Quality of Parental Consent in a Ugandan Malaria Study

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Objectives. We surveyed Ugandan parents who enrolled their children in a randomized pediatric malaria treatment trial to evaluate the parents' levels of understanding about the treatment trial and the quality of the parents' consents to allow their children to participate in the study.

Methods. We conducted 347 interviews immediately following enrollment at 4 Ugandan sites.

Results. A majority (78%) of the parents, most of whom where mothers (86%) had at most a primary school education. Of the participating mothers, a substantial percentage reported that they remembered being told about the study's purpose (77%), the required number of visits (88%), the risks involved (61%), treatment allocation (84%), and their ability to discontinue their children's participation (64%). In addition, most reported knowing the trial's purpose (80%) and the required number of visits (78%); however, only 18% could name possible side effects from the drugs being administered, and only 19% knew that children would not all be administered identical treatments. Ninety-four percent reported that they made the enrollment decision themselves, but 58% said they felt pressure to participate because of their child's illness, and 15% said they felt some type of pressure to participate from others; 41% reported knowing that they did not have to participate.

Conclusions. The consent Ugandan parents provided to allow their children to participate in the malaria study was of mixed quality. Parents understood many of the study details, but they were not very aware of the risks involved or of randomization. Many parents felt that they could not have refused to participate because their child was sick and they either did not know or did not believe that their child would receive treatment outside of the study. Our results indicate that further debate is needed about informed consent in treatment studies of emergent illnesses in children. (*Am J Public Health*. 2005;95:1184–1189. doi:10.2105/AJPH.2004.053082)

There is concern that illiteracy and limited education, lack of familiarity with research, and limited access to health care can jeopardize the ability of study participants, especially those in developing countries, to provide fully informed and voluntary consent.[1–4] Despite this concern, few studies have been conducted to examine the quality of informed consent in the aforementioned settings.[5–10] In developing countries, where children are involved in vital research on diseases such as malaria and dysentery, even fewer studies have evaluated the quality of informed parental consent for pediatric trial participants unable to provide their own consent. This aspect of informed consent also is understudied in developed countries.

At 4 separate sites in Uganda, we interviewed parents and guardians whose children were participating in a randomized study of antimalarial treatments. Immediately after parents consented to enroll their child in the antimalarial study, we interviewed those parents about their motivations for enrolling their child in the study, their experiences with the informed consent process, their comprehension of the trial, and the extent to which the enrollment decision was voluntary.

METHODS

Design and Setting

Children aged 6 months or older were enrolled in a randomized, single-blind treatment study that assessed the efficacy of different oral antimalaria drug regimens. Because of increasing *Plasmodium falciparum* resistance to chloraquine (CQ) and sulfadoxine pyrimethamine (SP), the standard first-line treatments for malaria in Uganda, this study compared the efficacy of CQ and SP with that of amodiaquine plus SP and, at 1 site, with that of amodiaquine plus artesunate. The trial, conducted, at 3 rural sites (Mubende, Kyenjojo, and Kanungu) and 1 periurban site (Jinja), was led by the Uganda Malaria Surveillance Project, a partnership between the Makerere University Institute of Public Health; the Makerere University–University of California, San Francisco Malaria Research Collaboration; the Ugandan Ministry of Health, and the University of California, Berkeley.

Informed Consent Process

Parents or guardians of children who met the study's eligibility criteria received copies of the trial consent forms in both English and the local language. Parents participated in a discussion with a nurse-coordinator or investigator during which the consent form was reviewed. The form, about 5 pages and 1200 words long, contained information on the study's purpose, its risks and benefits, its procedures (e.g., randomization and storage of blood for future research), the voluntary nature of participation, and the participants' freedom to withdraw from the study. A shorter consent form provided further details on collection and storage of blood for future research.

Participants

Our study involved the use of a convenience sample. All parents or guardians enrolling a 6-month-old to 12-year-old child in the malaria study between October 2002 and March 2003 were invited to participate. In-person interviews were conducted immediately after consent was provided for the malaria study. Respondents provided verbal informed consent to complete in-person interviews.

Survey Development and Administration

The survey instrument, developed by the authors in conjunction with the National Opinion Research Center (NORC) at the University of Chicago, was based on relevant domains from the research literature and the malaria study consent form.[11–13] The final instrument (available from the authors on request) consisted of 60 questions that focused on 6 domains. With the exception of questions gathering data on sociodemographic characteristics, the question formats used were multiple choice (17 questions), yes or no (22 questions), or open ended (9 questions). The data from these interviews provided (1) parents' motivations for enrolling their children in the malaria study; (2) parents' experiences with the informed consent process; (3) parents' comprehension of study details, including procedures, possible side effects, and randomization; (4) the extent to which the decision to participate was voluntary; and (5) sociodemographic characteristics. Data on a sixth domain, attitudes regarding samples stored for future research, are reported elsewhere.[14]

The instrument was translated into the Luganda, Rukiga, and Rutooro languages by professional translators in Uganda, who then back-translated the instrument into English. It was then tested among the 8 Ugandan interviewers to determine its comprehensibility. The instrument was pretested with parents who had been research participants at the site where the Luganda version of the survey was used. The in-person interview format allowed participation regardless of literacy level.

Specially trained Ugandan personnel, fluent in both English and the language spoken at their assigned site, conducted the interviews. Interviewers were paid and supervised separately from the malaria study and clinical staff. Neither the malaria study nor clinical staff had access to completed questionnaires, which were sent to NORC for data entry.

Of the 353 individuals invited to participate, 347 completed interviews, 5 terminated their interviews before completion, and 1 individual refused to be interviewed (response rate: 98%). The mean duration of the interviews was 33 minutes, and the range was 7 to 152 minutes.

Statistical Analysis

We used descriptive statistics to summarize the data. In the case of categorical variables, we calculated and compared proportions in each category via χ^2 tests. Seven variables (gender, marital status, head of household, education, previous research participation of other children, site, and pressure because of child's sickness) were examined in regard to associations with (1) knowledge about treatment allocation and side effects of the malaria drugs and (2) the voluntariness of the enrollment decision. The statistical significance (α) level was set at .05.

RESULTS

Overall, 85% of respondents identified themselves as the participating child's mother, 7% as the child's father, and 19% as the head of their household. Most owned the house they lived in (70%), and these homes were primarily dwellings with tin roofs (76%) but no electricity (90%). Other respondent sociodemographic characteristics are shown in Table 1.

TABLE 1—Characteristics of Study Respondents

	Percentage
Female	86
Parent of child in study	92
Head of household	19
Education	
None	20
Some primary school	40
Primary school	18
Some secondary school	14
Secondary school	4
Any college/university	4
Rural dweller	71
Electricity in house	10
Homeowner	70
Previous enrollment of 1 or more children in a research study	25

Experience With the Informed Consent Process

Most respondents remembered being told by study personnel about the study purpose (77%), study risks (61%), number of visits (88%), treatment assignment (84%), and the ability to discontinue participation (64%). Similarly, most reported that they felt informed about the study risks (65%), the number of visits (84%), the ability to quit (67%), the study purpose (67%), and treatment assignment (71%) (Table 2). Seventy-nine percent of the respondents reported that they received all of the information they wanted; 67% reported being given a chance to ask questions, of which two thirds (45% of respondents overall) actually asked questions.

Comprehension of Study Information

Eighty percent of the respondents correctly identified the study purpose as determining which malaria drugs are most effective for children; 20% chose finding the cheapest drugs, collecting data for the Ugandan government, or making money for the research team. Most knew they would have to bring their child to the clinic 7 times for the study (78%), that drugs would be administered

TABLE 2—Respondent's Experience With the Informed Consent Process

Topic	Reported Being Told About Topic by Study Staff, %	Felt Informed About Topic, %	Demonstrated Knowledge of Specific Details, %
Purpose of the study	77	67	80[a]
Risks of the study	61	65	18–45[b]
No. of clinic visits	88	84	78
Way treatments are assigned	84	71	19[c]
Option of quitting	64	67	65

[a]Recognized that the reason the study was being conducted was to find the best treatment for children with malaria.
[b]18% were able to name 1 or more side effects; 45% recognized 1 or more in multiple-choice questions (Table 3).
[c]Although 88% knew that all children would receive treatment for malaria, only 19% knew that not all children would receive the same drugs (Table 3).

TABLE 3—Comprehension of Study Details

	Percentage
Identified no. of required clinic visits	78
Identified treatment administration as oral	79
Knew child's blood would be taken	98
Knew child's blood would be used for future research	52
Named 1 or more side effects	18
Accurately identified the following symptoms as possible side effects	
Fainting	20
Skin rash or itching	32
Knew the following symptoms were not possible side effects	
Red eyes	65
Hearing problems	70
Knew that all children would be treated, but not with the same drug	19
Knew that doctors would determine treatment allocation according to chance	7[a]

[a]This question was asked only of the 19% who knew that not all children would receive the same drug; 39% of that group knew that treatment would be allocated by chance.

orally (79%), and that the investigators would take blood samples to study (98%). Only 52% knew that these samples would be used for future research. In addition, only 18% could name 1 or more side effects of the study drugs when asked an open-ended question. When asked about treatment side effects in a question involving a yes-or-no format, 20% knew that fainting was possible, and 32% knew that their children could experience a skin rash or itching (Table 3).

While most of the respondents (88%) knew that all children taking part in the study would receive malaria treatment, only 19% responded that not all children would receive the same treatment. Seven percent of the respondents (39% of those who knew that not all children would receive the same treatment) knew that treatment assignments would be determined according to chance, and 10% (59% of those who knew that not all children would receive the same treatment) believed that treatment would be decided on the basis of what the doctors thought was best for each child.

Univariate analyses indicated that feeling pressure because of the child's sickness ($P<.001$) and, to a lesser extent, having completed more years of education ($P=.042$) were significantly associated with understanding that not all children would receive the same malaria treatment. Feeling pressure because of the child's sickness was also significantly associated with recognizing possible side effects ($P<.001$ for each side effect). Knowledge that not all children would receive the same malaria treatment was significantly lower at 1 of the rural sites than at the other sites ($P<.001$).

Decisionmaking and Volition

The primary reason most respondents gave for enrolling their child in the study was to obtain malaria treatment. Several respondents mentioned specifically that they enrolled their child because previous treatment attempts had failed. A small number of parents (7%) reported that their primary motivation was the opportunity to learn about their child's sickness. One respondent said, "In this study, they teach a lot of things related to malaria." Another said that she enrolled her child "in order to enable researchers to get the best treatment for future kids," and still another said that "when the doctor explained, I saw the importance of this study." Others commented that malaria was a major problem for their region (e.g., "In this village we have been suffering a lot").

Almost all of the respondents (94%) reported that they personally made the decision to enroll their child, although 22% indicated that another person helped them with the decision (Table 4). Most commonly, help came from the malaria study team (13% overall), other doctors and nurses (13%), or the health center (11%) rather than from spouses (6%) or family and friends (8%).

Many of the respondents (58%) felt pressure to join the study because their child was sick, yet most (85%) reported no pressure from other people (Table 4). Among the 47 respondents who indicated feeling pressure from others, family and friends, the study team, or respondents' spouses (6% from each source), or a combination of these sources, created the pressure. A smaller percentage of respondents reported feeling pressure from other doctors or nurses (5%) or health center staff (4%).

TABLE 4—Decisionmaking and Volition

	Percentage
Made decision to join her- or himself	94
Knew she or he could have refused if so desired	41
Degree of pressure felt from others to join the study	
A lot of pressure	12
A moderate amount of pressure	2
A little pressure	1
No pressure	85
Felt pressure to join because child is sick	58[a]
Knew she or he could quit the study	65
Knew she or he could quit at any time	17[b]

[a]53% specified that they felt "a lot of pressure" because of their child's illness.
[b]Asked only of the 25% of those who knew they could quit at all.

Just 41% of the respondents reported they could have refused to enroll their child in the malaria study, and 86% of this group (36% of the respondents overall) stated that it would have been at least moderately easy to refuse. Overall, 25% of the respondents (56% of those who reported that they could have refused) reported that if they had refused to participate, their child would still have received malaria treatment. Of those who stated that they could *not* have refused to participate, nearly all reported the reason as being their child needed malaria treatment. No one attributed it to pressure from others.

Sixty-five percent of the respondents knew that they could quit the study, but only a quarter of these individuals (17% of respondents overall) knew that they could quit at any time, instead of when the treatment had been completed or the doctor said they could (Table 4). Fifty-three percent of respondents thought that their child would still receive malaria treatment if they quit the study.

Those who felt pressure from others to join the trial were more likely to feel pressure because of their child's sickness ($P<.001$)

and to belong to a household headed by the child's other parent ($P=.049$). Female respondents were more likely than male respondents to feel pressure because of their child's sickness ($P=.002$), and they also were more likely to know that they could quit the study ($P=.05$). Those with more education were more likely to know that they could quit at any time ($P=.008$).

The site variable showed a significant association with respondents' belief that they could have refused to join the study (all Ps $<.001$). Significant variation by site was noted in (1) the amount of pressure respondents felt because of their child's illness, (2) previous research experience, (3) education, and (4) beliefs regarding whether the child could be treated if not enrolled in the study. However, there was no consistent variation by site. At 1 of the sites, many respondents felt pressure from others and from their child's sickness and did not know they could quit if they wanted, whereas many participants at another site did not know that they could have refused to join the study or when they could quit.

DISCUSSION

To our knowledge, this is the largest study to date of the quality of informed consent in a developing country. Our data show that a parent or guardian's informed consent for a child enrolled in this malaria treatment study was of uneven quality. Most respondents had a high level of comprehension of some of the study procedures, and most respondents reported having made an autonomous decision to enroll, with few feeling any pressure from others. Conversely, respondent's comprehension of risks and randomization was relatively poor, and responses regarding availability of malaria treatment outside of the study and the possibility of discontinuing participation raise questions about the extent to which respondents' decisions were voluntary. This mixed portrait illustrates the complexity of both obtaining informed consent and assessing its quality in the context of an active controlled trial of treatment for an emergent condition in children.

Respondents understood what the study required of their children, such as number of clinic visits, administration of oral treatment, and blood to be drawn. However, their level of understanding about the possible side effects of study medications was substantially lower. Only 61% of the respondents recalled being told about risks, and many fewer (18%) could accurately name 1 or more side effects of the study drugs. While most (84%) remembered being told how malaria treatments would be assigned, 69% *incorrectly* thought that all children would receive the same treatment. Of the small number who knew not all children would receive the same treatment, many fewer knew that treatment assignment would be "based on chance, like pulling a number out of a hat," although assignment was explicitly described in this way in the consent form.

Previous informed consent studies conducted in both developed and developing countries have revealed people's understanding of randomization and of side effects often is poor.[8,15–20] Such poor understanding may not be surprising in the context of an active controlled trial in which risks associated with different study arms are similar and, most important, similar to the risks of treatment outside the trial. Furthermore, parents were probably aware that malaria treatment, even with side effects, is less risky than not treating malaria. These children were ill, and their parents were informed that all children would receive treatment. Knowledge of the particular drugs' side effects or randomization may therefore have played no or only a minor role in parents' decisions to enroll their children, or it may at least have played understandably less of a role than it might play in decisions about enrolling in placebo-controlled or high-risk trials or studies of nonurgent interventions.

Indeed, it may be difficult for investigators to impress such details upon parents who are worried, first and foremost, about treating their children's sickness. From an ethical standpoint, these details may not be critical for parents in making an informed decision about participation. Focus group discussions (conducted in a parallel study [E. Okiria, unpublished data, May 2003]) with mothers whose children were already participating in the malaria study suggest, in fact, that for many parents the greatest burden of participation was the time commitment and number of clinic visits rather than concerns about drug side effects. Because our respondents understood the nature of their time commitment far better than the risks involved with the study, their decision may have been based on information they found most salient.

A common worry among commentators focusing on informed consent is that women in Africa, and Uganda in particular, do not make independent decisions for themselves or their families because of accepted gender roles in their societies.[21–23] Yet, in our study, nearly all of the predominantly female respondents themselves made the decision to enroll their child, with only 8 of 347 respondents reporting that the enrollment decision was made by their spouse. Furthermore, among respondents who reported that although they decided about enrollment themselves, they received some help with the decision, spouses were the least common source of help. Most respondents felt no pressure from anyone to enroll their child in the study, and, among those few who did feel pressure, spouses were infrequently the source. In addition, women knew more often than men that they could quit the study.

However, similar to our data on comprehension, our data on the extent to which respondents' enrollment decisions were voluntary reveal a complex picture. More than half of the respondents felt pressure to join the study because of their child's sickness, and most cited their child's need for treatment as their main reason for enrolling. This may be surprising because the malaria study consent form emphasized that children who did not participate would still receive malaria treatment from the clinic, and in theory this treatment was also free. Yet, fewer than half of the respondents indicated that they could have refused to join the study, and only 56% of these individuals reported that if they had refused, their child could still have received treatment.

To the extent that these responses reflect parents' failure to grasp what they were told (or investigators' failure to thoroughly explain alternatives to participation), this finding has worrisome implications for the parents' consent. Possibly, however, drug access *was* more limited among nonparticipants owing to dif-

ferent funding sources. If so, respondents' answers may say more about their unfortunate health care situation than about problems with informed consent. Although parents may have felt that their options were constrained by their children's sickness and limited access to treatment, it does not necessarily follow that enrollment choices were not voluntary.[11] Indeed, limited treatment options are one reminder of the importance, in this trial and others, of taking into account other critical aspects of research ethics even before anyone is asked to provide informed consent, including whether short- and long-term benefits of research are appropriately responsive to the needs of a community with few health care resources.[24]

In previous informed consent studies, participants were interviewed months or years after the informed consent process,[6] so recall rather than comprehension was assessed. Conversely, immediately after parents or guardians gave consent for their children to be enrolled in the malaria study, we interviewed those parents and guardians to assess their knowledge, experience, and perspectives concomitant with their decision to allow their children to participate. Nonetheless, there are limitations associated with our data. The urgent nature of the malaria treatment trial is a crucial context for interpreting our results and may limit the generalizability of our findings to different types of trials. Furthermore, although 4 different sites in Uganda were involved, these sites may not represent all of Uganda or other African settings.

Conducting the study at 4 different sites provided us with a broad sample of respondents but also resulted in site variability for which we could not entirely account. For example, more people at 2 of the sites than at the other 2 sites reported pressure to join the study because their child was sick, whereas, at a third site, more people responded that their child could not be treated if they refused to join. Site variations were not statistically associated with differences in respondents' characteristics, but they may have been associated with differences in the informed consent process or access to health services, or they may even have been influenced by the use of different interviewers or different translations to accommodate the languages spoken in each region. Finally, although the same written consent materials and procedures were used at all of the sites, we did not observe the consent process itself. Variation in communication styles and clarity of disclosure may have influenced site-specific differences.

In conclusion, Ugandan parents or guardians who consented to enroll their children in a malaria study had mixed comprehension of the study details and felt some pressure to enroll their children because their children were sick and needed treatment that the parents were not confident they could otherwise obtain. Although these data raise questions about the quality of informed consent, they must be interpreted in the context of an active controlled trial of an emergent intervention, in a setting where it may not always have been possible to obtain treatment outside the trial. Further debate is needed on what is ethically necessary for informed consent in such a context. Such debate can pave the way for future studies involving thoughtful assessments of these aspects of informed consent and evaluations of strategies designed to improve the quality of consent in diverse trial settings. ■

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Contributors

C. Pace, A. Talisuna, D. Wendler, E. Emanuel, and C. Grady designed and planned the study and developed the interview script. F. Maiso monitored the day-to-day operations of the study in Uganda and coordinated data entry. F. Wabwire-Mangen and N. Bakyaita reviewed the proposed design and identified sites and procedures for implementation in Uganda. E. Okiria helped recruit and train interviewers, conducted parallel focus groups with parents of children in the malaria study, assisted with analysis of open-ended questions, and reviewed the article. E.S. Garrett-Mayer was responsible for the statistical analysis in collaboration with C. Pace, E. Emanuel, and C. Grady. C. Pace and C. Grady prepared the article. All of the authors contributed substantially to the editing of the article.

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