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ORIGINAL PAPER

Legitimacy, Trust and Stakeholder Engagement: Biobanking in South Africa

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Abstract Biobanking has become a global activity of growing relevance to research. The African continent is part of this global effort to collect, store and re-use samples and data. International research and capacity development efforts such as the Human Health and Heredity Africa (H3 Africa) project seek to empower African researchers and research participants alike. Given that African genetic diversity is a unique global resource, retaining samples and data on the continent is critical to building trust in communities who have been historically exploited in the name of research. Diverse and multiple stakeholders are involved in biobanking. Engaging authentically with these various stakeholder groups is a pre-requisite to building trust. Likewise, establishing legitimacy of biobanks also contributes to development of trust in communities. This paper reflects on the concepts of trust, legitimacy and stakeholder engagement. Empirical research conducted on researchers in South Africa as well as on research participants and Community Advisory Board (CAB) members is briefly presented. The development of educational pamphlets on genetics, genomics and biobanking and an educational video on biobanking in conjunction with CAB members is described. These tools were used to engage research participants and CAB members in discussions around biobanking. Establishing biobanks in African settings is challenging. However, efforts must be made to engage with relevant stakeholders on the basis of mutual respect and trust.

Keywords Legitimacy · Trust · Stakeholder engagement · Biobanking · South Africa

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Introduction

Biobanking has become a core resource for medical research globally as it has enormous transformative potential. Since the late 1990s, large biobanks have been established in resource rich environments predominantly in the USA and Europe—Iceland, Estonia and the UK, in particular. More recently, in 2016, biobank development has occurred in China (China Genebank in Shenzen). The Human Health and Heredity Africa (H3 Africa) project funded jointly by the National Institutes of Health (NIH) and the Wellcome Trust began biobank development in Africa. This project seeks to develop research capacity in Africa by encouraging African scientists to develop biorepositories in various African countries including South Africa.

Historically, Africa lies at the core of the controversy that surrounds data and sample mining. As a consequence of our rich African genetic diversity, samples and data from Africa are highly sought after internationally. The unidirectional flow of samples out of Africa, even as recently as the Ebola epidemic in West Africa, has raised huge concerns about exploitation. Undoubtedly, biobanking in Africa presents an incredible opportunity for researchers, pathology companies, the pharmaceutical industry and patients. Powerful questions emerge though, around who the ultimate beneficiaries of African samples and data actually are.

Several bioethical challenges lie at the core of biobanking. Some argue that "[g]enomic biobanks present ethical challenges that are qualitatively unique and quantitatively unprecedented." (Conley et al. 2012). It has become evident that trust in health researchers is waning globally and this is acutely expressed in resource poor environments. This crisis in trust has resulted in the erosion of legitimacy of biobanking and has been fuelled by a history of exploitation in medical research that exploits vulnerabilities of developing world communities. Rapid advances in genetic and genomic research require large volumes of biological samples but also exacerbate vulnerability as they raise concerns about data privacy and discrimination based on genetic risk and susceptibility. The growing trend of commodification of health and commercialisation of new technologies in the absence of benefit sharing is eroding trust.

Legitimacy and Biobanking

Legitimacy has been defined as "the capacity of the system to engender and maintain the belief that the existing political institutions are the most appropriate ones for the society" (Lipset 1959). Biobanking is dependent on the cooperation of various stakeholders. Public trust is a pre-requisite for such cooperation. Any initiative that depends on the active cooperation of its citizens requires legitimacy. Citizens may decide not to cooperate at all, to cooperate partially or to actively oppose a specific policy or initiative. In biobanking, such opposition may be couched in genuine concerns about privacy, discrimination and commercialization. The extent to which a governance framework can protect society from such perceived vulnerabilities impacts directly on public trust in biobanking (Salter and Jones 2005).

Scientific advances in biobanking are dependent on "the construction of novel forms of regulatory legitimacies" (Salter and Jones 2005). Uncertainty about future research poses challenges for scientists, regulators and custodians who are seeking to establish legitimacy of biobanks (Gottweis 2008). The "notion of an explicit dependency" between biobanking and ethical self-regulation to maintain public trust highlights the problem of legitimation faced by biobanks globally. Ensuring legitimacy is important when designing, implementing and enforcing regulatory structures. Public support for new technology is often harnessed using regulations introduced by governments. These regulations are informed by scientific experts. This technocratic approach has not worked with green biotechnology (genetically modified foods and crops). It is unlikely to work with red biotechnology (health applications of genetic science). The development of regulations must therefore be accepted by scientists and society. While industry might be satisfied with regulations that foster its economic interests, citizens might feel that their rights have been compromised by commercialisation (Moodley et al. 2014). On the other hand, while civil society may feel content with specific regulations and ethical protection, industry may perceive these to be restrictive. This calls for "novel forms of regulatory legitimacies" (Salter and Jones 2005).

Increasingly bioethics has developed a prominent role in "engendering public consent and legitimacy for projects"(Corrigan and Petersen 2008). Bioethics has considerable political value because it incorporates different interests of civil society, science and industry in the context of a neutral discursive domain (Salter and Jones 2005). If biobanks and bioethics oversight committees engage with broader lay values, they will authentically represent the public interest and achieve a broader public legitimacy. The European Group on Ethics (EGE) in embracing quality, openness and effectiveness has broadened the legitimacy base of EU decisions (Mohr et al. 2012).

Establishing Trust in Biobanking

Historically, researchers have "failed to obtain informed consent, modified protocols without consulting participants, withheld information, and failed to follow up as planned". Consequently, fear and mistrust of investigators have been identified as "deterrents to participation in research" (Pacheco et al. 2013). Participation in and support for biobanking is critically determined by trust. This is so because a research biobank represents a "collection of quite personal health and lifestyle information and genetic sampling of yet unknown but possibly large information potential about the participant" (Ursin 2010). Public support for science is determined to a large extent by perceptions. Recent surveys in the UK and Australia indicate that the public places significant trust in the university-based scientific community. However, the surveys also indicated that "trust evaporated quickly if scientists worked for either industry or government" (Caulfield et al. 2014). A focus group study with participants in a Norwegian biobank revealed that commercialisation was the main threat to trustworthiness (Ursin 2010). This could, however, be remedied if private research was approved by institutional research ethics committees and if such private research occurred in addition to and not instead of publicly funded research.

Trust is a confident belief in and reliance upon the ability of and moral character of another person (Beauchamp and Childress 2001). Building trust requires transparency in informing patients about intended and actual use of data (Erlich et al. 2014). Appealing to altruism in collecting samples without disclosing future use by end users including commercial entities is regarded as a betrayal of trust. It is clear that to many, trust refers to “a state of mind, a belief, or an expectation held by one trading partner about another that the other will behave in a mutually acceptable manner” (Dodgson 1993).

“Maintaining mutual commitment to the invention of a shared future” leads to productive teamwork (Flores 2012) or in the case of biobanking, to successful relationships with stakeholders. When trust is built in a relationship, we know that partners in the relationship will be sensitive to the concerns of each other and will fulfil promises made (Flores 2012). Trusting people unreservedly in all domains is not usual. In our assessments of trust in partnerships, the following are important: sincerity, competence, reliability and engagement. Different types of trust must be inculcated in collaborative partnerships—contractual trust (adherence to agreement and contracts), competence trust (expectations of ability and performance) and goodwill trust (mutual commitment to partners) (Davenport et al. 1999). These layers of trust are relevant to biobanking as we interact with donors/patients/members of the public, funders, clients/researchers and regulators. Historically, a mistrust of science has developed. Furthermore, failure of regulation in biotechnology has engendered mistrust. Scientists are now keen to exploit technology to advance medical science without undermining public trust. Concerns about a “crisis of trust” were expressed in the UK when UK Biobank was being established. In one of our empirical studies, one of my interviewees summed up the crux of the concern in biobanking: “It’s all about trust” (Moodley and Singh 2016).

Stakeholder Engagement in Biobanking

Engaging with stakeholders and including them in decision-making around biobanking is critical to the success of a biobank. Stakeholder engagement reflects the extent to which multiple stakeholders are involved in a project and the extent to which their diverse perspectives are acknowledged. Because biobanks are a public good, several stakeholders must be included and be involved in active participation during every step of the process for the endeavour to succeed (Porteri et al. 2014).

Public engagement may take the form of individual interviews, focus groups, community advisory groups, public meetings, surveys and deliberative democratic processes. If public engagement is effective, trust will be fostered and social justice will improve. This recognises the “Kantian perspective that all people and their viewpoints matter”(O’Doherty and Hawkins 2010). However, many forms of public engagement “fail to give sufficient authority to the conclusions arising from the engagement”. There have been serious deficits in deliberative democracy which requires that “participants are informed, try to understand the perspectives of others, demand and provide warrants for their positions and are willing to attempt to find a policy or other conclusion that they agree is fair”(O’Doherty and Hawkins 2010). Stakeholders have expectations that their deliberative efforts will be taken seriously.

The prototype biobank was formed in Iceland in 1998. It suffered several setbacks due to exclusion of medical doctors and resistance to issues of consent and governance. This phenomenon was described as the “biopolitics of the dispossessed”. Medical doctors felt excluded and refused to hand over medical records to the biobank (Palsson 2008). Although the public was initially supportive, when the biobank became a contested issue, many members of the public started to opt out. This was powerful because the entire population was involved. It has been argued that if the Icelandic project had been launched as a collaborative venture between government, academia and industry, the outcome may have been different (Palsson 2008). Likewise, Biobank Japan failed to collaborate with national universities and university hospitals and chose private hospitals as partners and this impacted negatively on the project both economically and scientifically (Triendl and Gottweis 2008).

Benefitting from these early experiences, UK Biobank placed high value on engagement via consultation with experts with strong positive results. However, public engagement may not have been sufficient. The stakeholder model of "consultation" reflects a restricted version of engagement as it involves "only those with an established stake or interest in the issues". Involving civil society at large including those members of the public who are not aware of the biobank is important (Corrigan and Petersen 2008). Rawls' concept of deliberative democracy provides justification for the democratic involvement of civil society in decision-making. This forms the basis for a "just and moral society". In France, the AFM Biobank involves a patient organisation who are engaged in research as a "partnership model".

Involving the public in the science, research and governance of biobanking has the potential to lead to the "co-production" of health science knowledge (Porteri et al. 2014). Information centres linked to biobanks could produce pamphlets and posters, hold press conferences and address issues and concerns of the public through a website and a toll free number"(O'Doherty and Hawkins 2010).

The ultimate form of community engagement is community-based participatory research (CBPR). According to Pacheco et al. (2013), "employing the methods of CBPR can aid in developing trust". CBPR can be defined as

> a partnership approach to research that equitably involves community members, organizational representatives and researchers in all aspects of the research process and in which all partners contribute expertise and share decision making and ownership.

A true partnership is created between academic institutions and the community. Most importantly, there is an "equitable distribution of all aspects of research, shared decision-making, and ownership of data". Developing culturally appropriate programs is nearly impossible without the full participation of community members.

In South Africa, this is the only approach that can be used with the San community—the earliest hunter gatherers in the country whose ancestors are regarded as the first inhabitants in South Africa with languages distinctly different from the other ethnic groups in the country. In research involving the San people, members of the San Council must be involved in RECs and steering committees. The Working Group for Indigenous Communities in Southern Africa requires inclusionary involvement of the San people in research. Researchers must meet with San community leaders first. Researchers must then speak to the community to explain the research. The community must vote about their desire to participate or not. Then only can consent be sought from individuals. Results of the research must be fed back to the community. The San Council is the gatekeeper to this process. Recently, the San Council has published its own Code of Ethics in which the values of honesty, respect, care, justice and fairness are outlined (Callaway 2017).

Empirical Research: Stakeholder Perspectives from South Africa

As a consequence of research funding from the National Research Foundation (South Africa) and the National Institutes of Health (NIH) in the USA, our centre undertook empirical research in South Africa to elicit the perspectives of various stakeholder groups in biobanking.

Researcher Perspectives

In 2015, soon after Research Ethics Committee approval was obtained from three different institutions, in-depth interviews were conducted with a purposive sample of 21 researchers in South Africa. Interviews lasted approximately 40–60 min and were audiotaped with consent. Thematic analysis of the transcribed interviews was conducted.

Results indicated that most researchers interviewed articulated serious concerns over standardised regulatory approaches that failed to consider the heterogeneity of biobanks. Given that biobanks differ considerably, they felt that guidelines and Research Ethics Committees (RECs) needed to stratify risk accordingly. It was also important for governance processes and structures to be flexible. While RECs were regarded as an important component of the governance structure, some researchers expressed concern about their expertise in biobanking. It was felt that specialised biobanking committees needed to be established. Interestingly, operational management of biobanks was regarded as an ethical imperative and a pre-requisite to building trust during consent processes. While broad general consent was preferred by some researchers, tiered consent, where research participants or potential biobank donors had a choice, was thought to be more consistent with respect for autonomy and building trust.

Some respondents indicated that Material Transfer Agreements (MTAs) were often lacking when bio-samples were exported and this was perceived to impact negatively on trust. They noted:

> When we export material from SA or from underdeveloped countries to the developed countries, we have no control over its eventual fate. Are we being used as experimental collection depots for the third world?
>
> Some researchers in Europe and the US try to bully us … they think all African institutions are backward and they are not very respectful towards the sample providers. They are quite taken aback when we actually insist on an MTA.

On the other hand, most researchers believed that authentic community engagement would help to build trust and improve understanding of consent processes. A respondent indicated:

> Consent forms should evolve in consultation with Community Advisory Boards so that the consent form can actually contain the information that would be really important from the patient and community perspective.
>
> At the moment the consent form is the product of the researcher/research team and biobank perspectives … it contains literature from an ethics and legal perspective … it may not be important from the patient's perspective.

The study concluded that building trust will best be achieved via a system of governance structures and processes that precede the establishment of a biobank and monitor progress from the point of sample collection through to future use, including export. Such governance structures must be robust and must include comprehensive national legislation, policy and contextualised guidelines. Given that such governance infrastructure appears to be lacking in many African countries, including South Africa (Staunton and Moodley 2013), much work needs to be done. Capacity development of all stakeholders including REC members will hopefully enhance expeditious and efficient review of biobanking protocols which in turn will reinforce trust in the researcher-donor relationship. It is clear that science translation and community engagement in biobanking is integral to the success of biobanking in South Africa (Moodley and Singh 2016).

Bridging the Gap Between Scientists and Patients/Research Participants and Community Members

While researchers involved in the first empirical study described above were well informed about genetics and genomics research as well as biobanking, research participants, patients and Community Advisory Board (CAB) members were not. Due to the technical language involved, it can be difficult to discuss genomic research with non-scientists. Despite this, there is evidence to suggest that by framing the topic in a way that the community will understand, such as by focusing on the inheritability of diseases rather than discussing the molecular biology of genes, the community can and will understand the concept of genomic research (Marsh et al. 2010; Chokshi et al. 2007). In this regard, recent work indicates that though most community members are not familiar with genomic terminology; they are indeed conceptually aware of patterns of inheritance and gene-environment interactions (Roman Isler et al. 2013).

As a result, we started off the process of engagement with patients with the development of five educational pamphlets on genetics and genomics research and biobanking. These pamphlets were developed in conjunction with the CAB members and experts in science translation of genetics and genomics information. In addition, an educational video (Stellenbosch Faculty of Medicine and Health Sciences 2016) on biobanking was developed in collaboration with CAB members.

The video was filmed at the tertiary academic hospital that houses the biobank collecting samples from HIV lymphoma patients. All participants in the video were actual staff working in the clinic and the biobanks. The roles of patients (potential research participants) were played by medical students. The script was written in a manner that reflected patients asking doctors and biobank staff several questions to encourage potential biobank donors to ask questions before donating samples to a biobank. This was done to empower potential research participants to engage fully with the research process as active participants in a context where patients often play a passive role in the healthcare system. Both the pamphlets and the video were used to engage with patients/research participants. In addition, a genogram was co-constructed with patients/research participants to focus on inheritability of diseases and character traits. This worked well in helping patients to realise how character traits, physical features and diseases pass from one generation to another in families.

Perspectives of Patients/Research Participants and CAB Members

In 2016, we conducted 41 semi-structured in-depth interviews with 30 lymphoma patients/research participants and 11 CAB members at a tertiary hospital in South Africa. In general, the interviews were challenging as participants had a very basic understanding of medical research in general and limited awareness of genomic research, in particular. Despite the low levels of knowledge on the topic, the majority of participants expressed willingness to donate a sample for research. In this study population, religious beliefs were not an important factor in decision-making to participate in biobanking research except for one participant who was a Jehovah's Witness. In South Africa, there is great cultural and linguistic diversity. There are 11 official languages spoken in the country. In the Western Cape, the predominant local ethnic language is isiXhosa. Although cultural beliefs were a significant factor among the isiXhosa speaking participants, this would not prevent them from participating in genomic research. As the research team was interested in learning how best to engage with communities participants proposed a variety of community engagement strategies specific to their community and alluded to potential challenges with community engagement. This study concluded that there was an overall poor understanding and awareness of genetic research in this community. Despite this, participants were willing to participate in biobanking studies, occasionally for perceived personal benefit but mainly for altruistic reasons, and despite some fears arising from cultural beliefs and traditions. The need for science translation and intense community engagement was evident (unpublished data).

Conclusion

Establishing biobanks in settings with vulnerable participants is challenging. South Africa has a history of exploitation where research is concerned. One such example of genomic research in 2009/2010 allegedly prompted the development of the San Code of Ethics in 2016. Communities and participant advocacy groups are becoming more empowered and proactive. Going forward, engaging with communities in an authentic manner would be critical even when the idea of a research project is just being conceived. This level of respect is highly valued by communities and will go a long way in building trust in biobanking.

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References

Beauchamp, Tom L., and James F. Childress. 2001. *Principles of biomedical ethics*. England: Oxford University Press.

Callaway, Ewen. 2017. South Africa's San people issue ethics code to scientists. *Nature* 543 (7646): 475–476. https://doi.org/10.1038/543475a.

Caulfield, Timothy, Sarah Burningham, Yann Joly, Zubin Master, Mahsa Shabani, Pascal Borry, Allan Becker, Michael Burgess, et al. 2014. A review of the key issues associated with the commercialisation of biobanks. *Journal of Law and the Biosciences* 1 (1): 94–110. https://doi.org/10.1093/jlb/lst004.

Chokshi, Dave A., Mahamadou A. Thera, Michael Parker, Mahamadou Diakite, Julie Makani, Dominic P. Kwiatkowski, and Ogobara K. Doumbo. 2007. Valid consent for genomic epidemiology in developing countries. *PLoS Medicine* 4 (4): e95. https://doi.org/10.1371/journal.pmed.0040095.

Conley, John M., Mitchell Robert, R. Jean Cadigan, Arlene M. Davis, Allison W. Dobson, and Ryan Q. Gladden. 2012. A trade secret model for genomic biobanking. *Journal of Law, Medicine and Ethics* 40 (3): 612–629. https://doi.org/10.1111/j.1748-720X.2012.00694.x.

Corrigan, Oonagh, and Alan Petersen. 2008. UK biobank: Bioethics as a technology of governance. In *Biobanks: Governance in comparative perspective*, ed. Herbert Gottweis and Alan Petersen, 143–158. New York: Routledge.

Davenport, Sally, John Davies, and Charlotte Grimes. 1999. Collaborative research programmes: Building trust from difference. *Technovation* 19 (1): 31–40. https://doi.org/10.1016/S0166-4972(98)00083-2.

Dodgson, Mark. 1993. Learning, trust and technological collaboration. *Human Relations* 46 (1): 77–95. https://doi.org/10.1177/001872679304600106.

Erlich, Yaniv, James B. Williams, David Glazer, Kenneth Yocum, Nita Farahany, Maynard Olson, Arvind Narayanan, et al. 2014. Redefining genomic privacy: Trust and empowerment. *PLoS Biology* 12 (11): 1–5. https://doi.org/10.1371/journal.pbio.1001983.

Flores, Fernando. 2012. On trust. In *Conversations for action and collected essays: Instilling a culture of commitment in working relationships*, ed. Maria Flores Letelier, 69–74. South Carolina: CreateSpace Independent Publishing.

Gottweis, Herbert. 2008. Biobanks in action: New strategies in the governance of life. In *Biobanks: Governance in comparative perspective*, ed. Herbert Gottweis and Alan Petersen, 22–38. New York: Routledge.

Isler, Roman, Karey Sutton Malika, R. Jean Cadigan, and Giselle Corbie-Smith. 2013. Community perceptions of genomics research: Implications for addressing health disparities. *North Carolina Medical Journal* 74 (6): 470–476.

Lipset, Seymour Martin. 1959. Some social requisites of democracy: Economic development and political legitimacy. *The American Political Science Review* 53 (1): 69–105. https://doi.org/10.2307/1951731.

Marsh, Vicki M., Dorcas M. Kamuya, Albert M. Mlamba, Thomas N. Williams, and Sassy S. Molyneux. 2010. Experiences with community engagement and informed consent in a genetic cohort study of severe childhood diseases in Kenya. *BMC Medical Ethics* 11: 13. https://doi.org/10.1186/1472-6939-11-13.

Mohr, Alison, Helen Busby, Tamara Hervey, and Robert Dingwall. 2012. Mapping the role of official bioethics advice in the governance of biotechnologies in the EU: The European Group on Ethics' Opinion on commercial cord blood banking. *Science and Public Policy* 39 (1): 105–117. https://doi.org/10.1093/scipol/scs003.

Moodley, Keymanthri, and Shenuka Singh. 2016. "It's all about trust": Reflections of researchers on the complexity and controversy surrounding biobanking in South Africa. *BMC Medical Ethics* 17: 57. https://doi.org/10.1186/s12910-016-0140-2.

Moodley, Keymanthri, Nomathemba Sibanda, Kelsey February, and Theresa Rossouw. 2014. "It's my blood": Ethical complexities in the use, storage and export of biological samples: Perspectives from South African research participants. *BMC Medical Ethics* 15: 4. https://doi.org/10.1186/1472-6939-15-4.

O'Doherty, Kieran, and Alice K. Hawkins. 2010. Structuring public engagement for effective input in policy development on human tissue biobanking. *Public Health Genomics* 13 (4): 197–206. https://doi.org/10.1159/000279621.

Pacheco, Christina M., Sean M. Daley, Travis Brown, and Melissa K. Filippi. 2013. Moving forward: Breaking the cycle of mistrust between American Indians and researchers. *American Journal of Public Health* 103 (12): 2152–2159. https://doi.org/10.2105/AJPH.2013.301480.

Palsson, Gísli. 2008. The rise and fall of a biobank: The case of Iceland. In *Biobanks: Governance in comparative perspective*, ed. Herbert Gottweis and Alan Petersen, 41–55. New York: Routledge.

Porteri, Corinna, Patrizio Pasqualetti, Elena Togni, and Michael Parker. 2014. Public's attitudes on participation in a biobank for research: An Italian survey. *BMC Medical Ethics* 15: 81. https://doi.org/10.1186/1472-6939-15-81.

Salter, Brian, and Mavis Jones. 2005. Biobanks and bioethics: The politics of legitimation. *Journal of European Public Policy* 12 (4): 710–732. https://doi.org/10.1080/13501760500160623.

Staunton, Ciara, and Keymanthri Moodley. 2013. Challenges in biobank governance in Sub-Saharan Africa. *BMC Medical Ethics* 14: 35. https://doi.org/10.1186/1472-6939-14-35.

Stellenbosch Faculty of Medicine & Health Sciences. 2016. Biobanking and beyond. Published 28 November 2016 on Youtube. Video, 13:13. https://www.youtube.com/watch?v=QjSfIA6_bfc.

Triendl, Robert, and Herbert Gottweis. 2008. Governance by stealth: Large-scale pharmacogenomics and biobanking in Japan. In *Biobanks: Governance in comparative perspective*, ed. Herbert Gottweis and Alan Petersen, 123–140. New York: Routledge.

Ursin, Lars O. 2010. Privacy and property in the biobank context. *HEC Forum* 22 (3): 211–224. https://doi.org/10.1007/s10730-010-9138-1.