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Study manual and data book

Coordinating center, Finland

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PREFACE

The study 'Exposure and risk assessment for fine and ultrafine particles in ambient air', acronym ULTRA, is a European collaborative project which aims to improve knowledge on human exposure to ambient air particulate matter of different sizes and different chemical composition in Europe, and to evaluate the associated health risks.

This study manual and data book has three parts. The first part is 'Study manual' and it describes the background, rationale, and methods of the ULTRA project. In the project, standard operation procedures (SOP) were developed and used to standardize the methods. These SOPs are included as appendices in this book. The chapters 1-8 and the appendices A1 – A13 have been written before the field work of the project, and the chapter 9 'Statistical analyses' has been written during the preliminary phase of the statistical analyses of the data. The second part of the manual 'Remarks and recommendations' has been written after the field work of the study in order to discuss and comment the methods used, and when appropriate, to give recommendations for future studies. The third part 'Data book' gives descriptive statistics of the data collected.

The development of the methods used in ULTRA and the writing of this book was a truly collaborative effort, which involved intense discussions and participation from all partners. However, some key players and their role can be pointed out. Gerard Hoek, Ph.D., was responsible for the PM2.5 and spirometry SOPs. Jyrki Mäkelä, Ph.D., from the Department of Physics, University of Helsinki, together with Marko Vallius, M.Sc., was responsible for the CPC SOP. The SOP for determination of absorption coefficient using reflectometric method was developed by Marko Vallius. Kirsi Timonen, M.D., was responsible for the ambulatory ECG and clinic visit SOPs. The operation procedure for DAS was finalized by Andrey Khlystov, Ph.D., for MAS by Wolfgang Kreyling, Ph.D., and for EAS by Aadu Mirme, Ph.D. Annette Peters, Ph.D., coordinated the development of the diary and Joachim Heinrich, Ph.D., the characterization questionnaires. Pekka Tiittanen, M.Sc., designed the procedures for the data transfer and management of the health data and Timo Lanki, M.Sc., did the same for the air hygiene data. Juha Pekkanen, M.D., drafted the chapters 1.1-1.3 of this manual and the chapter 1.5 together with Marko Vallius. Kirsi Timonen drafted the chapters 1.4 and 1.6 and edited the second part 'Remarks and recommendations'. Pekka Tiittanen wrote the chapters 1.7-1.9. For the part 'Remarks and recommendations' those who were responsible for a particular SOP drafted a paragraph on that SOP first. After that, all participants gave their comments. Mr. Harri Sinkko did the tables for the data book.

The study was coordinated at National Public Health Institute, Kuopio, Finland, by Juha Pekkanen with the help of Kirsi Timonen. At the coordinating center, Pekka Tiittanen was responsible for the overall data management. Timo Lanki was responsible for air hygiene data and Kirsi Timonen for the health data. Esko Vanninen, M.D., and Tuula Tarkiainen, M.D., at the Kuopio University Hospital, Department of Clinical Physiology and Nuclear Medicine, were responsible for the analyses of the ambulatory ECG recordings. The urinary CC16 samples were analysed in the laboratory of prof. Alfred Bernard at the Unité de Toxicologie Industrielle et de Médicine du Travail, Brussels, Belgium. During the field work in Helsinki, Aadu Mirme, Ph.D., was responsible for the EAS measurements, Gintautas Buzorius, Ph.D., and Ismo Koponen, M.Sc. for CPC measurements, and Marko Vallius for other central site measurements. Kirsi Timonen was responsible for the clinic visits with the help of the study nurse Mr. Sami Penttinen, and Timo Lanki, Ms. Kati Oravisjärvi, and Annalea Lohila, M.Sc.

Mrs Anita Tyrväinen weighed the PM2.5 filters and measured the absorption coefficients from them. Päivi Aarnio, Lic.Tech., and Tarja Koskentalo, Lic.Tech., Helsinki Metropolitan Area Council, Helsinki, were responsible for the network air pollution data in Helsinki.

At GSF - Forschungszentrum für Umwelt und Gesundheit, Neuherberg, Germany, Joachim Heinrich was the principal investigator. He was helped by Annette Peters and Wolfgang Kreyling. Dr. Kreyling was also responsible for the overall coordination of the aerosol measurements in ULTRA. Angela Ibald-Mulli, M.P.H. was responsible for the data management and quality control. Gabi Wölke, MA, coordinated the fieldwork in Erfurt. Martina Stadeler, M.D., was the physician overseeing the study conducted at the FSA with the help of the nurses Regina Müller and Cornelia Engel. Thomas Tuch, Ph.D., was responsible for the ambient air pollution measurements.

At the University of Utrecht, the Netherlands, prof. Bert Brunekreef was the principal investigator. He delegated most of the task to Gerard Hoek. Jeroen de Hartog, M.Sc., was responsible for the field study in Amsterdam, including data management. He was assisted by Carolien Mommers, M.Sc., Marloes Jongeneel, M.Sc., Ms Boukje de Wit, Ms Isabella van Schothorst and Ms Veronique van den Beuken for the clinical visits. Ms Marieke Oldenwening performed the ambient PM2.5 measurements. Nicole Janssen, Ph.D., and Mr Jean Pierre van Mulken contributed to the PM2.5 measurements. Saskia van der Zee, Ph.D., Willem Roemer, Ph.D., and Joop van Wijnen, M.D., from Environmental Medicine, Municipal Health Service Amsterdam, contributed significantly to the selection of the study population, the examination site, the sampling location and supplied data on ambient air quality of Amsterdam. Measurements of particle number counts were the responsibility of Gerard Kos, M.Sc., Andrey Khlystov and Harry ten Brink, Ph.D., (ECN).

The project has been funded by European Commission contract No ENV4-CT97-0568 (DG 12 – ESCY). In addition, the coordinating center got funds from the Finnish Research Programme on Environmental Health (SYTTY), Academy of Finland.

The field work of the ULTRA project was conducted during October 1998 – June 1999. Before this, intercomparisons of the aerosol spectrometers used in the current project were done during a previous ULTRA project funded by the European Commission contract No ENV4-CT96-0205.

December, 2000

Juha Pekkanen Kirsi Timonen

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1 STUDY MANUAL

1 STUDY MANUAL

1.1 INTRODUCTION

A large number of studies have reported that daily changes in particulate air pollution are associated with a variety of adverse respiratory outcomes, like symptoms, declines in lung function, hospital emergency admission and mortality (Dockery et al, 1993; Dockery and Pope, 1994; A Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society, 1996). Recently, similar associations have also been reported with cardiovascular outcomes, like hospital admissions and mortality (Schwartz, 1994; Burnett et al, 1995).

The goal of the project is to improve knowledge on human exposure to particulate matter of different sizes and of different chemical composition in Europe, and to evaluate the associated health risks. These results can then be used to develop standards for air quality in Europe, for better and more efficient monitoring of air quality, and as a bases for designing control strategies to improve urban air quality and reduce the health effects associated with exposure to particulate matter in ambient air.

Specifically, the aims of the project are

1. to improve exposure assessment to fine particles in Europe by assessing the size distributions, including ultrafine particles, and elemental compositions of fine particles in ambient air in three European cities with different sources of particulate air pollution, i.e.
    a) to describe the levels, variations in time, and intercorrelations of different types particles with each other and with other air pollutants
    b) to describe the elemental composition of particle mass collected with PM2.5 impactors

2. to improve risk assessment of exposure to fine particles of different sizes and of different elemental composition with focus both on respiratory and cardiovascular outcomes. Specifically, to test the following null hypotheses:
    a) there is no difference between the health effects associated with all fine particles (PM2.5) or size fractions of ultrafine and fine particles
    b) there is no difference between the health effects associated with fine particles of varying elemental composition

1.2 JUSTIFICATION AND DEFINITIONS OF MAIN EXPOSURE AND OUTCOME VARIABLES

1.2.1 Exposure variables

In addressing the above aims, the main variables used in the final analyses are 24-hour averages of PM2.5 and PM10, total particle number concentration, particle number concentration in size ranges 0.01-0.1 μm, 0.1-1 μm, and 1-2.5 μm, elemental composition and blackness of PM2.5 particles.

It is unknown, what characteristics of the airborne particles are responsible for their health effects. Currently, the two probably most hotly debated theories are the findings that suggest that the large number of ultra-fine particles in urban air are responsible for the health effect of particulate air pollution (Oberdörster et al, 1995; Peters et al, 1997). The second possibility is that the chemical composition of particles, especially the transition metal content on the surface of the particles determines their health effects (Tepper et al, 1994; Dusseldorp et al, 1995; Dreher et al, 1996; Osornio-Vargas et al, 1996). Both of these issues are addressed in the present study.

Particles in air tend to follow a trimodal distribution. Particles smaller than 2.5 μm in diameter are generally referred to as 'fine' and those greater than 2.5 μm in diameter as 'coarse'. Fine particles can be divided into two modes: ultrafine particles, with diameter below 0.1 μm, and the accumulation mode, particles between 0.1 and 1 μm in diameter. Coarse particles are mainly wind blow dust, e.g. Scandinavian countries suffer from high levels of PM10 (total mass of particles with an aerodynamic diameter below 10 μm) in late fall and early spring. These particles are mainly resuspended dust from street sanding and dust created from the use of studded tires. Ultrafine particles are mostly generated by local traffic exhaust emission and the particles in the accumulation mode are (outside inversion situations) mainly from long-range transport. Particle size affects exposure to particles by influencing lung deposition rates, indicates the source of the particles and possible chemical composition.

The main size ranges used in the analyses of the present ULTRA study are therefore 0.01-0.1 μm, 0.1-1 μm, and 1-2.5 μm. As the cut point 0.5 μm was used in the previous ULTRA study and the cut point 0.03 μm has been used in previous analyses (Peters et al. 1997, Pekkanen et al. 1997), data are calculated for these cut points. Also one hour averages of particle number concentrations will be analyzed to more clearly define the lag time of different health effects.

1.2.2 Respiratory end points

The main variables used in the final analyses are FVC, FEV1, PEF, MMEF from biweekly measurements of spirometry and respiratory symptoms from daily diaries. These end points have been repeatedly used in previous studies.

1.2.3 Cardiovascular end points

Main outcomes are 1) the angina pectoris (AP) symptom and medication data collected in the daily diary and during the clinic visit and 2) electrocardiograph (ECG) data collected with ambulatory ECG recordings (Holter) during the clinic visits. The main ECG variables used in the final analyses are ST-changes, ectopic beats / arrhythmia and indexes of heart rate variability (HRV, see below).

Especially HRV analyses provide a large number of indexes. One method to validate different measures of HRV is to look at predictive capability: those measures of ambulatory ECG recordings that predict future risk of death because of cardiovascular disease (CVD) are the most important. Based on the literature, most measures of HRV (both time and frequency domain analyses) predict mortality in elderly subjects (Tsuji et al.1994) or survival in MI patients (Bigger et al. 1993). The VLF seems to have best predictability, but the differences

are not large (Task Force 1996). Also, the correlations between different measures of HRV are very high, often above 0.75. Also measurements taken for a random 2-, 5- or 10-minute time frame have high correlations with 24-h measurements (Bigger et al.1993).

High frequency (HF) component of HRV is thought to reflect mainly vagal (parasympathetic) and low frequency (LF) component both sympathetic and parasympathetic part of the autonomous nervous function. The physiological basis of very low frequency (VLF) component is not well understood. HF is defined as frequencies 0.15-0.40 Hz, LF as 0.04-0.15 Hz, and VLF as 0.04 Hz or below. (Task Force 1996).

Air pollution could be hypothesized to lead to two different types of changes in HRV, either a change in the measured indexes of HRV measured during the whole 1 hour recording or 5 minute recording on rest (this is the kind of measurements that are done to evaluate prognoses after MI), or to changed responsiveness of HRV indexes to different stress tests causing autonomic modulation, i.e. the variable of interest would be the difference between the 5 minute resting HRV and 5 minute exercise HRV.

HRV is decreased early after myocardial infarction and begins to recover within a few weeks (Task Force 1996) and depressed SDNN is associated with survival after myocardial infarction. Also spectral analyses of HRV after myocardial infarction show a decrease both in the total power and in the individual power of spectral components. Therefore, a decrease in these indicators can be interpreted as an adverse outcome. However, also an increase in heart rate variability may indicate overreaction of autonomic control. Given the limited knowledge of the effects of air pollution on heart and that air pollution most likely does not have a beneficial effect on the heart, this can also be a harmful effect.

ST-changes reflect degree of myocardial ischaemia and have also prognostic value (Dekker et al. 1995). Daily variations of air pollutants can result in increased myocardial ischaemia with several mechanisms (arrhythmias, effect on haemostatic factors). QT-time reflects repolarization of the heart and long QT-time increases the risk of sudden death. PR-interval is a measure of atrio-ventricular conduction of the heart. Carbon monoxide (CO) can specifically increase myocardial ischaemia by forming carboxyhemoglobin. Ectopic beats reflect directly the status of the heart.

Due to the relative simplicity of the time domain analyses of HRV, HRV analyses will focus first on time domain analyses, and only in the second phase on spectral analyses. Based on the above considerations, the end points for the ECG analyses are:

Definitions:
-SDNN (ms): standard deviation of the length of all NN intervals
-RMSSD (ms): square root of the mean of the squared differences between adjacent NN intervals
-area of ST-depression: cumulative area of ST-depressions (ST-depression is defined as depressions over 0.05 mV (”0.5 mm”) lasting longer than 1 minute, when measured 60 ms after the J-point)
-max ST- depression: largest amplitude of ST- depression during the measuring period
(both area of ST- depressions and max ST- depressions are coded as absolute units and corrected for the baseline level during the 5 minute rest).
-QT-intervals (ms): is measured in three different ways: Absolute QT-interval, corrected QTc

interval (corrected for heart rate using Bazett's formula: QT divided by square root of R-R interval), and QT-peak.
-pNN50 (%): number of pairs of adjacent N-N intervals differing by more than 50 ms divided by the total number of N-N intervals
-PR-interval: average of three PR intervals during the rest

1. During 5 minutes of exercise:

Primary:
-SDNN
-RMSSD

Secondary:
-LF/HF ratio
-pNN50
-high frequency (HF)
-low frequency (LF)
-normalized HF
-normalized LF
-total power
-ventricular ectopic beats
-supraventricular ectopic beats
-area of ST-depression
-max ST-depression
-QTc-time

2. During 5 minutes of rest, paced breathing, standing up and rest after exercise:

As during exercise, but *not*:
-ventricular and supraventricular ectopic beats
-ST-depressions
-QTc-interval (only rest and rest after exercise)
In addition, *only* from the 5-minute rest period:
-Heart rate (HR)
-PR-interval

3. During the whole Holter monitoring period (incl. exercise)

Primary:
-ventricular ectopic beats
-supraventricular ectopic beats
-area of ST-depression
-very low frequency (VLF)

Secondary:
-QTc interval
-Heart rate (HR)
-SDNN
-SDANN

-RMSSD
-pNN50
-high frequency (HF)
-low frequency (LF)
-normalized HF
-normalized LF
-total power
-LF/HF ratio

1.2.3.1 Additional variables/analyses

In addition to the above variables/analyses, following exploratory analyses will be done and following data made available:

-difference in the HRV indexes calculated between the 5 minute rest and exercise and standing up

-RR interval data for each recording in ASCII format

-from all Holter analyses following information will be also be provided: details of each ST-depression episode (duration, max amplitude, slope, area, data on heart rate, extrasystolia)

1.2.4 Biomarkers

There has previously been no toxicity biomarker to monitor populations exposed to pneumotoxicants at the workplace or in the environment. A lung toxicity biomarker, Clara cell protein (CC16), applicable not only on bronchoalveolar lavage (BAL) fluid but also on serum or sputum has recently been identified (Hermans and Bernard, 1996). When no serum samples can be obtained, changes of CC16 in serum could yet be estimated by measuring the protein in urine. The influence of the renal function can be neutralized by dividing the urinary concentration of CC16 by that of retinol-bing protein (RBP). The concentration of Clara cell protein CC16 and RBP will be measured on spot urine samples by an automated nonisotopic assay relying on the agglutination of latex particles (Bernard and Lauwers, 1983; Bernard et al. 1991). In addition, measures of renal function will be determined from urine at the beginning and at the end of the study.

1.2.5 Blood pressure

Blood pressure will be measured both in rest and after standing up.

1.3 PLACE AND TIME

The field work of the ULTRA study will be carried out in three cities: in Helsinki, Finland, Erfurt, Germany, and Amsterdam, the Netherlands. It will last six months. In Helsinki, the field work will take place from November, 1998 to April, 1999; in Erfurt it will be from October, 1998 to March, 1999, and in Amsterdam from mid October, 1998 to mid April, 1999.

The participating centres of the ULTRA study are Unit of Environmental Epidemiology, National Public Health Institute, KTL, Kuopio, Finland (coordinator); Institute of Epidemiology, GSF-Forschungszentrum für Umwelt und Gesundheit (contractor), Neuherberg, Germany; Environmental and Occupational Health Unit, University of Utrecht, Utrecht, the Netherlands (contractor); the Energy Research Foundation, Petten, the Netherlands (associated contractor) and Environmental Medicine, Municipal Health Service Amsterdam (associated contractor), Amsterdam, the Netherlands. The other participating parties are Unité de Toxicologie Industrielle et de Médicine du Travail, Bruxelles, Belgium; Department of Environmental Sciences, University of Kuopio, Kuopio, Finland; Department of Environmental Physics, University of Tartu, Tartu, Estonia (subcontractor for KTL); Department of Physics, University of Helsinki, Helsinki, Finland; Helsinki Metropolitan Area Council, Helsinki, Finland; Department of Clinical Physiology, Kuopio University Hospital, Kuopio, Finland; Institute of Inhalation Biology, GSF-Forschungszentrum für Umwelt und Gesundheit, Neuherberg, Germany;

1.4 OVERALL QUALITY CONTROL

1.4.1 General

The aim of the quality control in ULTRA is to ensure that those procedures done similarly in all centers will be conducted in a comparable way to allow pooling of the data in the combined analyses. Therefore, the quality control puts less emphasis on procedures that are not done exactly the same way in different centers, e.g. aerosol spectrometry or are done only in one center or laboratory, e.g. Clara protein analyses, analyses of the ambulatory ECG recording, or the analysis of the elemental composition of the PM2.5 filters. In these cases, quality control measures of each individual unit or laboratory will be used.

The main ways to ensure comparability between centers are the introduction of standard operating procedures (SOP) for the main procedures, the training of the field workers in a common session, the site visits by the coordinating center, and the quality control procedures of individual measurements, as specified in the respective sections. For aerosol spectrometers, operating procedures (OP) will be available.

Within each center, the number of field workers should be as few as possible to avoid between worker variation. Further, in each center, a daily log book or diary should be kept throughout the study. In this diary, all exceptions from the protocols and other remarks should be mentioned. All deviations form the SOPs have to be reported on the form >Local and temporal deviation from or local change of a SOP= of the respective SOP.

1.4.2 SOP for making SOPs

All SOPs in ULTRA study are done according to SOP for making SOPs, Appendix A1.

1.4.3 Training session

The field workers who will take care of the clinic visits will be trained in a common workshop in Kuopio in 28.9. - 29.9.1998. The programme of the training session is in Appendix A9. A special emphasis will be given on ambulatory ECG recording. The training session will be guided by the Department of Clinical Physiology, Kuopio University Hospital.

1.4.4 Site visits

Kirsi Timonen from the coordinating center will visit all centers by the mid of December 1998 to ensure that all instructions in this manual are followed. In addition, Wolfgang Kreyling, the coordinator of the air hygiene in ULTRA, will visit all centers by the end of February -99 to check the air quality measurements. The form to be completed during these visits is attached as Appendix A10.

1.4.5 Quality control in individual procedures

The individual SOPs or OPs of the procedures include the respective quality control measures. When possible, cross comparisons will be conducted between the study centers, e.g. in weighing the filters, determining the reflectance of the filters, and comparing the spirometers used to a >reference= spirometer that circulates in all centers.

As quality control of CC16 urine measurements, one urine sample from one person in each center is divided into 5 tubes to control for laboratory error. This is done twice, both in the first and second half of the field work.

Data checks and data transfer checks will follow the instructions of the PEACE study (Roemer et al. 1995)

1.5 AIR HYGIENE MEASUREMENTS

1.5.1 Overview of measurements

This section of the ULTRA field work manual describes the air hygiene measurements which are carried out during the study. The measurement of PM2.5 and determination of absorption coefficients from PM2.5 filters are done according to specific Standard Operating Procedures (Appendices A2, A5). Operating procedures will be followed for aerosol spectrometers and CPC 3022A particle counter (Appendices A3-1, A3-2, A3-3, A4). Measurements of PM10, NO_X, CO, SO_2 and O_3 will be collected from existing networks.

Comprehensive data of the features of all air pollution and meteorological measurements, their location and measurement equipment will be included in the descriptive report on the measurement site and equipment (Appendix A11-a, A11-b). Descriptive reports should be sent to the coordinating center not later than in December 1998.

1.5.2 Sampling site

The most important criterion is that the selected site is representative of the exposure to ambient air of the target population. Sites that are not strongly influenced by local sources in the vicinity of the site will be used. In air pollution monitoring literature this type of site is referred to as "urban background". Concentrations of pollutants with urban sources measured at such a site will be higher than the "regional background" measured outside the city. All sampling sites are at least 40 meters away from busy streets. In addition, within 40 meters of the site no other important sources of combustion gases or particulate matter are present (construction work, small industries).

All sites have been selected to fulfill as closely as possible the following criteria; samplers are located at least twice the distance from an obstacle as the height of the obstacle (buildings, etc.), air flow around the sampler is unrestricted, sampling inlets are at least 2 meters away from a high volume sampler inlet, samplers are not placed near exhaust flues or vents.

The measurement sites used in ULTRA study centers are described in separate report sheets (Appendix A11-a).

1.5.3 Aerosol spectrometers

In Germany, MAS consists of two different sensors covering different size ranges. Fine particles are measured using a differential mobility analyzer (DMA, TSI model 3071) in combination with a condensation particle counter (CPC, TSI model 3760). Larger particles are classified by a Laser Aerosol Spectrometer (LAS, PMS model LAS-X).

In the Netherlands, DAS will be used, i.e., Mobility Analyzer together with a Laser aerosol spectrometer. Fine particles are measured and classified by the Mobility analyzer, and larger particles are measured and classified by the Laser aerosol spectrometer (LAS, PMS model LAS-X).

Electric Aerosol Spectrometer (EAS) used in Finland is based on an electric measurement principal similar to the principle of EAA model 3030 of TSI. EAS is significantly modified in order to take into account the needs of atmospheric aerosol studies in urban and rural environment.

More detailed descriptions of the aerosol spectrometers and their operation are given in the respective operating procedures (Appendix A3- 1-3; parts A3– 1-3 -a, A3- 1-3 -b and A3- 1-3 -c).

1.5.4 CPC 3022A

Condensation Particle Counter (CPC) TSI 3022A is used in all centers to measure the total concentration of particles. Upon entering the instrument, the sample passes through a heated saturator, where butanol evaporates into the air stream and saturates the flow. The aerosol sample then passes into a cooled condenser tube, where vapor supersaturates and condenses onto the airborne particles. This produces large, easily detectable aerosol droplets. These droplets pass through an optical detector immediately after leaving the condenser.

Instructions for operation and maintenance of CPC's are given in operation procedure 'Measurement of particle number concentration in ambient air using the Condensation Particle Counter' (Appendix A4).

1.5.5 PM2.5

During ULTRA, 24-hour samples of PM2.5 will be collected with Harvard impactors (Appendix A2). Filter change should take place at 12:00 a.m. ∀ 1.50 hours (resulting in a minimum of 21 hours and maximum of 27 hours of effective sampling time per one diurnal sample).

The filter type used should have a collection efficiency of at least 99% for 0.3 μm particles. Weight losses due to filter handling should be less than what corresponds with 5 $\mu g/m^3$. In addition, no artifact formation as observed on glass fibre, cellulose and many quartz filters (resulting from SO_2, HNO_3 and NO_2) should occur. Teflon filter with a polymethylpentene support ring and 2 μm pore size are therefore used in sampling. Low chemical background, low pressure drop during sampling and excellent aerosol retention ability are the properties which make it the best choice for this study.

1.5.6 SO_2, NO, NO_2, CO, O_3 and PM10

Concentrations of gaseous pollutants SO_2, NO, NO_2, CO, O_3 must be measured continuously at the measurement site or at another representative site (existing monitoring networks).

Measurement of PM10 can be done either continuously (Finland, The Netherlands) or as diurnal sampling (Germany).

For continuous monitors probably the most important determinant of performance is the calibration practice. Detailed documentation of calibration practice in all centers is considered necessary, in order to determine whether differences can be expected. The guiding principle is that measurements should be conducted according to the manual of the manufacturer. As measurements are conducted in the framework of existing networks, no major changes can be introduced for this study. Standard calibration procedures are done according to the instructions of the local authorities.

1.5.7 Meteorological data

For meteorological variables, data measured in networks operated by meteorological institutes or air pollution monitoring agencies can be used, but the most recommended method is to use a movable meteorological station located close to the sampling site. Temperature and humidity data should preferably be collected at a height of about 1.50-3 meters. Wind speed and wind direction are generally collected higher above the ground.

At least hourly average values of ambient temperature, relative humidity, ambient air pressure and wind speed and direction should be collected.

1.5.8 Reflectance

Reflectance of all of the PM2.5 filters are measured. This measurement is a good surrogate for measurement of Black Smoke. The reflectance of the filters reflects the ambient concentration of elemental carbon.

A detailed description of the measurement method is given in the SOP ULTRA/KTL-L-1.0 ‘Determination of absorption coefficient using reflectometric method’ (Appendix A5).

1.5.9 Elemental composition

Every second PM2.5 filter will be analyzed for a set of elements by ICP-MS or XRF. The elemental analysis will be done together in the same laboratory after the sampling periods. The proper storage of the filter samples has to be provided to avoid contamination, losses etc. After the measuring period the filters should be stored (e.g. in the plastic petri dishes) for chemical analyses at -20 EC. Detailed instructions on how to transport the filter samples to the analytical laboratory will be distributed by the coordinating center.

1.5.10 Submitting data to coordinating center

Cleaned datasets are sent to coordinating center from all study centers for combined analyses. Submitted data must be in MS-Excel 5.0 format (if Excel is not possible, ASCII with comma (,) separator should be used). The coordinating center will send a blank Excel data entry sheet with variable names to all study centers. Study centers have to fill in the sheet and send it back to the coordinating center. The data should be stored on 3.5≅ discs and unnecessary compression of the data should be avoided. A sample file will be distributed to all centers before the end of the field work periods.

At least 2/3 (66 %) of valid raw data are required to calculate hourly averages. Daily average number concentrations are valid, if at least 16 hourly average values are available from noon to noon.

Definitely erroneous data must be cleaned from the dataset. If there are data points with special features, but which should not be rejected from the data, it is advisable to insert an elucidating remark into the corresponding data cell.

The timescale of the data must be continuous and shift to summertime corrected by inserting a missing hour into the data files. Data are marked by the starting time of the corresponding measurement period. For example, hourly datum from 4th of January 14:00 to 15:00 is marked as 4.1.1997 (first column in Excel data sheet) 14:00 (second column in Excel data sheet).

The datasets must contain data of following variables:

A. AS HOURLY ARITHMETIC AVERAGES

1) Meteorological data:
a. Mean temperature (^{0}C)
b. Relative humidity (%)
c. Wind speed (m/s)
d. Wind direction (^{0})
e. Ambient air pressure (mbar)

2) Gaseous pollutants:
a. NO ($\mu g/m^3$)
b. NO_2 ($\mu g/m^3$)
c. CO (mg/m^3)
d. SO_2 ($\mu g/m^3$)
e. O_3 ($\mu g/m^3$)

3) Particles:
a. Particle total number concentration, CPC3022A
b. Aerosol spectrometers, number concentrations
Main particle size ranges
$NC_{0.01-0.1}$; $NC_{0.1-1.0}$; $NC_{1.0-2.5}$; $NC_{0.01-2.5}$
Sub particle size ranges
$NC_{0.01-0.03}$; $NC_{0.03-0.1}$; $NC_{0.1-0.5}$; $NC_{0.5-1.0}$
c. Aerosol spectrometers, mass concentrations from MAS (Germany) and DAS (the Netherlands), volume concentrations from EAS (Finland)
Main particle size ranges
$MC_{0.01-0.1}$; $MC_{0.1-1.0}$; $MC_{1.0-2.5}$; $MC_{0.01-2.5}$
Sub particle size ranges
$MC_{0.01-0.03}$; $MC_{0.03-0.1}$; $MC_{0.1-0.5}$; $MC_{0.5-1.0}$

d. PM10 (only Finland and the Netherlands)

B. DAILY ARITHMETIC AVERAGES FROM NOON TO NOON

1) Meteorological data:
a. Mean temperature (^{0}C)
b. Relative humidity (%)
c. Wind speed (m/s)
d. Wind direction (^{0})
e. Ambient air pressure (mbar)

2) Gaseous pollutants:
a. NO ($\mu g/m^3$)
b. NO_2 ($\mu g/m^3$)
c. CO (mg/m^3)
d. SO_2 ($\mu g/m^3$)
e. O_3 ($\mu g/m^3$)

3) Particles:
a. Particle total number concentration, CPC3022A
b. Aerosol spectrometers, number concentrations

Main particle size ranges
$NC_{0.01-0.1}$; $NC_{0.1-1.0}$; $NC_{1.0-2.5}$; $NC_{0.01-2.5}$
Sub particle size ranges
$NC_{0.01-0.03}$; $NC_{0.03-0.1}$; $NC_{0.1-0.5}$; $NC_{0.5-1.0}$

c. Aerosol spectrometers, mass concentrations from MAS (Germany) and DAS (the Netherlands), volume concentrations from EAS (Finland)

Main particle size ranges
$MC_{0.01-0.1}$; $MC_{0.1-1.0}$; $MC_{1.0-2.5}$; $MC_{0.01-2.5}$
Sub particle size ranges
$MC_{0.01-0.03}$; $MC_{0.03-0.1}$; $MC_{0.1-0.5}$; $MC_{0.5-1.0}$

d. PM2.5, 24-hour data from noon to noon
e. Absorption coefficients from PM2.5 filters
f. Elemental composition data from PM2.5 filters
g. PM10

C. DAILY ARITHMETIC AVERAGES FROM MIDNIGHT TO MIDNIGHT

h. Mean daily aerosol size distribution spectra, 24-hour data calculated from midnight to midnight

1.6 PANEL STUDY

1.6.1 Study population

In the ULTRA study, people with coronary artery disease will be selected. Specifically, the inclusion criteria for the study population are:

-free living people of an age of 50 or more years
-a self report of a doctor diagnosed CHD (coronary heart disease), e.g. angina pectoris, past myocardial infarction (MI), a PTCA (percutaneous transluminal coronary angioplasty) or a coronary by-pass surgery
-non-smoking
-able to perform spirometry in an acceptable way
-preferably, people who also have respiratory problems will be selected, but this is not an inclusion criteria

The specific exclusion criteria of the study are:

-fresh (less than 3 months) cardiac event (MI, stroke, by-pass)

-exclusion based on a physician evaluation: subjects that are too sick i.e. have an unstable angina (NYHA 4) or are unable to perform the exercise challenge; have poor cooperation e.g. dementia, have Parkinson disease, or have difficulties in filling in the diaries and questionnaires (cooperation can also be checked as the ability to blow to the spirometer); or for any other reason are likely to have problems with the study, e.g. leaving for holidays during the winter for weeks or months or have a severe infectious disease such as HIV or tuberculosis, should not be included; (Standard questions could be included in the characterization questionnaire filled in/ checked during the first (screening) clinical visit when also ability to blow to the spirometer and to do the exercise challenge are checked)
-insulin-dependent diabetes mellitus (DM), as DM affects autonomic nervous system, which in turn regulates HRV (remark: adult onset DM also affects HRV, but the prevalence is so high that excluding these may cause problems)
-there will be no exclusion based on medication. However, preferably patients without beta-blockers should be selected. Beta-blockers affect the sympathetic nervous input to the heart, and therefore affects HRV, as do beta-agonists, too. Beta-blockers also lower HR and affect exercise capacity. Due to sympatho-vagal interactions, sympathetic outflow, affected by beta-agonists, is able to reduce the variations in HR generated by vagal modulation, too. During the course of the study, changes in medication are not preferably, but we cannot affect this.
-bundle branch block is not included in the exclusion criteria, but it can be used as an optional exclusion criteria, as it disturbs ST-analyses
-subjects with cardiac pacemakers are also preferably excluded, as HRV analyses can not be done in these subjects

The aim of the study is to achieve at least 500 repeated ambulatory ECG recordings per center. Considering drop out, this could be achieved with 12 - 13 biweekly recordings over a 6-month period in 50 subjects.

1.6.2 Characterization

The subjects will be characterized with a questionnaire (Appendix A12). In addition, resting 12-lead ECGs are taken from all subjects.

1.6.3 Instructing the subjects on the first visit

After screening, every possible subject is invited to a clinical visit. The purpose of this first visit is to check for the eligibility criteria and let the subjects go through the procedures before deciding whether to participate to the study or not. During this visit, a physician will interview the subject and check for inclusion and exclusion criteria. If the criteria are met, there will also be a medical examination and the whole clinical visit procedure will be followed. If there are not any problems in following the flow of the visit, the subject will be guided to fill in the diary. After this, the subject is asked if he/she is willing to continue in the ULTRA study. If yes, a written consent is asked, a diary will be given to the subject and the clinical visits scheduled. If problems emerge, the subject will not be asked to participate.

1.6.4 Daily measurements at home

The panelists will fill in a diary on symptoms every day. The diary will be changed during the clinical visits. The diary is attached as Appendix A13. It will be taken care of that a panelist will always have a diary to fill even if she or he would not attend the clinical visit at a certain time, e.g. by having spare diaries at home.

Instructions for filling out the diary:
The diary should be filled out every day in the evening before going to bed. Your answers should reflect the occurrence of symptoms over the whole day. Please use a black marker and write clearly and legible in each square. Please fill out all squares, even if you did not experienced the symptom at this day. Please bring the filled out diaries with you to each examination. You will be supplied with new diary forms at the visit. Please fill out a diary on the evening of the day at which the examination has taken place. The diary contains additional questions which are important for the study.

1.6.5 Biweekly visit to the clinic

The subjects will have a clinical visit every two weeks. The visit will last about 1.5 hours. For each subject, the visit is aimed to be always on the same weekday at the same time (∀ 1 h). If this is not possible, e.g. because of an illness, the next choice is to move the particular visit to another day at the same time. When the latter is also impossible, the clinical visit should be placed whenever possible. During the visit, autonomous nervous system will be stimulated by paced breathing (parasympathetic stimulation) and standing up from supine position (sympathetic stimulation), urine samples will be collected, spirometric lung function of the subject will be measured, and electrocardiograph (ECG) will be recorded over the time of the visit. The visit includes also a at least 6-minute exercise challenge at a pace aiming at a level of 90 - 100 heart beats / min (Appendix A7). The field worker, e.g. a nurse, will take care of the visit, but a consulting physician should be easily available. The detailed flow of the visit, instructions for specific procedures, and safety precautions are described in respective SOPs (Appendices A6, A7, A8).

1.7 DATA MANAGEMENT

This chapter gives guidelines for data management. A proper data management is important to reduce the number of errors in data. It is also important to achieve standardization in data management, because the data sent from the participants to the coordinating center have to be in identical format. Finally, a proper data protection is required.

1.7.1 Limiting errors in data during the fieldwork

Errors in data can be reduced already during the fieldwork before the actual data entry. Field personnel have to be clearly instructed and well trained. Field protocols have to be as detailed as possible and they have to be followed. All exceptions from a protocol have to be marked in a fieldwork diary. All basic data (diaries, questionnaires) have to be checked as soon as

possible after a researcher has them to detect obvious errors. Detailed fieldwork instructions are given in separate standard operating procedures (Appendixes A2, A3- 1-3, A4, A5, A6, A7, A8).

1.7.2 Data entry

1.7.2.1 Limiting errors in data entry

It is not necessary to standardize the software to be used for the data entry. However, it is preferable to use such software (e.g. SPSS Data Entry), which offers a possibility to use build-in checks of impossible values. The subject numbers and study dates should be filled in advance to limit the amount of routine work.

A researcher has to check all the forms before a keyboard operator starts the data entry. Especially, forms with blank spaces which should have been filled in, all forms with written remarks and forms with crossed/changed questions have to be checked carefully. Unclear responses have to be clarified. If a response is questionable, it has to be coded as missing.

Keyboard operators have to be given clear guidelines how to enter the data. The keyboard operators have to contact the researcher if things have to be interpreted. The keyboard operators have to keep track of unclear diaries detailing what item was unclear and how it was coded. This is important specially if the researcher cannot be contacted immediately in unclear situations.

1.7.2.2 Double entry

The quality of data entry has to be checked by a double entry of a 10% random sample of at least the original diary and clinic visit forms. Double entry has to be done preferably by a different person in order to check the amount of typing errors. The values that have been entered twice have to be compared. The error rate is calculated as follows:

1. Determine the number of pairs with different values for the same variable for the same observation (d).
2. Determine the total number of entered variables (n).
3. Calculate error rate as d/n * 100%.

For example, when diary data have been collected from 50 subjects for 25 weeks (total of 1250 weeks), 125 randomly selected weeks should be entered for a second time. The diary contains 20 variables per day. Thus, the total number of entered variables is 2 entries * 125 weeks * 7 days * 20 variables = 35000 (=n). First, the logical checks on possible values have to be conducted and all unclear values have to be checked by the researcher on both sets of entered data. Suppose that after these checks there are 400 pairs for which the value of a variable is not the same for the same observation. The error rate is then calculated as (400/35000)*100 = 1.14%.

An error rate of 1% is considered acceptable for diaries and questionnaires. If the calculated error rate exceeds that value (as in the example), first the reasons for this should be

investigated. For example, it may be that one of the keyboard operators has performed badly. The data of that keyboard operator should then be entered again. Alternatively, specific variables might have been entered badly. These could then be entered again. However, if no specific reason could be detected, all data should be entered a second time. Differences between data entered twice for documenting error rates should not be used to correct errors in the data, as all data have not been checked. The observed error rate has to be marked in the data transfer form.

1.7.3 Data validation and verification

The following checks for impossible values and the logical checks in Appendix A15 have to be done before transferring data to the coordinating center:

After the data entry has been completed a checking program has to be run to check impossible values. Summary statistics (number of observations, arithmetic mean, standard deviation, minimum and maximum values) of all variables have to be calculated. Also, frequencies of all categorical variables have to be checked. Observations with impossible values have to be checked on the forms and typing errors have to be corrected.

There are logical connections between some variables in questionnaires. Observations with impossible combinations have to be displayed and checked. If the impossible combination is due to the typing error, it has to be corrected. If an impossible combination has been saved as it is in the questionnaire, then the inconsistency has to be solved according to the decision rules in the Appendix A15.

It is important to store original data in order to be able to go back to the original data in case of doubt or inconsistencies in the data. Therefore, all the changes should be made in a working copy of the original data. A log should be kept of all the changes made in the working copy of the original data.

1.7.4 Data transfer

1.7.4.1 Data to be transferred

The individual centers need to send following data to the coordinating center:

- baseline questionnaires 1 and 2 (physician and self-administered)
- diary
- clinical visit questionnaire
- clinical visit log book
- medication sheet
- spirometry

Each data have to be transferred in separate files. The guidelines and check forms are in Appendices A16 and A17. Because of the data protection, a subject’s name must not be included in data. All data have to be identified only by a subject’s identification number. The variables needed and the coding of the responses are described in the Appendices A14 and A15. The variables in files have to be in same order as in the Appendix A14.

Of diary data all available days of all study subjects have to transferred. Those days when a subject has not answered to any question have to be also included to preserve the time structure in the data.

The data files have to be named as follows:

	Amsterdam	Erfurt	Helsinki
Baseline questionnaire 1	BQ1AMS.DAT	BQ1ERF.DAT	BQ1HEL.DAT
Baseline questionnaire 2	BQ2AMS.DAT	BQ2ERF.DAT	BQ2HEL.DAT
Diary	DIARYAMS.DAT	DIARYERF.DAT	DIARYHEL.DAT
Clinical visit questionnaire	CLQAMS.DAT	CLQERF.DAT	CLQHEL.DAT
Clinical visit log book	CLLOGAMS.DAT	CLLOGERF.DAT	CLLOGHEL.DAT
Medication sheet	MEDICAMS.DAT	MEDICERF.DAT	MEDICHEL.DAT
Spirometry	SPIROAMS.DAT	SPIROERF.DAT	SPIROHEL.DAT

The correctness of the data transfer is checked by data transfer check forms (Appendix A17). The individual centers have to fill in the forms and send them to the coordinating center by fax. The individual centers also have to send summary statistics (number of observations, arithmetic mean, standard deviation, minimum and maximum values) for all variables and also frequencies of categorical variables.

1.7.4.2 Form of data transfer

Data files have to be transferred in comma-delimited ASCII format. The files can be zipped (PKZIP 2.04 or WinZip 6.3) before sending them to the coordinating center. Files can be sent by E-mail or alternatively by well packed 3.5 inch floppy disks. The data transfer check forms have to be sent by fax to the coordinating center.

An example of a file to be transferred (diary):

101,8,12,1998,0,0,0,1,0,0,2,0,0,0,2,1,1,4,.,1,0.5,1,.,.,.,.,.,.,.,1,1,0
102,8,12,1998,0,0,0,0,0,0,0,0,0,0,0,0,0,0,1,.,.,.,.,.,.,.,.,.,.,.,10,0

1.8 ANALYSES

1.8.1 Analyses of the ambulatory ECG recordings in Kuopio

From all centers, the recorded ambulatory ECG tapes are sent weekly to Kuopio University Hospital, Department of Clinical Physiology, for analyses. In the department, there are trained nurses who take care specifically of the ULTRA Holter analyses. The tapes recorded last with each recorder should have been marked before sending and are analyzed first in order to check the functioning of the recorders. If malfuctioning occurred, the nurses will inform the study centre immediately.

All recordings consist of the following periods:

-Rest, supine, spontaneous breathing (= REST SPONTANEOUS BREATHING)

-Rest, supine, paced breathing (=REST PACED BREATHING)

-Standing (=STANDING)

-Bicycle exercise (=STRESS)

-Rest, supine, spontaneous breathing (=REST RECOVERY)

In the recordings, there are event marks in the beginning and at the end of each period. In addition, all time points are marked also in the clinical visit log book. A stopwatch and the recorder's clock should have been started at the same time, but in practice there are small differences between these two times. Primarily, the event marks will be used to identify the beginning and the end of each period.

Some of the analyses are based on the whole recorded data, some on both specific short periods and the whole recorded data.

The short analyses are done from selected, representative 5-minute epochs (high signal quality, as few ectopic beats as possible).

Step-by-step flow of the analysis:

1. The ULTRA preference file is used in the Oxford II Medilog workstation.
2. The tape is read into the database in the workstation.
3. The templates are checked and corrected if necessary.
4. The correctness of the shortest and longest R-R –intervals are checked.
5. Specific analyses are performed as follows:

Heart rate variability

-The whole period and all five specific 5-minute periods (rest spontaneous breathing, rest paced breathing, standing, stress, and rest recovery) will be analyzed.

-If the subject has atrial fibrillation or large number of ectopic beats (e.g. bigeminy) the HRV analysis will be omitted (because the results are useless).

ST-analysis

-The whole recording will be analyzed. Only channel 1 will be used for the analysis.

-If the true baseline is below isoelectric level (0-level), the baseline will be set according to the true baseline level during the rest spontaneous breathing period.

-If a new baseline is set, the actual baseline will be marked in the ST-trend figure (in mV).

-A significant ST-depression is defined as a more than 1 min ST-depression below 0.053 mV (= 0.53 mm). ST-depression is measured 63 ms after J-point (slope 55 ms).

-ST-analysis will be done also to subjects with bundle branch blocks, WPW-syndrome, non-specific intraventricular conduction defects or prior myocardial infarcts (Q-, non-Q-wave).

The effect of these abnormalities will be taken into account in the final statistical analyses.

QT-analysis

-The whole recording and 3 specific periods (rest spontaneous breathing, stress, rest recovery) will be analyzed.

-Primarily, the channel 1 will be used for the analysis. If the amplitude of the T-wave is very low, and it is difficult to detect the end of T-(U)-wave, the channel 2 will be used. The use of the same channel in every subsequent recordings will be taken care of.

-The measurement points with a 5-minute window (whole recording) and with a 30 sec window (specific 5 min periods) will be check.

-QT-analysis will be done also to subjects with bundle branch blocks, WPW-syndrome, non-specific intraventricular conduction defects or prior myocardial infarcts (Q-, non-Q-wave). The effect of these abnormalities will be taken into account in the final statistical analyses.

VES, SVES

-The whole recording and the stress period will be analyzed. The latter has to be done by manual counting from the full disclosure screen.

-The number of the ectopic beats will be marked on the front page of the printout.

PR-interval

-The PR-interval will be measured manually from 3 consecutive beats during the rest spontaneous breathing period.

-The PR-interval from subjects with atrial fibrillation or with atrio-ventricular conduction defects (except patients with first-degree block) will not be measured.

-The PR-interval (average of 3 measurements) will be marked on the front page of the printout.

6. All ECG data will be converted to ASCII format for possible further analysis.
7. The original and converted ASCII data will be saved on the KLF-server (NT-server; directory T:\users\KLF-OXFORD\ULTRA). A DAT-recorder will be used for back-up. Ultimately, all data will be written on CD-R:s.

After the analyses, all the tapes will be stored in the National Public Health Institute, Kuopio. A printout of the results will be stored in the Department of Clinical Physiology, and a copy of it will be sent to the respective study center. All the ECG data will be keypunched by the coordinating center.

1.8.2 Analyses of the PM2.5 filters

The filters will be weighed according the PM2.5 SOP. In addition, the absorbance of the filters will be measured according the respective SOP. The absorbance of the Finnish filters will be measured at the National Public Health Institute, Finland, and of the Dutch and German filters in the University of Utrecht, the Netherlands. The elemental composition analyses will be conducted in a laboratory in Antwerpen, Belgium, using the XRF method.

1.8.3 Urinary samples

After the field work all urinary samples will be sent to Brussels for analyses according instructions in the SOP. The results will be sent to the coordinating center. Urinary CC16 concentrations will measured by an automated latex immunoassay (Bernard A, et al. 1992). From all samples, creatinine concentrations will also be determined.

1.9 STATISTICAL ANALYSES

The most essential part of the ULTRA data consists of repeated measures (i.e. longitudinal). The diary data is a typical example of longitudinal data: the subjects have kept diary on their symptoms on a daily basis about six months. The clinic visit data are rather similar to diary data. However, there are some differences: the response variables are mainly continuous, the number of observations per subject is much smaller and the time between repeated observations is longer (two weeks). Basically, both the diary and clinic data will be analysed in a similar way, although above mentioned small differences affect the modeling.

1.9.1 Regression models

Longitudinal models are models in which all observations from subjects are used as such. In aggregated models a daily mean response (eg. daily prevalence or incidence of cough) is used as a dependent variable. In longitudinal data it is important to take into account the dependence of the observations from a same subject, which can be modeled with a proper covariance structure. It is also important to pay attention to differences between subjects, especially individual levels.

In the analyses of ULTRA data, mainly longitudinal models will be used because they are more powerful, they include more information and differences between subjects can be taken into account. However, aggregated models can be used to examine long-term time trends, seasonal effects and other possible covariates, and they can be used also as a part of sensitivity analysis. In general, fixed effects model will be used for taking care of the differences in average level across subjects. The convergence may really be a problem in the random effects model, especially if the number of cases is small (eg. when modeling incidence of symptoms).

The dependence of the observations within a subject has to be taken into account using a proper covariance structure. If the correlation fades away with time, then an autoregressive

structure (eg. AR(1) or AR(2)) could be used. If the correlation between observations in a subject arise mainly as a consequence of variation in the regression intercept between individuals then compound symmetry could be the correct structure. Autoregressive covariance structure is typically used in diary studies. However, if the number of symptoms is small (eg. incidence of symptoms in diary) or the number of observations per subject is small (as in clinic visit data), compound symmetry may be the correct choice. Log likelihood can be used for comparing different covariance structures.

Subject spesific levels of response variable will be handled by including in a model a dummy variable for each subject. Another alternative would be to explicitly spesify the covariance structure as compound symmetry and to leave out the dummies for the subjects.

Both S-PLUS and SAS will be used. S-PLUS will be used as a main tool, because non-linear associations will be explored with generalized additive models (gam), which are available only in S-PLUS. Generalized linear regression models (gam and glm functions in S-PLUS, the GENMOD procedure in SAS) will be used for continuous (eg. HRV variables), binary (eg. symptoms in diary) and count response variables (eg. arrhytmias in ECG). The appearance of ST-segment depression can be examined with survival analyses, like Cox regression (the PHREG procedure), as earlier appearance of ST-depression during the exercise test can be interpreted as more severe ischaemia. For survival analyses a variable, which indicates the time to onset of the ST-depression during the exercise test, is created. Subject is used as strata. The assumption of proportional hazards needs to be tested by plotting log(-log) survival curves.

1.9.2 Modeling strategy

Confounder models for different health endpoints will be established for each center separately. First, covariates are used to build a ‘basic model’ without an air pollution variable in the model. Then individual pollutants are added to the model one at a time.

If long term effects (such as trend) are still disturbing the short-term confounders (such as temperature) no proper estimate can be made for the function of the latter. Thus, only before long-term confounding is dealt with properly, shorter term effects can be filtered out. Therefore, the sequence of modelling will start with long-term confounders towards short-term confounders.

In modeling the diary data at least following covariates will be considered: a dummy for each subject, long-term time trend, influenza (external data), weather (temperature, relative humidity and ambient air pressure, lags 0, 1, 2 and 3), weekday (or weekend) and public holidays. In modeling the clinic visit data at least following covariates will be considered: a dummy for each subject, long-term time trend, weather (temperature and relative humidity, lags 0, 1, 2 and 3), weekday, time of visit and public holidays, infections (from clinic visit questionnaire).

The basic model will be build by entering covariates into the model one by one according to the order above. In each step the association of the covariate entered last will be evaluated and the most appropriate form of the covariate will be included in the following steps. Trend, temperature, relative humidity and ambient air pressure are going to be included as

confounders in the model independent of the direction of the association. Influenza/infections will only be included when a relationship in the expected direction occurs in the exploring analyses. The shape and lags of these covariates will be explored in S-Plus using lowess functions.

The criteria for building the basic model are AIC, partial autocorrelation (PACF) plots of the residuals (only for diary) and exposure-response plots. In principle the model with the lowest AIC is selected from a predefined range of alternatives. In previous analyses it has been observed that AIC may select a too detailed trend model. Therefore, the exposure-response and PACF plots will be checked. If the response trend plot is too detailed (patterns with a period of less than a month) or at smaller lags (0-10 days) of the autocorrelation plots of the residuals negative autocorrelation occurs, a less detailed model than the one indicated by the lowest AIC will be selected.

In the analysis of both the clinic visit and diary data 24-h mean concentrations of the pollutants (lags from 0 to 3 days and 5-day average) will be used first as an exposure estimate. In the analysis of the clinic visit data also subject specific exposure estimates will be used as concentrations of the previous 1 hour (the hour before coming to the clinic), the averages of the previous 1-2, 3-4, 1-4, 5-8, 9-12, 13-16, 17-20, 21-24 hours and the average of the previous 24 hours.

Sensitivity analyses will be done using different lags and functions of trend, influenza, temperature, relative humidity and ambient air pressure for interesting combinations of exposure and health outcome. As we are looking for robust results, the results from the selected basic model should not give substantially different results from other reasonable models. Pollen counts will also be included in the sensitivity analyses to check possible confounding. However, it is the assumption that this variable does not confound the model because of the probably low correlation with air pollution; the lacking of summer period in Germany and Finland; and the nature of the population with probably low numbers of allergic subjects. The effect of ambient air pressure will be examined. Also the effect of imputed air pollution will be checked. The interaction of temperature and air pollution will be explored and two-pollutant models will be checked. A part of the analysis will be run for the subpopulations of the subjects (e.g. prior MI, diabetes, medication: use of beta-blockers, antiarrhythmic, asthma medication).

1.10 TIME TABLE

-Meeting in Helsinki 29.-30.6.1997
    -planning of the project

-Telephone meeting 17.2.1998
    -outline of the field work

-Meeting in Athens 21.3.-22.3.1998
    -the first draft of the health study protocol

-Air hygiene meeting in June 25-26, 1998 in Munich, organized by Wolfgang Kreyling

-air hygiene protocols and SOPs / OPs

-Telephone meeting in 9.6.1998
-draft of the study protocol, instrumentation

-Meeting in Helsinki 31.8. - 1.9.1998
-final protocols

-Training workshop in Kuopio 28.9. - 29.9.1998
-training of the field workers / clinical visit

-Field work of the study October 1998- June 1999

-Telephone meeting 18.5.1999
-status of the study

-Meeting in Athens 5.9.1999
-statistical analyses plan

- Aim: Data in the coordinating center by the end of 1999

-Telephone meeting 10.1.2000
-status of the data

-Workshop in Kuopio 27.2.-1.3.2000
-analyses of the almost final data, publication plan

-Telephone meeting 25.5.2000
-discussion on SOP deviations

-Telephone meeting 17.8.2000
-status of analyses and manuscripts

-Meeting in Munich 28.-30.9.2000
-draft manuscripts

-Telephone meeting 14.12.2000
-draft manuscripts

-End of the contract - end of year 2000

-Telephone meeting 8.2.2001
-Final report to EU- 2/2001

1.11. REFERENCES

Bernard A, Marchandise FX, Depelchin S, Lauwerys R, Sibille Y. Clara cell protein in serum and bronchoalveolar lavage. Eur Resp J 1992; 5:1231-1238.

Bernard A and Lauwerys R. Continuous flow for the automation of latex immunoassay by particle counting. Clin Chem 1983; 29: 1007-1011.

Bernard A, Lauwerys R, Noel A, Van de Leene B, Lambert A. Determination by latex immunoassay of protein 1 in normal and pthological urine. Clin Chem Acta 1991; 201: 231-246.

Bigger JT. Fleiss JL. Rolnitzky LM. Steinman RC. The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. Circulation. 1993; 88: 927-934.

Burnett RT, Dales R, Krewski D, Vincent R, Dann T, Brook JR. Association between ambient particulate sulfate adanddmissions to Ontario hospitals for cardiac and respiratory diseases. Am J Epidemiol 1995; 142: 15-22.

A Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Health effects of outdoor air polution. Am J Respir Crit Care Med 1996; 153: 3-50.

Dekker JM. Schouten EG. Klootwijk P. Pool J. Kromhout D. ST segment and T wave characteristics as indicators of coronary heart disease risk: the Zutphen Study. J Am College Cardiol 1995; 25:1321-1326.

Dockery DW and Pope CA III. Acute respiratory effects of particulate air pollution. Annu Rev Public Health 1994; 15:107-132.

Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. Association between air pollution and mortality in six U.S. cities. N Engl J Med 1993; 329: 1753-1759.

Dreher K, Jaskot R, Richards J, Lehman J, Winsett D, Hoffman A, Costa D. Acute pulmonary toxicity of size-fractionated ambient air particulate matter. Am J Respir Crit Care Med 1996; 153 (pt 2 of 2): A15.

Dusseldorp A, Kruize H, Brunekreef B, Hofschreuder P, de Meer G, van Oudvorst AB. Associations of PM10 and airborne iron with respiratory health of adults living near a steel factory. Am J Respir Crit Care Med 1995; 152: 1932-1939.

Hermans C, Bernard A. Clara cell protein: characteristics and potential applications as marker of lung toxicity. Biomarkers 1996; 1: 7.12.

Oberdörster G, Gelein RM, Ferin J, Weiss B. Association of particulate air pollution and acute mortality: involvement of ultrafine particles? Inhal Toxicol 1995; 7: 111-24.

Osornio-Vargas AR, Alfaro-Moreno E, Rosas I, Lindroos PM, Badgett A, Dreher K, Bonner JC. The in vitro toxicity of ambient PM10 particles form the souther, central and northern regions of Mexico City to lung fibroblasts is related to transition metal content. Am J Respir Crit Care Med 1996; 153 (pt 2 of 2): A15.

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

Peters A, Wichmann E, Tuch T, Heinrich J, Heyder J. Respiratory effects are associated with the number of ultra-fine particles. Am J Respir Crit Care Med 1997; 155: 1376-1383.

Roemer, Hoek, Brunekreef for the PEACE study team, Draft Study Manual PEACE Project, June 1995, Wageningen, the Netherlands

Schwartz J. What are people dying of on high air pollution days? Environ Res 1994; 64: 26-35.

Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation and clinical use. Circulation 1996; 93: 1043-1065.

Tepper JS, Lehmann JR, Winset DW, Costa DL, Ghio AJ (1994). The role of surface complexed iron in the development of acute lung inflammation and airway hyperresponsiveness. Am J Resp Crit Care Med 1994; 149: A839.

Tsuji H. Venditti FJ Jr. Manders ES. Evans JC. Larson MG. Feldman CL. Levy D. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. Circulation 1994; 90: 878-883.

2 REMARKS AND RECOMMENDATIONS

2 REMARKS AND RECOMMENDATIONS

As in all studies, in advance carefully prepared plans may change during the course of the field work for a reason or another. The field work in practice can reveal things that could be done better or could be taken into account in another way as planned. In this chapter these topics are discussed and some recommendations are given.

All SOP deviations are listed in the respective SOPs on the SOP deviation sheet.

2.1 MEASUREMENT OF PM2.5

PM2.5 measurements using the SOP have been of good quality in the three centers, judged by the limits of detection and precision of field duplicates. The SOP is therefore in principle suitable. At some points the SOP could be improved. We prescribed the use of Andersen Teflon filters instead of the more widely available Gelman Teflon filters based upon previous experiences that Andersen filters were much less curved (which is advantageous for reflectance measurements). The current batch was as curved as the earlier Gelman filters, so that there is no advantage anymore in using Andersen filters. More detailed criteria with respect to flow meter calibration and use (ambient temperature and pressure adjustment) should be provided (section 7.1). If the pump does not leak, an alternative configuration including a dry gas meter at the outlet of the pump could be used to determine sample volumes. In addition, it is recommend that all participating centers would use the same method to measure flow. In 7.1.3 the target weight from the external mass piece should be specified as the (certified) weight provided by the manufacturer. In 7.1.3 point 6 it should read that ‘the same’ instead of ‘other’ filters should be reweighed at the end of the session. In calculations, the formulas for adjusting for buoyancy should be added.

2.2 AEROSOL SPECTROMETERS

2.2.1 Aerosol measurements in Erfurt by MAS

Aerosol spectrometer measurements have been of good quality and were performed according to the OP. It proved very suitable that the performance of the MAS was checked multiple times during work shifts of working days due to the presence of operating staff and also once at both days of weekends. This resulted in a minimal number of missing data (4%). The missing data was caused predominantly by usual maintenance like flow controls, mobility calibration, laser alignment and monodisperse particle calibration. More importantly, the concept of comparing the total number concentration determined by MAS and the CPC multiple times per weekday provided an additional instantaneous information of the operator on the performance of either instrument.

Laser of the LAS-X and its adjustment caused some difficulties. However, both the mobility calibration and the routine checks of the LAS-X using monodisperse Latex spheres provided a means to control and correct for those deviations.

The site visit of the coordinator for aerosol measurements after about one third of the study period proved useful to stimulate efforts of the operators to improve maintenance and control of MAS.

2.2.2 Aerosol measurement in Amsterdam by DAS

DAS measurements have been of good quality and were performed according to the OP with a few exceptions. DAS was not physically checked every day by an operator but only once a week. However, the performance of DAS was checked daily by remote control. A malfunction which resulted in a severe lack of data during more than a week occurred in the beginning of the study. This happened because of two consecutive power failures within a minute. After the first failure the PC that controlled all the instruments and communications via the modem started to reboot when yet another power failure occurred resulting in a severe corruption of several system files and the PC had to be taken away from the site. Overall, during the whole study period a total of 14 % of data are missing. A substantial improvement of quality assurance was the continuous monitoring of essential flows of the instruments of DAS, which is far superior to periodically performed checks of the various flows. The lessons for the future out of the long malfunction period are 1) use UPS to avoid such cases; 2) have a duplicate PC with all the software installed such it can be used for replacement if the PC at the site fails.

The version of LAS-X used in Amsterdam appeared to have a principal short come because of the low aerosol sampling flow and the limited number of channels for particle sizes. The former resulted in a limitation of the upper detectable aerosol concentration of < 5000 cm^{-3}. This could be compensated by (1) using the LAS in 3 separate size ranges (one integrated was used), such that the high counts in the smallest size channel will not interfere with the other two ranges. In this way the smallest range can be discarded without affecting the other two larger particle size ranges, and (2) discarding LAS-X data when SMPS showed high concentrations in the according size channels – the latter was possible due to the overlap of SMPS and LAS-X in the size range of 0.1 – 0.4 µm.

Principally the concept of comparing the total number concentration measured by DAS and CPC provides an excellent option on data quality assurance to remotely control for changes in the performance of either of the instruments on a daily basis.

The site visit of the coordinator for aerosol measurements after about one third of the study period proved useful to stimulate efforts of the operators to improve maintenance and control of DAS.

2.2.3 Aerosol measurement in Helsinki by EAS

EAS measurements have been of good quality and were performed according to the OP with a few exceptions. EAS requires far less maintenance than the other spectrometers. Another big advantage is the fact that Dr. Mirme, who had constructed the EAS performed the measurements during the study. EAS is therefore particularly useful for these kinds of studies because it has less vulnerable parts, and check controls every ten minutes are stored on file for eventually necessary later reconstruction. Therefore less effort was undertaken than required in the OP, e.g. field forms of EAS and CPC were combined. As a permanent modem

connection was not available, only a very limited bi-daily check was done followed by a more thorough check every week. The transfer of the data to processing center in Tartu was made manually by a servicing person regularly downloading the data files from EAS computer and sending them via Electronic Mail to the center.

There was a major loss of data (a 5-day break) that resulted from a mechanical failure of the level on which EAS was placed. Still, overall there was a minimal number of missing data (3%).

After the site visit at about the middle of the study period, comparison between the total number concentration measured by EAS and CPC were introduced on a weekly base which had not occurred before. These comparisons indicated a slightly non-linear relation between the EAS and CPC at higher particle concentration. Calibration of the CPC at the end of the measurement period suggested that this was not due to the calibration of CPC. A similar association has been observed earlier, and it may be due to a relative decrease in ambient particle concentration in size range below 20 nm at high particle concentrations, particularly in the size range between the cut off sizes of the two instruments that are 6-7 nm for CPC and ~10 nm for EAS.

The site visit of the coordinator for aerosol measurements after about the middle of the study period proved useful to stimulate efforts of the operators to improve maintenance and control of EAS.

2.3 MEASUREMENT OF NC WITH CPC

The CPC SOP was basically suitable for the ULTRA study and the measurements were of good quality. Some of the details need, however, some discussion.

First of all the SOP is based on the assumption that the details of instruments are known. For a less experienced scientist, this is not necessarily true and therefore some reference material should be pointed out. An example of this is the use of flow meter (7.3. b).

A second general comment is that the campaign time was not clearly defined (e.g. UTC, local time, local winter time, etc.). In addition, some guidelines are needed for setting the computer time, e.g. what is acceptable inaccuracy of time (10 sec., 1 min).

A third general comment is that this SOP was based on the fact that there was a complementary aerosol instrument available, namely aerosol spectrometer. Therefore this guide can not be taken as general instructions for using a CPC.

Detailed comments:
7.2. Item c, it is recommended that all the leds are checked (Temperatures, laser and liquid level). If any of them is not green, it is advisable to check that parameter at the site.

7.2. item d, to check the flow one should first see that the leds are green.

7.2. One should also check that the particle led is flashing or on all the time, indicating that CPC is detecting particles.

7.2.1. It should be added that the incorrect sample flow can be detected first from the flow led being yellow.

7.3. item b, both aerosol flow (low flow) and total flow (high flow) should be measured. It is advisable to run the instrument at the high flow mode.

Additionally the voltage of the photometric mode zero should be checked. This can be done by switching of the flow and checking the voltage in the status menu.

8.2. The data should be plotted weekly, in order to check that it looks appropriate. Any strange behavior, e.g. high spikes, very low concentration, very little variation in concentration, should make the user aware of a potential problem.

The form A. daily maintenance:
All the leds should be checked.

2.4 DETERMINATION OF ABSORPTION COEFFICIENT USING REFLECTOMETRIC METHOD

As the results of the intercomparison samples measured both in the Netherlands and Finland were very close to each other, the SOP seems to have worked in securing the uniformity of the measurements. In Finland there was some uncertainty in the interpretation of chapters 7.1.2 and 7.2. The original idea was to measure several control filters only in the beginning of the study, and then to use the selected primary control filter during the whole study period. In this case, it would be reasonable to check every now and then that the primary control filter's reflective properties do not change during the study. In Finland this was done by comparing the reflectance of the primary control filter to the other control filters occasionally. In chapter 7.3, there should be added a limit for the deviation of the primary control filter during series of 25 samples, exceeding of which would result in a remeasurement of the filters. The measurement of humidity during measurement session is not necessary (chapter 8.0).

2.5 RECORDING OF THE AMBULATORY ECG

The ambulatory ECG SOP functioned properly. In Erfurt the SOP was deviated so that the time of the Holter recorder was not set to 00:00 in the beginning of the recording (instead, the real time was used). According the SOP in the beginning and at the end of the recording a 1 min rhythm strip was recorded. However, the speed of the ECG paper could perhaps be slower after a 10-20 second period of recording with a faster speed. This would save quite an amount of ECG paper.

The crucial point in the recording of good quality Holter tapes is a careful preparation of the recording, especially how the electrodes and patient cables are attached to the skin and fixed.

It can never be emphasized too much that the electrodes and wires must be fixed properly, in order that there will not be unnecessary disturbances in the recording. In the future, a digital registration system should be preferred to analog system used in the present study to improve the measurements and analyses. For example, a digital system enables a more exact determination of time points during a registration. In addition, direct transfer of the results from the Holter analyses to a dataset does save costs and also would increase data security.

2.6 FLOW OF THE CLINICAL VISIT

In principal, the flow of the visit was fluent. However, there have been some differences between the centers. In Finland, the urinary samples were collected sometimes at home just before the clinical visit. This was possible because the fieldworkers visited the subjects the day before the visit to take indoor and personal PM2.5 measurement equipment to the subjects and took the sample collection container with them at the same time. The fieldworkers came back the next day to collect the equipment and drive the subject to the clinical visit.

There were also differences in the work load during the exercise challenge test. Based on the mean HR during the exercise the target HR was not achieved always in all three centers. In addition, the criteria for not conducting the exercise test varied between the centers, so that especially in Finland no exercise test was done during a large proportion of the visits. This complicates many analyses. In future studies, it should be ensured that the subjects and the nurse feel comfortable in performing the exercise test. Further standardization of the exercise period would be needed for a future study.

2.7 URINARY CC16

The field workers gave urinary samples for quality control purposes, i.e. divided one sample into several tubes and labeled the tubes differently. However, the quality control plan had to be changed as the CC16 concentrations in these control samples were close to the detection limit. Therefore, as duplicate samples were collected from the study subjects during the field work in Helsinki, 50 duplicate samples were sent later to Brussels for CC16 analyses. These duplicate samples were selected based on the values of the already analyzed original samples to cover the whole range of the CC16 concentrations.

In the clinical visit SOP it was stated that the urinary samples are stored during the day in room temperature, and are put into the refrigerator (-18 °C) in the end of the day for storage. However, because of its anionic character CC16 is extremely stable in urine and it stays stable for days at room temperature, months at 4°C and years at -18C°. Thus it does not matter whether the urinary samples are put into a freezer immediately or not.

2.8 SPIROMETRY

It is difficult to evaluate whether the SOP has functioned properly. Review of the tracings of the first tests of each subject by the SOP coordinator revealed that the measurements were generally conducted according to the SOP and they were of good quality. Some changes would be useful. It should be prescribed more clearly that in addition to the best selected values also the reproducibility of the test should be available for analysis. Time of the test should be available for analysis as well. In 7.5.2 the selection procedure could be adapted such that the acceptable attempts are not reduced to two attempts but are all available for analysis. Only tests with really low PEF values (e.g. 20% below the maximum) should be excluded.

2.9 STUDY POPULATION

In Amsterdam, the study population was recruited in cooperation with the municipal health center. Subjects were initially recruited by distribution of information letters and screening questionnaires in senior residences. These residences are apartment buildings for free living elderly with special facilities like a little supermarket, hairdresser and a mobile bank. In six of these homes an information meeting was held. Participants were invited for a first introduction, which consisted of a check of inclusion criteria by a physician and a trial spirometry test. This first recruitment step resulted in 11 participating subjects. Because of this response a call for participants was published in a local newspaper and letters were distributed in areas mainly inhabited by the elderly. By the end of 1998, 33 subjects were included in the study. Eight persons more could be included by the end of February/early March 1999 via the department of cardiology of the Academical Medical Center (AMC) nearby. In total, 41 subjects started the study but four dropped out after the first measurement, resulting in a total of 37 subjects. To approach the designed number of measurements the study period was prolonged until 18 June, 1999.

In Erfurt, the study population was recruited through Dr. Bischoff, a local cardiologist. Out of 62 subjects that were recruited, a total of 12 had to be excluded according to the exclusion criteria: 6 were current smokers, 4 subjects had an insulin dependent diabetes and 2 subjects were too ill. Further, one person did not want to take part because of time reasons.

In Helsinki, the study population was sought through a patient organization 'Suomen Sydäntautiliitto' – The Finnish Heart Association. There was an advertisement in their journal 'Sydän', and information letters were distributed through gymnastic groups of the association. Letters were also mailed through the local division of the association to members with a postal code representing the study area in Helsinki. In addition, there was an advertisement in a local newspaper 'Alueuutiset'.

The potential subjects were advised to call the researchers in order to inform of the interest in participating to the study. The inclusion criteria were checked during the telephone discussion and the contact information was collected. About 95 telephone calls were received. Some 60 subjects fulfilled the inclusion criteria and were asked to participate to information meetings held on two evenings. In the two meetings, 48 subjects made an appointment for the first clinical visit. One subject did not start the study after the first visit. As a consequence, 47

subjects started the study in November, three of them did not continue until April: One moved to another town, one was excluded based on the criterion of the health study (pace-maker), and the third had to quit because of an illness. One new subject started in the beginning of January 1999.

Two minor deviations concerning inclusion and exclusion criteria were allowed in the panels. In the German panel, there were 3 subjects who were younger than 50 years. They were 40, 47 and 49 years old. In the Finnish panel, there were two subjects who had an adult onset diabetes mellitus that was treated with insulin.

2.10 AIR HYGIENE DATA

The ULTRA measurement sites, where particles were monitored (except PM10, which was network data in Finland and in the Netherlands) are described in the appendix A-11a. All study subjects lived within 4 km from the measurement site in Amsterdam and within 11 km in Erfurt. In Helsinki 43 subjects lived within 2 km and 4 subjects within 5 km from the site.

The measurement periods of the air hygiene data in the book are 31.10.98-1.5.99 (Finland), 25.10.98-19.6.99 (the Netherlands) and 6.10.98-1.4.99 (Germany).

2.10.1 Gaseous air pollution and continuous PM10 monitoring

In Finland the gaseous air pollution and continuous PM10 data came from the network measurement site of Helsinki Metropolitan Area Council located 70 m away from the ULTRA measurement site. In the Netherlands the measurements were taken from the National Air Quality Monitoring Network, operated by the National Institute of Public Health and the Environment, and the distance to the other measurement site was 15 km. In Germany all measurements except CO were made by the study personnel. The CO data came from the measurement site of Thüringer Landesanstalt für Umwelt, situated 2 km away.

MONITOR TYPES:

FINLAND:
Measuring height 4 m, except PM10 4.5 m
NO_x: Environnement SA, AC 30 M (chemiluminescense)
CO: Environnement SA, CO 11 M (IR gasfilter correlation)
O_3: Thermo Environmental Instruments, 49 (UV-absorption)
SO_2: Thermo Environmental Instruments, 43 A (UV-fluorescense)
PM10: ESM Eberline, FH 62 I-R (β-attenuation)

GERMANY:
Measuring height 4 m
NO_x: Environnement SA, AC 30 M (chemiluminescense)
CO: Horiba 350 E APMA (IR-absorption)
O_3: Environnement SA, O3 41 M (UV-absorption)

SO_2: Environnement SA, AF 21 M (UV-fluorescense)

THE NETHERLANDS:
Measuring height 3 m
NO_x: TECO, 42 (chemiluminescense)
CO: Thermo Environmental Instruments, 48 W (IR gasfilter correlation)
O_3: TECO 49 W: SO_2: TECO, 43 W (UV-absorption)
PM10: FAG Eberline, FH 62 I-N (β-attenuation)

2.10.2 Remarks on air hygiene data

It was decided that the 24-h value of wind direction is not used. This is because during the days with fluctuating wind direction the average wind direction would give a misleading figure. It would be possible to use the average value by restricting its use to those days, when the standard deviation of hourly values is below 75^o. However, by doing this, the amount of data gets inconveniently low.

It turned out that the network air pollution data were normalised differently in the centers (either 0 ^{o}C or 20 ^{o}C was used as normal condition). The network data were not changed, but remarks will be made in the publications when appropriate.

Data on elemental composition of the particles were not yet available at the time of the completion of this manual.

Because the amount of missing data in air pollution measurements was not negligible, it was decided to impute the missing hours in the data. For a pollutant, a regression equation was created between the primary measurement site and a secondary one, and the estimated values were used for imputation. The criteria for allowing the imputation were: less than 10% of the data missing, R^2 for the pollutant between the two measurement sites >0.5. Usually, only the same pollutant was used in the imputing. The only exceptions were PM2.5 (only in Finland) and $NC_{0.01\text{-}0.1}$, which were imputed using Eberline and CPC data, respectively. The imputed data were 1-h data (except PM2.5), which were then used to calculate the 24-h data.

Imputed variables and percentages of the 1-h values imputed (R^2):

FINLAND:
PM2.5: 7.1 % (0.94); PM10: 1.5 % (0.59); $NC_{0.01\text{-}0.1}$ 3.3 % (0.95); NO: 1.7 % (0.56); NO_2: 1.7 % (0.68); O_3: 1.6 % (0.83); temperature: 2.2 % (0.99); RH 1.1 % (0.87).

THE NETHERLANDS:
$NC_{0.01\text{-}0.1}$: 6.8 % (0.89); NO: 2.8 % (0.69); NO2: 4.2 % (0.52); CO: 1.2 % (0.55); O3: 5.6 % (0.77).

GERMANY:
$NC_{0.01\text{-}0.1}$: 1.1 % (0.93).

2.11 STATISTICAL ANALYSES

2.11.1 Ambulatory ECG

During the course of the study it came clear that both time domain and frequency domain variables will be used as primary endpoints. HRV-variables for the whole Holter monitoring and recovery periods should not be used unless all 5-minute periods (spontaneous breathing, paced breathing, standing, exercise and recovery) exist. HRV frequency domain variables (power) during exercise will not be used at all, because there is a basic assumption of a stable heart rate in the frequency domain analyses. Also frequency domain variables for the two lowest frequencies (POW1 and POW2) should not be used for the analysis, because the analyses period of 5 min is too short for the very low frequency analyses i.e. there are too few cycles at these frequencies during the short time. However, they can be used when analyzing the whole monitoring period. Usually in the analyses, time domain variables are used as such and frequency domain variables are log-transformed.

In the analyses of ST-segment depressions, the primary outcome variable is the appearance of ST-segment depression during the exercise test. In ULTRA, ST-depressions are recorded, when the ST-segment is 0.05 mV below baseline. In contrast, in clinical practice a 0.1 mV depression is required. If the ST-segment depression is horizontal or downward sloping, the depression is even more specific for ischaemia. Therefore, sensitivity analyses are run using different definitions of ST-depression.

As several subjects have a ST-depression already at the beginning of the exercise test, a worsening of ST-segment depression by 0.05 (or 0.1) mV during stress test can be used as an endpoint for them.

Subjects with no exercise test during the visit should be excluded from the ST-analyses. However, as a sensitivity analysis, the association of air pollution with failure to complete the exercise test should also be analyzed.

2.11.2 CC16

CC16/creatinine -ratio (log-transformed) should be used as an outcome variable when analyzing CC16 to take diuresis into account.

2.11.3 Diary data

Because the prevalence of a symptom in the diary data is for most symptoms rather low, slight and severe categories will be combined for the analysis. Recoding of the chest pain variables is necessary since in both the Dutch and Finnish data the prevalence of chest pain is lower than the more specific chest pain in exercise. Therefore, chest pain and chest pain in exercise will be combined into one variable.

Most symptoms will be analyzed separately (recoded as 0/1). However, chest pain and chest pain in exercise will be combined into one variable (1, if chest pain or chest pain in exercise), because of the reasons above, and fever will be combined with common cold (1, if fever or

cold), because of the low prevalence of fever.

‘Overall health today’ will be analyzed also as a binary variable. In the first place, in the German and Finnish data ‘Overall health today‘ should be categorized as good/average (codes 1-3) and bad (4-5), and in the Dutch data as good (codes 1-2) and average/bad (3-4) (no observations in category 5). Also the change to a worse grade (worse than subject-specific mode) could be used as an endpoint.

3 DATA BOOK

3 DATA BOOK

3.1 BASELINE QUESTIONNAIRE 1

1. Subject identification number (ID)

	Amsterdam	Erfurt	Helsinki
Number	101 - 144	301 - 362	514 - 580

2. Sex (B1Q3)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Female	13	35	4	9	23	49	40	31
Male	24	65	43	91	24	51	91	69

3. Are you currently working? (B1Q4)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	35	95	43	91	46	98	124	95
Yes	2	5	4	9	1	2	7	5

4. Do you work? (B1Q4P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Full time	0	0	3	6	0	0	3	2
Part time	2	5	2	4	1	2	5	4
Not working	35	95	42	89	46	98	123	94

5. Are you exposed to fumes, gases, dust or smoke at work? (B1Q4P1A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	2	5	3	6	1	2	6	5
Yes	0	0	2	4	0	0	2	2
Not Working	35	95	42	89	46	98	123	94

6. Unable to work (B1Q4P2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
Unable to work	2	5	4	9	0	0	6	5
Unemployed	0	0	5	11	1	2	6	5
Retired	29	78	33	70	44	94	106	81
Housewife/-man	4	11	0	0	0	0	4	3
Working	2	5	5	11	1	2	8	6

7. Age: 50+ (B1Q5)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	0	0	3	6	0	0	3	2
Yes	37	100	44	94	47	100	128	98

8. Did a doctor diagnose coronary heart disease? (B1Q6)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	0	0	4	9	1	2	5	4
Yes	37	100	43	91	46	98	126	96

9. Did a doctor diagnose angina pectoris? (B1Q7)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	13	35	21	45	17	36	51	39
Yes	24	65	26	55	30	64	80	61

10. Did a doctor diagnose a myocardical infarction? (B1Q8)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	0	0	1	1
No	11	30	14	30	20	43	44	34
Yes	25	68	33	70	27	57	86	66

11. How many infarctions did you have? (B1Q8P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	2	5	14	30	0	0	16	12
0	11	30	0	0	21	45	32	24
1	16	43	24	49	15	32	54	41
2	4	11	7	15	10	21	21	16
3	3	8	3	6	1	2	7	5
9	1	3	0	0	0	0	1	1

12. When did you have last infarction (year)? (B1Q8P2YY)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	13	35	14	30	21	45	48	37
Before 79	0	0	3	6	0	0	3	2
79-83	1	3	1	2	1	2	3	2
84-88	4	11	5	11	2	4	11	8
89-93	7	19	7	15	7	15	21	16
94	2	5	3	6	4	9	9	7
95	3	8	1	2	2	4	6	5
96	5	14	7	15	5	11	17	13
97	1	3	3	6	4	9	8	6
98	1	3	3	6	1	2	5	4

13. Have you had a coronary by-pass surgery or a balloon-dilatation? (B1Q9)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	20	54	13	27	24	51	57	44
Yes	17	46	34	72	23	49	74	56

14. When did you have your last coronary by-pass surgery (year)? (B1Q9P1YY)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	28	76	19	40	28	60	75	57
Before 89	1	3	3	6	1	2	5	4
89-93	3	8	2	4	1	2	6	5
94	0	0	0	0	2	4	2	2
95	1	3	4	9	3	6	8	6
96	0	0	6	13	6	13	12	9
97	2	5	8	17	6	13	16	12
98	2	5	5	11	0	0	7	5

15. When did you have your last balloon-dilatation (year)? (B1Q9P2YY)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	24	65	38	81	39	83	101	77
Before 90	2	5	0	0	1	2	3	2
90-94	6	16	2	4	2	4	10	8
95	1	3	1	2	0	0	2	2
96	3	8	3	6	3	6	9	7
97	0	0	1	2	2	4	3	2
98	0	0	2	4	0	0	2	2
99	1	3	0	0	0	0	1	1

16. Did a doctor diagnose a stroke? (B1Q10)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	36	97	43	91	46	98	125	95
Yes	1	3	4	9	1	2	6	5

17. How many strokes did you have? (B1Q10P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
0	33	89	43	91	46	98	122	93
1	1	3	4	9	1	2	6	5
2	3	8	0	0	0	0	3	2

18. When did you have your last stroke (year)? (B1Q10P2Y)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	33	89	43	91	46	98	122	93
78	0	0	1	2	0	0	1	1
92	1	3	0	0	0	0	1	1
93	1	3	0	0	0	0	1	1
96	1	3	3	6	0	0	4	3
97	1	3	0	0	1	2	2	2

19. Do you suffer diabetes? (B1Q11)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	35	95	40	85	42	89	117	89
Yes	2	5	7	15	5	11	14	11

20. Is your diabetes treated with insulin? (B1Q11P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	2	5	7	15	3	7	12	9
Yes	0	0	0	0	2	4	2	2
Don’t have diabetes	35	95	40	85	42	89	117	89

21. Do you have a pace maker? (B1Q12)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	37	100	47	100	47	100	131	100

22. Do you smoke now? (B1Q13)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	37	100	47	100	47	100	131	100

23. Check of NYHA criteria: cardiac diseases and symptoms (B1Q14)

1 = Only on severe exertion
2 = On moderate exertion
3 = On mild exertion
4 = Occur frequently even at rest

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	13	35	7	15	0	0	20	16
1	7	19	16	34	31	66	54	41
2	11	30	22	47	14	30	47	36
3	4	10	2	4	1	2	7	5
4	2	5	0	0	1	2	3	2

24. Are you prepared to come every second week at the same time to the examination for 1.5 hours? (B1Q15)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes	37	100	47	100	47	100	131	100

25. Do you plan to leave the city for holidays for weeks or months during the next 6 months? (B1Q16)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
No	30	81	45	96	47	100	122	93
Yes	7	19	2	4	0	0	9	7

26. Are you prepared to complete the diary daily? (B1Q17)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

27. The patient understood all questions and could complete the diary. (B1Q18)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

28. Is the patient able to perform an acceptable lung function test? (B1Q19)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

29. Is the patient able to perform the exercise challenge? (B1Q20)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

30. Are there other reasons for exclusion? (B1Q21)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	37	100	47	100	47	100	131	100

31. Is the patient suitable for the study? (B1Q22)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

32. The written consent was signed and the patient got a copy. (B1Q23)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Yes	37	100	47	100	47	100	131	100

33. Height (B1Q24)

		Amsterdam	Erfurt	Helsinki	Total
Female	Mean(sd)	161 (6.6)	163 (3.8)	160 (6.6)	160 (6.2)
	Min-Max	153-176	160-168	147-172	147-176
Male	Mean(sd)	174 (7.7)	173 (5.5)	175 (5.2)	174 (6.1)
	Min-Max	154-186	160-187	167-187	154-187

34. Weight (B1Q25)

		Amsterdam	Erfurt	Helsinki	Total
Female	Mean(sd)	71 (11.8)	72 (3.5)	72 (11.6)	71 (11.0)
	Min-Max	52-94	68-76	50-92	50-94
Male	Mean(sd)	83 (10.8)	81 (9.2)	90 (11.5)	84 (10.7)
	Min-Max	55-102	65-107	67-115	55-115

3.2 BASELINE QUESTIONNAIRE 2

1. Marital status (B2Q2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Married	20	54	39	83	27	57	86	66
Single	2	5	0	0	4	9	6	5
Divorced/separated	6	16	3	6	6	13	15	11
Widowed	9	24	5	11	10	21	24	18

2. Years of education (B2Q3)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	0	0	1	2	1	1
9 or less	12	32	5	11	26	55	43	33
10-12	11	30	30	64	10	21	51	39
13 or more	14	38	12	26	10	21	36	27

3. Have you had wheezing or whistling in your chest at any time in the last 12 months? (B2Q4)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	1	2	4	9	5	4
No	25	68	36	77	28	60	89	68
Yes	12	32	10	21	15	32	37	28

4. Have you been at all breathless when wheezing noise was present? (B2Q4P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	1	2	4	9	5	4
No	5	14	0	0	2	4	7	5
Yes	7	19	7	15	13	28	27	21
No wheezing at all	25	68	39	83	28	60	92	70

5. Have you had this wheezing or whistling when you did not have a cold? (B2Q4P2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	1	2	5	11	6	5
No	5	14	0	0	4	9	9	7
Yes	7	19	7	15	10	21	24	18
No wheezing at all	25	68	39	83	28	60	92	70

6. Have you had an attack of shortness of breath that came on during the day when you were at rest at any time in the last 12 months? (B2Q5)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	27	73	37	79	32	68	96	73
Yes	10	27	10	21	14	30	34	26

7. Do you usually cough first thing in the morning in the winter? (B2Q6)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	2	4	2	2
No	31	84	43	91	34	72	108	82
Yes	6	16	4	9	11	23	21	16

8. Do you usually cough during the day, or at night, in the winter? (B2Q7)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	2	4	2	2
No	30	81	35	74	26	55	91	69
Yes	7	19	12	26	19	40	38	29

9. Do you cough like this on most days for as much as three months each year? (B2Q7P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	1	3	9	19	10	21	20	15
Yes	6	16	3	6	12	26	21	16
Usually no cough	30	81	35	74	24	51	89	68

10. Do you usually bring up phlegm immediately after getting up? (B2Q8)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	23	62	42	89	30	64	95	73
Yes	14	38	5	11	17	36	36	27

11. Do you bring up phlegm like this on most days as much as three months each year? (B2Q8P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	2	5	2	4	3	6	7	5
Yes	12	32	3	6	14	30	29	22
Usually no phlegm	23	62	42	90	30	64	95	73

12. Did a doctor ever tell you that you had high blood pressure? (B2Q9A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	19	51	16	34	18	38	53	40
Yes	18	49	31	66	29	62	78	60

13. Did a doctor ever tell you that you had diabetes? (B2Q9B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	1	2	0	0	1	1
No	35	95	38	81	42	89	115	88
Yes	2	5	8	17	5	11	15	11

14. Did a doctor ever tell you that you had cardiac rhythm disturbances? (B2Q9C)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	2	4	2	2
No	20	54	22	47	23	49	65	50
Yes	17	46	25	53	22	47	64	49

15. Did a doctor ever tell you that you had myocardial infarction? (B2Q9D)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	0	0	1	1
No	10	27	14	30	20	43	44	34
Yes	26	70	33	70	27	57	86	66

16. Did a doctor ever tell you that you had stroke? (B2Q9E)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	36	97	43	91	46	98	125	95
Yes	1	3	4	9	1	2	6	5

17. Did a doctor ever tell you that you had angina pectoris? (B2Q9F)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	13	35	23	49	7	15	43	33
Yes	24	65	24	51	40	85	88	67

18. Did a doctor ever tell you that you had chronic ischemic heart disease? (B2Q9G)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	4	9	4	3
No	35	95	33	70	37	79	105	80
Yes	2	5	14	30	6	13	22	17

19. Did a doctor ever tell you that you had cor pulmonale? (B2Q9H)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	3	6	3	2
No	36	97	47	100	43	91	126	96
Yes	1	3	0	0	1	2	2	2

20. Did a doctor ever tell you that you had cardiac insufficiency? (B2Q9I)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	3	6	3	2
No	36	97	41	87	29	62	106	81
Yes	1	3	6	13	15	32	22	17

21. Did a doctor ever tell you that you had congestive heart failure? (B2Q9J)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	2	4	2	2
No	37	100	41	87	45	96	123	94
Yes	0	0	6	13	0	0	6	5

22. Did a doctor ever tell you that you had valvular defect? (B2Q9K)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	4	9	4	3
No	30	81	44	94	41	87	115	88
Yes	7	19	3	6	2	4	12	9

23. Did a doctor ever tell you that you had other heart problems? (B2Q9L)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	5	11	5	4
No	35	95	34	72	31	66	100	76
Yes	2	2	13	28	11	23	26	20

24. Did a doctor ever tell you that you had asthma? (B2Q9M)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	36	97	47	100	37	79	120	92
Yes	1	3	0	0	9	19	10	8

25. Did a doctor ever tell you that you had chronic bronchitis? (B2Q9N)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	33	89	45	96	43	91	121	92
Yes	4	11	2	4	4	9	10	8

26. Did a doctor ever tell you that you had COPD? (B2Q9O)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	28	76	46	98	47	100	121	92
Yes	9	24	1	2	0	0	10	8

27. Did a doctor ever tell you that you had emphysema? (B2Q9P)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	35	95	46	98	46	98	127	97
Yes	2	5	1	2	1	2	4	3

28. Did a doctor ever tell you that you had pneumioconiosis? (B2Q9Q)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	37	100	48	100	43	91	127	97
Yes	0	0	0	0	3	6	3	2

29. Did a doctor ever tell you that you had nasal allergy including hay fever? (B2Q9R)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	26	70	42	89	30	64	98	75
Yes	11	30	5	11	16	34	32	24

30. Did a doctor ever tell you that you had chronic renal diseases? (B2Q9S)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	37	100	44	94	42	89	123	94
Yes	0	0	3	6	4	9	7	5

31. Did a doctor ever tell you that you had other chronic diseases? (B2Q9T)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	3	6	3	2
No	29	78	35	74	24	51	88	67
Yes	8	22	12	26	20	43	40	31

32. In general, would you say your health is: (B2Q10)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Excellent	0	0	0	0	1	2	1	1
Very good	2	5	0	0	2	4	4	3
Good	18	49	23	49	14	30	55	42
Fair	16	43	23	49	29	62	68	52
Poor	1	3	1	2	1	2	3	2

33. How much does your health limit vigorous activities, such as running, lifting heavy objects, particpating in strenouos sports? (B2Q11A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	N	%
Yes limited a lot	19	51	30	64	27	57	76	58
Yes limited a little	14	38	16	34	20	43	50	38
No not limited at all	4	11	1	2	0	0	5	4

34. How much does your health limit moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? (B2Q11B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	5	14	5	11	7	16	17	13
Yes limited a little	17	46	27	57	15	34	60	46
No not limited at all	15	41	15	32	24	51	54	41

35. How much does your health limit lifting or carrying groceries? (B2Q11C)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Yes limited a lot	9	24	6	13	6	13	21	16
Yes limited a little	15	41	21	45	20	43	56	43
No not limited at all	13	35	20	43	21	45	54	41

36. How much does your health limit climbing several flights of stairs? (B2Q11D)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	10	27	18	38	15	32	43	33
Yes limited a little	18	49	22	47	26	55	66	50
No not limited at all	9	24	7	15	6	13	22	17

37. How much does your health limit climbing one flight of stairs? (B2Q11E)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
Yes limited a lot	2	5	3	6	1	2	6	5
Yes limited a little	15	41	16	34	10	21	41	31
No not limited at all	20	54	28	60	35	74	83	63

38. How much does your health limit bending, kneeling or stooping? (B2Q11F)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	8	22	12	26	10	21	30	23
Yes limited a little	14	38	20	43	14	30	48	37
No not limited at all	15	41	15	32	23	49	53	40

39. How much does your health limit walking more than a mile? (B2Q11G)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	1	2	1	1
Yes limited a lot	7	19	5	11	9	19	21	16
Yes limited a little	11	30	18	38	15	32	44	34
No not limited at all	19	51	24	51	22	47	65	50

40. How much does your health limit walking several blocks? (B2Q11H)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	4	11	2	4	4	9	10	8
Yes limited a little	9	24	14	30	16	34	39	30
No not limited at all	24	65	31	66	27	57	82	63

41. How much does your health limit walking one block? (B2Q11I)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	2	5	0	0	1	2	3	2
Yes limited a little	3	8	7	15	10	21	20	15
No not limited at all	32	86	40	85	36	77	108	82

42. How much does your health limit bathing or dressing yourself? (B2Q11J)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Yes limited a lot	1	3	1	2	1	2	3	2
Yes limited a little	3	8	8	17	13	28	24	18
No not limited at all	33	89	38	81	33	70	104	79

43. How much bodily pain have you had during the past 4 weeks? (B2Q12)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
None	5	14	10	21	8	17	23	18
Very mild	5	14	6	12	12	26	23	18
Mild	10	27	13	28	12	26	35	26
Moderate	11	30	12	26	10	21	33	25
Severe	6	16	5	11	3	6	14	11
Extremely	0	0	1	2	1	2	2	2

44. During the past 4 weeks, how much did pain interfere with your normal work (Including both work outside and housework)? (B2Q13)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	0	0	2	4	2	2
Not at all	10	27	13	28	19	40	42	32
A little bit	16	43	22	47	10	21	48	37
Moderately	6	16	9	19	10	21	25	19
Quite a bit	5	14	3	6	5	11	13	10
Extremely	0	0	0	0	1	2	1	1

45. Does your well-being depend on the weather? (B2Q14)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Not at all	14	38	10	21	17	36	41	31
Some what	18	49	23	49	22	47	63	48
A lot	5	14	14	30	8	17	27	21

46. Are you taking any capsules containing vitamins? (B2Q15)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
No	20	54	37	79	14	30	71	54
Yes	17	46	10	21	32	68	59	45

47. How often are you taking capsules containing vitamins? (B2Q15P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	1	2	1	1
Daily	16	43	8	17	20	43	44	34
Once a week	0	0	1	2	1	2	2	2
As needed	1	3	1	2	11	23	13	10
Never	20	54	37	79	14	30	71	54

48. Is your home/apartment facing: (B2Q16)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Street	2	5	16	34	11	23	29	22
Backyard/park	17	46	2	4	12	24	31	24
Street and backyard	18	49	29	62	24	54	71	54

49. Is your dwelling: (B2Q17)

1 = one family house detached from any other house
2 = one family house attached to one or more other houses
3 = apartment / more family house
4 = Neubaublock (only in Germany)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
1	0	0	5	11	0	0	5	4
2	7	19	5	11	1	2	13	10
3	30	81	12	26	46	98	88	67
4	0	0	25	53	0	0	25	19

50. When was this building originally built? (B2Q18)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	1	2	1	1
1990-1997	0	0	3	6	2	4	5	4
1980-1989	20	54	12	26	7	15	39	30
1970-1979	15	40	9	19	7	15	31	24
1960-1969	2	5	8	17	12	26	22	17
1945-1959	0	0	2	4	10	21	12	9
Before 1945	0	0	13	28	8	17	19	16

51. How many floors are in this building? (B2Q19)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
1	1	3	3	6	1	2	5	4
2-3	9	24	11	23	2	4	22	17
4 or more	27	73	33	70	44	94	104	79

52. At which floor is your home? (B2Q20)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
1	16	43	23	49	5	11	44	34
2-3	12	32	10	21	17	36	39	30
4 or more	9	24	14	30	25	53	48	37

53. Does your home have central heating? (B2Q21)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	0	0	5	11	0	0	5	4
Yes	37	100	42	89	47	100	126	96

54. Do you use coal or wood for heating? (B2Q21P1A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	37	100	42	89	47	100	126	96
No	0	0	4	9	0	0	4	3
Yes	0	0	1	2	0	0	1	1

55. Do you use gas for heating? (B2Q21P1B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	37	100	42	89	47	100	126	96
No	0	0	3	6	0	0	3	2
Yes	0	0	2	4	0	0	2	2

56. Do you use electric for heating? (B2Q21P1C)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	37	100	42	89	47	100	126	96
No	0	0	5	11	0	0	5	4

57. Do you use oil for heating? (B2Q21P1D)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	37	100	42	89	47	100	126	96
No	0	0	3	6	0	0	3	2
Yes	0	0	2	4	0	0	2	2

58. Do you regularly use a gas range or gas oven for cooking? (B2Q22)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	1	2	1	1
No	9	24	36	77	41	87	86	66
Yes	28	76	11	23	5	11	44	34

59. Do you sleep with the windows open at night mostly during the winter months? (B2Q23)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	13	35	12	26	40	85	65	50
Yes	24	65	35	74	7	15	66	50

60. How much are you annoyed by the traffic noise at home if the windows are kept open? (B2Q24)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
0	14	38	2	4	17	36	33	25
1	5	14	3	6	3	6	11	8
2	4	11	4	9	8	17	16	12
3	2	5	9	19	2	4	13	10
4	4	11	3	6	0	0	7	5
5	1	3	7	15	5	11	13	10
6	1	3	4	9	5	11	10	8
7	3	8	3	6	2	4	8	6
8	2	5	5	11	3	6	10	8
9	1	3	1	2	2	4	4	3
10	0	0	6	13	0	0	6	5

61. How much are you annoyed by air pollution at home i.e. smell of the traffic and industry, when you keep the window open? (B2Q25)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
0	24	65	1	2	16	34	41	31
1	1	3	5	11	4	9	10	8
2	3	8	10	21	6	13	19	15
3	3	8	10	21	5	11	18	14
4	0	0	3	6	5	11	8	6
5	2	5	4	9	2	4	8	6
6	0	0	3	6	1	2	4	3
7	2	5	4	9	3	6	9	7
8	2	5	2	4	3	6	7	5
9	0	0	0	0	1	2	1	1
10	0	0	5	11	1	2	6	5

62. Does anyone regularly smoke inside your home? (B2Q26)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	33	89	39	83	47	100	119	91
Yes	4	11	8	17	0	0	12	9

63. How many people in your household smoke inside your home regularly? (B2Q26P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
0	33	89	39	83	47	100	119	91
1	4	11	7	15	0	0	11	8
2	0	0	1	2	0	0	1	1

64. How many cigarettes are smoked daily inside your home? (B2Q26P2A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
0	33	89	39	83	47	100	119	91
5	0	0	1	2	0	0	1	1
6	0	0	2	4	0	0	2	2
10	0	0	5	11	0	0	5	4
20	3	8	0	0	0	0	3	2
30	1	3	0	0	0	0	1	1

65. How many pipes or cigars are smoked daily inside your home? (B2Q26P2B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
0	37	100	47	100	47	100	131	100

66. Do people smoke regularly in the room where you work? (B2Q27)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	1	2	4	9	5	4
No	1	3	3	6	11	23	15	11
Yes	1	3	1	2	0	0	2	2
Don’t work	35	95	42	89	32	68	109	83

67. Have you ever smoked for as long as a year? (B2Q28)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	7	19	10	21	21	45	38	29
Yes	30	81	37	79	26	55	93	71

68. How old were you when started smoking? (B2Q28P1)

	Amsterdam	Erfurt	Helsinki	Total
Mean (sd)	18 (6.2)	20 (6.1)	22 (9.3)	20 (7.1)
Min-max	7-45	14-46	15-53	7-53

69. When have you stopped smoking? (B2Q28P2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	19	10	21	21	45	38	29
96-99	6	16	10	21	2	4	18	14
89-95	6	16	5	11	4	9	15	11
79-88	9	24	6	13	4	9	19	15
69-78	5	14	10	21	6	13	21	16
59-68	2	5	5	11	6	13	13	10
49-58	2	5	1	2	3	6	6	5
Before 49	0	0	0	0	1	2	1	1

70. Before you stopped smoking, how much did you smoke on average: number of cigarettes per day. (B2Q28P3A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	10	21	0	0	10	8
0	8	22	2	4	21	45	31	24
1-4	3	8	0	0	1	2	4	3
5-9	2	5	5	11	4	9	11	8
10-14	4	11	7	15	4	9	15	11
15-19	3	8	9	19	2	4	14	11
20-24	12	32	9	19	9	19	30	23
25 or more	5	14	5	11	6	12	16	12

71. Before you stopped smoking, how much did you smoke on average: number of cigarillos per day. (B2Q28P3B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	10	21	0	0	10	8
0	36	97	36	77	47	100	119	91
5	1	3	1	2	0	0	2	2

72. Before you stopped smoking, how much did you smoke on average: number of cigars per day. (B2Q28P3C)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	10	21	0	0	10	8
0	33	89	34	72	47	100	114	87
1	2	5	0	0	0	0	2	2
2	0	0	2	4	0	0	2	2
4	1	3	0	0	0	0	1	1
5	0	0	1	2	0	0	1	1
10	1	3	0	0	0	0	1	1

73. Before you stopped smoking, how much did you smoke on average: pipe of tobacco in grams per week. (B2Q28P3D)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	N	%
Missing	0	0	10	21	0	0	10	8
0	36	97	37	79	46	98	119	91
50	1	3	0	0	0	0	1	1
200	0	0	0	0	1	2	1	1

74. Age

		Amsterdam	Erfurt	Helsinki	Total
Female	Mean(sd)	74 (7.6)	67 (5.1)	69 (7.4)	70 (7.7)
	Min-Max	63-84	59-70	54-78	54-84
Male	Mean(sd)	70 (8.5)	64 (8.3)	68 (5.4)	67 (8.0)
	Min-Max	54-83	40-78	58-83	40-83

3.3 BASELINE, DOCTOR ADMINISTRATED DAILY MEDICATION

1. β-blockers (BETABLBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	24	65	12	26	16	34	52	40
Yes	13	35	35	74	31	66	79	60

2. Ca^{++} -blockers (CABLOBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	26	70	29	62	34	72	89	68
Yes	11	30	18	38	13	28	42	32

3. ACE-inhibitors and AT-blockers (ACEBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	25	68	22	47	37	79	84	64
Yes	12	32	25	53	10	21	47	36

4. Nitrates (NITROBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	30	81	30	64	28	60	88	67
Yes	7	19	17	36	19	40	43	33

5. Anti-arrhythmic medication (ARRBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	35	94	46	98	41	87	122	93
Yes	2	5	1	2	6	13	9	7

6. ASA (ASABA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	15	41	11	23	11	23	37	28
Yes	22	59	36	77	36	77	94	72

7. Digitalis (DIGITABA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	35	95	38	81	40	85	113	86
Yes	2	5	9	19	7	15	18	14

8. Dipyridamole (DIPYRIBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	37	100	47	100	46	98	130	99
Yes	0	0	0	0	1	2	1	1

9. Diuretics (DIURETBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	31	84	27	57	34	72	92	70
Yes	6	16	20	43	13	28	39	30

10. Moksonidine (MOKSOBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	37	100	46	98	47	100	130	99
Yes	0	0	1	2	0	0	1	1

11. Inhalable β_2-agonist (AGONBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	35	95	46	98	44	94	125	95
Yes	2	5	1	2	3	6	6	5

12. Inhalable anticholinergs (ANTICBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	37	100	47	100	46	98	130	99
Yes	0	0	0	0	1	2	1	1

13. Inhalable glucocorticosteroids (GLUCORBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	35	95	46	98	37	79	118	90
Yes	2	5	1	2	10	21	13	10

14. Inhalable dinatriumcromoglicate / nedocromile (CROMOGBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	37	100	47	100	46	98	130	99
Yes	0	0	0	0	1	2	1	1

15. Leukotriene receptor blockers (RECBLOBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	37	100	47	100	46	98	130	99
Yes	0	0	0	0	1	2	1	1

16. Hyperlipidaemia medication (HYPLIPBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	25	68	27	57	26	55	78	60
Yes	12	32	20	43	21	45	53	40

17. Warfarine (WARFARBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	31	84	47	100	44	94	122	93
Yes	6	16	0	0	3	6	9	7

18. Diabetes medication(DIAPETBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
No	35	95	40	85	44	94	119	91
Yes	2	5	7	15	3	6	12	9

19. Medication affecting central nervous system (CNSBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	33	89	44	94	43	91	120	92
Yes	4	11	3	6	4	9	11	8

20. Other medication (OTHMEDBA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
No	18	49	12	26	24	51	54	41
Yes	19	51	35	74	23	49	77	59

3.4 RESTING ECG

1. Q and QS Patterns:
Anterolateral site (leads I, aVL, V_6) (QLAT)

0 = not diagnosed.
111 = Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.03 sec in lead I or V_6.
121 = Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.02 sec and < 0.03 sec in lead I or V_6.
122 = Q duration ≥ 0.03 sec and < 0.04 sec in lead I or V_6.
131 = Q/R amplitude ratio ≥ 1/5 and < 1/3, plus Q duration ≥ 0.02 sec and < 0.03 sec in lead I or V_6.
133 = Q duration ≥ 0.03 sec and < 0.04 sec, plus R amplitude ≥ 3 mm in lead aVL.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	30	81	40	85	45	96	115	88
111	1	3	2	4	1	2	4	3
121	0	0	1	2	0	0	1	1
122	2	5	2	4	0	0	4	3
131	1	3	2	4	0	0	3	2
133	2	5	0	0	0	0	2	2

2. Q and QS Patterns:

Posterior (inferior) site (leads II, III,aVF) (QINF)

0 = not diagnosed.

111 = Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.03 sec in lead II.

114 = Q duration ≥ 0.05 sec in lead III, plus a Q-wave amplitude ≥ 1.0 mm in the majority of beats in lead aVF.

115 = Q duration ≥ 0.05 sec in lead aVF.

121 = Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.02 sec and < 0.03 sec in lead II.

122 = Q duration ≥ 0.03 sec and < 0.04 sec in lead II,

123 = QS pattern in lead II.

124 = Q duration ≥ 0.04 sec and < 0.05 sec in lead III, plus a Q-wave ≥ 1.0 mm amplitude in the majority of beats in aVF. 125 = Q duration ≥ 0.04 sec and < 0.05 sec in lead aVF.

131 = Q/R amplitude ratio ≥ 1/5 and < 1/3, plus Q duration ≥ 0.02 sec and < 0.03 sec in lead II.

134 = Q duration ≥ 0.03 sec and < 0.04 sec in lead III, plus a Q-wave ≥ 1.0 mm amplitude in the majority of beats in lead aVF.

135 = Q duration ≥ 0.03 sec and < 0.04 sec in lead aVF.

136 = QS pattern in each of leads III and aVF.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	20	54	37	79	39	83	96	73
111	4	11	3	6	1	2	8	6
114	1	3	2	4	0	0	3	2
115	0	0	1	2	0	0	1	1
121	2	5	0	0	1	2	3	2
122	1	3	2	4	0	0	3	2
123	1	3	0	0	1	2	2	2
124	0	0	0	0	3	6	3	2
125	1	3	0	0	0	0	1	1
131	0	0	0	0	1	2	1	1
134	2	5	1	2	0	0	3	2
135	0	0	1	2	0	0	1	1
136	3	8	0	0	0	0	3	2

3. Q and QS Patterns:

Anterior site (leads V_1, V_2, V_3, V_4, V_5) (QANT)

0 = not diagnosed.

111 = amplitude ratio ≥ 1/3 plus Q duration ≥ 0.03 sec in any of leads V_2, V_3, V_4, V_5.

112 = Q duration ≥ 0.04 sec in any of leads V_1, V_2, V_3, V_4, V_5. 116 = QS pattern when initial R-wave is present in adjacent lead to the right on the chest, in any of leads V_2, V_3, V_4, V_5, V_6.

117 = QS pattern in all of leads $V_1 – V_4$ or $V_1 – V_5$.

121 = Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.02 sec and < 0.03 sec, in any of leads V_2, V_3, V_4, V_5.

122 = Q duration ≥ 0.03 sec and < 0.04 sec in any of leads V_2, V_3, V_4, V_5.

127 = QS pattern in all of leads V_1, V_2, and V_3.

128 = Initial R amplitude decreasing to 2.0mm or less in every beat between any of leads V_2 and V_3, V_3 and V_4, or V_4 and V_5.

131 = Q/R amplitude ratio ≥ 1/5 and < 1/3 plus Q duration ≥ 0.02 sec and < 0.03 sec in any of leads V_2, V_3, V_4, V_5.

132 = QS pattern in lead V_1 and V_2.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	32	86	36	77	44	94	112	86
111	1	3	3	6	1	2	5	4
112	0	0	1	2	0	0	1	1
116	1	3	0	0	0	0	1	1
117	0	0	1	2	0	0	1	1
121	0	0	1	2	0	0	1	1
122	0	0	2	4	0	0	2	2
127	0	0	1	2	0	0	1	1
128	1	3	0	0	0	0	1	1
131	1	3	0	0	0	0	1	1
132	0	0	2	4	1	2	3	2

4. QRS Axis Deviation (QRSAXIS)

0 = not diagnosed.

21 = Left. QRS axis from –30° trough -90° in leads I, II, III.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	33	89	45	96	46	98	124	95
21	3	8	2	4	0	0	5	4

5. High Amplitudes R Waves (HIRWAVE)

0 = not diagnosed.

31 = Left: R amplitude > 26 mm in either V_5 or V_6, or R amplitude > 20.0 mm in any of leads I, II, III, aVF, or R amplitude > 12.0 mm in lead aVL measured only on second to last complete normal beat.

33 = Left: R amplitude > 15.0 mm but ≤ 20.0 mm in lead I, or R amplitude in V_5 or V_6, plus S amplitude in V_1 > 35.0 mm.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	32	86	44	94	43	91	119	91
31	4	11	1	2	1	2	6	5
33	0	0	2	4	2	4	4	3

6. ST Junction (J) and Segment Depression: Anterolateral site (leads I, aVL, V_6) (STDEPLAT)

0 = not diagnosed.

42 = STJ depression ≥ 0.5 mm and < 1.0 mm and ST segment horizontal or downward sloping in any of leads I, aVL, or V_6.

43 = No STJ depression as much as 0.5 mm but ST segment downward sloping and segment or T-wave nadir ≥ 0.5 mm below P-R baseline, in any of leads I, aVL, or V_6.

44 = STJ depression ≥ 1.0 mm and ST segment upward sloping or U-shaped, in any of leads I, aVL, or V_6.

412 = STJ depression ≥ 1.0 mm but < 2.0 mm and ST segment horizontal or downward sloping in any of leads I, aVL, or V_6.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	26	70	32	68	33	70	91	69
42	3	8	6	13	7	15	16	12
43	5	14	5	11	5	11	15	11
44	1	3	0	0	0	0	1	1
412	0	0	4	9	1	2	5	4

7. ST Junction (J) and Segment Depression:
Posterior (inferior) site (leads II, III, aVF) (STDEPINF)

0 = not diagnosed.
42 = STJ depression ≥ 0.5 mm and < 1.0 mm and ST segment horizontal or downward sloping in lead II or aVF.
43 = No STJ depression as much as 0.5 mm, but ST segment downward sloping and segment or T-wave nadir ≥ 0.5 mm below P-R baseline in lead II.
412 = STJ depression ≥ 1.0 mm but < 2.0 mm and ST segment horizontal or downward sloping in lead II or aVF.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	33	89	40	85	41	87	114	87
42	1	3	4	9	2	4	7	5
43	1	3	1	2	3	6	5	4
412	0	0	2	4	0	0	2	2

8. ST Junction (J) and Segment Depression:
Anterior site (leads V_1, V_2, V_3, V_4, V_5) (STDEPANT)

0 = not diagnosed.
42 = STJ depression ≥ 0.5 mm and < 1.0 mm and ST segment horizontal or downward sloping in any of leads V_1, V_2, V_3, V_4, V_5.
43 = No STJ depression as much as 0.5 mm, but ST segment downward sloping and segment or T-wave nadir ≥ 0.5 mm below P-R baseline in any of leads V_2, V_3, V_4, V_5.
44 = STJ depression ≥ 1.0 mm and ST segment upward sloping or U-shaped in any of leads V_1, V_2, V_3, V_4, V_5.
412 = STJ depression ≥ 1.0 mm but < 2.0 mm and ST segment horizontal or downward sloping in any of leads V_1, V_2, V_3, V_4, V_5.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	33	89	35	74	40	85	108	82
42	2	5	4	9	3	6	9	7
43	0	0	3	6	0	0	3	2
44	0	0	1	2	1	2	2	2
412	0	0	4	9	2	4	6	5

9. T-Wave Items:

Anterolateral site (leads I, aVL, V_6) (TWAVELAT)

0 = not diagnosed.

52 = T amplitude negative or diphasic (positive-negative or negative-positive type) with negative phase at least 1.0 mm but not as deep as 5.0 mm in lead I or V_6, or in lead aVL when R amplitude is ≥ 5.0 mm.

53 = T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1.0 mm negative phase in lead I or V_6, or in lead aVL when R amplitude is ≥ 5.0 mm.

54 = T amplitude positive and T/R amplitude ratio < 1/20 in any of leads I, aVL, V_6; R wave amplitude must be ≥ 10.0 mm.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	23	62	28	60	30	64	81	62
52	7	19	10	21	4	9	21	16
53	5	14	9	19	11	23	25	19
54	0	0	0	0	1	2	1	1

10. T-wave Items: Posterior (inferior) site (leads II, III, aVF) (TWAVEINF)

0 = not diagnosed.

52 = T amplitude negative or diphasic with negative phase (negative-positive or positive-negative type) at least 1.0 mm but not as deep as 5.0 mm in lead II, or in lead aVF when QRS is mainly upright.

53 = T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1.0 mm negative phase in lead II; not coded in lead aVF.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	2	5	0	0	1	2	3	2
0	30	81	39	83	41	87	110	84
52	2	5	6	13	2	4	10	8
53	3	8	2	4	3	6	8	6

11. T-Wave Items:

Anterior site (leads V_2, V_3, V_4, V_5) (TWAVEANT)

0 = not diagnosed.

52 = T amplitude negative (flat), or diphasic (negative-positive or positive-negative type) with negative phase at least 1.0 mm but not as deep as 5.0 mm, in any leads V_2, V_3, V_4, V_5.

53 = T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1.0 mm negative phase, in any of leads V_3, V_4, V_5.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	29	78	33	70	36	77	98	75
52	2	5	12	26	6	13	20	15
53	4	11	2	4	4	9	10	8

12. A-V Conduction Defect (AVCDEF)

0 = not diagnosed.

63 = P-R (P-Q) interval ≥ 0.22 sec in the majority of beats in any leads I, II, III, aVL, aVF.

65 = Short P-R interval. P-R interval < 0.12 sec in all beats of any two of leads I, II, III, aVL, aVF.

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	1
0	32	86	42	89	40	85	114	87
63	3	8	5	11	6	13	14	11
65	1	3	0	0	0	0	1	1

13. Ventricular Conduction Defect (VENTCDEF)

0 = not diagnosed.

73 =Incomplete right bundle branch block. QRS duration < 0.12 sec in each of leads I, II, III, aVL, aVF, and R' > R in either of leads V_1, V_2.

74 = Intraventricular block. QRS duration ≥ 0.12 sec in a majority of beats in any of leads I, II, III, aVL, aVF.

75 = R-R' pattern in either of leads V_1, V_2 with R' amplitude ≤ R.

77 = Left anterior hemiblock (LAH). QRS duration < 0.12 sec in the majority of beats in leads I, II, III, aVL, aVF, plus Q-wave amplitude ≥ 0.25 mm and < 0.03 sec duration in lead I, plus left axis deviation of -45° or more negative.

711 = Complete left bundle branch block (LBBB). QRS duration ≥ 0.12 sec in a majority of beats (of the same pattern) in any of leads I, II, III, aVL, aVF, plus R peak duration ≥ 0.06 sec in a majority of beats (of the same QRS pattern) in any leads I, II, aVL, V_5, V_6.

721 = Complete right bundle branch block (RBBB). QRS duration ≥ 0.12 sec in a majority of beats (of the same QRS pattern) in any of leads I, II, III, aVL, aVF, plus: R' > R in V_1 or QRS mainly upright, plus R peak duration ≥ 0.06 sec in V_1 or V_2; or V_2; S duration > R duration in all beats in lead I or II.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	25	68	35	74	40	85	100	76
73	0	0	3	6	1	2	3	2
74	1	3	1	2	1	2	3	2
75	3	8	3	6	3	6	9	7
77	2	5	1	2	0	0	3	2
711	0	0	2	4	0	0	2	2
721	5	14	2	4	1	2	8	6

14. Arrhytmias (ARRHY)

0 = not diagnosed.
87 = Sinus tachycardia (over 100/min).
88 = Sinus bradycardia (under 50/min).
811 = Presence of frequent atrial or junctional premature beats (10 % or more of recorded complexes).
812 = Presence of frequent ventricular premature beats (10 % or more of recorded complexes).
831 = Atrial fibrillation (persistent).

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	30	81	42	89	42	89	114	87
87	0	0	1	2	0	0	1	1
88	1	3	0	0	1	2	2	2
811	2	5	0	0	0	0	2	2
812	1	3	1	2	0	0	2	2
831	1	3	3	6	3	6	7	5

15. ST Segment Elevation:
Anterolateral site (leads I, aVL, V_6) (STELELAT)

0 = not diagnosed.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	35	95	47	100	46	98	128	98

16. ST Segment Elevation:
Posterior (inferior) site (leads II,III, aVF) (STELEINF)

0 = not diagnosed.
92 = ST segment elevation ≥ 1.0 mm in any of leads II, III, aVF.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	35	95	46	98	46	98	127	97
92	0	0	1	2	0	0	1	1

17. ST Segment Elevation:

Anterior site (leads V_1, V_2, V_3, V_4, V_5) (STELEANT)

0 = not diagnosed.

92 = ST segment elevation ≥ 1.0 mm in lead V_5 or ST segment elevation ≥ 2.0 mm in any of leads V_1, V_2, V_3, V_4.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	2	5	0	0	1	2	3	2
0	35	95	45	96	45	96	125	95
92	0	0	2	4	1	2	3	2

18. Miscellaneous Items (MISC)

0 = not diagnosed.

95 = T-wave amplitude > 12 mm in any leads I, II, III, aVL, aVF, V_1, V_2, V_3, V_4, V_5, V_6.

941 = QRS transition zone at V_3 or to the right of V_3 on the chest.

942 = QRS transition zone at V_4 or to the left of V_4 on the chest.

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	1	3	0	0	1	2	2	2
0	20	54	23	49	19	40	62	47
95	0	0	1	2	0	0	1	1
941	6	16	18	38	24	51	48	37
942	10	27	5	11	3	6	18	14

3.5 CLINICAL VISIT QUESTIONNAIRE

1. Did you have chest pain yesterday? (CQ1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	400	93	381	78	446	86	1227	85
Yes	22	5	110	22	65	13	197	14

2. Did you have chest pain or other symptoms of angina pectoris during the preceding hour? (CQ2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	8	2	0	0	7	1	15	1
No	413	96	456	93	503	97	1372	95
Yes	8	2	35	7	8	2	51	4

3. Did you have shortness of breath yesterday? (CQ3)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	7	1	14	1
No	356	83	409	83	412	80	1177	82
Yes	66	15	82	17	99	19	247	17

4. Did you have shortness of breath during the preceding hour? (CQ4)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	7	1	14	1
No	398	93	470	96	483	93	1351	94
Yes	24	6	21	4	28	5	73	5

5. Did you have wheeze during the preceding hour? (CQ5)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	417	97	487	99	500	97	1404	98
Yes	5	1	4	1	11	2	20	1

6. Did you have an airway infection in the past two weeks? (CQ6)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	8	2	0	0	7	1	15	1
No	328	77	427	87	415	80	1170	81
Yes	93	22	64	13	96	19	253	18

7. Do you have an airway infection today? (CQ6P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	343	80	427	87	424	82	1194	83
No	35	8	39	8	21	4	95	7
Yes	51	12	25	5	73	14	149	10

8. Did you have fever in the last week? (CQ7)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	79	15	86	6
No	411	96	484	99	427	82	1322	92
Yes	11	3	7	1	12	2	30	2

9. Question for nurse: Do you think the subject can perform the exercise? (CQ8)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	35	8	19	4	82	16	136	9
Yes	387	90	472	96	429	83	1288	90

10. Why the subject cannot perform the exercise? (CQ8A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	394	92	474	97	436	84	1304	91
Resp. infection	2	0	9	2	20	4	31	2
Does not want to	4	1	0	0	2	0	6	0
Other	29	7	8	2	60	12	97	7

11. Did you visit a doctor for any acute illness during the 2 weeks? (CQ9)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	371	86	445	91	449	87	1265	88
Yes	51	12	46	9	62	12	159	11

12. Reason for visiting doctor (see table 11): Angina Pectoris (CQ9A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	378	88	445	91	457	88	1280	89
No	49	11	46	9	57	11	152	11
Yes	2	0	0	0	4	1	6	0

13. Reason for visiting doctor (see table 11): other cardiac (CQ9B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	378	88	445	91	457	88	1280	89
No	47	11	42	9	60	12	149	10
Yes	4	1	4	1	1	0	9	1

14. Reason for visiting doctor (see table 11): respiratory condition (CQ9C)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	378	88	445	91	457	88	1280	89
No	43	10	36	7	53	10	132	9
Yes	8	2	10	2	8	2	26	2

15. Reason for visiting doctor (see table 11): urinary tract infection (CQ9D)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	378	88	445	91	457	88	1280	89
No	39	9	46	9	59	11	144	10
Yes	12	3	0	0	2	0	14	1

16. Reason for visiting doctor (see table 11): other reason (CQ9E)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	378	88	445	91	457	88	1280	89
No	24	6	13	3	11	2	48	3
Yes	27	6	33	7	50	10	110	8

17. Did you stay in the hospital because of this illness? (CQ10)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	418	97	488	99	502	97	1408	98
Yes	4	1	3	1	9	2	16	1

18. Has there been any changes made in your prescriptions? (CQ11)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	9	2	0	0	8	2	17	1
No	356	83	432	88	474	91	1262	88
Yes	64	15	59	12	36	7	159	11

19. Did you take your medication today as prescribed? (CQ12)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	26	6	5	1	3	1	34	2
Yes	396	92	486	99	508	98	1390	97

20. Did you use any inhalator in the last 4 hours? (CQ13)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	7	1	14	1
No	411	96	488	99	449	87	1348	94
Yes	11	3	3	1	62	12	76	5

21. Inhalable β-agonist used in the last 4 hours (see table 20) (CQ13A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	420	98	488	99	459	89	1367	95
No	0	0	2	0	27	5	29	2
Yes	9	2	1	0	32	6	42	3

22. Inhalable corticol steroids used in the last 4 hours (see table 20) (CQ13B)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	420	98	488	99	459	89	1367	95
No	1	0	1	0	15	3	17	1
Yes	8	2	2	0	44	8	54	4

23. Inhalable anti-cholinergic used in the last 4 hours (see table 20) (CQ13C)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	420	98	488	99	459	89	1367	95
No	9	2	3	1	44	8	56	4
Yes	0	0	0	0	15	3	15	1

24. Did you smoke during the past 2 weeks? (CQ14)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	7	1	14	1
No	411	96	490	100	511	99	1412	98
Yes	11	3	1	0	0	0	12	1

25. How many cigarettes in total did you smoke during the past 2 weeks? (CQ14P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	7	1	14	1
Didn’t smoke at all	411	96	490	100	511	99	1412	98
1-5	8	2	1	0	0	0	9	1
6-10	1	0	0	0	0	0	1	0
11-20	2	0	0	0	0	0	2	0

26. Did you smoke in the last hour? (CQ14P2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	8	2	0	0	7	1	15	1
No	9	2	1	0	0	0	10	1
Yes	1	0	0	0	0	0	1	0
Didn't smoke at all	411	96	490	100	511	99	1412	98

27. Have you been in rooms where people smoked during the last 24 hours? (CQ15)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	7	1	14	1
No	320	75	432	88	484	93	1236	86
Yes	102	24	59	12	27	5	188	13

28. How long did you stay there? (CQ15P1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	8	2	0	0	7	1	15	1
0	320	75	432	88	484	93	1236	86
1-2	28	7	43	9	20	4	91	6
3-11	36	8	16	3	4	1	56	4
12+	34	8	0	0	0	0	34	2

29. How did you arrive to the clinical visit? (CQ16)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	8	2	15	1
Walking/cycling	100	23	124	25	5	1	229	16
Car/bus/tram	322	75	367	75	505	97	1194	83

30. How many cups of coffee did you drink during the last 4 hours? (CQ17A)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	7	2	0	0	25	5	32	2
0	189	44	293	60	237	46	719	50
1	94	22	90	18	103	20	287	20
2	108	25	105	21	138	27	351	24
3	8	2	3	1	15	3	26	2
4 or more	23	5	0	0	0	0	23	2

31. How many cups of tea did you drink during the last 4 hours? (CQ17B)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	9	2	0	0	81	16	90	6
0	220	51	461	94	395	76	1076	75
1	69	16	7	1	11	2	87	6
2	94	22	23	5	27	5	144	10
3	24	6	0	0	1	0	25	2
4 or more	13	3	0	0	3	1	16	1

32. Did you drink coffee during the last hour? (CQ17P1)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	8	2	293	60	7	1	308	21
No	358	83	149	30	486	94	993	69
Yes	63	15	49	10	25	5	137	10

33. Did you drink tea during the last hour? (CQ17P2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	9	2	461	94	7	1	477	33
No	367	86	11	2	509	98	887	62
Yes	53	12	19	4	2	0	74	5

34. Did you drink alcohol during the last 24 hours? (CQ18)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	8	2	0	0	9	2	17	1
No	231	54	303	62	433	83	967	67
Yes	190	44	188	38	76	15	454	32

3.5 CLINICAL VISIT LOG BOOK

1. Nurse filling out the questionnaire (QUNURSE)

Amsterdam		Erfurt		Helsinki	
Nurse	n	Nurse	n	Nurse	n
.	7	.	0	.	7
11	105	1	48	50	466
12	105	2	179	51	45
13	5	3	262		
14	30	4	2		
15	149				
16	28				

2. Was interview done? (INTERVIEW)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	15	3	22	2
Yes	422	98	491	100	503	97	1416	98

3. Was diary changed? (DIARYCH)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	19	4	0	0	25	5	44	3
No	0	0	47	10	0	0	47	3
Yes	410	96	444	90	493	95	1347	94

4. Was urine sample taken? (URINESA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	19	4	0	0	51	10	51	5
No	0	0	7	1	0	0	7	0
Yes	410	96	484	99	467	90	1361	95

5. ECG nurse identification number (ECGNURSE)

Amsterdam		Erfurt		Helsinki	
Nurse	n	Nurse	n	Nurse	n
.	7	.	0	.	7
11	83	1	48	50	466
12	103	2	179	51	45
13	8	3	262		
14	48	4	2		
15	149				
16	31				

6. Number of Holter recorder (HOLTREC)

	Amsterdam		Erfurt		Helsinki	
	n	%	n	%	n	%
Missing	7	2	5	1	8	2
1	137	32	176	36	438	85
2	161	38	141	29	2	0
3	124	29	85	17	70	14
4	0	0	84	17	0	0

7. Number of patient cable (CABLE)

	Amsterdam		Erfurt		Helsinki	
	n	%	n	%	n	%
Missing	7	2	5	1	8	2
1	137	32	176	36	438	85
2	161	38	141	29	2	0
3	124	29	85	17	70	14
4	0	0	84	17	0	0

8. Were there difficulties to locate the electrodes like previously? (ELECTROD)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	8	2	5	1	54	10	67	5
No	369	86	480	98	453	87	1302	91
Yes	52	12	6	1	11	2	69	5

9. The hour of real time of start of Holter recording (STRTHOUR)

	Amsterdam	Erfurt	Helsinki	Total
N	421	468	511	1418
Mean (sd)	13 (2.3)	11 (2.1)	12 (2.1)	12 (2.3)
Min-max	8-17	8-15	9-16	8-17
Median	13	10	12	12
25%-75%	11-15	9-13	10-14	10-14

10. Breathing frequency for 1 min, between about 3-4 min (BRFREQ1)

	Amsterdam	Erfurt	Helsinki	Total
N	420	486	491	1397
Mean (sd)	14 (3.7)	14 (2.5)	14 (3.1)	14 (3.1)
Min-max	3-27	8-21	6-26	3-27
Median	14	14	13	14
25%-75%	11-16	12-16	12-16	12-16

11. Systolic blood pressure 1 in supine position (SYSTSUP1)

	Amsterdam	Erfurt	Helsinki	Total
N	422	486	510	1418
Mean (sd)	140 (20)	133 (18.5)	140 (23.0)	137 (20.9)
Min-max	99-206	81-179	77-223	77-223
Median	137.5	132.5	139.5	136
25%-75%	125-152	119-145	123-153	122-150

12. Diastolic blood pressure 1 in supine position (DIASSUP1)

	Amsterdam	Erfurt	Helsinki	Total
N	422	486	510	1418
Mean (sd)	83 (11.5)	80 (8.9)	77 (9.8)	80 (10.4)
Min-max	57-118	54-108	54-118	54-118
Median	83	80	76	79
25%-75%	75-90	74-85	70-80	73-86

13. Systolic blood pressure 2 in supine position (SYSTSUP2)

	Amsterdam	Erfurt	Helsinki	Total
N	414	486	506	1406
Mean (sd)	141 (20.6)	133 (18.7)	143 (22.5)	139 (21.1)
Min-max	96-225	84-178	84-207	84-225
Median	137.5	133	143	138
25%-75%	127-153	119-147	125-158	123-152

14. Diastolic blood pressure 2 in supine position (DIASSUP2)

	Amsterdam	Erfurt	Helsinki	Total
N	414	486	506	1406
Mean (sd)	84 (11.4)	80 (8.3)	78 (9.6)	80 (10.1)
Min-max	62-126	54-101	53-118	53-126
Median	83	80	77	80
25%-75%	76-91	75-85	72-83	74-87

15. Systolic blood pressure at 3 min standing (SYSTSTAN)

	Amsterdam	Erfurt	Helsinki	Total
N	399	484	504	1387
Mean (sd)	144 (22.3)	138 (20.4)	150 (25.8)	144 (23.6)
Min-max	81-217	72-205	94-236	72-236
Median	143	138	147	142
25%-75%	128-158	124-151	132-165	128-158

16. Diastolic blood pressure at 3 min standing (DIASSTAN)

	Amsterdam	Erfurt	Helsinki	Total
N	399	484	504	1387
Mean (sd)	86 (12.1)	84 (9.5)	87 (11.0)	86 (10.9)
Min-max	59-119	45-113	61-130	45-130
Median	86	85	85	85
25%-75%	78-94	78-90	79-93	79-92

17. Heart rate in the end of 6 min exercise (HR)

	Amsterdam	Erfurt	Helsinki	Total
N	377	478	418	1273
Mean (sd)	79 (14.1)	87 (10.5)	91 (8.5)	86 (12.2)
Min-max	41-114	56-118	50-140	41-130
Median	77	86	92	87
25%-75%	69-89	81-93	86-96	78-94

18. Load in the end of 6 min exercise (LOAD)

	Amsterdam	Erfurt	Helsinki	Total
N	0	460	419	879
Mean (sd)	-	52 (17.7)	53 (12.1)	52 (15.3)
Min-max	-	20-100	0-100	0-100
Median	-	50	50	50
25%-75%	-	40-60	50-50	50-60

19. Exercise test completed (EXEOK)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	40	9	11	2	92	18	143	10
No	6	1	11	2	10	2	27	2
Yes	383	89	469	96	416	80	1268	88

20. Exercise test had to be stopped because (EXESTOP)

1=development of severe symptoms
2=equipment problems
3=other reason

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	423	99	480	98	508	98	1411	98
1	5	1	6	1	9	2	20	1
2	0	0	2	0	0	0	2	0
3	1	0	3	1	1	0	5	0

21. Did the patient experience shortness of breath during exercise? (EXESHBR)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	47	11	15	3	95	18	157	11
No	371	86	454	92	339	65	1164	81
Yes	11	3	22	4	84	17	117	8

22. Did the patient experience chest pain during exercise? (EXECHPA)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	47	11	13	3	95	18	155	11
No	380	89	452	92	414	80	1246	87
Yes	2	0	26	5	9	2	37	3

23. Breathing frequency for 1 min, between about 7-8 min (during 10 min rest in supine position) (BRFREQ2)

	Amsterdam	Erfurt	Helsinki	Total
N	415	486	482	1383
Mean (sd)	13 (3.6)	14 (2.4)	14 (3.2)	14 (3.1)
Min-max	5-28	7-21	8-26	5-28
Median	13	14	14	14
25%-75%	11-16	12-16	12-16	12-16

24. Number of spirometry (SPIROMET)

	Amsterdam		Erfurt		Helsinki	
	n	%	n	%	n	%
Missing	7	2	0	0	98	19
1	0	0	491	100	0	0
2	0	0	0	0	420	81
6	422	98	0	0	0	0

25. Spirometry nurse identification number (SPINURSE)

Amsterdam		Erfurt		Helsinki	
Nurse	n	Nurse	n	Nurse	n
.	9	.	1	.	80
11	98	1	48	50	393
12	104	2	187	51	45
13	1	3	253		
14	38	4	2		
15	148				
16	31				

26. Spirometry maneuver completed (SPIROOK)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	7	2	0	0	80	15	87	6
No	72	17	7	1	17	3	96	7
Yes	350	82	484	99	421	81	1255	87

27. The spirometry maneuver had to be stopped, because (SPISTOP)

1=the patient was unable to perform
2=equipment problems
3=development of severe symptoms
4=other reason

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	367	86	480	98	501	97	1348	94
1	46	11	1	0	8	1	55	4
2	7	2	10	2	1	0	18	1
3	3	1	0	0	3	1	6	0
4	6	1	0	0	5	1	11	1

28. Completeness of exercise test (EXERCISE)

1=test completed and no restraints in clinic questionnaire
2=test completed in spite of restraints in clinic questionnaire
3=test completed, but the tape has bad quality
4=test stopped because of development of symptoms
5=test stopped because of equipment or other problems
6=test not done because of cardiorespiratory symptoms
7=test not done because of other symptoms or the subject did not want to

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	8	2	0	0	7	1	15	1
1	327	77	380	77	362	70	1069	74
2	6	1	46	9	12	2	64	4
3	50	12	46	9	43	8	136	9
4	5	1	6	1	9	2	20	1
5	0	0	4	1	1	0	5	0
6	28	7	6	1	47	9	81	6
7	5	1	6	1	37	7	48	3

3.7 SPIROMETRY AND URINE SAMPLE DATA

1. Forced vital capacity (l) (FVC)

	Amsterdam	Erfurt	Helsinki	Total
N	386	491	417	1294
Mean (sd)	3.4 (1.0)	3.7 (0.8)	3.0 (0.7)	3.4 (0.9)
Min – Max	1.4 – 5.6	2.1 – 6.6	1.6 – 5.0	1.4 – 6.6
Median	3.4	3.7	2.9	3.3
25%-75%	2.5 – 4.2	3.2 – 4.2	2.5 – 3.4	2.8 – 4.0

2. Forced expiratory volume in one second (l) (FEV1)

	Amsterdam	Erfurt	Helsinki	Total
N	386	491	417	1294
Mean (sd)	2.4 (0.8)	2.8 (0.6)	2.2 (0.6)	2.5 (0.7)
Min – Max	1.0 – 4.6	1.4 – 4.5	1.1 – 4.0	1.0 – 4.6
Median	2.4	2.8	2.2	2.5
25%-75%	1.6 – 3.0	2.4 – 3.2	2.0 – 2.5	2.0 – 3.0

3. Peak expiratory flow (l/s) (PEF)

	Amsterdam	Erfurt	Helsinki	Total
N	386	491	417	1294
Mean (sd)	6.9 (2.5)	7.5 (1.9)	7.0 (1.8)	7.1 (2.1)
Min – Max	1.9 – 12.8	3.0 – 11.6	3.6 – 12.5	2.0 – 12.8
Median	7.1	7.6	6.6	7.1
25%-75%	4.6 – 8.7	6.3 – 8.8	5.7 – 7.9	5.7 – 8.5

4. Maximal mid-expiratory flow (l/s) (MMEF)

	Amsterdam	Erfurt	Helsinki	Total
N	384	491	417	1292
Mean (sd)	1.5 (1.0)	2.2 (0.9)	1.9 (0.8)	1.9 (1.0)
Min – Max	0.3 – 5.3	0.7 – 9.1	0.6 – 4.5	0.3 – 9.1
Median	1.2	2.1	1.7	1.8
25%-75%	0.7 – 1.9	1.6 – 2.8	1.4 – 2.2	1.2 – 2.4

5. Urinary CC16 (µg/l) (CC16)

	Amsterdam	Erfurt	Helsinki	Total
N	416	483	453	1352
Mean (sd)	21 (47)	48 (81)	22 (34)	31 (60)
Min – Max	1 – 330	1 – 783	1 – 271	1 – 783
Median	5	18	6	9
25%-75%	1 – 16	6 – 61	1 – 27	2 – 33

6. Urinary creatinine (g/l) (CREAT)

	Amsterdam	Erfurt	Helsinki	Total
N	416	483	453	1352
Mean (sd)	0.9 (0.5)	1.2 (0.6)	1.0 (0.6)	1.0 (0.6)
Min – Max	0.2 – 3.2	0.1 – 3.7	0.1 – 3.4	0.1 – 3.7
Median	0.8	1.1	1.0	0.9
25%-75%	0.5 – 1.1	0.7 – 1.5	0.6 – 1.4	0.6 – 1.4

3.8 AMBULATORY ECG (HOLTER)

1. Total duration of ambulatory ECG monitoring (ECGTIME)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	41 (4.4)	38 (2.1)	35 (4.6)	38 (4.5)
Min – Max	1 – 55	31 – 50	21 – 47	1 – 55
Median	40	38	36	38
25%-75%	38 – 43	37 – 39	35 – 37	36 – 40

2. Average heart rate during the whole monitoring period (HRAVE)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	66 (10.1)	70 (8.9)	67 (8.3)	68 (9.3)
Min – Max	37 – 89	53 – 104	45 – 103	37 – 104
Median	65	69	67	67
25%-75%	59 – 74	63 – 76	62 – 72	62 – 74

3. Maximum heart rate during the whole monitoring period (HRMAX)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	93 (18.9)	96 (12.3)	99 (16.9)	96 (16)
Min – Max	50 – 178	73 – 153	56 – 175	50 – 178
Median	91	95	100	96
25%-75%	80 – 101	88 – 101	90 – 105	86 – 104

4. Minimum heart rate during the whole monitoring period (HRMIN)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	53 (8.2)	57 (8.4)	54 (6.8)	55 (8.0)
Min – Max	32 – 73	35 – 93	39 – 76	32 – 93
Median	53	57	54	55
25%-75%	47 – 59	52 – 62	49 – 59	49 – 60

5. Ventricular ectopic beats during 5 min of exercise (VES)

	Amsterdam	Erfurt	Helsinki	Total
N	376	464	405	1245
Mean (sd)	2.2 (5.6)	6.7 (21.4)	3.4 (11.1)	4.3 (15.0)
Min – Max	0 – 69	0 – 223	0 – 121	0 – 223
Median	0	0	0	0
25%-75%	0 – 2	0 – 2	0 – 1	0 – 2

6. Supraventricular ectopic beats during 5 min of exercise (SVES)

	Amsterdam	Erfurt	Helsinki	Total
N	355	442	404	1201
Mean (sd)	2.1 (6.5)	0.9 (3.4)	1.4 (3.5)	1.4 (4.6)
Min – Max	0 – 50	0 – 38	0 – 25	0 – 50
Median	0	0	0	0
25%-75%	0 – 1	0 – 0	0 – 1	0 – 1

7. Average PR-interval during the rest (PRINTERV)

	Amsterdam	Erfurt	Helsinki	Total
N	393	444	479	1316
Mean (sd)	189 (28)	185 (31)	189 (31)	188 (30)
Min – Max	108 – 273	109 – 307	114 – 308	108 – 308
Median	188	180	188	185
25%-75%	172 – 208	167 – 198	164 – 206	169 – 203

8. Total ventricular ectopic beats during the whole monitoring period (TOTALVE)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	18 (35)	27 (91)	18 (61)	21 (68)
Min – Max	0 – 215	0 – 903	0 – 580	0 – 903
Median	2	2	1	2
25%-75%	0 - 17	0 – 15	0 – 5	0 – 12

9. Single ventricular ectopic beats during the whole monitoring period (SINGLEVE)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	17 (32)	22 (61)	12 (33)	17 (44)
Min – Max	0 – 215	0 – 651	0 – 283	0 – 651
Median	2	2	1	1
25%-75%	0 – 16	0 – 15	0 – 5	0 – 11

10. Paroxysmal supraventricular tachycardias during the whole monitoring period (PSVT)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	0.044 (0.20)	0.023 (0.18)	0.159 (1.03)	0.079 (0.64)
Min – Max	0 – 1	0 – 2	0 – 16	0 – 16
Median	0	0	0	0
25%-75%	0 – 0	0 – 0	0 – 0	0 – 0

11. Single supraventricular ectopic beats during the whole monitoring period (SINGLSVE)

	Amsterdam	Erfurt	Helsinki	Total
N	413	472	509	1394
Mean (sd)	7.8 (17.5)	4.6 (14.1)	5.1 (11.1)	5.8 (14.3)
Min – Max	0 – 131	0 – 123	0 – 99	0 – 131
Median	2	1	1	1
25%-75%	0 – 5	0 – 3	0 – 4	0 – 4

12. Correction in ST level (STLEVEL)

	Amsterdam	Erfurt	Helsinki	Total
N	165	236	231	632
Mean (sd)	-0.42 (0.44)	-1.00 (1.24)	-0.47 (0.56)	-0.65 (0.90)
Min – Max	-2.16 - -0.04	-5 - -0.04	-3.52 - -0.04	-5 - -0.04
Median	-0.24	-0.56	-0.24	-0.32
25%-75%	-0.6 - -0.08	-1.24 - -0.22	-0.52 - -0.12	-0.8 - -0.16

13. 1st ST-depression episode (EPISODE1)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	N	%
Missing	404	94	451	92	345	67	1200	83
1	25	6	40	8	173	33	238	17

14. Duration of 1st ST-depression episode (DUR1)

	Amsterdam	Erfurt	Helsinki	Total
N	24	37	167	228
Mean (sd)	6:04 (5:0)	4:41 (4:55)	6:14 (5:00)	5:58 (5:00)
Min – Max	0:30 - 22:30	0:30 - 19:30	0:30 – 25:30	0:30 - 25:30
Median	5:00	2:30	5:30	5:00
25%-75%	2:00 – 7:30	1:00 – 7:00	1:30 –9:30	1:30 – 9:30

15. Deviation of ST level in 1st ST-depression episode (STLEDEV1)

	Amsterdam	Erfurt	Helsinki	Total
N	26	38	173	238
Mean (sd)	-1.06 (0.61)	-1.10 (0.98)	-1.17 (0.55)	-1.14 (0.64)
Min – Max	-3.52 - -0.56	-5 - -0.56	-3.24 - -0.56	-5 - -0.56
Median	-0.84	-0.82	-1	-0.96
25%-75%	-1.24 - -0.72	-1.12 - -0.68	-1.44 - -0.76	-1.36 - -0.72

16. Slope of 1st St-depression episode (SLOPE1)

1 = less than -0.2mV/s
2 = between -0.2 and +0.2mV/s
3 = more than +0.2mV/s

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	N	%	n	%	n	%
Missing	404	94	451	92	345	67	1200	83
1	14	3	9	2	60	12	83	6
2	8	2	22	4	63	12	93	6
3	3	1	9	2	50	10	62	4

17. Area of 1st ST-depression episode (INTEGRA1)

	Amsterdam	Erfurt	Helsinki	Total
N	24	37	167	228
Mean (sd)	5.6 (7.3)	3.6 (4.4)	5.8 (6.5)	5.4 (6.3)
Min – Max	0.6 – 34.7	0.3 – 20.5	0.3 – 55.6	0.3 – 55.6
Median	3.6	1.6	3.7	3.6
25%-75%	1.4 – 5.6	0.7 – 4.8	1.1 – 8.0	1.0 – 7.7

18. 2nd ST-depression episode (EPISODE2)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	422	98	475	97	479	92	1376	96
2	7	2	16	3	39	8	62	4

19. Duration of 2nd ST-depression episode (DUR2)

	Amsterdam	Erfurt	Helsinki	Total
N	7	15	36	58
Mean (sd)	7 :04 (5:28)	4:38 (5:55)	4:45 (4:31)	5:00 (4:59)
Min - Max	1:30 - 16:00	1:00 - 22:30	0:30 - 23:30	0:30 - 23:30
Median	5:00	2:00	3:15	3:00
25%-75%	2:30 - 11:00	1:00 - 5:30	1:30 - 8:00	1:30 - 8:00

20. Deviation of ST level in 2nd ST-depression episode (STLEDEV2)

	Amsterdam	Erfurt	Helsinki	Total
N	7	16	39	62
Mean (sd)	-1.03 (0.34)	-0.84 (0.41)	-1.07 (0.46)	-1.01 (0.44)
Min – Max	-1.6 - -0.68	-2.24 – 0.56	-2.28 - -0.56	-2.28 - -0.56
Median	-1	-0.7	-1	-0.82
25%-75%	-1.28 - -0.72	-0.82 - -0.64	-1.36 - -0.68	-1.16 - -0.68

21. Slope of 2nd St-depression episode (SLOPE2)

1 = less than -0.2mV/s
2 = between -0.2 and +0.2mV/s
3 = more than +0.2mV/s

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	422	98	475	97	479	92	1376	96
1	5	1	0	0	11	2	16	1
2	2	0	13	3	16	3	31	2
3	0	0	3	1	12	2	15	1

22. Area of 2nd ST-depression episode (INTEGRA2)

	Amsterdam	Erfurt	Helsinki	Total
N	7	15	36	58
Mean (sd)	6.4 (6.0)	3.8 (6.0)	4.1 (5.2)	4.3 (5.5)
Min – Max	1.0 – 17	0.6 – 20.3	0.3 – 29.3	0.3 – 29.3
Median	3.4	0.9	2.2	1.9
25%-75%	1.7 – 10.6	0.6 – 3.5	1.0 – 5.9	0.9 – 6.2

23. 3rd ST-depression episode (EPISODE3)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	427	100	483	98	512	99	1422	99
3	2	0	8	2	6	1	16	1

24. Duration of 3rd ST-depression episode (DUR3)

	Amsterdam	Erfurt	Helsinki	Total
N	2	8	5	15
Mean (sd)	10:45 (3:11)	4:53 (3:39)	3:18 (5:12)	5:08 (4:34)
Min - Max	8:30 - 13.00	0:30 - 10:30	0:30 - 12:30	0:30 - 13:00
Median	10:45	4:30	0:30	3:00
25%-75%	8:30 - 13:00	1:45 - 7:45	0:30 - 2:30	0:30 - 8:30

25. Deviation of ST level in 3rd ST-depression episode (STLEDEV3)

	Amsterdam	Erfurt	Helsinki	Total
N	2	8	6	16
Mean (sd)	-1.14 (0.82)	-0.81 (0.21)	-0.94 (0.53)	-0.90 (0.41)
Min – Max	-1.72 - -0.56	-1.04 - -0.56	-1.96 - -0.64	-1.96 - -0.56
Median	-1.14	-0.79	-0.66	-0.67
25%-75%	-1.72 - -0.56	-1.02 - -0.62	-1.08 - -0.64	-1.04 - -0.64

26. Slope of 3rd St-depression episode (SLOPE3)

1 = less than -0.2mV/s
2 = between -0.2 and +0.2mV/s
3 = more than +0.2mV/s

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	N	%	n	%	N	%
Missing	428	100	483	98	512	99	1423	99
1	1	0	0	0	2	0	3	0
2	0	0	6	1	1	0	7	0
3	0	0	2	0	3	1	5	0

27. Area of 3rd ST-depression episode (INTEGRA3)

	Amsterdam	Erfurt	Helsinki	Total
N	2	8	5	15
Mean (sd)	9.8 (7.2)	3.4 (2.6)	2.7 (4.1)	4.0 (4.2)
Min – Max	4.8 – 14.9	0.6 – 8.0	0.3 – 9.9	0.3 – 14.9
Median	9.8	3.0	1.0	1.9
25%-75%	4.8 – 14.9	1.2 – 5.0	0.6 – 1.6	1.0 – 5.3

28. 4th ST-depression episode (EPISODE4)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	429	100	488	99	516	100	1433	100
4	0	0	3	1	2	0	5	0

29. Duration of 4th ST-depression episode (DUR4)

	Amsterdam	Erfurt	Helsinki	Total
N	0	3	2	5
Mean (sd)	-	0:50 (0:17)	4:45 (4:36)	2:24 (3:09)
Min – Max	-	0:30 – 1:00	1:30 – 8:00	0:30 – 8:00
Median	-	1:00	4:45	1:00
25%-75%	-	0:30 – 1:00	1:30 – 8:00	1:00 – 1:30

30. Deviation of ST level in 4th ST-depression episode (STLEDEV4)

	Amsterdam	Erfurt	Helsinki	Total
N	0	3	2	5
Mean (sd)	-	-0.67 (0.02)	-1.16 (0.11)	-0.86 (0.28)
Min – Max	-	-0.68 - -0.64	-1.24 - -1.08	-1.24 - -0.64
Median	-	-0.68	-1.16	-0.68
25%-75%	-	-0.68 - -0.64	-1.24 - -1.08	-1.08 - -0.68

31. Slope of 4th St-depression episode (SLOPE4)

1 = less than -0.2mV/s
2 = between -0.2 and +0.2mV/s
3 = more than +0.2mV/s

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	429	100	488	100	516	100	1433	100
1	0	0	0	0	0	0	0	0
2	0	0	1	0	0	0	1	0
3	0	0	2	0	2	0	4	0

32. Area of 4th ST-depression episode (INTEGRA4)

	Amsterdam	Erfurt	Helsinki	Total
N	0	3	2	5
Mean (sd)	-	0.5 (0.2)	4.9 (4.1)	2.3 (3.2)
Min – Max	-	0.3 - 0.6	2.0 - 7.8	0.3 – 7.8
Median	-	0.6	4.9	0.6
25%-75%	-	0.3 - 0.6	2.0 - 7.8	0.6 – 2.0

33. 5th ST-depression episode (EPISODE5)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	429	100	489	100	518	100	1436	100
5	0	0	2	0	0	0	2	0

34. Duration of 5th ST-depression episode (DUR5)

	Amsterdam	Erfurt	Helsinki	Total
N	0	1	0	1
Mean (sd)	-	1:00 (0)	-	1:00 (0)
Min – Max	-	-	-	-
Median	-	-	-	-
25%-75%	-	-	-	-

35. Deviation of ST level in 5th ST-depression episode (STLEDEV5)

	Amsterdam	Erfurt	Helsinki	Total
N	0	2	0	2
Mean (sd)	-	-0.7 (0.14)	-	-0.7 (0.14)
Min – Max	-	-0.8 - -0.6	-	-0.8 - -0.6
Median	-	-0.7	-	-0.7
25%-75%	-	-0.8 - -0.6	-	-0.8 - -0.6

36. Slope of 5th St-depression episode (SLOPE5)

1 = less than -0.2mV/s
2 = between -0.2 and +0.2mV/s
3 = more than +0.2mV/s

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	429	100	489	100	518	100	1436	100
1	0	0	0	0	0	0	0	0
2	0	0	2	0	0	0	2	0
3	0	0	0	0	0	0	0	0

37. Area of 5th ST-depression episode (INTEGRA5)

	Amsterdam	Erfurt	Helsinki	Total
N	0	1	0	1
Mean (sd)	-	0.6 (0)	-	0.6 (0)
Min – Max	-	-	-	-
Median	-	-	-	-
25%-75%	-	-	-	-

38. Mean of all filtered RR intervals during the whole monitoring period (TOTMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	367	429	433	1229
Mean (sd)	939 (160)	857 (102)	901 (103)	897 (127)
Min – Max	663 – 1580	571 – 1109	679 – 1310	571 – 1580
Median	929	862	885	886
25%-75%	817 – 1025	783 – 934	831 – 954	811 – 963

39. Standard deviation of all filtered RR intervals during the whole monitoring period (TOTSDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	94 (37)	88 (31)	125 (47)	103 (43)
Min – Max	28 – 213	14 – 192	29 – 261	14 – 261
Median	89	84	123	97
25%-75%	67 – 114	65 – 108	90 – 161	71 – 128

40. Mean of the standard deviations of all filtered RR intervals for all 5 minute segments during the whole monitoring period (TOTSDNNI)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	56 (21)	50 (17)	57 (20)	54 (20)
Min – Max	20 – 168	5 – 108	18 – 129	5 – 168
Median	54	49	55	53
25%-75%	40 – 70	38 – 59	43 – 66	40 – 65

41. Standard deviation of the means of all filtered RR intervals for all 5 minute segments during the whole monitoring period (TOTSDANN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	68 (30)	64 (26)	97 (41)	77 (36)
Min – Max	12 – 170	8 – 156	9 – 217	8 – 217
Median	63	62	94	72
25%-75%	47 – 85	46 – 82	68 – 125	50 – 97

42. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during the whole monitoring period (TOTRMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	36 (27)	29 (18)	35 (23)	33 (23)
Min – Max	9 – 224	8 – 129	10 – 139	8 – 224
Median	27	24	27	26
25%-75%	20 – 43	17 – 34	20 – 39	19 – 39

43. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during the whole monitoring period (TOTPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	9.2 (10.3)	6.9 (8.3)	8.7 (10.9)	8.2 (9.9)
Min – Max	0 – 54.6	0 – 52.3	0 – 67.9	0 – 67.9
Median	4.5	3.7	5.0	4.4
25%-75%	1.3 – 14.1	1.1 – 9.8	1.8 – 10.1	1.4 – 11.1

44. Number of RR intervals during the whole monitoring period (TOTINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	2685 (490)	2735 (376)	2406 (412)	2604 (450)
Min – Max	1516 – 4663	1975 – 4482	1088 – 3294	1088 – 4663
Median	2674	2698	2470	2602
25%-75%	2368 – 2991	2451 – 2951	2223 – 2675	2357 – 2872

45. Power from spectral analysis of heart rate variability, overall band (0-0.4 Hz), the whole monitoring period (TOTPOWER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	2618 (1770)	2149(1535)	2446 (1924)	2393 (1759)
Min – Max	338 – 9913	99 – 11537	310 – 12048	99 – 12048
Median	2218	1759	1950	1942
25%-75%	1284 – 3590	1039 – 2782	1190 – 2914	1151 – 3108

46. Power from spectral analysis of heart rate variability, band 1 (0-0.0033 Hz), the whole monitoring period (TOTPOW1)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	276 (212)	300 (294)	404 (312)	329 (285)
Min – Max	24 – 1274	14 – 3258	10 – 1985	10 – 3258
Median	212	210	313	244
25%-75%	124 – 356	117 – 398	176 – 564	133 – 440

47. Power from spectral analysis of heart rate variability, band 2 (0.0033-0.04 Hz), the whole monitoring period (TOTPOW2)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	1505 (1069)	1286 (968)	1240 (858)	1335 (969)
Min – Max	217 – 6132	66 - 8337	100 – 6548	66 – 8337
Median	1170	1070	1065	1089
25%-75%	772 – 1969	616 – 1628	690 – 1547	684 – 1680

48. Power from spectral analysis of heart rate variability, band 3 (0.04-0.15 Hz), the whole monitoring period (TOTPOW3)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	522 (472)	357 (345)	433 (639)	433 (506)
Min – Max	29 – 2982	14 – 2925	17 – 5948	14 – 5948
Median	389	249	218	264
25%-75%	174 – 721	138 – 446	116 – 431	136 – 533

49. Power from spectral analysis of heart rate variability, band 4 (0.15-0.4 Hz), the whole monitoring period (TOTPOW4)

	Amsterdam	Erfurt	Helsinki	Total
N	366	430	433	1229
Mean (sd)	316 (390)	216 (306)	369 (598)	300 (456)
Min – Max	12 – 2664	5 – 1991	12 – 4318	5 – 4318
Median	174	110	155	143
25%-75%	74 – 406	57 – 237	76 – 332	68 – 314

50. Average absolute QT interval, the whole monitoring period (TOTQTAV)

	Amsterdam	Erfurt	Helsinki	Total
N	403	448	454	1305
Mean (sd)	372 (32)	361 (33)	379 (34)	371 (34)
Min – Max	277 – 486	283 – 478	189 – 511	189 – 511
Median	373	359	380	372
25%-75%	349 – 396	339 – 382	357 – 398	346 – 393

51. Average absolute QTc interval, the whole monitoring period (TOTQTCAV)

	Amsterdam	Erfurt	Helsinki	Total
N	403	448	454	1305
Mean (sd)	388 (28)	389 (28)	399 (31)	392 (29)
Min – Max	308 – 508	242 – 494	172 – 548	172 – 548
Median	387	390	400	391
25%-75%	372 – 400	370 – 404	379 – 416	374 – 408

52. Mean of all filtered RR intervals during the rest, spontaneous breathing (SPOMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	427	468	1261
Mean (sd)	983 (175)	907 (124)	995 (126)	962 (147)
Min – Max	656 – 1650	602 – 1193	718 – 1340	602 – 1650
Median	967	902	979	948
25%-75%	848 – 1088	818 – 1002	901 – 1086	860 – 1055

53. Standard deviation of all filtered RR intervals during rest, spontaneous breathing (SPOSDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	427	468	1261
Mean (sd)	48 (24)	40 (19)	44 (23)	44 (22)
Min – Max	10 – 221	8 – 139	12 – 180	8 – 221
Median	44	36	39	39
25%-75%	32 – 60	27 – 51	28 – 53	28 – 54

54. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during the rest, spontaneous breathing (SPORMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	366	427	468	1261
Mean (sd)	33 (31)	29 (24)	35 (30)	32 (28)
Min – Max	7 – 266	6 – 251	9 – 228	6 – 266
Median	23	22	25	24
25%-75%	16 – 39	15 – 32	17 – 38	16 – 37

55. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during the rest, spontaneous breathing (SPOPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	366	427	468	1261
Mean (sd)	8.1 (11.1)	7.3 (11.1)	10.8 (16.1)	8.8 (13.3)
Min – Max	0 - 57.1	0 – 70.1	0 – 92.5	0 – 92.5
Median	2.9	2.4	4.1	3.1
25%-75%	0.6 – 11.1	0.4 – 9.6	0.9 – 12.8	0.6 – 11.1

56. Number of RR intervals during the rest, spontaneous breathing (SPOINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	427	468	1261
Mean (sd)	308 (55)	332 (53)	302 (41)	314 (51)
Min – Max	63 – 456	81 – 497	107 – 416	63 – 497
Median	305	330	303	312
25%-75%	271 – 348	297 – 364	273 – 331	280 – 345

57. Power from spectral analysis of heart rate variability, overall band (0-0.4 Hz), the rest, spontaneous breathing (SPOPOWER)

	Amsterdam	Erfurt	Helsinki	Total
N	359	426	465	1250
Mean (sd)	2147 (1997)	1665 (1734)	2002 (2402)	1930 (2085)
Min – Max	87 – 18981	44 – 14921	120 – 18633	44 – 18981
Median	1603	1096	1226	1289
25%-75%	846 – 2831	624 – 2042	630 – 2315	669 – 2418

58. Power from spectral analysis of heart rate variability, band 1 (0-0.0033 Hz), the rest, spontaneous breathing (SPOPOW1)

	Amsterdam	Erfurt	Helsinki	Total
N	359	426	465	1250
Mean (sd)	137 (222)	91 (143)	115 (214)	113 (196)
Min – Max	0 – 1649	0 – 1176	0 – 2099	0 – 2099
Median	60	40	48	47
25%-75%	20 – 157	15 – 99	13 – 124	16 – 124

59. Power from spectral analysis of heart rate variability, band 2 (0.0033-0.04 Hz), the rest, spontaneous breathing (SPOPOW2)

	Amsterdam	Erfurt	Helsinki	Total
N	359	426	465	1250
Mean (sd)	1180 (1257)	912 (1088)	843 (986)	963 (1112)
Min – Max	51 – 13138	23 – 8684	24 – 13182	23 – 13182
Median	820	555	545	651
25%-75%	475 – 1531	303 – 1074	287 – 994	330 – 1194

60. Power from spectral analysis of heart rate variability, band 3 (0.04-0.15 Hz), the rest, spontaneous breathing (SPOPOW3)

	Amsterdam	Erfurt	Helsinki	Total
N	359	426	465	1250
Mean (sd)	513 (600)	410 (489)	581 (964)	503 (732)
Min – Max	8 – 4758	7 – 3542	14 – 8769	7 – 8769
Median	303	251	268	268
25%-75%	123 – 684	136 – 463	119 – 553	125 – 567

61. Power from spectral analysis of heart rate variability, band 4 (0.15-0.4 Hz), the rest, spontaneous breathing (SPOPOW4)

	Amsterdam	Erfurt	Helsinki	Total
N	359	426	465	1250
Mean (sd)	318 (528)	254 (484)	466 (900)	351 (685)
Min – Max	7 – 3329	3 – 5398	11 – 5764	3 – 5764
Median	125	95	161	128
25%-75%	56 – 324	43 – 219	66 – 372	55 – 305

62. Mean of all filtered RR intervals during the rest, paced breathing (PACMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	468	1266
Mean (sd)	1006 (422)	926 (133)	995 (132)	975 (255)
Min – Max	647 – 8327	371 – 1246	714 – 1380	371 – 8327
Median	968	925	974	954
25%-75%	854 – 1087	831 – 1027	900 – 1089	868 – 1065

63. Standard deviation of all filtered RR intervals during rest, paced breathing (PACSDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	468	1266
Mean (sd)	40 (24)	33 (19)	37 (22)	36 (22)
Min – Max	9 – 287	6 – 143	8 – 137	6 – 287
Median	36	28	31	31
25%-75%	24 – 47	21 – 39	22 – 44	22 – 43

64. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during the rest, paced breathing (PACRMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	468	1266
Mean (sd)	33 (32)	28 (27)	34 (31)	32 (30)
Min – Max	6 – 304	7 – 216	7 – 250	6 – 304
Median	23	20	23	22
25%-75%	15 – 36	13 – 31	15 – 38	15 – 35

65. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during the rest, paced breathing (PACPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	468	1266
Mean (sd)	9.0 (13.3)	7.4 (12.4)	10.4 (16.9)	9.0 (14.5)
Min – Max	0 – 70.5	0 – 74.7	0 – 85.1	0 – 85.1
Median	2.5	1.8	2.3	2.1
25%-75%	0.3 – 13.5	0 – 8.5	0.3 – 11.7	0.3 – 10.9

66. Number of RR intervals during the rest, paced breathing (PACINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	468	1266
Mean (sd)	308 (54)	326 (49)	303 (41)	312 (49)
Min – Max	119 – 463	212 – 496	179 – 419	119 – 496
Median	304	321	302	310
25%-75%	272 – 348	289 – 353	273 – 330	277 – 343

67. Power from spectral analysis of heart rate variability, overall band (0-0.4 Hz), the rest, paced breathing (PACPOWER)

	Amsterdam	Erfurt	Helsinki	Total
N	358	431	465	1254
Mean (sd)	1293 (1324)	1134 (1759)	1496 (2061)	1314 (1777)
Min – Max	51 – 11281	21 – 17947	63 – 13834	21 – 17947
Median	1004	606	715	737
25%-75%	378 – 1620	332 – 1205	368 – 1495	355 – 1454

68. Power from spectral analysis of heart rate variability, band 1 (0-0.0033 Hz), the rest, paced breathing (PACPOW1)

	Amsterdam	Erfurt	Helsinki	Total
N	358	431	465	1254
Mean (sd)	80 (142)	64 (160)	62 (210)	68 (176)
Min – Max	0 – 966	0 – 1705	0 – 3578	0 – 3578
Median	33	22	19	23
25%-75%	11 – 86	6 – 57	7 – 57	7 – 63

69. Power from spectral analysis of heart rate variability, band 2 (0.0033-0.04 Hz), the rest, paced breathing (PACPOW2)

	Amsterdam	Erfurt	Helsinki	Total
N	358	431	465	1254
Mean (sd)	505 (570)	412 (583)	423 (533)	443 (562)
Min – Max	19 – 4330	6 – 5750	15 – 6603	6 – 6603
Median	330	230	262	262
25%-75%	158 – 645	123 – 438	146 – 489	143 – 526

70. Power from spectral analysis of heart rate variability, band 3 (0.04-0.15 Hz), the rest, paced breathing (PACPOW3)

	Amsterdam	Erfurt	Helsinki	Total
N	358	431	465	1254
Mean (sd)	285 (460)	313 (737)	378 (817)	329 (704)
Min – Max	5 – 4490	4 – 8558	7 – 7837	4 – 8558
Median	162	126	114	128
25%-75%	54 – 332	59 – 275	56 – 290	57 – 294

71. Power from spectral analysis of heart rate variability, band 4 (0.15-0.4 Hz), the rest, paced breathing (PACPOW4)

	Amsterdam	Erfurt	Helsinki	Total
N	358	431	465	1254
Mean (sd)	423 (624)	345 (745)	633 (1168)	474 (907)
Min – Max	6 – 5254	6 – 6831	10 – 8145	6 – 8145
Median	176	126	205	161
25%-75%	80 - 480	49 – 298	75 – 586	68 – 436

72. Mean of all filtered RR intervals during standing (STAMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	464	1262
Mean (sd)	912 (162)	833 (107)	928 (140)	891 (143)
Min – Max	643 – 1519	531 – 1138	611 – 1346	531 – 1519
Median	894	830	904	880
25%-75%	791 – 1003	753 – 911	830 – 1024	789 – 973

73. Standard deviation of all filtered RR intervals during standing (STASDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	464	1262
Mean (sd)	53 (25)	47 (18)	51 (20)	50 (21)
Min – Max	12 – 185	14 – 124	15 – 172	12 – 185
Median	48	44	47	47
25%-75%	36 – 63	32 – 58	37 – 62	35 – 60

74. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during standing (STARMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	464	1262
Mean (sd)	38 (123)	25 (15)	29 (23)	30 (68)
Min – Max	7 – 2336	7 – 142	7 – 168	7 – 2336
Median	24	20	22	21
25%-75%	16 – 40	15 – 29	16 – 32	15 – 33

75. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during standing (STAPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	464	1262
Mean (sd)	7.5 (9.7)	5.8 (8.4)	7.3 (11.0)	6.8 (9.8)
Min – Max	0 – 57.7	0 – 55.2	0 – 63.0	0 – 63.0
Median	3.2	2.2	2.7	2.7
25%-75%	0.6 – 11.6	0.5 – 7.6	0.9 – 8.3	0.6 – 8.5

76. Number of RR intervals during standing (STAINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	432	464	1262
Mean (sd)	335 (56)	360 (52)	321 (51)	339 (55)
Min – Max	196 – 466	246 – 564	175 – 461	175 – 564
Median	334	354	322	336
25%-75%	295 – 378	322 – 395	285 – 356	300 – 376

77. Power from spectral analysis of heart rate variability, overall band (0-0.4 Hz), standing (STAPOWER)

	Amsterdam	Erfurt	Helsinki	Total
N	360	430	462	1252
Mean (sd)	2560 (2564)	1887 (1593)	2321 (2047)	2241 (2092)
Min – Max	125 – 17549	99 – 13757	183 – 16478	99 – 17549
Median	1749	1382	1751	1657
25%-75%	913 – 3282	791 – 2558	1011 – 2757	893 – 2801

78. Power from spectral analysis of heart rate variability, band 1 (0-0.0033 Hz), standing (STAPOW1)

	Amsterdam	Erfurt	Helsinki	Total
N	360	430	462	1252
Mean (sd)	250 (557)	170 (288)	228 (375)	214 (413)
Min – Max	1 – 6608	1 – 3416	1 – 4390	1 – 6608
Median	84	72	105	88
25%-75%	29 – 221	25 – 202	38 – 274	30 – 235

79. Power from spectral analysis of heart rate variability, band 2 (0.0033-0.04 Hz), standing (STAPOW2)

	Amsterdam	Erfurt	Helsinki	Total
N	360	430	462	1252
Mean (sd)	1514 (1664)	1114 (1057)	1306 (1088)	1300 (1280)
Min – Max	35 – 10676	31 – 11767	69 – 8785	31 – 11767
Median	964	803	998	930
25%-75%	531 – 1765	431 – 1530	558 – 1724	508 – 1659

80. Power from spectral analysis of heart rate variability, band 3 (0.04-0.15 Hz), standing (STAPOW3)

	Amsterdam	Erfurt	Helsinki	Total
N	360	430	462	1252
Mean (sd)	544 (643)	430 (461)	496 (711)	487 (616)
Min – Max	17 – 5176	11 – 3126	10 – 5779	10 – 5779
Median	334	266	261	285
25%-75%	139 – 705	136 – 521	109 – 592	128 – 593

81. Power from spectral analysis of heart rate variability, band 4 (0.15-0.4 Hz), standing (STAPOW4)

	Amsterdam	Erfurt	Helsinki	Total
N	360	430	462	1252
Mean (sd)	251 (373)	174 (257)	292 (642)	239 (466)
Min – Max	5 – 3530	4 – 2302	6 – 7686	4 – 7686
Median	110	78	88	90
25%-75%	47 – 297	39 – 193	47 – 225	44 – 239

82. Mean of all filtered RR intervals during stress (STRMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	327	411	371	1109
Mean (sd)	802 (148)	735 (78)	672 (60)	734 (112)
Min – Max	567 – 1395	529 – 1052	536 – 893	529 – 1395
Median	783	737	653	716
25%-75%	698 – 868	687 – 780	633 – 700	652 – 784

83. Standard deviation of all filtered RR intervals during stress (STRSDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	327	411	371	1109
Mean (sd)	36 (18)	37 (15)	34 (19)	35 (18)
Min – Max	9 – 152	10 – 103	11 – 150	9 – 152
Median	31	34	29	31
25%-75%	23 – 43	26 – 45	22 – 39	24 – 43

84. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during stress (STRRMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	327	411	371	1109
Mean (sd)	29 (21)	21 (15)	24 (15)	25 (17)
Min – Max	8 – 149	7 – 97	7 – 103	7– 149
Median	23	16	21	20
25%-75%	15 – 35	11 – 26	15 – 30	13 – 30

85. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during stress (STRPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	327	411	371	1109
Mean (sd)	7.8 (11.9)	4.7 (9.5)	5.0 (7.2)	5.7 (9.7)
Min – Max	0 – 74.2	0 – 79.9	0 – 58.2	0 – 79.9
Median	2.6	0.7	2.4	1.7
25%-75%	0.3 – 9.9	0 – 4.7	0.6 – 6.1	0.2 – 6.7

86. Number of RR intervals during stress (STRINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	327	411	371	1109
Mean (sd)	384 (62)	410 (46)	446 (45)	414 (56)
Min – Max	214 – 528	255 – 559	160 – 559	160 – 559
Median	382	405	458	417
25%-75%	345 – 429	383 – 435	426 – 472	379 – 459

87. Mean of all filtered RR intervals during the rest, recovery (RECMEAN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	431	463	1260
Mean (sd)	996 (181)	903 (121)	941 (116)	944 (144)
Min – Max	660 – 1679	604 – 1198	645 – 1350	604 – 1679
Median	970	911	927	932
25%-75%	866 – 1095	810 – 995	861 – 1004	845 – 1021

88. Standard deviation of all filtered RR intervals during rest, recovery (RECSDNN)

	Amsterdam	Erfurt	Helsinki	Total
N	366	431	463	1260
Mean (sd)	51 (26)	43 (19)	44 (24)	45 (23)
Min – Max	11 – 200	8 – 135	13 – 192	8 – 200
Median	47	39	38	40
25%-75%	33 – 63	29 – 53	28 – 52	29 – 55

89. Square root of the mean of the sum of squares of differences between adjacent filtered RR intervals for all 5 minute segments during the rest, recovery (RECRMSSD)

	Amsterdam	Erfurt	Helsinki	Total
N	366	431	463	1260
Mean (sd)	38 (41)	28 (22)	34 (26)	33 (30)
Min – Max	8 – 547	6 – 237	8 – 157	6 – 547
Median	26	23	25	25
25%-75%	18 – 46	15 – 35	18 – 39	17 – 38

90. Percentages of differences between adjacent filtered RR intervals that are greater than 50 ms during the rest, recovery (RECPNN50)

	Amsterdam	Erfurt	Helsinki	Total
N	366	431	463	1260
Mean (sd)	10.3 (12.7)	7.5 (10.9)	9.1 (13.8)	8.9 (12.6)
Min – Max	0 – 63.2	0 – 79.2	0 – 78.1	0 – 79.2
Median	4.4	3.2	3.6	3.6
25%-75%	0.8 – 16.8	0.5 – 9.6	0.9 – 10.8	0.7 – 12.3

91. Number of RR intervals during the rest, recovery (RECINTER)

	Amsterdam	Erfurt	Helsinki	Total
N	366	431	463	1260
Mean (sd)	309 (51)	337 (47)	318 (43)	322 (49)
Min – Max	178 – 453	250 – 495	117 – 464	117 – 495
Median	308	328	321	319
25%-75%	273 – 345	300 – 369	292 – 346	292 – 353

92. Power from spectral analysis of heart rate variability, overall band (0-0.4 Hz), the rest, recovery (RECPOWER)

	Amsterdam	Erfurt	Helsinki	Total
N	361	426	458	1245
Mean (sd)	2478 (2546)	1786 (1863)	1932 (2562)	2040 (2357)
Min – Max	114 – 23124	46 – 16662	85 – 18510	46 – 23124
Median	1733	1171	1091	1269
25%-75%	862 – 3107	631 – 2344	572 – 2153	651 – 2501

93. Power from spectral analysis of heart rate variability, band 1 (0-0.0033 Hz), the rest, recovery (RECPOW1)

	Amsterdam	Erfurt	Helsinki	Total
N	361	426	458	1245
Mean (sd)	171 (408)	108 (170)	101 (182)	124 (267)
Min – Max	0 – 5112	0 – 1537	0 – 1490	0 – 5112
Median	66	51	39	49
25%-75%	24 – 184	17 – 124	15 – 103	18 – 128

94. Power from spectral analysis of heart rate variability, band 2 (0.0033-0.04 Hz), the rest, recovery (RECPOW2)

	Amsterdam	Erfurt	Helsinki	Total
N	361	426	458	1245
Mean (sd)	1267 (1389)	947 (1185)	819 (1071)	992 (1222)
Min – Max	61 – 8986	24 – 12447	32 – 10797	24 – 12447
Median	787	572	479	586
25%-75%	416 – 1504	318 – 1205	259 – 992	322 – 1205

95. Power from spectral analysis of heart rate variability, band 3 (0.04-0.15 Hz), the rest, recovery (RECPOW3)

	Amsterdam	Erfurt	Helsinki	Total
N	361	426	458	1245
Mean (sd)	616 (687)	485 (594)	589 (1087)	561 (833)
Min – Max	15 – 4437	1 – 6126	7 – 8309	1 – 8309
Median	383	308	244	300
25%-75%	143 – 833	138 – 625	107 – 553	125 – 652

96. Power from spectral analysis of heart rate variability, band 4 (0.15-0.4 Hz), the rest, recovery (RECPOW4)

	Amsterdam	Erfurt	Helsinki	Total
N	361	426	458	1245
Mean (sd)	366 (533)	248 (451)	423 (815)	347 (634)
Min – Max	5 – 3537	4 – 4474	6 – 6200	4 – 6200
Median	150	110	144	130
25%-75%	63 – 416	51 – 236	63 – 338	57 – 324

97. Average absolute QT interval, the rest spontaneous breathing (SPOQTAV)

	Amsterdam	Erfurt	Helsinki	Total
N	413	452	507	1372
Mean (sd)	372 (38)	368 (43)	383 (42)	375 (42)
Min – Max	264 – 542	281 – 770	133 – 531	133 – 770
Median	371	363	386	374
25%-75%	343 – 401	344 – 390	355 – 408	347 – 401

98. Average absolute QTc interval, the rest spontaneous breathing (SPOQTCAV)

	Amsterdam	Erfurt	Helsinki	Total
N	413	452	507	1372
Mean (sd)	380 (32)	388 (39)	388 (37)	385 (37)
Min – Max	267 – 554	282 – 808	119 – 556	119 – 808
Median	381	387	388	385
25%-75%	361 – 397	367 – 402	366 – 410	366 – 403

99. Average absolute QT interval, stress (STRQTAV)

	Amsterdam	Erfurt	Helsinki	Total
N	372	450	385	1207
Mean (sd)	319 (29)	340 (38)	307 (28)	323 (35)
Min – Max	219 – 403	243 – 544	233 – 438	219 – 544
Median	320	337	305	321
25%-75%	300 – 337	317 – 359	290 – 322	299 – 341

100. Average absolute QTc interval, stress (STRQTCAV)

	Amsterdam	Erfurt	Helsinki	Total
N	372	450	385	1207
Mean (sd)	361 (28)	397 (39)	375 (32)	379 (37)
Min – Max	257 – 489	265 – 606	282 – 571	257 – 606
Median	360	394	373	374
25%-75%	344 – 372	374 – 416	360 – 389	357 – 397

101. Average absolute QT interval, the rest recovery (RECQTAV)

	Amsterdam	Erfurt	Helsinki	Total
N	411	456	504	1371
Mean (sd)	347 (32)	360 (41)	355 (38)	354 (38)
Min – Max	228 – 448	273 – 682	166 – 580	166 – 682
Median	346	355	355	352
25%-75%	325 – 370	335 – 385	334 – 374	331 – 376

102. Average absolute QTc interval, the rest recovery (RECQTCAV)

	Amsterdam	Erfurt	Helsinki	Total
N	411	456	504	1371
Mean (sd)	353 (28)	381 (38)	368 (36)	368 (36)
Min – Max	248 – 481	260 – 738	153 – 662	153 – 738
Median	351	380	367	364
25%-75%	337 – 364	358 – 400	350 – 385	347 – 386

103. Atrial fibrillation in the ambulatory ECG (ATRFIBR)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Not reported/missing	416	97	463	94	489	94	1368	95
Yes	13	3	28	6	29	6	70	5

3.9 DIARY

1. Chest pain today (CHPAIN)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	163	3	0	0	126	2	289	1
No	5755	92	5716	76	7249	93	18720	87
Slight	279	4	1678	22	413	5	2370	11
Severe	31	1	97	1	40	0	168	1

2. Chest pain at physical exertion today (CHPAINPH)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	129	2	288	1
No	5672	91	5886	79	7038	90	18596	86
Slight	370	6	1479	20	629	8	2478	12
Severe	27	0	126	2	32	0	185	1

3. Shortness of breath today (SHBREATH)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	120	2	279	1
No	5155	83	5705	76	6353	81	17213	80
Slight	797	13	1664	22	1105	14	3566	17
Severe	117	2	122	2	250	3	489	2

4. Feeling tired or weak today (TIRED)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	159	3	0	0	129	2	288	1
No	4797	77	5402	72	5962	76	16161	75
Slight	1164	19	1970	26	1520	19	4654	22
Severe	108	2	119	2	217	3	444	2

5. Tripping or racing heart today (TRIHEART)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	160	3	0	0	150	2	310	1
No	5675	91	6625	88	6819	87	19119	89
Slight	383	6	788	11	699	9	1870	9
Severe	10	0	78	1	160	2	248	1

6. Cold hands or feet today (COLDHAND)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	141	2	300	1
No	5443	87	6135	82	5113	65	16691	77
Slight	621	10	1313	18	2059	26	3993	19
Severe	5	0	43	1	515	7	563	3

7. Cough today (COUGH)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	92	1	251	1
No	4625	75	6780	91	6008	77	17413	81
Slight	1310	21	656	9	1558	20	3524	16
Severe	134	2	55	1	170	2	359	2

8. Phlegm today (PHLEGM)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	159	3	0	0	109	1	268	1
No	4017	64	6479	86	5901	75	16397	76
Slight	1920	31	972	13	1685	22	4577	21
Severe	132	2	40	1	133	2	305	1

9. Woken up with breathing problems today (WAKEUP)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	148	2	307	1
No	5792	93	6921	92	7176	92	19889	92
Slight	179	3	547	7	457	6	1183	5
Severe	98	2	23	0	47	1	168	1

10. Wheeze today (WHEEZE)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	159	3	0	0	134	2	293	1
No	5681	91	7001	93	7102	91	19784	92
Slight	299	5	460	6	530	7	1289	6
Severe	89	1	30	0	62	1	181	1

11. Common cold or flu today (COMMCOLD)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	161	3	0	0	137	2	298	1
No	5374	86	6730	90	7032	90	19136	89
Slight	670	11	703	9	581	7	1954	9
Severe	23	0	58	1	78	1	159	1

12. Fever today (FEVER)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	160	3	0	0	146	2	306	1
No	5951	96	7441	99	7623	97	21015	98
Slight	110	2	45	1	42	1	170	1
Severe	7	0	5	0	17	0	29	0

13. Did you avoid physically demanding activities because of symptoms today? (AVOIDACT)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	293	5	0	0	169	2	462	2
No	5173	83	6388	85	6827	87	18388	85
Slight	711	11	826	11	679	9	2216	10
Severe	51	1	277	4	153	2	481	2

14. How would you rate your overall health today? (HEALTH)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	256	4	0	0	107	1	363	2
Good	2607	42	2484	33	2771	35	7862	36
Quite good	2558	41	3021	40	1639	21	7218	34
Average	739	12	1734	23	2872	37	5345	25
Bad	68	1	225	3	422	5	715	3
Very bad	0	0	27	0	17	0	44	0

15. How long have you been outside today? (OUTSIDE)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	227	4	0	0	160	2	387	2
0	1760	28	621	8	1328	17	3709	17
1	1861	30	1637	22	3159	40	6657	31
2	1148	18	2113	28	2028	26	5289	25
3 or more	1232	20	3120	41	1153	14	5505	26

16. Have you been out of town for more than 8 hrs today? (AWAY)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	166	3	0	0	151	2	317	1
No	5653	91	7048	94	7168	92	19869	92
Yes	409	7	443	6	509	7	1361	6

3.10 ON NEED / ADDITIONAL MEDICATION (BASED ON THE DIARY)

1. Nitrates (NITROEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	5995	96	7295	97	7017	90	20307	94
Yes	233	4	196	3	608	8	1037	5

2. Inhalable β_2-agonists AGONEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	151	2	151	1
No	6219	100	7490	100	7192	92	20901	97
Yes	9	0	1	0	433	6	443	2

3. Inhalable anticholinergs (ANTICEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6193	99	7491	100	7504	96	21188	98
Yes	35	1	0	0	121	2	156	1

4. Inhalable dinatriumcromoglicate / nedocromile (CROMOGEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7625	97	21344	99

5. Inhalable glucocorticosteroids (GLUCOREX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6173	99	7491	100	7549	96	21213	98
Yes	55	1	0	0	76	1	131	1

6. Leukotriene receptor blockers (RECBLOEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7625	97	21344	99

7. Anti-arrhythmic medication (ARREX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6229	100	7491	100	7614	97	21333	99
Yes	0	0	0	0	11	0	11	0

8. β-blockers (BETABLEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6146	99	7482	100	7625	97	21253	99
Yes	82	1	9	0	0	0	91	0

9. Ca++ -blockers (CABLOEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6226	100	7472	100	7625	97	21323	99
Yes	2	0	19	0	0	0	21	0

10. ACE-inhibitors (ACEEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6227	100	7491	100	7625	97	21343	99
Yes	1	0	0	0	0	0	1	0

11. ASA (ASAEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6194	99	7477	100	7624	97	21295	99
Yes	34	1	14	0	1	0	49	0

12. Digitalis (DIGITAEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7622	97	21341	99
Yes	0	0	0	0	3	0	3	0

13. Dipyridamole (DIPYRIEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7625	97	21344	99

14. Diuretics (DIURETEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6109	98	7402	99	7623	97	21134	98
Yes	119	2	89	1	2	0	210	1

15. Moksonidine (MOKSOEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	N	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7625	97	21344	99

16. Warfarine (WARFAREX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	6162	99	7491	100	7625	97	21278	99
Yes	66	1	0	0	0	0	66	0

17. Hyperlipidaemia medication (HYPLIPEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7487	100	7625	97	21340	99
Yes	0	0	4	0	0	0	4	0

18. Diabetes medication (DIABETEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6228	100	7491	100	7625	97	21344	99

19. Medication affecting central nervous system (CNSEX)

	Amsterdam		Erfurt		Helsinki		Total	
	N	%	n	%	n	%	n	%
Missing	0	0	0	0	203	3	203	1
No	6093	98	7458	100	7579	97	21130	98
Yes	135	2	33	0	46	1	214	1

20. Other medication (OTHMEDEX)

	Amsterdam		Erfurt		Helsinki		Total	
	n	%	n	%	n	%	N	%
Missing	0	0	0	0	203	3	203	1
No	5460	88	5450	73	6586	84	17496	81
Yes	768	12	2041	27	1039	13	3848	18

3.11 AIR HYGIENE 24-HOUR DATA (FROM NOON TO NOON)

1. Number concentration of particles in size range 0.01-0.1 μm (1/cm^3) (NC1)

	Amsterdam	Erfurt	Helsinki	Total
N	216	177	182	575
N missing	21	0	0	21
Mean	17 338	21 124	17 040	18 409
Sd	6 069	11 992	9 328	9 414
Min	5 699	3 867	2 305	2 305
Max	37 195	96 678	50 306	96 678
Median	17 147	19 198	14 886	16 580
25%	12 614	12 401	11 052	12 296
75%	21 322	27 933	20 879	22 392

2. Number concentration of particles in size range 0.01-0.1 μm (1/cm^3) without any imputations (NC1NOIMP)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean	17 456	20 902	17 223	18 481
Sd	6 137	11 714	9 399	9 376
Min	5 699	3 867	2 305	2 305
Max	37 195	89 295	50 306	89 295
Median	17 233	18 289	15 132	16 586
25%	12 766	12 348	11 004	12 296
75%	21 639	27 715	21 055	22 514

3. Number concentration of particles in size range 0.1-1.0 μm (1/cm^3) (NC2)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean (sd)	2131 (1139)	1829 (1277)	1390 (674)	1800 (1107)
Min - Max	413 - 6413	303 - 6848	344 - 3782	303 - 6848
Median	1874	1492	1200	1492
25%-75%	1212 - 2795	964 - 2237	909 - 1672	1012 - 2276

4. Number concentration of particles in size range 1.0-2.5 μm (1/cm^3) (NC3)

	Amsterdam	Erfurt	Helsinki	Total
N	209	177	176	562
N missing	28	0	6	34
Mean (sd)	0.3 (0.3)	0.7 (1.2)	2.3 (1.1)	1.1 (1.3)
Min - Max	0.01 - 1.9	0.1 -10.5	0.5 - 6.6	0.01 - 10.5
Median	0.2	0.4	2.1	0.6
25%-75%	0.1 - 0.5	0.3 - 0.8	1.5 - 2.9	0.2 - 1.6

5. Total number concentration of particles in size range 0.01-2.5 μm (1/cm^3) (TNC)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean	19 588	22 732	18 616	20 282
Sd	6 437	12 577	9 824	9 937
Min	6 836	4 656	3 027	3 027
Max	40 142	94 861	54 092	94 861
Median	20 078	19 847	16 596	18 263
25%	14 496	13 378	12 426	13 601
75%	23 904	30 008	22 455	24 484

6. CPC particle total number concentration (1/cm^3) (CPCTNC)

	Amsterdam	Erfurt	Helsinki	Total
N	212	162	174	548
N missing	25	15	8	48
Mean	24 536	23 724	22 594	23 679
Sd	8 521	12 749	9 655	10 295
Min	9 117	4 827	4 594	4 594
Max	51 861	111 771	58 919	111 771
Median	24 212	21 323	20 843	22 119
25%	17 906	15 299	16 290	16 659
75%	29 631	29 608	26 103	29 335

7. Number concentration of particles in size range 0.01-0.03 μm (1/cm^3) (NC1A)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	7	41
Mean	10 403	16 409	11 097	12 539
Sd	4 269	8 792	6 257	7 116
Min	2 991	2 787	1 182	1 182
Max	24 448	64 592	34 009	64 592
Median	9 829	14 933	9 980	10 780
25%	6 953	9 701	6 747	7 599
75%	13 431	21 278	13 891	15 706

8. Number concentration of particles in size range 0.03-0.1 μm (1/cm^3) (NC1B)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean	7 054	4 493	6 126	5 943
Sd	2 695	3 382	3 378	3 317
Min	1 468	895	1 123	895
Max	16 985	24 703	19 930	24 703
Median	7 019	3 429	5 320	5 382
25%	5 195	2 253	4 088	3 458
75%	8 778	5 623	7 249	7 595

9. Number concentration of particles in size range 0.1-0.5 μm (1/cm^3) (NC2A)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean (sd)	2127 (1136)	1807 (1257)	1381 (670)	1788 (1099)
Min - Max	412 - 6369	295 - 6797	342 - 3766	295 - 6797
Median	1873	1485	1194	1487
25%-75%	1210 - 2783	958 - 2216	902 - 1661	1002 - 2265

10. Number concentration of particles in size range 0.5-1.0 μm (1/cm^3) (NC2B)

	Amsterdam	Erfurt	Helsinki	Total
N	210	177	176	563
N missing	27	0	6	33
Mean (sd)	4.7 (6.6)	22.2 (31.5)	9.5 (4.7)	11.7 (19.7)
Min - Max	0.2 - 42.7	0.7 - 174.7	1.9 - 28.3	0.2 - 174.7
Median	2.3	9.0	8.7	6.1
25%-75%	1.3 - 4.6	4.2 - 25.3	6.0 - 11.6	2.7 - 12.1

11. Mass concentration* of particles in size range 0.01-0.1 μm (μg/m^3) (MC1)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean (sd)	1.8 (0.7)	0.5 (0.4)	0.7 (0.4)	1.0 (0.8)
Min - Max	0.4 - 4.5	0.1 - 2.8	0.2 - 2.3	0.1 - 4.5
Median	1.7	0.4	0.6	0.8
25%-75%	1.2 - 2.3	0.3 - 0.7	0.5 - 0.8	0.4 - 1.4

* In Helsinki volume concentration.

12. Mass concentration of particles in size range 0.1-1.0 μm (μg/m^3) (MC2)

	Amsterdam	Erfurt	Helsinki	Total
N	193	177	176	546
N missing	44	0	6	50
Mean (sd)	14.3 (9.3)	21.1 (18.4)	5.9 (2.8)	13.8 (13.4)
Min - Max	2.3 - 63.0	2.6 - 88.6	1.4 - 16.5	1.4 - 88.6
Median	12.0	14.6	5.2	9.5
25%-75%	7.0 - 18.4	9.2 - 27.3	3.9 - 7.5	5.6 - 17.1

13. Mass concentration of particles in size range 1.0-2.5 μm (μg/m^3) (MC3)

	Amsterdam	Erfurt	Helsinki	Total
N	209	177	176	562
N missing	28	0	6	34
Mean (sd)	1.0 (1.0)	1.2 (1.8)	4.3 (2.1)	2.1 (2.2)
Min - Max	0.04 - 7..0	0.1 - 14.4	1.0 - 13.3	0.04 - 14.4
Median	0.7	0.8	3.7	1.3
25%-75%	0.3 - 1.6	0.5 - 1.3	3.0 - 5.2	0.5 - 3.1

14. Total mass concentration of particles in size range 0.01-2.5 μm (μg/m^3) (TMC)

	Amsterdam	Erfurt	Helsinki	Total
N	193	177	176	546
N missing	44	0	6	50
Mean (sd)	17.1 (10.0)	22.9 (19.8)	10.9 (4.9)	16.7 (13.9)
Min - Max	3.2 - 68.0	2.9 - 98.7	2.6 - 28.7	2.6 - 98.7
Median	15.3	15.7	9.6	12.8
25%-75%	9.6 - 22.1	10.7 - 29.4	7.5 – 13.2	8.6 - 20.3

15. Mass concentration of particles in size range 0.01-0.03 μm (μg/m^3) (MC1A)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean	0.075	0.050	0.042	0.057
Sd	0.028	0.029	0.023	0.031
Min	0.023	0.009	0.005	0.005
Max	0.168	0.219	0.125	0.219
Median	0.075	0.043	0.038	0.050
25%	0.052	0.028	0.026	0.033
75%	0.093	0.066	0.052	0.078

16. Mass concentration of particles in size range 0.03-0.1 μm (μg/m^3) (MC1B)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean (sd)	1.7 (0.7)	0.5 (0.4)	0.6 (0.4)	1.0 (0.8)
Min - Max	0.4 - 4.4	0.1 - 2.6	0.1 - 2.2	0.1 - 4.4
Median	1.6	0.4	0.6	0.7
25%-75%	1.2 - 2.2	0.2 - 0.6	0.4 - 0.8	0.4 - 1.4

17. Mass concentration of particles in size range 0.1-0.5 μm (μg/m^3) (MC2A)

	Amsterdam	Erfurt	Helsinki	Total
N	202	177	176	555
N missing	35	0	6	41
Mean (sd)	12.9 (8.0)	17.1 (13.7)	4.5 (2.2)	11.6 (10.6)
Min - Max	2.0 - 53.6	2.4 - 75.6	1.1 - 13.4	1.1 - 75.6
Median	11.2	12.7	4.0	8.1
25%-75%	6.6 - 17.4	8.1 - 22.3	3.0 - 5.7	4.5 - 15.4

18. Mass concentration of particles in size range 0.5-1.0 μm (μg/m^3) (MC2B)

	Amsterdam	Erfurt	Helsinki	Total
N	210	177	176	563
N missing	27	0	6	33
Mean (sd)	1.2 (1.5)	4.0 (6.0)	1.4 (0.7)	2.1 (3.7)
Min – Max	0.1 - 9.2	0.2 - 38.3	0.3 - 4.4	0.1 - 38.3
Median	0.7	1.7	1.3	1.2
25%-75%	0.3 - 1.3	0.9 - 4.3	0.9 - 1.8	0.6 - 2.1

19. Mass of particles less than 10 µm in diameter (µg/m^3) (PM10)

	Amsterdam	Erfurt	Helsinki	Total
N	208	155	182	545
N missing	29	22	0	51
Mean (sd)	36.2 (16.6)	27.1 (20.2)	19.5 (9.6)	28.0 (17.3)
Min - Max	13.6 - 112.0	5.2 – 104.2	6.4 - 67.4	5.2 - 112.0
Median	31.9	20.0	17.5	24.2
25%-75%	25.7 - 41.9	13.0 – 32.7	12.4 - 23.8	15.8 - 34.1

20. Mass of particles less than 2.5 µm in diameter (µg/m^3) (PM25)

	Amsterdam	Erfurt	Helsinki	Total
N	228	161	181	570
N missing	9	16	1	26
Mean (sd)	20.0 (13.3)	23.1 (18.9)	12.7 (6.7)	18.5 (14.2)
Min - Max	3.8 - 82.2	4.5 – 118.1	3.1 - 39.8	3.1 - 118.1
Median	16.9	16.3	10.6	14.1
25%-75%	10.4 - 23.9	10.5 – 27.4	8.1 - 16.0	9.6 - 22.6

21. Coarse particulate matter (2.5-10 µm) (PMC)

	Amsterdam	Erfurt	Helsinki	Total
N	199	154	181	534
N missing	38	23	1	62
Mean (sd)	15.3 (8.1)	3.7 (6.2)	6.7 (5.9)	9.0 (8.5)
Min - Max	-16.3 – 45.3	-28.7 - 51.3	-0.2 – 37.0	-28.7 - 51.3
Median	14.9	2.9	4.8	6.7
25%-75%	10.1 – 19.4	0.6 - 5.8	3.0 – 8.5	3.0 - 13.7

22. Absorption coefficient for PM2.5 filter (*10^{-6}) (PM25BS)

	Amsterdam	Erfurt	Helsinki	Total
N	229	160	168	557
N missing	8	17	14	39
Mean (sd)	17 (9)	25 (15)	20 (8)	20 (11)
Min - Max	3 – 55	5 - 78	5 - 49	3 - 78
Median	15	20	19	18
25% - 75%	10 – 23	13 - 34	14 - 25	12 - 26

23. Carbon monoxide (mg/m^3) (CO)

	Amsterdam	Erfurt	Helsinki	Total
N	237	176	173	586
N missing	0	1	9	10
Mean (sd)	0.6 (0.2)	0.4 (0.4)	0.4 (0.2)	0.5 (0.3)
Min – Max	0.4 - 1.6	0.1 - 2.5	0.1 - 1.0	0.1 - 2.5
Median	0.6	0.3	0.4	0.5
25%-75%	0.5 - 0.7	0.2 - 0.5	0.3 - 0.6	0.3 - 0.6

24. Nitrogen monoxide (μg/m^3) (NO)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N missing	0	0	0	0
Mean (sd)	25.0 (33.4)	19.3 (31.5)	20.4 (20.8)	21.9 (29.6)
Min – Max	0 - 208.2	0.2 - 264.6	2.3 - 172.7	0 - 264.6
Median	11.9	7.2	14.0	12.0
25%-75%	5.8 - 28.9	2.8 - 22.4	8.8 - 23.0	5.5 - 25.5

25. Nitrogen dioxide (μg/m^3) (NO2)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N missing	0	0	0	0
Mean (sd)	42.7 (15.8)	28.9 (14.4)	31.1 (11.9)	35.0 (15.6)
Min - Max	8.5 - 93.5	6.7 - 81.7	10.7 - 67.5	6.7 - 93.5
Median	42.5	26.5	29.7	32.4
25%-75%	30.8 - 53.9	18.5 - 36.8	22.8 - 35.5	23.4 - 44.5

26. Ozone (μg/m^3) (O3)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N missing	0	0	0	0
Mean (sd)	31.1 (20.4)	32.1 (18.2)	38.2 (19.7)	33.5 (19.8)
Min - Max	1.4 - 85.5	0 - 67.9	5.7 - 94.3	0 - 94.2
Median	28.5	31.5	36.3	31.8
25%-75%	13.3 - 45.8	18.1 - 46.5	22.9 - 54.2	17.4 - 47.6

27. Sulphur dioxide (μg/m^3) (SO2)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	180	594
N missing	0	0	2	2
Mean (sd)	6.7 (4.5)	5.6 (5.8)	5.8 (4.5)	6.1 (5.0)
Min – Max	0.2 - 32.8	0.5 - 46.7	0.2 - 35.0	0.2 - 46.7
Median	5.5	3.8	4.6	4.7
25%-75%	3.5 - 8.8	2.7 - 6.0	2.8 - 7.5	3.0 - 8.1

28. Mean temperature (^{o}C) (TEMP)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N missing	0	0	0	0
Mean (sd)	7.8 (4.9)	3.7 (4.8)	-1.7 (6.4)	3.7 (6.7)
Min - Max	-4.0 - 20.1	-7.8 - 13.6	-24.3 - 11.5	-24.3 - 20.1
Median	7.5	4.4	-0.4	4.2
25%-75%	4.6 - 11.6	0.8 - 6.7	-4.6 - 2.2	-0.2 - 7.9

29. Relative humidity (%) (RH)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N missing	0	0	0	0
Mean (sd)	86 (8.6)	86 (6.6)	86 (9.0)	86 (8.2)
Min – Max	48 - 100	64 - 99	51 - 98	48 - 100
Median	87	86	88	87
25%-75%	81 - 92	82 - 90	82 - 92	81 - 91

30. Ambient air pressure (mbar) (AP)

	Amsterdam	Erfurt	Helsinki	Total
N	237	176	181	594
N missing	0	1	1	2
Mean (sd)	1014 (10)	1016 (10)	1012 (14)	1014 (12)
Min – Max	988 - 1041	992 – 1040	961 - 1040	961 - 1041
Median	1014	1016	1011	1014
25%-75%	1008 - 1021	1008 – 1023	1001 - 1022	1006 - 1022

31. Wind speed (m/s) (WS)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	181	595
N missing	0	0	1	1
Mean (sd)	5.4 (2.5)	1.6 (0.9)	4.3 (1.8)	3.9 (2.5)
Min – Max	1.4 - 15.7	0.4 - 5.1	0.3 - 10.9	0.3 - 15.7
Median	5.1	1.4	3.9	3.5
25%-75%	3.3 - 6.6	0.9 - 2.1	3.1 - 5.2	1.9 - 5.3

32. Daily pollen counts (sum of all species) (POLLEN)

	Amsterdam	Erfurt	Helsinki	Total
N	237	177	182	596
N of days with pollen	195	44	30	269
Mean (sd)	51 (88)	5 (16)	69 (445)	42 (253)
Min – Max	0 – 566	0 - 140	0 – 4952	0 - 4952
Median	13	0	0	0
25%-75%	2 – 52	0 - 0	0 – 0	0 - 13

Spearman correlations of air pollutants and meteorological factors (24-hour averages). All correlations statistically significant (p-value<.05) except those marked with *.

		PM10	PM25	PM25BS	NC1	NC2	CPCTNC	NO	NO2	CO
PM25	AMS	.78								
	ERF	.95								
	HEL	.76								
PM25BS	AMS	.61	.73							
	ERF	.88	.82							
	HEL	.51	.71							
NC1	AMS	-.06*	-.15	.28						
	ERF	.65	.62	.77						
	HEL	.07*	.14*	.54						
NC2	AMS	.71	.80	.80	.16					
	ERF	.83	.84	.87	.67					
	HEL	.65	.80	.86	.53					
CPCTNC	AMS	-.09*	-.18	.27	.95	.08*				
	ERF	.64	.61	.79	.97	.70				
	HEL	.05*	.09*	.53	.98	.49				
NO	AMS	.36	.48	.83	.44	.59	.44			
	ERF	.74	.68	.93	.80	.80	.82			
	HEL	.03*	.11*	.58	.83	.50	.86			
NO2	AMS	.39	.49	.82	.49	.67	.48	.91		
	ERF	.84	.82	.87	.82	.82	.80	.87		
	HEL	.31	.35	.69	.72	.72	.74	.73		
CO	AMS	.42	.58	.83	.22	.60	.25	.80	.76	
	ERF	.76	.77	.81	.72	.78	.72	.77	.86	
	HEL	.22	.40	.55	.35	.51	.35	.54	.32	
SO2	AMS	.52	.48	.63	.48	.67	.50	.63	.72	.50
	ERF	.63	.69	.63	.56	.57	.58	.56	.63	.68
	HEL	.27	.44	.46	.49	.49	.46	.33	.41	.19
O3	AMS	-.43	-.58	-.79	-.24	-.59	-.22	-.86	-.82	-.76
	ERF	-.68	-.67	-.85	-.65	-.75	-.66	-.87	-.80	-.76
	HEL	.13*	-.06*	-.41	-.56	-.31	-.57	-.74	-.33	-.60
TEMP	AMS	.07*	-.14	-.37	-.18	-.10*	-.28	-.57	-.49	-.59
	ERF	-.33	-.44	-.22	-.34	-.36	-.37	-.15	-.42	-.62
	HEL	.16	-.07*	-.25	-.55	-.17	-.55	-.42	-.29	-.08*
RH	AMS	.10*	.27	.34	.18	.22	.13*	.50	.45	.46
	ERF	.20	.24	.33	.19	.24	.24	.37	.35	.47
	HEL	-.30	-.03*	-.12*	-.24	-.09*	-.21	.05*	-.17	.14*
AP	AMS	.38	.34	.32	-.06*	.35	-.08*	.16	.12*	.28
	ERF	.61	.59	.58	.42	.54	.42	.47	.58	.56
	HEL	.17	.23	.17	.08*	.25	.03*	-.01*	.15	.07*

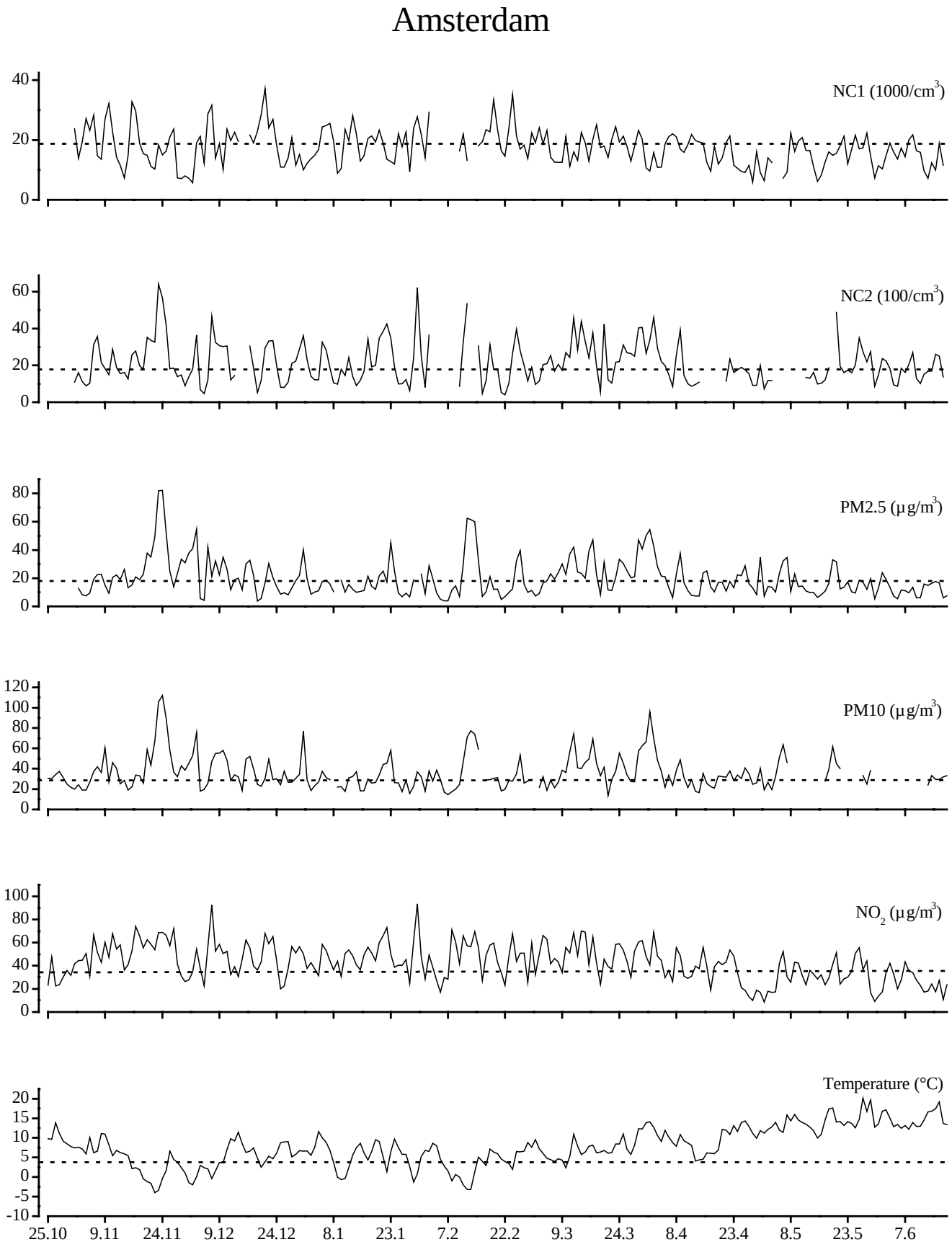

Figure 1. Levels of air pollutants and temperature in Amsterdam. Horizontal line is the average over all centers and over the whole study periods. NC1 = number concentration of particles in size range 0.01-0.1 µm; NC2 = number concentration of particles in size range 0.1-1.0 µm; PM2.5 = mass of particles less than 2.5 µm in diameter; PM10 = mass of particles less than 10 µm in diameter; NO_2 = nitrogen dioxide.

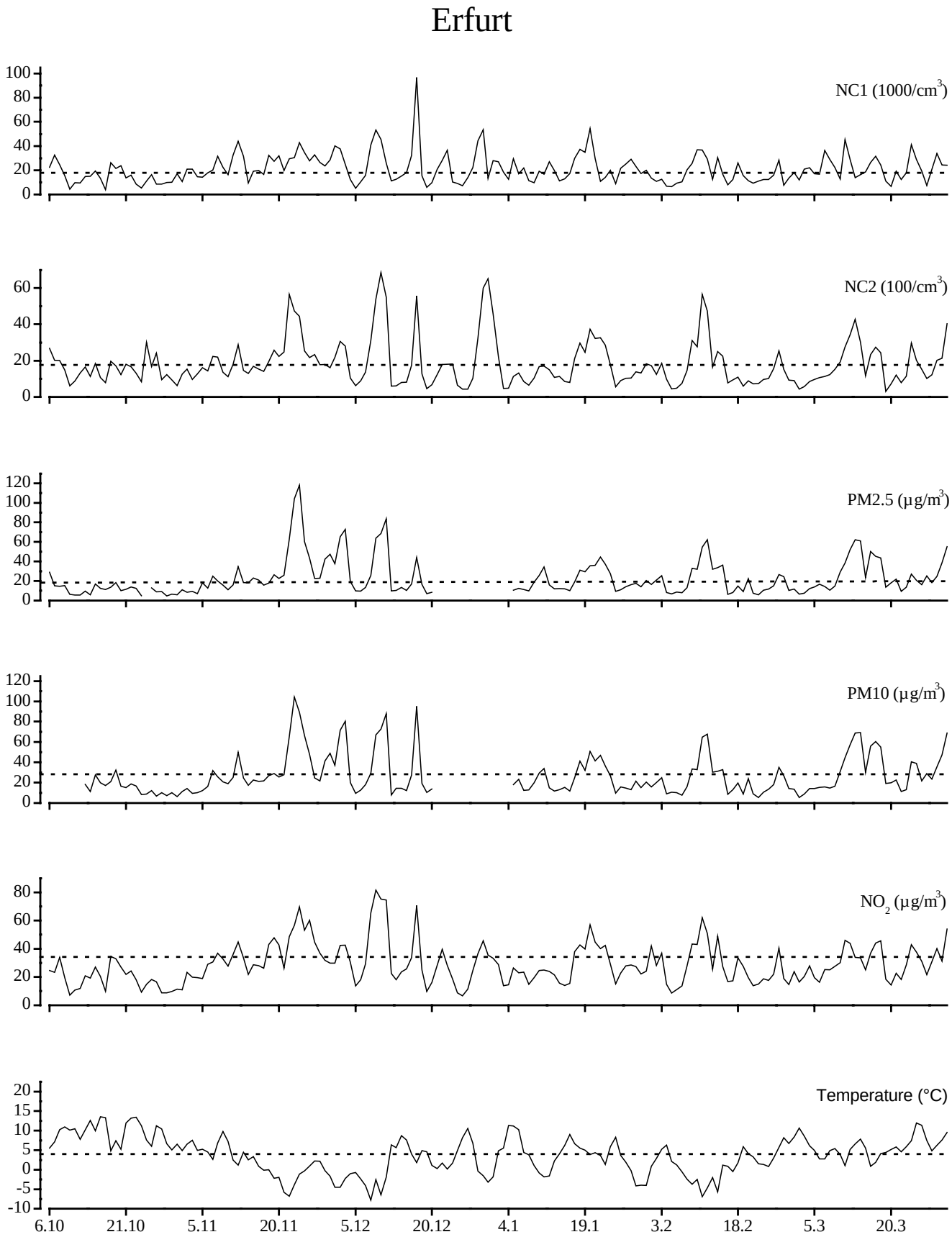

Figure 2. Levels of air pollutants and temperature in Erfurt. See figure 1 for legends.

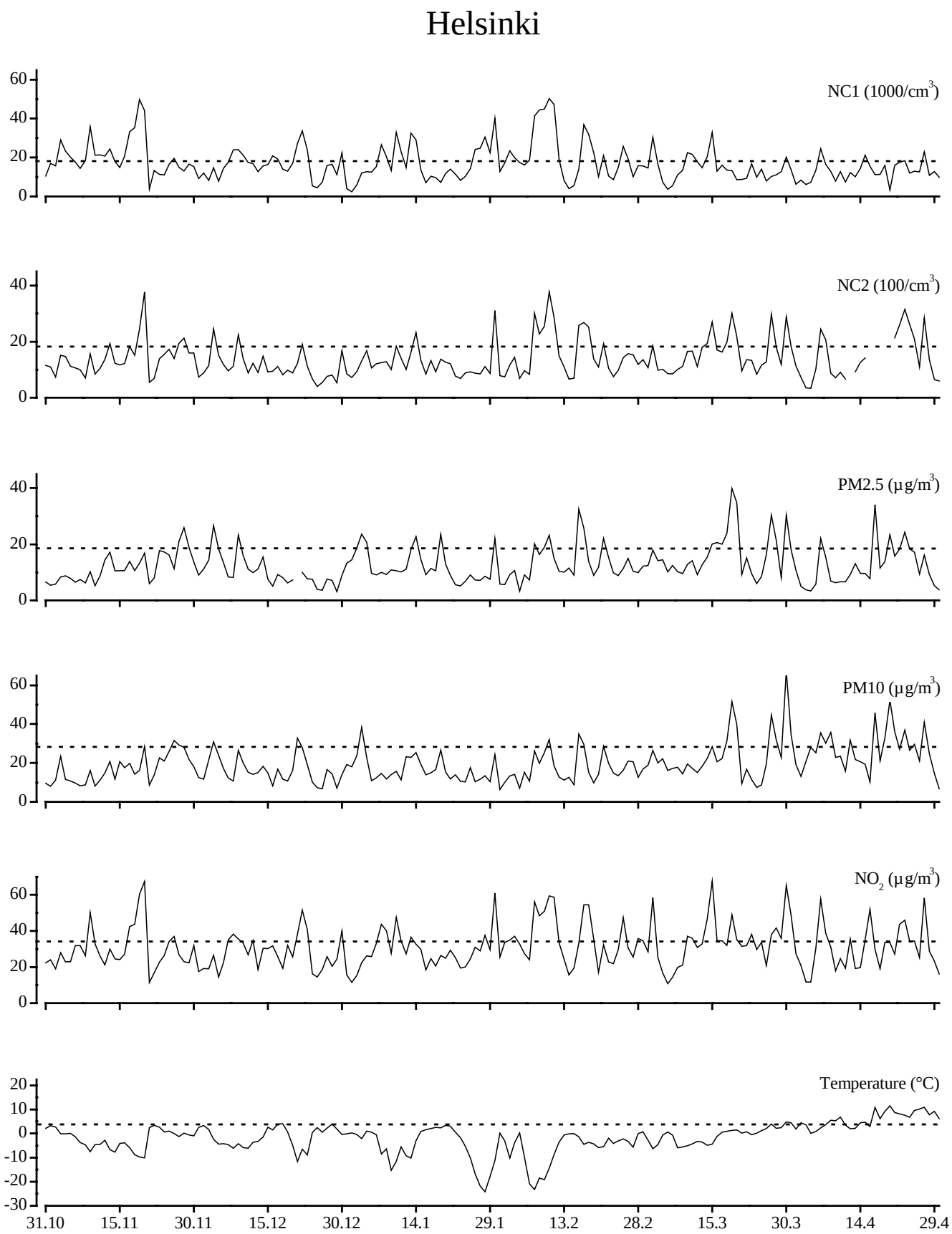

Figure 3. Levels of air pollutants and temperature in Helsinki. See figure 1 for legends.

4 APPENDICES

Can be found as separate links on the web site