



Developing a Child Cohort Research Strategy for Europe

## Strategy for European birth cohort research

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## ***Executive summary***

More than 70 birth cohorts across Europe are prospectively studying more than 500,000 mothers, fathers and children at repeated time points and over long time periods. These studies are gathering a wealth of important, policy relevant, information on childhood diseases and their determinants and are contributing increasingly to Europe-wide research and results.

Considering existing European birth cohorts, CHICOS found a lack of data from minority groups, Southern and Eastern European countries, and older children and adolescents.

CHICOS proved that pooling cohort data across countries is possible and valuable, but has also highlighted practical obstacles in international collaborative initiatives. In fact, **currently there is no common European database with prospective, individual-level, data on child health and determinants.**

Harmonizing existing data collections, improving the use of existing resources, filling data gaps, and increasing availability of registry data that can be combined with cohort data have also proved extremely beneficial.

**CHICOS has shown that the groundwork now exists for ongoing birth cohort research in Europe including more than 500,000 mother-child pairs which can lead to scientific advances of great relevance to European child health policy making.**

CHICOS recommends **establishing a collaborative European Birth Cohort**, using data from **existing and new** cohorts. Such a cohort will lead to a permanent Europe-wide data resource containing longitudinal, individual-level information about child health in Europe. It will provide key statistics on child health and determinants to enable health surveillance and to provide rapid responses to knowledge gaps that have to be tackled to inform policies. The collaborative European Birth Cohort should include support to:

- **Establish the infrastructure for a Europe-wide database platform** – including database platform, data sharing and harmonisation rules, biobank access guidelines, exchange of methods and expertise – resulting in more efficient use of existing and newly established cohorts;
- **Include new cohorts that cover groups of the population that are currently underrepresented in birth cohort research.** There should be efforts to fund, develop, include and improve cohorts from specific European regions (e.g. Eastern Europe) and minority groups.
- **Continue follow-up of existing European cohorts.** This is the most efficient way to obtain information on health and disease in older children, adolescents, and adulthood.
- **Combine data from cohorts, routine registries, and other data sources.** This would enhance the contribution of both birth cohorts and population based registries.
- **Integrate knowledge translation and public and policy engagement.** This would support the translation of research findings into political and public health priorities and policies.

# **1. Context**

## **1.1. Aims and objectives**

The aim of this report is to present the European-wide strategy for birth cohort research developed by the CHICOS project.

Specific objectives were:

1. To evaluate current birth cohort data and research across Europe;
2. To compare alternative Europe-wide strategies for birth cohort research;
3. To present recommendations for future birth cohort research.

There are four sections to the report: in the first section we outline what a birth cohort is and how cohorts contribute to policy relevant research; in the second section we describe the current status of birth cohort research in Europe; in the third section we compare alternative European birth cohort strategies; and the final section lists recommendations.

## **1.2. What is a birth cohort?**

Birth cohorts are longitudinal studies that follow participants (parents and their children) from the intrauterine period, birth or shortly after, through childhood into adolescence and sometimes adulthood. CHICOS only includes cohorts with a focus on health. Such studies collect information on a range of topics related to the social and environmental characteristics of children's and their parents' lives, such as parents' employment and education, child care, diet, air pollution, and physical activity. At repeated time points throughout childhood, child growth, behaviour, and cognitive development are measured, and information on a variety of other health related topics, such as asthma and infectious diseases is gathered. Most studies also collect biological specimens, which provide the opportunity to measure biological markers of a variety of environmental or nutritional factors, and obtain genetic information from parents and children.

For the purposes of this strategic document we restricted our definition of a European birth cohort to be a study with the following features:

- a. Participants are recruited from a European country.
- b. Participants (mothers and children) are recruited during or before pregnancy, at birth, or in the first 12 months of the child's life.
- c. Initial recruitment of participants took place in 1990 or thereafter. Selected cohorts have information on pregnancy, infancy, childhood, adolescence and potentially early adulthood in Europe from 1990 to 2012.
- d. Recruitment of at least 300 participants.
- e. To have completed follow-up assessment at least once during the first years of life of the child (by questionnaire, hands on assessment, medical record review or linkage to health related data) or to have certain and earmarked funding to complete the afore described follow-up.

### **1.3. How can birth cohorts contribute to policy relevant research?**

Policy and decision makers need a sound evidence base for the development and implementation of public health policies and interventions, including those focused on child health. The economic and societal costs associated with non-optimal child health are substantial and investing in children's health has been recognised as essential to human and economic development. Wide differentials in child health exist within and between European countries, indicating considerable scope for improvement.

There are several unique features of the birth cohort study design that make it particularly important as a contribution to understand the causes of disease and ill-health. Cohort studies have been particularly important in establishing causal relationships in areas where for practical or ethical reasons randomised controlled trials are not possible, such as maternal cigarette smoking, foetal and infant growth, or environmental toxin exposure.

The **long follow up** in birth cohorts makes them ideally suited to address new scientific or policy related questions. For example, birth cohort studies with stored biological samples from birth are increasingly answering questions about the role of epigenetic changes in the development of disease, even though the potential importance of this was not widely considered at the time that many of these cohorts were established. Similarly, their breadth and long term nature means that they can provide data on otherwise unexplored relationships such as that between patterns of child care and health outcomes.

Cohort studies are **prospective**, measuring risk factors at an early age (point in time) **before** disease onset or before information of health related outcome are collected at an older age (later time). This prospective approach can more clearly delineate the causal direction of an association. Whereas retrospective studies reconstruct the past histories of individuals, they may be subject to biased or inaccurate recall, and missing information by the subjects while prospective studies collect data at the time. Cross-sectional study designs cannot separate exposure and outcome assessment in time and are thus unable to tell whether a risk factor caused a disease or if vice versa is true: for example, whether vitamin D levels in the blood cause asthma or if asthma resulted in the child being less able to play outdoors and thus be exposed to sunlight which determines vitamin D levels (Text box 1).

#### ***Text box 1. Vitamin D and Asthma***

Recent mother and birth cohort studies observed that low levels of vitamin D during pregnancy or in childhood are associated with an increased risk of asthma and asthma exacerbations, as well as impaired lung function (Camargo et al 2007; Morales et al 2012). These results suggest that intervention to ensure adequate vitamin D levels may reduce the development of asthma outcomes in childhood.

Another example of how birth cohorts can **swiftly provide answers for policy making** is the concern raised about the role of early life exposure to peanuts in the development of allergic disease. When this suspicion was raised, one birth cohort study was able to rapidly identify peanut oils in skin products as a cause (Lack et al. 2003, Text box 2).

### ***Text box 2. Peanut allergy***

The ALSPAC cohort in the UK determined that the use of skin products containing peanut oils in the first six-months of life was related to the development of peanut allergy; consequently peanut oil is now a banned ingredient in skin products for children (Lack et al 2003). Previous studies had not been able to show this relationship as they were not longitudinal and could not identify the antecedents of the allergy.

Birth cohort studies have data that could be used in programmes to **monitor key health outcomes or determinants** to assist in **responses to current policy issues**. Birth cohorts have already contributed to research in the following child health policy areas:

- Understanding **health inequalities**. The persistent social inequality in health in adult life may (partly) have its origin early in life. Social gradient in gestational age at birth and in foetal growth, have been proved to both be predictors of later health. It has been suggested that socioeconomic differences in simple lifestyle factors, e.g. maternal smoking, may be the mechanism behind the gradient and this has proved to be likely for foetal growth (Mortensen et al. 2009). When birth cohort data were used to explore the mechanisms behind the social gradient in preterm births, this very explanation was not confirmed (Text box 3). Comparative studies using birth cohort data from different settings may provide clues to identify possible preventable factors underlying social gradients in preterm births.

### ***Text box 3. Social inequalities and preterm birth***

An educational gradient was found in preterm birth risk in the Danish National Birth Cohort (as in most other data). Cohort data were used to estimate how maternal pre-pregnant BMI and maternal smoking, weight gain, and alcohol intake during pregnancy affected the gradient (Morgen et al. 2008). The effect of these maternal lifestyle factors accounted for only a minor part of the educational inequality in preterm births and, consequently, better explanations are needed.

- Identifying healthy and unhealthy environments, such as research on lead pollution influencing cognitive development in children (Lanphear et al. 2005), contributing to the ban on lead in petrol and the subsequent dramatic decreases in blood lead levels in mothers and children over the past decades. In other areas, such as air pollution (Dadvand et al. 2013) and food contaminants (Grandjean et al. 1997; Toft et al. 2004), birth cohort research is now producing new results which may influence future policy-making.
- Identifying the role of lifestyle-related behaviour, such as breast feeding, parental smoking, parenting methods, parents' stress and anxiety, consumption of fish during pregnancy, child's diet and physical activity, for normal growth, development and health in childhood. For example, cohorts have established a probable causal link between breastfeeding and child IQ (Text box 4), which can help to underpin breastfeeding promotion programmes.

#### ***Text box 4. Breastfeeding and child health and development***

By comparing the effects of breastfeeding on child health and development in birth cohorts from high and low/middle income countries, researchers have shown that the association between breastfeeding and higher IQ in the child is likely to be causal. This is because results are consistent in the different cultural settings where socio-economic patterns in breastfeeding differ. Associations with blood pressure and BMI of children were not likely to be causal (Brion et al. 2011).

- Identifying the role of specific exposures. For example, the role of peanut oil in lotions/ointments for children and its relationship with the onset of peanut allergy (Text box 2) and the controversy about intake of small amounts of alcohol during pregnancy (Text box 5). Birth cohorts are producing important policy-relevant evidence on health effects of many specific exposures, from contaminants (mercury, lead, many others) to nutrients (vitamin D, omega-3 fatty acids), and their biobanks make it possible to define exposure-response relationships accurately.
- Identifying characteristics related to major mortality and morbidity risks in infancy or childhood. For example, research from birth cohorts and registries has been a key influence on health policy in preventing sudden infant death syndrome (Gilbert 2005).

#### ***Text box 5. Alcohol consumption during pregnancy***

In contrast to most other European countries, Denmark was not strict about warning against moderate intake of alcohol during pregnancy in the early 21st century. Compared to other cohorts, a substantial proportion of women in the Danish National Birth Cohort reported that they drank small amounts of alcohol whilst pregnant. This made it possible to study foetal health associated with such levels of intake. Studies showed that the risks of preterm birth, congenital anomalies and infant death were unaffected. However, a strong increase in miscarriage risk was observed with an intake of two or more drinks a week (Andersen et al. 2012). Further work will enable determining the association of moderate alcohol consumption with longer term offspring outcomes such as cognitive function and educational attainment. This will provide policy makers and couples with relevant information to make informed decisions regarding 'safe' levels of alcohol consumption in pregnancy

### ***1.4. Why is a European birth cohort research strategy needed?***

There are now many pregnancy and birth cohort studies in Europe, that when pooled have information gathered from more than 500,000 mothers and children (Larsen et al 2013). Most birth cohorts have collected pregnancy, perinatal, infancy and childhood data on lifestyles, socioeconomic position, growth, adiposity and many have genetic data (section 2 of this report). Most have biological specimens from mothers and children (and sometimes fathers) stored in large biobanks.

New European birth cohort studies are currently being planned. For example, two very large birth cohorts are currently at the development stage in Germany and the UK, and likely to start recruitment in 2012-13. Data collection and methods vary across cohorts and there has traditionally been little coordination to structure and consolidate research across these different birth cohorts. It is becoming increasingly clear that considerable added value can be gained from collaboration between birth cohort studies:

1. *Discovering causes of disease* – By including cohorts with a range of genetic factors, culture, socioeconomic levels, living habits, etc., associations that are replicated would supply stronger causal evidence and that would make them more relevant to child health policy. Collaboration of birth cohorts and registers across Europe would enable replication to become routine practice and only findings with robust replication should be influence policy-making.
2. *Speedy response to key policy questions* – Frequently, speedy responses are needed to address policy concerns (Text box 2). Greater collaboration among European mother-child cohorts will enable a better and more coordinated response across Europe.
3. *Understanding inequalities in disease and health related behaviours* - Many diseases of relevance to childhood health vary in their prevalence across Europe. For example, childhood obesity levels vary considerably across regions of Europe ([www.iotf.org](http://www.iotf.org)) and, within European countries they vary by socioeconomic position (Lawlor et al 2005). Differences in prevalence, such as those seen for childhood obesity, suggest that interventions could reduce these prevalences to those seen for the countries with lowest prevalence. Only by comparing risk factors and policies across countries and by targeting research at the relevant geographic areas, we can hope to understand how to reach this goal. Comparisons will have to make use of standardised measurements of risk factors and outcomes and this can only be achieved through European coordination.
4. *Large sample sizes* – Very large sample sizes are required to understand the epidemiology and prevention of rare but important disease outcomes in infancy and childhood, such as congenital anomalies and childhood cancers. Cross European collaborations are required to examine major causes for such diseases. Similarly, very large sample sizes are required to fully understand the role of infrequent risk factors and how risk factors interact in determining child health and disease status - for example interactions of environmental and genetic factors.
5. *Improving methodology* – By sharing ideas across a wider group of scientists involved with birth cohorts across Europe and also involving child-health policy, research and practice experts, methodological approaches to data collection and analysis are likely to improve. Researchers from different disciplines will likely share a range of methodological approaches each with their own strengths and limitations.
6. *Greater & more efficient use of existing cohorts* – Commonly individual birth cohorts repeatedly collect many hundreds of different variables on individuals: the potential contribution to science of these data goes well beyond what any group of principal investigators envisage. Principal investigators for any one cohort are unlikely to include researchers with expertise in all areas that the study could contribute to. Thanks to widespread cross European cooperation, a greater number of scientists drawn from a wider range of expertise could address issues and make use of available data, which individual cohorts may not have thought of.

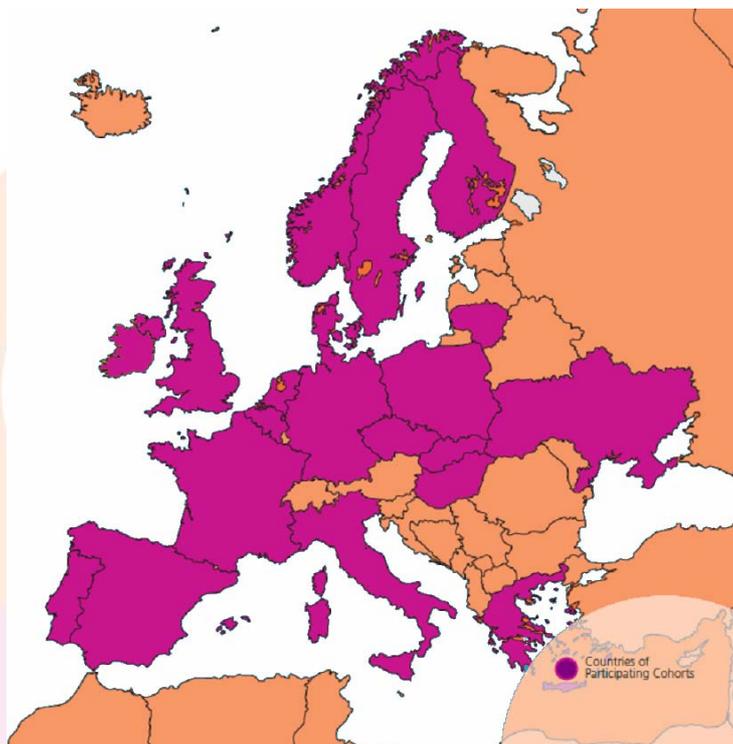
In summary, improved collaboration across Europe will enhance research and knowledge obtained from individual birth cohorts and their ability to contribute policy relevant findings. The ways to achieve and sustain this are less clear. One of the reasons why the EC funded the CHICOS (“Developing a Child Cohort Research Strategy for Europe”) project through its 7th framework programme was to develop a strategy for birth/mother-child cohort research in Europe.

## 2. The current state of European birth cohort research

### 2.1. Birth Cohorts in Europe

There are many birth cohorts in Europe: their aims vary considerably with some being general cohorts with multiple aims, whilst others focus on specific health or exposure-related research issues; design (e.g. time of recruitment) and size also vary. However, an inventory of birth cohorts showed that the number of birth cohorts exceeds 70 and they encompass more than 500,000 children (Larsen et al, 2013). This is an impressive number but of course it is only a small percentage of all births in Europe (>5 million births annually in 25 EU countries – <http://epp.eurostat.ec.europa.eu/>). Most cohorts were located in Northern and Western Europe, though all regions of Europe have birth cohorts that are suitable for research purposes.

An overview of existing cohorts and the data they have collected from parents and children can be found at [www.birthcohorts.net](http://www.birthcohorts.net), a webpage that aims to make relevant basic information available to the public, to stakeholders and to researchers in order to increase the scientific exploitation of these valuable data as well as facilitate collaboration and comparative analyses between the studies.



**Fig. 1. Countries of identified birth cohorts in Europe included in this overview.**

CHICOS has evaluated available data on health outcomes and determinants in the European birth cohorts, reaching the following conclusions:

- The majority of cohorts collect data on **perinatal outcomes**, such as birth weight, gestational duration, and perinatal mortality. Several of the perinatal outcomes are associated with social inequality, the quality of health services, and living conditions. Furthermore, they are closely related to future health outcomes, and serve as key exposures in life course studies (Kuh et al. 2003). Birth registries are essential for monitoring of these outcomes, while pregnancy cohorts are needed to address aetiology and validation. European birth cohorts substantially contribute to research within modifiable risk factors for adverse birth outcomes, such as smoking, diet and other environmental exposures;
- Many cohorts collect data on **asthma, respiratory health, and allergies**, and standardised tools for assessment of these outcome are either available or under development in large European projects (Bousquet et al. 2011; Keil et al. 2006). Pooled analyses have been carried out, for example examining the effect of exposure to maternal smoking on the risk of asthma in children (Neuman et al. 2012, Text box 6);
- Measures of **weight and height** are available in the majority of existing European birth cohorts, although other measurements of **adiposity** or its distribution (e.g. waist, skinfold thicknesses, directly assessed fat mass, visceral fat) are less available. **Blood pressure** is commonly measured, but relatively few cohorts have performed blood based or vascular function/structure measurements;
- European birth cohorts offer varied assessments of child **neuropsychological and behavioural development**, thus precluding combined analyses; there is a strong need to harmonize the neuropsychological assessment;
- In **injury** research, birth cohorts have so far played a limited role and no standardised questionnaires or protocols are available although the cohorts have the potential to provide valuable information on determinants of injuries, for instance social inequalities, and safety , e.g. parental behaviour;
- Data on **infectious outcomes** have been collected by several existing European birth cohorts through questionnaires and biological samples; linking data from existing birth cohorts with surveillance data can provide a rapid and very flexible response to emerging infections and pandemics;
- **Childhood cancers** are rare and can only be studied in cohort studies by combining data from many projects inside and outside Europe (Brown et al. 2007). Birth cohorts have the potential to play an important role in the development of childhood cancer-related biomarkers;
- **Social and cultural conditions and inequalities** are well described determinants of child health, growth, and development (Text box 3). All European birth cohorts collect information, albeit in a range of formats and depths. Few cohorts include sufficiently large minority groups such as low-income, ethnic minority to draw conclusions about the child health problems in these groups;
- Information on **diet** at different time points (pregnancy, early infancy and later childhood) is widely collected, but populations with particular dietary patterns are often underrepresented, e.g.

those from lower income groups, Eastern European regions and minority ethnic groups. Dietary assessment methods need harmonising across cohorts in order to facilitate comparisons between countries;

- Few cohorts record **physical activity** data in pregnancy or childhood. A combination of objective measures of physical activity and validated questionnaires is needed including questions on sedentary activities and access to green spaces;
- Almost all cohorts have questionnaire data on **smoking and alcohol consumption** of parents before, during and after pregnancy, while **illicit drug use** is more rarely assessed. A better understanding of the complex causal pattern behind initiation and continuation of substance abuse is needed for preventive purposes;
- For **environmental pollutant exposures**, data in more than 40 cohorts are available and summarised by the ENRIECO project (Gehring et al. 2013; Vrijheid et al. 2012). Pooled analyses have been feasible for some of these exposures: e.g. on the effects of persistent organic pollutants on foetal growth (Govarts et al. 2012), and on the effects of smoking on asthma (Neuman et al. 2012, Text box 6). For other exposures such as radiations, noise, new chemicals, data and methods are not sufficiently standardised to compare countries;
- Many birth cohorts collect **biological and genetic samples** and make major investments to establish **biobanks**. Information about exposures using biomarkers might overcome the potential for bias from studies using self reported data, increase power for association studies, and might give insight in the underlying causal mechanisms. However, collaboration on logistics of biological and genetic sample collection, storage and use is scarce. Many birth cohorts have biological samples but cannot make optimal use of them because of financial restrictions. Scientific collaborations especially those using genetic samples have proven to be extremely successful (Horikoshi et al. 2013; Paternoster et al. 2012).

***Text box 6. Maternal smoking and asthma in children: a pooled analysis of 8 European birth cohorts***

Previous, smaller, studies were unable to differentiate effects of prenatal and postnatal maternal smoking on childhood asthma. A large pooled analysis of 8 European birth cohorts with data on more than 21,000 children showed that maternal smoking during early pregnancy is associated with increased risk of wheeze and asthma in children, even among children who are not exposed to smoking late in pregnancy or after birth (Neuman et al. 2012). Policy makers should be aware of the importance of promoting smoking cessation before pregnancy.

**Gaps** common to all topics include:

1. **Lack of data on minority ethnic groups and in certain regions of Europe** (namely Eastern Europe, to a lesser extent Southern Europe) where the prevalence of many adverse child health outcomes and high-risk behaviour and life-style factors is highest;
2. **Lack of tracking of results into later childhood, adolescence and adulthood.** Birth cohorts provide a wide range of information and biological samples which are useful when studying the relationship between early life influences on the risk of developing chronic diseases such as

cardiovascular disease and cancer. Several adult diseases start developing many years before symptoms occur, and early life risk factors have been found to play an important role in disease development. However, very few cohorts have been followed-up for long enough to study disease causation over the life course.

3. **Lack of comparable assessment tools and data**, hampering the comparison of data and findings across European birth cohorts, especially for neuropsychological development, diet, and physical activity.
4. **Improved links to routine surveillance systems and registries** have been highlighted as an important need for birth outcomes, injuries, infections, and childhood cancers. Further, the development of cohorts in combination with other study designs (case-control, clinical trial) is desirable.

## **2.2. Birth cohort coordination**

Recent years have seen an increase in the willingness to share data among birth cohorts, and in the development of methods for doing this efficiently and within correct research governance frameworks. This has been achieved through coordination and networking projects (such as CHICOS) and through collaborative EU research projects. These are the important **lessons** that have been learnt from these collaborative efforts and that are important for maintaining and enhancing such collaborative research:

- **Existing European birth cohorts represent enormous investments** in terms of money, time, intellectual resources, commitment of participants and their parents;
- **Coordination efforts have created a positive attitude towards data sharing**, but such efforts are almost always limited by the time span of funded projects. Nevertheless, they have laid the groundwork for an ongoing infrastructure that includes more than 500,000 mother-child pairs with longitudinal repeat data on a very wide range of child health topics. **Continuity** is important to develop this into a permanent Europe-wide resource for child health surveillance and research;
- **Europe has different types of birth cohorts that can be used to complement each other**: e.g. older cohorts for life-course research, newer cohorts to tackle emerging concerns, large cohorts embedded in registries, smaller cohorts with more in depth data collection;
- **Combining, pooling, comparing data from cohorts is possible and can bring scientific advances** which will in turn bring greater relevance of results to European child health policy making. CHICOS has carried out 8 case studies on important public health issues in which data from many birth cohorts have been combined successfully to give larger analysis populations and thus more conclusive findings than those based on single cohorts (Text box 7: list of CHICOS case study topics). Other European projects have made similar contributions (e.g. Text box 6);
- **Collaborative analyses require adequate funding** over and above the funding available for each individual cohort study. Exploring whether relevant data exist, whether they are sufficiently similar for collaboration, agreeing standardised analysis protocols, producing a correct datasets for a specific collaboration from each study, analysing each study dataset in exactly the same way and then combining results appropriately is not trivial and requires adequate funds. This funding should include the real cost of establishing a data management and analysis protocol (that ensures

results are as equivalent as possible for each individual cohort) for each project, all stages required within a each cohort to get to the stage of having results and then the costs of pooling results across all of the cohorts. It is important to recognize that the growing demand, by funders, national governments and international policy makers for data sharing across research studies, which the vast majority of researchers support, is currently putting excessive pressure on local data management personnel. It is reaching the stage where for some studies it is impossible to comply with data sharing expectations because of these pressures / lack of funding;

- **Considerable progress has been made in standardizing data of a wide variety of cohorts**, most successfully in projects that focus on fairly narrow topic areas (genetics, air pollution, asthma). In these areas, large efforts have gone into comparing available variables across cohorts and deciding on how best to use common variables in combined analyses. These efforts must be well documented and made available for future studies. There are still many extremely heterogeneous or mixed areas with scarce comparability of variables across cohorts, for example neurodevelopment, diet, and physical activity;
- **There is a need to reduce obstacles related to judicial, governance and practical issues.** This involves agreeing on clear data sharing, transfer, and authorship guidelines, as well as a mechanism to build a Europe-wide cohort database. CHICOS has published case study guidelines that are a first step towards this;
- **There is a need to develop a strategy and action plan** for cohort collaboration as a basis for speedy response to key research and policy questions.

**Text box 7. CHICOS case studies, pooling data from European birth cohorts** (number of cohorts; estimated number of participating mother-child pairs):

1. Alcohol consumption during pregnancy and birth weight (9 cohorts; >100,000 participants)
2. Socioeconomic inequalities in preterm delivery (12 cohorts; >100,000 participants)
3. Maternal occupation during pregnancy and adverse birth outcomes (12 cohorts; >200,000 participants)
4. Persistent organic pollutants (measured in blood during pregnancy), birth outcomes, and children's respiratory health (12 cohorts; 8,000 participants)
5. Fish consumption during pregnancy and foetal growth (20 cohorts; 152,000 participants)
6. Adiposity and vascular and metabolic health in children (17 cohorts; 47,000 participants)
7. Early growth and childhood asthma (31 cohorts; 147,000 participants)
8. Maternal complications during pregnancy and childhood wheezing (14 cohorts; 114,000 participants)

### **2.3. Links between birth cohorts and registries**

Health information systems describe and monitor health conditions in a society. Birth registries and other routine registries, for example registries on vaccinations (example Text Box 8), use of medication and primary health care, and hospital diagnosis, provide key information on child and adult health and

can be used for evaluation of health programs. The number and quality of national registries vary across European countries. In Scandinavia health information is traditionally collected from the population in nationwide routine registries, such as birth, patient and vaccination registries. In contrast, Southern and Eastern Europe have very few nationwide, routine health registries available to monitor national health conditions and for research. Furthermore, there are very few pan-European registers that contain individual-level data needed for aetiologic research. Although many risk factors and effects discovered through research based on Scandinavian registries are also valid for other countries, it would be very important to set up reliable surveillance systems also in Southern and Eastern European countries and provide prevalence of important health indicators, for example birth outcomes. Such registries would also make it possible to investigate country-specific subgroups to further elucidate important health issues. Population based birth cohorts embedded in birth registries can provide in depth information by following subgroups intensively over longer periods of time.

***Text box 8. Decline in early childhood respiratory tract infections after introduction of pneumococcal conjugate vaccination.***

The pneumococcal conjugate vaccine (PCV7) was introduced into the Norwegian Childhood Immunization Program in 2006. By linking the Norwegian mother and child cohort study (MoBa) with the national vaccination registry in Norway, it was shown that among the children immunized with PCV7 through the childhood immunization program there was reduced incidences of acute otitis media and lower respiratory tract infections in their first 36 months of age. The vaccine was introduced to reduce severe and invasive pneumococcal infections, and the reduced incidence of less severe infections is an added benefit (Magnus et al. 2012). The results from this study contribute with valuable information for evaluation of the national immunization program in Norway.

## **2.4. Privacy protection and legal framework**

Basic regulatory infrastructure has to be in place to establish and build up cohorts and registries and thus regulate and protect the privacy and integrity of personal information. The regulatory infrastructure varies across European countries today. In 2012 the European Commission proposed a new data protection directive to strengthen and harmonize data protection rules throughout Europe. The new directive will replace the EU's Data Protection Directive introduced in 1995 (95/46/EC). EU Member States have implemented the 1995 rules differently, resulting in divergences in enforcement. With the new directive one law will apply to all member states.

## **2.5. Knowledge translation and public and policy engagement**

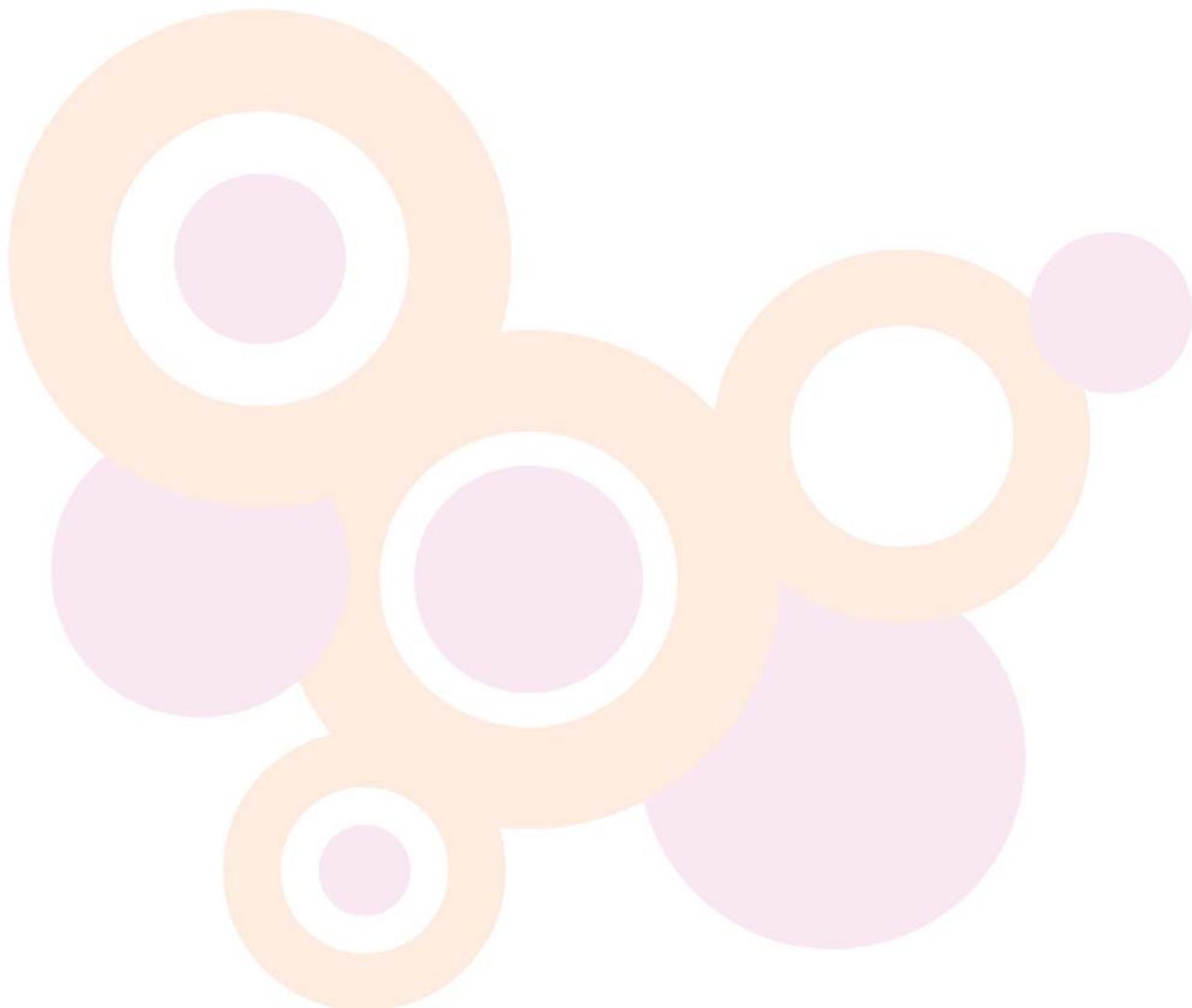
The CHICOS review of the links between birth cohort research and policy found that while the potential of cohorts to contribute to policy is generally clear, barriers remain: policy-makers need unequivocal answers quickly, while researchers are cautious about generalising and need time to complete scientifically rigorous research. Furthermore, policy makers and politicians consider 'evidence' from a wide-range of sources that take public acceptability, cost, political pressures and ideology into account in both understanding and responding to policy problems. Our work suggests there is low agreement in both the research and policy community on the priorities for child health that birth cohorts have to address, and that the potential for policy makers to contribute to cohort planning is

currently underused. On the other hand, research from the current European child health cohorts has made important contributions to current policy within the EU (section 1.3).

Increased and improved communication between policy makers, the public, and the scientific community bring advantages to all by ensuring that the best use is made of existing research undertaken. Investment in knowledge translation as part of a European Birth Cohort would facilitate an efficient use of the existing resource of cohort studies. While individual scientists and cohorts make concerted efforts to publish their research findings and to engage with a broader audience, a combined effort is likely to be more effective. Furthermore, given the frequent moves in the typical career of national and international policy makers (i.e. moving through policy briefs), links at an organisational rather than individual level are crucial. Organisations with the mandate to translate research into evidence for policy (such as Comparative Effectiveness Research organisation, knowledge brokers and scientific advisory committees) already perform this role for specific topics at different levels of government.

Hence the need for a forum to:

1. Exploit existing birth cohort data by creating a new opportunity for those outside the scientific community to raise questions;
2. Disseminate findings of research to a wider audience by creating non-scientific outputs from across the community of cohort studies.



### **3. Comparing different European birth cohort strategies**

As mentioned in the previous sections, we have outlined the rationale for a European birth cohort strategy and evaluated the current status of birth cohort data and coordination. One of the following approaches could be adopted:

- a. Support for **continued collaboration** between existing cohorts. Such collaboration would work most efficiently through topic-specific task forces focusing on data sharing mechanisms, exchanging methodology and birth cohort researchers, and improving data comparability and harmonisation. It may be achieved by setting up an infrastructure for collaboration;
- b. Support for a **new large Pan-European birth cohort** to collect appropriate new data across all geographical areas and key populations in the region. This new cohort would take considerable time to plan, obtain relevant funding, pilot data collection and begin recruitment. Results may not be expected until 10-15 years from now;
- c. A combination of the two above. Support for a **collaborative European Birth Cohort**, using data from **existing and new** cohorts. This approach would build a permanent Europe-wide data resource, containing a minimum set of prospective, individual-level information about child health in Europe which will provide key statistics on child health and determinants to enable health surveillance and as a basis for research. A core database with tightly governed access policies respecting each individual cohort's integrity should form part of this, and could be set up relatively rapidly. It would include additional support for establishing new cohorts in geographical areas or in populations that are currently underrepresented in existing cohorts. It should also try to fill the research and data gaps indicated in section 2 of this report, that is support for follow-up of children into adolescence and young adulthood, links to routine registries, and an action plan for rapid response and knowledge translation

The table below summarises the advantages and disadvantages of these three strategies. It could be argued that following both strategy (a) and (b) forward would be the best approach. Importantly, both carry costs, and whilst (a) is less costly than (b) it does still require appropriate resourcing for the above described potential to be achieved. Given the current global (and European) economic climate we do not think it realistic to suggest that both approach (a) and (b) are taken forward. Because of the wealth of data in existing cohorts (see Section 2 of this report) and emerging collaborations among them that are starting to contribute important research for European child health policy (section 2), together with the fact that recent experience from the USA demonstrates how difficult and slow it is likely to be to obtain adequate funding and then establish a new pan-European birth cohort, **we believe approach (c) – i.e. developing a new pan-European birth cohort study from existing birth cohorts supplemented by new birth cohorts that fill gaps in populations currently not covered – is the most appropriate approach for providing a clear research base relevant to EU policy to improve and maintain maternal and child health.**

**This would imply that a collaborative European birth cohort is established, based largely on existing cohort data, but with support for establishing new cohorts in regions and/or populations that are currently underrepresented.**

**Table 1. Comparison of different approaches to a European wide Birth Cohort Strategy (1/2)**

Need addressed	Support for continued collaboration between European birth cohorts (Strategy (a))	Support for a new pan-European birth cohort (Strategy (b))	Combination of (a) and (b): the collaborative European Birth Cohort (Strategy (c))
<b><i>Time</i></b>	Substantial amounts of data and collaborations already exist and so this could continue now.	Would take considerable time to plan, obtain relevant funding, pilot data collection and then begin recruitment. Realistically it would be 5-10 years before recruitment began and 10-15 years before data were able to contribute to policy relevant research.	Substantial amounts data and collaborations already exist in cohorts, but time is needed to build a core database and agree access policies. Strategy c) would make use of existing data (with all provisions listed under a)), while planning for additional cohorts to complement these (for example by recruiting under-represented groups and regions).  Any new data collection will, however, be less extensive than in alternative (b).  Alternative (c) would take more time to set up and deliver policy relevant results than (a), but much faster than (b).
<b><i>Financial consequences</i></b>	Least costly, though still requires funding for coordination, maintenance of birth cohorts database, data sharing, harmonisation of data, and completing collaborative research.	Most costly, and would likely require EU level funding and funding from government sources within each country. Some countries may not see this as a spending priority.	A minimum set of information on European child health would require that data collection from groups that are not represented in cohorts today. Existing cohorts and registries will be used as data sources when available. Building of a core database would require funding but less substantial than (b). This approach would require EU level funding.  Alternative (c) would be more expensive than (a) but less expensive than (b).
<b><i>European coverage</i></b>	Coverage of existing cohorts shows important lack of data on minority ethnic groups and in certain regions of Europe (namely Eastern Europe, to a lesser extent Southern Europe) where the prevalence of many adverse child health outcomes and high-risk behaviour and life-style factors is highest.	If it were possible to get agreed funding from all European countries (or a minimum set of countries would provide sufficient coverage of each region) and to develop methods that would ensure adequate numbers of key European minority ethnic groups were recruited and supported to remain participants in the study this strategy would be more representative than (a).	The purpose of the approach is to collect a minimum set of data from existing cohorts and from groups that are not represented in existing cohorts: e.g. minority groups and Eastern European populations.  This would minimize the current gaps in coverage.

Table 1. Comparison of different approaches to a European wide Birth Cohort Strategy (2/2)

Need addressed	Support for continued collaboration between European birth cohorts (Strategy (a))	Support for a new pan-European birth cohort (Strategy (b))	Combination of (a) and (b): the collaborative European Birth Cohort (Strategy (c))
<b>Gaps in knowledge</b>	This strategy is based on existing data only and is thus appropriate for tackling knowledge gaps for which data has already been collected, or is being collected by cohorts individually. It will thus not include support for collecting new data on emerging risk factors.	A new birth cohort could ensure that all data to fill knowledge gaps is collected from the start in a standardized way across cohorts.	<p>Similar to approach (a), this approach would initially be based on existing data. However, the database and infrastructure should also ensure that knowledge gaps are identified early and that ongoing data collection in the cohorts is directed towards filling these gaps in a coordinated manner across Europe.</p> <p>Because this approach includes support for continued follow-up of existing cohorts it will also be particularly useful to fill knowledge gaps related to later childhood, adolescence, early adulthood and onwards. Follow-up of the existing cohorts is by far the most efficient way of obtaining these data.</p>
<b>Policy needs</b>	The varying data available in existing cohorts may be an advantage for emerging policy / scientific questions. For example, a well maintained and updated database of existing cohorts and the data contained within them could be searched to identify any with relevant data. Having had different investigators involved in each study is likely to have increased the potential for some “unusual at the time” measurements to have been undertaken.	Potential to ensure that collected data are relevant to identified key areas of scientific and policy need. However, the gap between agreeing this is the way forward and beginning recruitment may mean some of this potential is lost. Also if all data collection are standardized this cohort may be less able to respond to newly emerging areas.	The minimum set of data from a European cohort would provide basic and representative health information for monitoring child health and related policies in Europe. More detailed information on specific topics/scientific questions can be collected from smaller cohorts so that emerging policy concerns can be responded to rapidly.
<b>Collaboration</b>	Persuading scientists from different countries to effectively collaborate with each other and share data can be difficult, because of time-constraints, lack of resources for such work, a sense of data-ownership, and real ethical/governance issues that restrict this type of work. Approaches to overcome these barriers are increasingly available, but if this strategy is adopted there would need to be investment in methods to overcome them.	Having a Pan-European cohort would engage relevant researchers in a collaborative way from the start. Though efforts would still be necessary to ensure that all relevant researchers did have a sense of ownership and were keen to input and that data were made widely available within an appropriate governance framework.	Efforts to support collaboration would be necessary. See (a) and (b).

## 4. Recommendations

CHICOS shows that the groundwork now exists for an ongoing infrastructure for birth cohort research in Europe that includes more than 500,000 mother-child pairs with the ability to bring scientific advances of great relevance to European child health policy making.

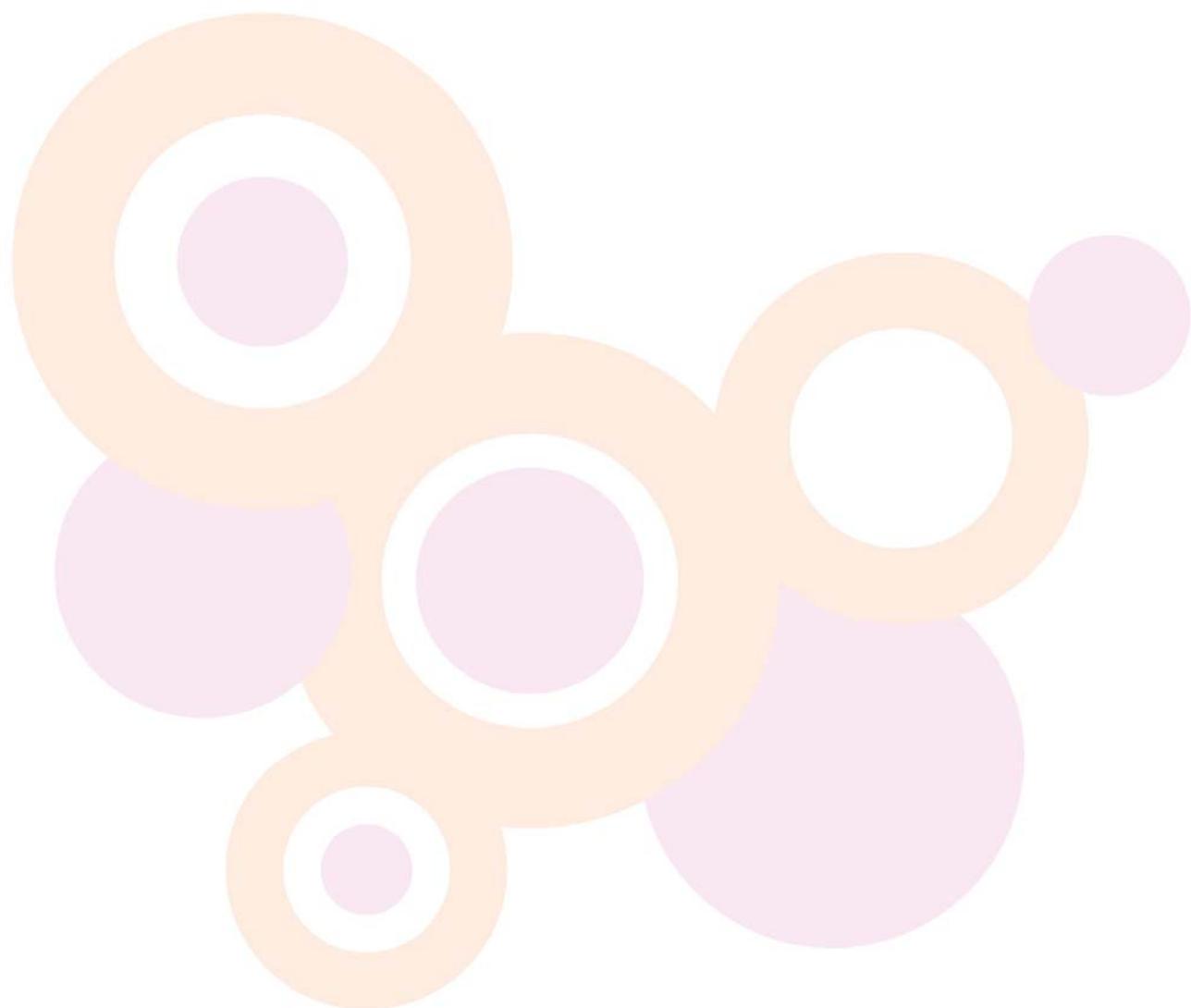
Our strategic analysis of the current state of European birth cohort research has resulted in a set of recommendations that address needs for birth cohort coordination and research at the European level over the next 10 to 15 years:

CHICOS recommends **establishing a collaborative European Birth Cohort**, using data from **existing and new** cohorts. This cohort will build a permanent Europe-wide data resource for longitudinal, individual-level information on child health in Europe. It will provide key statistics on child health and determinants to enable health surveillance and to provide rapid responses to knowledge gaps that should be tackled to inform policy.

The collaborative European birth cohort should include support for:

1. ***Establishing the infrastructure for Europe-wide database platform*** – including a core database platform, data sharing and data harmonisation rules, biobank access guidelines, exchange of methodology and expertise - resulting in more efficient use of existing and newly established cohorts;
2. ***Including new cohorts that cover groups of the European population that are underrepresented in birth cohort research*** – There is a lack of data from minority groups, and some regions in Europe (e.g. Eastern Europe) are underrepresented in cohort research. There should be efforts to fund, develop, include and improve cohorts from these regions and minority population groups;
3. ***Continuing follow-up of existing European cohorts*** – There are especially good opportunities in Europe for longer term follow-up of the existing cohorts and the European research communities and funding bodies have an obligation to exploit these opportunities and thereby contribute to insight in which mechanisms, acting over the life course, are responsible for creation of health and disease in childhood, adolescence, adulthood and older ages. Follow-up of the existing cohorts is by far the most efficient way of obtaining these data;
4. ***Combining data from cohorts, registries and other data sources*** – Birth registries and other routine registries can provide key information on child and maternal health and be used as instruments for evaluation of health programs. Registries with individual child health data on the European level are largely lacking. Birth cohorts embedded in birth registries can provide in depth information on subsets of mothers and children, following up subgroups intensively over defined periods of time. This would enhance the contribution of both birth cohorts and population based registries;
5. ***Integrating knowledge translation, public and policy engagement*** – A key role within a European birth cohort infrastructure would be that of undertaking knowledge translation, public and policy engagement. Alongside support for infrastructure scientific collaborations, we believe investment in knowledge translation would lead to an efficient use of the existing

resource of cohort studies. This would improve efficiency in communication between the scientific community and a broader audience, including policy makers at both national and international levels. A **knowledge translation forum** could monitor topics of interest to the public or within policy communities and use knowledge of existing data to identify opportunities for rapid responses. Such a forum could, in turn, organise publication of briefing documents written in a style and format appropriate to public and policy audiences. This would have the further advantage of supporting the increased impact of less well resourced cohorts (often those based in less affluent countries).



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