

Should donors be allowed to give broad consent to future biobank research?

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Large international biobank studies can make substantial contributions to scientific research by validation of the biological importance of previous research and by identification of previously unknown causes of disease. However, regulations for patient consent that are too strict and discrepancies in national policies on informed consent might hinder progress. Therefore, establishment of common ground for ethical review of biobank research is essential. In this essay, broad consent is defined on a scale between strictly specified (eg, for a specific study) and blanket consent (ie, with no restrictions regarding the purpose of the research). Future research includes that which might not be planned or even conceptualised when consent is obtained. In conclusion, broad consent and consent for future research are valid ethically and should be recommended for biobank research provided that: personal information related to research is handled safely; donors of biological samples are granted the right to withdraw consent; and new research studies or changes to the legal or ethical authority of a biobank are approved by an ethics-review board.

Introduction

Local and national research for genetic risk factors for cancer frequently lack statistical power, and specific traits might be identified when their prevalence in a population or in specific families is merely a confounding factor. Validation of the biological importance of genes thought to be associated with cancer and the identification of previously unknown causes of cancer need analyses of large numbers of familial cases and controls—preferably from multiple populations. International collaboration is needed, but regulations for patient consent that are too strict and discrepancies in national policies on informed consent might hinder progress in cancer research (figure 1).^{1–3} Establishment of common ground for review of the ethics of biobank research is essential. Here, we argue that broad consent to multiple purposes of biomedical research and future consent to as yet unspecified biomedical research by

donors for use of human blood and tissue samples in future biobank-based research is legitimate.

The conceptual issue

Arguments against allowing broad consent and future consent state that consent should be based on information relevant to an assessment of benefits and risks associated with participation in a research project. Vilhjalmur Arnason argues that “the more general the consent is, the less informed it becomes. It is misleading to use the notion of informed consent for participation in research that is unforeseen and has not been specified in a research protocol”.⁴ However, this claim raises the question: what is appropriate information? If the information covers all issues that are relevant for a person’s choice, then that person’s consent is appropriately informed. If the risks and benefits are common to several studies, then general information on these studies might be sufficient for the donor of the sample to make an informed decision.

Furthermore, Arnason argues that the “standard meaning of informed consent”⁴ cannot accommodate broad consent and future consent. However, several legitimate procedures for information and consent exist in practice, depending on the nature of the research and the risks thought to be at stake.⁵ When there are more risks and high risks, information must be more detailed and the consent procedure more strict. For research that involves less risk for research participants, less-strict information and consent procedures are appropriate.^{6,7}

Respect for donors

A further argument against broad consent and future consent states that the practice of giving specific information and asking for specific consent shows respect for patients and donors. This argument would indeed be true if the process of obtaining specific consent did not jeopardise the amount and quality of research that can be done. Since the response for collection of data (eg, sending out questionnaires or

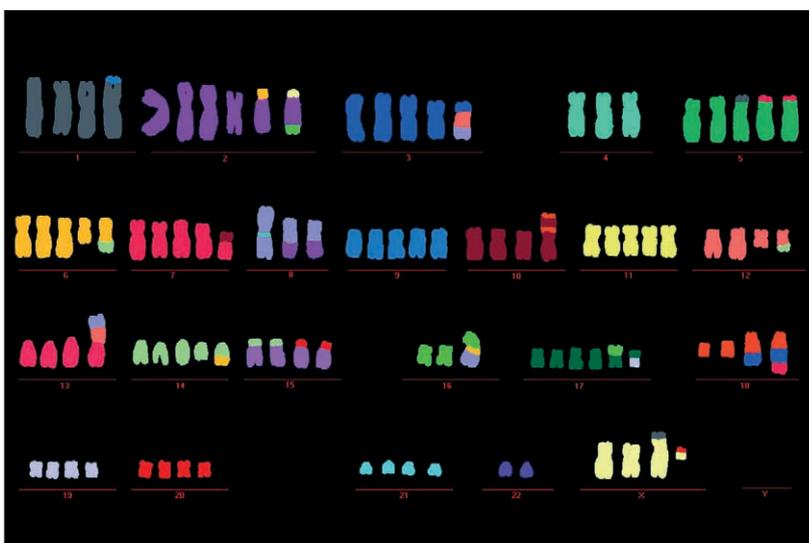


Figure 1: Cytogenetic analysis (multicolour fluorescence in-situ hybridisation) of breast carcinoma cell. Karyotype shows several numerical and structural chromosome aberrations.

asking for renewed consent to use biobank samples obtained previously) from any large population commonly ranges between 50% and 90%, the need for renewed consent for use of biobank material would reduce the number of participants available, possibly introducing selection bias and decreasing the scientific importance of the studies. Most participants are unlikely to benefit directly from biobank research because of lead times in treatment development and low probabilities that tissue donors will have the relevant diseases studied. Nonetheless, most donors have a general interest in research—ie, in medical progress. General research interests are promoted by facilitation of large-scale population studies with access to samples from appropriate controls and cases. Such studies are in turn promoted by allowing donors to submit broad consent and future consent.^{8,9}

The informed and voluntary assumption of risk

An argument against broad consent and future consent is risk exposure. The basic idea of informed consent, emanating from the Nuremberg trials, is that any risk associated with a research protocol must be accepted on a voluntary basis. The need for an informed and voluntary assumption of risk seems to preclude broad consent and future consent. However, if the risk of harm from future biomedical research is low and sufficiently well controlled, if the participant voluntarily accepts this level of risk, and if there is a mechanism for withdrawal, then there is no reason why broad consent and future consent to such studies should not be acceptable.

Broad consent for future biobank research

Strong arguments for allowing broad consent and future consent include the importance of biobank-related research, respect for the autonomy of donors, and consistency with current practice.

The importance of biobank research

Several studies have shown the great potential of biobank-related research in epidemiology.¹⁰ Biobank records of neoplasms allow investigation of large populations as new technology becomes available. For example, the large genetic heterogeneity of acute leukaemias was discovered by use of molecular and molecular cytogenetic analyses of retrospective biobank samples obtained 10–20 years ago. The clinical use of these findings was later verified in prospective clinical trials.¹¹ Biobanks of samples from large families that were obtained over several decades have been essential for the identification of breast-cancer genes (figures 1 and 2).¹² The association relation between infection with *Helicobacter pylori* and risk of gastric carcinoma,¹³ the causal relation between human papillomavirus and cervical cancer,^{14,15} and the link between Epstein-Barr virus and multiple sclerosis^{16,17} highlight the importance of biobank-related research.

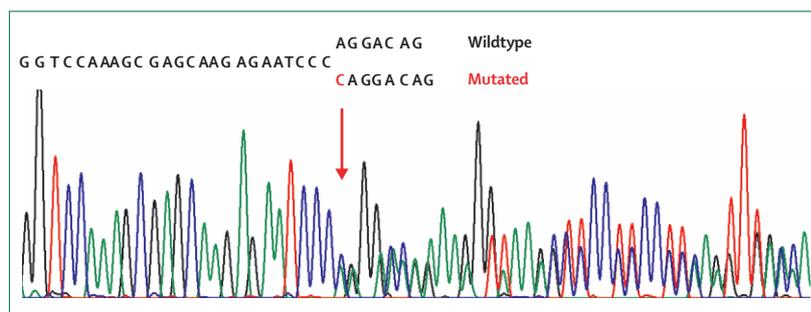


Figure 2: BRCA1 germline mutation in an individual with family history of breast carcinoma
Sequence analysis shows insertion of cytosine (5385_5386insC), producing a frameshift in mutated allele compared with wildtype.

Respect for autonomy

The primary motive for the requirement of informed consent in research is respect for autonomy (ie, self-determination).⁵ To interfere with self-determination is to disrespect autonomy. From this perspective, to allow broad consent for future research would be laudable. Acceptance of broad consent and future consent implies a greater concern for autonomy than if such consents are prohibited.

Respect for autonomy does not imply total self-governance when a decision also affects others (eg, family members). However, infringement on autonomy should be done only with good cause. Provided that information is coded and handled safely, that secrecy is maintained, and that donors and families are protected from harm, no limitation of autonomy is necessary. Although the protection of communities might imply other potential infringements on autonomy,¹⁸ this question is complex, and provided that the above criteria are met, no limitation of autonomy is necessary for community members.⁸

Biobank research done without consent—an argument from consistency

Consistency with current practice lends further support to the idea that sample donors should be entitled to give broad consent and consent to future research, provided that the risks of harm are well controlled by a secure coding system and by secrecy laws that protect the confidentiality of personal information. In the UK, Estonia, and Sweden, ethics-review boards have a mandate to approve a biobank study without requiring informed consent;³ in Iceland, the national bioethics committee can grant this permission.

Regulations in Canada, Germany, Norway, the Netherlands, and the USA permit biobank research without consent provided that samples are not identifiable.³ Thus, when risks of harm to donors in a research project are low (ie, when protected sample codes prevent the spread of information), or when obtaining consent is impractical—a provision stated in several ethical guidelines—research without consent is

usually permitted. Given that ethics-review boards might grant biobank research without consent, it seems odd that participants themselves should not be allowed to give broad consent to future biobank research.

Acknowledgment of the view of actual donors and potential donors

Few studies have investigated the perceptions of actual donors and potential donors regarding the use of broad consent or specific consent to biobank research.¹⁹ Interviews²⁰ of 1038 members of a so-called people's panel by the UK human genetics commission suggested that most panel members (ie, four in five) wanted specific consent for every new project on existing samples. In a study²¹ of 100 healthy volunteers, 35% reported that they wanted to be consulted if their tissue samples were to be used for further research; they also noted a preference for consenting to specific research (eg, cancer research). In a nationally representative survey²² of US households, 1635 (84%) of 1947 eligible participants consented in 1999 to have their blood samples included in a national repository for genetic research. In 2000, 2501 (85%) of 2933 consented²²—proportions that can be interpreted as acceptance of broad consent.

The Swedish MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) study showed that those who gave informed consent, participated in research, and had access to information on the progress of the research had a greater acceptance of broad-consent forms.²³ 1494 (94%) of the original 1583 participants gave initial consent and donated a blood sample for a specific purpose in 1990. In 2001, 85 (6%) people had died, moved abroad, or had an unknown address, and the remaining 1409 (94%) eligible participants received a questionnaire 10 years later about attitudes to research that had a broader purpose. 1311 (93%) were willing to consent to use of donated blood samples for academic research on the heredity of cardiovascular diseases, 292 (22%) of whom wanted to be informed about, and give new consent for, every new genetic study.

Some biobank projects are associated with information campaigns aimed at large sections of society, and have substantial media coverage. Two Swedish studies^{24,25} suggest a favourable effect of such exposure to broad consent. In one study,²⁴ 790 (86%) of 920 blood donors to the medical biobank of Umeå, Sweden, chose to waive their right to informed consent and to allow the ethics-review board to make a surrogate decision on their behalf. In a random sample²⁵ of citizens aged 18–85 years in a region of Umeå called Västerbotten county, the same researchers found that 388 (66%) of 589 respondents accepted surrogate decision-making. Regarding concerns for biobank research, potential sample donors²⁵ emphasised greater concern for the safe handling of sensitive information than for the specific purpose of the research. Although these studies suggest no consensus of opinion, most actual donors seem to

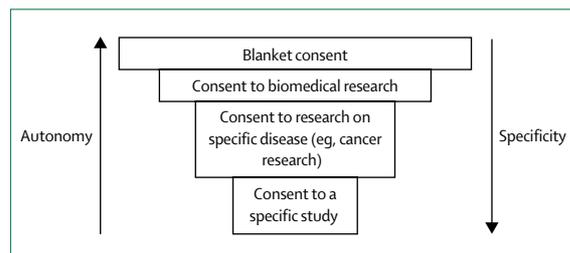


Figure 3: Consent procedures can be thought of as a continuum from highly specific consent to blanket consent

Less restriction on the types of consent allowed implies increased respect for autonomy.

favour a procedure of broad consent. Allowing broad consent at the time of recruitment leaves this decision to the individual. The right to withdraw consent later, and the mechanisms by which to do so, protect regretful participants.

Broad consent and future consent: a scale from specified to blanket consent

Although we argue for broad consent and future consent, we do not suggest a policy where anything goes. If respect for autonomy was the only argument for the need for informed consent, blanket consent permitting any use of a sample would be a logical solution. Our argument against blanket consent is the societal importance of biobank-related biomedical research: blanket consent could lead to the consumption of important samples, potentially allowing commercial, purely technical or political applications (eg, development of new methods for criminal investigations, for refinement of paternity tests, or for helping immigrant authorities to identify the ethnic origin of immigrants). Although some donors might be willing to accept such use of their samples, it might jeopardise substantially public trust in biomedical research. We think that limiting the use to biomedical research is consistent with the widely accepted restriction of access to medical biobanks for any purpose other than medical diagnosis, treatment, or research.

Consent procedures can be regarded as a continuum from highly specific consent to blanket consent (figure 3). A donor of human tissue should be able to submit consent to a range of research—eg, cancer research or cardiovascular research. However, for potential donors who base their decisions on risk assessment, there is no difference between these broad areas of research provided that the same safety measures apply. On the basis of the arguments given, individuals should be allowed to consent to biomedical research in general—a possibility that might be provided for by legislation, such as that proposed in the new Norwegian law on health research, or by the action of ethics-review boards who have authority to select appropriate information and consent procedures.^{26,27}

Withdrawal of consent

We suggest that consent should be regarded as valid until further notice. There should be a realistic opportunity for withdrawal of consent for those who have donated identifiable samples and data, which can be an issue with biobank-based research that can last for many decades (eg, contact information to the biobank might have changed, and donors are unlikely to save contact information for decades).

The Swedish national biobanking programme has established regional biobank registries that act as contact points for withdrawal of consent for all biobanks established within defined geographical regions (www.biobanks.se). The right to withdraw consent does not imply a right to withdraw results that have already accumulated, rather it implies that new data cannot be obtained and that existing data must be maintained in an impersonalised form. When the right to withdraw consent at any time includes a realistic practical possibility to exert this right, perhaps many decades after the original consent, no time limits are needed in the original consent.

Broad consent: not broad permissions from ethics-review boards

The option of broad consent and future consent does not imply once-and-for-all permission for broad research proposals by ethics-review boards. For an ethics-review board to assess the risk–benefit relation for a donor, it must review the coding measures, information security, and other potential risks for the donor that might arise from, for example, changes in legal status, principal investigators, or organisation of the original biobank.

Conclusion

Broad consent and consent to future research studies are valid ethically and should be recommended for biobank research, provided that personal information related to the research is handled safely, that donors of biological samples are granted the right to withdraw consent, and that every new study is approved by the ethics-review board; all three criteria must be fulfilled. Giving donors the option of broad consent and future consent facilitates important research and shows respect for the autonomy of individuals.

Conflict of interest

We declare no conflicts of interest.

Acknowledgments

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