

# Ethical considerations in genomic research in South Africa

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The conduct of genomic research in South Africa (SA) raises a number of ethical challenges that need to be addressed in its design and execution. These include, for example, considerations of consent, community engagement, stigmatisation, feedback of findings and ensuring that genomic research is of benefit to patients and researchers in SA. We provide an overview of the current debates on some of these issues and pointers for further reading.

*S Afr Med J* 2019;109(6):375-377. DOI:10.7196/SAMJ.2019.v109i6.14067

Genetic and genomic methods are now integral to our study of the biology and epidemiology of disease and can offer insight into diseases that develop in the body and how these spread in communities. Genomic research methods can also assist in the identification of new targets for drug and vaccine development and can reveal valuable information regarding drug effectiveness and potential drug toxicity in particular persons or groups.

There are several ways in which genomic research can be of relevance to patients in clinics, in addition to providing high-level information about disease at the population level. For instance, researchers are increasingly exploring how personal genomic tests could be used to better attune the care that a person receives. This could be done by predicting the drug dose that may be most effective for that person by identifying specific individuals more at risk of spreading viruses<sup>[1]</sup> or by predicting which individuals are more at risk of developing particular conditions and should therefore be subjected to more regular screening.

Against this background, there are a number of important ethical considerations that need to inform both the conduct of genomic research, but also the gradual introduction or expansion of genomic medicine in South African (SA) clinics. We describe a selection of these in this article. A more detailed description of some of these challenges can be found in a recent consensus study report by the Academy of Science of South Africa (ASSaf) on the ethical, legal and social implications of genetics and genomics in SA.<sup>[2]</sup>

## Informed consent

Consent is a key pillar of health research, which is always required in SA unless an ethics committee has waived the need to obtain consent in exceptional circumstances. Valid consent is consent voluntarily given by a competent person on the basis of sufficient information. The test case for the latter is that the consent process should provide information that a reasonable person would possibly want to know – which is different from requiring ‘all’ information.

A particular challenge in the context of genetic and genomic research is that samples and data can be stored and re-used for multiple projects over long periods of time, including projects that are far removed from the original purpose for which samples and data were collected. The possibility for the broad future re-use of samples and data is in conflict with the traditionally specific nature of consent, where data and samples were collected for a specific purpose.

One response to this matter is the introduction of a so-called ‘broad consent’ model that allows for future re-use of samples and data for a number of specific purposes. Broad consent is described as being a permissible consent model in the SA National Ethics in Health Research guidelines.<sup>[3]</sup> It is different from ‘blanket consent’; broad consent is subject to a number of clearly defined process and content restrictions.<sup>[4]</sup> These include limitations on the kinds of purposes the samples and data will be used for, which can be set to accommodate identified concerns, e.g. from a patient group or community. An example could be that the consent form for samples collected for a schizophrenia genomic study indicates that samples and data will also be used for other future *psychiatric* genomic research. Another important restriction that should accompany the use of broad consent is that it be used only when researchers have already described how and where samples and data will be stored, who will have access to these resources, and who will make decisions. Details regarding this governance framework should be included in the consent process.

## Community engagement

Genomics research has seen an evolving recognition to focus on the protection of individual research participants and on that of their communities. One reason why this is considered important is that community engagement recognises more communitarian values traditionally strong in African societies.<sup>[5]</sup> Community engagement requires, for example, including communities in discussions on the ethics of genomic research, developing benefit-sharing arrangements and acknowledging the contributions of study populations. Community engagement is based on principles of solidarity, reciprocity, inclusiveness and mutual respect, which are characteristic of communitarian settings.

A range of approaches have been developed to foster community engagement for genomic research.<sup>[6]</sup> For example, Stellenbosch University’s Centre for Medical Ethics and Law has developed a range of tools to support community engagement around biobanking. This includes an educational video that is freely available for download and use (<https://www.sun.ac.za/english/faculty/healthsciences/cmcl/elsi>). The SA National Bioinformatics Institute is also piloting a bilingual (English-Xhosa and English-Afrikaans) book that uses a combination of text, colourful illustrations and recorded audio (‘speaking book’) to communicate concepts in genomics, informed consent, biobanking and medical research ([www.uwc.ac.za/Faculties/NS/News/Pages/SANBI-pilots-it's-biobank-bilingual-speaking-books.aspx](http://www.uwc.ac.za/Faculties/NS/News/Pages/SANBI-pilots-it's-biobank-bilingual-speaking-books.aspx)). Another

helpful resource was created by researchers in Botswana, who developed a series of 4 comic books that together introduce key concepts in genomic research ([http://botswanabaylor.org/genome\\_adventures.html](http://botswanabaylor.org/genome_adventures.html)). These resources are freely available and could be adapted to better fit the SA research context.

### The possibility for genetic discrimination and stigmatisation

A recurring fear in the context of genetic and genomic research relates to the possibility that it could cause or increase stigma for patient or population groups. Specifically, the concern is that genetic information could be used to 'taint' or 'mark' members of those groups.<sup>[7]</sup> A recent SA example<sup>[8]</sup> suggests that, as a minimum, genomic research could reveal information about a population group that was considered private by members of that group, translating into a potential for reputational harm. While it is important to consider that the process of stigmatisation involves more than just 'marking' a group,<sup>[9]</sup> genomic researchers need to be cognisant of the risk of their research and the presentation of the results being perceived as offensive or stigmatising by participants and communities.

### Feedback of findings

Genomic research has the potential to identify a select number of individual findings that could be relevant to the health of the individual.<sup>[10]</sup> Lists of mutations that should be considered for feedback are available in the USA ([https://www.snpedia.com/index.php/ACMG\\_recommendations\\_for\\_reporting\\_of\\_incidental\\_findings\\_in\\_clinical\\_exome\\_and\\_genome\\_sequencing](https://www.snpedia.com/index.php/ACMG_recommendations_for_reporting_of_incidental_findings_in_clinical_exome_and_genome_sequencing)) and in the UK (<https://www.genomicsengland.co.uk/information-for-participants/findings/>). Overall, the consensus seems to be that individual genetic findings that are: (i) medically actionable or have clinical utility; (ii) robustly associated with disease causation; and (iii) unlikely to have been diagnosed without the genetic finding, should be fed back to participants.<sup>[11]</sup> Ideally, there should be some indication that participants would want to receive findings, e.g. because they were asked during the consent process.

A particular challenge in determining which findings should be fed back in SA genomic research, however, relates to the relative scarcity of population-level genomic data that can help to predict whether detected variants are possibly benign or pathogenic. A second challenge relates to possibilities for diagnostic validation of research results in accredited National Health Laboratory Service (NHLS) laboratories in SA. Such validation will possibly be costly and could increase the burden on these genetic diagnostic laboratories. If there is no possibility to validate the research results, the question is whether it is appropriate to return unvalidated results. The question is whether, if there is no possibility to validate the research result, it is appropriate to return unvalidated research results. In light of these uncertainties, the current preference seems to be to inform participants that no individual genetic research results will be fed back.

### Genomic research for the benefit of South Africans

Debates on the ethics of genomic research in Africa are strongly premised on the notion of equity. This comes to the fore, for instance, in terms of the scientific imperative for extending genomic studies to African populations to ensure that genomic research is fair and inclusive.<sup>[12]</sup> There is also the representation of SA researchers in population genomic studies carried out in this country. It is almost impossible to discuss ethical issues in genomics without taking into consideration the differences in resources and capacity between SA researchers and their collaborators in high-income countries, as

well as the historical narrative of exploitation of African scientists in international health research collaborations. Suggestions have been made to minimise exploitation of African researchers and to achieve equitable research collaborations,<sup>[13]</sup> some of which include: leadership of genomic projects by local researchers; capacity building; giving voice to local researchers in decision-making within genomic collaborations; and allowing local researchers to define the research agenda. An important component of ensuring fairness is also the equitable sharing of research resources, which may include data, biological samples, intellectual property and financial resources.

Equally important is the need to ensure that collaborations between SA research institutions are equitable. Otherwise, concerns of exploitation, which have plagued global health research, may be replicated in in-country collaborations. Developing models and resources for equitable genomic collaborations for in-country and global research is important. The Council on Health Research for Development provides a number of resources and guidelines that could help in navigating some of the tensions in research collaborations.<sup>[14]</sup>

The importance of genomics in SA populations will be more visible if genomic medicine is available in clinics and if it is accessible and affordable. This will require that healthcare practitioners receive specialised training in genetics and genetic counselling, as well as local investment in genomic medicine. But first and foremost, genomic research in SA should be tailored to the health needs of the SA population. It will therefore be important to identify national priorities for genomic research.

### Regulation of genomic research in South Africa

The law governing genomic research is contained in several pieces of legislation, including the SA Constitution, which grants a right to privacy, the National Health Act, 2008 and the Protection of Personal Information Act (PoPIA), 2013, once it has been enacted.<sup>[2]</sup> Importantly, SA legislation comprehensively protects against discrimination (and stigmatisation as a form of discrimination), including discrimination on the grounds of one's genetic material. Regulations regarding sample export are in place and need to be followed by researchers conducting genomic research that requires export, including seeking an export permit from the National Department of Health.<sup>[15]</sup> An important question relating to the conduct of genomic research is whether and how the use of broad consent will be allowed once the PoPIA becomes effective, which is expected in 2020. There is a possibility that rigorous interpretation of the PoPIA would prevent the use of genetic samples and data for research projects not specifically described in consent forms used in their collection and would thus effectively dampen genomic research.<sup>[16]</sup>

### Conclusions

Genomic research raises a range of ethical challenges that need to be considered in its design and execution. Some of these relate to how samples and data are collected and include considerations of consent and community engagement. Others more broadly relate to the research process, and include considerations of justice and fairness, including ensuring that research is of benefit to the SA population.

**Declaration.** None.

**Acknowledgements.** Both authors are members of the H3Africa consortium and have gained valuable insight into the ethics of African genomic research through this affiliation. The views are solely those of the authors.

**Author contributions.** JdV developed the first draft of the manuscript, and NSM provided critical feedback on the manuscript.

**Funding.** JdV and NSM are supported by H3Africa grants from the National Institutes of Health (through the ‘Stigma in African genomics’ grant, award no. U01HG008226, and the ‘Individual findings in African genomics’ grant, award no. U54HG009790).

**Conflicts of interest.** None.

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Accepted 2 April 2019.