

## **Executive summary:**

Child health has been identified as one of the overarching issues of the Seventh Framework Programme (FP7) Health Research theme, which focuses on improving the health of European citizens. Policy and decision makers need a solid evidence base to develop and implement public health interventions and incorporate health goals in the definition and implementation of all policies, including those focused on child health. More than 70 birth cohorts are collecting a wealth of information on childhood diseases and their determinants across Europe. However, there has been little coordination of research and results between countries, and the large potential for policy implications does not always filter through to policy at national and European level.

CHICOS was commissioned to improve child health across Europe by developing an integrated strategy for mother-child cohort research through coordination of the most important European cohorts. CHICOS is structured into work packages to make an overview of all mother-child cohorts in Europe (WP1), evaluate existing information on outcomes and determinants from these cohorts, evaluate links between cohorts and routine registers, identify gaps in knowledge, and develop recommendations for research action at European level for the next 15 years focusing on key areas of policy concern (WP2 and 3) and to review the extent to which mother-child cohorts and registries have contributed to current European child health policies and make recommendations to improve the contribution of mother-child cohort research to policy at the European level (WP4). Working groups focused on the availability of information of key child health outcomes including: perinatal outcomes, asthma, obesity, cognitive and behavioural development, injuries, infections, childhood cancer. Key determinants include: social inequalities, nutrition and exercise, lifestyle exposures, environmental toxin exposures, genetic factors and biobanks, multiple risk factors. WP5 is dedicated to the dissemination of project results to stakeholders, as well as evaluation of new technologies for cohort research dissemination.

Following three years of intense collaboration, the project came to conclusion in February 2013. In short, CHICOS has shown that pooling of cohort data across countries is possible and valuable, but that there are still substantial practical obstacles in international collaborative initiatives. A lack of data was identified from minority groups, southern and eastern European countries, as well as from older children and adolescents. Considerable benefits would be derived from a European database with prospective, individual-level, data on child health and determinants. As well as in 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. CHICOS shows that the groundwork now exists for ongoing birth cohort research in Europe including more than 500,000 mother-child pairs with the ability to bring scientific advances of great relevance to European child

health policy making. This final document outlines in our findings and recommendations for future birth cohort research and its' role in policy development.

## **Project Context and Objectives:**

Birth cohorts are prospective longitudinal studies that follow participants (parents and their children) from the intrauterine period, birth or shortly after birth, through childhood into adolescence and sometimes adulthood. Such studies collect information on diverse 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 during childhood they measure child growth, behaviour, and cognitive development, and they collect information on a variety of other health related topics, such as asthma and infectious diseases. 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.

CHICOS includes only cohorts with a focus on health. In the context of the project the definition of a European birth cohort was restricted to be a study with the following features:

- a) Participants are recruited from a European country.
- b) Participants (mothers and children) are recruited in or before pregnancy, at birth, or in the first 12 months of the child's life.
- c) Initial recruitment of participants had taken place in 1990 or more recently. Selected cohorts will 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 some 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 definite funding for completing such follow-up.

## **HOW CAN BIRTH COHORTS CONTRIBUTE TO POLICY RELEVANT RESEARCH?**

Policy and decision makers need a valid evidence base for the development and implementation of public health 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 potential for improvement.

There are several unique features of the birth cohort study design that make it particularly important for contributing to understanding 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, for example maternal cigarette smoking, fetal 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 such data at the time. Cross-sectional study designs cannot separate exposure and outcome assessment in time and are thus not able to distinguish whether a risk factor caused a disease or if the association is the other way round. For example, whether vitamin D levels in the blood cause asthma or if asthma resulted in the child being less able to play outside and be exposed to sunlight which determines vitamin D levels. 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, and impaired lung function. 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 rapidly provide answers for policy making is the concern raised regarding the role of early life exposure to peanuts in 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). 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 product in skin products for children. 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 rather persistent social inequality in health in adult life may (partly) have its origin early in life. Social gradient have been demonstrated in gestational age at birth and in fetal growth, both predictors of later health. It has been suggested that social patterning of simple lifestyle factors, e.g. maternal smoking may be the mechanism behind the gradient and this has proved to be likely for fetal growth. However, when birth cohort data was used to explore the mechanisms behind the social gradient in preterm birth, so such simple explanation could be confirmed. An educational gradient was found in preterm birth risk in the Danish National Birth Cohort (as in most other data). Cohort data was used to estimate how maternal pre-pregnant BMI and maternal smoking, weight gain, and alcohol intake during pregnancy affected the gradient (Ref). The effect of these maternal lifestyle factors explained only a minor part of the educational inequality in preterm birth and, consequently, better explanations are needed. Comparative studies using birth cohort data from different settings may provide clues to identify possible preventable factors behind that social gradient in preterm birth.

-Identifying healthy and unhealthy environments, such as research on lead pollution influencing cognitive development in children, contributing to the ban on lead in petrol and the subsequent dramatic decreases in blood lead levels in mothers and children over the last decades. In other areas, such as air pollution and food contaminants, birth cohort research is now producing new results which have the potential to influence future policy

-Identifying the role of lifestyle-related behaviours, such as breast feeding, parental smoking, child's diet and physical activity, for normal growth and development and health in childhood. For example, cohorts have established a probable causal link between breastfeeding and child IQ, which can help to underpin breastfeeding promotion programmes. By comparing the effects of breastfeeding on child health and development between 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 were consistent in the different cultural settings where socio-economic patterns in breastfeeding are different. 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 to developing peanut allergy (see earlier example) and the controversy about intake of small amounts of alcohol during pregnancy. In contrast to most other European countries, a small intake of alcohol during pregnancy was not strictly warned against in Denmark during the first years of the 21st century. Compared to other cohorts, a substantial proportion of women in the Danish National Birth Cohort reported to drink small amounts while pregnant. This allowed to study fetal health associated with such intake. These studies revealed that the risks of preterm birth risk, congenital anomalies and infant death was unaffected, but a strong increase in miscarriage risk was found with intake of two drinks a week or more.

-Identifying characteristics related to major mortality and morbidity in infancy or childhood. For example, research from birth cohorts has been a key influence on health policy for preventing sudden infant death syndrome.

## **WHY IS A EUROPEAN BIRTH COHORT RESEARCH STRATEGY NEEDED?**

There are now many pregnancy and birth cohorts in Europe that together have information collected 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. The majority of cohorts have biological specimens of the mothers and children (and sometimes fathers) stored in large biobanks.

New European birth cohorts 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 2013. 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 differences in genetic factors, culture, socioeconomic levels, living habits, etc, associations that are replicated would give stronger causal evidence and that would make them more relevant to child health policy. Collaboration of birth cohorts and registers across Europe will enable such replication to become routine practice and only findings with robust replication should be put forward to influence policy.

### **2) Speedy response to key policy questions**

Frequently, speedy responses are necessary to policy concerns (as in the case of peanut allergy). Greater collaboration of European mother-child cohorts will enable a better and more coordinated response across Europe.

### **3) Large sample sizes**

Very large sample sizes are required to understand the epidemiology of, and how best to prevent, rare but important disease outcomes in infancy and childhood, such as congenital

anomalies and childhood cancers. Only with collaborations across Europe can we examine major causes for such diseases. Similarly, to fully understand the role of infrequent risk factors or how risk factors interact with each other to determine child health and disease status (for example interactions of environmental and genetic factors), we need very large sample sizes.

#### 4) Improving methodology

By sharing ideas across a wider group of scientists involved with birth cohorts across Europe and also involving experts from research and practice in child-health policy, it is likely that methodological approaches to data collection and analysis will improve. Researchers from different disciplines will likely share different methodological approaches with different strengths and limitations.

#### 5) Greater and more efficient use of existing cohorts

Individual birth cohorts commonly have many hundreds of different variables on individuals collected repeatedly. The potential contribution to science of these data go well beyond what any group of principal investigators could imagine doing. Principal investigators for anyone cohort are unlikely to include those with expertise in all areas that the study could contribute to. With widespread collaboration across Europe a greater number of scientists from a wider range of expertise would be able to address questions, and make use of available data, that 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. Therefore, the EC funded the CHICOS ('Developing a Child Cohort Research Strategy for Europe') project through its 7th framework programme to develop a strategy for birth/mother-child cohort research in Europe.

In this context, the CHICOS remit was therefore based on following objectives:

- To make an overview of birth and mother-child cohorts in Europe, including the opportunities to link these cohorts to existing pan-European registries.
- To evaluate existing information on child health outcomes and determinants from cohorts, to evaluate links to routine registries, to identify gaps in knowledge, and to develop recommendations for research action at European level for the next 15 years, focusing on key areas of policy concern.

-To review the extent to which mother-child cohorts and registries have contributed to current European child health policies and make recommendations to improve the contribution of mother-child cohort research to policy at the European level.

-To disseminate results of the project to stakeholders and to evaluate new technologies for cohort research dissemination.

## **Project Results:**

### **CURRENT STATE OF EUROPEAN BIRTH COHORT RESEARCH**

#### **BIRTH COHORTS IN EUROPE**

A large number of birth cohorts exist in Europe. Their aims vary considerably with some being general cohorts with multiple aims, whilst others focus on specific health or exposure-related research questions. The design (e.g. time of recruitment) and size also vary. Nevertheless, an inventory of birth cohorts showed that the number of birth cohorts exceeds 70 and the cohorts encompass more than 500,000 children (Larsen et al 2013). This is an impressive number but of course only a small percentage of all births in Europe (greater than five million births annually in 25 EU countries - see <http://epp.eurostat.ec.europa.eu/> online). The majority of 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 the existing cohorts and the data they have collected from parents and children, can be found at <http://www.birthcohorts.net>, a webpage that aims to make basic information about the birthcohorts available to the public, to stakeholders (researchers in particular), in order to increase the scientific exploitation of these valuable data as well as facilitate collaboration and comparative analyses between the studies.

CHICOS has evaluated available data on health outcomes and determinants in the European birth cohorts. The full detailed reports are available from the CHICOS website; Research priorities for childhood diseases (see <http://tinyurl.com/cqb48ga> online), and Research priorities for child health determinants (see <http://tinyurl.com/bw5pt6b> online):

-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. Also, they are closely related to future health outcomes, and serve as key exposures in life course studies (Kuh et al 2003; Saigalet al 2008). Birth registries are essential for monitoring of these outcomes, while pregnancy cohorts are needed to address aetiological issues and validation. European birth cohorts have given a substantial contribution to research within modifiable risk factors for adverse birth outcomes, for example smoking, diet and other environmental exposures.

-Many cohorts collect data on asthma, respiratory health, and allergies, and some standardised tools for assessment of these outcome are available or under development in large European projects. Pooled analyses of these data have been carried out, for example examining the effect of maternal smoking on asthma in children (Neuman et al 2012).

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

-Measures of weight and height are available in the majority of existing European birth cohorts, but the availability of other measurements of adiposity or its distribution (e.g. waist, skinfold thicknesses, directly assessed fat mass, visceral fat) is more limited. Blood pressure is commonly measured, but relatively few cohorts have measurements of blood based measures or vascular function/structure measures.

-European birth cohorts are very heterogeneous in their assessment of neuropsychological and behavioural development of the children, which precludes combined analyses, and there is a strong need to harmonize the neuropsychological assessment.

-In injuries research, birth cohorts have had a limited role up to now and no standardised questionnaires or protocols exist in this field, but the cohorts have the potential to provide valuable information on determinants (ie. social inequalities) and safety behaviours (ie. parental behaviour).

-Data on infectious outcomes has 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 studies inside and outside Europe. The 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. All European birth cohorts collect information, albeit in different format and depth. Few cohorts include sufficiently large minority groups (low-income, ethnic minority) to draw conclusions about the particular child health problems in these groups.

-Information on diet in different time points, (pregnancy, early infancy and later childhood) is widely collected in the cohorts, 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.

-There are few cohorts with 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. For preventive efforts, better understanding of the complex causal pattern behind initiation and continuation of substance abuse is needed.

-For environmental pollutant exposures, there is data in more than 40 cohorts, summarised by the ENRIECO project (Vrijheid et al 2012, Gehring et al 2013). For some of these exposures, pooled analyses have been feasible (e.g. the effects of persistent organic pollutants on fetal growth - Govarts et al 2012 -, and the effects of smoking on asthma - Neuman et al 2012), whereas for others (e.g. radiations, noise, new chemicals) data and methods are not sufficiently standardised to compare between countries.

-Many birth cohorts collect biological and genetic samples and had major investments for establishing 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 do have biological samples available but cannot make optimal use of them because of financial restrictions. Scientific collaboration using especially genetic samples has proven to be extremely successful.

Gaps common to all topics include:

-Lack of data in minority ethnic groups and in certain regions of Europe (namely Eastern Europe, to a lesser extent Southern Europe) where the prevalence of many of the adverse child health outcomes are highest;

-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.

-Lack of comparable assessment tools and data, impeding the comparison of data and findings across Europe, especially for neuropsychological development, diet, and physical activity.

-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.

## **BIRTH COHORTS COORDINATION**

Recent years have seen an increase in the willingness to share data between 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:

- The 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 these efforts are almost always limited by the time span of funded projects. Nevertheless, they have built the groundwork now 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 further develop this into a permanent Europe-wide resource for child health surveillance and research.
- Europe has different types of 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. Other European projects have made similar contributions.
- Collaborative analyses require adequate funding over and above the funding available for each individual cohort study. Exploring whether relevant data exist, where it does whether it is sufficiently similar for collaboration, agreeing standardised analysis protocols, pulling out datasets from each study, analysing these and then combining results appropriately is not trivial and requires adequate funds. Such funds should include not just the cost of central data management and analysis but also those required by the individual cohorts to participate in combined analyses. Growing demand for data sharing puts increasing pressure on local data management personnel to prepare data.
- 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. It is important that these efforts are well documented and made available for future studies. There are still many topic areas where is very large heterogeneity and little comparability in 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 clear guidelines on data sharing, transfer, and authorship, as well as a mechanism for building 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 that can provide a basis for speedy response to key research and policy questions.

## **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, 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. An example of vaccination is the pneumococcal conjugate vaccine (PCV7), 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 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 (Magnus et al. 2012). The results from this study contribute with valuable information for evaluation of the national immunization program in Norway.

The number and quality of national registries vary across European countries. In the Scandinavian countries there is a long tradition of collecting health information from the population in nationwide routine registries like birth registries, patient registries and vaccination registries. In contrast, Southern and Eastern Europe has very few nationwide, routine health registries available for monitoring national health conditions and for research. Furthermore, there are very few pan-European registers that contain individual-level data needed for etiologic research. Although many risk factors and effects discovered through research based on Scandinavian registries are valid for other countries, it would be of great importance to obtain reliable surveillance system also in Southern and Eastern European countries to 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.

## **PRIVACY PROTECTION AND LEGAL FRAMEWORK**

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

## **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 account of public acceptability, cost, political pressures and ideology in both understanding and responding to policy problems. Our work carried out in WP4 (see <http://tinyurl.com/c7ffez6> online) suggests there is low agreement in either the research or policy community about the priorities for child health cohorts 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.

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 research already undertaken. Investment in knowledge translation as part of a collaborative European Birth Cohort effort 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. Further, given frequent moves the typical career of policy makers at both national and international levels (ie moving through policy briefs) links at an organisational rather than individual level are crucial. Organisations with the purpose of translating

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. There is a need for the creation of a forum for:

- 1) exploitation of existing cohort data by creating a new opportunity for those outside of the scientific community to raise questions and
- 2) dissemination of findings of research to a wider audience by creating non-scientific outputs from across the community of cohort studies.

## **A COMPARISON OF DIFFERENT EUROPEAN BIRTH COHORT STRATEGIES**

Above, we have outlined the rationale for having a European birth cohort strategy and evaluated the current status of birth cohort data and coordination. One of the following approaches could be taken to this:

- a. Support for continued collaboration between existing cohorts. Such collaboration would work most efficiently through topic-specific task forces that focus on mechanisms for sharing of existing data, exchanging methodology, exchanging birth cohort researchers, and improving data comparability and harmonisation.
- b. Support for a new large Pan-European birth cohort that collects appropriate new data across all geographical areas and key populations in the region.
- c. A combination of the two approaches above. Support for a 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. This approach should be pragmatic/flexible when it comes to size of a European cohort and data collection methods. It should include additional support for establishing new cohorts in geographical areas or in populations that are currently underrepresented in existing cohorts.

Of course it could be argued that taking 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 potential described above to be realised. 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 and emerging collaborations between them that are starting to contribute important research for European child health policy, 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 that a combination of alternative (a) and (b) would be the best approach - i.e. approach (c). This would imply that a 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. The issues then are how, within this cohort, to best support collaboration between existing cohorts and at the same time establish a European cohort database with a minimum set of child health information available from countries or populations that are currently underrepresented in an efficient way. Our recommendations for these are provided below.

## **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 and that can bring scientific advances of great relevance to European child health policy making.

Our strategic analysis of the current state of European birth cohort research have 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 European Birth Cohort collaboration, using data from existing and new cohorts. This cohort should build a permanent Europe-wide data resource to contain prospective, 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 should be tackled to inform policy.

This European birth cohort should include support for:

### **1) Establishing the infrastructure for a European Birth Cohort**

This infrastructure should include 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 groups of the European population that are underrepresented in birth cohort research today

There is a lack of data from minority groups, and some regions in 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 particularly 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) Linking cohorts, registries and other relevant 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.

5) Integrating knowledge translation, public and policy engagement

A key role within a European birth cohort infrastructure should be that of undertaking knowledge translation, public and policy engagement. Alongside support for infrastructure scientific collaborations, we believe investment in knowledge translation would 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 force 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).

## **Potential Impact:**

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. They are collecting a wealth of important, policy-relevant information on childhood diseases and their determinants, but there has been little coordination of research and results between countries.

The aim of CHICOS was to coordinate the most important European birth cohorts to develop an integrated strategy for birth cohort research in Europe for the next 15 years. The project has gathered together members from more than 50 birth cohorts at workshops, meetings, as well as through the activities of the working groups and case-studies. It has stimulated new links and exchanges between existing and planned birth cohorts, contributing to the establishment and reinforcement of new or existing collaborations at the European level.

CHICOS has updated and enlarged the existing European birth cohort inventory (see <http://www.birthcohort.net> online). For each cohort, information is included on methodological aspects, contact details, availability of information on determinants and health outcomes, and availability of biological samples. This information is publicly available for consultation, for birth cohort researchers and policy makers, as well as other potential stakeholders. This inventory will have a large impact in many ways. It will be used by birth cohort researchers to identify cohorts relevant for pooled analyses and replication studies. For example, the inventory, and the 'Cohort' section of the CHICOS website, has been used in many of the CHICOS case-studies to identify cohorts of potential interest to answer the specific research questions. A complete list of European birth cohorts can also be used to identify gaps in birth cohort research on specific topics. For example, the working group on obesity, vascular and metabolic health, concluded that although weight and height measurements are available in the majority of existing birth cohorts, other measures of adiposity or its distribution are more limited. Policy makers and other stakeholders will be able to use the inventory to identify birth cohorts that can provide specific information on particular child health determinants and outcomes, both at a national and international level. This is a pre-requisite for the process of implementation of a structure for a rapid response to key policy questions.

Individual working groups have produced reports on research priorities on selected child health determinants and childhood diseases. Each working group provided a set of specific recommendations, which have been gathered together in the final reports of WPs 2 and 3, which are publicly available on the CHICOS website. The detailed reports represent the most up-to-date information available on the status of birth cohort research in Europe, including areas for future support of existing cohorts and development of new cohorts. They provide

indications for data collection during follow-up of existing birth cohorts; suggest gaps in knowledge that could be filled in by new cohorts (e.g. inclusion of minority groups) and by investigating understudied health determinants (e.g. mixtures of exposures or social and cultural indicators); emphasize the need for European collaboration on specific topics (e.g. biobanks and genetic analyses) and the need for sharing of expertise and data between cohorts. CHICOS has also produced methodology and protocols for the assessment of specific health outcomes and exposures. These protocols will have an impact on new data collections and on the possibility of future collaborative pooled analyses. Areas have been identified in which there is a need for protocol harmonization (e.g. for neuropsychological assessment). Overall, the reports also represent a starting point and a reference for further improvement of exposure and outcome assessment.

CHICOS case-studies have demonstrated that pooling data from different cohorts at the European level is possible, despite posing important challenges. Apart from the scientific impact of the results and the possibility of their translation into policies, case-studies have demonstrated the feasibility of large European pooled analyses between birth cohorts, and have created connections between birth cohort researchers. Empirically, it has been indicated that coordination between birth cohorts may result in a more efficient and valid use of the collected data and an added value of shared expertise.

CHICOS has evaluated potentialities and challenges in the links between birth cohort research and policy, conducting reviews of the influence of research on policies, and a Delphi study to establish information needs and analysing case-studies of the role of policy makers in the design of birth cohorts. The project has identified challenges in knowledge translation, and has provided recommendations for enhancing translation of research results into policies. Increased and improved communication between policy makers, the public, and the scientific community will benefit everyone by ensuring that the research already undertaken is used in the most effective manner.

To enhance the potential impact of the project and improve dissemination at all levels, CHICOS has released a clear set of recommendations.

The project has recommended establishing a European Birth Cohort, using data from existing and new cohorts. Particular emphasis was placed on the need of support for:

- (i) Establishing the infrastructure,
- (ii) Inclusion of groups of the population that are under-represented in current birth cohort research,
- (iii) Continuing follow-up of existing European cohorts,

- (iv) Combining data from birth cohorts, routine registries, and other data sources,
- (v) Integrating knowledge translation and public and policy engagement.

## **SUPPORT OF CURRENT EC POLICIES**

One of the CHICOS workpackages was specifically focused on the link between birth cohort research and the development of policies to promote child health in Europe. A review of current EU policy regarding child health was conducted, covering 149 policy documents located using structured searches. Within existing activities (workshops and meetings) we have raised the awareness of the importance of policy transfer within the group of CHICOS studies, and highlighted key areas within EC policies where their research could have impact.

Six overlapping policies presented the following broad areas of action:

- (i) Together for Health: A Strategic Approach for the EU 2008-2013. This forms the basis for all direct action in the field of public health
- (ii) EC Strategy on Nutrition, Overweight and Obesity and
- (iii) Platform on Diet, Physical Activity and Health. These two policies respond to the rise in overweight and obesity among the European population, identifying children as a key group for action (iii) The Environment and Health Action Plan 2004-2010. This highlights the need to protect children from environmental pollution.
- (iv) The EU Consumer Policy Strategy 2007-2013, which defines children as vulnerable consumer groups.
- (v) The Science, Children Awareness, Legal instruments and Evaluation initiative (under the Sixth Environment Action Programme and The European Environment and Health Strategy 2004-2010). This addresses the susceptibility of children and fetuses to environment risks.

In in-depth analysis of specific aspects involved in these policies, namely 'regulation of particulate matter to protect child health' and 'policies to promote physical activity for children', the working group identified calls for future research to

1. improve knowledge of the extent of the problem, and
2. increase knowledge of the nature of the problem or solutions.

Birth cohort research is expected to play an important role for both of these goals

In 2004, WHO Europe developed the Children's Environment and Health Action Plan (CEHAPE) which has been greatly influential and was endorsed by the EU in the same year. The EU's Environment and Health Action Plan 2004-2010 (listed as no. (ii) above) was developed at this time to coincide with and support the work of WHO. The CHICOS project was in line with many of the Actions reported in the Plan, in particular: (Action 4) Enhance coordination and joint activities on environment and health; (Action 5) Integrate and strengthen European environment and health research; (Action 6) Target research on diseases, disorders and exposures.

Being based on birth cohorts and involving different regions and populations in Europe, CHICOS activities have attempted to be coherent with the guiding principles of the 2005 WHO European strategy for child and adolescent health, and especially with the two principles of

- (i) a Life-course approach - policies and programmes should address the health challenges at each stage of development from prenatal life to adolescence; and
- (ii) Equity - the needs of the most disadvantaged should be taken into account explicitly when assessing health status and formulating policy and planning services.

Specifically on part of multiple exposure research in birth cohorts, CHICOS has provided foundation for the new Seventh Framework Programme (FP7) project 'The Human Early-Life Exposome - Novel tools for integrating early-life environmental exposures and child health across Europe' (in short 'HELIXv'). This project follows up on the complex and multifactorial pathways involving more 'integrative' methods of environmental exposures. Results from HELIX (estimates of burden of disease, a.o.) will feed into public health policy in areas of environmental pollution and child health. CHICOS further fostered the initiative 'Kids in Cohorts' through the infrastructure that allowed the facilitation of interaction with cohorts. This initiative concentrates on the involvement of children and families in cohort research in relation to the development of research agendas. This shows the utility of creating a collaborative network: using the CHICOS network it was possible to raise seed funding to conduct a small piece of research with senior cohort investigators from the UK. The pilot has thus far a manuscript in print for publication in BMC Medical Research Methodology, and convened on two occasions with UK funding bodies about the possibility of funding follow up work.

The long-term project impact will be greatly dependent on effective dissemination of project results and recommendations of which WP5 was dedicated. Associated activities are described in the next chapter

## **MAIN DISSEMINATION ACTIVITIES**

WP5 is responsible for dissemination to ensure that the results of the project are made widely available and accessible to a wide community of users, comprised of partners and birth cohort, as well as academics, public health departments and policy makers throughout Europe. The objective was to ensure efficient communication to raise awareness of the project and its results among stakeholders and to maximize the impact of communication efforts.

### **Dissemination strategy.**

The strategy defined the principles of the project communication by defining clear objectives and establishing target audiences as well as by defining the problems to be tackled, the appropriate communication partners, and the relevant channels and tools. The list of deliverables of 'Work Package 5 - Dissemination' was specifically designed to promote and disseminate the results of the work. The updated version of the dissemination strategy was delivered at Month 16 of the project (May 2011), although the tools used for dissemination were presented to the Project Executive Committee at each meeting for update and approval.

### **CHICOS logo.**

The logo was created for the CHICOS project as one of the first dissemination activities at an early phase of the project. Graphic designers produced a number of different logos which were evaluated for their strength and affinity to the objectives of CHICOS. The one chosen, based on circles of different colours and sizes, aims at transmitting the following different messages:

- i. connections and collaborations (the circles are connected),
- ii. biological mechanisms (the circles represent cells),
- iii. childhood (the circles represent balloons), and
- iv. the added value of large-scale collaborations (the circles represent a gear).

Templates for word documents, posters and slides were prepared and the logo was used for all presentations and reports concerning CHICOS. It is now a recognised project brand in the birth cohort community.

CHICOS website. The CHICOS project website was launched at the start of the project, <http://www.chicosproject.eu>. The website has a non-technical layout and a simple language to stress its connection to childhood health and to reach both the scientific and the lay audience. Special care has been taken into making the website accessible and interactive. It has both a public access area, divided into six sections ('The project', 'Workpackages', 'Cohorts', 'Pubs&Docs', 'Communications', 'News'), and a reserved area that is only accessible by project partners by means of a login and password. The website has been managed throughout the duration of the project to ensure efficient communication and to provide information on the project, updates on progress and results, as well as to be a gateway to other relevant research. In particular, news from the project and from participating cohorts, as well as reports and documents have been regularly released on the website. The cohort section of the website represented a gateway to the list of European birth cohorts and the inventory birthcohort.net.

Following completion of the project, the CHICOS website will continue to be actively managed and updated for at least 2 more years (i.e. until February 2015). It will therefore continue to provide regular news and reports related to the project to be shared with the wider birth cohort community, the broader scientific community, policy makers, NGOs, the general public, and all related stakeholders. The cohort and stakeholder sections will be also kept updated.

CHICOS brochure. Two versions (b/w and coloured) of a web-based project brochure announcing the project, and providing simple information about the project for interested parties were prepared as part of the initiative. The online versions of the brochures were uploaded on the communication section of the CHICOS website. Hard copies of the coloured version were distributed to the partners for local dissemination to the EC officer for dissemination at the EU level, as well as to all the participants during CHICOS-related workshops and meetings.

CHICOS Mailing list. A contact management system was created to handle the mailing list of stakeholders and to circulate emails and monitor the campaigns. The list includes CHICOS partners, birth cohort researchers, researchers involved in European projects related to CHICOS, International and National scientific societies, International organizations, selected policy makers and other stakeholders. Stakeholders could also subscribe directly via the CHICOS website. The mailing list was actively managed with frequent updates and inclusion of new recipients.

CHICOS Newsletters. Newsletter No. 1 was published in February 2011. It was uploaded on the website and distributed to a list of 214 recipients registered in the mailing list, including partners, registered stakeholders and EU birth cohort researchers. This newsletter

introduced the project to stakeholders and advertised the first CHICOS workshop. Newsletter No. 2 was published in December 2012 to describe the CHICOS case-studies and to announce the European Child health Conference in Dublin, May 2013, during which the final CHICOS report will be launched. The newsletter was uploaded on the website and distributed to a list of 530 subscribers of the CHICOS mailing list.

CHICOS meetings and workshops.

(I) The CHICOS kick-off meeting was held on April 26-27, 2010, at CREAL, Barcelona, Spain. The meeting brought together the cohort members and evaluated the inventory and protocols for the work packages. Antonio Plasencia (Public Health Director, Ministry of Health, Catalonia) and Marco Martuzzi (WHO Europe Office) took part in the kick-off meeting as external experts/stakeholders.

(II) The first CHICOS workshop entitled 'Towards improved coordination of birth cohort research in Europe' was held on April, 11-12 2011 at CREAL, Barcelona. The workshop was attended by 80 delegates to discuss on-going work in CHICOS, namely the inventory of birth cohorts in Europe; birth cohort research in main topic areas of child health and child health determinants; the link between birth cohort research and policy; and proposals for collaborative case-studies among EU birth cohorts.

The workshop also included two keynote lectures:

- i) on birth cohort research in low- and middle-income countries, held by Linda Richter (University of the Witwatersrand, South Africa), and
- ii) on the role of birth cohorts in policy relevant research, by Debbie Lawlor (CHICOS project and University of Bristol, UK).

(III) The 2nd CHICOS workshop entitled 'Birth Cohort Research in Europe - Current and Future Strategic Priorities' was held on May 24-25, 2012, in Turin, Italy.

The workshop was organized to discuss the interim results from workpackages, working groups and case studies carried out as part of CHICOS research efforts. Recommendations and strategic priorities for birth cohort research in Europe were also discussed. More than 70 delegates from 14 countries attended the workshop that also included two keynote lectures: i) on economic determinants of child health and cognitive development in Europe, held by Daniela del Boca (University of Turin, Italy) and ii) on birth cohort research in Central and Eastern Europe held by Wojciech Hanke (Nofer Institute of Occupational Medicine, Lodz, Poland).

In total, some 50 birth cohorts participated in at least one of the two workshops organized by CHICOS.

Additional meetings were also organized. CHICOS partners met in Copenhagen, Denmark, on November 28-29, 2011 in order to start discussing about the project recommendations and the aims of the project strategic document. A meeting was held in Rotterdam, The Netherlands as well, on December 2012, to finalize the strategic document and discuss dissemination activities of the CHICOS results. Together with colleagues from EUCCONET, a workshop on how to combine European birth cohort data was organized at CREAL, Barcelona, Spain, on March 29-30, 2012.

Other activities. Poster and oral presentations at scientific conferences or meetings of related projects have been presented throughout the duration of the project. To raise media awareness, a press release for the first CHICOS Workshop was prepared and submitted to the press offices of the University of Turin and CREAL in Barcelona.

A summary poster and a one-page brochure have been prepared to efficiently deliver the final CHICOS recommendations to the scientific community as well as to policy makers and international organizations.

## **FURTHER EXPLOITATION OF CHICOS FINDINGS**

Long-term comprehension of the project outcomes and implementation of its recommendations both within the scientific community and by policy makers require that knowledge of the project is acquired by a broad range of users, along with continued dissemination efforts. To reach these objective results of the CHICOS project, a number of media tools and approaches will be exploited.

The CHICOS website will be actively maintained and updated for at least two more years (i.e. until February 2015). It will continue to provide regularly news and reports related to the project and share these with birth cohort community, the broader scientific community, policy makers, NGOs, the general public, and all related stakeholders. The cohort and stakeholder sections will be also kept updated. The website will thus serve as a gateway to birth cohort research in Europe, including links to the inventory of birth cohorts: [birthcohort.net](http://birthcohort.net). All reports produced within CHICOS, including the reports from WPs 2 and 3 on research priorities for child health determinants and outcomes and the report from Workpackage 4 on the interaction between mother-child cohort research and policy will be available for download from the website.

The dissemination materials produced at the latest stage of the project will be uploaded onto the CHICOS website and publicly available to relevant stakeholders and social groups. They will be specifically disseminated through the CHICOS mailing list to partners, birth cohort researchers, academic (e.g. paediatric) organizations, and research, regulatory, governmental or health-related organizations.

These materials will include:

- (i) The Newsletter No. 3 including the final recommendations of the CHICOS project. It will be published on May 2013 and will target a broad audience;
- (ii) A one-page brochure presenting in a succinct way the final CHICOS recommendations to be used for both electronic and traditional postal distribution;
- (iii) An overview poster providing the key results of the project;
- (iv) Scientific papers published in the following years.

The CHICOS strategic document and executive summary will be available at the CHICOS website following the presentation during the European Child Health Conference 'Child Health Research, the Key to a Healthier European Society'. The conference is organized

together with colleagues from RICHE, TACTIS and EURO-PERISTAT, and will be held in Dublin, Ireland on 30-31 May 2013. The strategic document will be disseminated through the CHICOS mailing list before the conference, and media awareness will be raised compiling a press release in conjunction with the congress. A lay version of the strategic report written in non-technical language is being prepared to reach a broader audience, which is to be used as an efficient tool for diffusion beyond the scientific community, including policy makers, NGOs, organizations of patients, regulatory organizations, and international organizations. This report will be distributed through the mailing list and uploaded onto the CHICOS website.

In April 2013, CHICOS and RICHE joined forces to present project conclusions and recommendations during a roundtable meeting with MEPs from the Commission on Environment, Public Health and Food Safety in Brussels (and others? Update..).

The roundtable was intended to actively engage with MEPs, to receive responses and discuss perspectives on child health issues in Europe, and how to most effectively steer European child health research funding to meet the short and long-term health needs of the EU population.

Further diffusion of the understanding of knowledge transfer in Europe (when and why research evidence used to develop recommendations and regulation) is planned during the 8th International Conference in Interpretive Policy Analysis 2013 in Vienna.

The CHICOS mailing system will play a key role in disseminating the newsletter, final brochure, strategic document and the non-technical report. The mailing system currently includes 535 subscribers. The list will be regularly updated as well as being enriched by stakeholders registering directly through the CHICOS website. The list of stakeholders of potential interest for CHICOS is publicly available at the CHICOS website ('Cohort' section for birth cohort researchers and 'Communication' section for other stakeholders) and currently includes:

(i) birth cohort researchers - 77 birth cohorts identified,

(ii) other related international projects - more than 50 projects identified, such as: PANCARE, ENRIECO, ESCAPE, HELIX, I4C, EARNST, GAALEN, NEW GENERIS, RICHE, TACTIS, MOMI, MEDALL, OBELIX

(iii) international organizations - several European or International organizations identified, including DG SANCO, the WHO Regional Office for Europe (Child and Adolescent Health and Development), EURO-PERISTAT, Child Health Field of The Cochrane Collaboration, the International Agency for Research on Cancer

(iv) international scientific societies and professional organizations - about 20 societies identified, such as the European Society for Paediatric Research or the European Society for Paediatric Endocrinology

(v) national scientific societies - paediatric and related national societies of EU Member States

(vi) health ministries and national agencies - ministries of the EU Member States

(vi) other organizations - miscellaneous groups of other potential stakeholders, such as the ICCCP (International Confederation of Childhood Cancer Parent Organizations), or the portal Europe for Patients

Materials will be also sent to the Network of the National Contact Points (NCPs) in Member States and Associated States. A news item regarding the CHICOS recommendations is to be submitted to the CORDIS database.

CHICOS results will be presented in international conferences on different aspects of child health and epidemiology, and published in international peer-reviewed journals. Because of the broad scope and interdisciplinary nature of the project, publication will deliberately be aimed at journals from different fields, including public health and epidemiology, paediatrics, obstetrics and gynaecology, general medicine, respiratory diseases, multidisciplinary sciences, and biostatistics.

A preliminary list of publications under preparation is as follows:

'Pregnancy and birth cohort resources in Europe: a large opportunity for aetiological child health research.' Accepted by Paediatric and Perinatal Epidemiology.

'How are European birth-cohort studies engaging and consulting with young cohort members?' Accepted by BMC Medical Research Methodology.

'Adverse birth outcomes associated with selected maternal occupations in 12 European birth cohorts - a CHICOS initiative.' Intended journal: under discussion

'Polychlorinated biphenyls (PCBs), dichlorodiphenyldichloroethylene (p,p'-DDE) and birth outcomes in 11 European birth cohorts: dose-response relationship and effect modifiers.' Intended journal: Environmental Health Perspective

'Prenatal exposure to DDE and PCB153 and infant's respiratory health: A European meta-analysis.' Intended journal: Epidemiology

'Fish intake during pregnancy and birth outcomes: A Meta-analysis within 20 European Birth Cohorts Studies.' Intended journals: Lancet, Am J Clin Nutrition

'Adiposity, vascular and metabolic health. ' Intended journal: under discussion

' Preterm birth, birth weight and infant growth and the risk of childhood asthma: a meta-analysis of 147,000 European children. 'Intended journal: under discussion

'Maternal complications and conditions in pregnancy and wheezing in early childhood: a combined analysis of 14 European birth cohorts' Intended journal: a respiratory journal

In the long-run, exploitation of the CHICOS results and the knowledge acquired during the CHICOS project will be achieved via involvement of partners in other international projects, including those funded by the EU. Furthermore, the involvement of partners in policy networks at the national and international level, including different Directorates of the EU, Member States' health ministries and their commissions, and regional health authorities, will facilitate the awareness of CHICOS results and their possible use for the development and implementation of policies related to child health.

**List of Websites:**

<http://www.chicosproject.eu>