*Original Research Article*

# Understanding of Critical Elements of Informed Consent in Genomic Research: A Case of a Paediatric HIV-TB Research Project in Uganda

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**Abstract**

Several studies have reported inadequate comprehension of informed consent for genomic research. This study aimed to assess research participants' understanding of critical elements of informed consent for genomic research. A cross-sectional survey involving 123 parents/caregivers of children participating in a paediatric genomic TB/HIV study was conducted**.** Only 47.2% of the participants had adequate understanding of consent information. The mean objective (actual) and subjective (perceived) understanding scores were 78.7% and 91.7% respectively. Participants adequately understood most elements of consent however, some elements were poorly understood including foreseeable risks, protection of confidentiality and compensation for research related injury. Overall there was inadequate comprehension of critical elements of informed consent and there was dissonance between actual and perceived comprehension of informed consent.

**Keywords**

informed consent, genomic research, understanding, research participants, biobanking

## Introduction

Valid informed consent requires that participants voluntarily make decisions to participate in research after adequately understanding the information provided (Wendler, 2004). Yet several studies have shown that participants in biomedical research including biobanking fail to understand vital aspects of research to which they consented (Afolabi et al., 2014; Bergenmar et al., 2011; Beskow et al., 2015; Klima et al., 2014; McCaughey et al., 2016; Robinson et al., 2013; Traore et al., 2015). Genomic research challenges the traditional consenting process because of its complexity, difficulty in accurately translating scientific concepts and terminologies into local languages (Marshall et al., 2014; Mystakidou et al., 2009; Ngwenya et al., 2020) and difficulties with processing large amounts of information in a time-limited setting (Corneli et al., 2012). Further, there are challenges in understanding information related to the use of stored samples for unknown future research, and other issues that relate to risk/benefit assessment. In low resourced settings, this is compounded by low literacy levels that make comprehension of consent information difficult (de Vries et al., 2015; Ramsay et al., 2014; Tindana et al., 2012). Some scholars have argued that participants do not have to understand everything because a lot of information could confuse them (Beskow et al., 2015; Beskow et al., 2010; Emanuel et al., 2000); they opine that focus should be drawn to what participants need to know in order to make an informed decision. Others have proposed the use of simplified informed consent forms as a means of enhancing understanding of consent (Beskow et al., 2010; Garrett et al., 2017).

Literature from Uganda has also reported several challenges to informed consent processes in health research (Kiguba et al., 2012; Pace et al., 2005; Ssali et al., 2015). Rutakumwa et al. (2019) in a qualitative study, reported inadequate understanding of consent by participants of genomic research. He reported that some participants actually could not even recall that they had participated in research. This raises the ethical question of whether consent achieves the purpose for which it is intended. It is from this viewpoint that this study sought to assess informed consent comprehension by examining parents/caregivers who enrolled their children in an HIV/TB genomic study. This study aimed to assess genomic

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research participants' understanding during the informed consent process and identify predictors of comprehension so as to inform best practices for enhancing comprehension of informed consent.

## Methods

This was a cross-sectional study that was conducted between May to September 2019. Data were collected using quantitative methods. Participants were consecutively recruited from the Ugandan site of the Collaborative African Genomic Network (CAfGEN) study that is currently being implemented at the Baylor College of Medicine Children's Clinical Centers of Excellence (COEs) in Botswana, Uganda, and Swaziland; as well as Baylor College of Medicine, Texas. The CAfGEN study is a collaborative project within the Human Heredity and Health for Africa (H3Africa) Consortium (H3Africa, 2014) that is using genomics methods to identify host genetic factors that are important for the progression of HIV and HIV-TB co-infection in sub-Saharan Africa (Mboowa et al., 2018). The CAfGEN study also seeks to "uncover specific genetic markers and genes that reflect the greatest risk for progression in HIV disease and to gain new insights into the pathophysiology of HIV and HIV-TB coinfection, in order to ultimately facilitate development of new treatment strategies" (Mboowa et al., 2018, p. 7). The study recruited more than 1000 children and adolescents. Informed consent for the CAfGEN study was obtained by a team comprising of two trained counsellors and two graduate nurses who had receive basic short-course training in genetic counselling. The risks incorporated in the CAfGEN study informed consent documents included: physical risks of the phlebotomy procedure; a possibility of coming across genes that are not related to the study (incidental findings), breach of confidentiality, and social risks such as discord within the family in case there are findings about diseases that can be passed on in families. Informed consent documents were translated into Luganda, the most widely spoken language in Central Uganda. Informed consent was administered in either English or Luganda depending on the participants preference and ease of understanding. No audiovisual aids were used. Participants were given the opportunity to ask questions; to which researchers gave appropriate responses. Those who desired were provided with a copy of the informed consent form to take home for consultations with family and friends. Lastly, assessment of understanding was performed using a checklist before signing of the informed consent form. On average the consent process for the CAfGEN study lasted between 45–60 min.

The study population comprised of parents and caregivers, above 18 years of age, who had consented to their children's participation in the CAfGEN study and voluntarily provided written informed consent. One hundred twenty-three participants were consecutively recruited until the sample size was realized. The sample size was obtained assuming that 50% of the parents and caregivers comprehended informed consent, for a design effect of 1% (Wejnert et al., 2012), confidence limits of 5% and power of 80% for a total pooled population of 500 research participants from the Ugandan CAfGEN study site. This sample size was obtained using the online calculator for sample size based on proportions available on www.openepi.com. Eligible participants who declined to give written consent were excluded from the study.

Data were collected using the Quality of Informed Consent (QuIC) questionnaire (Joffe et al., 2001) that was initially developed and validated for assessing objective and subjective understanding of informed consent in cancer clinical trials. The QuIC questionnaire has been widely used and validated for assessment of understanding of informed consent in genetics research (Klima et al., 2014; McCarty et al., 2007; Ormond et al., 2009). The QuIC questionnaire has 13 domains which include: nature of project, purpose, duration, procedures, experimental nature of study, foreseeable risks and discomforts, benefits to participants, benefits to future patients, alternatives, privacy and confidentiality, compensation, voluntary nature of participation, contacts in case of concerns about the study, participants' rights and welfare. The questionnaire comprised of two parts: Part A that evaluated objective understanding (how well-informed participants were) and Part B that evaluated subjective understanding (how well-informed participants believed they were). Part A contained 21 questions based on the facts of the study and the content of the informed consent document and process for the CAfGEN study. Part B contained 14 questions on participants' perceived understanding of the content of the informed consent documents for the CAfGEN study. The questionnaire was translated into Luganda. The questionnaire was pre-tested to ensure that the questions are appropriate, easy to administer and could assess participants' understanding. Participants were recruited immediately after completing all study recruitment procedures for the CAfGEN study. The questionnaire was administered in either English or Luganda depending on the participants' preference.

For Part A, each response was assigned a score as follows: 100 for a correct response, 50 where participants were unsure and 0 for an incorrect response. For Part B responses were score as follows: 100 for "Understood", 50 for "Unsure" and 0 for "Did not understand". Scores for each domain were obtained by averaging the scores for all completed questions in that domain (Joffe et al., 2001). The overall scores were classified as follows; 80–100% for "Adequate understanding", 50–79% for "moderate understanding" and less than 50% for "inadequate understanding". These score ranges were adapted from a systematic review on comprehension of informed consent for surgery and clinical research (Falagas et al., 2009).

## Statistical Analysis

Descriptive statistics were used to summarize the data. At bivariate analysis, the association between participants' characteristics and understanding of critical elements of informed consent was assessed using the Chi square test and Fishers' exact test for frequencies less than five. At multivariate analysis, logistic regression was used to assess the factors likely to influence participants' understanding of informed consent information. The level of significance was set at $p < 0.05$.

This research was reviewed and approved by Makerere University School of Biomedical Sciences Research Ethics Committee (SBS-HDREC 626). Written informed consent was obtained from all participants prior to enrollment in the study. Participants were assured of confidentiality. Participants received transport reimbursement and compensation for time and inconvenience. The authors of this paper were independent of the CAfGEN study.

## Results

One hundred twenty-three parents/care givers participated in this study, a majority were female (100/123, 81.3%). The mean age of the participants was 38.9 years (SD = 11.8, interquartile range 30–46 years). Most participants were employed (73.2%); 68/123 (55.3%) had at least attained secondary level of education; 102/123 (89.2%) had participated in research before; and 94/123 (76.9%) read the informed consent forms themselves. Most informed consent discussions lasted between 30 min to one hour and a vast majority of participants (95.9%) found the consent information easy to understand (See Table 1).

**Table 1.** Parents/Caregivers' Characteristics.

| Characteristic (N = 123) | Categories | Freq (%) |
|---|---|---|
| Gender | Male | 23 (18.7) |
| | Female | 100 (81.3) |
| Marital status | Single | 56 (45.5) |
| | Married | 60 (48.8) |
| | Widowed | 7 (5.7) |
| Highest level of education | No formal education | 7 (5.7) |
| | Primary | 48 (39) |
| | Secondary | 55 (44.7) |
| | Tertiary | 13 (10.6) |
| Employment status | Unemployed | 33 (26.8) |
| | Employed | 90 (73.2) |
| Participated in research before | Yes | 21 (17.1) |
| | No | 102 (82.9) |
| Duration of the consent discussion | Less than 30 min | 18 (14.6) |
| | 30 min–1 h | 99 (80.5) |
| | More than 1 h | 6 (4.9) |
| Who read for you the consent form | I read the consent form | 94 (76.4) |
| | Read for me | 29 (23.6) |
| Ease understanding disclosed information | Very easily | 118 (95.9) |
| | Very difficult | 5 (4.1) |

## Assessment of Objective Understanding of Consent Information

Only 58/123 participants (47.2%) had adequate objective understanding of critical elements of informed consent, the rest had moderate understanding (65/123, 52.8%). The objective understanding scores for the different consent elements are shown in Table 2. The informed consent elements that were adequately understood and answered correctly by participants included; nature of research (A1), purpose of the study (A2), benefits to participants (A14) and study duration (A3). Conversely, the informed consent elements that were poorly understood and answered incorrectly included the anticipated risks and discomforts (A13), protection of confidentiality (A16), and compensation for study related injury (A18). The mean domain score for objective understanding was 78.7% (IQR 69.6–84.6) suggesting that overall objective understanding of the critical elements of informed consent was moderate.

At bivariate analysis, none of the demographic factors significantly influence objective understanding of informed consent information as shown in Table 3. Multivariate logistic regression analysis revealed age above 35 years as the only significant predictor of participants objective understanding of informed consent information (OR 0.51, 95% CI 0.17–0.88, $p = 0.023$). The odds of understanding informed consent was 41% lower in participants aged 35 years and above than the odds of understanding informed consent in participants less than 35 years (Table 3).

## Assessment of Subjective (Perceived) Understanding of Critical Elements of Informed Consent

Table 4 presents the subjective assessment of understanding of the critical elements of informed consent. Overall, participants felt that they understood the information included in the informed consent document (mean subjective domain score = 91.7). They felt that they understood that they were participating in genomic research (B1), that participation was voluntary (B13), the study procedures the children would undergo (B4) and the benefits of the study to the children (B7) and future patients (B8). However, participants felt less certain about compensation for research related injury (B11) and anticipated risks of participation (B6).

The proportion of participants who answered the questions correctly in QuIC part A items was compared with how well the participants thought they had understood the

**Table 2.** Responses to Part A of the QuIC Assessment (Objective Understanding).

| Domain | Question (N = 123) | Disagree Freq (%) | Unsure Freq (%) | Agree Freq (%) | Mean Score | Domain Score |
|---|---|---|---|---|---|---|
| Nature of project (research) | **A1**: When I signed the consent form for the CAfGEN study, I knew I was giving consent for myself or my child to participate in a research project | 0 | 0 | 123 (100) | 100 | 100 |
| Purpose | **A2**: The main goal of the CAfGEN study is to understand why some children with HIV progress to severe disease faster than others. | 1 (0.8) | 1 (0.8) | 121 (98.4) * | 98.8 | 98.5 |
| | **A5**: In this research project, one of the main goals is to understand how genes contribute to the progression of children with HIV to AIDS. | 0 | 2 (1.6) | 121 (98.4) * | 99.2 | |
| | **A6**: In the research project, one of the major goals is to investigate why some children living with HIV can stay without symptoms for a long time while others frequently fall sick | 1 (0.8) | 1 (0.8) | 121 (98.4) * | 98.8 | |
| | **A7**: The genetic testing in this study will result in knowing whether my child is among those who do not fall sick frequently | 3 (2.4) | 1 (0.8) | 119 (96.8) * | 97.2 | |
| Duration | **A3**: I have been informed how long my participation in the study is likely to last | 1 (0.8) | 0 | 122 (99.2) * | 99.2 | 99.2 |
| Study procedures | **A8**: My blood will not be stored as part of this research study | 121 (98.4) * | 2 (1.6) | 0 | 99.2 | 94.9 |
| | **A9**: The researcher will provide me with results of genetic tests conducted on my blood samples | 118 (95.9) * | 2 (1.6) | 3 (2.4) | 96.7 | |
| | **A10**: The researcher will store my child's sample and use it for undefined research in the future | 4 (3.3) | 6 (4.9) | 113 (91.9) * | 94.3 | |
| | **A11**: As part of this study, researchers will have access to my child's medical records and information, including genetic information that might be shared with other researchers. | 11 (8.9) | 3 (2.4) | 109 (88.6) * | 89.8 | |
| | **A12**: The blood sample my child gives during participation in this study will be labeled with his/her name in order to identify it | 114(92.7) * | 4 (3.3) | 5 (4.1) | 94.3 | |
| Experimental nature of the study | **A4**: All the procedures in the research project are standard for any genetic routine testing | 12 (9.8) | 6 (4.9) | 105 (85.4) | 87.8 | 87.8 |
| Foreseeable risks and discomforts | **A13**: This research project does not carry any risks or discomforts to my child | 21 (17.1) | 4 (3.3) | 98 (79.7) | 18.7 | 18.7 |
| Benefits to participants | **A14**: There may not be direct medical benefit to my child from his/her participation in this research study | 41 (33.3) | 3 (2.4) | 79 (64.2) * | 65.4 | 65.4 |
| Benefits to future patients | **A15**: By participating in this research study, my child is helping the researchers learn information that may benefit him/her or other future patients | 0 | 1 (0.8) | 122 (99.2) * | 99.6 | 99.6 |
| Alternatives to participation | **A17**: The researchers did not offer me any alternatives besides involvement in this research study | 91(74.0) * | 1 (0.8) | 31 (25.2) | 74.4 | 74.4 |
| Confidentiality | **A16**: Because my child is participating in the CAfGEN study, it is possible that the study sponsor, various government agencies or others that are not directly involved in his/her care could view his/her medical records | 77 (62.6) | 3 (2.4) | 43 (35.0) * | 36.2 | 36.2 |

*(continued)*

**Table 2. (continued)**

| Domain | Question (N = 123) | Disagree Freq (%) | Unsure Freq (%) | Agree Freq (%) | Mean Score | Domain Score |
|---|---|---|---|---|---|---|
| Compensation for injury | **A18**: The consent form that I signed described who will pay for my child's treatment if he/she gets injured or become ill as a result of participation in the CAfGEN study | 55 (44.7) | 4 (3.3) | 64 (52.0) * | 53.7 | 53.7 |
| Contacts in case of questions or concerns | **A19**: The consent form I signed lists the name of the person (persons) whom I should contact if I have any questions or concerns about the CAfGEN study | 0 | 3 (2.4) | 120 (97.6) | 98.8 | 98.8 |
| Voluntary participation | **A20**: If I had not wanted my child to participate in the CAfGEN study, I could have declined to sign the consent form | 1 (0.8) | 2 (1.6) | 120 (97.6) | 98.4 | 95.6 |
| | **A21**: I will have to remain in this research study even if I decide someday that I want to withdraw | 114 (92.7) | 0 | 9 (7.3) | 92.7 | |
| **Overall objective understanding (mean domain score)** | | | | | | **78.7** |

*Denotes correct responses.

item in QuIC part B. Low similarity (proportion of participants answering incorrectly who thought they understood the question) was noted for A13/B6 (Risks and discomforts; 17.1%), A14/B7 (benefits to the participant, 64.2%), and A16/B10 (Sharing of medical data; 35%).

## Discussion

Findings from this study show that most participants did not adequately understand informed consent. A greater majority of participants believed themselves to be well informed, their self-perceived level of understanding was generally higher than their actual understanding as determined by objective measures. This is consistent with what other scholars have reported (Joffe et al., 2001; MacQueen et al., 2014; Ormond et al., 2009; Shiono et al., 2014) (Klima et al., 2014; McCarty et al., 2007). The most understood aspects of consent were: the nature of research, benefits to future patients and duration of the study. While the least understood included: anticipated risks and discomforts, confidentiality and compensation for research related injury. Higher age (35 and above) was the only variable that significantly influenced participants' understanding of informed consent.

The inadequate understanding of informed consent information observed in this study is not unique; several studies have shown that participants often fail to adequately understand important aspects of the research to which they consented (Mandava et al., 2012; McCarty et al., 2007; Rahm et al., 2013; Richter et al., 2018). There was low concordance between the actual and perceived understanding of the benefits of participation in the CAfGEN study. This means that participants might not have adequately understood that there may not be any direct benefits to their children. Conversely, they clearly understood that their children's participation in research could be of benefit to future research endeavors and the community. These incongruences may indicate therapeutic misconception, defined as when a research participant expects direct benefits, even when the aim to benefit only future patients has been explained (Eisenhauer et al., 2019). This observation is not surprising because Baylor-Uganda offers quality HIV care and treatment to thousands of children living with HIV and some parents/caregivers could have ascribed the routinely given ancillary care as a direct benefit to their participation in the genetic study.

There was discordance between actual and perceived understanding of the risks and discomforts of participating in genomic research. Actual understanding of the risks of participating in the CAfGEN study was the least understood aspect with a domain score of 18.7. Much as participants thought that they had understood the risks of participating in the study, they could not correctly answer the questions on the potential risks. Inadequate understanding during informed consent for genetics and biobanking, particularly the risks, has been reported by several authors (Eisenhauer et al., 2019; Klima et al., 2014; Moodley & Singh, 2016; Tindana et al., 2015). This might be due to the non-physical nature of risks involved in genomic and genetics research and the uncertainty of the future studies at the time of consenting. Generally, the poor understanding of genetics-related information is not limited to research participants only, studies have shown that various stakeholders, including investigators have limited understanding of genetic and genomic concepts (Kengne-Ouafo et al., 2016; Mwaka et al., 2021; Ogunrin et al., 2019; Tindana et al., 2012). Therefore, we would not expect a research participant to adequately understand informed consent when the investigator obtaining it does not sufficiently understand genetics and genomic research and its implications. On the other

**Table 3.** Correlation of Parents/Caregivers' Understanding of Critical Element of Informed Consent in a Multivariate Ordered Logistic Regression Model.

| | Unadjusted model | | | Adjusted model | | |
|---|---|---|---|---|---|---|
| Characteristics | OR | 95% CI | p-value | OR | 95% CI | p-value |
| **Grouped age** | | | | | | |
| Less than 35 years | *Ref* | | | *Ref* | | |
| 35 years and above | 0.51 | 0.25–1.06 | 0.072 | 0.39 | 0.17–0.88 | 0.023 |
| **Gender** | | | | | | |
| Male | *Ref* | | | *Ref* | | |
| Female | 0.78 | 0.31–1.94 | 0593 | 0.54 | 0.19–1.54 | 0.250 |
| **Marital status** | | | | | | |
| Unmarried | *Ref* | | | *Ref* | | |
| Married | 0.65 | 0.32–1.32 | 0.235 | 0.60 | 0.27–1.34 | 0.21 |
| **Education Level** | | | | | | |
| None | *Ref* | | | *Ref* | | |
| Primary | 0.75 | 0.15–3.72 | 0.725 | 0.77 | 0.14–4.29 | 0.763 |
| Secondary | 0.63 | 0.13–3.06 | 0.562 | 0.47 | 0.08–2.66 | 0.397 |
| Tertiary | *0.47* | *0.07–3.04* | *0.427* | *0.45* | *0.06–3.48* | *0.448* |
| **Employment status** | | | | | | |
| Unemployed | *Ref* | | | *Ref* | | |
| Employed | *1.09* | *0.49–2.44* | *0.819* | *1.09* | *0.45–2.61* | *0.853* |
| **Is this your first study** | | | | | | |
| Yes | *Ref* | | | *Ref* | | |
| No | *1.56* | *0.59–4.09* | *0.363* | *1.78* | *0.63–5.01* | *0.275* |
| **Duration of consent discussion** | | | | | | |
| Less than 30 min | *Ref* | | | *Ref* | | |
| 30 min – 1 h | 1.54 | 0.55–4.29 | 0.410 | 2.23 | 0.73–6.82 | 0.160 |
| More than 1 h | 0.78 | 0.11–5.48 | 0.808 | 1.18 | 0.13–10.54 | 0.883 |
| **Who read for you the consent form** | | | | | | |
| I read the consent form | *Ref* | | | *Ref* | | |
| Read for me | 0.74 | 0.32–1.71 | 0.477 | 0.76 | 0.28–2.01 | 0.574 |
| **Ease understanding the information disclosed** | | | | | | |
| Very easily | *Ref* | | | *Ref* | | |
| Very difficult | 0.74 | 0.12–4.58 | 0.744 | 0.61 | 0.08–4.93 | 0.643 |

hand, sub-optimal comprehension of informed consent may not necessarily be due to the complexity of genetic research, but may as well be caused by inadequate informed consent forms lacking key components (Alkaraki et al., 2020; Al-Riyami et al., 2011). It could also be caused by the questionable quality of translation of consent information into local languages (Ngwenya et al., 2020); much as this study did not explore this issue. Translation of genetic and genomic concepts and terminologies into local languages or wording that can better be understood by participants in settings with low literacy levels is a big challenge. This is particularly the case when research is implemented in ethnically diverse populations like ours (Marshall et al., 2014; Upjohn & Wells, 2016). Translation of consent documents is problematic because several genomic terminologies have no direct translation in Ugandan local languages (e.g., Luganda). Therefore, innovative tailored local narratives have to be given to enhance adequate understanding (Nabukenya et al., 2022; Ndebele et al., 2012). Lastly, poor communication skills and inadequate education and training of research team members responsible for obtaining informed consent have also been reported to contribute to inadequate comprehension during the informed consent process (Nusbaum et al., 2017). Personal interaction between the researcher and research participant is critical in maintaining the integrity of the informed consent process and is also key in enhancing comprehension of consent information (Albrecht et al., 2005). However, exploration of researchers' communication skills was beyond the scope of this study. Per Ugandan ethics guidance, consent language should be easily understood by a child in the final year of elementary school education.

## Factors That Influence Understanding of Consent Information

In this study participants aged 35 years and above were less likely to understand consent information than those below

**Table 4.** Responses to Part B of the QuIC Assessment (Subjective Understanding).

| Domain | Questions (N = 123) | Did not Understand Freq (%) | Unsure Freq (%) | Understood Freq (%) | Domain score |
|---|---|---|---|---|---|
| Nature of project (research) | **B1**: How well did you understand that the CAfGEN study is genetic research? | 0 | 0 | 123 (100) | 100 |
| Purpose | **B2**: How well did you understand what the researchers are trying to find out in the CAfGEN study? | 1 (0.8) | 1 (0.8) | 121 (98.4) | 98.8 |
| Duration | **B3**: How well did you understand for how long your child will be in the study? | 1 (0.8) | 0 | 122 (99.2) | 99.2 |
| Study procedures | **B4**: How well did you understand the procedures that your child would undergo as part of the research study? | 1 (0.8) | 8 (6.5) | 114 (92.7) | 95.9 |
| Experimental nature of the study | **B5**: How well did you understand which of the study procedures are experimental? | 7 (5.7) | 8 (6.5) | 108 (87.8) | 91.1 |
| Foreseeable risks and discomforts | **B6**: How well did you understand the possible risks and discomforts of participating in the CAfGEN study? | 42 (34.2) | 0 | 81 (65.9) | 65.9 |
| Benefits to participants | **B7**: How well did you understand the possible benefits of participating in the study? | 7 (5.7) | 1 (0.8) | 115 (93.5) | 93.9 |
| Benefits to future patients | **B8**: How well did you understand that your child's participation in this study may benefit future patients? | 0 | 1 (0.8) | 122 (99.2) | 99.6 |
| Alternatives to participation | **B9**: How well did you understand the alternatives to participation in the study? | 6 (4.9) | 2 (1.6) | 115 (93.5) | 94.3 |
| Confidentiality | **B10**: How well did you understand the effect of the study on the confidentiality of your child's medical records? | 13 (10.6) | 3 (2.4) | 107 (87.0) | 88.2 |
| Compensation for injury | **B11**: How well did you understand who will pay for you/ your child's treatment if you are injured or become ill as a result of participation in the CAfGEN study? | 47 (38.2) | 3 (2.4) | 73 (59.4) | 60.6 |
| Contacts in case of questions or concerns | **B12**: How well did you understand who you should contact if you have any questions or concerns about the study? | 1 (0.8) | 2 (1.6) | 120 (97.6) | 98.4 |
| Voluntary participation | **B13**: How well did you understand the fact that your child's participation in the study is voluntary? | 0 | 2 (1.6) | 121 (98.4) | 99.2 |
| Overall understanding | **B14**: Overall, how well did you understand the study when you signed the consent form? | 0 | 2 (1.6) | 121 (98.4) | 99.2 |
| **Overall subjective understanding (mean domain score)** | | | | | **91.7** |

35 years. There are conflicting results on association of age and informed consent comprehension in biobanking and genomic research. Whereas some studies report younger age as a predictor of understanding informed consent comprehension (Beskow et al., 2017; McCarty et al., 2007; Robinson et al., 2013), others report the contrary (Hoover-Regan et al., 2013; Klima et al., 2014). This is an issue that may require further exploration in our setting. Higher education has been associated with better comprehension of informed consent in genomic research (Campbell et al., 2017), however in this study, education level had no significant influence on understanding of informed consent information. It is also important to note that the majority of our participants were literate, with more than half having secondary level education.

The main limitation of this study was the small sample size, these findings may, therefore, not be applicable to parents/caregivers in the wider Ugandan community. However, our findings have given a glimpse at the comprehension of informed consent in this low resourced setting and present an opportunity for further research on enhancing understanding of critical elements of informed consent.

The main strength of this study was the fact that assessment of understanding of informed consent information was done immediately after the parents/caregivers had completed the

informed consent procedures for the CAFGen study. This reduced the probability of recall bias.

## Conclusion

This study adds to the existing evidence on research participants sub-optimal comprehension of informed consent in biobanking and genomic research in low resource settings. The dissonance between actual and perceived understanding during the informed consent process calls for the innovation of more contextualized and objective methods of information delivery; and assessment of comprehension of informed consent.

## Best Practices

These findings suggest that it is not enough to just ask a participant a question, "Have you understood?" Most certainly they will answer in the affirmative because they feel that they have understood, even if they have not really understood adequately. It reiterates the need for more objective ways of assessing comprehension of consent in biobanking and genomic research especially in low resource settings. Several innovative approaches aimed at enhancing comprehension of informed consent have been suggested and can be adapted for genomic research in Uganda. For example, use of visual and audio imageries to explain highly technical and complex language (Nabukenya et al., 2022; Taylor et al., 2021); electronic video consent (Naeim et al., 2021), use of Computer-based education modules (Shelton et al., 2015), and summarizing of consent information and delivering it in a conversational and interactive manner (Nabukenya et al., 2022). The revised common rule also introduced the concept of "key information" (HHS.gov, 2018) where participants should be given focused and concise information presented in a way that facilitates comprehension. This encourages clarity and honesty, and creativity in information disclosure (King, 2019).

The Ugandan national ethics guidelines (UNCST, 2014) do not clearly pronounce themselves on the use of checklists and other tools for assessing comprehension of informed consent. Therefore, there is a need to develop more efficient and innovative ways to convey complicated concepts, explain the benefits and risks of genomic research and assess participant understanding to improve the overall informed consent process (Klima et al., 2014; Tabor et al., 2012). Assessment of comprehension of informed consent, preferably by standardized tools, should also become a mandatory requirement per local ethics guidance. We hope our findings will contribute to the development of contextualized and culturally appropriate consent approaches to genomic research in low resource settings, that enhance comprehension during the consenting process in genomic research and biobanking.

## Research Agenda

Less than half of participants in this study had adequate comprehension of informed consent. More research is needed on how best comprehension can be enhanced during the informed consent process for genomic research and biobanking in these settings. To meaningfully achieve this, there is a need for a larger mixed-method study. The quantitative aspect of the study will allow for generalization of findings to low resourced settings. The qualitative aspect will provide an in-depth exploration of the possible facilitators and barriers to comprehension of informed consent in these settings. Findings from the proposed study will provide valuable empirical data to inform research ethics policy and practice.

## Educational Implications

Genomics is an emerging field of research in sub-Saharan Africa that is not fully understood by several stakeholders, including researchers. Valid informed consent requires that the one obtaining consent is knowledgeable and capable of answering all the questions that research participants may ask. Therefore, there is a need for training of research teams in the basic concepts and the ethical, legal and social issues in genomic research. Research teams should also undertake short course training in research ethics and/or good clinical practices with particular emphasis on informed consent processes that enhance informed consent comprehension.

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FAA and MES participated in the conceptualization, design, data collection, analysis and interpretation, and manuscript writing. FNN and JB were supervisors to AFA and participated in the design, data analysis and interpretation. IGM participated in the design, data analysis and interpretation. All authors participated in the writing of this manuscript and approved the final draft. ESM, FNN and JB were supervisors to AFA from whose master's thesis this manuscript was developed.