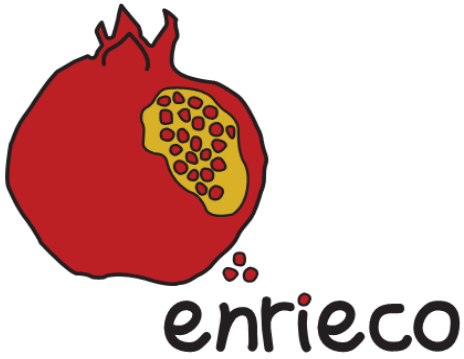
The ENRIECO Project:

ENVIRONMENTAL HEALTH **R**ISKS IN **E**UROPEAN BIRTH **CO**HORTS



ENV-FP7-2008-226285

Deliverable 15

Scientific Paper

Evaluation of Environmental Information and Recommendations

Work Package 2

Work Package Leader:	Ulrike Gehring, PhD
Working Group leaders:	Cecile Chevrier, Sylvaine Cordier, Ulrike Gehring, Joachim Heinrich, Thomas Keil, Mark Nieuwenhuijsen, Jordi Sunyer, , Gunnar Toft, Martine Vrijheid, Magnus Wickman
Participants:	Ferran Ballester, Anna Bergström, Jens Peter Bonde, Jeremie Botton, Bert Brunekreef, Lex Burdorf, Elisabeth Cardis, Maribel Casas, Chih-Mei Chen, Cécile Chevrier, Ann Colles, Sylvaine Cordier, Payam Dadvand, Yvonne de Kluizenaar, Elly Den Hond, Anke Huss, Merete Eggersbo, Maria Pia Fantini, Ulrike Gehring, Regina Grazuleviciene, Eva Hallner, Kiviranta Hannu, Cynthia Hohmann, Ilias Kavouras, Thomas Keil, Lorenza Luciano, Åsa Neuman , Mark Nieuwenhuijsen, Anne-Marie Nybo-Andersen, Mattias Öberg, Vicky Patelarou, Göran Pershagen, Claire Petit, Frank Pierik, Kinga Polanska, AC Santos, Greet Schoeters, Remy Slama, Claudia Snijder, Jordi Sunyer, Christina Tischer, Gunnar Toft, Stéphanie Vandentorren, Constantine Vardavas, Martine Vrijheid, Tanja Vrijkotte, Michael Wilhelm,
Deliverable:	15
Title:	Environmental exposure information in European birth cohorts: results from the ENRIECO project
Nature:	R
Dissemination level:	PU (following scientific publication)
Planned:	Month 21
Actual:	30 November 2010 (original) 27 February 2011 (revised)

Abstract

Many European pregnancy and birth cohorts are studying environment-health relationships. In order to improve the collaboration among these birth cohort studies and the use of existing data within these studies and to facilitate collaborative projects, an inventory of the environmental exposure and health data in existing European birth cohort studies was made as part of the European Union funded **EN**vironmental health **RI**sks in **E**uropean birth **CO**horts (ENRIECO) project.

Small working groups consisting of experts in the field evaluated the information from the inventory regarding different exposures (outdoor air pollution, water contamination, allergens and biological organisms, metals, pesticides, smoking and second hand tobacco smoke, persistent organic pollutants and other chemical pollutants, noise, and occupational exposures) and made recommendations for future research. This paper presents a summary of the experts' evaluations and recommendations with regard to environmental exposure assessment in European birth cohort studies.

Data from 34 cohorts was evaluated. All cohorts had some information on second hand tobacco smoke exposure and many cohorts assessed occupational exposures (n=29), exposure to allergens and biological organisms (n=27) and outdoor air pollution (n=23). Assessment of exposure to water contaminants, metals, pesticides, radiations, persistent organic pollutants, and noise was limited to fewer (n=11-16) cohorts. Exposure to cat and dog allergens, moulds, radiations, smoking and second hand tobacco smoke, noise, and occupation were mainly assessed by means of questionnaires. Exposure to metals, persistent organic pollutants and other chemicals such as Bisphenol A, phthalates and phenols was mainly assessed by means of biomonitoring. Exposure to house dust mites was exclusively assessed by means of environmental monitoring and exposure to water contaminants was mostly assessed by means of a combination of environmental measurements and questionnaire information on water-related behaviors. Because exposure to pesticides occurs through varying pathways (household use, food, occupational exposure, residential exposure through agricultural activities, etc.) the assessment methods used in the cohorts are multiple and variable. There is little standardization of exposure assessment methods between cohorts, as these were usually funded locally, and for different reasons. Some exceptions include collaborative studies

within the more established fields of outdoor air pollution, water contamination, and indoor exposure.

Recommendations for future research within cohorts include the performance of validation studies, the assessment of the role of the timing of the exposure in addition to the level, the inclusion of time-activity pattern and non-residential exposures in the exposure assessment; recommendations for future research with existing data as well as new data and new follow-ups.

Introduction

Epidemiological studies have shown associations between environmental hazards and adverse child health outcomes. The fetus and infant are especially vulnerable to the exposure to environmental risk factors that disrupt developmental processes. Major environmental hazard such as ambient air pollution, water contaminants, allergens/ biological organisms, environmental tobacco smoke (ETS), noise pollution, pesticides, radiation, toxic wastes, and ultraviolet (UV) light may lead to serious health problems including premature birth, low birth weight, respiratory diseases, cancer, learning disabilities, behavioral problems, cancer, and birth defects, and may affect health in later life.

The economic and societal costs associated with children's environmental health disorders are substantial. Many birth cohohrt studies conducted in Europe have attempted to address these issues. However, generally, the wealth of available information has only been partially exploited, partly because of the lack of statistical power of single studies to study rare health outcomes or exposures with a low prevalence. Therefore, there is an urgent need to evaluate, and where possible combine, the existing exposure response data, methods and tools from European birth cohort studies in order to reveal any causal links between exposing agents and health and to provide recommendations for effective policy decisions to improve children's environmental health and reduce economic and societal costs.

Many European pregnancy and birth cohorts are studying environment-health relationships, but many times sample sizes are too small to lead to conclusive results on their own in particular if health outcomes and exposures with low prevalence are studied. Sometimes apparently inconsistent or opposite results are reported. Environmental exposure assessment often is thought to be the weakest part in the studies as a result of lack of funding and expertise, and could be improved. Nevertheless, these cohorts often contain high quality data in many areas such as health outcomes and possible confounders and have a team of highly experienced researchers working on them with great expertise and commitment.

In order to improve the collaboration between existing birth cohort studies and the use of existing data within these studies and to facilitate collaborative projects, an inventory of the environmental exposure and health data in existing European birth cohort studies was made as part of the European Union funded ENvironmental health RIsks in European birth COhorts

(ENRIECO) project. Small working groups consisting of experts in the field evaluated the information from the inventory regarding different exposures (outdoor air pollution, water contamination, allergens and microbial agents metals, pesticides, other chemicals, smoking and second hand tobacco smoke, persistent organic pollutants, noise, and occupational exposures) and made recommendations for future research. This paper presents a summary of the experts' evaluations and recommendations with regard to environmental exposure assessment in European birth cohort studies.

Methods

Participating cohorts

A detailed description of the definition and identification of cohorts for the ENRIECO project can be found elsewhere (ref inventory paper). In brief, cohorts were included in an inventory if they a) collected data on at least one of the following exposures: air pollution, water contamination, allergens and biological organisms, metals, pesticides, persistent organic pollutants, other chemical pollutants, noise, and radiations ; b) started enrolment of mothers into the cohort during pregnancy or at birth; c) included in their protocol at least one follow-up point after birth with direct contact with mothers and children; d) included at lest 200 mother-child pairs; and d) were based in a European country. All cohorts fitting these criteria were considered regardless of whether data had been published or recruitment of subjects was still ongoing. An overview of the inventory is published elsewhere (ref). A web-based searchable inventory database is now publically available on www.birthcohorts.eu (also accessible through www.birthcohorts.net).

Evaluation of exposure information

The work was divided in 11 exposure groups: outdoor air pollution, water contamination, allergens and microbial agents metals, pesticides, other chemical pollutants (e.g. Bisphenol A, phthalates and phenols), smoking and second hand tobacco smoke, persistent organic pollutants, noise, and occupational exposures. Small working group consisting of experts in the field evaluated the information for the different exposure topics. A list of the names of the

experts who participated in the different working groups is presented in supplementary Table 1.

The main aims of the evaluations were a) to provide a review of the available environmental exposure data from European birth cohort studies and b) to give recommendations for future research in European birth cohorts, either as individual cohorts or by pooling cohorts. For the evaluations a detailed protocol was developed, which is available on the ENRIECO website www.enrieco.org.

The evaluations of the exposure information that is available in the cohort studies were largely based the ENRIECO inventory. In brief, between March 1, 2009 and February 14, 2011 cohorts completed inventory questionnaires with detailed information on the study protocol, exposure and health outcome assessment. Evaluations included a description of the current available data of European birth cohorts; details on protocols; and evaluations of assessment methods including the comparability of methods and protocols between studies. For the evaluation of available assessment methods, other sources of information such as (where available) existing review articles; CDC; WHO (Air quality guidelines for Europe); IPCS (International Programme on Chemical Safety-Environmental Health Criteria Monographs (EHCs)-Chemical Safety Information from Intergovernmental Organizations (INCHEM)) were included.

The recommendations for future research in European birth cohorts given by the working groups, to a large extent depended on expert judgment. Recommendations included recommendations for individual cohorts as well as recommendations for pooling cohorts and recommendations for exposure assessment methods. It also included recommendations for potential further use of methods and tools in cohorts where they did not exist or where there had been insufficient use with an emphasis on methods that are appropriate and feasible within the context of birth cohort studies.

The full working group reports are available on the project's website www.enrieco.org . In the reports some other studies that did not strictly match our criteria of a birth cohort study were included. For example, some studies that have not conducted follow-up after birth (Aarhus Birth Cohort Study in Denmark and APREG in Hungary) and others that did not collect data on the environmental exposures defined in our criteria, but do have data on, for example, maternal occupation and passive tobacco smoke exposure. These cohorts are not described in

this paper. Data for three other cohorts (ArcRisk in Norway, DARC in Denmark, PARIS in France) became available after the reports had been written and therefore are not included in the reports, but will be included in this paper.

Results

On February 14, 2011, data were collected from a total of 36 different birth cohorts in Europe (counting the cohorts of the Faroes, the old INMA cohorts and the new INMA cohorts as one cohort each) and entered into the database. All cohorts did have some information on smoking and second hand tobacco smoke exposure and many cohorts assessed occupational exposures (n=32), exposure to allergens and biological organisms (n=26) and outdoor air pollution (n=26). Fewer cohorts assessed exposure to metals (n=19), persistent organic pollutants (including persistent organochlorine pesticides, n=17) and other chemical exposures (Bisphenol A, phthalates and phenols, n=19) and very few cohorts assessed exposure to water contaminants (n=11), radiations (n=12), and noise (n=14).

Table 1 provides an overview of the contribution of the birth cohorts to the different exposure topics, the methods used and the status of the work. A more detailed description of the exposure assessment in the cohorts is provided in Table 2 and in the full reports. Exposure modeling is becoming the method of choice for air pollution exposure assessment. Exposure to cat and dog allergens, moulds, radiations, smoking and second hand tobacco smoke, noise, and occupation were mainly assessed by means of questionnaires. Exposure to metals, persistent organic pollutants and other chemicals such as Bisphenol A, phthalates and phenols was mainly assessed by means of biomonitoring. Exposure to house dust mites was exclusively assessed by means of environmental monitoring and exposure to water contaminants was mostly assessed by means of a combination of environmental measurements and questionnaire information on water-related behaviors. Because exposure to pesticides occurs through varying pathways (household use, food, occupational exposure, residential exposure through agricultural activities, etc.) the assessment methods used in the cohorts are multiple and variable. The assessment of household use and occupational exposures to pesticides by means of questionnaires and the assessment of persistent organochlorine pesticides by means of biomonitoring were most common in the cohorts.

Exposure information was generally available for the vast majority of the study participants if exposure is assessed by means of exposure modeling, questionnaires, routinely collected data or a combination of these. Biomonitoring was sometimes performed in addition (e.g. for assessment of exposure to water contaminants, smoking and second hand tobacco smoke exposure) usually for a small subset of the study population for validation purposes. For other exposures such as pesticides, persistent organic pollutants, Bisphenol A, phthalates and phenols, where exposure assessment largely relied on biomonitoring, the situation was different. Most of the smaller cohorts (ArcRisk, Duisburg, Faroes, FLEHS, INMA old and new, LUKAS, PCB cohort, and REPRO_PL) with roughly up to 1,300 participants tried to measure at least some of the biomarkers in the whole cohort, whereas the larger cohorts performed biomonitoring in a subset of a cohort's population.

There was little standardization of exposure assessment methods between cohorts and even if the same method was used, protocols varied largely between cohorts. For example, different questionnaires were used in different cohorts; there were no standardized protocols for the collection and analysis of individual environmental samples (e.g. house dust samples were collected from different surfaces at different locations in the participants' homes and analyzed for allergens with different assays); and biomonitoring was done in different media (e.g. polychlorinated biphenyls (PCBs) were analyzed in breast milk, cord blood, placenta, serum and whole blood). Some exceptions include studies in which a standardized exposure assessment was part of a collaborative effort, such as the TRAPCA and ESCAPE studies for outdoor air pollution, the HIWATE study for water contamination, the AIRALLERG and HITEA studies for indoor exposures including allergens and microbial agents; combustion products; and second hand tobacco smoke.

Exposure to water contaminants and noise was mainly assessed during pregnancy; exposure to metals was mainly assessed at birth (Table 3). Exposures to persistent organic pollutants, pesticides, other chemicals, and occupational exposures were often assessed during pregnancy and/or at birth. Information on occupational exposures before pregnancy is also available in many cohorts. Exposure to outdoor air pollution has mainly been assessed for pregnancy and/or early life; exposure to allergens and biological contaminants was mainly assessed during infancy and early childhood (Table 3). Repeated exposure assessments that allow the study of changes in exposure as well as the role of the timing of exposure were available for

some exposure topics (e.g. outdoor air pollution, allergens and biological organisms, smoking and second hand tobacco smoke exposure).

A number of exposures (cat and dog allergens, moulds, household use of pesticides, radiations, smoking and second hand tobacco smoke, noise, and occupation) were mainly assessed by means of questionnaires, sometimes in combination with environmental measurements (water contamination). Very often, these questionnaires have not been validated against a more direct exposure assessment method such as biologic or environmental monitoring. Exceptions are the validation of questionnaire data on smoking and second hand tobacco smoke against air nicotine levels [1,2] and urine cotinine levels [1] and the validation of questionnaire data on water contamination against biomonitoring data in some cohorts. Likewise, there are few validations of modeled exposures (ambient air pollution) or surrogate variables (e.g proximity to agricultural activities as a proxy for bystander exposure to pesticides) against individual environmental monitoring. Since the validity of the exposure assessment is crucial in the study of health effects related to a certain exposure, the implementation of validation studies is strongly recommended (Table 3).

Other recommendations for methods as well as recommendations for future work with existing and new data are presented in Table 3. Recommendations for future work vary between exposures and largely depend on the amount of research that has already been done within the European birth cohort studies. While for some exposures, combined analyses have been performed/are being performed within the framework of EU-collaborative projects (e.g. for outdoor air pollution, water contamination, allergens and biological contaminants) there is currently not sufficient data for data pooling/combined analyses for others (e.g. radiations, Bisphenol A, phtalates and phenols).

Discussion

The European birth cohorts collected a wealth of data on environmental exposures. All 36 cohorts had some information on smoking and second hand tobacco smoke exposure many cohorts assessed occupational exposures (n=32), exposure to allergens and biological organisms (n=26) and outdoor air pollution (n=26). Fewer cohorts assessed exposure to metals (n=19), persistent organic pollutants (including persistent organochlorine pesticides, n=17) and other chemical exposures (Bisphenol A, phthalates and phenols, n=19) and very few cohorts assessed exposure to water contaminants (n=11), radiations (n=12), and noise

(n=14). Main assessment methods were exposure modeling (outdoor air pollution), questionnaires (cat and dog allergens, moulds, radiations, smoking and second hand tobacco smoke, noise, and occupation), biological monitoring (metals, persistent organic pollutants and other chemicals such as Bisphenol A, phthalates and phenols), environmental monitoring (house dust mites) and a combination of environmental measurements and questionnaires (water contamination). Because exposure to pesticides occurs through varying pathways assessment methods used in the cohorts were multiple and variable. Few validation studies comparing estimated exposures from questionnaires and models with more direct exposure assessment methods such as biological and environmental monitoring have been performed so far and therefore, the performance of validation studies is strongly recommended. Other recommendations including recommendations for methods and recommendations for future research with existing and new data are summarized and discussed below.

Standardization

There is little standardization of exposure assessment methods between cohorts, as these were usually funded locally, and for different reasons. Some exceptions include collaborative studies within the more established fields of outdoor air pollution, water contamination, and indoor exposure where a standardized exposure assessment was added to varying numbers of existing birth cohort studies (e.g. TRAPCA [3-5], ESCAPE, HIWATE, AIRALLERG [6,7] and HITEA). Heterogeneity in exposure assessment methods may result in inconsistencies in exposure-response relationships between studies and limit the possibilities for combined and/or meta-analyses. Therefore, the standardization of exposure assessment methods has been recommended by many groups. For exposures that were (mainly) assessed by means of biomonitoring (i.e. metals, pesticides, persistent organic pollutants, and other chemical pollutants), the performance of inter-laboratory comparisons and either the standardization of the exposure assessment with regard to the sampling medium or the development of conversion factors has been recommended to facilitate combined analyses (Table 3). However, it should be noted that standardization may reduce the possibility of comparing different methods, and this may not in all cases be beneficial.

Validity

Exposure assessment by means of individual environmental or biological measurements is costly and therefore usually not feasible in large cohort studies. Often, questionnaires are used instead to assess exposures. The validity of questionnaires for the assessment of pet allergen and mould exposure as well as second hand tobacco smoke and water contaminants exposure has been assessed in a number of studies. Despite some misclassification, questionnaire reports were found to be an inexpensive and valid estimate of residential environmental tobacco smoke exposure among preschool and school children [1,2,8]. The specificity of questionnaire information on cat- and dog-ownership for cat and dog allergen levels in settled house dust was found to be high, but the sensitivity was found to be low.[9-12] Similarly, it has been shown that questionnaire data cannot be used as a surrogate for measurements of specific microbial components such as endotoxin, gram positive bacteria and mould components in house dust[13-15]. In other fields (e.g. household use of pesticides, non-ionizing radiation) where exposure assessment largely relies on questionnaires, such validation studies are still lacking and were recommended by the experts involved in this project.

Furthermore, often little is known about the long(er)-term validity of a single exposure assessment for a longer period. For example, land-use regression models that are currently used very often for outdoor air pollution exposure assessments are based on one measurement campaign during which air pollution concentrations are measured at a number of locations. Few validation studies have been performed so far. Some evidence comes from the Dutch PIAMA study, where it has been shown that the original TRAPCA-model was highly predictive (R^2=0.80) of NO_2 concentrations measured at the same sites almost ten years later [16]. Similarly it has been shown that there is a high correlation between measurements of persistent organic pollutants performed as much as 10 years apart [17]. Furthermore, there is some evidence that a single endotoxin measurement is a valid estimate of exposure for longer time periods. [18-21] Within-home correlation was found to be considerable for living room floor dust samples over a period of 6 years (r=0.5 for endotoxin loads [21]) and somewhat higher for bed (r=0.7-0.8) [18] and bedroom floor dust samples (r=0.6) [20] over periods of up to13 months. For non-persistent compounds such as bisphenol A and phtalates, that have short half lives and that are rapidly excreted from the body, the long(er)-term validity of a single measurement is limited and therefore it is recommended to collect multiple samples at different time points.

Timing of exposure assessment

For many exposures, we presently know very little about the relevance of the timing of the exposure in addition to the level of exposure, and it is unclear whether exposure during a specific period when organs develop and are considered being more susceptible, is more important than later exposure. Prospective birth cohort studies with repeated exposure and health outcome assessments offer a unique possibility to increase our knowledge with regard to the temporal variability of exposure and the relevance of exposure during different time periods. Therefore repeated exposure assessments have been recommended by several groups (e.g. air pollution, allergens and biological contaminants, second hand tobacco smoke exposure, noise, and persistent organic pollutants). Collecting data before birth or before any adverse health event is crucial whenever exposure assessment relies on maternal self-report (i.e. occupational exposures, exposure to persistent organic pollutants and pesticides).

Time-activity pattern, exposure at non-residential addresses and residential mobility

Individual assessment of exposures such as air pollution, water contaminants, noise and bystander pesticide exposure individual by means of personal or biomonitoring alone will generally not be feasible in birth cohorts, as the study populations generally comprise several hundreds to thousands of subjects, living or attending school/daycare at different places. Therefore, environmental exposure assessment in the European birth cohorts currently is often limited to residential exposure although study participants regularly spend considerable amounts of their time outside their homes for instance at day care centers or schools where they may be exposed as well, possibly to higher levels of exposure (e.g. to higher levels of air pollution if a school is located in the vicinity of a highway). Consequently, little is known about the role of residential and non-residential exposure in the association between these exposure and health. Validation studies comparing estimated residential exposures with personal exposure measurements are scarce for basically all exposures. Some recent publications on the effects of ambient air pollution where exposure was estimated as a time-weighted average of several addresses where the participants spent considerable amounts of time indicated little differences between the estimated exposure at the home address and the time-weighted average exposure.[14-17] This needs further evaluation and therefore, we recommend collecting information on residential history in birth cohort studies. Time-activity pattern, exposure at non-residential addresses and residential mobility are currently rarely

included in the assessment of air pollution, water contaminants, noise and bystander pesticide exposure, but should be included in future studies to improve exposure assessment.

Recommendations for future analyses

Statistical power of analyses of relationship between exposure and health outcomes in single cohorts can be low if the number of subjects is small or the frequency of the exposure is low. Data pooling and/or meta-analysis of multiple cohorts can overcome this problem. Combined analyses have been performed/are being performed within the framework of EU-collaborative projects such as TRAPCA (air pollution) [3,4,22] GA2LEN (allergens) [23], AIRALLERG (allergens and biological contaminants) [6,7], ESCAPE (air pollution) and HIWATE (water contamination). In addition, for exposures to moulds, second hand tobacco smoke, and persistent organic pollutants, combined analyses have been performed as part of the case studies of the current ENRIECO project to explore the feasibility, potentials and difficulties of merging partly heterogeneous data from different European pregnancy and birth cohort studies. Moreover, the possibility of performing a combined analysis of the impact of occupational exposures on birth weight has been identified as part of another ENRIECO case study. One conclusion from the case study is that combining data from various cohorts requires careful consideration of the aims, protocols, data, ethical issues, analyses and management, and it is time and labor intensive but potentially fruitful. One challenge of the case study on persistent organic pollutants was the development of conversion factors to facilitate combined analyses with persistent organic pollutant measurements performed in different media. Lessons learned from these case studies are very valuable when considering/planning similar case studies on other exposures such as metals. For ionizing, non-ionizing and UV radiations, there is currently not sufficient data available in the cohorts for data pooling. Likewise, for non-ionizing radiations and other chemical contaminants, there is currently not enough data in the cohorts for data pooling exercises, but many measurements are ongoing and comparison studies may be feasible within the next few years. For the other chemical exposures, especially for brominated flame retardants and polyfluorinated compounds, conversion models will be needed to transfer between different biological media and between different time points. Few cohorts performed objective assessments of noise exposure. Combined analyses are considered possible, but should be carefully balanced against the loss of validity due to differences in exposure assessment. Further opportunity to study the environmental exposures such as water contaminants and pesticides in the cohorts

making use of routinely collected data and data from Geographical Information Systems, respectively, have been identified

Recommendations for future work with new data, new follow-ups and new cohorts vary largely between exposure topics and are generally very specific. The recommendation to perform (some of) the validations studies discussed above and the inclusion of non-residential exposures and time-activity pattern in exposure assessment have been made by several groups. Moreover, some working groups recommended the assessment of exposures that have not been assessed in the cohort studies (e.g. outdoor air pollution: ultrafine particles; water contamination: non-regulated substances such as pharmaceuticals, PFOS/PFOA and (other) endocrine disruptors; radiation: medical radiation exposure; use of mobile phones and other telecommunication equipment). Recommendations for exposure assessment by questionnaire have been made by several groups (UV, non-ionizing radiations, second hand tobacco smoke, noise, and occupational exposures). Inter-laboratory comparisons have been recommended by the group working on persistent organic pollutants. Recommendations for future work with new data also include recommendations for the use of new technologies such as Geographical Information Systems and satellite imaging for assessment of pesticide exposure and molecular methods or DNA fingerprinting for assessment of microbial exposures. For chemical exposures the need to develop a framework in Europe for the detection and prioritization of new chemicals in cohort studies, closely linked to toxicologists, has been expressed. The evaluation of possible links with other cohort studies has been recommended for ionizing radiations.

References

1. Gehring U, Leaderer BP, Heinrich J, Oldenwening M, Giovannangelo ME, Nordling E et al. Comparison of parental reports of smoking and residential air nicotine concentrations in children. *Occup Environ Med* 2006; 63:766-72.

2. Brunekreef B, Leaderer BP, van Strien R, Oldenwening M, Smit HA, Koopman L et al. Using nicotine measurements and parental reports to assess indoor air: the PIAMA birth cohort study. Prevention and Incidence of Asthma and Mite Allergy. *Epidemiology* 2000;11:350-2.

3. Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer PH, Wijga A et al. Air pollution from traffic and the development of respiratory infections and asthmatic and allergic symptoms in children. *Am J Respir Crit Care Med* 2002;166:1092-8.

4. Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U et al. Estimating Long-Term Average Particulate Air Pollution Concentrations: Application of Traffic Indicators and Geographic Information Systems. *Epidemiology* 2003;14:228-39.

5. Gehring U, Cyrys J, Sedlmeir G, Brunekreef B, Bellander T, Fischer P et al. Traffic-related air pollution and respiratory health during the first 2 yrs of life. *Eur Respir J* 2002;19:690-8.

6. Chen CM, Gehring U, Wickman M, Hoek G, Giovannangelo M, Nordling E et al. Domestic cat allergen and allergic sensitisation in young children. *Int J Hyg Environ Health* 2008;211:337-44.

7. Gehring U, Heinrich J, Hoek G, Giovannangelo M, Nordling E, Bellander T et al. Bacteria and mould components in house dust and children's allergic sensitisation. *Eur Respir J* 2007;29:1144-53.

8. Marbury MC, Hammond SK, Haley NJ. Measuring exposure to environmental tobacco smoke in studies of acute health effects. *Am J Epidemiol* 1993;137:1089-97.

9. Chew GL, Burge HA, Dockery DW, Muilenberg ML, Weiss ST, Gold DR. Limitations of a home characteristics questionnaire as a predictor of indoor allergen levels. *Am J Respir Crit Care Med* 1998;157:1536-41.

10. Gehring U, Triche E, Van Strien RT, Belanger K, Holford T, Gold DR et al. Prediction of residential pet and cockroach allergen levels using questionnaire information. *Environ Health Perspect* 2004;112:834-9.

11. Bollinger ME, Eggleston PA, Flanagan E, Wood RA. Cat antigen in homes with and without cats may induce allergic symptoms. *J Allergy Clin Immunol* 1996;97:907-14.

12. Nafstad P, Magnus P, Gaarder PI, Jaakkola JJ. Exposure to pets and atopy-related diseases in the first 4 years of life. *Allergy* 2001;56:307-12.

13. Sordillo J, Alwis U, Hoffman E, Gold D, Milton D. Home characteristics as predictors of bacterial and fungal microbial biomarkers in house dust. *Environ Health Perspect* 2011;119:189-95.

14. Giovannangelo M, Gehring U, Nordling E, Oldenwening M, Terpstra G, Bellander T et al. Determinants of house dust endotoxin in three European countries - the AIRALLERG study. *Indoor Air* 2007;17:70-9.

15. Giovannangelo ME, Gehring U, Nordling E, Oldenwening M, van Rijswijk K, de Wind S et al. Levels and determinants of beta(1-->3)-glucans and fungal extracellular polysaccharides in house dust of (pre-)schoolchildren in three European countries. *Environ Int* 2007;33:9-16.

16. Eeftens M, Beelen R, Fischer P, Brunekreef B, Meliefste K, Hoek G. Stability of measured and modelled spatial contrasts in NO2 over time. *Occup Environ Med* 2011;In press.

17. Hagmar L, Wallin E, Vessby B, Jonsson B, Bergman A, Rylander L. Intra-individual variations and time trends 1991-2001 in human serum levels of PCB, DDE and hexachlorobenzene. *Chemosphere* 2006;64:1507-13.

18. Park JH, Spiegelman DL, Burge HA, Gold DR, Chew GL, Milton DK. Longitudinal study of dust and airborne endotoxin in the home. *Environ Health Perspect* 2000;108:1023-8.

19. Heinrich J, Holscher B, Douwes J, Richter K, Koch A, Bischof W et al. Reproducibility of allergen, endotoxin and fungi measurements in the indoor environment. *J Expo Anal Environ Epidemiol* 2003;13:152-60.

20. Abraham JH, Gold DR, Dockery DW, Ryan L, Park JH, Milton DK. Within-home versus between-home variability of house dust endotoxin in a birth cohort. *Environ Health Perspect* 2005;113:1516-21.

21. Topp R, Wimmer K, Fahlbusch B, Bischof W, Richter K, Wichmann HE et al. Repeated measurements of allergens and endotoxin in settled house dust over a time period of 6 years. *Clin Exp Allergy* 2003;33:1659-66.

22. Gehring U, Bolte G, Borte M, Bischof W, Fahlbusch B, Wichmann H-E et al. Correction: Exposure to endotoxin decreases the risk of atopic eczema in infancy: A cohort study. *J Allergy Clin Immunol* 2002;109:648.

23. Eller E, Roll S, Chen CM, Herbarth O, Wichmann HE, von Berg A et al. Meta-analysis of determinants for pet ownership in 12 European birth cohorts on asthma and allergies: a GA(2)LEN initiative. *Allergy* 2008;63:1491-8.

Table 1. Methods used for assessment of environmental exposures in the European birth cohorts.

Cohort	N[a]	Exposure										
		Outdoor air pollution	Water contamination	Allergens & biol. organisms	Metals	Pesticides [b]	POPs [c]	Other chemicals [d]	Radiations	Smoking and Second hand tobacco smoke [e]	Noise	Occupation
ABCD	78,63	M			Q	Q			Q, M*, E*	Q		Q
ALSPAC	14,062			Q	B	Q	B*	B*	Q, G	Q, B	Q, E	Q
ArcRisk	431				B		B	?*		Q		Q
BAMSE	4,089	M, E, S		Q, E						Q, B, E		Q
BiB	13,000	M*, E	E, Q, B							Q		Q
Co.N.ER	654	S*		Q						Q	Q	Q
Czech	7577	E								Q, B		Q
DARC	562	S		Q						Q		Q
DNBC	96,986	M, S		Q		Q		B	Q	Q		Q
Duisburg	234	S	Q	Q	B		B	B		Q, B*		Q
EDEN	1873	M, E, S	E*, Q*		B, Q			B	Q	Q		Q
ELFE	20,000	M*, E*	Q*	E *	B*	Q*, B*	B*	B*, Q*	Q*, M*, G*	Q*, B*		Q*, B*
Cohorts of the Faroes												
Cohort I	1,022				B, Q		B			Q		Q
Cohort II	182				B		B			Q		Q
Cohort III	656				B, Q		B			Q		Q
Cohort V	491				B*, Q	Q	B*	B*		Q		Q
FLEHS	1,196	E, S		Q	B, Q	Q	B	Q		Q		Q
GAPS II	708	M, S		Q						Q	Q, M	
Generation R	9,778	M		Q		Q, E, B*	B*	B, Q		Q	Q, M	Q, B
Generation XXI	8,666			Q						Q		Q
GINIplus	5,991	M		Q						Q, B, E		
HUMIS	2,500	S		Q	Q	Q	B	B, Q	Q, E	Q		Q
INMA old												
Granada	668	M, S	E, Q, B	Q	B*	Q	B	B, Q	Q	Q, B	Q	Q
Menorca	482	?*		Q, E	B*		B	B	Q	Q		Q
Ribeira Ebre	102		E, Q	Q	B*, Q		B	B*, Q	Q*	Q, B*		Q
INMA new												
Asturias	485	M, E, S	E, Q	Q, E	B, Q	Q	B	B	Q	Q, B*	Q	Q
Gipuzkoa	611	M, E, S	E, Q	Q	B, Q	Q	B	B	Q	Q, B*	Q	Q
Sabadell	622	M, E, S	E, Q	Q, E	B, Q	Q	B	B	Q	Q, B*	Q	Q
Valencia	787	M, E, S	E, Q	Q	B, Q	Q	B	B	Q	Q, B*	Q	Q
INUENDO	1,322				?*	Q*	B*	B		Q		Q
KANC	4,000	M	E, Q							Q	Q, M	Q
KOALA	2,934		Q	Q					Q*	Q	Q	Q

Table 1. (continued).

Cohort	N[a]	Exposure										
		Outdoor air pollution	Water contamination	Allergens & biol. organisms	Metals	Pesticides [b]	POPs [c]	Other chemicals [d]	Radiations	Smoking and Second hand tobacco smoke [e]	Noise	Occupation
Leicester Respiratory Cohorts	5,400	M, S		Q						Q		Q
LISAplus	3,097	M, S		Q, E		Q*				Q, B, E	Q, M	
LUKAS	442			Q, E	B, Q	Q	B	B, Q		Q		Q
MAS	1,314			Q, E						Q, B	Q	Q
MoBa	107,400	M	Q	Q*	Q*	Q, B	B*	B	Q	Q	Q	Q
NINFEA	7,500	M*, S		Q	Q	Q		Q*	Q*	Q	Q	Q
PARIS	3,840	M	Q	Q, E						Q, E		Q
PCB cohort	1,134				B	Q	B	B*		Q		Q
PELAGIE	3,460		Q, E, B		B*	Q, E, B	B*	B		Q		Q
PIAMA	3,963	M, S		Q, E						Q, E		
REPRO_PL	1,800	E, B, S		Q	B, Q		B*			Q	Q	Q
RHEA	1,500	M*, S	Q, E	Q	B	Q	B*	B*	Q	Q, B	Q	Q, B

[a] Number of children participating in the study; [b] Organochlorine pesticides are under POPs; [c] Persistent Organic Pollutants; [d] Bisphenol A, phthalates and phenols; [e] prenatal and/or postnatal active and/or passive smoking

M: modeling, E: environmental monitoring, B: biomonitoring, Q: questionnaires; G: Geographical data; S: surrogate variables from questionnaires or Geographical Information Systems; ? unknown

* planned

Table 2. Description of exposure assessment in the ENRIECO birth cohorts by exposure topic.

Exposure topic	N *	Description
Outdoor air pollution	26	• Air pollution modeling is becoming increasingly the method of choice: land-use regression modeling (16 cohorts) and dispersion modeling (9 cohorts) • Fifteen cohorts are currently participating in the collaborative EU-funded ESCAPE project that adds land-use regression modeling of nitrogen oxides, particulate matter, soot and particle composition to existing cohort studies using a standardized protocol • Most cohorts currently have data on exposure during pregnancy and/or early life
Water contamination	12	• Disinfection by-products were studied most • Exposure assessment usually by means of a combination of questionnaires and individual measurements or routinely collected measurement data • Validation by means of biomonitoring in a small number of subjects • Most studies assessed exposure during pregnancy
Allergens & biological organisms	26	• Exposure to cat and dog allergen was assessed by means of questionnaires in all cohorts; by means of measurements in house dust samples in 7 cohorts • Mite allergen levels were measured in settled house dust samples in 8 cohorts • Mould exposure was mainly assessed by means of questionnaires • Exposure was assessed during infancy and/or early childhood in most studies
Metals	19	• Most cohorts have analyzed the effects of low-level environmental exposure to Hg and Pb; little attention to other metals (As, Cd, etc) • There are well-standardized protocols for most of the metals • The ICP-MS and the AAS analytical techniques were used most • Most measurements were performed in cord blood; other non-invasive matrices such as hair and urine are gaining attention
Pesticides [a]	18	• Many studies assessed household use (14 cohorts); fewer studies assessed occupational (11 cohorts) or dietary exposure (7 cohorts) • Exposures via household use, occupational exposure and diet, were mainly assessed by means of questionnaires
Persistent organic pollutants	17	• Exposure assessment by means of high performance liquid chromatography (HPLC) measurements in biological samples with adjustment for lipid content • Variation between studies with regard to sampling medium, timing of sample collection and lipid adjustment • Most data available for polychlorinated biphenyl (PCB) and dichlorodiphenyltrichloroethane (DDT)
Other chemical exposures [b]	19	• Few cohorts have measured these contaminants, but this is a rapidly developing field and many cohorts are planning to assess exposure to emerging contaminants • There is heterogeneity with regard to the type of biological media used and the timing of the exposure measurements

Table 2. Description of exposure assessment in the ENRIECO birth cohorts by exposure topic.

Exposure topic	N *	Description
Outdoor air pollution	26	• Many cohorts assessed outdoor air pollution exposure • Air pollution modeling is becoming increasingly the method of choice: land-use regression modeling (16 cohorts) and dispersion modeling (9 cohorts) • Fifteen cohorts are currently participating in the collaborative EU-funded ESCAPE project that adds land-use regression modeling of nitrogen oxides, particulate matter, soot and particle composition to existing cohort studies using a standardized protocol • Most cohorts currently have data on exposure during pregnancy and/or early life
Water contamination	12	• Disinfection by-products were studied most • Exposure assessment usually by means of a combination of questionnaires and individual measurements or routinely collected measurement data • Validation by means of biomonitoring in a small number of subjects • Most studies assessed exposure during pregnancy
Allergens & biological organisms	26	• Exposure to cat and dog allergen was assessed by means of questionnaires in all cohorts; by means of measurements in house dust samples in 7 cohorts • Mite allergen levels were measured in settled house dust samples in 8 cohorts • Mould exposure was mainly assessed by means of questionnaires • Exposure was assessed during infancy and/or early childhood in most studies
Metals	19	• Most cohorts have analyzed the effects of low-level environmental exposure to Hg and Pb; little attention to other metals (As, Cd, etc) • There are well-standardized protocols for most of the metals • The ICP-MS and the AAS analytical techniques were used most • Most measurements were performed in cord blood; other non-invasive matrices such as hair and urine are gaining attention
Pesticides [a]	18	• Many studies assessed household use (14 cohorts); fewer studies assessed occupational (11 cohorts) or dietary exposure (7 cohorts) • Exposures via household use, occupational exposure and diet, were mainly assessed by means of questionnaires
Persistent organic pollutants	17	• Exposure assessment by means of high performance liquid chromatography (HPLC) measurements in biological samples with adjustment for lipid content • Variation between studies with regard to sampling medium, timing of sample collection and lipid adjustment • Most data available for polychlorinated biphenyl (PCB) and dichlorodiphenyltrichloroethane (DDT)
Other chemical exposures [b]	19	• Few cohorts have measured these contaminants, but this is a rapidly developing field and many cohorts are planning to assess exposure to emerging contaminants • There is heterogeneity with regard to the type of biological media used and the timing of the exposure measurements

Table 2. (continued).

Exposure topic	N *	Description
Radiations	12	*Non-ionizing radiations* • *Mainly assessed by questionnaire:* maternal occupational exposures (3 cohorts), prenatal medical ionizing radiation exposures (6 cohorts); 2 cohorts currently plan to ask questions about medical radiation exposures in children • 1 cohort is planning to assess residential radon exposure using geographical methods • No standardized questionnaires or protocols in this field *UV* • Only *six* cohorts are collecting UV-related data through questionnaire questions on sunburn in children, use of sun beds during pregnancy, and time spent outdoors. • *None* of the cohorts collect data on maternal and child skin type, sunscreen use, or clothing. • Standard questionnaires are not available. *Non-ionizing radiations* • Very few cohorts assess exposure to non-ionizing radiations: 2 cohorts include occupational EMF exposure in their questionnaires, 2 cohorts assess ELF exposure to overhead high-voltage power lines through geographical information from electricity companies, 2 cohorts include questions about mobile phone use of the mother during pregnancy and 4 on children's mobile phone use. • A few cohorts have started using base-station maps combined with information from home appliances and personal RF exposimeters, in order to estimate whole body RF/ELF-EMF exposure. • There are no standardized or validated questionnaires, models or protocols in use at this moment.
Smoking and second hand tobacco smoke	36	• All cohorts have information about exposure during pregnancy and 30 cohorts in addition assessed exposure at different periods during infancy and childhood • Assessment mainly by questionnaire; cotinine measurements in biological samples (mainly urine) in 11 cohorts
Noise	14	• All cohorts used questionnaire assessments, mainly annoyance • 5 cohorts used noise propagation modeling or noise maps • Traffic is the source of noise that has been studied most • Most cohorts assessed exposure during pregnancy

Table 2. (continued).

Exposure topic	N *	Description
Occupational exposures	32	• All cohorts have information on maternal occupation and most cohorts (n=26) have information on paternal occupation at at least one point in time • Data mainly collected by means of questionnaires (most often job title; sometimes checklist occupation or occupational exposures) • Coding of maternal job title (n=16) or use of Job Exposure Matrices (JEM) (n=6) planned/done in a number of studies

* N = Number of cohorts with exposure assessment; [a] Organochlorine pesticides are under persistent organic pollutants; [b] Bisphenol A, phthalates and phenols

Table 3. Recommendations for methods, future work with existing data and future work with new data by exposure topic.

Exposure topic	Methods	Future work with existing data	Future work with new data
Outdoor air pollution	• Exposure modeling is currently the state-of the art method • Few studies so far compared land-use regression models with dispersion models; results are inconsistent • Residential mobility, time-activity pattern, and exposure at non-residential addresses should be evaluated in exposure assessment • Assessment of long-term validity of land-use regression models which are based on one measurement campaign • There is currently little validation of modeled exposures against personal exposure measurements	• Within the ESCAPE project, a standardized exposure assessment is being added to a number of birth cohort studies and will soon be linked to existing health data in these cohorts; pooled analyses will be performed for a number of health endpoints	• Assessment of long-term exposure to ultrafine particles, which are currently not being assessed within cohort studies.
Water contamination	• Best method for exposure assessment is to combine information of water-related behaviors obtained by questionnaire with newly or routinely collected water contaminant measurements • Validation of questionnaires against biomonitoring since it has been conducted in only a few subjects • Assessment of variability and measurement error of questionnaires by repeated assessments	• Further opportunity to study exposure to water pollutants in cohorts without water exposure assessment; routinely collected water pollutants are often available • Consideration of source of water as an exposure indicator (ground water vs surface water) • Data pooling currently being done in the HIWATE project • Access to publicly collected data should be increased and European databases should be made available to researchers	• Assessment of exposure to non-regulated substances such as pharmaceuticals, PFOS/PFOA and (other) endocrine disrupters in addition to assessment of regulated substances

Table 3. (continued).

Exposure topic	Methods	Future work with existing data	Future work with new data
Allergens & biological organisms	• Measurements in house dust or air samples are recommended • Use of questionnaires is inexpensive, but questionnaires were found to have a low sensitivity • Exposure at non-residential locations and timing of exposure should be taken into account	• Meta-analyses in the framework of the GA2LEN (allergens) and AIRALLERG projects (allergens and biocontaminants) and ENRIECO case study on mould and dampness	• Use of newly developed analysis techniques such as molecular methods or DNA fingerprinting
Metals	• Human biological monitoring is the state of the art method for estimation of total dose. • ICP-MS is more sensitive and faster than AAS. • In general labs are using well standardized protocols. It is recommended to validate the analytical technique in each lab including a sample with known concentration of metal/s every X number of samples. This will be useful to validate both the pre-treatment and the analytic process. • Some studies compared Hg levels in biological samples with fish/shellfish consumption assessed through validated food frequency questionnaires with encouraging results. More studies are needed to confirm these findings. For other metals, validation of other exposure assessment methods must be further explored.	• Data pooling and/or meta-analysis of the data available in the European birth cohorts can overcome this problem if conversion models can be developed to transfer between different biological media (hair, cord blood, urine, etc.).	• Validation of questionnaire data against human biological monitoring is needed.

Table 3. (continued).

Exposure topic	Methods	Future work with existing data	Future work with new data
Pesticides	• There are multiple pesticides and multiple pathways of exposure conducing to varying exposure assessment • Biomonitoring hardly feasible for large cohorts, but recommended on sub-populations for validation purposes and identification of main exposure sources • There is a need for standardization of exposure assessment by biomonitoring (choice of molecules of interest, biological matrices, sampling and storage conditions, chemical analyses controlled by international comparison programs, etc.) between studies • Validation of questionnaires needed • Inclusion of exposure at non-residential locations may improve exposure assessment	• Since few cohorts assessed exposure to pesticides there is a large scope of doing more work on pesticide exposure within the European birth cohorts, particularly by analyzing available biological samples • Use of Geographical Information System technologies with existing European data on soil occupancy and satellite imagings/maps of crops to assess bystander exposure due to agricultural activities	• Include validation studies in exposure assessment • Assessment of time-activity pattern and exposure at non-residential locations
Persistent organic pollutants	• HPLC derived methods are the state of the art for measurements of POPs • All analyzing laboratories should participate in inter-laboratory calibration tests. • Especially for detecting POPs in low concentrations in small volumes equipment with a high sensitivity is needed. • The persistence of organochlorines makes sample degradation a lesser problem as for other more readily degradable compounds. However, it is recommended to store samples at -80 ºC at least, if measurements are planned to be performed after several years.	• The possibility to perform a pooled or meta-analysis on the association between exposure to POPs and birth outcomes in the European birth cohorts have been evaluated within a case study that is part of ENRIECO. • Data pooling was possible for PCB, DDT and hexachlorbenzene. For other POPs there is little data or too much heterogeneity with regard to the sampling media or the timing of exposure assessment. • Conversion factors needed to be developed to allow pooling of data.	• There is high degree of variability between studies in study design including timing of sample collection and collection medium. Therefore additional data collection according to a standardized protocol may be needed, especially if the outcomes of interest are hypothesized to be related to exposure at specific time windows during fetal life or early childhood.

Table 3. (continued).

Exposure topic	Methods	Future work with existing data	Future work with new data
Other chemical exposures (Bisphenol A, phtalates and phenols)	• Human biological monitoring is the state of the art method for estimation of total dose • Lipophilic *BFRs*, particularly PBDEs, are best measured in blood serum (maternal, cord, or child) or breast milk; *PFCs* are best analyzed in blood (serum or plasma, maternal or cord) • Since PBDE levels are low, extremely sensitive methods are needed. • It is highly recommended that conversion factors are developed to transfer from concentrations in one medium/time point to another. Pooling of studies for future analyses will then be possible. • For non-persistent exposures with very short half-lives, such as *phthalates* and *BPA*, multiple measurements of these chemicals at different time points during pregnancy will greatly improve exposure assessment. • Issues of contamination from storage materials and lab equipment, and storage conditions are of great importance and need to be addressed in depth. • It is recommended to conduct a European evaluation of inter- and intra-laboratory variability. • Validation of other exposure assessment methods such as questionnaires, occupational JEMs, environmental measurements, and/or toxicokinetic models is needed.	• There is currently not enough data in the cohorts for data pooling exercises, but many measurements are ongoing and within 1 or 2 years there will be possibilities for comparison studies. • For pooling or meta-analysis studies, conversion models will need to be developed to transfer between different biological media and between different time periods, especially for *BFRs* and *PFCs* where very different media and time periods are being measured. • As most cohorts use urine for their measurement of *BPA* and *phthalates*, pooling studies will be possible in this field but these will require more information on inter laboratory variability. •	• This is an emerging field and there is a rapidly growing expertise in the cohorts, which would benefit from continued communication and coordination. • Cohorts should work together on developing conversion models and inter laboratory comparisons that will allow future comparison and pooling studies. • Mechanisms need to be developed for the detection and prioritization of new chemicals in cohort studies. • Coordination with other European projects will be crucial to harmonize research on emerging exposures in the birth cohorts in Europe • Assessment of medical radiation exposure •

Table 3. (continued).

Exposure topic	Methods	Future work with existing data	Future work with new data
Radiations	*Ionizing radiations* • Assessment of medical radiation exposures (X-ray, CT-scan) by standardized questionnaires • Assessment of occupational exposure by means of badge dose information or if not possible by questions on x-ray equipment and protective equipment used • Assessment through job-exposure matrices probably difficult	• Existing data are not sufficient for pooled studies.	• Evaluation of link with other EUROPEAN cohorts of children exposed to CT scans
	UV • ENRIECO has developed a set of core questions on sun exposure for different exposure-time windows that is recommended for use in cohort studies	• Existing data are not sufficient for pooled studies	• Inclusion of vitamin D and UV exposure related questions in cohort questionnaires.
	Non-ionizing radiations • Use of core set of standardized questions to assess mobile and cordless phone use • Validation of questionnaires using information of other types of studies • Coordination between cohorts in developing validated exposure models for RF and ELF-EMF • Future collaborative efforts focusing on design of questions related to other RF-EMF sources (e.g. WiFi, new communication technologies, microwave ovens, baby phones)	• Comparison studies with existing data comparing questionnaire data between cohorts	• Integration of standardized questions on use of mobile phones and other telecommunications equipment in future questionnaires to facilitate future combined analyses of non-cancer effects
Smoking and second hand tobacco smoke	• Questionnaires are most suitable method for larger epidemiological studies and for assessment of long-term exposure • Relevance of the timing of the exposure (before conception; during pregnancy, infancy, childhood or later in life) is not clear. Large studies can enhance knowledge if exposure is assessed repeatedly during different time periods.	• Combined analyses on the effects of pre- and postnatal exposure to second hand tobacco smoke have been performed within a case study that is part of ENRIECO	• Large studies with close monitoring of second-hand tobacco smoke exposure before conception, during trimesters of pregnancy and during the first year of life to disentangle the role of exposure during different periods • Specific questions recommended for the different exposure periods

Table 3. (continued).

Exposure topic	Methods	Future work with existing data	Future work with new data
Noise	• Objective measures should be in accordance with END guidelines • Noise propagation modeling is recommended for large studies • Subjective noise assessments by questionnaire e.g. annoyance related to specific sources of noise should be performed in addition to objective measures • Standard scales for the assessment of noise annoyance can be recommended • Information on non-residential exposures, time-activity pattern and insulation of buildings, window opening behavior, position of bedroom in relation to source of noise should be included in exposure assessment	• Few European cohorts currently have data from objective noise assessments that could be combined • The accuracy gained by pooling data should be carefully balanced against the loss of validity due to differences in assessments	• Inclusion of objective and subjective exposure assessments • Assessment of time-activity pattern
Occupational exposures	• A number of Job Exposure Matrices (JEMs) have been built in Europe that cover different periods of time and different types of exposures. • JEMs need to be validated against objective measures of exposure (work environment, biomarkers) • If JEMs are used country- and agent-specific JEMs should be since work environments differ between countries and time periods. • To avoid any influence of birth outcome on the availability of occupational information and on its quality, we recommend that data should be collected before birth. This is mandatory when questionnaires on occupational exposures are used and optional for job title. • The period of interest is around conception and each trimester - or at least one trimester of pregnancy (depending on the health outcome studied) for mothers, and before conception for fathers.	• Within the ENRIECO project, the possibility to perform pooled/meta-analyses of the association between adverse health outcomes and selected occupations of mothers and fathers during vulnerable periods has been explored; 14 cohorts are eligible for this analysis, 12 have already expressed their interest. A protocol for the analysis has been developed.	• For an adequate data collection on occupational exposures job title is not sufficient. In addition, one should collect description of task, type of industry, number of hours per week, and if possible name of company, existence of biomonitoring data. Free text should be kept in the data base for additional details. • A good training of coders should be organized for standardization. • Standardized questionnaires for physical load should be published

Supplemetary Table 1. Experts who participated in the different working groups.

Exposure	WG-group leader	Participants (birth cohort)
Outdoor air pollution	Ulrike Gehring u.gehring@uu.nl	Ferran Ballester, Ann Colles, Vicky Patelarou, Frank Pierik, Kinga Polanska, Bert Brunekreef
Water contamination	Mark Nieuwenhuijsen mnieuwenhuijsen@creal.cat	Sylvaine Cordier, Vicky Patelarou, Maribel Casas, Jeremie Botton
Allergens & biological organisms	Joachim Heinrich joachim.heinrich@helmholtz-muenchen.de	Chih-Mei Chen, Christina Tischer, Ulrike Gehring, Constantine Vardavas
Metals	Jordi Sunyer jsunyer@creal.cat	Ferran Ballester, Kinga Polanska, Constantine Vardavas, Michael Wilhelm, Maribel Casas
Pesticides	Cecile Chevrier cecile.chevrier@rennes.inserm.fr	Frank Pierik, Stephanie Vandentorren, Sylvaine Cordier, Claire Petit
Persistent organic pollutants	Gunnar Vase Toft gunntoft@rm.dk	Jens Peter Bonde, Remy Slama, Michael Wilhelm, Greet Schoeters, Vicky Patelarou, Stephanie Vandentorren, Hannu Kiviranta, Merete Eggersbo
Other chemical exposures	Martine Vrijheid mvrijheid@creal.cat	Maribel Casas, Elly Den Hond, Ilias Kavouras, Frank Pierik, Stéphanie Vandentorren, Gunnar Vase Toft, Michael Wilhelm
Radiations	Martine Vrijheid mvrijheid@creal.cat	Maribel Casas, Elisabeth Cardis, Payam Dadvand, Mark Nieuwenhuijsen; External Experts: Anke Huss, Roel Vermeulen
Smoking and second hand tobacco smoke	Magnus Wickman magnus.wickman@ki.se	Anna Bergström, Ulrike Gehring . Eva Hallner, Cynthia Hohmann, Thomas Keil, Åsa Neuman, Göran Pershagen, Mattias Öberg
Noise	Thomas Keil thomas.keil@charite.de	Cynthia Hohmann, Yvonne de Kluizenaar, Maria Pia Fantini, Lorenza Luciano, Frank Pierik
Occupation	Sylvaine Cordier sylvaine.cordier@univ-rennes1.fr	Jens Peter Bonde, Lex Burdorf, Frank Pierik, Claudia Snijder, Merete Eggesbo, Mark Nieuwenhuijsen, Anne-Marie Nybo-Andersen, Manolis Kogevinas, Vicky Patelarou, Tanja Vrijkotte, AM Garcia, Martine Vrijheid, Regina Grazuleviciene, Ana Cristina Santos; External experts : J Févotte, Hans Kromhout, Nel Roeleveld, Martie Van Tongeren