INFORMED CONSENT IN CLINICAL TRIALS: PERCEPTIONS AND EXPERIENCES OF A SAMPLE OF SOUTH AFRICAN RESEARCHERS

Authors:
Katherine van Loon
Graham Lindegger

Affiliations:
1Department of Medicine, Beth Israel Deaconess Medical Centre, USA
2School of Psychology, University of KwaZulu-Natal, South Africa

Correspondence to:
Graham Lindegger
lindegger@ukzn.ac.za

Postal address:
University of KwaZulu-Natal, Pietermaritzburg, P/Bag X01, Scottsville, 3209, South Africa

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ABSTRACT

The implementation of informed consent (IC) in clinical trials presents many challenges, especially in developing countries. This study explored the experiences and reported practices regarding the implementation of IC in clinical trials in South Africa. Data were gathered through semi-structured interviews with a range of stakeholders in clinical trials in two provinces. The interviews were analysed to identify themes and issues relating to IC. The findings show that IC practices involve attention being paid to both formal requirements and informal practices to attain IC. Research assistants or trial counsellors were found to play a critical role in facilitating the IC process. It is recommended that more recognition be given to the important role of trial counsellors in clinical trials, and that they be given more formal training, support and supervision.

INTRODUCTION

First articulated in the Nuremberg Code in 1947, informed consent (IC) has been accepted as an essential ethical requirement for all research on human subjects, particularly for participation in clinical trials. Founded upon the principle of respect for the autonomy of persons, IC seeks to protect the individual’s right to make a voluntary, informed decision regarding participation in research. Faden and Beauchamp (1986), in their seminal work on IC, suggested that it can be understood in both legal and moral terms. The legal notion, seen as a formal contract between researcher and participant, is expressed in formal requirements such as signed consent forms. The moral notion is concerned with optimising the process of decision making by participants about whether and how they wish to participate in research. Satisfaction of the legal requirements for IC does not necessarily guarantee satisfaction of the ethical requirements, and vice versa. Recent literature on IC has used phrases such as ‘genuine informed consent in practice’ (Molyneux et al. 2004), implying that even though the formal conditions for IC may have been satisfied, the spirit of IC may not necessarily have been achieved in practice. There have also been suggestions that the regulatory requirements for IC may be insufficient and ‘may fail to address the realities’ of people making decisions about IC (Dawson & Kass 2005:1221).

For consent to be valid, five components are usually required:
• disclosure of all appropriate information about the research study
• ensuring that the prospective participant comprehends the disclosed material
• ensuring that the prospective participant has the legal and mental capacity to decide about and consent to participation in the research
• ensuring that the decision about participation is freely given
• formal consent with written documentation or an acceptable alternative.

The requirement for legal and mental capacity appears to be the least contentious and is therefore not addressed in this paper.

Despite general agreement on these components of IC, there continues to be much debate surrounding the substantive aspects of consent and its procedural implementation. The substantive aspects, viz. the need for first-person consent, founded on the principle of respect for the autonomy of persons, is generally seen as universal and immutable, although there have been some culture-based challenges to this substantive requirement. The procedural aspects, concerned with the optimum practical implementation of IC, should be guided by local conditions, including cultural considerations, in order to achieve true IC. There are many challenges to achieving genuine IC in practice (Molyneux et al. 2005), especially in resource-poor and developing countries, in settings where a large portion of the prospective participants have little formal education, where there is a history of social or political oppression, in contexts where research is not a familiar concept or experience, and in diverse cultural settings.

Debates and controversies driven by cultural considerations in IC have been amongst the most virulent and contentious and have covered all five components described above, e.g. what information should be provided and by whom, who should be required to consent, and how to obtain valid consent from adults who are culturally defined as minors (Hyder & Wali 2006; Lindegger & Richter 2008).
Moodley 2002; Onvomaha, Kass & Akweongo 2006). With the commencement of international HIV vaccine trials, UNAIDS has given particular attention to cultural considerations in practice of IC in resource-poor settings (Richter et al. 1999). The question has also arisen whether IC is universally applicable or whether it is a culture-bound notion. There have been claims that first-person consent, the very cornerstone of IC, derives from an individualistic notion of personhood specific to Western culture (Christakis 1988; Moodley 2002; Onvomaha et al. 2006). It has been argued that, in these latter contexts, it may be more appropriate to obtain IC from community representatives such as traditional leaders. But recent studies have found that there is little support for the notion of bypassing individual consent in either developed or developing countries (Molyneux et al. 2005).

In the light of the increasing number of questions raised by IC and its implementation in international clinical research, and the apparent difficulty in obtaining genuine or authentic consent, especially in developing countries, it is necessary to carefully examine the practices and experiences of researchers obtaining IC in diverse socio-cultural contexts, including South Africa. The questions and concerns about the ethics of clinical research, and about IC in particular, are highly pertinent to South Africa. The significant increase in the number of clinical trials, the history of political oppression, the relatively poor education of a large section of the population and the multicultural population all present numerous challenges to the attainment of IC in health care research in South Africa.

The aim of this study was to explore the experiences, including perceived difficulties, challenges and solutions, regarding the implementation of IC in clinical trials in South Africa. Through the examination of these experiences it is our intent to identify critical issues facing the implementation of IC in South Africa and other developing countries.

METHOD

Study design

This was an exploratory, qualitative study, designed to identify challenges to the implementation of IC in clinical trials. The rationale for choosing a qualitative methodology for this study was twofold. Firstly, the qualitative methodology is particularly appropriate for exploratory investigations as it generates rich data for developing hypotheses that can later be tested with quantitative data. Secondly, the use of qualitative methods rather than structured questionnaires allows for the emergence of novel information from the participants, an important goal of the study.

Sample

As this was an exploratory, qualitative study, there was no attempt to gain a representative sample. A diverse sample was collected, consisting of pharmaceutical company representatives, principal investigators (PI) and research assistants (RA). (As RAs functioned largely as trial counsellors (TC), the latter concept will be used throughout this paper.) It was thought that each of these groups might have different and complementary perspectives on IC and its implementation. All interviewees were recruited through a series of referrals and networking. Only two provinces were used for the study, viz. Gauteng and KwaZulu-Natal. As a convenience sample was used, numbers were ultimately determined by the number of people willing to volunteer. A total of 60 respondents agreed to participate, consisting of 22 principal investigators (PI), 27 trial counsellors (TC) and 11 pharmaceutical representatives (PR). All the PIs and PRs were white or Indian English-speaking people, whereas the TCs were all black people whose home language was an African language. These demographics reflect the historical distribution of staff in clinical trials in South Africa, although this is changing rapidly. The clinical research experiences represented by the participants included microbiology, intensive care, paediatric, surgical, antibiotic and HIV research.

Procedure and data collection

Following the granting of ethical approval for the study, researchers at various trial sites were contacted, informed about the study and invited to participate. Following an initial expression of interest, an information sheet and consent form describing the project was provided to potential participants. Before each interview the study was thoroughly discussed with each prospective participant. They were fully informed prior to the commencement of the interview that all names and affiliations would remain confidential.

In-depth, semi-structured and open-ended interviews were conducted in person with the participants. All interviews were conducted by the first author in English and were audiotaped, with the explicit consent of the participants. Following an opening invitation, ‘Tell me about your experience with the IC process’, the interviews focussed on the participants’ experiences and perceptions of each of the main components of IC. For each component the respondents were also invited to give specific instances of both difficulty and success in relation to IC. In some cases the interviews deviated substantially from the interview guide (reflecting the open-ended part of the interview) in order to accommodate unanticipated insights and experiences provided by the interviewees. All interviews were conducted with a single respondent and lasted 45 to 90 minutes.

Data analysis

Data was coded using NUD*IST VIVO (QSR 1999) through a series of iterative steps. An initial code list was established on the basis of preliminary reading of three randomly selected transcripts, one from each subgroup. The code list was then refined by the co-author and a research assistant reviewing the remaining transcripts. The process of refining the code structure included adding and reconstructing codes as new insights emerged. During its development, the code structure was reviewed three times. All the transcripts were then coded using the final version of the code structure. Coding of the transcribed interviews allowed for the making of associations amongst the themes, and selecting supporting quotations.

Trustworthiness

In order to enhance the trustworthiness of this study, the following processes were used. At the outset of the study, the participants were assured that the goal of the research project was not to audit the adequacy of IC procedures, but rather to survey the researchers’ experiences of IC in order to better understand and improve IC processes and practices in future research. It was hoped that this would allow the participants to be honest, and thus to improve the credibility of the findings. The fact that the first author conducted all the interviews ensured consistency in data collection. In order to enhance the reliability of the study, the interviews were all conducted using a standard semi-structured interview guide, constructed using texts describing each of the five components of IC. However, the interview also invited participants to give examples from their own experience in order to enhance the credibility of the findings (De Vos 2005:346). Interviews were conducted in English. Even though the participants were all fluent in English, this was not the home language for most of the TCs, and this may have influenced the reliability of the findings.

In order to enhance the trustworthiness of the data analysis, the second author and a research assistant independently re-coded a sample of the transcribed interviews in order to check the reliability of the coding. In the interests of the credibility of the findings, the second author also checked that the interview data supported the findings, and that the final quotes selected
adequately represented the range of views expressed in the data (Miles & Huberman 1994).

FINDINGS

The results of the study will be presented in two major sections. In the first section, the findings regarding the broad process of obtaining IC are described. In the second section, the results are presented under the broad categories of: (1) transmission of information; (2) understanding; (3) autonomy; and (4) formal consent. As there is a fair degree of overlap between these two sections, some issues are reported in both but are described more fully in only one section.

Context and process of obtaining IC

Double agenda of IC

The findings clearly reveal that the process of implementing IC procedures and of obtaining IC from participants in clinical trials is driven by two separate, albeit related, agendas, one being a formal, legal agenda, and the other being a more informal, personal agenda. Many participants described the use of formal, structured procedures, e.g. information leaflets and informed consent forms approved by research ethics committees. It was reported that these procedures were used to formalise and standardise IC across research participants, and that these components were relatively easy to operationalise, monitor and check. It was no surprise that it was especially PIs and PRs who were concerned about these formal components.

Alongside this formal IC process, the interviewees also described the subtle, informal processes that occur or are employed specifically in the process of obtaining IC for trial participation. It was especially the TCs who described these informal processes as a crucial, but often unrecognised, part of obtaining IC in clinical trials. Many TCs reported that they felt the responsibility to make informal and subtle, ethical decisions when obtaining IC from potential participants. For example, some mentioned their dilemmas about how much time to give the participants to think before deciding about participation in a trial. Others reported times when the participants claimed to have a good understanding of participation in a trial, but they personally thought that these people understood little about the real meaning of trial participation and should therefore not be recruited into the trial. TCs were often acutely aware of psychological and social factors impacting on the decision of potential participants to participate in trials. A typical example reported was the situation where people were asked to make decisions about trial participation when they had only recently discovered that they were infected with HIV and were still in a state of severe shock. These findings suggest that TCs carry considerable, additional burdens as part of the process of obtaining IC. Understandably, the formal requirements for IC were the greater concern of the PIs and PRs, given that they carried the ultimate responsibility for the trials.

The language used by some interviewees offered useful insights into how the IC process itself was implicitly seen. For example, some interviewees used the phrase ‘consenting the subjects’, which revealed a tendency to see trial participants as passive agents and consent as a relatively passive process done to them, as part of a legal/ethical requirement, with little sense of active decision making by them.

Relational context of informed consent

One of the most recurrent findings of this study was the relational context of IC. The interviews revealed the central importance of the relationship between the research staff and potential participants in the IC process. This is the most important part of the subtle, informal process of IC described above, and a vital backdrop against which IC is obtained. Many respondents spontaneously referred to the importance of the relationship between the researchers and the participants in the trial in obtaining IC, constructing the relationship in various ways, e.g. as trusting, confident and free to ask questions, or as deferential, guarded and hesitant to ask questions regarding participation, either because of the perceived power differential between the researchers and the participants or out of a desire to please. PIs and PRs tended to describe the relationship in more positive terms, but they were also aware of the possible tension in their relationship with potential participants in the trial. The TCs often gave more descriptions of the challenges and difficulties in the relationships between the researchers and trial participants, probably because of their closer personal contact with them.

Various social and cultural processes were described as impacting on the IC process, often through the impact on the relationship between the researcher and prospective participants. TCs, in particular, reported various forms of social desirability on the part of trial participants, often informed by patterns of cultural etiquette. A typical example reported was the way in which participants responded to questions about whether they understood the information explained to them. Some counsellors explained that statements such as ‘I do understand’ or ‘I do not understand’ are often not statements of personal understanding as such, but rather statements expressing respect. ‘I do understand’ may sometimes be seen as an expression of respect for the researcher who has just carefully explained information. Equally, the statement ‘I do not understand’ may also be seen as a statement of respectful awe for the researcher, who has a much greater ability to understand the material, and thus that the trial participant should not be so bold and disrespectful as to claim equal understanding.

One PI provided insight into her experience of this power differential affecting the IC process:

‘I think that in many cases they have too much respect or fear for the doctor or the health professional. I do think there is a barrier, and while we do encourage them to ask as many questions as they can, I do feel they might be shy. It’s their culture that they’re not going to challenge me… That’s the barrier: who am I to challenge the doctor and his knowledge? The other fear of mine is that the people in the African culture are usually very, very obliging. They want to please me. So, if I go and ask them to consent for a study, there is always the fear that they might be doing it because they have been my patients for years, and they might feel like they have to please me. They may think that they are doing me a favour by participating.’

Not surprisingly, a lower level of formal education and illiteracy were reported as complicating the process of obtaining true IC. However, what was especially novel was the explanation by some TCs that claims of illiteracy by potential participants sometimes needed to be understood as a statement about researcher-participant relationships, or apprehension about clinical trials, rather than as factual statements about illiteracy. According to these TCs, at times the statement ‘I can’t sign’ (because of illiteracy) really means ‘I am hesitant to sign’. This may have to be seen as an expression of self-protection in the face of the perceived power discrepancy between the researchers and the potential participants, rather than as a factual statement about illiteracy.

Some TCs reported that, given their greater similarity to the trial participants in cultural background and home language, they often felt the responsibility to create a context within which potential trial participants would feel more free to raise questions or concerns as part of the decision-making process, or to decline to participate in trials. The impact of these processes will be illustrated further in some of the findings regarding specific components of IC reported in the next section.

Components of informed consent

Table 1 provides a summary of factors perceived to affect the implementation of the various components of IC.
Transmission of information

Due to illiteracy in some of the populations involved in clinical trials, the researchers reported relying primarily upon verbal communication to provide information about trials. But it was reported that even verbal communication posed challenges, principally between members of different ethnic/language groups. In many cases, the transmission of information was delegated entirely to the TCs, who were more likely to be able to speak the home language of the research participants. Some investigators reported a dialogue process, whereby the TC served as a translator of information and/or questions. However, many respondents emphasised the need for the counsellor to facilitate the process.

Communication is further complicated by the lack of precise translations for scientific terminology (i.e. placebo, vaccine, etc.) in indigenous languages. It was reported by some respondents, especially TCs, that formally translated research documents were often not altogether intelligible to participants, who rather spoke a ‘street language’. The researchers described novel strategies employed for overcoming the challenge of translating scientific vernacular, viz. the use of other familiar ideas to convey the essential meaning of technical concepts. One PI reported:

‘With placebo, we are calling it “spaza” here. Spaza is something that is not real in an African language. That was the word that we found that they use in the townships for something that is not real, and [the subjects] understood immediately.’

The respondents frequently remarked on the excessive length and complexity of the IC forms given to potential trial participants. Because the forms must meet the requirements of international guidelines, sponsor companies and local ethics committees, brevity is difficult to achieve. In addition, forms must include all information considered relevant for legal indemnification. The result is overlong forms that overwhelm trial participants. One PI described the form as follows:

‘It’s too big. If it’s a document from the United States, you can forget it. For some of these pharmaceutical trials, the informed consent forms are like a book. The patients don’t want that. They want a little thing that they can read and understand in lay language. The consent forms for these trials need to be simple – that you can read and understand.’

Many participants emphasised that, in addition to the translation of IC forms into the person’s home language, there was a need for this translation to be in everyday language. One PI reports: ‘When I give [the form] to my nursing staff to read, they say, “It’s like university Zulu or university Sotho. We don’t use these words any more! Who translated this?” One counsellor suggests, ‘The form should be made simpler using street language, because we deal with street people from the local townships who are not learned and are not used to medical terms.’

The respondents reported that they transmitted information in both one-on-one and group settings, emphasising that the trial participants appeared to benefit from involvement in a group information session as a result of the solidarity and empowerment conferred by the group setting. As members of a group with common experiences, the trial participants were more likely to ask questions about the research, or they may vicariously benefit from questions asked by others.

Understanding

Factors that were identified as affecting the understanding of trial information included: educational level, scientific literacy, prior exposure to research, and the interactions between the researcher and participants. Prior exposure to research was especially identified as a factor affecting understanding. Investigators struggle to convey research aims and methods to individuals who have not previously been exposed to scientific and research concepts. However, the counsellors reported higher levels of understanding in participants with higher levels of formal education. The respondents also claimed that the interaction between the researcher and the participants played an important role in facilitating understanding. The counsellors were especially conscious of the subtle, cultural features of communication affecting the transmission of information and understanding. They reported that creating a reciprocal relationship, wherein the trial participants felt comfortable to enter into dialogue or ask questions, facilitated the understanding of the material.

Regarding the assessment of understanding, few of the respondents in this study reported using formal tools to assess understanding. However, most indicated that, due to the tendency of trial participants to claim understanding even when they did not fully understand, informal methods to assess understanding were commonly used during the IC process. The verbal assessment of understanding commonly involves asking open-ended questions and/or requiring summarisation of the information. Counsellors also reported paying simultaneous attention to non-verbal cues to assess the understanding of the trial participant during the consent process. As an example, one counsellor remarked,
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Autonomy
Factors that were identified as influencing the autonomy of people’s decisions regarding participation in clinical trials include: family and community membership; vulnerability due to poverty and disease; benefits or incentives, including payment and access to care; and power differentials between participants and researchers.

As this data was collected before the Medicine Control Council policy of a flat rate of reimbursement of trial participants, the researchers reported commonly offering reimbursement for travel expenses and meals, and occasionally reimbursement for wages lost. While such reimbursements might seem meagre by the standards of a developed country, some of the researchers conjectured that, in the resource-poor settings from which many trial participants come, they may subtly put pressure on people to participate in a trial. Similarly, the researchers also thought that intangible incentives, such as medical care, as well as the need to please her/him, might be compromised by reliance on the physician for care and the need to please her/him.

The previous section described the power differential between the researchers and trial participants, and the potential impact on the IC process in general. During the interviews it was commonly suggested that this differential may impact on the degree of autonomy of the decisions taken by people about whether to participate in trials. For example, in the case of a patient whose physician invites his/her participation in a clinical trial, the self-determination of the patient might be compromised by reliance on the physician for care and the need to please her/him.

Formal consent
The signature on the consent form represents the capstone and culmination of the consent process. Apart from the inability of some participants to read or write, as reported above, the researchers also reported a reluctance by some trial participants to enter into any agreement via signature, with some going so far as to falsely claim illiteracy in order to avoid applying a signature to an IC form, as described in the previous section.

Confidentiality is a major concern of people during the process of granting formal consent, especially in HIV-related trials. Several counsellors reported that people are unwilling to take the consent form away from the trial site or into their homes. The fear of losing one’s anonymity requires the person to place a high level of trust in the researchers. One counsellor said:

“When I talk to the patient, I check out her body language to see if she understands. Some simply stare at me with blank faces, but if the patient keeps nodding while I speak and asks more questions, then I can see that she understands... A person who does not understand will simply not look at me.’

Another counsellor reported that even when trial participants explicitly claim understanding, ‘[i]t is evident in their eyes that they do not understand’.

DISCUSSION
While IC is widely accepted as an essential ethical requirement for clinical trials, there are multiple challenges to the practical implementation of IC, especially in developing countries and as has been reported previously (Onvomaha et al. 2006). There have been calls for empirical research into these issues and challenges (Hyder & Wali 2006) in order to understand them more fully. Many of the findings of this study replicate those of other empirical studies on IC, confirming many of the challenges in obtaining genuine IC. These issues include wariness in relation to lengthy and complex IC forms, translations that are unreadable and difficult to understand (Dawson & Kass 2005; Moodley 2002; Onvomaha et al. 2006), and time being allowed between the transmission of information and the granting of formal consent (Moodley 2002). The findings regarding the power discrepancies between doctors/researchers and patients/participants and their impact on the IC process also mirror the findings of previous studies (Moodley 2002).

The findings of this study also confirm the double agenda of IC as a formal, legal requirement, and as a personal decision-making process. The findings suggest that obtaining IC for participation in clinical trials often involves the subtle interweaving of the formal/legal and informal/personal processes, with some aspects being emphasised more by some members of the research team than by others.

One of the most consistent findings throughout this study was the central role of the researcher-participant relationship in obtaining IC. If authentic IC is about good decision making, as was suggested earlier in this paper, then there is a need for trial staff to attend carefully to the interpersonal processes that will facilitate or delay this decision-making process. While some respondents in this study perceived the relationship with trial participants as being positive, others perceive it as being more guarded and fearful. Both are likely to be true. But the findings also highlight the subtle complexities in the communicational relationship between researchers and trial participants, seen in the claim by some interviewees that what trial participants say is not always what they mean (e.g. ‘I understand’ may be an expression of respect rather than a statement of cognitive understanding). The trial counsellors consistently emphasised the importance of the relationship in transmitting information, as a good relationship would make it easier for the participants to ask questions or raise concerns about trial participation, would facilitate and assess understanding, and would encourage autonomous decision making. Together, these findings suggest the importance of trial researchers acquiring interpersonal skills training, based on cultural sensitivity, to enhance their competence in obtaining IC. The findings regarding the importance of the researcher-participant relationship can be seen as being parallel to the findings in other studies in Africa of the importance of a trusting relationship between communities and research organisations (Gikonyo et al. 2008; Onvomaha et al. 2006) in order to be able to obtain IC and conduct research. The findings also lend weight to the argument of Gikonyo et al. (2008:708) that the trend towards increased formal standards of IC needs to be ‘counterbalanced with greater attention to the diverse social relationships that are essential to the successful application of these procedures’.

The findings suggest that the transmission and understanding of information is an important challenge to authentic IC.
While illiteracy and language barriers undeniably affect the transmission of information to trial participants, they should be seen as negotiable obstacles that can be overcome with sufficient attention and trained personnel (Abdool Karim et al. 1998; Preziosi et al. 1997). This might be accomplished through close collaboration with community advisory boards (CAB) and skilled community members in the formulation of sound translations and explanations of scientific concepts, and the identification of the most appropriate methods for providing information. As mentioned, the risk that excessively long consent forms retard rather than facilitate the understanding of information. There is also a need to employ appropriate methods to share information about trials and to promote understanding of this information. In fact, this study reflects the findings of other studies that have pointed out that the very nature of research itself is not understood (Molyneux et al. 2004, 2005). However, some interesting examples emerged of the use of concepts familiar to communities that may be used as metaphors to explain research concepts, reflecting the findings of other researchers (Moodley 2002). To this end, the assistance of communities (e.g. CABs) is very helpful.

Overall, while recognising the importance of participant understanding for trial participation, few interviewees reported the use of formal assessment tools. This is consistent with the findings of other, multinational studies (Hyder & Wali 2006). However, the findings do highlight the need for appropriate methods to reliably measure understanding of the information shared, rather than to rely on self-reported understanding or quantitative methods alone. Such formal assessment procedures have become more common, especially in the HIV-prevention trials that are underway in South Africa. A recent study by Lindegger et al. (2006) has provided evidence of a range of culturally sensitive and novel ways in which understanding may more appropriately be assessed for trial participation.

It has often been argued that persons from African cultures are more collective and relational in their construction of personal identity and that this impacts on IC (Gikonyo et al. 2008; Hyder & Wali 2006; Moodley 2002; Onvomaha et al. 2006). There have been heated debates about who should consent to participation in research, and whether individual consent is necessary or acceptable in African contexts. Recent studies (Dawson & Kass 2005; Molyneux et al. 2005) have argued that individual consent cannot be bypassed or replaced by the consent of community leaders or household heads. However, they do defend the need for cultural sensitivity to collective norms. In the present study there were no claims of the irrelevance of first- or proxy-person consent for trial participation, or suggestions that more culturally appropriate forms of proxy consent should rather be used. In fact, all the interviewees concurred that the individual participant had to consent to participation in the trial. However, they simultaneously reported that the participants often indicated that they wished to involve partners, family or others in the consent process, or that they were expected to also obtain the agreement of their partners. This finding echoes the findings of other, similar studies in Africa and other developing countries (Hyder & Wali 2006; Onvomaha et al. 2006), revealing the parallel consent process involving traditional leaders, household heads and individual participants. This parallel process of obtaining first-person consent, while simultaneously respecting the need to consult with leaders, partners or family, can be seen as a good expression of the plea by Loue et al. (1996) to ‘take into account local customs and traditions that should be incorporated into the research process’ (cited by Moodley 2002:213).

One of the aims of the study was to compare the perspectives and perceptions of different groups of researchers on IC, viz. PRs, PIs and TCs. While most of the interviewees were aware of the impact of relationships on IC, it was no surprise that the former two groups, who carry greater legal and managerial responsibility, tended to focus more on the formal aspects of IC, whereas the TCs especially focussed on details of the participant-researcher interaction. Overall, the findings of this study reveal the critical role played by TCs in obtaining IC from prospective research participants, and especially their implicit role in the ethical conduct of trials. There were many indications of the central role that TCs perceive themselves to play in obtaining consent. This parallels the report by Gikonyo et al. (2008) of the central role played by fieldworkers in establishing and maintaining the social interactions and relationships that are critical to successful research. Many TCs gave indications of the informal personal decisions that they had to make in obtaining IC, e.g. in relation to whether the person adequately understood the information, whether they needed more time, and whether they wanted others involved in the process. Many of these decisions had ethical aspects. This again echoes the findings of Gikonyo et al. (2008:718), who pointed to the ‘critical role (of fieldworkers) in ethical practice at the field level... (which is)... often under-recognised and under-supported’. In fact, many counsellors felt that the central role that they played in making important, but subtle, ethical decisions was not always recognised. The findings also reveal the burden of responsibility these TCs carry because of these subtle decisions. On the basis of these findings we would recommend that TCs, or research assistants, should be given more extensive training, including in some of the practical aspects of bioethics, as well as ongoing professional supervision and support to carry out these subtle, but crucial, roles. The provision of such professional training and support would also help to ease the emotional burden carried by TCs. This parallels other calls for more extensive training of researchers in the consent process (Allmark & Mason 2006).

There are definite limitations to this study. The language differences between the interviewers and TCs and the fact that the findings were not checked with the study participants may raise questions about their trustworthiness. Further, no attempt was made to confirm with the participants that the findings accurately reflected their perspectives and experiences, which may raise questions about the trustworthiness of the conclusions (Ulin et al. 2002). Given that a convenience sample was employed in this study, and that the study was limited to only two provinces, the findings cannot be generalised to all trial researchers in South Africa. However, the strength of the study probably lies in the use of the in-depth qualitative methodology, which has allowed novel findings to emerge. This study has especially revealed the importance of the IC process itself, based on the relationship between researchers and participants.

CONCLUSION
IC has been the most widely accepted ethical requirement for clinical trials since the establishment of the Nuremberg Code. However, there has been growing recognition of the multifaceted and complex nature of IC. Recent literature has highlighted the importance of IC being a genuine process based on personal decision making, not only a legal formality. This study attempted to identify some of the challenges in the implementation of genuine IC as perceived by researchers involved in clinical trials in South Africa. The findings identify a number of important issues, especially regarding research-participant relationships, which potentially complicate the implementation of IC in clinical trials in developing countries. The findings also highlight the need for the training, supervision and professional support of research staff involved in obtaining IC. Finally, the study demonstrates the commitment needed by trial researchers to make IC a genuinely ethical process.

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