td>
<td>88.9</td>
<td>70.0</td>
<td>77.5</td>
<td>61.9</td>
</tr>
<tr>
<td>Moderately annoyed</td>
<td>7.9</td>
<td>15.8</td>
<td>12.2</td>
<td>24.4</td>
</tr>
<tr>
<td>Highly annoyed</td>
<td>3.2</td>
<td>14.3</td>
<td>10.3</td>
<td>13.7</td>
</tr>
</tbody>
</table>

*SAPALDIA, Swiss Study on Air Pollution and Lung Diseases in Adults.
†Annual mean values (fixed monitoring sites).
‡Slightly annoyed = Annoyance Scale scores of 0-3; moderately annoyed = score of 4-7; highly annoyed = score of 8-10.
Table 3. Coefficients from linear (Annoyance Scale scores) and logistic (high levels of annoyance) regression models (individual level): SAPALDIA* diary study, 1992-1993.

<table>
<thead>
<tr>
<th></th>
<th>Annoyance Scale scores</th>
<th>Highly annoyed†</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β          (95% CI*)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude estimate (n = 400)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>0.40       (-0.39, 1.20)</td>
<td></td>
<td>1.81</td>
<td>(1.48, 2.22)</td>
</tr>
<tr>
<td>NO₂ home outdoors‡</td>
<td>0.92       (0.68, 1.16)</td>
<td>1.72</td>
<td>1.23</td>
<td>(2.42)</td>
</tr>
<tr>
<td>Multivariate Model (n = 399)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>1.08       (-0.64, 2.81)</td>
<td>0.87</td>
<td>0.72</td>
<td>(2.42)</td>
</tr>
<tr>
<td>NO₂ home outdoors‡</td>
<td>0.87       (0.48, 1.25)</td>
<td>1.72</td>
<td>1.23</td>
<td>(2.42)</td>
</tr>
<tr>
<td>Area§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wald</td>
<td>-1.39      (-2.69, -0.09)</td>
<td>0.36</td>
<td>0.10</td>
<td>(1.30)</td>
</tr>
<tr>
<td>Davos</td>
<td>-0.57      (-1.90, 0.77)</td>
<td>0.62</td>
<td>0.18</td>
<td>(2.12)</td>
</tr>
<tr>
<td>Lugano</td>
<td>-1.29      (-2.46, -0.12)</td>
<td>0.60</td>
<td>0.25</td>
<td>(1.42)</td>
</tr>
<tr>
<td>Montana</td>
<td>-1.56      (-3.12, -0.00)</td>
<td>0.22</td>
<td>0.02</td>
<td>(2.02)</td>
</tr>
<tr>
<td>Payerne</td>
<td>-0.45      (-1.77, 0.87)</td>
<td>0.56</td>
<td>0.17</td>
<td>(1.78)</td>
</tr>
<tr>
<td>Aarau</td>
<td>-1.00      (-2.15, 0.15)</td>
<td>0.73</td>
<td>0.30</td>
<td>(1.81)</td>
</tr>
<tr>
<td>Geneva</td>
<td>-2.22      (-3.75, -0.70)</td>
<td>0.29</td>
<td>0.08</td>
<td>(1.05)</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.50       (-0.14, 1.15)</td>
<td>1.31</td>
<td>0.72</td>
<td>(2.38)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>-0.98      (-1.73, -0.22)</td>
<td>0.58</td>
<td>0.29</td>
<td>(1.16)</td>
</tr>
<tr>
<td>Dust exposure work</td>
<td>1.06       (0.28, 1.83)</td>
<td>2.00</td>
<td>1.04</td>
<td>(3.85)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>1.33       (0.28, 2.39)</td>
<td>2.42</td>
<td>1.10</td>
<td>(5.34)</td>
</tr>
<tr>
<td>Phlegm day and night</td>
<td>1.24     (0.03, 2.45)</td>
<td>3.96</td>
<td>1.56</td>
<td>(10.08)</td>
</tr>
<tr>
<td>Asthma $</td>
<td>-1.30      (-2.36, -0.23)</td>
<td>0.34</td>
<td>0.10</td>
<td>(1.14)</td>
</tr>
</tbody>
</table>

*SAPALDIA, Swiss Study on Air Pollution and Lung Diseases in Adults; CI, confidence interval.
†A score of 8-10 on the Annoyance Scale.
‡Change associated with a 10-µg/m³ increment in NO₂ level.
§Reference area = Basel.
$Doctor diagnosed asthma.

The prevalence of asthma was significantly higher compared with the other areas (16.5% vs. 7.6%, χ² 0.004), we conducted a sensitivity analysis excluding the alpine areas. This resulted in only minor changes in the estimates, with a somewhat reduced effect of asthma (β=-1.12, p=0.11). Whereas women tended to score approximately 0.5 points higher than men in all tested models, age, nationality, and educational level could not be identified as significant predictors and/or confounders. In the multivariate model, a 10 µg per m³ increment in nitrogen dioxide level at home outdoors was associated with an average increase in annoyance score of 0.87 points, similar to the crude estimate of 0.92.
Investigation of the model for potential interactions between nitrogen dioxide and the other covariates revealed workplace dust exposure to be an effect modifier. In stratified analysis, persons exposed to dust at work were found to be more sensitive air pollution "graders" (/\beta=1.2 per 10 \mu g/m^3 nitrogen dioxide) than the nonexposed (\beta=0.74). Furthermore, interactions of workplace dust exposure with sex and with phlegm were observed. Men scored 1.7 points higher when exposed to dust at work, whereas for women such exposure had no significant impact on annoyance-scoring (\beta=0.4, p=0.48). The multivariate model presented explains 22 percent of the variance in individual annoyance scores. Nitrogen dioxide-level at home outdoors has the highest share and contributes 7.5 percent, followed by area with 3.1 percent. The other predictors explain between 0.5 percent (phlegm) and 1.5 percent (workplace dust exposure) of the variance.

The assumptions of homoscedascity, independence, and normality of residuals were found to be met. Omitting two influential observations (Annoyance Scale=0, nitrogen dioxide>78 \mu g/m^3) slightly increased both, the observed effects and the total explained variability.

Similar results were obtained from the multivariate logistic regression analysis using the "high annoyance" rating (scores of 8-10 on the Annoyance Scale) as the outcome measure (Table 3). The fit of the model was found to be satisfactory according to the Hosmer- Lemeshow $\chi^2$ (8df).

### 6.4.2 Population Means Across Areas

Figure 2 shows the regression lines between population mean scores of annoyance and annual mean PM$_{10}$ and nitrogen dioxide levels across areas. When all participants in the cross-sectional survey were included for calculation of the population mean Annoyance Scale scores, correlation between measured air pollution levels and subjective assessment of air pollution was high (PM$_{10}$: $r = 0.85$; nitrogen dioxide: $r = 0.88$) (Figure 2, top).

In a next step, only participants living close (in the same neighborhood) to the fixed monitoring site of a study area were selected for calculation of mean annoyance scores (Figure 2, bottom). Correlation between objective and subjective air pollution measures
Figure 2. Mean Annoyance Scale scores (bars, 95% confidence interval) among all participants (top) and among participants living close to the fixed monitoring sites (FMS) (bottom), according to annual mean levels of particulate matter less than 10 μm in diameter (PM$_{10}$) and nitrogen dioxide (NO$_2$) (measured at fixed monitoring sites), for eight areas in the Swiss Study on Air pollution and Lung Diseases in Adults (SAPALDIA), 1991 and 1993. (B1=Basel - St. Johann, B2=Basel-Feldbergstrasse, W=Wald, D=Davos, L=Lugano, M=Montana, P=Payerne, A=Aarau, G=Geneva).
Table 4: Estimated effects (population level) of annual neighborhood mean nitrogen dioxide levels* on neighborhood mean Annoyance Scale scores within each SAPALDIA† area and across all areas.

<table>
<thead>
<tr>
<th>Subjects (n)</th>
<th>Neighborhoods (n)</th>
<th>Range NO₂ [µg/m³]</th>
<th>Range of %highly‡</th>
<th>Change in mean A-Scale scores§</th>
<th>rPearson</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban/Suburban areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geneva</td>
<td>989</td>
<td>9</td>
<td>54-68</td>
<td>14-31</td>
<td>1.04 (0.64, 1.45)</td>
</tr>
<tr>
<td>Lugano</td>
<td>1309</td>
<td>10</td>
<td>38-59</td>
<td>24-43</td>
<td>1.01 (0.61, 1.42)</td>
</tr>
<tr>
<td>Basel</td>
<td>1487</td>
<td>13</td>
<td>29-63</td>
<td>13-38</td>
<td>0.97 (0.65, 1.29)</td>
</tr>
<tr>
<td>Aarau</td>
<td>1293</td>
<td>11</td>
<td>32-49</td>
<td>8-21</td>
<td>0.82 (0.26, 1.39)</td>
</tr>
<tr>
<td>Rural areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Payerne</td>
<td>1495</td>
<td>6</td>
<td>25-39</td>
<td>10-18</td>
<td>0.58 (-0.50, 1.67)</td>
</tr>
<tr>
<td>Wald</td>
<td>1515</td>
<td>12</td>
<td>16-31</td>
<td>0-17</td>
<td>1.36 (0.56, 2.16)</td>
</tr>
<tr>
<td>Alpine areas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davos</td>
<td>741</td>
<td>10</td>
<td>8-29</td>
<td>0-28</td>
<td>0.83 (0.04, 1.63)</td>
</tr>
<tr>
<td>Montana</td>
<td>792</td>
<td>10</td>
<td>13-21</td>
<td>0-6</td>
<td>0.12 (-1.17, 1.41)</td>
</tr>
<tr>
<td>Across all areas</td>
<td>9208</td>
<td>81</td>
<td>8-68</td>
<td>0-43</td>
<td>0.77 (0.67, 0.86)</td>
</tr>
</tbody>
</table>

* estimates based on passive sampler measurements in 1993.
†SAPALDIA, Swiss Study on Air Pollution and Lung Diseases in Adults.
‡Persons with a score of 8-10 on the Annoyance Scale.
§Change associated with a 10-µg/m³ increment in NO₂ level.

was higher than it was with all participants (PM₁₀: r = 0.92; nitrogen dioxide: r = 0.93).

In addition, the change associated with a 10-µg/m³ increment in PM₁₀ or nitrogen dioxide level was higher for participants living close to the fixed site monitor than for all participants (PM₁₀: 1.90 vs. 1.31; nitrogen dioxide: 0.84 vs. 0.64).

Regression between the percentage of highly annoyed subjects and mean concentrations of PM₁₀ and nitrogen dioxide showed similar associations. Again, restricting the analysis to participants living close to the monitoring site strengthened the relation.

6.4.3 Subpopulation Means within Areas

For each area, neighborhood mean annoyance scores were regressed against corresponding estimated annual mean nitrogen dioxide values based on passive sampler measurements (Table 4). Correlation was high in urban areas (0.90 - 0.97), intermediate in sub-urban and rural areas and Davos, (0.6 - 0.7) but low in Montana (0.08). Overall correlation including all neighborhoods (n=81) was high as well (r=0.88). Common
slope models were found to appropriately fit the data; however, an individual intercept model provided a better fit of the data than did a simple model with common intercepts and common slopes.

6.5 Discussion

6.5.1 Association Between Population Mean Scores and Measured Air Pollution Levels

We have shown that, although individuals rate annoyance due to air pollution very differently, given the same objective level of air pollution, population mean annoyance scores are strongly correlated with annual mean air pollution levels. In fact, across areas the average rating of persons living close to the fixed site monitors showed even stronger associations with the nitrogen dioxide measures. The same conclusion holds for the percentage of subjects reporting a high level of annoyance. Within areas, people living in the same neighborhood had, on average, a subjective rating scheme of air pollution which was correlated with the corresponding neighborhood levels. These observations support the hypothesis that reported annoyance is a function of true exposure, though it is distorted by subjective factors, which are apparently leveled out when population average scores are used.

Except for Montana, where only a small range of air pollution levels was observed, estimated slopes varied only slightly between areas (0.6-1.4) and were consistent with the adjusted estimate for nitrogen dioxide (0.9) in the multivariate model based on individual data. The heterogeneity of intercepts between areas suggests that, apart from individual characteristics, local and possibly cultural factors may influence the relation between objective and subjective measures of ambient air pollution. Evidence for some cultural impact could also be found in the multivariate model: in some areas, subjects tended to score significantly lower compared with the reference area, Basel. When replacing area with a dichotomous variable „Swiss German-speaking areas“ as opposed to the French- and Italian-speaking parts of Switzerland, the Swiss German speakers tended to score 0.6 points higher.

The contrast between our individual-level and grouped scores analysis is corroborated by recent reports on poor individual cross-sectional correlation between personal
exposure and ambient air pollution levels as opposed to high longitudinal correlation within subjects\textsuperscript{22,23}. A large number of individual factors have an impact on both personal exposure and individual annoyance scores. These are not taken into account in the (crude) cross-sectional analysis, resulting in poor correlations. Whereas individual factors affecting personal exposure may be explained to a large extent by indoor sources and exposure-relevant activities, predictors of individual annoyance are to a large extent subjective and may not easily be accessible through questionnaires. However, the work of Janssen et al.\textsuperscript{22,23} supports the use of ambient air pollution levels as exposure estimates in air pollution epidemiology and, indirectly, the applicability of grouped annoyance scores, which correlate well with measured ambient levels.

6.5.2 Consistency with Similar Studies

A small-scale urban study carried out in the city of Zurich, Switzerland, in 1995\textsuperscript{9} investigated the associations between measured levels of ambient air pollution (8-week average of $\text{PM}_{10}$ and nitrogen dioxide levels) and traffic-noise on the one hand and degree of annoyance, assessed with the Annoyance Scale, on the other hand at four sites with different traffic densities. In a postal survey, 324 subjects living in houses adjacent to the fixed monitoring sites assessed their level of annoyance due to air pollution on the Annoyance Scale. The results of the Zurich study are consistent with the present findings. In fact, even stronger correlations between measured and self-reported data ($\text{PM}_{10}$: $r=0.97$; nitrogen dioxide: $r=0.96$) and steeper slopes ($\beta=1.6$ per 10 $\mu$g/m$^3$ nitrogen dioxide) were observed. In a study based on random population samples in 55 urban areas in Sweden, Forsberg et al.\textsuperscript{8} used the frequency of annoyance due to traffic exhaust for quantifying the relation between subjective and objective measures of air pollution. Similarly, they found a significant correlation ($r=0.56$) between the percentage of subjects reporting being annoyed daily or almost daily by traffic exhaust in their residential area and measured nitrogen dioxide-levels (6-month averages) at nearby fixed monitoring sites. In another study\textsuperscript{24}, where similar annoyance scores (a seven-point bi-polar semantic differential scale) were applied to the assessment of disturbance due to smoke, fumes, and odors from road traffic in selected population groups, median scores ranging from 0 to 4 were observed in neighborhoods across the
United Kingdom, but the association with measured air pollution levels was not reported.

6.5.3 Validity of Annoyance Scores

The validity of an exposure estimate \( (x) \) refers to the agreement between this measured exposure surrogate \( (x) \) and the true exposure \( (z) \). Because the true exposure \( (z) \) of study subjects could not be obtained, we validated population mean Annoyance Scale scores against measured ambient air pollution levels. The observed high correlation, especially within areas \( (r > 0.85) \), suggests, that population mean Annoyance Scale scores could be valid indicators for ambient air pollution.

However, the underlying mechanism of the "exposure-response" relation, observed in both SAPALDIA and the Zurich study, is not fully understood. Is olfactory perception of air-quality a main factor, or is the reported level of annoyance due to air pollution at home determined by traffic-related noise or visible traffic volume on adjacent streets? In SAPALDIA and the Zurich study, annoyance due to traffic noise, in addition to air pollution, was also assessed with the Annoyance Scale. Correlation coefficients between population mean scores for annoyance due to air pollution and annoyance due to traffic-noise (SAPALDIA: \( r=0.90 \); Zurich-study: \( r=0.96 \)), as well as between mean \( \text{PM}_{10} \)-concentrations and annoyance due to traffic-noise (SAPALDIA: \( r=0.87 \); Zurich-study: \( r=0.99 \)) were high and significant. These findings are plausible, given the obvious association between traffic-related noise and air-pollution. However, other factors, such as home environment (green space, construction density), might act as confounders.

6.5.4 Possible Role and Limitations of Annoyance Scores

Our findings suggest that population mean annoyance scores do reflect gradients of air pollution levels between and within areas in Switzerland. On the other hand, a high level of annoyance indicates an impairment of well-being. This ambiguity of annoyance relating to both exposure and health outcome opens up two main fields of application: 1) exposure estimation in semi-individual studies and 2) evaluation of environmental policies.

In semi-individual studies, within-area variability of air pollution levels could be assessed using neighborhood population mean Annoyance Scale score, and thus the
establishment of expensive monitoring networks within areas may not be needed. In questionnaire surveys, the marginal costs for this additional measure would be very low. The fact that the association between annoyance scores and air pollution levels across areas was improved when analysis was restricting to subjects living close to the monitors suggests that assigning exposure estimates based on neighborhood mean scores to subjects living in those neighborhoods would mitigate non-differential exposure misclassification\(^5\). However, the annoyance scores could not replace personal exposure measurements, because of the high between-person variability of annoyance rating, which could only partly be explained by smoking status, respiratory health status and workplace exposure. Moreover, the observed interactions illustrate the complexity of individual scoring and it will hardly be possible to use individual scores as exposure estimates, even when adjusting for known confounders. Forsberg et al.\(^8\) also reported individual characteristics (female sex, asthma, lack of access to a car) to have a significant impact on annoyance reporting. We found some evidence for reporting bias as subjects affected by respiratory symptoms scored higher given the same nitrogen dioxide level. The anomalous finding that asthmatics scored lower, on average, may partially be explained by the fact that in Davos 44 percent of the asthmatics stated that they had moved there because of the positive effect of the alpine climate on their asthma\(^{13,26}\). In fact, only in alpine areas did asthmatics score lower than non-asthmatics (mean score 0.8 vs. 2.4; \( p \) (t test) = 0.02), whereas in the other areas no difference could be observed (mean score = 3.7 vs. 3.8; \( p = 0.42 \)). In general, the emerging problem for the semi-individual study design of using an exposure measure which might be related to the health outcome of interest may be solved by excluding subjects with positive health outcomes when calculating the grouped scores assigned to all participants in a neighborhood.

The observed exposure-response-relation should not be extrapolated to areas with considerably higher pollution levels than those encountered in Switzerland, because of the limited range of the Annoyance Scale. Therefore, the question of whether our findings hold in general should be evaluated in international studies including areas covering a large range of air pollution levels and cultural settings. Furthermore, in this analysis the Annoyance Scale was evaluated in the context of long-term exposure to air
pollution, estimated by recent annual mean levels. The validity of the Annoyance Scale for short-term exposure assessment remains to be evaluated.

The aspect of health outcome might be a disadvantage for the use of annoyance scores as an exposure estimate. From a public health and regulatory perspective, however, the health relevance of annoyance may be its real strength, since it relates to a broader understanding of environmental quality. Annoyance lacks pollutant-specific information, and therefore it cannot be used for etiologic inference or direct pollutant-oriented air quality management decisions. However, the focus on single pollutants which may allow implementation of effective risk management strategies may fall short from a broader public health perspective. Annoyance due to air pollution, by default, is an indicator for a complex environmental condition. Through the addition of the Annoyance Scale question to regular nationwide population surveys, the change over time in the prevalence of highly annoyed subjects might be monitored and the successful implementation of environmental policy strategies evaluated.

6.6 References


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7 GENERAL DISCUSSION

In this chapter, first, the results elucidating the research questions raised in section 1.2 are summarized, and limitations and possible bias of the empirical work briefly recapitulated (section 7.1). Then, the validity of the three evaluated measures of exposure is discussed in the context of air pollution epidemiology and health risk assessment (section 7.2). In section 7.3, possible improving strategies for assessing human exposure to different aspects of air pollution are proposed. A brief outlook concludes the discussion (section 7.4).

7.1 Main Findings and Limitations of the Empirical Work

7.1.1 Feasibility of Personal Monitoring

The successful implementation of the European multicentre study EXPOLIS, described in chapter 3, proofs, that personal exposure measurements of fine particles technically are feasible on a small-scale level, for short time periods (days)\(^1\). Quality assurance tests ascertained that the measurement techniques used in EXPOLIS for personal (Buck IH pump, GK2.05 cyclone) and microenvironmental (PQ100 pump, EPA-WINS) PM\(_{2.5}\) measurements yield comparable and reliable results (section 3.5.3).\(^1\) Given the high correlation observed in side-by-side tests between the EXPOLIS-MEM (PQ100 pump, EPA-WINS) and the FSM (Digitel), the home outdoor and fixed site levels are also directly comparable (section 5.3.1).\(^2\)

Yet, in the EXPOLIS center in Basel, only short-term personal exposure measurements of one subject at the time have been collected. Therefore, these data allow only to directly assess the validity of measures of short-term exposures. The validity regarding measures of long-term exposures may be different, depending on the study design, the related error model and the aspect of air pollution under consideration. Limitations of personal exposure assessment due to the burden imposed on study subjects, which may result in low response rates\(^3\) and changes of behavior\(^4\), will be discussed in section 7.2.1.
7.1.2 Representativity of Participants of Personal Monitoring

Random population sampling has been implemented in the EXPOLIS centers Basel and Helsinki. In chapter 4, it could be shown, that in Basel, selection bias towards lower traffic volume at home has occurred when recruiting participants for both, the demanding personal exposure assessment protocol and the less tedious diary-only protocol. In Helsinki, the exposure sample did not importantly differ from the target population regarding the observed characteristics, while the diary sample showed some clear differences. Although in Helsinki, traffic volume was not significantly related to participation in EXPOLIS, the point estimates and selection trends across the multistage sampling process indicate, similar to Basel, a tendency to decreased participation with increasing traffic intensity at home. These findings suggest, that demanding personal exposure assessment studies are likely to yield biased population exposure distributions. However, the analysis of the associations between the collected personal exposure data and the measured outdoor fine particle levels in the observed range of exposure must not necessarily be impaired.

Traffic volume at home seems a rather crude surrogate for exposure to traffic-related air pollution, since it does not take into account the time effectively spent at home or close to traffic of study participants. Nevertheless, in a study on the association of respiratory health and exposure to automobile exhaust, significant associations between distance of the home from trunk roads and personal NO$_2$ exposures have been observed, supporting the use of traffic data as exposure surrogate. There is some potential for misclassification regarding traffic volume at home, though. The street of the participant’s address (Basel) or the closest link (Helsinki) may not reflect the street with the highest traffic volume around the home of the participant. Furthermore, for 695 (27%) Basel subjects, mostly living at small streets, the noise register did not provide measured traffic volumes, but assigned standard values. In section 4.5 it could be shown, though, that 14 % missing traffic data in Basel, and subjects living at a large distance to the traffic link in Helsinki, are not likely to having distorted the analysis of selection bias.
7.1.3 Associations between Ambient Fine Particle Levels and Personal Exposures

Chapter 5 reports that the observed associations between short-term fixed site fine particle levels and personal exposures differ, depending on what aspect of fine particle air pollution is considered. While ambient levels of indicators for regional air pollution (sulfur, potassium) were highly correlated to corresponding personal exposures, the associations were weaker for indicators of ultrafine primary traffic-related (lead, bromine) and crustal (calcium) particles. This contrast is consistent with the spatial variation of the chemical composition of fine particles (PM$_{10}$) observed in the region of Basel. Within the framework of the Basel Risk Study on Ambient Air (BRISKA), PM$_{10}$ mass concentrations, sulfur (S) and potassium (K) have been found to be rather homogeneously distributed across the city, whereas indicator elements for primary traffic-related (Pb, Elemental Carbon) and for mostly mechanically generated coarse particles (Ca) showed more spatial variability.

In quality assurance tests, described in chapter 3 and 5, it could be ascertained that the different PEM, MEM and FSM technologies yield comparable results, and therefore should not impair the analysis of the associations between personal, home outdoor, and fixed site fine particle concentrations. However, as pointed out in section 5.5., the different averaging and starting times for each of the samples present a drawback for the comparison of personal exposures and home outdoor levels of fine particle mass and trace elements. While there is evidence that for fine particle mass concentrations, correlation analysis seems robust against not fully identical measuring periods, the more pronounced diurnal variability of ultrafine primary particles (< 0.1 μm) as compared to accumulation mode particles in the size range between 0.1 and 0.4 μm suggests differential measurement error for the different fractions of fine particles. Therefore, compared to the true correlation, the different monitoring periods may have attenuated the correlations for lead and bromine reported in chapter 5. Differences in short-term infiltration for the three particle modes observed by Long et al. may have acted in the same direction. Another drawback in the analysis of source specific exposures are the rather large number of values below detection limit for potassium (28%), lead (28%), bromine (14%) and calcium (39%). However, the computed medians and Spearman correlations coefficients should yield robust estimates.
7.1.4 Annoyance Scores as Measure of Air Pollution Exposure

Although individuals were found to rate annoyance due to air pollution very differently, given the same objective level of air pollution, population mean annoyance scores were found to be associated with annual mean ambient air pollution levels, both within (NO$_2$) and between (NO$_2$, PM$_{10}$) regions (chapter 6).\textsuperscript{11}

The distribution of the annoyance scores was clearly skewed to the right in Montana, Davos and Wald and, to a lesser extent, in Payerne and Aarau. This is reflected in lower median values (0-2) compared to population means in these areas (1.1-3.1) (section 6.4, table 2). However, because of the upper limit of 10 of the annoyance scale, extreme values introducing strong bias could not occur. In fact, the population mean scores better discriminate the annoyance levels in the eight SAPALDIA areas than the median values. The same is true for the percentage of highly annoyed subjects, which is a relevant measure for public health. Therefore, mean scores and prevalence of high annoyance were used for linear regression. The assumptions of independence, homoscedasticity and normal distribution of residuals were met in the presented models. Excluding one influential observation when regressing mean neighbourhood scores against neighbourhood NO$_2$-levels across all areas (section 6.4, table 4) only slightly changed the estimates of the regression parameters.

Across areas, the average rating of those living close to the FSMs, whose exposures probably are best captured by the FSM-levels, showed even stronger associations with PM$_{10}$ and NO$_2$ (section 6.4.2). Within areas, people living in the same neighborhood had on average a subjective rating scheme of air pollution which was correlated with the corresponding neighborhood levels of the traffic-indicator NO$_2$ (section 6.4.3). These observations support the hypothesis, that reported annoyance is a function of true exposure, though distorted by subjective factors. The latter are apparently leveled out when using population average scores. Thus, population mean annoyance scores seem to reflect the between-city and the between-neighborhood variability of the air pollution mixture. The high correlation observed between population mean scores of annoyance by air pollution and annoyance by traffic\textsuperscript{11,12} suggest, that, at least in urban settings, population mean annoyance scores most likely reflect differences of traffic-related exposures.
The most important limitation of the annoyance scores is that they cannot be used as surrogate of individual exposures of study participants, since individual annoyance scores where not associated with average home outdoor NO₂ levels. There is some evidence for reporting bias related to health outcome, as subjects affected by respiratory symptoms scored higher given the same NO₂ level (section 6.4.1). This would impair the use of mean population annoyance scores in the semi-individual study design. By excluding subjects with positive health outcomes for calculating grouped neighborhood scores, as suggested in section 6.5.4, this problem may be solved, though. Because of the limited range of the Annoyance-scale (from 0 [no disturbance] to 10 [unbearable disturbance]), the scores do not indicate an absolute level of air pollution. Therefore, the associations observed between mean population annoyance scores and ambient air pollution levels in Switzerland should not be extrapolated to areas with considerably higher or lower pollution levels. Furthermore, the validity of annoyance scores for short-term exposure assessment remains to be evaluated.

7.2 Validity of Evaluated Measures of Exposure

Based on empirical data, this thesis investigated the validity of i) measured short-term personal exposure to fine particle mass and trace elements, ii) outdoor levels of fine particle mass and trace elements, and iii) questionnaire based annoyance scores. In the following, the validity of these exposure variables in epidemiological studies will be discussed under the perspective of average long-term versus short-term (peak) exposures and of individual versus population level assignment. In addition, their applicability in health risk and impact assessment will be considered.

7.2.1 Measured Personal Exposure to Fine Particles

As pointed out before, measured personal exposure to fine particle mass concentrations is the sum of exposures to particles from various outdoor and indoor sources and due to individual activities. It provides an estimate of individual exposure to particle mass per se, which would be useful to assess the health effects of total particle mass, irrespective of the sources of the particles contributing to the mass and irrespective of their chemical composition. However, to investigate the specific health effects of particles (or other air pollutants) generated by different sources, the total personal exposure to fine particle
mass (or to other air pollutants) is not appropriate. Therefore, a clever personal monitor would distinguish between air pollutants generated indoors and outdoors and identify ultrafine, fine and coarse mode particles. For air pollution epidemiology, this would provide estimates of exposure to different fractions of ambient particles as well as to possible confounding exposures. However, even if such a device was available, the burden imposed on study subjects would make it difficult to recruit representative population samples, as described in chapter 3.2. In addition, changes in behavior of study subjects under investigation are likely. Boudet et al.4 have shown, that participants of EXPOLIS Grenoble on monitoring days as compared to non-monitoring days spent more time at home indoors (871.38 vs. 797.37 Minutes; p_{paired T-test} = 0.02), and less time in other indoor environments (63.75 vs. 130.07 Minutes; p = 0.03), outdoors (56.45 vs. 76.58 Minutes; p = 0.2) and commuting (93.16 vs. 107.96 Minutes; p = 0.3). Such change of time activity patterns during participation in personal exposure measurements impairs the derived exposure estimates and introduces error in individual level exposure assignment. Given the burden on study subjects, but also the high expenses, only short-term exposure assessment of limited population samples seems feasible with personal monitors. At the maximum, repeated measurements over several days might be envisaged. Overall, personal long-term exposure measurements of large population samples have inherent limitations and do not seem realistic, despite the development of smaller and lighter personal monitors in recent years13. Regarding the assessment of population exposure distributions for risk assessment, chapter 3.2 provides evidence that exposure-relevant selection bias is likely to occur in typical multi-cultural populations of modern western urban areas3. Such bias would impair risk assessment, in particular, extreme exposures might be missed. Selection toward lower traffic volumes at home, observed in the exposure sample of EXPOLIS Basel, suggests, that population exposure rather would be under- than overestimated. The integration of personal exposure measurements in an epidemiological study may reduce the range of exposures, but the exposure-response analysis in the observed range of exposure must not necessarily be impaired. Still, biased health effect estimates might occur if the association between exposure and health outcome is not constant over the whole range of exposure. Another scenario of bias, introduced by personal exposure measurements, could occur if the association between exposure and health outcome was different for respondents and
non-respondents. This may be the case, if, for example, indicators of socioeconomic status, in chapter 4 reported to be associated with non-response, would act as effect-modifier.

### 7.2.2 Ambient Fine Particle Levels

Human exposure to air pollutants stemming from outdoor sources is the measure of interest in health effect and risk assessment of ambient, outdoor air pollution. Time-activity data collected within the framework of the EXPOLIS study, though, confirm, that in western urban societies people spend the major part of their time indoors. On average, EXPOLIS participants (n = 1335) in Athens, Basel, Grenoble, Helsinki, Milan and Prague spent during the 48-hour monitoring period 42 hr (87.5%) in indoor environments, 4 hr (8%) in transfer and 2 hr (4%) outdoors. These time activity patterns of European adult urban populations are strikingly consistent with data from American and Canadian populations, recently reported to spend 88.6% and 87.3% of their time indoors, 6% and 6.9% outdoors and 5.3% and 5.7% in vehicles, respectively. The high proportion of time spent in indoor environments highlights, that the penetration of particles (and of ambient air pollution in general), from outdoors to indoor environments is a key factor for human exposure to ambient air pollutants. Within the EXPOLIS-EAS study, also the association between concurrently measured (identical measuring periods) home outdoor and indoor levels of tracer elements has been investigated. Outdoor levels of indicators of secondary, accumulation mode (S) and primary traffic (Pb) particles were found to be highly correlated to indoor levels (n=45) with Pearson correlation coefficients of r=0.91 and r=0.90, respectively. The indoor/outdoor ratios were 0.89 and 0.82, respectively. Indoor calcium, an indicator of crustal particles which has also major indoor sources, was not related to outdoor levels. This suggests that the composition of accumulation and ultrafine mode particles found indoors is determined by the local outdoor fine mode particle mixture.

The differences reported for short-term associations regarding different aspects of particle exposure suggest, that FSM-levels are not equally valid surrogates for short-term exposures to ultrafine, fine and coarse mode particles.2 Regarding outdoor ultrafine and coarse mode particles, their spatial heterogeneity, observed within the city of Basel in combination with time activity patterns of populations, impairs the use of FSM-levels.
as measure of short-term exposure. The more homogeneously distributed ambient fine particle mass levels\textsuperscript{18}, however, seem to reflect population exposure to secondary, accumulation mode particles, including accumulated traffic-related particles. A prerequisite to obtain valid surrogates for exposure to regional air pollution from FSMs is, however, that the monitor represents the average PM\textsubscript{2.5} level of an urban area.\textsuperscript{19}

Inferences from individual, short-term to long-term or population exposures seem possible for compounds with strong short-term associations. If personal exposures track ambient levels on a short-term basis, as observed for the spatially homogeneous compounds PM\textsubscript{2.5}-sulfur and potassium, this is probably also true on the long run. In contrast, inferences to long-term exposure are more difficult for compounds with high spatial variability. The weaker short-term associations observed for traffic-related and crustal trace elements must not necessarily imply equally weak associations for long-term average or population exposures. In fact, long-term differences in time-activity patterns between subjects may be less pronounced than short-term, day-to-day variability within one subject.

As argued in section 5.5.3, in the semi-individual study design, where the Berkson error model applies, an unbiased point estimate of the exposure-response association could be obtained for both, spatially homogeneous and heterogeneous compounds. However, for the spatially heterogeneous compounds, the power to detect an association would be reduced. Moreover, if the location of the FSM does not represent the city-average of spatially heterogeneous compounds, this may be a source of systematic errors. In cross-sectional analysis of long-term exposures to heterogeneous compounds, Berkson error might be mitigated if the contrast of average exposures between areas is clearly larger than the within-city or between-individual differences in one city. However, traffic-exposed sites in different cities with equal traffic volume may show more similar air pollution levels than traffic and background sites in one city. This may result in quite overlapping population distributions of the areas under investigation regarding traffic-related exposures, weakening the power to detect the respective health effects. This suggests, that exposure assessment strategies for investigating long-term effects of traffic-related air pollution should aim at capturing the within-area variability of the heterogeneous compounds.
7.2.3 Questionnaire Based Annoyance Scores

As could be shown in chapter 6, annoyance scores may not be used as measures of exposure on the individual level, because of the wide range of individual perception at a given level of ambient air quality. However, on a population level, mean annoyance scores seem to capture differences in air pollution, both between areas and within areas. The observed within-area association between mean annoyance scores and NO₂ levels (an indicator of traffic-related air pollution) suggests, that mean population annoyance scores indicate also differences in the composition of the complex air pollution mixture, in particular of traffic-related compounds, which are not showing in the spatially quite homogeneous fine particle mass concentrations across urban areas. Therefore, as pointed out in section 6.5.4, population mean annoyance scores seem a promising tool for assigning long-term exposures to the complex mixture of air pollution on a population or group level. As an indicator, they may capture health relevant exposure patterns in a population. However, high annoyance indicates also an impairment of well being and thus bears a component of health outcome. For computing population mean annoyance scores, it was therefore suggested to rather exclude subjects with positive health outcomes, as subjects with respiratory symptoms have been found to score systematically higher (section 6.5.4). Still, while the health component may be a disadvantage for exposure assessment in the semi-individual study setting, such an encompassing measure of environmental quality seems a useful tool to monitor the implementation of environmental policy strategies. Furthermore, in epidemiological studies, annoyance scores might be used as a measure of individual, subjective perception of environmental exposures. If an objective exposure measure was available, confounding due to subjective perception of exposure might be evaluated and, if necessary, adjusted for in multivariate analysis.

7.3 Implications for Improving Strategies in Exposure Assessment

Numerous studies investigating the health effects of ambient, outdoor particulate air pollution throughout the last decade, have relied on ambient fine particle mass concentrations. Yet, fine particle mass is rather a crude measure of exposure to ambient air pollution, since it does not take into account the spatio-temporal differences in the
chemical composition of particulate matter and time-activity patterns of populations. The different sources, transformation, transport and removal processes of ultrafine, fine and coarse mode particles result in distinct chemical profiles of the three particle modes, which are probably related to different health effects. A prerequisite to separately assess the health effects associated with each of the particle modes are specific exposure surrogates or indicators of primary traffic-related particles, secondary accumulation mode particles and coarse mode particles, the latter including crustal and biogenic particles. Differences in spatial variability of the different particle modes also imply differential measurement errors when assigning fixed site levels on a group or population level. This has in particular an impact on the ability to identify the specific health effects related to the three particle modes in the semi-individual study design.

In the following, the relevance of improving strategies in exposure assessment will be discussed separately for different aspects of ambient air pollution, on the one hand in the epidemiological context, on the other hand for risk and impact assessment and regulatory purposes. However, the findings of this work cannot give evidence about the noxious compounds of fine particles or ambient air pollution; they can only indicate, which exposure measures could be useful to disentangle the health effects of the air pollution mixture.

### 7.3.1 Exposure to Accumulation Mode Particles

The accumulation mode particles in the size range of 0.1 - 1 μm show the most uniform distributions of particulate air pollution across urban areas and penetrate well into indoor environments. They are indicated by fine particle sulfur (S) and sulfates (SO₄²⁻), but also by fine particle mass concentrations (PM₂.₅). In ambient air, PM₁₀ and PM₂.₅ are highly correlated in areas without major sources of coarse particles. In Basel, a correlation of 0.97 was found between simultaneously measured PM₁₀ and PM₂.₅ concentrations, for other regions correlation coefficients of r>0.89 have been reported. In these areas, also PM₁₀ may be used as an indicator of fine mode particles. To assess population exposure to this regional, secondary aerosol, fixed site fine particle mass concentrations seem to be valid exposure surrogates, with a minor potential of measurement error, provided the fixed site represents the city average. Epidemiological studies relying on fixed site fine particle mass therefore most likely
reveal health effects related to regional or long-range transboundary air pollution. For risk and impact assessment purposes, a reasonable approach to describe population exposure distributions of long-range transboundary air pollution seem GIS-applications, which model the spatial distribution (1-2 km-grid) of fine particle mass concentrations. Such an approach has already successfully been implemented for estimating the public health impact of ambient air pollution for Switzerland\textsuperscript{32}, and, in a tri-national study, additionally for France and Austria\textsuperscript{33,34}.

7.3.2 Exposure to Primary Traffic-Related Particles

Exposure assessment regarding ultrafine particles seems a more difficult task. Nucleation mode particles rapidly convert to accumulation mode particles and therefore show high spatial variability with elevated concentrations mostly close to sources. Fine particle mass is dominated by fine mode particles and does not reflect differences in ultrafine particle levels. Moreover, even a perfect indicator of ultrafine particles, measured at a FSM, would not capture their spatial variability. In exposure assessment on a group or population level, this would result in substantial Berkson error. Therefore, improving strategies should aim at measuring specific indicators of primary traffic-related air pollution and at better characterizing their spatial distributions. A possibility would be a monitoring network of several fixed monitoring stations within a city and the characterization of the chemical composition of the fine particle levels. Alternatively, models could be developed characterizing the spatial variability of different compounds of ambient air pollution and taking into account individual time-activity patterns. A promising tool are GIS- (Geographic Information System) applications, with the possibility to link source specific exposure estimates to study populations under investigation. Hruba et al.\textsuperscript{35} have recently shown, in a study on long-term effects of particulate matter, that individual-level assignment is feasible with a GIS-model. The GIS-application provided concentrations (100 m x 100 m grid) of total PM\textsubscript{2.5}, PM\textsubscript{10} and TSP mass, which then where assigned by address codes to the children participating in the study. Analysis of the elemental composition of the fine particles would allow to expand such a model to source-specific exposures. Also by means of a GIS, different measures of traffic flows (flow on the closest street to the residence, highest flow and sum of flows within a 170 m radius of the residence), were assigned to the subjects of a
case-control study. However, when assigning traffic-related exposures on an individual level, the classic error model would apply for health effect assessment. This may lead to biased, most likely attenuated, effect estimates. An alternative to the individual level assignment or the grouping by regions (with FSM-assignment) could be grouping according to traffic or other source-related exposures. For example, subjects living in different cities in homes with high traffic volume could be compared to subjects living in residential areas with low traffic density. In order to ascertain that the whole range of exposure is covered, and that the groups to be compared have equal sample sizes, participants could be selected according to their exposures. Such improving strategies for group estimates would be an alternative to the common between-city and within-city analysis and would help to avoid classic errors and probably to mitigate Berkson errors. Also for risk assessment purposes, GIS-applications could provide a better description of traffic-related population exposure distributions within areas.

7.3.3 Exposure to Coarse Particles

Coarse particles have received far less attention than ultrafine and fine particles in health effect assessment. Since they include such different species as mechanically generated crustal particles and biological material such as pollen or debris of insects, the characterization of exposure to coarse particles needs further specification than indicating the particle size range between 2.5 and 10 μm. Given the spatial variability of coarse particles, successful strategies for improving exposure assessment for this fraction should be similar to those proposed for the primary traffic-related fraction, namely several FSMs in a city, exposure modeling, the use of GIS-applications and grouping according to source-specific exposures.

7.3.4 Exposure to the Air Pollution Mixture

Population mean annoyance scores seem to be a promising tool to capture within-area differences in long-term population exposure to the complex mixture of air pollution. In an urban setting, as tentatively discussed in sections 7.1.4 and 7.2.3, they most likely reflect differences in traffic-related exposures. They are an inexpensive measure of exposure which may be included at minor marginal costs in epidemiological studies on
the long-term effects of air pollution. Their use implies a broader understanding of exposures to adverse environmental conditions and they may neither be used for etiologic inference nor pollutant specific risk assessment. However, their inclusion in regular nation-wide population surveys would allow to monitor the change over time of the prevalence of highly annoyed subjects, and thus to evaluate the successful implementation of environmental policy strategies.

7.3.5 Possible Confounding Exposures

In cross-sectional study designs, individually different exposures related to indoor sources or to exposure-relevant activities such as smoking and gas appliances may act as confounders. These exposures therefore should be assessed separately and their impact on effect estimates thoroughly evaluated. Questionnaires seem to be useful tools to assess such exposures.

7.4 Outlook

Currently, new personal monitors are being developed to measure concurrently and continuously exposures to several compounds of the air pollution mixture. Personal exposure studies with these new monitors, conducted in selected population samples, will further contribute to our understanding of the relation between personal exposures and the outdoor air pollution mixture. The data collected will be useful to validate potential indicators for use in air pollution epidemiology and health risk and impact assessment. For risk assessment purposes, exposure models could be developed allowing for different input parameters in order to alternatively simulate population exposures to air pollution stemming from outdoor sources, from indoor sources or to describe total exposure, depending on the health risk under consideration.

The concurrent development on the one hand of GIS models for use in health effect and risk assessment and, on the other hand, of improved analytical methods to specify the chemical composition of particulate matter at low environmental concentrations, suggests, that in the near future, powerful tools will become available to assign source specific exposures in high spatial resolution to (sub)-populations or individual study participants. The application of such exposure surrogates in epidemiological studies may ascertain the emerging evidence regarding the health effects of different compounds of
the air pollution mixture. In recent years, an increasing number of studies have reported adverse health effects to be related to indicators of secondary (sulfur/sulfates) and of traffic-related compounds. Several studies have observed stronger and more consistent health effects for fine particles (PM2.5) than for the coarse fraction (PM2.5-10). In contradiction to these findings, Mar et al. report also associations for the coarse fraction. Loomis provides evidence, that stronger associations for fine particles, observed in western urban areas, must not necessarily apply for areas with different climates and cultural settings. Meta-analysis of future studies, representing the world’s major climates and different social and cultural settings, and investigating the associations between health outcomes and indicators for the aspects of regional air pollution, of traffic-related particles and of coarse mode particles, hopefully will allow to disentangle the relative (public) health impact of the different compounds of the air pollution mixture and to identify effective abatement strategies.

7.5 References


12. Oglesby, L. Atembarer Schwebestaub (PM10) in der Stadt Zürich: Messungen von Luftschadstoffen und Lärm sowie Beurteilung durch die Anwohnerinnen und Anwohner an verschieden stark verkehrslasteten Standorten in der Stadt Zürich (German) [Master Thesis]. Department of Environmental Sciences, Swiss Federal Institute of Technology, 1995.


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8 CONCLUSIONS

In this thesis, different measures of air pollution exposure, which may be applied in health effects and risk assessment, have been evaluated. It could be shown, that the validity of a surrogate for human exposure to air pollutants very much depends on the context it is used in. Key factors that determine the validity of an exposure measure are the aspect of air pollution under consideration, the time-frame, i.e. short-term versus long-term exposures, and, in air pollution epidemiology, the study design with it's related error structure.

Although the implementation of the European EXPOLIS study proved that personal exposure measurements technically are feasible on a short-term basis (48 hr), and in small population samples (50-200 subjects), alternatives are needed for assessing long-term exposures of large populations. The burden imposed on study subjects and the observed exposure-relevant selection bias suggest, that individual exposure levels may only directly be measured in selected groups of the population. Non-representative study samples and changes of behavior of subjects while monitored, jeopardize the generalizability of the results of personal monitoring studies. This impairs the use of the results, in particular for risk assessment purposes.

The empirical data of the EXPOLIS-EAS study Basel suggest, that short-term FSM-levels of spatially homogeneous air pollution compounds - in this work measured as fine particle mass, sulfur or potassium - are valid surrogates for individual short-term exposure to regional air pollution. This finding can probably be extrapolated to long-term and population exposures. Therefore, FSM-fine particle levels, which have been used as exposure surrogate in numerous epidemiological studies, seem to have been reasonable estimates for short-term and long-term population exposures to regional air pollution, which includes also accumulated primary traffic-related particles.

Regarding spatially heterogeneous compounds of ambient air pollution, the empirical data of EXPOLIS-EAS indicate weaker associations between short-term ambient levels and individual exposures for trace elements of traffic-related (Pb and Br) and crustal (Ca) particles. This makes inferences regarding long-term or population exposures to traffic related pollutants more difficult. In epidemiological studies probably both, short-term and long-term exposures to compounds with high spatial variability, have not been
adequately described by one FSM in a region. This may be particularly true for exposure to primary traffic-related particles, where time spent in proximity to the source is another important factor. As a consequence, in semi-individual study designs, the power to detect health effects of air pollution compounds with high spatial variability probably has been reduced.

Population mean annoyance scores, evaluated in the framework of SAPALDIA, provide direct evidence regarding the validity of a measure of long-term population exposure to spatially heterogeneous aspects of air pollution. In contrast to the investigated trace elements, the annoyance scores are not pollutant specific. In an urban setting, though, differences in mean population annoyance scores between neighborhoods most likely reflect differences in traffic-related aspects of exposure. Population mean annoyance scores could be applied as a simple, but useful tool for assessing long-term within-city differences of population exposure to the air pollution mixture at minor costs.

In conclusion, future epidemiological studies may rely on FSM-data for assessing human exposure to the aspect of regional, long range air pollution. Because individual exposures to these spatially homogeneous compounds seem to closely track ambient levels, extrapolation of the findings from short-term to long-term exposures and from individual to population levels should be possible. Also for risk assessment purposes, ambient fine particle levels seem useful to estimate meso-scale (km-grid) population exposure distributions to regional air pollution. Regarding spatially heterogeneous compounds of ambient air pollution, two different improving strategies could be implemented: first, exposure assessment strategies capturing their spatial variation, such as small-scale GIS-models (100m grid), secondly, grouping by source-specific exposures, e.g. by traffic density at home. In semi-individual studies, both strategies may reduce Berkson error, and thus increase the power to detect the specific health effects associated with ultrafine and coarse mode particles, respectively. For risk assessment purposes, refined modeling techniques, including GIS-applications, could be developed to describe small-scale (100m-grid) source specific population exposure distributions.

Overall, the findings of this thesis add plausibility to the health effects of ambient air pollution, observed at low outdoor air pollution levels in a large body of epidemio-
logical research throughout the last decade. Yet, it could be shown, that there is still a potential for improved assessment of human exposure to outdoor air pollution. The implementation of the suggested improving strategies in exposure assessment could help to identify the specific, potentially different, health effects of different aspects of the air pollution mixture, in particular for traffic-related compounds, and to evaluate the associated public health impact.
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