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Critical assessment of the research outcomes of European birth cohorts: linking environmental factors with non-communicable diseases

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ABSTRACT

Objectives: The objective of this review paper was to stimulate collaborative discussions toward the development of a general concept of an open source protocol for a feasible and efficient longitudinal birth cohort study exploring non-communicable diseases (NCDs), their multifactorial etiology and relations between various risk factors.

Study design: The present paper systematically reviews the design of existing birth cohorts in Europe containing environmental exposure data, and assesses a quantity and quality of their research outcomes as their potential to be an effective tool for studying non-communicable diseases and their risk factors.

Methods: European birth cohorts with more than 3000 participants have been included in the study. A total number of scientific papers published in the internationally recognized journals and their impact factors and citation records were evaluated for all cohorts as surrogates for their efficiency to contribute to NCDs understanding and thus their prevention.

Results: The birth cohorts contributing most significantly to the NCD understanding shared common features: (i) study size between 10,000 and 15,000 mother–child pairs; (ii) repeated assessment of children from prenatal into adulthood; and (iii) availability of biological samples. Smaller cohorts and cohorts with a specific focus generated a lower number of publications; however, these often received considerably a higher number of citations.

Conclusions: General cohort studies with 10,000–15,000 mother–child pairs allow a broader context interpretation, publish a higher number of articles, and often lead to the formation of infrastructures for ‘spin-off (nested) studies’.

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Introduction

Non-communicable diseases (NCDs) with not-fully-understood multifactorial etiologies are increasingly important determinants of population health globally.^{1–6} These include for

example asthma and allergic diseases, neurodevelopmental disorders, obesity, metabolic syndrome, diabetes, or cancers. While the control of communicable diseases (CDs) has significantly improved,⁷ the burden of ill health due to NCDs has been increasing.⁸

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There is growing evidence suggesting that the risk of many NCDs is linked to early-life exposure to toxic chemicals, nutrition imbalances, and psychosocial stress.^{9–11} Individuals are often exposed to cumulative levels of these factors over long periods. Despite low levels of exposure in early life, the NCD can develop many years or even decades later. For example, exposure to toxic or endocrine-disrupting chemicals in early life can affect the metabolism that influences brain growth or controls weight and, with other exposure factors, increase the subsequent risks of cardiovascular disease, obesity, diabetes, and cancer.^{12–14}

To adequately investigate aspects of an individual's life contributing to NCD development, a study group has to be observed systematically for a number of years. The tool that enables such observation is a longitudinal birth cohort study, which may provide information on the relationship between diverse risk factors and health outcomes from the time of conception until adult age.¹⁵ Pregnancy and early childhood are very sensitive periods crucial for a child's development and any exposure during this time period may significantly affect health in adolescence and adulthood.¹⁶ A number of studies demonstrated the important role of maternal exposures during pregnancy with regard to the child's morbidity.^{17,18} The identification of factors that cause or considerably contribute to the development of chronic diseases and disorders may prevent their future epidemics.

To build and sustain a birth cohort study that produces relevant high-quality scientific outputs requires a clear study concept, substantial funding, and rigorous management. Taking into consideration the long duration and enormous effort required, birth cohorts should be designed in a way that enables the study of multiple factors and health outcomes, many of which are not apparent at the time of the study initiation. Several birth cohort studies assessing children's health have been initiated during the past two decades in Europe and have recently been described in two papers.^{19,20} These studies describe the number of participants, the duration, the follow-up frequency, information regarding the collection of biological materials, investigated biomarkers, and environmental factors. The most frequently studied topics include immune disorders (such as asthma, atopic eczema, other allergic disorders, etc), neurobehavioral disorders (such as attention deficit hyperactivity disorder [ADHD], attention deficit disorder [ADD], autism spectrum diseases [ASD]), nutrition and obesity, as well as other general parameters (birth outcomes, postnatal adaptation, and specific health problems of adolescents). However, existing reviews do not provide information regarding the relationship between the overall design, size, and studied topics of an individual cohort and the quantity and quality of its research results and outcomes.

The main goal of the presented analysis was to systematically review the design, the underlying hypotheses, and especially the research outcomes of existing birth cohorts in Europe containing environmental exposure data that enrolled more than 3000 children with the specific focus on NCDs. The research outcomes, peer-reviewed research publications, and their citations by other researchers were evaluated in order to identify the study characteristics

contributing to the cohorts' short- as well as long-term scientific potential. Emphasis was placed on the quality of the scientific outcomes. We realize that more important would be the evaluation of actual impacts in terms of policy, prevention and changes in medical practice. However, this assessment would be extremely difficult and non-systematic, and therefore quantity and quality of research outcomes is used as a proxy. The review was conducted with the aim of opening the discussion and initiating possible collaboration in order to establish a general concept of, and open source protocol for feasible, efficient, and long-term birth cohorts with high scientific potential.

Methods

The overall approach

Information on birth cohort studies in Europe and their outcomes was collected from existing design papers,^{19,20} from the internet pages of individual cohorts, as well as directly from the leaders of individual cohort studies (Table 1). Then, the ISI Web of Science and PubMed were searched for referenced peer-reviewed publications and their citations in order to identify the most frequent research topics and the relationship between study design and research outcomes in terms of quantity and quality.

Birth cohorts

All selected studies had to (a) focus at least on one NCD; (b) be based in Europe; (c) consider an environmental topic (such as air pollution, water contamination, pesticides, metals, persistent pollutants, or other contaminants, noise, radiation, allergens, and/or other biological stressors); (d) have more than 3000 participants (in order to have sufficient power with respect to infrequent health outcomes);²¹ (e) enroll mothers during pregnancy or at birth; (f) make at least one direct contact between mother and child during the course of the study; and (g) plan at least one follow-up point after birth. We also wanted to evaluate the effect of collecting biological samples (e.g. blood, cord blood, urine, breast milk, hair, faeces, and nails) on the overall performance of the study. A general description of the analyzed European birth cohorts is presented in Table 1.

Publication outcomes

In the next step, a list of publications (up to December 2012) for each cohort study was created based on information on the respective cohort web page, through the web search and through the direct contact of the study teams.

Bibliographic records

Bibliographic records (title, authors, journal, subject category, impact factor, date of publication, volume, issue, total number of citations from 1990 to 2012, average citation per year, nickname of the cohort) for 1926 papers were extracted from

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