Stigma, Risk Behaviors and Health Care among HIV-infected Russian People Who Inject Drugs (SCRIPT)

Principal Investigator: Karsten Lunze, MD, MPH, DrPH – Boston Medical Center

Clinicaltrials.gov Registration: NCT03695393

Statistical Analysis Plan (SAP): pages 26-27

NIDA Award Number: R00DA041245

Boston University Medical Campus IRB Protocol Number: H-38069

Protocol Version: July 20, 2021

TABLE OF CONTENTS

1. INTRODUCTION

1.1 SUMMARY

People who use drugs (PWID) often experience multiple layers of stigma when they are living with HIV.[1] Stigma is defined as the social exclusion and dehumanization of individuals in an undesirable social category.[2] Interventions to help affected PWID living with HIV cope with the dual stigma related to HIV and substance use have not been studied specifically in this population. Among people living with HIV, stigma adversely impacts all aspects of the care cascade: timely HIV testing, diagnosis, treatment, adherence and retention in care.[3-5] Among PWID, drug use may add to adverse social factors and create particular stigma vulnerability. Russia is a country where PWID and other HIV key populations are highly stigmatized and face discrimination. Furthermore, agonist treatment for opioid use disorder is illegal in the Russian Federation. People with substance use disorders and those living with HIV have to register with the local authorities for treatment. While many try to avoid registration, most PWID and people living with HIV (PLWH) are known to the authorities. Further qualitative findings suggest that in the absence of public anti-stigma campaigns in Russia, stigma reduction interventions should address internalized stigma and their determinants to help affected people cope with the dual stigma. Stigma interventions should be adapted to address not only affected people's shame and guilt, but also their felt hopelessness. These emotions and related feelings such as avoidance and fear of being rejected may negatively affect people's agency and mental health.[7, 8] We are proposing *Acceptance and Commitment Therapy* (ACT) as a potential behavioral intervention to target the emotions underlying internalized stigma and thus empower affected people. ACT has been shown to increase engagement in addiction care.[9] Its use and efficacy to reduce stigma has not yet been explored among HIV-positive PWID.[10] The objective of this study, "Stigma, Risk Behaviors and Health Care among HIV-positive Russian People Who Inject Drugs (SCRIPT)," is to implement and evaluate the feasibility of an adapted form of ACT targeted to PWID living with HIV in Russia as an intervention to reduce intersectional HIV and substance use stigma via a two-armed randomized controlled trial among 100 HIV-positive PWID. The central hypothesis is that ACT is feasible and can be delivered to decrease HIV and substance use stigma scores.

SCRIPT aims to evaluate: 1) the feasibility of ACT with a HIV-positive PWID population in Russia via measures of satisfaction with the intervention, general participation in intervention sessions, and fidelity to the intervention; 2) the impact of ACT on the reduction of HIV and substance use stigma scores, entry into HIV care, substance use frequency, and mental health.

The study's goal is to examine the feasibility of a new intervention and to compare this intervention's effectiveness of reducing internalized stigma with the current standard of care provided by civil society organizations (CSOs) in Russia.

SCRIPT proposes to study a stigma intervention specifically among HIV-positive PWID, broadening its scope to not only HIV-related, but also substance use-related stigma in this key population. By measuring the intervention's effect size on stigma variables and related behavioral outcomes in this population, we will better understand how to intervene on the phenomenon of stigma and ultimately inform the dissemination of stigma interventions in similar health care contexts.

1.2 SIGNIFICANCE

The SCRIPT study will assess the feasibility of an intervention designed to decrease intersectional internalized stigma among HIV-positive PWID. Potential results from this study in Russia should be applicable to comparable countries attempting to reduce stigma within this population.

2. OVERVIEW OF STUDY DESIGN

2.1 STUDY AIMS

SCRIPT's Specific Aims are as follows:

Aim 1: ***Evaluate the feasibility of an ACT stigma intervention*** compared to standard of care via a 2-armed RCT of 100 HIV-positive Russian PWID on the following outcomes:

a. Primary: Satisfaction with the intervention at 1 month
b. Secondary:
    a. Participation in three intervention sessions;
    b. Fidelity to the intervention, using the Adherence Raters' Manual for Stigma Treatment Study (Kohlenberg et al, 2004) and an intervention adherence score

Aim 2: ***Measure changes in internalized stigma***

a. Primary: HIV Stigma via the Simbayi HIV internalized shame scale at 1 month;
    Substance Use Stigma via Modified Substance Abuse Self-Stigma Scale at 1 month
b. Secondary:
    a. Any initiation of HIV care (ART) at 6 months
    b. Engagement in substance use care at 6 months
    c. Change in last 30 days injection drug use at 6 months
c. Exploratory
    a. Depression as measured by the PHQ-9 at 6 months
    b. Anxiety as measured by the GAD-7 at 6 months
    c. Intersectional stigma as measured by both substance use stigma and HIV stigma scales at 6 months
    d. Psychological flexibility as measured via the Acceptance and Action Questionnaire at 6 months

2.2 STUDY HYPOTHESIS

We hypothesize that the SCRIPT intervention, which utilizes an adapted form of ACT targeted to PWID living with HIV in Russia, is feasible and can be delivered to decrease HIV and substance use stigma scores.

2.3 STUDY OUTCOMES

Aim 1. The primary outcome for aim 1 is satisfaction with the intervention at month 1, assessed by a satisfaction scale. Secondary outcomes are participation in intervention sessions and fidelity to the intervention, assessed via audio-recording. This will be scored with an ACT Adherence Checklist and the Adherence Raters' Manual for Stigma Treatment Study (Kohlenberg et al, 2004) to rate the recorded intervention audio recordings.

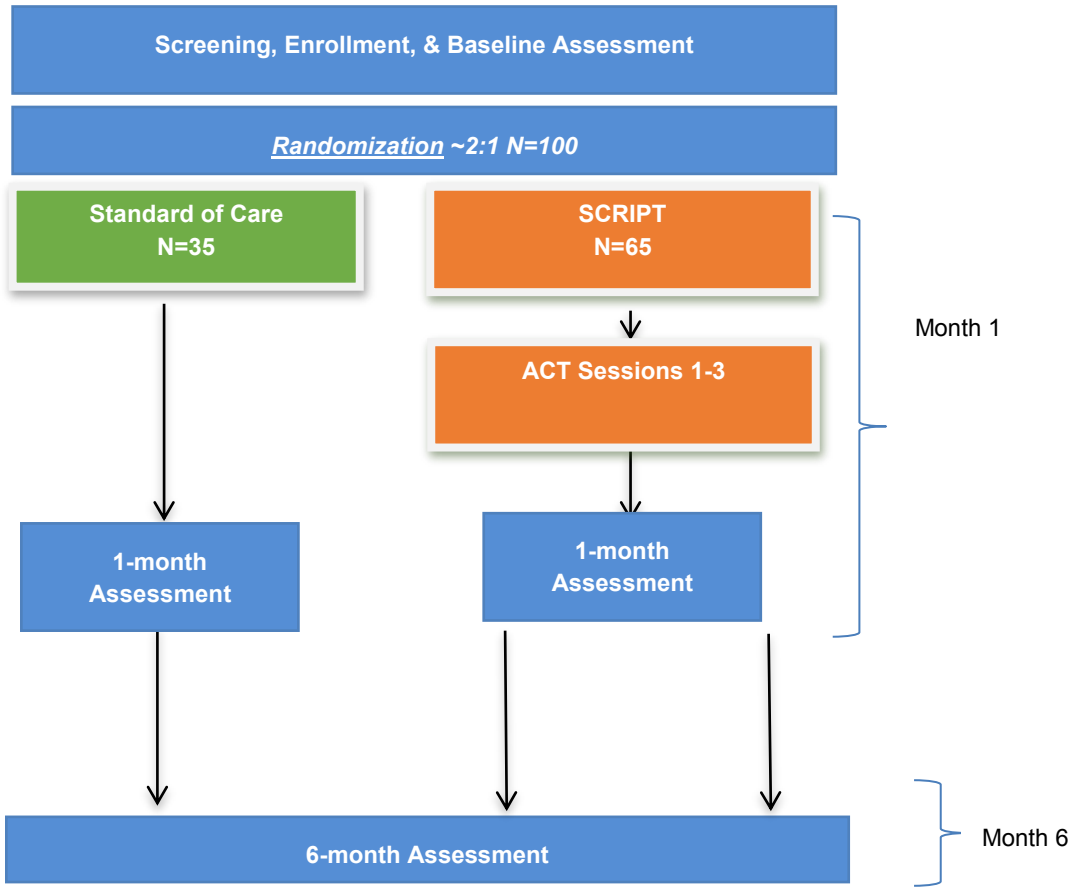
Aim 2. The primary outcome for aim 2 is measured change in internalized HIV stigma and substance use stigma at 1 and 6 months assessed by the Berger HIV Stigma Scale, the Leickness HIV internalized shame scale, the modified Substance Abuse Self-Stigma Scale, and the Acceptance and Action Questionnaire – Substance Abuse. Secondary outcomes are initiation of ART, recent (last 30 days) injection drug use frequency at 1 and 6 months, and mental health as measured by the PHQ-9 and GAD-7.

2.4 STUDY DESIGN

SCRIPT is a Randomized Controlled Trial (RCT) among 100 HIV+ PWID, which aims to test the feasibility of the SCRIPT intervention and evaluate its effectiveness on the reduction of internalized stigma as well as self-reported entry into substance abuse treatment or initiation of ART. Eligible participants will be randomly assigned into one of two groups: 1) Control group receiving CSO site standard of care or; 2) ACT intervention. Both the intervention group and the control group will receive standard of care counseling and referral to addiction treatment and HIV treatment at the CSO sites. Following their baseline assessment, participants assigned to the intervention group will meet with the interventionist three times over one month in approximately 13 groups of 5 people each. All three sessions will be in groups, except for the occasional individual make-up 2nd session (more details in section 3.6B). Study outcomes will be assessed at 1 and 6 months (Figure 1).

Figure 1 illustrates the design of this 2-arm RCT with 65 participants in the SCRIPT intervention arm and 35 participants in the standard of care arm.

Figure: SCRIPT Study Design



Throughout the course of the study, participants in both groups will be expected to participate in three in-person assessments (baseline, 1 month and 6 months).

2.5 PILOT TESTING

Prior to enrollment of the 100 participants, we will perform 2 pilot intervention groups; each will include 3 group sessions with approximately 5 participants each. The groups will be led by trained SCRIPT interventionists. The purpose of this pilot phase is to ensure that our intervention is culturally appropriate, feasible to conduct, and relevant to our participants. We will use feedback from the pilot study to make improvements to our study before we begin recruiting participants.

For the pilot phase of the study, we will recruit approximately 10 participants from the same study population as outlined above to conduct two pilot intervention group trainings. Thus, no control groups will be pilot tested. These pilot participants will receive the same study procedures as the main study participants (recruitment, screening, informed consent, baseline assessment, compensation, group sessions), except they will not receive the 1-month nor the 6-month assessments. The pilot participants will provide informed consent using a form that is specific to the pilot phase of the study. The study flyer and pamphlet will not be used for recruitment during the pilot phase. All data collected during this pilot phase will not be used for feasibility or intervention effectiveness analyses, but may be used for secondary analyses of baseline data.

2.6 STUDY SITES

Participants will be recruited through a civil society organization (CSO) providing street outreach services to PWID and people living with HIV in St. Petersburg, Russia. CSOs serving PWID and PLWH have been historically funded by the Global Fund; currently, they are financed mostly by foundations and private donations. All are closely monitored by the Russian authorities. They have no specific rules on medical privacy, other than providing an inviting, safe haven for affected people, who congregate at the CSOs for support and mutual help. The latter offer counseling, but usually have no medical staff and do not offer therapy.

All assessments and group trainings will be conducted at a rehabilitation center. Street outreach CSOs do not have facilities to conduct study procedures, but have connections with other organizations, such as rehabilitation centers, and thus participants recruited from the CSOs will be transported to these organizations for all other study procedures. The rehabilitation centers have the resources and capacity to conduct the assessments and intervention. Therefore, this collaboration with the CSOs is a multi-institutional approach to reach individuals in a highly stigmatized population and help them address the negativity in their lives related to other people's attitudes about their HIV status and substance use.

Recruitment will be completed by the CSO staff and phone-screening will be completed by the rehabilitation center staff, who are trained as research assessors (RAs) by academic staff at PMSU. In-person screening, informed consent, and assessments will also be completed by RAs. Intervention sessions will be completed by trained ACT interventionists on site at the rehabilitation center or at the Laboratory of Clinical Pharmacology of Addictions at the First St. Petersburg Pavlov State Medical University (PSMU) in St. Petersburg, Russia. PSMU is the major educational, scientific, and clinical medical institution for northwestern Russia. The ACT interventionists are both rehabilitation center staff and PMSU staff, who were trained in ACT for this study by the PI and master trainer consultants in a workshop modified for the Russian context, conducted from March 2 through March 9, 2019.

2.7 INCLUSION CRITERIA

To be eligible to participate in the trial, participants will need to meet the following inclusion criteria:

1. 18 years old or older
2. HIV-positive
3. Current injection drug use (past 30 days)
4. Not currently on ART
5. Provision of contact information for two contacts to assist with follow-up
6. Address within 100 kilometers of St. Petersburg
7. Not enrolled in any other research studies
8. Possession of a telephone (home or cell)
9. Able and willing to comply with all study protocols and procedures over 6 months
10. Available at the specific days of the week and times that the group sessions will be occurring for the subsequent 3-4 weeks (to ensure that participants randomized into the intervention arm will be able to receive the intervention)

2.8 EXCLUSION CRITERIA AT STUDY ENTRY

1. Not fluent in Russian
2. Cognitive impairment resulting in inability to provide informed consent based on research assessor (RA) assessment
3. Acute severe psychiatric illness as determined from screening questions (i.e., answered yes to any of the following: past three month active hallucinations; mental health symptoms prompting a visit to the ED or hospital; mental health medication changes due to worsening symptoms; presence of suicidal plans) and research assessor clinical observation (i.e. clinical observation or prior knowledge of severe personality disorder; past three months active mania; past three months active psychosis)
4. Participants in the main study did not participate in the pilot portion of the study.

2.9 RECRUITMENT GOALS

We aim to randomize 100 participants over 13 months into the trial. We will approach potential participants at CSOs serving PWID and people living with HIV (PLWH) in St. Petersburg.

3. INTERVENTION

3.1 INTERVENTION OVERVIEW

The study will randomize 100 PWID living with HIV in the St. Petersburg area. We will approach potential participants at CSOs serving PWID and people living with HIV (PLWH). After a phone-screening, potential participants will be given clear transportation instructions to the location of the remainder of the procedures (in-person screening, consent, enrollment, assessments, intervention sessions). After in-person screening, consent, enrollment, and the baseline assessment, participants will be randomly assigned to either the SCRIPT intervention or standard of care. Following randomization, participants in both groups will receive standard of care at the study site.

Following randomization by RAs at the rehabilitation center, participants in the intervention group will be scheduled to engage in group ACT sessions. These will consist of three 2-hour group sessions of culturally adapted ACT to reduce stigma and related manifestations in weeks 1, 2 and 3. The ACT sessions are described in further detail in 3.3.A.

Throughout the course of the study, participants will be expected to participate in three in-person assessments (baseline, 1 month [4 weeks], and 6 months [24 weeks]). Participants in the intervention groups will receive three ACT sessions over one month in approximately 13 groups of 5 people each (n=65), with a final assessment conducted at 6 months.

3.2 RANDOMIZATION

Randomization is not stratified by any factor. Blocked randomization with randomly selected block sizes was used to reduce selection bias and make the sequence less predictable. We generated a random sequence of 34 blocks, sizes 3 and 6. Then, we randomized assignments within each block with an allocation ratio of 2:1. A greater number of blocks was created than is necessary in the event that the investigator continues enrollment beyond the initially planned sample size. Randomization sequence was created in R, version 3.5.2 (Copyright (C) 2018 The R Foundation for Statistical Computing) and uploaded to REDCap platform, electronic data collection tool.

3.3 INTERVENTION

The SCRIPT intervention is comprised of a culturally adapted ACT intervention designed to reduce stigma and related manifestations. Both ACT and standard of care groups will receive the usual care at the CSO and study sites, which includes counseling and referral to addiction treatment clinics (for detox and rehabilitation; opioid agonist treatment is not available in Russia) and to HIV treatment clinics (for ART and HIV care) in St. Petersburg (standard of care).

3.3.A. ACCEPTANCE AND COMMITMENT THERAPY (ACT)

The ACT intervention will consist of three sessions scheduled for 2 hours each. Sessions will occur in groups of approximately 5 and will follow an intervention manual, based on the one developed in Luoma et al. (2008) and Luoma et al. (2012) and culturally adapted to a Russian context by the study team. Participants are told that the groups are intended to help them overcome stigmatization, shame and judgments of self and others. Standard ACT exercises are modified to focus on how to respond to shame and self-stigmatizing thoughts in a

way that would not obstruct recovery from SUD or health care seeking. In an ACT approach, rather than trying to reduce or eliminate manifestations of internalized stigma (such as shame), acceptance techniques encourage participants to notice these feelings and reduce their conditioned link to potentially adverse outcomes such as risk behaviors or avoidance of care.[49] The initial phase of the intervention focuses on the workability of suppression and avoidance, and provides a rationale for defusion and acceptance skills. Well known ACT exercises will be adapted as needed for the Russian cultural context in which this study is conducted. The intervention then proceeds to teach defusion and acceptance skills through such exercises as 30 seconds of word repetition focused on a negative self-judgment, a procedure known to reduce both fusion with thoughts and the distress they evoke (Masuda, Hayes, Sackett, & Twohig, 2004). This phase also includes mindfulness exercises, acting out a tug of war with a negative thought, and publicly sharing negative self-judgments by writing them on name tags. The third phase of the treatment focuses on helping participants identify life goals and values. They are guided to respond and refocus on actions related to their values, such as self-care activities that would reduce their HIV risks and support care seeking.[10] It also includes a focus on building a positive agenda of human connection and values related to treatment participation. Finally, participants write out an epitaph for their life and share their values, goals, needed actions, and expected barriers. Follow up sessions will review this material with clients, as well as address barriers to implementing these skills in their lives. When speaking to participants, we will refer to ACT as Acceptance and Commitment Training, as the goal of the sessions is to *train* participants how to overcome stigmatization.

The ACT stigma intervention will be delivered by clinical psychologists. Supervision will be provided by site PI and ACT trainer. Interventionists and supervisors will be trained by ACT trainers and PI. To assess interventionist fidelity to ACT for quality assurance, we will use the Adherence Raters' Manual for Stigma Treatment Study (Kohlenberg et al, 2004) to rate the recorded intervention audio tapes, with a focus on interventionist behavior and competency. The measure classifies three different targets of clinician behaviors, openness, awareness, engagement, as well as interventionist stance. The coding will be conducted by an ACT clinician who is also a certified ACT trainer. This will also allow us to investigate how combinations of interventionist behaviors relate to outcomes and help train future interventionists in Russia and Russian speaking countries. Fidelity will be measured by an adherence checklist completed by interventionists after each session.

The ACT sessions will be scheduled to take place at the rehabilitation center. The First St. Petersburg Pavlov State Medical University is an alternative location where sessions can be conducted. Sessions will be planned to occur in a weekly succession, with a goal of 3 sessions within the first month of study participation.

The sessions will entail exercises on values, goal setting, psychological flexibility and commitment, led by an ACT-trained interventionist.

All sessions will be audio recorded for quality assurance purposes. The interventionist will use discretion to turn the recorder off if a participant feels uncomfortable disclosing certain sensitive information, in which case she will turn it back on as soon as appropriate. Audiorecordings of intervention sessions will be deleted seven years after the completion of study analyses and publication of all study manuscripts.

Study participants will be invited to refer to each other by a nick name or pseudonym in the groups, however, participants can use their real first names, if preferred. Interventionists will instruct participants to not repeat anything they have heard in these sessions.

3.4 Control Group

Participants in the control group will receive standard care as normally provided to patients by civil society organizations. This could include information on HIV and substance use disorders, counseling, referral to addiction treatment clinics, and referral to HIV treatment clinics. They might also be given printed information, including phone numbers, on places that provide HIV medical care and substance use treatment.

3.5 Schedule of Data collection

		Phone Screener	Screener and Baseline		ACT Sessions 1-3	1-month assessment (4 weeks)	6 month visit (24 weeks)
			In-person Screener	Baseline			
Screening	Verification of HIV and hx of IDU	X	X				
	Screening Questions	X	X				
Enrollment	Sign Informed Consent		X				
	Complete contact information/verify numbers			X			
Assessment	Baseline Study Assessment			X			
	1-Month Study Assessment **incl ACT satisfaction questions**					X	
	6-Month Study Assessment						X
	Interventionist Checklist				X		
Randomization	Randomization			X			
Intervention	Adverse Events			X		X	X
	ACT Intervention				X		
Other	Compensate for Participation			X	X	X	X
	Provide Resource Card			X			
	Report Adverse Events			X	X	X	X
	Complete Tracking Forms		X	X	X	X	X

Control Group

		Phone Screener	Screener and Baseline Visit		1 mo (4 weeks)	6 mo (24 weeks)
			In-person Screener	Baseline		
Screening	Verification of HIV and substance use	X	X			
	Screening Questions	X	X			
Enrollment	Sign Informed Consent		X			
	Complete contact information/verify numbers			X		
Assessment	Baseline Study Assessment			X		
	1-Month Study Assessment				X	
	6-Month Study Assessment					X
Randomization	Randomization			X		
Other	Provide Resource Card			X		
	Compensate for Participation			X	X	X

	Complete Tracking Forms			X	X	X

3.5.A. VISIT WINDOWS

ACT Intervention Session Windows for Intervention Group

1st ACT Session

- Window open: 1 day post baseline
- Target date: 7 days post baseline
- Window close: 31 days post baseline
- Window length: 30 days

2nd ACT Session

- Window open: 8 days post baseline
- Target date: 14 days post baseline
- Window close: 29 days post baseline
- Window length: 21 days

3rd ACT Session:

- Window open: 15 days post baseline
- Target date: 21 days post baseline
- Window close: 36 days post baseline
- Window length: 21 days

Research Assessment Windows for Intervention and Control Group

Intervention Group 1 Month (4-week) Visit

- Window open: 16 days post first group session
- Target date: 30 days post first group session
- Window close: 90 days post first group session
- Window length: 74 days

Intervention Group 6 Month (24-week) Visit

- Window open: 151 days post first group session
- Target date: 180 days post first group session
- Window close: 240 days post first group session
- Window length: 89 days

Control Group 1 Month (4-week) Visit

- Window open: 16 days post baseline
- Target date: 30 days post baseline
- Window close: 90 days post baseline
- Window length: 74 days

Control Group 6 Month (24-week) Visit

- Window open: 151 days post baseline
- Target date: 180 days post baseline
- Window close: 240 days post baseline
- Window length: 89 days

Windows listed above are used as guides for scheduling visits, but deviations may occur due to participant scheduling.

3.6 DATA SOURCES

3.6.A QUESTIONNAIRES

Questionnaires will be administered at baseline, 1-, and 6-month study visits to collect information about participant demographics (e.g., age, gender), stigma scores, sex risks, substance use risk behaviors, care utilization, general and mental health.

3.6.B SESSION AUDIO RECORDINGS

We will audio-record all intervention sessions and will code a subset of these recordings for quality assurance and fidelity monitoring, i.e., to document adherence to the intervention study procedures.

3.6.C INTERVENTIONIST ADHERENCE CHECKLIST

Interventionists will fill out an intervention adherence checklist to document the items of the intervention that were covered (i.e. specific metaphors, emphasis on homework, etc.)

4. STUDY PROCEDURES

4.1 RECRUITMENT

Participants enrolled in the Stigma, Risk Behaviors and Health Care among HIV-positive Russian People Who Inject Drugs (SCRIPT) study will be recruited by staff from a civil society organization (CSO) in St. Petersburg, Russia.

4.2 PHONE SCREENING

Participants who express interest in joining the study at the CSO, will be given the opportunity to participate in a phone screening. The CSO staff will call the rehabilitation center and notify the SCRIPT RA that a CSO client is potentially interested in the study and would like to complete a phone screening. The rehabilitation center RA will conduct a Brief Screening Agreement specific to the phone screening. If deemed eligible from the phone screening, the staff at the CSO will provide clear instructions to using the public transportation system to get to the rehabilitation center. The instructions will have contact information for the rehabilitation center if any issues arise. The potential participant may also receive help from the CSO outreach worker for transportation (i.e. metro card, taxi).

If a participant is acutely sick and/or still in withdrawal when approached for phone screening, the CSO staff will re-approach that person later (if the person is interested) when this person presents again at the CSO.

4.3 SCREENING

In-person screening for the SCRIPT study will take place at a rehabilitation center by rehabilitation staff. Rehabilitation staff will be appropriately certified in human subjects research and trained as research assessors (RA) to do the screening procedures. They will be on the local protocol as staff under the Pavlov IRB.

A RA will conduct screening, and will meet with the potential participant in a private room to briefly describe the study and conduct in-person screening to confirm the presence of inclusion criteria and the absence of exclusion criteria.

If a potential participant arrives at the rehabilitation center for in-person screening acutely sick and/or still in withdrawal, the RA will invite the individual to come back later (if the person is interested) when this person presents again at the rehabilitation center (i.e., once the person is eligible for screening and/or eligible for the study, they can be enrolled once they are feeling better).

The rehabilitation center will keep a list of names phone-screened to prevent re-screening. This list will contain no other information other than names, contact information (if eligible), and eligibility status and will not be linked to screening data. This list only serves to avoid repeat screening. We will ask CSO staff and RAs to not refer potential participants again who previously did not screen into the study. However, we will not link participants' reasons for ineligibility to their names (or any other identifiable information). Informed consent will take place immediately after screening and if, for some reason it cannot, the data from the screening will not be retained. Answers to phone screening questions will be recorded in a different REDCap project than the basic personal information (name and contact information). Participants who were phone screened as eligible, will be asked to come in for an in-person screening which will serve as the documentation data.

Protocol for ensuring double randomization and double enrollment do not occur

1. Prior to screening, the RA verifies that the participant was not previously referred for screening.

2. The RA searches the name of the participant in the SCRIPT tracking system in REDCap to confirm that the patient has not been previously enrolled in the SCRIPT Study. If a match appears, the RA checks DOB and address. (This will be done confidentially, so that the patient does not know that there is someone with the same last name already in the study, to protect the confidentiality of the enrolled participant.) If no match is found, the RA proceeds with screening.

4.4 INFORMED CONSENT

An RA will conduct the consent process as well as obtain written consent. After eligibility and interest in enrollment is determined, an RA will administer and document the informed consent of the participant in a private location, such as a private room at the study site or at a location of the potential participant's preference. If participants are unsure whether they would like to participate, they will be allowed any amount of time they wish to consider participation in the study. If the participant is not able to make a decision on the day of the initial visit, s/he will be invited to contact the study team once s/he have made their decision. The

study will be explained to eligible participants who will be offered participation in the study. Research assessors will answer any questions the patients may have including risks, benefits and alternatives (including non-participation) to participation, and will provide written materials describing the study. The written informed consent (in Russian), including the risks, benefits and alternatives, will be signed and dated by the participant and the research assessors. A signed copy of the informed consent will be provided to the participant, and a copy will be maintained by the research team. Potential participants will be informed that refusal to participate will not affect their medical care in any way and they will be informed of their right to drop out of the study at any time.

4.5 VISIT FLOW

We aim to screen and consent eligible participants, followed by baseline assessment (about 60 minute duration) on the same day. The first ACT group session (about 120 minute duration) will occur once five participants have been randomized into the intervention group and are all available for the pre-scheduled group session. After eligible participants are consented and enrolled, the following will take place at the **Baseline visit**:

- Collection of locator/contact information and verification of contact phone numbers
- Administration of assessment questionnaire
- Randomization
- Compensation and scheduling next visit

Intervention Group:

- Participants randomized into the intervention group will have their group ACT sessions consecutively on weeks 1, 2, and 3.

Intervention and Control Group:

- During the **1-, and 6-month in-person assessments,** the Research Assessor will:
    - Review and update locator/contact information, verifying new numbers, as necessary
    - Administer assessment questionnaire
    - Compensate participant and schedule next visit (1-month visit only)

4.6 QUALITY ASSURANCE

Informed consent quality assurance

The Research Assessor will review Informed Consent Forms (ICFs) for completeness with the participant present. Items to check will include, but are not limited to: responses/initials collected for all questions, correct version of ICF used, signed and dated by both participant and Research Assessor. The Local Study Coordinator, who will oversee all RAs, will review all completed consent forms weekly and will complete the Consent Form Deviation log if any errors are identified.

Assessment quality assurance

During the assessment, if the participant provides conflicting answers or answers that did not make logical sense (either within the same section or between sections), the Research Assessor will gently try to help the participant arrive at more logical answers. However, the Research Assessor will not force the participant to change his or her answers. Certain quality assurance checks are built into the assessment. The system will flag any inappropriate responses and prevent the Research Assessor from continuing until the issue is resolved. If many "refused" options are selected, the RA will offer the participant the opportunity to complete those sections (the Research Assessor will accept the participant's refusal if he or she does not wish to complete the section). The Research Assessor will never guess to correct a mistake. The only instance when a change can be made to the completed assessment is in the event that the Research Assessor is 100% certain that an error was made in data entry. Local data manager will QC all paper forms used for the assessment (i.e., rulers for VAS). Upon completion of QC of paper forms, the reviewer will write their initials and date of review at the bottom of the forms.

ACT intervention quality assurance

The ACT stigma intervention will be delivered by clinical psychologists. Supervision will be provided by site PI and an ACT trainer. Interventionists and supervisors will be trained by ACT trainers. To assess interventionist fidelity to ACT, we will use an ACT Fidelity Measure to rate the recorded intervention videos/tapes, with a focus on interventionist behavior and competency. The measure classifies three different targets of clinician behaviors, openness, awareness, engagement, as well as interventionist stance. This will also allow us to investigate how combinations of interventionist behaviors relate to outcomes and help train future interventionists in Russia and Russian speaking countries.

3.6.B MISSED VISITS

The following procedures will take place in the event of an intervention participant missing their group session. If they miss their:

1st session: We will schedule them into the next available group.

2nd session: We will ask them if they would like to participate in an individual make-up session. This will be an adapted session conducted by one of the interventionists who is trained specifically in this individual session. If they choose to not participate in the make-up session, they will still be scheduled for their 3rd session and for their 1-month and 6-month assessments.

3rd session: This will be a missed session, but they will still be invited for their 1-month and 6-month assessments.

4.7 COMPENSATION

Participants will be compensated for their time and travel with 2000 rubles (approx. USD 30) in currency each for their baseline assessment and for their participation at 1- and 6-month follow-up visits. Participants who complete an ACT session without an assessment will receive the same amount. Participants who complete phone assessments for the follow-up visits will be compensated 500 rubles for their participation with cash or a phone card (this will be offered as a last resort option for the 1-month and 6-month assessments). All participants who conduct their follow-up assessments over the phone due to COVID-19, will still receive full compensation (2000 RUB). Participants who arrive 1 hour late or more to a session will receive partial

compensation (1000 rubles). Participants who arrive with only 30 minutes remaining in the session will receive no compensation.

Similar compensation has been used in a previous collaborative Russian-Boston research study and was deemed by the PSMU IRB to be an appropriate, non-coercive amount of funds for involvement in a clinical research project.

4.8 RETENTION

Baseline visit: Retention begins at baseline by ensuring that the participant enjoys the experience of participating in the study, by explaining the informed consent and what would happen in the study, and by carefully collecting contact information, including both the address where the participant is registered and the address where the participant is currently staying. Participants will be asked to provide contact information for up to 4-5 alternative contacts (although only 2 will be required as per eligibility criteria), who may know their whereabouts. Alternative contacts can include friends, family members, and social workers. Participants will be asked if any of their friends are participating in the study and to include them as alternative contacts, if possible. Contact numbers must be verified by calling the numbers with the participant present, using the following script: "I work with a team at the Center of Medical Rehabilitation #1. Your friend/relative [NAME] is here with me and just enrolled in a study. He/she has listed you as an alternative contact. We will only call you if we are having trouble reaching [NAME] to see if you can help us connect with them. Today I am just calling to confirm that this number is active."

Participants will also be asked for their email address and membership to any social networking platforms.

All visits: Participants will be offered tea, coffee, water, and snacks at each study visit to make their experience in the research study more enjoyable.

RA will offer to help participants add the next scheduled study visit to the calendar in their phone and set a reminder in their phone.

Follow up visits: Contact information for participant and alternatives will be reviewed and updated at every visit.

Other strategies: Participants will be contacted by telephone with appointment reminders and email if one is provided. The study team will also utilize social networking to connect with participants. If participants are unable to be reached via phone, in addition to attempting to reach them via text messaging and email, participants will be sent private messages on Vkontakte (Russian social network) utilizing an existing standard script to remind them of their upcoming study visit. No sensitive information will be revealed or ascertained using this method.

Standard reminder text: This is a reminder that your visit to the Center of the Medical Rehabilitation #1 is scheduled for_____at_____. Please reply to confirm or call 973-53-96 to reschedule.

Study participants will be asked to contact the study team if their phone number changes between study visits; participants will be compensated 200 rubles (USD 3) in currency for this information. All no-shows will be followed up to reschedule appointments.

Participants will receive a card with clear instructions on how to arrive to the study site.

5. ASSESSMENTS

5.1 BASELINE ASSESSMENT

The baseline assessment will be conducted immediately following the screening and informed consent. The assessment will be interviewer-administered.

Participants will be assessed as part of this study using validated interview instruments covering the following topics, which will take approximately 60 min:

- Demographics, modified from the ASI Lite-CF Clinical/Training Version and Addiction Severity Index[7]
- ART Medication Use and Adherence
- HIV Sex Risk Behaviors, questions are adapted from the Women's Health Coop Baseline Questionnaire
- HIV Risk Categories, using questions adapted from the American Red Cross and Navaline et al.[17]
- HIV Disclosure, using questions from Stein et al. (1998)[18] and Raj et al. (2006)[19]
- HIV Stigma, using the Berger et al. HIV stigma scale[20] and Leickness et al.
- Substance Use Stigma[21, 22], via a modified Substance Abuse Self-Stigma Scale
- Substance Use enacted interpersonal stigma, through the Stigma-Related Rejection Scale (SRS)
- Psychological flexibility, by the Acceptance and Action Questionnaire – Substance Abuse (AAQ-SA)
- Mental health through the Patient Health Questionnaire (PHQ-9)
- Anxiety by the GAD-7
- Partner Violence and Sexual Assault, adapted from the TAJ assessment
- Alcohol Use, via the AUDIT-C[28]
- Perceived alcohol stigma, using questions from Luoma et al. (2010)
- Drug use by an adapted version of the Risk Behavior Survey[30, 31]
- Overdose and Suicide, using adapted questions from Britton et al. (2012)[34]
- Social Support, using the harmonized STTR document[35, 36]
- VR-12 Health Survey & MOS-HIV[37, 38]
- Care utilization
- Post-Traumatic Stress Disorder via the Abbreviated PTSD Checklist
- Police involvement
- HIV Testing History

5.2 FOLLOW UP ASSESSMENTS

Phone assessments will be permitted for 6 month assessments, as a last resort, for participants who are unable to come in-person. The 1 month assessment will take about 45 minutes, the final assessment at 6 months will take about 60 min.

Administered Assessment	Baseline	1-Month	6-Month
Demographics	X		
ART Use and Adherence	X	X	X
HIV Sex Risk Behaviors	X	X	X
HIV Risk Categories	X		
HIV Disclosure	X		X
HIV Stigma	X	X	X
Substance Use Stigma	X	X	X
Substance Use Daily Life Experience (SRS)	X		
Acceptance and Action (AAQ-II – SA)	X	X	X
Patient Health Questionnaire (PHQ-9)	X	X	X
Anxiety (GAD-7)	X	X	X
Partner Violence and Sexual Assault	X		
Alcohol Use: AUDIT-C	X		
Perceived Alcohol Stigma	X		
Drug Use	X	X	X
Overdose	X		X
Social Support Scale	X		X
VR-12 Health Survey	X		X
Health Care Utilization	X		X
Abbreviated PTSD Checklist	X		
Involvement with Police	X		X
[‡]Satisfaction with the Intervention		X	
*HIV Testing History	X		
[a]COVID-19 testing history, risk behaviors, and perceptions			X

[‡]Intervention group participants only

*If this information is not collected at baseline, RAs will collect this information at a later study visit.

[a] Not administered to all 6-month participants

6. PARTICIPANT SAFETY

Boston Medical Center, First St. Petersburg Pavlov State Medical University/Global Health Institute and their Institutional Review Boards (IRB), the Principal Investigator (Dr. Karsten Lunze) and the site PI and project manager are responsible for monitoring the pilot RCT proposed for the R00 phase and for ensuring the safety of participants. As the research is conducted in Russia, Dr. Lunze will verify at each weekly conference call meeting if any adverse events or unanticipated problems occurred. The Russian investigators will notify the PI by email of serious incidents the same day. Discussion will take place on whether or not the incident meets the definition of an Unanticipated Problem (UP): is unexpected, possibly related to being in the research, and places subjects or others at greater risk of harm. Discussion will also take include if protocols or consents need to be modified, and if/when the incident should be reported to the IRBs. The principal risk of the study is breach of confidentiality. The remaining risks are minimal.

Participation in this study presents “minimal risk” which is defined as “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests,” (from 45 CFR 46.102(i)). The primary risk of the study is the risk of loss of confidentiality. This risk and

any other risk of study participation are addressed above and within Protection of Human Subjects. The risk of breach of confidentiality is best addressed by appropriate study procedures; however, the PI will be responsible for assuring that study procedures are adhered to regarding data security, data transfer, and communications in tracking participants by meeting regularly with study staff, reviewing procedures, and performing quality control reviews of study forms as described above.

6.1. SPECIFICATION OF SAFETY PARAMETERS

An **Adverse Event (AE)** is defined as any abnormal or harmful behaviors, increasing severity of symptoms that are identified by the interventionist, suicidal behaviors or attempts, breach in the protection of participant data or breach of confidentiality whether or not considered related to the subject's participation in the research.

Stable chronic conditions that were present prior to study entry and do not worsen are not considered AEs.

SERIOUS Adverse Event (SAE) – is any adverse event that

(1) results in death;

(2) is life-threatening;

(3) results in inpatient hospitalization or prolongation of existing hospitalization;

(4) results in a persistent or significant disability/incapacity;

(5) results in a congenital anomaly/birth defect; or

(6) based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

Life-threatening means that the event places the subject at immediate risk of death from the event as it occurred.

Unanticipated Problem (UP) – is defined as an event, experience or outcome that meets all three of the following criteria:

- is unexpected; AND
- is related or possibly related to participation in the research; AND
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

  Possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research

Unexpected means the nature, severity, or frequency of the event is not consistent with either:

- the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent

document, and (b) other relevant sources of information, such as product labeling and package inserts; or

- the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

6.2 Study Monitoring

Since there is no data to be reviewed regularly in this behavioral trial and no stop-rule, as the main concern being loss of confidentiality, the PI will have access to an existing URBAN ARCH Data Safety Monitoring Board (DSMB) if issues arise as needed for the R00 SCRIPT pilot behavioral intervention trial. If there are no issues, the DSMB will not review.

General description of URBAN ARCH DSMB

To ensure the safety of the participants and the validity and integrity of the data, the URBAN ARCH consortium established an external DSMB to assume oversight of the entire URBAN ARCH Consortium and any studies originating from the URBAN ARCH Cohorts, in accordance with NIH guidelines. The K99 used URBAN ARCH data for its quantitative analysis, and the R00 study originated from this work. Although risks with the R00 SCRIPT pilot behavioral intervention trial are essentially limited to loss of confidentiality, due to the vulnerable population of HIV-positive and substance using individuals, the URBAN ARCH DSMB can advise on special precautions to ensure the safety of all R00 study participants. Should any issues be raised by either the PI, any co-investigator or any key study personnel in the R00 SCRIPT behavioral intervention trial, the PI will consult with the URBAN ARCH DSMB. The URBAN ARCH DSMB is responsible for ensuring participant safety (by reviewing blinded and unblinded safety data on a regular basis and assessing the safety of study procedures) and for monitoring the overall conduct of the URBAN ARCH studies.

The DSMB is an independent group advisory to the URBAN ARCH PIs and the NIAAA, and is required to provide recommendations about starting, continuing, temporarily suspending the trial until certain conditions are met, and stopping the studies. Most importantly for the SCRIPT interventional behavioral trial, the DSMB can be asked to make recommendations, as appropriate, about:

- Benefit/risk ratio of procedures and participant burden
- Selection, recruitment, and retention of participants
- Protocol violations and adherence to protocol requirements
- Completeness, quality, and analysis of measurements
- Amendments to the study protocol and consent forms
- Participant safety
- Notification of and referral for abnormal findings

The DSMB meets by conference call at a minimum of every 6 months. The Board is charged with evaluating the quality of trial administration, monitoring safety issues, and providing guidance on scientific, methodological and ethical issues. Specifically, the Board reviews investigators' plans and processes for

identifying individual or patterns of adverse events and review accumulating safety data. Following each meeting, the DSMB will make recommendations on modification, or termination of the study.

The Board will be composed of three full members (inclusive of the DSMB Chair) and 1 adjunct member.
Full Members of the DSMB are:
1. Theodore Colton, ScD (Professor of Epidemiology and Biostatistics, BUSPH), Chair of DSMB
2. Josiah Rich, MD (Professor of Medicine, Brown Medical School)
3. Jesse Stewart, PhD (Associate Professor of Psychology, Indiana University-Purdue University Indianapolis)

Consulting with the DSMB as needed for this trial will be valuable for further ensuring the quality and scientific validity of the study. An agenda will be provided detailing the studies to be discussed. If any issues arise with the R00 SCRIPT study, it will be added to the agenda. It is estimated that the meeting will be scheduled for 1.5 hours. Communication in the interim will be as needed. Unscheduled meetings can be requested by any party with the responsibility of overseeing the study. Requests can be made to the DSMB Chair, PIs, or NIAAA officials. The Chair, in collaboration with the URBAN ARCH Administrative Coordinating Core or NIAAA, will schedule any unplanned meetings.

The Methods and Time for Assessing, Recording, and Analyzing Safety Parameters

All AEs will be assessed to determine if they meet criteria for a Serious Adverse Event (SAE). All AEs will be reported to Dr. Lunze at weekly phone meetings. Dr. Lunze will be designated to distinguish a serious adverse event (SAE) from a non-serious adverse event. The site PI and project manager (both MDs) will monitor SAE and AE on site. If the AE is serious, then the SAE form must be completed and appropriate reporting measures followed. Investigators are encouraged to consult with the PI, if they are uncertain how to classify an event.

Suicide Safety Protocol: Any participant who voices current suicidality or is experiencing a psychiatric emergency during the interview or group session in the presence of a Research Assessor or Interventionist, will be reported to the site PI or his designee immediately. The site PI or the assessor (Research Assessor or Interventionist) will determine the appropriate course of action, which will depend on location of the event and the clinical situation. If clinically indicated, the participant will be referred to acute suicide intervention services.

- Information of risk for suicide may be obtained by either impromptu information, from question 9 of the Mental Health Survey: PHQ-9 in the study assessment, or question 1f in Section B of the screener.
- If the participant answers any option that is not “Not at all” for question 9, a suicide safety question will autopopulate, assessing suicidal plans. If the participant answers “Yes” or “Refused” for the suicide safety question, the Research Assessor will move forward with the above suicide safety protocol.
    - If the participant answers “Yes” or “Refused” for the suicide safety question (post question 9 of the PHQ-9) during the baseline assessment, the participant will be disenrolled from the study. They will not be disenrolled during the 1-month or 6-month assessment, as they will no longer be receiving the intervention, however they will still be clinically assessed.
- If a potential participant answers “Yes” or “Refused” for question 1f of section B of the screener, the Research Assessor will move forward with the above suicide safety protocol.

The study will take place in a setting where standard procedures are in place to assist patients who experience acute events. The research assessors and interventionists are trained clinical psychologists, specialists in social work, and addiction psychiatrists. If consequences arise due to research procedures (e.g., distress, anxiety, suicidal ideation), the physician investigators will be available to assess participants and make appropriate interventions or referrals based on the clinical circumstances. Any participant who voices current suicidality or is experiencing a psychiatric emergency during the assessments will be evaluated by that physician investigator, who will determine the appropriate course of action, which will depend on location of the event and the clinical situation. Patients will be escorted to receive care by appropriate staff if deemed necessary.

- If an event is discovered outside of the scheduled study visits, it must still be recorded accordingly.
- Action to be taken will be determined by the RAs for all AEs that are mild and moderate (unless specified below) and by the site PI or project manager for SAEs and AEs that are severe, life-threatening or fatal.

SAE Reporting

If the SAE is not resolved or stabilized at this time or new information becomes available after the SAE form is completed, the SAE form should be updated as soon as possible. Any changes or updates to the SAE form will need to be re-reviewed and re-authorized by the study clinician.

In some cases, the study clinician may be unsure upon first learning of an SAE whether it is study related and/or expected, because study staff are awaiting more complete medical records. In such cases, the study clinician should make his/her best estimate of relatedness and expectedness, understanding that these determinations can be updated later. When updating determinations at a later date, the rationale for the change should be included in the SAE narrative.

SAEs and unanticipated events which are considered “at least possibly related” during the treatment and follow-up phases will be reported to the local IRB and to NIDA within 48 hours of knowledge of the SAE and all other SAEs and unanticipated events will be reported within the time period mandated by the local IRB as indicated below.

The site must actively seek information about the SAE until the SAE is resolved, stabilized or until the participant is lost to follow-up and terminated from the study.

To summarize: upon determining an Adverse Event is Serious, the following procedures should be followed:

- The study staff, while meeting/talking with the participant or person providing details on the event, will gather as much information about the event from the participant as possible and complete the appropriate forms.
- The completed AE and SAE forms will be reviewed by key personnel on the Pavlov team. Any relevant clinical documents (labs, physician notes) available at that time will be provided to key personnel on the Pavlov team within 24 hours of finding out about the event.
- After initial notification, the SAE must be updated with any additional information.

All unanticipated problems must be reported to the US team immediately.

Reporting Procedures to the IRB and NIDA

Each site will follow reporting guidelines set forth by their Institutional Review Boards regarding unanticipated problems, adverse events, and serious adverse events. Deaths and serious breaches of confidentiality reported to research staff will be reviewed by the site PI and reported to the PI the same day, who will then report to the IRB. The co-investigators and PI will review aggregate data every 6 months. Should any irregularities arise, the PI will consult with the DSMB, as described above. According to the minimum standards for AE and SAE reporting to NIDA, we will report AEs and SAEs once per year through the annual progress report.

Reporting mechanisms of IRB actions to NIDA: The PI will provide a summary of safety-relevant events to NIDA on an annual basis as part of the progress report.

Report of changes or amendments to the protocol. All changes or amendments to the protocol will be submitted to both IRBs prior to changing study procedures.

BUMC Reporting Guidelines:

The Principal Investigator at BMC/BU Medical Campus will report Unanticipated Problems and Adverse Events to the BMC/BU Medical Center IRB in accordance with IRB policies:

- Unanticipated Problems involving a fatal or life-threatening event will be reported to the IRB within 2 days of the investigator learning of the event.
- Unanticipated Problems not involving a fatal or life-threatening event will be reported to the IRB within 7 days of the investigator learning of the event.
- Adverse Events (including Serious Adverse Events) will be reported in summary at the time of continuing review, along with a statement that the pattern of adverse events, in total, does not suggest that the research places subjects or others at a greater risk of harm than was previously known.

Pavlov Reporting Guidelines:

What Event is Reported	When is Event Reported
Fatal or life-threatening unexpected, suspected serious adverse reactions	Within 7 calendar days of initial receipt of information
Non-fatal, non-life-threatening unexpected, suspected serious adverse reactions	Within 15 calendar days of initial receipt of information
AEs and UPs	On a quarterly basis

7. DATA MANAGEMENT

7.1 DATA COLLECTION

All study data will be captured electronically on computers via a secure, web-based data capture system. All computers for data collection and analysis will have encryption. Audiorecordings to code adherence to the study protocol and the study manual will be made with a dedicated, portable audiorecorder. Recordings will be transferred to a secure server immediately following the session and deleted from the portable devise. Coding will be directly from audiorecordings by a Russian-speaking, certified ACT trainer. All audiorecordings

will be kept on the secure server until seven years after completion of study analyses and publication of study manuscripts and then deleted.

7.2 QUALITY CONTROL PROCESS

Quality control measures will include: detailed and unambiguous specifications for completion of data forms, including rules for coding skipped questions and missing data, training of study staff responsible for data collection and built-in validation rules, error checks, question skips for electronic data capture, and computer algorithms to check for out-of-range codes and internal inconsistencies. All data, regardless of capture method, will be converted to SAS datasets and reviewed for logic, skip patterns, response ranges, out-of-range codes, and internal inconsistencies. The RAs will be queried regarding any noted inconsistencies.

7.3 DATA SECURITY, WEB SYSTEMS, AND CONFIDENTIALITY

Screening forms and most other research paperwork will not include the participant's name; instead, a unique ID will be assigned to each person screened, and another number assigned to those who enrolled. Any documents with identifiable participant data will only be accessible to the Russian Co-Investigators, the project management staff, and the RAs who recruit and follow participants.

Tracking information will be kept similarly. Computer data will be password protected, and accessible only to research associates needing the information for follow-up purposes.

The Ukrainian Institute on Public Health Policy (UIPHP) will design, develop and maintain the electronic data collection forms, participant and data tracking, and underlying database systems, and implement procedures for data quality control, including multiple checks for entered data. Electronic data collection forms will be designed to read easily, have clear instructions, preprogrammed skip patterns, real-time range checks and internal logic to minimize missing data and result in "cleaner" data at capture. Electronic data collection forms, including randomization module, participant and data tracking, will be developed in REDCap (Research Electronic Data Capture), a web application located at UIPHP server. The REDCap platform has no hard requirements with regard to server processing power, memory or hard drive space since it is not resource-intensive and requires very little initial drive space by either the web server or database server. The application employs various methods to protect against malicious users who may attempt to identify and exploit any security vulnerabilities in the system. The REDCap users have access only to data and information that they are supposed to have within the application by identifying user privileges. Each user has their own account, and their user account will only have access to REDCap projects that they have created themselves or to projects which other users have granted them access. REDCap contains an auto-logout setting, which is customizable (default auto-logout time is 30 minutes), and will automatically log a user out of the system if they have not had any activity (e.g. typing, moving the mouse) on their current web page for the set amount of time. This prevents someone else from accessing their account and their project data if they leave a workstation without properly logging out or closing their browser window. REDCap maintains a built-in audit trail that logs all user activity and all pages viewed by every user, including contextual information (e.g. the project or record being accessed). Therefore, a REDCap project administrator will be able to monitor any activity in the project, e.g. entering data, exporting data, modifying a field, running a report, or add/modifying a user. Study forms will be completed according to the schedule below.

After completion of data collection in REDCap, all data that we collect from participants will be de-identified and transferred to the URBAN ARCH repository for future research. When investigators want to perform a study on repository data they will submit a study plan for review and approval and will need to obtain any necessary approvals, such as approval from their IRB, to carry out the work with repository data. Prior to receiving the data, the researchers will agree not to share the data and not to attempt to identify any individual participants. In all cases, the data will be released from the repository in coded form (i.e., names and contact details will not be included and data/samples will be identified by a subject ID number).

FORM	Phone Screen	Screen & Baseline Visit		ACT Sessions 1-3	1-month visit (4 weeks)	6-month visit (24 weeks)	As Needed
	Screen	Screen	Baseline				
Screener	X	X					
Consent and enrollment form		X					
Contact info			X	X	X	X	X
Baseline assessment			X		X	X	
1-month assessment					X		
6-month assessment						X	
Contact log							X
Baseline tracking form			X				
Follow-up tracking form			X	X	X	X	
Participant tracking overview							X
SAE form (Web)							X
Incarceration Form							X
Study conclusion form							X
ACT interventionist fidelity checklist				X			X
All forms are electronic, unless indicated otherwise							

8. STATISTICAL ANALYSIS

This study will use an intent-to-treat analysis that includes all participants according to their randomized assignment. Descriptive statistics will be calculated for variables at baseline and each follow-up time to assess whether there appear to be any differences across treatment arms.

Our Specific Aims are to compare the effects of SCRIPT and standard of care on following outcomes:

Aim 1: ***Evaluate the feasibility of an ACT stigma intervention*** compared to standard of care via a 2-armed RCT of 100 HIV-positive Russian PWID on the following outcomes:

a. Primary: Satisfaction with the intervention at 1 month
b. Secondary:
    a. Participation in three intervention sessions;
    b. Fidelity to the intervention, using the Adherence Raters' Manual for Stigma Treatment Study (Kohlenberg et al, 2004) and an intervention adherence score

Aim 2: ***Measure changes in internalized stigma***

Primary:

a. HIV Stigma via the Simbayi HIV internalized shame scale at 1 month;
b. Substance Use Stigma via Modified Substance Abuse Self-Stigma Scale at 1 month

Secondary:

a. Any initiation of HIV care (ART) at 6 months
b. Engagement in substance use care at 6 months
c. Change in last 30 days injection drug use at 6 months

Exploratory:

a. Depression as measured by the PHQ-9 at 6 months
b. Anxiety as measured by the GAD-7 at 6 months
c. Intersectional stigma as measured by both substance use stigma and HIV stigma scales at 6 months
d. Psychological flexibility measured via the Acceptance and Action Questionnaire at 6 months

8.1 PRIMARY ANALYSES

The primary outcome for this aim is satisfaction with the intervention. We will calculate descriptive statistics for all variables at baseline and follow-up. Initial analyses will compare binary outcomes between groups using a chi-square test and comparing continuous outcomes (i.e. satisfaction scores) using two sample t-tests. Because ACT intervention is delivered in the form of group sessions, individuals within the same groups will be correlated. All analyses will use the intention-to-treat approach and analyze participants according to randomized group, accounting for intra-group correlation.

9. STAFF TRAINING

9.1 TRAINING OF STUDY STAFF

All study staff will be trained on the study protocol. Training will take place in-person in Tbilisi, Georgia, St. Petersburg, Russia, and via webinars.

Recruitment will be performed by a CSO outreach worker who has extensive experience working with this population. In-person screening, enrollment, and all assessments will be performed by Research Assessors (RAs) who have experience working with this population. The staff are trained to assess for adverse events and will follow established protocols for identifying and monitoring any ongoing adverse events.

9.2 TRAINING OF INTERVENTIONISTS

The SCRIPT intervention training will be led by a certified ACT trainer who has substantial experience conducting behavioral intervention trainings, and a certified ACT trainer native in Russian, together with the BMC PI, who is trained in ACT and has relevant experience with conducting research internationally to engage HIV-positive PWID in medical care. Over the course of 5 days, the trainers will train the interventionists in

Tbilisi, Georgia, providing them with an overview of the theoretical framework, assessment techniques and the SCRIPT intervention; and practice the intervention delivery to assure the appropriate use of ACT in this context. As per previous trainings in earlier studies, simultaneous translation may be used to allow multiple role-playing sessions to be critiqued. Booster trainings will be conducted bi-annually and as necessary based on findings from quality assurance efforts. These intensive trainings as well as the monitoring and observation for quality assurance are designed to limit potential variability due to individual interventionists.

10. STUDY CONTACTS

Dr. Lunze will be responsible for the financial management of the study and communication between NIH and the rest of the leadership team. He will manage the implementation of the study in Russia and oversee all components of the study. He will lead the weekly study team research meetings. He will help create the study protocol, oversee its administration, and assist in training interventionists. He will participate in analysis and presentation of study results and preparation of papers for publication.