PROTOCOL COVER PAGE

Official Grant Title: Improving HIV treatment outcomes for people who use drugs: adapting and piloting a drug-use stigma-reduction intervention in HIV care and treatment clinics in Tanzania

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Abstract

Background
Globally, people who used drugs (PWUD) face high levels of drug use stigma. Drug use stigma, including experienced, anticipated, perceived, and internalized, has been documented as a barrier to linkage and retention in Medication Assisted Treatment (MAT), needle and syringe exchange programs, HIV care and treatment services, and general health care and is negatively associated with physical and mental health outcomes among PWUD.

Reducing drug use stigma in HIV care and treatment clinics (CTCs) will improve access to and retention in HIV treatment services for PWUD, a key population at elevated risk for HIV, thereby improving individual health outcomes, reducing onward transmission of HIV, and contributing to achievement of the global and national 95-95-95 targets. We propose to address the drug use stigma barrier in HIV CTCs by adapting and testing an HIV stigma-reduction intervention to focus on drug use stigma-reduction.

Objectives (AIMS)
1. To adapt a health facility HIV stigma-reduction participatory training intervention to address drug use stigma in HIV CTCs.
2. To evaluate the acceptability, appropriateness, and feasibility of the adapted drug use stigma-reduction intervention.

Methods
Study design and procedures: Guided by the ADAPT-ITT model, which provides a framework and prescriptive method for adapting evidence-based interventions (EBIs), we will employ a mixed methods design to adapt, and pilot test the intervention, including pre-post surveys with CTC staff and post intervention focus group discussions. A formative (qualitative) phase of research will be conducted with PWUD and clinical and non-clinical CTC staff to inform the first step in the adaption of the HIV stigma-reduction intervention to focus on drug-use stigma. We will pilot the adapted participatory training intervention for health care staff in seven high-volume HIV clinics in areas with the highest concentration of PWUD in Dar-es-Salaam, the Ilala, Kinondoni, and Temeke Municipal Councils.

Measurements: The key outcome measures will be three scales to measure stigma and a self-assessed and reported measure of knowledge of drug use. In addition, we propose to collect socio-demographic characteristics, a measure of social desirability bias, and level of contact with PWUD. The implementation outcome measures will be feasibility, acceptability, and appropriateness of the intervention.

Data analysis: Qualitative data will be analyzed using a multi-stage, modified grounded theory approach. To confirm the validity of the scales we will conduct confirmatory factor analyses (CFA) on the scales we do not modify and exploratory factor analyses (EFA) on those that we do. To examine the intervention effect, we will fit linear mixed effect regression models using the R package lme4 to examine changes in outcome measures from pre- to post-intervention while controlling for repeated measurements via random intercepts by individual. Each model will control for type of clinic, type of staff (clinical vs. non-clinical), gender, age, years of service in health facilities, years of service in an HIV

clinic, social desirability, level of contact with PWUD, and number of clients who use drugs treated within the last month. In addition, to identify possible effect modifiers (e.g., staff type, gender, level of contact with drug users), we will test time by modifier interaction terms within these models.

1. Introduction

1.1 Background

The goal of this study is to adapt and pilot an effective health facility HIV stigma-reduction intervention to address drug use stigma in HIV Care and Treatment clinics (CTCs) in Tanzania, a barrier to linkage and retention in HIV care for People Living with HIV (PLWH) who use drugs. In Tanzania, there are an estimated 300,000 People who use Drugs (PWUD), primarily heroin. Although most heroin is inhaled or ingested, an estimated 10% (30,000) of PWUD inject. HIV prevalence among PWUD who do not inject (18-25%) and those who do inject (35%) is 4-7 times higher than in the general population (5%). PWUD face high levels of stigma, including when they try to seek HIV treatment at HIV CTCs, presenting a barrier to linkage and retention in HIV treatment for this highly HIV vulnerable group. Therefore, reducing drug use stigma in HIV CTCs is critical to improving access to and retention in HIV treatment services for PWUD. In response to this need, the investigators will:

AIM 1: Adapt a health facility HIV stigma-reduction participatory training intervention to address drug use stigma in HIV CTCs

AIM 2: Pilot test the adapted drug use stigma-reduction intervention for acceptability, appropriateness, and feasibility

The investigators will achieve Aim 1 through a systematic, multi-stage adaptation process that will include a formative phase of in-depth interviews with PLWH who use drugs and CTC staff to inform initial adaptation of the Health Policy Plus (HP+) intervention. Stakeholders, including PLWH who use drugs and CTC staff, will provide feedback on the initial materials through a participatory workshop, leading to a training manual that will be reviewed by topic experts and then finalized. Experienced Tanzanian HIV stigma-reduction trainers will deliver the intervention to CTC staff. The pilot test will include health workers based in seven CTCs in Dar-es-Salaam. A mixed methods evaluation will comprise pre-post surveys, observation of trainings, and post-training focus group discussions with intervention participants and trainers. Changes in CTC staff's mean scores on stigma scales from pre- to post-intervention will be assessed, along with measures of intervention acceptability, appropriateness, and feasibility. Focus groups will explore themes around the experience of participating in the drug use stigma-reduction training.

1.2 Study Description:

The goal of this R21 application is to adapt and pilot an effective health facility HIV stigma reduction intervention to address drug use stigma in HIV CTCs in Tanzania, a barrier to linkage and retention in HIV care PLWH who use drugs. Reducing drug use stigma in HIV CTCs will improve access to and retention in HIV treatment services for PWUD, a key

population at elevated risk for HIV, thereby improving individual health outcomes, reducing onward transmission of HIV, and contributing to achievement of the global and national 95-95-95 targets. The investigators propose to do this by adapting (Aim 1) and testing for acceptability, appropriateness and feasibility (Aim 2) a drug use stigma-reduction intervention for HIV CTCs, guided by the eight-step ADAPT-ITT model. The study has two phases. First, the investigators will adapt the participatory training from an evidence-based health facility HIV stigma-reduction intervention (the HP+ total facility approach) to address drug use stigma among HIV CTC staff and then pilot test it in seven CTCs in three municipalities of Dar-es-Salaam. The first seven steps of the ADAPT-ITT model will guide AIM 1—the adaptation process, and step eight will guide AIM 2.

Step 1: Assess. Formative research will provide contextual information from PLWH who use drugs and CTC staff, to inform the adaptation of the HP+ intervention to focus on drug use stigma. Given the sensitivity of the topic and concerns about privacy and confidentiality, the investigators will employ individual in-depth interviews with both PLWH who use drugs and CTC staff.

In-depth interviews with PLWH who use opioids: 18 respondents aged 18 or older in the following categories: Medicated Assisted Therapy (MAT) clients living with HIV who get HIV treatment at CTCs; MAT clients not on HIV treatment; PLWH who use opioids who are not on MAT or HIV treatment. With PLWH the investigators will seek to understand the types of drug use stigma (experienced, anticipated, and perceived) that they encounter in relationship to CTCs, the specific manifestations of those types of stigma, and how this stigma influences HIV care linkage and retention among respondents living with HIV. The investigators will also explore what respondents view as driving drug use stigma in CTCs.

In-depth interviews with CTC staff: Fourteen staff from the high-volume clinics located in areas where people who use drugs congregate or live, who have direct interactions with clients split by type of staff (clinical and non-clinical). The in-depth interviews will focus on capturing stigmatizing attitudes and practices toward PWUD and understanding the underlying drivers of drug use stigma in CTCs (e.g., fear, lack of knowledge, attitudes and beliefs), as well as the who, when, and where drug use stigma occurs in the course of staff-client interactions.

All interviews will be recorded, transcribed, and translated. A multi-stage modified grounded theory approach to analysis will be deployed. An initial rapid qualitative analysis will be conducted followed by inductive and deductive development of initial codebooks. Coding and analysis will continue iteratively to discover additional themes and issues. The findings will be described in thematic summaries, tables, and diagrams.

Step 2: Decision. Guided by the formative results and the study team's experience working with service delivery for PWUD and developing and adapting stigma-reduction intervention tools for a range of audiences, the study team will conduct the first round of adaptation of the HP+ intervention training curriculum materials. The investigators will develop five, 2.5-hour participatory training modules that can be delivered flexibly across multiple partial days of training. Existing HP+ participatory training modules will be assessed for their appropriateness in terms of training modality (e.g., discussion, role play, reflection) and the specific content that needs to be adjusted (e.g., case studies, pictures, drivers of stigma) to

focus on drug use stigma. New materials for identified gaps will be developed, for example, around drug use as a medical condition.

Step 3: Administer. Next, the training materials will be put through a dry run—a 2-day participatory stakeholder workshop with key stakeholders, including HIV CTC staff, people with lived experience of drug use, Community Based Organization staff providing services to PWUD, MAT medical providers, and municipality and ministry of health representatives. Workshop participants will be asked to provide feedback on their overall perceptions and experience of the training (e.g., did it resonate, was it engaging, did it cover the right topics, exercises that should be dropped, gaps that remain to be filled). They will also be asked to comment on the approach and content of each specific exercise, including relevance, appropriateness, and content (including any visual materials).

Step 4: Produce. The study team will review and discuss stakeholder workshop feedback, refining the training manual in response.

Step 5: Topical experts. Two HIV stigma-reduction training experts will review the adapted manual to provide feedback on its congruence with stigma-reduction training principles, the scientific literature, and observed experience of PWUD trying to access HIV treatment.

Step 6: Integrate will involve a final revision of the manual incorporating feedback from the topical experts.

Step 7: Trainers, Kimara Peer's two stigma-reduction master trainers and a MAT provider expert and the Principal Investigator (PI) and site PI will work together to finalize training plans.

Step 8: Pilot test. The drug-use stigma-reduction intervention will be delivered in seven HIV CTCs with high client loads located in areas within the three identified municipalities where PWUD congregate or live. These types of CTCs have on average 20 to 25 staff (clinical and non-clinical) who come into direct contact with clients. Staff of all levels will be trained together, which has been shown to have multiple benefits. Training will be on site at the facility and delivered to all relevant staff together in five, 2.5-hour participatory sessions. Timing of the sessions will be negotiated with each facility to ensure minimal disruption to service delivery, as has been done successfully for the HP+ intervention. Training will be delivered by two master trainers from a local community-based organization (Kimara Peers) who have 20 years of delivering HIV stigma-reduction training, including to health workers, and who also run outreach services and a drop-in center for PWUD and a MAT provider, and an addiction specialist. The training team will include people of lived experience of drug use, who will participate as a panel in one of the sessions.

A mixed-methods approach will be used for assessment: pre-post intervention surveys, training observation, and focus group discussions with intervention participants and trainers. Trainers will complete a process rating form at the end of each session focusing on issues of feasibility, coverage of session content, 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 whether and when they return. The site PI and a member of the field staff will each observe, between them, half of all sessions across the seven facilities, recording observations on the same issues

captured by the facilitators, as well as facilitator fidelity to the training manual material and facilitator-participant interaction. Participant views on the training will be captured through focus groups, one in each facility (8-12 intervention participants per group of clinical and non-clinical staff). Focus groups will be recorded, transcribed, translated, and analyzed using the same process described above for formative work in Aim 1. Topics will focus on acceptance and appropriateness of training modalities and content, as well as areas where participants wanted more focus. Questions on the length and timing of sessions will also be discussed.

2. Methods

2.1 Study design

This is a mixed methods pre-post study design (single arm) with HIV care and treatment clinic (CTC) staff, both clinical and non-clinical. Data collection will include a pre(baseline) survey and a post-intervention (endline) survey conducted three months after completion of an intervention in a clinic and focus group discussions with CTC staff who participated in the training post intervention. A mixed methods approach is used because of the nature of the proposed study which combines adapting an HIV stigma-reduction intervention to address drug-use stigma and conducting a preliminary pilot study to test the intervention adaptation. Hence, we will employ surveys to collect pre and post intervention data and then conduct focus groups to help us deepen our understanding of how staff who participated in the intervention experienced it.

2.2 Study population for the pilot study (Inclusion and Exclusion criteria)

The pilot training intervention will be delivered to CTC staff.

The inclusion criteria for CTC staff will be having duties of provision of health services that include having direct contact with clients seeking HIV treatment services, whether they are dedicated CTC staff or shared staff within the wider facility (e.g., lab, guards) and being 18 years or older. The exclusion criteria will be being mentally incompetent or refusal to consent.

2.3 Study area and clinic selection

The study will be conducted in Dar-es-Salaam, in the Ilala, Kinondoni, and Temeke Municipal Councils. These are the areas the highest concentration of PWUD. The study area has 140 CTCs and three MAT clinics. CTCs and MAT clinics are governed by the municipalities. The intervention will be piloted in seven high-volume HIV clinics in areas with the highest concentration of PWUD. The seven clinics will be selected through a two-step process. Based on existing data on location of where higher concentrations of PWUD live, we will map each CTC's distance from a high drug use area. We will then take the list of all CTCs that would provide close and easy access to the largest concentrations of PWUD (within 5Km) and randomly select the 7 study facilities.

2.4 Sample size for the pilot study

Sample size for the pre- and post-surveys of the intervention was calculated using the PASS software program,(98) we estimated the power for comparisons of mean scale scores from pre- to post-intervention, assuming a p-value of 0.05 and a final sample size of 131 with both measurements (i.e., 13% attrition from the initial sample size of 150). We would have 85% power to detect a small-to-medium sized effect based on standardized mean difference (d=0.32).(99)

We are therefore targeting baseline enrollment of a150 health workers working in seven CTCs in Dar-es-Salaam. Health workers will be randomly selected on the day of baseline data collection at each facility. A mixed methods evaluation will comprise pre-post surveys (n=150 at each round), observation of trainings, and post-training focus group discussions with intervention participants (n=7; 8–12 participants each) and trainers (n=1; 6 participants).

2.5 Measures

Primary Outcome Measures

The Primary Outcome measures for this study include one to measure stigma and three to measure acceptability, appropriateness and feasibility of the pilot stigma reduction training intervention.

To measure stigma, we will use a modified Opening Minds Scale for Health Providers (OMS-HC) which is an 8-item scale measuring stigma amongst health workers toward people who use drugs. Each item consists of a 5-point Likert scale, with 5 indicating the highest degree of agreement with the statement. The score is calculated additively with a range of 8-40. Higher scores indicate a higher level of stigma. Included items are:

- If I were under treatment for drug addiction, I would not disclose this to any of my colleagues.
- If I had drug addiction, I would seek treatment at a health facility away from the one I work in.
- I would see myself as weak if I had drug addiction and could not fix it myself
- I would be reluctant to seek help if I had drug addiction
- Despite my professional beliefs, I have negative reactions towards people who use drugs
- I would not want a person with addiction, even if it were managed, to work with children.
- Healthcare providers do not need to be advocates for people who use drugs.
- I am afraid to provide health services to people who use drugs

We will measure implementation outcomes at endline by assessing feasibility, acceptability and appropriateness of the intervention. Each measure has 4 items. They are measured in a five Likert scale including the following responses with scale values ranging from 1 to 5: completely disagree (1), disagree (2), neither agree nor disagree (3), agree (4), and completely agree (5). No items need to be reverse coded. Higher scores indicate greater acceptability, appropriateness, or feasibility.

Secondary Outcome Measures

We will include two secondary outcome measures:

1) A modified *Drug and Drug Problems Perceptions Questionnaire* to capture self-assessed and self-reported knowledge about drug use and how to provide services to people who use drugs. The measure uses a Likert scale (1-5) and has 8 (for non-clinical staff) and 10 (for clinical staff) items. Clinical staff receive 2 additional items. Scores (range:1-5) and are calculated by taking the mean value of responses to all questions. Higher scores correspond to higher degrees of knowledge and therefore a better outcome.

Items include the following:

I feel

- I have a working knowledge of drugs and drug related problems.
- safe providing HIV services to people who use drugs (PWUD)

I feel I know enough about {insert below item} to carry out my role providing HIV services to PWUD

- the causes of drug problems
- the physical effects of drug use
- the psychological effects of drugs
- the factors which put people at risk of developing drug problems

I feel I know enough about {insert below item} to provide appropriate services to PWUD

- drug addiction as a brain disease
- the social effects of drug use
- drug-to drug interactions (CS only)
- co-occurring conditions (CS only)

2) A modified *Bogardus Social Distance Scale*
This is a 6-item scale measuring social distance, or (un)willingness to interact with a person who uses drugs in different social interactions. The response options are on a 4-point Likert scale, with 4 indicating a response of "definitely yes" and 1 indicating "definitely no". The score is calculated additively with a range of 6-24. Higher scores correspond to higher degrees of social distance and therefore a worse outcome.
Included items:

- Would you feel ashamed if people knew someone in your family has drug addiction?
- Would you be afraid to have a conversation with someone who uses drugs?
- Would you be disturbed about working at the same health facility with someone who uses drugs?
- Would you stop being friends with someone who uses drugs?
- Would you feel upset or disturbed being in the same room with someone who uses drugs?
- Would you marry someone who uses drugs? (reverse coded)

<u>Other measures</u>

Marlowe-Crowne Social Desirability Scale (MCSDS)
Due to the sensitive nature of the topic, social desirability bias in responses at endline of the intervention is a possibility. We therefore will include the MCSDS, which has been adapted and validated in East Africa, to control for this possibility.

Level of contact report
A 5-item scale that measures the amount that a respondent comes into contact with people who use drugs in professional, social, and personal situations. Each item consists of a dichotomous true/false response, with true indicating that the person agrees with the statement. Scores are calculated dichotomously: agreement with none of the 5 items indicates a low degree of contact ("low contact"), and agreement with one or more of the 5 items indicates a high degree of contact ("high contact").

Sociodemographic characteristics
These include sex, age, and education. Other characteristics which will be assessed will include position of a health worker in CTC (clinical vs non-clinical staff), length of service in health care, length of service in CTC, and frequency of contact in the CTC with clients who use drugs.

Participation in stigma reduction training
Participants will be asked to self-report if they have ever had training on stigma and discrimination reduction (baseline) and then at endline more detailed questions will be asked about participation in the pilot study intervention.

2.6 Data collection
Five research assistants will be recruited to assist with data collection. Two will be for qualitative data collection and three for quantitative data collection. They will receive training for three days on the study protocol, procedures and ethics, interviewing techniques, as well as practice with the instruments.

Based on the results of the formative research phase, a focus group discussion guide will be developed to capture participant views on the training through focus groups, one in each facility (8–12 intervention participants per group of clinical and non-clinical staff). Potential topics of the focus groups discussions could be acceptance and appropriateness of training modalities and content, as well as areas where participants wanted more focus. Questions on the length and timing of sessions will also be discussed.

2.7 Data analysis (see Statistical Analysis Plan)

2.8 Ethical considerations
Ethical approval will be sought from, MUHAS Senate Research and Publications Committee and National Review Ethics Committee (NatREC) of NIMR. The RTI IRB will rely upon the MUHAS Senate Research and Publications Committee as detailed in a letter to the funder, the National Institutes of Health (NIH) as part of the Just-In-Time documentation for the grant. This is because the MUHAS Senate Research and Publications Committee is better situated to provide IRB oversight to a study being conducted in Tanzania as they are familiar with the local context in which the research will occur. The MUHAS Senate Research and Publications Committee and the RTI IRB have entered into an Institutional Review Board (IRB) Authorization Agreement (IAA). Permission to conduct the study will be sought from the Municipal councils and health facilities. For the formative phase of the research (part of AIM 1) which is to inform intervention adaptation, informed oral consent will be collected with people who use drugs because of the illegality of drug use in

Tanzania. This is considered the most ethical approach when conducting interviews with highly stigmatized populations who engage in criminalized behavior. There is precedent for oral consent from previous studies with PWUD in Tanzania. Written informed consent will be collected from all CTC staff.

2.10. Study limitations and mitigation

Recruiting PWUD to participate in research, in a context where drug use is criminalized, is a potential complication. The study team has done this successfully for previous studies through MAT clinics and CBOs, so we do not anticipate an issue for this study. Social desirability bias in responses from any health provider to sensitive questions around stigmatizing beliefs or actions toward clients is a challenge for any study on stigma. To minimize this, questionnaires will be self-filled unless a CTC respondent prefers a face-to-face interview or when there are literacy challenges. We will also collect the Marlowe-Crowne Social Desirability Scale (MCSDS) to measure and control for social desirability bias.

3. Dissemination plan

The investigators will work together to disseminate study findings widely, at local, national, and international conferences and through publications in peer-reviewed scientific journals. Presentations and publications will be a focus of the capacity strengthening aspect of this project with a focus on building Dr. Mlunde writing and presentation skills. We anticipate a minimum of two publications from this study covering the adaptation process and final results of the pilot study. We will target dissemination in multidisciplinary HIV, global health, substance use, and/or human rights journals. The study team will target national, regional, and international conferences and also leverage opportunities within Tanzania and the east and southern Africa region to present to government, donor, and implementing organizations working in HIV and with people who use drugs (PWUD) through various fora to ensure that the results are available quickly on the ground to inform programs and policy.