

ISSUES IN MEDICINE

Biobank research: Time for discussion and debate

A Dhai, S Mahomed

Ames Dhai is Director of the Steve Biko Centre for Bioethics in the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. Safia Mahomed is a specialist in Biotechnology Law and has a special interest in human tissue ethics.

Corresponding author: A Dhai (amaboo.dhai@wits.ac.za)

The establishment of biobanks is gaining prominence globally. The open and evolving nature of biobanks has profound ethical, legal and social implications for individual and group autonomy, informed consent, privacy, confidentiality, secondary use of samples and data over time, return of results, data sharing, benefit sharing with communities, and premature or unplanned closure. Complexities also emerge because of increasing international collaborations, and differing national positions. Public consultation and involvement are very necessary to the success of biobanks. Implementing national laws in an internationally consistent manner is problematic.

S Afr Med J 2013;103(4):225-227. DOI:10.7196/SAMJ.6813

The importance of research involving human genetic or genomic information analysed together with other personal or health data for the understanding of multifactorial diseases has increased significantly over the past few decades. This type of research is vital for improvements in disease detection, prevention, diagnosis, intervention, treatment and cure, including the development of new products and services. It is therefore not surprising that growing prominence is being placed on the establishment and sharing of resources comprising data, human biological material (HBM) and information derived from their analysis.^[1] This paper opens with a brief description of biobanks and then discusses some associated ethical and legal complexities in this context; it also attempts to stimulate debate on problems that may arise as a result of unforeseen biobank closure, a situation that has to date received very little attention in scholarly exploration. South Africa cannot afford to lag in this 'new wave' of research while several biobank initiatives are already underway, and one of the objects of this paper is to kindle deliberation on the subject.

What are biobanks?

Biobanks are repositories where organised collections of HBM and associated data from large numbers of individuals are collected, stored and distributed for the purpose of health research. Data

include health, environment and lifestyle information, and often individuals are followed up over long periods. The repositories range from large national biobanks which cater for research into a range of conditions, to smaller units within institutions. The latter are used for research into a limited number of diseases or for disease-specific conditions.^[2] Biobanks are further distinguished into being either public or private in nature. Public biobanks are often called population biobanks. HBM and associated data from public biobanks are used for the promotion of the health of the population.^[2] Hence, biobanks may be one of the following, or a combination thereof: cross-sectional, longitudinal, large-scale, disease-specific or population-based; and they provide platforms for international collaborations on a scale not previously achieved.^[1] While the notion of biobanking is not new, the reliance on the use of biobanks involving an intersection of disciplines and generating knowledge across disciplines has increased significantly.^[3] However, the open and evolving nature of biobanks has profound ethical, legal and social implications for individual and group autonomy, informed consent, privacy, confidentiality, secondary use of samples and data over time, return of results, data sharing, and benefit sharing with communities.^[3-5] There has been much discussion on these issues, but very little has been said about premature or unplanned closure which, in the context of biobanks, is fraught with challenges. In addition, another

layer of complexities emerge because of increasing international collaborations and differing national positions.

How does biobank research differ from conventional established research with biological specimens?^[6]

Conventional research usually entails:

- one researcher or an already recognised set of researchers
- samples obtained and used in defined ways for research in discrete areas
- informed consent from each research participant for use of their sample, and permission to obtain, use and disclose the participants' health information.

With biobank research:

- those obtaining the samples may be brokers or intermediaries who may supply specimens without necessarily being involved in the research
- the biobank sample repository can be used for many research projects and often in numerous scientific areas
- future research activities, including research by investigators who cannot be specified at the time of sample collection, are considered
- because several studies could use the biobank's samples and data, a move from the classic research ethics paradigms on informed consent towards a format of broad or even blanket consent needs to be considered.

Risks of biobank research

While physical risks are rare, potential risks extend beyond the individual participant to population groups that the participant is associated with as well as the general public at large.^[6] Common risks are usually social and dignitary. Social risks include stigmatisation and discrimination, are frequently group-based, and implicate both research participants and non-participants. Stigma and discrimination could arise when research findings indicate that members of certain sub-populations are more likely to have a genotype conferring an increased risk of disease or other traits. Genetic discrimination is widely feared. When identifiable samples are used in research, disclosure of sensitive information will result in an invasion of the participant donor's privacy. Dignitary risks occur when religious or personal values are violated. Unidentifiable samples could lead to research that the donor may not approve of, e.g. use of samples for research on termination of pregnancy, to which the donor could have strong religious objections.^[6] When analysing risks and benefits, it would be important to weigh the potential benefits of knowledge to be gained from the research against potential harm for participants and society at large.

Implications for informed consent

Informed consent is an ethical principle and a legal doctrine of shared decision making, and a central tenet of conventional traditional research. It allows individuals to exercise their fundamental right to decide whether and how their body, body parts and associated data will be used in research.^[3] Classic research ethics focuses on individual consent which can only be obtained after the research has been approved by a research ethics committee (REC). Biobanks introduce a new paradigm that frequently separates the sample collection process (i.e. the informed consent process) from the actual research on the sample.^[6] The research could be conducted many years later and may involve research questions and methods that could not have been contemplated at the time of sample collection. Samples

are exchanged and data are distributed across complex databases. Samples may undergo transformation into specific cell lines that can themselves be duplicated and exchanged.^[3] The supremacy of consent itself is challenged as it is ill-equipped to protect rights in the world of networks and extensive computerised processing of personal and health data over prolonged periods.^[3] Use of informed consent language is also problematic. What is obtained is permission and not informed consent, as it is difficult for donors to make informed and voluntary choices throughout the life cycle of HBM in a biobank.^[5]

To address the bottleneck between classic research ethics paradigms and the wider societal goals of biobank research, new guidelines and amendments to existing ones have proposed solutions to the informed consent impasse. Solutions include broad/blanket consent; multilayered consent with secondary use statements; recontact/reconsent mechanisms; presumed consent/opting out; and waived consent.^[7] Biobank research entails a balanced choice between autonomy and the public good as the benefits of this type of research involve broader societal concerns of scientific advancements for diagnosis, prevention and treatment of disease, and increasing knowledge.

Property rights – some considerations

Property rights surrounding HBM, commoditisation of human tissue and medical data continue to be discussed at length, with competing values of fairness to donors and maintaining access to research materials dominating. Deep moral significance is attached to the donation of body parts, tissue and organs. Biobanks evoke the notion that property which is shared by all humanity must bear in mind population and individual considerations.

Current research ethics regulations are based on the principle of autonomy which is independent of any property right in one's tissue.^[1] Moreover, the traditional role of informed consent does not include that of soliciting and obtaining gifts of HBM. In exceptional situations, specimens can be so unique as to become the source of immortalised cell lines and other valuable products. Current case law demonstrates instances where disputes have arisen because researchers used samples without the necessary permission or when donors were exploited for financial and scientific gain.^[8-10] It is difficult to apply traditional principles of delict, contract and property law to biobanks as knowledge generated by donated specimens and other information derived is not adequately categorised by property and contract dogma.^[11]

Biobanks – 'end of life' issues

Biobank closure, sale, bankruptcy, end of funding and transfer of materials to other entities are issues that have not yet been explored adequately. Biobanks need to develop plans for appropriate transfer, disposition and destruction of HBM and data in the event of unexpected discontinuation, such as termination of funding, or if the bank no longer served a scientific or valuable purpose. Destroying specimens and samples under the control of the biobank is less complex than ensuring the destruction of resources that have been provided to third parties. While every effort could be made to retrieve and destroy all such specimens, data and samples, there may be circumstances where this is not feasible (e.g. if pooled samples are prepared or cell lines have been developed and disseminated anonymously). In addition, destroying all data may also be quite difficult as backup files may cover lengthy periods.^[1] Different cultural and religious groups may have different attitudes to biological material, and these could change over time. Some cultural or religious groups may follow traditional practices in the disposal or destruction of HBM. While this will most probably be addressed

during the consent process, it will also be an important consideration at the point of disposal.^[1]

Commercial biobanks, because they are a relatively new development, could be viewed as start-up ventures with the concomitant risk of business failure. Should a biobank company become bankrupt, the HBM and medical records may be its only substantial assets. Where a biobank files for bankruptcy, creditors would require that the sale and distribution of the assets are maximised – a situation that could be perceived as morally repugnant. Furthermore, there are complexities regarding the consent and confidentiality agreements obtained during donation and how these ethical values would now be protected. Currently, the trustee in the bankruptcy is legally in a position to breach any pre-existing contract to sell off assets. Legislation will have to be enacted to limit the ability of the biobank to accept donations only where the donor retains certain non-waivable property rights that would bind transferees of the information. Such a law would restrict the donor's ability to make unconditional gifts, but there does not seem to be any other alternative.^[6]

With increasingly long-term research, donor death in the context of biobanking must also be considered. Questions arise as to whether HBM and data should be returned to family members. In addition, consideration will have to be given to whether results from research should be provided to biological family members. Currently, most international guidelines have not considered the effect of donor death and the rights of persons enrolled in research who have already died. Neither is there any guidance on the rights of family members or the estate over the HBM, data and research results of the deceased donor.^[12] It is recommended that these issues be discussed with the donor and be included in the informed consent process. The donor's wishes in the event of death should be recorded and respected.

Public engagement and trust

The above issues make it clear that public consultation and involvement are very necessary to the success of biobanking. Public and community participation in research is not a new phenomenon. The public and

even patient support groups are being increasingly recognised as active participants in the research process. Ongoing dialogue between the public, researchers and biobank managers is essential.^[3]

Conclusion

A multitude of research questions remain unanswered. Much more transdisciplinary knowledge of genetic, environmental, psychosocial and lifestyle factors that contribute to the development and progression of chronic diseases is necessary for advances in public health. Biobanks, with their HBM and databases, will play a critical role in answering these questions. While recognising the importance of pursuing scientific knowledge as essential to and in parallel with human progress, human wellbeing and the relief of suffering, it is vital that human dignity is respected and upheld. Currently, implementing national laws in an internationally consistent manner is problematic. National and international laws and policy guidelines will need to be amended or enacted to ensure that rights are protected in the world of networks and extensive computerised processing of personal and health data.

1. OECD Guidelines on Human Biobanks and Genetic Research Databases. Paris: OECD, 2009. <http://www.oecd.org/sti/biotechnology/policies/44054609.pdf> (accessed 22 November 2012).
2. O'Doherty KC, Hawkins AK, Burgess MM. Involving citizens in the ethics of biobank research: Informing institutional policy through structured public deliberation. *Soc Sci Med* 2012;75:1604-1611. [<http://dx.doi.org/10.1016/j.socscimed.2012.06.026>]
3. Cambon-Thomsen A, Rial-Sebbag E, Knoppers BM. Trends in ethical and legal frameworks for the use of human biobanks. *Eur Respir J* 2007;30(2):373-382.
4. Murphy J, Scott J, Kaufman D, Geller G, LeRoy L, Hudson K. Public perspectives on informed consent for biobanking. *Am J Public Health* 2009;99(12):2128-2134. [<http://dx.doi.org/10.2105/AJPH.2008.157099>]
5. Winickoff DE, Winickoff RN. The charitable trust as a model for genomic biobanks. *N Engl J Med* 2003;349:1180-1184. [<http://dx.doi.org/10.1056/NEJMs030036>]
6. Rothstein MA. Expanding the ethical analysis of biobanks. *J Law Med Ethics* 2005;33(1):89-101. [<http://dx.doi.org/10.1111/j.1748-720X.2005.tb00213.x>]
7. Tasse AM, Budin-Ljosne I, Knoppers BM, Harris JR. Retrospective access to data: the ENGAGE consent experience. *Eur J Hum Genet* 2010;18:741-745. [<http://dx.doi.org/10.1038/ejhg.2010.30>]
8. Moore v. Regents of the Univ. Of Cali., 793 P.2d 479. Cal 1990.
9. Greenberg v. Miami Children's Hospital, 264 F.Supp.2d 1064. S.D. Fla. 2003.
10. Dalton R. When two tribes go to war. *Nature* 2004;430(6999):500-502.
11. Palmer LL. Should liability play a role in the social control of biobanks? *Journal of Law, Medicine and Ethics*. 2005; 3: 70-78. [<http://dx.doi.org/10.1111/j.1748-720X.2005.tb00211.x>]
12. Knoppers BM, Hudson TJ. The art and science of biobanking. *Hum Genet* 2011;130(3):329-332. [<http://dx.doi.org/10.1007/s00439-011-1067-9>]