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Assessment of Parents'/Guardians' Initial Comprehension and 1-Day Recall of Elements of Informed Consent Within a Mozambican Study of Pediatric Bacteremia

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Abstract

Participants' understanding of key elements of a research protocol is essential to their ethical enrollment in the study. Ongoing participation should be based on continued comprehension and consent, which presumes a high degree of recall. Many obstacles can prevent full understanding of information about the research protocol. This study's aim was to evaluate the comprehension and 1-day recall of the elements of informed consent by the parents/guardians of children enrolled in a clinical study in Mozambique. We developed a 10-question test based on the study's informed consent document. We asked participants to answer questions shortly after being read the informed consent document and again the following day. Participants who did not demonstrate good or reasonable understanding at enrollment were provided the information again as a refresher. Overall high rates of initial comprehension demonstrate that attention to the informed consent process can result in Mozambicans's informed, voluntary participation in clinical trials.

Keywords

ethics, informed consent, understanding, recall, elements of informed consent, Mozambique

Introduction

Today's international ethical codes and regulations on biomedical research involving human participants were born from the growing complexity of biomedical investigation and successive scandals that occurred during the development and implementation of different types of research. Currently, the most widely recognized national and international guidelines, such as the Nuremberg Code, the Declaration of Helsinki, the Belmont Report, and the International Ethical Guidelines of the Council of International Organizations of Medical Sciences (CIOMS), emphasize that study participants must knowingly agree to take part in research (The Belmont Report, 1979; CIOMS, 2016; "The Nuremberg Code", 1947/1949; World Medical Association, 2013).

Informed consent in research is the voluntary decision to participate without being forced, intimidated, or coerced (American Cancer Society, 2016; CIOMS, 2016; Hallinan, Forrest, Uhlenbrauck, Young, & McKinney, 2016; Pozón, 2015). Traditionally, the quality of the informed consent process and its effects have been assessed in three important dimensions: information, comprehension, and voluntariness (The Belmont Report, 1979; Joglekar et al., 2013). Yet, many factors can influence a research participant's understanding and experience of the information provided, such as the type of study, its cultural setting, local beliefs and customs, as well as the participant's language, religion, level of education, and socioeconomic status (Lavery, Grady, Wahl, & Emanuel, 2007; Minnies et al., 2008).

The way in which information is transmitted to the participant is crucial for his or her good comprehension, because each individual's maturity and intellectual abilities, education, and personal beliefs may be different (The Belmont Report, 1979). The readability of an informed consent document is not determined only by the terminology and number of pages but also by whether it provides sufficient but concise information regarding the study in a way that the potential participant can grasp. What may be an acceptable informed consent document in a high-literacy context is unlikely to be acceptable in settings that have a

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low literacy rate (Bottrell, Alpert, Fischbach, & Emanuel, 2000; Ezeome, Ezeome, & Chuke, 2011). Moreover, in low- and middle-income countries (LMIC), participants' reading levels and the acceptability of any single informed consent document may vary significantly across multiple settings where an individual trial is conducted.

Mozambique is one such challenging setting for medical research. The United Nations ranks Mozambique 181st of 188 countries worldwide in the 2016 Human Development Index (United Nations Development Programme [UNDP], 2016). Mean length of schooling in Mozambique is 3.2 years (UNDP, 2016), and the illiteracy rate is approximately 60% for women and 30% for men aged 15 to 49 years (Ministério da Saúde [MISAU], Instituto Nacional de Estatística [INE], & ICF International [ICFI], 2013; U.S. Agency for International Development [USAID], 2016). The official language in Mozambique is Portuguese, but in addition, there are more than 40 local languages (Simons & Fennig, 2017), of which the following five are commonly used: Emakhuwa (25.3%), Xishangana (10.3%), Cisena (7.5%), Elomwe (7%), and Chuabo (5.1%; Central Intelligence Agency, 2017). Outside of urban areas where people speak Portuguese and are more likely to have had formal education; few have the ability to read, discuss, and understand the aims and procedures of a scientific study described in an informed consent document. In addition, many local languages, such as Xishangana and Chuabo are not commonly used in written form.

Over the past several years, a growing number of biomedical studies involving human participants have been conducted in Mozambique, particularly research on infectious diseases. Mozambican regulations governing human subjects research are based on the World Medical Association's Declaration of Helsinki, CIOMS' Guidelines, and World Health Organization's (WHO) Operational Guidelines for Ethics Committees (Schwalbach, 2014; Training and Resources in Research Ethics Evaluation [TRREE], 2014) and include a requirement for written informed consent, with a document in Portuguese.

There has been little evaluation of informed consent practices in biomedical research in Mozambique, or assessment of how effective those practices are. A recent systematic review and meta-analysis of participants' comprehension of informed consent, in 103 studies over 30 years and across multiple countries, described participants' comprehension rates that varied between 52% and 76% (Tam et al., 2015). Other more targeted research, including a study in the West African country of Mali, have found that participants in clinical trials have general knowledge deficits and misunderstand specific elements of the informed consent document including study-related risks, distinctions between research and treatment, and the notion of voluntary participation and the right of withdrawal from the study (Joglekar et al., 2013; Krosin, Klitzman, Levin, Cheng, & Ranney, 2006; Shiono et al., 2014).

The Mozambican National Bioethics Committee (*Comité Nacional de Bioética em Saúde* [*CNBS*]) has paid careful attention to the quality of informed consent documents it approves for use in biomedical research and has dedicated resources to educating researchers and members of its eight subordinate institutional research ethics committees (RECs), on best practices in informed consent (Schwalbach, 2014). Recognizing that assessment of informed consent practices can be useful to this national effort, we sought to evaluate the effects of the informed consent process on participants' understanding and recall of the elements of informed consent in a currently ongoing pediatric clinical study in Mozambique. We were particularly interested in identifying factors that might facilitate or hinder participants' understanding of information provided in the informed consent document, as well as steps that might provide further evidence to strengthen researchers' commitment to improving the quality of informed consent practices in similar settings or studies.

Method

Our informed consent study was a "secondary study" of parents or guardians whose children were being recruited into a larger study, the aim of which was to evaluate the causes of bacteremia in HIV-infected children below age 5 years, hospitalized in the pediatric units of four hospitals in Mozambique. It was a prospective cohort study that sought to evaluate parents'/guardians' understanding of an approved informed consent document and their 24-hr recall of the document's main elements.

Participants

Participants for the informed consent study were recruited from among the parents/guardians who were approached to enroll their child in the primary bacteremia study. Recruitment occurred between November 2016 and March 2017, at the point of the child's admission into the pediatric urgent care unit of Mavalane General Hospital and Maputo Central Hospital in Maputo city, as well as the Quelimane General Hospital and Quelimane Central Hospital in Quelimane city (Figure 1).

Procedures

All participants were recruited into the primary study by one or more members of the study team following an approved recruitment protocol. Each person recruited was provided a written copy of the primary study's approved informed consent document, which outlined the study's goals, eligibility criteria, anticipated risks and benefits, and

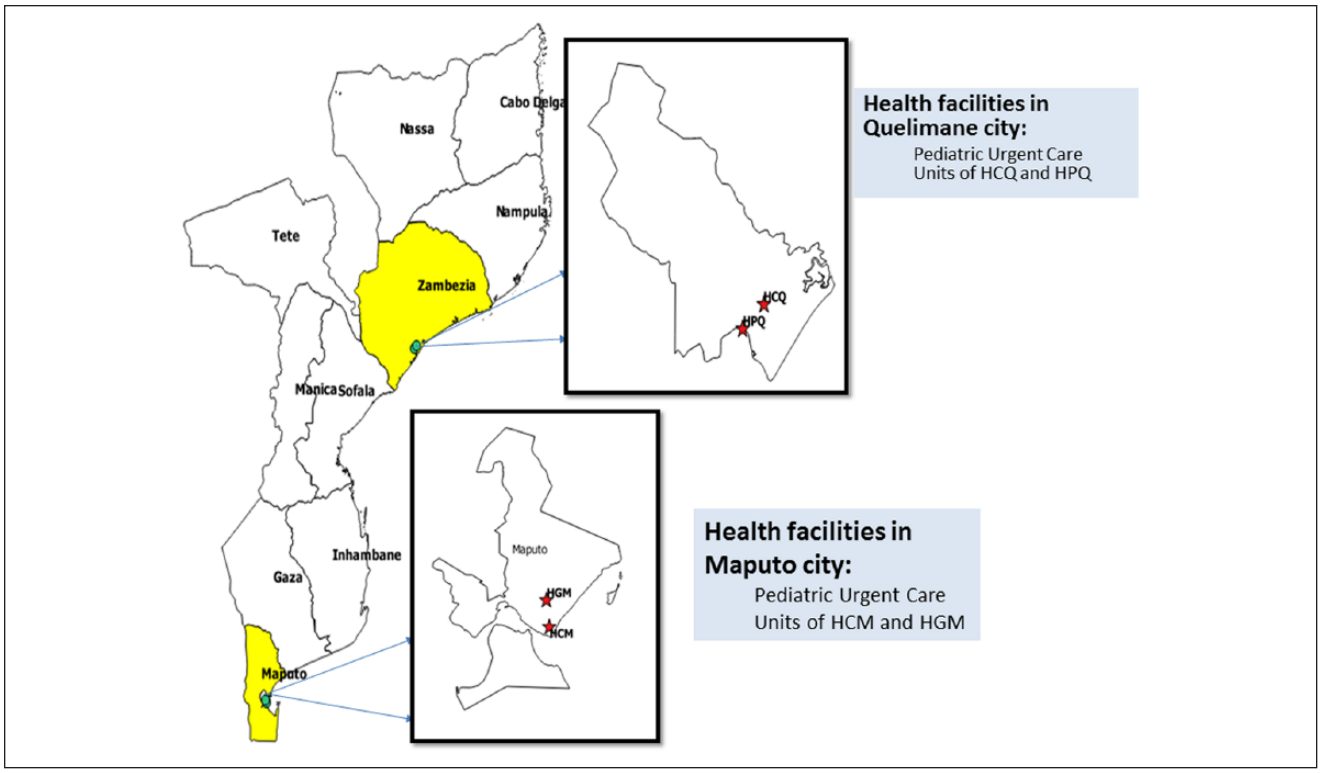

Figure 1. Map of Mozambique with study hospitals identified in Maputo and Quelimane.

other information required under Mozambican research regulations, and which was adapted and approved to include consent for the secondary study. Informed consent was obtained for the primary study and secondary study at the same time and included asking the individual whether they were also willing to be interviewed about their recall of the elements of the primary study's informed consent document on the following day. Subsequently, the nurse invited the individual to talk with a member of our team.

We met with each child's parent or guardian in a private room for the interview when the child was able to come with them. For those parents or guardians of children who were seriously ill and in Urgent Care, we conducted the interviews at the child's bedside. Before each interview began, we asked the participant which language he or she found most comfortable. Sometimes the interview took place in two languages, such as when the participant initially stated that they spoke Portuguese but slipped into another language while speaking or when the interviewer shifted into another language after realizing that the participant was struggling to speak or understand Portuguese.

At the beginning of the interview, one of the team members read aloud and orally explained the content of the primary study's six-page informed consent document. We utilized two trained interviewers at each hospital, with one conducting the interview at enrollment and the other conducting the interview at Day 2. At the end of the presentation, the participant was asked to answer questions related to each of the 10 elements of the informed consent document; if he or she did not answer the questionnaire correctly, the interviewer re-read the relevant section(s) to ensure that the participant understood it prior to signing. The average length of the interview was between 10 and 15 min.

Measurements and Data Collection

We developed an instrument with 21 questions based on the informed consent document from the principal study, where the first 11 questions addressed demographic information and the remaining 10 questions addressed key elements provided within the informed consent document. For each specific section or element, we asked the participant to explain the information that had been provided before advancing to the next section. We developed a guide for the interviewers that outlined an ideal answer for each of the 10 content informed consent element questions and bolded four to five keywords that we expected the participant to use in answering correctly. We then provided either a dichotomous (yes/no) assessment of whether the participant's answer was correct or a 4-point Likert-type scale assessment of the participant's answer, based on how closely it matched the ideal. We used the same instrument to assess both the participant's understanding of the informa-

tion after its initial presentation and recall of that information on the following day.

Statistical Analysis

Statistical analysis was performed using R version 3.3.3 software (R core team, 2015). Descriptive statistics were used to summarize the participants' sociodemographic characteristics. Open-ended questions were coded and analyzed thematically as either "adequate or inadequate understanding/recall" based on the 4-point Likert-type scale. For each question, we aggregated responses as 4 = "good understanding/recall", if the participant could respond using three or more of the bolded keywords; as 3 = "reasonable understanding/recall", if they responded with two of the bolded keywords; as 2 = "poor understanding/recall", if they responded with only one bolded keyword; and as 1 = "no understanding/recall", if they could not respond using any of the bolded keywords. If responses did not include the identified bolded keywords, responses with a similar meaning were accepted based on the interviewer's interpretation of the response and then classified into the above categories. Interviewers received prestudy training with guidance on what responses would be acceptable to limit the variability of interpretation between interviewers. Categorical variables/responses were reported as frequency and percentages.

We then expressed the quality of informed consent by further aggregating responses into "adequate understanding/recall" if ≥80% of all responses to each of the 10 questions were assessed to be either good or reasonable, and as "inadequate understanding/recall," if the participant did not meet the 80% threshold. Although the 80% threshold was regarded as "adequate" understanding for the purposes of our analysis, we again highlight that all participants were able to show initial understanding of all essential elements of informed consent prior to enrollment in the study.

To further explore participant characteristics associated with comprehension, we summed the 10 Likert-type scale points as an overall measurement of their comprehension. As the same participants were interviewed at different times, at enrollment and again the next day, we analyzed data using a linear mixed-effects model with R lme4 package, with the response as a continuous variable (Bates, Maechler, Boler, & Walker, 2015). Participant ID was treated as a random intercept, and all other variables included in the model were treated as fixed effects.

Two groups of participants were defined by whether they had adequate understanding at enrollment and then two types of interviews were further categorized by when they had been conducted (at enrollment or on Day 2). Reinforcement of the concepts of informed consent for those with inadequate initial understanding at enrollment was the interaction term between the two binary variables, indicating that only those participants who had inadequate understanding at enrollment received a refresher on the elements of consent that they had not understood. Other patient characteristics were also included in the model as fixed effects. Gender, age group, language, and relationship to the child were binary variables, whereas education level was treated as a continuous variable with a value of 1 to 5 (corresponding to the five education levels). To be conservative, profile confidence intervals (CIs) of the model coefficients are reported. Values of p are reported of likelihood ratio F tests with Kenward–Roger approximation of degree of freedom using R package "car" (Fox & Weisber, 2011).

Ethics

The protocols for the present study on informed consent and the parent study on pediatric bacteremia, on which this project was based, were both approved by the Mozambican National Committee of Bioethics in Health (CNBS) and the Vanderbilt University Institutional Review Board. Interviewers in Mozambique completed the Portuguese-language educational modules on the ethics of human subject's research and protection of research participants provided by the TRREE course (available at http://elearning.trree.org/).

Results

Participant Characteristics

A total of 138 participants were enrolled in our study to assess initial comprehension and next-day recall of the elements of informed consent. Of these, 120 participants completed both questionnaires. Ninety-five percent of participants were female, with a median age of 27 years. Among those, 88 (64%) were between 18 and 30 years and 122 (88%) were the hospitalized child's mother. Eighty-eight (64%) participants completed the primary study's informed consent process in Portuguese with their subsequent knowledge and recall of the elements of informed consent also assessed in Portuguese. Nineteen (14%) participants were interviewed in a combination of Portuguese and another local language. Thirty-four (25%) participants had no formal education, whereas an additional 58 (42%) reported only some primary school (Table 1).

Comprehension and Recall of Informed Consent

Overall, 76 (78%) participants had adequate understanding (≥80% of responses correct) of all the elements of informed consent at both enrollment and at recall the day following enrollment. A total of 21 (22%) participants had adequate understanding at enrollment but were unable to maintain adequate understanding at recall on Day 2. Twenty-three

Table 1. Sociodemographic Characteristics of the Study Participants.

Variables	Maputo *n* = 68 (%)	Quelimane *n* = 70 (%)	Total *n* = 138 (%)
Age, median (IQR), years	28 (24-34)	25 (22-30)	27 (22-32)
18-30	43 (63)	45 (64)	88 (64)
31-40	17 (25)	12 (17)	29 (21)
>40	7 (10)	13 (19)	20 (14)
Missing data	1 (2)	—	1 (1)
Sex			
Female	68 (100)	63 (90)	131 (95)
Male	—	7 (10)	7 (5)
Relationship with child			
Mother	61 (90)	61 (87)	122 (88)
Father	—	5 (8)	5 (4)
Brother/Sister	—	1 (1)	1 (1)
Aunt	1 (1)	—	1 (1)
Grandmother	4 (6)	3 (4)	7 (5)
Other	2 (3)	—	2 (1)
Language			
Portuguese	41 (60)	47 (67)	88 (64)
Chuabo	1 (1)	18 (26)	19 (14)
Xishangana	8 (12)	—	8 (6)
More than one	18 (27)	1 (1)	19 (14)
Missing data	—	4 (6)	4 (2)
Level of education			
No formal education	10 (15)	24 (34)	34 (25)
Primary	38 (56)	20 (29)	58 (42)
Secondary	19 (28)	20 (29)	39 (28)
Pre-University	1 (1)	5 (7)	6 (4)
University	—	1 (1)	1 (1)

Note. IQR = interquartile range.

(19%) participants showed inadequate understanding of the elements of informed consent during the initial informed consent process, requiring refresher instruction prior to signing the informed consent documents. At repeat questioning on Day 2, seven (30%) of these 23 participants were subsequently classified as having maintained an adequate level of understanding, whereas 16 of the 23 (70%) were classified as having poor recall and thus inadequate understanding (Table 2).

Initial Understanding and Recall of Individual Elements of Informed Consent

The proportion of participants with adequate understanding and 1-day recall for each of the individual elements of informed consent are shown in Table 3. At initial enrollment, 85 (71%) participants demonstrated adequate understanding of the purpose of the document being read to them.

Table 2. Overall Parent/Guardian Understanding of Informed Consent at Enrollment and Recall on Day 2.

Understanding at enrollment	Understanding on Day 2	(%)
n = 120	*n* = 97	
Adequate (97)	Adequate (76)	78
	Inadequate (21)	22
	n = 23	
Inadequate (23)	Adequate (07)	30
	Inadequate (16)	70

Of these, 27 (32%) were unable to maintain adequate recall the following day. On the purpose or objective of the study, 93 (78%) demonstrated adequate understanding at initial enrollment, of whom 29 (31%) were unable to maintain adequate recall the following day. Rates were higher for understanding and recall of the primary study's eligibility criteria, with 111 (93%) participants demonstrating adequate understanding at enrollment and of these, 88 (79%) having adequate recall the following day. The possible risks of the study were adequately understood by 107 (89%) participants at enrollment, with 91 (79%) demonstrating adequate recall the following day. The number of participants who had adequate understanding at enrollment of their right to withdraw their child from the primary study was 110 (92%), with 93 (85%) able to recall this information on Day 2. Finally, of the 88 (73%) participants who had adequate initial understanding, 70 (80%) maintained adequate recall of the purpose of collecting blood or other biological samples that were part of the primary study.

Overall, among the participants who had an inadequate understanding of a particular point at enrollment and received reinforcement of the information before proceeding, two-thirds were able to recall that information on Day 2 for six of the 10 questions.

Predictors of Comprehension and Recall

In our linear mixed-effects model, overall there was a 2.36 (95% CI = [3.22, 1.49]) point reduction in the sum of the Likert-type scale scores between enrollment and recall on Day 2 (Table 4). If the participant had inadequate understanding at enrollment, then the sum of their Day-2 Likert-type scale score was 7.36 (95% CI = [8.84, 6.05]) points lower than that of participants who had adequate understanding at enrollment. The characteristic most significantly associated with comprehension and recall of the elements of informed consent was education level. As educational level increased, there was a 1.13 (95% CI = [0.57, 1.70]) point increase in the sum of Likert-type scale scores (Figure 2a). Participants with a lower education level were more likely to have inadequate understanding of the elements of

Table 3. Parent/Caregiver Understanding of Informed Consent at Enrollment and Recall on Day 2 of Each Element of Informed Consent..

Understanding at enrollment	Understanding on Day 2	(%)
1. What is the purpose of this document that I am reading to you?		
Adequate (85)	Adequate (58)	68
	Inadequate (27)	32
Inadequate (35)	Adequate (14)	40
	Inadequate (21)	60
2. Please describe the *purpose or objective of this study*.		
Adequate (93)	Adequate (64)	69
	Inadequate (29)	31
Inadequate (27)	Adequate (12)	44
	Inadequate (15)	56
3. Who is *eligible to participate* in this study?		
Adequate (111)	Adequate (88)	79
	Inadequate (23)	21
Inadequate (09)	Adequate (03)	33
	Inadequate (06)	67
4. Please describe the *possible risks* related to this study.		
Adequate (107)	Adequate (91)	85
	Inadequate (15)	15
Inadequate (13)	Adequate (07)	54
	Inadequate (06)	46
5. Is there any *kind of benefit to you* or your child for study participation?		
Adequate (105)	Adequate (80)	76
	Inadequate (25)	24
Inadequate (15)	Adequate (10)	67
	Inadequate (05)	33
6. What will it happen if you decide to *withdraw from the study*?		
Adequate (111)	Adequate (93)	85
	Inadequate (17)	15
Inadequate (09)	Adequate (03)	33
	Inadequate (06)	67
7. Will you receive anything for participating in this study?		
Adequate (113)	Adequate (109)	96
	Inadequate (04)	4
Inadequate (07)	Adequate (05)	71
	Inadequate (02)	29
8. Who can you contact later if you have any questions about this study?		
Adequate (98)	Adequate (83)	85
	Inadequate (15)	15
Inadequate (22)	Adequate (15)	68
	Inadequate (07)	32
9. Will your name be used in the report related to this study?		
Adequate (111)	Adequate (96)	86
	Inadequate (15)	14
Inadequate (09)	Adequate (07)	78
	Inadequate (02)	22
10. What is the *purpose of the blood/biological samples* we intend to collect from your child?		
Adequate (88)	Adequate (70)	80
	Inadequate (18)	20
Inadequate (32)	Adequate (17)	53
	Inadequate (15)	47

Table 4. Linear Mixed-Effects Model for Associations With Understanding and Recall at Day 2 of Elements of Informed Consent..

	Estimate	95% CI	*p* value
Day 2 recall compared with enrollment	−2.36	[−3.22, −1.49]	<.0001
Inadequate understanding at enrollment	−7.43	[−8.84, −6.05]	<.0001
Age group (≥25)	0.23	[−0.73, 1.15]	.6393
Portuguese language	−0.87	[−1.99, 0.27]	.1411
Male gender	1.72	[−4.22, 0.79]	.1896
Relationship to child	1.61	[−0.01, 3.22]	.0565
Education level	1.13	[0.57, 1.70]	.0001
Day 2 recall if had inadequate understanding at enrollment	2.78	[0.89, 4.65]	.0044

Note. CI = confidence interval.

informed consent at enrollment and thus required reinforcement on these topics before being enrolled (Figure 2b). However, participants who received reinforcement at enrollment, after initially giving inadequate answers, had an additional increase of 2.78 (95% CI = [0.89, 4.65]) points in their Likert-type scale score on the Day 2 interview.

Discussion

This study was motivated in part by our concern that important elements of informed consent may not be well comprehended by research participants in Mozambique. We found that following a structured informed consent process, participants had a relatively high level of understanding of the key elements of our primary clinical study immediately after enrollment (81%), followed by a drop in overall recall on Day 2 for those who showed adequate understanding at enrollment (22%). Although this level of misunderstanding is worrisome to the investigators, it is consistent with levels of comprehension described in other studies conducted in LMIC and high-income countries (HIC; Lynöe, Hyder, Chowdhury, & Ekström, 2001; Mandava, Pace, Campbell, Emanuel, & Grady, 2012; Minnies et al., 2008; Sánchez, Salazar, Tijero, & Díaz, 2001; Upvall & Hashwani, 2001), which suggests the overall picture of informed consent is complex.

Other studies have found that participants' understanding of a study in which they are enrolled can be improved with multiple meetings between participant and researcher that reinforces key information (Mystakidou, Panagiotou, Katsaragakis, Tsilika, & Parpa, 2009). In our study, when we identified a participant who had difficulty comprehending any of the key elements of the informed consent document following our initial reading, we repeated that particular section until we were confident the participant had appropriate understanding of all the different key informed consent elements of the primary study. We attempted to ensure that anyone identified as not fully informed was not inappropriately enrolled in the study. We also sought to ensure that our attempts to evaluate the informed consent process did not prejudice recruitment into the primary study by inadvertently identifying persons who would subsequently become ineligible for study participation based on their lack of being able to provide informed consent.

Participants seemed to have no trouble comprehending and recalling four of the study's 10 elements: eligibility criteria, possible risks of participation, potential benefits, and what would happen if they decided to withdraw from the study. Although participants demonstrated adequate initial comprehension for the different elements of informed consent, even before being provided any necessary reinforcement, our data show a consistent decrease in participants' ability to answer questions on the same key elements on the following day. What is most troublesome about our results is the extent of participants' misconception with regard to the purpose of the collection of blood for the primary study.

Consent to the collection of blood and other biological material as part of medical research is an increasingly ethically charged issue in sub-Saharan Africa, as many countries including Mozambique, work to develop national policies on the use, storage, and sharing of biological samples. In settings like Mozambique, drawing blood can be seen as standard diagnostic procedure for clinical laboratory analyses, but in addition to the diagnosis of blood stream infections, one goal of the primary study was also to store blood samples for future analyses. This is a sensitive issue for informed consent and the child's parents/guardians were told about the difference between collecting blood for future research and for standard clinical procedures. Thus, it was of special concern that participants demonstrated relatively poor understanding at enrollment of the purpose for which blood was drawn from their children (32 of 120 [27%]).

We explored sociodemographic characteristics that can influence comprehension and recall of a study's features. Prior studies have found that illiteracy is one of the most important predictors of inadequate comprehension or recall of elements of informed consent (Joglekar et al., 2013; Krosin et al., 2006; Minnies et al., 2008). Our findings were consistent with the prior literature, in that increased education level was associated with improved initial

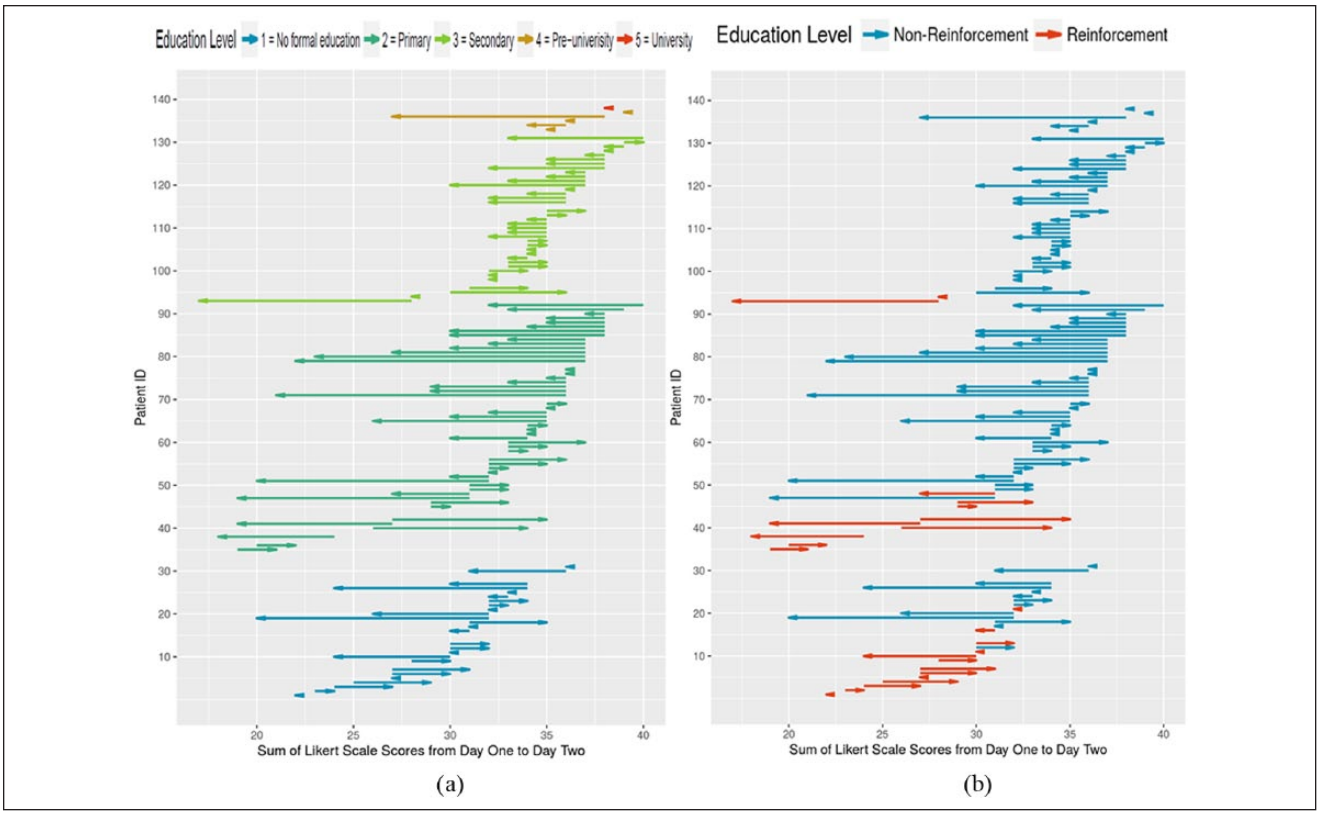

Figure 2. Likert-type scale scores by education level.

understanding and ability to maintain understanding at Day 2 following the informed consent process.

Language is often a proxy for educational level, and language barriers have also been identified as a factor in participants' understanding of information provided during the informed consent process. In Mozambique, someone who speaks Portuguese is assumed to have some formal education. In both the primary and secondary studies, the informed consent process and subsequent assessments were conducted in Portuguese and two local languages. Our study, however, found no difference in understanding or recall between participants who were given the informed consent materials in Portuguese and in other, local languages.

Best Practices

Administering informed consent in LMICs, where participants' levels of literacy and formal education are low, raises many questions for best practices. To maximize the quality of the informed consent process and its many benefits, it is important to reflect deeply on the recommendations provided by the different internationally recognized guidelines and codes of ethics. Starting from the assumption that to participate in a study, a participant must first comprehend the different elements included in the informed consent document, we suggest that the participants' understanding of key issues be assessed formally as part of the informed consent process and, as necessary, be reinforced with additional information and explanation, before they are enrolled. In areas where access to health care is limited, potential participants may be driven to nod or even proclaim that they understand the nature and specific aspects of a study when, in reality they cannot explain or even repeat what they have been told. Our efforts at providing participants with refresher information on elements of the informed consent document when they were identified as having difficulty comprehending proved to reinforce some participants' comprehension in the short term. However, it did not prevent many from being unable to recall that information the following day. Hence, particularly for longitudinal studies, we strongly recommend meeting with participants routinely, to talk about the study and to provide refresher information about the different elements of informed consent as needed. Although the information that participants should remember over time will depend on the study, they typically need to remember that they are taking part in a research project, the study's risks and benefits, and the fact they can withdraw without penalty.

In addition, RECs in Mozambique may need to consider adopting the following practices: (a) paying special attention to the language used in "approved" informed consent documents to aid comprehension among members of

populations with limited formal education, (b) requiring investigators to evaluate participants' understanding of the different elements of informed consent using such approaches as "teach-back" methodologies to ensure comprehension before enrollment, and (c) requiring investigators to submit periodic reports on the quality of the consent process in their studies and on efforts to improve quality wherever appropriate.

Research Agenda

This study was conducted in collaboration with a study on the diagnosis of pediatric bacteremia. Extending this work to more complex randomized clinical trials, interventional research, or cross-sectional studies in similar settings might identify additional nuances in what participants understand and recall about clinical research protocols. Moreover, future studies in Mozambique are needed that further analyze why participants do not understand certain elements of informed consent, investigators' ability to explain the elements of informed consent in an intelligible way, and how participants' primary language affects translation and delivery of the elements of informed consent, including that many of Mozambique's local languages have no written form.

Educational Implications

This study will improve and strengthen general knowledge about the limits of the informed consent process in biomedical research, specifically in LMIC settings like Mozambique. It also suggests a model for the training of researchers and study staff in the delivery of information essential to the informed consent process. The informed consent process should be seen as a two-way communication between the participants and researchers, both to convey knowledge and to preserve the integrity and social values of the communities in which research is conducted.

Our preliminary data suggest that certain aspects of research may be harder for Mozambican participants to understand than others. This knowledge can help investigators tailor their informed consent processes and documents to address these areas of misunderstanding. Because research is crucial in low-income countries such as Mozambique, where high rates of disease reduce the quality and length of life, it is essential to develop clear guidelines and tools to improve participants' comprehension of research and to implement the informed consent process in a way that addresses local cultural values and constraints.

Limitations

Our study had several limitations. First, our tool for assessing participants' understanding and recall was developed for this study without external validation, raising the possibility of interviewer bias, in which the interviewer's assessment of a participant's answers was subject to under- or over-scoring. Second, it is possible that our telling individuals at recruitment that we would test their understanding of the elements of informed consent focused their attention and improved their understanding of that information over what would have been the case in a standard study. Next, recall was assessed on the day following enrollment and may not be a reliable proxy for longer term recall. Furthermore, the Likert-type scale scores were converted into points, added up, and then treated as a continuous variable. Although it is acceptable to treat a Likert-type score as a continuous variable, the distance between two scales is not necessarily equal. Our primary outcome was the sum of 10 scores as a representation of overall level of understanding. However, this may not be wholly accurate as some questions may have been correlated. Finally, the same issue exists for the treatment of education level, as the distance between two consecutive levels of education is not necessarily equal.

Conclusion

This study adds to a growing body of evidence related to the quality of informed consent in developing country contexts and is the first for Mozambique. Overall high rates of initial comprehension at enrollment followed by a declining level of recall on the day following enrollment in this study demonstrate that it is possible in Mozambique to attain satisfactory levels of comprehension for informed consent, but the lack of evidence for the long-term retention of this information remains worrisome. Special concern is noted for participants' apparent poor understanding and/or recall of the purpose for which their child's blood was drawn in a study to investigate blood stream infections. Why some of the elements of informed consent were less well comprehended in our study should be examined in future research, with the goal of helping Mozambican RECs focus on specific areas where comprehension appears to be deficient.

Authors' Note

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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