

# Children and Population Biobanks

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Population biobanks, which store and distribute human DNA, cell lines, and tissue samples collected from large cohorts, are being established and are growing in size (1). These population biobanks are often funded wholly or in part by governments and are envisaged as novel resources for national and international biomedical research programs. Such programs include studies on associations between genotypes, environmental exposure measures, socioeconomic parameters, and phenotypes of human health and disease.

Knowledge obtained from such population cohorts as, for example, those in the UK Biobank, with donors' samples prospectively linked to continuously updated electronic health records, is expected to facilitate advances in personalized medicine, including preventive medicine and safer, more effective drug-prescribing (2). The UK biobank, launched in 2007, targets half a million adult Britons (3); similarly large cohorts are being enlisted in Canada, China, Norway, Netherlands, Denmark, Ireland, and the United States.

Many of these biobanks collect samples and data from children, often along with their parents (see table, p. 819). Some aim to provide longitudinal resources for the study of gene-environment interactions on child growth and development, such as in the Norwegian Mother and Child Cohort (4), or to follow specific diseases throughout childhood (5).

However, the large-scale collection and use of such data has raised some concerns. Some newborn screening programs launched from the 1960s onward in the United States and elsewhere, with the primary goal of early detection of treatable disorders in newborn children, have recently discovered the research potential of their huge blood-spot

card stocks, which has created public outcry over presumed breach of trust and privacy (6). Inclusion of children's samples in population biobanks, even with the authorization of parents or guardians, raises specific concerns. Children are a vulnerable research population, in the sense that they lack the capacity for consenting to their participation (7). But they are different from other vulnerable populations, such as mentally disabled individuals, or patients with schizophrenia or dementia, or individuals with other conditions affecting their capacity to appreciate the risks and benefits of donating DNA samples and phenotypic data to a biobank. Unlike members of such other populations, children's vulnerability is temporary and does not arise from a disorder; most children will become healthy adult members of society.

DNA remains unique as a permanent identifier throughout an individual's life. Thus, appropriate safeguards are needed when collecting and distributing children's DNA samples and data (8). A child whose DNA sample is donated by her parents today and distributed over the next few decades for research projects around the world can potentially be in the public eye decades later. As sequencing of entire genomes becomes a routine procedure, DNA donors' privacy can never be completely ensured within biobanks (9). Individuals can be traced even in very large aggregate data sets spanning thousands of donors (10, 11). As a consequence, there is no true "opting out" from biobanks once DNA sequences have been published and deposited with public databases. Even when the DNA sample itself is destroyed, researcher-generated data—including identifying markers or sequences—may not be irrevocably eliminated. By the time children are recontacted for their consent as adults (if one assumes that this approach is taken by the biobank), their identifying DNA sequences along with their phenotypic data sets may already have been shared with other resources around the world. Apart from biobanks, some direct-to-consumer personal genomics providers that share results with clients via protected Web sites are already analyzing children's DNA samples (12), creating another avenue by which personal privacy might be compromised.

Kohane and Altman have argued that individuals who donate genotype and phenotype information to research databases must be

Access to samples and individual DNA sequence data from children included in population biobanks should, when feasible, await their consent as adults.

perceived as "health information altruists" (13). Biobanks that collect children's DNA, and possibly phenotype data, do so with the authorization of parents or guardians. Obviously, parents are making many important decisions that affect their children's future, but in the case of biobank participation, the consequences of their nonvoluntary altruism may have unpredicted consequences decades later. For example, although the 2008 U.S. Genetic Information Nondiscrimination Act protects individuals by prohibiting employers or health insurance providers from acquiring or using their genetic information, it does not fully protect them from other modes of discrimination by bankers, life or disability insurance providers, schools, immigration authorities, and so on (14).

New policies—not just new consent language—are therefore needed for recruiting participants and for the inclusion of children in population biobanks (15). Without such changes, lack of openness about potential risks on the part of researchers may lead to the loss of public trust in population research. Among the adverse effects may be costly delays (in terms of public and individual health) in the realization of personalized medicine—including that for children.

When considering new policies concerning the inclusion of DNA samples and data from children in biobanks, it is crucial to distinguish between disease-specific and population biobanks. Disease-specific biobanks are an integral part of therapeutic research involving children with specific conditions. The decision about storage and future use of samples and data are part of the decision-making process concerning diagnosis and treatment of the affected child and similarly affected family members. The balancing of potential harms and benefits is therefore fundamentally different from that for voluntary participation in population research. We propose that disease-specific biobanks—in particular, when dedicated to childhood diseases and disabilities—should continue to collect and share children's DNA samples and data within the limits authorized by parents and bound by continuous oversight, including ethics review. Records should be kept regarding the use of distributed samples and data.

Ideally, the affected children themselves should be recontacted once they reach the age of consent or maturity to allow contin-

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## Biobank Features

Name	Country	Year	Target participants (1000s)
Norwegian Mother and Child Cohort Study	Norway	1999	260 (F, N)
Danish National Birth Cohort	Denmark	1996	100 (M, C)
National Children's Study	U.S.A.	2010	100 (M, C)
European Longitudinal Study of Pregnancy and Childhood	Several	Various	40 (P, C)
Avon Longitudinal Study	U.K.	1991	23 (M, N)
All Babies in Southeast Sweden	Sweden	1997	22 (F)
Northern Finland Birth Cohorts 1966/1986	Finland	1966/86	21 (M, N)
Etude Longitudinale Française depuis l'Enfance	France	2010	20 (N)
Guangzhou Twin Project	China	2005	20 (T 7–15 y)
National Child Development Study	U.K.	1958	19 (N)
Child and Adolescent Twin Study in Sweden	Sweden	2004	15 (F, T 9–12 y)
Generation R Study	Netherlands	2002	10 (F)
Born in Bradford	U.K.	2007	10 (M, N)

**Largest biobank projects collecting children's samples** (target population of at least 10,000 individuals, arranged by target size). Not all donors are children. The list was prepared by using surveys returned to the P<sup>3</sup>G and information provided on the biobanks' Web sites. A full catalog of P<sup>3</sup>G member biobanks and further details are available (15). Year, year of recruitment or initial data collection started; numbers of target populations are rounded to the nearest thousands. F, families; N, newborns; C, children; M, mothers; T, twins; P, parents; y, years of age.

ued research on their samples and data. There is evidence that this would be in accord with the desires of the general population. In a recent U.S. survey, 1186 adults were asked about hypothetical samples collected from them as children with their parent's permission; 46% responded that they would want to be contacted as adults for consent to continue research with those samples. Moreover, 33% were concerned or very concerned about research conducted without their consent as adults (16). More study is needed regarding the desirability or feasibility of recontact. Moreover, the logistics will be complex and costly. The possibility of recontacting entails the need to use a method for coding that is both secure and allows for reidentification.

In contrast to policies for disease-specific research, we feel that an overhaul is needed for the collection and distribution policies of DNA samples and data from children that have been included in population biobanks. We propose that population biobanks continue to collect, store, and analyze children's DNA and phenotypic data with the appropriate authorization by parents or guardians, but that they may not make these DNA samples (or individual genetic sequence data) accessible outside the biobank until donors are recontacted as adults and give their own informed consent.

Pediatric population biobanks could publish and give access to aggregate phenotypic data and results, including from genetic studies, in order to advance pediatric research. Individual DNA sequence data could not

be released. For example, published studies might include reports on genetic deletions or duplications affecting health, giving their chromosomal locations and approximate sizes but not specific sequences, an approach taken by a recent study on the role of chromosome 1q21.1 in mental retardation in children (17). Such policies would minimize the risks of revealing children's identifying genetic data, thus protecting their privacy, while still allowing the advancement of pediatric research. Such arrangements could align with current developments in many places, such as the European Union (EU), which has opted against a centralized EU biobank but is striving for harmonization of sample collection and distribution policies (18).

There are no perfect solutions: We have to choose the best possible policies even as we evaluate risks and benefits both to the individual donors and to the research community and society at large. Limiting the distribution of children's DNA samples and their individual genetic sequence data by population biobanks while waiting for their own consent as adults may negatively impact research. Some donors whose DNA samples and data were donated by their parents may not be traceable decades later, whereas others may not wish to consent as adults (16). Moreover, building in-house genetic capacities within existing population biobanks to minimize delays in research while maximizing privacy protection may be costly. However, we believe that research will only be affected marginally by adopting such a

policy and only in the short term, as biobanks are foreseen as long-term projects. Consider that we are still enjoying the fruits of the Framingham Heart Study, six decades after the initial cohort was recruited, and research is ongoing because of the trust that has been built over generations (19).

This proposal may seem provocative. However, there are good reasons for devising the best possible strategies for the inclusion of children in population biobanks. For adults, there exists broad consensus on voluntariness, altruism, and consent being essential requirements for morally justifiable participation in population biobanks. Why

accept lower standards for children? Children are vulnerable, but unique, for their vulnerability is temporary. The long-term benefits of maintaining public trust in biomedical research by waiting for participating children to consent as adults justify extra governance efforts and added costs.

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