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Using discrete choice experiments to design interventions for heterogeneous preferences: protocol for a pragmatic randomized controlled trial of a preference-informed, heterogeneity-focused, HIV testing offer for high-risk populations

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Abstract

Introduction. Approximately one million undiagnosed persons living with HIV (PLWH) in Southern and Eastern Africa need to test for HIV. Novel approaches are necessary to identify HIV testing options that match the heterogeneous testing preferences of high-risk populations. This pragmatic randomized controlled trial (PRCT) will evaluate the efficacy of a preference-informed, heterogeneity-focused HIV counseling and testing (HCT) offer, for improving rates of HIV testing in two high-risk populations.

Methods and Analysis. The study will be conducted in Moshi, Tanzania. The PRCT will randomize 600 female barworkers and 600 male Kilimanjaro mountain porters across three study arms. All participants will receive an HIV testing offer comprised of four preference-informed testing options, including one "common" option – comprising features that are commonly available in the area and, on average, are most preferred among study participants – and three options that are specific to the study arm. Options will be identified using mixed logit and scale-adjusted latent class analyses of data from a discrete choice experiment (DCE). Participants in Arm 1 will be offered the common option and three "targeted" options that are predicted to be more preferred than the common option and combine features widely available in the study area. Those in Arm 2 will be offered the common option and three "enhanced" options, which also include HCT features that are not yet widely available in the study area.

Participants in Arm 3 will be offered the common option and three predicted "less preferred" testing options. The primary outcome will be uptake of HIV testing.

Ethics and Dissemination. Ethical approval was obtained from Institutional Review Boards in the United States and in Tanzania. Findings will be published in peer-reviewed journals. The use of rigorous DCE methods for the preference-based design and tailoring of interventions could lead to novel policy options and implementation science approaches.

Strengths and limitations of this study

- The pragmatic randomized controlled trial described in this protocol paper includes males and females at high risk of HIV infection; the implementation of the trial in collaboration with all HIV testing providers in the study area allows for the evaluation of testing uptake in a nearly closed system.
- The study goes beyond the traditional approach of evaluating single-offer ("one-size-fits-all") interventions by identifying combinations of testing options that explicitly target preference heterogeneity in the target population.
- The methods used to identify the intervention conditions evaluated in the trial, including the scale-adjusted latent class (SALC) analysis of data from the discrete choice experiment (DCE) used to elicit heterogeneous population preferences for HIV testing, may be applied to other contexts and may lead to the development of new implementation science approaches for systematically adapting effective interventions to local contexts.

- The study design will allow for separate estimates of the effects of SMS reminders, the issuance of physical HIV testing invitation cards, the heterogeneity-focused testing offer, and an incentive offer on HIV testing rates.
- Potential limitations include loss to follow-up during the multi-phase study, the finite range of HIV testing characteristics that can be include in a DCE, exogenous events during the study period that may influence rates of HIV testing across study arms, and limited generalizability of specific study findings to other populations and settings.

Keywords (longer list)

HIV counseling and testing; Discrete choice experiment; Preference heterogeneity; Latent class analysis; Pragmatic randomized controlled trial; Mobile health (mHealth); Conditional financial transfers; Policy design; Tanzania; sub-Saharan Africa

Background

In 2018, 37.9 million people were living with HIV worldwide, and 770,000 died of HIV-related illnesses.[1] HIV counseling and testing (HCT) is a cost-effective intervention for increasing HIV serostatus awareness,[2,3] a point of entry into HIV care and treatment, and an important means of primary and secondary HIV prevention.[4] HIV Prevention Trials Network Protocol 052 conclusively demonstrated a marked reduction in HIV transmission among serodiscordant couples in which the HIV-infected partner was begun on antiretroviral therapy early in the course of infection.[5] Subsequently, public health officials and policymakers, considering treatment as prevention, have called for dramatic increases in HIV testing — as frequently as annually in many populations and semi-annually among individuals at high risk.[6]

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set for 2020 the ambitious 90-90-90 target: diagnosing 90% of all persons living with HIV (PLWH), initiating treatment for 90% of those diagnosed, and achieving viral suppression for 90% of those treated.[7] While substantial progress has been made toward these targets since 2014, most countries remain short of at least one target, and the number of undiagnosed HIV infections in every region are considered a major hindrance to achieving the UNAIDS targets and ending the epidemic.[8] Novel approaches are needed to increase testing uptake, especially among high-risk groups.

In order to establish the diagnosis of HIV in 90% of all PLWH in Eastern and Southern Africa, more than 1 million undiagnosed infected persons need to test, including 190,000 in Tanzania.[4,6,9] Tanzania's 2017-22 Health Sector HIV and AIDS Strategic Plan (HSHSP-IV) lists as a key challenge that HIV testing services "need to be more efficient and ambitious to meet the 90-90-90 targets through more targeted testing approaches."[10] Evaluations of population preferences for testing have typically focused on the acceptability of specific testing options, such as home-based,[11-13] provider-initiated,[14-17] or workplace testing,[18,19] usually without

consideration or offer of other options. Results from these narrow assessments do not probe the potential diversity in testing preferences among target populations and cannot characterize which testing options will maximize uptake of testing.[20-22]

Discrete choice experiments (DCEs), grounded in the economic theory of utility maximization, are specifically designed to provide information about individuals' preferences for varying characteristics of multi-attribute products. The DCE method is based on the assumption that a product or service such as HCT can be described in terms of its characteristics, namely attributes and levels within attributes. Participants are repeatedly asked to choose between two or more alternatives in choice scenarios simulating real choice decisions. Each alternative differs in the arrangement of attribute levels presented to the participant. The choice scenarios are systematically varied by means of an experimental design.[23-26] Relative attribute importance, the utility that respondents derive from the diverse options, and trade-offs, i.e., the willingness to trade between attribute levels, can be quantified analytically.[27] DCEs are used increasingly to understand patient perspectives and to design patient-centered interventions. Although DCEs have been used in various contexts related to HIV, including testing,[20,28-32] prevention,[33-36] service delivery,[37-39] and treatment,[40-43] to our knowledge DCEs have not yet been used to systematically design HIV counseling and testing interventions.

Below we describe the study protocol for a pragmatic randomized controlled trial (PRCT) that evaluates the efficacy of a targeted, preference-informed HCT offer for improving rates of HIV testing in high-risk populations. The testing offer is developed using data from a discrete choice experiment (DCE) and designed to match the heterogeneous HIV testing preferences in the target population. To our knowledge this is the first PRCT in which the study conditions are optimized using data from a DCE, and the first PRCT that evaluates an intervention explicitly targeting preference heterogeneity. Our hypothesis is that a preference-informed,

heterogeneity-focused HIV testing offer increases uptake of HIV testing relative to an offer designed to target the average preferences of high-risk populations.

Methods/Design

Study aim and hypothesis

The aim of this study is to evaluate the efficacy of a preference-informed, heterogeneity-focused HCT offer for improving rates of HIV testing among two high-risk populations. We hypothesize that an HIV testing offer matched to the specific preferences of the intended target population and explicitly accounting for preference heterogeneity within these populations will increase rates of testing relative to a control offer.

Study setting

The study is conducted in Moshi, Tanzania. Moshi is the commercial center and administrative capital of the Kilimanjaro Region in Northern Tanzania and has an estimated population of about 200,000.[44] Moshi has 25 HCT facilities, including 8 care and treatment centres (CTCs), which provide free HIV care to persons living with HIV.[45] The study is implemented with support from the Regional Medical Officer and the Regional AIDS Control Coordinator of the Kilimanjaro Region.

Study participants

The study population comprises women employed in bars, restaurants and guesthouses serving alcohol to patrons ("female barworkers", FBW), and male mountain porters who are supporting climbers of nearby Mount Kilimanjaro ("Kilimanjaro mountain porters", KMP). The Regional

AIDS Control Coordinator identified these groups as populations at high risk of HIV infection who could benefit from increased rates of testing; we subsequently showed that FBW and KMP engage in higher rates of HIV risk behaviors than randomly selected male and female community members in the same setting.[20] A census of bars and female barworkers, conducted by the study team between February and June of 2016, identified 612 venues within Moshi, with 2,059 age-eligible FBW. There are an estimated 10,000 porters in the Kilimanjaro Region.[46,47] Eligible study participants are ages 18 or older, reside in Moshi, are able to read, and have no plans to leave the study area during the 12-15 month period following study enrollment.

Outcome measure

The primary outcome measure is uptake of HIV testing. During the study, the outcome measure will be ascertained repeatedly through a combination of self-reports from study participants and the documentation of HIV tests and test results by HIV testing providers.

Study design

The study is comprised of 5 sequential phases (**Figure 1**). The target duration for each phase is 13 weeks (91 days). The outcome measure will be observed in each phase.

Phase A: Reference phase. Phase A includes no intervention. The purpose of this phase is to inform estimates of background rates of HIV testing among individuals participating in a research study focusing on HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase A.

Phase B: SMS phase. In Phase B, a Short Messaging System (SMS) reminder message to test for HIV will be sent to participants 4 weeks (28 days) after the beginning of Phase B. The purpose of this phase is to inform estimates of the effect of an SMS reminder on rates of HIV

testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase B.

Phase C: Invitation phase. In Phase C, participants will be given a credit card-sized invitation card describing an HIV testing option that combines features commonly available in the study area, and that, on average, are most preferred among study participants ("**common option**"). This option will be the same for FBW and KMP. Four weeks (28 days) after the beginning of Phase C, participants will be sent an SMS reminder to test for HIV as shown on the invitation card given to them. The purpose of this study phase is to inform estimates of the effect of a testing invitation on rates of HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase C.

Phase D: The pragmatic randomized controlled trial. Phase D is a PRCT that includes three parallel study arms (**Table 1**). All participants will receive an HIV testing offer comprised of four invitation cards describing preference-informed HIV testing options. Options will be identified using mixed logit and scale-adjusted latent class (SALC) analyses of data from a discrete choice experiment (DCE) with members of the target populations (see below). **Arm 1** will be offered the common option and three "**targeted**" options, predicted to be jointly more preferred than the common option and comprising testing features widely available in the study area. **Arm 2** will be offered the common option and three "**enhanced**" options, which are also predicted to be jointly more preferred than the common option but include additional features that are not yet widely available in the study area. **Arm 3** will be offered the common option and three options that are jointly predicted to be "**less preferred**" than the common option. Participants will be asked to test for HIV using the most preferred of the 4 testing options given to them. Arms 1 and 2 are intervention arms. Arm 3 represents an active control arm: study involvement in Arm 3 is the same as in Arms 1 and 2. Four weeks (28 days) after the beginning of Phase D, participants will be sent an SMS reminder to test for HIV using any of the testing

options given to them. The purpose of this study phase is to obtain estimates of the effect of a heterogeneity-focused HIV testing offer on rates of HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase D.

Phase E: Incentive phase. In phase E, participants will be offered an incentive to test for HIV using their choice of any of the testing options remaining to them from Phase D. An SMS reminder will be sent to participants 4 weeks (28 days) after the beginning of Phase E. The purpose of this phase is to inform estimates of the effect of a conditional financial transfer (CFT) on testing decisions and identify the most preferred testing option among those offered, among participants who did not test during Phase D.

The study design will allow for separate estimates of the effects on HIV testing rates of:

(1) an SMS reminder message,
(2) a testing invitation,
(3) a heterogeneity-focused testing offer, and
(4) a conditional financial transfer (CFT) offer.

Assignment to study arms

Participant IDs will be randomly assigned to study arms using a random number generator. The testing offer in Phase D will reflect the study arm assigned to the respective Participant ID. The random assignment is expected to result in approximately equal numbers of participants in each study arm.

Design of the intervention

Overview. A DCE with a representative sample of members of the target population will be used to elicit information on the distribution of preferences for feasible and modifiable

characteristics of HIV testing options in the target population. DCE data will be analyzed, and results of these analyses will be used to identify four types of testing options that will be offered to participants in the PRCT:

1) ***A "common" option.*** This single testing option combines testing features that are widely available in the study area, and, on average, are most preferred among study participants. This option will be offered to all participants in Phases C and D.
2) ***Three "targeted" options.*** This set of testing options, comprising features widely available in the study area, is predicted to be jointly more preferred than the common option by the largest possible share of participants.
3) ***Three "enhanced" options.*** Enhanced testing options include additional features that are not yet widely available in the study area (e.g., oral testing). The set of enhanced testing options is predicted to be jointly more preferred than the common option by the largest possible share of participants.
4) ***Three "less preferred" options.*** This set of testing options includes options that are predicted to be equally or less preferred than the common option by the largest possible share of participants.

Testing options will not differ between FBW and KMP. The design decision to offer three targeted, enhanced, and less preferred options was driven by practical considerations: (1) a choice from 4 alternatives (the common option plus 3 options specific to the study arm) is expected to be cognitively feasible for participants, (2) the implementation of 10 testing options (one common option, plus 3 targeted, 3 enhanced, and 3 less preferred options) as part of this study is feasible from a logistical and budgetary perspective; and (3) the widespread implementation of 3 testing options that target preference heterogeneity in the two high-risk populations is feasible in the study area. Similarly, the decision to offer the same options to

FBW and KMP was made because, in practice, a gender- or risk group specific implementation of testing options is not feasible.

Development and fielding of the DCE

A DCE with 300 FBW and 300 KMP recruited prior to the PRCT will characterize the patterns and variability in HIV testing preferences in the target population. The DCE development will follow established guidelines and procedures established in our prior studies of HIV testing preferences.[21,23,48] Focus group discussions with members of the target populations will be used to prioritize HIV testing features with respect to their expected influence on HIV testing decisions, and to establish levels of features that represent plausible trade-offs in actual or hypothetical HIV testing interventions.

In the DCE survey, respondents will be introduced to each attribute and level and asked to complete 12 to 16 choice tasks. Each choice task will include 3 hypothetical testing options; participants will be asked to identify their preferred alternative. The combination of alternatives presented to respondents as part of the DCE will be varied according to a *d*-efficient, orthogonal statistical design,[49] generated in Ngene software (ChoiceMetrics). Survey content and presentation will be tested in up to 40 guided individual pretest interviews. Pilot studies with at least 200 participants will yield statistical priors that inform the statistical design of the final DCE. DCE surveys will be administered in-person, in Kiswahili (a language commonly used in the study area), using tablet devices, by trained research staff using the custom-built survey software, *comet* (Selway Labs).

Analysis of DCE data

The analysis of DCE data will follow established guidelines.[23,48] To estimate mean (average) preferences in the study population, DCE data will be first analyzed using mixed, or random

parameters, logit models using Stata (StataCorp) version 15,[50] which traditionally were considered best practice for analyzing DCE data,[51] but focus on average preferences. To model systematic variation in preferences across respondents, a scale-adjusted latent class (SALC) model will be estimated in Latent Gold Choice version 5.0 (Statistical Innovations Inc. 2018). SALC models allow for the joint modeling of preference heterogeneity (systematic variation in preferences across respondents) and variation in response certainty or consistency (normal response variation within an individual); these two sources of variation are confounded in traditional multinomial logit models. The Bayesian Information Criterion (BIC) will be used to identify which model yields the best fit for the data.

Selection of testing options for inclusion in the PRCT

Results from the mixed logit model will be used to identify the common option; results from the best-fitting latent class model will be used to identify the combinations of targeted, enhanced, and less-preferred options to be in included in the PRCT.

Common option: The common option will combine the most preferred (on average) levels of each attribute included in the DCE, as described by the mean parameter estimates from the mixed logit model.

Targeted, enhanced, and less-preferred options: The latent class analysis will identify statistical groupings of individuals with similar sets of preferences; these groupings are referred to as classes. Using parameter estimates from the latent class model, we will predict class-specific relative preferences for all feasible combinations of feature levels (i.e., testing options), which, in turn, will be converted into predicted choice probabilities in a simulated choice between the respective testing option and the “common option”. Class-specific predicted choice probabilities will be aggregated across classes (taking into consideration the estimated class sizes) to calculate the share of the population predicted to prefer each testing option over the

common option. These shares are used, as follows, to generate population-based rankings of all feasible combinations of three testing options. For targeted options, we will select from all options that combine features currently available in the study area those three options that jointly maximize the share of participants predicted to choose at least one of the three targeted options over the common option. Similarly, for enhanced options, we will select from all options that include additional features not yet widely available in the study area those three options that jointly maximize the share of participants predicted to choose at least one of the three enhanced options over the common option. For less preferred options, we will select those three options that jointly maximize the share of participants predicted to prefer the common option over all less preferred options.

Presentation of testing options to study participants

Testing options will be presented to participants on physical invitation cards. Each participant will be personally given 4 cards; each card will describe the characteristics of the testing option in a format similar to that presented in the DCE. The combination of cards given to a participant will be determined by the study arm assigned to the participant; references to specific testing venues may be varied according to participants' location of residence or preferred testing venue. Cards will have unique codes that allow for the tracking of participants' testing uptake across testing venues in the study area.

SMS delivery

SMS messages will be sent via a highly versatile, low-cost, mHealth system, called *mobile phone based appointment reminder and incentive system* (*mParis)*, which can autonomously send large numbers of SMS messages according to pre-specified algorithms and is based in the study area.[52,53]

Testing incentive

During Phase E, an incentive in the amount of TSH 5000 (~US $2.20) will be given in cash to participants presenting for testing with a coded testing invitation card at any of the testing venues in the study area. The amount is based on a prior willingness-to-accept study in the same area.[54]

Sample size

The target sample size for the PRCT is 1200 participants, comprising equal numbers of FBW and KMP. Randomization across study arms is expected to result in three groups with approximately 400 participants each.

Recruitment

Participants in formative work will be recruited using convenience and snowball sampling. For DCE surveys and the PRCT, mountain porters will be recruited from the Mweka gate of Kilimanjaro National Park. The Mweka gate is selected because of its proximity to Moshi (~15 kilometers); four of six popular climbing routes descend through this gate. Porters exiting the gate will be approached sequentially, and eligible porters will be handed an invitation card containing contact information and an invitation to the study's research office for consent and enrollment. For the recruitment of female barworkers, bars will be randomized and visited in the order of randomization. Eligible FBW will be consented at their place of work or given invitation cards containing contact information and an invitation to the study's research office for consent and enrollment. Recruited participants may receive reminder phone calls or SMS messages to come to the study offices for more information and study enrollment.

Enrollment and informed consent

Eligible individuals contacted for participation in the study will be informed by trained study personnel of the study purpose, procedures, as well as risks and benefits during the informed consent process. Only consenting individuals will be included in the study. Study participants' mobile phone numbers and the name and phone number of a contact person through whom they can be reached will be recorded to allow for phone-based follow-up.

Blinding

Participants will be blinded with respect to their assignment across the three study arms. While research staff are not blinded to participants' study arm assignment, study procedures are the same for all arms except for the characteristics of the testing offer.

Study activities

Study activities and their schedule are shown in **Table 2**.

Participants providing informed consent will be enrolled in the study. At the time of enrollment, a baseline survey will be conducted with all participants to assess socio-demographic characteristics, testing history, testing preferences, HIV serostatus, and HIV risk.

After enrollment, participants will progress through up to 5 study phases. Phase A represents a no-intervention phase. Phase B starts with the completion of a Phase A follow-up survey. Phase C starts with the distribution of a physical invitation card that describes the "common" option. Phase D starts with the distribution of four physical invitation cards that describe the preference-informed HIV testing options, namely the "common" option and three "targeted", "enhanced", or predicted "less preferred" options, depending on the study arm. Phase E starts with a phone call or SMS message offering a financial incentive to test. SMS reminder messages will be sent 28

days after the beginning of Phases B, C, D, and E. Phases A and B will end with a short phone-based survey with study participants. Phases C, D, and E will end with a phone-based survey or the collection of a testing invitation card from testing sites, whichever occurs earlier. After the completion of Phases B and C, participants will be contacted by phone and SMS and invited to come to the local study office for receipt of testing options.

HIV testing will be done in accordance with Tanzania's National AIDS Control Program (NACP) guidelines.[55] As per NACP guidelines, participants testing positive for HIV will be linked to care at a local CTC. Participants who report having tested positive for HIV, or those for whom documentation of a positive HIV test is collected from testing sites, will discontinue participation in HIV testing related components of the study and will instead be asked a brief survey about their linkage to HIV care and treatment.

Study timeline

The schedule of activities implies a minimum time of 15 months for participants to progress through all 5 study phases. Delays in reaching participants by phone and delays in participants returning to study offices will extend the duration of follow-up. In order to minimize loss to follow-up prior to the PRCT and reduce variability in the timing of the PRCT across participants, all participants in Phases A, B or C who are 91 or more days late for a follow-up assessment will transition to Phase D during their next in-person visit. Additionally, participants may be directly enrolled into Phases C and D (**Figure 1**). Study enrollment will continue until the target number of N=1200 participants in the PRCT (Phase D) has been reached. Follow-up will continue until 6 months after the last participant enters Phase D.

Participant retention

To maximize retention, study participants due for follow-up may receive multiple phone calls and SMS reminders to come to the study offices. Escalating incentives, i.e., incentive amounts that increase across consecutive study phases, will be used. Differences in baseline characteristics between participants retained and participants lost to follow-up will be analyzed statistically to evaluate selection biases.

Statistical analysis

The primary analysis involves the comparison of testing rates between study arms in Phase D. The effect of the intervention — a preference-informed, heterogeneity-focused, HIV testing offer — will be described by differences in testing uptake between those offered targeted or enhanced options, relative to those offered predicted less preferred options. Statistical significance will be evaluated in a bivariate analysis using a chi-squared test. Logistic regression analysis will evaluate the statistical significance of differences in a multivariate framework. Uptake of HIV testing within 3 months of the beginning of Phase D will be the binary outcome variable; study arm will be the key explanatory variable. Systematic variation in the efficacy of the intervention, e.g., by gender or with HIV risk, can be modeled using interactions between study arm and the respective covariates.

Survival models with up to 5 observations per participant (one each for Phases A, B, C, D, and E) will be used to estimate the differential effects of study arm assignment, SMS reminders, invitations, and conditional financial incentives, on rates of HIV testing. The time until an HIV test following the beginning of the respective study phase constitutes the dependent variable. “Exposure” to SMS reminders, invitations, and a financial incentive are hypothesized to increase the “hazard” of testing relative to no intervention.

Statistical power

DCE. Statistical power in DCEs varies with sample size, the number of choice tasks, the number of alternatives per task, and the number of attributes and levels, among other characteristics. An empirical power-test formula by Yang et al (2015) suggests that the DCE sample size (N=600) allows us to estimate the utility difference between the most and least-preferred testing options with a precision that is better than that of 'the average' DCE study.[56] A sample size guidance by Orme [57] suggests that the three cohorts (N=400 each) are sufficiently large to derive independent estimates for each sub-cohort.

PRCT. The sample size for the three-arm trial (N=1200) was selected to ensure adequate statistical power to identify the statistical significance of policy-relevant differences in testing uptake between study arms. We expect testing rates in Arm 3 to range from 25% among porters (as in our preliminary data) to 40% among barworkers (lower than the 59% in our preliminary data where barworkers were enrolled at a health facility).[20] Assuming an equal split between study arms, 400 participants per arm yield 65-72% power to detect a difference of 10 percentage points, 94-96% power for a difference of 15 points and >99% power for difference of 20 percentage points between the targeted, respectively enhanced, arms and the comparison arm (alpha=0.05, two-sided).

Reporting of results

Methods and results will be reported in accordance with the *CONSORT* reporting guidelines and its extensions for pragmatic randomized controlled trials (**see Supplemental File**).[58]

Data security and confidentiality

A research data security plan (RDSP) will ensure that data are kept in compliance with relevant privacy regulations, including HIPAA; access to identifying information will be strictly limited.

Study personnel will be instructed to keep the identity of all research subjects confidential and will sign confidentiality agreements.

Monitoring and quality assurance

Adherence to intervention protocols and the completeness and quality of study data will be continuously monitored by the principal investigators and a study monitor. Electronic data capture on tablet devices and daily uploads to secure servers allow for the continuous monitoring of study activities in near real time. All paper documents will be scanned. Rigorous quality assurance / quality control procedures will be established, including interviewer observation, validation and range checks during data entry, verification of entered data, and the monitoring of time stamps for DCE choice tasks.

Discussion

This study will evaluate whether an HIV testing intervention, which is uniquely designed using data from a DCE and explicitly targets preference heterogeneity, will improve testing uptake. If testing rates differ between study arms, the results will support our hypothesis that DCE-derived preference data can be used to systematically design HIV testing interventions that target heterogeneous preferences among and within high-risk populations, and that offering such interventions will increase testing uptake in target populations. With novel approaches to testing urgently needed to reach the 90-90-90 targets, the DCE and targeted methods used in this study may be broadly used to develop cost-effective testing offers that match the preferences of high-risk populations across diverse settings.

To our knowledge this is the first PRCT in which the intervention conditions are designed using data from a DCE, and the first PRCT that evaluates an intervention explicitly targeting preference heterogeneity. If successful, the methods used to understand how different groups of users value key characteristics of a health intervention can readily be applied to other settings in which interventions are being developed or adapted to optimize their efficacy. This work may demonstrate the utility of DCEs as a tool in implementation research to replace the costly practice of iteratively evaluating narrowly focused interventions. Thus, even as we apply this approach to the specific area of HIV testing, the study has potential to significantly advance the fields of patient-oriented research and implementation science. The methods could be used to develop new approaches to adapt effective interventions to local contexts, by informing a priori which interventions should be rolled out, and with which modifications, in order to maximize uptake across different populations and sub-populations.

Our study design and implementation approach have several unique components. First, the implementation of the study, in collaboration with all HCT providers in the study area, allows for the evaluation of testing uptake in a nearly closed system. Second, the use of an automated mHealth system to send large numbers of SMS messages according to pre-specified algorithms reduces both error potential and cost. Third, the similarity between HIV testing options given to participants and hypothetical choice scenarios presented in the DCE allows for explicit comparisons between stated and revealed preferences. Fourth, the study design allows for separate estimates of the effects of reminder SMS, the issuance of physical HIV testing invitation cards, and an incentive offer, on HIV testing rates. Finally, the approach for identifying the targeted, enhanced, and less-preferred options is not contingent on the use of SALC analysis and Latent Gold proprietary software; instead it can be approximated using open source alternatives e.g., in R. In a sensitivity analysis we will evaluate the effect of specific assumptions on the selection of testing options for the PRCT.

The study is subject to several limitations, although some of these are specific to our particular application and are not necessarily limitations of the DCE-informed approach in general. First, feasibility considerations limit the study area to include only HCT facilities in Moshi municipality, and testing uptake will be measured using a combination of provider documentation and self-report. While coded invitation cards collected from all HCT providers offer definitive evidence of a completed HIV test, participants may test without invitation cards, and may test outside the study area. Phone-based follow-up surveys will assess overlap between provider documentation and participant reports of testing and the extent to which participants test outside the study area. Second, study eligibility criteria include literacy, and study procedures involve phone- and SMS-based contact with participants. While literacy in the region was 94.4% in 2000, and, in 2017, 93% of urban households had a mobile phone,[59-61] the exclusion of illiterate persons and limited mobile phone access may influence the results. Third, multiple follow-up assessments increase the potential for loss-to-follow-up; sensitivity analyses will be conducted to describe the effects of selection bias on estimates. Finally, DCE surveys contain a limited set of testing characteristics; the finite range of attributes and levels is a limitation of DCEs in general. Preference- and choice-relevant testing characteristics may differ in other settings, and changes in the testing environment and available testing options may occur during the study period. While adaptations to the preference survey and analysis of DCE data may be necessary and require technical expertise, such costs are expected to be far smaller than costs associated with large-scale, iterative trials of potentially ineffective HCT testing interventions.

In conclusion, this study evaluates the critical link between preference-based intervention design and efficacy. If the PRCT indicates that a preference-informed, heterogeneity-focused HCT offer increases testing rates, the testing options evaluated in this study can be offered to high-risk populations in the study area, and the preference elicitation method and tools can be

used to inform the design of testing options that better match the preferences of other high-risk populations, both locally and in other settings.

Declarations

Ethics approvals

The protocol was registered in ClinicalTrials.gov (Protocol NCT02714140) on March 21, 2016. The protocol was approved by the Institutional Review Boards at Duke University (Duke Health IRB, Protocol Pro00075996, version 7, 16-Dec-2019) and the University of South Carolina (Health Sciences South Carolina IRB, facilitated review, Pro00060760) in the United States; as well as the Ethics Review Committee at Kilimanjaro Christian Medical University College (Protocol #901), the National Institute for Medical Research (NIMR/HQ/R.8a/Vol. IX/2603), and the Tanzania Food & Drugs Authority (now Tanzania Medical Devices Administration, Authorization No. TZ18CT0017) in Tanzania. Protocol amendments will be submitted to these entities as required.

Patient and public involvement

Focus group discussions with members of the target populations will be used to prioritize HIV testing features with respect to their expected influence on HIV testing decisions, and to establish levels of features that represent plausible trade-offs in actual or hypothetical HIV testing interventions. The results will inform the development of the DCE and the testing options in the PRCT.

Data availability

Findings from this study will be published in peer-reviewed journals. Data from the proposed study will be stored in a data repository; these data will be de-identified so that they cannot be linked back to individuals. Investigators wishing to use study data to answer new research questions may submit data analysis concept proposals for consideration by the Principal Investigators. The Principal Investigators will review the proposal and will provide those submitting scientifically rigorous and promising proposals access to the data repository to address their research questions.

Consent for publication

All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with ICMJE criteria.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JO, NT, and BN conceptualized the study. AH, AM, BF, BN, DB, JO, and NT were involved in the development and submission of the funding application. All authors contributed to the

development of the study protocol. JO and NT contributed equally to the development of this manuscript, wrote the first draft of the manuscript, and led subsequent revisions. AH, AM, AS, BF, BN, DB, JO, MM, MZ, NT, and TM read the manuscript and provided critical input. All authors read and approved the final manuscript.

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List of abbreviations

CTCs	HIV care and treatment centres
CFTs	Conditional financial transfers
DCE	Discrete choice experiment
FBW	Female barworkers
FGD	Focus group discussion
FU	Follow-up
HCT	HIV counseling and testing
HIV	Human Immunodeficiency Virus
HSHSP-IV	Tanzania's 2017-22 Health Sector HIV and AIDS Strategic Plan
IRB	Institutional Review Board
KCRI	Kilimanjaro Clinical Research Institute
KMP	Kilimanjaro mountain porters
LMICs	Low- and middle-income countries
mHealth	Mobile health
mParis	Mobile phone assisted reminder and incentive system
NIMR	National Institute for Medical Research
PLWH	Persons living with HIV
PRCT	Pragmatic randomized controlled trial
SALC	Scale adjusted latent class
SMS	Short messaging system (text messages)
UNAIDS	Joint United Nations Programme on HIV and AIDS

Table 1. HIV testing options offered across the three study arms in the pragmatic randomized controlled trial

Arm	Offers	Description
1	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from the mixed logit model.
	3 targeted options	Comprise features *widely available* in the study area and are predicted to be jointly more-preferred than the common option by the largest possible share of participants.
2	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from the mixed logit model.
	3 enhanced options	Include additional features that are *not yet widely available* in the study area and predicted to be jointly more-preferred than the common option by the largest possible share of participants.
3	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from the mixed logit model.
	3 less preferred options	Includes options that are widely available in the study area and jointly predicted to be equally or less-preferred than the common option by the largest possible share of participants.

Table 2. Schedule of activities

Phase	Time point	Target timing	Key activity	Key information collected
A	t_A	Enrollment	Baseline survey	HIV testing preferences, history, HIV risk, socio-demographics
	$t_{Afu} = t_B$*	t_A + 91 days	Phone-based FU	HIV testing uptake since t_A
B	t_{Bs}	t_B + 28 days	SMS reminder	
	t_{Bfu}	t_B + 91 days	Phone-based FU	HIV testing uptake since t_B
C#	$t_{Bx} = t_C$	t_{Bfu} + < 91 days	Testing invitation ("common" option)	
	t_{CS}	t_C + 28 days	SMS reminder	
	t_{Cfu}	t_C + 91 days	Card collection from testing sites, phone-based FU	HIV testing uptake since t_C
D#	$t_{Cx} = t_D$	t_{Cfu} + < 91 days	4 testing invitations, study arm specific	
	t_{Ds}	t_D + 28 days	SMS reminder	
	t_{Dfu}	t_D + 91 days	Card collection from testing sites, phone-based FU	HIV testing uptake since t_D
E	t_E	t_{Dfu} + < 91 days	Phone call and SMS message with incentive offer	
	t_{Es}	t_D + 28 days	SMS reminder	
	t_{Efu}	t_E + 91 days	Card collection from testing sites, phone-based FU	Choice among testing options offered, HIV testing uptake since t_E

* The phone-based follow-up at the end of Phase A constitutes the beginning of phase B
# To reduce variability across participants in the timing of Phase D, some participants may be enrolled directly into Phases C and D. FU: follow-up

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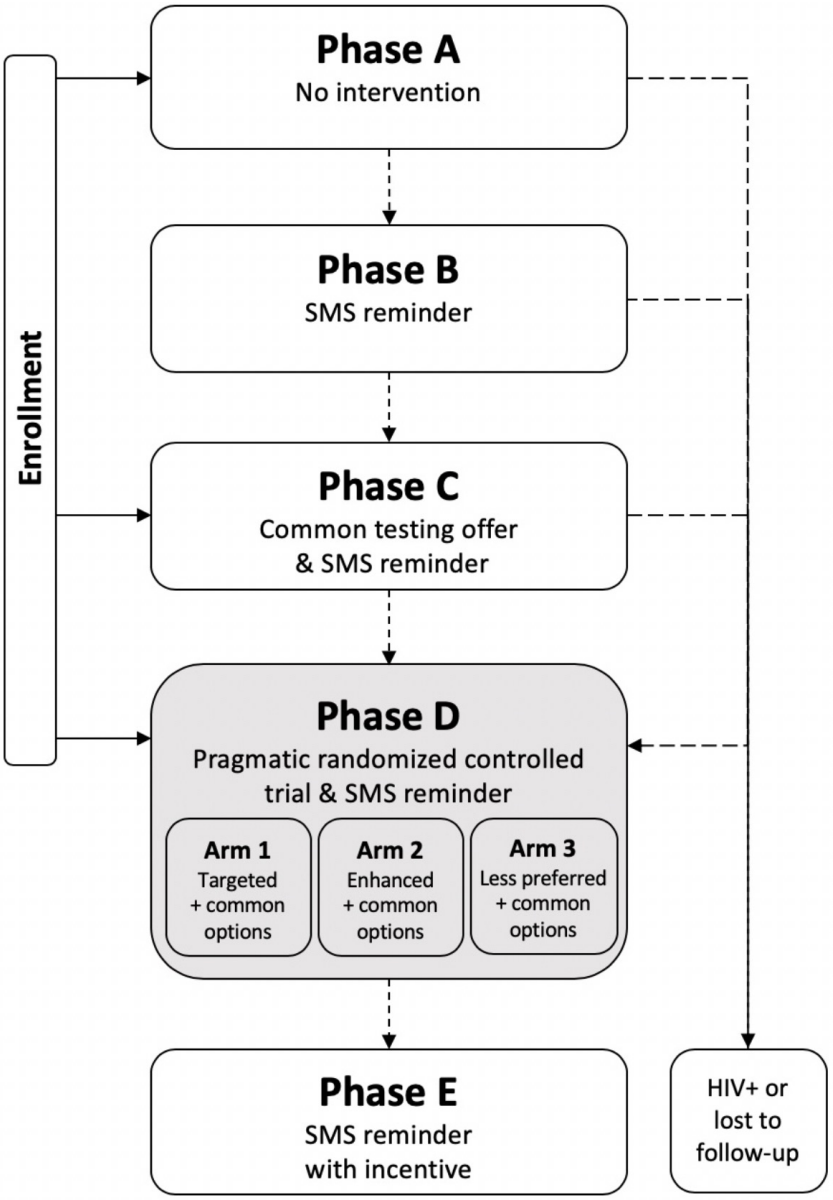

Figure 1. Study design

205x294mm (144 x 144 DPI)

Supplementary Table S1. CONSORT checklist for pragmatic randomized controlled trials

SECTION and topic	Item #	Descriptor[1]	Reported on page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., random allocation", "randomized", or "randomly assigned").	2
INTRODUCTION			
Background	2	Scientific background and explanation of rationale. **EXT**: Describe the health or health service problem that the intervention is intended to address and other interventions that may commonly be aimed at this problem.	5
METHODS			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected. **EXT**: Eligibility criteria should be explicitly framed to show the degree to which they include typical participants and/or, where applicable, typical providers (eg, nurses), institutions (eg, hospitals), communities (or localities eg, towns) and settings of care (eg, different healthcare financing systems).	7

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered. **EXT**: Describe extra resources added to (or resources removed from) usual settings in order to implement intervention. Indicate if efforts were made to standardise the intervention or if the intervention and its delivery were allowed to vary between participants, practitioners, or study sites. Describe the comparator in similar detail to the intervention	8, 11
Objectives	5	Specific objectives and hypotheses.	7
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors). **EXT**: Explain why the chosen outcomes and, when relevant, the length of follow-up are considered important to those who will use the results of the trial	5, 20
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. **EXT**: If calculated using the smallest difference considered important by the target decision maker audience (the minimally important difference) then report where this difference was obtained	19

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Randomization:			
Sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification).	10
Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	10
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	10
Blinding (Masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated. **EXT**: If blinding was not done, or was not possible, explain why	16
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	18
RESULTS			

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons. **EXT**: The number of participants or units approached to take part in the trial, the number which were eligible, and reasons for nonparticipation should be reported	17
Recruitment	14	Dates defining the periods of recruitment and follow-up.	n/a
Baseline data	15	Baseline demographic and clinical characteristics of each group.	n/a
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	15
Outcomes and Estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	n/a

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	n/a
Adverse events	19	All important adverse events or side effects in each intervention group.	n/a
DISCUSSION			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	n/a
Generalizability	21	Generalizability (external validity) of the trial findings. **EXT**: Describe key aspects of the setting which determined the trial results. Discuss possible differences in other settings where clinical traditions, health service organisation, staffing, or resources may vary from those of the trial.	n/a
Overall evidence	22	General interpretation of the results in the context of current evidence.	n/a

[1] EXT denotes a pragmatic trial extension of the CONSORT statement.

https://www.bmj.com/content/bmj/337/bmj.a2390.full.pdf

Supplementary Table S2: WHO Trial Registration Data Set

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT02714140
Date of registration in primary registry	March 21, 2016
Secondary identifying numbers	N/A
Source of monetary/material support	National Institute of Mental Health (R01MH106388) 6001 Executive Boulevard Bethesda, MD 20892-9663
Primary sponsor	University of South Carolina, USA
Secondary sponsor(s)	Kilimanjaro Christian Medical Centre, Tanzania
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Public title	Does Preference-based HIV Testing Increase Uptake in High Risk Populations?
Scientific title	Using DCEs to Identify and Match Preferences for HIV/AIDS Counseling and Testing (DCE-IMPACT)
Countries of recruitment	Tanzania
Health conditions or problems studied	HIV, HIV testing
Intervention(s)	Behavioral: Invitation cards Behavioral: Reminders Behavioral: Conditional economic transfers
Key inclusion and exclusion criteria	Ages Eligible for Study: 18 Years and older Sexes Eligible for Study: Any Accepts Healthy Volunteers: Yes Inclusion criteria: Women employed in bars, restaurants and guesthouses serving alcohol to patrons (“female barworkers”) and male mountain porters who are supporting climbers of nearby Mount Kilimanjaro (“Kilimanjaro mountain porters”) Exclusion criteria: Unable to read
Study type	Interventional (Clinical Trial)
Date of first enrolment	12-February-2019
Target sample size	1200
Recruitment status	Ongoing
Primary outcome(s)	Uptake of HIV testing
Key secondary outcomes	N/A

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Supplemental Table S3. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	23
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary Table S2
Protocol version	3	Date and version identifier	23
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	24
	5b	Name and contact information for the trial sponsor	Supplementary Table S2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	24
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-7
	6b	Explanation for choice of comparators	8
Objectives	7	Specific objectives or hypotheses	7
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	19
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 and Table 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	19
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	15
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	10,16
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	10
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	16
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 2
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	18

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	19
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	18
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	18
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	23
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	23

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	16
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	19
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	24
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	24
	31b	Authorship eligibility guidelines and any intended use of professional writers	24
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	24
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Using discrete choice experiments to design interventions for heterogeneous preferences: protocol for a pragmatic randomized controlled trial of a preference-informed, heterogeneity-focused, HIV testing offer for high-risk populations

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Using discrete choice experiments to design interventions for heterogeneous preferences: protocol for a pragmatic randomized controlled trial of a preference-informed, heterogeneity-focused, HIV testing offer for high-risk populations

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Keywords: HIV counseling and testing; Discrete choice experiment; Preference heterogeneity; Latent class analysis; Pragmatic randomized controlled trial

Using discrete choice experiments to design interventions for heterogeneous preferences: protocol for a pragmatic randomized controlled trial of a preference-informed, heterogeneity-focused, HIV testing offer for high-risk populations

Abstract

Introduction. Approximately one million undiagnosed persons living with HIV (PLWH) in Southern and Eastern Africa need to test for HIV. Novel approaches are necessary to identify HIV testing options that match the heterogeneous testing preferences of high-risk populations. This pragmatic randomized controlled trial (PRCT) will evaluate the efficacy of a preference-informed, heterogeneity-focused HIV counseling and testing (HCT) offer, for improving rates of HIV testing in two high-risk populations.

Methods and Analysis. The study will be conducted in Moshi, Tanzania. The PRCT will randomize 600 female barworkers and 600 male Kilimanjaro mountain porters across three study arms. All participants will receive an HIV testing offer comprised of four preference-informed testing options, including one "common" option – comprising features that are commonly available in the area and, on average, are most preferred among study participants – and three options that are specific to the study arm. Options will be identified using mixed logit and latent class analyses of data from a discrete choice experiment (DCE). Participants in Arm 1 will be offered the common option and three "targeted" options that are predicted to be more preferred than the common option and combine features widely available in the study area. Those in Arm 2 will be offered the common option and three "enhanced" options, which also include HCT features that are not yet widely available in the study area. Participants in Arm 3,

an active control arm, will be offered the common option and three predicted “less preferred” options. The primary outcome will be uptake of HIV testing.

Ethics and Dissemination. Ethical approval was obtained from the Duke University Health System IRB, the University of South Carolina IRB, the Ethics Review Committee at Kilimanjaro Christian Medical University College, Tanzania’s National Institute for Medical Research, and the Tanzania Food & Drugs Authority (now Tanzania Medicines & Medical Devices Authority). Findings will be published in peer-reviewed journals. The use of rigorous DCE methods for the preference-based design and tailoring of interventions could lead to novel policy options and implementation science approaches.

Registration. The protocol was registered in ClinicalTrials.gov (Protocol NCT02714140) on March 21, 2016.

Strengths and limitations of this study

- The pragmatic randomized controlled trial described in this protocol paper includes males and females at high risk of HIV infection; the implementation of the trial in collaboration with all HIV testing providers in the study area allows for the evaluation of testing uptake in a nearly closed system.
- The study goes beyond the traditional approach of evaluating single-offer ("one-size-fits-all") interventions by identifying combinations of testing options that explicitly target preference heterogeneity in the target population.
- The methods used to identify the intervention conditions evaluated in the trial, including the latent class analysis of data from the discrete choice experiment (DCE) used to elicit heterogeneous population preferences for HIV testing, may be applied to other contexts and may lead to the development of new implementation science approaches for systematically adapting effective interventions to local contexts.
- The study design will allow for separate estimates of the effects of SMS reminders, the issuance of physical HIV testing invitation cards, the heterogeneity-focused testing offer, and an incentive offer on HIV testing rates.
- Potential limitations include loss to follow-up during the multi-phase study, the finite range of HIV testing characteristics that can be included in a DCE, ordering effects and exogenous events during the study period that may influence rates of HIV testing across study arms, and limited generalizability of specific study findings to other populations and settings.

Keywords (longer list)

HIV counseling and testing; Discrete choice experiment; Preference heterogeneity; Latent class analysis; Pragmatic randomized controlled trial; Mobile health (mHealth); Reminders; Conditional financial transfers; Policy design; Implementation science; Tanzania; sub-Saharan Africa

Background

In 2018, 37.9 million people were living with HIV worldwide, and 770,000 died of HIV-related illnesses.[1] HIV counseling and testing (HCT) is a cost-effective intervention for increasing HIV serostatus awareness,[2,3] a point of entry into HIV care and treatment, and an important means of primary and secondary HIV prevention.[4] HIV Prevention Trials Network Protocol 052 conclusively demonstrated a marked reduction in HIV transmission among serodiscordant couples in which the HIV-infected partner was begun on antiretroviral therapy early in the course of infection.[5] Subsequently, public health officials and policymakers, considering treatment as prevention, have called for dramatic increases in HIV testing — as frequently as annually in many populations and semi-annually among individuals at high risk.[6]

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set for 2020 the ambitious 90-90-90 target: diagnosing 90% of all persons living with HIV (PLWH), initiating treatment for 90% of those diagnosed, and achieving viral suppression for 90% of those treated.[7] While substantial progress has been made toward these targets since 2014, most countries remain short of at least one target, and the number of undiagnosed HIV infections in every region are considered a major hindrance to achieving the UNAIDS targets and ending the epidemic.[8] Novel approaches are needed to increase testing uptake, especially among high-risk groups.

In order to establish the diagnosis of HIV in 90% of all PLWH in Eastern and Southern Africa, more than 1 million undiagnosed infected persons need to test, including 190,000 in Tanzania.[4,6,9] Tanzania's 2017-22 Health Sector HIV and AIDS Strategic Plan (HSHSP-IV) lists as a key challenge that HIV testing services "need to be more efficient and ambitious to meet the 90-90-90 targets through more targeted testing approaches."[10] Evaluations of population preferences for testing have typically focused on the acceptability of specific testing options, such as home-based,[11-13] provider-initiated,[14-17] or workplace testing,[18,19] usually without

consideration or offer of other options. Results from these narrow assessments do not probe the potential diversity in testing preferences among target populations and cannot characterize which testing options will maximize uptake of testing.[20-22]

Discrete choice experiments (DCEs), grounded in the economic theory of utility maximization, are specifically designed to provide information about individuals' preferences for varying characteristics of multi-attribute products. The DCE method is based on the assumption that a product or service such as HCT can be described in terms of its characteristics, namely attributes and levels within attributes. Participants are repeatedly asked to choose between two or more alternatives in choice scenarios simulating real choice decisions. Each alternative differs in the arrangement of attribute levels presented to the participant. The choice scenarios are systematically varied by means of an experimental design.[23-26] Relative attribute importance, the utility that respondents derive from the diverse options, and trade-offs, i.e., the willingness to trade between attribute levels, can be quantified analytically.[27] DCEs are used increasingly to understand patient perspectives and to design patient-centered interventions. Although DCEs have been used in various contexts related to HIV, including testing,[20,28-32] prevention,[33-36] service delivery,[37-39] and treatment,[40-44] to our knowledge DCEs have not yet been used to systematically design HIV counseling and testing interventions.

Below we describe the study protocol for a pragmatic randomized controlled trial (PRCT) that evaluates the efficacy of a targeted, preference-informed HCT offer for improving rates of HIV testing in high-risk populations. The testing offer is developed using data from a discrete choice experiment (DCE) and designed to match the heterogeneous HIV testing preferences in the target population. To our knowledge this is the first PRCT in which the study conditions are optimized using data from a DCE, and the first PRCT that evaluates an intervention explicitly targeting preference heterogeneity.

Methods and analysis

Study aim and hypothesis

The aim of this study is to evaluate the efficacy of a preference-informed, heterogeneity-focused HCT offer for improving rates of HIV testing among two high-risk populations. We hypothesize that an HCT offer matched to the specific preferences of the intended target population and explicitly accounting for preference heterogeneity within these populations will increase rates of testing relative to a control offer.

Study setting

The study is conducted in Moshi, Tanzania. Moshi is the commercial center and administrative capital of the Kilimanjaro Region in Northern Tanzania and has an estimated population of about 200,000.[45] Moshi has 25 HCT facilities, including 8 care and treatment centres (CTCs), which provide free HIV care to persons living with HIV.[46] The study is implemented with support from the Regional Medical Officer and the Regional AIDS Control Coordinator of the Kilimanjaro Region.

Study participants

The study population comprises women employed in bars, restaurants and guesthouses serving alcohol to patrons ("female barworkers", FBW), and male mountain porters who are supporting climbers of nearby Mount Kilimanjaro ("Kilimanjaro mountain porters", KMP). The Regional AIDS Control Coordinator identified these groups as populations at high risk of HIV infection who could benefit from increased rates of testing; we subsequently showed that FBW and KMP engage in higher rates of HIV risk behaviors than randomly selected male and female

community members in the same setting.[20] For example, compared to randomly selected community members, FBW and KMP reported 2–3 times as many lifetime sexual partners, higher rates of sexually transmitted illnesses, and higher rates of having sex in exchange for money or gifts, but similar numbers of lifetime HIV tests.[20] A census of bars and female barworkers, conducted by the study team between February and June of 2016, identified 612 venues within Moshi, with 2,059 age-eligible FBW. There are an estimated 10,000 porters in the Kilimanjaro Region.[47,48]

Inclusion criteria

Eligible study participants are ages 18 or older, reside in Moshi, are able to read, and have no concrete plans to leave the study area during the 12- to 15-month period following study enrollment.

Outcome measure

The study outcome of interest is uptake of HIV testing. During the multi-phase study (see below), the outcome is ascertained repeatedly by counselors' documentation of participants' HIV tests, self-reports from study participants, or both. In the PRCT and one preceding study phase, coded HIV testing invitation cards will be distributed to participants and HIV tests will be tracked on the basis of cards returned to any HIV testing center in the study area. Self-reports capture tests outside the study area and tests without cards. The primary outcome measure is counselor-documented uptake of testing. A secondary outcome measure is counselor-documented or self-reported uptake of testing.

Study design

The study is comprised of 5 sequential phases (**Figure 1**). The target duration for each phase is 13 weeks (91 days).

Phase A: Reference phase. Phase A includes no intervention. The purpose of this phase is to inform estimates of background rates of HIV testing among individuals participating in a research study focusing on HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase A.

Phase B: SMS phase. In Phase B, a Short Messaging System (SMS) reminder message to test for HIV will be sent to participants 4 weeks (28 days) after the beginning of Phase B. The purpose of this phase is to inform estimates of the effect of an SMS reminder on rates of HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase B.

Phase C: Invitation phase. In Phase C, participants will be given a credit card-sized invitation card describing an HIV testing option that combines features commonly available in the study area, and that, on average, are most preferred among study participants ("**common option**"). Four weeks (28 days) after the beginning of Phase C, participants will be sent an SMS reminder to test for HIV as shown on the invitation card given to them. The purpose of this study phase is to inform estimates of the effect of a testing invitation on rates of HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase C.

Phase D: The pragmatic randomized controlled trial. Phase D is a PRCT that includes three parallel study arms (**Table 1**). All participants will receive an HIV testing offer comprised of four invitation cards describing preference-informed HIV testing options. Participants will be asked to test for HIV using their individually most preferred of the 4 testing options given to them. Options will be identified using mixed logit and latent class analyses of data from a discrete choice experiment (DCE) with members of the target populations (see below). **Arm 1** participants will be offered the common option and three "**targeted**" options, predicted to be jointly more preferred than the common option and comprising testing features widely available in the study

area. **Arm 2** participants will be offered the common option and three "**enhanced**" options, which are also predicted to be jointly more preferred than the common option but include additional features that are not yet widely available in the study area. **Arm 3** participants will be offered the common option and three options that are jointly predicted to be "**less preferred**" than the common option. In other words, for arm 3 participants, the common option is the predicted most preferred of the four options; the other three options, on average, provide no additional value. Arms 1 and 2 are intervention arms. Arm 3 represents an active control arm: study involvement in Arm 3 is the same as in Arms 1 and 2. Four weeks (28 days) after the beginning of Phase D, participants will be sent an SMS reminder to test for HIV using any of the testing options given to them. The purpose of this study phase is to obtain estimates of the effect of a heterogeneity-focused HIV testing offer on rates of HIV testing. A phone survey after 13 weeks (91 days) will ask participants about any HIV test during Phase D.

Phase E: Incentive phase. In phase E, participants will be offered an incentive to test for HIV using their choice of any of the testing options remaining to them from Phase D. An SMS reminder will be sent to participants 4 weeks (28 days) after the beginning of Phase E. The purpose of this phase is to inform estimates of the effect of a conditional financial transfer (CFT) on testing decisions and identify the most preferred testing option among those offered, among participants who did not test during Phase D.

The study design will allow for separate estimates of the effects on HIV testing rates of:

(1) an SMS reminder message,

(2) a testing invitation,

(3) a heterogeneity-focused testing offer, and

(4) a conditional financial transfer (CFT) offer.

Assignment to study arms

Participant IDs will be randomly assigned to study arms using a random number generator. The testing offer in Phase D will reflect the study arm assigned to the respective Participant ID. The random assignment is expected to result in approximately equal numbers of participants in each study arm.

Design of the intervention

Overview. A DCE will be used to elicit information on the distribution of preferences for feasible and modifiable characteristics of HIV testing options in the target population. DCE data will be analyzed, and results of these analyses will be used to identify four types of testing options that will be offered to participants in the PRCT:

1) ***A "common" option.*** This single testing option combines testing features that are widely available in the study area, and, on average, are most preferred among study participants. This option will be offered to all participants in Phases C and D.
2) ***Three "targeted" options.*** This set of testing options, comprising features widely available in the study area, is predicted to be jointly more preferred than the common option by the largest possible share of participants.
3) ***Three "enhanced" options.*** Enhanced testing options include additional features that are not yet widely available in the study area (e.g., oral testing). The set of enhanced testing options is predicted to be jointly more preferred than the common option by the largest possible share of participants.
4) ***Three "less preferred" options.*** This set of testing options includes options that are predicted to be equally or less preferred than the common option by the largest possible share of participants.

The design decision to offer three targeted, enhanced, and less preferred options was driven by practical considerations: (1) a choice from 4 alternatives (the common option plus 3 options specific to the study arm) is expected to be cognitively feasible for participants, (2) the implementation of 10 testing options (one common option, plus 3 targeted, 3 enhanced, and 3 less preferred options) as part of this study is feasible from a logistical and budgetary perspective; and (3) the widespread implementation of 3 testing options that target preference heterogeneity is feasible in the study area. The statistical analysis of the DCE data (see below) will determine whether the testing offers differ between FBW and KMP.

Development and fielding of the DCE

A DCE with 300 FBW and 300 KMP recruited prior to the PRCT will characterize the patterns and variability in HIV testing preferences in the target population. The DCE development will follow guidelines and procedures established in our prior studies of HIV testing preferences.[21,23,49] Focus group discussions with members of the target populations will be used to prioritize HIV testing features with respect to their expected influence on HIV testing decisions, and to establish levels of features that represent plausible trade-offs in actual or hypothetical HIV testing interventions. Reconciling prior qualitative work[22] with the objectives of the PRCT, the DCE is expected to include feasible attributes and levels across three domains: privacy and confidentiality (e.g. testing venue, different types of counseling), accessibility and value (testing availability, additional services provided), and perceived quality and accuracy (e.g. type of sample for the HIV test).

In the DCE survey, respondents will be introduced to each attribute and level and asked to complete 12 to 16 choice tasks. Each choice task will include 3 hypothetical testing options; participants will be asked to identify their preferred alternative. The combination of alternatives presented to respondents as part of the DCE will be varied according to a *d*-efficient statistical

design,[50] generated in Ngene software (ChoiceMetrics). Survey content and presentation will be tested in up to 40 guided individual pretest interviews. Pilot studies with at least 200 participants will yield statistical priors that inform the statistical design of the final DCE. DCE surveys will be administered in-person, in Kiswahili, using tablet devices, by trained research staff using the custom-built survey software, *comet* (Selway Labs).

Continuous recruitment and enrollment may result in overlap between DCE survey respondents and PRCT participants. All PRCT participants will complete the DCE survey to allow for comparisons of stated preferences (DCE survey responses) and revealed preferences (testing decisions).

Analysis of DCE data

The analysis of DCE data will follow established guidelines.[23,49] To estimate mean (average) preferences in the study population, DCE data will be first analyzed using mixed, or random parameters, logit models using Stata (StataCorp) version 15,[51] which traditionally were considered best practice for analyzing DCE data,[52] but focus on average preferences. To model systematic variation in preferences across respondents, a random effects latent class logit (RELCL) model will be estimated in Latent Gold Choice version 5.0 (Statistical Innovations Inc. 2018). RELCL models allow for the joint modeling of systematic variation in preferences (latent classes) and random variation in preferences (random effects) across respondents.[53] The Bayesian Information Criterion (BIC) will be used to identify which model yields the best fit for the data.

To evaluate whether the distribution of preferences differs significantly between the two groups of participants (FBW vs. KMP), participant type will be included in the model as a covariate. If the distributions of preferences differ significantly across groups, separate preference-informed testing options may need to be identified for FBW and KMP. On the other hand, if the

preference distributions are broadly similar, the testing offer can be optimized for the joint preferences of both populations.

Selection of testing options for inclusion in the PRCT

Results from the mixed logit model will be used to identify the common option; results from the best-fitting latent class model will be used to identify the combinations of targeted, enhanced, and less-preferred options to be in included in the PRCT.

Common option: The common option will combine the most preferred (on average) levels of each attribute included in the DCE, as described by the mean parameter estimates from the mixed logit model.

Targeted, enhanced, and less-preferred options: The latent class analysis will identify statistical groupings of individuals with similar sets of preferences; these groupings are referred to as classes. Using parameter estimates from the latent class model, we will predict class-specific relative preferences for all feasible combinations of feature levels (i.e., testing options), which, in turn, will be converted into predicted choice probabilities in a simulated choice between the respective testing option and the "common option". Class-specific predicted choice probabilities will be aggregated across classes (taking into consideration the estimated class sizes) to calculate the share of the population predicted to prefer each testing option over the common option. These shares are used, as follows, to generate population-based rankings of all feasible combinations of three testing options. For targeted options, we will select from all options that combine features currently available in the study area the three options that jointly maximize the share of participants predicted to choose at least one of those three targeted options over the common option. Similarly, for enhanced options, we will select from all options that include additional features not yet widely available in the study area the three options that jointly maximize the share of participants predicted to choose at least one of those three

enhanced options over the common option. For less preferred options, we will select the three options that jointly maximize the share of participants predicted to prefer the common option over all less preferred options.

Presentation of testing options to study participants

Testing options will be presented to participants on physical invitation cards. Each participant will be given 4 cards; each card will describe the characteristics of the testing option in a format similar to that presented in the DCE. The combination of cards given to a participant will be determined by the study arm assigned to the participant; references to specific testing venues may be varied according to participants' location of residence or preferred testing venue. Cards will have unique codes that allow for the tracking of participants' testing uptake across testing venues in the study area.

SMS delivery

SMS messages will be sent via a highly versatile, low-cost, mHealth system, called *mobile phone based appointment reminder and incentive system* (*mParis)*, which can autonomously send large numbers of SMS messages according to pre-specified algorithms and is based in the study area.[54,55]

Testing incentive

During Phase E, an incentive in the amount of TSH 5000 (~US $2.20) will be given in cash to participants presenting for testing with a coded testing invitation card at any of the testing venues in the study area. The amount is based on a willingness-to-accept study previously conducted in the same area.[56]

Sample size

The target sample size for the PRCT is 1200 participants, comprising equal numbers of FBW and KMP. Randomization across study arms is expected to result in three groups with approximately 400 participants each.

Recruitment

Participants for formative work will be recruited using convenience and snowball sampling. For DCE surveys and the PRCT, the goal is to employ a systematic recruitment approach that minimizes biases. Mountain porters will be recruited from the Mweka gate of Kilimanjaro National Park. The Mweka gate is selected because of its proximity to Moshi (~15 kilometers); four of six popular climbing routes descend through this gate. Porters exiting the gate will be approached sequentially, and eligible porters will be handed an invitation card containing contact information and an invitation to the study's research office for consent and enrollment. For the recruitment of female barworkers, bars will be randomized and visited in the order of randomization. Eligible FBW will be consented at their place of work or given invitation cards containing contact information and an invitation to the study's research office for consent and enrollment. Recruited participants may receive reminder phone calls or SMS messages to come to the study offices for more information and study enrollment.

Enrollment and informed consent

Eligible individuals contacted for participation in the study will be informed by trained study personnel of the study purpose, procedures, as well as risks and benefits during the informed consent process. Only consenting individuals will be included in the study. Study participants' mobile phone numbers and the name and phone number of a contact person through whom they can be reached will be recorded to allow for phone-based follow-up.

Enrollment into the trial will be conducted in three sequential stages. Approximately half the participants will be enrolled into Phase A and one quarter each into Phases C and D. This approach ensures variation in the exposure to pre-PRCT intervention components across participants, thereby allowing for the estimation of potential ordering effects as participants move through the different study phases. The staggered enrollment also ensures a better alignment of study timelines for Phases D and E across participants.

Blinding

Participants will be blinded with respect to their assignment across the three study arms. While research staff are not blinded to participants' study arm assignment, study procedures are the same for all arms except for the characteristics of the testing offer.

Study activities

Study activities and their schedule are shown in **Table 2**.

Participants providing informed consent will be enrolled in the study. At the time of enrollment, a baseline survey will be conducted with all participants to assess socio-demographic characteristics, testing history, testing preferences, HIV serostatus, and HIV risk.

After enrollment, participants will progress through up to 5 study phases. Phase A represents a no-intervention phase. Phase B starts with the completion of a Phase A follow-up survey. Phase C starts with the distribution of a physical invitation card that describes the "common" option. Phase D starts with the distribution of four physical invitation cards that describe the preference-informed HIV testing options, namely the "common" option and three "targeted", "enhanced", or predicted "less preferred" options, depending on the study arm. Phase E starts with a phone call or SMS message offering a financial incentive to test. SMS reminder messages will be sent 28 days after the beginning of Phases B, C, D, and E. Phases A and B will end with a short phone-

based survey with study participants. Phases C, D, and E will end with a phone-based survey or the collection of a testing invitation card from testing sites, whichever occurs earlier. After the completion of Phases B and C, participants will be contacted by phone and SMS and invited to come to the local study office for receipt of testing options.

HIV testing will be done in accordance with Tanzania's National AIDS Control Program (NACP) guidelines.[57] Since 2013, Tanzania's National Comprehensive Guidelines for HIV Testing and Counselling describe specific retesting intervals ranging from 4 weeks to 6 months for most persons at elevated risk of HIV infection.[58] Our own survey of HIV testing sites in the study area revealed that most counselors continue to recommend retesting after 3 months for all clients testing negative for HIV, regardless of risk. As per NACP guidelines, participants testing positive for HIV will be linked to care at a local CTC. Participants who report having tested positive for HIV, or those for whom documentation of a positive HIV test is collected from testing sites, will discontinue participation in HIV testing related components of the study and will instead be given a brief survey about their linkage to HIV care and treatment.

Study timeline

The schedule of activities implies a minimum time of 15 months for participants to progress through all 5 study phases. Delays in reaching participants by phone and delays in participants returning to study offices will extend the duration of follow-up. In order to minimize loss to follow-up prior to the PRCT and reduce variability in the timing of the PRCT across participants, all participants in Phases A, B or C who are 91 or more days late for a follow-up assessment will transition to Phase D during their next in-person visit. Additionally, participants may be directly enrolled into Phases C and D (**Figure 1**). Study enrollment will continue until the target number of N=1200 participants in the PRCT (Phase D) has been reached. Follow-up will continue until 6 months after the last participant enters Phase D.

Participant retention

To maximize retention, study participants due for follow-up may receive multiple phone calls and SMS reminders to come to the study offices. Escalating incentives, i.e., incentive amounts that increase across consecutive study phases, will be used. The effect of selective attrition on estimates will be evaluated in sensitivity analyses (see below).

Statistical analysis

The primary analysis involves the comparison of testing rates between study arms in Phase D. The effect of the intervention — a preference-informed, heterogeneity-focused, HIV testing offer — will be described by differences in testing uptake between those offered targeted or enhanced options, relative to those offered predicted less preferred options. Statistical significance will be evaluated in a bivariate analysis using a chi-squared test. Logistic regression analysis will evaluate the statistical significance of differences in a multivariate framework. Uptake of HIV testing within 3 months of the beginning of Phase D will be the binary outcome variable; study arm will be the key explanatory variable. Systematic variation in the efficacy of the intervention, e.g., by gender or with HIV risk, can be modeled using interactions between study arm and the respective covariates.

Survival models with up to 5 observations per participant (one each for Phases A, B, C, D, and E) will be used to estimate the differential effects of study arm assignment, SMS reminders, invitations, and conditional financial incentives, on rates of HIV testing. The time until an HIV test following the beginning of the respective study phase constitutes the dependent variable. “Exposure” to SMS reminders, invitations, and a financial incentive are hypothesized to increase the “hazard” of testing relative to no intervention. To control for potential ordering effects, participants exposure to intervention components in prior study phases (Phase B and C SMS reminders, Phase C testing offer, recent testing uptake) will be included as covariates.

Statistical power

DCE. Statistical power in DCEs varies with sample size, the number of choice tasks, the number of alternatives per task, and the number of attributes and levels, among other characteristics. An empirical power-test formula by Yang et al (2015) suggests that the DCE sample size (N=600) allows us to estimate the utility difference between the most and least-preferred testing options with a precision that is better than that of 'the average' DCE study.[59] A sample size guidance by Orme [60] suggests that the two study populations (N=600 each) and three cohorts (N=400 each) are sufficiently large to derive independent estimates for each sub-cohort.

PRCT. The sample size for the three-arm trial (N=1200) was selected to ensure adequate statistical power to identify the statistical significance of policy-relevant differences in testing uptake between study arms. We expect testing rates in Arm 3 to range from 25% among porters (as in our preliminary data) to 40% among barworkers (lower than the 59% in our preliminary data where barworkers were enrolled at a health facility).[20] Assuming an equal split between study arms, 400 participants per arm yield 65-72% power to detect a difference of 10 percentage points, 94-96% power for a difference of 15 points and >99% power for difference of 20 percentage points between the targeted, respectively enhanced, arms and the comparison arm (alpha=0.05, two-sided).

Reporting of results

Methods and results will be reported in accordance with the *CONSORT* reporting guidelines and its extensions for pragmatic randomized controlled trials (**see Supplemental Files 1-4**).[61]

Sensitivity analyses

Extensive sensitivity analyses will describe the sensitivity of our estimates to the definition of the outcome variable, model specification, and selective attrition. Estimates from the analysis of the secondary outcome measure (counselor-documented or self-reported testing uptake) will be presented alongside the analysis of the primary outcome measure (counselor-documented HIV testing). The DCE choice data will be analyzed using a broad range of models in order to describe the sensitivity of the selected PRCT testing offers to model specification and assumptions. The effect of attrition will be estimated by modeling attrition as a function of observable characteristics at the time of enrollment and weighing individual-level predictions of the intervention effect by the inverse probability of attrition. Differences between the average intervention effect and the attrition-weighted average effect will characterize the effects of selective attrition on our estimates.

Data security and confidentiality

A research data security plan (RDSP) will ensure that data are kept in compliance with relevant privacy regulations, including HIPAA; access to identifying information will be strictly limited. Study personnel will be instructed to keep the identity of all research subjects confidential and will sign confidentiality agreements.

Monitoring and quality assurance

Adherence to intervention protocols and the completeness and quality of study data will be monitored by the principal investigators and a study monitor. Electronic data capture on tablet devices and daily uploads to secure servers allow for the continuous monitoring of study activities in near real time. All paper documents will be scanned. Rigorous quality assurance / quality control procedures will be established, including interviewer observation, validation and

range checks during data entry, verification of entered data, and the monitoring of time stamps for DCE choice tasks.

Patient and public involvement

Focus group discussions with members of the target populations will be used to prioritize HIV testing features with respect to their expected influence on HIV testing decisions, and to establish levels of features that represent plausible trade-offs in actual or hypothetical HIV testing interventions. The results will inform the development of the DCE and the testing options in the PRCT.

Ethics and Dissemination

Ethical approval was obtained from the Duke University Health System IRB, the University of South Carolina IRB, the Ethics Review Committee at Kilimanjaro Christian Medical University College, Tanzania's National Institute for Medical Research, and the Tanzania Food & Drugs Authority (now Tanzania Medicines & Medical Devices Authority). Findings will be published in peer-reviewed journals. The use of rigorous DCE methods for the preference-based design and tailoring of interventions could lead to novel policy options and implementation science approaches.

Discussion

This study will evaluate whether an HIV testing intervention, which is uniquely designed using data from a DCE and explicitly targets preference heterogeneity, will improve testing uptake. If testing rates differ between study arms, the results will support our hypothesis that DCE-derived preference data can be used to systematically design HIV testing interventions that target

heterogeneous preferences among and within high-risk populations, and that offering such interventions will increase testing uptake in target populations. With novel approaches to testing urgently needed to reach the 90-90-90 targets, the DCE and targeted methods used in this study may be broadly used to develop cost-effective testing offers that match the preferences of high-risk populations across diverse settings.

To our knowledge this is the first PRCT in which the intervention conditions are designed using data from a DCE, and the first PRCT that evaluates an intervention explicitly targeting preference heterogeneity. If successful, the methods used to understand how different groups of users value key characteristics of a health intervention can readily be applied to other settings in which interventions are being developed or adapted to optimize their efficacy. This work may demonstrate the utility of DCEs as a tool in implementation research to replace the costly practice of iteratively evaluating narrowly focused interventions. Thus, even as we apply this approach to the specific area of HIV testing, the study has potential to significantly advance the fields of patient-oriented research and implementation science. The methods could be used to develop new approaches to adapt effective interventions to local contexts, by informing *a priori* which interventions should be rolled out, and with which modifications, in order to maximize uptake across different populations and sub-populations.

Our study design and implementation approach have several unique components. First, the implementation of the study, in collaboration with all HCT providers in the study area, allows for the evaluation of testing uptake in a nearly closed system. Second, the use of an automated mHealth system to send large numbers of SMS messages according to pre-specified algorithms reduces both error potential and cost. Third, the similarity between hypothetical choice scenarios presented in the DCE and actual HIV testing options given to participants allows for explicit comparisons between stated and revealed preferences. Fourth, the study design allows for separate estimates of the effects of reminder SMS, the issuance of physical HIV testing

invitation cards, and an incentive offer, on HIV testing rates. Finally, the approach for identifying the targeted, enhanced, and less-preferred options is not contingent on the use of RELCL analysis and proprietary software; instead it can be approximated using open source alternatives e.g., in R. In a sensitivity analysis we will evaluate the effect of specific model assumptions on the selection of testing options for the PRCT.

The study is subject to several limitations. First, feasibility considerations limit the study area to include only HCT facilities in Moshi municipality. While coded invitation cards collected from all HCT providers offer definitive evidence of a completed HIV test, participants may test without invitation cards, and may test outside the study area. Sensitivity analyses will characterize the effect of using only provider-documented testing uptake (primary outcome) vs. provider-documented or self-reported testing uptake (secondary outcome) on estimates.

Second, the preference estimates from the DCE, preference informed testing options, and estimated effect sizes are not generalizable to other high-risk groups in Tanzania or other parts of Africa. However, if this study is successful, it will support the broader use of stated preference methods to systematically elicit the preferences of key populations and facilitate corresponding adaptations to HIV testing options. We acknowledge that study eligibility criteria include literacy, and study procedures involve phone- and SMS-based contact with participants. While literacy in the region was 94.4% in 2000, and, in 2017, 93% of urban households had a mobile phone,[62-64] the exclusion of illiterate persons and limited mobile phone access may influence the results. It is also possible that individuals who are likely to move (and thus may not be enrolled or are lost to follow-up) may have different preferences and opportunities for HIV testing.

Third, participants' progression through multiple study phases may influence testing uptake in the PRCT. Ideally, all tangential intervention components (SMS reminders, invitation cards, incentives) could be evaluated alongside the preference-informed HIV testing offer as part of a

multi-arm RCT, however, the sample size required for such a trial is not feasible. A multi-stage enrollment approach and the inclusion of variables describing participants' exposure to SMS reminders, testing offers, and HIV tests in prior study phases as covariates allow us to estimate the direction and magnitude of such ordering effects on uptake. In our study we will not be able to estimate an unconditional effect of incentives on HIV testing uptake, as concurrent incentivized and non-incentivized testing offers were not considered viable among potentially closely-knit community members (e.g., barworkers in the same bar, porters climbing together).

Finally, DCE surveys contain a limited set of testing characteristics; the finite range of attributes and levels is a limitation of DCEs in general. Preference- and choice-relevant testing characteristics may differ in other settings, and changes in the testing environment and available testing options may occur during the study period. While adaptations to the preference survey and analysis of DCE data may be necessary and require technical expertise, such costs are expected to be far smaller than costs associated with large-scale, iterative trials of potentially ineffective HCT testing interventions.

In conclusion, this study evaluates the critical link between preference-based intervention design and efficacy. If the PRCT indicates that a preference-informed, heterogeneity-focused HCT offer increases testing rates, the testing options evaluated in this study can be offered to high-risk populations in the study area, and the preference elicitation method and tools can be used to inform the design of testing options that better match the preferences of other high-risk populations, both locally and in other settings.

Declarations

Ethics approvals

The protocol was registered in ClinicalTrials.gov (Protocol NCT02714140) on March 21, 2016. The protocol was approved by the Institutional Review Boards at Duke University (Duke University Health System IRB, Protocol Pro00075996) and the University of South Carolina (University of South Carolina IRB, facilitated review, Pro00060760) in the United States; as well as the Ethics Review Committee at Kilimanjaro Christian Medical University College (Protocol #901), the National Institute for Medical Research (NIMR/HQ/R.8a/Vol. IX/2603), and the Tanzania Food & Drugs Authority (now Tanzania Medicines and Medical Devices Authority, Authorization No. TZ18CT0017). Protocol amendments will be submitted to these entities as required.

Data availability

Findings from this study will be published in peer-reviewed journals. Data from the proposed study will be stored in a data repository; these data will be de-identified so that they cannot be linked back to individuals. Investigators wishing to use study data to answer new research questions may submit data analysis concept proposals for consideration by the Principal Investigators. The Principal Investigators will review the proposal and will provide those submitting scientifically rigorous and promising proposals access to the data repository to address their research questions.

Consent for publication

All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with ICMJE criteria.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

JO, NT, and BN conceptualized the study. AH, AM, BF, BN, DB, JO, and NT were involved in the development and submission of the funding application. All authors contributed to the development of the study protocol. JO and NT contributed equally to the development of this manuscript, wrote the first draft of the manuscript, and led subsequent revisions. MM developed the *comet* software for the collection of DCE data on iPads. AH, AM, AS, BF, BN, DB, JO, MLM, MM, MZ, NT, and TM read the manuscript and provided critical input. All authors read and approved the final manuscript.

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List of abbreviations

CTCs	HIV care and treatment centres
CFTs	Conditional financial transfers
DCE	Discrete choice experiment
FBW	Female barworkers
FGD	Focus group discussion
FU	Follow-up
HCT	HIV counseling and testing
HIV	Human Immunodeficiency Virus
HSHSP-IV	Tanzania's 2017-22 Health Sector HIV and AIDS Strategic Plan
IRB	Institutional Review Board
KCRI	Kilimanjaro Clinical Research Institute
KMP	Kilimanjaro mountain porters
LMICs	Low- and middle-income countries
mHealth	Mobile health
mParis	Mobile phone assisted reminder and incentive system
NIMR	National Institute for Medical Research
PLWH	Persons living with HIV
PRCT	Pragmatic randomized controlled trial
RELCL	Random effects latent class logit
SMS	Short messaging system (text messages)
UNAIDS	Joint United Nations Programme on HIV and AIDS

Table 1. HIV testing options offered across the three study arms in the pragmatic randomized controlled trial

Arm	Offers	Description
1	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from a mixed logit model.
	3 targeted options	Comprise features *widely available* in the study area and are predicted to be jointly more-preferred than the common option by the largest possible share of participants.
2	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from a mixed logit model.
	3 enhanced options	Include additional features that are *not yet widely available* in the study area and predicted to be jointly more-preferred than the common option by the largest possible share of participants.
3	1 common option	Combines the on average most preferred levels of each attribute included in the DCE, as described by the mean parameter estimates from a mixed logit model.
	3 less preferred options	Includes options that are widely available in the study area and jointly predicted to be equally or less-preferred than the common option by the largest possible share of participants.

DCE = Discrete Choice Experiment

Table 2. Schedule of activities

Phase	Time point	Target timing	Key activity	Key information collected
A	t_A	Enrollment	Baseline survey	HIV testing preferences, history, HIV risk, socio-demographics
	$t_{Afu} = t_B$*	t_A + 91 days	Phone-based FU	HIV testing uptake since t_A
B	t_{Bs}	t_B + 28 days	SMS reminder	
	t_{Bfu}	t_B + 91 days	Phone-based FU	HIV testing uptake since t_B
C#	$t_{Bx} = t_C$	t_{Bfu} + < 91 days	Testing invitation ("common" option)	
	t_{CS}	t_C + 28 days	SMS reminder	
	t_{Cfu}	t_C + 91 days	Card collection from testing sites, phone-based FU	HIV testing uptake since t_C
D#	$t_{Cx} = t_D$	t_{Cfu} + < 91 days	4 testing invitations, study arm specific	
	t_{Ds}	t_D + 28 days	SMS reminder	
	t_{Dfu}	t_D + 91 days	Card collection from testing sites, phone-based FU	HIV testing uptake since t_D
E	t_E	t_{Dfu} + < 91 days	Phone call and SMS message with incentive offer	
	t_{Es}	t_D + 28 days	SMS reminder	
	t_{Efu}	t_E + 91 days	Card collection from testing sites, phone-based FU	Choice among testing options offered, HIV testing uptake since t_E

* The phone-based follow-up at the end of Phase A constitutes the beginning of phase B

To reduce variability across participants in the timing of Phase D, some participants may be enrolled directly into Phases C and D. FU: follow-up

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Figure Legend

Figure 1. Study design

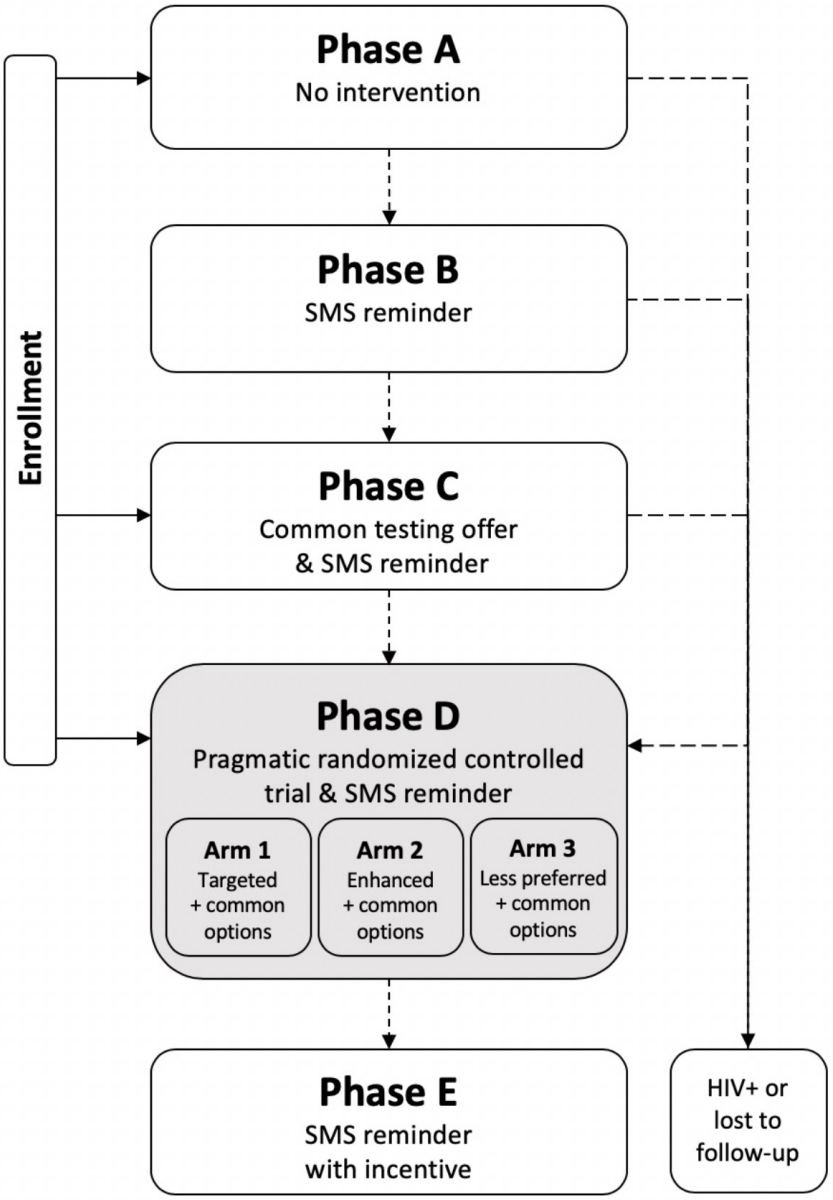

Figure 1. Study design

205x294mm (144 x 144 DPI)

Supplemental File 1. CONSORT checklist for pragmatic randomized controlled trials

SECTION and topic	Item #	Descriptor[1]	Reported on page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., random allocation", "randomized", or "randomly assigned").	2
INTRODUCTION			
Background	2	Scientific background and explanation of rationale. **EXT**: Describe the health or health service problem that the intervention is intended to address and other interventions that may commonly be aimed at this problem.	6
METHODS			
Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected. **EXT**: Eligibility criteria should be explicitly framed to show the degree to which they include typical participants and/or, where applicable, typical providers (eg, nurses), institutions (eg, hospitals), communities (or localities eg, towns) and settings of care (eg, different healthcare financing systems).	8

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered. **EXT**: Describe extra resources added to (or resources removed from) usual settings in order to implement intervention. Indicate if efforts were made to standardise the intervention or if the intervention and its delivery were allowed to vary between participants, practitioners, or study sites. Describe the comparator in similar detail to the intervention	9, 12
Objectives	5	Specific objectives and hypotheses.	8
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors). **EXT**: Explain why the chosen outcomes and, when relevant, the length of follow-up are considered important to those who will use the results of the trial	5, 22
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. **EXT**: If calculated using the smallest difference considered important by the target decision maker audience (the minimally important difference) then report where this difference was obtained	21

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Randomization:			
Sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification).	12
Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	12
Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	12
Blinding (Masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated. **EXT**: If blinding was not done, or was not possible, explain why	18
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	20
RESULTS			

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons. **EXT**: The number of participants or units approached to take part in the trial, the number which were eligible, and reasons for nonparticipation should be reported	19
Recruitment	14	Dates defining the periods of recruitment and follow-up.	n/a
Baseline data	15	Baseline demographic and clinical characteristics of each group.	n/a
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	17
Outcomes and Estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	n/a

SECTION and topic	Item #	Descriptor[1]	Reported on page #
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	n/a
Adverse events	19	All important adverse events or side effects in each intervention group.	n/a
DISCUSSION			
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	n/a
Generalizability	21	Generalizability (external validity) of the trial findings. **EXT**: Describe key aspects of the setting which determined the trial results. Discuss possible differences in other settings where clinical traditions, health service organisation, staffing, or resources may vary from those of the trial.	n/a
Overall evidence	22	General interpretation of the results in the context of current evidence.	n/a

[1] EXT denotes a pragmatic trial extension of the CONSORT statement.

https://www.bmj.com/content/bmj/337/bmj.a2390.full.pdf

Supplemental File 2: WHO Trial Registration Data Set

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT02714140
Date of registration in primary registry	March 21, 2016
Secondary identifying numbers	N/A
Source of monetary/material support	National Institute of Mental Health (R01MH106388) 6001 Executive Boulevard Bethesda, MD 20892-9663
Primary sponsor	University of South Carolina, USA
Secondary sponsor(s)	Kilimanjaro Christian Medical Centre, Tanzania
Contact for public queries	Jan Ostermann, PhD Ph: 8037778747 jano@mailbox.sc.edu Nathan Thielman, MD Ph: 9196681721 n.thielman@duke.edu
Contact for scientific queries	Jan Ostermann, PhD Ph: 8037778747 jano@mailbox.sc.edu Nathan Thielman, MD Ph: 9196681721 n.thielman@duke.edu
Public title	Does Preference-based HIV Testing Increase Uptake in High Risk Populations?
Scientific title	Using DCEs to Identify and Match Preferences for HIV/AIDS Counseling and Testing (DCE-IMPACT)
Countries of recruitment	Tanzania
Health conditions or problems studied	HIV, HIV testing
Intervention(s)	Behavioral: Invitation cards Behavioral: Reminders Behavioral: Conditional economic transfers
Key inclusion and exclusion criteria	Ages Eligible for Study: 18 Years and older Sexes Eligible for Study: Any Accepts Healthy Volunteers: Yes Inclusion criteria: Women employed in bars, restaurants and guesthouses serving alcohol to patrons (“female barworkers”) and male mountain porters who are supporting climbers of nearby Mount Kilimanjaro (“Kilimanjaro mountain porters”) Exclusion criteria: Unable to read
Study type	Interventional (Clinical Trial)
Date of first enrolment	12-February-2019
Target sample size	1200
Recruitment status	Ongoing
Primary outcome(s)	Uptake of HIV testing
Key secondary outcomes	N/A

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

Supplemental File 3. SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	26
	2b	All items from the World Health Organization Trial Registration Data Set	Supplementary File 2
Protocol version	3	Date and version identifier	26
Funding	4	Sources and types of financial, material, and other support	28
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	28
	5b	Name and contact information for the trial sponsor	Supplementary File 2
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	28
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-8
	6b	Explanation for choice of comparators	8
Objectives	7	Specific objectives or hypotheses	8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	8
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	22
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Figure 1 and Table 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	21
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	17
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	12
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	12,18
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	12
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	18
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Table 2
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	20

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	22
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	20
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	20
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	20
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	26
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	26

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	17
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	22
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	27
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	27
	31b	Authorship eligibility guidelines and any intended use of professional writers	27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	27
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	**Supplemental File 4**
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Form M0345

DUKE UNIVERSITY HEALTH SYSTEM

Tumaini University
Kilimanjaro Christian Medical College

ID: ___ ___ - ___ ___ ___ - ___

Name: _____

Fingerprint:

Consent to participate in a research study: **Identifying and Matching Individuals' Preferences for HIV/AIDS Counseling**
Survey Consent, Version Date 13-Dec-2019

Concise Summary

This is a research study to learn about preferences for HIV testing.

If you decide to enroll in this study, you will be asked to complete a survey administered by a study interviewer. The survey will ask you questions about your background (such as age and marital status), HIV testing history, and what you like or don't like about different HIV testing options.

At the end of the survey, we will describe several free testing options that you might want to use in the future. We will contact you periodically during the next 24 months to see if, and how, you decided to test for HIV.

There are no major risks involved with study participation.

If you are interested in learning more about this study, please continue reading below.

Introduction:
You are asked to take part in a research study about preferences for HIV testing. This study is under the direction of Dr. Bernard Njau at Kilimanjaro Christian Medical Centre and Drs. Jan Ostermann and Nathan Thielman at Duke University and the University of South Carolina in the United States. This study is sponsored by the United States' National Institutes of Health.

Research studies are voluntary. As your study staff member reads this form to you, please take your time deciding whether to participate. Please ask him/her to explain anything that you do not clearly understand. The purpose of the study, procedures, risks, and benefits are described below.

The research team will give you a copy of this form. It is important that you know:

- Your participation is entirely voluntary;
- You may decide not to take part or to withdraw from the study at any time

Form M0345

DUKE UNIVERSITY HEALTH SYSTEM

Tumaini University
Kilimanjaro Christian Medical College

ID: ___ ___ - ___ ___ ___ - ___

Name: _____

Fingerprint:

Consent to participate in a research study: **Identifying and Matching Individuals' Preferences for HIV/AIDS Counseling**
Survey Consent, Version Date 13-Dec-2019

Purpose:
The purpose of this study is to determine which characteristics of HIV testing programs influence HIV testing decisions.

Who Will Be In This Study and How Long Will This Study Last?
Approximately 2,500 persons will participate in surveys about HIV testing. After the completion of today's survey, you may be contacted again during the next 24 months with follow-up questions and offers for HIV testing.

Procedures:
The survey will last approximately 60 minutes. After you have signed and dated the consent form we will ask you questions about issues such as:

- Age and marital status,
- HIV risk behaviors,
- HIV testing, and
- Attitudes toward different HIV testing options
- Experiences with HIV treatment

Some participants will receive invitation cards to test for HIV. You may receive SMS reminders or incentives to test, and you will be periodically re-contacted to answer questions about your risk behaviors and testing decisions. You may also be offered other testing options in the future. HIV test results will be linked to your study data without your name.

Risks and discomforts:
Talking about HIV testing may cause some people to experience discomfort. You can refuse to answer any questions, and you can stop the interview at any time.

Benefits:
You will not receive any direct benefit from participating.

Confidentiality:
Study records will be kept confidential as required by law. Your records will be assigned a unique study number. If you choose to test for HIV using any of the options offered to you, only this number will be used to link your HIV test result to your study data. If we collect your fingerprints today, they may be used to verify your identity. All information is stored in a secure database. Information that links your name to the study number will be kept in a locked cabinet that can only be accessed by members of the research team. Your survey data will be shared with members of the research team at Duke University and the University of South Carolina in the U.S. When information is sent to the U.S. it is sent through a secure

Form M0345

DUKE UNIVERSITY HEALTH SYSTEM

Tumaini University
Kilimanjaro Christian Medical College

ID: ___ ___ - ___ ___ ___ - ___

Phone: 0_____

Fingerprint:

internet connection. When information from this study is presented at scientific meetings or in scientific journals, your identity will not be revealed.

A description of this clinical trial will be available on *www.ClinicalTrials.gov*, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Voluntary Participation/Right to Withdraw:
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you agree to participate, you may refuse to answer any question or stop the interview at any time. Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits and will not affect your access to health care.

Cost to you:
There is no cost to you for taking part in this research study.

Payments to participants:
You will receive a minimum of TSH 10,000 after the completion of today's survey, and after any other survey for which you are asked to return to the study offices. After receiving the compensation you may be offered choices that could result in a higher or lower amount.

Whom do I call if I have questions or problems?
For questions about this study or if you have problems, concerns, questions, or suggestions about the research, contact Dr. Bernard Njau at KCMC (telephone number 0784-300-846). For questions about your rights as a research participant or to discuss problems or concerns related to the research contact the KCMC Ethics Committee at 027-275-3616.

Form M0345

DUKE UNIVERSITY HEALTH SYSTEM

Tumaini University
Kilimanjaro Christian Medical College

ID: ___ ___ - ___ ___ ___ - ___

DOB: ___ ___ / ___ ___ / 19 ___ ___
(dd / mm / yyyy)

Fingerprint:

Consent to participate in a research study: **Identifying and Matching Individuals' Preferences for HIV/AIDS Counseling**
Survey Consent, Version Date 13-Dec-2019

Optional permission for future contact:
I give permission for members of the research team for this study to contact me about other components of this study, or about other studies, in the future. It will be my choice whether or not to participate in those studies at that time.

_____ Yes _____No _____Initials

STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____
Name of Participant in block letters

_____ _____ _____
Signature of Participant Date Time

_____
Name of Interviewer in block letters

_____ _____ _____
Signature of Interviewer Date Time