Defining fair and acceptable randomisation procedure in trials targeting vulnerable populations: Qualitative evidence from the POWER trial in Cameroon

Authors: Fanny Procureur[1], Emile Nitcheu[2], Sandie Szawlowski[1], Chimène Mangoua Chimsgueya[2], Laetitia Laure Toukam[2], Julienne Noo[2], Eric Defo Tamgno[2], Iliassou Mfochive[2], Stephanie Moyoum[2], Serge Billong[3], Ubald Tamoufe[2], Aurélia Lépine[1]

Affiliation:

1. Institute for Global Health, University College London, London, United Kingdom
2. John Hopkins Cameroon Programme, Yaounde, Cameroon
3. University of Yaoundé I, Yaounde, Cameroon

Corresponding author: Aurelia Lepine, a.lepine@ucl.ac.uk

University College London
Faculty of Population Health Sciences
Institute of Global Health
3rd floor, Institute of Child Health, 30 Guilford Street, London WC1N 1EH

Abstract

Context and aims: Important ethical issues have been consistently highlighted in randomised controlled trials (RCTs). Although RCTs are widely used in non-clinical health research, there is little research on participants' perceptions of the fairness and transparency of RCTs.

Methods: Data were collected as part of the POWER trial, which aims to test the effectiveness of health shock prevention for HIV prevention among women who engage in commercial and transactional sex in urban Cameroon. This qualitative study was carried out in 2 phases. In the pre-randomisation phase (phase 1), we conducted 25 focus groups and 8 in-depth semi-structured interviews to determine the most acceptable randomisation strategy for our study participants. In the post-randomisation phase (phase 2), 41 in-depth semi-structured interviews were conducted with participants to assess their perceptions and satisfaction with their group allocation status (e.g. treatment or control).

Results: We found that participants understood the rationale for randomisation of the intervention and were satisfied with the randomisation strategy. This latter finding was mainly due to i) the involvement of participants in the chosen randomisation method and ii) the fact that the control group would receive the intervention at the end of the study.

Conclusion: It is important that researchers conduct similar studies before designing RCTs in vulnerable populations to minimise ethical issues related to the conduct of RCTs. Conducting pre- and post-randomisation qualitative research is an effective approach to improve RCT design and to assess and address potential problems with RCTs.

1. Introduction

Ethical issues in randomised controlled trials (RCTs) have been reported extensively (Khera, 2021; Ravallion, 2016), especially when measuring the effectiveness of behavioural interventions. A key concern is the choice of randomisation method used to allocate participants to the treatment or control group. There are many methods for allocating participants to the treatment or control group within an RCT. Computerised randomisation is the simplest and most reliable method, but it can be perceived as opaque by participants, which can lead to resistance to the randomisation process and non-acceptance of group allocation. This perceived lack of transparency can have important implications for the effectiveness of an intervention and is of particular concern where there is a lack of trust in research by participants, which is often the case in settings where participants come from vulnerable and stigmatised groups. There are many risks associated with using a poor randomisation strategy. It may discourage participants in the control group from continuing in the study, leading to differential attrition between the treatment and control groups, which will complicate the evaluation design. Allocation to the control group can also worsen participants' mental health and cause frustration towards the research team and participants allocated to the treatment group. For example, in our trial, 35% of participants are minors (under 21 years of age) and 18% are moderately depressed, as measured by the Patient Health Questionnaire PHQ-9 Depression Scale (Kroenke K, 2001). Finally, the participants' environment (sex work) is violent, which may also increase the risk of perpetuating violence against the research team or other participants during the randomisation process, given the disappointment and frustration generated by the randomisation process.

To date, there has been no qualitative study that has explored vulnerable populations' perceptions of the randomisation strategy. This study aims to determine the best approach to determining the randomisation procedure. To this end, we propose a strategy based on the use of qualitative methods to define and evaluate the randomisation process in the context of an intervention aimed at preventing sexually transmitted infections (STIs) and HIV among vulnerable women in Africa. The trial is called 'Protecting women from economic shocks to fight HIV in Africa' (POWER). POWER aims to test the effectiveness of health shock prevention in preventing HIV among women who engage in commercial and transactional sex in Cameroon.

Like many other behavioural economic interventions, the POWER trial lacks equipoise, which raises additional questions about the ethics of randomisation. Indeed, while the effect of the intervention we are testing - free health insurance for treated participants and up to six of their economic dependents - on the primary outcomes (HIV and STI infection) is uncertain, there is evidence in the literature of the benefits of health insurance on other outcomes. For example, it is well documented in the health economics literature that free health care increases health care utilisation and improves financial protection (Erlangga D, 2019). Based on this evidence, and assuming that there was no negative effect of the intervention on the primary outcomes, it was decided to roll out the intervention to the control group at the end of the trial, even if there was no effect of the intervention on the primary outcomes. This information was provided to participants when they were first recruited into the trial.

This paper identifies several research questions that should be addressed by researchers using RCTs to evaluate behavioural interventions in contexts where the randomisation strategy poses risks to both the population and the validity of the results. First, we examine whether participants understand and accept randomisation. Second, we collect preferences regarding the preferred randomisation method (computerised versus private participatory versus public draw randomisation) to determine the best randomisation strategy in the study setting. Thirdly, we assess participants' perceptions of the fairness and transparency of the preferred randomisation strategy in both the treatment and control groups.

2. Methodology

2.1. Qualitative methods and sampling

The study was conducted in two phases, the first before randomisation and the second after randomisation. Phase 1, conducted prior to randomisation, explored the perceptions of our research participants (sex workers and transactional sex workers) about the randomisation process. The aim was to assess their preferences regarding the randomisation method in order to maximise the acceptability of randomisation, particularly in terms of fairness and transparency of the process. Participants were selected using purposive sampling. We stratified the sample on the basis of observable characteristics (e.g. age, number of economic dependents, location). Phase 1 explored participants' perceptions and experiences of the following issues

1. How should randomisation be explained to participants?

2. Do participants prefer a participatory or computerised randomisation strategy?

3. Do participants prefer a private or public draw?

4. What are the main potential risks and what strategies should be implemented to avoid these risks?

Phase 1 and Phase 2 took place on the premises of our partner CBOs in Yaoundé, Cameroon. All data collection and randomisation for POWER takes place on the premises of the partner CBOs.

We sought answers to these questions through focus groups, individual in-depth interviews and self-administered questionnaires. Self-administered questionnaires were used to minimise potential social desirability bias and to assess the internal consistency of the results. During this phase, 33 respondents were interviewed and completed the paper-based questionnaire (see Appendix 1).

Table 1: Total number of participants of formative/ pre-randomisation study

Women who engage in transactional sex	**Female sex workers**
Focus group 1: n=6 Focus group 2: n=6	Focus group 1: n=7 Focus group 2: n=6
Individual interview: n = 4	Individual interview: n = 6
Total = 16	Total = 17
Total participants = 33	

Phase 2 was conducted immediately after randomisation. Exit interviews were used to evaluate the fairness, transparency, and acceptability of the randomisation process for both treatment and control group participants. The study's descriptive component aimed to evaluate the understanding and acceptance of randomisation by all participants. Additionally, it aimed to assess the counselling and support provided by partner community-based organizations (CBOs) to participants allocated to the control group.

For the post-randomisation descriptive research (phase 2), purposive sampling was chosen. Participants were selected based on specific characteristics to ensure a representative sample. These characteristics included the number of economic dependents, relationship to main economic dependents, occupation, fatalism, belief in luck, determinism, risk aversion, perception about own and economic dependents' health status, and poverty level (measured by food expenditures and income level). The data used for selection was collected during the baseline

quantitative survey conducted 2-4 months prior to randomisation. To implement this, we created a list of participants to interview based on the baseline data, varying the mentioned characteristics. Additionally, we intentionally oversampled participants from the control group as our primary goal was to comprehend and investigate the reactions of those who would not benefit from the intervention, as well as the quality of CBO counselling provided to the control group. A list of eligible participants was available on-site, and those selected were sent to participate in an exit interview after the randomisation process.

Table 2: Number of participants for post-randomisation study

Women who engage in transactional sex	**Female sex workers**
Control group participants: n= 12 Treatment group participants: n=10 Individual interviews: n = 22	Control group participants: n=8 Treatment group participants: n= 11 Individual interviews: n = 19
Total participants = 41	

2.2. Data collection

Phase 1, the exploratory phase, took place in March 2021 and involved face-to-face interviews and focus groups. The interviews and focus groups were recorded with the participants' permission using voice recorders. Information sheets and consent forms were available in both English and French. Our qualitative research collaborators in Cameroon conducted the interviews in French, using a semi-structured interview guide developed by the research team. The interviews commenced with open-ended questions aimed at comprehending the participants' interpretation of the term 'random'. Subsequently, we posed closed questions regarding their preference for various randomisation methods. The interviews and focus groups lasted approximately 45 minutes each, and the questionnaire took an average of 10 minutes to complete. Post-randomisation exit interviews (phase 2) were conducted between October and November 2021, during the randomisation phase. Voice recorders were used to record in-depth interviews with participants' permission. Local qualitative researchers, who were not directly associated with the local CBOs, conducted the interviews in French. Semi-structured interview guides were used to encourage participants to be open and honest about their experience of randomisation and counselling offered by the CBO to control group participants.

2.3. Data analysis

During phase 1, semi-structured interviews and focus groups were conducted with flexibility. We explored topics further when participants required probing or brought up unanticipated subjects. This process ensured comprehensive coverage of all potential and relevant topics. The research team discussed interview and focus group data after each data collection day to identify emerging themes and adapt the research approach and topic guide if necessary. The data collectors themselves developed recording transcriptions shortly after data collection to preserve meaning and remain faithful to the participants' thoughts and words. Manual analysis was conducted on the interview data, which mainly consisted of focus groups. We applied a simple coding system using thematic analysis based on our topic guide. We classified the gathered information by theme of exploration and summarised it into categories.

During phase 2, we structured topic guides for the interviews to collect specific information on participants' reactions to their group allocation, which was identified during phase 1. We conducted transcription simultaneously with data collection, and all transcripts were uploaded to Nvivo 12. We defined coding based on the topic guide themes, and the data was grouped to facilitate framework analysis. We performed two framework analyses: one for treatment group participants and one for control group participants. This approach aided in identifying various perceptions in the interview data concerning the most relevant characteristics used to stratify our sample, namely (1) fatalism, (2) risk aversion, and (3) perception of insurance needs.

(1) Participants were classified as fatalist or non-fatalist based on their responses to two questions using a 5-point Likert scale: whether they believed that life events were determined by God (Franklin, 2008), and whether they believed in the inevitability of events (Esparza, 2015). Fatalists were those who generally agreed with the statements, while non-fatalists were those who generally disagreed.

(2) The study measured participants' risk aversion by self-rated preference for risk in their daily lives on a scale of 0 to 10. Those who rated 0 to 4 were classified as risk-averse, while those who scored 7 to 10 were considered risk-takers (Dohmen, 2011).

(3) The perceived need for health insurance was determined by three categories: the individual's perception of their own health (rated on a 5-point Likert scale ranging from

very good to very bad), their perception of their main economic dependent's health (also rated on a 5-point Likert scale ranging from very good to very bad), and their perceived poverty, which was based on their ability to meet daily expenses (answered with a yes or no response). Participants who perceived a high need for insurance had low scores on the health perception scale and answered 'no' to the question about their ability to cover daily expenses. Conversely, those who perceived a low need for insurance had high scores on the health perception scale and were able to cover daily expenses.

The interviews focused on main themes, with participant characteristics presented in columns and summarised data in the cells. Pseudonyms were used for all participant names mentioned in this paper.

2.4. Ethical considerations

This study is part of POWER trial which was approved by the National Ethics Committee (CNERS) in Cameroon, as well as the University College London ethics committee. The scientific advisory committee for POWER comprises members from Johns Hopkins University, UNAIDS, the National AIDS Control Committee (CNLS) in Cameroon, and the HIV/AIDS Division of the Ministry of Public Health in Cameroon. Participants in both qualitative studies were provided with an explanation of the research purpose and processes prior to giving their consent. Informed consent was obtained from all participants, who signed a form agreeing to take part in the study. Respondents were informed that they could withdraw from the study at any time without affecting the intervention package they would receive. All interviews were conducted in private rooms and strict confidentiality was maintained. The personal information of the respondents was not linked to the recorded interviews in any way. Once the audio recordings were transcribed, they were stored on the UCL external server. Respondents received a transport reimbursement of CFAF 3,000 (~£5) for their participation.

3. Results

3.1. Pre-randomisation explorative research

Participants were asked questions regarding the randomisation process and we classified results per theme of exploration.

3.1.1. How best to explain randomisation processes?

Participants were given a comprehensive explanation of the scientific benefits of randomisation. Following this, respondents emphasised the importance of all study participants receiving a substantial information session before undergoing the randomisation process. Some respondents also enquired about the rationale behind randomisation, as they believed that everyone should receive treatment.

IDI04 expressed concern, stating *"Honestly, if I'm not lying, it's going to hurt me (if I do not receive the intervention), because it will be a little…it's weird... we can treat one family for free and then we don't treat another family. » IDI04*

"Because you simply cannot give something to one person, and nothing to the other." IDI03

The researchers defined randomisation using different metaphors, such as lottery or random games played in Cameroon, until all participants understood the concept. Subsequently, respondents were asked to describe randomisation and aleatory procedures to a lay person. The lottery, which was the most popular metaphor, was recommended by most respondents.

For instance, one participant said, "*The best way to describe it as we do it at random. We pick at random". FGD1*. Another participant suggested "*As if you played the lottery. You either lose or win." FGD1*

3.1.2. Computer-assisted versus participative randomisation

When participants were given the choice between a computer-assisted draw, in which a computer randomly allocates groups prior to participants' arrival, and a participative draw, in which participants needed to physically draw themselves, all participants unanimously preferred the participative draw. They felt that participative randomisation, a physical draw, provided a more tangible opportunity for every person to win. Additionally, participants expressed the importance of feeling in control of their fate.

"*With a draw it's simple, everyone takes their destiny into their own hands.* » IDI07

3.1.3. Individual draw versus public draw

Most participants expressed a preference for an individualised or private draw. A physical and private draw provides a sense of control and helps to avoid any doubts about the impartiality of the randomisation process. Furthermore, respondents expressed discomfort with the idea of a public draw if they were assigned to the treatment group. This could potentially trigger negative emotions from those assigned to the control group and harm their relationships with other participants. It could even put them at risk of emotional or physical violence.

"There'll be more jealousy when it's the group draw than when I'm alone right? If I am alone, there will be less jealousy because I control what I do, and I see everything; while if there are people next to me, if I win, maybe at the exit, they can end up waiting for me there outside, I don't know. So, I prefer to be alone." IDI09

"If we do it in public, there are people who can get really emotional; there are a lot of emotional people out here [sex workers who come to the CBO], *so I prefer to draw in private." IDI02*

3.1.4. Potential risks identified

Respondents identified three main risks of randomisation. The first risk was the potential negative impact on participants' mental health if they were allocated to the control group. Women involved in commercial and transactional sex are more vulnerable to poor mental health and depression, and not receiving health insurance could further deteriorate their mental health.

Participants noted that winning brings a sense of pride and weightlessness, while losing can lead to feelings of being overwhelmed and uncomfortable.

"When you win, you're proud of yourself, your body does not weigh, but if you lose; in your head you're overloaded, you're disturbed it's like a fight that knocks you down, you're not comfortable, you're wondering why you didn't win, you want to be in the place of the others." IDI05

This emotional response may also result in acts of rage or violent behaviour at the CBO premises. However, it is important to note that the comment mentioned above was made by a small number of participants and may not be representative of the majority. Additionally, it is unlikely to occur.

"On the cry of anger, everyone can react violently at the moment, if there is a counsellor who can bring the person back to normal it will be good." IDI08

Moving on, another potential risk identified was that participants may drop out of the project upon discovering that they have been assigned to the control group, as they may not perceive any benefits from remaining in the project. To reduce these risks, respondents recommended that CBO staff conduct exit interviews with the control group on the day of randomisation. These counselling sessions would inform participants of all the services they could still benefit from if they chose to remain in the study, such as free STI and HIV testing, free treatment if positive, and phone credit. It was also noted that participants found it important to have someone who could provide comfort and support.

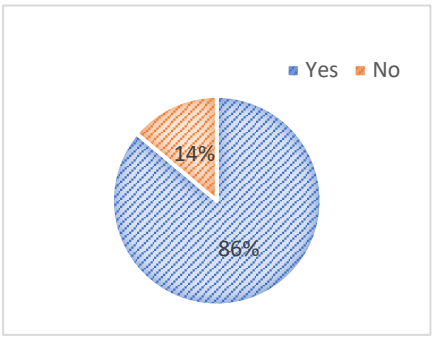
"I suggest that those who will not receive insurance should be told that this does not mean that they will not benefit from other services that the project offers, because a girl like me for example, if I'm not winning, I'm sure I'm going to stop, as soon as I find out that I've lost I'm going to leave. If someone can take and cheer me up it will be better." IDI06

The results of the paper-based survey, which was distributed to participants at the end of the focus group, were confirmed by the findings presented in Figure 1. The quantitative survey revealed that participants were more indifferent towards being in the control group than they were during the focus group discussions (FGDs).

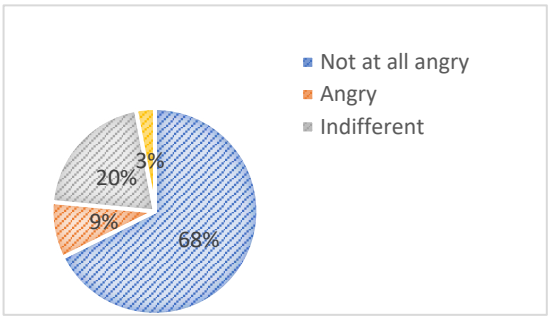
Figure 1 displays the expectations of participants in the event that they were allocated to the control group.

Figure 1: Expectations of participants if allocated to control group

Would you need to talk to a CBO staff if allocated to the control group?



How would you feel if allocated to the control group?



3.1.5. Retention strategies and randomisation procedures chosen

Based on the findings of the exploratory research, we have established the following retention strategies to be implemented on the day of and after randomisation. Firstly, we informed participants that random insurance allocation was chosen for scientific purposes. Secondly, we made participants aware that while there were benefits to receiving free care, the effects of this intervention on HIV infections and STIs were not yet known, hence the need for testing. Thirdly, the intervention was not fully defined and the benefits of study participation were emphasised over the intervention itself. Additionally, a counselling service was set up and provided by CBO staff throughout the randomisation period for control group participants.

Finally, the study offered health insurance to control group participants at the end of the study if the intervention was found to be safe. It was anticipated that this approach would enhance the retention of participants in the control group and address the ethical concern of equipoise in the trial. Participants would be incentivised to remain in the study and complete all data collection waves until the end of the project, as it would provide them with access to the intervention. This information was conveyed to all participants on the day of randomisation.
During the randomisation study site visit, all participants followed the same participant flow, which included:

1. Welcoming and registration of participants,
2. Informed consent procedure with an information sheet

3. Randomisation process, which involved a random draw from a ball sack containing two coloured balls. One ball assigned the participant to the control group (white), and the other assigned them to the treatment group (orange)
4. Treatment group: reconsenting procedure and information package on insurance product, Control group: the opportunity to speak with a counsellor and receive information on other study benefits.

3.2. Post-randomisation qualitative exit interviews

This section evaluates the perception of the randomisation procedure and compares reactions and attitudes towards randomisation across selected participant characteristics that may affect perceptions and preferences.

3.2.1. Fairness of randomisation process

All participants believed that our randomisation process was fair and unbiased, confirming the results from pre-randomisation. The draw was conducted in front of three research team staff, including two enumerators and a site supervisor. The enumerators carried out the survey, and the site supervisor witnessed the conduct of the randomisation.

"It is a fair method because I don't see what I am picking, we put the balls in one bag, I just turned, turned my hand, and I picked. It's just someone's fate." 2181000 (control)

"I really prefer that it happens by random draw, each for herself facing her destiny yet if it had to be a person who selects such and such, we could say that there is fraud." 218000 (control)

Participants particularly appreciated the role of witnesses from both our research team and the CBO during each individual draw as it reflected special formality and thus reliability.

"When there are many people there when I draw the ball, I don't mind, actually it can certify my outcome." 110223 (control)

"The supervisors presence shows that it is fair and well organised." 2171100 (control)

3.2.2. Reaction on randomisation outcome and perceived impact on life

The participants in the control and treatment groups had different reactions upon learning about the randomisation outcome. The majority of treatment participants expressed feelings of joy, satisfaction, and relief, while the majority of control group participants expressed disappointment.

For instance, one treatment participant stated, "I was very happy when I drew the ball, I directly thought about my sisters, to help them." (2271312, treatment)

"I felt really proud, and grateful that now it is guaranteed I am going to receive the insurance, with all those sicknesses in my family." 2173220 (treatment)

Despite the majority of the control group expressing general disappointment, there were noticeable differences within this group based on specific characteristics. Participants with fatalistic tendencies tended to attribute the outcome of randomisation to divine intervention, believing that it guided them to draw a certain ball and thus be assigned to a specific group.

For example, one participant stated, *'It was the Lord who allowed, if he had allowed me to pick up the orange ball, I would have had it'* (2181000, control).

Another participant expressed gratitude, stating *'I thought thank God (...) what a joy in my heart that I won (smile) and it has already started to give me joy in my head'* (132000, treatment).

"I just consider it like that, it was just not my day, because if I were to come here again, il will come and play the game again and God will help and I will have the insurance." 2213313 (control)

In contrast, non-fatalistic participants attributed the outcome to chance, with one stating that each person faces their own destiny.
When asked about the impact of the randomisation outcome on their life, fatalistic participants expressed detachment. *"According to me it's not because of that* (God)*, it is just every person facing their own destiny." 217100 (control)*

One participant stated, *"We must always think of God, each one because he has chosen that... I wait until next year and until then I have to endure it." 112233 (control)*

Another participant responded, *"No impact in my life at all...since before that, I had a child who was constantly sick. So that's not what will change much." 2173132 (control)*

The second characteristic we examined regarding heterogeneity was attitude towards risk. Participants who scored 7 to 10 on the self-reported risk scale were considered risk takers. When asked about their reaction to the randomisation outcome, they described the process as a form of gambling and their attitude reflected their playful nature. They were also more accepting of the group allocation outcome than risk-averse participants.

They stated, *"I was not sure about what this would bring, but I played my part, it's just chance, so I play the game." 2102300 (control)*

In contrast, when the white ball came out, a participant exclaimed, *"I only shouted, (haha) as soon as the white ball came out, I was surprised, I wanted the insurance but hey, better late than never!" 112000 (control)*

Risk averse participants (scoring from 0 to 4 out of 10 on the risk scale) had a rather down-to-earth discourse, in which they showed limited acceptance of the randomisation outcome.

"Maybe it's justified, maybe it's not justified, but yeah it still hurts me." 1153113 (control)

The final characteristic examined was the participant's perceived need for insurance, which was captured by health status and poverty level. A high perceived need for insurance corresponded to a poor perception of their own health and that of their economic dependents, and a belief that they could not afford their weekly expenses at the time. Participants with a high perceived need expressed feelings of relief, directly mentioned sick relatives or argued that being in the control group was problematic because they felt they really needed the insurance as soon as possible.

"I was relieved, I immediately thought of my mother who has had eye problems for some time". 2281333 (treatment)

"I was really upset, I'm not jealous, but I'm sad, why? Because I really had problems this year. So I really wanted to be there." 140000 (control)

Participants with a low perceived need for insurance were more tolerant of the randomisation outcome and were either happy to be in the control group or happy to be in the treatment group

because they could now either save money or spend money on other things, such as beauty products. It is interesting to see that a sense of economic relief had a positive effect on reactions to group allocation, and that the insurance was seen as a 'bonus' by this subgroup.

"I don't really mind if it comes later". 1132120 (treatment)

"*I don't know if it was a good thing anyway, because I've already asked myself 1,000 questions since the beginning, I don't know if I'm going to benefit so much from it..."* 2102300 (control)

*"I don't know... it can help, can't it? To buy what you need, since I am a woman there, from haircuts to soap, ointment, stuff like that."*2271312 (treatment)

3.2.3. Ethical acceptability of the trial

The perceived impact of randomisation on control group participants was strongly influenced by the fact that they knew they would receive the health insurance product at the end of the trial. Feelings of disappointment were often qualified by participants by the fact that they were simply part of 'wave 2'. The CBO-based part of the research team was not instructed to use the term 'wave 2', but during randomisation the research team found that using the terminology of 'wave 1' and 'wave 2' for receiving the health insurance product was more efficient and effective than laboriously explaining that we would be able to provide insurance to the control group at the end of the research project. This also generated more trust in the research among the control group. We found that the certainty of receiving the insurance was very reassuring and a tangible prospect for control group participants, but also an effective way to maximise retention in the study.

"Hmm first reaction I was disappointed but, it's just for the next wave, I know it's going to come eventually, it's not definitive it's just for a time." 2171100 (control)

"I didn't feel too weak because it's always the same it's only that we can miss this year for next year so it didn't hurt me so much, so in fact I was even a little happy." 211210 (control)

"I was not thrilled because I wanted to benefit from it now, so like that's gonna be a little extended... But I am satisfied, because no matter what, I know I will also be a beneficiary of health insurance." 121200 (control)

3.2.4. Optional CBO-based counselling post-randomisation

Given the results of our pre-randomisation study and the need to minimise adverse effects and maximise retention, our research team decided to also offer optional counselling sessions. These post-randomisation counselling sessions were delivered by CBO-trained counsellors on site to control group participants. The main aim of these sessions was to reassure control group participants, but also to remind them of the benefits they would still receive from participating in the POWER trial. Only 12% of the control group participants chose to attend the counselling sessions. Participants who did not want to be referred mostly said that they had received all the information they needed from the research staff and had no further questions. However, we found that participants who chose to receive post-randomisation counselling were satisfied, as it helped them put the outcome into perspective and restored a sense of trust in the project.

"*The interview with the CBO was good, it was related to what I had drawn, she reassured me, saying that I am not really losing anything, that I will still benefit from the insurance but not now, later and that I can benefit from other advantages*." 2173132 (control)

The counselling service was also mentioned by some participants as a unique space for one-to-one counselling and an opportunity to ask health-related questions that they would not normally have the time or inclination to ask.

"*The HIV test, I had never done it before... but when I was here today, we talked a lot about women's bodies and I just said ah! I never thought I should do this HIV test, it never crossed my mind, but since it was explained to me, I can just go and have a test, I won't be stressed anymore*". 2173310 (control)

4. Discussion

In this article we have explored how best to prepare for and conduct an RCT with vulnerable populations to minimise risk and frustration for participants by involving them in the design of the randomisation process. We found that the best way to explain randomisation to this population was to use the metaphor of a lottery, as this was locally accepted, relevant and best reflected the random element of the process. This was also the case in other African contexts (Jepson M, et al., 2018; Kombe, 2019).

In line with the study by Kombe (2019), we found in our pre-randomisation study that it was also important for participants to understand why we decided that study participants would not be selected according to their need for the intervention, but rather randomly, and for participants to be able to understand the scientific justification for the randomisation.

With regard to the randomisation method, our respondents unanimously opted for an individual draw. Participants opted for a 'hat draw', where a coloured ball was drawn from a bag to determine group allocation in the presence of external witnesses from the research team. This method was chosen by participants to limit jealousy, increase a sense of control, transparency and fairness, and to eliminate the possibility of major adverse effects, including the risk of violence. Post-randomisation analysis showed that participants appreciated the transparency of the process and the presence of external witnesses. The additional external witnesses gave participants a sense of the integrity and trustworthiness of the randomisation process. Participants also appreciated having a sense of control over the randomisation process.

Ethical considerations regarding the allocation of an intervention to a group in development contexts have been widely debated by behavioural economists (Goldberg, 2014; Mulligan, 2014; Ravallion, 2016). For these reasons, we also decided that the best approach was to explain the health insurance of the control group participants at the end of the project, and we called this 'Wave 2' of the research project. This explanation reinforced trust and encouraged retention of the control group. The use of this term was suggested by our local research team, who had noticed some reluctance within the control group cohort in informal exchanges. In addition, there were rumours that there was a high risk of control group participants being abandoned during data collection and that promises of health insurance would not be kept by the researchers. To dispel these beliefs, the term 'Wave 2' indicated that this stage of the project was a tangible part of the research project and therefore more plausible.

In exploring the responses of participants with different characteristics, we found interesting differences in participant profiles. The 'fatalistic' participants had a very tolerant attitude towards the process and the control group participants in this category did not express strong feelings of disappointment. In terms of risk aversion, we also observed that 'risk takers' were more playful and light-hearted after randomisation than 'risk averse' participants. In terms of perceived need for insurance, we noticed quite a gap between some participants who expressed that it would relieve a real burden for those who were more deprived and in poorer health, and others who saw the

insurance as a 'bonus' that would allow them to spend more money on materialistic expenses or to start saving money.

5. Conclusion

RCTs targeting vulnerable populations, such as sex workers in low-income countries, may carry many risks and have the potential to cause major adverse effects. The results of our study confirm that RCTs can worsen the mental health of vulnerable groups. Conducting such RCTs with vulnerable populations may increase vulnerability if not properly thought through and without consideration of contextual strategies (e.g. choice of appropriate vocabulary, randomisation method and setting). Our results also show that reactions to group allocation can be strongly influenced by personality traits and preferences, as well as participants' perceived need for treatment. This means that participants' reactions to group allocation may be better understood and explained if they are linked to specific participant characteristics. Qualitative formative research is strongly recommended to anticipate and mitigate the risks associated with participation in RCTs. Best practices for RCTs with vulnerable populations include: thorough explanation of the need for randomisation, transparency during the randomisation process, private lottery, adequate compensation and benefits for control group participants, including assuring post-study treatment for the control group, and provision of counselling for control group participants.

References

Burke, M., Gong, E., & Jones, K. (2015). *Income shocks and HIV in Africa.* . The Economic Journal. 125(585): p. 1157-1189.

Cameroon Ministry of Public Health. (2016). *Analyse Situationnelle du financement de la santé au Cameroun, Stratégie de Financement de la Santé 2017-2021.*

Dohmen, T. H. (2011). *Individual Risk Attitudes: Measurement, Determinants, and Behavioural Consequences.* . Journal of the European Economic Association, 9(3), 522–550. http://www.jstor.org/stable/2.

Erlangga D, S. M. (2019). *The impact of public health insurance on health care utilisation, financial protection and health status in low- and middle-income countries: A systematic review.* . PLoS One. Aug 28;14(8):e0219731. doi: 10.1371/journal.pone.0219731. Erratum in: PLoS One. 2019 Nov 7;14(11):e0225237. PMID: 31461458; PMCID: PMC6713352.

Esparza, O. W. (2015). *Simultaneous Development of a Multidimensional Fatalism Measure in English and Spanish.* . Current Psychology. 34, 597–612. https://doi.org/10.1007/s12144-014-9272-z.

Franklin, M. D. (2008). *Developmentand validation of a religious health fatalism measure for the African-American faith community.* . Journal of Health Psychology,13(3), 323–335.https://doi.org/10.1177/1359105307088137.

Goldberg, J. (2014). *The R-word is not dirty.* Blog post, Centre for Global Development, Washington DC.

INS, I. N. (2012). *Cameroun Enquête Démographique et de Santé et à Indicateurs Multiples (EDS-MICS).* INS/Cameroun and ICF International: Calverton, Maryland, USA.

International Labour Organization. (2015). *ATELIER DE DIALOGUE NATIONAL POUR LA VALIDATION DU PROJET DE PLAN D'ACTIONS POUR LA MISE EN ŒUVRE D'UNE ASSURANCE MALADIE DE BASE A ACCÈS UNIVERSEL AU CAMEROUN.*

Jepson M, E. D., group, C. s., group, C. s., group, P. s., group, A.-2. s., & group., O. p. (2018). *An observational study showed that explaining randomization using gambling-related metaphors and computer-agency descriptions impeded randomized clinical trial recruitment.* . Journal of Clinical Epidemiology 99:75-83. doi: 10.1016/j.jclinepi.2018.02.018. Epub 20.

Khera, R. (2021). *Some Questions of Ethics in Randomised Controlled Trials.* Available at SSRN: http://dx.doi.org/10.2139/ssrn.3780908.

Kombe, M. Z. (2019). *Community perspectives on randomisation and fairness in a cluster randomised controlled trial in Zambia.* . BMC Medical Ethics 20, 99. https://doi.org/10.1186/s12910-019-0421-7.

Kroenke K, S. R. (2001). *The PHQ-9: validity of a brief depression severity measure.* . Journal of General Internal Medicine. Sep;16(9):606-13. doi: 10.1046/j.1525-1497.2001.016009606.x. PMID: 11556941; PMCID: PMC1495268.

Mulligan, C. (2014). *The Economics of Randomized Experiments* . Blog post, Economix, New York Times.

Pettifor, A., MacPhail, C., Hughes, J., Selin, A., Wang, J., & Gómez-Olivé, F. (2016). *The effect of a conditional cash transfer on HIV incidence in young women in rural South Africa: a phase 3, randomised controlled trial.* Lancet Global Health. ;4(12):e978–88. DOI:https://doi.org/10.1016/S2214-109X(16)30253-4.

Prudden, H. e. (2015). *Factors Associated with Variations in Population HIV Prevalence across West Africa: Findings from an Ecological Analysis.* . PloS one. 10(12): p. e0142601.

Ravallion, M. (2016). *The Economics of Poverty: History, Measurement, and Policy* . pp. 312. Oxford University Press.

Robinson, J. a. (2011). *Transactional sex as a response to risk in Western Kenya.* . American Economic Journal: Applied Economics. 3(1): p. 35-64.

Sandøy, I. M. (2016). *Effectiveness of a girls' empowerment programme on early childbearing, marriage and school dropout among adolescent girls in rural Zambia: study protocol for a cluster randomized trial.* Trials 17, 588. https://doi.org/10.1186/s13063-016-1682-9.

UNAIDS. (2013). *Global report: UNAIDS report on the Global AIDS Epidemic 2013.*

Wamoyi, J. e. (2016). *Transactional sex and risk for HIV infection in sub-Saharan Africa: a systematic review and meta-analysis.* . Journal of the international AIDS society 19(1): p. 20992.

Appendix

- Fatalism question: combined responses from 2 questions linked with predetermination and religious beliefs.

M13q90	The events of my life are determined by God.	Strongly Disagree Disagree Neither agree nor disagree Agree Strongly agree
M13q88	If someone is supposed to have a serious illness, they will have it.	

- Participants who were 'risk averse' had rated their preference for risk in their everyday life to be from 0 to 4 on a scale from 0 to 10 (0 being no risk at all and 10 being a lot of risk), and risk takers scored from 7 to 10.

M2q10	When it comes to your attitude towards risk, how do you rate on a scale of 0 to 10 in general your everyday life? 0 is very conservative people who try to limit the risks of living. 10 corresponds to the most adventurous people who like to take risks.	Select a number from 0 to 10.

- Perception of insurance needs were grouped into 3 categories:

1) perception of own health (5-point Likert scale)

M4q01	How would you rate your current state of health?	Very poor Poor Fair Good Very good

2) Perception of their main economic dependent's health (5-point Likert scale)

M4q040	How would you rate your main economic dependent's current state of health?	Very poor Poor Fair Good Very good

3) Perceived poverty, which was based on their ability to cover daily expenses

M1q65	Do you currently have enough money today to meet daily expenses?	YES/ NO