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Developing a Child Cohort Research Strategy for Europe

STRATEGIES FOR EUROPEAN BIRTH COHORT RESEARCH **NON TECHNICAL REPORT**



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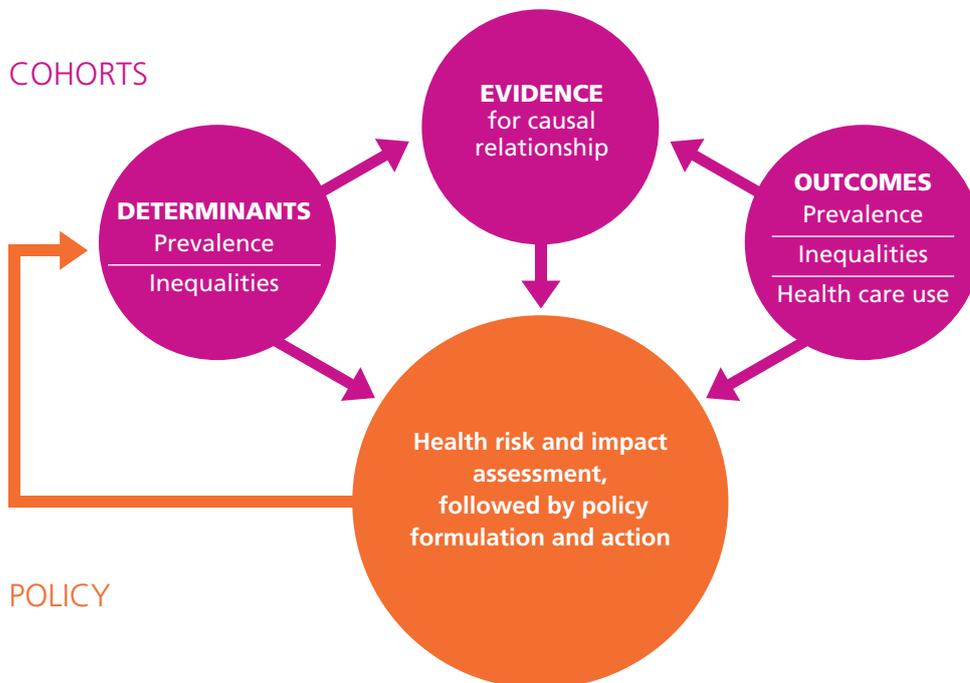
Comparing European birth cohort strategies

CHICOS (Developing a **Child Cohort Research Strategy** for Europe) is a project funded under the European Union's 7th Framework Programme.

It was launched in January 2010 with the aim to **improve child health across Europe** by developing an integrated European strategy for birth cohort research. Beside optimizing the work of the different birth cohorts that were already active in Europe, **CHICOS** would **provide policy- and decision-makers with data** based on solid scientific evidence, thus supporting public health interventions to improve child health. The project was completed in February 2013.

What you will find in this Report:

- **CHICOS** recommendations (Key messages);
- the context of **CHICOS** research (What is a birth cohort?, How can birth cohorts contribute to policy-relevant research?, Why is a European birth cohort research strategy needed?);
- the current state of European birth cohort research (Birth cohorts in Europe, Birth cohort coordination);
- alternative strategies for birth cohort coordination.





Developing a Child Cohort Research Strategy for Europe

Key Messages

- Birth cohorts are valuable potential sources of policy-relevant research, since they collect a wealth of key information on childhood diseases and their determinants.
- Today, there are more than 70 birth cohorts across Europe, studying over 500,000 mothers, fathers, and children at repeated time points and over long time periods.
- Pooling of cohort data across countries is possible and valuable, but there is currently no common European database.
- Improved collaboration across Europe will enhance research and knowledge obtained from individual birth cohorts and their ability to contribute policy-relevant findings and respond rapidly to new policy concerns.
- Based on strategic analysis of the current state of European birth cohort research, **CHICOS** has drafted a set of recommendations for the next 10 to 15 years.

RECOMMENDATIONS

ESTABLISHING A COLLABORATIVE EUROPEAN BIRTH COHORT

this cohort shall use data from existing and new cohorts and:

- **establish an infrastructure for a Europe-wide database platform**
for more efficient use of both existing and newly established cohorts
- **include new cohorts that cover groups of the European 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 adults
- **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, public and policy engagement**
this would support the translation of research findings into political and public health priorities and policies

What is a birth cohort?

Birth cohorts are **longitudinal studies**: this means that participants are followed through the years. In this specific case, cohort monitoring spans from the intrauterine period, birth, or shortly after birth, through childhood and into adolescence and sometimes adulthood.

What kind of information is gathered?

Birth cohort studies collect information on diverse topics related to the social and environmental characteristics of children’s and their parents’ lives. Most studies also collect biological specimens, which provide the opportunity to measure biological markers of a variety of environmental or nutritional factors, and to obtain information on the genetic profile of parents and children.

Follow-up

Child growth, child behaviour, and cognitive development are measured at **repeated time points** during childhood, and information is collected on a variety of other health-related topics, such as asthma and infectious diseases.

CHICOS took into account birth cohort studies with the following characteristics:

- a. Study focus is on health and participants are recruited from a European country.
- b. Participants are recruited during or before pregnancy, at birth, or in the first 12 months of a child’s life.
- c. Initial recruitment of participants took place in 1990 or thereafter.
- d. The birth cohort includes at least 300 participants.
- e. The birth cohort must have completed some follow-up assessment, at least during the first years of life or have certain, earmarked funding to complete the aforementioned follow-up.

CHICOS focused in particular on the following child health outcomes and determinants:

- social and cultural conditions
- nutrition and physical activity
- life-style and substance exposures
- environmental exposures
- biological and genetic factors
- perinatal outcomes
- respiratory health
- obesity, and vascular and metabolic health
- neuro-cognitive and behavioural development
- accidents and injuries
- infectious diseases
- childhood cancer



How can birth cohorts contribute to policy-relevant research?

Investing in children's health has increasingly been recognised as essential to human and economic development.

Wide differentials in child health exist within and between European countries, indicating considerable potential for improvement.

In order to implement public health interventions in the field of child health, policy- and decision-makers need to refer to a **sound evidence base**.

Birth cohort studies offer this kind of base

Their prospective nature (i.e., the fact that they measure risk factors before information on health outcomes is collected and, in most instances, even before disease onset) and the large variety of exposures and outcomes assessed make these studies particularly valuable when it comes to:

understanding the causes of disease and ill-health rapidly providing of answers for policy making

because:

1. birth cohort studies imply a **long follow-up**: this makes them particularly well-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 biochemical changes induced by the environment in the development of disease, even though the potential importance of this approach was not widely considered at the time many of these cohorts were established.

2. cohort studies are **prospective**: they measure risk factors at an early age (point in time) **before** disease onset or before information of health-related outcome is collected at an older age (later time).

This approach can more clearly delineate the causal direction of an association. An example is the relationship between vitamin D levels and asthma.

Vitamin D and asthma

Recent 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. These results suggest that intervention to ensure adequate vitamin D levels may reduce the development of asthma outcomes in childhood.



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 a number of child health policy areas, including:

- Understanding **health inequalities**.
The rather persistent social inequality in health in adult life may (partly) have its origin early in life. Social gradient in gestational age at birth and foetal growth have both been proved to be predictors of later health.
- Identifying **healthy and unhealthy environments**.
For example, research on lead pollution influencing cognitive development in children contributed to the ban on lead in petrol and the subsequent dramatic decreases in blood lead levels in mothers and children over the past decades.
- Identifying the role of **lifestyle-related behaviours**.
Examples are the studies on the effects of breastfeeding, parental smoking, children’s diet and physical activity on normal growth development and health in childhood.
- Identifying the role of **specific exposures**.
An example is the controversy about the health effects to the foetus of the intake of small amounts of alcohol during pregnancy.
- Identifying characteristics related to major **mortality and morbidity risks** in infancy or childhood.
For example, research from birth cohorts and registries (surveillance systems which monitor a population’s health conditions, such as birth and vaccination registries) has been key to health policy health policy in preventing sudden infant death syndrome.

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 body mass index and maternal smoking, weight gain, and alcohol intake during pregnancy affected the gradient. The effect of these maternal lifestyle factors accounted for only a minor part of the educational inequality in preterm births; consequently, better explanations are needed.

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 found that breastfeeding is associated with a higher IQ in the child. Results were consistent in the different cultural settings where socio-economic patterns in breastfeeding differ. Associations with blood pressure and body mass index of children were not likely to be causal.

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 moderate drinking while pregnant. This made it possible to study foetal health associated with moderate alcohol intake. Studies showed that the risks of preterm birth, congenital anomalies and infant death, were unaffected. However, a strong increase in the risk of miscarriage was observed with an intake of two or more drinks a week.





Developing a Child Cohort Research Strategy for Europe

Why is a European birth cohort research strategy needed?

Most birth cohorts have collected pregnancy, perinatal, infancy, and childhood data on lifestyle, socioeconomic position, growth, adiposity, and many have genetic data, as well. Most have biological specimens of the mothers (and sometimes fathers) and children stored in large **biobanks**. Data collection and methods vary across cohorts and there has traditionally been little coordination to structure and consolidate research across the different birth cohorts.

It is becoming increasingly clear that considerable added value could be gained from collaboration between birth cohort studies:

- **Discovering causes of disease**
Risk factors that are associated with diseases in diverse cohorts are more likely to be real causes of those diseases. Collaboration of birth cohorts and registries across Europe would enable replication of this kind to become routine practice, and only findings with robust replication should influence policy.
- **Speedy response to key policy questions**
Greater collaboration among European birth cohorts would enable a better, more coordinated response across Europe.
- **Large sample sizes**
Very large sample sizes are required to understand the epidemiology of, and how best to prevent, rare but important diseases in infancy and childhood, such as congenital anomalies and childhood cancer. Cross-European collaboration is required to examine major causes for this type of 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 between environmental and genetic factors).
- **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.
- **Greater and more efficient use of existing cohorts**
Thanks to widespread cross-European collaboration, a greater number of scientists drawn from a wider range of fields of expertise would address issues, and make use of available data, which individual cohorts may not have thought of.

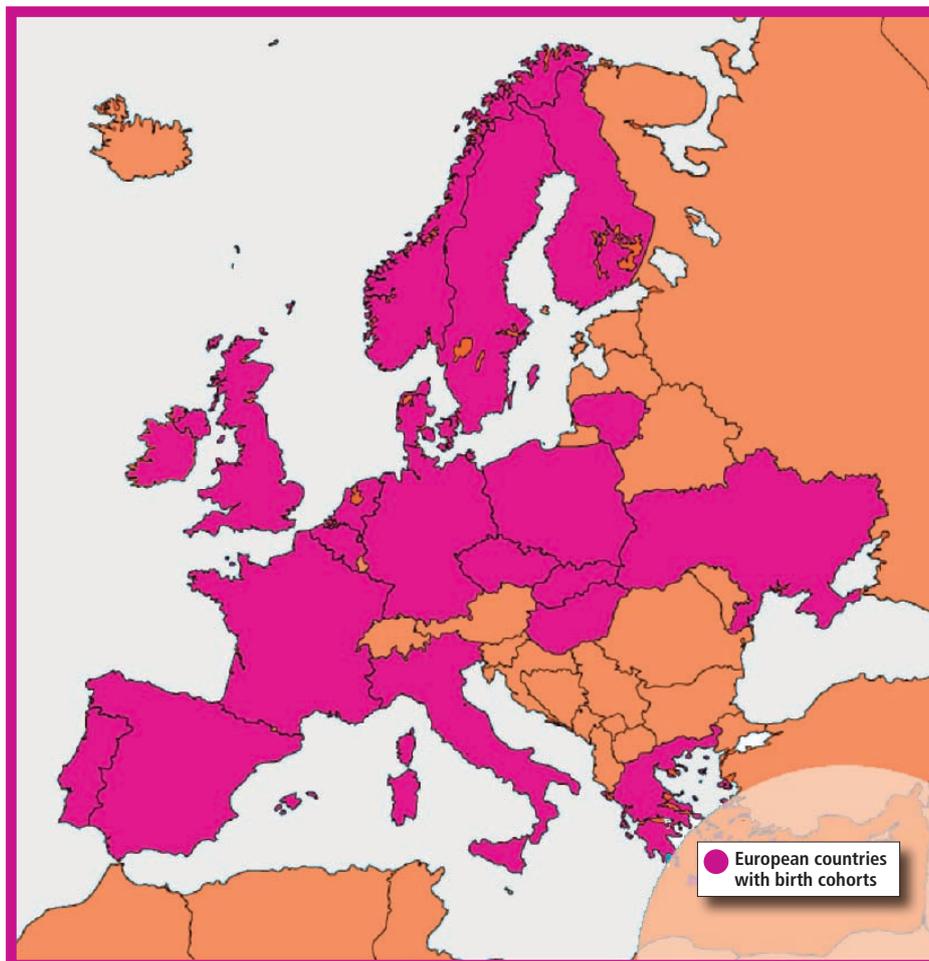
Improved collaboration across Europe will
enhance research and knowledge
obtained from individual birth cohorts and their
ability to contribute policy-relevant findings

The current state of European birth cohort research

Birth cohorts in Europe

There are over 70 birth cohort studies in Europe today, and they follow more than 500,000 children. Objectives, time of recruitment, size, and geographical distribution of the cohorts vary considerably throughout the continent:

- some are general cohorts with multiple aims, others focus on specific health or exposure-related research issues;
- the majority of cohorts is located in Northern and Western Europe, though all regions of Europe have birth cohorts that are suitable for research purposes;
- the number of children followed by each cohort spans from less than 1,000 to more than 100,000.



There are some **shortcomings** that are common to most, if not all birth cohorts:

- **lack of data on minority ethnic groups and certain regions of Europe** (namely Eastern Europe, to a lesser extent Southern Europe) where the prevalence of some adverse child health outcomes, high-risk behaviour and life-style factors is highest;
- **lack of tracking of results into later childhood, adolescence and adulthood:** very few cohorts have been followed up for long enough to study disease causation over the life course;
- **lack of comparable assessment tools and data**, hampering the comparison of data and findings across European birth cohorts, especially for neuropsychological development;
- **lack of links to routine surveillance systems and registries** that are needed for birth outcomes, injuries, infections, and childhood cancer.

VALUE OF LINKS BETWEEN BIRTH COHORTS AND REGISTRIES

Decline in early childhood respiratory tract infections after introduction of pneumococcal conjugate vaccination

■ The pneumococcal conjugate vaccine (PCV7) was introduced into the Norwegian Childhood Immunisation Programme in 2006. By linking the Norwegian Mother and Child cohort study (MoBa) with the national vaccination registry in Norway, it was shown that, among children immunised with PCV7 through the childhood immunisation programme, there was reduced incidence of acute otitis media and lower respiratory tract infections before 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. The results from this study have contributed valuable information for evaluation of the national immunisation programme in Norway.



Birth cohort coordination

Collaboration between birth cohort studies is fundamental. In recent years, networking projects (such as **CHICOS**), and collaborative EU research projects have helped to approach this goal.

In order to make the most of the enormous investments represented by existing European birth cohorts in terms of money, time, intellectual resources, commitment of participants and their parents, the following topics need to be addressed:

- **Coordination efforts** have created a positive attitude towards data sharing, but efforts of this kind are almost always limited by the time span of funded projects.
- **Continuity** is important to further 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 included in registry data, smaller cohorts with more in-depth data collection.

- **Combining, pooling, and 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 study populations and thus more conclusive findings than those based on single cohorts.
- **Collaborative analyses require adequate funding** over and above funding available for each individual cohort study.
- **Considerable progress has been made in standardising data of a wide variety of cohorts**, most successfully in projects that focus on fairly narrow topic areas (genetics, air pollution, asthma), but there are still many extremely heterogeneous or mixed areas with scarce comparability of variables across cohorts (for example, neurodevelopment, diet, and physical activity). Greater collaboration and creation of specific task forces of experts would help creating common tools for exposure and outcome assessment.
- **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.
- **A strategy and action plan for cohort collaboration needs to be developed** as a basis for speedy response to key research and policy questions.

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) and birth outcomes and 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 infant growth and childhood asthma (31 cohorts; 147,000 participants)
8. Maternal complications during pregnancy and childhood wheezing (14 cohorts; 114,000 participants)



Comparing European birth cohort strategies

A European birth cohort strategy is a necessity. Given the existence of different birth cohorts already active in Europe, which approach is best suited to reach this goal?

Would it be better:

a. to support **continued collaboration between existing cohorts,**

or:

b. to focus on the creation of a **new large pan-European birth cohort** that would collect new pertinent data across all geographical areas and key populations in the region?

Based on a thorough analysis of the pros and cons of the above strategies, including their financial requirements and the current economic crisis in Europe, **CHICOS** has come to the conclusion that the best choice would be a combination of the two approaches, i.e., to focus on the establishment of a **Collaborative European Birth Cohort using data from both existing and new cohorts.**

This would involve the creation of a cooperative European birth cohort based largely on existing cohort data, but with support for establishing new cohorts in regions and/or populations that are currently underrepresented.





Developing a Child Cohort Research Strategy for Europe

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