Long-term exposure to air pollution and cardiovascular mortality: an analysis of 22 European cohorts within the ESCAPE project

eAppendix

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eAppendix 1: Description of each cohort and study area

Figure 1 shows the location of all cohorts. Below are brief descriptions of each cohort and study area.

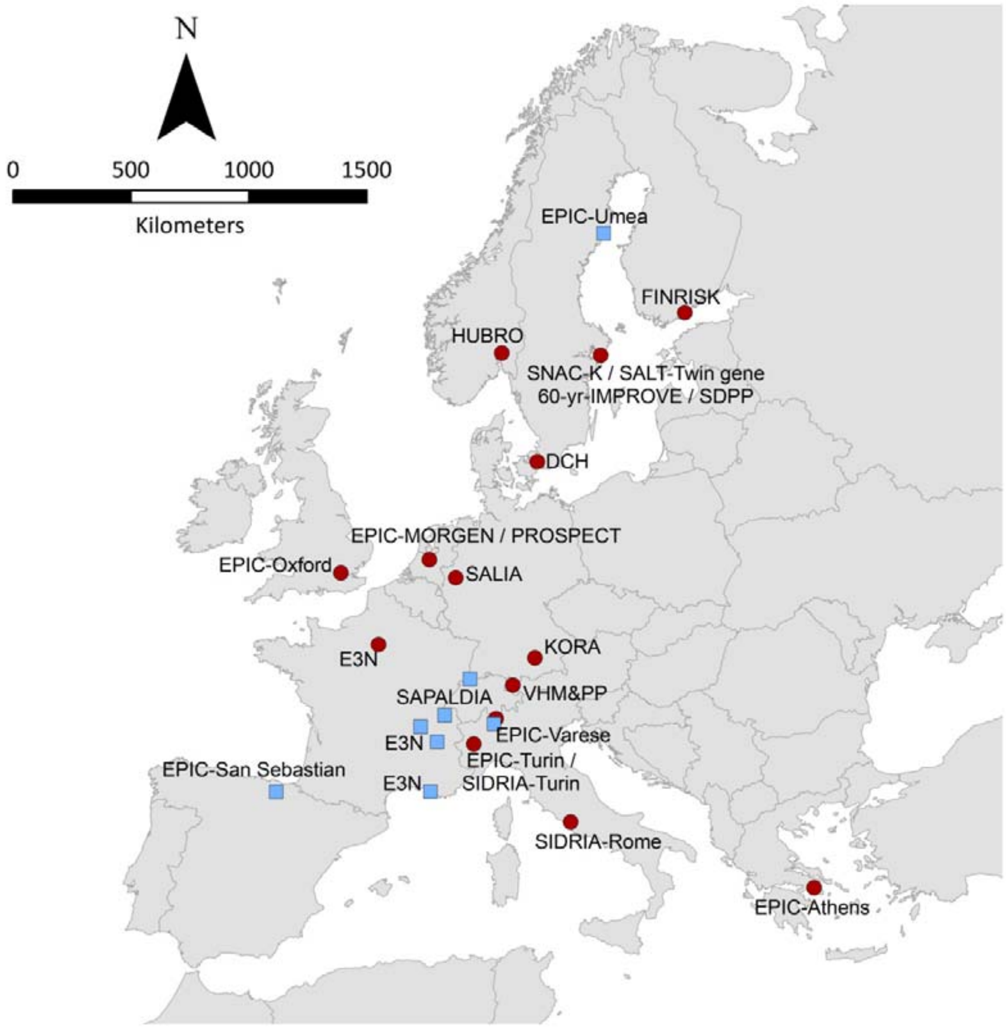

Figure 1: Cohort locations. Dark circles mark the cohort areas in which both PM and nitrogen oxides were measured. Blue squares indicate cohort areas where NO_2 and NO_x were measured.

The National FINRISK Study *(FINRISK)*, Finland

FINRISK surveys have been conducted every five years since 1972 to monitor the risk factor trends of chronic diseases, including cardiovascular diseases, diabetes, cancer, asthma, and allergy. For each survey, a stratified random sample has been selected from the 25-64 (74 since 1997) year old inhabitants in different regions of Finland. The ESCAPE study used FINRISK data from four surveys (1992, 1997, 2002, and 2007) and two study regions (the cities of Helsinki and Vantaa, and Turku city with its nearby municipalities). The FINRISK study protocol has been described elsewhere.[1]
The surveys included a self-administered questionnaire (the questions focus mainly on socioeconomic factors, medical history, health behaviour, and psychosocial factors) and a clinical examination including measurements of height, weight and blood pressure and blood sampling. The participants have been annually followed up through 31 December, 2008 (up to 16 years) for fatal and nonfatal coronary and stroke events, and total mortality. The National Hospital Discharge Register and the National Causes of Death Register were used to identify these events. These registers cover every hospitalization in Finland and every death of permanent residents in Finland, yielding in practice 100% coverage of the follow-up events.[2,3] In addition, we used the drug reimbursement records from the Social Insurance Institution of Finland to identify subjects who had developed diabetes or hypertension during the follow-up period.

The population-based Oslo Health Study (HUBRO), Norway

HUBRO was designed to identify health needs and the priorities of the health sector within Oslo, to monitor the developments and trends of diseases and their associated risks, to estimate the prevalence and later the incidence of chronic diseases, to investigate the social and geographical differences in health and associated risk factors and to initiate research to further investigate the aetiology of major health problems.[4] HUBRO was carried out in the city of Oslo from May 2000 to September 2001. All men and women born in the following years: 1924, 1925, 1940, 1941, 1954, 1955, 1960, 1969, and 1970, who resided in Oslo on December 31, 1999, were invited to participate. 58,178 subjects were invited and 22,699 individuals (39%) participated in the study. The questionnaires covered the following topics: health and chronic diseases, family history of disease, risk factors and lifestyles, social network, education, occupation, use of health services, and use of medicine. A physical exam was performed to obtain data on blood pressure, pulse recording, and collection of venous non-fasting blood samples. HUBRO was linked to the Norwegian Cause of Death Registry including deaths up to December 31, 2010, and was also linked to the Cancer Registry of Norway including cancers up to December 31, 2009.

SNAC-K, The Swedish National study of Aging and Care in Kungsholmen (SNAC-K), Sweden

SNAC-K is an ongoing longitudinal study aiming to investigate the ageing process and identify possible preventive strategies to improve health and care in elderly adults.[5] The study population consists of randomly sampled individuals >=60 years old and in a central area of Stockholm (Kungsholmen) between March 2001 and June 2004. The sample was stratified for age and year of assessment giving sub-cohorts with 60, 66, 72, 78, 81, 84, 87, 90, 93, 96, and 99+ year olds. Information was collected through social interviews, assessment of physical functioning, clinical examination (incl. geriatric, neurological and physical assessments) as well as cognitive assessment. At baseline, information regarding events prior to the study period was gathered. The follow-up interval is six years for the younger age cohorts, and three years for the older age cohorts (81+). During the follow-up intervals, medical events of all subjects are registered through linkage with primary care registry and hospital discharge registry (available for all subjects in Sweden). In case of death, hospital and cause of death registries provide the clinical information, and informant interviews are carried out. The same protocol as for the baseline data collection is used during the follow-up, though only concerning the follow-up period. Website of study: http://www.aldrecentrum.se/snack/index.htm. Any outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register and the national patient register) have been used.

Stockholm Screening Across the Lifespan Twin study (SALT) & Twin GENE (subcohort), Sweden

The SALT study was set-up to screen all twins born in Sweden before 1958 for the most common complex diseases with a focus on cardiovascular diseases.[6,7] Twin Gene is a sub-study involving establishing a biobank with DNA and serum from SALT participants. SALT is a telephone interview, which took place between 1998-2002. For the purposes of this study, only twins living in Stockholm County are included in the analyses. Information concerning birth order and weight, zygosity, contact with twin partner and family constellation, diseases, use of medication, occupation, education, life style habits, gender- and age-specific (hormone replacement therapy) and memory problems (age > 65) was collected. In Twin Gene, twins born before 1958 were contacted 2004-2008, a total number of ~2500 participants was available. Health and medication data were collected from questionnaires. Blood sampling material was mailed to study subjects, who contacted a local health care centre for blood sampling and a health check-up. Height, weight, circumference of waist and hip, and blood pressure was measured and blood was collected. Any outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register and the national patient register) have been used.

Stockholm 60 year olds & IMPROVE, Sweden

The 60 year olds cohort is a study aiming to identify biological and socio-economic risk factors and predictors for cardiovascular diseases.[8] Recruitment took place between August 1997 and March 1999. A random sample of every third man and woman living in Stockholm County, who was born between 1 July 1937 and 30 June 1938, was invited to the 60 year olds study. In total ~4100 subjects were included. Height, weight, BMI, Waist/Hip ratio and resting ECD, blood pressure and fasting blood samples were taken during a physical examination, while a comprehensive questionnaire was completed, including information on socioeconomic, medical and life-style factors. The study was supplemented 2003 by the IMPROVE project (an ongoing multi cohort study into genetics and CVDs). In Stockholm, IMPROVE is a sub-cohort consisting of ~500 participants from the 60 year olds cohort with inclusion criteria of having at least three risk factors for the metabolic syndrome. For IMPROVE, three follow-ups were conducted, blood and urine were collected, socio-economic data, quantitative B-mode ultra sound examination of carotid arteries and replicate B-mode ultrasound was performed, and vascular events were recorded. Any outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register and the national patient register) have been used.

Stockholm SDPP, - Stockholm diabetes preventive programme (SDPP), Sweden

The Stockholm diabetes prevention programme, a population-based prospective study, aimed at investigating the aetiology of type 2 diabetes and developing prevention strategies for type 2 diabetes.[9] An initial survey included all men and women in the targeted age group in Stockholm County; for men in four municipalities (Värmdö, Upplands Bro, Tyresö and Sigtuna), and for women these four plus a fifth municipality (Upplands Väsby). All were screened by a questionnaire regarding presence of own diabetes and diabetes in relatives. Subjects with family history of diabetes (FHD) and randomly selected subjects without FHD, all without previously diagnosed diabetes, were invited to a health examination. This baseline study, 1992-1994 for men and 1996-1998 for women, comprised 7949 subjects, aged 35-56 years, and about 50% had FHD. In the follow-up study 8-10 years later, 2383 men (2002-2004) and 3329 women (2004-2006) participated. At the health examinations, both at baseline and follow-up, an extensive questionnaire (information on lifestyle factors, such as physical activity, dietary habits, tobacco use, alcohol consumption, health status, socioeconomic status and psychosocial conditions) was completed. Diabetes heredity was confirmed and measurements of weight, height, hip and waist circumference as well as blood pressure were performed. In addition, an oral glucose tolerance test (OGTT) was made, and blood was sampled at fasting state and 2 hour after glucose intake. Outcomes based on the Swedish nationwide health registries (such as the myocardial infarction and stroke registries, the cause-of-death register, and the national patient register) have been used.

Danish Diet Cancer and Health study (DCH), Denmark

The primary aim of the DCH study is to investigate diet and lifestyle in relation to incidence of cancer and other chronic diseases.[10] The study combines the collection of questionnaire data with storing of biological specimen in order to investigate genetic susceptibility and gene-environment interactions with regard to diet, dietary compounds, and the risk of cancer, and indeogenous markers of nutritional, metabolic, and hormonal characteristics of study participants. Historical residential history of the study participants is available, which facilitate studies of air pollution and noise. The study enrolled participants in two areas, Copenhagen and Aarhus, Denmark. 160,725 individuals aged 50-64 years were invited to participate between December 1993 and May 1997. All participants were Danish-born, living in the Copenhagen or Aarhus areas and without medical history of cancer diagnosis registered in the Danish Cancer Registry at the time of invitation. Out of the 160,725 people invited, which were a random sample of all eligible individuals in the specified areas, 57,053 were enrolled. Due to the geographical limitations of the land use regression, only the almost 40,000 participants from the Copenhagen area were included in the ESCAPE analyses. On enrolment, each participant completed self-administered questionnaires (in Danish) that included questions on dietary habits, health status, family history of cancer, social factors, reproductive factors, smoking, environmental smoking, and lifestyle habits. Anthropometric measurements including blood pressure and blood samples were also obtained. The DCH cohort is followed up regularly by use of complete nationwide registers hence the loss to follow-up is virtually nil. Data on cancer incidence from the Danish Cancer Registry and data on cause-specific mortality from the Danish Mortality Registry were used.

Study on the influence of Air pollution on Lung function, Inflammation and Aging (SALIA), Germany

The SALIA study was initiated in 1985 as part of Environmental Health surveys to monitor health effects of outdoor air pollution in the heavily polluted Ruhr Area.[11,12] It was an element of the Clean Air Plan initiated by the Government of North-Rhine Westphalia in Germany. The geographic regions covered were parts of Dortmund (1985, 1990), Duisburg (1990), Essen (1990), Gelsenkirchen (1986,1990) and Herne (1986). They were chosen to represent a range of polluted areas with high traffic load and steel and coal industries. Two non-industrial small towns, Dülmen (1985) and Borken (1985, 1986, 1987, 1990, 1993, 1994) were chosen as reference areas. The Research Institute for Environmental Medicine in Düsseldorf (then Medical Institute of Environmental Hygiene) coordinated the studies. The baseline investigations of SALIA were cross-sectional surveys. They were conducted on 4757 women in the local health departments in March and April between 1985 and 1994. Sampling included all women of German nationality aged 54 to 55 residing in the selected areas. Women were selected because men in these areas mainly worked in the mining industry with very high occupational exposure probably masking the effects of air pollution. Postal questionnaires were sent out and included information about airway diseases and covariates. The filled in questionnaires were checked at the day of investigation. Overall questionnaire response was 70%. Specific measurements (lung function, determination of immunological markers, and xenobiotics) were added in subgroups. All investigations were done according to standardized operating procedures.
Height and weight was measured at the day of investigation. These measurements are not available for more than 10% of all women. Therefore BMI was not included in the ESCAPE analysis, after having demonstrated that BMI did influence the results only marginally.
Follow-ups were set up to investigate the effects of outdoor air pollution and changes in pollution on respiratory health and mortality. In 1990, women investigated in 1984/1986 had a first follow-up investigation including a questionnaire and a lung function testing. A mortality follow-up of all women having participated in the baseline investigation was conducted in 2003 and in 2008 by the Institute of Epidemiology Helmholtz Munich. All surviving women were asked to participate in a questionnaire follow-up in 2006 and invited to eventually participate in a follow-up investigation. All women with lung-function available at baseline were invited to a more detailed follow-up investigation, which started in 2007.
The mortality analyses of ESCAPE use questionnaire data from the baseline investigation and the data from the mortality follow-ups. All these data were available to be included in the ESCAPE analysis.
All women with geocoded addresses at baseline were included in the analysis (4663). Two continuous covariates were used as year of recruitment, early (1985, 1986, and 1987) and late (1990, 1993, and 1994) years. Coding was year of recruitment – 1900, recruitment before 1990 was coded as 90 in the late variable, recruitment after 1990 was coded as 87 in the early variable. No dietary covariates were available, environmental tobacco smoke was a combined variable from home and work place, occupational exposure was extreme temperature and dust. Area SES was defined as income-rate per five-digit postcode-area.

The Cooperative Health Research in the Region of Augsburg (KORA), Germany

KORA is a cohort study based on four cross-sectional surveys of a random sample of inhabitants of the Augsburg region.[13] Main objectives of the baseline study were to investigate cardiovascular and other chronic diseases regarding: 1) to assess health indicators (morbidity, mortality) and health care (utilization, costs), 2) to quantify the prevalence of risk factors, and 3) to study the impact of lifestyle, metabolic and genetic factors. The follow-up studies aimed to assess also time-trends in risk factors and health over a period of seven to ten years. Two cross-sectional population-representative surveys were conducted in 1994-1995 (survey S3) and 1999-2001 (survey S4) in the city of Augsburg and two adjacent rural counties to include all inhabitants of the Augsburg region with German nationality aged 25 to 74 (n=400,000). Follow-up examinations of survey S3 and S4 participants were carried out seven to ten years later. Baseline examination included standardized interviews, physical examination, and blood sampling. All investigations were done according to standardized operating procedures.

Follow-up investigations were conducted in 2004-2005 for survey S3 and in 2006-2008 for survey S4. 2974 and 3080 of survey S3 and S4 participants attended the follow-up examinations including standardized computer-assisted interview, self-administered questionnaire, physical examination, and blood sampling. Survival was ascertained for S3 participants in 2008 through Population Registry search and is available from the time of recruitment until December 31 2007. Survival of S4 participants was ascertained through a combination of returned questionnaires and subsequent Population Registry search and is available from recruitment until December 31, 2008. Causes of death are abstracted for all deaths from the death certificates. For the ESCAPE analyses a study/baseline indicator was included instead of calendar time.

The Vorarlberg Health Monitoring and Prevention Program (VHM&PP), Austria

The VHM&PP study is a prevention program routinely performed by the Agency of Social and Preventive Medicine and covers all adults of the whole province.[14,15] It has been ongoing since 1985 and data are presently available until 2005. Recruitment and follow-up has been ongoing that means during the whole period new persons were recruited and already recruited persons came for follow-up visits. The total adult population of the state Vorarlberg is covered, with voluntary enrolment. Data are available from 1985 to 2005 at present on 185,330 persons, corresponding to about 65% participation. Their age at recruitment ranges from 18-97 years (mean=42). The screening examination takes place in the practice of the local physicians; a self-administered questionnaire is also applied. The same protocol was applied at baseline and follow-up examinations.
A total of 132,242 geocodes were assigned exposures. 30,718 geocodes (18.85%) were omitted if: 1) they were entirely outside of the Vorarlberg state, 2) within 300m of the state boundary (lack of GIS data in neighboring countries), and 3) if their elevation was > 600m.

Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), Switzerland

SAPALDIA is a multi-center study performed in eight geographic areas representing the range of environmental, meteorological, and socio-demographic conditions in Switzerland.[16] A random population sample across eight geographic areas (Aarau, Basel, Davos, Geneva, Lugano, Montana, Payerne, and Wald) was obtained in 1991, with follow-ups in 2002 and 2010. The main aim of the study was to assess the effect of air pollution (outdoor and indoor) on respiratory and cardiovascular health, with a special focus on how the respiratory and cardio-vascular systems interact in this regard, and on the role of lifestyle and genetic background. In 1991, 9651 subjects, aged 18 to 60 years, were recruited via detailed interviews and more than 90% provided valid spirometry results. The follow-up in 2002 obtained health information and anthropometric data from physical re-examination with spirometry and blood sampling, blood pressure measurement, and heart rate variability in a subsample (<50yrs). The most recent follow-up (SAPALDIA 3) was in 2010. In the third assessment, study subjects were also asked in detail about chronic diseases having been diagnosed and treated since the second survey. Questionnaire domains are the following: respiratory health and disease, cardiovascular health and disease, chronic disease and relevant risk factors, women's health, allergies, medications, drug use, exposure to air pollutants, sleep apnea, and health care resources used. SAPALDIA did not obtain information on physical activity, alcohol intake, and nutrition at baseline in 1991. Within ESCAPE, only the areas of Basel, Geneva, and Lugano were included, with PM measurements in Lugano only.

Italian Studies on Respiratory Disorders in Childhood and Environment (SIDRIA)

The SIDRIA study has been an extension of the ISAAC initiative in Italy (International Study on Asthma and Allergies in Childhood), a worldwide survey to analyse variations in prevalence of symptoms asthma, rhinitis, and atopic eczema.[17] A cross-sectional survey was carried out between October 1994 and March 1995 in eight centres in northern and central Italy using standardised questionnaires (response rate=94%). Parents of first and second graders from a representative sample of primary schools, and adolescents in the third year of a representative sample of junior high schools answered a self-administered questionnaire on the child's health status, as well as their personal respiratory health status and various risk factors, including education, occupation, housing conditions, smoking habits, and traffic intensity in their area of residence. The data used within ESCAPE are from the subset of parents recruited in two metropolitan areas: Rome and Turin, in the context of a project co-funded by the Ministry of Health (Programma Strategico Ambiente e Salute, Ricerca Finalizzata ex-art.12, 2006). A record linkage has been performed with the Municipal Registry Office Databases to collect the residential history of parents who were living in Rome and Turin with their children at the time of the survey. In the city of Turin the project was performed through a collaboration between SIDRIA and the regional Unit of

Epidemiology (ASL TO3), in the context of the Turin Longitudinal Study, a census-based cohort study following up health outcomes of people censused in Turin since 1971. It was possible to identify ~16,000 adults.

European Prospective Investigation into Cancer and Nutrition (EPIC)

The European Prospective Investigation into Cancer and Nutrition (EPIC), which covers a large cohort of half a million men and women from 23 European centers in 10 Western European countries, was designed to study the relationship between diet and the risk of chronic diseases, particularly cancer.[18] Eight of these centers were included in ESCAPE. The selection of ESCAPE participants was done centrally at Imperial College, UK using the central EPIC database.

EPIC-Umeå, Sweden

EPIC-Umeå is a collaborative effort between three health studies in NSHDS, the Västerbotten Intervention Program (VIP), the Northen Sweden MONICA project, and the Västerbotten Mammary Screening Program.[19] Since 1985 all individuals 40, 50 and 60 years of age (with subsets at age of 30 and 70) in the population of the county have been invited for screening within the VIP cohort. They were asked to answer questions about general health, psychosocial factors, physical activity, use of tobacco, and nutritional intake (including five questions about alcohol). At screening, blood pressure, blood lipids, BMI, a glucose intolerance test, and, in recent years, also a measurement of the waist circumference is registered. Follow-up was aimed at identifying new cancer cases; deaths is based on national and local cancer registries. A subsample recruited 1992 – 1996 was included in the ESCAPE project.

EPIC- Monitoring Project on Risk Factors and chronic diseases in the Netherlands (MORGEN), The Netherlands

The MORGEN cohort consists of a general population sample of 10,260 men and 12,394 women aged 20–59 years from three Dutch towns (Amsterdam, Doetinchem and Maastricht).[20] From 1993 to 1997 each year a new random sample, consisting of 6000 subjects, was examined. A total of 50,766 persons were invited to participate in the MORGEN cohort. Those who replied received two questionnaires by mail (a general questionnaire on socio-demographic factors, lifestyle and health indicators, and an FFQ and were invited to visit the local Public Health Service for a medical examination). The EPIC-MORGEN cohort and the EPIC-PROSPECT cohort have been joined to form the EPIC-NL cohort. All members of the EPIC-NL cohort are followed for changes in vital status and the occurrence of diseases by linkage with several registries, including the Municipality registry for vital status, the Dutch National Cancer registry for occurrence of cancer, the Central Bureau of Statistics registry for causes of death, and a National Hospital Discharge Diagnosis registry for occurrence of cardiovascular diseases or type 2 diabetes. Changes in some exposure status are assessed by questionnaires during follow-up. Part of the MORGEN cohort (Doetinchem participants) is re-invited every five years for a physical examination in addition to questionnaire information. The MORGEN cohort of EPIC-NL is linked to the Dutch Cancer Registry because participants are residing in several geographical areas covered by different regional integral cancer centres.

EPIC-Prospect, the Netherlands

A total of ~17,500 healthy women, living in Utrecht and surroundings, were enrolled.[21] Women were recruited from breast cancer screening participants, age 50-70 years at enrolment. The purpose of the EPIC-PROSPECT study is to assess the relation between nutrition and cancer and other chronic diseases. Baseline information was collected between 1993-1997 on the basis of two self-administered questionnaires and a medical examination. The general questionnaire contains questions on demographic characteristics, presence of chronic diseases of interest, and risk factors for chronic diseases of interest, i.e. blood pressure, serum cholesterol, reproductive history of women, family history, smoking habits, drinking of alcohol, and physical activity. Dietary intake was assessed using detailed food frequency questionnaires. A medical examination was performed including measurement of blood pressure, anthropometric measurements and taking of blood. All EPIC-PROSPECT participants are followed-up by questionnaire at 3-5 year intervals. The questionnaire collects information on changes in lifestyle habits as well as on health status. All incident and prevalent cancer cases were identified through linkage to the regional cancer registry, IKMN (Integraal Kankercentrum Midden Nederland), then from the National Cancer Registry from 2008 onwards. Vital status and cause-specific mortality information is obtained through linkage to the municipality registries and Central Buro of Statistics.

European Prospective Investigation into Cancer and Nutrition (EPIC) –Oxford, UK

The Oxford cohort was recruited from the nationwide general population in urban and rural areas throughout the United Kingdom, although a large percentage comes from Southern parts of England and big cities such as London.[22] The cohort contains 65,429 men and women over 20 years of age recruited through medical general practices or by post between 1993 and 1999, with an emphasis on vegetarians. The questionnaires gathered information on diet (FFQ and 24hr recall), social and demographic factors, lifestyle, anthropometrics, medical history of diseases, and prevalent cancers; approximately 20,000 gave a blood sample. Participants who consented were followed-up from recuitment by "flagging" on the NHS Central Registers (NHSCRs) in England and Wales (via the Office for National Statistics), Scotland (via the General Registry Office) and Northern Ireland (via the Northern Ireland Cancer Registry) via automatic notifications. The date of each event and coding of the cancer site or type and the causes of death were recorded according to the 10th revision of the International Classification of Diseases (ICD-10). For incident cancers, tumour morphology is also coded, according to WHO ICD-O. EPIC-Oxford website: http://www.epic-oxford.org. The study population was restricted to ~45,650 participants living within 400Km threshold of ESCAPE monitoring sites.

EPIC- Italy

Two centers in the EPIC-Italy participated in the ESCAPE project: Varese and the city of Turin.[23]

EPIC -Turin: Recruitment took place from 1993 and involved blood donors and other healthy volunteers, accruing 10,604 participants by 1998.[24] Co-operation with the local cancer registry and the local health authority allows for access to hospital discharge information and all newly diagnosed cancer cases. Follow-up started in 1998, including collaboration with the local cancer registry, the demographic computerized archives of the Torino area and the discharge report database for hospital patients.

EPIC –Varese: Recruitment was carried out at two hospital centres in Varese province and took place between 1993 and 1997. 12,083 volunteers were recruited through general practitioners' records, factories, and schools or through letters sent at home. A blood sample was provided by each participant. Follow-up started in 1998, including collaboration with the local cancer registry, the regional population database of the National Health Service, the mortality database of Varese province, and the discharge report database for hospital patients. Participants came from the cities of Varese and Milano, and rural areas of Sesto Calende and Busto Arsizio. A total of 568 geocodes were omitted because they were: 1) within 1000m of the W or NE boundaries of the province where land use data were not available, and 2) located at elevation >459m.

EPIC- San Sebastian, Spain

EPIC-San Sebastian recruited 8417 persons (4158 men and 4259 women) between 1992 and 1996, with the age range of 35 and 65 years.[25] The participants are healthy volunteers (mainly blood donors), who had received a letter of invitation and agreed to participate. Face to face interviews collected baseline information on dietary intake, anthropometric measurements, lifestyles (tobacco smoking, physical activity, level of education, medical history eg heart attack, diabetes, cancer, hypertension, etc), and family history of cancer. A blood sample was also taken. Follow-up was through computerized follow-up questionnaire, via two phases: firstly by phone interviews between 1996 and 1999; and secondly in 2003, via emails. Follow-up for identification of cancer cases is done every two years, based on a computerized record-linkage programme with population cancer registries of Basque Country; other sources of information including hospital discharge data and pathology reports. The main source of mortality data is the National Mortality Registry from the National Institute of Statistics (INE), while other regional sources, as well as letters to the members of the Spanish cohort, are being sent each year in some centres to update the vital status.

EPIC-Greece

Recruitment of volunteers in EPIC-Greece started in 1994, and was completed in 1999.[18] In total, 16,619 women and 11,953 men were recruited from Greece nationwide. Data collection on medical and reproductive history, socio-demographic and lifestyle factors and habitual diet was performed via interview and a baseline examination that recorded measurement of anthropometric data and collection of blood samples. The follow-up of study participants was initiated in January 1997 and focused on the update of information on lifestyle factors and the health status. Due to the lack of a national cancer registry and the country-wide nature of EPIC-Greece, information is being collected through self-administered questionnaires or telephone interviews. Reported diagnoses of interest were further ascertained through consultation of medical files in hospitals and clinics all over Greece, or through the collection of death certificates from the regional death registries, in case of death. Participants that contribute to the ESCAPE analyses are residents from the Prefecture of Attica (which comprises mainly the Greater Athens Area, and hence called EPIC-Athens in the manuscript). Based on GIS availability, we included only the members if the EPIC cohort who were residents of 16 municipalities, specifically Athens, Agios Ioannis Rentis, Amaroussion, Egaleo, Galatsi, Halandri, Ilioupolis, Kalithea, Moschato, Nea Ionia, Nea Smyrni, Nikaia, Peristeri, Pireaus, Tavros, and Zografou.

Etude Epidémiologique auprès de femmes de la Mutuelle Générale de l'Education Nationale (E3N), France

E3N is a large ongoing prospective cohort consisting of 98,995 French women born between 1925 and 1950, subscribing to the health insurance plan for public education system employees, and who voluntarily enrolled in 1990-1991.[26] The main objective of the study was to investigate the risk factors for breast cancer among women in particular hormonal factors and diet. This study began in 1990 when a baseline questionnaire (Q1) was sent to the 103,089 out of the 494,458 women subscribed to the health insurance plan for public education system employees women aged 40–65 years who agreed to participate. Follow up questionnaires were sent in January 1992 (Q2) and then approximately every two years thereafter. The most recent update questionnaires was sent in June 2008 (Q9) and another one in 2010. The base population covers the whole country of France and participation was based on voluntary agreement. To date, participants have been followed for 18 years (from 1991 to 2008) with complete data available from 2005. All the questionnaires are self-administered and are sent by mail to participants in French language and returned to the study centre at IGR, Paris. Biological material was collected in 1996 on 25,000 women out of the 68,000 (who lived in communes with at least 1000 participants) invited to participate in the setting up of the biological bank. While the E3N study includes a large population in all France, exposure assessment for the ESCAPE project was available only for 4 cities: Paris, Lyon, Grenoble and Marseille. PM measurements were only done in Paris. E3N is the French component of EPIC.

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eAppendix 2: Description of definition of mortality outcomes

Table: Description of definition of mortality outcomes

Outcome	**ICD-9**	**ICD-10**
CVD	*400-440*: • 401-405: Hypertensive disease • 410-414: Ischemic heart disease • 415-417: Diseases of pulmonary circulation • 420-429: Other forms of heart disease • 430-438: Cerebrovascular disease	*I10-I70*: • I10-I15: Hypertensive diseases • I20-I25: Ischemic heart diseases • I26-I28: Pulmonary heart disease and diseases of pulmonary circulation • I30-I52: Other forms of heart disease • I60-I69: Cerebrovascular diseases
IHD	*410-414*: • 410: Acute myocardial infarction • 411: Other acute and subacute forms of ischemic heart disease • 412: Old myocardial infarction • 413: Angina pectoris • 414: Other forms of chronic ischemic heart disease	*I20-I25*: • I20: Angina pectoris • I21: Acute myocardial infarction • I22: Subsequent myocardial infarction • I23: Certain current complications following acute myocardial infarction • I24: Other acute ischemic heart diseases • I25: Chronic ischemic heart disease
MI	*410*: • Acute myocardial infarction	*I21, I21*: • I21: Acute myocardial infarction • I22: Subsequent myocardial infarction
CBV	*430-438*: • 430: Subarachnoid hemorrhage • 431: Intracerebral hemorrhage • 432: Other and unspecified intracranial hemorrhage • 433: Occlusion and stenosis of precerebral arteries • 434: Occlusion of cerebral arteries • 435: Transient cerebral ischemia • 436: Acute, but ill-defined, cerebrovascular disease • 437: Other and ill-defined cerebrovascular disease • 438: Late effects of cerebrovascular disease	*I60-I69*: • I60: Subarachnoid hemorrhage • I61: Intracerebral haemorrhage • I62: Other nontraumatic intracranial haemorrhage • I63: Cerebral infarction • I64: Stroke, not specified as hemorrhage or infarction • I65: Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction • I66: Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction • I67: Other cerebrovascular diseases • I68: Cerebrovascular disorders in diseases classified elsewhere • I69: Sequelae of cerebrovascular disease

eAppendix 3: Exposure assessment procedures and land use regression model results for all study areas

Exposure assessment

Air pollution concentrations at the baseline residential addresses of study participants were estimated by land use regression models following a standardized procedure that has been described elsewhere.[1,2] In brief, air pollution monitoring campaigns were performed between October 2008 and May 2011 in all study areas. Three two-week measurements of nitrogen dioxide (NO_2) and nitrogen oxides (NO_x) were performed at 40 sites within one year in each study area. In addition, simultaneous measurements of $PM_{2.5}$ absorbance (marker for Black Carbon) and particles less than 2·5µm ($PM_{2.5}$), less than 10µm (PM_{10}) were performed at 20 sites in 19 of the 22 study areas.[3,4] PM_{coarse} was calculated as PM_{10} - $PM_{2.5}$. In the remaining three areas only NO_x was measured. The three measurements were then averaged, adjusting for temporal trends using data from a background monitoring site with continuous data. [3,4] Predictor variables on nearby traffic intensity, population/household density and land use were derived from Geographic Information Systems (GIS), and were evaluated to explain spatial variation of annual average concentrations using regression modeling. Land use regression model results for all study areas are shown below. The land use regression models were used to estimate ambient air pollution concentration at the participants' addresses. If values of predictor variables for the cohort addresses were outside the range of values for the monitoring sites, values were truncated to the minimum and maximum values at the monitoring sites. Truncation was performed to prevent unrealistic predictions (e.g. related to too small distance to roads in GIS) and because we did not want to extrapolate the derived model beyond the range for which it was developed. Truncation has been shown to improve predictions at independent sites.[5]

Pollution measurements were performed in 2008-2011, but follow-up from baseline addresses was in all cohorts covering earlier time periods. We therefore extrapolated predicted concentrations back in time using the absolute difference and the ratio between the baseline and 2008-2011 periods, based on data from routine background monitoring network site(s) in the study areas. We did not use another pollutant (e.g. PM_{10} trend from routine background monitoring site to assess a $PM_{2.5}$ trend), because this introduces too much uncertainty due to different trends for different pollutants. The procedures for each area were:

1. Daily air pollution data for background routine monitoring site(s) that cover the year before and after the baseline period as well as the period of the ESCAPE measurements were collected (covering at least 75% of the year with valid data).
2. The annual average concentration for the routine monitoring site(s) covering the measurement period, based on the exact dates of ESCAPE measurements, were calculated: $C_{routine\text{-}ESCAPE}$
3. For each study participant the average concentration for the routine monitoring site(s) based on the year before and the year after the recruitment date was calculated: $C_{routine\text{-}baseline}$. In case of trends during the recruitment period of all subjects, this resulted in different, but gradual changes in the correction.
4. For each study participant the absolute difference and the ratio between the average one year before and one year after the recruitment date and the annual average covering the ESCAPE measurement period were calculated for the routine monitoring site(s):

$Diff_{routine} = C_{routine\text{-}baseline} – C_{routine\text{-}ESCAPE}$

$Ratio_{routine} = C_{routine\text{-}baseline} / C_{routine\text{-}ESCAPE}$

5. For each study participant the back-extrapolated concentration based on the absolute difference ($C_{extrapolated\text{-}difference}$) was calculated by adding $Diff_{routine}$ to the modeled annual mean ESCAPE concentration (C_{ESCAPE}):

$C_{extrapolated\text{-}difference} = C_{ESCAPE} + Diff_{routine}$

For each study participant the back-extrapolated concentration based on the ratio ($C_{extrapolated\text{-}ratio}$) was calculated by multiplying the modeled ESCAPE annual mean concentration (C_{ESCAPE}) with the ratio:

$C_{extrapolated\text{-}ratio} = C_{ESCAPE} * Ratio_{routine}$

Details on this procedure can be found on the website http://www.escapeproject.eu/manuals/. Please find below example calculations for both procedures.

	Absolute difference method					
Subject ID	Baseline date	$C_{routine\text{-}ESCAPE}$	$C_{routine\text{-}baseline}$	$Diff_{routine}$	C_{ESCAPE}	$C_{extrapolated\text{-}difference}$
1	1-2-1998	20	35	35 – 20 = 15	40	40 + 15 = 55
2	5-2-1998	20	36	36 – 20 = 16	35	35 + 16 = 51
3	8-2-1998	20	37	37 – 20 = 17	25	25 + 17 = 42
	Ratio method					
Subject ID	Baseline date	$C_{routine\text{-}ESCAPE}$	$C_{routine\text{-}baseline}$	$Ratio_{routine}$	C_{ESCAPE}	$C_{extrapolated\text{-}ratio}$
1	1-2-1998	20	35	35 / 20	40	40 * 35/20 = 70
2	5-2-1998	20	36	36 / 20	35	35 * 36/20 = 63
3	8-2-1998	20	37	37 / 20	25	25 * 37/20 = 46.3

In addition to predicted concentrations, traffic intensity on the nearest road (vehicles/day) and total traffic load (intensity*length) on all major roads within a 100m buffer were used as indicators of exposure.

Since 2002 member states of the EU are obliged to produce every 5th year noise maps for major roads, major railways and major airports and for larger agglomerations. ESCAPE made use of data from local assessments for road traffic noise carried out for the first round of noise mapping in the EU (2007). For specific cohorts where the EU noise maps were not available, (additional) road traffic noise calculations were carried out in accordance with the EU-Directive. The noise level (L_{den}: day-evening-night equivalent level) was calculated for the most exposed façade of dwellings. National calculations methods were used in the study areas of the Finnish, Swedish, Norwegian, Danish, Dutch and German cohorts; the interim method of the EU was applied for EPIC-Turin and SIDRIA-Turin.

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Table 1: Land use regression model results: model explained variance (R^2) and between parentheses leave-one-out cross-validation explained variance (CV R^2) for the different pollutants for each study area.[a]

Cohort	NO_2	NO_x	$PM_{2.5}$ absorbance	PM_{10}	$PM_{2.5}$	PM_{coarse}	NO_2 background
EPIC-Umeå, Sweden	87% (83%)	87% (82%)	NA	NA	NA	NA	73% (64%)
FINRISK, Finland	83% (75%)	85% (74%)	65% (47%)	67% (42%)	67% (53%)	61% (33%)	78% (69%)
HUBRO, Norway	76% (64%)	76% (67%)	91% (84%)	77% (65%)	81% (62%)	67% (57%)	57% (48%)
SNAC-K, Sweden	82% (78%)	83% (79%)	89% (85%)	82% (77%)	87% (78%)	72% (65%)	89% (83%)
SALT/Twin gene, Sweden	82% (78%)	83% (79%)	89% (85%)	82% (77%)	87% (78%)	72% (65%)	89% (83%)
60-y/IMPROVE, Sweden	82% (78%)	83% (79%)	89% (85%)	82% (77%)	87% (78%)	72% (65%)	89% (83%)
SDPP, Sweden	82% (78%)	83% (79%)	89% (85%)	82% (77%)	87% (78%)	72% (65%)	89% (83%)
DCH, Denmark	88% (83%)	83% (73%)	92% (86%)	75% (64%)	62% (55%)	71% (54%)	75% (64%)
EPIC-MORGEN, Netherlands	86% (81%)	87% (82%)	92% (89%)	68% (60%)	67% (61%)	51% (39%)	84% (78%)
EPIC-PROSPECT, Netherlands	86% (81%)	87% (82%)	92% (89%)	68% (60%)	67% (61%)	51% (39%)	84% (78%)
SALIA, Germany	89% (84%)	88% (81%)	97% (95%)	69% (63%)	88% (79%)	66% (57%)	64% (47%)
EPIC-Oxford, UK	89% (87%)	91% (88%)	96% (92%)	90% (88%)	82% (77%)	68% (57%)	71% (66%)
KORA, Germany	86% (67%)	88% (76%)	91% (82%)	83% (75%)	78% (62%)	81% (69%)	59% (32%)
VHM&PP, Austria	74% (66%)	60% (51%)	81% (73%)	83% (71%)	57% (42%)	53% (31%)	64% (53%)
SAPALDIA, Switzerland							
- Basel	67% (58%)	61% (52%)	NA	NA	NA	NA	78% (63%)
- Geneva	87% (81%)	81% (73%)	NA	NA	NA	NA	81% (75%)
- Lugano	87% (82%)	87% (82%)	79% (71%)	87% (80%)	83% (77%)	77% (65%)	65% (58%)
E3N, France							
- Paris	77% (67%)	75% (67%)	91% (81%)	87% (77%)	89% (73%)	81% (73%)	81% (73%)
- Grenoble	83% (78%)	82% (74%)	NA	NA	NA	NA	76% (71%)
- Lyon	90% (72%)	75% (65%)	NA	NA	NA	NA	86% (76%)
- Marseille	59% (46%)	53% (39%)	NA	NA	NA	NA	85% (77%)
EPIC-Varese, Italy	72% (61%)	74% (52%)	NA	NA	NA	NA	82% (61%)
EPIC-Turin, Italy	78% (70%)	78% (72%)	88% (81%)	78% (69%)	71% (59%)	65% (58%)	94% (89%)
SIDRIA-Turin, Italy	78% (70%)	78% (72%)	88% (81%)	78% (69%)	71% (59%)	65% (58%)	94% (89%)
SIDRIA-Rome, Italy	87% (76%)	80% (69%)	84% (79%)	72% (59%)	71% (60%)	70% (57%)	67% (53%)
EPIC-San Sebastian, Spain	58% (50%)	49% (39%)	NA	NA	NA	NA	89% (83%)
EPIC-Athens, Greece	70% (55%)	67% (46%)	56% (40%)	78% (60%)	86% (69%)	44% (23%)	35% (20%)

[a] NA = Not available

eAppendix 4: Study population characteristics at baseline for each cohort (variables included in main model 3)

Table 1: Study population characteristics at baseline for EPIC-Umeå with complete confounder information in main model 3 (N = 22,136)

Variable	Mean (SD)
Age at baseline	46.0 (10.2)
Number of cigarette equivalents/day (current)	2.4 (5.6)
Years of regular smoking	8.8 (13.0)
Intake of fruit (g/day)	163.0 (132.6)
Intake of vegetables (g/day)	93.5 (90.1)
Alcohol consumption (g/day)	3.2 (4.0)
BMI (kg/m^2)	25.0 (4.0)
Unemployment rate (neighborhood)	0.3 (0.1)
	N (%)
Gender	
- Women	11,561 (52%)
- Men	10,575 (48%)
Calendar year	
- 1992	1804 (8%)
- 1993	5319 (24%)
- 1994	4896 (22%)
- 1995	5489 (25%)
- 1996	4628 (21%)
Smoking status	
- Current	4187 (19%)
- Former	4223 (19%)
- Never	13,726 (62%)
Marital status	
- Single	2087 (9%)
- Married/living with partner	18,215 (82%)
- Divorced/separated	1376 (6%)
- Widowed	458 (2%)
Educational level	
- Low	6209 (28%)
- Medium	11 184 (50%)
- High	4743 (21%)
Employment status	
- Employed	18,900 (85%)
- Unemployed	1399 (6%)
- Homemaker/housewife	451 (2%)
- Retired	1386 (6%)

Table 2: Study population characteristics at baseline for FINRISK with complete confounder information in main model 3 (N = 10,224)

Variable	Mean (SD)
Age at baseline	47.9 (13.2)
Number of cigarette equivalents/day (current)	3.8 (7.8)
Years of regular smoking	8.6 (12.2)
Alcohol consumption[a]	0.9 (1.3)
BMI (kg/m^2)	26.4 (4.6)
Average income (3km) (EUR)	22,954 (5459)
	N (%)
Gender	
- Women	5501 (54%)
- Men	4723 (46%)
Calendar year	
- 1992	2783 (27%)
- 1997	2941 (29%)
- 2002	2418 (24%)
- 2007	2082 (20%)
Smoking status	
- Current	2638 (26%)
- Former	2947 (29%)
- Never	4639 (45%)
Marital status	
- Single	1611 (16%)
- Married/living with partner	7170 (70%)
- Divorced/separated	1100 (11%)
- Widowed	343 (3%)
Educational level	
- Low	3167 (31%)
- Medium	5291 (52%)
- High	1766 (17%)
Environmental tobacco smoke at work and/or home	
- No	8322 (81%)
- Yes	1902 (19%)
Intake of fruit	
- Daily	6783 (66%)
- Weekly	2639 (26%)
- Seldom	592 (6%)
- Never	210 (2%)
Intake of vegetables	
- Daily	6973 (68%)
- Weekly	2550 (25%)
- Seldom	488 (5%)
- Never	213 (2%)
Occupational class	
- Blue collar	1528 (15%)
- White collar	5435 (53%)
- Students/housewives/retired/ unemployed	3261 (32%)
Employment status	
- Employed/Self-employed	7073 (69%)
- Unemployed	621 (6%)
- Homemaker/housewife	347 (3%)
- Retired	2183 (21%)
Area indicator	
- Helsinki and Vantaa	4935 (48%)
- Turku area	5289 (52%)

[a] Number of glasses of alcoholic drink during last week

Table 3: Study population characteristics at baseline for HUBRO with complete confounder information in main model 3 (N = 18,234)[a]

Variable	Mean (SD)
Age at baseline	48.3 (15.2)
Number of cigarette equivalents/day (lifetime average)	6.7 (8.4)
Years of regular smoking	11.5 (14.4)
BMI (kg/m^2)	25.7 (4.1)
Unemployment rate (municipality level) (%)	1.8 (0.7)
	N (%)
Gender	
- Women	10,236 (56%)
- Men	7998 (44%)
Calendar year	
- 2000	7928 (44%)
- 2001	10,306 (56%)
Smoking status	
- Current	4752 (26%)
- Former	5094 (28%)
- Never	8388 (46%)
Alcohol consumption	
- Weekly	9228 (51%)
- Occasionally	7358 (40%)
- Never/not past year	1648 (9%)
Intake of fruit	
- Daily	7284 (40%)
- Weekly	8881 (49%)
- Rarely	2069 (11%)
Intake of vegetables	
- Daily	2646 (15%)
- Weekly	12,503 (69%)
- Rarely	3085 (17%)
Marital status	
- Single	5645 (31%)
- Married/living with partner	9089 (50%)
- Divorced/separated	2474 (14%)
- Widowed	1026 (6%)
Educational level	
- Low	3234 (18%)
- Medium	6597 (36%)
- High	8403 (46%)

[a] Number of observations in CVD mortality analyses differs from number of observations in natural cause mortality analyses because confounder model for CVD mortality excluded variable Employment status related to convergence problems especially for the more specific CVD mortality causes.

Table 4: Study population characteristics at baseline for SNAC-K with complete confounder information in main model 3 (N = 2401)

Variable	**Mean (SD)**
Age at baseline	70.3 (8.1)
Number of cigarette equivalents/day (lifetime average)	7.1 (9.5)
Years of regular smoking	9.8 (15.2)
BMI (kg/m^2)	26.0 (4.1)
Average income (neighborhood) (SEK)	352,638 (26,928)
	N (%)
Gender	
- Women	1441 (60%)
- Men	960 (40%)
Calendar year	
- 2001	512 (21%)
- 2002	691 (29%)
- 2003	798 (33%)
- 2004	400 (17%)
Smoking status	
- Current	378 (16%)
- Former	960 (40%)
- Never	1063 (44%)
Marital status	
- Single	305 (13%)
- Married/living with partner	1301 (54%)
- Divorced/separated	364 (15%)
- Widowed	431 (18%)
Educational level	
- Low	509 (21%)
- Medium	1039 (43%)
- High	853 (36%)
Environmental tobacco smoke at work	
- No	810 (34%)
- Yes	1591 (66%)
Environmental tobacco smoke at home	
- No	
- Yes	1094 (46%)
	1307 (54%)
Occupation class	
- Blue collar	387 (16%)
- White collar	2014 (84%)
Employment status	
- Other	1714 (71%)
- Employed	687 (29%)
Alcohol consumption	
- Daily	524 (22%)
- Weekly	643 (27%)
- Seldom	1060 (44%)
- Never	174 (7%)

Table 5: Study population characteristics at baseline for SALT / Twin gene with complete confounder information in main model 3 (N = 5473)

Variable	Mean (SD)
Age at baseline	58.0 (9.9)
Number of cigarette equivalents/day (lifetime average)	8.5 (9.7)
Years of regular smoking	16.7 (17.3)
BMI (kg/m^2)	28.6 (4.1)
	N (%)
Gender	
- Women	3050 (56%)
- Men	2423 (44%)
Calendar year	
- 1998	262 (5%)
- 1999	1467 (27%)
- 2000	1410 (26%)
- 2001	1177 (22%)
- 2002	1157 (21%)
Smoking status	
- Current	1295 (24%)
- Former	2059 (38%)
- Never	2119 (39%)
Marital status	
- Single	784 (14%)
- Married/living with partner	3723 (68%)
- Divorced/separated	612 (11%)
- Widowed	354 (7%)
Educational level	
- Low	1179 (22%)
- Medium	2360 (43%)
- High	1934 (35%)
Individual level socioeconomic status	
- Low	1643 (30%)
- Medium	2842 (53%)
- High	988 (18%)
Mean income (municipality level) (SEK)	
- Quartile 1	1528 (28%)
- Quartile 2	2366 (43%)
- Quartile 3	221 (4%)
- Quartile 4	1358 (25%)

Table 6: Study population characteristics at baseline for 60-yr/IMPROVE with complete confounder information in main model 3 (N = 3612)

Variable	**Mean (SD)**
Age at baseline	60.4 (0.1)
Number of cigarette equivalents/day (lifetime average)	8.0 (9.1)
Years of regular smoking	15.2 (16.4)
Alcohol consumption (g/day)	8.9 (9.7)
BMI (kg/m^2)	26.8 (4.2)
Average income (municipality) (SEK)	290,838 (46,103)
	N (%)
Gender	
- Women	1897 (53%)
- Men	1715 (47%)
Calendar year	
- 1997	757 (21%)
- 1998	2772 (77%)
- 1999	83 (2%)
Smoking status	
- Current	761 (21%)
- Former	1371 (38%)
- Never	1480 (41%)
Environmental tobacco smoke at work and/or home	
- No	
- Yes	1898 (53%)
	1714 (47%)
Marital status	
- Single	161 (5%)
- Married/living with partner	2587 (72%)
- Divorced/separated	617 (17%)
- Widowed	247 (7%)
Educational level	
- Low	995 (28%)
- Medium	1596 (44%)
- High	1021 (28%)
Occupation class	
- Blue collar	820 (23%)
- Low white collar	1977 (55%)
- High white	815 (23%)
Employment status	
- Employed/Self-employed	1857 (51%)
- Unemployed	351 (10%)
- Homemaker/housewife	276 (8%)
- Retired	1128 (31%)
Intake of fruit	
- Daily	2318 (64%)
- Weekly	1015 (28%)
- Seldom/never	279 (2%)
Intake of vegetables	
- Daily	476 (13%)
- Weekly	3085 (85%)
- Seldom/never	51 (1%)

Table 7: Study population characteristics at baseline for SDPP with complete confounder information in main model 3 (N = 7408)

Variable	Mean (SD)
Age at baseline	47.1 (5.0)
Number of cigarette equivalents/day (lifetime average)	8.5 (8.8)
Years of regular smoking	12.3 (12.4)
Alcohol consumption[a]	1.3 (1.9)
BMI (kg/m^2)	25.6 (4.0)
Average income (municipality) (SEK)	277,069 (18,711)
	N (%)
Gender	
- Women	4570 (62%)
- Men	2838 (38%)
Calendar year	
- 1992	292 (4%)
- 1993	1741 (24%)
- 1994	805 (11%)
- 1996	1815 (25%)
- 1997	2378 (32%)
- 1998	377 (5%)
Smoking status	
- Current	1928 (26%)
- Former	2711 (37%)
- Never	2769 (37%)
Marital status	
- Single/living alone	1217 (16%)
- Married/living with partner	6191 (84%)
Educational level	
- Low	1892 (26%)
- Medium	3321 (45%)
- High	2195 (30%)
Occupation class	
- Worker/blue collar	2451 (33%)
- White collar	4957 (67%)
Employment status	
- Not employment	606 (8%)
- Employed	6802 (92%)
Intake of fruit	
- Daily/weekly	6845 (92%)
- Seldom	482 (7%)
- Never	81 (1%)

[a] Number of glasses of alcoholic drink per day.

Table 8: Study population characteristics at baseline for DCH with complete confounder information in main model 3 (N = 35,458)

Variable	Mean (SD)
Age at baseline	56.7 (4.4)
Number of cigarette equivalents/day (current)	6.3 (10.4)
Years of regular smoking	18.7 (17.1)
Intake of fruit (g/day)	183.2 (151.2)
Intake of vegetables (g/day)	175.9 (99.2)
Alcohol consumption (g/day)	21.7 (22.8)
BMI (kg/m^2)	26.0 (4.1)
Average income (municipality) (100,000 Dkr)	1.9 (0.4)
	N (%)
Gender	
- Women	19,171 (54%)
- Men	16,287 (46%)
Calendar year	
- 1993	86 (1%)
- 1994	3712 (11%)
- 1995	11,034 (31%)
- 1996	14,726 (42%)
- 1997	5900 (17%)
Smoking status	
- Current	12,737 (36%)
- Former	9851 (28%)
- Never	12,870 (36%)
Marital status	
- Single	2317 (7%)
- Married/living with partner	24,544 (69%)
- Divorced/separated	6539 (18%)
- Widowed	2058 (6%)
Educational level	
- Low	10,490 (30%)
- Medium	16,844 (48%)
- High	8124 (23%)
Environmental tobacco smoke at work and/or home	
- No	12,654 (36%)
- Yes	22,804 (64%)
Employment status	
- Not employment	7073 (20%)
- Employed	28,385 (80%)

Table 9: Study population characteristics at baseline for EPIC-MORGEN with complete confounder information in main model 3 (N = 16,446)

Variable	Mean (SD)
Age at baseline	43.9 (10.9)
Number of cigarette equivalents/day (lifetime average)	10.4 (11.1)
Years of regular smoking	14.3 (13.7)
Intake of fruit (g/day)	171.9 (129.2)
Intake of vegetables (g/day)	126.6 (51.8)
Alcohol consumption (g/day)	12.7 (18.0)
BMI (kg/m^2)	25.2 (4.0)
Percentage of people with low income (neighborhood)	41.6 (7.4)
	N (%)
Gender	
- Women	8946 (54%)
- Men	7500 (46%)
Calendar year	
- 1993	3566 (22%)
- 1994	2948 (18%)
- 1995	3568 (22%)
- 1996	3365 (21%)
- 1997	2999 (18%)
Smoking status	
- Current	5923 (36%)
- Former	4762 (29%)
- Never	5761 (35%)
Marital status	
- Single	3669 (22%)
- Married/living with partner	11,118 (68%)
- Divorced/separated	1311 (8%)
- Widowed	348 (2%)
Educational level	
- Low	1954 (12%)
- Medium	10,752 (65%)
- High	3740 (23%)

Table 10: Study population characteristics at baseline for EPIC-PROSPECT with complete confounder information in main model 3 (N = 15,670)

Variable	Mean (SD)
Age at baseline	57.7 (6.0)
Number of cigarette equivalents/day (lifetime average)	5.7 (7.4)
Years of regular smoking	15.2 (16.5)
Intake of fruit (g/day)	231.6 (139.2)
Intake of vegetables (g/day)	136.3 (52.5)
Alcohol consumption (g/day)	9.0 (12.4)
BMI (kg/m^2)	25.5 (4.1)
Percentage of people with low income (municipality)	35.9 (2.7)
Percentage of people with low income (neighborhood)	35.8 (7.2)
	N (%)
Gender	
- Women	15,670 (100%)
- Men	0 (0%)
Calendar year	
- 1993	1354 (9%)
- 1994	4071 (26%)
- 1995	4023 (26%)
- 1996	4102 (26%)
- 1997	2120 (14%)
Smoking status	
- Current	3454 (22%)
- Former	5166 (33%)
- Never	7050 (45%)
Marital status	
- Single	888 (6%)
- Married/living with partner	12,046 (77%)
- Divorced/separated	1252 (8%)
- Widowed	1484 (10%)
Educational level	
- Low	3478 (22%)
- Medium	9685 (62%)
- High	2507 (16%)

Table 11: Study population characteristics at baseline for SALIA with complete confounder information in main model 3 (N = 4352)

Variable	**Mean (SD)**
Age at baseline	54.5 (0.6)
Number of cigarette equivalents/day (current)	2.6 (6.6)
Years of regular smoking	4.4 (10.5)
Average income (postal code area) (EUR)	973.6 (69.1)
	N (%)
Gender	
- Women	4352 (100%)
- Men	0 (0%)
Calendar year	
- 1985-1987	1667 (38%)
- 1990-1994	2685 (62%)
Smoking status	
- Current	729 (17%)
- Former	379 (9%)
- Never	3244 (75%)
Educational level	
- Low	1255 (29%)
- Medium	2094 (48%)
- High	1003 (23%)
Environmental tobacco smoke at work and/or home	
- No	2141 (49%)
- Yes	2211 (51%)
Occupational exposure to dust	
- No	3923 (90%)
- Yes	429 (10%)

Table 12: Study population characteristics at baseline for EPIC-Oxford with complete confounder information in main model 3 (N = 38,941)

Variable	Mean (SD)
Age at baseline	45.8 (13.7)
Number of cigarette equivalents/day (lifetime average)	5.0 (8.3)
Years of regular smoking	6.7 (11.2)
Intake of fruit (g/day)	259.9 (204.5)
Intake of vegetables (g/day)	281.0 (156.4)
Alcohol consumption (g/day)	9.1 (11.7)
BMI (kg/m^2)	24.0 (3.9)
Carstairs index 2001 (continuous)	-1.5 (2.3)
	N (%)
Gender	
- Women	30,178 (78%)
- Men	8763 (22%)
Calendar year	
- 1993	311 (1%)
- 1994	5345 (14%)
- 1995	7009 (18%)
- 1996	13,399 (34%)
- 1997	7854 (20%)
- 1998-2001	5023 (13%)
Smoking status	
- Current	4016 (10%)
- Former	10,294 (26%)
- Never	24,631 (63%)
Marital status	
- Single	6336 (16%)
- Married/living with partner	27,554 (71%)
- Divorced/separated	3474 (9%)
- Widowed	1577 (4%)
Educational level	
- Low	14,194 (37%)
- Medium	9391 (24%)
- High	15,356 (4%)
Employment status	
- Employed/self-employed	28,230 (73%)
- Unemployed	958 (3%)
- Stay at home	4593 (12%)
- Retired	5160 (13%)

Table 13: Study population characteristics at baseline for KORA with complete confounder information in main model 3 (N = 8399)

Variable	Mean (SD)
Age at baseline	49.5 (13.8)
Number of cigarette equivalents/day (lifetime average)	9.2 (13.3)
Years of regular smoking	12.0 (14.2)
Alcohol consumption (g/day)	16.3 (22.3)
BMI (kg/m^2)	27.2 (4.6)
Percentage of people with low income (5km grid)	28.2 (18.4)
	N (%)
Gender	
- Women	4270 (51%)
- Men	4129 (49%)
Calendar year	
- 1994-1995	4299 (51%)
- 1999-2001	4100 (49%)
Smoking status	
- Current	2183 (26%)
- Former	2546 (30%)
- Never	3670 (44%)
Marital status	
- Single	872 (10%)
- Married/living with partner	6356 (76%)
- Divorced/separated	635 (8%)
- Widowed	536 (6%)
Educational level	
- Low	1059 (13%)
- Medium	6270 (75%)
- High	1070 (13%)
Environmental tobacco smoke at home	
- No	6390 (76%)
- Yes	2009 (24%)
Environmental tobacco smoke at work	
- No	6328 (75%)
- Yes	2071 (25%)
Employment status	
- Employed/self-employed	4894 (58%)
- Unemployed	273 (3%)
- Stay at home	1170 (14%)
- Retired	2062 (25%)
Intake of fruit	
- Daily	4995 (60%)
- Weekly	2547 (30%)
- Seldom/never	857 (10%)
Intake of vegetables	
- Daily	3953 (47%)
- Weekly	3821 (46%)
- Seldom/never	625 (7%)

Table 14: Study population characteristics at baseline for VHM&PP with complete confounder information in main model 3 (N = 117,824)

Variable	Mean (SD)
Age at baseline	41.9 (14.9)
BMI (kg/m^2)	24.8 (4.3)
Average income (municipality) (EUR)	25,119 (1273)
	N (%)
Gender	
- Women	66,042 (56%)
- Men	51,782 (44%)
Calendar year	
- 1985-1989	58,490 (50%)
- 1990-1994	26,393 (22%)
- 1995-1999	18,414 (16%)
- 2000-2005	14,527 (12%)
Smoking status	
- Current	28,255 (24%)
- Former	7233 (6%)
- Never	82,336 (70%)
Marital status	
- Single	20,134 (17%)
- Married/living with partner	80,572 (68%)
- Divorced/separated	8962 (8%)
- Widowed	8156 (7%)
Occupational class	
- White collar	66,348 (56%)
- Blue collar	40,961 (35%)
- Others (mainly self-employed)	10,515 (9%)
Employment status	
- Employed/self-employed	81,705 (69%)
- Unemployed	4126 (4%)
- Retired	31,993 (27%)

Table 15: Study population characteristics at baseline for SAPALDIA with complete confounder information in main model 3 (N = 3473)

Variable	**Mean (SD)**
Age at baseline	41.1 (11.8)
Number of cigarette equivalents/day (lifetime average)	11.5 (14.5)
Years of regular smoking	10.7 (12.4)
BMI (kg/m^2)	23.7 (4.0)
Average educational level (neighborhood)[a]	3.2 (0.3)
	N (%)
Gender	
- Women	1807 (52%)
- Men	1666 (48%)
Calendar year	
- 1991	3473 (100%)
Smoking status	
- Current	1259 (36%)
- Former	740 (21%)
- Never	1474 (42%)
Marital status	
- Single	1214 (35%)
- Married/living with partner	1885 (54%)
- Divorced/separated	305 (9%)
- Widowed	69 (2%)
Educational level	
- Low	522 (15%)
- Medium	2222 (64%)
- High	729 (21%)
Environmental tobacco smoke at home	
- No	3000 (86%)
- Yes	473 (14%)
Environmental tobacco smoke at work	
- No	3163 (91%)
- Yes	310 (9%)
Employment status	
- Employed	2931 (84%)
- Unemployed	54 (2%)
- Stay at home or retired	488 (14%)

[a] Average of a 7-categories (1-7) level of education variable, calculated for participants living within the same neighborhood zone

Table 16: Study population characteristics at baseline for E3N with complete confounder information in main model 3 (N = 14,313)

Variable	Mean (SD)
Age at baseline	53.0 (6.7)
Intake of fruit (g/day)	242.0 (164.7)
Intake of vegetables (g/day)	242.0 (126.8)
Alcohol consumption (g/day)	12.0 (15.1)
BMI (kg/m^2)	22.8 (3.2)
Unemployment rate (regional scale)	9.4 (1.0)
	N (%)
Gender	
- Women	14,313 (100%)
- Men	0 (0%)
Calendar year	
- 1993	10,751 (75%)
- 1994	2257 (16%)
- 1995	917 (6%)
- 1996	388 (3%)
Smoking status	
- Current	2364 (17%)
- Former	4886 (34%)
- Never	7063 (49%)
Educational level	
- Low	710 (5%)
- Medium	856 (6%)
- High	12,747 (89%)

Table 17: Study population characteristics at baseline for EPIC-Varese with complete confounder information in main model 3 (N = 9871)

Variable	Mean (SD)
Age at baseline	51.7 (8.3)
Number of cigarette equivalents/day (lifetime average)	4.0 (6.4)
Years of regular smoking	9.4 (13.3)
Intake of fruit (g/day)	303.8 (172.2)
Intake of vegetables (g/day)	158.0 (58.4)
Alcohol consumption (g/day)	11.4 (15.7)
BMI (kg/m^2)	25.7 (4.2)
Unemployment rate (municipality scale)	4.2 (0.6)
	N (%)
Gender	
- Women	8487 (86%)
- Men	1384 (14%)
Calendar year	
- 1993	756 (8%)
- 1994	3561 (36%)
- 1995	2432 (25%)
- 1996	1599 (16%)
- 1997	1523 (15%)
Smoking status	
- Current	2035 (21%)
- Former	1939 (20%)
- Never	5897 (60%)
Marital status	
- Single	437 (4%)
- Married/living with partner	8574 (87%)
- Divorced/separated	241 (2%)
- Widowed	619 (6%)
Educational level	
- Low	6030 (61%)
- Medium	3127 (32%)
- High	714 (7%)

Table 18: Study population characteristics at baseline for EPIC-Turin with complete confounder information in main model 3 (N = 7261)

Variable	Mean (SD)
Age at baseline	50.4 (7.5)
Number of cigarette equivalents/day (lifetime average)	7.2 (8.2)
Years of regular smoking	17.6 (16.3)
Intake of fruit (g/day)	318.2 (182.2)
Intake of vegetables (g/day)	181.8 (100.2)
Alcohol consumption (g/day)	18.1 (20.3)
BMI (kg/m^2)	25.3 (3.8)
	N (%)
Gender	
- Women	3,461 (48%)
- Men	3,800 (52%)
Calendar year	
- 1993	457 (6%)
- 1994	1264 (17%)
- 1995	2318 (32%)
- 1996	1541 (21%)
- 1997	1432 (20%)
- 1998	251 (4%)
Smoking status	
- Current	1830 (25%)
- Former	2339 (32%)
- Never	3092 (43%)
Marital status	
- Not married (single, widowed, separated, divorced)	1045 (14%)
- Married	6216 (86%)
Educational level	
- Low	3168 (44%)
- Medium	3104 (43%)
- High	989 (14%)
Deprivation index (quintiles) (census block)	
- I (less deprived)	1876 (26%)
- II	1659 (23%)
- III	1350 (19%)
- IV	1411 (19%)
- V (more deprived)	965 (13%)

Table 19: Study population characteristics at baseline for SIDRIA-Turin with complete confounder information in main model 3 (N = 5054)

Variable	Mean (SD)
Age at baseline	44.2 (6.2)
Number of cigarette equivalents/day (current)	9.3 (10.2)
Years of regular smoking	11.3 (10.6)
	N (%)
Gender	
- Women	2620 (52%)
- Men	2434 (48%)
Calendar year	
- 1999	5054 (100%)
Smoking status	
- Current	2110 (42%)
- Former	1047 (21%)
- Never	1897 (38%)
Marital status	
- Married/living with partner	4820 (95%)
- Single/divorced/separated/ widowed	234 (5%)
Educational level	
- Low	884 (18%)
- Medium	3604 (71%)
- High	566 (11%)
Environmental tobacco smoke at home	
- No	4389 (87%)
- Yes	665 (13%)
Occupational class	
- Blue collar	2120 (42%)
- White collar	1529 (30%)
- Other	1405 (28%)
Employment status	
- Employed	3649 (72%)
- Unemployed	351 (7%)
- Homemaker/housewife/retired	1054 (21%)
Deprivation index (quintiles) (census block)	
- I (less deprived)	878 (17%)
- II	1049 (21%)
- III	931 (18%)
- IV	1097 (22%)
- V (more deprived)	1099 (22%)

Table 20: Study population characteristics at baseline for SIDRIA-Rome with complete confounder information in main model 3 (N = 9177)

Variable	**Mean (SD)**
Age at baseline	44.3 (6.0)
Number of cigarette equivalents/day (current)	10.1 (10.5)
Years of regular smoking	11.7 (10.4)
	N (%)
Gender	
- Women	4848 (53%)
- Men	4329 (47%)
Calendar year	
- 1999	9177 (100%)
Smoking status	
- Current	3898 (43%)
- Former	2106 (23%)
- Never	3173 (35%)
Marital status	
- Married/living with partner	9177 (100%)
Educational level	
- Low	4121 (45%)
- Medium	3681 (40%)
- High	1375 (15%)
Occupation class	
- Non-manual	4783 (52%)
- Manual	1179 (13%)
- Worker unspecified	521 (6%)
- Unemployed	392 (4%)
- Housewife	2302 (25%)
Index of socioeconomic position (census block)	
- 1 (=High)	1703 (19%)
- 2	1684 (18%)
- 3	1667 (18%)
- 4	1797 (20%)
- 5 (=Low)	2326 (25%)

Table 21: Study population characteristics at baseline for EPIC-San Sebastian with complete confounder information in main model 3 (N = 7464)

Variable	Mean (SD)
Age at baseline	49.4 (7.7)
Number of cigarette equivalents/day (life time average)	6.9 (10.0)
Years of regular smoking	11.4 (14.3)
Intake of fruit (g/day)	330.2 (258.5)
Intake of vegetables (g/day)	243.7 (137.1)
Alcohol consumption (g/day)	18.3 (24.0)
BMI (kg/m^2)	27.3 (3.9)
Average income (municipality) (EUR)	12,670 (1396)
	N (%)
Gender	
- Women	4003 (54%)
- Men	3461 (46%)
Calendar year	
- 1992	155 (2%)
- 1993	2865 (38%)
- 1994	2877 (39%)
- 1995	1567 (21%)
Smoking status	
- Current	2031 (27%)
- Former	1413 (19%)
- Never	4020 (54%)
Marital status	
- Single	603 (8%)
- Married/living with partner	6533 (88%)
- Divorced/separated	264 (4%)
- Widowed	64 (1%)
Educational level	
- Low	5272 (71%)
- Medium	1532 (21%)
- High	660 (9%)

Table 22: Study population characteristics at baseline for EPIC-Athens with complete confounder information in main model 3 (N = 4192)

Variable	Mean (SD)
Age at baseline	49.4 (11.7)
Number of cigarette equivalents/day (lifetime average)	1.7 (15.0)
Years of regular smoking	10.8 (13.1)
Intake of fruit (g/day)	402.6 (258.2)
Intake of vegetables (g/day)	609.5 (288.6)
Alcohol consumption (g/day)	9.2 (14.5)
BMI (kg/m^2)	27.5 (4.5)
	N (%)
Gender	
- Women	2306 (55%)
- Men	1886 (45%)
Calendar year	
- 1994	1582 (38%)
- 1995	1100 (26%)
- 1996	367 (9%)
- 1997	457 (11%)
- 1998	278 (7%)
- 1999	408 (10%)
Smoking status	
- Current	1707 (41%)
- Former	830 (20%)
- Never	1655 (40%)
Marital status	
- Single	394 (9%)
- Married/living with partner	3270 (78%)
- Divorced/separated	266 (6%)
- Widowed	262 (6%)
Educational level	
- Low	990 (24%)
- Medium	1753 (42%)
- High	1449 (35%)
Occupation class	
- Blue collar	493 (12%)
- White collar	1990 (48%)
- Other	1709 (41%)
Employment status	
- Employed/self-employed	2804 (67%)
- Unemployed	28 (1%)
- Homemaker/housewife	669 (16%)
- Retired	691 (17%)
Educational level (municipality level)	
- 1: Low (primary)	214 (5%)
- 2: Medium (secondary)	3277 (78%)
- 3: High (higher)	701 (17%)

eAppendix 5: Description of exposure to $PM_{2.5}$, $PM_{2.5}$ absorbance, PM_{10}, PM_{coarse}, NO_2, and NO_x concentrations, and traffic intensity on the nearest road (motor vehicles/day) and traffic intensity on major roads in 100m buffer (motor vehicles*m/day) at participant addresses in each cohort.
The boundary of the box closest to zero indicates the 25th percentile, line within the box marks the median, and the boundary of the box farthest from zero indicates the 75th percentile. Whiskers (error bars) above and below the box indicate the 90th and 10th percentiles.

Figure 1: Description of exposure to $PM_{2.5}$ concentration ($\mu g/m^3$) at participant addresses in each cohort. PM not available for EPIC-Umeå, EPIC-Varese, and EPIC-San Sebastian.

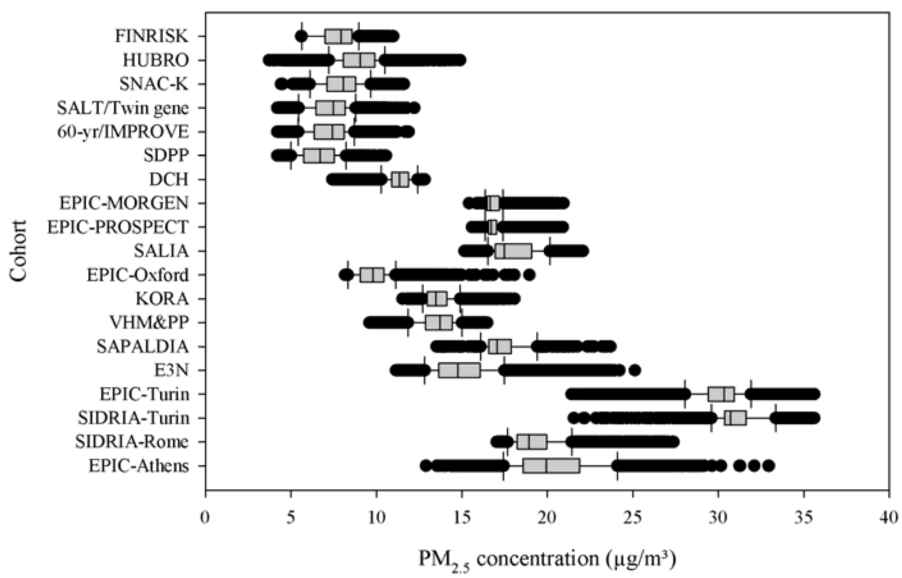


Figure 2: Description of exposure to $PM_{2.5}$ absorbance concentration (10^{-5} m^{-1}) at participant addresses in each cohort. PM not available for EPIC-Umeå, EPIC-Varese, and EPIC-San Sebastian.

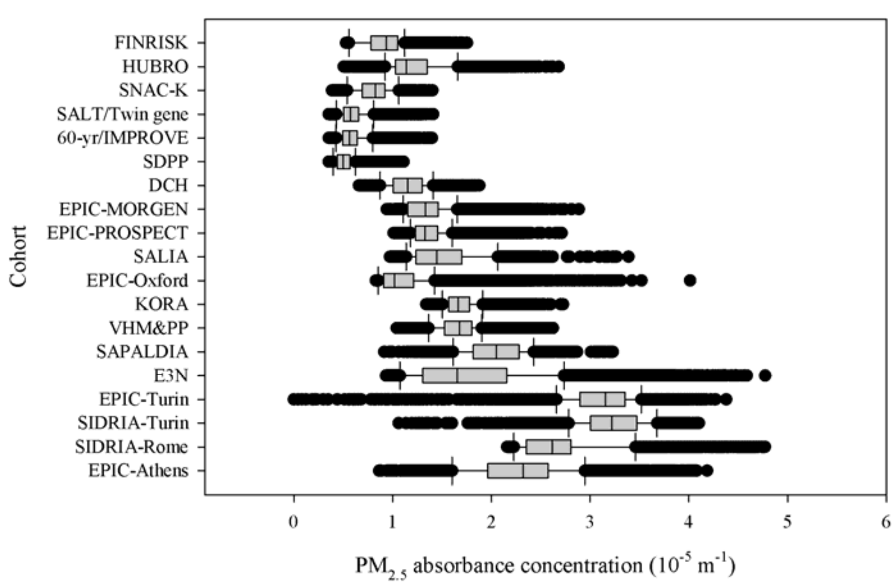


Figure 3: Description of exposure to PM_{10} concentration (µg/m^3) at participant addresses in each cohort. PM not available for EPIC-Umeå, EPIC-Varese, and EPIC-San Sebastian.

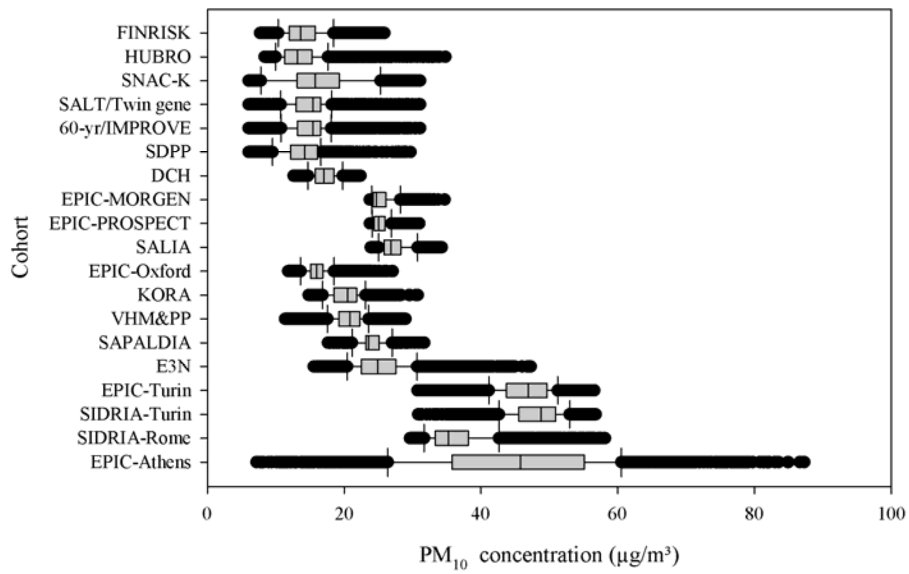


Figure 4: Description of exposure to PM_{coarse} concentration (µg/m^3) at participant addresses in each cohort. PM not available for EPIC-Umeå, EPIC-Varese, and EPIC-San Sebastian.

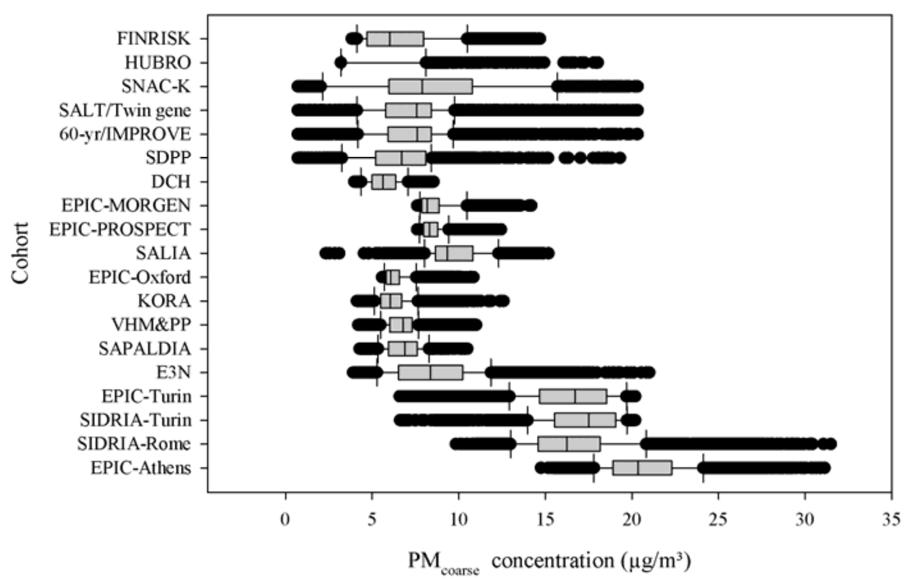


Figure 5: Description of exposure to NO_2 concentration (μg/m^3) at participant addresses in each cohort

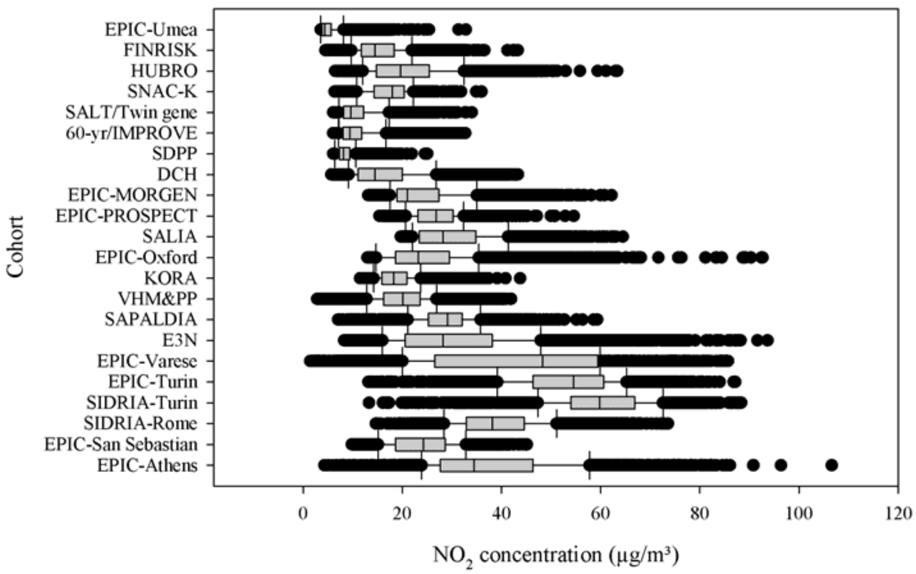


Figure 6: Description of exposure to NO_x concentration (μg/m^3) at participant addresses in each cohort

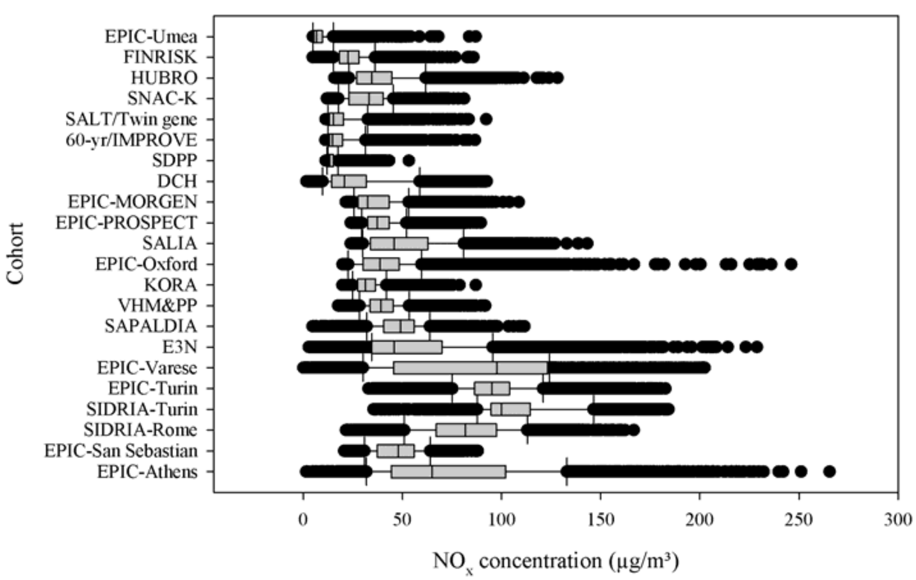


Figure 7: Description of traffic intensity on the nearest road (motor vehicles/day) at participant addresses in each cohort. Not available for EPIC-Varese and EPIC-San Sebastian.

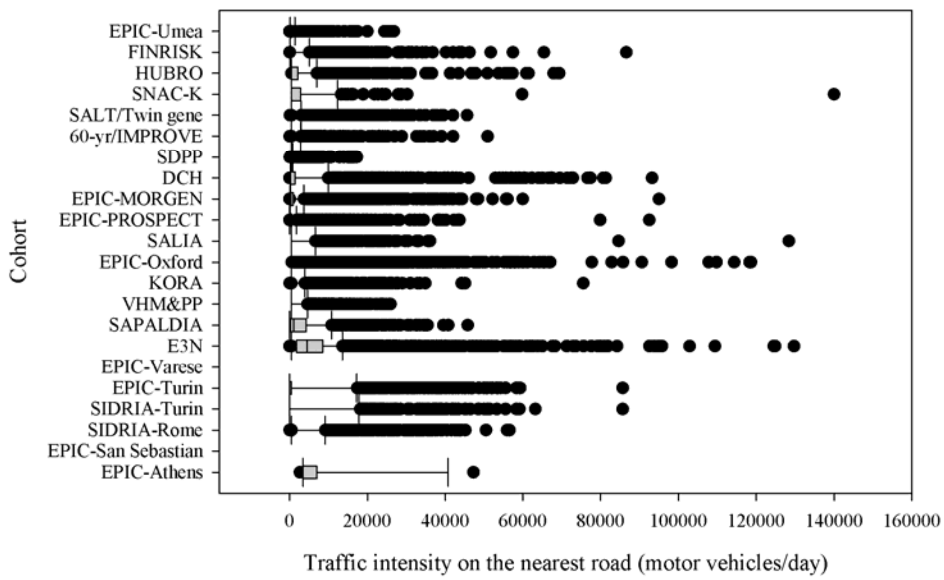
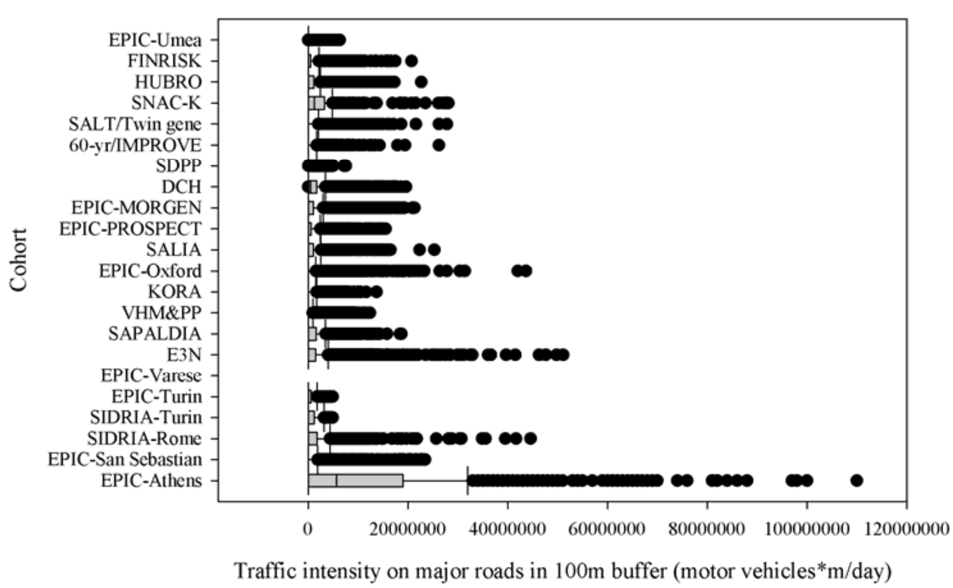


Figure 8: Description of traffic intensity on major roads in 100m buffer (motor vehicles*m/day) at participant addresses in each cohort. Not available for EPIC-Varese



eAppendix 6: Correlations between modeled NO_2 (µg/m^3), NO_x (µg/m^3), $PM_{2.5}$ (µg/m^3), $PM_{2.5}$ absorbance (10^{-5} m^{-1}), PM_{10} (µg/m^3) and PM coarse (µg/m^3) concentrations, and traffic intensity on the nearest road (trafnear) (motor vehicles/day) and traffic intensity on major roads in 100m buffer (major100) (motor vehicles*m/day) at participant addresses in each cohort.

Table 1: Pearson correlations between exposure measures in EPIC-Umeå (N = 22,136)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.99	1.00						
$PM_{2.5}$	-	-	-					
$PM_{2.5}$ abs	-	-	-	-				
PM_{10}	-	-	-	-	-			
PM coarse	-	-	-	-	-	-		
trafnear	0.25	0.26	-	-	-	-	1.00	
major100	0.48	0.48	-	-	-	-	0.46	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 2: Pearson correlations between exposure measures in FINRISK (N = 10,224)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.91	1.00						
$PM_{2.5}$	0.42	0.40	1.00					
$PM_{2.5}$ abs	0.49	0.49	0.98	1.00				
PM_{10}	0.71	0.73	0.67	0.72	1.00			
PM coarse	0.63	0.68	0.11	0.21	0.81	1.00		
trafnear	0.29	0.36	0.17	0.29	0.33	0.37	1.00	
major100	0.46	0.53	0.29	0.41	0.47	0.45	0.57	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 3: Pearson correlations between exposure measures in HUBRO (N = 18,234)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.93	1.00						
$PM_{2.5}$	0.39	0.41	1.00					
$PM_{2.5}$ abs	0.75	0.74	0.44	1.00				
PM_{10}	0.36	0.50	0.71	0.26	1.00			
PM coarse	0.55	0.73	0.27	0.41	0.70	1.00		
trafnear	0.40	0.38	0.08	0.22	0.37	0.51	1.00	
major100	0.43	0.59	0.24	0.27	0.47	0.59	0.47	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 4: Pearson correlations between exposure measures in SNAC-K (N = 2401)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.92	1.00						
$PM_{2.5}$	0.82	0.63	1.00					
$PM_{2.5}$ abs	0.82	0.67	0.98	1.00				
PM_{10}	0.63	0.66	0.70	0.78	1.00			
PM coarse	0.63	0.67	0.71	0.79	1.00	1.00		
trafnear	0.54	0.62	0.31	0.33	0.33	0.34	1.00	
major100	0.29	0.22	0.36	0.37	0.24	0.26	0.40	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 5: Pearson correlations between exposure measures in SALT/Twin gene (N = 5473)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.93	1.00						
$PM_{2.5}$	0.60	0.48	1.00					
$PM_{2.5}$ abs	0.87	0.74	0.84	1.00				
PM_{10}	0.51	0.50	0.49	0.61	1.00			
PM coarse	0.52	0.51	0.49	0.63	1.00	1.00		
trafnear	0.56	0.68	0.27	0.42	0.38	0.40	1.00	
major100	0.45	0.45	0.33	0.50	0.35	0.37	0.43	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 6: Pearson correlations between exposure measures in 60y/IMPROVE (N = 3612)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.94	1.00						
$PM_{2.5}$	0.61	0.50	1.00					
$PM_{2.5}$ abs	0.88	0.76	0.84	1.00				
PM_{10}	0.56	0.54	0.50	0.63	1.00			
PM coarse	0.58	0.56	0.50	0.65	1.00	1.00		
trafnear	0.59	0.71	0.30	0.47	0.45	0.47	1.00	
major100	0.51	0.51	0.36	0.56	0.40	0.43	0.47	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 7: Pearson correlations between exposure measures in SDPP (N = 7408)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.80	1.00						
$PM_{2.5}$	0.61	0.29	1.00					
$PM_{2.5}$ abs	0.76	0.39	0.90	1.00				
PM_{10}	0.45	0.30	0.31	0.43	1.00			
PM coarse	0.45	0.31	0.31	0.44	1.00	1.00		
trafnear	0.47	0.69	0.11	0.21	0.14	0.15	1.00	
major100	0.30	0.31	0.15	0.28	0.18	0.20	0.34	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 8: Pearson correlations between exposure measures in DCH (N = 35,458)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.97	1.00						
$PM_{2.5}$	0.57	0.49	1.00					
$PM_{2.5}$ abs	0.70	0.65	0.49	1.00				
PM_{10}	0.76	0.67	0.74	0.69	1.00			
PM coarse	0.71	0.67	0.60	0.61	0.66	1.00		
trafnear	0.62	0.70	0.20	0.41	0.30	0.43	1.00	
major100	0.68	0.67	0.32	0.49	0.47	0.49	0.63	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 9: Pearson correlations between exposure measures in EPIC-MORGEN (N = 16,446)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.91	1.00						
$PM_{2.5}$	0.20	0.38	1.00					
$PM_{2.5}$ abs	0.79	0.84	0.71	1.00				
PM_{10}	0.92	0.89	0.37	0.87	1.00			
PM coarse	0.92	0.84	0.17	0.71	0.90	1.00		
trafnear	0.42	0.47	0.28	0.42	0.36	0.45	1.00	
major100	0.58	0.61	0.33	0.61	0.57	0.52	0.48	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 10: Pearson correlations between exposure measures in EPIC-PROSPECT (N = 15,670)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.77	1.00						
$PM_{2.5}$	0.42	0.54	1.00					
$PM_{2.5}$ abs	0.78	0.80	0.80	1.00				
PM_{10}	0.79	0.86	0.72	0.96	1.00			
PM coarse	0.60	0.67	0.59	0.61	0.66	1.00		
trafnear	0.24	0.23	0.31	0.31	0.22	0.38	1.00	
major100	0.39	0.36	0.43	0.48	0.41	0.38	0.41	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 11: Pearson correlations between exposure measures in SALIA (N = 4352)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.97	1.00						
$PM_{2.5}$	0.83	0.82	1.00					
$PM_{2.5}$ abs	0.82	0.72	0.82	1.00				
PM_{10}	0.76	0.74	0.89	0.86	1.00			
PM coarse	0.74	0.71	0.84	0.81	0.86	1.00		
trafnear	0.29	0.30	0.19	0.29	0.19	0.19	1.00	
major100	0.51	0.33	0.31	0.68	0.34	0.34	0.48	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 12: Pearson correlations between exposure measures in EPIC-Oxford (N = 38,941)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.93	1.00						
$PM_{2.5}$	0.88	0.87	1.00					
$PM_{2.5}$ abs	0.78	0.71	0.63	1.00				
PM_{10}	0.53	0.54	0.57	0.57	1.00			
PM coarse	0.19	0.22	0.19	0.37	0.77	1.00		
trafnear	0.25	0.36	0.18	0.22	0.23	0.22	1.00	
major100	0.37	0.50	0.33	0.36	0.32	0.28	0.60	1

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 13: Pearson correlations between exposure measures in KORA (N = 8399)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.95	1.00						
$PM_{2.5}$	0.46	0.51	1.00					
$PM_{2.5}$ abs	0.75	0.82	0.51	1.00				
PM_{10}	0.72	0.72	0.43	0.68	1.00			
PM coarse	0.84	0.89	0.40	0.85	0.78	1.00		
trafnear	0.36	0.39	0.30	0.30	0.18	0.29	1.00	
major100	0.45	0.50	0.28	0.47	0.25	0.41	0.45	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 14: Pearson correlations between exposure measures in VHM&PP (N = 117,824)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.49	1.00						
$PM_{2.5}$	0.47	0.47	1.00					
$PM_{2.5}$ abs	0.68	0.51	0.70	1.00				
PM_{10}	0.59	0.40	0.69	0.75	1.00			
PM coarse	0.85	0.49	0.31	0.65	0.56	1.00		
trafnear	0.23	0.18	0.00	0.34	0.06	0.32	1.00	
major100	0.22	0.21	0.03	0.18	0.08	0.18	0.41	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 15: Pearson correlations between exposure measures in SAPALDIA (N = 1250)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.93	1.00						
$PM_{2.5}$	0.80	0.76	1.00					
$PM_{2.5}$ abs	0.81	0.80	0.75	1.00				
PM_{10}	0.88	0.80	0.81	0.78	1.00			
PM coarse	0.85	0.76	0.59	0.80	0.80	1.00		
trafnear	0.47	0.42	0.32	0.21	0.36	0.33	1.00	
major100	0.55	0.56	0.68	0.51	0.57	0.37	0.20	1

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 16: Pearson correlations between exposure measures in E3N (N = 10,915)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.92	1.00						
$PM_{2.5}$	0.60	0.49	1.00					
$PM_{2.5}$ abs	0.72	0.58	0.58	1.00				
PM_{10}	0.56	0.49	0.81	0.32	1.00			
PM coarse	0.86	0.67	0.68	0.74	0.66	1.00		
trafnear	0.38	0.38	0.45	0.35	0.40	0.29	1.00	
major100	0.54	0.55	0.36	0.74	0.32	0.54	0.41	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 17: Pearson correlations between exposure measures in EPIC-Varese (N = 9871)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	1.00	1.00						
$PM_{2.5}$	-	-	-					
$PM_{2.5}$ abs	-	-	-	-				
PM_{10}	-	-	-	-	-			
PM coarse	-	-	-	-	-	-		
trafnear	-	-	-	-	-	-	-	-
major100	-	-	-	-	-	-	-	-

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 18: Pearson correlations between exposure measures in EPIC-Turin (N = 7261)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.82	1.00						
$PM_{2.5}$	0.72	0.81	1.00					
$PM_{2.5}$ abs	0.93	0.79	0.77	1.00				
PM_{10}	0.63	0.47	0.62	0.60	1.00			
PM coarse	0.47	0.31	0.51	0.45	0.95	1.00		
trafnear	0.26	0.50	0.39	0.22	0.15	0.02	1.00	
major100	0.40	0.76	0.59	0.35	0.20	0.00	0.67	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 19: Pearson correlations between exposure measures in SIDRIA-Turin (N = 5054)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.72	1.00						
$PM_{2.5}$	0.67	0.88	1.00					
$PM_{2.5}$ abs	0.98	0.71	0.73	1.00				
PM_{10}	0.68	0.46	0.55	0.69	1.00			
PM coarse	0.35	0.16	0.31	0.38	0.88	1.00		
trafnear	0.30	0.56	0.47	0.28	0.13	-0.06	1.00	
major100	0.49	0.92	0.79	0.47	0.28	-0.05	0.62	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 20: Pearson correlations between exposure measures in SIDRIA-Rome (N = 9177)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.61	1.00						
$PM_{2.5}$	0.69	0.51	1.00					
$PM_{2.5}$ abs	0.63	0.50	0.78	1.00				
PM_{10}	0.62	0.48	0.92	0.72	1.00			
PM coarse	0.80	0.54	0.90	0.71	0.93	1.00		
trafnear	0.42	0.28	0.68	0.76	0.64	0.57	1.00	
major100	0.53	0.44	0.61	0.63	0.52	0.51	0.47	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

Table 21: Pearson correlations between exposure measures in EPIC-San Sebastian (N = 7464)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.99	1.00						
$PM_{2.5}$	-	-	-					
$PM_{2.5}$ abs	-	-	-	-				
PM_{10}	-	-	-	-	-			
PM coarse	-	-	-	-	-	-		
trafnear	-	-	-	-	-	-	-	-
major100	0.01	0.01	-	-	-	-	-	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

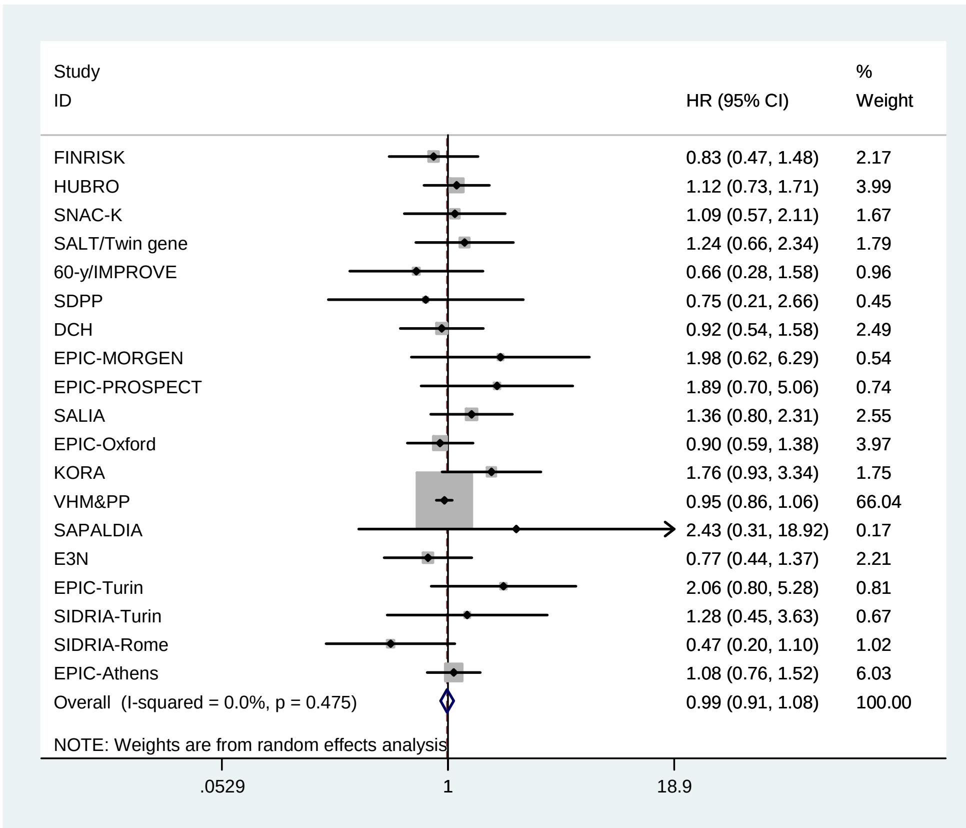
Table 22: Pearson correlations between exposure measures in EPIC-Athens (N = 4192)[a]

	NO_2	NO_x	$PM_{2.5}$	$PM_{2.5}$ abs	PM_{10}	PM coarse	trafnear	major100
NO_2	1.00							
NO_x	0.94	1.00						
$PM_{2.5}$	0.66	0.70	1.00					
$PM_{2.5}$ abs	0.70	0.77	0.67	1.00				
PM_{10}	0.75	0.69	0.62	0.80	1.00			
PM coarse	0.57	0.60	0.41	0.59	0.55	1.00		
trafnear	0.24	0.38	0.34	0.40	0.12	0.20	1.00	
major100	0.31	0.41	0.44	0.50	0.31	0.73	0.40	1.00

[a] Based on number of observations without missing value in any confounder variable of model 3 (main model).

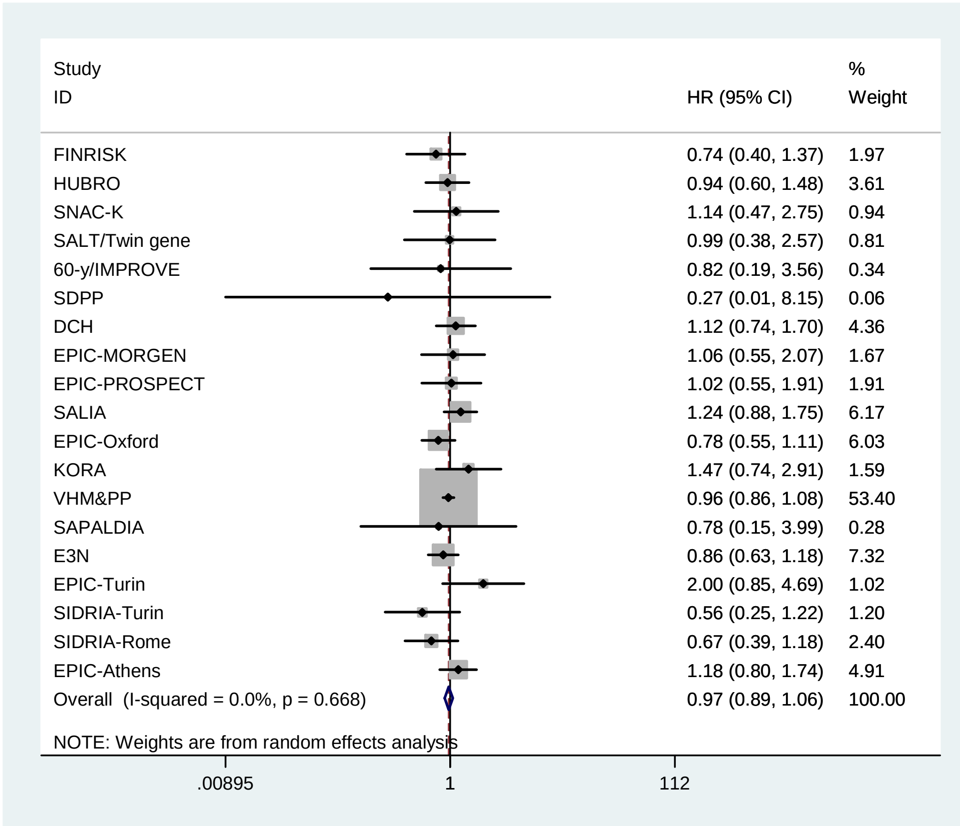
eAppendix 7: Forest plots (HRs and 95%-CIs) of association between CVD mortality and exposure to $PM_{2.5}$, $PM_{2.5}$ absorbance, PM_{10} PM_{coarse}, NO_2 and NO_x, and traffic indicators (using main confounder model 3)

Figure 1: Adjusted association between CVD mortality and exposure to $PM_{2.5}$ (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



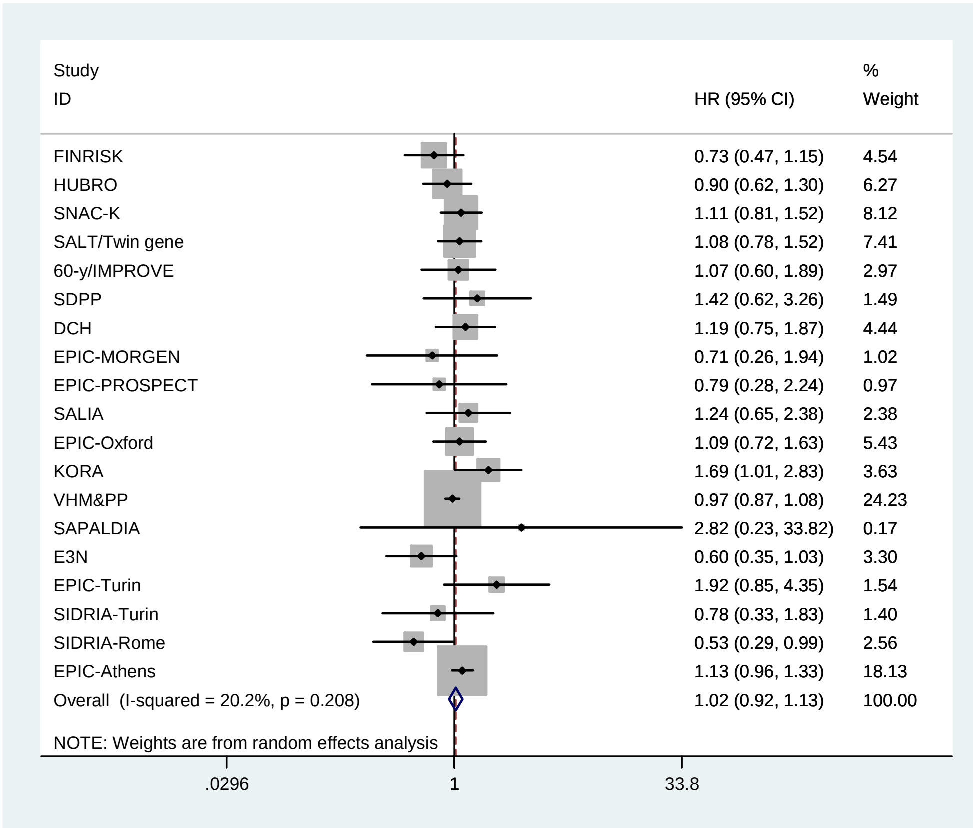
[a] HRs are presented per 5 µg/m³ for $PM_{2.5}$.
PM not available for EPIC-Umeå, EPIC-Varese and EPIC-San Sebastian. For E3N and SAPALDIA PM was available for part of the cohort

Figure 2: Adjusted association between CVD mortality and exposure to $PM_{2.5}$ absorbance (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



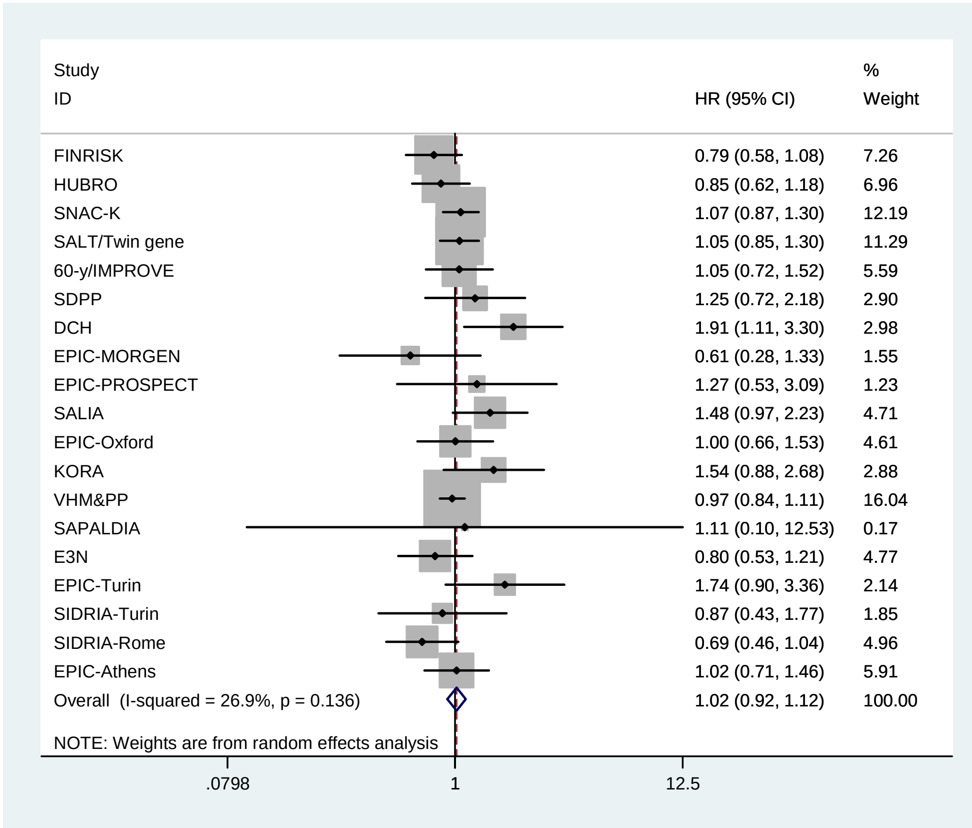
[a] HRs are presented per 10^{-5} m^{-1} for $PM_{2.5}$ absorbance.
PM not available for EPIC-Umeå, EPIC-Varese and EPIC-San Sebastian. For E3N and SAPALDIA PM was available for part of the cohort

Figure 3: Adjusted association between CVD mortality and exposure to PM_{10} (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



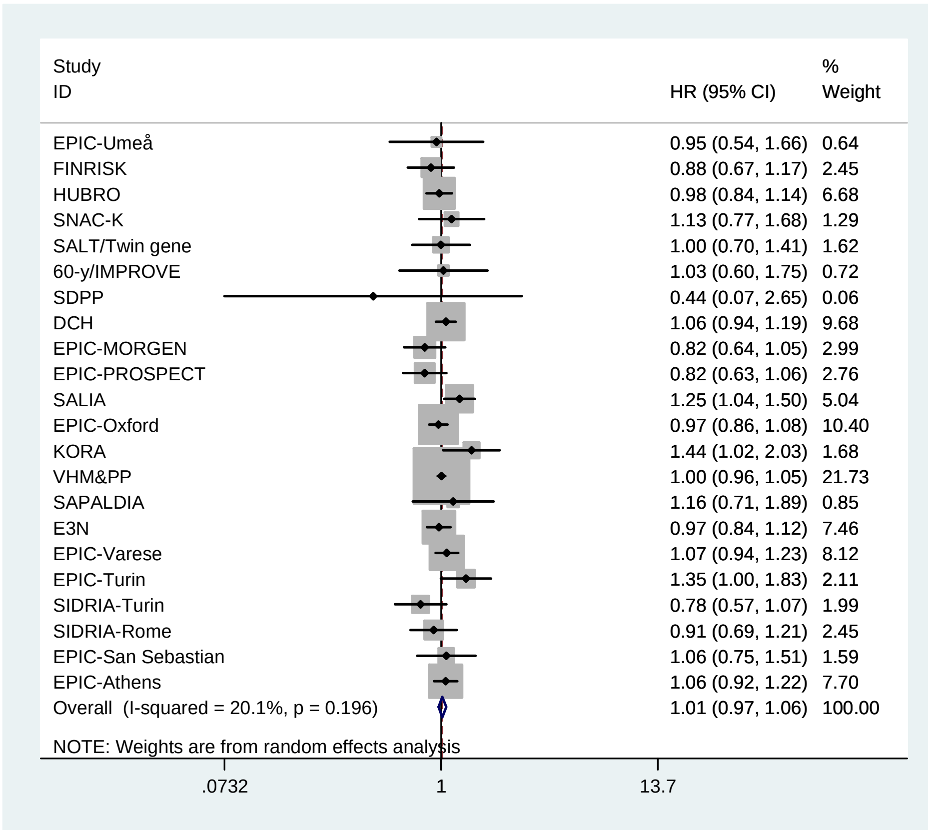
[a] HRs are presented per 10 µg/m³ for PM_{10}.
PM not available for EPIC-Umeå, EPIC-Varese and EPIC-San Sebastian. For E3N and SAPALDIA PM was available for part of the cohort

Figure 4: Adjusted association between CVD mortality and exposure to PM_{coarse} (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



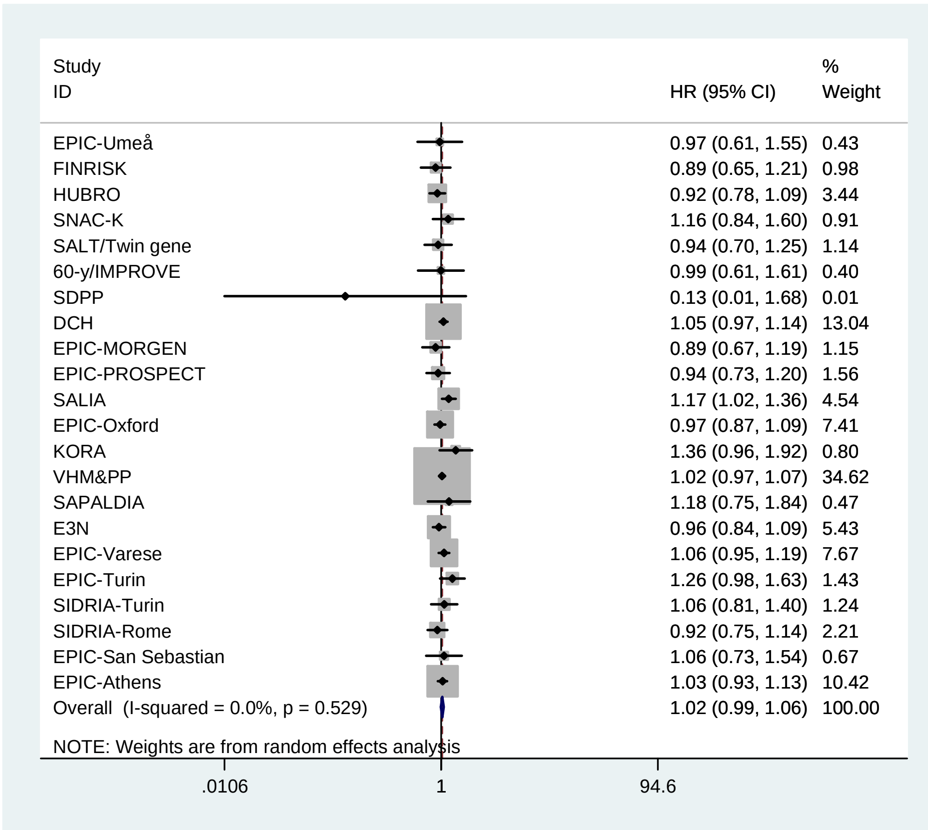
[a] HRs are presented per 5 $\mu g/m^3$ for PM_{coarse}.
PM not available for EPIC-Umeå, EPIC-Varese and EPIC-San Sebastian. For E3N and SAPALDIA PM was available for part of the cohort

Figure 5: Adjusted association between CVD mortality and exposure to NO_2 (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



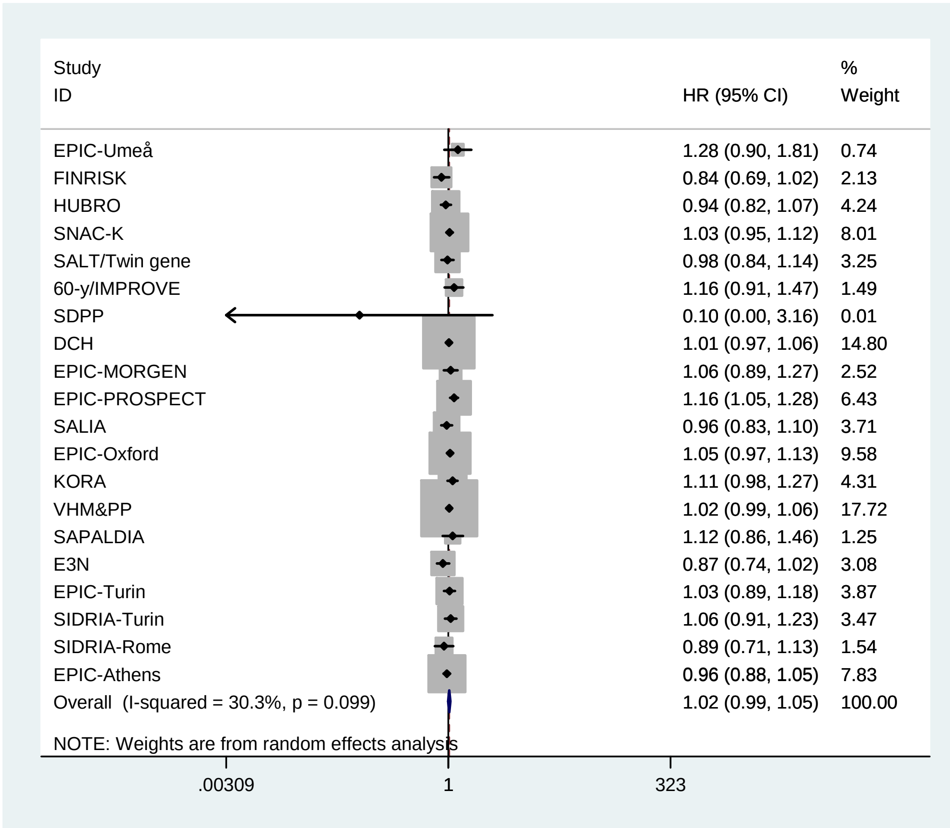
[a] HRs are presented per 10 $\mu g/m^3$ for NO_2

Figure 6: Adjusted association between CVD mortality and exposure to NO_x (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



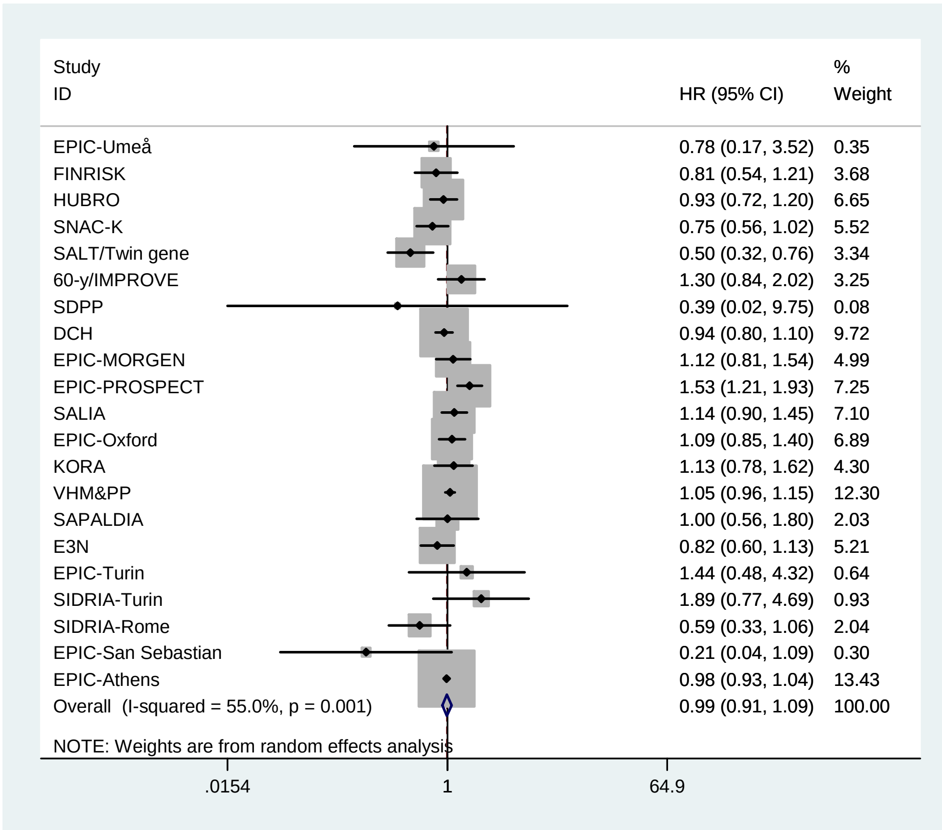
[a] HRs are presented per 20 μg/m^3 for NO_x

Figure 7: Adjusted association between CVD mortality and traffic intensity on the nearest road (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



[a] HRs are presented per 5000 motor vehicles/day for the traffic intensity on the nearest road. Traffic intensity data on the nearest road not available for EPIC-Varese and EPIC-San Sebastian

Figure 8: Adjusted association between CVD and total traffic load on all major roads within a 100m buffer (using main model 3): Results from cohort-specific analyses and from random-effects meta-analyses.[a]



[a] HRs are presented per 4,000,000 motor vehicles*m/day for the total traffic load on all major roads within a 100m buffer.

Total traffic load on all major roads within a 100m buffer not available for EPIC-Varese

eAppendix 8: Meta-analysis results (HRs and 95%-CIs) of association between CVD mortality and exposure to air pollution and traffic indicators for the extended confounder models

Table 1: Association between CVD mortality and exposure to air pollution and traffic indicators: Results from random-effects meta-analyses (HRs and 95%-CIs) for the extended confounder models. Results for main model 3 and extended confounder models are based on exactly same number of observations.[a]

Exposure	**Model 3**	**Model 3 + prevalent hypertension and physical activity[e]**
$PM_{2.5}$[b]	0.99 (0.90 – 1.07)	0.97 (0.89 – 1.05)
$PM_{2.5}$ abs[b]	0.97 (0.89 – 1.06)	0.95 (0.87 – 1.04)
PM_{10}[b]	1.02 (0.91 – 1.15)	1.01 (0.91 – 1.13)
PM coarse[b]	1.02 (0.91 – 1.14)	1.00 (0.90 – 1.12)
NO_2	1.01 (0.95 – 1.07)	1.00 (0.95 – 1.06)
NO_x	1.02 (0.98 – 1.06)	1.01 (0.98 – 1.05)
Traffic intensity on the nearest road[c]	1.01 (0.97 – 1.05)	1.01 (0.97 – 1.05)
Traffic intensity on major roads 100m buffer[d]	0.99 (0.88 – 1.11)	0.99 (0.88 – 1.10)
	Model 3	**Model 3 + prevalent hypertension, physical activity , prevalent diabetes, and cholesterol level[f]**
$PM_{2.5}$[b]	0.98 (0.90 – 1.07)	0.97 (0.89 – 1.06)
$PM_{2.5}$ abs[b]	0.96 (0.86 – 1.08)	0.94 (0.85 – 1.04)
PM_{10}[b]	1.01 (0.91 – 1.12)	1.00 (0.92 – 1.10)
PM coarse[b]	1.02 (0.91 – 1.14)	0.99 (0.88 – 1.11)
NO_2	1.00 (0.94 – 1.06)	1.00 (0.94 – 1.05)
NO_x	1.02 (0.97 – 1.06)	1.01 (0.97 – 1.05)
Traffic intensity on the nearest road[c]	1.02 (0.98 – 1.05)	1.01 (0.97 – 1.05)
Traffic intensity on major roads 100m buffer[d]	0.99 (0.88 – 1.12)	0.99 (0.88 – 1.11)
	Model 3	**Model 3 + noise (continuous)[g]**
$PM_{2.5}$[b]	1.14 (0.92 – 1.40)	1.11 (0.89 – 1.39)
$PM_{2.5}$ abs[b]	1.00 (0.83 – 1.21)	0.90 (0.73 – 1.11)
PM_{10}[b]	1.05 (0.89 – 1.23)	1.04 (0.87 – 1.24)
PM coarse[b]	1.06 (0.89 – 1.25)	1.04 (0.91 – 1.19)
NO_2	0.99 (0.90 – 1.09)	0.96 (0.85 – 1.09)
NO_x	1.03 (0.97 – 1.09)	0.99 (0.91 – 1.08)
Traffic intensity on the nearest road[c]	1.03 (0.99 – 1.08)	1.02 (0.98 – 1.06)
Traffic intensity on major roads 100m buffer[d]	1.04 (0.88 – 1.23)	0.97 (0.79 – 1.19)
	Model 3	**Model 3 + noise (categorical (5 dB))[g]**
$PM_{2.5}$[b]	1.14 (0.92 – 1.40)	1.12 (0.90 – 1.41)
$PM_{2.5}$ abs[b]	1.00 (0.83 – 1.21)	0.94 (0.76 – 1.16)
PM_{10}[b]	1.05 (0.89 – 1.23)	1.04 (0.87 – 1.24)
PM coarse[b]	1.06 (0.89 – 1.25)	1.04 (0.90 – 1.22)
NO_2	0.99 (0.90 – 1.09)	0.97 (0.85 – 1.10)
NO_x	1.03 (0.97 – 1.09)	0.99 (0.91 – 1.08)
Traffic intensity on the nearest road[c]	1.03 (0.99 – 1.08)	1.02 (0.98 – 1.07)
Traffic intensity on major roads 100m buffer[d]	1.04 (0.88 – 1.23)	0.98 (0.80 – 1.20)

[a] HRs are presented for the following increments: 10 µg/m^3 for NO_2, 20 µg/m^3 for NO_x, 5 µg/m^3 for $PM_{2.5}$, 10^{-5} m^{-1} for $PM_{2.5}$ absorbance, 10 µg/m^3 for PM_{10}, 5 µg/m^3 for PM_{coarse}, 5,000 motor vehicles/day for the traffic intensity on the nearest road, and 4,000,000 motor vehicles*m/day for the total traffic load on all major roads within a 100m buffer

[b] PM not available for EPIC-Umeå, EPIC-Varese and EPIC-San Sebastian. For E3N and SAPALDIA PM was available for part of the cohort (see Table 1)
[c] Not available for EPIC-Varese and EPIC-San Sebastian
[d] Not available for EPIC-Varese
[e] Hypertension and physical activity available for all cohorts, except SALIA, VHM&PP, SIDRIA-Turin and SIDRIA-Rome (only hypertension), and SAPALDIA (no info)
[f] Diabetes available for all cohorts, except SALIA, VHM&PP, and SAPALDIA. Cholesterol level available for EPIC-Umeå, FINRISK, HUBRO, KORA, VHM&PP, and E3N.
[g] Noise data available for FINRISK, HUBRO, SNACK, SALT, 60-yr/IMPROVE, DCH, EPIC-MORGEN, EPIC-PROSPECT, SALIA, KORA, SIDRIA-Turin, and EPIC-Turin

eAppendix 9: Meta-analyses results (HRs and 95%-CIs) for association between CVD mortality and exposure to NO_2 and $PM_{2.5}$ stratified for age, gender, smoking status, educational level, fruit intake and BMI

Table 1: Adjusted association between CVD mortality and exposure to NO_2 and $PM_{2.5}$ stratified for age, gender, smoking status, educational level, fruit intake and BMI: Results from random-effects meta-analyses (HRs and 95%-CIs). Last column denotes p-value whether there is statistical difference between strata.
Only cohorts with results for each stratum for a variable were included in the meta-analysis for that variable.

	NO_2[a]	$PM_{2.5}$[a]	p-value
Age[b]			
- <60 years	0.99 (0.88 – 1.11)	0.88 (0.64 – 1.21)	NO_2: 0.52
- 60-75 years	1.05 (0.97 – 1.15)	1.10 (0.92 – 1.30)	$PM_{2.5}$: 0.48
- >= 75 years	0.99 (0.92 – 1.07)	1.02 (0.86 – 1.20)	
Gender[c]			
- Women	1.00 (0.95 – 1.05)	0.88 (0.78 – 1.00)	NO_2: 0.75
- Men	1.01 (0.95 – 1.08)	1.08 (0.96 – 1.22)	$PM_{2.5}$: 0.02
Smoking status[d]			
- Current	0.98 (0.90 – 1.07)	1.00 (0.78 – 1.29)	NO_2: 0.72
- Former	1.02 (0.95 – 1.10)	1.01 (0.82 – 1.24)	$PM_{2.5}$: 0.94
- Never	1.01 (0.97 – 1.06)	0.97 (0.88 – 1.08)	
Educational level[e]			
- Low	1.04 (0.97 – 1.13)	1.13 (0.91 – 1.39)	NO_2: 0.13
- Medium	1.05 (0.98 – 1.13)	1.18 (0.92 – 1.51)	$PM_{2.5}$: 0.22
- High	0.93 (0.83 – 1.03)	0.81 (0.57 – 1.16)	
Fruit intake[f]			
- < 150 g/day	0.99 (0.90 – 1.08)	1.04 (0.72 – 1.50)	NO_2: 0.59
- 150-300 g/day	1.05 (0.96 – 1.14)	1.06 (0.75 – 1.50)	$PM_{2.5}$: 0.99
- >= 300 g/day	0.98 (0.86 – 1.12)	1.03 (0.75 – 1.41)	
BMI[g]			
- < 25 kg/m^2	1.02 (0.96 – 1.08)	0.89 (0.77 – 1.02)	NO_2: 0.98
- 25-30 kg/m^2	1.01 (0.96 – 1.06)	1.04 (0.91 – 1.19)	$PM_{2.5}$: 0.17
- >= 30 kg/m^2	1.01 (0.94 – 1.09)	1.08 (0.89 – 1.30)	

[a] HRs are presented for the following increments: 10 μg/m^3 for NO_2, and 5 μg/m^3 for $PM_{2.5}$
[b] Included cohorts: FINRISK, SALT, EPIC-PROSPECT, SALIA, EPIC-Oxford, KORA, VHM&PP, E3N, EPIC-Varese, EPIC-Athens
[c] Included cohorts: All cohorts, except EPIC-PROSPECT, SALIA, E3N (which consisted of women only)
[d] Included cohorts: All cohorts
[e] Included cohorts: All cohorts, except VHM&PP
[f] Included cohorts: EPIC-Umeå, DCH, EPIC-MORGEN, EPIC-PROSPECT, EPIC-Oxford, E3N, EPIC-Varese, EPIC-Turin, EPIC-San Sebastian, EPIC-Athens
[g] Included cohorts: All cohorts, except SALIA, SIDRIA-Turin, SIDRIA-Rome