Published in final edited form as:
IRB. 2005 ; 27(6): 1–8.

Motivations, Understanding, and Voluntariness in International Randomized Trials

Nancy E. Kass, ScD,
Phoebe R. Berman Professor of Bioethics and Public Health at the Department of Health Policy and Management, Johns Hopkins University Bloomberg School of Public Health and Johns Hopkins University Berman Bioethics Institute, Baltimore, MD, USA

Suzanne Maman, PhD, and
Assistant Professor at the Department of Behavior and Health Education, University of North Carolina, Chapel Hill, NC, USA

Joan Atkinson, RN, MPH
United States Government Coordinator for HIV/AIDS, Lesotho, USAID, Pretoria, South Africa

Research on informed consent conducted in wealthy countries has found that subjects' understanding of research often is incomplete or, at times, inaccurate.[1] Other studies reveal a subtler clouding of the distinction between treatment and research, whereby patient/subjects know they are in research, but view research as treatment for their disease.[2] Such a misunderstanding may compromise meaningful decision- making about participation in clinical trials.[3]

The minimal empirical research on informed consent that exists from developing countries suggests that trial subjects in the developing world encounter similar challenges. Research participants in resource poor regions may face additional barriers in informed consent related to language, education, culture, beliefs, and/or decision-making styles.[4] For example, in a study in Haiti on HIV transmission, only three of 15 potential participants scored well enough on a true-false comprehension test to be enrolled,[5] and investigators in The Gambia found that 90% of participants in a vaccine trial knew the purpose of the vaccine, but only 10% understood placebos.[6]

Autonomous decision-making, a standard goal of existing national and international research ethics guidelines, may be especially challenging for research conducted in international settings. It is expected that autonomous decision-makers voluntarily agree to participate in clinical trials. Yet voluntariness can be compromised by a variety of factors, including poverty, limited access to medical care, and patterns of decision-making related to gender, socioeconomic status, or culture.[7] The political and human rights context of studies can also compromise voluntariness.[8] Moreover, in some contexts, potential participants may feel they cannot say no to a professional's recommendation that they enroll in a study.[9] It has been well documented in both U.S. and international research that trust in researchers contributes significantly to participation in research, regardless of whether participants understand the study.[10] Finally, concerns have been raised that financial or medical incentives may create undue influence to participate in research,[11] although the degree to which inducements are problematic remains a matter of debate.[12]

Given the limited empirical data documenting understanding and voluntariness in international research, we conducted a qualitative pilot study to learn how participants in international clinical trials define research and why they enroll. We interviewed participants in three developing countries who were participants in six different randomized, controlled

infectious disease trials. We hope future studies will lead to interventions to improve informed consent, research review, and policy.

Study Methods

Sampling Frame and Recruitment

In-depth interviews were conducted with 26 research participants from six different randomized controlled trials studying a clinical intervention designed to prevent or ameliorate an infectious disease in developing countries. Trials spanned three countries, two in Africa and one in the Caribbean.[13] Two trials were selected from each country. Two studies tested drugs to prevent tuberculosis (TB) in HIV-infected populations, two tested interventions to reduce maternal to child transmission (MTCT) of HIV, one tested the efficacy of a vaginal microbicide in preventing heterosexual transmission of HIV, and one examined the efficacy of a malaria treatment for young children in a drug-resistant region. We deliberately sought interviews with participants in trials in different countries studying different infectious diseases in order to determine whether our findings transcended study topic and geographic region. We also deliberately chose randomized controlled trials (three were placebo-controlled) from which to recruit participants because the literature on randomization shows it is a difficult concept to communicate and understand. U.S. or European sources funded all the trials, which were collaborations with one of four different U.S. or European research institutions. All the trials were conducted at an established referral hospital or health center in the relevant country. These facilities served poor communities who generally lacked access to basic infrastructure such as running water and electricity. Access to regular, quality health care outside the study ranged from minimal to nonexistent.

Participants selected for this pilot study were enrolled in a clinical trial or had completed trial participation within the last year. Using convenience sampling, we asked research staff of the ongoing parent trials to refer participants to us who attended the research clinic on the days interviewers from our study were visiting. For completed trials, research staff from parent trials invited up to five former participants to be interviewed for this pilot project. Everyone referred to us agreed to participate and gave witnessed, oral consent. Interviews were conducted in the hospital or clinic setting where the six studies occurred. Participants were not paid to participate in the study. However, after the interview was completed they were given a small thank you gift such as barrettes for their children or a bar of soap.

Interview Guide Development and Interview Conduct

We used a semistructured interview guide based on the general theme of motivations, understanding, and voluntariness. Interviewing began with general questions (such as “Tell me about a typical day for you”) and moved to increasingly specific questions about the research trial and the individual’s participation. The interview guide outlined general topics for discussion (see Appendix); interviewers continued with probing follow-up questions as appropriate. We modified the interview guide as the study progressed and as new themes emerged during interviews. One or two study members (JA and/or NK) conducted interviews in a private room that generally lasted 30–40 minutes. All interviews were audiotaped for subsequent transcription.

Translation

All participants spoke and responded in a local language. In one country (two trials), the interviewer/investigator for this study spoke the local language and was able to conduct interviews in the local language. In this setting, interviews were audiotaped, and the investigator translated interviews into English. The English versions then were transcribed.

In the other two countries (four trials), the staff of the parent trial provided a translator of convenience. A research nurse was a translator for one of the trials, a nonresearch nurse was a translator for two of the trials, and for the other trial the translator was a visiting relative of one of the research staff who was a university student and spoke English. For these four trials, the interviewer, the subject-respondent, and the translator sat together in a private room. The interviewer from our staff asked questions in English, the translator repeated the question in the local language, the respondent answered in his/her local language, the translator repeated the answer in English, and then the next question was asked. Only English sections of audiotapes were transcribed for analysis.

Data Analysis

An inductive coding approach was used, whereby the coding scheme was developed from patterns and themes that emerged from the data.[14] Data were segmented manually into categories or groups according to the coding scheme. In the final stage of analysis, a matrix was developed to compare major themes, patterns, and connections within and across interviews and across studies.[15]

Study Findings

Demographic and Background Information

All but one of the respondents was female. We have demographic information for approximately half of respondents. Of these respondents, almost all had less than eight years of formal education, and about half had less than five years of education. About two-thirds were between 20– 30 years old and about one-third were between 31–40. Of the 16 for whom we have employment information, five were unemployed, seven were street vendors, and four had domestic positions. About three-fourths were married and all had children.

Major Themes in Data

Five major themes emerged from the data, each of which will be described in greater detail below: 1) participants generally understood the purpose of the clinical trial in which they were or had been enrolled; 2) respondents generally did not understand randomization, treatment allocation, or that different trial participants would receive different interventions; 3) the opportunity to receive better medical care was a major incentive to participate in the clinical trials; 4) respondents often extrapolated from their beliefs about their personal outcome to their beliefs about the outcome of the trial; and 5) most participants understood that joining the trial was voluntary, but several felt they could not leave the trial once enrolled. Of note, due to the iterative nature of the interview process, we did not ask every respondent every question. Where possible, we report the numbers of respondents with whom each topic was discussed as well as the general direction and range of responses within each theme.

Study Purpose Generally Understood—Twenty-five respondents were asked to define research and/or the activity in which they were participating. Nine explicitly stated that the research or activity was to learn about a new medicine, or to learn if a new medicine works. A woman in an MTCT HIV trial said, “They did give us something to drink so that our babies cannot be affected,” and a woman in the microbicide trial said, “This research was about the product … like the gel that you put into the vagina if it can prevent STDs.” Another three respondents appreciated that the activity was to learn about the condition in question, but never mentioned the testing of a particular intervention. One respondent in the MTCT HIV prevention trial initially said she could not explain research. When probed she said, “Research is great in learning about HIV.” A woman whose child was in the malaria treatment trial said, “The researchers would like to know what’s really causing malaria.”

Nine respondents knew they were at the clinic or hospital because of a particular illness they had, but none mentioned anything about research, learning, uncertainty, or investigation. For example, a woman in the MTCT HIV trial said the activity is "for the baby to take the medicine"; another woman in the same trial said, "She is attending for HIV." A woman in the TB/HIV prevention trial said the project was for "medicines, things for health, to keep us alive." Five of these respondents, and four others, said they had no idea whatsoever what research was. One respondent said, "Research project? They build houses?" A translator for a woman whose child was in the placebo-controlled malaria trial explained, "She does not know what research is. She thought they have already done the research, and they are trying to implement the results of the research with these children."

Treatment Assignment Not Well Understood—Interviewers asked respondents whether all participants in the same trial get the same drugs. Only if a respondent answered no did we ask how researchers assigned treatments or interventions in the trial. It was typical for respondents across different studies to say they did not know how researchers decided to give which participants which treatment. Three specifically said all participants get the same drug, and four specifically said participants get different treatments. Another said that, while she did not know, it would make sense to her that people with different amounts of malaria in their blood might get different interventions. Two women enrolled in the same MTCT HIV trial responded that women received different drugs. They believed this meant they were in different studies, however. Another thought the researchers selected the drug specifically for her because of her particular medical history. According to the translator, "She said they decided to give her AZT because she had had a miscarriage." Most of the mothers of children in the placebo-controlled malaria study thought all the children were receiving the same treatment. One mother told the translator the children "are getting the same kind of medicines because they were suffering from the same kind of malaria. She said they might be getting different amounts of the same medicine." Another woman from the malaria trial who referred to the consent form said she "is sure that they are all getting the same drugs because the paper says they are all given the same drugs." None of the respondents who were subjects in the three placebo-controlled trials mentioned the possibility that they had received a placebo or no treatment as part of the study.

Hope for Access to Treatment or Care Is Primary Motivation for Participation —Seventeen of 18 respondents who provided reasons why they joined the research or activity cited the desire for help or for treatment. Most of the comments reflect the view that the primary motivation was to obtain medical care. Two respondents said they thought the treatment provided through research was *better* than the available medical care. Said one participant in a TB/HIV trial, "I thought that they would help us." Another trial participant told the translator, "She doesn't know any place [besides the study] that she could get help." A participant in a different TB/HIV trial said, "They work with you. Whatever illness you have, they help you … they gave you a whole bunch of medicine." She told the translator "if she hadn't been in the project she would have died already." A mother of a child in the malaria trial reported: "She came because her two kids were sick with malaria. So she went to the outpatient clinic and they referred her to come in." Among those who thought care in research was better than what they could obtain outside a clinical trial, we heard, "[Care is] better in the research than in the clinics" and "She signed the form because the medicines they are giving are new and it may be helpful." Two respondents, both in the microbicide trial, said their desire to be tested for HIV motivated them to join that study.

Several participants volunteered that their experiences as trial participants confirmed to them that the trial provided good medical care. A participant in a TB study said, "When I was at the clinic and felt bad, every time I went the doctors took care of me." Another respondent

had a similar experience: “There were lots of advantages. There was nothing I didn’t like. The doctor was free and the medicines were free. There was nothing I didn’t like.”

Extrapolating from Beliefs about Personal Outcome to Beliefs about Trial Outcome—Six respondents volunteered a belief that the research intervention worked because they had experienced a positive outcome. For example, a woman in the placebo-controlled microbicide trial said she was “sure the drug worked because she tested HIV-negative.” When asked if the gel will prevent STDs, she said “yes because she used it and was sure it was a good product.” We asked, “How does she know it was a good product?” and were told, “Because when she used the product there was no problem with the product, and when it was given to the partner there was no problem.”

Participants Did Not Feel Forced to Enroll in the Research Studies—We asked all but three respondents whether their participation in the clinical trial was voluntary. One respondent said she did not remember; three did not directly answer the question. Of the remaining 19 respondents, all indicated they had participated voluntarily. Eight specifically said they had been told that participation was up to them and/or that no one had forced them to join. For example, the translator for a participant in a TB prevention study reported the woman said she “did not feel forced into the study. If you don’t want to enter you don’t have to.” Ten respondents referred to the consent form as evidence that the choice to enroll was theirs. According to the translator for a participant from the malaria study, the woman “said the paper said she had a right to say no. After thinking about the situation with her child she decided to join.” Another woman reported that she had signed the paper “to show the study she agreed to do the research … she only does that in this clinic, not the other clinics.” The notion was that for regular medical care, there are no forms to sign, but in research, the papers are there to say one can refuse.

Four respondents said they did not realize they could quit the trial if they wanted to. Moreover, two suggested that because of the benefits the trial provided, it would be ridiculous to leave the study once enrolled. According to the translator for a participant in a placebo-controlled TB trial, “Nobody forced her into the project. She said she cannot leave at any time because it is bad. But that is because they give you the gift of life and, therefore, it is bad to leave.”

Discussion

In interviews with 26 clinical trial participants from three countries, we found variation in their understanding about the purpose of the clinical trial and about the voluntariness of trial participation. Many of the respondents viewed research as a “learning” activity, though some were specifically aware that research is designed to test the effectiveness of a new product. In almost all cases, respondents knew that the trial in which they participated focused on a specific disease that they could name. Most seemed eager to have joined the trial in order to obtain benefits from participation. None reported being forced to participate.

Ten of the 26 respondents said that the consent form for the clinical trial symbolized to them that they could drop out of the study or activity. However, it is somewhat troubling that a few respondents said that once enrolled in a trial, they believed they could not withdraw from the study. This finding is consistent with other published accounts of trial participation in resource poor countries. For example, an investigation in Bangladesh revealed that 48% of research participants did not know they could withdraw after joining a trial, and in an HIV trial in South Africa, only 24% believed they could leave after enrollment.[16]

Respondents generally knew that the clinical trial in which they were enrolled was a research study. However, there was no evidence across interviews that participants knew they were being randomized. Moreover, no participant in any of the three placebo-controlled trials mentioned the possibility of receiving a placebo, and no participant expressed uncertainty about whether the research intervention would work. When respondents were aware that different trial participants might receive different medications, they provided their own explanations to make sense of differences in allocation. Featherstone and Donovan have shown that research participants often make sense of difficult research concepts such as randomization or equipoise by developing detailed narratives. They further suggest that even providing seemingly clear and accurate information does not ensure accurate understanding of research concepts. Indeed, many studies have documented that research subjects do not understand randomization and placebos, even when research staff specifically explain these concepts and practices to them.[17]

There were limitations to this study. Although respondents were participants in several different clinical trials conducted in three resource poor countries, it is difficult to generalize our findings based on the responses from 26 individuals. Additional empirical research on informed consent in resource poor settings is needed to validate or refute our findings and recommendations, including studies that focus on individuals invited to participate in clinical trials who chose not to enroll. Our sample was limited to those who agreed to participate in a clinical trial; it is possible that those who rejected research participation would add important insights about motivation, understanding, and voluntariness.

A significant limitation of our findings is that, for the four studies in which we used translators of convenience, we were unable to validate the accuracy of translation. Particularly for qualitative research, where the exact quotes are themselves the data, accurate translation is critical to the validity of the conclusions drawn. While we asked all translators to translate verbatim, it is possible that, rather than doing so, some translators summarized the respondents' answers in a way that did not accurately reflect their responses. Finally, two limitations exist in all informed consent research of this sort. First, we did not know what the research staff told respondents about the clinical trial in which they participated. Thus, if they misunderstood an aspect of the trial, we do not know whether this was due to how the research was described to them or to their inability to understand the information they were given. Second, since we conducted some of the interviews several months after respondents had enrolled in the study in question, what we interpreted as a lack of understanding may have been a problem of recall.

Recommendations

We recommend that future research examine creative approaches to *improve* understanding in international, resource poor settings. Furthermore, formative research should guide the development of such interventions, as well as assess how well participants understand the information ultimately provided. Perhaps most importantly, we recommend that a higher bar be used to judge research acceptability when conducting research where participants may not understand key research procedures, as well as the defining feature of clinical research. We offer specific recommendations along these lines.

1. Conduct more empirical research testing interventions to improve understanding of research conducted in resource poor countries

It is essential that scholarly work be conducted measuring the effect of creative interventions to improve participants' understanding of research, particularly in settings where individuals are not very familiar with the concept of research and thus may conflate research with health care delivery. We are aware of no published studies documenting the effect of consent

interventions in developing countries. In U.S.-based studies, requiring patients to verbalize risks and benefits themselves[18]or having research staff provide "corrected feedback" to participants has been shown to be effective.[19] Use of simplified material[20] and pictures improved understanding,[21] and another study found patients preferred simplified consent forms.[22] Two studies found that the use of video did not result in improvement of understanding but improved recall one to two months later.[23] While these studies demonstrated improvement in certain aspects of research understanding, we are aware of no studies that improved understanding of the critical fact that clinical benefit and/or treatment allocation were *uncertain*. Creating and evaluating alternative means of conducting informed consent procedures is critical. U.S. Institutional Review Boards (IRBs) should remember that a variety of approaches, either in addition to, or instead of, written consent forms, can be legally acceptable means of educating participants and documenting consent. Alternative approaches seem particularly important in light of the finding from one published study that, where more than 80% of international participants are illiterate, 60% of investigators still use written consent forms.[24]

2. Test participant understanding and engage in formative research

"Formative research" is a form of rapid ethnographic assessment involving target populations before a study is initiated, particularly in large or multisite trials.[25] This approach can help identify appropriate terminology and locally relevant analogies to explain challenging concepts and generally highlight what participants find difficult to understand. Once a study begins, researchers should, as a matter of course, conduct informal assessments of participants' understanding and why they enroll. Research staff can then engage in group and/or individual discussions to try to clarify misunderstandings. We know from previous work that, while 65% of researchers think it is desirable to build formal mechanisms to test participant understanding into a study's design, only 16% of U.S. investigators working in developing countries do so.[26] If investigators asked qualitative questions before or during a study to assess understanding, they could provide "corrected feedback,"[27] ultimately improving understanding. Formative research in the planning stages of a study can also be invaluable in identifying what participants do and do not understand about research, both generally and in relation to particular protocols. Learning not only what participants find unfamiliar, but also what their beliefs are regarding health care, research, malaria, HIV, and other relevant conditions, may influence the content of informed consent materials. Formative research also can identify preferred methods for learning information, such as group sessions, involvement of family members, and use of peer educators.

3. Give more attention to risks and benefits when participants do not fully understand

Until further empirical research can suggest additional strategies to improve understanding, researchers will continue to conduct clinical trials even though participants may not fully understand the nature of research or that clinical benefit is uncertain. The normative question becomes whether researchers should continue to enroll participants under such circumstances, and/or what safeguards might be put in place.[28] An incomplete understanding of research can raise concern in two ways. Conducting research with someone who fundamentally does not understand they are in research and/or that efficacy is uncertain is potentially exploitive, in that the researcher is using the participant to further the agenda of others without having obtained valid consent to do so. Second, without a full understanding of what research is about, participants may experience harms. Those who do not understand, for example, that a vaginal microbicide may not be efficacious, or that half the women get placebo, may be more likely to engage in unprotected intercourse. Mothers who mistakenly believe their child's malaria has been cured may be less vigilant about seeking medical care when symptoms persist. Indeed, it was jarring to learn from our respondents who participated in the microbicide trial that they enjoyed sex more because

they felt protected by the microbicide or that their husbands were happy because the women were using something to protect against HIV transmission when we knew that half of the women in the trial received placebo, and that trial results revealed that the microbicide *increased* the risk of HIV transmission.[29]

However, while participants' lack of understanding is *prima facie* ethically problematic, one should not conclude that incomplete understanding necessarily ought to forbid the conduct of all research, or that incomplete understanding is of equal concern in all types of research. Indeed, requiring full understanding might lead to the termination of the bulk of health research in *all* regions of the globe, rich and poor alike. Instead, we propose that to adequately determine how much understanding is necessary for particular studies to go forward, studies should be evaluated on a case-by-case basis, based primarily but not exclusively on the risks posed by lack of understanding. The determination should be what the effect of the risk of misunderstanding would have on the subject or the community and what the risks and benefits of the study are overall. High-risk studies demand careful assessments of participant understanding, greater demonstrated levels of participant understanding, and greater expectations of benefit than do studies that pose lesser risks to research participants. If a misunderstanding could lead to potentially dangerous outcomes—as in the example of the microbicide trials or with HIV vaccine trials—researchers must always assess participant understanding. When individuals do not fully understand the critical components of a trial, they must be excluded from participation.

Conversely, for some lower risk studies, after first ensuring that investigators devote sincere effort to improving participant understanding, it may be appropriate for them to proceed even with the knowledge that some participants don't understand they will receive a placebo or why the study is being conducted. The justification for going forward is that the research might produce important generalizable results without undue risk to trial subjects. In populations where it is questionable whether there is understanding of essential concepts, and thus whether valid consent is obtained, a more vigilant examination of risks and benefits must be undertaken.

4. Make careful distinctions between provision of benefit in research and coercion

Our respondents generally felt free to join or to refuse to participate in a clinical trial, and most viewed enrollment as being in their (or their children's) best interests. Indeed, several explicitly said they had nowhere else to turn for medical care, and a few said without the research intervention, they would have died. While respondents may have been correct in believing that joining would be to their benefit, the notion of voluntary "choice" inevitably is different in settings where there are few reasonable alternatives for medical care. Moreover, given that settings of deprivation are fertile ground for public health problems to be highly prevalent and severe—and thus will and ought to be the settings for public health research—they raise challenging moral questions about what are appropriate levels of benefit for those with so few health care or material resources.[30] Researchers and IRBs are right to consider appropriate levels of benefit, or inducement, in research studies in resource poor settings. At the same time, it is critical not to conflate the provision of beneficial research in a community with few good alternatives for medical care with coercion. As always, it is incumbent on researchers and reviewers to examine the study's risks and the acceptability of all individual study procedures.[31] The provision of benefit to participants is a good thing. No amount of benefit, however, can be used to justify unacceptably risky research or otherwise morally problematic study procedures.

Appendix

Interview Field Guide

- Tell me a bit about yourself. What do you do? Do you have children?
- Why did you come here today?
- Can you tell me about this activity/study/project?
- What is the goal of the activity/study/project?
- What is a research study?
- Who first talked to you about the study? What did they say?
- Did you consult with anyone (family or friends) before you decided to join this study?
- Why did you decide to join the study?
- What are the possible advantages/disadvantages of being in a study?
- Do family and friends know about your participation in this study? Did you tell them about it? Why or why not? How did they react?
- Do you feel like any person forced you to be in this study? If so, whom? How did they do that?
- Do you remember signing a form? Can you tell me what that was for?
- If you want to stop being in this study, do you think that is possible?
- Would you recommend to a friend of yours to join/not join a research study? Why/why not?

Acknowledgments

This work was supported in part by a grant from the National Institute for Allergy and Infectious Diseases, National Institutes of Health: R01 AI/T15AI07560. We are extremely grateful to the investigators who gave us permission to speak with participants in their research studies.

References

1. Riecken HW, Ravich R. Informed consent to biomedical research in Veterans Administration Hospitals. JAMA. 1983; 248:344–348. [PubMed: 7045434] Joffe S, Cook EF, Cleary PD, et al. Quality of informed consent in cancer clinical trials: A cross-sectional survey. Lancet. 2001; 358(9295):1712–1777.
2. Appelbaum PS, Roth LH, Lidz CW, et al. False hopes and best data: Consent to research and the therapeutic misconception. Hastings Center Report. 1987; 17(2):20–24. [PubMed: 3294743] Kass N, Sugarman J. Are research subjects adequately protected? A review and discussion of three projects conducted by the Advisory Committee on Human Radiation Experiments. The Kennedy Institute of Ethics Journal. 1996; 6:271–282.Appelbaum PS, Lidz CW, Grisso T. Therapeutic misconception in clinical research: Frequency and risk factors. IRB: Ethics & Human Research. 2004; 26(2):1–8. [PubMed: 15069970]
3. Miller FG, Rosenstein DL. The therapeutic orientation to clinical trials. NEJM. 2003; 348(14): 1383–1386. [PubMed: 12672867] Moreno JD. Abandon all hope? The therapeutic misconception and informed consent. Cancer Investigation. 2003; 21(3):481–482. [PubMed: 12901293]
4. Preziosi MP, Yam A, Ndiaye M, et al. Practical experiences in obtaining informed consent for a vaccine trial in rural Africa. NEJM. 1997; 336:370–373. [PubMed: 9011793] Benatar SR. Reflections and recommendations on research ethics in developing countries. Social Science &

Medicine. 2002; 54(7):1131–1141. [PubMed: 11999507] Molyneux CS, Wassenaar DR, Peshu N, et al. Even if they ask you to stand by a tree all day, you will have to do it (laughter) …! Community voices on the notion and practice of informed consent for biomedical research in developing countries. Social Science & Medicine. 2005; 61:443–454. [PubMed: 15893058]

5. Fitzgerald DW, Marotte C, Verdier RI, et al. Comprehension during informed consent in a less-developed country. Lancet. 2002; 360:1301–1302. [PubMed: 12414207]
6. Leach A, Hilton S, Greenwood BM, et al. An evaluation of the informed consent procedure used during a trial of a Haemophilus influenzae type B conjugate vaccine undertaken in The Gambia, West Africa. Social Science & Medicine. 1999; 48(2):139–148. [PubMed: 10048773]
7. See ref. 4, Benatar 2002.
8. Beyrer C, Kass N. Human rights, politics, and research ethics review. Lancet. 2002; 360:246–251. [PubMed: 12133674]
9. National Bioethics Advisory Commission. Ethical and Policy Issues in Research Involving Human Participants. Bethesda, MD: NBAC; 2001.
10. Kass N, Sugarman J, Faden R, et al. Trust: The fragile foundation of contemporary biomedical research. Hastings Center Report. 1996; 26:25–29. [PubMed: 8891706] Tindana P, Kass N. The informed consent process in a rural African setting: A case study of the Kassena-Nankana district of Northern Ghana. IRB: Ethics & Human Research. forthcoming.
11. Macklin R. Due and undue inducements: On paying money to research subjects. IRB: A Review of Human Subjects Research. 1981; 3(9):1–6.
12. Emanuel EJ. Ending concerns about undue inducement. Journal of Law, Medicine, and Ethics. 2004; 32:100–105.
13. Investigators who allowed us to conduct interviews at their sites were promised confidentiality with regard to study title, institutional affiliation, funder, and country.
14. Bernard, HR. Social Research Methods: Qualitative and Quantitative Approaches. London, UK: Sage Publications; 2000.
15. Miles, MB.; Huberman, AR. An Expanded Sourcebook, Qualitative Data Analysis. 2nd ed.. London, UK: Sage Publications; 2003.
16. Lynoe N, Hyder Z, Cowdhury L, et al. Obtaining informed consent in Bangladesh. NEJM. 2001; 344:460–461. [PubMed: 11221611] Joubert G, Steinberg H, van der Ryst E, et al. Consent for participation in the Bloemfontein Vitamin A trial: How informed and voluntary? American Journal of Public Health. 2003:582–584. [PubMed: 12660201]
17. Featherstone K, Donovan K. Why don't they just tell me straight, why allocate it? The struggle to make sense of participating in a randomized controlled trial. Social Science & Medicine. 2002; 55:709–719. [PubMed: 12190265] See also Gray B. Human Subjects in Medical Experimentation. 1975New YorkWiley-Interscience Appelbaum PS, Lidz CW, Meisel A. Informed Consent: Legal Theory and Clinical Practice. 1987New YorkOxford University Press See ref. 4, Preziosi 1997; See ref. 6, Leach et al. 1999.
18. Wadey V, Frank C. The effectiveness of patient verbalization on informed consent. Canadian Journal of Surgery. 1997; 40(2):124–128.
19. Taub HA, Kline GE, Baker MT. The elderly and informed consent: Effects of vocabulary level and corrected feedback. Experimental Aging Research. 1981; 7(2):137–146. [PubMed: 7274320]
20. Rogers CG, Tyson JE, Kennedy KA. Conventional consent with opting in versus simplified consent with opting out: An exploratory trial for studies that do not increase patient risk. Journal of Pediatrics. 1998; 132(4):606–611. [PubMed: 9580757]
21. Murphy DA, O'Keef ZH, Kaufman AH. Improving comprehension and recall of information for an HIV vaccine trial among women at risk for HIV: Reading level simplification and inclusion of pictures to illustrate key concepts. AIDS Education and Prevention. 1999; 11(5):389–399. [PubMed: 10555623]
22. Davis TC, Holcombe HJ, Berkel HJ, et al. Informed consent for clinical trials: A comparative study of standard versus simplified forms. Journal of the National Cancer Institute. 1998; 90(9): 668–674. [PubMed: 9586663]
23. Fureman I, Meyers K, McLellan AT, et al. Evaluation of a video-supplement to informed consent: Injection drug users and preventive HIV vaccine efficacy trials. AIDS Education and Prevention.

1997; 9(4):330–341. [PubMed: 9376207] Weston J, Hannah M, Downes J. Evaluating the benefits of a patient information video during the informed consent process. Patient Education and Counseling. 1997; 30(3):239–245. [PubMed: 9104380]

24. Kass N, Dawson L, Loyo-Berrios NI. Ethical oversight of research in developing countries. IRB: Ethics & Human Research. 2003; 25(2):1–10. [PubMed: 12833901]
25. Bentley ME, Pelto GH, Straus WL, et al. Rapid ethnographic assessment: Applications in a diarrhea management program. Social Science & Medicine. 1988; 27(1):107–116. [PubMed: 3212501]
26. See ref. 24, Kass et al. 2003.
27. See ref. 19, Taub et al. 1981.
28. Sreenivasan G. Does informed consent to research require comprehension? Lancet. 2003; 362:2016–2018. [PubMed: 14683665]
29. Wilkinson, D.; Ramjee, G.; Tholandi, M.; Rutherford, G. Nonoxynol-9 for preventing vaginal acquisition of sexually transmitted infections by women from men. Oxford: Update Software; 2003. Cochrane Review CD003939 [2]
30. Richardson HS, Belsky L. The ancillary care responsibilities of medical researchers. Hastings Center Report. 2004; 34:24–33. [PubMed: 15553395]
31. See ref. 4, Benatar 2002 Faden R, Beauchamp TL, King NM. A History and Theory of Informed Consent. 1986New YorkOxford University Press