

Review Article

Pregnancy and Birth Cohort Resources in Europe: a Large Opportunity for Aetiological Child Health Research

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Abstract

Background: During the past 25 years, many pregnancy and birth cohorts have been established. Each cohort provides unique opportunities for examining associations of early-life exposures with child development and health. However, to fully exploit the large amount of available resources and to facilitate cross-cohort collaboration, it is necessary to have accessible information on each cohort and its individual characteristics. The aim of this work was to provide an overview of European pregnancy and birth cohorts registered in a freely accessible database located at <http://www.birthcohorts.net>.

Methods: European pregnancy and birth cohorts initiated in 1980 or later with at least 300 mother–child pairs enrolled during pregnancy or at birth, and with postnatal data, were eligible for inclusion. Eligible cohorts were invited to provide information on the data and biological samples collected, as well as the timing of data collection.

Results: In total, 70 cohorts were identified. Of these, 56 fulfilled the inclusion criteria encompassing a total of more than 500 000 live-born European children. The cohorts represented 19 countries with the majority of cohorts located in Northern and Western Europe. Some cohorts were general with multiple aims, whilst others focused on specific health or exposure-related research questions.

Conclusion: This work demonstrates a great potential for cross-cohort collaboration addressing important aspects of child health. The web site, <http://www.birthcohorts.net>, proved to be a useful tool for accessing information on European pregnancy and birth cohorts and their characteristics.

Keywords: *European pregnancy birth cohort, cohort characteristics, cross-cohort collaboration.*

Introduction

Early-life exposures, such as environmental and parental lifestyle factors, may affect growth and development in fetal life and in childhood, and health across the life course.¹ Identification of key causal exposures during intrauterine and early life, as well as effective methods for preventing their adverse effects, have the potential to benefit both the individual and the society.² Over the last five decades, child mortality and morbidity have decreased in Europe, but considerable variation in these parameters still exists within and between countries, possibly due to variations in adverse exposures, as well as variations in disease prevention, e.g. through childhood vaccination. Also,

the fact that access to health care is free of charge in some countries but not in others, likely impacts childhood morbidity and mortality. Whereas eastern European countries mainly struggle with injuries and respiratory infections, other parts of Europe are challenged by asthma, allergies, obesity and neurodevelopmental disorders.²

In parallel with an increased interest in the early-life developmental origins of disease, many European pregnancy and birth cohorts have been established over the last 25 years. Cohort studies offer a unique opportunity to monitor early-life factors associated with variation in growth and development. With long-term follow-up, cohorts render it possible to explore exposures – including genetic, epigenetic,

socio-economic and lifestyle factors and environmental toxins – for later development of diseases. However, cohorts are expensive to maintain, and in order to fully exploit their potential in a cost-efficient way, existing cohorts and their characteristics should be made accessible to the global scientific community.

There is increasing evidence of the value of cross-cohort collaboration using pooled data from existing cohorts for determining robust genetic associations.³ The value of pooling data from two or more cohorts to address research questions on environmental or lifestyle exposures has also been illustrated in previous studies.^{4–6}

Accessible information on characteristics of existing pregnancy and birth cohorts, including basic details about enrolment, inclusion criteria and the data and biological samples collected, is essential for improving collaboration to better understand causality, e.g. through cross-cohort comparisons, and for improving statistical precision, e.g. by pooling data from different cohorts where this is appropriate. In addition, investigators of new pregnancy and birth cohorts could benefit from knowing about existing resources. Some cohort profile papers have been published in the *International Journal of Epidemiology* to improve access to and collaboration between cohorts.^{7–11} However, we are aware of only a few previous publications that summarise existing cohorts across geographical regions. These publications are mostly focused on subgroups of cohorts with specific exposures or outcomes of interest, such as environmental exposures and atopic diseases.^{12–14}

The main aim of this work was to provide an overview of pregnancy and birth cohorts in Europe and to summarise the characteristics of each cohort. This may facilitate greater collaboration across cohorts for the benefit of the global scientific community. Furthermore, the aim was to evaluate the potential of doing pooled analyses and to demonstrate the statistical implications of such cross-cohort collaboration.

Methods

Identification of cohorts

European pregnancy and birth cohorts were identified from multiple sources. First, we searched the web-based database located at <http://www.birthcohorts.net>. This database was founded in 2005 as part of the European FP5 programme research action: the Chil-

drenGenoNetwork. As part of the CHICOS project (<http://www.chicosproject.eu>) within the European FP7 programme, the database was redesigned to include detailed information on each cohort. This allows for identification of cohorts which collect information on specific exposures, outcomes or biological samples of interest. The database, <http://www.birthcohorts.net>, is not limited to include European cohorts only, but is open for registration of cohorts from around the world.

Second, we searched the list of cohorts that were identified by two EU funded research projects – the ENRIECO project (<http://www.enrieco.org>) and EUCCONET (<http://www.euconet.com>). The objective of the ENRIECO project was to advance knowledge on specific causal relationships between environmental exposures and child health through the coordination of pregnancy and birth cohorts.¹⁴ EUCCONET brings together leaders of international child cohorts in order to compare practices, exchange experience and share questionnaires and other tools.

Third, we identified published literature in PubMed using the following search terms: birth cohort, Europe, mother–child cohort, prospective cohort study. Also, we searched the reference lists of all identified papers retrieved via the earlier searches. Finally, we advertised <http://www.birthcohorts.net> at relevant conferences and workshops, and made contact with people whom we knew worked with pregnancy and birth cohorts in order to identify additional cohorts.

Between 1 September 2011 and 1 June 2012, we contacted all principal investigators (PIs) of the identified cohort. PIs of cohorts not already registered at <http://www.birthcohorts.net> were encouraged to register, and PIs of registered cohorts were encouraged to update their cohort profile through completion of a web-based questionnaire at <http://www.birthcohorts.net>. Each cohort was sent up to four reminders in order to be included in the present overview.

All identified European pregnancy and birth cohorts were included if they: (i) were initiated in 1980 or later; (ii) had enrolled at least 300 mother–child pairs either during pregnancy or at birth; (iii) had collected some postnatal data; and (iv) had completed the cohort profile questionnaire.

Extraction of information on cohort characteristics

The cohort profile questionnaire was divided into the following sections: (i) identification and contacts; (ii)

basic cohort description including sample size, enrolment and expected follow-up of the children; (iii) birth outcomes, child development and child health; (iv) child and parental exposures; (v) parental characteristics and reproductive history; (vi) parental health; and (vii) child and parental biological samples collected. The time point was recorded for each assessment of exposure and outcome, as well as for biological samples collected. For the purpose of this overview, characteristics of each of the included cohorts were extracted directly from <http://www.birthcohorts.net>, as of June 2012.

Identified cohorts and their characteristics

Identified cohorts

Initially, we identified 70 potentially eligible pregnancy and birth cohorts. Of these, 56 cohorts fulfilled the inclusion criteria (Table 1). The restriction to cohorts initiated in 1980 or later guarantees that these will reflect relatively contemporary exposures and practices across Europe, whilst allowing for some cohorts to have follow-up into early adulthood already. Cohorts with a sample size of fewer than 300 were excluded because we assumed that these would be unlikely to provide robust result. However, we admit that even small cohorts can contribute importantly to a number of research questions. Also, cohorts enrolling participants after birth or without follow-up of the children, as well as cohorts, which did not respond to the cohort profile questionnaire were excluded (Figure 1). Therefore, this overview is not completely comprehensive. Moreover, other cohorts not described here may exist, but given our extensive literature search and network of pregnancy and birth cohort researchers, we find it unlikely that we have missed substantial number of cohorts in this overview that fulfil our inclusion criteria.

Characterisation of included cohorts

In total, the 56 cohorts included in this overview together encompassed around half a million live-born European children. For many of the cohorts, extensive data on maternal exposures (and some on both parents) during pregnancy, as well as data on early-life developmental periods are available. The sample size of each cohort varied considerably from fewer

than 500 to more than 100 000 children. More than a third of the cohorts ($n = 22$) were general, in that they cover a broad range of exposures related to all aspects of child development, health and well-being. The remaining cohorts were established to address research questions related to one or two areas, such as environmental exposures and atopic disorders (Table 1).

Cohorts from all European regions (European regions as defined by the United Nations Statistics Division) were included, representing 19 European countries. The majority of the cohorts were, however, located in Northern and Western Europe ($n = 41$), and in high-income (Income-level as defined by The World Bank Group based on the country's gross national income per capita, in USD) countries ($n = 53$). The three largest cohorts were located in Scandinavia (Figure 2).

As of 1 June 2012, the majority of cohorts ($n = 47$) had completed enrolment of participants, three were open (or dynamic) cohorts with continuous enrolment, and six were still enrolling participants. One cohort enrolled participants before pregnancy, 34 enrolled during pregnancy and 21 enrolled at birth. Fifteen of the cohorts with enrolment at birth collected data on pregnancy exposures retrospectively (Table 1).

The oldest cohort enrolled participants during the period from 1982 to 1984,¹⁵ and the youngest cohort had just started enrolment.¹⁶ Most of the cohorts had completed several waves of follow-up of the children at different ages. More than half of the cohorts ($n = 32$) expected a lifelong follow-up, while the remaining only expected to follow-up the children during childhood and adolescence because child health was the focal point of these cohorts (Figure 3).

The majority of cohorts collected information on parental lifestyle exposures (e.g. diet, smoking, alcohol consumption, physical activity) during intrauterine and in the early period of life as well as information on parental occupational and environmental exposures (e.g. air pollution). Most of the cohorts collected information on maternal demographic and obstetric characteristics. Information on a wide range of pregnancy outcomes and information on child health was collected by all cohorts. Exposure and outcome data were collected from medical files or directly from participants either by questionnaires, interviews or by clinical assessments, but some cohorts also relied on information from routine

Table 1. Overview of included European pregnancy and birth cohorts and their characteristics

Cohort (Full name of cohort)	Country	Regions covered	Timing of enrollment	Prospective/retrospective collection of information on pregnancy exposures	Number of live-born children	Key scientific area
<i>ABC</i> (^a Aarhus Birth Cohort ²³)	Denmark	Aarhus	Pregnancy	Prospective	106 370	General with multiple aims
<i>ABCD</i> (Amsterdam-born Children and their development cohort ⁸)	Netherlands	Amsterdam	Pregnancy	Prospective	6161	General with multiple aims
<i>ABIS</i> (All babies in Southeast Sweden ²⁴)	Sweden	South Eastern Sweden	^d Birth	Retrospective	17 045	General with multiple aims
<i>ALSPAC</i> (Avon Longitudinal Study of Parents & Children/Children of the 90 s ⁷)	United Kingdom	Avon	Pregnancy	Prospective	14 062	General with multiple aims
<i>BAMSE</i> (Stockholm Children Allergy and Environmental Prospective Birth Cohort Study ²⁵)	Sweden	Stockholm	^d Birth	Retrospective	4089	Environmental exposures and asthma
<i>BASILINE</i> (Babies after scope: evaluating the longitudinal impact using neurological and nutritional endpoints ²⁶)	Ireland	Cork	Pregnancy	No collection of information on pregnancy exposures	2185	Fetal growth, early life exposures, multidisciplinary outcomes
<i>BIB</i> (Born in Bradford ²⁷)	United Kingdom	Bradford	Pregnancy	Prospective	13 776	General with multiple aims. A specific aim of comparing South Asian to White British populations
<i>BILD</i> (^a Bern-Basel-Infant Lung Development Cohort ²⁸)	Switzerland	Bern, Basel	Pregnancy	Prospective	488	Wheezing/asthma/allergy
<i>CCC2000</i> (Copenhagen Child Cohort ²⁹)	Denmark	Copenhagen	^d Birth	Retrospective	6090	Developmental trajectories of psychopathology and physical health
<i>CHEF-1</i> (Children's health and the environment in the Faeroes ³⁰)	Faroe Islands	Faroe Islands	Pregnancy	Prospective	1022	Environmental exposures and neurodevelopment
<i>CHEF-3</i> (Children's health and the environment in the Faeroes ³⁰)	Faroe Islands	Faroe Islands	Pregnancy	Prospective	656	Environmental exposures and neurodevelopment
<i>CHEF-5</i> (Children's health and the environment in the Faeroes ³⁰)	Faroe Islands	Faroe Islands	^d Birth	Retrospective	491	Environmental exposures and neurodevelopment
<i>CHOPIN</i> (Childhood Obesity: Early Programming by Infant Nutrition)	Germany	Munich	^d Birth	Retrospective	1678	Nutritional exposures and obesity
<i>Co.N.E.R.</i> (Bologna Birth Cohort ³¹)	Italy	Bologna	^d Birth	Retrospective	654	Environmental/nutritional exposures and wheezing/asthma/allergy
<i>CZECH</i> (Czech early childhood health ³²)	Czech Republic	Teplice, Prachatice	Birth	No collection of information on pregnancy exposures	7577	Environmental exposures and growth

Table 1. Continued

Cohort (Full name of cohort)	Country	Regions covered	Timing of enrolment	Prospective/retrospective collection of information on pregnancy exposures	Number of live-born children	Key scientific area
<i>DNBC</i> (Danish National Birth Cohort ³³)	Denmark	Denmark	Pregnancy	Prospective	94 837	General with multiple aims
<i>EDEN</i> (Study on the pre- and early-postnatal determinants of child health and development ³⁴)	France	Nancy, Poitiers	Pregnancy	Prospective	1907	General with multiple aims
<i>EHL</i> (^b Growing up in Wales: environments for healthy living ³⁵)	United Kingdom	Swansea	Pregnancy	Prospective	615	General with multiple aims
<i>ELFE</i> (Etude Longitudinale Française depuis l'Enfance ³⁶)	France	France	^d Birth	Retrospective	18 326	General with multiple aims
<i>FCOU</i> (Family and children of Ukraine ³⁷)	Ukraine	Kyiv, Dniprodzerzhynsk, Mariupol	Pregnancy	Prospective	4510	General with multiple aims
<i>G2I</i> (Generation XXI ³⁸)	Portugal	Porto	^d Birth	Retrospective	8647	General with multiple aims
<i>GASPII</i> (Genetic and environment: prospective study on infancy in Italy ^{31,39})	Italy	Rome	^d Birth	Retrospective	708	Environmental/nutritional exposures
<i>GECKO</i> (Groningen Expert Center for Kids with Obesity Drenthe Cohort ⁴⁰)	Netherlands	Drenthe	Pregnancy	Prospective	2997	Obesity
<i>Generation R⁴¹</i>	Netherlands	Rotterdam	Pregnancy	Prospective	9749	Environmental exposures, genetic factors and multidisciplinary outcomes
<i>GINIplus</i> (German Infant Study on the influence of Nutrition Intervention ⁴²)	Germany	Munich, Wesel	Birth	No collection of information on pregnancy exposures	5991	Lifestyle exposures
<i>GMS</i> (Gateshead Millennium Study ⁴³)	United Kingdom	North Eastern England	Birth	No collection of information on pregnancy exposures	1029	Lifestyle exposures
<i>HHF2</i> (Healthy habits for two ⁴⁴)	Denmark	Aalborg, Odense	Pregnancy	Prospective	11 144	Lifestyle exposures
<i>HUMIS</i> (Norwegian Human Milk Study ⁴⁵)	Norway	Rogaland, Telemark, Troms, Finnmark, Oppland, Akershus, Østfold	^d Birth	Retrospective (half the cohort)	2500	Microbial/POPs/ other environmental exposures and child health outcomes
<i>INMA</i> (INMA-Environment and Childhood Project ⁴⁶)	Spain	Ribera Ebre, Menorca, Granada, Valencia, Sabadell, Asturias, Gipuzkoa	Pregnancy	Prospective	3768	Environmental/nutritional exposures, genetic factors, and birth outcomes/ wheezing/ asthma/allergy/ growth/ neurodevelopment

Table 1. Continued

Cohort (Full name of cohort)	Country	Regions covered	Timing of enrolment	Prospective/retrospective collection of information on pregnancy exposures	Number of live-born children	Key scientific area
^a INUENDO (Human fertility at risk from biopersistent organochlorines in the environments ⁴⁷)	Sweden, Poland, Ukraine, Greenland, Lithuania	Sweden (east & west coast), Warsaw, Kharkiv, all regions in Greenland, Kaunas	Pregnancy	Prospective	1322	Environmental exposures semen quality and fertility
KANC (Kaunas Cohort ⁴⁸)			Pregnancy	Prospective	4405	Environmental exposures, genetic factors and birth outcomes, children wheezing/asthma/allergy/growth/ neurodevelopment
KOALA (KOALA Birth Cohort Study ⁴⁹)	Netherlands	Southern Netherlands	Pregnancy	Prospective	2834	Wheezing/asthma/allergy/growth/development
Kraków Cohort ⁵⁰	Poland	Kraków	Pregnancy	Prospective	505	Environmental exposures and birth outcomes/ neurodevelopment
^b LIFE Child <i>Lifeways Cross-Generation Cohort Study</i> ⁵¹	Germany	Leipzig	Pregnancy	Prospective	~2000	General with multiple aims
LISAplus (Influence of lifestyle factors on the development of the immune system and allergies in East and West Germany ⁵²)	Ireland, Germany	Dublin, Galway, Munich, Leipzig, Wesel, Bad Honnef	Pregnancy, Birth	Prospective, No collection of information on pregnancy exposures	1094, 3097	General with multiple aims, Environmental/nutritional exposures and wheezing/asthma/allergy
LRC (Leicester Respiratory Cohorts ⁵³)	United Kingdom	Leicestershire and Rutland	Birth	No collection of information on pregnancy exposures	10 650	Wheezing/asthma/cough/ growth/allergy
LUKAS ⁵⁴	Finland	Kuopio, Jyväskylä, Joensuu, Iisalmi	Pregnancy	Prospective	442	Microbial exposure and wheezing/asthma/allergy
MAS-90 (Multizentrische Allergie Studie ⁵⁵)	Germany	Berlin, Munich, Freiburg, Mainz, Düsseldorf	Birth	No collection of information on pregnancy exposures	1 314	Wheezing/asthma/allergy
<i>Merthyr Allergy Study</i> ⁵⁵	United Kingdom	Southern Wales	Pregnancy	Prospective	497	Environmental/nutritional exposures and wheezing/asthma/allergy
MoBa (Norwegian Mother and Child Cohort Study ⁵⁶)	Norway	Norway	Pregnancy	Prospective	108 500	General with multiple aims
MUBICOS (^b Multiple Births Cohort Study ⁵⁷)	Italy	Rome, Turin, Trieste, Bologna, Pisa, Foggia, Palermo	^d Birth	Retrospective	~1000	General with multiple aims
NINFEA (^b Nascita e INFanzia: gli Effetti dell'Ambiente ⁵⁸)	Italy	Italy	Pregnancy	Prospective	~7500	General with multiple aims
OCC (^b Odense Child Cohort)	Denmark	Odense	Pregnancy	Prospective	2 578	General with multiple aims

Table 1. Continued

Cohort (Full name of cohort)	Country	Regions covered	Timing of enrollment	Prospective/retrospective collection of information on pregnancy exposures	Number of live-born children	Key scientific area
PARIS (Pollution and Asthma Risk: an Infant Study) ²⁸⁾	France	Paris	^d Birth	Retrospective	3 840	Environmental exposures and wheezing/asthma/allergy
PÉLAGIE (Endocrine disruptors: longitudinal study on pathologies of pregnancy, infertility and childhood) ⁶⁶⁾	France	Brittany	Pregnancy	Prospective	4 000	Environmental exposures and
PIAMA (Prevention and incidence of asthma and mite allergy) ⁶¹⁾	Netherlands	Netherlands	Pregnancy	Prospective	3 963	Environmental/nutritional exposures and wheezing/asthma/allergy
<i>b</i>Piccoli⁴⁶⁾	Italy	Rome, Trieste, Firenze, Torino	^d Birth	Retrospective	2 000	General with multiple aims
PRIDE Study	Netherlands	Netherlands	Pregnancy	Prospective	502	General with multiple aims
^b PRenancy and Infant DEvelopment Study ¹⁶⁾	Poland	Lodz, Lask, Legnica Wrocław, Lublin, Szczecin, Piekary	Pregnancy	Prospective	1 647	General with multiple aims
REPRO_PL (Polish Mother and Child Cohort Study) ⁶⁵⁾		Slaskie, Katowice, Mikolow	Pregnancy	Prospective	1 590	General with multiple aims
RHEA (Mother child cohort in crete) ⁶⁴⁾	Greece	Heraklion	Pregnancy	Prospective	1 924	Nutritional exposures and wheezing/asthma/allergy
SEATON (Study of eczema and asthma to observe the effects of nutrition) ⁶⁵⁾	United Kingdom	Aberdeen	Pregnancy	Prospective	1 139	Environmental exposures
Slovak PCB Study (Early childhood development and PCB exposures in Slovakia) ⁶⁶⁾	Slovak Republic	Michalovce, Stropkov, Svidnik	^d Birth	Retrospective	1 139	Environmental exposures
SWS (Southampton Women's Survey) ⁶⁷⁾	United Kingdom	Southampton	Pre-pregnancy	Prospective	3 159	General with multiple aims
Trieste Cohort (Trieste child development cohort)	Italy	Trieste	Pregnancy	Prospective	900	Neurodevelopment
WHISTLER (Wheezing Illnesses Study in Leidsche Rijn) ⁶⁸⁾	Netherlands	Leidsche Rijn	^d Birth	Retrospective	2 923	Wheezing/asthma/allergy

^aOpen cohort – numbers of live-born children as of June 2012.

^bEnrolment not completed.

^cExpected number of children that will be enrolled in the cohort. The actual numbers may be slightly lower.

^dBirth cohorts that collect information on pregnancy exposures retrospectively.

^eThe INJENDO represents Greenland that is however not a part of the European continent geographically, but it is an autonomous country within the kingdom of Denmark and is therefore associated with Europe politically.

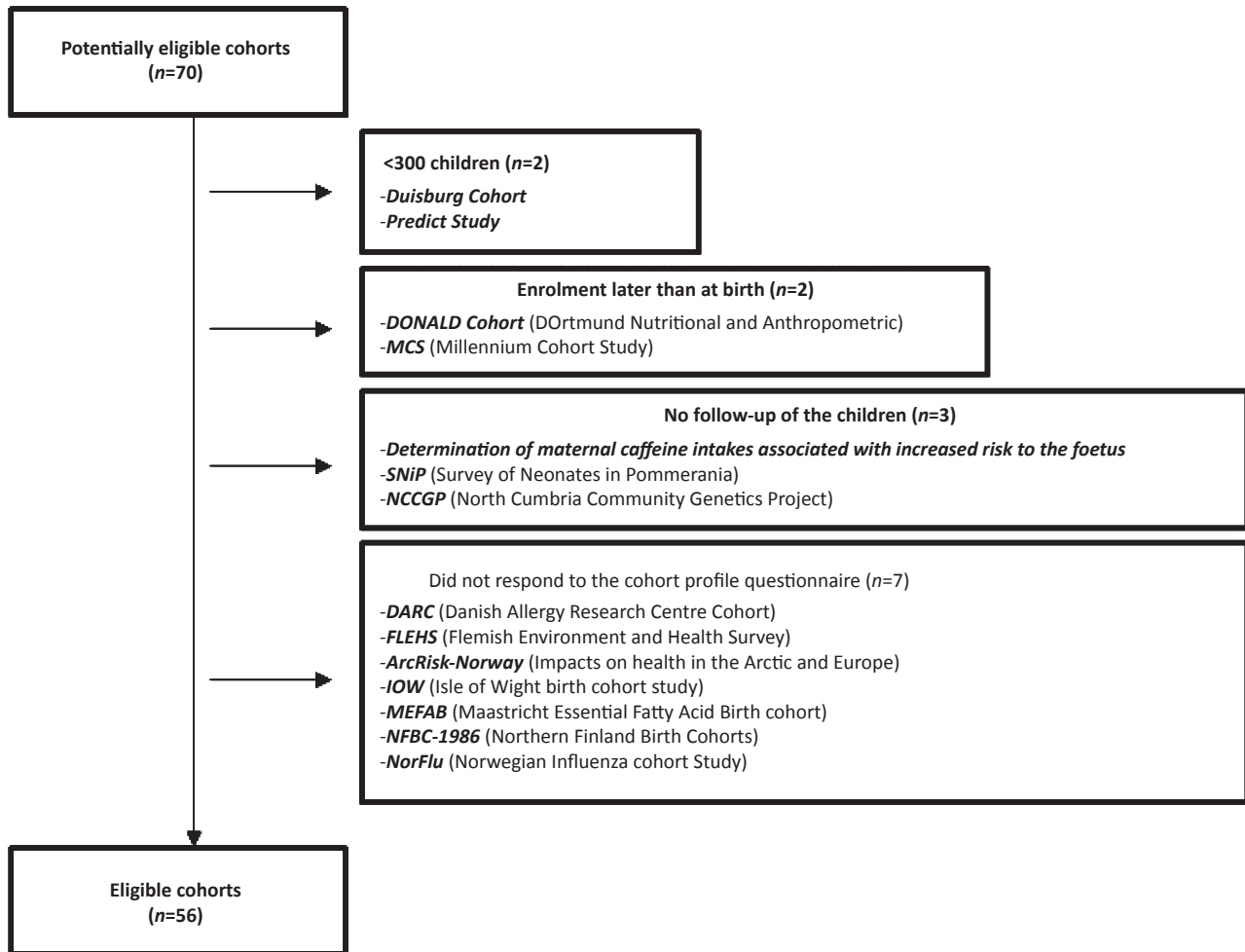


Figure 1. Overview of excluded pregnancy and birth cohorts.

health registers. Many of the cohorts collected biological samples, such as DNA from mother and/or child, although not all cohorts yet have DNA available for, say, genome-wide association studies and epigenome-wide association studies (Table 2). Also, several cohorts have analysed biological samples for biomarkers of environmental exposures, such as water contamination, metals, persistent organic pollutants (POPs) and smoking.¹⁷ It has, however, not been possible to determine the number or which of the included cohorts that have assessed environmental as well as nutrient exposures by means of biomonitoring.

From Figure 3, the data collection waves for each of the cohort appear. It should be noticed that not all exposure and outcome information, as well as biological samples have been collected at each follow-up of the children. What has been collected by the cohorts at

different ages of the children can be found at <http://www.birthcohorts.net>.

Why collaborate across cohorts?

The aetiology of some rare conditions, such as congenital heart defects and childhood epilepsy, could be, and has been explored using large cohorts built from existing disease and related registers which can be linked.^{18–20} For some research questions these registers are however unlikely to have data on relevant exposures. For example, biological samples as well as detailed questionnaire and physical examination data are rarely available in registers, which can assess exposures such as diet, physical activity, smoking, alcohol and body composition with reasonable accuracy. However, there are also other major reasons for using data from existing cohorts on a collaborative

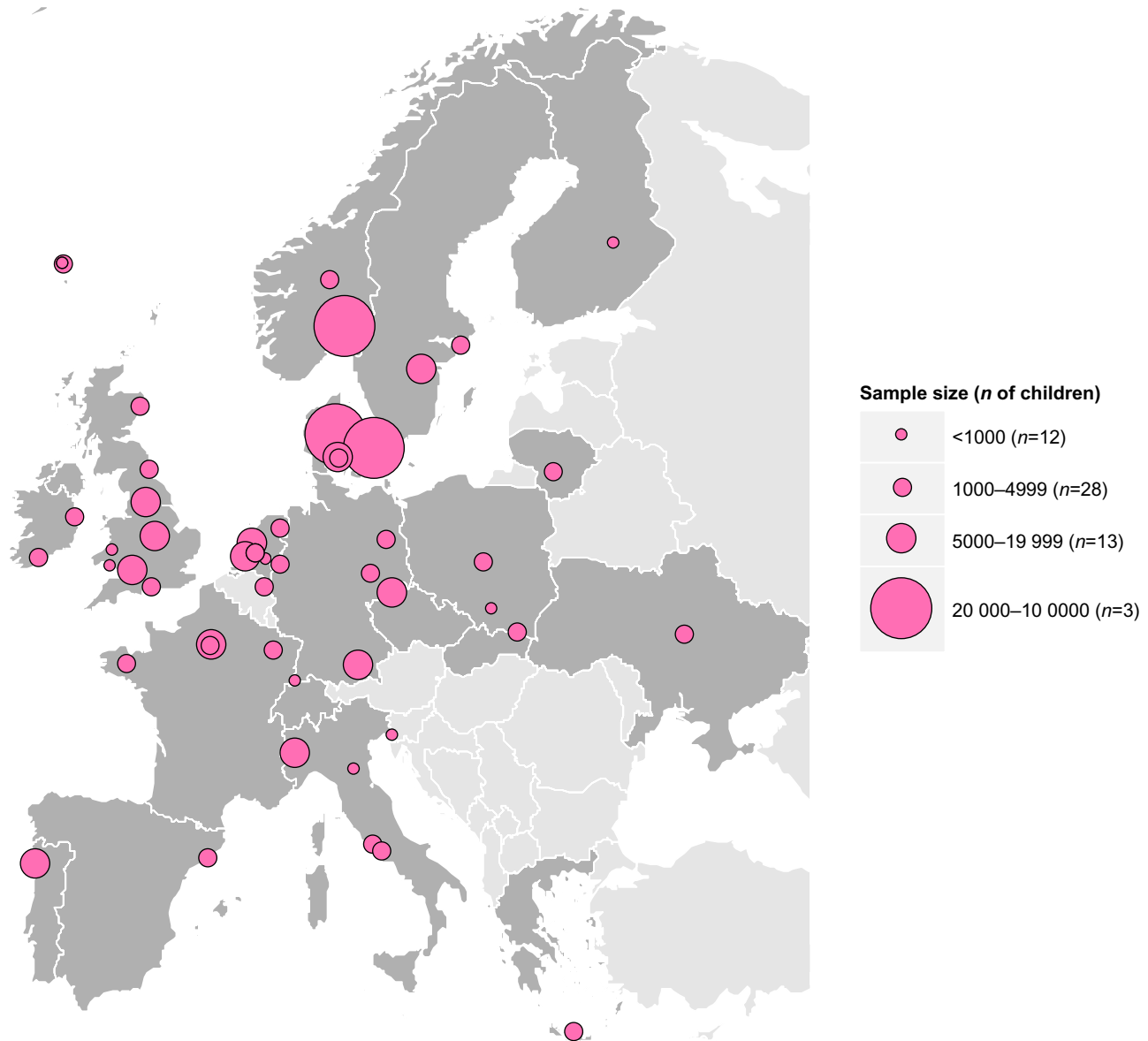


Figure 2. Location and sample size (No. of children) of included European pregnancy and birth cohorts.

basis: (i) the variation in geography and time periods make it likely that confounding structures would differ between cohorts, and thus cross-cohort comparisons could strengthen causal inference;⁴ (ii) many cohorts have collected biological samples with DNA and could explore genetic associations with rare phenotypes in collaboration, as well as biological samples for biomonitoring of environmental and nutrient exposures; (iii) replication of findings is increasingly recognised as important, and the European pregnancy and birth cohorts provide ample opportunity for doing this; (iv) the cohorts provide the opportunity for doing pooled analyses in order

to increase statistical precision, which is likely to be particularly valuable for exploring associations with rare outcomes; and finally (v) funding for single cohorts, encompassing very large samples, is rarely feasible.

Statistical precision

We have performed a number of power calculations under different assumptions in order to demonstrate the statistical implications of pooling data across cohorts. Figure 4 illustrates that a study of 200 000 mother–child pairs would have a statistical power of

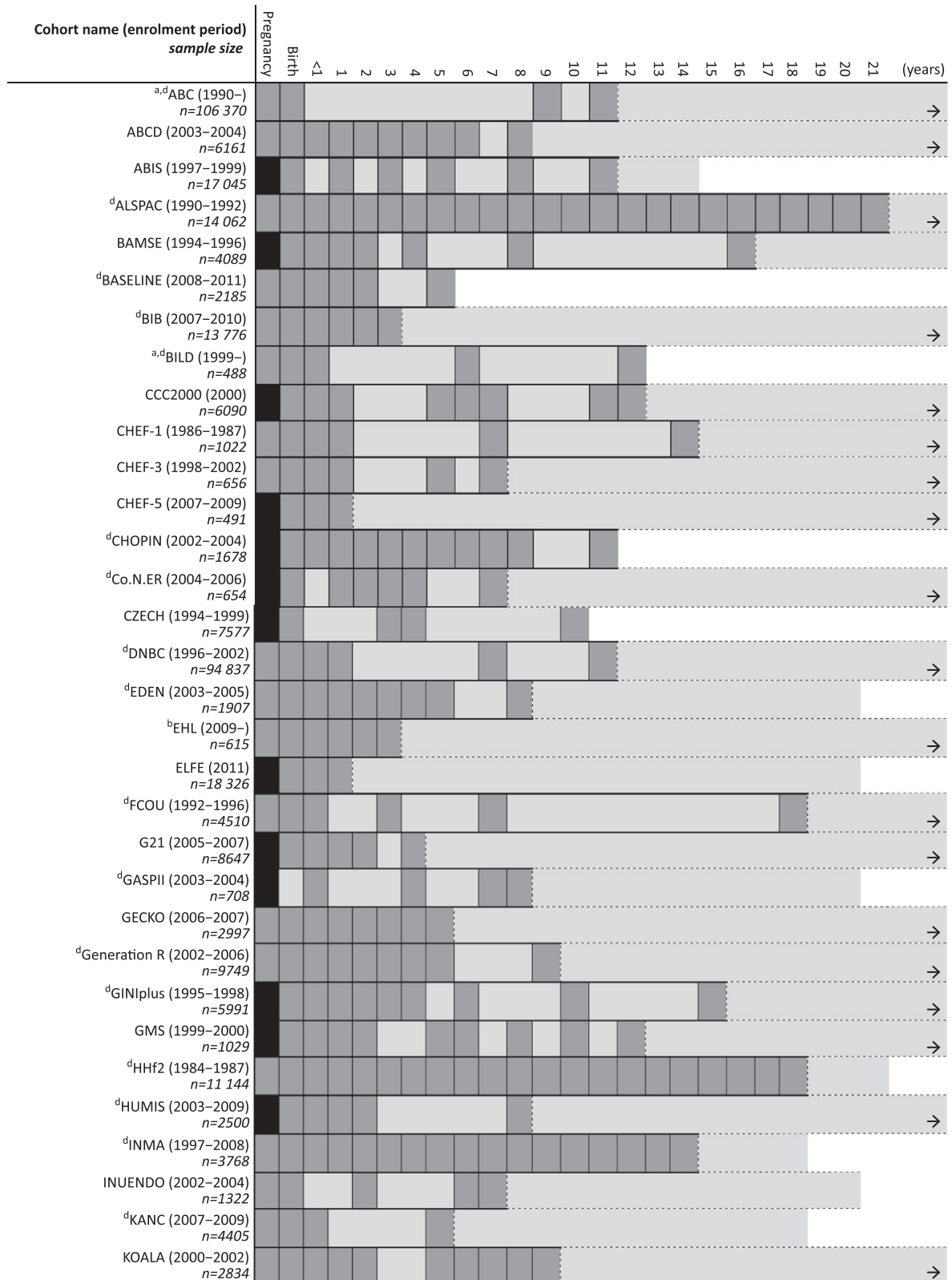


Figure 3. Enrolment and follow-up of the children in the included European pregnancy and birth cohorts.

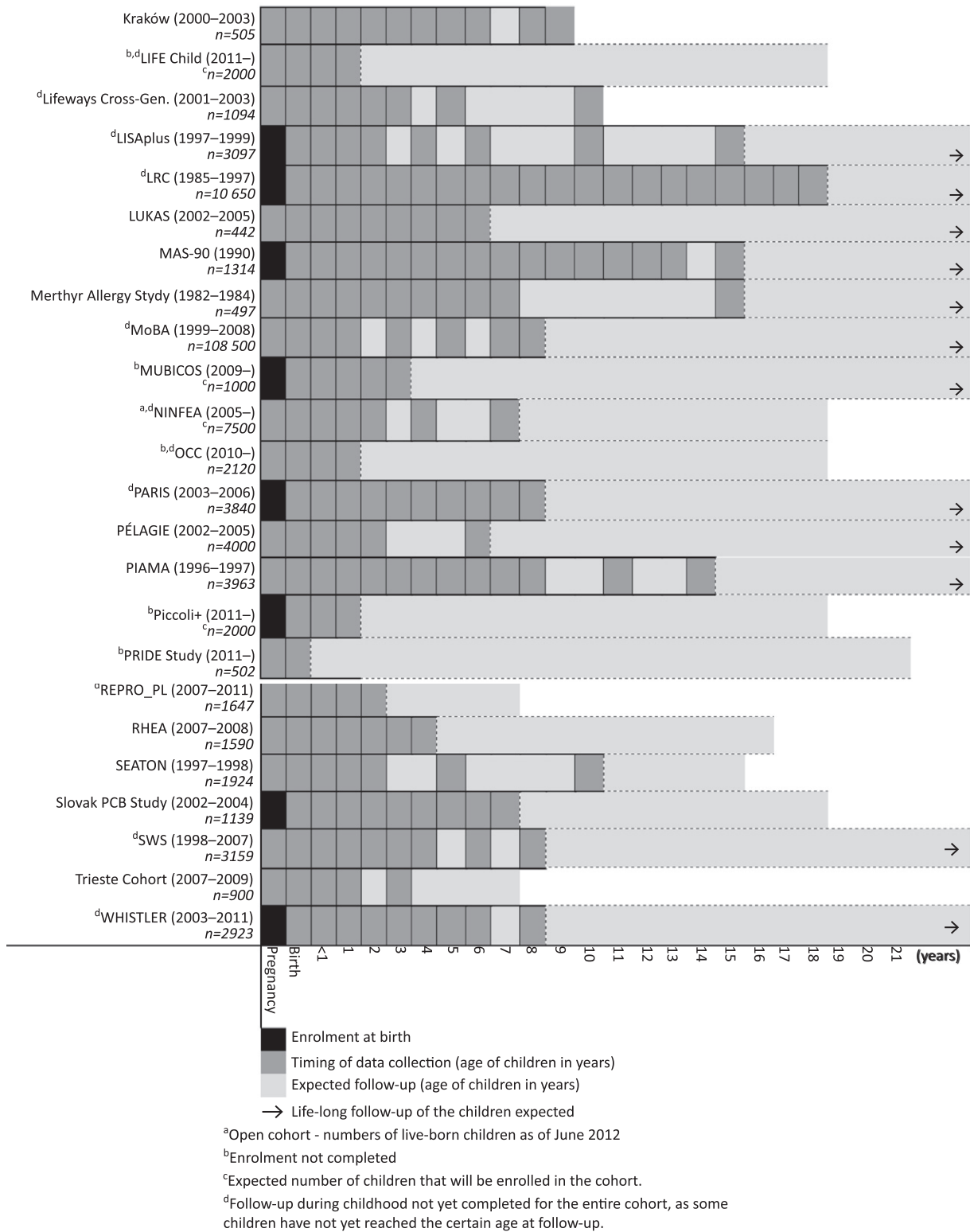


Figure 3. Continued

Table 2. Selected exposure and outcome data and biological samples collected by the included European pregnancy and birth cohorts

Maternal demographic characteristics	Name/acronym	No. of cohorts
Age at birth	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PIAMA, PRIDE Study, Piccoli+, PÉLAGIE, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	54
Ethnicity	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, CZECH, EHL, FCOU, GASPII, GECKO, Generation R, GMS, HUMIS, INMA, INUENDO, KANC, KOALA, LIFE Child, LRC, LUKAS, MUBICOS, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	41
Education	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	51
Occupation	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	48
Income	ABC, ABCD, ABIS, ALSPAC, BASELINE, BIB, CCC2000, EDEN, EHL, ELFE, G21, GECKO, Generation R, HUMIS, LIFE Child, Lifeways Cross-Gen., LRC, MoBa, PÉLAGIE, PRIDE Study, Slovak PCB Study, WHISTLER	21
Maternal obstetric characteristics	Name/acronym	No. of cohorts
Fertility treatment	ABC, ABCD, ALSPAC, CHEF-5, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, HHf2, HUMIS, INMA, MoBa, MUBICOS, NINFEA, OCC, PELAGIE, Piccoli+, PRIDE Study, RHEA	24
Parity	ABC, ABCD, ABIS, ALSPAC, BAMSE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Cohort, SWS, Trieste Cohort	49
Waiting time to pregnancy	ABC, ABCD, ALSPAC, CHEF-5, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GECKO, Generation R, HHf2, HUMIS, INMA, INUENDO, KOALA, LIFE Child, MoBa, NINFEA, OCC, PÉLAGIE, Piccoli+, PRIDE Study, RHEA,	25
Mode of delivery	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, KOALA, Kraków Cohort, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, Merthyr Allergy Study, Moba, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	52
Prenatal diagnostics	ABCD, ALSPAC, BIB, CCC2000, CHEF-3, CHEF-5, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GECKO, Generation R, HHf2, Life Child, Lifeways Cross-Gen., MUBICOS, MoBa, NINFEA, OCC, Piccoli+, PRIDE Study, PÉLAGIE, REPRO_PL, RHEA, WHISTLER	29
Maternal lifestyle characteristics	Name/acronym	No. of cohorts
Weight and height	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	47

Table 2. Continued

Maternal lifestyle characteristics	Name/acronym	No. of cohorts
Smoking	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	53
Alcohol consumption	ABC, ABCD, ABIS, ALSPAC, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., MoBa, MUBICOS, NINFEA, OCC, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	44
Diet	ABC, ABCD, ABIS, ALSPAC, BASELINE, BILD, CHEF-1, CHEF-3, CHEF-5, Co.N.ER, DNBC, EDEN, EHL, ELFE, FCOU, GASPII, Generation R, GMS, HHf2, HUMIS, INMA, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LUKAS, MoBa, NINFEA, OCC, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort	39
Physical activity	ABC, ABCD, ALSPAC, BASELINE, BIB, CHOPIN, DNBC, EDEN, EHL, ELFE, FCOU, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, KOALA, Lifeways Cross-Gen., MoBa, MUBICOS, NINFEA, OCC, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SWS, WHISTLER	30
Medication	ABC, ABCD, ABIS, ALSPAC, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	47
Maternal environmental exposures	Name/acronym	No. of cohorts
Occupational hazards	ABC, ABCD, ALSPAC, BIB, Co.N.ER, CZECH, DNBC, EDEN, ELFE, FCOU, GASPII, Generation R, HUMIS, INMA, INUENDO, KANC, Kraków Cohort, MoBa, MUBICOS, NINFEA, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, Trieste Cohort, WHISTLER	27
Outdoor air pollution	ABCD, BIB BILD, CZECH, DNBC, EDEN, GASPII, Generation R, INMA, KANC, Kraków Cohort, Lifeways Cross-Gen., NINFEA, PIAMA, Piccoli+, REPRO_PL, RHEA, Trieste Cohort, WHISTLER	19
Indoor air pollution	ABCD, BILD, Co.N.ER, DNBC, EDEN, ELFE, FCOU, GASPII, Generation R, INMA, KOALA, Kraków Cohort, LUKAS, NINFEA, OCC, PIAMA, Piccoli+, REPRO_PL RHEA, Trieste Cohort, WHISTLER	21
Infant and child exposures	Name/acronym	No. of cohorts
Childcare attendance	ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-3, CHEF-5, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, HHf2, INMA, INUENDO, KOALA, LIFE child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MoBa, MUBICOS, NINFEA, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, WHISTLER	42
Passive smoking	ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BILD, CCC2000, CHEF-1, CHOPIN, DNBC, EDEN, ELFE, FCOU, GASPII, Generation R, GINIplus, GMS, HHf2, INMA, KANC, KOALA, LIFE Child, LISApplus, LRC, LUKAS, Merthyr Allergy Study, MoBa, NINFEA, PARIS, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, SEATON, Slovak PCB Study, SWS	36
Breast feeding	ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	55

Table 2. *Continued*

Infant and child exposures	Name/acronym	No. of cohorts
Diet	ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHOPIN, Co.N.ER, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	51
Physical activity	ABCD, ABIS, BAMSE, BIB, BILD, CCC2000, CHEF-1, CHOPIN, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MoBa, MUBICOS, OCC, PARIS, PÉLAGIE, PIAMA, RHEA, SEATON, SWS, WHISTLER	40
Medication	ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INUENDO, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, SWS, WHISTLER	46
Vaccination	ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, Co.N.ER, DNBC, EDEN, ELFE, FCOU, GASPII, Generation R, HHf2, INUENDO, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, Slovak PCB Study, SWS, WHISTLER	38
Prenatal and perinatal outcomes	Name/acronym	No. of cohorts
Birth weight and gestational age	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MAS-90, Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort, WHISTLER	56
Congenital malformation	ABC, ABCD, ABIS, ALSPAC, BASELINE, BIB, CCC2000, CHEF-1, CHEF-3, CHEF-5, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, HHf2, HUMIS, INMA, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., Merthyr Allergy Study, MoBa, MUBICOS, NINFEA, OCC, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, SWS, Trieste Cohort, WHISTLER	39
Miscarriage (<20 or <22 weeks)	ABC, ABCD, ALSPAC, Co.N.ER, DNBC, EDEN, ELFE, FCOU, GASPII, GECKO, Generation R, HHf2, INMA, INUENDO, KANC, LIFE Child, MUBICOS, OCC, PRIDE Study, REPRO_PL, RHEA	21
Stillbirth	ABC, ABCD, ALSPAC, BIB, CCC2000, Co.N.ER, DNBC, EDEN, FCOU, GECKO, Generation R, INMA, Lifeways Cross-Gen., LRC, MoBa, OCC, PÉLAGIE, PRIDE Study, RHEA, SEATON, SWS	22
Development and child health outcomes	Name/acronym	No. of cohorts
Asthma/allergy	ABCD, ABIS, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, Merthyr Allergy study, MoBa, MUBICOS, NINFEA, OCC, PARIS, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, WHISTLER	51
Weight and height	ABCD, ABIS, BAMSE, BASELINE, BIB, BILD, CCC2000, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, GECKO, Generation R, GMS, HHf2, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, WHISTLER	48
Sexual maturation	ALSPAC, BAMSE, CCC2000, CHEF-1, CHEF-3, CHOPIN, DNBC, EDEN, FCOU, GINIplus, GMS, HHf2, INMA, KOALA, LIFE Child, LISApplus, LRC, LUKAS, PIAMA	19
Mental health	ABCD, ABIS, BIB, CCC2000, CHEF-1, CHEF-5, CHOPIN, DNBC, EDEN, ELFE, FCOU, Generation R, HHf2, HUMIS, KANC, KOALA, LIFE Child, MoBa, Trieste Cohort	20

Table 2. *Continued*

Development and child health outcomes	Name/acronym	No. of cohorts
Neuro-development	ABCD, BASELINE, BIB, CCC2000, CHEF-1, CHEF-3 CHEF-5, CHOPIN, Co.N.ER, DNBC, EDEN, ELFE, FCOU, GASPII, Generation R, HHf2, HUMIS, INMA, KANC, KOALA, LIFE Child, MoBa, MUBICOS, NINFEA, PÉLAGIE, Piccoli+, PRIDE Study, REPRO_PL, RHEA, Slovak PCB Study, SWS, Trieste Cohort	31
Infectious disease	ABCD, ABIS, BAMSE, BASELINE, BIB, BILD, CHEF-3, CHEF-5, Co.N.ER, CZECH, DNBC, EDEN, EHL, ELFE, FCOU, G21, GASPII, Generation R, GINIplus, HHf2, HUMIS, INMA, INUENDO, KOALA, Kraków Cohort, LIFE Child, Lifeways Cross-Gen., LISApplus, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PÉLAGIE, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, WHISTLER	41
Biological samples	Name/acronym	No. of cohorts
Maternal whole blood	ABC, ALSPAC, BIB, CZECH, CHEF-1, CHEF-3, CHEF-5, DNBC, EDEN, ELFE, G21, Generation R, HUMIS, INMA, INUENDO, KANC, KOALA, Kraków Cohort, MoBa, PIAMA, PRIDE Study, REPRO_PL, RHEA, SWS	24
Maternal serum/plasma	ABC, ABCD, ABIS, ALSPAC, BIB, CHEF-3, CHEF-5, Co.N.ER, DNBC, EDEN, ELFE, G21, GASPII, Generation R, INMA, INUENDO, KOALA, LIFE Child, LUKAS, MoBa, OCC, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort	29
Maternal DNA	ABC, ALSPAC, Co.N.ER, CZECH, DNBC, EDEN, GASPII, Generation R, GSM, INMA, INUENDO, KANC, KOALA, LIFE Child, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PIAMA, Piccoli+, PRIDE Study, REPRO_PL, RHEA, SWS	25
Breast milk	ABIS, CHEF-1, CHEF-3, CHEF-5, EDEN, ELFE, FCOU, HUMIS, INMA, KOALA, LIFE Child, LUKAS, OCC, PIAMA, REPRO_PL, Slovak PCB Study, Trieste Cohort	17
Child whole blood	ABC, ABCD, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CHOPIN, DNBC, EDEN, FCOU, GECKO, Generation R, GINIplus, GMS, INMA, KANC, KOALA, Kraków Cohort, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MoBa, PARIS, PIAMA, RHEA, Slovak PCB Study	32
Child serum/plasma	ABC, ABIS, ALSPAC, BAMSE, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CHOPIN, Co.N.ER, DNBC, EDEN, FCOU, G21, GASPII, GECKO, Generation R, GINIplus, INMA, KOALA, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MoBa, OCC, PARIS, Piccoli+, RHEA, SEATON, Slovak PCB Study	34
Child DNA	ABC, ABIS, ALSPAC, BAMSE, BASELINE, BILD, CHOPIN, Co.N.ER, CZECH, DNBC, EDEN, GASPII, GECKO, Generation R, GINIplus, GSM, INMA, INUENDO, KANC, KOALA, LIFE Child, Lifeways Cross-Gen., LISApplus, LRC, LUKAS, MoBa, MUBICOS, NINFEA, OCC, PARIS, PIAMA, Piccoli+, SWS	33
Umbilical cord blood	ABC, ABIS, ALSPAC, BASELINE, BIB, BILD, CHEF-1, CHEF-3, CHEF-5, CZECH, DNBC, EDEN, ELFE, G21, GASPII, GECKO, Generation R, HUMIS, INMA, KANC, Kraków Cohort, LIFE Child, LUKAS, MoBa, OCC, PÉLAGIE, Piccoli+, REPRO_PL, RHEA, SEATON, Slovak PCB Study, SWS, Trieste Cohort	33
Paternal DNA	BIB, EDEN, Generation R, INUENDO, KOALA, LIFE Child, MoBa, MUBICOS, OCC, PIAMA, RHEA, SWS	12

80% to detect a relative risk of 1.5 for a rare outcome (0.2%), given an exposure prevalence of 10%, at a 5% significance level. For an exposure prevalence of 2%, and an outcome prevalence of 0.2%, a sample size of around 300.000 would render it possible to detect a relative risk of 2.0 with a statistical power of 80%, at a 5% significance level. To illustrate the opportunities provided, a total of 39 cohorts, which collected information on congenital malformation can be identified at <http://www.birthcohorts.net>, varying from small ($n = 491$ children) to large ($n = 108\,500$ children)

cohorts, encompassing a total of 473 152 children. This provides a unique opportunity for exploring early-life determinants of rare anomalies. It is, however, far from likely that information on specific anomalies are available in all 39 cohorts, and since <http://www.birthcohorts.net> can only indicate broad categories of collected data, the details may reveal that some cohorts that are seemingly eligible for a specific study may not be. Hence, direct contact with PIs to obtain exact information about individual characteristics of each cohort is needed, also to discuss the possibilities

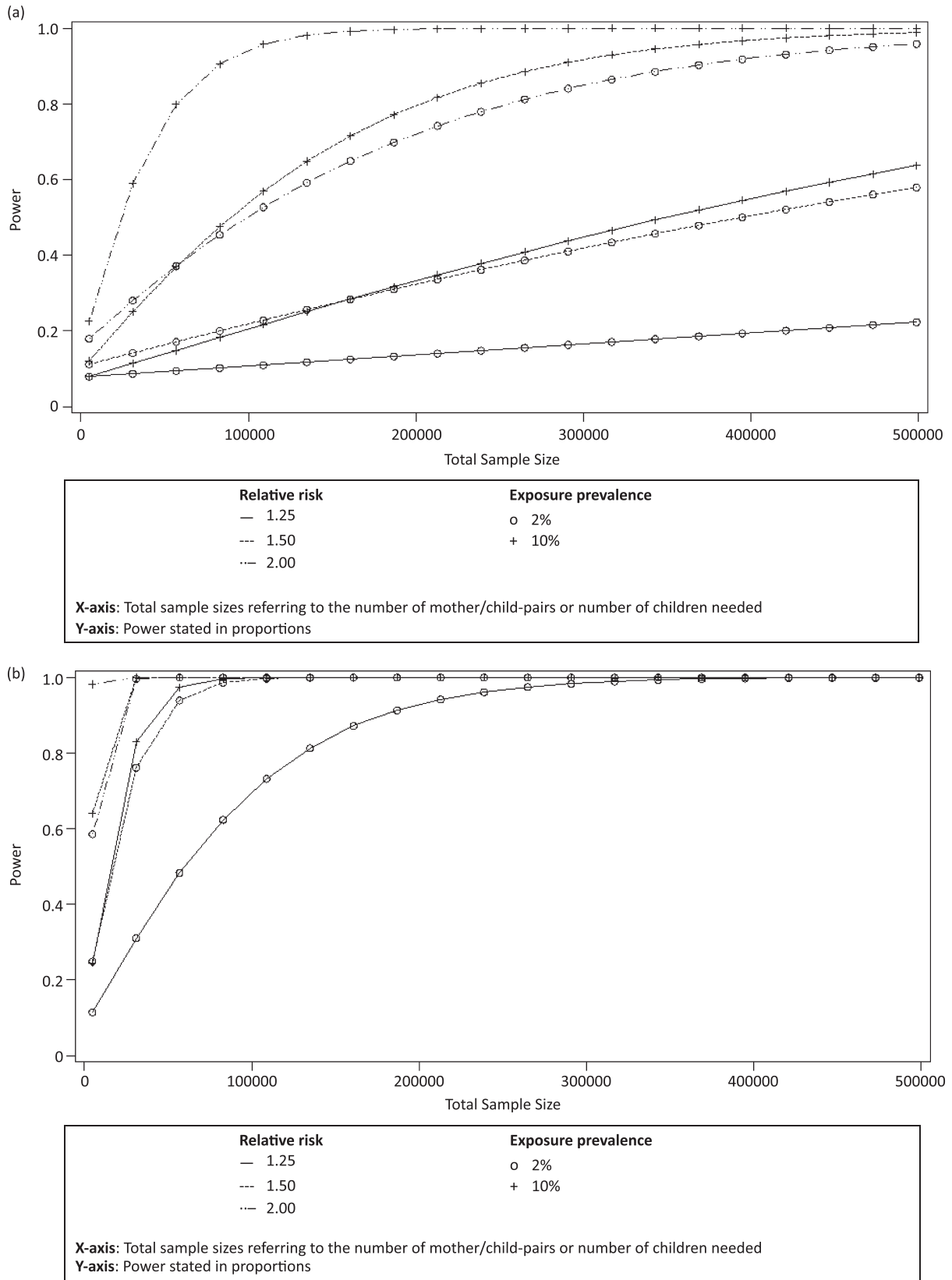


Figure 4. Statistical implications of combining of data across cohorts. (a) Assumptions: outcome prevalence 0.2%, significance level 5%. (b) Assumptions: outcome prevalence 5%, significance level 5%.

of data sharing, since registration at <http://www.birthcohorts.net> not necessarily implies easy or open access to data. However, the above calculations importantly illustrate the value of efforts to work collaboratively across cohorts.

Data collection methods – a great challenge

The wide range of data collection methods that have been used poses a great challenge when pooling data from different cohorts. Therefore, there is a need to develop methods that are suitable to support the use of currently collected data for pooled analyses in epidemiology, and also for considering which exposures and outcomes should be collected by similar items/procedures in future cohorts. Difficulties or challenges in trying to harmonise measures across all or most upcoming cohorts can be that: (i) some cohorts have obtained funding to use the most up to date and most expensive tool for a given exposure, while others only have funds for a much cheaper possibly proxy measure; and (ii) the available resources for different cohorts may reflect the true priorities in different populations in terms of how important different exposures and outcomes are, which will not be the same across Europe. On the other hand, a variety of different measurement methods can be useful for exploring how response and reliability differs between them, and how robust associations are despite differences in methods.

Experiences from ongoing cross-cohort studies

Currently, information from <http://www.birthcohorts.net> has been used for the identification of cohorts for a number of ongoing collaborative studies in Europe, e.g. a pooled analysis of associations between moderate maternal alcohol consumption and fetal effects in low-risk pregnancies, a comparative study of socio-economic gradients in preterm birth, and a study of occupational hazards and adverse reproductive outcomes. Experiences from these studies have demonstrated remarkable willingness to share data and to do collaborative studies across European cohorts. However, these studies have also highlighted a number of discrepancies between the information about cohort sample sizes at <http://www.birthcohorts.net> and the actual number of whom data are available. For example, not surprisingly, the number of available participants estimated, based on

information at <http://www.birthcohorts.net>, will commonly reflect the total number of pregnancies/births at the time of enrolment or the expected number of children who will be enrolled, whereas less data for any specific variable will often be available. Furthermore, information on attrition in every single follow-up of the children does not appear anywhere. Since attrition is a major drawback of cohort studies, future updates of the <http://www.birthcohorts.net> should include this important information.

Another major experience of the difficulties in post-harmonisation of data was that otherwise eligible cohorts had to be excluded from the studies using pooled data, because it was impossible to harmonise data. For example, the study on fetal effects of maternal alcohol consumption included only eight cohorts ($n \approx 270\,000$), as data on maternal alcohol consumption particularly proved impossible to harmonise. The methods used to collect data on alcohol consumption during pregnancy, were different in almost all of the existing cohorts, since some cohorts asked for type and some for total intake, some used open response categories, while others had predefined response categories that moreover differed between the cohorts, and finally the data were collected at different time points during pregnancy. In order to facilitate data harmonisation, the PhenX project has provided the scientific community with a core set of 21 research domains, such as anthropometrics, environmental exposures, nutrition, reproductive health etc., each of which includes up to 16 measures. The PhenX toolkit is freely accessible and for efficient use of data, it could be suggested to apply standard measures as provided by PhenX when planning future cohort studies.²¹ However, the measures in the PhenX toolkit have been developed for adults (and parents), and there is a need for additional measures developed specifically for children. On the other hand, many cohorts are at various stages, as in some cohorts the offspring are young adults, while other cohorts have recently started enrolment, and most cohorts would probably use tools corresponding to those used at earlier stages. In these respects, data from existing cohorts have to be post-harmonised in the best possible way. Moreover, a broad coverage of different context-specific exposures may also be highly relevant in the long run.

Another efficient approach of using existing data sources and handling difficulties of data harmonising could be to pool aggregated data obtained separately

in different cohorts. However, this arises the risk of aggregation bias that may not reflect the association existing at the individual level. Also, it may be problematic to estimate biologic effects due to heterogeneity in exposure level or level of covariates across cohorts, but this could partly be taken into account if using internal or external information.

Finally, when pooling data from both general cohorts and cohorts that address specific exposures or outcomes, it should be considered that cohorts with specific aims presumably relate to selected groups. For example, some cohorts have excluded ethnic minority groups, while other cohorts include different ethnic groups. This is an issue of major concern for the validity of cross-cohort studies doing pooled analyses, and this need to be carefully considered when interpreting the results.

Conclusions

In conclusion, we have summarised the characteristics of existing pregnancy and birth cohorts in Europe. The database, <http://www.birthcohorts.net>, proved to be a useful tool for identification of cohorts, but it cannot replace direct contact with PIs to obtain detailed information about individual characteristics of each cohort. Previous publications have similarly summarised characteristics of cohorts that are located in low and middle-income countries and of cohorts which address specific exposures and outcomes.^{12–14} The value of these overviews is that they illustrate the potential to address key research questions which require or would greatly benefit from collaboration across cohorts. Whilst we have emphasised the potential added-value of cross-cohort collaboration, we recognise that there are hindrances to such collaborative work. It is simplistic to assume that just because data are available, such collaborative research is available to the scientific community. Clearly, there are costs associated with preparing data sets and completing pooled analyses, and it is important for funders to recognise these requirements. Where key research questions can be addressed by collaboration across existing data sources, it is clearly more cost-effective to support this than to undertake a new European mega-cohort. Other issues, such as whether ethical and governance issues permit data sharing, difficulties in harmonisation of data across cohorts, as well as incomplete recognition of important collaborators to be included may impede high quality collaborative research. Both

in the genetic and non-genetic field, an increasing number of examples exist on how these issues can be overcome.²² Thus, we envisage useful collaborations being realised between European pregnancy and birth cohorts, and we encourage publications of similar overviews from other geographical regions, so that cohorts from all over the globe are ultimately documented. Furthermore, <http://www.birthcohorts.net> is still open for registration of new cohorts as well as for cohorts registered elsewhere, so that it may serve as a global platform for collaboration. A global overview of the possibilities offered by existing cohorts in life-course research would be of great value, and this would support the vision of active cross-cohort collaboration in order to improve statistical precision, to replicate findings, to share knowledge and to develop strong scientific networks across cohorts.

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