Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in an HIV-TB Genomic Research Project in Botswana

by

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DECLARATION

I, Dimpho Ralefala, hereby declare that the work on which this thesis is based, is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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1. **Ralefala, D.,** Kasule, M., Wonkam, A., Matshaba, M. and de Vries, J., 2020. Do solidarity and reciprocity obligations compel African researchers to feedback individual genetic results in genomics research?. *BMC medical ethics*, *21*(1), pp.1-11. (Published).
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ABSTRACT

Background: There has been tremendous progress in the use of genomics[1] in biomedical research and medical care since the launch of the Human Genome Project in 1990. However, it has also introduced new ethical challenges regarding the feedback of findings generated in genomic sequencing. While some would argue in support of the return of individual findings generated from genomics research, participants' preferences regarding which findings should be fed back differs. Most literature discusses feedback of findings in high income countries and very few address this issue in lower and middle-income countries (LMICs). As a result, it remains unclear whether and how individual findings from genomic studies in Africa should be fed back, who should provide these results and when.

Methods: In order to contribute to addressing this gap, an empirical study was conducted to explore expectations and preferences for feedback of individual genetic findings in an HIV-TB genomics research project in Botswana. A qualitative study methodology involving deliberative focus group discussions (dFGDs) and in-depth interviews (IDIs) was used. Participants for this study were adolescents involved in an HIV-TB genomics study being conducted at the Botswana-Baylor Children's Clinical Centre of Excellence (BBCCCE). Parents and caregivers of children enrolled in that same genomic study were also enrolled in this study. A total of 93 participants (44 adolescents and 49 parents and caregivers) were enrolled in 12 dFGDs (6 groups of adolescents and 6 groups of parents and caregivers). Each group of participants met twice within a week, resulting in a total of 24 dFGD meetings. Participants of the dFGDs and in-depth interviews were selected purposively. Additionally, in-depth interviews were conducted with 12 dFGD participants (6 adolescents and 6 parents or

[1] In this thesis, the terms genomics and genetics are used. Genomics is used to refer to the research itself which focuses on the entire genome. The terms genetics results and genetics research results are used interchangeably in relation to results that are being fed back.

caregivers). The dFGDs and IDIs were conducted in Setswana, audio-recorded, transcribed and translated into English. Data were imported into NVivo 12 and analysed using the framework approach for qualitative data analysis.

Results: The study findings revealed that participants' desire to receive individual genetic results is underpinned by their cultural values, mainly solidarity and reciprocity. Participants viewed research participation as a mutual relationship and considered the return of research results to be one way of reciprocating their efforts. This seems to be underpinned by the principle of Ubuntu which advocates for solidarity and reciprocity within communities. Participants noted that when reciprocity obligations are respected, participants feel valued and expressed that not respecting reciprocity expectations could undermine participants' trust and participation in future studies.

Almost all participants wanted to receive individual genetic results. While parents and caregivers wanted to receive individual genetic results regardless of their severity, preventability or actionability, adolescents were reluctant to receive results for genetic conditions that are severe and non-preventable, especially if they are also unactionable. Participants advanced different reasons for feedback of results including for awareness, improving lifestyle, accepting one's' situation, and preparing for the future. The findings also reveal the importance of taking into account participants' context, relations and empowerment when making decisions about whether and which results ought to be fed back.

When asked about practical considerations for feedback of results, both adolescents and parents expressed that they would prefer to receive individual genetic results in person, with adolescents preferring researchers to provide feedback, while parents preferred feedback from doctors associated with the study. Adolescents and parents both expressed that feedback should be supported by counselling, but they differed on the timing of feedback.

Most participants shared that they would like to be informed about the possibility of discovering individual genetic results during the consent process and that consent be obtained for feedback during the enrolment process. They further expressed that in cases where prior consent to feedback was not obtained, then participants should be re-contacted where life-saving genetic information is discovered. Participants emphasized the need for researchers to ensure that participants' decisions regarding feedback of results are well-informed. Autonomy, transparency, and communication were identified as key values to uphold during the consent process.

Conclusion: In conclusion, expectations of solidarity and reciprocity could translate into an obligation to feedback selected individual genetic results in African genomics research. Decisions on practicalities for feedback of results should take into account participants' context and considerations of participants' preferences. For example, in settings like BBCCCE it might be feasible for the study team to relay participants' results to treating doctors in the same centre, while also organising counselling services if necessary. However, in cases where a study is done in a public facility with limited resources, that could be difficult to implement. Consequently, researchers may have to take up the responsibility of feeding back individual results as well as providing genetic counselling in such settings. To make these decisions, researchers should engage with relevant stakeholders including policymakers and local Institutional Review Boards (IRBs) so as to make informed decisions regarding the feasibility and acceptability of their approach to feedback of results. Obtaining participants' consent for feedback of results is important to ensure that their rights and wellbeing are protected in research. This is critical in building trust relationships between participants and researchers. Lastly, although this study is focused in Botswana, these findings could also be generalised to similar contexts in Africa and provide an authoritative voice to H3Africa to be able to mandate

projects with potential to generate individual genetic results to make provisions to feedback these results to study participants.

Keywords: expectations, preferences, feedback, genomics research, individual genetic results, solidarity, reciprocity, practical considerations, reasons, informed consent, parents, adolescents, HIV-TB, Botswana, Africa.

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DEDICATION

This thesis is dedicated to my late parents, Boithatelo and Olebile Njadingwe, who both lacked the opportunity to receive a formal education. My mother, a brilliant woman who was denied an education due to her gender and ultimate marriage into another family, was only permitted to study up to standard three. While my father, as the family's firstborn and heir, was unable to attend school due to his responsibility for the family livestock. This meant that both of my parents were unable to pursue skilled employment when the country transitioned from an agricultural to a skills-based economy. As a result, my mother worked as a shop assistant for the most of her adult life and cultivated the family fields seasonally to supply food and sold any leftovers to augment the family income, while my father did several manual jobs throughout his life. Nonetheless, my parents were ardent believers in the value of education and were prepared to make whatever sacrifice necessary to ensure their children's education. As a youngster, my mother used to tell me that "education is an inheritance that no one can take away from you," and so when she passed on, I understood that, unlike other children whose parents left them riches, my inheritance was in being educated. As a result, education became the focal point of my existence. I have made it a point to take advantage of every educational opportunity that is availed to me. As such, obtaining this qualification is a manifestation of my parents' potential, and not only a fulfilment of their dreams. I hope that this accomplishment serves as an inspiration to young girls and as a reminder to parents to believe in their daughters' capabilities. It is for this reason that I dedicate this thesis to my parents and the female child and commit to use this achievement to positively benefit my community and country as a whole.

Table of Contents

LIST OF FIGURES

LIST OF TABLES

LIST OF APPENDICES

ABBREVIATIONS AND ACRONYMS

AIDS: Acquired Immunodeficiency Syndrome

BBCCCE: Botswana-Baylor Children's Centre of Clinical Excellence

CAB: Community Advisory Board

CAfGEN: Collaborative African Genomics Network

DFGDs: Deliberative Focus Group Discussions

ES: Exome Sequencing

GS: Genome Sequencing

GWASs: Genome Wide Association Studies

H3Africa: Human Hereditary and Health in Africa

HICs: High Income Countries

HIV: Human Immunodeficiency Virus

IDIs: In-Depth Interviews

IFGeneRA: Individual Findings in Genetics Research in Africa

IRB: Institutional Review Board

LMICs: Lower- and Middle-Income Countries

NHGRI: National Human Genome Research Institute

PhD: Doctor of Philosophy

RECs: Research Ethics Committees

TB: Tuberculosis

UB: University of Botswana

UCT: University of Cape Town

US: United States

WES: Whole Exome Sequencing

WGS: Whole Genome Sequencing

CHAPTER 1: INTRODUCTION

1.1. Background

Since the Human Genome Project's inception in 1990, tremendous progress has been achieved in the use of genomics in science and medicine (NHGRI, 2018). It has developed from a fledgling field of study to a significant area of biomedical research and is increasingly becoming a crucial component of medical treatment, with far-reaching implications for society. The completion of the human genome sequence in April 2003 accelerated and facilitated biomedical research significantly, as researchers worldwide now have access to and utilize this data to inform their investigations (NHGRI, 2018). As a result of genomic research, we now have a better understanding of the genetic architecture of a variety of illnesses and of human history. Technological advancements combined with cost reductions in genetic research have resulted in new knowledge about the genesis, diagnosis, and treatment of some of the world's most prevalent and deadly illnesses, including malaria, cancer, HIV/AIDS, TB, and diabetes (H3Africa, 2014).

Exome and genome sequencing (ES/GS) are being more integrated into healthcare (Saunders et al., 2012; Vassy et al., 2014; Worthey et al., 2011). Genomics research is being accelerated, particularly in the areas of cancer and pharmacogenetics, with the goal of producing a future of "precision medicine" in which therapies are tailored to the unique characteristics of each patient (Collins & Hamburg, 2013; Kandoth et al., 2013).

However, the majority of these genetic advances have been spearheaded by high-income nations with little or no investment in Africa. Until recently, only seven studies were conducted entirely on African populations, out of the numerous genome-wide association studies (GWAS) conducted internationally (www.genome.gov/gwastudies/). This generated fears that

the African continent might miss out on possible health and economic gains associated with genetic scholarship (H3Africa, 2014; Popejoy & Fullerton, 2016). In response to this challenge, the Human Heredity and Health in Africa (H3Africa) project was launched in June 2010 as a collaboration between the African Society of Human Genetics, the National Institutes of Health in the United States of America, and the Wellcome Trust, a global charity based in the United Kingdom. H3Africa was founded to assist African academics in conducting genomic studies on African diseases in order to better understand the genetic factors that influence the risk of sickness in African populations (NHGRI, 2018). Over the past decade, this initiative has funded 51 projects across 30 African nations to perform genomics investigations on prevalent non-communicable and communicable illnesses, as well as ethics research. It is anticipated that samples from 50,000 to 75,000 individuals would be collected and analyzed as part of this initiative (H3Africa, 2014).

One key ethical challenge in genomics research is the likelihood of generating genetic information relevant to the health of the individual. Whole Genome Sequencing (WGS) often uncovers information about individuals that is not related to the issue being studied, and these discoveries may be important for patient care (Presidential Commission for the Study of Bioethical Issues, 2013). These findings are often referred to as ‘secondary’, ‘unsolicited’ or ‘incidental’ genomic findings (Green et al., 2013b; Presidential Commission for the Study of Bioethical Issues, 2013; Van El et al., 2013). For example, misattributed paternity may be found in an assessment of the segregation of mutation in a family. In this situation, it is impossible for the clinician to avoid noticing the result, although the intention was not to specifically look for this information. Likewise, researchers may discover that a participant has mutations that put them at a risk of acquiring a certain condition. The ability to find results relating to diseases that were not the primary purpose of study is unique to genomic studies, in

the sense that more traditional genetic research was normally tailored to a certain disease. In South Africa, healthcare practitioners and researchers continue to struggle with deciding what to do with individual genetic data (Van Der Merwe, Ramesar, & De Vries, 2022).

A considerable amount of empirical and conceptual ethics work has been conducted around this topic, mostly in the United States (US) and to a lesser extent in Europe. However, there has been very little work done in this area in Low-and Middle-Income Countries (LMICs), especially in Africa. At the time of conducting this study, only a few studies have been conducted in Africa (Marsh, Kombe, Fitzpatrick, Molyneux, & Parker, 2013; Marsh, Kombe, Fitzpatrick, Williams, et al., 2013), with a few more studies having been published recently (Kasule, Matshaba, Mwaka, Wonkam, & de Vries, 2022; Mwaka et al., 2021; Ochieng et al., 2021; Spies et al., 2021) and none addressed views of participants in Botswana. Yet this is an equally important challenge in the African research context that pushes the boundaries between research and clinical care and leads to questions about issues like ancillary care obligations and so forth. It also came up as one of the more pressing ethical challenges in H3Africa research. To elucidate this question and gather an evidence base that could inform the development of appropriate policies for the return of individual genetic findings in African genomics research, this study focused on exploring expectations and preferences for feedback of individual genetic findings with adolescents as well as parents and caregivers of children involved in an HIV-TB genomics research project in Botswana.

1.2. Thesis outline

This thesis reports on empirical findings for a study that explored the views and expectations of adolescents, parents and caregivers of children and adolescents in a genomic study in Botswana with regards to feedback of individual genetic findings.

The thesis is outlined as follows:

Chapter 1 presents the background of the study, providing an overview of the advancement of genomics research in recent years as well as the status of African genomics research. The chapter describes the Human Heredity and Health in Africa (H3Africa) initiative, which is one of the largest genomics research initiatives taking place in Africa. It introduces the challenge of unanticipated findings emerging in the context of H3Africa research and presents the challenges that African researchers face in dealing with feedback of these results.

Chapter 2 discusses the literature on the ethical, legal and social implications of individual genetic results generated from genomics research. A general overview of genomics research is provided, describing how genetic findings are generated and classified. Following that, current debates on the feedback of genetic findings drawing from both theoretical and empirical literature are discussed. This chapter concludes by contextualising the discussion on feedback of findings to the African context.

Chapter 3 describes the study rationale, main aim, objectives and methods of the thesis. It provides a description of the study design, study population as well as data collection and analysis procedures. This chapter concludes by describing how the relevant stakeholders were engaged as well as measures put in place to ensure that the study was conducted responsibly and ethically.

Chapter 4 is the first results chapter and contains a published peer reviewed article on participants' views regarding researchers' obligations for feedback of individual genetic findings. Empirical data presented in this chapter reveal that participants' expectations for feedback of findings are underpinned by African values of solidarity and reciprocity.

Chapter 5 is the second results chapter and presents empirical data on participants' views on which results to feedback and why. The chapter contains a published peer reviewed article.

Chapter 6, the third results chapter in the thesis, documents empirical evidence on participants' views on practical considerations for feedback of individual genetic results. The chapter contains a manuscript that has recently been accepted for publication.

Chapter 7, the fourth and final results chapter in the thesis, provides empirical data on participants' views on informed consent regarding feedback of individual results from genomics research. The data presented in this chapter have been published in a peer reviewed journal.

Finally, *Chapter 8* provides a discussion and conclusion. It summarises the key issues identified by participants for consideration in decisions about feedback of individual findings from genomics research. These are discussed in relation to the Botswana research context as well as available literature. Implications for practice and future research are discussed as well as the study limitations. The chapter ends with a conclusion.

CHAPTER 2: LITERATURE REVIEW

2.1. General overview of findings from genomics research

The use of genomics research methods on the African continent is on the rise. Whilst not all of these projects use whole-genome or whole-exome sequencing (WGS/WES) methods, those that do risk identifying genetic findings that are directly relevant to the health of the individual. For every causative mutation identified in the human genome, there are thought to be no fewer than 18,000 other mutations, the majority of which are of unconfirmed significance; in the entire genome, these are estimated to be about three million mutations (Grody, Thompson, & Hudgins, 2013; Kohane, Masys, & Altman, 2006). Amidst this huge number of potential variants are a small number of variants that are known to be disease-causing - and even when genomic research projects are discovery-driven and aimed at the identification of new associations between genetics and disease, the possibility exists that the participants included in the projects carry variants that are known to be pathogenic (Kang, Spector-Bagdady, Caplan, & Braithwaite, 2016).

As a result, projects that do whole exome or whole genome sequencing often generate primary, secondary or incidental findings. Primary findings are those that are related to the condition under investigation (Loud et al., 2016). Secondary findings are usually defined as results that are unrelated to the primary reason for conducting the study but are nonetheless intentionally sought, whereas incidental findings are variants that are discovered accidentally (Darnell et al., 2016). This possibility of inevitably discovering unexpected variants while doing a whole exome and whole genome sequencing causes one of the more intractable ethical challenges of genomics research (Grody et al., 2013; Kang et al., 2016), which is whether and to what extent geneticists have a moral responsibility to probe for variants of clinical importance (Kang et al., 2016).

As a result of the huge amount of data generated in exome/genome sequencing, computer software is used to do the initial filtering as it is impossible to analyse the huge amount of data manually. This process involves the disposal of those variants deemed as unlikely to be pathogenic using a couple of rules. Even after that initial filtering, it is still common to be left with several hundred variants that could possibly be pathogenic, and sifting through them requires the collective expertise of clinical geneticists, bioinformaticists and molecular biologists (Grody et al., 2013). Establishing whether a participant carries pathogenic variants therefore may be a costly and time-consuming endeavour. A complicating factor for African genomics research is that the scarcity of relevant reference data makes it difficult to establish whether variants are likely benign or pathogenic – meaning it is more difficult for researchers to decide whether participants should be told about the findings or not (Wonkam & de Vries, 2020). It is this ethical challenge that this thesis seeks to shed light on.

Generally, genomics research results fall into three categories: (1) results that are clinically actionable; (2) results with clinical validity for disease but not often anticipated to be clinically actionable; and (3) results with little or no clinical validity for disease and harms (Berg, Khoury, & Evans, 2011). The ethical question arises about what to do with findings in this first category, which concerns findings that inform on the future health of research participants. The ethics debate uses different terms to describe these kinds of findings – including for instance ‘incidental findings’, ‘secondary results’, ‘pertinent results’ and other terms (Christenhusz, Devriendt, & Dierickx, 2013; Ortiz-Osorno, Ehler, & Brooks, 2015; Presidential Commission for the Study of Bioethical Issues, 2013; Shkedi-Rafid, Dheensa, Crawford, Fenwick, & Lucassen, 2014; Wolf et al., 2012). For the purposes of this thesis, what is of interest is the collection of individual genetic results that have a bearing on the health of the research

participant – whether anticipated or not – and I will call these 'individual genetic results'. These includes both primary and secondary findings.

Over the past years, the generation of individual genetic results in genomics research has brought about some ethical dilemmas including - whether or not individual results from genomics research should be fed back to participants or not, which results to feedback, why, when and how. The reason this is an issue is because some genetic results (incidental findings) may not be related to the condition under study, also genetic results present probability and not certainties. A systematic review of the ethical reasons presented in the literature for and against the disclosure of incidental findings, arising in research showed that the strongest reason in favour of the disclosure of an incidental finding is its confirmed clinical utility and the probability of treatment or prevention (Caulfield et al., 2008; Clayton, 2008; Hens, Nys, Cassiman, & Dierickx, 2011; Kaye, Boddington, De Vries, Hawkins, & Melham, 2010; McGuire, Caulfield, & Cho, 2008; Van Ness, 2008). Other ethical reasons advanced in this debate include beneficence, autonomy, reciprocity among others (Bredenoord, Kroes, Cuppen, Parker, & van Delden, 2011). In addition, some authors have emphasised that there may be an ethical obligation to return results flowing from ancillary care obligations (Richardson, 2008; Richardson & Belsky, 2004b) and duty to rescue (Mackay, 2018).

In this literature, arguments against disclosing individual findings include a lack of expertise essential to evaluate and analyse incidental findings, possible therapeutic misconceptions, uncertain net benefit, and concerns about the impact on family members (Cho, 2008; Kaye et al., 2010; McGuire et al., 2008; Van Ness, 2008; Wachbroit, 1998). While some contend that individual findings should be disclosed with caution. This suggestion is offered under particular circumstances, such as whole genome sequencing and other emerging genetic technologies,

genetic testing of minors, and findings identified in the future based on data obtained now (Ali-Khan, Daar, Shuman, Ray, & Scherer, 2009; Clayton, 2008; Hens et al., 2011; Kohane et al., 2006; McGuire et al., 2008; Tabor & Cho, 2007; Wachbroit, 1998). It is also made while attempting to strike a balance between the autonomy of patients in making their own decisions and the greater skill and knowledge of healthcare professionals (Botkin, 1995; Parker & Majeske, 1995). With regards to genomic sequencing of minors, prominent issues in these discussions are whether or not minors' expectations and preferences are the same as those of parents or caregivers as well as whether there might be a need to reconsent them for feedback of their individual results once they have reached the age of majority.

2.2. Empirical results from literature on feedback of findings from genomics research

As a result of the ethical dilemmas discussed above, several empirical studies have been conducted to establish participants' views and preferences regarding what type of results they would like to receive from genomics studies, when and how. Most studies found that participants typically would like to receive their individual results from genomics research. (Bollinger, Scott, Dvoskin, & Kaufman, 2012; Coors, Raymond, McWilliams, Hopfer, & Mikulich-Gilbertson, 2015; Facio et al., 2013; Regier et al., 2015; Yu, Crouch, Jamal, Tabor, & Bamshad, 2013; Yushak et al., 2016). However, opinions from research participants vary from wanting to receive all findings to receiving only subsets of genetic information. For instance, several studies indicated that whilst some research participants would like to receive incidental results, often regardless of negative consequences of such results (C. V. Fernandez et al., 2015; Miller, Hayeems, & Bytautas, 2010; Murphy et al., 2008), some reasoned that receiving such information is empowering (Clift et al., 2015; Facio et al., 2013; Kaphingst, Ivanovich, Biesecker, et al., 2016; Levenseller et al., 2014), while others felt entitled to it (Clift

et al., 2015; Daack-Hirsch et al., 2013; Conrad V Fernandez et al., 2014; Hitch et al., 2014; Kleiderman et al., 2014; Sapp et al., 2014).

The commonly reported reason for desiring incidental results was the capacity to act on them, however the notion of "actionability" varied widely (Mackley, Fletcher, Parker, Watkins, & Ormondroyd, 2017). It covered access to treatment (Daack-Hirsch et al., 2013; Middleton et al., 2016; Sapp et al., 2014) and prevention (Daack-Hirsch et al., 2013; Facio et al., 2013; Conrad V Fernandez et al., 2014), while others acknowledged the possibility to plan or change lifestyles (Clift et al., 2015; Daack-Hirsch et al., 2013; Conrad V Fernandez et al., 2014; Hitch et al., 2014; Oberg et al., 2015) or inform reproductive decision-making (Facio et al., 2013; Kaphingst, Ivanovich, Biesecker, et al., 2016; Kleiderman et al., 2014; Middleton et al., 2016; Shahmirzadi et al., 2014). Additionally, participants in Bollinger et al. (2012), indicated that they could use the information to monitor the progress of other research studies that could be relevant to the conditions that they have learnt about upon being provided with their results. Other participants also described that the findings may be useful to them in the future as research advances and leads to better understanding of the data and that the results could also provide them with some personal utility (Bollinger et al., 2012).

In the empirical evidence available, it transpires that participants were however concerned about what the results really meant, especially the possibility that the results could be inaccurate. Participants also seem concerned about the uncertainty of these results (Yu et al., 2013). On the other hand, most participants in a study conducted by Bollinger et al. (2012) prioritised receiving results that they could understand, and they put less significance on the magnitude of the risk and actionability of the result. Only a small group of participants in Regier et al. (2015) did not want to receive incidental results, irrespective of the potential

implications for their health. Overall, participants in Bollinger et al. (2012) believed that researchers have a responsibility to provide feedback on incidental findings and that the study should endeavour to fulfil this perceived obligation. Many participants were willing to settle for the return of a limited set of results, even though most of them would wish to be provided with as much information as possible (Bollinger et al., 2012). Failure to provide feedback of results was seen as a potential deterrent for participants to enrol in genetic or genomic research (O'Daniel & Haga, 2011).

Additionally, empirical evidence also showed that participants often cite family as a reason for receiving incidental results and, more specifically, for initiating involvement in WES/WGS (Clift et al., 2015; Facio et al., 2013; Yu et al., 2013). However, it also revealed that some participants may filter information on incidental results in the following ways: they may share only actionable results with relatives (Conrad V Fernandez et al., 2014; Hitch et al., 2014), decide on the impact of the results on specific relatives (Hitch et al., 2014), or choose which relatives to share information with (Conrad V Fernandez et al., 2014). For example, a survey of cancer patients indicated that the majority (75%) would discuss genetic data indicating vulnerability to preventable diseases with family members while 62% would share information about unpreventable conditions. In this study, what worried most participants regarding incidental findings were implications for health insurance (48%) or life insurance (41%). Only 21 % worried about privacy of their information (Yushak et al., 2016).

Kaphingst, Ivanovich, Elrick, et al. (2016) in a study that explored preferences among women diagnosed with breast cancer at a young age, revealed that many participants preferred to receive their sequencing results within the shortest time possible. Generally, participants would prefer to have face-to-face interactions with a professional who is knowledgeable about

genetics and the consequences of incidental findings (Hitch et al., 2014). While some participants would prefer to have healthcare providers engaged in managing their results by assisting them to understand results in consideration of their current health status and by offering counselling support (J. H. Yu, Julia Crouch, Seema M Jamal, Michael J Bamshad, & Holly K Tabor, 2014b). In another study, participants indicated that they would prefer to discuss the results in person and did not put any emphasis on the kind of personnel they would prefer to deliver the results but were rather concerned about the communicative skills and knowledge of that individual. Participants underscored the significance of having in place a process for returning results which is customised to an individual's situation and one that he/she has a say in determining (Kaphingst, Ivanovich, Biesecker, et al., 2016).

A study by Bijlsma et al. (2018) demonstrated that providing participants with background information can enhance their decision making and enable them to select subsets of findings that should be reported to them. Although most participants in Bijlsma et al. (2018) initially showed a positive attitude to receiving unsolicited results, they eventually changed their preferences to receiving only subsets of genetic information after being provided with detailed information on next-generation sequencing and a binning model of four classifications of unsolicited results. After being provided with information, participants were mainly concerned about their ability and that of family members to deal with increased possibility of having a genetic condition. Most participants preferred receiving their individual results even though they recognised that there could be certain complexities (Bijlsma et al., 2018).

With regards to consent, published evidence suggests that participants generally emphasized the value of autonomy - having the freedom to select which incidental findings (if any) they should receive (Christenhusz, Devriendt, Van Esch, & Dierickx, 2015; Clift et al., 2015;

Daack-Hirsch et al., 2013; Conrad V Fernandez et al., 2014; Hitch et al., 2014; Kleiderman et al., 2014; Yu, Crouch, et al., 2014b). They also exhibited a strong sense of ownership of their genetic information and a desire to have control over it (Christenhusz et al., 2015; Clift et al., 2015; Daack-Hirsch et al., 2013; Conrad V Fernandez et al., 2014; Hitch et al., 2014; Kleiderman et al., 2014; Sapp et al., 2014). Available evidence from the United States of America and Europe further suggests that participants would like to be notified when interpretation of results change or if new information become available, such as when they reach the age when a screening program for a genetic condition may start (Christenhusz et al., 2015; Kaphingst, Ivanovich, Biesecker, et al., 2016; Yu, Crouch, et al., 2014b). However, in a study exploring the views of genetics health professionals on the return of genomic results by Grove et al. (2014), there was no agreement with regards to who should initiate re-contact although some genetics health professionals expressed that participants and researchers should share this obligation (Grove, Wolpert, Cho, Lee, & Ormond, 2014).

2.3. Guidelines for feedback of results

Several guidelines for feedback of individual genetic research results have been developed by academic societies and consortia involved in genetic and genomic research. For instance, the American College of Medical Genetics and Genomics (ACMG), stipulated recommendations of the ACMG Working Group on Incidental Findings in Clinical Exome and Genome Sequencing. These recommendations were based on a consensus-driven evaluation of clinical utility and validity of genetic results. Through this process, the Working Group developed a list of illnesses, related genes and specific categories of mutations which should be disclosed to patients who would have undergone exome or genome sequencing for clinical purposes. For this purpose, the Working Group gave priority to conditions with available treatments or preventative measures, as well as conditions where people with pathogenic variants may be

asymptomatic for a very long time (Green et al., 2013a). Nonetheless, as previously mentioned, these guidelines were specifically developed for the feedback of genetic results generated in a clinical setting and cannot be generalised to the research context. On the other hand, the Presidential Commission for the Study of Bioethical Issues (2013) also issued some key recommendations regarding ethical management of incidental and secondary findings in the research context. These recommendations specified that (a) researchers should explain to participants during the informed consent process the range of potential incidental or secondary findings that might be identified in the conduct of genome sequencing. In this context, participants should be informed if such findings will be reported, the procedure for reporting such findings, and whether and how participants may choose not to receive findings (b) the management of incidental results that are expected should be planned for by researchers in advance, including but not limited to those that are known to be important and clinically useful. Additionally, an institutional review board should evaluate and approve the plan, and this should also be shared with participants during the informed consent process ("Presidential Commission for the Study of Bioethical Issues," 2013). Accordingly, following the increase of genomic studies conducted by the H3Africa consortium, Guidelines for the Return of Individual Genetic Research Findings (H3Africa, 2016; Matimba et al., 2022), were developed as an attempt to develop Africa-specific guidelines. These guidelines stipulated key principles and procedures that H3Africa researchers could follow to inform decisions related to feedback of individual genetic results. Although these guidelines encourage researchers to include feedback policy and consent in their protocols for ethics clearance, the current approach of these guidelines is to proceed with caution, with primary emphasis on feedback of pertinent results. The guidelines recommend that findings with potential medical actionability should be fed back as soon as they are validated, and that feedback should be done by clinicians or other healthcare professionals involved in the study until others are sufficiently trained (H3Africa,

2016; Matimba et al., 2022).The guidelines provide a decision tree as a practical guidance to researchers intending to feedback results to research participants, which stipulates the following steps for researchers to follow; (a) determine if there is substantial evidence to inform on the pathogenicity and clinical relevance of the identified variant (b) assess whether the finding has personal value or clinical relevance. (c) assess whether the finding can be acted upon (d) confirm whether the participant consented to feedback or to be re-contacted (e) ensure that results can be confirmed in a diagnostically accredited lab or with alternative genotyping methods, such as using a second sample to confirm the findings (f) as well as ensuring the availability of genetic counsellors or other medical professionals trained to provide feedback, such as clinicians (H3Africa, 2016; Matimba et al., 2022). Although these guidelines provide an important guidance for the return of genetic results, they were developed on the basis of expert consultations and without evidence hence they are quite open-ended. As a result, the way that this thesis pushes that debate is that it provides a robust evidence base.

2.4. Considerations for return of results in African genomics

Although there are several papers that have discussed issues related to return of individual genetic results, most of these are not specific to Africa or LMICs. However, when genomics research is conducted in Africa, there are several important elements of the research context as well as of African ontological worldviews that need to be considered in decisions about whether and how results are returned. Several scholars from Asia and Africa argue that bioethics has cultural underpinnings. According to Christakis (1992), the content and form of ethical principles along with the way moral tensions are resolved, are shaped by culture. Onuoha (2007) refers to culture as the "*dominant values, symbols, social practices, and interpretative categories of a community*." This means that people often solve ethical problems that they are faced with either in medicine or research, using their cultural beliefs, values and

practices. This approach of understanding culture suggests that moral considerations are informed by culture as the former is infused with values and symbolic connotations (Onuoha, 2007).

Therefore, the importance of culture and its capability to impact and mould the meanings attached to a public's experiences of health and sickness should be taken into consideration in bioethics discourse (Marshall & Koenig, 2004). For example, in African settings, disease is often explained in terms of a causal relationship between the "visible" and "invisible world", while in other parts of the world, disease tends to be understood more in relation to the functioning of the body (Sindiga, 1995). Therefore, a dependable diagnosis of disease in the African context may have to take into consideration the inseparability of the physical and the spiritual (Murove, 2005). In another example, Gbadegesin (1993) describes that in the Yoruba culture, whenever there is a problem, it is often believed that it is because of some evil power and the search for the cause of the problem usually leads to the supernatural realm, where it is believed there are spirits and powerful forces that are in charge of human destinies. As a result, diviners and traditional healers have so much influence as they are believed to possess deep knowledge and ultimate reality (Gbadegesin, 1993). Similarly in Botswana, many people believe in witchcraft such that it is often thought to lie at the basis of any problem or tragedy and traditional doctors may be approached to connect with the spiritual realm and correct the adversity.

Consequently, a number of scholars (Christakis, 1992; Metz, 2010; Onuoha, 2007) argue for a bioethics discourse that is contextualized to the African setting and worldview. Onuoha (2007) for instance, argues that an African Bioethics framework should guide Africa in addressing a number of new ethical challenges facing the continent, emanating from science and technology,

including issues arising from genomic studies. Metz (2010), has also argued for Ubuntu philosophy as a framework for addressing ethical issues in the African context. In the words of Saule, as quoted by Mufune (2003), this promotes the notion of assisting others as a means of assisting oneself, community action and well-being over individuality, unity over division, reverence for elders and sharing.This is so because traditional African societies are bound by a very strong sense of community (Mawondo, 2007). This notion of an African person and community is embodied in a well-known saying by John S. Mbiti who said, "I am because we are; and since we are therefore I am" (Mbiti, 1989, p. 141). The Setswana version of this proverb is 'Motho ke motho ka batho' or 'Motho ke motho ka batho ba bangwe,' while in Xhosa is 'Umuntu ngumuntu ngabantu' (Jensen & Gaie, 2010).

This conception of a person is believed to be shared across many African cultures and languages (Shutte, 1993, p. 46). Mbiti (1989) argues that this orientation is the compass of the African perspective. For many Africans, this communal concept of a person is celebrated as one of the cornerstones of the African worldview (Jensen & Gaie, 2010). It obligates community members to treat one another with respect, compassion, kindness and care (Murove, 2012) and to act in solidarity with one another (Metz, 2012). The principle of solidarity inspires individuals and communities to consider the interests of others in their actions (Onuoha, 2007). This discussion is embraced by (Metz, 2010 p. 3), when he says "*an action is right just insofar as it is a way of living harmoniously or prizing communal relationships, ones in which people identify with each other and exhibit solidarity with one another; otherwise, an action is wrong".* Metz highlights that individuals show solidarity with one another by helping or behaving in ways that benefit others. In this context, solidarity is described as a reciprocal relationship in which community members, who recognize their shared vulnerabilities and interdependence decide to collaborate with one another in order to

alleviate suffering, reduce health disparities, and ensure the well-being of all parties (Tosam, Chi, Munung, Oukem-Boyer, & Tangwa, 2018).

In terms of medical care, solidarity necessitates that each individual's basic healthcare needs be met and for each person to contribute to a healthier society (Onuoha, 2007). In addition, any research carried out in communities should recognize and appreciate the members' participation in that research as a way of showing solidarity and ascertain benefits and burdens are distributed fairly amongst the members (Onuoha, 2007). The principle of solidarity as discussed by Metz (2010) contends that the sponsoring agencies and the researcher should perceive themselves as one with communities hosting the research in that they are working collectively to accomplish a shared goal. This expectation of solidarity in African settings is evidenced by a study conducted by Amurwon, Hajdu, Yiga, and Seeley (2017) in rural Uganda which found that providing and receiving generalised reciprocal support preserved communal linkages. Some participants in the study considered an opportunity to give and receive support as an 'investment' with benefits that can be derived in the future when the need arose. Likewise, those participating in genomics research in the African context could have an expectation to have their individual findings returned to them as a way of showing reciprocity and appreciating their participation in such studies. As a result, it is important to consider these theoretically underpinnings in the interpretation of participants views about whether and how individual results from African genomics research are returned.

Apart from considerations of theoretical underpinnings in African context, there are also practical issues that need to be considered. According to Wonkam and de Vries (2020), the socioeconomic context of Africa, inadequately resourced healthcare systems, and overstretched healthcare professionals, all of which have a significant impact on access to

healthcare, limit the ability to determine what genetic results are actionable in the African context and by whom. There is also a severe shortage of trained medical genetics experts who can help validate genomic research results in a diagnostic setting, assess their relevance, relay pertinent information in a comprehensible and non-directive manner, and act on individual genetic results. A further issue is that in most African countries, there are not enough healthcare personnel and institutions that are prepared to return individual research results, posing the question of how and who should return individual research results from African genomics research (Wonkam & de Vries, 2020).

In a 2015 paper discussing actionability issues for research conducted in LMICs by HICs researchers, Ortiz-Osorno et al. (2015) also observed noticeable variations concerning circumstances of research participants in low- and high-income countries that change the analysis of when and why incidental findings ought to be offered to research participants (Ortiz-Osorno et al., 2015). The return of incidental findings is founded on the notion that the information might result in some clinical benefits; this is often termed actionability (Eckstein, Garrett, & Berkman, 2014). Although actionability is always pertinent when considering obligations to return incidental findings, in deliberations about incidental findings and research in low-income countries, actionability is usually combined with access to care. Just because a clinical or behavioural action is available that can prevent, alleviate, or treat the illness it does not imply that an individual is always able to access the resources to take that action (Sullivan & Berkman, 2018). For example, some basic preventative amenities such as mammography, which would be a recommended preventative service should there be an incidental finding associated to BRCA1 and an increased risk of heritable breast and ovarian cancer, are not usually accessible in African countries, where there are usually a few facilities offering services for a whole region. Whereas in several settings in the United States and other high-income

countries, there could be numerous alternatives available to assist in managing the cancer risk (Lawal, Murphy, Hogg, Irurhe, & Nightingale, 2015).

Genetic research in low-income countries is both valuable and critical as the move towards personalized medicine continues. Nonetheless, as research increases in low-resource settings, researchers will have to address the issue of actionability; there is a tension between the diminished benefit of returning incidental findings in low-resource countries and the notion of upholding justice by not denying medical information to populations that already have restricted access to health care (Sullivan & Berkman, 2018). The success of clinical research does not only depend on the ability of researchers to design and address research problems of relevance for the populations where the research is being conducted, but also on how well the research study and related processes attend to the needs and cultural practices of each local community. Planning for anticipatable incidental findings should take into consideration the significance and relevance of the incidental findings' actionability at the local research setting where the participant lives (Ortiz-Osorno et al., 2015). Taken together, these observations pose important questions for the return of individual genetic findings to African participants.

Chapter summary

The literature reviewed in this chapter addressed a variety of pertinent issues in genomics research. It began with an overview of genetic findings and highlighted key categories of genetics findings. This was followed by the current debates over whether or not to feedback these findings. Additionally, empirical data on participants' views about receiving feedback of their individual genetic findings were reviewed, revealing that participants typically desire feedback of their individual genetic findings. This chapter concludes by explaining various critical aspects of the African setting as well as the African ontological worldviews that should

be taken into account when determining if and how findings should be returned in African genomics. The following chapter will discuss the rationale for this study and the methods employed to collect data.

CHAPTER 3: STUDY RATIONALE AND RESEARCH DESIGN

3.1. Problem statement

As discussed above, there is presently a paucity of evidence, and no consensus on whether and how to feedback individual results in African genomics research. This gap is increasingly becoming a concern, as projects are left to devise ad hoc strategies to return relevant individual genetic results, indicating the necessity for a coordinated strategy for the return of individual genetic results in African genomics research (Wonkam & de Vries, 2020). At the same time, it is important that policies and practices regarding the return of individual genetic results in African genomics research, take account of African values and research contexts, as well as the preferences of African research participants. As a result, it is critical to investigate expectations and preferences of African participants for feedback of individual findings from genomic research. These findings are essential for both directing patient-physician interactions and decision-making, as well as shaping the development of guidelines for genomic research (Kang et al., 2016).

3.2. Research aim

This study aimed at exploring expectations and preferences for feedback of individual genetic findings with adolescents as well as parents and caregivers of children involved in an HIV-TB genomics research in Botswana.

3.3. Specific research objectives

The specific objectives of this study were;

a. To explore participants views on important values for consideration in feedback of individual results in African genomics research.

b. To explore participants preferences and reasons for feedback of individual genetic results.
c. To investigate participants views on practical considerations for feedback of individual genetic results.
d. To investigate participants views on important considerations for informed consent in feedback of individual genetic results.

Key questions that were investigated relate to;

a. What are participants views on important values for consideration in feedback of individual results in African genomics research?
b. What are participants preferences and reasons for feedback of individual genetic results?
c. What are participants views on practical considerations for feedback of individual genetic results?
d. What are participants views on important considerations for informed consent in feedback of individual genetic results?

3.4. Research design

This was a prospective qualitative study which utilised in-depth interviews (IDIs) and deliberative focus group discussions (dFGDs) to collect data. A qualitative design was chosen for this study because I was exploring a topic that is complex and has never been studied in Botswana population. As indicated by J. Ritchie, & Lewis, J. (2003), qualitative approaches are especially suited to investigating topics that are complex in nature since they allow for a more in-depth investigation of the issues under consideration. They provide unique instruments for investigating what motivates or underpins a choice, attitude, or behaviour (J. Ritchie, &

Lewis, J., 2003). In this study, the views and perspectives of adolescents participating in a genomic study at the Botswana-Baylor Children's Clinical Centre of Excellence (BBCCCE), as well as those of parents and caregivers of children participating in the same study were explored regarding feedback of individual findings from genomic research.

3.5. Study setting and population

This study was part of a larger project coordinated by the Individual Findings in Genetics Research in Africa (IFGeneRA) project, a collaborative project between the University of Cape Town, the Botswana-Baylor Children's Clinical Centre of Excellence (BBCCCE) and the Universities of Botswana and Yaounde in Cameroon. This study was conducted in Botswana, a country in Southern Africa with an upper middle-income status and a Gross Domestic Product (GDP) per capita of 7080.12 US Dollars (USD) (Botswana, 2018b). According to 2017 estimates, Botswana has a population of more than 2 million people, with 86.7% of the population being Christians, and 63.9% of the population residing in urban areas (Botswana, 2018a). Adult literacy rates in the nation stood at 90% in 2014 (Botswana, 2016). HIV and TB continue to be among the most significant illnesses afflicting children in Botswana, and research on these ailments has a long history. Overall, Botswana's HIV prevalence is 17.6%, with a rate of 20.3% in towns and cities, 16.6% in urban villages, and 16.9% in rural areas (Kandala, Campbell, Rakgoasi, Madi-Segwagwe, & Fako, 2012). This is compounded by a high proportion of HIV/TB co-infection, which is estimated to be 60% (WHO, 2014). Of concern is the increasing prevalence of HIV among adolescents from 3.7% in 2008 to 5.0% in 2013 (Botswana, 2013). This is despite the country's comprehensive health care infrastructure, which includes hospitals, clinics, health posts, and mobile health stops distributed over 27 health districts. Health care (including hospitalization, laboratory testing, and medicines) is offered free of charge to all people in public sector institutions, and about 95% of Botswana's

population resides within 8 kilometres of a health centre (Botswana, 2015). Currently, genetic sequencing in Botswana is mostly used in research contexts and is not widely available.

Due to the high prevalence of HIV/TB and other factors described above, the Collaborative African Genomics Network (CAfGEN) was established to study the genes of children living with HIV and TB in order to inform the development of new therapies to prevent or suppress these diseases (BBCCCE, 2020c). The CAfGEN study is a joint project which is part of the Human Heredity and Health for Africa (H3Africa) Consortium (H3Africa, 2014). It employs genomic techniques to uncover host genetic variants that influence HIV and HIV-TB progression in African children and adolescents (Mboowa et al., 2018). The CAfGEN project is being undertaken at the BBCCCE, a paediatric and adolescent clinic that offers children, adolescents, and their families free state-of-the-art HIV care, treatment, and support (BBCCCE, 2020a). As a result, many of the adolescents who took part in the CAfGEN study and were recruited for this study also receive treatment from BBCCCE.

Study participants

The CAfGEN project was chosen as a case study because it is one of the few genomic studies currently being undertaken in Botswana and provided an opportunity to examine issues surrounding the feedback of individual genetic findings from genomics research. The CAfGEN cohort was chosen because they are more informed about health and genetics than the general public and are more equipped to engage in meaningful discussions about genetic findings due to their involvement in a genomics study with a significant community engagement component. Over the years, the CAfGEN project has provided information about the relationship between heredity and health to the adolescent cohort, as well as their parents and caregivers. For example, as part of a community engagement effort for the CAfGEN study, four Genome

Adventure Comic books were produced and translated into other languages (BBCCCE, 2020d). Additionally, the adolescent cohort in this study provided an opportunity to explore perspectives of adolescents regarding these issues, as well as those of the parents and caregivers.

Participants recruited into this study included: 1) parents and caregivers of children involved in the CAfGEN study and aged 2 - 18 years and 2) adolescents aged 15 - 18 years, involved in the same study. According to Geller, Tambor, Bernhardt, Fraser, and Wissow (2003), previous research has revealed that age may influence how research participants think about participating in genetic studies. In most cases, adolescents aged 14 or 15 years are able to reason at the level similar to that of adult research participants (Petersen & Leffert, 1995; Santelli et al., 1995). As a result, deciding on the age of adolescents to recruit in this study was important to ensure that I recruited a group that will be able to understand the complex issues related to feedback of results in genomics research and be able to provide well-thought opinions. However, it should be noted that in Botswana minors under the age of 18 are not allowed to consent to participate in research without their parents or caregivers' permission nor can they be given results directly without the parents' involvement. As a result, when children are involved in research, the assent of the child and the consent of the parent(s) or guardian needs to be obtained. Since participants were recruited from the CAfGEN study, all the adolescents in this study were HIV positive, as well as majority of parents.

3.6. Development of data collection tools

Deliberative focus group discussions (dFGDs) (Rothwell, Anderson, & Botkin, 2016) were primarily used for data collection, supplemented by in-depth interviews (IDIs). The dFGD method was chosen for this study because it provided an opportunity for learning and

discussions, with the goal of allowing participants to engage more deeply with the issue under discussion. This was particularly important given that this study examined a complex topic. The IDIs were used to complement the dFGDs to investigate any remaining unresolved issues in the dFGD data. These techniques were used to explore a broad range of issues relating to the return of individual genetic results including participants' views on whether or not to feedback results, which results to feedback and why, who to feedback how and when. A dFGD manual with step-by-step instructions for data collection was developed for this study by the larger IFGeneRA team that I was a part of, and I collaborated in that process. The manual was developed after an extensive literature review (see Appendix O), and I ran the pilot testing for its appropriateness. The manual included various scenarios and questions to elicit participants' perspectives on a variety of ethical issues surrounding the feedback of results. The scenarios addressed a range of topics, including the return of results to adults and children; the return of adult-onset and early-onset conditions; and the roles and responsibilities associated with the identification and return of results.

Following the dFGD data collection, I prepared and piloted an interview topic guide to investigate any remaining unresolved issues in the dFGD data. The interview guides were developed de novo in consultation with the supervisors, based on the themes probed during the dFGDs. The dFGD manual, in-depth interview guide, as well as consent forms were all translated into Setswana (the local language of Botswana) by the research assistant, and I verified them. This included translation of diseases listed in Table 1 of the manual, most of which were already known to us as native Setswana speakers and proficient in English. For diseases that their Setswana words were not known to us, I searched for their translations in the English-Setswana online dictionary. I also had a colleague with a medical background confirm the translations. The English and Setswana versions of the Table were further shared

with participants during the pilot testing to verify the translations and assess understanding. I piloted the dFGD manual with 2 groups of parents and caregivers in Botswana (16 participants in total) and 1 group of adolescents (5 participants), as well as the IDI instrument with 3 parents or caregivers and 2 adolescents. The pilots assessed the practicality of the dFGD and IDI methodologies, as well as the suitability of the scenarios and topic guides for usage in Botswana. They also assessed participants' grasp of the issues discussed and were used to estimate the length of the dFGDs and IDIs sessions. The dFGD pilot guided my decision to include a 30-minute break during the approximately 3-hour-long first session of the dFGD. Additionally, with the assistance of participants, several phrases and Setswana translations were modified in the dFGD and IDI tools. Participants of the pilot testing were excluded from the actual study.

3.7. Sampling and recruitment procedures

Participants for the dFGDs were recruited in person during their visits to the BBCCCE, as well as through telephone where necessary. For those recruited in person, the CAfGEN employees, notably the study nurse and research assistant, screened through their clinic cards to check if they met the inclusion criteria for this study, as they registered for their clinic visit. They were then informed about this study. Those interested in learning more were directed to me or my research assistant. After confirming that a participant fits the inclusion criteria, I described the study's goal and obtained consent with the assistance of the research assistant.

Participants recruited via phone, were screened from the CAfGEN database by the CAfGEN research assistant and contacted to inform them about this study. Prior to participation in the dFGDs, they were also taken through the consent process in person.

Participants for the IDIs were selected from the dFGDs. I selected participants who were more interactive or had unusual opinions, as well as a few others who were less participatory in the dFGDs, to allow them to share their perspectives in a more private setting. There were, however, no formal criteria for determining the amount of participation in the dFGDs.

These participants were also recruited by phone and taken through the consent process in person prior to participation in the IDIs. In each event, participants had a choice to use Setswana or English or a combination. English and Setswana are both official languages used in Botswana, with English being the language of choice for most official communications.

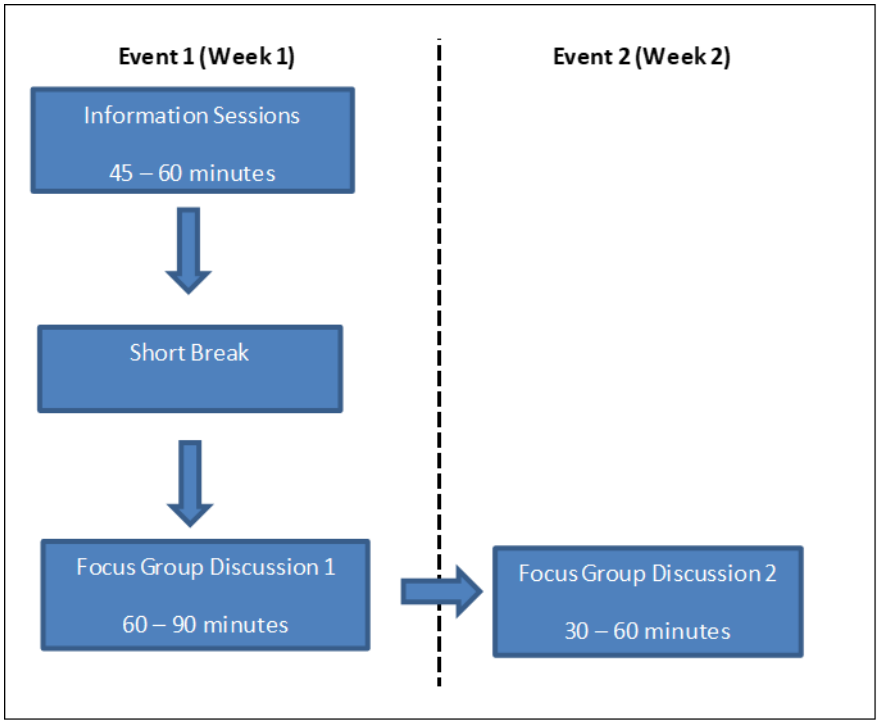
3.8. Data collection procedures

The method of deliberative focus group discussions utilized in this study is a hybrid of standard FGD and prolonged periods for learning and discussion, with the goal of allowing participants to engage more deeply with the issue under discussion. The dFGD technique utilized in this study engaged participants in an interactive information-sharing session. During the first meeting, case studies illustrating specific ethical concerns associated with the return of individual genetic findings were utilized to facilitate information sharing. This provided participants with an opportunity to learn about genes, their functions, and their impact on health. The first session lasted around 45 to 60 minutes and was followed by a brief break. The follow-up session included initial conversations to elicit participants' first reactions to the feedback of individual genetic results from genomics research. This session lasted around 60 to 90 minutes. In order to assist the participants in reflecting on the material and topics covered during the meeting, participants were provided with an information booklet including basic genetic facts. This booklet served as a reference for them during the discussion (See Appendix N). They were then invited to participate in a second dFGD meeting a week later, during which

their perspectives on feedback of findings were elicited further. This second dFGD lasted around 30 to 60 minutes (see figure 1 for a schematic overview).

While dFGDs for parents and caregivers were conducted separately from those for adolescents, both groups of participants (adolescents, parents, and caregivers) were asked the same questions on their views toward feedback of individual genetic findings. Even where pairs of parents and children were recruited in certain circumstances, they participated in separate activities. While these participants may have discussed the dFGD questions among themselves at home, potentially influencing one another's views, I could not rule out the possibility that other participants who were not paired did not, as both groups were encouraged to discuss study issues with family members between the first and second meetings, which were held a week apart. There were no parent/child pairings recruited for the IDIs.

Figure 1 Overview of research process



The purpose of conducting the dFGDs in two stages was to: allow sufficient time for engagement with participants and information sharing, particularly given that this study examined a complex topic; ii) allow participants to reflect on the issue being discussed in between the sessions; and iii) allow participants opportunity to revisit their views over time (Marsh, Kombe, Fitzpatrick, Molyneux, et al., 2013; Marsh, Kombe, Fitzpatrick, Williams, et al., 2013). While this study investigated a broader range of issues concerning the return of individual genetic results, participants were also specifically interrogated on solidarity and reciprocity, for example, in response to questions about why participants believed individual genetic results should be returned, whether, how, and why participants should be appreciated for their participation, and who they believed was responsible for covering the costs of follow-up care and why.

The dFGD data were transcribed on a rolling basis. The data collection continued until saturation was attained. Data saturation was discussed with my supervisors (MK and JDV). I conducted a total of 24 dFGD meetings, with 12 groups of participants (6 groups of adolescents and 6 groups of parents and caregivers). In addition, 12 in-depth interviews were conducted with 6 adolescents and 6 parents/caregivers who had participated in the dFGDs. The IDIs focused on delving deeper into some of the study's early findings. IDI sessions lasted between 30 and 80 minutes. The data were collected between February 2019 and March 2020. I conducted all the dFGDs and IDIs while the research assistant helped with meeting logistics and note-taking. All study materials were available in both Setswana and English, as both the research assistant and I are fluent in both languages. I discovered that although Setswana was favoured by the older generation, the younger generation preferred English.

In this qualitative study, 93 participants were purposively selected (44 adolescents and 49 parents and caregivers of children and adolescents enrolled in the CAfGEN study). Parents and caregivers' initial dFGD sessions had a group size of around 4 to 11 people, whereas adolescents' initial dFGD meetings had a group size of approximately 5 to 12 individuals. The follow-up dFGD meetings were attended by a total of 34 adolescents and 38 parents and caregivers. For these meetings, parents and caregivers' groups consisted of 4 to 8 participants, whereas adolescents' groups consisted of between 2 to11 participants. The 21 participants who were unable to attend the follow-up dFGD meeting (10 adolescents and 11 parents and caregivers) had other conflicting interests. A total of 24 dFGD sessions were held, including 12 dFGD meetings with 6 groups of parents and caregivers and another 12 dFGD meetings with 6 groups of adolescents. IDIs were held with 6 adolescents and 6 parents or caregivers, following the dFGDs (see table 1 below).

Table 1 Summary of dFGDs and IDIs meetings

	dFGD				**IDI**
	# Groups	# Events	# Participants		# Participants
			Meeting 1	Meeting 2	
Parents/caregivers	6	12	49	38	6
Adolescents	6	12	44	34	6
Total	12	24	93	72	12

3.9. Data management and analysis

In order to prepare for data analysis, all audio recordings of the dFGDs and IDIs were transcribed. The content of the recordings made in Setswana was translated into the English language. The audio recording was transcribed verbatim. Codes were utilised to identify each participant in the transcript. These codes included the participant's type ("P" for parent and "A" for adolescent), a speaker number, and a dFGD number. For instance, in the first dFGD, P1G1 marked the first parent to talk. Data were transcribed by the research assistant who is a native Setswana speaker proficient in English. I double-checked each transcription by listening to the audio while reading the transcript. Any erroneous quotations and typographical mistakes were corrected. Transcripts were uploaded into NVivo qualitative data analysis software Version 12 (QSR International Pty Ltd, 2012) following data cleaning and verification to allow data organization and analysis.

The study objectives and the Framework Method for data analysis were used to guide the data analysis in this study. The Framework Method is a systematic and flexible qualitative data analysis approach (Gale, Heath, Cameron, Rashid, & Redwood, 2013), in the sense that it is not limited to any epistemological position, allowing it freedom and flexibility to tie well with specific aims of any piece of research (J. Ritchie, Spencer, Bryman, & Burgess, 1994). This approach falls within a wide family of qualitative sociological data analysis methods usually referred to as thematic analysis or qualitative content analysis. These methods establish common issues and differences in qualitative data, before focusing on how different parts of the data relate with each other and intends to bring out descriptive and/or explanatory conclusions gathered around themes (Gale et al., 2013). The Framework analysis draws themes from both predefined issues and emergent data. As a result, I had predefined areas of interest which were guided by the literature, but also remained open to discovering any new

information shared by the participants (Parkinson, Eatough, Holmes, Stapley, & Midgley, 2016).

One important distinction between more conventional data analysis and framework analysis is the production of a matrix in which cells of summarised data are presented in rows (cases) and columns (codes) to provide a layout into which the data can be systematically reduced, so that it can be easily analysed both by case (in this case, the dFGD event) and by code. For instance, the matrix produced allowed me to quickly assess how (the code) reciprocity was understood or spoken about in each dFGD event. Similarly, it allowed me to quickly have an overview of the combined perspectives on all the codes within an event.

The Framework Method for data analysis utilised in this study entails five critical steps as described by Rabiee (2004):

a) Familiarisation with the data – this involved listening to the audio recordings, reading all transcripts a couple of times as well as the observational transcripts made during the interviews and summary notes scribbled at the end of the interview. This process allowed me to plunge into the details of the data and appreciate the interview in its entirety before organising it. Through this process the main themes started to surface.

b) The following step involved establishing a thematic framework. Themes were created both from the research questions and from the accounts of research participants. At this point descriptive reports were developed, and an analysis was conducted on the data taking note of the questioning route.

c) Indexing, consisted of sifting the data, highlighting and sorting out quotes and making internal and external comparisons of the cases.

d) The fourth stage, charting, involved lifting the quotes from their original context and re-arranging them under the newly developed appropriate thematic content. One of the most important aspects of this undertaking was data reduction, which was accomplished by comparing and contrasting data and cutting and pasting similar quotes together.

e) After the data were organised, cleaned and verified it was interpreted (Rabiee, 2004).

I applied both an inductive and deductive approach to coding. For the deductive approach, I specifically looked for common themes in the international empirical literature around feedback of findings, to ensure I was able to comment about the extent to which these international themes also came up in Botswana. For the inductive approach, I followed a more conventional process in the Social Sciences, where I did the initial coding of the data, and open codes were discussed with my supervisors (JDV and MK). Following open coding, the team (DR, JDV and MK) worked together to develop the hierarchical coding scheme, that I then applied to the entire dataset. I worked with my supervisors (JDV and MK) to develop a coding handbook. Eight transcripts of the dFGDs (4 from the 1st session and 4 from the 2nd session of the dFGD – 2 from adolescents and 2 from parents and caregivers for each session) were read and coded to derive initial codes. Reading through the coded data, I looked for emerging patterns and the nature of participants' expectations and preferences. I interrogated patterns in the data and started to formulate a set of themes to capture peoples' expectation and preferences. The data was analysed collectively by observing the overall views of participants (parents and caregivers, as well as adolescents) regarding a particular issue. A comparison between parents and caregivers' views versus adolescents' views regarding an issue was also performed and where significant differences were found these were included in the write-up of data. Views and values which were compelling to the community were mapped out to note

what people's values are and how they work together. The literature was used to make sense of issues that were outstanding in the data (Parkinson et al., 2016).

Participants' demographics

In the adolescent category, the majority (61%) of participants were female. The majority of adolescents (36%) were 16 years old, and 93 % were enrolled in junior or high school or had completed the qualifications. Half of the adolescents resided in settlements around Gaborone, the city in which this research was based, 39% in the city, and 11% did not indicate their address.

Similarly, 92% of participants in the category of parents and caregivers were female. One possible explanation for this is because in Botswana, women are typically the primary caretakers (Kang'ethe, 2011; Kang'ethe, 2013; Maundeni, Osei-Hwedie, Mukaamambo, & E. & Ntseane, 2009). Most parents and caregivers (39%) were between the ages of 41 and 50, and 94% held educational credentials ranging from primary to tertiary qualifications. As with the adolescent population, the majority of parents and caregivers (57%) resided in villages around the city, while 43% lived in Gaborone (see table 2).

Table 2 Summary of participants' demographics

Adolescents	**Frequency**	**Parents and Caregivers**	**Frequency**
Male	17 (39%)	Male	4 (8%)
Female	27 (61%)	Female	45 (92%)
Total	44 (100)	Total	49 (100%)
Age		**Age**	
15 years	8 (18%)	21 - 30 years	6 (12%)
16 years	16 (36%)	31 - 40 years	17 (35%)
17 years	11 (25%)	41 - 50 years	19 (39%)
18 years	7 (16%)	51 - 60 years	6 (12%)
Unknown	2 (5%)	Above 60 years	1 (2%)
Total	44 (100%)	Total	49 (100%)

Educational level		**Educational level**	
Primary education	0 (0%)	Primary education	6 (12%)
Junior School	31 (70%)	Junior School	19 (39%)
High School	10 (23%)	High School	12 (25%)
Tertiary	0 (0%)	Tertiary	9 (18%)
None	1 (2%)	None	2 (4%)
Unknown	2 (5%)	Unknown	1 (2%)
Total	44 (100%)	Total	49 (100%)
Residence		**Residence**	
City/Town	17 (39%)	City/Town	21 (43%)
Village	22 (50%)	Village	28 (57%)
Unknown	5 (11%)	Unknown	0 (0%)
Total	44 (100%)	Total	49 (100%)

3.10. Engagement meetings with stakeholders

I attended monthly meetings for the CAfGEN study Community Advisory Board (CAB). The first meeting was to inform them about this study and consult them about the materials developed for this study; including the background information that was provided to participants as well as the dFGD and IDI guides that were used to collect data. The meeting with the CAB members also helped in addressing any concerns about the study and potential solutions to issues surrounding genomics research in Botswana were identified. Subsequent meetings were mainly aimed at updating the CAB on the study progress and get guidance on some of the study procedures. These meetings were held at BBCCCE and organised by the CAfGEN staff.

3.11. Ethical considerations

Before the research team made contact with potential participants, the study proposal, informed consent forms, and associated study documents were approved in writing by the RECs at the University of Cape Town (HREC REF: 010/2019), the University of Botswana (UBR/RES/IRB/BIO/118), the National Health Research and Development Committee of the

Ministry of Health and Wellness in Botswana (HPDME: 13/18/1), and the Botswana-Baylor Children's Clinical Centre of Excellence (BBCOE-IRB 1810-11), in accordance with their Research Ethics Policies and international guidelines. Approval was also obtained for subsequent amendments to the protocol and supporting documents before being implemented.

Informed consent procedures

The majority age in Botswana is 18 years. As a result, assent was obtained from all minors aged 15-17 who were invited to participate in the study. Formal consent was sought from their parents or caregivers. To avoid pressuring the adolescents to participate, it was emphasized repeatedly that the adolescents were under no pressure to participate even if their parents had consented; that a decision to participate should be theirs alone and that I would not report back to their parents if they refused to participate. Informed consent was obtained from those aged 18 years, as well as parents who participated in the dFGDs and IDIs. Consent was obtained following internationally accepted best practices for obtaining informed consent as well as national regulations and guidelines.

Assent or consent were recorded on a form, in writing in English or Setswana, according to the preference of the participant. Each participant was provided with a copy of the informed consent form to take home after the study. Each participant had an opportunity to ask any questions from the research team about the research before being asked to sign a copy of the consent form. Participants were asked for permission to record the conversation as well as permission to re-contact individuals at a future date if further information was needed.

Protection of participant confidentiality

In order to protect participants' privacy and to keep their data confidential, names and other identifying information were not recorded on any data collection instrument. Instead, each participant was allocated a unique identifier which was recorded on the demographic information sheet and the informed consent form. An electronic document linking participant names with their unique identifiers was kept on a password protected computer and only ever used or accessed by the student. Any printed documents linking participants' names with their unique identifiers were kept in separate locked file cabinets from those containing data to ensure confidentiality.

Both the research assistant and I were trained in procedures relating to the seeking of informed consent and the protection of participant confidentiality. To mitigate potential risks regarding breaches of confidentiality, the importance of keeping the discussion confidential was emphasised to participants. The main purpose of the study was also explained to potential participants, as well as procedures for maintaining confidentiality and the right to refuse or withdraw participation at any time (which were emphasized once again immediately before focus group discussions began, to allow for individuals to leave if they knew other individuals in the group who they would not want to speak in front of). Focus group participants were also encouraged to use a pseudonym in the focus group, to protect their identity. Participants were given numbers to identify them during the focus group discussions as a way to protect their identity. Any identifying information inadvertently mentioned during data collection was cleaned from the transcripts before importing into NVivo software for data analysis.

The only personal identifiers collected from participants were their names and a telephone number. This information was accessible only to me and the research assistant for the purposes

of scheduling interviews and dFGDs and reminding participants of scheduled meetings. The information was contained in one contact list that I kept in a locked filing cabinet, separate from any data collected. The list will be kept for a period up to five years after completion of the study and then destroyed. No participants were mentioned by name in the thesis or publications that resulted from this data. The contact details will only be used for any dissemination activities that will be held to share the outcomes of the research project.

Summary descriptions of participants included in the thesis and publications present total counts of representatives per category (e.g. total number of male parents and caregivers, education level of adolescents etc.) and participants are not identified by names.

All digital voice recordings from both types of activities (dFGDs and IDIs sessions) will be destroyed after publication of the study's main findings. Electronic copies of all data will be stored securely at the University of Botswana and University of Cape Town for up to 5 years after the completion of the study or as long as necessary to complete all publications.

Potential risks

This was a minimal risk study that posed few potential risks to participants. There were no physical or legal risks anticipated for research participants. However, there was a small chance for participants to experience some psychological or social discomfort while discussing their experiences or their HIV condition (which was not required for participation but may have come up in the course of the discussions). The study involved focus groups and interviews, as a result, by participating in the group discussion, other people who also participated knew the diagnosis of the child. This was discussed during the informed consent process, and participants were asked to discuss any concerns at the conclusion of the data collection event with me or

the research assistant, so that they can be referred to locally available care as necessary. Specifically, arrangements were made to have participants who could become stressed during the dFGDs or IDIs referred to the BBCCCE counsellor for help.

Participants were informed that they were free to decline to answer any question(s) and could stop participation at any point. All participants were told that agreeing or refusing to participate in the study will not affect their care or their relationship with BBCCCE. Also, participants were asked to report any social harms that they may experience as a result of participating in this project, but none were reported.

Potential benefits to participants

There were no direct benefits to participants in either of the activities included in this project. Possible benefits of the study included the potential to help in understanding which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, researchers will be able to do better genomics research in the future. It may also have been a benefit for participants to have participated in a group of people who have the same disease as themselves or their children. These possible benefits are small but reasonable to the minimal risks associated with study participation.

Reimbursement

Participants were reimbursed for their time and transport according to the reimbursement rate set by the parent study (CAfGEN study) and approved by the RECs. Adolescent participants were given BWP 30.00 per study visit, while parents and caregivers were given BWP 50.00 per study visit.

3.12. Researcher's positionality

It is important to highlight my background and position as a researcher as it may have influenced how people responded to the dFGD and interview questions as well as my own interpretation of the study findings. Firstly, I am a young Motswana woman and have lived most of my childhood in rural Botswana setting. I moved to the city at the age of 18 years to pursue my bachelor's degree at the University of Botswana and have lived in the city since. Nonetheless, I occasionally go to the village to visit my family and spend special holidays. Therefore, this combination of my age, gender and experience could have made me relatable to most of my study participants who were representative of the average Motswana woman and female adolescents. This position could have influenced them to be more comfortable to openly discuss their views on this complex issue.

Secondly, to interpret the study findings, I relied heavily on my understanding of Botswana culture and healthcare context as well as my bioethics education and work experience. I have completed a one-year intensive bioethics fellowship at the Johns Hopkins University in the United States of America, a Masters degree in Social Sciences in Health Research Ethics at the University of Kwa Zulu Natal in South Africa and have over 10 years' experience of research ethics administration at the University of Botswana. As a result, having been exposed to both American and African bioethics philosophies allowed me to make well-considered and balanced interpretations to my study findings. Furthermore, my supervisory team comprised of three experts with different educational background, experience, age and gender.

Thirdly, one of my supervisors is the Executive Director of Botswana-Baylor Children's Clinical Centre of Excellence and the Principal Investigator of the CAfGEN study from which participants in my study were recruited. As a result, this may have unintentionally encouraged

some participants to participate in my study as they receive clinical care from BBCCCE. Nonetheless, the Executive Director did not participate in the recruitment nor data collection with participants. Although CAfGEN study nurse and research assistant assisted with notifying participants about my study, the informed consent and data collection was done by myself with the assistance of my research assistant in a separate room. Participants were informed that they are free to participate or refuse to participate in the study and that their refusal or participation will not affect their relationship with BBCCCE. They were also informed that the study is conducted towards the fulfilment of a PhD qualification and that I do not work for BBCCCE. I believe that this allowed participants freedom to decide on whether to participate in my study or not, as evidenced by 36 people who declined to participate in the study because they either had other commitments or were not interested in the study and 21 participants who attended the 1st dFGD meeting but could not attend the follow-up dFGD meeting due to other commitments. Although, having a supervisor at BBCCCE might have introduced some unintentional bias in the interpretation of the study results, this was also mitigated by having a primary supervisor and co-authors who are not affiliated with BBCCCE and are not from Botswana. Additionally, although participants in the CAfGEN study were specifically informed at the time of obtaining their consent for the CAfGEN study that no results will be fed back and that this study is based on a hypothetical situation, it is possible that interrogating participants views regarding this issue might have prompted some of them to feel disappointed in their participation in the CAfGEN study.

Lastly, this study was funded through a grant whose principal investigators are Prof Ambroise Wonkam and Associate Professor Jantina de Vries, received from the National Human Genome Research Institute of the National Institutes of Health as part of the H3Africa initiative. I also received a stipend from this grant. However, I do not believe that this introduced any bias in

my analysis and interpretation of the study results. Also, the funders did not participate in any of the study activities including the analysis and interpretation of the research results. The content of this thesis and publications that resulted from it are solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Chapter summary

This chapter discussed the data collection techniques employed in this thesis. It justified the methodologies chosen, placing a particular emphasis on the use of a qualitative design that included deliberative focus group discussions and in-depth interviews. Additionally, the study's setting and population are explained, as are the sampling and data collection processes. Furthermore, the data management and analysis techniques, including the framework approach for analysis employed in this study, as well as ethical considerations and the researcher's positionality, have been detailed in depth. The following chapters present peer-reviewed published articles based on data from this study, in order to convey the expectations and desires of Botswana genomics research participants about feedback of individual genetic results.

CHAPTER 4: IMPORTANT VALUES FOR CONSIDERATION IN FEEDBACK OF INDIVIDUAL RESULTS IN AFRICAN GENOMICS RESEARCH

4.1. Title of paper: Do solidarity and reciprocity obligations compel African researchers to feedback individual genetic results in genomics research?

Authors: Dimpho Ralefala, Mary Kasule, Ambroise Wonkam, Mogomotsi Matshaba, Jantina de Vries

Abstract

Background: A key ethical question in genomics research relates to whether individual genetic research results should be disclosed to research participants and if so, which results are to be disclosed, by whom and when. Whilst this issue has received only scarce attention in African bioethics discourse, the extension of genomics research to the African continent has brought it into sharp focus.

Methods: In this qualitative study, I examined the views of adolescents, parents and caregivers participating in a paediatric and adolescent HIV-TB genomic study in Botswana on how solidarity and reciprocity obligations could guide decisions about feedback of individual genetic research results. Data were collected using deliberative focus group discussions and in-depth interviews.

Results: Findings from 93 participants (44 adolescents and 49 parents and caregivers) demonstrated the importance of considering solidarity and reciprocity obligations in decisions about the return of individual genetic research results to participants. Participants viewed

research participation as a mutual relationship and expressed that return of research results would be one way in which research participation could be reciprocated. They noted that when reciprocity obligations are respected, participants feel valued and not respecting reciprocity expectations could undermine participant trust and participation in future studies.

Conclusions: I conclude that expectations of solidarity and reciprocity could translate into an obligation to feedback selected individual genetic research results in African genomics research.

Nature of publication: Peer- reviewed Original Full Journal Article

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Candidate contribution: Contributed to the conceptualisation of this work and designed the study. Collected the data and developed the data analysis strategy. Prepared the first draft of the manuscript and incorporated revisions from co-authors. Read and approved the final manuscript.

Co-author contribution:

AW, JDV, MK and MM: Contributed to the conceptualisation of this work.

JDV and MK designed the study and contributed to development of the data analysis strategy.

JDV, MK, MM and AW: commented on the first draft of the manuscript.

JDV, MK, MM and AW: read and approved the final manuscript.

JDV, MK and MM supervised the overall work.

Background

Feedback of individual genetic research results to research participants has increasingly become a topic of debate in bioethics, not in the least because such results may be relevant to the health of participants and their families (Renegar et al., 2006). Whilst some researchers have expressed a concern that feeding back individual genetic research results contravenes the traditional goal of producing generalizable knowledge for the good of society (Laurino, 2016), there appears to be a growing consensus regarding both moral and legal obligations of researchers, to feedback particular results (Eckstein et al., 2014; Holm et al., 2014; Wolf et al., 2008). Key values that are discussed in this literature are respect, autonomy, charity, mutuality, and reciprocity (Solberg, 2012).

Amongst the plethora of papers that have commented on issues relating to the feedback of individual genetic results in genomics research, only a small subset is specific to low and middle-income countries (LMICs). Of those, Kerasidou's paper (2015) seems to engage most with the peculiarities of the LMIC research context, yet it focuses on the return of aggregate and not individual findings. The others (Mackay, 2018; Ortiz-Osorno et al., 2015; Richardson, 2008; Sullivan & Berkman, 2018) seem to largely frame their work in terms of the poverty and vulnerability of African research participants. Richardson and Cho (2012) elaborate an entrustment model for the return of results, in which they premise an obligation to return results on the inability of participants to afford or access healthcare through other means. As such, this account is premised on participants' vulnerability, with the vulnerability arising out of poverty. Ortiz-Osorno and colleagues (2015) limit their discussion of feedback of individual clinical results to a question of actionability, with specific focus on the inability of some research participants to afford the healthcare that the individual results would mandate. Similar to Richardson, this work is also largely premised on the poverty and potential vulnerability of the

LMIC research participants taking part in research. Finally, Mackay (2018) advances a "do the most good" principle to guide decisions about the return of research results and specifically ties this notion to the perceived poverty and vulnerability of African research participants. Of note is that all of these accounts seem to be specific to genomics research that is led by principal investigators based in high-income countries (HICs) where the main question is whether and to what extent HIC researchers have an obligation to return results to participants in poorer countries (Mackay, 2018; Ortiz-Osorno et al., 2015; Richardson & Cho, 2012; Sullivan & Berkman, 2018).

The focus on the poverty and vulnerability of African research participants has two effects. First, it categorically treats all Africans as poor or vulnerable and of course the reality is not that simple. Second, and perhaps more importantly, it tends to disregard some of the fundamental ethical norms that guide Africans' way of life, as it does the life of others, namely solidarity and reciprocity. Although there is a fledging literature that advances reciprocity arguments with regards to feedback of results in genomics research, this issue is often mentioned in passing and neither elaborated nor contextualised to the African setting (Bredenoord, Kroes, et al., 2011; Bredenoord, Onland-Moret, & Van Delden, 2011; Kerasidou, 2015). Richardson and Cho (2012) briefly explain reciprocity as an attribute of relationships which involves an exchange of burdens and benefits. Bredenoord and colleagues (Bredenoord, Kroes, et al., 2011; Bredenoord, Onland-Moret, et al., 2011) state that even though participants often participate in research for altruistic or other reasons, they may anticipate a reward for instance in the form of feedback of individual genetic research results. Overall, in this literature, reciprocity seems to be advanced merely as a way of appreciating research participants or showing gratitude for their participation in research. Importantly, the discretion to appreciate participants seems to mostly lie with the researchers. This differs with accounts of reciprocity

in the African research context, where it is not only seen as a moral obligation but a fundamental social norm where deviance has a consequence.

The concepts of solidarity and reciprocity in African societies are grounded in the principle of Ubuntu (Mufune, 2003) or Botho, as commonly known in Setswana. According to Saule as cited by Mufune (Mufune, 2003), this *"emphasizes the principle of helping others as a way of helping oneself, collective activity and well-being rather than individualism, unification rather than division, respect for elders and sharing"* (p. 21). Although some of these themes like a sense of community may also be present elsewhere, the dominant philosophies there do not generally consider these values as fundamental in prescribing obligations, as is the case in Ubuntu philosophy (Ewuoso, 2020). As highlighted by Metz (2012), the communal nature of the African way of life which is centred around Ubuntu, is fundamental in defining personhood, dictates ethical obligations, and requires members of the community to identify with others as well as demonstrate solidarity towards each other. In this context, solidarity is defined as a reciprocal relationship in which members of a community who recognise their similarities, including their shared vulnerabilities and that they are dependent on one another, decide to collaborate with each other with the goal of avoiding suffering, reducing health inequalities and ensuring that all parties flourish (Tosam et al., 2018). This form of solidarity is not directed by sympathy for the disadvantaged. Instead, people in solidarity treat each other as equals in a balanced relationship, especially in relation to the shared interest, goal or situation (West-Oram & Buyx, 2017). Solidarity and reciprocity are interconnected, for solidarity to grow there must be a certain level of reciprocity (Prainsack & Buyx, 2016). Therefore, honouring reciprocity obligations is seen as one way of showing Ubuntu and solidarity and is of key importance in maintaining societal relationships and stability in the African context.

Yet although the concept of solidarity has steadily gained more attention in bioethics literature (Hoedemaekers, Gordijn, & Pijnenburg, 2007; Prainsack, 2017, 2018; Prainsack & Buyx, 2011, 2013; Prainsack & Buyx, 2016; S. M. Ritchie & Rigano, 2007; West-Oram & Buyx, 2017), again few papers addresses this issue in research in LMICs (Pratt, Cheah, & Marsh, 2020; Tosam et al., 2018). No empirical study has explored how these two concepts that are integral to the African way of life, could impact on African researchers' obligations to feedback individual genetic research results. In our study, we were interested in understanding better how solidarity and reciprocity feature in relation to discussions around the feedback of individual genetic research results particularly from the view of participants in an African genomic research study.

Methods

The work presented in this paper was part of a larger study aimed at exploring expectations and preferences for feedback of individual genetic research results with parents and caregivers of participants and adolescents involved in an HIV-TB genomics research in Botswana.

Study setting and population

This study was conducted as part of the Individual Findings in Genetics Research in Africa (IFGENERA), a collaborative project between the University of Cape Town, University of Botswana and Botswana-Baylor Children's Clinical Centre of Excellence (BBCCCE). The study was based in Botswana, a country with an estimated population size of just over 2 million people, majority of which are Christians (86.7 percent) with 63.9 percent living in urban areas (cities, towns and urban villages) as of 2017 statistics (Botswana, 2018a). The country's adult literacy rate stood at 90 percent in 2014 (Botswana, 2016). For many years, Botswana has been challenged with one of the worst HIV/AIDS burdens in the world with an estimated prevalence

of 18. 5 percent (Botswana, 2013) coupled with a high HIV/TB co-infection estimated at 60 percent (WHO, 2014).

As a result of this HIV/TB burden, the Collaborative African Genomics Network (CAfGEN) conducted at BBCCCE, was initiated to study genes of children with HIV and TB, to inform the development of new therapies to prevent or supress these infections (BBCCCE, 2020c). The CAfGEN study is a collaborative project within the Human Heredity and Health for Africa (H3Africa) Consortium (H3Africa, 2014) and uses genomics approaches to identify host genetic factors that are important for the progression of HIV and HIV-TB infection in paediatric and adolescent African populations (Mboowa et al., 2018). This genomic study was selected as a case study because it is amongst the few genomic studies being conducted in Botswana and offered an opportunity to explore questions around the feedback of individual results in genomics research. The adolescent cohort in this study provided an opportunity to explore perspectives of adolescents regarding these issues, as well as of the parents of younger children.

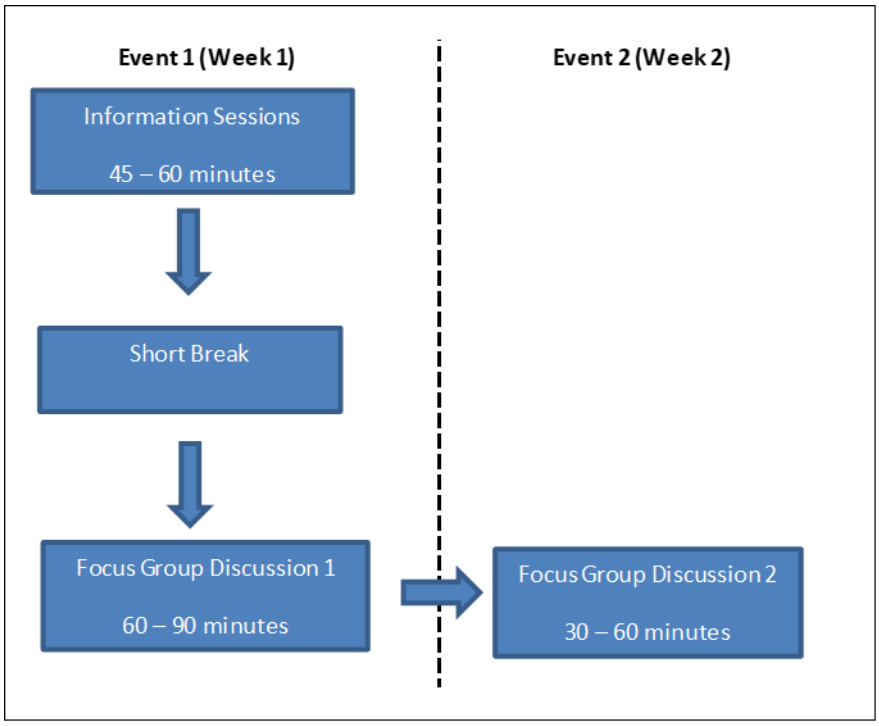
Data collection

Participants of this study were purposively selected. Recruitment of participants was done face-to-face during participants' clinic visits at the BBCCCE as well as telephonically where necessary. This study targeted 1) parents and caregivers of children (aged 2-18 years) involved in the CAfGEN study and 2) adolescents (aged 15-18 years) involved in the same study. BBCCCE is a clinical centre that provides HIV/AIDS treatment and support to children, adolescents and their families. As a result, all of the adolescents who participated in the CAfGEN study, who were also recruited into our study, received care from BBCCCE.

We used a qualitative study methodology involving deliberative focus group discussions (dFGDs) (Rothwell et al., 2016) and in-depth interviews (IDIs). Deliberative Focus Groups combine a traditional FGD approach with extended opportunities for learning and discussion, in an attempt at allowing participants to engage with the study topic in more depth. A dFGD manual with step by step instructions for the dFGD process was developed after a rigorous literature review. The tool was then piloted with 3 groups of participants (2 groups of parents and caregivers and 1 group of adolescents) to ensure content validity and practicability, after which it was used for the main study. The data was collected from February 2019 up to March 2020. The dFGD technique adopted for this study involved an interactive information sharing session with participants during the initial meeting, where the provision of information was iterated with discussion of a few scenarios. Participants were provided with information about genes and what they are, how they work, what happens when there are problems with genes, how genes impact on health as well as what genomics research is. This information session took about 45 – 60 minutes (see figure 1 for a schematic overview).

DFGDs for parents and caregivers were held separate from adolescents dFGDs, although in some instances we recruited pairs of parent/children who participated in separate events. While these participants may have discussed the dFGD questions between themselves at home, and possibly influencing each other's views, we could not rule out that other participants who were not paired did not do so, as both groups were encouraged to discuss issues raised in the study with family members between the 1st meeting and the 2nd meeting, which were held a week apart. No parent/children pairs were recruited for the IDIs.

Figure 2 Overview of research process



Holding the dFGDs in two separate stages was intended to: i) create enough time for engagement with participants and support information sharing especially because we were investigating a topic with which participants were unfamiliar; ii) provide participants with an opportunity to reflect on the issue being studied in-between the discussions; and iii) allow revisiting of views over time (Marsh, Kombe, Fitzpatrick, Molyneux, et al., 2013; Marsh, Kombe, Fitzpatrick, Williams, et al., 2013). Whilst we interrogated a broader range of issues relating to the return of individual genetic research results, we also specifically probed solidarity and reciprocity, for instance in relation to questions about why participants thought that individual genetic results should be returned, whether how and why participants should be appreciated for their participation and who they thought was responsible for covering costs of follow-up care and why.

Transcription of the dFGD data was done on a rolling basis. A topic guide was developed for the IDIs after completing 12 dFGD events (6 groups) and the remaining 12 dFGD events

followed as per the dFGD manual. The IDIs were conducted after completion of the dFGD data collection, to ensure that in-depth data about areas of controversy was collected. The IDI topic guide was piloted with 5 participants (3 parents/caregivers and 2 adolescents). Although we did not have a strict criteria to assess this, we mostly selected participants who either held uncommon views or who engaged more in the discussions. This approach was taken to explore such views at depth and ensure that we had a rich data. We also selected a few other participants who were mostly quiet in order to give them a chance to express their opinions but did not find that they engaged more during the interviews than during the dFGDs. IDI sessions took between 30 – 80 minutes. Data saturation was discussed by DR and JDV. The dFGDs and IDIs for parents and caregivers were conducted in Setswana while a mixture of Setswana and English was used in the adolescents' dFGDs. Field notes were made both during and after the dFGDs and IDIs. All discussions were audio-recorded, transcribed and translated into English.

Participant demographics

This study enrolled a total of 93 participants; 44 adolescents and 49 parents and caregivers attended the initial dFGD meetings. The group size for parents and caregivers' initial dFGD meetings consisted of about 4 – 11 participants, while adolescents initial dFGDs had about 5 – 12 participants. A total of 34 adolescents and 38 parents and caregivers were retained to attend the follow-up dFGD meetings. For these meetings, parents and caregivers' groups ranged between 4 – 8 participants, and 2 – 11 for adolescents. The 21 participants (10 adolescents and 11 parents and caregivers) who could not attend the follow-up dFGD meeting had other competing interests. Twelve dFGD meetings with 6 groups of parents and caregivers, and another 12 dFGD meetings with 6 groups of adolescents were conducted, making a total of 24 dFGD meetings. Follow-up IDIs were conducted with 6 adolescents and 6 parents or caregivers (see table 1 below).

Table 1 Summary of dFGDs and IDIs meetings

	dFGD				IDI
	# groups	# events	# participants		# participants
			Meeting 1	Meeting 2	
Parents/caregivers	6	12	49	38	6
Adolescents	6	12	44	34	6
Total	12	24	93	72	12

Majority of the adolescents (61 percent) were female, while 39 percent were male. Most adolescents (36 percent) were 16 years old and 93 percent were either attending junior school or high school or had completed the qualifications. Half of the adolescents lived in villages surrounding the city of Gaborone where this study was based, while 39 percent lived in the city.

On the other hand, parents and caregivers' participants were mostly female at 92 percent, with only 8 percent of male participants. One reason for this may be that women are usually the primary caregivers in Botswana (Kang'ethe, 2011; Kang'ethe, 2013; Maundeni et al., 2009). Most parents and caregivers (39 percent) were aged between 41 – 50 years and 94 percent had attained educational qualifications ranging from primary to tertiary education. Similar to the adolescent population, majority of the parents and caregivers (57 percent) lived in villages surrounding the city and 43 percent lived in the city of Gaborone (see table 2).

Table 2 Summary of participants' demographics

Adolescents	**Frequency**	**Parents and Caregivers**	**Frequency**
Male	17 (39%)	Male	4 (8%)
Female	27 (61%)	Female	45 (92%)
Total	44 (100)	Total	49 (100%)
Age		**Age**	
15 years	8 (18%)	21 - 30 years	6 (12%)
16 years	16 (36%)	31 - 40 years	17 (35%)
17 years	11 (25%)	41 - 50 years	19 (39%)
18 years	7 (16%)	51 - 60 years	6 (12%)
Unknown	2 (5%)	Above 60 years	1 (2%)
Total	44 (100%)	Total	49 (100%)
Educational level		**Educational level**	
Primary education	0 (0%)	Primary education	6 (12%)
Junior School	31 (70%)	Junior School	19 (39%)
High School	10 (23%)	High School	12 (25%)
Tertiary	0 (0%)	Tertiary	9 (18%)
None	1 (2%)	None	2 (4%)
Unknown	2 (5%)	Unknown	1 (2%)
Total	44 (100%)	Total	49 (100%)
Residence		**Residence**	
City/Town	17 (39%)	City/Town	21 (43%)
Village	22 (50%)	Village	28 (57%)
Unknown	5 (11%)	Unknown	0 (0%)
Total	44 (100%)	Total	49 (100%)

Analysis

All audio recordings of the dFGDs and IDIs were transcribed verbatim and exported into NVivo qualitative data analysis software Version 12 (QSR International Pty Ltd, 2012) for coding and data analysis. The data was coded by two members of the research team (DR and JDV), following an agreed description of the coding framework. Themes were derived both from the literature (deductive approach) and from the data (inductive approach). The qualitative data was analysed using the Framework Method for data analysis (Gale et al., 2013). This method encompasses five key stages that are closely aligned with the traditional analytical

process of thematic analysis and involves: a) Familiarisation with the data b) establishing a thematic framework c) indexing d) charting and e) data interpretation. The Framework method results in the production of a matrix in which cells of summarised data are presented in rows (cases) and columns (codes) ensuring that data can be easily analysed both by theme and by participant or event (J. Ritchie, Lewis, Nicholls, & Ormston, 2013).

Results

Almost all participants considered that feedback of individual genetic research results could be a way of appreciating participants' contribution to research. Whilst they gave a range of reasons to support this view, what seemed to lie at the basis of these views were expectations of solidarity and reciprocity.

Awareness of genetics

As indicated under the methods section, the dFGD method that we used involved an interactive information session to equip participants with a basic knowledge about genetics and genomics research. During the information session, we established participants' understanding of genetics and found that a couple of them already had a fair knowledge of what genes and genomics are. These participants described genes in relation to family traits, like how people look, how their noses are shaped, intelligence, and diseases that run in the family. After the information session participants were also able to integrate the information, they had learnt to make informed responses to the discussions. For example, using a scenario about a mother for whom researchers discovered a genetic predisposition for breast cancer while taking part in a genetic study on mental health, participants were asked about what researchers should do with this extra genetic result. In response one parent said:

"My thinking is that, it has been said that a gene doesn't mean sickness, but I think researchers can investigate and find something that they did not expect. […] So, what I think they could do is to tell her, also taking note of the outcomes, that this is just a gene and not sickness, but it could happen that it could develop into sickness as time goes on. This will help her to prepare herself mentally, knowing that she is living with that gene. And if they tell her when there is still time, she could also take care of herself before the sickness develops. It's important for her to know before she gets sick, so that she can try to prevent the sickness" (P4G5).

In the above quote, the participant was able to clearly articulate that having a gene for a particular disease does not mean one has that sickness and that behaviour impacts on whether or not a genetic predisposition develops into a disease. We found that most of our participants had similar perspectives. Additionally, participants were aware that genes are passed on from both parents and that it is possible for a gene to skip some children and be found in others or skip an entire generation.

Research participation should be reciprocated

Participants generally reported that they would want to receive their individual genetic research results in exchange for their participation in research. For instance, one adolescent expressed that they "should get something in return if they are taking part in a study" (A1G1). Most adolescents specifically indicated that they would like to get their individual genetic research results back so that they could know how to take care of themselves and behave in ways that would improve their health. Both parents and adolescents often reasoned that researchers should feedback their individual genetic research results because the research would not have happened without them. In particular, they mentioned that they gave blood to be used in the study as well as their time and opinions. One parent noted that:

"… They have to tell you what they have found after doing the investigations and you also have to be satisfied, because when doing research, the researcher comes to me to request for my participation…all the questions and answers come from me so I also expect that, after you have investigated on me… that package that you are going to give me should include answers to me, especially what you have found in your investigations including overall findings from participants" (P4G5).

A few parents also added that, although research participants usually take up risks that other people would not take, research usually benefits researchers, the university and the nation while participants do not usually benefit directly from research. They viewed feedback of individual genetic research results as a possible way to off-set the potential risks that they could have incurred. They pointed out that receiving individual genetic research results could help them know their genetic make-up. One parent mentioned that:

"..it was painful for the children when blood was drawn, it is uncomfortable to be in that position but since we have taken a stand, I think we should be the first ones to get help when we need it because we stepped up […] taking part in research involves everything in you, it is emotional, physical and spiritual. Research should be tit-for-tat, help me, I will help you because we are on a mission that should be accomplished" (P4G3).

Research participation is a mutual relationship that works both ways

While participants were aware that their participation in research could help the nation at large as well as future generations, some adolescents reported that they would like to get their individual genetic research results because otherwise "some people might think that researchers

just wanted to know their results only…" (A4G3). This highlights a concern by participants that if researchers do not give participants their individual genetic research results, it would appear like researchers only needed participants to achieve their agenda, without having any concern for their wellbeing. Furthermore, participants expressed viewing research participation as a relationship in which both researchers and the participants are helping each other out. They expressed that since participants helped researchers to advance their agenda by participating in the study, it was therefore appropriate to also expect researchers to advance the knowledge of participants by giving them back their individual research results. One parent expressed that:

"Appreciation should be both ways, the researchers have helped me as the participant to find out about genes I didn't know I had and the participant has also helped the researchers complete their studies by taking part in the research" (IDI-P003).

Participants also viewed the research process as a team effort, which meant that they were working together with researchers as a team and helping one another to achieve the goal of promoting good health. One parent expressed that:

"…Both the participant and researcher are helping each other out. That we are working as a team. We have to work as a team because we would be working together and agree on issues as you would have helped me with information I didn't know about" (IDI-P003).

When reciprocity obligations are respected, participants feel valued

Participants additionally expressed a view that receiving their individual genetic research results would show them that their participation was valued. One adolescent reported that "participants want to feel appreciated and motivated to do the right thing" (IDI-A002). A couple

of parents also shared this view and added that giving participants their individual genetic research results shows "the participant the results of their participation and that it was valued" (P12G5). Parents also expressed that this would be a learning experience for them but will also show that researchers care about them enough to give them information that could improve the quality of their life. They further pointed out that showing appreciation could encourage participants by knowing that their participation was adding to something and has yielded results. One parent noted:

"Yes, it shows the participant the results of their participation and that it was valued. It won't be right for our blood to be taken for testing and we don't receive results, because if we were told that they will be testing something then when results are returned, we will know whether we have that thing or not. And this will motivate me, knowing that my participation was beneficial" (P12G5).

Receiving individual genetic research results was valued over financial rewards

Obviously, there are other ways to respect reciprocity obligations in research. Some participants also mentioned other ways of showing appreciation for their participation in genetic research including: giving financial rewards; a gift basket; food; T-shirts; certificates; and a party. We therefore specifically probed whether those kinds of contributions would be an acceptable, alternative to respecting reciprocity obligations.

Both adolescents and parents generally did not support the idea of getting financial rewards beyond compensation for transport and meals and stated that participation in research is voluntary. Most participants indicated that they would rather get their individual genetic research results back so that they can gain knowledge from participating in the study and know

how the research is going as well as how their samples are helping. They also mentioned several objections to sharing financial rewards. One adolescent said:

"I don't know about financial rewards because what if it's not enough money because there are people who are never satisfied by what they receive. I would be so happy to get results because it shows that you guys care, I don't agree with financial rewards, it's a no" (IDI-A006).

Additionally, participants expressed that such financial rewards may not be a good way to appreciate participants' contribution as "people might think that their participation was bought" (A4G3). Also, a lot of people may end up wanting to participate in the study only because of the financial reward. They pointed out that research participants "shouldn't get anything else except their results because they were in the study" (A5G6). Nonetheless, one parent with professional research experience cautioned that even asking to receive individual genetic research results could be problematic for the reasons shared below:

"If you now say I want my results then at the end you will say, no…for me to take part in the study, I need 50, 000 Pula [referring to Botswana currency], its going there and you will wonder if you can get the best sample or question the quality of the information from such a sample, in most cases it's a no, and imagine in that case we take prostitutes because they want money, taking people who want to go and drink, so you will not just take anyone, so the statistics principles would already be violated" (IDI-P004).

As a result, he pointed out that he would rather have a situation where research is voluntary, and researchers have the discretion to decide to give participants whatever information they

deem to be important to share. However, even with this view, this participant also seemed to have held some hope of receiving some form of indirect benefits sometime in the future as a result of having participated in this study:

"The research is not necessarily for me as an individual but for the nation so I will benefit in one way or the other. The benefit is in my society that I live in, I have a generation that will keep on moving even when I am gone, that is the generation that will benefit, that is what is important. It's not me, that is why even today it is said to give generously but by doing so you shouldn't expect to be given anything back but your reward will come, someone, somewhere will give to me or my generation; my children to what I have given today" (IDI-P004).

Not respecting reciprocity expectations could have consequences

Participants also expressed that there is a general feeling that researchers often need help from participants but would not want to help them when they need help. However, they expressed that failing to reciprocate to participants by researchers could have some negative consequences as it will reveal that researchers do not want to help participants after participants helped them to achieve their agenda. When asked about who they thought was responsible for covering costs of follow-up care and why, one parent said:

"I think it's because they feel that you need their help but wouldn't want to help them when they need you, that is why they expect you to help in getting other tests because you would have found what you were looking for so at least help with subsequent tests, that help you offer the participants could encourage others to keep volunteering for other researches as this isn't the only research that will be conducted, there could come another study that needs participants, I could discourage others from taking part in studies because of the way I was handled during

my time when I was participating in this research and if they hear me say that, then they might not take part, or I could tell them that I benefited from taking part in a study and people would be motivated to take part in more research studies, that is why they expect that sort of assistance from the researchers, so that they don't lose motivation and keep advising others to take part in researches" (IDI-P006).

Discussions

In this study, we sought to understand how solidarity and reciprocity impact on African researchers' obligations to feedback individual genetic research results by examining views of adolescents and parents in an HIV-TB genomic study in Botswana. We found out that almost all participants considered that feedback of individual genetic research results would be a way of appreciating participants' contribution to research. Whilst they gave a range of reasons to support this view, what seemed to lie at the basis of these views were expectations of solidarity and reciprocity. Participants viewed research participation as a mutual relationship that needs to be respected. They also saw themselves as working together with researchers as a team, helping one another to achieve the ultimate goal of promoting good health. The principle of solidarity calls for team members to look out for each other and act in ways that could benefit one another. As Metz (2017) indicated, "*once a researcher and a participant have begun to think of themselves as a 'we' engaged in the joint project of a study, they have formed a tie that imposes special obligations to care for one another's quality of life that can go beyond those listed in a participant agreement form (with the one in a greater position to aid naturally having more of a duty to do so)*"(p 117.) As result since participants helped researchers advance their knowledge, it would be appropriate for them to also help participants advance their knowledge by giving them their individual genetic research results. This finding resonates with the ancillary care model developed by Richardson (2008) who highlighted that research

participation means that researchers enter into a relationship with participants, in which they take on limited responsibility for the health of research participants. The nature of this relationship is such that they have ancillary care obligations for findings that are relevant to the health of the condition under study. However, the ancillary care model advanced by Richardson is slightly different from the solidarity and reciprocity argument advanced in this paper, as pointed out by Metz (2017) the nature of the relationship advanced in Richardson's ancillary care model is a result of research participants' having entrusted researchers with their bodies and information, therefore it is this "reduced privacy or compromised autonomy" (p.121) that obligates researchers to provide support to participants. As a result, this limits the range of support that a researcher could provide to participants as it could exclude other conditions that participants may have, even if they were known to the researcher prior to the study (Metz, 2017). On the other hand, while solidarity and reciprocity argument advanced in this study are also relational, the difference is that the relationship here is communal. According to Metz (2017), "*upon sharing a way of life with participants, a researcher has established part of a morally significant relationship that demands respect and hence full-blown realization in the form of caring for their quality of life as well*" (p.117). Unlike the entrustment model where the duty to provide help is a result of the disclosure of private information, this appeal to communion could possibly have a much broader reach (Metz, 2017). In our study, participants were less worried about ancillary care obligations but framed that the nature of reciprocity obligations required that researchers return the value of their research participation *in kind.* Importantly, what that means to them is that where their research participation helped researchers improve knowledge, so too should researchers help them improve their knowledge.

In addition, participants noted that providing them with their individual genetic research results could off-set the risks that they would have taken up by participating in the study. According

to Prainsack (2018), a solidarity-based viewpoint means that we can recognize that those who volunteer to help others, often take-up some costs, and that even though such acts are often viewed as gifts that are voluntarily given (Zeiler, 2014), the nature of the gift is influenced by social relations and shared responsibilities that exist between the giver and the recipient (Prainsack, 2018). Therefore, once the gift is given, it often creates a "web of indebtedness and future reciprocity" (Simpson, 2014, p. 342). Our participants' balancing the risk that they took on with their views on return of results could perhaps be understood in this light.

Our findings further revealed that, when reciprocity obligations are respected, participants feel appreciated and valued. This in turn enhances solidarity between participants and researchers and could motivate participants to participate in future research, knowing that their participation was beneficial and has yielded results. Participants highlighted that they need to feel that they are part of something larger and that their contribution fed into a reciprocal, respectful and beneficial relationship. Honouring reciprocity obligations is important in maintaining societal relationships and stability.

While there are many ways to reciprocate participants, including financial incentives, many participants in our study did not consider monetary rewards beyond compensation for transport and meals; as an appropriate way to reciprocate. They mentioned that such financial incentives could undermine the voluntary nature of the contribution. This is particularly important, as it means that participants appreciate that research participation is a voluntary endeavour and that getting money for research participation may make it seem like a commercial exchange rather than a relationship based on solidarity and reciprocity, where any exchange of gifts is based on caring for one another. Prainsack (2018), states that in a solidarity model, what the gift giver should be able to anticipate from the one who receives it, is that in reciprocating, the recipient

will treat her as per the same standards that have been accorded to her. As a result, a solidarity outlook requires that we work toward attaining balance and reciprocity between those who are within the organisational and institutional context in which the "gift" is given. This suggests that it makes sense to expect researchers to compensate the knowledge-based benefit that participants have accorded them by providing a knowledge-based benefit to participants. Returning overall study results is another way of achieving that, but participants in our study specifically expressed that they would want to receive individual genetic research results as a form of appreciation for their contribution. These views are consistent with findings by Marsh et al (2013) in Kenya, who found that disclosing individual genetic findings about sickle cell disease was strongly supported by participants due to perceived health and social benefits. Several other studies conducted elsewhere also revealed that participants generally would like to be provided with feedback on their individual genetic results (Bollinger et al., 2012; Coors et al., 2015; Facio et al., 2013; Regier et al., 2015; Yu et al., 2013; Yushak et al., 2016).

Conclusions

Overall, our findings seem to suggest that our Batswana research participants conceptualise participation in genomics research in terms of a reciprocal relationship. They articulated an expectation that their gift of research participation, which helped researchers produce knowledge, should be reciprocated by sharing knowledge-based benefit – as would be provided when sharing individual genetic research results. They were therefore overwhelmingly in support of an obligation for researchers to share individual genetic research results. As a result, these expectations of solidarity and reciprocity by participants could mean that African researchers do have an obligation to return selected individual genetic research results. However, we could not exclude that there are other reasons for the high-level of support for feedback of results.

Obviously, in this paper we did interrogate other, broader aspects relating to the feasibility of returning individual genetic research results – and so, even if in this paper we have established that there seems to be an ethical obligation to return individual genetic research results, we cannot comment on the extent to which this is practicable or feasible.

CHAPTER 5: PREFERENCES AND REASONS FOR FEEDBACK OF INDIVIDUAL GENETIC RESULTS

5.1. Title of paper: Participants' preferences and reasons for wanting feedback of individual genetic research results from an HIV-TB genomic study: A case study from Botswana.

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Abstract

The feedback of individual results of genomics research is an ethical issue. However, which genetic results African participants would like to receive and why, remains unclear. A qualitative study was conducted to collect data from 44 adolescents and 49 parents/caregivers of adolescents enrolled in a genomic study in Botswana. Almost all the participants wanted to receive genetic results. Parents and caregivers wanted to receive results across all categories of genetic conditions discussed in the study, while adolescents were reluctant to receive results for severe, non-preventable, and unactionable conditions. Participants expressed different reasons for wanting feedback of results, including for awareness, improving lifestyle, accepting one' situation, and preparing for the future. Our findings also reveal that participants' context, relations, and empowerment are important to consider in interpreting their preferences for feedback of results.

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Candidate's contribution: The candidate contributed to the conceptualisation of this work and collected the data. She also developed the data analysis strategy and analysed the data. DR prepared the first draft of the manuscript and all authors commented. Revisions were made by DR and all the other authors read and approved the final manuscript. JdV, MK and MM supervised the overall work. This study was conducted to fulfil requirements of a PhD degree for DR.

Co-author contribution:

All the authors contributed to the conceptualisation of this work.

JdV and MK contributed to the development of the data analysis strategy.

All authors commented on the first draft of the manuscript.

All authors read and approved the final manuscript.

JdV, MK and MM supervised the overall work.

Introduction

Whole Genome Sequencing (WGS) sometimes reveals information about individuals that are unrelated to the original research question but may be important for patient care (Bijlsma et al., 2018; Green et al., 2013b; Presidential Commission for the Study of Bioethical Issues, 2013). For example, researchers may identify that a participant carries a mutation that predisposes them to a particular illness or that influences their drug metabolism (Hegde et al., 2015). These findings are usually categorized as "incidental" or "secondary" findings (Ortiz-Osorno, Ehler, & Brooks, 2015). Secondary findings often refer to results that are not associated with the primary motive of testing but are, nevertheless, intentionally sought, while incidental findings involve variants that were discovered unintentionally (Darnell et al., 2016).

Generally, incidental and secondary findings from genomic sequencing are classified into the following three main groups: (a) clinically actionable results, (b) results with clinical validity for a disease but not usually expected to be clinically actionable, and (c) results with little or no clinical validity for disease and harm (Berg, Khoury, & Evans, 2011). Most studies conducted in high-income countries (HICs) revealed that participants generally would like to be provided with feedback of their individual results (Bollinger, Scott, Dvoskin, & Kaufman, 2012; Coors, Raymond, McWilliams, Hopfer, & Mikulich-Gilbertson, 2015; Facio et al., 2013; Regier et al., 2015; Yu, Crouch, Jamal, Tabor, & Bamshad, 2013; Yushak et al., 2016). However, opinions from research participants vary from wanting to receive all findings to only certain subsets of genetic information. Some studies and reports in clinical trials indicated that research participants recommend the return of results, regardless of their negative implications (Fernandez et al., 2009; Miller, Hayeems, & Bytautas, 2010; Murphy et al., 2008). Other participants mainly wanted to receive genetic results that they were able to act on or "do

something about". In this case, "actionability" is generally defined as the ability to treat or prevent the disease (Yu et al., 2013).

Many of the studies conducted on this topic originate in high-income countries and such work has hardly been extended to low- and middle-income countries (LMICs), particularly in Africa (Marsh, Kombe, Fitzpatrick, Molyneux, & Parker, 2013; Marsh, Kombe, Fitzpatrick, Williams, et al., 2013). According to Beskow and Burke (2010), the research context needs to be taken into consideration in discussions around the feedback of individual genetic results from genomics research as the findings cannot be generalized across different contexts. With the increase in genomics research in the continent brought about by initiatives such as the Human Heredity and Health in Africa (H3Africa), this issue has become more urgent than before. H3Africa has provided funding to 51 projects spread across 30 African countries to conduct population-based genomics studies of common non-communicable and communicable diseases. It was envisaged that samples from 50,000 to 75,000 participants would be analyzed through this initiative (H3Africa, 2014), generating extensive individual (secondary and incidental) genetic results that could be beneficial to participants' clinical and personal utility. As a result, this has brought about ethical challenges regarding the feedback of findings generated in African genomic sequencing. Whether participants in African genomic studies would like to receive genetic results, and if they do, which type of result and why, are still unclear. To address this gap in knowledge, we conducted an empirical study to explore the preference of adolescent participants, their parents and caregivers, regarding receiving feedback of genetic results of an HIV-TB genomics research project in Botswana. In this paper, we present participants' views on receiving genetic results, their preference and reason for wanting certain results.

Methods

Study setting and population

We conducted an empirical qualitative study using data from individuals that participated in a genomics research study based in Botswana, an upper-middle-income country in Southern Africa with a gross domestic product per capita of US$7080.12 United States dollars (USD) (Botswana, 2018). For many years, HIV and TB have remained among the most serious diseases confronting children in Botswana, and there is a long track record of research on these conditions. The overall HIV prevalence in Botswana is 17.6%, with 20.3% in cities and towns, 16.6% in urban villages, and 16.9% in rural areas (Kandala, Campbell, Rakgoasi, Madi-Segwagwe, & Fako, 2012). This is coupled with a high HIV/TB co-infection rate estimated at 60% (WHO, 2014). The rising prevalence of HIV among adolescents, from 3.7% in 2008 to 5.0% in 2013 (Botswana, 2013), is concerning. This situation prevails despite the country's extensive healthcare system including hospitals, clinics, health posts, and mobile stops spread across 27 health districts. Health care (inclusive of hospital care, laboratory tests, and medications) is provided free of charge in public sector facilities for all citizens, and almost 95% of Botswana's population lives within 8 kilometers of the nearest health facility (Botswana, 2015). However, genetic testing in Botswana is limited to the context of research.

As a result of the HIV/TB burden and other aforementioned characteristics, the Collaborative African Genomics Network (CAfGEN) was initiated to study genes in children with HIV and TB, for the development of new therapies to prevent or suppress these infections (BBCCCE, 2020b). The CAfGEN study is a collaborative project which is part of the H3Africa consortium (H3Africa Consortium, 2014), and uses genomics approaches to identify host genetic factors that are important for the progression of HIV and HIV-TB infection in pediatric and adolescent

African populations (Mboowa et al., 2018). The CAfGEN study was conducted at Botswana-Baylor Children's Clinical Center of Excellence (BBCCCE), which is a pediatric and adolescent clinic that provides free of charge state-of-the-art HIV care, treatment, and support to children, adolescents, and their families (BBCCCE, 2020a).

As a result, many of the adolescents participating in the CAfGEN study recruited into our study also received care from BBCCCE. The adolescent cohort in this study provided an opportunity to explore adolescents' perspectives regarding questions around the feedback of results, as well as that of their parents and caregivers. The participants in our study included: 1) parents and caregivers of children aged 2-18 years and 2) adolescents aged 15-18 years enrolled in the CAfGEN study. Previous research has suggested that age may play a role in adolescents' views on participating in genetic studies (Geller, Tambor, Bernhardt, Fraser, & Wissow, 2003). According to Petersen and Leffert (1995) and Santelli et al. (1995), under most circumstances, adolescents aged at least 14 or 15 years are able to make conscious decisions similar to adult participants. As a result, recruiting adolescents of appropriate age was important to ensure that they could comprehend the complex issues related to feedback of results as well as provide sound opinions. However, in Botswana, minors below the age of 18 cannot consent to participate in research nor can receive results without the permission of their parents or caregivers. As a result, for this study, we obtained assent from both adolescents and their parents or caregivers.

Considering that the CAfGEN study included only adolescents who had been perinatally infected with HIV, all the adolescents in our study and probably most parents, were HIV positive. The number of HIV-positive non-parent caregivers is not known because their HIV status was not assessed in the study. The CAfGEN cohort was targeted for this study because

they were likely generally knowledgeable about health and genetics than the general population. Consequently, they could participate better in meaningful discussions regarding feedback of genetic research results as they are part of a genetic study that has a strong community engagement aspect. Over the years, the BBCCCE has empowered the adolescent cohort as well as their parents and caregivers with information regarding the association between heredity and health. For example, four Genome Adventure Comic books were published by the institution (BBCCCE, 2020c) and translated into various languages as part of a community engagement project for the CAfGEN study.

Data Collection

We purposively selected 93 participants (44 adolescents enrolled in a genomic study in Botswana and 49 parents and caregivers of children and adolescents enrolled in the same study). While some adolescents were recruited with their parents or caregivers, they participated in separate meetings. No comparative responses from parent-adolescent dyads were conducted, as it was not the focus of the study. The study primarily used deliberative focus group discussions (dFGDs) (Rothwell, Anderson, & Botkin, 2016) for data collection. These were augmented with in-depth interviews (IDIs) to explore a broad range of issues relating to the return of genetic research results, including participants' views on receiving results, and their preference and reasons for certain results. A dFGD manual providing a step-by-step guide for data collection was developed for this study based on an extensive literature review (see Annex 1). The manual provided several scenarios and questions to elicit participants' views regarding a range of ethical issues related to return of results. The scenarios explored several issues, including those relating to the return of results to adults and children, the return of adult-onset and early-onset conditions, roles and responsibilities for the identification and return of results. The interview topic guides were developed after identifying

gaps in the dFGD data to further probe any issues that still needed clarification. The dFGD manual, in-depth interview guide, and consent forms were all translated into Setswana (the local language spoken in Botswana) by a research assistant who is a native speaker also fluent in English. The guides were also checked for consistency by the lead author, a native speaker of Setswana and fluent in English. The dFGD manual was pilot tested with 2 groups of parents and caregivers (16 participants in total) and 1 group of adolescents (5 participants), and the IDI tool was pilot tested with 3 parents or caregivers and 2 adolescents. The pilot testing aimed at the following: (i) assessing the feasibility of the dFGD and IDI methods, (ii) ensuring the fitness of the scenarios and topic guides with the study purpose, (iii) assessing participants' comprehension concerning the issues discussed, and (iv) estimating the duration of the dFGDs and IDIs. The pilot dFGD suggested the introduction of a 30-minute break in the first session of the dFGD that lasted approximately 3 hours. In addition, some sentences and Setswana translations were revised both in the dFGD and the IDI tools with guidance from participants. Data from the pilot dFGDs and IDIs were excluded from the analysis.

The participants were recruited in person during their visit to the BBCCCE as well as telephonically, where necessary. The CAfGEN staff, particularly the study nurse and research assistant, was responsible for recruiting participants. The participants were informed about the study and interested parties were referred to the researchers. The purpose of the study was then explained to prospective participants, and consent was obtained by the primary author and the research assistant. Participants recruited by phone were taken through the consent process in person before participating in the dFGDs or IDIs. In each event, the participants decided whether to use Setswana or English. English and Setswana are both official languages in Botswana, and most official communication involves English. The members of the study team conducting these events were fluent in both languages, and all study materials were available

in both languages. The parents and caregivers preferred Setswana for their discussions, the younger generation preferred English. Data were collected from February 2019 to March 2020.

The research team used deliberative focus group discussions because it combines a traditional FGD approach with extended opportunities for learning and discussion in an attempt to allow participants to engage with the study topic in an in-depth manner. The dFGD technique adopted for this study involved an interactive information-sharing session with the participants. Case studies elaborating on particular ethical considerations in the return of genetic results were used for information sharing during the first meeting. This allowed participants to learn about genes, their functions, and their impact on health. Data were collected until saturation was reached. Data saturation was discussed by DR, MK, and JDV. A total of 24 dFGD meetings were held with 12 groups of participants (6 groups of adolescents and 6 groups of parents and caregivers). These were complemented with 12 in-depth interviews (6 adolescents and 6 parents or caregivers) with people that had also participated in the dFGDs. The interviews were conducted on a one-on-one basis. The authors selected a range of participants from the dFGDs, from those that were quieter in the discussions to those that were more engaged. The IDIs focused on further clarifying and probing some of the early insights from the study.

Both groups of participants (adolescents, parents and caregivers) were asked the same questions about their views on wanting the feedback of genetic results. They were asked questions about their preference on the feedback of results for adult participants as well as those of children. A scenario of a mother found with a breast cancer gene while participating in a mental health study was used to solicit participants' opinions on this topic (see Annex 1). This was followed up with a scenario where a daughter participating in an HIV-TB genomic study was found to be a carrier of a breast cancer gene. Participants were then asked about issues

related to returning early-onset and adult-onset results. However, in this paper, we do not present the data pertinent to the feedback of pediatric genetic results but only the views of adolescents, parents and caregivers on wanting to receive feedback of results, and the preference and reasons for certain results.

To get participants' preference on receiving feedback of results, we gave each participant a print-out of Table 1 with four categories that genetic results could fall into. This approach was guided by findings from Holm et al. (2015) who found that allowing research participants to make choices about which genetic conditions they would like to receive feedback of enhanced their satisfaction as compared to giving them no options for feedback or allowing them to choose either "yes" or "no" regarding receiving results.

This table categorizes genetic conditions by severity, that is, how sick can the condition make a person and preventability, that is, the likelihood that the condition will develop in a person. We used the table to concretize the kinds of findings genomics research could reveal among the participants. We then moderated discussions around each category, exploring whether participants would want to receive such results and why.

Not severe & preventable 1. Pet dander (dog) allergy 2. Iron deficiency anaemia 3. Kidney stones 4. Lactose intolerance 5. Gastroesophageal reflux disease 6. Reduced response to ibuprofen 7. Chronic mild constipation 8. Delayed response to local anaesthetic 9. Increased susceptibility to cavities	**Severe & preventable** 1. Alcoholism * (mental health) 2. Asthma 3. Deep vein thrombosis 4. Familial hypercholesterolemia 5. Melanoma 6. Peanut allergy 7. Types II Diabetes 8. Malignant hyperthermia 9. Childhood onset hereditary colon cancer 10. Aortic aneurism
Not severe & non-preventable 1. Attention deficit hyperactivity disorder* (learning disability) 2. Essential tremor 3. Generalized anxiety * (mental health) 4. Hypothyroidism 5. Poor vision 6. Seasonal allergies 7. Turner Syndrome 8. Vitiligo 9. Mitral valve prolapse 10. Obstructive sleep apnoea	**Severe & non-preventable** 1. Autism * (developmental and learning disability) 2. Bipolar disorder * (mental health) 3. Duchenne Muscular Dystrophy 4. Juvenile (Type I) Diabetes 5. Juvenile rheumatoid arthritis 6. Polycystic Ovarian Syndrome 7. Rett Syndrome * (Childhood-onset degenerative) 8. Acute lymphoblastic leukaemia 9. Batten disease (NCL) * (Childhood-onset degenerative) 10. Alzheimer's disease * (adult-onset) 11. Huntington's disease* (adult-onset)

Table 1: Categories of possible individual genetic research results. Table copied from Holm et al. (2015), reproduced here with permission.

Most participants in the study were females among both adolescents (61%) as well as parents and caregivers (92%). The 16-17 age group represented 61% of the adolescent participants while the most represented age group among parents and caregivers was 41-50 (39%). As most of the adolescents were in the 16-17 age group, the majority were either in junior secondary school or senior secondary school or had attained either of the qualifications (93%). Most (94%) of the parents and caregivers had educational qualifications ranging from primary to tertiary education. There was near uniformity in the residential location of participants in both categories—they were from villages around the city of Gaborone where this study was conducted (adolescents = 50%, parents and caregivers = 57%) or the city of Gaborone (adolescents = 39%, parents and caregivers = 43%). A few adolescents (11%) did not record

their place of residence (for more details on the study procedures and methods, see Ralefala, Kasule, Wonkam, Matshaba, and de Vries (2020).

Data Analysis

All audio recordings of the dFGDs and IDIs were transcribed for data analysis. The content recorded in Setswana was translated to English. Each transcript comprised verbatim transcription of the audio recordings. Codes denoting the type of participant ("P" for parent and "A" for adolescent), speaker number, and group number were used to describe each participant in the transcript. For example, P1G1 denoted the first parent to speak in the first group of dFGD. The data were transcribed by the research assistant. Transcribed data from the dFGDs and IDIs were verified by the primary author (DR) by listening to the recordings while reading the transcripts. Any misquoted text and typographical errors were corrected. Upon completion of data cleaning and verification, transcripts were uploaded into the NVivo qualitative data analysis software Version 12 (QSR International Pty Ltd, 2012) to facilitate data organization and analysis. Both inductive and deductive approaches were applied to the coding. Data analysis for this study was guided by the stipulated study objectives and the framework method for data analysis (Gale, Heath, Cameron, Rashid, & Redwood, 2013).

However, the dFGD data relevant to this paper drew heavily from Holm et al. (2015). For instance, each participant in our study was given a print-out of the Table extracted from Holm et al. (2015) to demonstrate the four categories in which genetic results could fall into and it was found to be very compelling. Consequently, themes that emerged during discussions on which genetic results participants would want to receive aligned with those of Holm et al. (2015).

Ethical Review

This study was reviewed and approved for ethics compliance by the Health Research Ethics Committee of the Faculty of Health Sciences at the University of Cape Town, the University of Botswana Institutional Review Board, the Health Research and Development Committee of the Ministry of Health and Wellness in Botswana, and the Institutional Review Board of Botswana-Baylor Children's Clinical Centre of Excellence. Written assent was obtained from all adolescents, as well as written permission from their parents or caregivers before enrolling them in the study. Parents and caregivers also provided written informed consent for their participation in the study. Verbal permission for audiotaping was obtained from all participants. Separate written consent was obtained for participating in the dFGDs and IDIs in Setswana or English, according to the participant's preference. All participants were offered a snack and reimbursement for transport. Unique identifiers were used to protect participants' identities during dFGDs and IDIs.

Results

Participants' preferences for feedback of individual genetic research results

Overall, the majority of adolescents, and parents and caregivers expressed that they would like to receive genetic results, except a few adolescents and one parent preferring to not receive any genetic results. These findings are consistent with some studies and reports in clinical trials that document that research participants recommend the return of genetic results, often regardless of possible negative implications of the results (Fernandez et al., 2009; Miller et al., 2010; Murphy et al., 2008). After ascertaining whether or not participants wanted to receive results, the research team was interested in knowing which kinds of results the participants would prefer receiving. An investigation guided by Holm et al. (2015) was carried out to

engage participants on which kinds of research findings they would like to receive. The four categories include the following genetic conditions: a) not severe and preventable, b) severe and not preventable, c) severe and preventable, and d) severe and not preventable. Parents and caregivers showed a desire to receive results across all four categories regardless of severity, preventability, or actionability. Interestingly, adolescents indicated preference to receive results encompassing three categories (a, b, and c) and reluctance to receive results for genetic conditions that are severe, not preventable, and unactionable.

Participants' reasons for wanting feedback of individual genetic research results

It is important to know.

When probed about receiving unactionable results, a parent said, *"For me, knowledge is power, irrespective of the consequences that come with it because you can exercise some proper management practices that will enhance the quality of your life…" (IDI P004).* Parents and caregivers shared that knowledge about the genetic conditions that they are predisposed to and their cause could help to dispel the misconceptions of witchcraft. In Setswana culture and other cultures in Africa, it is common to associate certain ailments with witchcraft, especially where the cause of the disease is unknown. Parents and caregivers also expressed that knowing their genetic results could save them money and time as it would prevent them from searching for treatment of a genetic condition with no cure yet. These findings are in line with results from a study conducted in the United States of America by Sanderson et al. (2016) among healthy adults who had their genomes sequenced, wherein 94% of the participants wanted to receive all types of results. In a study by Christensen et al. (2017), two-thirds of participants wanted to receive all categories of genetic results about their children, including for non-preventable

conditions. Participants gave several reasons for wanting to receive genetic research results, as outlined below.

Improve lifestyle or look for help.

Adolescents expressed that even though some genetic results could reveal unexpected information, it could facilitate them to take better care of themselves and improve their health. Parents and caregivers also wanted to know their own results so that they could engage in healthy lifestyles that could help prevent the progression of genetically predisposed diseases, such as exercising, being aware of their environment to avoid any triggers, and taking up any other necessary preventative measures. This view was particularly strong for preventable conditions. Both adolescents and parents and caregivers also shared that once they knew their results, they could look for help to address the genetic condition, including going for counseling, looking for treatment, and exploring other ways of managing the condition. One parent expressed the following:

"When (you are) told you have a certain gene, since it's a gene, it doesn't mean you have the illness. There is a 50/50 chance you might get it, so you would keep on going for regular tests to make sure that you treat the illness. You take care of yourself by always checking since you would have been informed on it…' (IDI-P002).

Similar reasons have been reported elsewhere, in which participants expressed willingness to adopt healthier lifestyles, undertake preventive measures to reduce their future risk of getting sick, or look for treatment (Bijlsma et al., 2018; Facio et al., 2013; Sanderson et al., 2016).

Accept one's situation.

Adolescents also expressed that knowing their genetic results could help them accept their condition and prepare for the future. One adolescent said that *"it's just like when you have HIV, you accept your situation and live on" (A5G4)*, while another shared that, *"I would want to know so that I accept the possibilities of what could happen in the future, so that when it develops, I would already be in a good state of mind" (A5G2)*. Similarly, parents and caregivers also shared that knowing their genetic results could help them *"stay mentally prepared to accept the situation if the gene develops into an illness"*. According to a parent,

"…You see accepting your situation is powerful, you have to consider yourself blessed to have known your status, the best medication even better than a pill is accepting oneself, then everything becomes better despite the results one receives…"(P8G4).

Prepare for the future.

One adolescent also said, *"I want my results back because like I said, I want to be prepared for whatever might come my way, if it's breast cancer then I should be prepared for what will happen" (IDI-A006)*. Likewise, parents and caregivers also wanted to know their genetic results so that they could get their affairs in order in cases where the worst is expected to come. According to them, this will also help them to be alert about their health and prepare themselves for any situation that might arise. The importance of accepting one's situation and preparing for the future was mostly expressed with regard to receiving genetic results that are severe and non-preventable, as well as those that are unactionable. This finding resonates with views from participants in the study by Sanderson et al. (2016) where some participants wanted their personal genetic risk information, including for conditions that they could do nothing to prevent or treat so that they could prepare or plan for the future. Similar views were also shared in

studies by Holm et al. (2015), Basson, Futter, and Greenberg (2007); Futter, Heckmann, and Greenberg (2009). In addition, one parent reasoned that treatment for an unactionable genetic condition today could be developed in the future and they could benefit from it. According to her,

"Knowing your results is very important, even when there is no treatment, it can be developed at a later stage, like when HIV started in our country there wasn't any treatment. Then it was discovered at a later stage. So just because the doctors tell you that the genetic disease doesn't have any treatment doesn't mean you shouldn't receive the results" (P4G2).

Some participants in the study by Bollinger et al. (2012) and Sanderson et al. (2016) also shared a similar view, indicating that their genetic information could be useful to them in the future as research advances.

Participants' reasons for not wanting feedback of individual genetic research results

Although many participants expressed that they would like to receive their genetic results, some adolescents and a few parents and caregivers were uncomfortable with receiving results, especially those that were severe, non-preventable, and unactionable. Their main concern about receiving such results was the subsequent psychological implications. Some adolescents shared that it is not very useful to know about genetic conditions that are unactionable because, *"…there is no help […], then it's the same as not knowing anyway' (A1G2)*. A couple of other adolescents also expressed that they would not want to know their genetic results *"if there is no treatment or cure"* as it would be traumatizing and could make one lose hope in life. This view resonated with several parents and caregivers. One parent indicated the following:

"…this will really disturb my mind because it will be too emotional. The human mind gets afraid when it receives certain news, I will get so confused even when you know it's just in the genes and there are possibilities I do not get the illness or has not developed, I guess its human nature" (P3G4).

Likewise, some participants in the Sanderson et al. (2016) study were also concerned about possible negative psychological implications of receiving genetic results, especially for conditions or diseases that are untreatable.

Few adolescents and one parent in our study also indicated that it is not necessary for them to know the results of genetic conditions that are not severe because if the condition develops, they will experience some changes or discomforts in their bodies that are not life-threatening, and they could always get help for them. A parent said*, "I see it as not that important to know, you know it is not dangerous; they are just signs that you will just realize and take action to that so there is no need to be told" (P4G5).*

Only one parent strongly opposed receiving feedback of extra genetic results in general. He said,

"…they [researchers] should keep those results to themselves, I would not want to know them, I will find out some other time. I would not want to be stressed by something that might occur in 20 years that would disrupt my life in the present" (P1G1).

He also believed that *"a lot of things are driven by faith, if you tell me and I believe I will get sick, then I will get sick (P1G1)."* This parent was also concerned that knowing his genetic results could also place a burden on his children as genetic conditions are hereditary. However, stigma was not a concern for almost all participants. Only one adolescent expressed that some people may not want to know their results because they would not want to be *"…stigmatized,*

ignored, or rejected by people since they would have seen that they have a certain gene. This may embarrass them, while some may just accept it since it concerns their health" (IDI-A001).

Context matters for interpretation of preferences for feedback of individual genetic research results

It seems that the choice of the kind of results people want is influenced by their experiences. For instance, parents and caregivers in our study wanted to receive all genetic results, while adolescents were reluctant to receive genetic results for conditions that are severe and not preventable, especially if they are unactionable. This may be because the parents and caregivers in our study survived a time where there was no treatment for HIV and have experienced a period where there is treatment and other ways to manage the disease. This experience seems to have influenced their views on receiving genetic results despite their severity, preventability, and actionability. One parent attributed their ability to *"accept their situation"* to their HIV experience and said, *"…if we were able to accept our HIV status and counsel ourselves then what more can you fear…" (P9G3).* This observation is similar to other observations (Kleiderman et al., 2014; Sapp et al., 2014) seen in the case of parents of children with rare genetic diseases. Parents in the study by Kleiderman et al. (2014) wanted to be notified about all results affecting their children's health, regardless of the severity of the disease. Likewise, Sapp et al. (2014) reported that parents also preferred to receive all types of results for their children and ascribed this to their success in coping with their child's condition for managing any other negative health information. The adolescents' real time experience of learning about their HIV status and how it affects their health differs from those of the parents and caregivers as most adolescents were only recently learning to live with the knowledge of their HIV status. During dFGD meetings, we learned that most parents disclosed their children's HIV status to them during their adolescent years. This situation seems to have affected adolescents' views

on wanting feedback of unactionable genetic results, that, unlike their parents, are living in a period where HIV is manageable and may not easily imagine dealing with an unactionable result. The other reason could be that having a life-long condition could already be burdensome for these adolescents and may have made them fearful of knowing about the possibility of having another condition that they could do nothing about. When asked about wanting feedback on severe, non-preventable, and unactionable results, there was often a sobering silence during the adolescents' dFGDs, indicating their apprehension in processing the information, with some of them eventually expressing that receiving such results would be emotionally traumatizing.

Participants' placed value in sharing their genetic research results with family members

Both adolescents, parents and caregivers expressed that as the results may also be relevant to other family members, it is imperative that they are also made aware of the genetic research results. According to a parent,

"I believe that I want to get all the results back. I wouldn't want to be in the dark about my health or my family's health. I have to have information that could save our lives. If one of the family members has cancer, diabetes, or any illness in the family, it is important to know if the family has that gene and the possibility of anyone getting sick. So, it is important to have that information" (IDI-P003).

Participants described that their lives are not theirs alone and that there are people in their lives who should know about their health. Others indicated that it is important for them to know their results so that they could inform their caretakers, should they get sick, so that they know their situation upfront and be informed about the care that would be needed. Almost all participants

preferred to receive results with limited direct benefit to themselves but potential clinical benefits to their family members. For example, in the case of a breast cancer predisposition in males that elevates their risk to disease only slightly but increases the risk for their children and female siblings considerably. According to a participant,

"Yes, it is important that the results are returned even if the gene won't affect the participant. (As) They would still be helpful to others, and even (if) his children might not be at risk, his grandchildren could be at risk. So, the results are important to be returned to the participant" (PIDI-P001).

This highlights the interconnection of lives. Similarly, other studies have found that participants consider sharing their results with family members. For instance, a questionnaire administered to oncology patients revealed that most patients (75%) would share hereditary results revealing susceptibility to preventable conditions with family members and 62% would share information regarding unpreventable conditions (Yushak et al., 2016). In addition, participants in the study by Bijlsma et al. (2018) suggested that they would like to receive their genetic results so that they could share them with *"their close family members, with some feeling responsibility towards their children"* (p. 313).

Discussion

This study revealed that the research participants in Botswana generally wanted to receive genetic results, which largely resonates with empirical data from other studies (Bollinger et al., 2012; Coors et al., 2015; Facio et al., 2013; Regier et al., 2015; Yu et al., 2013; Yushak et al., 2016). In this study, we discovered three significant reasons for participants wanting feedback of genetic research results. First, the preference of the participants in receiving feedback of

genetic results changes depending on their context, hence, must be inquired before reporting results. This is evident in our finding wherein most adult participants (parents and caregivers) that have lived with the knowledge of their HIV status for a long time and who experienced the transition from HIV being an 'unactionable' condition to a manageable one, wanted to receive their genetic research results regardless of severity, preventability, and actionability. Whereas adolescents that do not share this experience may have only recently come to terms with the knowledge of their HIV status are more reluctant to receive results relating to severe, non-preventable, and unactionable conditions. Long-term HIV patients may have developed resilience and may better handle challenges, including dealing with unactionable genetic research results.

Second, the participants valued the importance of sharing genetic information with family members. The participants seemed to view their lives to be interconnected with others, especially family members. This view is consistent with the African way of life, which is communal and where there is a strong emphasis on solidarity. The principle of solidarity encourages people and societies to account for the interests of others in their actions (Onuoha, 2007). In this context, individuals demonstrate solidarity with each other by assisting one another or acting in ways that profit others (Metz, 2017). With regard to medical care, solidarity requires that each individual's basic healthcare requirements be satisfied and each individual contribute towards a healthier society (Onuoha, 2007); this was reflected in our participants' interest in sharing their genetic results with family members. Therefore, there may be an increased obligation for researchers to return results of genetic conditions, such as familial kidney disease or breast cancer genes in male participants, which often have implications in other family members.

Third, the participants in our study attributed a lot of power to knowledge. They wanted to know their genetic results for the sake of knowledge. These findings reflect the status and value of knowledge in Botswana culture as depicted in commonly used expressions like "education is a shield," "education is an inheritance that cannot be taken from you" or "knowledge is power," as expressed by some participants. According to Foucault (1977), the expression "knowledge is power" means that "power and knowledge directly imply one another…there is no power relation without the correlative constitution of a field of knowledge, nor any knowledge that does not presuppose and constitute at the same time power relations" (p. 27). Therefore, providing knowledge permits one to act; hence, power is present only in action (Gordon, 1980, p. 248). This raises questions regarding the meaning of returning meaningful knowledge. Drawing on this study, it is considered that knowledge about genetic predispositions is knowledge that emancipates and empowers. In this case, this could mean receiving feedback of genetic results that could explain the cause of a genetic condition that participants may be predisposed to, genetic results for conditions that participants may either prevent or treat, or those that could inform them to prepare for their future. This information could empower participants to make decisions about their lives or help those around them. Consequently, this suggests that the results from all the four aforementioned categories of genetic conditions should be considered for receiving feedback, except those with unknown significance or interpretation. Such results may neither have any importance to participants nor would they be of use to improve health. The desire by participants to receive all the four aforementioned categories of genetic conditions challenges the recommendation of several guidelines to report only genetic results that are clinically actionable (providing dependable information about medical conditions that can be clinically averted or treated) (Knoppers, Zawati, & Senecal, 2015).

Although our findings are similar to those of other studies, they contribute to the literature on preference for wanting feedback of results of genomic research in Botswana and Africa. The emphasis on reciprocity and solidarity expectations for researchers to report genetic results is different from what has been reported previously (Ralefala, Kasule, Wonkam, Matshaba, & de Vries, 2020). In addition, participants' strong desire to receive genetic results could be influenced by Botswana's universal health care system and degree of reliance on the government to provide treatments, which is different from that in the US and other places but similar to Europe.

Conclusion

Participants in genomic studies often have varying preferences as well as reasons for receiving feedback of individual genetic results. Although participants in this study also presented various perspectives surrounding feedback of genetic results, most perspectives suggested that the participants wanted feedback of their genetic information but the kind of information preferred varied based on severity, preventability, and actionability of the results. As a result, there seems to be a stronger case to have actionable genetic results returned to participants, regardless of age, as this information was highly desired. Our findings also reveal that participant' context, relations and empowerment are important aspects to consider in interpreting participants' preferences for wanting feedback of genetic results. During the study, other issues related to the feasibility of feedback of results and cost for the study as well as issues related to the actionability of results were discussed. However, these findings have not been presented in this paper.

Best Practice

There is a need for Africa-specific guidelines for the feedback of individual genetic research results that takes into account the African genetic variation and context (Wonkam & de Vries, 2020). The findings from this study are an initial step toward achieving this goal.

Research Agenda

The mitigation of mistrust between participants and researchers warrants further research that consider the preferences of African participants on the kind of genetic results they want to receive. Further studies examining the views of healthy participants regarding wanting feedback of individual genetic results also need to be conducted. Quantitative studies with larger samples also need to be conducted to investigate participants' preferences and priorities in the feedback of individual genetic results. This will allow for generalization and contribute to the scarce African literature on this topic.

Educational Implication

Findings from this study will be important to research professionals conducting genomic research in Africa. They will provide guidance on why and which individual genetic results must be reported to research participants. This is important in building trust between researchers and participants. Institutional review board members should also be aware of participants' preferences and expectations for receiving feedback of individual genetic results to ensure their consideration in protocols developed for reporting the results of African genomics studies.

CHAPTER 6: PRACTICAL CONSIDERATIONS FOR FEEDBACK OF INDIVIDUAL GENETIC RESULTS

6.1. Title of paper: Participant views on practical considerations for feedback of individual genetic research results: A case study from Botswana

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Abstract

Key to discussions around feedback of individual results from genomics research are practical questions on how such results should be fed back, by who and when. However, there has been virtually no work investigating these practical considerations for feedback of individual genetic results in the context of low-and middle-income countries (LMICs), especially in Africa. Consequently, we conducted deliberative focus group discussions with 6 groups of adolescents (n=44) who previously participated in a genomics study in Botswana as well as 6 groups of parents and caregivers (n=49) of children who participated in the same study. We also conducted in-depth interviews with 6 adolescents and 6 parents or caregivers. Our findings revealed that both adolescents and parents would prefer to receive their individual genetic results in person, with adolescents preferring researchers to provide feedback, while parents preferred doctors who are associated with the study. Both adolescents and parents further expressed that feedback should be supported by counselling but differed on the timing of feedback, with preferences ranging from feedback as quickly as possible to feedback at project

end. In conclusion, decisions on practicalities for feedback of results should be done in account of participants' context and considerations of participants' preferences (word count: 198).

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Candidate's contribution: The candidate contributed to the conceptualisation of this work and the study design. Collected the data and developed the data analysis strategy. Prepared the first draft of the manuscript and sent it to all authors for comments. Incorporated revisions into the manuscript and sent to all authors to read and approve the final manuscript.

Co-author contribution:

All authors contributed to the conceptualisation of this work.

JDV and MK designed the study.

MK and JDV contributed to the development of the data analysis strategy.

All authors commented on the first draft of the manuscript.

All authors read and approved the final manuscript.

JDV, MK and MM supervised the overall work.

Background

Whilst there is a growing body of critical scholarship investigating ethical challenges in African genomics research, the majority of such work focuses on a small number of challenges relating for instance to informed consent (Marshall et al., 2014; Munung et al., 2016; Tindana et al., 2012; Tindana & de Vries, 2016) and community engagement (Folayan, Oyedeji, & Fatusi, 2015; Rotimi et al., 2007; Tindana et al., 2015). However, equally important to ethical deliberations around genomics research are questions on how individual results from genomic studies should be fed back, by who and when. While there is a developing consensus that some research results ought to be fed back, what remains unclear is specifically with whom this obligation lies. Generally, no individual is identified specifically to perform this task (Knoppers, Joly, Simard, & Durocher, 2006).

Most literature on this topic is from high-income countries (HICs). Nonetheless, these studies have generated varying results on delivery preferences for returning different types of genetic and genome sequencing results. With regards to sources of information, previous research on feedback of genetic results has suggested preferences for different types of clinicians. For example, findings from a US-based focus group discussion with some members of the general public, identified that doctors or physicians were mostly preferred, followed by genetic counsellors, and then psychiatrists or therapists (Yu, Crouch, et al., 2014b). Similarly, other studies from the US which specifically address feedback of genetic results have also yielded varied findings, with preferences for results to be returned in-person, via the internet, mail, phone or through a combination of these techniques (Bui, Anderson, Kassem, & McMahon, 2014; Levenseller et al., 2014; Wright et al., 2014; Yu et al., 2013; Yu, Harrell, Jamal, Tabor, & Bamshad, 2014). Few studies have explored patients preferences for when they would like to have their genetic results fed back, although concerns have been raised that patients might

not be emotionally ready to find out about secondary genetic results at an initial disclosure meeting (Kaphingst, Ivanovich, Elrick, et al., 2016).

There has been virtually no work investigating these practical considerations for feedback of individual results from genomics research in the context of low-and middle-income countries (LMICs), particularly in Africa, despite increasing genomic research in these settings. As a result, there is currently no evidence for how individual genetic research results can feasibly be fed back, nor is there practical insight into how participants expect feedback to be given - both of which are essential to the development of a feedback practice in African genomics research. In order to contribute to this discussion, we undertook an empirical study to explore participants' preferences for feedback of individual results in an HIV-TB genomic research project in Botswana. Specifically, we sought to generate an evidence base regarding participants' preferences on how individual results from genomic studies should be fed back, by who and when.

Methods

Ethical Review

Ethics approval for this study was obtained from the Faculty of Health Sciences Health Research Ethics Committee (HREC REF: 010/2019) at the University of Cape Town, the University of Botswana Institutional Review Board (UBR/RES/IRB/BIO/118), the Health Research and Development Committee (HPDME: 13/18/1) of the Ministry of Health and Wellness in Botswana and the Botswana-Baylor Children's Clinical Centre of Excellence IRB. Written assent was obtained from all adolescent participants along with written consent by their parents or caregivers. Parents and caregivers also provided signed informed consent for their own participation in the study.

Study population

This study was conducted in Botswana, an upper middle-income country in Southern Africa, with a Gross Domestic Product per capita of 7080.12 United States Dollars (USD) (Botswana, 2018b). In 2014, the country spent about 5.4 percent of its GDP on health expenditure (WHO, 2016) for an estimated population of over 2 million people. This is reflected by an extensive health-care system across the country including hospitals, clinics, health posts and mobile stops spread across 27 health districts. Health care (inclusive of hospital care, laboratory tests and medications) is provided free-of-charge in public sector facilities for all citizens and almost 95 percent of Botswana's population lives within 8 kilometers of the nearest health facility (Botswana, 2015). Although, private healthcare is also available in Botswana, about 98 percent of all health facilities are operated by the government (Tapera, Moseki, & January, 2018). Nationally, most out-patients services are offered through a network of clinics. In 2009, 66 percent of outpatients were attended in clinics, 21 percent at health posts, 7 percent at hospitals while only 6 percent were attended at primary hospitals. This pattern is in line with the government's policy of promoting the utilization of clinics and health post services before visiting hospitals. As a result clinics and health posts are spread across the country, and are the most accessible of all types of health facilities (Botswana, 2010). As of 2009, Botswana's public healthcare system had a total of 819 professional doctors, 5 816 professional nurses, 52 Social Workers, 13 Social Workers Technicians, and 7 psychologists among other professionals (Botswana, 2010). It is through this system that patients are provided with a comprehensive care and treatment of common problems (Tapera et al., 2018).

Nonetheless, our study was conducted at Botswana-Baylor Children's Clinical Centre of Excellence, which is a public-private partnership between the government of Botswana and Baylor College of Medicine's Baylor International Paediatric AIDS Initiative. Botswana-

Baylor Children' s Clinical Centre of Excellence is a paediatric and adolescent clinic specialising in HIV treatment. As such, it is the main care unit for children, adolescents, and young adults with HIV and has been caring for these patients for almost two decades. The BBCCCE also conducts research, including a genomic study which is part of the Collaborative African Genomics Network (CAfGEN), which studies genes of children and adolescents with HIV and TB, to inform the advancement of new treatments to prevent or supress these infections (BBCCCE, 2020b). It is from the CAfGEN study that our participants were recruited. The CAfGEN study was chosen as a case study because it is one of the few genomic studies being carried out in Botswana and presented an opportunity to explore issues related to feedback of individual results in genomics research. Consequently, adolescents enrolled in the CAfGEN study, who participated in our study, also receive medical care from BBCCCE. In our study, we specifically recruited adolescents aged 15-18 years as well as parents and caregivers of children and adolescents aged 2 – 18 years. We purposively enrolled 93 participants; 44 adolescents who previously participated in the CAfGEN study and 49 parents and caregivers of children and adolescents who participated in the same study.

Data collection procedures

Participants were recruited in person during their visits to the BBCCCE as well as over the telephone where necessary. Recruitment was done by the CAfGEN study nurse and research assistant who briefed participants about our study and relayed those interested to us, for the consent process and enrolment into the study.

In our study, we used deliberative focus group discussions (dFGDs) (Rothwell et al., 2016) and in-depth interviews (IDIs) to explore a wide range of issues relating to the feedback of individual genetic research results including participants' views on how and when they would

like to receive results and by whom. A dFGD manual with detailed instructions was developed to guide the discussions. This was piloted with 2 groups of parents and caregivers, as well as 1 group of adolescents, while the IDI tool was piloted with 3 parents/caregivers and 2 adolescents.

The deliberative focus group discussions method used for this study, is a combination of a traditional FGD method with extended opportunities for learning and discussion, in an effort to allow participants to engage with the topic under discussion in more depth. The dFGD approach used in this study involved an interactive information-sharing session with participants which lasted about 45 – 60 minutes. Case studies elaborating particular ethical considerations in the return of individual genetic results were used for information sharing during the first meeting. This allowed participants to learn about genes, their functions and impact on health. After a short break, this was followed by a discussion to get participants' immediate thoughts about feedback of results from genomics research. This session lasted about 60 – 90 minutes. At the end of this meeting, participants were given an information leaflet covering basic information on genetics as a reference to help them reflect on the information and issues discussed during the meeting. They were later invited for a second dFGD meeting a week later, where their opinions about feedback of findings was interrogated further. This second dFGD took about 30 – 60 minutes. Data was collected until saturation was reached. Data saturation was discussed by DR, MK and JDV. dFGD meetings were held with 12 groups of participants (6 groups of adolescents and 6 groups of parents and caregivers), resulting in 24 dFGD meetings in total. These were complemented with 12 in-depth interviews (6 adolescents and 6 parents/caregivers) with people who had also participated in the dFGDs. The IDIs focused on probing some of the early insights from the study. These were conducted with participants from the dFGDs who either engaged more in the discussions or held uncommon

views, as well as a few others who were less interactive in the dFGDs so as to give them an opportunity to share their views in a more private conversation. However, no strict criteria were used to assess participants' level of engagement in the dFGDs. IDI sessions took 30 – 80 minutes. The dFGDs and IDIs for parents and caregivers were conducted in Setswana using translated tools, while a combination of Setswana and English was used in the dFGDs and IDIs with adolescents. The choice of language for discussions was decided by participants. Data was collected from February 2019 to March 2020.

Participants' demographics

The majority of adolescents (61 percent) in our study were female. Adolescents in our study were aged between 15 – 18 years; with 18 percent aged 15 years, 36 percent aged 16 years, 25 percent aged 17 years, 16 percent were 18 years old, and the rest (5 percent) did not record their age. Most adolescents (93 percent) were either attending or had completed junior school or high school. Half of the adolescents lived in villages surrounding the city of Gaborone where this study was based, 39 percent lived in the city while 11 percent did not report their place of residence. Almost all parents and caregivers (92 percent) were female. One likely reason for this could be that women are usually the primary caregivers in Botswana (Kang'ethe, 2011; 2013; Maundeni et al., 2009) owing to sociocultural and legal factors (Jorosi-Tshiamo, Mogobe, & Mokotedi, 2013). Majority of parents and caregivers (39 percent) were aged between 41 – 50 years and 94 percent had educational qualifications ranging from primary to tertiary education. Similar to the adolescent study population, most parents and caregivers (57 percent) resided in villages surrounding the city of Gaborone while 43 percent lived in the city.

Data analysis procedures

All discussions were audio-recorded, transcribed, translated into English and imported into NVivo qualitative data analysis software Version 12 (QSR International Pty Ltd, 2012) for coding and data analysis. Data was transcribed by a Research Assistant and verified by the primary author (DR), both being native Setswana speakers and proficient in English. We applied both an inductive and deductive approach to coding. The Framework Method for data analysis was used to guide the analysis of the data (Gale et al., 2013). This followed five key stages that are closely aligned with the analytical process of thematic analysis, and which involve: a) familiarisation with the data b) establishing a thematic framework c) indexing d) charting e) data interpretation (J. Ritchie et al., 1994). See Ralefala, Kasule, Wonkam, Matshaba, and de Vries (2020), for more information on the methodological approach used in this study.

Results

When deciding on which results should be returned, a key question relates to practical aspects of how results should be fed back, by whom and when. Decisions in relation to these practical questions impact on the feasibility and cost of returning individual genetic research results – for instance, if the preference is for telephonic consults then this would be more cost-effective than in-person consultations. In this paper, we specifically report on our research participants' preferences for these practical elements of returning results. Although we also discussed other issues, including those related to feasibility of feedback of results and cost for the study as well as actionability of results, these findings have not been presented in this paper.

Participant views on how to feedback and by whom

Our findings revealed that most adolescents expressed that researchers should feedback results because they are the ones who conducted the study and are more knowledgeable about genes and their outcomes. In addition, adolescents described that over the course of their participation in a research project, they developed a relationship with the research team, and they considered that it would make sense for them to receive information about the study from those team members. However, there were also divergent views with some other adolescents recommending that a treating doctor should be the one to feedback results because they know more about the health of the research participant and could give them further information on what to do. Only one adolescent shared a view that a counsellor should feedback results.

By contrast, most parents and caregivers expressed that researchers should relay results to a doctor who would then give them to the participant. Their view was that a doctor is better placed to advise the participant on their condition in light of their medical history and advice on steps or precautions to be taken. Yet in this case also, parents seem to be referring to medical staff who are linked to the study in some way. This is evidenced by the statement below from one of the parents:

"The researcher could tell those that they would have been working with, if it's a doctor so that they inform the participant about the results of the research, the medical staff could be the ones giving back the results because they would know how to handle such cases" (IDI-P005).

Another parent said:

"As the researcher you will give the findings back to the partner you are working with, just like you have partnered with Baylor clinic, so you will give Baylor the findings and they will know how to contact their clients and give them their results" (P4G5).

As seen from above quote, this view seems to be influenced by the setup at Botswana-Baylor Children' s Clinical Centre of Excellence which is a public-private paediatric and adolescent clinic specialising in HIV treatment. As such, it is the main care unit for patients with HIV and has been caring for these patients for almost two decades. Yet the BBCCCE also conducts research, including the CAfGEN study in which (the children of) all of our research participants had participated. In the BBCCCE, adolescent patients are seen regularly by doctors who are often well-acquainted with the participant's medical history. Against that setting, feeding back individual genetic research results through the BBCCCE could make sense. However, patients in the national health care system do not have regular doctors as doctors work on rotation, making it difficult for the suggested arrangement to be feasible. Similarly, other genomic research projects that are not embedded within a clinical care programme also may not have the kind of clinical relationship with patients that would enable the return of individual genetic research results.

In addition to preferring results being shared by the BBCCCE doctor, some parents expressed that feedback of results should rather be done by a team comprising of the researcher, doctor and counsellor, while others shared that this responsibility should be assigned to a counsellor. Only a few parents shared that the researchers should be the ones to feedback. In this context, a researcher was described to participants as a scientist who may not have a medical background, for example a geneticist. This explanation was given to help participants differentiate between doctors and researchers.

All the adolescents expressed that they would prefer to have their genetic results fed back in person (face-to-face), so that they could receive counselling if they need it. They shared that if researchers *"... use any other method, the information could get lost" (A2G3)*. Similarly, parents expressed that they would prefer to be given their results in person so that they could be given counselling.

Although most adolescents initially expressed that results should be fed back by the researchers, they additionally pointed out that there should be further counselling for feedback of results done by a counsellor, with only a few indicating preference for their mother, a social worker or a psychologist. One adolescent emphasised the importance of counselling by saying:

"…I think it would help if participants were sat down and spoken to rather than just giving them their results and have them be on their way. There are good listeners who will benefit from comforting counselling sessions on issues like if I have this gene I shouldn't lose hope…" (IDI-A001).

Other adolescents also expressed that a counselling session could provide an opportunity for them to be given more information about the genetic condition as well as how to take care of themselves so that the genetic condition does not affect them. They also shared that going through counselling could clarify that having a gene does not mean one is already ill, but that there is a possibility of having that condition in future, comfort them and help them accept their condition. When probed about what kind of information participants would need to make sense of individual genetic findings in genomic research, adolescents expressed that they would like to know as much information related to genes as possible. One adolescent shared that

"…researchers should give more information on what a gene is and what it means to have a gene of a certain illness and how to prevent and treat that illness" (IDI-A002). Others indicated that participants should be taught about different genetic illnesses and whether they are preventable or not and that participants should be counselled on how to *"…handle the situation when they receive bad results…* (*IDI-A006)"*, keep a positive mind and not worry much about what is going to happen in their future.

Similar to adolescents, whilst most parents and caregivers think that doctors should do the actual feeding back, there are also many parents and caregivers who think that this should be done in conjunction with counselling support. When asked about who should provide counselling for feedback of results, one parent stated that:

"It will be the counselling team, in most cases people are not trained to be counsellors, even the doctors don't have the counselling skills, they just know the medicine so, that one I would say participants should be taken straight to the trained professionals" (IDI-P004).

One other participant mentioned that a counsellor could help them emotionally while a pastor could help to prepare them spiritually. Parents and caregivers further pointed out that providing counselling as part of the feedback process is very important in helping participants accept their situation. They shared that as part of counselling, participants should be provided with information about the discovered mutation. Parents additionally mentioned the need for pre-counselling to prepare the participants to receive their results, but also highlighted that counselling should be a step-by-step process that should continue after feedback of results so as to guide participants on what they could do to manage the mutation from developing into an illness. One parent suggested that:

"They sit down with me and counsel me about the possible outcomes of the results and that whatever outcome, there could be help, so as to calm my emotions down. I don't think you can be told such results without any counselling. They should tell you that although the study was looking for this and that, we also found some other things that we did not expect. One strategy is to ask the participant how they would receive the results if anything else were to be found in their blood sample..." (P12G5).

In addition, parents were also probed about what kind of information participants would need to make sense of individual genetic findings in genomic research and one parent shared that *"…a lot of information about genes should be given..[…]..you should teach people about the different genetic illnesses so that people don't assume that they are bewitched or whatever" (IDI-P001).* Another shared that in returning results, *"…researchers could start of by teaching people about illnesses that pass from one person to the next in the family due to genes" (IDI-P003).* Additionally, some parents shared that researchers could:

"…cover that genetic studies can unearth some illnesses that you didn't know you had, that way you could have a resolution to the situation, and I would also have that important information that explains that having a certain gene of a particular illness doesn't mean that you have that illness, but it could develop into an illness at the end" (IDI-P005).

Overall, there seemed to be an expectation by both adolescents, parents and caregivers for the research team to make provision for counselling support by the trained professionals, who were mostly identified as counsellors. However, in this context, participants were not probed on whether counsellors would need to be trained in genetics or not.

Participants views on when to feedback

Our findings revealed that adolescents generally would like to receive their results at the end of the study. They reasoned that this would allow researchers ample time to do their investigations. However, others were concerned that delaying feedback may not be ideal as some genetic conditions are life-threatening hence waiting till the end of the study may be too late. To resolve this, one adolescent suggested that *"if the results are not that life threatening you can wait before telling her, if the results are very risky then the researchers should tell the participant right away" (A2G6)*. On the contrary, most parents would prefer to be given results as early as possible and not to wait for the study to be completed. Their concern was that waiting for the completion of the study would be too late and that timely feedback could enable them to look for the necessary help, should there be any. Nonetheless, one parent shared that *"researchers shouldn't be rushed because their job is complex; they should be left to do their job thoroughly, even if it takes them 3 years" (P2G6)*. This view was shared by other parents. Similar to adolescents' discussions, these conflicting views were mediated by one parent who suggested that:

"... it will depend on the kind of the illness, if it is an illness that requires immediate attention then they should let you know in a timely manner, but if it is something that you can live with and have it not affect you, then they should continue with their study and give results at the end".

Discussion

Our study revealed that almost all the adolescents and parents would prefer to have their results fed back in person. This is consistent with views expressed by participants in Kaphingst,

Ivanovich, Elrick, et al. (2016) and O'Daniel and Haga (2011). Participants shared that a face-to-face feedback meeting provides an opportunity for counselling. Whilst most adolescents in our study would prefer to have these results fed back by researchers, parents would rather have researchers work with doctors to relay the results to participants. This is because they thought that doctors are better placed to advise participants on their condition, taking note of their medical history, and providing guidance on risk management and follow-up steps. Such views were also expressed by some participants in Yu et al (2014b) who would prefer to have their results fed back by healthcare providers, so that they could assist them to understand results in consideration of their current health status and by offering counselling support. Additionally, a majority (42%) of participants in O'Daniel and Haga (2011) also chose to learn their results from their physician.

In our study, the parents did not seem to refer to a family physician, but rather to doctors associated with the clinical programme at BBCCCE. At this centre, patients have regular doctors who are well-acquainted with their patients' medical history. This is not the case in the national health care system, especially in main hospitals where doctors rotate and where electronic health records are not used consistently, making it difficult for doctors to be well acquainted with their patients' medical background. This was also identified as a limitation for most African settings by Wonkam and de Vries (2020).

Although participants indicated wanting results fed back by researchers or medical staff, both adolescents and parents expressed that feedback should be supported by counselling. Counselling is expected to provide participants with background genetic information to help participants understand their situation as well as information that could help them cope. This is in line with a recommendation by O'Daniel and Haga (2011), who shared that the feedback

of these results could imitate a genetic counselling session involving an overview of genetics as well as the specifics of the study and limitations for interpreting the results. Again, the feasibility of implementing this through the national health care system in Botswana is questionable due to lack of genetic counsellors in the country. Although most major hospitals in Botswana' would normally have a psychologist or a social worker or both depending on the size of the hospital, they are not usually trained in genetics counselling. This is true even in a setup like BBCCCE where there are both a counsellor and a clinical psychologist whom patients may be referred to. As a result, projects intending to feedback genetic research results may need to work with these professionals and train them in the basic principles of genetics as well as the complexities of genetic results for them to provide meaningful feedback to participants. Elsewhere, it has been suggested that nurses could also be trained to provide basic genetic counselling in addition to their current roles (Barr et al., 2018; Nembaware, African Genomic Medicine Training, & Mulder, 2019). This is because nurses are usually at the forefront of many healthcare settings in Africa and often have comprehensive information about patients, families, as well as communities (Prows, Glass, Nicol, Skirton, & Williams, 2005). Nonetheless, where taking advantage of available professionals to provide genetic counselling is not possible due to limited resources in the public healthcare system, researchers may need to make arrangements to provide such services through budgeting to employ a counsellor who will be trained to assist with the return of results at project end. In this case, the obligation for researchers to provide ancillary care to participants in the form of counselling support, may be stronger. According to Richardson (2008), in doing research, researchers often take on some responsibility with regard to the health of research participants as a result of having entered into a researcher-participant relationship. The nature of this relationship is such that researchers have ancillary care obligations for findings that are related to the health condition being studied. As further highlighted by Richardson and Belsky (2004a), this

obligation may be strengthened by participants' degree of vulnerability and the extent to which the duty to rescue reinforces these grounds.

Lastly, our findings revealed that both adolescents and parents described preferences for the timing of feedback, ranging from feedback as soon as possible to feedback at project end. Most adolescents were more inclined to having feedback of results at the end of the study as compared to parents who preferred to have results fed back as soon as possible. Participants who preferred to have results fed back immediately argued that waiting for the completion of the study could be too late for certain serious and urgent genetic conditions that might need immediate action. These views are consistent with findings from the study by (Kaphingst, Ivanovich, Elrick, et al., 2016) which revealed that many participants preferred to receive their sequencing results within the shortest time possible. While a few suggested for feedback of results to be staged, to provide immediate feedback for results that need urgent attention only, and have the rest fed back at the end of the study. According to participants in Yu et al (2014a), prioritizing and staging return of results could help in avoiding information overload.

Conclusions

In conclusion, our participants preferred that feedback of individual genetic results should be done in person. Decisions about who to feedback and counsel participants are project-dependent and should be done in account of study setting. For example, in settings like BBCCCE it might be feasible for the study team to relay participants' results to treating doctors in the same centre to feedback to participants, while also organising a counsellor for counselling if necessary. However, in cases where a study is done in a public facility with limited resources, that could be difficult to implement. Consequently, researchers may have to take up the responsibility of feeding back individual results as well as providing genetic

counselling in such settings. To make these decisions, researchers should familiarise themselves with their research settings up-front and engage with relevant stakeholders so as to make informed decisions regarding the feasibility and acceptability of their approach to feedback of results. Our participants also suggested that staggered feedback could be considered, where results that require urgent follow-up are fed back as soon as possible while others are fed back when the project ends.

CHAPTER 7: IMPORTANT CONSIDERATIONS FOR INFORMED CONSENT IN FEEDBACK OF INDIVIDUAL GENETIC RESULTS

7.1. Title of paper: Should feedback of individual results be integrated into the consent process in African genomics? Participants' views from an HIV-TB genomics research project in Botswana.

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Abstract

Background: Whilst informed consent is a key component of considering whether individual genomic research results could or should be fed back to research participants, little is known about the views of African research participants on its role.

Methods: We carried out a qualitative study to explore views of adolescents and parents or caregivers regarding informed consent for feedback of individual results from a genomics research project in Botswana. We conducted 24 deliberative focus group discussions with 93 participants (44 adolescents and 49 parents or caregivers) and 12 in-depth interviews (6 adolescents and 6 parents).

Results: Our findings revealed that most participants would like to be informed about the possibility of discovering individual genetic results during the consent process and that consent be obtained for feedback during the enrolment process. They further expressed that in cases where prior consent to feedback was not obtained, then participants should be re-contacted

where life-saving genetic information is discovered. Participants emphasized the need for researchers to ensure that participants' decisions regarding feedback of results are well-informed. Autonomy, transparency, and communication were identified as key values to uphold during the consent process.

Conclusion: In conclusion, obtaining participants' consent for feedback of results is important to ensure that their rights and wellbeing are protected in research. This is critical in building trust relationships between participants and researchers.

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Candidate's contribution: The candidate contributed to the conceptualisation of this work the study design. Collected the data developed the data analysis strategy. Prepared the first draft of the manuscript. Incorporated revisions and sent to co-authors to read and approve the final manuscript.

Co-author contribution:

All the authors contributed to the conceptualisation of this work.

JDV and MK contributed to the design of the study and development of the data analysis strategy.

JDV, MK, MM and AW commented on the first draft of the manuscript.

All the authors read and approved the final manuscript.

JDV, MK and MM supervised the overall work.

Introduction

Amidst a growing consensus in the research community that some individual genomic research results ought to be fed back, is growing emphasis on the importance of incorporating the possibility of feedback in the consent process. Yet the call to integrate information about the feedback of results in consent is set against concerns about the complexity of consent for genomics research and whether people effectively understand all elements of such research (Tindana & de Vries, 2016). Elements that would need to be effectively conveyed in the consent process is that most genetic information present risks not certainties, that a single gene has the ability to influence multiple traits or conditions and variants can have opposite effects. In addition, genetic variants may be reclassified or gain (or lose) significance (Bredenoord, Onland-Moret, et al., 2011). As a result, Rotimi and Marshall (2010) pointed out that uncertainties associated with the clinical relevance of genetic results has led to many genomic research projects conducted in the past not to feedback results to participants. This was also true for most projects in the Human Heredity for Health in Africa (H3Africa) consortium in 2016, which did not seek explicit consent for the return of results (Munung et al., 2016). However, this position is becoming more difficult to justify as many genomics studies are now likely to discover genetic information that is clinically relevant (Kengne Kamga et al., 2020; Rotimi & Marshall, 2010; Wonkam & de Vries, 2020). Many authors also now argue in favour of feedback of genetic results to participants. Affleck (2009)) reasons that participants should decide for themselves whether they would like to take up risks that come with knowing their results, and that where participants attach personal value to results, they should be fed back out of respect for their autonomy. This view is supported by Budin-Ljøsne (2012) who indicated that participants have a right to know their health information regardless of its utility. Other key values that are discussed in this literature are respect, charity, mutuality, and reciprocity (Solberg, 2012) as well as duty to rescue (Sullivan & Berkman, 2018).

Therefore, it is important that this issue be attended to, and participants views be accounted for, to ensure that their rights and wellbeing are protected in research. This is particularly important as many studies have revealed that participants would like their individual genetic research results to be fed back (Christensen et al., 2017; C. V. Fernandez et al., 2009; Sanderson et al., 2016; Shahmirzadi et al., 2014). Since the ultimate decision about whether to receive individual genetic research results rests with the participant, this suggests that some type of informed consent process will be needed for these decisions (Appelbaum et al., 2015). Even so, feedback of genetic research results to participants requires customised consent documents that sensibly accounts for ethical and social obligations to participants as well as those related to them (Rotimi & Marshall, 2010).

Our Africa-based study team was particularly interested in understanding how African genomics research participants view these issues. Specifically, we were interested to know a) whether or not to obtain consent for feedback of results and why, b) do participants have a right to know or not to know their genetic results? c) what should happen if consent was not initially obtained and d) what should happen when a preventable life-threatening gene is discovered for a participant who initially indicated not wanting to receive results. We carried out a qualitative study to explore views of adolescents and parents or caregivers regarding informed consent process for feedback of individual results from a genomics research project in Botswana.

Methods

In this qualitative study, we purposively selected 93 participants: 44 adolescents who had previously participated in an HIV-TB genomics study in Botswana and 49 parents and caregivers of children and adolescents who participated in the same study, which is a part of

the Collaborative African Genomics Network (CAfGEN). We decided to link our study to this larger genomic study mainly because genomics research is relatively new in Botswana and most people would likely not be very familiar with genomics concepts. The CAfGEN study had a quite extensive community engagement process in place, coupled with a robust consent process. This sensitized participants in the CAfGEN study to key concepts of genomics research. It also gave them a more direct interest in questions relating to what should be done with individual genetic research results. For these reasons, we specifically recruited participants who had enrolled in CAfGEN. For the purpose of this study, we recruited adolescents aged 15 – 18 years, involved in the CAfGEN study, as well as parents and caregivers of children involved in the same study, aged 2 – 18 years.

We used deliberative focus group discussions (dFGDs) (Rothwell et al., 2016) and in-depth interviews (IDIs) to explore a broad range of issues relating to the return of individual genetic research results including participants' views regarding the consent process. A dFGD manual developed for this study was piloted with 2 groups of parents and caregivers and 1 group of adolescents, while the IDI tool was piloted with 3 parents/caregivers and 2 adolescents. The dFGDs and IDIs for parents and caregivers were conducted in Setswana using translated tools, while a combination of Setswana and English was used in the dFGDs and IDIs with adolescents. The data was collected from February 2019 to March 2020.

Deliberative focus group discussions involve a combination of the conventional FGD methodology with expanded opportunities for learning and discussion, in an effort to enable participants to engage with the research topic in greater depth. The dFGD technique adopted for this study involved holding two dFGD meetings with each group of participants a week apart. The initial dFGD meeting involved an interactive information-sharing session with

participants. Case studies elaborating particular ethical considerations in the return of individual genetic results were used for information sharing during the first meeting. This allowed participants to learn about genes, their functions and impact on health. This information session took about 45 - 60 minutes. Participants were then given a 30 minutes break which was followed by a dFGD to get participants' initial or immediate thoughts about feedback of findings from genomics research. This dFGD took about 60 – 90 minutes. Overall, the first session of the dFGD took about 3 hours. Participants were then provided with information covering a summary of the content that was discussed in the workshop to take home to be used as a reference to help participants reflect on or revisit the information and questions interrogated during the first session. They were then invited for a second dFGD meeting a week later, where their opinions about feedback of findings was interrogated further. This second dFGD took about 30 – 60 minutes.

DFGD meetings were held with 12 groups of participants (6 groups of adolescents and 6 groups of parents and caregivers), resulting in 24 dFGD meetings in total. The initial dFGD meetings for parents and caregivers comprised of about 4 – 11 participants, while adolescents initial dFGDs meetings were attended by about 5 – 12 participants. Overall, 34 adolescents and 38 parents and caregivers were retained to participate in the follow-up dFGD meetings. The other 21 participants (10 adolescents and 11 parents and caregivers) had competing interests and were unable to attend the follow-up dFGD meetings. For these follow-up meetings, parents and caregivers' groups varied from 4 to 8 participants, and from 2 to 11 for adolescents. The dFGDs were complemented with 12 in-depth interviews (6 adolescents and 6 parents/caregivers) with people who had also participated in the dFGDs. The IDIs focused on clarifying and probing further some of the early insights from the study. These were conducted with participants from the dFGDs who either engaged more in the discussions or held uncommon views, as well as a

few others who were less interactive in the dFGDs so as to give them an opportunity to share their views in a more private conversation. However, no strict criteria were used to assess participants' level of engagement in the dFGDs. IDI sessions took 30 – 80 minutes (for more details on the methodology, see Ralefala et al. (2020).

All discussions were audio-recorded, transcribed, translated into English and imported into NVivo qualitative data analysis software (QSR International Pty Ltd. Version 12, 2018) for coding and data analysis. The Framework Method for data analysis was used to analyse the qualitative data resulting from this study (Gale et al., 2013). This method involves producing a matrix in which summarised data are displayed in rows (cases) and columns (codes) to create a layout in which data can be systematically presented and analysed both by theme and by participant or event. This process involves five key phases which are similar to the analytical process of thematic analysis, which are: (a) familiarisation with the data (b) establishing a thematic framework (c) indexing (d) charting and (e) mapping and interpretation of data (J. Ritchie et al., 1994).

Ethical Review

This study was reviewed and approved for ethics compliance by Institutional Review Boards in South Africa and Botswana. Written assent was provided for by all adolescent participants and permission by their parents or caregivers. Parents and caregivers also provided signed informed consent for study participation.

Results

Demographic data was collected from the study population including gender, age, educational level and residential location. Most adolescents (61 percent) in our study were female.

Adolescents' age ranged from 15-18 years, with most of them aged 16-17 years (61%), consequently most of them (70%) were either in junior secondary school or had completed, while 23 percent were either in senior secondary school or had completed. Half of the adolescents resided in villages nearby the city of Gaborone where this research was conducted, 39 percent resided in the city, while 11 percent did not indicate their place of residence. An overwhelming majority of parents and caregivers in our study were female (92 percent). One possible explanation for this could be that women are normally the main caregivers in Botswana (Kang'ethe, 2011; Kang'ethe, 2013; Maundeni et al., 2009), owing to social, cultural and legal factors (Jorosi-Tshiamo et al., 2013). A significant number of parents and caregivers (39 percent) were between 41 – 50 years of age and 94 percent had educational qualifications varying from primary to tertiary education. Like the adolescent population, most parents and caregivers (57 percent) resided in villages nearby the city and 43 percent resided in the city of Gaborone.

Our data revealed a range of important themes regarding the return of individual genetic research results, including (for instance) the importance of reciprocity in guiding expectations of feedback, the reasons why our participants overwhelmingly wanted to receive results and practical considerations around the return of results. These findings were the subject of other manuscripts submitted for publication elsewhere. This paper specifically focuses on exploring participants' views on the role of the consent process in the feedback process.

Prior consent for feedback of results

Our findings revealed that most adolescents expressed that it is important to obtain their informed consent regarding possible individual genetic results at enrolment, so that they could know their options and stay mentally prepared for whatever will be revealed by the genetic test. However, a few expressed that being informed about the possibility of finding individual

genetic results upfront may not be ideal as it could cause emotional anxiety. People of this view indicated that it may be better to discuss and obtain consent from the participant for feedback of results when they are available. Most parents also emphasized the need to be told about the possibility of discovering individual genetic results at the beginning of the study and having their consent obtained for feedback. One parent said:

"I think before I take part in the study, everything should be explained to me before any tests as you have explained these pamphlets to us. They should let me know of the possible results that might come up, so maybe I have positive results I would have already counselled myself and that I can prepare myself for any results that may come up, that way it becomes easy for me to receive the results because I have already been taught at the beginning. I would be ready for anything, negative or positive results, that way it becomes easy, when the doctor releases the results, I will tell him that I accept any result, this will make me not to collapse so being taught first is important to ready my heart" (P7G4).

Transparency in consent for feedback of results

In addition, both adolescents and parents also emphasized the importance of transparency in research. Adolescents shared that it is important for researchers to clearly inform them about the possibility of finding incidental results instead of providing information about the disease under study only. They worried that if there is no transparency in the consent process then participants could later interpret the discovery of incidental results to think that researchers have gone overboard to test them for other things to pursue a different research agenda. Others pointed out that some participants may not receive results well if they were not initially informed about the possibility of discovering incidental results. Likewise, parents also emphasised the importance of transparency between researchers and participants and shared that researchers should tell them all the information they need to know to make informed

decisions so that they could prepare themselves on what might come out. To highlight the importance of transparency in the consent process, one parent had this to say:

"…imagine we are 10 and none of us was told anything, what would you do as the researcher when you find a condition that you didn't expect? Will you hide it? If you are going to share it, how will you share it without having notified any of us who could be affected?" (P11G5).

The above view was also supported by other participants who also emphasised that "it is wrong for researchers to withhold information from participants".

Nonetheless, some participants observed that there could be limitations to informed consent in genomics research. One parent shared that genomics research is wide and complex and that researchers may not always be able to predict upfront what they may discover hence may not be able to inform the participants of what is expected at the beginning of the study but emphasized that what is key is for participants to be counselled when results become available so that they can decide whether to receive them or not.

"I think research is not as straightforward as it seems; however, if I take it in good faith then we shouldn't be worried that we were not told of the possibilities of extra results. Genomics studies are complex and it's difficult to focus on one thing. When you are looking at genes in a blood sample, you are looking at a vast sample, there are many different illnesses that can be found in the blood like cancer and many other different illnesses, so it could be difficult for them to explain it. Unless we did not understand what a genomics study entails, but if it has been explained like the way it has been explained to us and we understand it then we should expect anything. But as the ladies have mentioned, it is important however that there be counselling at a time when one is told about results that were not expected, to try and help her receive the unexpected results and avoid extreme reactions. What I know about genomics is

that it is a wide net, if it was a particular condition maybe that's when I will worry that one has gone overboard without telling me" (P11G5).

Recontacting participants for feedback of results

Additionally, adolescents expressed that in cases where prior consent to feedback individual genetic results was not obtained, researchers should re-contact the participant to get consent to feedback when information is discovered about genetic risk for a preventable harmful condition, because the participant could benefit from receiving that information. Similarly, most parents also pointed out that should such information be found, then the participant should be recontacted to get their consent on whether or not to feedback the result because doing so might save the participant's life. But one parent shared that:

"… I always consider the person's life as the key issue. The information available is for the quality of the participant's life that is why I say that irrespective of the consent, one needs to know because knowledge is power, having consented or not at the end you will say because I value the participant's life just as I value that which you have given me for me to get these findings and on top of my findings I have seen that you are under threat. Really those who want to consent are those who are saying we hear that South Africa has launched missiles but keep quiet or somebody hears about the elephants at the cattle post, they keep quiet while you go out and look for your goats, really you need the information" (IDI-P004).

Participants also expressed that even in cases where a participant had indicated that they would not want to receive their results, when a harmful variant for a preventable condition is discovered, then the participant should be re-contacted to check if they would reconsider their decision to feedback. They noted that "…this finding might not have been expected …" (P12G5) or "…maybe when they signed the agreement, they did not have enough information

or didn't think it through" (IDI-A002). They emphasised that researchers have an obligation to warn the participant. One parent said, "to me, this issue is about ethical considerations, we are human. I don't think someone would just sit on information that could potentially save a life" (P11G5).

Information-sharing and effective communication

Parents and caregivers also noted that some participants may refuse to receive results because they are scared or that they are not well informed. As a result, they pointed out that it is important for researchers to establish why an individual would not want to know their results, and that such individuals should be provided with information about the pros and cons of knowing their results so that they could make informed decisions. See a quote below from one of the parents:

"This is why I was saying that you could label those who want to know the results and those who don't want to know the results, then you could ask why they don't want to know the results and tell them the benefits of knowing their results and that you can take action but if you don't know your results then you won't have information [...] For those who don't want their results then you should find out why they don't want their results, how they are feeling and why they feel that way and give them the benefits and risks of knowing the information and not knowing the information" (PIDI-P002).

The importance of communication in the consent process for feedback of genetic results was also emphasised. One parent expressed that:

"...what is important is communication, in that case you have to call me again and revisit the issue of returning the results with me, make me aware of the implications of the study and what

was found in relation to my health, because it is important for me to know since I am going to live with that condition or could get it addressed. I don't think I will reject the results if you tell me that I have a cancer gene even if I had said I shouldn't be given the results, because it is important for me to know so that I can prevent it or take care of myself. So, it is important to make me aware" (P4G5).

Right to know or not to know

Inherent to a drive to include a discussion about feedback of results in the consent process is a question about whether people have a right to know or not to know, particularly for harmful, preventable conditions. As a result, we engaged participants on these discussions and found that most adolescents believed that they have a right to know their individual genetic results because these results could affect their lives and receiving results could empower them to act towards their health. Similarly, parents and caregivers shared that it is their right to know their results because researchers used their blood. As a result, they should know any health information that researchers have about them, so that they could take care of themselves. Others limited their right to know to genetic conditions that are actionable or those that are life-threatening. However, one parent expressed that their right to know applies only if there was prior agreement to feedback or if the discovered gene is related to the disease under study.

When asked on whether participants have a right not to know, many adolescents expressed that they do not have a right not to know as receiving genetic information could be lifesaving. This view was also expressed when participants were asked whether they have a right to change their mind and decide not to receive results after having signed a consent form indicating their desire for feedback. In this case they reasoned that having signed a consent form could have encouraged researchers to go an extra mile to look for help for them before delivering the

results hence participants seemed to view changing their mind as not being considerate or appreciative of the researchers' efforts. Participants' views on this issue could be influenced by the Setswana culture where being courteous is considered an indication of good manners. A refusal to receive results or to withdraw from disclosure of results may be viewed as being rude and is something that most participants may not feel comfortable to do. This is grounded in the African philosophy of Ubuntu which requires members of the community to treat other people with kindness, compassion, respect and care (Murove, 2012). Nonetheless, other adolescents pointed out that their right not to know exists even where consent to feedback was initially given and that participants have the right to change their minds. They also shared that their right not to know is especially relevant if there is no help for the participant. Likewise, most parents and caregivers expressed that participants do not have a right not to know genetic information that could be lifesaving. One parent expressed that "a person who refuses to receive results doesn't have responsibility towards themselves (P4G3)". Their reasoning seems to have been influenced by their HIV experience as demonstrated by this expression from one of the parents; "I don't think if you have accepted your HIV status you could be scared to receive any results at this point (P3G3)". They shared that it is through knowing their HIV results that they were able to get treatment for themselves and their children, and now they are doing well. Some participants also felt that refusal to receive feedback of individual genetic results is not right as not only the participant's life may be in danger, but those of their family members too. They also noted that refusal of participants to receive the results could be "…tough on the researchers as [they would] have seen the results and believe that the participant needs to know, but if he or she had said no, then [researchers] cannot force them..."(IDI-P002). They suggested that researchers should put an effort to ensure that participants are making informed decisions on whether or not to receive their genetic results. Nonetheless, some parents maintained that participants do have the right not to know even if a consent to feedback was provided and trying

to force results on those who have expressed that they do not want to know could attract lawsuits against the research team.

Discussion

Our findings revealed that most participants would like to be informed about the possibility of discovering individual genetic results during the consent process and that consent be obtained regarding whether to feedback results before enrolling in genomics research or not. This desire to be informed and to be given an opportunity to decide on feedback of results is consistent with the principle of autonomy which states that participants have a right to self-determination, to decide what should happen to their bodies, samples or information about them (CIOMS, 2002).

Participants also expressed that there should be transparency in research and that it is generally wrong for researchers to withhold information from participants. They further expressed that in cases where prior consent to feedback was not obtained, then participants should be re-contacted when life-saving genetic information is discovered. Re-contacting participants with lifesaving information was recommended even where a participant had initially indicated not to receive results. Similarly, participants in Appelbaum et al. (2014) supported having consent for potential re-contact obtained in the initial informed consent. Our participants argued that sometimes participants may have been ill-informed at the time of making a decision not to receive results and that participants could also change their minds over time. This suggests that our participants seemed to view consent as an ongoing process and not a one-time event. This view is consistent with the CIOMS guidelines which states that, "obtaining informed consent is a process that is begun when initial contact is made with a prospective subject and continues throughout the course of the study" (p. 33). These guidelines further state that investigators in

long-term studies should periodically seek informed consent from their study participants (CIOMS, 2002). In this case, researchers could make provision for re-consenting participants for feedback of results as the study progresses and not necessarily only when a preventable, life-threatening gene is discovered as suggested by our participants, but this can be done for all study participants at certain intervals as determined by the study team. This will provide an opportunity for participants to reflect on their previous decisions and allow those who would like to change their mind about previous choices to do so. This is particularly important in feedback of findings from genomics research where it might be impossible for researchers to anticipate which results will be found because of the complexity of genomic studies (Horton & Lucassen, 2019).

Participants' strong desire to be re-contacted with lifesaving information seems to be founded on the principle of duty to rescue and could be influenced by participants' HIV experience where knowledge of their HIV status has empowered them to get relevant help and survive the HIV virus. This finding is consistent with observations by Bredenoord, Onland-Moret, et al. (2011), who shared that there is often a strong case for researchers to feedback life-saving genetic information of immediate clinical utility. According to Bovenberg, Meulenkamp, Smets, and Gevers (2009), this obligation cannot easily be overruled by other moral considerations—except, for example, when the participant has expressed a prior wish not to be informed. Similarly, while our participants generally wanted to be re-contacted with lifesaving genetic information, some of them cautioned that re-contacting participants who had initially indicated that they would not want to receive results should be handled with sensitivity and that counselling should be used when returning results.

In addition, participants pointed out that researchers should ensure that participants' decisions regarding feedback of results are well-informed as some genetic information may be lifesaving. This view resonates with the H3Africa recommendations for feedback which describe that in cases where participants are given an opportunity to decide on their preferences for feedback, researchers need to make sure that participants are accurately informed about the possible information they may or may not receive, and how that information would affect their lives. If participants are not properly informed, they would make misinformed decisions which could have real consequences for their lives and wellbeing in future (H3Africa, 2018).

The importance of providing participants with information is also identified as a critical component of the informed consent process by international guidelines including The Belmont Report (*National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.*, 1979) and the CIOMS guidelines (2002). According to these guidelines, participants should be provided with pertinent information that could empower them to make an informed decision regarding their participation in research. Therefore, providing participants with information about the possibility of discovering genetic information as well as its possible implications could empower them to decide whether they would want to receive such results or not. This approach is also preferred by Bredenoord, Onland-Moret, et al. (2011) who expressed that there should be an effort by the researcher (or another professional) to help participants understand genetic information as this will enable them to express their preferences regarding feedback of results. Although our study did not discuss what sort of information participants would like to be provided with during the consent process, a study by Appelbaum et al. (2014) found that researchers and participants alike embraced disclosure of a wide range of benefits, risks, and ancillary information, including potential impact on family members, protections for confidentiality, and how genetic results will be dealt with in the event of death

or incapacity. The H3Africa guidelines also emphasise that value and validity of results should be well articulated to participants during the consent process as well as participants' right to decline receiving their results (H3Africa, 2018).

Furthermore, our participants also emphasized the importance of effective communication in handling consent issues. Kohane and Taylor (2010), also highlighted that effective communication between researchers and participants is imperative in understanding participants' preferences and the significance of results. They further advocated for an approach in which participants' ability to process appropriately communicated, complex, contingent information, is respected, rather than assuming that they will be unable to understand genomic complexities that are actually less intellectually taxing than some other issues they might encounter in clinical care (Kohane & Taylor, 2010).

Conclusion

In conclusion, obtaining participants' informed consent for feedback of results is important to ensure that their rights and wellbeing are protected in research. Therefore, this could mean that African genomics researchers should inform participants about the possibility of discovering individual genetic results in research and make provision for participants to decide whether they would like to receive such results or not. This could be done using a tiered consent model, where separate informed consent forms are developed for participants to consent, first for study participation and then for feedback of results. Doing this in stages, could address concerns about overloading participants with too many decisions to make during the consent process and create an opportunity for participants to be provided with relevant information that could empower them to make informed decisions. Autonomy, transparency and communication were

identified as key values to uphold during the consent process. This is critical in building trust relationships between participants and researchers.

CHAPTER 8: DISCUSSION AND CONCLUSIONS

8.1. Discussion

The advancement of genomics research has brought about ethical dilemmas relating to the feedback of individual genetic findings. While there is now a considerable evidence base to support the formulation of suitable policies and guidelines in HICs, hardly any evidence exists to help African genomics researchers understand how to approach individual genetic findings in their work. It is for this reason that I conducted this qualitative study to explore views and expectations of adolescents, parents and caregivers of children and adolescents enrolled in a genomic study in Botswana, regarding feedback of individual genetic results. The broad aim was to help contribute towards an evidence-informed guidance framework that could be used by future researchers and research ethics committees in making decisions about feedback of results in genomics research in Botswana specifically, and in other African countries more broadly.

In this study, I specifically asked participants for their views on whether or not individual genetic results should be fed back, which ones and why. I also explored participants' views on practical considerations and inquired on how to feedback, when to feedback and who should feedback. Issues of consent were also discussed with participants, including whether or not participants' consent should be obtained prior to feedback and what should happen in cases where a potentially harmful variant is discovered while prior consent to feedback was not obtained.

This study used deliberative focus group discussions and in-depth interviews to explore these questions with participants. In the previous chapters, the study results were presented and discussed in line with the objectives of the thesis. In this chapter, I present key insights

generated in the course of this study that inform on feedback of findings in genomics research in Botswana.

Important values for consideration in feedback of individual genetic results in Botswana genomics research

Almost all participants in this study agreed that providing feedback of individual genetic findings would be an effective way for researchers to demonstrate their appreciation for participants' contribution to research. These expectations appear to be underpinned by African values of solidarity and reciprocity, which are rooted in the African philosophy of Ubuntu (Mufune, 2003) or Botho, as commonly referred in Setswana. While there are descriptions of reciprocity and solidarity in the literature about feedback of findings in genomics research, this issue is often briefly discussed and not contextualised to the African setting (Bredenoord, Kroes, et al., 2011; Bredenoord, Onland-Moret, et al., 2011; Kerasidou, 2015).

Richardson and Cho (2012) describe reciprocity as a characteristic of interactions in which burdens and benefits are exchanged. Bredenoord and colleagues (Bredenoord, Kroes, et al., 2011; Bredenoord, Onland-Moret, et al., 2011) indicate that while participants usually take part in research for altruistic or other motives, they may expect a reward, such as receiving their individual genetic findings. In general, reciprocity appears to be discussed in this literature simply as a means of acknowledging research participants or expressing appreciation for their involvement in the study. Notably, in this literature, the decision to appreciate participants appear to be solely that of researchers. This is in contrast with accounts of reciprocity presented in this work, in which reciprocity is viewed not just as a moral responsibility but also as a basic social norm whose violation has consequences. For example, participants in this study voiced concern that researchers' inability to reciprocate may dissuade

them from participating in future studies. Participants considered themselves as members of a team with researchers, assisting one another in achieving the ultimate objective of promoting good health.

The principle of solidarity requires members of a team to watch out for each other's needs and act in ways that might be beneficial to each other (Metz, 2017). Consequently, given that participants contributed to the advancement of researchers' knowledge, it would be appropriate for researchers to also contribute to advancement of participants' knowledge by providing them with their individual genetic results. This finding differs slightly from Richardson's ancillary care model and is more in line with the solidarity and reciprocity argument advanced by Ubuntu philosophy. As Metz (2017) notes, the type of relationship presented in Richardson's ancillary care model results from research participants having entrusted researchers with their bodies and information; thus, this "reduced privacy or compromised autonomy" (p.121) compels researchers to provide support to participants. Consequently, the type of support that researchers can offer participants is limited to the condition under study, and may exclude additional conditions that participants might have, even if the researcher was aware of them before the conduct of the study (Metz, 2017).

On the contrary, solidarity and reciprocity argument advanced in this study are not only relational but also communal. According to Metz (2017), once a researcher interacts with participants and shares into their way of life, they constitute a morally significant relationship that needs to be respected and, requires complete awareness that their wellbeing would need to be cared for as well. Therefore, this appeal to communion may have a considerably broader reach as compared to the entrustment model, in which the obligation to assist is triggered by the revelation of private information (Metz, 2017). Participants in our study expressed less

concern about ancillary care obligations, but articulated their expectations in terms of reciprocity obligations, which compel researchers to reciprocate the value of their research participation in kind. For example, many participants did not regard financial rewards other than reimbursement for transportation and food as acceptable forms of reciprocation.

Importantly, they believed that if their engagement in research has aided researchers in improving knowledge, researchers should reciprocate by assisting them in improving their own knowledge. This would foster a reciprocal interaction between researchers and participants, therefore strengthening their relationship. Participants in my study further shared that receiving their individual genetic findings would reassure them that their contribution was appreciated and valued by the research team. Thus, reciprocating to participants in this manner would strengthen the relationship between researchers and participants and encourage participants to take part in future studies. This could ultimately lead to participants trusting more in science and not see it as an exploitative endeavour but rather a reciprocal, respectful and beneficial relationship.

It is imperative to note that the principles of reciprocity and solidarity in the African research context are not new to African populations, but they have perhaps not been taken seriously before in research ethics. These principles are grounded in the Ubuntu philosophy, which pre-exists the colonial era and has been prominent across a large geographical area in the Sub-Saharan Africa for a long time (Cilliers, 2008; Komparic, 2015; Metz, 2010). These principles dictate duties which could be elevated to the status similar to that given to the notion of rights in the global North (Gyekye, 2011) and should be taken more seriously.

In this thesis, I have demonstrated that solidarity and reciprocity are important in Botswana society and manifest in empirical work as a request to return individual genetic results. Secondly, I have described that there are existing arguments linking reciprocity and solidarity to the return of individual genetic results. Taking these two observations together, I recommend that in order to honour reciprocity obligations, African genomics research do have an a priori ethical obligation to return at least some individual genetic results.

Preferences of Botswana participants and reasons for wanting feedback of individual genetic results

Chapter 5 reported on participants' views on which results to feedback as well as reasons for feedback. It showed that participants value receiving feedback about their results and believed that doing so would help them know about their health status and accept their health condition. They expressed that receiving genetic results would empower them to make informed decisions about their health, for instance: changing lifestyles to prevent the condition where necessary, looking for help and treatment or prepare for the future. This strong desire by participants to receive information about their genetic results is entrenched in the Setswana culture which values knowledge as highlighted by most participants who emphasised that "it is important to know". For parents and caregivers, feedback of individual genetic results was emphasised regardless of severity, preventability or actionability of the genetic condition, while adolescents were reluctant to receive genetic results for conditions that are severe, non-preventable and unactionable.

These decisions seem to have been influenced by participants' experiences of living with HIV. While parents and caregivers lived through a time where HIV had no treatment to a time where there is treatment, adolescents never had to experience that situation as they were born in an

era where HIV is a treatable condition. The desire to receive all genetic results regardless of severity, preventability or actionability by parents and caregivers in this study is consistent with observations from other studies involving parents of children with rare genetic diseases (Kleiderman et al., 2014; Sapp et al., 2014) who ascribed their capacity to cope with their child's illness as proof of their ability to cope with any further negative health information (Sapp et al., 2014). Therefore, adolescents who did not have the experience of having HIV as an untreatable condition, were not able to relate with the idea of living with a condition that is severe, non-preventable and unactionable as compared to parents and caregivers.

Importantly, both parents and adolescents highlighted the need to share genetic results that could benefit family members even in cases where the individual participant may not benefit directly from knowing that finding. The example I used was that of a male participant found with a genetic predisposition to developing breast cancer, who may have only a small increased risk of getting breast cancer but knowing that result could benefit his female siblings or children. This desire to share results with family members is consistent with the African way of life which is relational and the concept of Ubuntu which requires members of the community to care for one another. As a result, I conclude that to honour the desire of African research participants as expressed in this study, results that are actionable (through clinical interventions or lifestyle changes) ought to be fed back, regardless of whether they benefit the individual participants or their family members.

Practical considerations for feedback of individual genetic results in Botswana context

In chapter 6, participants' views and preferences regarding practical considerations for feedback of results were reported. It was reported that both adolescents and parents would prefer to receive their individual genetic results in person, with adolescents preferring

researchers to provide feedback, while parents preferred doctors who are associated with the study to do so. This desire by parents to have their results fed back by doctors seems to have been influenced by the setup at BBCCCE, where patients have regular doctors who are well-acquainted with their patients' medical history. This is not the case in the national health care system, especially in main hospitals where doctors rotate and where electronic health records are not used consistently, making it difficult for doctors to be well-acquainted with their patients' medical background. As a result, it might be difficult for study team to relay participants' results to treating doctors in the public health system or other contexts that are different from BBCCCE. This was also identified as a limitation for most African settings by Wonkam and de Vries (2020).

The participants in this study also described preferring feedback of results to be supported by counselling and believe that this would help them understand and cope with the results. Again, the feasibility of implementing this in the national healthcare system in Botswana is questionable due to lack of genetic counsellors in the country. To the best of my knowledge, genetic counselling is not currently recognised as a medical profession in Botswana. Although most major hospitals in Botswana would normally have either a psychologist or a social worker or both, they are not usually trained in genetic counselling. This is true even in a setup like BBCCCE where there is a counsellor and a psychologist whom patients can be referred to, but these do not have specific genetic counselling training. As a result, projects intending to feedback genetic research results may need to work with these professionals and train them in the basic principles of genetics as well as the complexities of genetic results for them to provide meaningful feedback to participants. Where counsellors and/or psychologists are not available, it has been suggested that nurses could also be trained to provide basic genetic counselling in addition to their current roles (Barr et al., 2018; Nembaware et al., 2019).

In situations where working with available professionals to provide genetic counselling is not possible due to limited resources in the public healthcare system, the obligation for researchers to make arrangements to provide such services to participants as a way of reciprocating, may be stronger than where such services are already available in the public healthcare system.

Lastly, participants' preferences with regards to the timing of feedback ranged from feedback as quickly as possible to feedback at project end. While a few participants suggested for feedback of results to be staged, this seems to be the most viable option in Botswana context. This way, only results that need urgent attention will be fed back immediately and the rest fed back at the end of the study. According to participants in Yu et al (2014a), prioritizing and staging return of results could help in avoiding information overload.

In account of these findings, I recommend that results ought to be fed back in conjunction with some form of counselling support. Ideally, support would be given by a genetic counsellor but in their absence, can be provided by other trained professionals (psychologist, nurses, social workers). Such professionals should participate in some of the training programmes available on the continent that introduces healthcare workers to the basic principles of genetic counselling. Where working with available professionals (psychologist, nurses, social workers) to relay results and provide genetic counselling is not possible due to limited resources in the public healthcare system, researchers may need to make arrangements to provide such services through budgeting to employ a counsellor who will be trained to assist with feedback of results. Ideally, going forward, African health systems should consider building a cadre of genetic healthcare professionals. Lastly, to avoid information overload, feedback of results may be staggered, where results that require urgent follow-up are fed back as soon as possible while

others are fed back at project end. In order to decide on the practicality and acceptability of their strategy to feedback results, researchers should become familiar with their study settings upfront and engage with important stakeholders including policy-makers and local IRBs.

Important considerations for informed consent for feedback of individual genetic results in Botswana genomics

With regards to informed consent, most participants expressed a desire to be told about the likelihood of discovering individual genetic results during the consenting phase and that agreement to feedback results should be obtained during the enrolment process. Additionally, they stated that when potentially life-saving genetic information is uncovered, participants should be re-contacted, even if earlier agreement for feedback was not obtained or the participant indicated they did not wish to receive their genetic data. They reasoned that people often change their mind, and that they may not have been well-informed at the time of making a decision not to receive results. However, some of them warned that re-contacting individuals who had previously said that they would not like to receive their results should be handled carefully to ensure that participants' autonomy is not compromised, and that counselling should be employed when returning results. Accordingly, they highlighted that it is important for researchers to ascertain that participants are well-informed in making decisions for feedback of results, by providing them with information and communicating effectively.

Participants generally appeared to consider informed consent as a continuous process rather than a one-time occurrence. This view is in accordance with the CIOMS guidelines which describe that, *"obtaining informed consent is a process that is begun when initial contact is made with a prospective subject and continues throughout the course of the study"* (p. 33). These guidelines additionally stipulate that informed consent should be periodically sought

from participants in long-term studies (CIOMS, 2016). On the other hand, the Presidential Commission for the Study of Bioethical Issues (2013), advised that when a potentially life-saving unforeseen incidental genetic discovery is identified for a person who has chosen not to receive incidental findings, the IRB should be consulted to guide on whether or how to disclose that result. These recommendations differ with the recommendation made by Fabsitz et al. (2010), who recommended that when the participant has opted-in or out of receiving results, the investigators should honour that decision even in cases where lifesaving genetic information is discovered. These authors suggest that researchers should consult with the IRB only when the informed consent is silent.

Against this background, and with my knowledge of IRB review processes in Botswana and in consistent with the CIOMS guidelines, I recommend that the best way forward would be for genomics researchers to make provision to re-consent study participants for feedback of results at certain intervals during the conduct of the study and not necessarily only when a potentially lifesaving information is uncovered. This provides participants with the option to revise their previous choices and update them without threatening their autonomy. This is also in line with the principle of Ubuntu, which demands members of a group or community to act in the best interest of each other and help one another. In this case, that means researchers should do their best to aid participants to make informed choices about receiving their individual genetic results.

If accepted, then the H3Africa guidelines should be revised to require periodic reconsenting of participants in genomics research, as doing so is one way of achieving the guidelines' recommendation. The H3Africa guidelines stipulate that in situations where participants are given an opportunity to indicate their preferences for return of results, researchers should make

sure that participants are fully informed about the potential results they may or may not receive, as well as the possible implications of such information in their lives. According to these guidelines, participants could make ill-informed decisions which could affect their lives and wellbeing in future, if they are not accurately informed (H3Africa, 2018). To ensure that information is communicated effectively, researchers could explore opportunities to present information about feedback of findings in stages, including during the consent process and subsequently, for instance during community engagement events or a scheduled telephone call. This may alleviate worries about overwhelming participants with information during the consenting phase and create an opportunity to provide relevant information to participants as well as empower them to make well-informed choices.

Considering these findings, it may be opportune to suggest that researchers doing genomic research in Botswana should include the possibility of feedback of results in the original consent documentation. Further, researchers have the option to seek permission to return results at the time of enrolment, or at a later stage (for instance during ongoing engagement events or if life-saving information is found). Ideally, consent is a process which involves engagement with participants over time. Where the study setup allows, then information and decisions about feedback of results ought to be revisited. In any case, where lifesaving, actionable results are discovered, then participants ought to be recontacted and given the option to receive these results, regardless of whether they previously indicated a desire not to receive results with consultation of the IRB.

Overall, this study provided strong evidence about both the ethical obligations to feedback results in African genomics, as well as about participants' desire to receive such results. Whilst there are still many questions outstanding, what is important is that there appears to be an

ethical obligation and an expectation to feedback selected individual genetic results, especially those that are actionable (through clinical interventions or lifestyle changes), regardless of whether they benefit the individual participants or their family members. Feedback of results should be done in person in conjunction with some form of counselling support. To avoid information overload, feedback of results may be staggered, where results that require urgent follow-up are fed back as soon as possible while others could be fed back at project end. Researchers should include the possibility of finding genetic mutations (primary and secondary) in the original consent documentation and obtaining participants' consent on whether to feed back the results or not. Informed consent should be considered as a process which involve engagement with participants over time. Where the study setup allows, then information and decisions about feedback of results ought to be revisited regularly over the course of the project. In any case, where lifesaving, actionable results are discovered, then participants ought to be recontacted and given the option to receive these results, regardless of whether they previously indicated a desire not to receive results.

These results affirm recommendations of the H3Africa (2018) Guideline for the Return of Individual Genetic Research Findings, which indicates that genomics research projects should include provisions on feedback of results in their consent forms and that engaging with participants on feedback of results should start before the study commences. Similarly, these guidelines further recommends that the responsibility to feedback participants' individual genetic results lies with clinicians and other qualified health professionals who are part of the genomic research project, until other staff (for example, psychologists, nurses, social workers, etc.) are sufficiently trained to take over this task. However, where this study significantly deviates from the H3Africa guidelines is that those guidelines are written more broadly and open-ended, with the discretion to feedback results lying on the researchers. This thesis

demonstrates very clearly that researchers have to feedback results to honour participants' expectations of reciprocity and solidarity. Additionally, the guidelines put emphasis on feedback of primary findings, whereas participants in this study have expressed a strong desire to receive both primary and secondary findings. In that account, I recommend that a revision of the H3Africa Guidelines be considered to mandate all H3Africa projects with potential to generate individual genetic results (primary and secondary), to make provisions to return such results from genomics research.

8.2. Strengths and limitations of the study

Although this study has generated important findings that add to the body of knowledge on feedback of findings in genomics research in Botswana, these findings may not be generalisable to some contexts especially those having other diseases or disorders not related to HIV and AIDS or those with a different healthcare context from that of Botswana. Additional limitations should be noted as follows;

Importantly, the majority of participants (92% of parents and caregivers, and 61% of adolescents) were female. Participants were selected from the CAfGEN project database which also included a high proportion of female parents/caregivers and adolescents. Even though I actively sought to recruit male participants, this proved hard for different reasons discussed in the Methods Chapter. In future, and to the extent possible male participants should be actively recruited to obtain their views on issues like the ones discussed in this study.

Secondly, participants' experience of health care provision might be different from others in the country because all the participants have access to free cutting-edge medical treatment at Botswana-Baylor Children' s Clinical Centre of Excellence (a public-private clinic specialising

in paediatric and adolescent HIV care) which is different from elsewhere in the country. This could also have encouraged people to be interested in knowing their individual genetic findings with the expectation that they would receive assistance from BBCCCE. Consequently, some of the suggestions made by participants in my study with regards to practicalities for feedback of results may not be applicable in contexts different from BBCCCE. Future research addressing this issue should consider opinions of participants in the public healthcare system.

Thirdly, participants in this study might have been more familiar with consent procedures compared to the general population as they were enrolled in a genomic study with a robust programme for community engagement. As a result, their understanding of genomics research and the informed consent process may differ from that of the general public.

Fourthly, while I attempted to educate participants on the complexities of genetic results, feedback on genetic results was discussed as a hypothetical scenario. There is presently no strategy in place for the genetic study associated to my study to provide individual results to participants. As a result, when participants are confronted with a real-life situation, their perspectives may shift, and this is worth investigating when African genomics projects begin to apply return policies.

Lastly, for reasons of feasibility I was only able to focus on some aspects of feedback of results and not others. For instance, the rich literature around feedback of results also speaks to the trade-off between a quest to produce generalisable knowledge – which would benefit everyone – and the ethical obligations to return individual results – which benefit only one or few people. I did not interrogate this trade-off and how participants recommend that decisions are made in this regard. Similarly, I did not interrogate who should bear the cost of returning results –

whether that should be the funders, the institutions, the researchers or the patients themselves. Therefore, whilst my study is able to make some recommendations about what ought to happen going forward, what happens in practice needs to be balanced against those considerations.

On the other hand, one strength of this work is the dFGD method utilised in this study. It is an innovative technique that allows participants to be informed and involved in discussion for an extended amount of time, allowing them to feel more comfortable expressing their thoughts than they would in a standard FGD. As a result, I got to saturation much quicker than I anticipated. This could be a better way of engaging participants on difficult issues like genetics. Additionally, the scenarios utilised in the dFGDs allowed participants to communicate their ideas through an external character rather of speaking directly about their personal experiences at first. Finally, by utilising dFGDs and IDIs, I was able to conduct in-depth examinations of the research questions.

8.3. Implications for practice and future research

Whilst obligations of reciprocity and solidarity presented in this thesis are narrowly applied to feedback of results, these recommendations have potentially far-reaching implications, and could apply more broadly in the research ethics context especially with regards to the following areas:

- Researchers doing genomics research in Botswana would need to make arrangements for feedback of results in consideration of participants' expectations of reciprocity and solidarity as presented in this study. In addition, IRBs and relevant stakeholders should ensure that plans to feedback individual genetic results to participants are incorporated in protocols for genomics research as well as guidelines and policies that govern the conduct of genomics research.

- Further, these expectations could mean that community engagement should be taken more seriously as a step towards identifying what participants expectations are and how they could be met in the context of research in general. This also means that IRBs should take up a more active role in ensuring that general study findings are fed back to participants. In Botswana, for the IRBs that I manage, community engagement and dissemination of study results in general are currently recognised as a beneficial but not mandatory practice.
- Lastly, in section 8.1.1. I suggested that there may be a difference between how ancillary care is described in the literature and the account of reciprocity emanating from my empirical findings. Whilst that discussion falls out of the scope of this thesis, the implications of this suggestion merits further investigation comparing conceptual accounts as well as practices of ancillary care and reciprocity obligations in research.

8.4. Conclusions

In summary, my findings seem to imply that Botswana's study participants view involvement in genomics research as a reciprocal relationship. They stated that researchers should reciprocate their gift of study participation, which aided in the generation of knowledge, by offering a knowledge-based benefit – such as sharing individual genetic results. As a result of these participants' expectations of solidarity and reciprocity, people doing research in Africa may have an ethical duty to provide feedback on some individual genetic results. While participants reported a broad desire to get feedback on their genetic results, their preferences differed according to the severity, preventability, and actionability of the results. As a result, there appears to be a greater argument for returning actionable genetic data to participants regardless of their age, as this knowledge appears to be highly wanted. Additionally, my

findings indicated that the context, relationships, and empowerment of participants are critical factors to consider when interpreting participant preferences for return of genetic results.

Decisions about practicalities for feedback should be project-dependent and should be done in account of study setting. To make these determinations, researchers should become familiar with their study settings and communicate with important stakeholders to make educated judgments about the feasibility and acceptability of their strategy for feedback of results.

Informed consent is critical for ensuring that participants' rights and well-being are safeguarded throughout the study. As demonstrated by this study, people doing genomics research in Botswana should inform participants about the possibility of discovering genetic results during the research and create procedures for participants to opt in or out of receiving such information. This would encourage participants to trust more in science and enhance the relationship between participants and researchers. Even though my study is focused on Botswana, these findings could also be generalised to similar contexts in Africa and provide an authoritative voice to H3Africa to be able to mandate projects with potential to generate individual genetic results to make provisions to feedback these results to study participants.

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Appendix A: University of Cape Town HREC ethics approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.arlefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

25 February 2019

HREC REF: 010/2019

A/Prof J de Vries
UCT Centre for Clinical Research
J Floor, Office J52.16
OMB

Dear A/Prof de Vries

PROJECT TITLE: EXPECTATIONS AND PREFERENCES OF PARENTS AND ADOLESCENTS REGARDING FEEDBACK OF INDIVIDUAL GENETIC FINDINGS IN AN HIV-TB GENOMIC RESEARCH IN BOTSWANA (PHD CANDIDATE - MS D RALEFALA) SUB-STUDY LINKED 782/2017

Thank you for your response letter dated 18 February 2019, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 28 February 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Ms Dimpho Ralefala will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.

Appendix B: University of Botswana research permit recommendation

UNIVERSITY of BOTSWANA

Office of the Deputy Vice Chancellor (Academic Affairs)

Office of Research and Development

Corner of Notwane and Mobuto Road, Gaborone, Botswana

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Ref: UBR/RES/IRB/BIO/1 8

17th December 2018

Permanent Secretary
Ministry of Health and Wellness
The Permanent Secretary
Private Bag 0038
Gaborone, Botswana

RE: REQUEST FOR EXPEDITED REVIEW OF A RESEARCH PROPOSAL SUBMITTED BY Ms DIMPHO RALEFALA AND PROF JANTINA DE VRIES

Since it is a requirement that everyone undertaking research in Botswana should obtain a Research Permit from the relevant arm of Government, The Office of Research and Development at the University of Botswana has been tasked with the responsibility of overseeing research at UB including facilitating the issuance of Research permits for all UB Researchers inclusive of students and staff.

I am writing this letter in support of an application for a research permit by Ms Dimpho Ralefala and Prof Jantina de Vries. Ms Ralefala and Prof de Vries are collaborating with a team of researchers at the University of Botswana (UB) and Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE) to conduct a study titled **"Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in an HIV-TB Genomic Research Project in Botswana."** The overall objective of the proposed study is to explore expectations and preferences for feedback of individual genetic research findings with parents of participants and adolescents involved in an HIV-TB genomics research in Botswana. It is hoped that the findings of this study will contribute to literature on feedback of findings from genomics research as well as to the development of a framework for feedback of findings in genomics research in Africa.

The Office of Research and Development is satisfied with the process for data collection, analysis and the intended utilisation of findings from this research.

We will appreciate your kind and timely consideration of this application.

We thank you for your usual cooperation and assistance

Sincerely,

UNIVERSITY OF BOTSWANA
Office of Research & Development
2018 -12- 17
PRIVATE BAG 00708 GABORONE

Prof G. Hall
Director, Office of Research and Development

Appendix C: Botswana Ministry of Health ethics approval letter

PRIVATE BAG 0038
GABORONE
BOTSWANA
REFERENCE:

TEL: (+267) 363 2500
FAX: (+267) 391 0647
TELEGRAMS: RABONGAKA
TELEX: 2818 CARE BD

REPUBLIC OF BOTSWANA

MINISTRY OF HEALTH AND WELLNESS

REFERENCE NO: HPDME: 13/18/1 **19 December 2018**

Health Research and Development Division

Prof. Jantina de Vries
Associate Professor Bioethics
Department of Medicine
University of Cape Town

Dear Prof. Jantina de Vries

PERMIT: **EXPECTATIONS AND PREFERENCES OF PARENTS AND ADOLESCENTS REGARDING FEEDBACK OF INDIVIDUAL GENETIC FINDINGS IN AN HIV-TB GENOMIC RESEARCH IN BOTSWANA: VERSION 1, DATED 18 OCTOBER 2018**

Your application for a research permit for the above stated research protocol refers. We note that your proposal has been reviewed and approved by University of Botswana Review Board.

Permission is therefore granted to conduct the above mentioned study. This approval is valid for a period of 1 year effective 19 December 2018.

This permit does not however give you authority to collect data from the selected site(s) without prior approval from the management. Consent from the identified individuals should be obtained at all times.

The research should be conducted as outlined in the approved proposal. Any changes to the approved proposal must be submitted to the Health Research and Development Division in the Ministry of Health and Wellness for consideration and approval.

Furthermore, you are requested to submit at least one hardcopy and an electronic copy of the report to the Health Research, Ministry of Health Wellness within 3 months of completion of the study. Approval is for academic fulfillment only. Copies should also be submitted to all other relevant authorities.

Thank you for your cooperation and your commitment to the protection of human subjects in research.

Yours faithfully

MINISTRY OF HEALTH RESEARCH DIVISION 2018 -12- 19 P. BAG 0038 GABORONE REPUBLIC OF BOTSWANA

Ms S. Moeunyane
for /PERMANENT SECRETARY

Appendix D: Botswana-Baylor Children's Clinical Centre of Excellence ethics approval letter

Botswana-Baylor Children's Clinical Centre of Excellence
An Affiliate of Baylor College of Medicine International Pediatric AIDS Initiative at Texas Children's Hospital

Plot: 1836, Hospital Way
(Off Notwane Road)
Private Bag BR129 Gaborone
Tel: (+267) 319-0083
Fax: (+267) 319-0079
Website: www.bipai.org

DATE: 28/01/2020

TO: Jantina de Vries

FROM: Botswana-Baylor COE Institutional Review Board

PROJECT TITLE: Prospective analysis of parents and adolescents expectations and preferences regarding feedback of Individual Genetic Findings in genomics research in Botswana. IFGeneRA-02
PROTOCOL #: BBCOE-IRB 1810-11
FUNDING SOURCE:
BBCCOEIRB REVIEW DATE: 28/01/2020
EFFECTIVE DATE: 28/01/2020
EXPIRATION DATE: 27/01/2021
IRB REVIEW TYPE: REGULAR
IRB REVIEW ACTION: RENEWAL

Dear PI:

The Botswana-Baylor COE Institutional Review Board by [FULL BOARD] has considered the renewal for the project referenced above and **APPROVED.**

The renewal is valid for one year from the date of the IRB approval is granted or modification required. A final report must be provided to the IRB and all records relating to the research (including signed consent forms where applicable) must be retained and available for audit for at least 3 years after research has ended.

It is the responsibility of all investigators and research staff to promptly report any serious, unexpected and related adverse events and potential unanticipated problems involving risks to subjects or others. Please do note that the researcher is still required to seek administrative or other procedural that may vary per institution.

This approval is issued under the Botswana-Baylor COE's OHRP Federalwide Assurance# 00020346.

Should you have any queries or concerns, do contact the BBCOEIRB Secretary at otshume@baylorbotswana.org.bw and cc the acting chair a jtfarirai@baylorbotswana.org.bw. Include the project titled and IRB Reference number in all correspondence with IRB.

Regards,

Dr John T. Farirai
(MBChB, Dip HIV Man, PDM, Mphil, MPH)
Chairman- Botswana-Baylor COE Institutional Review Board

Appendix E: Permission email from Dr Ingrid A. Holm

From: Dimpho Ralefala <dnjadingwe@gmail.com>
Date: Monday, July 20, 2020 at 11:38 AM
To: Ingrid Holm <Ingrid.Holm@childrens.harvard.edu>
Cc: Jantina De Vries <jantina.devries@uct.ac.za>
Subject: Request to reproduce a figure in your published article [EXTERNAL]

*** External Email - Caution ***

Dear Dr Ingrid A. Holm,

I am a PhD candidate at the University of Cape Town and used *Figure 2. Hypothetical result report (p.417)* from your article titled "Participant Satisfaction With a Preference-Setting Tool for the Return of Individual Research Results in Pediatric Genomic Research" to explore participants views on which genetic results to feedback.

I am now writing to request permission to reproduce this figure in our manuscript which will be submitted for publication.

I look forward to hearing from you.

Sincerely,

Dimpho Ralefala.

From: Dimpho Ralefala <dnjadingwe@gmail.com>
Date: Monday, July 20, 2020 at 9:00 PM
To: Ingrid Holm <Ingrid.Holm@childrens.harvard.edu>
Cc: Jantina De Vries <jantina.devries@uct.ac.za>
Subject: Re: Request to reproduce a figure in your published article [EXTERNAL] [EXTERNAL]

*** External Email - Caution ***

Thank you very much.

We will definitely acknowledge the article and reference accordingly.

Best regards,

Dimpho.

On Tue, 21 Jul 2020, 02:44 Holm, Ingrid, <Ingrid.Holm@childrens.harvard.edu> wrote:

> Thanks for your email. Yes, that is fine with me. I assume you'll acknowledge the article and reference. Good luck!
>
> Best,
>
> Ingrid
>
> Ingrid A. Holm, MD, MPH
> Division of Genetics and Genomics | Division of Endocrinology | Boston Children's Hospital
> Professor of Pediatrics | Harvard Medical School

Appendix F: Assent form for DFGD participation

Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Assent Form

We are doing a project to explore what people participating in genomics research may like to learn from such research and why. We would like to speak with you about the kinds of things you may like to learn from genomics research. We are asking you to take part in a group discussion to explore what you might like to know and why. We hope you can help us understand better which kinds of results we should always give back to participants in genomics studies. This project is led by Drs. Mogomotsi Matshaba of the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE) and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

If you decide you want to be in this study, you will be part of a group discussion with other children with the same disease as you who participated in genomics research. The group will be small, about 6-10 people. In the group discussions, we will first ask you to tell us what you remember about the genomic research project you participated in. We will then give you some information about genomics research and the kind of things we can learn from it. After that, we will ask you to discuss some questions about which kinds of things you think you would like to learn from genomics research and why.

After we break up, we will give you some materials to read at home. We will then call you again for another group discussion about one week later. At the second meeting, we will again discuss the kinds of things you may want to learn from genomics research and why. We will talk about the things you may have learned since the last meeting, and we will give you some examples that we can discuss. If we break up and you still feel like you would like to discuss more, we may even organize the third meeting to discuss your thoughts.

By participating in the group discussion, other people who also participate will know the kind of disease you have, and it is important that you realise this. You are free to tell us as much or as little as you would like in the group discussions. Whilst there is no risk to participating in this study, you could find it upsetting to talk about your disease. To reduce the chances of that, you don't have to answer any question that you find upsetting. We will talk with you about how you feel after the group discussion, to make sure you are not upset. We will take you to a counsellor for help if you need counselling assistance. If you would like to talk to us after you have left, then you can call us on 3190083 and we will make sure to put you in touch with people who can help.

The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will be able to do better genetic research in the future. It may also be a benefit for you to be in a group of people who have the same disease as your child.

Other people will not know if you are in this study. We will put things we learn about you together with things we learn about other children, so no one can tell what things came from

you. When we tell other people about this research, we will not use your name, so no one can tell who we are talking about.

Your parents or guardian have to say it's OK for you to be in the study. After they decide, you get to choose if you want to do it too. If you don't want to be in the study, no one will be mad at you. If you want to be in the study now and change your mind later, that's OK. You can stop at any time.

Our telephone number is 3190083. You can call us if you have questions about the study or if you decide you don't want to be in the study anymore.

You can also contact the Office of Research and Development at the University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573, if you have any questions concerning this study or this assent form beyond those answered by the researchers, including questions about the research, your rights as a research participant; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team.

We will give you a copy of this form in case you want to ask questions later.

Agreement

I have decided to be in the study even though I know that I don't have to do it. I have been given the opportunity to ask questions and these have been answered.

_____	_____
Name and Signature of Study Participant	Date
_____	_____
Name and Signature of Researcher	Date

Appendix G: Parents' permission form for DFGD participation

Parent/Guardian Permission form

Title of the Study: Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Introduction and summary
You are approached to ask if your child may participate in a genomic study at the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE). We would like to speak with your child about the kinds of things he/she may like to learn from genomics research. We are asking you to allow your child to take part in a group discussion to explore what he/she might like to know and why. The other people in the group are also children with the same disease as your child who agreed to participate in the same study your child participated in. Together, we hope they can help us understand better which kinds of results we should always give back to participants in genomics studies.

Objective
We hope to use the findings of this study to understand better which kinds of genetic research results we should share with genomics research participants and why.

The Researchers
This project is led by Drs. Mogomotsi Matshaba of the BBCCCE and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

How many people will take part in this study?
A total of approximately 36 children with the same disease as your child will participate in 9 group discussions.

How long will your child's participation in this study last?
We will take about three hours for the discussion today. Following that, we will ask your child to come back again about one week from now to have another discussion. If we still have more to discuss, we may even ask him/her to come back again a third time. We hope that each time we meet to discuss, we will learn something more about his/her views on what results you think we should give back to participants and their families.

Methods
If you allow your child to participate, he/she will be part of a group discussion with other children with the same disease as your child who participated in genomics research. The group will be small, about 6-10 people. In the group discussions, we will first ask your child to tell us what he/she remember about the genomic research project he/she participated in. We will then give his/her some information about genomics research and the kind of things we can learn from it. After that, we will ask him/her to discuss some questions about which kinds of things he/she thinks he/she would like to learn from genomics research and why.

After we break up, we will give your child some materials to read at home. We will then call him/her again for another group discussion about a week later. At the second meeting, we will again discuss the kinds of things your child may want to learn from genomics research and why. We will talk about the things he/she may have learned since the last meeting, and we will give

him/her some examples that we can discuss. If we break up and your child still feels like he/she would like to discuss more, we may even organize the third meeting to discuss your thoughts.

What are the possible risks or discomforts involved from being in this study?
By participating in the group discussion, other people who also participate will know the diagnosis of your child, and it is important that you realise this. Your child is free to tell us as much or as little as he/she would like in the group discussions. Whilst there is no risk to participating in this study, your child could find it upsetting to talk about his/her disease. To reduce the chances of that, he/she doesn't have to answer any question that he/she finds upsetting. We will talk with your child about how he/she feels after the group discussion, to make sure he/she is not upset. We will take your child to a counsellor for help if he/she needs counselling assistance. If your child would like to talk to us after he/she has left, then he/she can call us on 3190083and we will make sure to put him/her in touch with people who can help.

What are the possible benefits of being in this study?
The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will be able to do better genetic research in the future. It may also be a benefit for your child to be in a group of people who have the same disease as him/her.

How will information about your child be protected?
We will record and write down the group discussion. At the start of the discussion, we would like to get some information about your child – including his/her name – but we will not share his/her name with anybody. When we write the discussion down it will not have your child's name on it. We will share the writings with all the researchers on the project. When we talk to others about our research, we may use some of the sentences that your child said but we will not use any other information that could identify him/her. However, it is important to know that the discussion will take place in a group. We will ask everybody in the group to keep the discussion confidential, but it is possible that somebody could talk to others about it. If your child wants, he/she can use another name for himself/herself during the discussion, so that nobody in the group will know his/her real name.

What if you want to stop before your child's part in the study is complete?
Your child does not have to answer all the questions during the group discussion. If we ask a question and it makes your child feel uncomfortable, he/she can just tell us. Also, your child can decide to leave the discussion at any time. Your child can withdraw from this study at any time, without penalty.

Will your child receive anything for being in this study?
We will pay for the cost of your child's transport.

Will it cost you anything to be in this study?
It will not cost you or your child anything to be in this study.

What if you have questions about this study?

If you have any questions or comments about this project, or if you want to speak more about the project, you can call us on 3190083. You can also call Ms Keofentse Mathuba. If you prefer, you can also send an email to Mogomotsi Matshaba at matshaba@bcm.edu .

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Office of Research and Development, University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573.

Key points to remember of this study:

- We are doing a project to explore what people participating in genomics research may like to learn from such research and why
- In South Africa, we will speak to parents of children with autism and adults living with schizophrenia or bipolar disorder. In Botswana, we will speak with children in the CAfGEN genomic study and their parents.
- We will ask your child to come back again in two weeks' time to have another group discussion. We may even ask your child to come back again a third time.
- Your child doesn't have to give us his/her real name if you would prefer for us not to know it
- We would like to record the conversation. This is for us to keep good track of what was discussed. We will not tell anyone your child's name.

  Please remember that your child's participation is voluntary, and there are no consequences if you do not want your child to participate. You can withdraw him/her in the future if you want. Please contact Keofentse Mathuba if you no longer want your child to participate, or if you would like to discuss any of the issues that came up when we spoke with you.

Consent Statement:

- I agree to allow my child to participate in the IFGENERA research project;
- I understand that his/her participation is voluntary and that I can withdraw him/her at any moment;
- I understand that my child is participating in research, and that he/she will not benefit from this;
- I have been given the opportunity to ask questions and these have been answered.

Participant name or pseudonym Participant signature Date

Name of researcher Researcher' signature Date

Appendix H: Consent form for DFGD participation

Title of the Study: Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Introduction and summary
You recently agreed for your child to participate in a genomic study at the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE). We would like to speak with you about the kinds of things you may like to learn from genomics research. We are asking you to take part in a group discussion to explore what you might like to know and why. The other people in the group are also parents of children with the same disease as your own child who agreed to participate in the same study your child participated in. Together, we hope you can help us understand better which kinds of results we should always give back to participants.

Objective
We hope to use the findings of this study to understand better which kinds of genetic research results we should share with genomics research participants and why.

The Researchers
This project is led by Drs. Mogomotsi Matshaba of the BBCCCE and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

How many people will take part in this study?
A total of approximately 54 parents of children with the same disease as your child will participate in 9 group discussions.

How long will your part in this study last?
We will take about three hours for the discussion today. Following that, we will ask you to come back again about one week from now to have another discussion. If we still have more to discuss, we may even ask you to come back again a third time. We hope that each time we meet to discuss, we will learn something more about your views on what results you think we should give back to participants and their families.

Methods
If you agree to participate, you will be part of a group discussion with other parents of children with the same disease as your child who participated in genomics research. The group will be small, about 6-10 people. In the group discussions, we will first ask you to tell us what you remember about the genomic research project you participated in. We will then give you some information about genomics research and the kind of things we can learn from it. After that, we will ask you to discuss some questions about which kinds of things you think you would like to learn from genomics research and why.

After we break up, we will give you some materials to read at home. We will then call you again for another group discussion about a week later. At the second meeting, we will again discuss the kinds of things you may want to learn from genomics research and why. We will talk about the things you may have learned since the last meeting, and we will give you some examples that we can discuss. If we break up and you still feel like you would like to discuss more, we may even organize a third meeting to discuss your thoughts.

What are the possible risks or discomforts involved from being in this study?
By participating in the group discussion, other people who also participate will know the diagnosis of your child, and it is important that you realise this. You are free to tell us as much or as little as you would like in the group discussions. Whilst there is no risk to participating in this study, you could find it upsetting to talk about your child's disease. To reduce the chances of that, you don't have to answer any question that you find upsetting. We will talk with you about how you feel after the group discussion, to make sure you are not upset. We will take you to a counsellor for help if you need counselling assistance. If you would like to talk to us after you've left, then you can call us on 3190083and we will make sure to put you in touch with people who can help.

What are the possible benefits from being in this study?
The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will be able to do better genetic research in the future. It may also be a benefit for you to be in a group of people who have the same disease as your child.

How will information about you be protected?
We will record and write down the group discussion. At the start of the discussion, we would like to get some information about you – including your name – but we will not share your name with anybody. When we write the discussion down it will not have your name on it. We will share the writings between all the researchers on the project. When we talk to others about our research, we may use some of the sentences that you said but we will not use any other information that could identify you. However, it is important to know that the discussion will take place in a group. We will ask everybody in the group to keep the discussion confidential, but it is possible that somebody could talk to others about it. If you want, you can use another name for yourself during the discussion, so that nobody in the group will know your real name.

What if you want to stop before your part in the study is complete?
You do not have to answer all the questions during the group discussion. If we ask a question and it makes you feel uncomfortable, you can just tell us. Also, you can decide to leave the discussion at any time. You can withdraw from this study at any time, without penalty.

Will you receive anything for being in this study?
We would like to thank you for the time that you took to be part of our study. We will pay for the cost of your transport.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you have questions about this study?

If you have any questions or comments about this project, or if you want to speak more about the project, you can call us on 3190083. You can also call Ms Keofentse Mathuba. If you prefer, you can also send an email to Mogomotsi Matshaba at matshaba@bcm.edu .

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant; or if you feel that you have been treated unfairly and would like to talk to someone other than a member

of the research team, please feel free to contact the Office of Research and Development, University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573.

Key points to remember of this study:

- We are doing a project to explore what people participating in genomics research may like to learn from such research and why
- In South Africa, we will speak to parents of children with autism and adults living with schizophrenia or bipolar disorder. In Botswana, we will speak with parents of children on the CAfGEN Study.
- We will ask you to come back again in two weeks' time to have another group discussion. We may even ask you to come back again a third time.
- You don't have to give us your real name if you would prefer for us not to know it
- We would like to record the conversation. This is for us to keep good track of what was discussed. We will not tell anyone your name.

Please remember that your participation is voluntary, and there are no consequences if you do not want to participate. You can withdraw in the future if you want. Please contact Keofentse Mathuba if you no longer want to participate, or if you would like to discuss any of the issues that came up when we spoke with you.

Consent Statement:

- I agree to participate in the IFGENERA research project;
- I understand that my participation is voluntary and that I can withdraw at any moment;
- I understand that I am participating in research, and that I will not benefit from this;
- I have been given the opportunity to ask questions and these have been answered.

Participant name or pseudonym	Participant signature	Date

Researcher name	Participant signature	Date

Appendix I: Assent form for IDI participation

Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

We are doing a project to explore what people participating in genomics research may like to learn from such research and why. We would like to speak with you about the kinds of things you may like to learn from genomics research. We are asking you to take part in an in-depth (one-on-one) interview to explore what you might like to know and why. We hope you can help us understand better which kinds of results we should always give back to participants in genomics studies. This project is led by Drs. Mogomotsi Matshaba of the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE) and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

A total of approximately 6 parents or guardians and at least 6 adolescents who participated in our previous deliberative group discussions will participate in this one-on-one interview.
If you decide you want to be in this study, we will ask you to discuss some further questions about which kinds of things you think you would like to learn from genomics research and why. We will take about 30 mins for this one-on-one discussion.

If we break up and you still feel like you would like to discuss more, we may even organize a third meeting to discuss your thoughts.

You are free to tell us as much or as little as you would like in the one-on-one interview. Whilst there is no risk to participating in this study, you could find it upsetting to talk about your disease. To reduce the chances of that, you don't have to answer any question that you find upsetting. We will talk with you about how you feel after the group discussion, to make sure you are not upset. We will take you to a counsellor for help if you need counselling assistance. If you would like to talk to us after you have left, then you can call us on 3190083 and we will make sure to put you in touch with people who can help.

The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will be able to do better genetic research in the future.

Other people will not know if you are in this study. We will put things we learn about you together with things we learn about other children, so no one can tell what things came from you. When we tell other people about this research, we will not use your name, so no one can tell who we are talking about.

Your parents or guardian have to say it's OK for you to be in the study. After they decide, you get to choose if you want to do it too. If you don't want to be in the study, no one will be mad at you. If you want to be in the study now and change your mind later, that's OK. You can stop at any time.

Our telephone number is 3190083. You can call us if you have questions about the study or if you decide you don't want to be in the study any more.

You can also contact the Office of Research and Development at the University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573, if you have any questions concerning this study or this assent form beyond those answered by the researchers, including questions about the research, your rights as a research participant; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team.

We will give you a copy of this form in case you want to ask questions later.

Agreement

I have decided to be in the study even though I know that I don't have to do it. I have been given the opportunity to ask questions and these have been answered.

_____	_____
Signature of Study Participant	Date
_____	_____
Signature of Researcher	Date

Appendix J: Parents' permission form for IDI participation

Title of the Study: Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Introduction and summary
You recently allowed your child to participate in a deliberative focus group discussion for our study at the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE). We would like to follow-up with your child on some of the things we discussed at the previous meeting and speak with him/her about the kinds of things he/she may like to learn from genomics research. We are asking your child to take part in an in-depth interview to explore what he/she might like to know and why. We hope that your child can help us understand better which kinds of results we should always give back to participants.

Objective
We hope to use the findings of this study to understand better which kinds of genetic research results we should share with genomics research participants and why.

The Researchers
This project is led by Drs. Mogomotsi Matshaba of the BBCCCE and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

How many people will take part in this study?
A total of approximately 6 parents or guardians and at least 6 adolescents who participated in our previous deliberative group discussions will participate in this in-depth interview.

How long will your child's participation in this study last?
We will take about 30 mins for this discussion.

Methods
If you agree for your child to participate, we will ask him/her further questions about which kinds of things he/she think they would like to learn from genomics research and why.

If we break up and your child still feel like she would like to discuss more, we may even organize another meeting to discuss his/her thoughts.

What are the possible risks or discomforts involved from being in this study?
Your child is free to tell us as much or as little as he/she would like in the interview discussion. Whilst there is no risk to participating in this study, your child could find it upsetting to talk about his/her disease. To reduce the chances of that, your child doesn't have to answer any question that he/she finds upsetting. We will talk with your child about how he/she feels after the group discussion, to make sure he/she is not upset. We will take your child to a counsellor for help if he/she need counselling assistance. If your child or you, would like to talk to us after he/she has left, then you can call us on 3190083and we will make sure to put you in touch with people who can help.

What are the possible benefits from being in this study?
The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will be able to do better genetic research in the future. Reflecting on the questions that we ask your child might also be eye-opening to him/her on issues related to feedback of findings in genomics research.

How will information about your child be protected?
We will record and write down our interview discussion. At the start of the discussion, we would like to get some information about your child. When we write the discussion down it will not have your child's name on it. We will share the writings between all the researchers on the project. When we talk to others about our research, we may use some of the sentences that your child said but we will not use any other information that could identify him/her.

What if you or your child wants to stop before his/her part in the study is complete?
Your child does not have to answer all the questions during the interview discussion. If we ask a question and it makes him/her feel uncomfortable, he/she can just tell us. Also, your child can decide to leave the discussion at any time. Your child can also withdraw from this study at any time, without penalty.

Will your child receive anything for being in this study?
We would like to thank your child for the time that he/she took to be part of our study. We will pay for the cost of your child's transport.

Will it cost you anything for your child to be in this study?
It will not cost you anything for your child to be in this study.

What if you have questions about this study?

If you or your child have any questions or comments about this project, or if your child wants to speak more about the project, you can call us on 3190083. You can also call Ms Keofentse Mathuba. If you prefer, you can also send an email to Mogomotsi Matshaba at matshaba@bcm.edu .

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your child's rights as a research participant; or if you feel that your child has been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Office of Research and Development, University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573.

Key points to remember of this study:

- We are doing a project to explore what people participating in genomics research may like to learn from such research and why
- In South Africa, we will speak to parents of children with autism and adults living with schizophrenia or bipolar disorder. In Botswana, we will speak with children in the CAfGEN genomic study and their parents.

- We will ask your child to come back again in two weeks' time to have another group discussion. We may even ask your child to come back again a third time.
- Your child doesn't have to give us his/her real name if you would prefer for us not to know it
- We would like to record the conversation. This is for us to keep good track of what was discussed. We will not tell anyone your child's name.

Please remember that your child's participation is voluntary, and there are no consequences if you do not want your child to participate. You can withdraw him/her in the future if you want. Please contact Keofentse Mathuba if you no longer want your child to participate, or if you would like to discuss any of the issues that came up when we spoke with you.

Consent Statement:

- I agree to allow my child to participate in the IFGENERA research project;
- I understand that his/her participation is voluntary and that I can withdraw him/her at any moment;
- I understand that my child is participating in research, and that he/she will not benefit from this;
- I have been given the opportunity to ask questions and these have been answered.

Participant name or pseudonym Participant signature Date

Name of researcher Researcher' signature Date

Appendix K: Parents' consent form for IDI participation

Title of the Study: Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Introduction and summary
You recently participated in a deliberative focus group discussion for our study at the Botswana-Baylor Children's Centre of Clinical Excellence (BBCCCE). We would like to follow-up with you on some of the things we discussed at the previous meeting and speak with you about the kinds of things you may like to learn from genomics research. We are asking you to take part in an in-depth interview to explore what you might like to know and why. We hope that you can help us understand better which kinds of results we should always give back to participants.

Objective
We hope to use the findings of this study to understand better which kinds of genetic research results we should share with genomics research participants and why.

The Researchers
This project is led by Drs. Mogomotsi Matshaba of the BBCCCE and Mary Kasule of the University of Botswana. They are working with colleagues at the University of Cape Town (UCT) in South Africa.

How many people will take part in this study?
A total of approximately 6 parents or guardians and at least 6 adolescents who participated in our previous deliberative group discussions will participate in this in-depth interview.

How long will your part in this study last?
We will take about 30 mins for this discussion.

Methods
If you agree to participate, we will ask you further questions about which kinds of things you think you would like to learn from genomics research and why.

If we break up and you still feel like you would like to discuss more, we may even organize another meeting to discuss your thoughts.

What are the possible risks or discomforts involved from being in this study?
You are free to tell us as much or as little as you would like in the interview discussion. Whilst there is no risk to participating in this study, you could find it upsetting to talk about your child's disease. To reduce the chances of that, you don't have to answer any question that you find upsetting. We will talk with you about how you feel after the group discussion, to make sure you are not upset. We will take you to a counsellor for help if you need counselling assistance. If you would like to talk to us after you've left, then you can call us on 3190083and we will make sure to put you in touch with people who can help.

What are the possible benefits from being in this study?
The benefit of this study is that it will help us understand which kinds of things people participating in genomic research may like to learn from it, and why. With the findings, we will

be able to do better genetic research in the future. Reflecting on the questions that we ask you might also be eye-opening to you on issues related to feedback of findings in genomics research.

How will information about you be protected?
We will record and write down our interview discussion. At the start of the discussion, we would like to get some information about you. When we write the discussion down it will not have your name on it. We will share the writings between all the researchers on the project. When we talk to others about our research, we may use some of the sentences that you said but we will not use any other information that could identify you.

What if you want to stop before your part in the study is complete?
You do not have to answer all the questions during the interview discussion. If we ask a question and it makes you feel uncomfortable, you can just tell us. Also, you can decide to leave the discussion at any time. You can withdraw from this study at any time, without penalty.

Will you receive anything for being in this study?
We would like to thank you for the time that you took to be part of our study. We will pay for the cost of your transport.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you have questions about this study?

If you have any questions or comments about this project, or if you want to speak more about the project, you can call us on 3190083. You can also call Ms Keofentse Mathuba. If you prefer, you can also send an email to Mogomotsi Matshaba at matshaba@bcm.edu .

If you have any questions concerning this study or consent form beyond those answered by the investigator, including questions about the research, your rights as a research participant; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Office of Research and Development, University of Botswana, on telephone number 355-2900, E-mail: research@mopipi.ub.bw, Telefax: 395-7573.

Key points to remember of this study:

- We are doing a project to explore what people participating in genomics research may like to learn from such research and why
- In South Africa, we will speak to parents of children with autism and adults living with schizophrenia or bipolar disorder. In Botswana, we will speak with parents of children on the CAfGEN Study.
- We will ask you to come back again in two weeks' time to have another group discussion. We may even ask you to come back again a third time.
- You don't have to give us your real name if you would prefer for us not to know it
- We would like to record the conversation. This is for us to keep good track of what was discussed. We will not tell anyone your name.

Please remember that your participation is voluntary, and there are no consequences if you do not want to participate. You can withdraw in the future if you want. Please contact Keofentse Mathuba if you no longer want to participate, or if you would like to discuss any of the issues that came up when we spoke with you.

Consent Statement:

- I agree to participate in the IFGENERA research project;
- I understand that my participation is voluntary and that I can withdraw at any moment;
- I understand that I am participating in research, and that I will not benefit from this;
- I have been given the opportunity to ask questions and these have been answered.

Participant name or pseudonym	Participant signature	Date

Researcher name	Participant signature	Date

Appendix L: Adolescents' demographic data form

1	Gender	Male		Female			
2	How old are you? (years)						
3	Where do you live?	Town/city		Village		Ward	
4	What is your highest level of education?	Tertiary	High school	Junior school	Non-formal education	Primary	None
5	Do you know how to read and write?	Yes	No				
6	Who do you stay with?	Mother		Father		Guardian	
7	If you stay with a guardian, what is his/her relationship to you?	Grandmother		Grandfather	Auntie	Uncle	Other
9	Have you been in other research studies?		Yes		No		
10	How many research studies have you ever been involved in?						
11	Who is the head of the house?						
12	What is the marital status of the head of the house?	Married		Single	Divorced	Other	
13	What type of job does the head of the house do?						

Appendix M: Parents' demographic data form

Thank you for agreeing to participate in this study. Before we start our discussions, we'd like to know a little bit about you, your child and your family

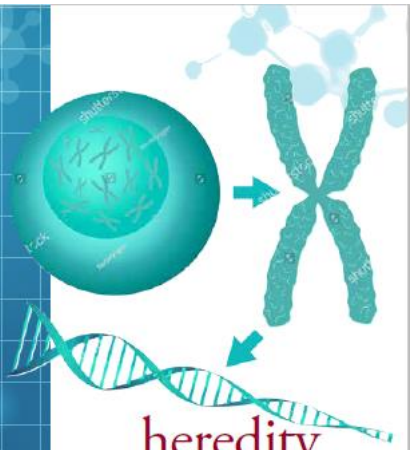
DEMOGRAPHIC DATA

1	Gender	Male		Female			
2	How old are you? (years)						
3	Where do you live?	Town/city		Village		Ward	
4	What is your highest level of education?	Tertiary	High school	Junior school	Non-formal education	Primary	None
5	Do you know how to read and write	Yes	No				
6	Are you the mother (father, parents/guardians) of this child?			Yes		No	
7	If you are the guardian to this child, what is your relationship to this child	Grandmother		Grandfather	Auntie	Uncle	Other
8	How old is the child?						
9	Has your child ever been in other research studies?		Yes		No		
10	How many research studies has your child ever been involved in?						
11	Have any of your other children been in any research studies?	Yes				No	
12	Who is the head of the house?						
13	What is your marital status?	Married		Single	Divorced	Other	
14	What type of job do you do?						
15	What is the job of the child's father (mother)?						

Appendix N: Participants' information brochure

gene problems

- Genes tell our bodies how to grow, work well and remain healthy
- Genes that we have can also make us sick or weak, so that we develop diseases
- Sometimes our genes can give problems in the body and cause disease or make the body weak
- This happens when genes are changed in some way so that they do not work properly
- The changes in genes are called mutations and can lead to diseases
  example: the gene that makes the heart weak, if that gene is passed on from a parent to a child, the child's heart can also be weak
- Some illnesses that seem to run in families are due to genetic mutations, but these still won't always pass from parent to child in very straightforward ways
  example: a child has the shape of his grandfather's face, but his parents don't
- Some illnesses are influenced by genetic mutations but also by other things, such as the kind of food you eat, or other illnesses that you have during your life. Some are not due to genetic mutations at all, but other things that might affect families over generations, like living near to a source of pollution, or always having eaten certain types of unhealthy food.



heredity is about chance

- This does not mean that if your one parent has a mutation that you will also get the mutated gene
  example: just because your parents are tall does not mean that you will be tall
- There will be characteristics and features that you get from your current and past family. Sometimes, a disease that a grandparent or aunt or uncle had can also affect a grandchild, even though the parent was healthy.

how genes impact on health

- Genetic information tells our bodies how to work. Sometimes, genes could also cause our bodies to be weak for a particular disease
- Sometimes people live in the same house and eat the same food and have the same behaviour, but one person gets ill and the other doesn't
  example: two people could both smoke a lot of cigarettes, but one may develop lung cancer and the other doesn't. This is partly because of their genes – for the one person, they may protect him from the lung cancer whilst for the other they may have made his body weaker
- But most times, the exact shape of the genes is not enough to give you an illness. You need to have the genes, but you also need to have a certain behaviour that can cause the illness
  example: if you have genes that mean that you are at risk of developing heart disease, that does not mean you will get heart disease. If you exercise, walk everywhere, and eat healthy food, then you can stay healthy. But if you eat unhealthily, don't move AND have genes that mean you can develop heart disease, then you could be at risk.

research

- Researchers and scientists are working hard to try and find out how genes work in our bodies
- If researchers can find out how genes do what they do, they can know what diseases are caused by genes that don't work properly
- To do this, we need people to participate in our research studies where some blood is drawn from different people who give their permission to use their blood in research
- Genes are carried in cells in the blood so by testing the blood we can find out more about genes and the genes that might play a role in why people get sick
- It is very important for us to do research about genes and which problems in genes (mutations) might make people sick because if we know this then we can start making plans of how to help people or how to keep people healthy
- Part of what we want to discuss with you today is what do you think about research where we test genes to look for any problems (mutations) so that we can help people to get better
- It is important for you to understand that the purpose of research is to learn about diseases in a way that benefits all people, not just individuals. When we spend time looking at results that could benefit individual people, that means we can spend less time learning about disease in a way that benefits all people.

the IFGeneRA study

This research project is being conducted in Gaborone, Botswana and Cape Town, South Africa. This project has two parts. The first part focusses on understanding the views and perspectives of people who take part in genomic research studies by finding out what individual genetic results they would like to get back and why. We would like to know how, where, when, why, who and by whom any individual genetic results found in genomics research should be fed back. This research project involves participants in current ongoing genomics research projects conducted on three conditions: (1) HIV; (2) Schizophrenia/Bipolar and (3) Autism.

The second part will explore the views of professionals who are involved in developing and implementing policies for the giving back genomic findings to participants. These professionals may be directly involved in research, or they could be policy makers, health care providers and members of ethics review committees. This could allow us to outlining the opportunities and challenges in developing policies for individual feedback of genetic results in African genomics research.

Appendix O: DFGD manual

Manual for Deliberative Focus Group Discussions (dFGDs) on Feedback of Individual Findings in Genomic Research among Lay Individuals who have Participated in Genomics Research in Gaborone, Botswana, and Cape Town, South Africa

Developed by members of IFGENERA project 2 with guidance from Vicki Marsh, between April 2018 and March 2019.

Important note: *This manual may not be published in any form. Sections of this Manual have been guided by the 'Manual for Community Consultation Information session on Benefits and Payments to Research Participants in Kilifi' by Vicki Marsh and colleagues. The manual may be used for the design of other dFGDs on topics similar to the one explored in the IFGENERA project.*

Version: January 2019

1. RESEARCH STUDY OUTLINE

1.1. The background and rational

The decision to feedback individual genetic findings is a complex issue. Researchers may be steered by the desire to respect research participants by feeding back relevant individual findings in genomics research. However, the final decision could be challenged by the responsibility to protect participants from the level of uncertainty associated with research findings that have not been validated for diagnostic purposes. Traditionally, researchers have opted to err on the side of caution and not to feedback too much of what has been found. The result is a phenomenon described as 'helicopter research' where research teams move into the lives of individuals or communities to collect personal information and then leave without any sort of feedback or communication thereafter.

Some research suggests that individuals carry varying levels of curiosity about themselves, particularly when it comes to their own health and wellbeing or that of their family. As such, participants might experience feelings of loss and frustration when research studies take information from them without sharing what was found. This is not only damaging to the work done at the time but could also hinder any future attempt for research or interventions in these same communities. In struggling with these competing and contrasting ideas, the objective of this research is to understand what African research participants think about disclosure of individual findings in genomics research. This knowledge holds important implications for engagement, collaboration, and transparency between research participants and researchers.

One important question in discussions around the feedback of individual genetic findings generated in the context of genomics research, relates to stakeholder expectations of and preferences for which findings are to be fed back, to and by whom, and when. This study will investigate key questions related to what people may want to know, why they want to know it, and how they would like to receive such results. Other questions relate to reciprocity / solidarity, whether research results need to be verified in a diagnostic laboratory, and how important it is that participants who receive results, have access to the interventions that would mediate the effects of the genetic finding.

1.2. The overall aim of the research

The specific aim of this study is to explore expectations and preferences for feedback of individual genetic research findings with (parents of) participants involved in genomics research in Botswana and South Africa.

1.3. How will the research be undertaken?

- **Encourage differing opinions**

We will achieve the aim of this study by conducting deliberative focus group discussions (dFGDs) with a diverse set of research participants in genomics research. Diversity among participants is important to ensure the collection of competing ideas that can challenge our current understanding of the issue, with the objective of generating a rich description of the range of perspectives on this topic. We can introduce diversity into the group by recruiting individuals who vary according to age, gender, level of education, experience of engaging with research, religion or culture.

- **Participants**

Specifically, dFGDs will be used to explore preferences for the extent, nature, timing and means of feedback of individual genetic research findings in African genomics research. This component of our study will take place in Gaborone, Botswana and Cape Town, South Africa, using three ongoing genomics research projects:

  - In Botswana, we will involve parents of children and adolescents involved in the H3Africa CafGen project;

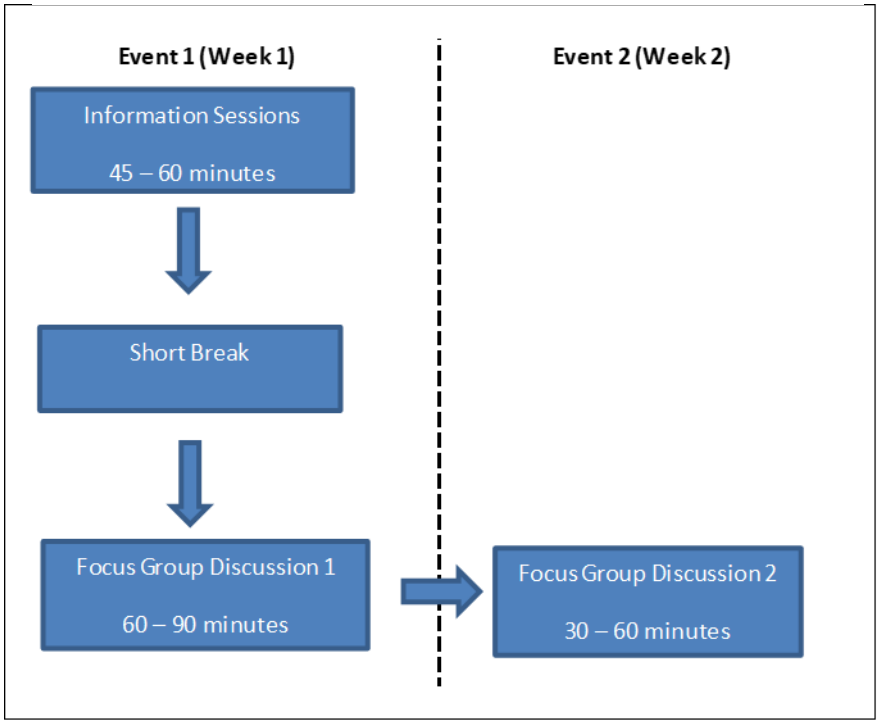
  - In South Africa, we will involve parents of children and adolescents involved in genomics research in the NeuroDEV (i.e. children with neurodevelopmental disorders) and the NeuroGAP (i.e. adults with psychotic disorders predominantly schizophrenia and bi-polar disorder) studies.

We will conduct 27 dFGDs with the a) parents of children, b) adolescents, and c) adult participants enrolled in genomics research in Botswana and South Africa. We will categorize findings that could potentially be fed back to research participants in categories varying in degree of actionability and predictability and discuss with participants whether and why they may want to receive those findings.

➢ **Data collection procedure**

We will engage each participant in three separate activities (as groups) namely 1) an information session and 2) two small group discussions (deliberative Focus Group Discussions or dFGDs) held over two days (see

Figure 3 Overview of research process



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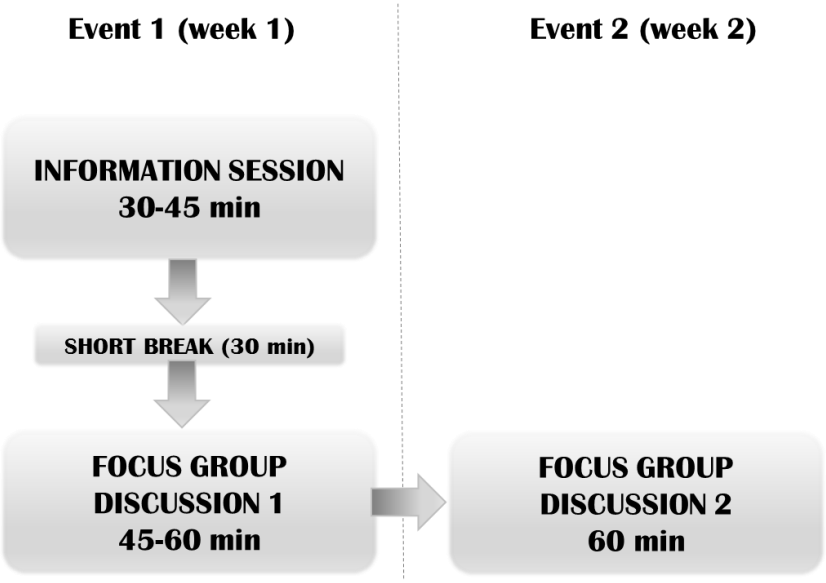

During the information session we will discuss genetics and heredity, how genetics may inform on health and what participants may expect from the research. During the information session, we will pay careful attention to how individuals make sense of genomics research and genes. This is important to gauge whether individuals are comfortable in discussing the material in the dFGD or if further information is necessary to prepare participants for the dFGDs. During the small group discussions participants will engage in discussions about what findings should be returned, when and why. The first small group discussion will take place on the same day as the initial information session. The second small group discussion will take place within two weeks of small group discussion 1. The reason for planning the dFGDs in two stages is: 1) to foster reflection and to allow enough time for information sharing on the topics discussed during the information session as well as the first round of dFGDs, and 2) for participants to go home and think about these issues, perhaps to talk to others, before returning for the second dFGDs.

- **Initial information session:**

We aim to conduct a short 30-45 minute initial information session. We will use this information session as a learning tool for participants and for the research team. This will also be an important opportunity to assess whether our planned research process is appropriate. We will hold information sessions at a venue convenient to participants – in Cape Town, they will be facilitated at the hospitals where NeuroDEV and NeuroGAP recruitment is taking place whilst in Botswana the research team may decide where the sessions are best held. During the information session we will take notes of the discussions, but these will not be audio-recorded.

The first part of the information session will be spent talking about genetics and heredity. During this part of the session we will: create a space where people can discuss that genes are things that are carried with us in our blood; talk about family inheritance; and weave in ideas that heredity is about chance / God's Will. The second part of the information session will be spent on explaining: that genomic research is predictive of something but it is not an absolute; that genomics research is not diagnostic; what findings can be expected from research; and what can be expected from the research process. Once we feel comfortable that participants have a fair understanding of what genomic research is about, we will complicate the narrative by explaining that sometimes research can find something about the health of a participant and providing some information about what genomics could reveal about a person's health.

Look out for: *During the information session we will make use of case studies to facilitate the discussion. These case studies will use indicator illnesses like breast cancer as an example of what can be found out about the health of a participant following their participation in genomics research. However, it is important to note that we are not primarily interested in knowing a lot about the conditions in the case studies (i.e. we're not fostering discussions about breast cancer) but that the indicator illnesses are used simply to facilitate a discussion about return of individual results in genomics research.*

- **First round of questioning:**

For the first round of questions we will conduct group discussions with groups of participants who have provided written informed consent that they would like to participate in the dFGDs and have completed the information session. The number of small groups enrolled for the dFGDs will depend on the number of people who participated in the initial information session. Each dFGD will consist of a maximum of 6 participants to give each participant an opportunity to partake in the discussion. The discussion will be recorded with permission.

- **Data analysis of dFGD 1:**

After dFGD 1 the interviews needs to be transcribed and analysed before the dFGD 2 meeting. This is important so that the interviewer can make notes of key relevant issues that need more clarity or can be explored / expanded on during the dFGD 2. If it is not possible for the interviews to be transcribed and studied carefully before the dFGD 2, then the interviewee needs to listen through the recording of dFGD 1 and make notes of key issues and areas that need more clarity or can be explored / expanded on during the dFGD 2.

- **Second round of questioning:**

Within 2 weeks of the information session and dFGD 1, all participants will be invited to attend a second round of questioning (dFGD 2) to further explore and reflect on views discussed in the information session and the first round of questioning. The discussion will be recorded with permission.

  - ***Phase 1:*** Phase 1 of the second round of questioning will be used to present case study 1 again in order to recap some of the answers participants provided during the first round of questioning. The aim of the recall is to challenge

participants about their views and opinions raised during the first round of questioning. The interviewer can use this space to introduce more complex questions and counter questions as possible probes that might enrich participants' answers during the first round of questions.

- ***Phase 2:*** Phase 2 of this session will be used to discuss relevant information that has come up during the data analysis of dFGD 1.

1.4. General outline of the information session guide and dFGDs tool

The information session will provide information about basic aspects of genomics research to ensure that participants have enough awareness of some of the key issues to sustain an informed discussion about feedback of individual findings during the dFGDs. Information sharing should be done in a way that participants feel comfortable and empowered to engage with sometimes complex issues in genomics research.

The information session guide comprises of different modules that work together to allow a combination of information sharing and exploration. The two modules that make up the information session are::

- **Module 1** provides an introduction and a rationale for why the research study will be undertaken.

- **Module 2** establishes some basic information about genomics research and what it can reveal about health. The module includes suggested questions that could be helpful to facilitate the discussion and check understanding among participants.

The small group discussion tool is a semi structured guide that will be used by the facilitator in navigating through the focus group discussions. The guide is carefully structured in a way that will allow a detailed probe into the views and reasoning of participants. There will also be an opportunity for other participants to share their opinions on the views raised by other participants.

Some instructions for the facilitator have been included in italics to highlight things to look out for or follow up on during the discussion.

The small group discussion tool consists of three modules:

- **Module 3:** presents questions and prompts for the first round of dFGD which is facilitated by the help of a case study scenario.

- **Module 4:** provides details on closing the information session, dFGD 1 and planning next steps for dFGD 2.

- **Module 5:** presents questions and prompts for the second round of dFGD to explore in more detail and challenge the views and ideas raised by participants during dFGD 1. Some additional questions to further complicate the session is also included. This session is facilitated with the help of notes made during the information session and preliminary analysis of the discussion for dFGD 1.

1.5. General guidelines for facilitating group discussions and sharing information

- Note that this discussion is not about getting participants to agree on the topics that are being discussed, instead we need to try and develop a comprehensive understanding of all views, concerns and opportunities around the feedback of individual genetic research results in African genomics. It is therefore essential to try and explore different issues while carefully considering the reasoning behind these issues;

- In order to understand how participants think about the views or opinions they share, it is important to probe why particular people hold certain views, to offer counterpoints and to work together with participants to interrogate assumptions;

- It is necessary to keep a watchful eye out for participants who dominate the discussion. The facilitator needs to remain in control of the group and give all participants an opportunity to share their views. This means that it will sometimes be necessary to direct questions at those participants who have not contributed to the discussion. Some caution is necessary when doing so in way that encourages view sharing but avoids discomfort among the participants;

- Take care not to lead participants during the discussion, we need participants to share their own views. Equally important is to not show reaction (i.e. positive or negative) to views shared by the participants, instead remain neutral and non-judgemental so that participants can feel comfortable to share their own views;

- It is important to take notes during the discussion. Carefully note the ways in which participants say things and try to write down any unique phrases or words. These notes can then be used to further guide the discussion or probe in more detail about relevant topics;

- Ideally each discussion group should have a co-facilitator. This is helpful because the co-facilitator may be able to ask questions and ask for clarification which the facilitator might have missed.

2. MANUAL FOR INFORMATION SESSION AND FOCUS GROUP DISCUSSIONS

MODULE 1: Starting the information session

Background to the module:

- In this module it is important to create an open, friendly and safe environment where participants feel free to participate in the discussions. This is important since we want participants to feel comfortable to share any opinions or views in an environment that is free from judgement or other negative factors that might limit participation.
- The data collected from notes and recording of the dFGDs, will primarily be used as the data for two PhD degrees, reports, and peer-reviewed published papers.
- It is essential that we obtained signed informed consent before the start of Module 2. This process will entail carefully reading through the informed consent, along with participants, and asking each participant to indicate their willingness to participate in the study by signing a paper-based version of the informed consent form. We will also provide a copy of the informed consent form for participants to take home and keep for their own record, with contact details for the primary investigator and ethics committee in case they have any concerns or further questions.

Outputs of this module: When this module has been completed, the facilitator: must have established an open, friendly and safe environment where participants feel free to participate in the discussions; must be sure that participants understand what will be expected from them and how this process will take place; and should feel confident that all participants are comfortable with the way in which the data will be used (e.g. obtaining degrees etc.). Each participant will also have had to sign an informed consent form.

The sections below should be explained in your own words but make sure to consistently check understanding (e.g. using open questions) among participants.

1. Welcome/Introductions:

- Welcome the participants to the dFGD and express your appreciation that they are willing to take part in the discussions. Facilitator(s) also need to make sure to introduce themselves;

- State the general aim of the information session as understanding how people think about genes, family inheritance, and genomics research as well as what is expected from our research to make sure that research is done in a way that is fair and safe;

2. Objectives of the information session and of the research:

- The information session is an important part of a process that will produce data that will form part of two separate PhD degrees and inform practice in the way the group conducts genomics research.

3. What to expect

- This information session should be used as an opportunity to tell participants about the research process. We will also conduct the first dFGD after the information session;
- All participants will be invited to attend a second dFGD within the 2 weeks following the information session and dFGD 1 to continue these discussions. During the information session, participants should also be given the names of participants to attend the various group discussions;
- There will be a reimbursement for time and travel costs (Give amount for SA and Botswana) for each session.

4. Informed consent process

Read through the informed consent carefully and make sure that every participant indicates they understand what is expected of them. Each participant should sign a copy of the informed consent form. The points below should be emphasised before going on to the next step of the informed consent form.

- **Remind the participant of study participation**

Your participation in this study is voluntary. If you agree to participate in this study, you will be asked to participate in a group discussion. The total time we will use today is about three hours. You will be asked questions about genomics and individual results. If the questions make you uncomfortable, you can tell us and you don't have to answer. You may withdraw your participation from the discussion at any point, even after you have initially agreed to participate in the study.

- **Remind the participant on confidentiality statement**

To help us with our research, we would like to record the conversation. We will write down the conversation, but we will not write down your name and any other information that can identify you. Therefore, no one will be able to identify you from the transcript. As a participant in this research study, you will be assigned a number. Therefore, no one will be able to identify you from the database. Any publications or other research outputs based on this data will not identify you directly. The data will only be accessible by the research staff working directly on this study. The research staff are researchers and PhD students working directly on this project.

- **Recordings or photographs**

We would like to ask for your permission to record the information session as needed and to take some photographs. If you provide your permission at the start but change your mind during the session you may ask us for any information you would like us to exclude. you are still aloud to change your mind at a later stage should you want to.

- Give participants an opportunity to ask any questions or raise issues about the recordings.
- Ask for written informed consent from each participant.

5. Housekeeping issues, including:

- Make sure that all participants know of any breaks (e.g. tea) and when the session will be completed;
- Provide clear instructions of where the bathrooms are;
- Address transport refund issues.

MODULE 2: Basic understanding of genetics and heredity

Background

- This module has the main aim of drawing out what participants understand about genes and heredity. We aim to listen to the way that participants describe the research components from what is necessary to understand our research. This is an important step in the information session as participants will not be able to comment on the how, what, when, why or why not of feedback on individual research findings if they do not have a basic understanding of what these findings relate to.
- Because genomics research is a complex issue that will be difficult to talk about among lay individuals (*also influenced by culture, language, personal life experiences*) in general, the discussions will focus on key concepts needed for a minimum understanding to participate in the dFGDs. Concepts will be explained with the help of a story that is more relatable for participants. Even though the story has been made to be simple, the content may be new and difficult for people to grasp immediately. To help understanding, the story box should be explained as a narrative on what happens to a particular named individual and with enough details of the family for participants to begin to build a mental picture of this situation. The facilitator can use the story to illustrate basic concepts in genomics research. Facilitators should probe comprehension by asking open questions and repeating information where needed. These reminders may continue to be needed throughout the discussion of the sessions, and the facilitator should be on the look-out for any signs that views are being expressed because participants have misunderstood or forgotten important aspects of the example story.
- The concepts discussed will also be used as the focus for discussions in the dFGDs, and one aim of introducing them in the information session is to help people to quickly pick up on these issues in these discussions.

Outputs from this session: By the end of the module, you should be fairly certain that people grasp the key points in genomics necessary to facilitate a discussion about the return of results.

Follow the instructions and use participatory methods to explore the issues described in the text below along with any other relevant issues that may come up.

1. **Genes and family inheritance**

- ***Introducing story 1: Genes and how they are passed on in a family***

In the next set of discussions, we would like to find out what you know and understand about our research and how we find out the things that we do. To understand this, you need to know a little bit about genes and how they are passed on in families. We know that you might not have heard of these things before but don't worry, we are going to talk about this now until every person knows what these things are.

To help us talk about these topics, we will give you some examples and explain these to you as a story, and we will ask you to talk about what you understand from what was said and what questions you might have. So, while you are listening to the story, please try to pick out anything that stands out to you.

For the facilitator: *At the end, check understanding of the main points in this scenario.*

Story 1[2]: Fezile meets the family and learns about genes and family inheritance. It is finally the day of the wedding. Fezile holds his mother's hand tightly as he feels excited to attend his first ever family wedding, but he is also a little nervous about all the mostly familiar faces starring back at him. Some of his aunts, uncles, and cousins he has not seen since he was younger come over to great them excitedly.

Aunt Noluthando pulls Fezile into a hug and says, "Look how you've grown! And you've got such a beautiful smile and big bright eyes! You remind me so much of my grandfather!"

Uncle Lwazi adds, "Look!, He is getting so tall and strong! You look just like your father. Only 11 years old, and you look like a soccer player! It runs in your blood!"

The wedding is beautiful, and the guests have lots of fun celebrating after the wedding ceremony. That night Fezile has trouble sleeping and wonders, "Aunt Noluthando's grandfather? It runs in your blood? What were they trying to say?"

The next day Fezile tells his mother what happened and asks her to explain what his family members were talking about. His mom, who is a science teacher at the local school, excitedly tells Fezile: "Genes! that is what they are talking about!"

- ***Discussion***

In a large group, use the topics highlighted throughout this section to discuss concepts around genes and heredity by using the information described in the rest of this section. In discussing each of the concepts below, the facilitator should use participatory group discussion methods to ensure that participants are comfortable with these topics. Participants do not need to

[2] Adapted from: Narcisa, L. (2014*). Kids Health: What is a gene?* Retrieved from https://kidshealth.org/en/kids/what-is-gene.html

understand the detail of genetics research and how genes work, only transfer a basic understanding of these points using the description that follows (*see descriptions below)*:

- What are genes?
- Where are our genes?
- Genes are passed on through families from parents to children;
- Genes that are passed on to children are from both parents – we inherit genes from both parents;
- Genes play a role in physical appearance e.g. the shape of our face and height but also other characteristics **AND** functions inside of the body that cannot be seen with the eye e.g. mechanism that controls breathing;
- Heredity is about chance (which participants may know or understand better as 'God's will'). This means that even if you carry a genetic factor, it doesn't mean you will actually develop the disease;
- Sometimes things go wrong in our genes – called mutations – that can make people sick;
- Mutations can be passed on from parents to their children through genes;
- Researchers study genes to understand how they work and to find out what mutations make people sick;
- To study genes they ask permission to test blood from people who are willing to take part in their studies.

What is a gene and where are they?

Starting questions:

- *Who in the group knows what genes or DNA are?*
- *What do genes do?*

  PROMPT: explore participants' basic understanding of genetics and inheritance

It can be fun to explore all of the ways that you are like others in your family – for example your height, the shape of your face, or the same talent for a sport like soccer. But why are we like others in our families? Well, because of our genes.

This is not the same thing as the 'jeans' that you buy at the shop. Genes are much more exciting than that. Genes are the recipe for making you the way that you are and they come from your mother and her family and from your father and his family. Your body is made up of cells. Every cell has about 25,000 to 35,000 genes inside of it. These genes hold the information that makes up the features or characteristics that are passed on to you (i.e. inherited) from your parents. The genes are made up of a material we call DNA – you may know that from CSI or other television shows. 'DNA' sort of means the same thing as 'Genes'.

Let us look at some examples. Say both of your parents have funny ears, you might also have funny ears if you inherit this feature from them. Similarly, if your father is very short, there is a chance that you could also be very short because you inherited the feature shortness. Genes do not only belong to human beings; we also find genes in animals and in plants.

You are probably wondering where in our bodies we can find these important genes? Well, genes are very small so we are not able to see them with the human eye. A cell is so small that we have to use a strong microscope to see it. Cells are everywhere in your body and there are billions of them. There are cells in blood, but also in your skin and muscles. Because there are cells in blood, and all cells contain genetic material, researchers can take a blood sample to get some of your genes out of your body.

Questions to group to probe comprehension:

- *Do you feel you have a better understanding of what genes are now?*
- *Can you tell me what genes do?*
- *Where can we find genes (or DNA) in the body?*

How do genes work:

Every gene is responsible for giving out specific instructions, sort of like a recipe handed down from your mother or grandmother, that tell our bodies to grow, work properly, and stay healthy.

Your parents each have two copies of each of their genes. Only one copy of their genes are then passed on to you so that you have one copy from your father and another from your mother. The pair of genes that you inherit from your parents are responsible for making you look like your parents and your family by making you have their type of body, face and so forth.

In the story that we told you earlier, Uncle Lwasi told Fezile that he is getting tall and strong just like his father. This means that Fezile's father is a tall and muscular man and that he has passed on some of what he looks like to his son.

Just because genes are passed on from your parents it does not mean that you will look and be exactly like them. For example, if both of your parents are tall you might be short. This is because we get different genes randomly passed down over generations – your grandparents might all be short, and even though your parents were tall, you got the genes for shortness from your grandparents. Remember in the story Aunt Noluthando told Fezile that he looks just like her grandfather.

Genes do not only make up how we look. Genes also work inside of our bodies on things we cannot see but that we need to be healthy. For example, we have special genes that help us to carry oxygen in our blood which we need to help our cells function well. We have genes that influence the shape of our heart or how strong our muscles are.

Question to the group: is this clear to you? Are there any questions?

When there are problems with genes:

So genes tell our bodies how to grow, work well and remain healthy. But sometimes, the genes that we have can also make us sick or weak, so that we can develop diseases.

Sometimes the genes from a mother and a father can give problems to the child. This happens when genes are changed in some way so that they do not work properly. Genes that have been changed are called mutations. This can lead to diseases.

Some of these gene problems can be passed on from a parent. For example, take a gene that can make the heart weak. If that gene is passed on from a parent to a child, the child's heart can also be weak.

Some illnesses that seem to run in families are due to genetic mutations, but these still won't necessarily pass from parent to child in very straightforward ways (e.g. skipped generations – people likely to recognise this in everyday life – as for height, skin colour). Some illnesses are influenced by genetic mutations but also by other things, such as the kind of food you eat, or other illnesses that you have during your life. Some are not due to genetic mutations at all, but other things that might affect families over generations, like living near to a source of pollution, or always having eaten certain types of unhealthy food.

Question to probe comprehension:

- *Do you know of any sicknesses that run in families?*

  PROMPT: heart disease, cancers, psychiatric conditions, other?

Heredity is about chance: But this does not mean that if your one parent has a mutation that you will also get the mutated gene. Remember that we said that just because your parents are tall does not mean that you will be tall? There will be characteristics and features that you get from your current and past family. Sometimes, a disease that a grandparent or aunt or uncle had can also affect a grandchild, even though the parent was healthy.

For South Africa NeuroDEV dFGD - De novo mutations: but we don't always inherit illnesses from our parents. It is also possible that a fault slips into the DNA when the child is still in the mother's tummy, before she even knows that she is pregnant. Sometimes it means that the baby is born with a disease that nobody in the family has.

How can my genes impact on my health?

As we said before, our genetic information tells our bodies how to work. But sometimes, our genes could also cause our bodies to be weak for a particular disease. We know this because sometimes people live in the same house and eat the same food and have the same behaviour, but one person gets ill and the other doesn't. For instance, you can get two people who both smoke a lot of cigarettes. But one may develop lung cancer and the other doesn't. We think that this is because of the exact shape of the genes they have – for the one person, they may protect him from the lung cancer whilst for the other they may have made his body weaker.

But most times, the exact shape of the genes is not enough to give you an illness. You need to have the genes, but you also need to have a certain behaviour that can cause the illness. For instance, if you have genes that mean that you are at risk of developing heart disease, then that does not mean you will get heart disease. If you exercise, walk everywhere, and eat healthy food, then you can stay healthy. But if you eat unhealthy, don't move AND have genes that mean you can develop heart disease, then you could be at risk. In a way, this is about God's will: even if you carry in your genes a susceptibility to developing a particular disease, this doesn't always mean that you will get it. Research that look at genes could help to identify if we are at risk of developing a particular diseases that can make us sick, but again, research cannot confirm that we will definitely get sick if we have a risk of getting a certain disease.

Questions to probe with the group:

- *Does having a gene for a particular disease always mean you get the disease?*
- *What does it mean for something to be 'God's will'?*
- *If a doctor were to tell you that you have a gene for this illness, what does that mean for your health?*

PROMPT: use example conditions such as heart disease, cancers

Research and why we are having this discussion

Researchers and scientists are working hard to try and find out how genes work in our bodies. If researchers can find out how genes do what they do, they can know what diseases are caused by genes that don't work properly.

In our research we are also trying to understand how some diseases work and which genes might be the reason for different diseases. To do this we need people like you to participate in our research studies. For the study researchers draw some blood from different people who give their permission to use their blood in research. Genes are carried in cells in the blood so by testing the blood we can find out more about genes and the genes that might play a role in why people get sick. It is very important for us to do research about genes and which problems in genes – mutation – might make people sick because if we know this then we can start making plans of how to help people or how to keep people healthy.

Part of what we want to discuss with you today is what do you think about research where we test genes to look for any problems (mutations) so that we can help people to get better.

It is important for you to understand that the purpose of research is to learn about diseases in a way that benefits all people, not just individuals. When we spend time looking at results that could benefit individual people, that means we can spend less time learning about disease in a way that benefits all people.

Questions to the group:

- *What is the purpose of research?*

  PROMPT: to benefit all people, not just individuals

- **Summary of module**

Conclude this module by summarising the main points about genes, heredity, and willingness to participate in research. By the end of this session participants should be comfortable with the idea of genes, that genes are passed on through families by chance and that research studies are done among lay individuals like themselves to explore genes and to identify problems in genes (mutations). A basic understanding of these concepts is important before going on to the next section where we will discuss in more detail how participants think about what is found in research studies and how, when, or why these findings should be communicated back to participants.

Short coffee break with some refreshments: 30 minutes

MODULE 3: FIRST DELIBERATIVE FOCUS GROUP DISCUSSION

Background to module:

- This module has the main aim of drawing out what participants understand about the return of research results, and what research does or does not do without being unduly influenced by researchers' ideas about these (e.g. 'many researchers believe that results which have limited value to participants should not be returned because this would entail a burden of cost or complexity to return'). We aim to listen to the way that participants describe findings we derive from our research. This is an important step in the information session as participants will not be able to comment on the how, what, when, why or why not of individual research findings if they do not understand what these findings are.
- Because genomics research is a complex issue that will be difficult to talk about among lay individuals (*influenced by culture, language, personal life experiences*) in general, the discussions will focus on key concepts needed for a minimum understanding to participate in the dFGDs. Each concept will be explained with the help of Case Study Scenarios that are more relatable for participants. These scenarios may be difficult for people to grasp at first. To help understanding, the Case Study Scenario boxes should be explained as a story i.e. a narrative on what happens to a particular named individual living in a particular named place and with enough details of the family for participants to begin to build a mental picture of this situation. After each story, the facilitator should check if the participants have understood the Case Study Scenario by asking open questions and repeating information where needed. These reminders may continue to be needed throughout the discussion of the sessions, and the facilitator should be on the look-out for any signs that views are being expressed because participants have misunderstood or forgotten important aspects of the Case Study Scenario.
- In addition to the case study scenarios, also make use of materials such as newspaper / magazine articles that report on e.g. celebrities who have talked about their own diagnosis of breast cancer. This can be a useful starting point for the first dFGD session.

Outputs from this session: By the end of the module, you should have: Generated a list of factors that would influence people's thinking about the return of individual finding; Understood/documented how these factors work as influences; Understood/documented the

reasoning behind the views regarding research findings. In addition, you should make sure that people grasp the key points within the three concepts well since they will be referred back to in the second dFGD (follow up activity).

Follow the instructions and use participatory methods to explore the issues described in the text below along with any other relevant issues that may come up.

1. **Case Study Scenario 1**

a) ***Introducing Case Study Scenario 1***

In the next set of discussions, we would like to find out what you know and understand about our research and how we find out the things that you do. We think that there are many different reasons why people take part in our research and that they might, or might not, expect to know what we found out from our research. We want to talk to you today about how you think about research findings where blood is tested to look at genes and how they work. In talking about these things, we will ask you some questions about if you think people should be told what is found in research, how would people like to be told, why or why not would people like to be told, and when should we tell people what was found.

To help us talk about these issues, we will give you some example scenarios from studies that are sometimes conducted in South Africa / Botswana. We will explain these to you as a story, and we will ask you to talk about what you understand from what was said and what questions you might have. So, while you are listening to the story, please try to pick out anything that stands out to you. *At the end, check understanding of the main points in this scenario.*

Question to the group: Probe whether people know what breast cancer is.

Case study scenario 1: A mother participates in research that is looking at psychiatric problems when it is discovered that she has a mutation in the BRCA1 gene which increases her risk of getting breast cancer.

Part 1 told before asking 'GENERAL QUESTION': In a creative way, tell a story about a mother who, after consulting with her family, participated in a research study that is looking at psychiatric problems. In the process of exploring her blood sample a researcher noticed that she carries the BRCA1 gene which means that there is a chance that she may develop breast cancer at some stage in her life. Breast cancer was not part of the focus for the study and the informed consent did not state that findings will be returned to participants.

For the facilitator: Go to page 18 and discuss the 'General question'.

Part 2 told after 'GENERAL QUESTION': The research team decides to ask the mother if she would like to know what they have found when they explored her blood sample. After talking to the researchers, the mother decides that she would like to hear what the researchers have found even if it was not related to the study. After telling the mother about the BRCA1 gene and that this increases her risk of developing breast cancer, the researchers explain that their study is not the same as a diagnostic test and that she will need to go for a test that specifically tests for the risk of breast cancer. They also explain to her that breast cancer is thought to be hereditary which means that it is caused by mutated genes passed from parent to child so she should also think about telling her 22 year old daughter to get a diagnostic test for the risk of breast cancer. The mother does not yet tell her daughter about the potential health risk but instead decides to go for the diagnostic test to find out if she is at risk for developing breast cancer, but the test is too expensive and she will not be able to pay for it.
The story is aimed to bring out the information that would be considered necessary for participants to answers questions on the how, what, when, or why on the return of individual research findings in genomics research.

The main points that should be included in the case study scenario:

- Individual findings from genomics research: sharing with participants;
- Findings unrelated to what is being studied;
- Research is not diagnostic;
- Findings that are clinically actionable;
- Feedback of findings for the sake of solidarity;
- Concerns about privacy or confidentiality;
- Practicalities of returning results;
- Sharing individual findings: issues related to autonomy and disrespect.

Note: To make the case study scenario more interesting, you could give the characters well known names (e.g. famous TV celebrity known to the participants) or to engage the participants you could ask them to provide these names and details of the fictional characters.

b) ***Discussion Case Study Scenario 1***

GENERAL QUESTION: What do you think the researchers should do about these extra results, and why?

PROMPT: What do you think about the fact that researchers had not explained about the possibility of finding this result before running tests that would show it? Why do you think they did that and in what situations would that be a reasonable or unreasonable strategy?'

AFTER TELLING PART 2 OF CASE STUDY CONTINUE WITH THE THEMES.

THEME 1: Research is not diagnostic

In the case study, the researchers told the mother that they think she might have a risk for developing breast cancer but that their test is not good enough to say this for sure because their test is not a diagnostic test. They suggest she goes for another test at a hospital and provide her with some details of where she can get this test.

- Do you think it was good enough for the researchers to suggest a place where the mother can get the right test to tell her if she is at risk for breast cancer?
- What other thing might have been right for them?
- Could the researchers have done more to help the mother find out if she is at risk for breast cancer?

PROMPT: Should researchers pay for the test? Should they pay for the treatment?

Look out for: *Responses related to the interpretation, misconception or expectation that research is diagnostic. Note whether there are expectations related to treatment but do not probe in detail about expectations of treatment as this is not at all the focus of this discussion. One of the major issues participants might raise is that the mother has now been found to have an increased risk of breast cancer and the researchers have an (arguable) responsibility to help her (straight to the duty of rescue).*

THEME 2: Findings that are clinically actionability

Remember from the case study that the researchers decided to tell the mother what they have found because it could affect her health but also that of her daughter if her daughter inherited the gene for breast cancer. Some people feel that they only want to know what was found by researchers who looked at their genes, if this directly affects their health, or that of a loved one,

and if something can be done to improve their health. In the case study, breast cancer is something that can be prevented and treated. Other diseases might not be preventable or treatable because they are so rare or because we do not yet know enough about how they work to make people sick.

- Thinking of this, would you want to know what was found after researchers have studied your genes even when there is no help for you? Why?

Look out for: *The literature states that some participants express the desire to receive feedback on findings when the findings have direct relevance to their own health or that of a loved one. Other participants have indicated that they agreed to participate in the study to advance research and do not expect to receive feedback on individual research findings. Here we are interested to know if participants only want to know about findings that are preventable and treatable. As stated before, do not go into detail about prevention or treatment as this is not the focus of the discussion. We only want to know what participants think about receiving feedback on findings that are actionable, or would they want to know even if they can do nothing about the findings? Note that some of the points discussed will be things that could be a standard for all participants where others could be context determined (i.e. a type of prevention or treatment might not be available in a specific area due to poverty etc.).*

THEME 3: Feedback of findings for the sake of solidarity

Some people who have participated in research feel that they participate in research to advance research but that they don't need to get anything back for their contribution. Others feel that if participants give of themselves by allowing researchers to draw blood from them, they then also deserve to get something back. In the story that we told you about the mother, it means that the researchers should be obligated to tell her what they found after studying her genes because she agreed to participate in the study and allowed them to take blood from her.

- Thinking of this, do you think that participants should get something back to recognise their role in the research and if so what?
- In genomics research, what would be a reasonable way to recognise the gift of a sample?
- Would feeding back information relevant to the participant's health be a good way to recognise the gift of a sample?

Look out for: *Ideas related to solidarity, the idea that researchers and community members should work collectively to accomplish a shared goal. This could mean that there is an expectation that if participants give of themselves, they should benefit in some way e.g. feedback of individual research findings.*

THEME 4: Findings unrelated to what is being studied

In the case study, you were told a story of a mother who participated in a research study that was looking at psychiatric problems, she was never told by the researchers or anyone else that they might find other problems too that are not related to psychiatric problems. The researchers then found a gene that put the mother at risk for developing breast cancer. Even though the researchers did not say that they will return any findings to the participants, and specifically said that they were looking at psychiatric problems and not breast cancer, they decided to tell the mother what they had found and told her to go for a test that can confirm a diagnosis.

- Do you think that it was right for the researchers to tell the mother what they had found out even if it was not at all what they said they were looking for?

PROMT: Why/ why not?

- Do participants have a right to know what researchers know about their health?

PROMPTS: Reciprocity: information as a recognition/reward to participating in research?

Duty to rescue: if the researcher knows something about me, then he has an obligation to also tell me OR to help me sort out the issue.

- How do you think the mother felt about being told that she might have a risk of developing breast cancer when no one told her that participating in this research study might give her this news?

PROMPT: Experiences of feelings such as worry, fear, anxiety, helplessness, indifference, or gratitude?

In order to find results such as the one reported in the case study, researchers have to do a lot of work to analyse their data. This takes a lot of time and effort, and it means that they cannot spend as much time doing their actual research.

- Thinking of this, do you think that it would be good for researchers to spend time to find relevant individual results in genomics research?

PROMPT: Genomics recruits usually >2000 people, so spending even 30 min per person means spending 1000 hrs (125 work days or half a year of a full-time person)

Look out for: *Some have argued that the research team has a "duty to warn" or a "duty to rescue" the participant as he or she is in a position to prevent potentially serious harm at little or no personal cost and that the participant might otherwise not discover the condition in time to change its course. But identifying these results in datasets takes time and resources. Probe here whether and how participants think these should be weighted.*

- When do you think people should be told that genomics research could tell us something about a person's health?

  PROMPT: at consent, when something is actually found, another time?

- Should a research participant have the right to say that they do not want to know what is found out about them after their genes have been studied?

  PROMPT: Even if the informed consent stated that people might be told what is found out after their genes have been looked at, could the mother have told the researchers that she doesn't want to know what they found?

Look out for: *Responses related to <u>autonomy</u> (i.e. do participants think and feel that they would have the freedom of determining their own action – whether or not they want to know or share what was fed back). Responses related to <u>disrespect</u> (i.e. "it would be a disrespectful action if research volunteers are treated as conduits for generating scientific data without giving due consideration to their interest in receiving information about themselves derived from their participation in research").*[3]

THEME 5: Concerns about privacy

In the story that we told you, the researchers suggested that the mother tell her daughter about what was found because the breast cancer gene can be passed from a parent to their child. For this reason, the researchers advised her to tell her daughter so that she can go for a diagnostic test. If the daughter also carries this gene, she could go to the doctor frequently to check her breasts and have surgery early. That could save her life. Although this could help to keep her daughter healthy, the mother is worried that she will now have to explain why she participated

[3] From: National Academies of Sciences, Engineering, and Medicine. 2018. Returning individual research results to participants: Guidance for a new research paradigm. Washington, DC: The National Academies Press. doi: https://doi.org/10.17226/25094.

in a study about psychiatric problems. The mother feels that this information is private and that she did not intend to tell people what was found from studying her genes.

- Do you think the mother has the right not to have to tell her daughter, or anyone else, about the news that she received?

- Do you think that it is wrong of the mother not to tell her daughter that she might be at risk of developing breast cancer, especially because it could affect her daughter's health too?

- Should the researchers call the daughter in and tell her what was found from studying her mother's genes?

Look out for: *Issues related to confidentiality (e.g. if people would feel comfortable disclosing a potential health risk even if it might put their child's health at risk too) – when this happens find out how people would think about sharing information that is private to help someone else.*

THEME 6: Practicalities of returning results

In the case study, the researchers did not tell the mother that she might be told what is found after studying her genes. The mother also did not ask the researchers specifically to tell her what was found after her genes were studied.

- If genomics research were to find something, what do you think the best way would be to tell people what was found?

PROMPTS: Telephone call or come into the clinic? Who should be allowed to know what information was found after studying a person's genes (i.e. participant only or other people also)?

- Should the researchers first ask the mother's permission to take a second sample to again look for the specific finding to make sure that they have indeed found this risk gene?

MODULE 4: Closing the information session and next steps

Background to this module:

- The main aim of this module is to have a final check that all the outputs from the earlier modules have been achieved and that any outstanding issues/questions from participants have either been addressed or a way of addressing them has been agreed. This means making sure that the timing and venue of the follow up dFGD 2 are all reasonable and agreed, and that everyone is clear about what to expect.

Outputs: By the end of this module, make sure participants leave with key points of understanding and views shared (including outputs from modules 2 and 3) and looking forward to next steps (dFGD 2) with clear understanding of what this will involve.

1. Debrief

Make sure that participants understand that these questions and case study scenarios are all hypothetical and that the NeuroGAP / NeuroDEV / CAFGEN studies are not actually feeding back information on individual genetic findings.

2. Making final summaries

- Summarise views on genetics and heredity and how these factors may influence participation on research studies.
- Summarise views on the fact that research findings are not diagnostic and note how this may or may not affect trustworthiness of research findings.
- Summarise views on whether people would want to know findings (i.e. on an individual or group level), and how these findings should be communicated if they are fed back and under what circumstances.
- Highlight any other main issues shared during the information session
- Address any questions that participants might have (e.g. about IFGENERA project 2).

3. Planning for next meeting

- Remind the participants that the information session will be followed by two dFGDs that relate back to the issues discussed in the information session.

- Discuss and agree on dates and venues for these meetings and transport arrangements. For example, suggest possible dates/places and ask participants to choose.

4. Closing the information session

- Thank the participants for their willingness to take part in the information session and that you look forward to further discussion during the dFGDs.
- Each participant should receive a handout highlighting the main issues discussed during the information session. They should also be encouraged to give these points some more thought before the dFGDs and to even talk to others about these issues.
- Make transport arrangements and provide transport reimbursement before participants leave.

MODULE 5: SECOND DELIBERATIVE FOCUS GROUP DISCUSSION

Background to module:

The aim of this module is to recall and further explore some of the answers that participants provided during the first dFGD. In this round of discussion, the interviewer should challenge participants about their views and opinions raised during the first round of questioning. For this reason, it is very important to complete a preliminary analysis of the qualitative data from dFGD 1 BEFORE dFGD 2 is undertaken so that the interviewer is sure to explore unique discussions that took place within each group during dFGD 1.

- The interviewer should also use this opportunity to introduce more complex questions and to ask counter questions that may be helpful to probe in more detail some of the answers that participants provided in the first dFGD.

The main points that should be covered in this module:

- Recap and explore discussion from dFGD1;
- Findings without a risk of imminent harm;
- Cost of identifying relevant results.

Outputs from this session: By the end of the module, you should have: probed and explored in more detail answers and views raised by participant during dFGD 1.

Follow the instructions and use participatory methods to explore the issues described in the text below along with any other relevant issues that may come up.

2. Recap and explore discussion from dFGD 1

c) ***Discussion of notes from information session and dFGD 1***

Remember in the previous meeting we talked about genes and how research can sometimes tell people things about their health after their blood has been tested. Today, we will again ask you some of the same questions from our last discussion to make sure that we have understood what you have told us but also to give you the opportunity to add anything new that you did not mention before but might have thought of in the meantime. *Consider recapping the case study scenario 1.*

Record key issues that came up from the informational session and dFGD 1 for reference here.

Explore each of these issues in more detail by for example asking "Thinking back to the workshop and also adding any new ideas you may have today. You mentioned [insert

statement from the information session or dFGD1]. Do the rest of you agree with that point?" For example, "When I listened to the recordings of our previous dFGD, you all seemed to agree [insert statement from the information session or dFGD1]. Is that right?"

d) ***Further complicate topics discussed in dFGD 1***

THEME 1: Findings without a risk of imminent or serious harm

In the case study, the researchers decided to tell the mother that she carries the gene for a risk of developing breast cancer because this is something that could affect her health. Although it is not for sure that the mother will develop cancer, the researchers thought it would be important for her to know this news since cancer is a severe but preventable disease, so she might want to make plans to get help sooner rather than later because this influences her chances of treating and surviving the cancer.

Some researchers would say that it was not necessary or right for the researchers to tell the mother this news because she had not yet shown any signs of being sick and that the researchers had no way of knowing if she would ever get sick. In our research there are a number of genetic conditions that researchers might find.

On the piece of paper that we have given you there is a table, where each block groups some examples of the genetic conditions that may come up grouped by preventability (i.e. the likelihood that the condition will develop in that person) and severity (i.e. how sick the person might become). Let's look at the table together to make sure that everybody understands what it is showing us.

In the top left corner of the table you will see conditions that are not severe and can be prevented. This means, that if someone has one of these conditions, they cannot die from it and there is help so that they don't suffer from these conditions. Some examples of these conditions in the table are: being allergic to animals such as dogs or cats; having too little iron in your blood making you feel tired all of the time; or having kidney stones. In the bottom left of the table there are some conditions that are also not severe but that cannot be prevented by doctors

or anyone else but could still be treated. Some examples of these conditions in the table are: not being able to see well and needing reading glasses; being an anxious person; or vitiligo (*show participants a picture of vitiligo and explain that it is when patches of skin on a person's body does not have any pigment and appears lighter as the rest of the skin)*. If we now look at the right side of the table, the top block shows examples of conditions that are serious problems but can also be prevented. Some of these conditions are: having a drinking problem / drinking too much and being drunk constantly which is a mental health problem; or some types of cancers like the mother in the case study. The last block at the bottom right of the table shows us some examples of conditions that are very serious and that cannot be prevented but that can be treated. Some examples of these conditions are: some psychiatric problems such as depression; learning difficulties or developmental problems such as autism where children are not able to go to mainstream schools because they are not on the same level as other children; or Alzheimer's disease which you might have seen some older people develop and they begin to be very confused or forget things or the names of family members.

- Thinking of this table and what we have just spoken about, do you think that researchers should always tell participants what they have found?
- Do you think that researchers should only tell participants if there is a chance that they will develop a disease or actually get sick?
- Do you think that researchers should tell participants about conditions that are severe and cannot be prevented but only managed to some extent?
- Do you think that researchers should tell participants about conditions that are severe but can still be prevented?
- Do you think that researchers should also tell participants about conditions that are not severe but can still be prevented?
- Do you think researchers should also tell participants about conditions that are not severe but also cannot be prevented?

Look out for: *This will be a complex question to discuss in the group so really try to take some time and care to make sure that all participants understand what is being asked / discussed. Some people argue that the return of individual genomic results should not be expected or be compulsory in the ethical principles for human research, except for the rare occasion when presumably reliable results are of significant clinical importance and where there is a risk of*

imminent or serious harm to the participant if they are not disclosed. If we are not sure that a participant will get sick, should this feedback still be given? One reason to share information is because of reciprocity, if participants gave their permission for their blood to be studied, then there can arguably be other mechanisms to achieve this same goal such as offering financial compensation for time and effort. The issue of reciprocity has been discussed in detail in Theme 2 of dFGD 2 and should not again be discussed in detail in this question. Also, do not go into a detailed discussion about benefits in return for participation as this is not the focus of this study. For this question, we are interested to further explore if participants feel that any and all feedback should be available or is it only if there is a direct and severe risk to their health.

For this discussion, give each participant a print out of the table below to demonstrate the four types of genomic conditions that could be reported. Again, be careful not to suggest that the current studies are reporting these conditions. This is only an example for the sake of our dFGDs.

Not severe & preventable	**Severe & preventable**
1. Pet dander (dog) allergy 2. Iron deficiency anemia 3. Kidney stones 4. Lactose intolerance 5. Gastroesophageal reflux disease 6. Reduced response to ibuprofen 7. Chronic mild constipation 8. Delayed response to local anaesthetic 9. Increased susceptibility to cavities	1. Alcoholism * (mental health) 2. Asthma 3. Deep vein thrombosis 4. Familial hypercholesterolemia 5. Melanoma 6. Peanut allergy 7. Types II Diabetes 8. Malignant hyperthermia 9. Childhood onset hereditary colon cancer 10. Aortic aneurism
Not severe & non-preventable	**Severe & non-preventable**
1. Attention deficit hyperactivity disorder* (learning disability) 2. Essential tremor 3. Generalized anxiety * (mental health) 4. Hypothyroidism 5. Poor vision 6. Seasonal allergies 7. Turner Syndrome 8. Vitiligo 9. Mitral valve prolapse 10. Obstructive sleep apnea	1. Autism * (developmental and learning disability) 2. Bipolar disorder * (mental health) 3. Duchenne Muscular Dystrophy 4. Juvenile (Type I) Diabetes 5. Juvenile rheumatoid arthritis 6. Polycystic Ovarian Syndrome 7. Rett Syndrome * (Childhood-onset degenerative) 8. Acute lymphoblastic leukemia 9. Batten disease (NCL) * (Childhood-onset degenerative) 10. Alzheimer's disease * (adult-onset) 11. Huntington's disease* (adult-onset)

Note: *This table was directly copied from Holm, I. A., Iles, B. R., Ziniel, S. I., Bacon, P. L., Savage, S. K., Christensen, K. D., … Huntington, N. L. (2015). Participant Satisfaction With a Preference-Setting Tool for the Return of Individual Research Results in Pediatric Genomic*

Research. Journal of Empirical Research on Human Research Ethics: JERHRE, 10(4), 414–426. https://doi.org/10.1177/1556264615599620
This article can be read as background for the questions in theme 3.

THEME 2: What about children?

In case study scenario 1 we talked about a mother who participated in the research, but we now wonder how your ideas might, or might not, differ when it is a child that participates in our research and in what way this changes what parents might, or might not, expect to know about what we found out from our research.

Complicating case study scenario 1: A mother is asked to allow her daughter to participate in research that is looking at genes that play a role in progression of HIV infection and TB infection when it is discovered that her daughter is a carrier of the BRCA1 gene believed to be a risk factor for developing breast cancer.

In a creative way, tell a story about a mother who has allowed that her daughter participate in a research study that is looking at genes that play a role in progression of HIV infection and TB infection. In the process of exploring the daughter's blood sample a researcher noticed that she carries the BRCA1 gene which means that there is a chance that she may develop breast cancer at some stage in her adult life. The researchers are not sure if they should tell the mother what they have found. The little girl might not develop breast cancer and will also not do so before she is an adult. However, if they do not tell the mother, the girl my never go for a diagnostic test when she is older which is a problem because early detection could save her life if she ever developed breast cancer.

The main points that should be included in the case study scenario:

- Ethical issues related to feedback findings that may not be actionable during childhood;
- Parents' right to know and a child's right to privacy.

Note: To make the case study scenario more interesting, you could give the characters well known names (e.g. famous TV celebrity known to the participants) or to engage the participants you could ask them to provide these names and details of the fictional characters.

Ask open ended questions to check that participants have understood these main points in the story.

e) Discussing the Complicated version of Case Study Scenario 1

Researchers working on a study focusing on HIV/TB discover that one of the children in the study is a carrier of the BRCA1 gene which means that she might be at risk of developing breast cancer when she is an adult.

- Do you think the researchers have a responsibility to tell the parent(s) of a child that she carries a gene that might make her sick when she is an adult?

  PROMT: Is it ok to tell parents information that will only affect the child when she is an adult, which then takes away the child's decision whether to tell her parents the news when she is an adult?
- Should the researchers tell the parents specifically what they have found or only that they think that she should go for a diagnostic test when she is an adult?
- Do you think the researchers have a responsibility to tell the parent(s) of a child that she carries a gene that might make her sick when she is an adult?
- Do you think the researchers have a responsibility to tell the parent(s) of a child that she carries a gene that might make her sick even if the parents won't be able to change anything about their child's condition?

Look out for: Any discussion whether findings should be available to parents where research results may not be actionable during childhood. Probe whether participants feel it is ethically sound to tell parents information that the child might have kept private if she participated as an adult participant.

Appendix P: In-depth interview guide

Title of the Study: Expectations and Preferences of Parents and Adolescents Regarding Feedback of Individual Genetic Findings in a Genomic Research in Botswana

Topic Guide for IDIs with lay people who have participated in genomics research in Botswana

Introduction and Purpose of the study

Thank you for your willingness to participate in our in-depth interviews focusing on preferred feedback on individual genetic findings. We are very grateful to you for taking the time to participate in our research study.
This interview is a follow-up on some of the issues that were discussed in the deliberative focus group discussions that you previously participated in. The purpose of this meeting is to conduct an in-depth interview to learn more from lay individuals who participate in genomic research what, when, how, and why they think individual genetic findings should be returned to participants or their parents (guardians). This information has important implications for developing best ethical practices for genomic research.
Therefore, in our interview, we will again ask you some more questions about feedback of individual genetic findings to find out more about your thoughts and preferences.

Introduction

- Introduce self, organisation
- Introduce study
- Why am I interviewing you?
- Length of Interview
- This interview part of a study that will conducted both in Botswana and in South Africa
- Explain why recording
- Confidentiality reminder – *interview transcripts only shared with research team*
- Voluntariness reminder – *no need to answer all questions*
- Compensation and potential harms
- Any questions?
- Consent form and signing of the form

1. Feedback of results to participants

1.1. In our previous group discussions, we have talked about the different categories of genetic conditions that may be discovered during participation in genomic research. However, there are other genetic results that are not health related that may also be discovered in genomics studies.

a. Considering this, do you think genetic results that relates to an individual's paternity should be fed back?
b. Do you think genetic results that relates to an individual's ancestry should be fed back?
c. In other cases, genetic results could inform reproductive choices, do you think such genetic results should be fed back?
d. What kind of genetic information should not be fed back to participants?
    - Information that is harmful? (Examples?)
    - E.g. false paternity?
e. Do you think parents have the right to know all of their child's individual genetic results OR only those genetic test results with clear and timely direct benefit?
    - If yes, why?
    - If no, why not?
f. Sometimes, researchers may want to feedback results not because it would help the participant but because it could help their family members. For instance, this would be the case if they find that one of their male participants carries variants relating to breast cancer – knowing that wouldn't help them, but it would help their sisters and daughters. In that case, do you think those results should be fed back?

2. Severe and non-preventable

2.1. In our previous focus group discussions, participants seemed to have differing opinions with regards to feedback of results for conditions that are severe and non-preventable. There were those who wanted to receive the results and those who did not want to know the results. Considering this, how then can researchers manage these divergent views to ensure that each participants' interest is protected in returning the results?

3. Actionability

3.1. Looking at the information collected in our previous group discussions, there seem to be a high expectation of assistance and support from researchers by research participants with regard to actioning results from genomics research. Do you agree that this is the case? And why is it so?

3.2. Also, some participants indicate that whenever they go for a medical test, even for those done in research, they are always expectant of extra results. What do you think could be the reasons for this expectation?

3.3. Internationally, the consensus is that only results that are 'actionable' should be fed back. This means that some kind of intervention is available that participants can take to prevent the illness from developing. This could be something concrete – for instance, an

operation to insert a device in the heart, or removing the breasts so that women don't develop cancer. It could also be something softer – for instance, regular screening, or changes in diet and exercise.

a. Do you agree with this criterion of 'actionability'? Is it right that only results that the person can do something about should be fed back?
    - E.g. Alzheimer's or Huntington's disease – ok not to feedback?
b. How do we know that something is actionable for each individual person though?
    - E.g. woman in a remote rural area may not have access to operation – still ok to feedback?
c. If something is actionable for some participants in a project, but not for others (e.g. in a different country) would it be ok to feedback information only to some people but not to others?

4. Reciprocity

4.1. Some participants in the group discussions pointed that they would expect researchers to reciprocate to them in one way or the other. What do you think are some of the reasons for participants to expect reciprocity from researchers?

5. Confidentiality issues

5.1. Again, information from the focus group discussions seems to indicate that both parents and adolescents believe that it is wrong for a parent to keep to themselves information on their breast cancer genetic results that could affect their daughter as the daughter could also be at risk of getting the breast cancer. As a result, some participants indicate that researchers should be able to notify the daughter themselves if the mother has no intentions to tell the daughter, while others think that doing so will be a breach of the mother's confidentiality and could also negatively affect the relationship between the mother and daughter. What then do you think researchers should do to balance between protecting the mother's confidentiality and the health of her daughter?

5.2. a. On the other hand, some parents feel that results for conditions that are severe and not preventable should be fed back to the parent alone and they can decide on the right time to tell the child. However, it is not clear if this applies to children of all ages, what about those that are over 18 years?

b. How about for other conditions, for example; those that are not severe and preventable? What should be the procedure for feeding back such results that relate to children?

6. Practicalities of returning results

a. According to you, who should ideally feedback individual findings from a genetic study?
    - The researcher?
    - Results to be given by a doctor?
b. Who should ideally provide participants with counselling, where needed?

c. Some participants pointed out that receiving feedback on individual genetic results could bring conflict in the family, that some family member is bewitching the participant, some parents may be in denial and take the child to traditional healers to seek help while other participants could lose hope for life and consider suicide. What do you think should be done to ensure that the above negative effects are minimised?

7. Cost of follow-up care

7.1. Even when researchers give back individual research results, the patients would still need to see a doctor to go for confirmation testing. They may also need an operation (for instance, if there is a risk of developing cardiomyopathy or breast cancer) or they need annual screening. That means there is a cost associated with knowing you have a genetic predisposition. It also mean that the information is not definite but indicates a risk.

a. Considering that there is a cost associated with receiving genetic research information, do you still think this information should be fed back? Why?
b. Who should pay for follow-up care? Why?
    - Explore the responsibilities of researchers, government, research participants
    - How far do the responsibilities of the researchers extend? E.g. should they only arrange a clinical appointment, should they pay for the consultation etc?
    - Only be responsible for mutations that fall into the research teams' area of expertise?
    - *Remember that the real interest here is understanding why, with a particular focus on reciprocity.*

8. Taking a second sample

8.1. When doing research, it is always possible that some of the tubes get mixed up, or that the results for different people get mixed up. For research, that is not a problem (the overall dataset is still the same) but it would be very bad for individuals to get the wrong results of course. Some people have proposed that the solution is to approach participants and ask them for a second sample, but this has implications for cost and logistics.

a. Re-contacting people, making appointments, taking another sample, screening the other sample – this is expensive. Who should bear the cost of this?
    - Researchers, funders, the healthcare system? Why?
b. If the trade-off is between not giving results or giving results with the warning that there may have been mix-up (but without collecting a second sample), do you still think researchers should feedback individual results?

9. Consent

9.1. During the focus group discussions some participants expressed that they only have the right to know results if that was agreed upon in the beginning or for conditions that relate to what is being studied. While others indicated that, their right to know applies even where there is no prior agreement to return back the results because it's their samples that are being studied and that they have to know their health status. What do you think could be done practically to manage these divergent views so as to avoid conflicts and ensure that each participant's interest is protected?

9.2. Most studies do not seek consent for feedback of results, partly because genomics studies are already difficult to explain.

a. Do you think going forward that participants should be asked for consent? For general feedback, individual feedback?

- But what if researchers find something that signal predisposition to something quite lethal (e.g. breast cancer in women) and people said 'no I don't want to know'. Have they really considered all the issues? What should be done in such a situation?

10. Educational needs of individual genetic findings for a feedback session

10.1. Now I want to ask you to share your thoughts on the use of educational material to facilitate a feedback session.

- How can we prepare lay individuals for the feedback on individual genetic results in genomic research?
- What kind of information would you need to make sense of individual genetic findings in genomic research?
- What other sources of information would be helpful for you to make sense of individual genetic findings in genomic research? [Other patients sharing their experiences? Online resources? Written materials?]

Closing Section

- We have now reached the end of this interview. Is there anything else you think is important that we have not talked about today?
- Do you have any questions about what we talked about? Is there anything you need more information about?

Thank the participant.