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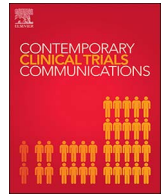
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Reasons for participating in a randomised clinical trial: The volunteers' voices in the COSTOP trial in Uganda

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ABSTRACT

Introduction: The reasons why research participants join clinical trials remains an area of inquiry especially in low and middle income countries.

Methods: We conducted exit interviews with participants who took part in a trial which aimed to evaluate whether long term prophylaxis with cotrimoxazole can be safely discontinued among adults who have been stabilised on antiretroviral therapy (ART). Participants were all reported to be stable on ART and had been participating in the trial for between 12 and 36 months; at the end of the trial participants were interviewed using a semi-structured questionnaire. One of the objectives of the exit interview was to find out what motivated the participants to join the research.

Results: Participants gave personal reasons for joining the trial, frequently linked to their health and well-being as well as reduction of pill burden.

Conclusion: We conclude that underlying reasons for joining clinical trials may extend beyond or can be different from the rationale given to the participants before enrolment by the research team. The reasons that motivate enrolment to clinical trials and research in general require further investigation in different settings.

Trial registration number: ISRCTN44723643.

1. Introduction

The sustained participation and cooperation of volunteers recruited to take part in clinical trials is essential for their success. While randomised controlled trials are considered to be the gold standard methodology to test medical interventions [1,2], the conduct of the trial is dependent on people's willingness to take part. There has, as a result, been considerable interest in what motivates a person to volunteer to take part in a trial. While Jenkins and Fallowfield [3], in their assessment of the reasons for participation in a cancer trial, concluded that people were motivated by a desire to help others and trust in their doctor, others have noted personal gain as an overriding motive for taking part in some trials [4–6] or a desire to please their doctor/health care team [7,8].

Jenkins and Fallowfield [3] noted that people are more likely to take part in a trial when there is active treatment in all trial arms. Mills and colleagues [4] concur, observing participants' dislike of placebo or 'no-treatment' groups, and there are concerns about randomisation, the research process and the chance of being placed on a no treatment arm.

A study on bladder cancer showed that patients may decline to join a randomised trial because of their desire for effective treatment [9]. However, the expected health benefits may be much broader. Indeed, several studies have found that participants anticipate improved access to health care through taking part [5,6,10,11]. This may be particularly important in settings where general health care provision is costly and/or of poor quality. In addition, the participants' perceptions about a trial may be very different from what the research team may be emphasising as the objective of the research [12] and their reason for participation has previously been reported to influence their adherence to trial medication and procedures [13].

We present in this paper data on the motivation to participate in a clinical trial conducted in Uganda, collected through exit interviews.

2. Background

2.1. COSTOP trial

The COSTOP trial was a randomised double blind placebo con-

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Table 1
Participants' motivation for joining COSTOP trial.

Reasons given for joining trial	Gender				Age group (years)						Total	
	Male		Female		< 35		35–54		55 or more		N	%
	N	%	N	%	N	%	N	%	N	%		
Predefined categories												
To see if stopping cotrimoxazole is safe	341	66.2%	935	63.3%	200	65.8%	957	63.4%	119	66.8%	1276	64.0%
To get treatment	157	30.5%	538	36.4%	102	33.6%	535	35.4%	58	32.6%	695	34.9%
To improve my health	117	22.7%	286	19.4%	49	16.1%	310	20.5%	44	24.7%	403	20.2%
To help others through research	110	21.4%	238	16.1%	37	12.1%	271	17.9%	40	22.5%	348	17.0%
To get CD4/other test results	52	10.1%	201	13.6%	42	13.8%	188	12.4%	23	12.9%	253	12.7%
To try out new medicine	53	10.3%	172	11.6%	38	12.5%	161	10.7%	26	14.6%	225	11.2%
To obtain financial benefits	21	4.1%	105	7.1%	23	7.6%	88	5.5%	15	8.4%	126	6.3%
Other categories												
Reduce pill burden	108	21.0%	286	19.4%	48	15.8%	305	20.2%	41	23.0%	394	19.8%
Expected better care, including past experience	43	8.4%	110	7.4%	26	8.6%	114	7.5%	13	7.3%	153	7.7%
To participate in research	8	1.6%	25	1.7%	4	1.3%	27	1.8%	2	1.1%	33	1.7%
Participant was told/encouraged to join	7	1.4%	20	1.4%	3	1.0%	19	1.3%	5	2.8%	27	1.4%
To obtain a cure	5	1.0%	14	1.0%	3	1.0%	16	1.1%	0	0.0%	19	1.0%
Because of HIV-infection	2	0.4%	16	1.1%	1	0.3%	17	1.1%	0	0.0%	18	0.9%
Personal cost of taking cotrimoxazole	1	0.2%	1	0.1%	0	0.0%	2	0.1%	1	0.0%	2	0.1%
Total assessed	515	100%	1477	100%	304	100%	1511	100%	178	100%	1993	100%

trolled trial to evaluate whether long-term prophylaxis with cotrimoxazole (CTX) can be discontinued without loss of efficacy and with a reduction in adverse drug reactions among adults who have been stabilised on antiretroviral therapy (ART). Volunteers were adults aged 18 years and above who had stabilised on ART and had no contraindication to taking CTX. They were randomised to continue CTX prophylaxis or receive a matching placebo. Participants were followed for a minimum of 12 and maximum of 36 months. They attended designated study clinics monthly at regular intervals; and if unwell could attend without an appointment. The trial was conducted at research clinics located in Entebbe and Masaka, in Uganda. Full details of the trial have been reported elsewhere [14,15].

Participants consented to participate in the trial after receiving detailed information about the study. This included details on study objectives, trial duration, why the participant had been invited to take part, trial procedures and the equal likelihood that they would be allocated to active treatment or placebo. They were compensated for the costs of transport according to the prevailing public transport rates and informed that there were no direct benefits for the individual. There was no compensation for time spent at the clinic. Participants in the trial were told that they were free to withdraw from the trial at any time.

The investigators were concerned that a positive outcome to the trial might be questioned if there was a possibility that the participants may have had access to cotrimoxazole from sources outside the trial. There was no simple test that could be applied to determine whether a participant was on active drug, so a small qualitative study was nested within the trial to investigate this concern; there was some evidence of open label drug being taken by the participants. The results from the participant interviews did not suggest that the trial results would have been seriously compromised [16]. Subsequently, exit interviews were conducted on all participants by field workers independent from the clinical intervention team to explore why they had agreed to participate in the trial, and whether they had adhered to the allocated treatment. This paper addresses the reasons given for joining the COSTOP trial.

3. Methods

The participant information document for COSTOP gave the primary reason for the research as determining whether stopping cotrimoxazole would be safe for patients who were already doing well on ART. This information was provided in the local language before

participants were asked for their consent to enrol in the study. Following the final study visit, all participants were invited to an exit interview. This paper addresses the question in the survey regarding the reason people joined the study. Participants were offered seven predefined responses but were encouraged to give additional reasons.

3.1. Ethical requirements

The study was approved by the Uganda Virus Research Institute Regulatory ethics committee and the Uganda National Council for Science and Technology. Each participant gave written/thumb print consent before taking part in the exit interview.

3.2. Procedure

Participants were randomised to be interviewed either by one of the four social science field assistants or one of the four trained peer HIV-positive participants (in Entebbe or Masaka, the two sites where the COSTOP trial was conducted). The interviewers were trained on the purpose and application of a structured questionnaire that included open and closed ended questions. They were all independent of the clinical intervention team with the expectation that this would enhance the willingness of participants to share information which they would have found difficult to give to the study team, for example about failure to adhere.

Responses were analysed both by total participants and stratified by gender and age (see Table 1), the most likely confounders. It was not our intention to test a hypothesis, rather to describe reasons given for joining the trial.

4. Results

Of 2180 participants enrolled into the trial 37 died before the final visit, 95 were lost to follow-up, 49 had withdrawn consent and six were not interviewed at their final study visit.

A total of 1993 (91%) participants were available for interview at the end of the study out of the 2180 randomised participants. Of the 1993 participants, 986 (49%) were randomised to be interviewed by peers and 1007 (51%) by the social scientists; 75% of the participants were female and 76% were aged between 35 and 54 years.

Most volunteers gave more than one reason for joining the clinical trial, 96%, chose at least one of the predefined categories (Table 1).

Twenty nine per cent gave other reasons that were not among the predefined categories and only 12 (< 1%) did not give a reason. There were some differences in the responses collected by social scientists and peer interviewers; this could possibly have been because the trained social scientists might have had more experience in probing for information than the peers. Social desirability could also be a possible explanation for the difference between the two groups.

The most common response given for joining the trial was to see if stopping cotrimoxazole would be safe; this was followed by a desire to get treatment for their illness. To improve health and reduce pill burden were other frequently reported reasons. Older people were more likely than younger participants to mention altruistic reasons and the desire to further improve their health through their participation. There were no major differences in the reasons given by men and women although there was a suggestion that more women joined the trial to receive treatment. There was some evidence of differences in response according to the category of interviewer; those interviewed by social scientists were more likely to give more than one reason than those interviewed by peer interviewers for joining the study, namely 43.2% and 33.3%. Participants interviewed by social scientists more often mentioned 'to see if cotrimoxazole is safe, 68.7% versus 59.3%' and 'to get treatment, 41.4% versus 28.2%.

5. Discussion

In addition to the primary question of assessing whether participants adhered to the study protocol the exit interview addressed a number of other issues including why the participants agreed to join the COSTOP trial. The main reasons given for participation were personal benefit, safety of discontinuing cotrimoxazole and to improve health and access care.

In addition to the anticipated responses, predefined by the research team, several other reasons were given. The most common of these were to reduce pill burden and the expectation of better care when obtained at a research centre (often based on past experience with the research group).

Other studies have shown that the ability to comprehend study information on account of a lack of clarity of the information provided, can be a barrier to participation in research. A study conducted in the United Kingdom, where formal literacy would not be expected to be a common problem in the general population, showed that health literacy varies between participants: at least a third of the older adults had some difficulty in understanding basic health related information [17].

In sub-Saharan Africa where literacy levels remain low in some populations, researchers have tried to improve the understanding of study information, but this remains a challenge [18,19].

Participant information requires translation into the local language to enable comprehension of the research and health terms used in research, and different vernaculars may be spoken at one study site [20]. Information needs to be simple and avoid ambiguity [12]. These principles are in keeping with Good Clinical Practice guidelines [21,22].

Access to good health care was an important motivation for taking part in the COSTOP trial. The public health services in Uganda still face limitations with respect to basic infrastructure, staff numbers and supplies [23]. The local improvements often associated with clinical research with regards to systems, expertise and staff attitudes may lead to improvement in the health outcomes for the research participants and the other people in the setting where research is being conducted [24]. Volunteers participating in the COSTOP trial recognised and appreciated this.

Although gender differences in relation to health seeking behaviour patterns sometimes occur [25], in this trial there was little evidence of differences in response.

Our study had some limitations. Participants may have misunderstood some of the questions; as these may have had different meanings

for different people. For example, the reason, "to see if stopping cotrimoxazole is safe" could be regarded as a research reason or a personal reason. It is also possible that some volunteers may have simply repeated the rationale given to them during the consent process rather than providing their own views. The majority of volunteers however, gave more than one reason for joining the trial which suggests that personal expectations have been expressed. The findings of this study may not be generalisable to all clinical trial settings however the trial did address both safety and efficacy endpoints and could be considered as typical of many such trials conducted in lower or middle income countries.

6. Conclusion

Participants join trials for various reasons. Participants of the COSTOP trial provided responses suggesting that their motivation may extend beyond or can be different from the rationale given to them before enrolment. This reflects the importance that researchers and sponsors should attach to understanding the culture and socio-economic context of the potential volunteers and their setting. Providing on-going study information to the participants by the research teams conducting clinical trials, particularly for trials that last for more than a year, is important. A participant may become uncertain about the basis of the investigation and will inevitably be most concerned about their health and wellbeing. Understanding underlying reasons for joining clinical trials and research in general may require investigation in different populations particularly in low and middle income countries [11]. There is still need for more research to understand better how cultural and socio-economic factors influence participation in research and to what extent participants may agree to enrolment simply because they have been asked to join.

Ethical approval and consent to participate

The study was approved by the Uganda Virus Research Institute (UVRI) Regulatory ethics committee (REC) and the Uganda National Council for Science and Technology (UNCST). The participants who took part in the exit interviews were asked for individual consent before the interview. Informed consent was obtained from all the participants.

Consent to publish

Written informed consent was obtained from the participants that indicated that data would be shared by the researchers for publication. The consent is held by the author's institution and is available for review by the Editor-in-chief.

Availability of supporting data

Data are available and can be accessed when required.

Competing interests

None of the authors has a conflict of interest; AN and ZA contributed to the monitoring and coordinating of the clinical trial.

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Authors' contributions

All the authors contributed towards writing this article. AN and JS

had the initial idea for the paper. All the authors (AS, MM, AN, ZA, JS) discussed the data and the insights of the paper. AS wrote the first draft of the manuscript. The manuscript was edited by all authors. All the authors approved the final version.

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List of abbreviations

ART	Antiretroviral Therapy
COSTOP	Safety of discontinuing Cotrimoxazole prophylaxis among HIV infected adults on ART in Uganda. A randomised controlled trial
CTX	Cotrimoxazole
DFID	Department for International Development
HIV	Human Immune-deficiency Virus
MRC	Medical Research Council
REC	Regulatory Ethics Committee
UK	United Kingdom
UNCST	Uganda National Council for Science and Technology
UVRI	Uganda Virus Research Institute

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