

Better health for mother and child – The Danish National Birth Cohort (DNBC), its structure, history and aims

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If you want to prevent disease and promote health you have to study man. You need data or information from people – often many people. There is no other way. If you want to study causes of disease and malfunction, you sometimes have to start data collection early in life, often at best before conception.

OPEN ACCESS TO DATA

When the DNBC started there was a growing body of evidence coming mainly from the UK, the Nordic countries and the US indicating that early exposure may have long lasting health consequences. The Nordic countries had the advantage that inexpensive long term follow-up is possible due to our personal ID numbers and a long history of a large variety of registers related to health, social conditions, occupational history and family conditions. Most of the health registers are outcome registers and lack data on putative causes for disease. These putative causes (exposures) can be collected by asking, measuring and by analyzing biological samples reflecting internal exposures or genetic/epigenetic markers.

A cohort study needs personal and sensitive data. At the same time the valuable data collected has to be as accessible as possible to make sure data is available and used for the public good. Not in order to promote individual epidemiologists, but to help preventing disease and promote help. This point of view requires a fundamental philosophy of open access to data given ethical conditions and principles of data protection are not to be violated. A cohort data collection has to be an open data source and collection of data for private research use only should not be encouraged.

In the DNBC only data dedicated to the principle of open access was and is accepted. From the start all data collected within the framework of the DNBC belonged to no one in particular. A Steering Committee to secure this principle was therefore established.

Open access to data is controversial. It is a way to obtain important information at a rapid speed, but it may also be a threat to privacy and researchers thirst for “ownership” and competitive advantages. Open access to data is also one of the most important quality assurance mechanisms we have and we invite and encourage people to check our and others' results.

In research we are interested in general laws of nature, not in private matters and competitive advantages, making it possible to combine care for privacy with productive science. Data should be stored in a central place without personal identifiers such as name, CPR-numbers, etc. These identifiers are needed to link and clean data, but not when doing research. Access to individual data for linking purposes should

therefore only be given to a limited set of data managers, who have signed a document stating they follow all principles laid down by the national Data authority and Good Epidemiologic Practice. We have no known examples of researchers in Denmark having misused personal data, and it is important we maintain this track record. Unless we are constantly alert, privacy will be violated sooner or later and such a violation may have serious consequences for most of us, especially for those running large scale cohorts.

ESTABLISHING THE DANISH NATIONAL BIRTH COHORT

A large study aiming at including 100,000 newborns needs a lot of public support and needs a slim operational structure. Rather few people were responsible for making decisions (to begin with the heads of the Danish Epidemiology Science Centre: Jørn Olsen, Mads Melbye, Thorkild I. A. Sørensen and Peter Aaby – later Sjurður F. Olsen, Anne-Marie Nybo Andersen, Allan Vaag and Ellen Aa. Nøhr joined the DNBC Management Group) and we had to realize from the start of the study that obtaining a representative sample of newborns was neither needed nor possible. Representativeness is a time and place specific concept and at the point in time where research data from the cohort would be ready to be translated into prevention, the population of pregnant women would look quite different, as everybody now can see.

The original ambitious idea was to establish a common Nordic Cohort with 450,000 children from Denmark, Norway, Sweden, Finland and Iceland back in 1994-96. This could have been done had we had a Nordic funding structure powerful enough to handle a study of these dimensions. It was the right thing to do at that time, but not all agreed.

During the establishment period the Danish National Birth Cohort received important support from the Chief Medical Officer at the National Board of Health (NBH), Palle Juul Jensen, but many others were skeptical, also within the NBH.

Most of the opposition, however, came from general practitioners (GPs) and midwives, strangely enough the main target groups to benefit from the knowledge generated by the study, given their key role in the Antenatal Care System (ANC). The ANC is still not widely guided by evidence, at least not for the prevention tasks. However, the GPs who took part in the data collection turned out to be very consistent and helpful in their support, perhaps because our ongoing interviews were well accepted by most of the women and did not cause anxiety that led to unexpected and unnecessary contacts with the GPs. Many GPs and midwives are

now keen users of data in the DNBC for their research.

The study had to be approved by each of the 15 counties in Denmark at that time (1994-5) since these local authorities paid for the blood sampling from GPs and midwives. Only in the last third of the recruitment period from 1998 to 2002 did we have a full scale national data collection. About 60% of the women who were informed about the study by the GP accepted the invitation. About 30% of all eligible pregnancies in Denmark were included in the cohort.

Collection of blood from the umbilical cord at hospitals was less successful with a participation rate of 60%, partly due to competing interest for blood to research projects in larger hospitals and some remaining resistance from midwives. Blood was stored in EDTA vials and shipped by ordinary mail to the biobank at Statens Serum Institut. The consequences of this sample handling procedure for many laboratory measurements is still unaccounted for, but research into this question is ongoing.

DNBC was part of the Danish Epidemiology Science Centre. The Centre had a time limited existence of 10 years, which does not fit well with a project that should run at least 90 years and perhaps longer. The cohort is hosted by the 3 largest universities in Denmark and Statens Serum Institut, which provide some guarantee for continuation, but also risks, since no long term commitments have been given and no agreement exists on how the commitment should be shared if research funding dries out over a long time period. Without stable financing it is difficult to secure a continuous updating of health data for the main target group: children born into the cohort. This is especially important since health problems in children and teenagers often remain untreated or are treated outside hospitals. Fathers do play an important role for the health and well-being of families and we need to establish a special data collection for fathers as it is now done for the mothers.

Data collection in the DNBC so far includes several follow-ups after the initial 4 telephone interviews planned in the first protocol. A more detailed description of the data collection can be found at our study website <http://www.dnbc.dk> (includes also references to published papers based on DNBC data and papers on the data collection).

The cohort homepage www.dnbc.dk was established very early in our history and has been an important source for documentation for our data collections and a vehicle for information to users of data and results. We also use the homepage and the email addresses collected to communicate with participants. We provide research results and we explain the background for our new data collections via our website.

FUTURE COLLABORATION AND CONDITIONS FOR REGISTER-BASED RESEARCH

Although our DNBC sample size is large we still lack power to study important but rare diseases like cerebral palsy, childhood cancers, etc. More collaboration is therefore needed, as it is done in the I4C group (International Childhood Cancer Cohort Consortium), and in the cerebral palsy studies using data from both

DNBC and MOBA. In later years we have seen not only publications based on pooled data from the Danish and Norwegian cohorts, but research results from one cohort have been replicated in the other, e.g. in the dietary field or within pharmaco-epidemiology. Researchers who have worked with data within a specific field in one cohort cooperate on projects based on data from the sister cohort. In several European projects (the Chichos child cohort research network or the European Study of Cohorts for Air Pollution Effects (ESCAPE) data from both the Norwegian and Danish cohorts are used. This is also the case for several gene-environment association studies, e.g. the Genetics of Obesity in Young Adults (GOYA) initiative in cooperation with epidemiologists from Bristol and within the NIH Gene Environment Association Studies (GENEVA) consortium.

The short term future is well secured unless EU rules on data protection or national political decisions make use of health data impossible or very difficult. This is always a risk. The long term future depends upon how important fetal programming is for health and function in adult life and this is still an open question.

Much of the research has focused on disease, but functional defects may be even more important from a societal viewpoint. A 10% drop in IQ induced by factors that interfere with fetal brain development may not be very important for the affected person, but if the exposure is frequent the consequences for society will be substantial. More focus on functional defects will require continuing data collections. Putting email, social media and mobile phones to use makes this achievable even with limited financial resources.

The legal and public attitude towards using personal data in research is unpredictable, but what we can do is to make personal information as well protected as possible. We must avoid storing data with personal ID numbers of any kind and we must prevent access to our data sources from unauthorized external people. The era when researchers kept personal and sensitive data on their PCs is hopefully gone. There is a risk associated with any data source whether it is used or not.

The Danish National Research Foundation took a strong stand on the principle of an open data source for research where nobody could have their "private" part of restricted use, at least not outside a short and well defined time limit. Nobody can own other people's data. Cohort participants own their own data and therefore have the right to withdraw this data at any point in time. The DNBC was established to serve the public good and we should keep it this way.

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