Efficacy Testing of a Culturally Relevant Stigma Intervention in WLWH in Tanzania
Approval Date: 04/23/2024
NCT05033002

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DUHS IRB Application (Version 1.7)

General Information

*Please enter the full title of your protocol:		
Efficacy Testing of a Culturally Relevant Stigma Intervention in WLWH in Tanzania		
***Please enter the Short Title you would like to use to reference the study:**		
Stigma Efficacy Trial, Tanzania * This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.		

Standard Research Summary

Purpose of the Study

- Objectives & hypotheses to be tested

The scientific premise of this program of research is that stigma has significant and negative effects on various psychosocial, behavioral, and clinical outcomes associated with prevention, care, and treatment among Tanzanian WLWH.

For this specific study, we will obtain the following feasibility information:

· Recruitment metrics: length of time to complete participant recruitment; barriers to recruitment; percent of total participants screened who meet screening criteria (median score of IHSS; intention to remain resident in study area for duration of study) to meet sample size requirements for future RO1;

· Retention metrics: attendance and completion of the five group intervention sessions, punctuality. We will also monitor the number of pre-session contacts for each study participant and the amount and type of follow-up required for participants who miss one or more study visits.

· Timing and Completeness of study instruments: time (minutes) it takes to complete the questionnaires; missing data from questionnaires.

· Fidelity: to evaluate fidelity to the study protocol and structured debriefing of each story, we will use detailed fidelity checklists. RAs will complete a process rating form at the end of each intervention session capturing issues of feasibility, coverage of debriefing session content, length of session, disruptions, issues raised during the session, and level of participant engagement with the material. The training team will maintain attendance rosters for each session, noting when participants leave the room and if/when they return.

Hypothesis: Although not formally articulated in the grant application, we hypothesis that the stigma intervention to be tested in this study (Labda Siku Moja) will reduce internalized stigma and improve coping self-efficacy, self-esteem, and hope among women living with HIV (WLWH) in Tanzania.

Background & Significance

- Should support the scientific aims of the research

HIV-related stigma yields a number of negative outcomes[1] among women living with HIV (WLHW) including a diminished self-efficacy for disclosing one's HIV status to family members, friends,

and sexual partners[7-8]; postponed or refused care (non-engagement in care) [1, 9-10]; healthcare services sought outside one's community for fear of confidentiality breaches[6]; delayed early initiation of antiretroviral therapy (ART)[9]; diminished ART adherence[1, 9-11]; diminished hope[12-13]; increased psychological distress, including depression[14-18]; and a reduced quality of life[18-20].

This highly significant study focuses on Tanzania – a country in east Africa – where the burden of HIV, and its related stigma, is disproportionately prevalent among WLWH[17]. In support of PAR-19-326, **this study will test the feasibility and preliminary efficacy of the internalized stigma reduction intervention, *Labda Siku Moja: Sauti za Wanawake Wanaoishi na VVU*** (Maybe Someday: Voices of Women Living with HIV) supporting the program announcement's goal "to improve health seeking behaviors across the HIV…care continuum and improve biologic and mental health outcomes" in Tanzanian WLWH. ***Labda Siku Moja* is a theoretically based, culturally relevant, linguistically sensitive, sex specific internalized stigma reduction intervention developed for Tanzanian WLWH**.

In Tanzania, where 80% of the population lives in rural areas[24] and HIV is the third leading cause of death[25], an estimated 880,000 women are living with HIV[26]. In sub-Saharan Africa, including Tanzania, **WLWH contract HIV at least 5 to 7 years earlier than men[27]** because they are more likely to have older partners, get married earlier, and have greater challenges in negotiating safer sex because of gender inequality[28]. In 2018, according to UNAIDS, 4.6% of Tanzanian adults between the ages of 15 and 49 were living with HIV with the **prevalence being higher among women** (♀ = 6.0%: ♂=3.6%)[26]. Although the prevalence is higher in urban areas (urban, 7.5% versus rural, 4.5%)[29], this study will also recruit rural WLWH since most of the Tanzanian population live in rural areas. Further, one could argue that the *Labda Siku Moja* intervention may be even more useful for women in isolated, rural areas, as they would have fewer opportunities to see women as portrayed in the stories[30]. There are **dispr oportionate rates of new infections among young women in Tanzania** (ages 15-24) compared to their male counterparts of the same age[26]. In 2012, women aged 23-24 were twice as likely to be living with HIV as men of the same age[28]. Data from the representative 2016-2017 Tanzania Impact Survey identified that **women between the ages of 15 and 39 are more than twice as likely to be living with HIV as their male counterparts[31]**. Additionally, **the highest HIV prevalence rate in Tanzania is among women aged 45-49, at 12%** (compared with 8.4% among men of this age)[31]. Thus, in the design of this proposed study, we are focusing on WLWH since they are disproportionately impacted and will purposively recruit based on geography (urban and rural) and age (18-24 and 25+).

The United Republic of Tanzania's *Fourth Health Sector HIV and AIDS Strategic Plan (HSHSP- IV) 2017-2022*[29] calls for the elimination of HIV related stigma and discrimination recognizing its negative impact on PLWH; and achieving the 90-90-90 targets (now the 95-95-95 targets for 2030). The most recent Tanzanian *PLWH Stigma and Discrimination Survey*[32] (2013; N = 2205, 57% of sample = WLWH) documented that:

- "Being gossiped, verbally insulted, exclusion from social, family as well as religious activities were the leading forms of stigmatization whereby Dar es Salaam indicated high levels of stigma (49.7%) as compared to (39.4%) from other regions, females experienced more gossiping than male counterparts in both regions" [32. p. vi].
- Compared to men, WLWH had higher rates of feeling ashamed (29.8%) and feeling suicidal (7.0%) or nearly equal rates for feeling guilty (13.8%), having a low self-esteem (42.9%), and believing they should be punished (5.4%)[32].

In appraising the current literature on HIV-related stigma interventions, Pantelic et al. (2019)[33] and Ma et al. (2019)[34] recently shifted the focus toward systematic examination of interventions specifically aimed at reducing self-stigma or internalized stigma in PLWH. Pantelic et al.[33] further differentiated their focus by only examining self-stigma or internalized stigma interventions (N=20) implemented in low- and middle-income settings. The parent intervention to the *Labda Siku Moja* intervention – the *Maybe Someday* intervention developed by Sandelowski and Barroso[4, 22] and tested by Barroso and Relf in the Southern US (R21NR021415)[23, 35] was identified in the Ma et al systematic review[34] as being one of the few to use an RCT design with sufficient power and include a qualitative evaluation of the intervention – the two identified limitations of the internalized stigma reduction interventions identified in this systematic review. **I n Tanzania, despite the negative impact of stigma on psychosocial, behavioral, and clinical HIV outcomes, rigorously tested, efficacious interventions to mitigate the negative effects of internalized stigma associated with HIV among women are limited, and critically needed.**

Design & Procedures

- Describe the study, providing details regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

This individually randomized, group-treatment feasibility and efficacy trial will compare the *Labda Siku Moja* internalized stigma intervention to treatment as usual (TAU). Treatment as usual will consist of routine care offered by each site; currently, there is no specific stigma reduction intervention delivered as part of routine care in Tanzania. Specifically, feasibility will utilize a process evaluation approach while efficacy and determination of effect sizes will utilize a 2x4 repeated measures randomized controlled trial (2 treatments x 4 time points [baseline, 30 days, 90 days, 180 days]) with a post-intervention focus group "to expand our understanding of how best to deliver the intervention, it is crucial to include the voices of the participants in the evaluation of the intervention" as advocated by Ma et al.[34]. By conducting a post-intervention focus groups, we can "elicit the participants' experiences with the intervention and their perceptions of it, and provide insights into the acceptability and feasibility of the intervention, and how to further improve it"[34, p. 739].

Intervention Procedures. Before implementing the intervention, we will work with the Community and Technical Advisory Board (CTAB) to finalize all study procedures. The CTAB will consist of 6 to 8 individuals and will be co-chaired by a social/ behavioral scientist experienced in HIV research, Dr. Lusajo Kajula, and a national HIV community advocate, Ms. Pfiriaeli Kiwia, Program Coordinator and Co-Founder, Kimara Peer Educators and Health Promoters (please see letters of support). Other CTAB members may include health center or dispensary staff, a representative from TACAIDS and/or the National AIDS Control Program/ MOH, and at least one WLWH. This CTAB will provide guidance on all study and human subjects protection procedures and will help identify mechanisms to recruit WLWH who may be disconnected from care.

The intervention will be delivered via in-person groups. These groups will be held at either the dispensary or health center where the WLWH were recruited or at MUHAS. Regardless of site, the group/cohort meetings will occur in a private room. The stories of the *Labda Siku Moja* intervention will be viewed on either a health facility/dispensary TV or projected from a laptop using existing equipment. During the 5 weekly meetings, intervention arm participants will view one story and have a structured debrief by the Tanzania MPI; the structured debrief will use Motivational Interviewing (MI)[42], a practical, empathetic, and short-term process that recognizes the difficulty of making life changes. MI utilizes a spirit of empathy, acceptance, respect, honesty, and caring, which helps in building warm, trusting relationships. MI will help the participants in the intervention arm of this study to explore and resolve issues, feelings, and insecurities associated with HIV-related stigma.

The recruited sample recruited will be comprised of both **urban and rural Tanzanian WLWH,purposively stratified by age (18-24/25+)**. Eligible participants will be individually randomized in 8 waves (8 waves x 10 participants/wave x 2 sites (urban site and rural site) yielding the sample of 160 participants (80 intervention arm and 80 control arm). Up to 200 may be consented to factor in for screen failures.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

Study Sample Recruitment.
We will recruit 160 WLWH in total for this study. The sample recruited will be comprised of both urban and rural Tanzanian WLWH, purposively stratified by age (18-24/25+). Eligible participants will be individually randomized in 8 waves (8 waves x 10 participants/wave x 2 sites (urban site and rural site) yielding the sample of 160 participants (up to 200 may be consented to factor for screen failures) (80 intervention arm and 80 control arm). We will recruit at community-based clinics, health centers, and dispensaries in the Kinondoni Municipal District (part of urban Dar es Salaam) and a rural area different that the current R21 study (recruited rural participants from Lushoto); for this proposed study, we will recruit from one or more of the following rural sites – Bagamoyo, Kigamboni, Mkuranga. At both the urban and rural sites, staff at these organizations who are already aware of the woman's HIV status will approach potential respondents to introduce the study. At health centers and dispensaries, staff will be particularly encouraged to refer WLWH who are not regularly engaged in care and/or not virologically suppressed to help facilitate reaching a population not stably engaged and retained in care. Study staff will only meet WLWH who, after learning about the study from the above agencies, indicate they are potentially interested in learning more the study. Convenience sampling will be employed, however purposively

ensuring both young women (18-24) and older women (25+) living with HIV and urban and rural WLWH will be a focus. This study team has successfully recruited from these sites in previous studies.

Inclusion Criteria.
The inclusion criteria for this study are: (1) women who are living with HIV; (2) age 18 (age of adulthood as defined by the Tanzanian government); (3) able and willing to voluntarily consent to participate in the study; (4) able to travel to a data collection in their local community (as described above); (5) demonstrate mental competence at time of informed consent; (6) verbally indicate that they plan to reside in their current community for at least 6 months after enrollment (necessary to prevent attrition); and (7) score at the median or higher level on the Swahili Version of the Multidimensional Measure of Internalized HIV Stigma Scale.

Exclusion Criteria.
At the time of obtaining informed consent, eligible participants will be excluded if there is (1) any acute psychological or physiological distress; if there is evidence of acute psychologic and/or physiologic, they will be excluded from this study and referred to an appropriate site for evaluation and treatment. (2) Transgender women living with HIV will not be eligible to participate in this study to reduce the potential for confounding sources of stigma recognizing that a transgender identity is highly stigmatized and culturally sensitive in Tanzania. Further, it would be exceedingly difficult to recruit a sufficient sample of transgender women living with HIV to conduct an appropriate analysis. (3) Participants may be enrolled in other HIV-related studies except cognitive-behavioral intervention studies addressing stigma, self-efficacy, self-esteem, and/or disclosure

Subject Recruitment and Compensation

- Describe recruitment procedures, including who will introduce the study to potential subjects. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about approximately how many DUHS subjects will be recruited. If subjects are to be compensated, provide specific prorated amounts to be provided for expenses such as travel and/or lost wages, and/or for inducement to participate.

Recruitment.
At both the urban and rural sites, staff at these organizations who are already aware of the woman's HIV status will approach potential respondents to introduce the study. At health centers and dispensaries, staff will be particularly encouraged to refer WLWH who are not regularly engaged in care and/or not virologically suppressed to help facilitate reaching a population not stably engaged and retained in care. Study staff will only meet WLWH who, after learning about the study from the above agencies, indicate they are potentially interested in learning more the study. Convenience sampling will be employed, however purposively ensuring both young women (18-24) and older women (25+) living with HIV and urban and rural WLWH will be a focus. This study team has successfully recruited from these sites in previous studies.

Retention.
At the time of enrollment, the study protocol, including the number of study visits will be explained in detail. To help facilitate retention, study participants will be asked to provide a mobile phone number to facilitate outreach to remind participants of upcoming study visits. We will obtain permission to contact them via this mobile phone (phone, SMS, WhatsApp) as part of the informed consent process. After each wave of data collection, participant information will be updated, in case they have changed their phone number or address.

Additionally, we will ask each study participant to provide the name and contact information for two persons from their social network who the participant has designated as a "safe contact". Using a "safe contact" locator form, the study staff will records the contact information for friends and family members who may be contacted in the event the participant misses a visit, with the consent of the participant.

This "safe contact" will only be contacted if we are unable to contact the individual study participant after 5 attempts over 5 different days. If this individual is contacted, we will use a standardized script developed with the study participant and documented in the participant's study protocol file with the informed consent document to explain the purpose of the call. In all situations, we will not discuss anything about HIV.

Particularly for follow-up study visits (30-60-90-180 days), we will offer flexible scheduling options. This may include early morning or late afternoon visits as well as visits on Saturday. During each study visit, in addition to the reimbursement for time and transportation reimbursement, participants will receive small tokens of appreciation for either themselves or a child. These small tokens of appreciation might be a pen, notebook, and/or personal hygiene product.

Community engagement through Community and Technical Advisory Board (CTAB) and relationship building with health centers/dispensaries will enable the broad support needed to better follow up with and retain participants.

Compensation.
UPDATED, 8 September 2022:

All women who are screened for the study, will receive an incentive as described below:

- not eligible-get incentive ($2.50)
- eligible-decline enrollment-get incentive ($2.50)
- eligible-enroll-complete rest of questionnaire-get incentive ($5)

ORIGINAL TEXT
Participants will receive 20,000 Tanzanian Schilling (TZA; equivalent of $8.50) USD for the baseline study visit and the 30 day study visit. For participants in the intervention arm, they will also receive $8USD for each of the 5 intervention study visits. At the 90 and 180 day study visits, participants will receive 30,000 Tanzanian Schillings (equivalent to ~$13.00USD). This compensation should cover transportation costs and loss of income for study participation.

Tanzania salary information for comparative purposes: In Tanzania, the average daily wage in Tanzania ranges from 3077 TZS for domestic workers to 15,3835 TZS for someone working in the mining sector /financial institution/international company. Reference: Etyang, D. (2017). An Analysis of Wages and Collective Bargaining in Tanzania - 2016. May 2017 - ALREI - WageIndicator Foundation, Amsterdam.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

This study will not enroll individuals who do not have capacity to provide informed consent. All study staff (PD, RAs), as a part of their orientation to the study protocol, will receive information about capacity to provide consent. The PD for the study will be an individual with an MSc in Clinical Psychology.

Study Interventions

- If not already presented in #4 above, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i.e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

This study will not use an investigational drug or biologic or device.

This study's intervention will include 5 ethnodramas identified to be culturally and linguistically acceptable through a mixed methods evaluation in a previous R21 with the same study team. These 5 ethnodramas associated with the Labda Siku Moja are described in detail **in Table 2 of the full grant application** which is attached. T**hey are also provided as an attachment/appendix**

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant individuals, imprisoned persons or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Participation in this study is completely voluntary. Those who personally select not to participate, if inclusion/criteria are met, will receive usual care associated with HIV. In this situation, there is no usual care condition for stigma.

This individually randomized, group-treatment feasibility and efficacy trial will compare the Labda Siku Moja internalized stigma intervention to treatment as usual (TAU). Treatment as usual will consist of routine care offered by each site; currently, there is no specific stigma reduction intervention delivered as part of routine care in Tanzania. Specifically, feasibility will utilize a process evaluation approach while efficacy and determination of effect sizes will utilize a 2x4 repeated measures randomized controlled trial (2 treatments x 4 time points [baseline, 30 days, 90 days, 180 days]) with a post-intervention focus group "to expand our understanding of how best to deliver the intervention, it is crucial to include the voices of the participants in the evaluation of the intervention" as advocated by Ma et al.34. By conducting a post-intervention focus groups, we can "elicit the participants' experiences with the intervention and their perceptions of it, and provide insights into the acceptability and feasibility of the intervention, and how to further improve it"34, p. 739. A flow diagram of the study is illustrated **in figure 3 of the full grant application which is attached**.

Risk:
There is minimal risk to human participants in this proposed study. Nonetheless, rigorous efforts will be made to protect them. We will recruit a total of 160 participants for this study. The WLWH will be recruited by a project team member across urban and rural areas in Tanzania. Community-based clinics and health centers/dispensaries providing HIV care and treatment services, and HIV/AIDS service organizations involving WLWH will be the primary recruitment sites.

The study team has successfully recruited from these sites/agencies previously. IRB approval will be sought in accordance with all domestic and foreign regulations. As such, in the Republic of Tanzania, the study will be reviewed by the IRB at Muhimbili University of Health and Applied Sciences (MUHAS) and will be registered with the National Institute of Medical Research (NIMR). The study will also obtain IRB approval from Duke University since this is the coordinating site of the project. In standard operating procedure, once approval is obtained from MUHAS, NIMR, and Duke University, RTI will defer IRB approval to Duke University.

We will obtain written informed consent, or thumb print confirmation for those who are illiterate, from the participants prior to initiating any study activities. The Tanzanian MPI, project director or research assistant will screen eligible participants with regard to inclusion/exclusion criteria.

Benefits:
There are possible benefits to participants of this study. All participants will help researchers better understand stigma, coping self-efficacy, ART medication adherence, engaging in care, sexual risk behaviors and quality of life. Completion of study instruments will allow the women an opportunity to express past/recent experiences. Participants will receive the equivalent of $8USD to $13USD for their time (lost wages) and to cover travel associated costs. The risks to participants are both minimal and reasonable in relation to the anticipated benefits to participants and others.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

Participants in this study will not incur any costs.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

STATISTICAL DESIGN AND POWER

Power Analysis. The proposed study is designed to assess the preliminary efficacy of the intervention and to generate pilot data to support the conduct of a larger trial. The sample size of 160 is, therefore, primarily determined by whether the intervention could be feasibly implemented in a larger, multi-site study and to calculate a pooled effect size for the primary outcomes so as to determine the sample size necessary for such a large study, rather than by the power to detect specified effect sizes. Nevertheless, we have conducted a power analysis using the Optimal Design[47] for mixed effects models on repeated measures of continuous outcomes, employing an intention-to-treatment analysis. The power analysis revealed that a total sample size of 160 (i.e, 80 in each treatment arm) would achieve 80% power to detect a standardized effect size δ of 0.51 with four repeated measurements, assuming an intra-class correlation of 0.70 and a two-tailed alpha of .05. The standardized effect size δ is analogous to Cohen's *d* for which Cohen defines 0.20 as a small effect, 0.50 as a medium effect size, and 0.80 as a large effect[48]. Thus, we will have sufficient power to detect a medium effect size of the longitudinal intervention effect on a linear trend of stigma, coping self-efficacy, and self-esteem over time. For comparing intervention effects at days 30, 90, and 180, cross-sectionally, the results from another power analysis with the G*Power[49] on independent-sample tests show that we will have 80% power to detect a close to medium effect size of Cohen's $d = 0.45$. Additionally, we expect the dropout rate will be less than 10% based on studies we have conducted in this area, and attrition between conditions will not differ. The sample size will not require an attrition adjustment because mixed-effects models allow for data missing at random.

Statistical Analysis, Aim #1, Feasibility: To assess the feasibility, the following parameters will be collected and evaluated:
·Recruitment: to identify the length of time to complete participant recruitment; identify barriers to recruitment; to assess the number of participants who meet screening criteria (median score of IHSS) to meet sample size estimation; to determine capacity to recruit women who may not be engaged in care
·Retention: to assess adherence to and completion of the intervention (high-intensity intervention), attendance and punctuality for group intervention sessions
·Measurement: to assess the time (minutes) it takes to complete the questionnaires; to evaluate missing data from questionnaires
·Fidelity: to evaluate fidelity to study protocol and structured debriefing using Motivational Interviewing will be done using detailed fidelity checklists. These fidelity checklists will evaluate delivery of a list of important teaching components in each session
·Process Evaluation: to conduct a qualitative evaluation with participants to identify barriers and facilitators, perceptions, and overall satisfaction with the *Labda Siku Moja* intervention

Statistical Analysis, Aim #2: We will conduct an intention-to-treat analysis which will include all women randomized to determine whether women living with HIV who viewed the video experience a greater reduction in internalized stigma and greater improvements in coping self-efficacy and self-esteem over the 180 days than women in the control condition. Two-tailed statistical tests will be performed using SAS 9.4. For this exploratory study, the significance level will not be adjusted for multiple tests. Student *t*-tests and chi-square tests will be used to test whether the randomization balanced the conditions on key baseline characteristics and baseline scores on the main outcomes. If treatment conditions differ significantly on any these characteristics, which is unlikely to happen though due to the random assignment, the baseline measure would be controlled as a covariate in subsequent analyses. Random coefficients regression models (a type of hierarchical mixed effects model for repeated measures) will be used to examine between-condition differences in change over time (trajectories across baseline, 30 days, 90 days, and 180 days) in the outcomes. Fixed effects will be condition, time, and condition-by-time, while random effects will be participant and participant-by-time. If necessary, baseline covariates will be included as fixed effects. We will also conduct *a priori* contrasts to examine differences between treatment conditions at 30, 90, and 180 days. Observed effect sizes will be calculated for the condition-by-time effects (rate of change) and between-condition differences at 30, 90, and 180 days.

Estimated Time to Target Accrual and Accrual Rate:
Study Sample Recruitment. We will recruit 160 WLWH in total for this study. The sample recruited will be comprised of both **urban and rural Tanzanian WLWH, purposively stratified by age (18-24/25+)** . Eligible participants will be individually randomized in 8 waves (8 waves x 10 participants/wave x 2 sites (urban site and rural site) yielding the sample of 160 participants (80 intervention arm and 80 control arm).

We will recruit at community-based clinics, health centers, and dispensaries in the Kinondoni Municipal District (part of urban Dar es Salaam) and a rural area different from a previous R21 study (recruited rural participants from Lushoto); for this proposed study, we will recruit from one or more of the following rural sites – Bagamoyo, Kigamboni, Mkuranga. At both the urban and rural sites, staff at these organizations who are already aware of the woman's HIV status will approach potential respondents to introduce the study. At health centers and dispensaries, staff will be particularly encouraged to refer WLWH who are not regularly engaged in care and/or not virologically suppressed to help facilitate reaching a population not stably engaged and retained in care.

Study staff will only meet WLWH who, after learning about the study from the above agencies, indicate they are potentially interested in learning more the study. Convenience sampling will be employed, however purposively ensuring both young women (18-24) and older women (25+) living with HIV and urban and rural WLWH will be a focus. This study team has successfully recruited from these sites in previous studies.

Time/Accrual Rate.
In accordance with the study timeline, we will recruit participants beginning in Year1/Month 6 and follow participants through Year 2/Month 9. Control and intervention eligible participants will be individually randomized in 8 waves (8 waves x 10 participants/wave x 2 sites (urban site and rural site) yielding the sample of 160 participants (80 intervention arm and 80 control arm). We estimate that it will take 6 months to complete recruitment.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

The MPIs (Relf, Nyblade, Kilonzo) will virtually meet bi-weekly with the Project Leadership Team (please refer to study team structure) to monitor the conduct of the study and ensure that the study protocol is implemented as written. All project team members will be instructed to notify either the Tanzanian MPI (Kilonzo) or contact MPI (Relf) if there is any adverse event. Once an adverse event is identified and/or reported, actual or potential, the MPI Steering Committee will virtually meet within 24 hours. The MPI Steering Committee will implement the appropriate course of action to remedy critical incidents and adverse events that may occur during the study. The MPI Steering Committee and the CRC, PD, Chief Statistician will conduct a data and safety review at mid-point of data collection and at any time a serious adverse event occurs.

During the study, if an adverse event were to be occur, the MPI Leadership Team, the CRC, and the Project Director will evaluate the adverse event and determine whether the event affects the risk/benefit ratio of the study and whether modifications to the protocol or consent form are required. A "Critical Incident Journal" will also be maintained during the project. This journal will contain information such as the nature of the critical incident, the personnel involved, the solutions considered, and the final action implemented to resolve the incident. When necessary, the study team will also seek the expert opinion of the Duke University Health System IRB, the Research Triangle International IRB, and/or the Muhimbili University of Health and Applied Sciences IRB. Safety concerns for participants in this protocol are minimal. However, non-serious adverse events will be summarized and reported to the IRB periodically. The summary will include the number of participants enrolled and a summary of graded adverse events to date. Should serious adverse events occur, they will be reported within 48 hours to the appropriate IRB as well as the NIH by the contact MPI (Relf).

All members of the investigative team have completed or will complete during the orientation/on-boarding process, in a standard program on the ethical conduct of human research that conforms to current NIH guidelines or the country-specific equivalent. This program included information on the history of human participant protection, ethical principles governing informed consent, risk/benefit evaluation, equitable selection of research participants, and regulatory oversight. The study protocol will be implemented by project staff that will receive standardized and verified training in study protocols and procedures and will be monitored in continued use of those protocols/procedures over the course of the study.
A project database will be constructed using participant study numbers. A separate file, cross-referencing participant identification with project ID numbers, will be maintained with access limited only to staff working directly with the participants. Participants will be assured that they can withdraw from the study at any time without adverse effects. The Tanzanian MPI will be responsible for on-going quality control of the project database. The Tanzanian MPI, in collaboration with the other members of the MPI Leadership Team and Tanzanian Project Director, will ensure the confidentiality of all data and the results of monitoring, and will assist NIH by commenting on any problems that arise around the conduct of the study, participant enrollment, and data collection.

Regarding quantitative data integrity, field data collected by participants will be uploaded to a central database housed at TRI via an encrypted, secured network stored on servers behind RTI's firewall. REDCap (Research Electronic Data Capture) is a secure, web-based application that is HIPAA compliant and secure designed to support data capture. Data capture in the field, via REDCap, will use a tablet device with instruments preloaded in the local language (Swahili) and English.

During the quantitative data collection/analysis period, the key team members (MPIs, CRC, Project Director, Database Coordinator, Chief Statistician) will meet bi-weekly (every 2 weeks), and as needed, to discuss issues related to data elements/data analysis and results. The quantitative database used for storing data will be saved and backed up nightly on a secure encrypted server behind the firewall at RTI.

The MPIs, CRC, and PD will enact several safeguards to ensure that office and other space needed for the conduct of the proposed research to ensure the confidentiality of participants. Safeguards include the following:
a) all computers will be password-protected;
b) screensavers on computers will automatically initiate after 60 seconds of non-use;
c) all computers will be located in positions and angled so that casual observers cannot read computer screens;
d) all computers will contain the most current virus and security software and receive regular updates of this software;
e) all data collection materials will be stored in locked file cabinets inside a locked office, and access to these offices is limited to key study personnel (who have completed human participants' protection certification);
f) all data will be backed up nightly on a secure server and a flash drive will be used to store data off-site in the event of a building catastrophe; and
g) all data documents will be shredded or destroyed by the Tanzania MPI or PD at the appropriate time.
We are confident that all research activities conducted for the study will protect the privacy and confidentiality of the study participants and will fully meet the requirements of human participants' protection.

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