MASLIHAT INTERVENTION FOR TAJIK MALE MIGRANTS WHO INJECT DRUGS

Protocol Number: 2020-0795

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Principal Investigator: Mary E. Mackesy-Amiti

Grant Title: MASLIHAT Intervention for Tajik Male Migrants Who Inject Drugs

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CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines, as described in the *Statement of Compliance* above.

Principal Investigator:

Signed: _____ Date: 11/18/2021

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Site Investigator:

Signed: _____ Date: 11/18/2021

Name: Mahbatsho Bahromov

Title: Director, PRISMA Research Center

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1 PROTOCOL SUMMARY

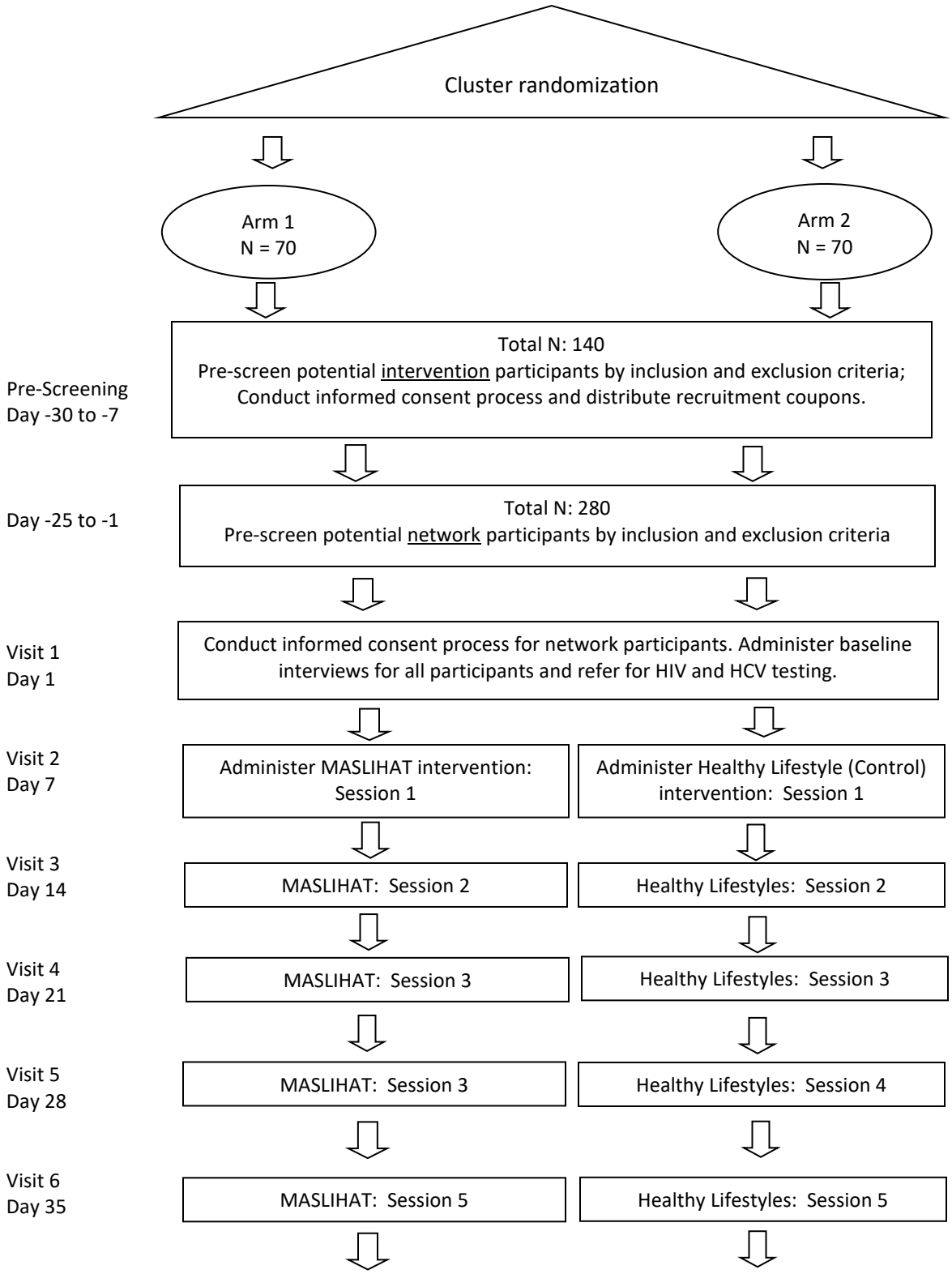
1.1 SYNOPSIS

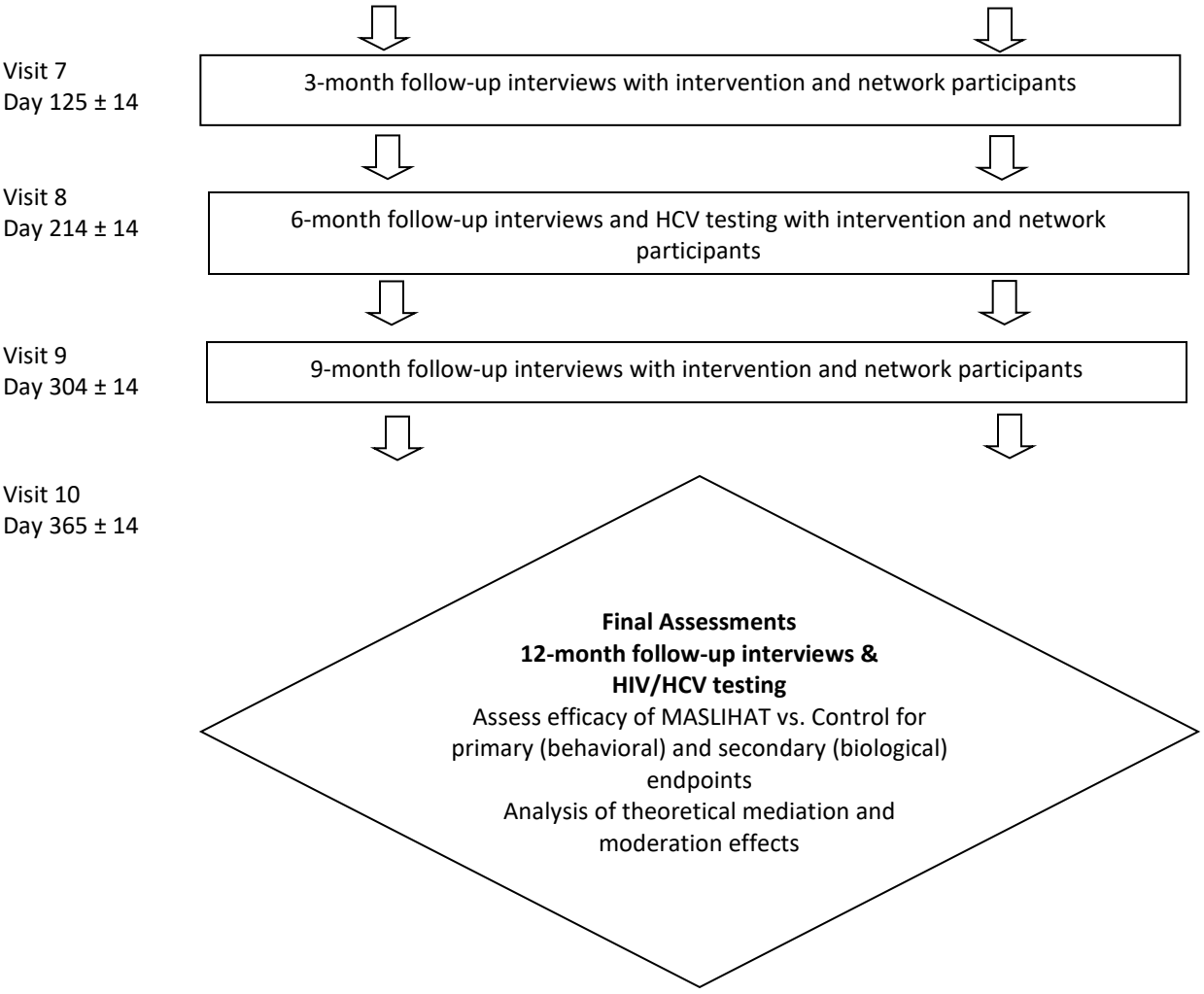
Title:	MASLIHAT Intervention for Tajik Male Migrants Who Inject Drugs
Grant Number:	1R01DA050464
Study Description:	This protocol will test the efficacy of the MASLIHAT peer education HIV prevention intervention for Tajik migrant laborers who inject drugs in the host country, against an attention control. The primary outcomes are self-reported risk behaviors among participants and network members over 12 months following the intervention, including syringe sharing, and sex without condom. Follow-up interviews will be conducted at 3, 6, 9, and 12 months. We will conduct HIV testing at baseline and 12-month follow-up, and HCV testing at baseline and 6- and 12-month follow-up. We expect the MASLIHAT intervention to be associated with greater reduction in injection and sexual risk behavior during follow-up compared with the control condition.
Objectives*:	Primary Objective: Assess the efficacy of the MASLIHAT intervention compared to the TANSIHAT control condition for reducing injection equipment sharing, condomless sex, and heavy alcohol use among intervention participants and among their network members. Secondary Objectives: Assess the efficacy of the MASLIHAT intervention compared to the TANSIHAT control condition for reducing the incidence of HIV and hepatitis C infection among intervention participants and among their network members
Endpoints*:	Primary Endpoint: Reduce the proportion of men sharing syringes or other injection equipment in the past 3 months to 10% or less; reduce the proportion of men engaging in condomless sex in the past 3 months to 10% or less. Reduce the proportion of men engaging in heavy alcohol use in the past 3 months to 10% or less. Secondary Endpoints: Reduce the 12-month incidence of HIV and HCV by 50% compared to the control group.
Study Population:	We will enroll a total of 420 male Tajik migrant workers who inject drugs in Moscow, including 140 intervention participants (70 MASLIHAT, 70 control group) and 280 network members recruited by the intervention participants for participation in the assessments.
Phase* or Stage:	Phase 2
Description of Sites/Facilities Enrolling Participants:	Participants will be enrolled at PRIZMA Research Center in Moscow, Russia.

Description of Study Intervention/Experimental Manipulation:	MASLIHAT is a small group peer education training HIV prevention intervention for Tajik migrant workers who inject drugs in the host country. It is delivered in 5 2-hour sessions delivered once a week for 5 weeks.
Study Duration*:	30 months
Participant Duration:	12 months.

1.2 SCHEMA

Flow Diagram




Visit 7
Day 125 ± 14
3-month follow-up interviews with intervention and network participants
Visit 8
Day 214 ± 14
6-month follow-up interviews and HCV testing with intervention and network participants
Visit 9
Day 304 ± 14
9-month follow-up interviews with intervention and network participants
Visit 10
Day 365 ± 14
Final Assessments
12-month follow-up interviews &
HIV/HCV testing
Assess efficacy of MASLIHAT vs. Control for primary (behavioral) and secondary (biological) endpoints
Analysis of theoretical mediation and moderation effects

1.3 SCHEDULE OF ACTIVITIES

	Pre-screening (Pre-consent)	Visit 1 Day 1	Visit 2 Day 7±3	Visit 3 Day 14 ±3	Visit 4 Day 21 ±3	Visit 5 Day 28±3	Visit 6 Day 35 ±3	Visit 7 Day 125 ±14	Visit 8 Day 214 ±14	Visit 9 Day 304 ±21	Visit 10 Day 365 ±30
Recruitment / pre-screening	X										
Network pre-screening	X										
Informed Consent		X									
CAPI interview		X						X	X	X	X
HIV testing		X									X
HCV testing		X							X		X
Intervention participation			X	X	X	X	X				
Adverse Events Reporting		X	X	X	X	X	X	X	X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

Labor migration is an important contributor to the continuing global AIDS epidemic and also the movement of HIV across country borders and populations.[1-3] Migrants who inject drugs while in a host country are at especially high risk due to behaviors that are exacerbated by social marginalization and lack of access to health care and preventive services.[4] Tajikistan, a small country in Central Asia with a high unemployment rate and growing drug epidemic, exports more than a million Tajiks annually, many of whom inject drugs, to work outside of their own country.[5, 6] Russia, with one of the world's highest drug-related HIV rates, is a major destination. Our earlier research showed alarmingly high normative and behavioral risk for HIV among Tajik migrant men who inject drugs (MWID) in Moscow due to risky drug use, needle sharing, alcohol consumption at behavior disinhibiting levels, and unsafe sex with casual and paid sex partners.[7] Yet, little exists in the way of HIV prevention programming for migrants who inject drugs in Russia[4] or even prevention models for migrants worldwide.[8] A grave need exists for a targeted culturally and contextually congruent HIV preventive intervention for labor migrants who inject drugs.[9] To help curb transmission in this vulnerable population, we developed and pilot tested the Migrants' Approached Self-Learning Intervention in HIV/AIDS for Tajiks (MASLIHAT) prevention model. The model recruits and trains Tajik migrants who inject drugs as peer educators in delivering the intervention to others in their social networks while simultaneously reducing their own risk. Pilot testing of the model (R21DA039068) with pre/post evaluation indicated that the intervention proved successful in reducing heavy alcohol use, condomless sex, and syringe sharing.

The current study will test the efficacy of the MASLIHAT Intervention to reduce risky drug, alcohol, and sexual behavior among Tajik male labor migrants in Moscow who inject drugs compared with a control intervention in a parallel design cluster-randomized trial. In the MASLIHAT intervention, we will train Tajik migrant MWID as peer educators who will deliver the intervention to their network members both during the five-week training and after completion. We will assess changes in drug, alcohol, and sexual risk behavior at 3, 6, 9 and 12 months post-intervention, and compare effects for MASLIHAT and control group participants, and their network members. We will also examine mechanisms of behavior change among MASLIHAT participants, including purported mediators and potential moderators. We will assess changes in HIV knowledge, risk awareness, prevention self-efficacy, psychosocial well-being, and behavioral norms among participants and network members, and test associations with injection drug use (IDU) social network interactions and mediation of behavior change outcomes. We hypothesize that the MASLIHAT intervention will influence behavior of both peer educators and network members by increasing knowledge and awareness of HIV transmission risks, modifying behavioral norms, and improving self-efficacy.

2.2 BACKGROUND

1.1. The role of labor migration in HIV acquisition and transmission is a high-priority issue for both developing and developed countries.[4, 10] Central Asia is the world's second largest migration pipeline,

and reports the fastest growing rates of HIV/AIDS globally.[11, 12] Tajikistan, a small impoverished country in Central Asia, is one of the most remittance dependent countries in the world.[13, 14] After a 2-year decline due to the economic downturn in Russia,[15] remittances are now rising again. Remittance inflow to Tajikistan through migrant labor in Russia accounted for an estimated $2.2 billion per year or 31% of its GDP in 2017.[13] It is estimated that almost one million Tajik citizens work outside the country; most of these migrants are men, and that one-third of men age 20 to 39 have left Tajikistan at least once in their lives to find temporary work.[14] Most of these migrant workers find employment in the Russian Federation, mainly working in construction, trade, agriculture, and maintenance.[16, 17] Most stay in Russia for 2-3 years due to the transportation costs in getting there plus legal restrictions that make it difficult to obtain visa papers that allow annual or frequent crossings. A World Bank study found that over a 2.5 year period (May 2015-December 2017), 26% of the households surveyed had a migrant worker at some time.[18] According to the Ministry of Health of Tajikistan, migrants make up 14.9% of the total number of HIV infected men and women, and 87% of HIV-infected are men.

As often true for labor migrants, life in Russia for Tajik male workers is hard. Previous research reveals that Tajik migrants perform Russia's most dangerous construction work and low-wage jobs.[19] They often are the focus of Russian hostility and violence including physical beatings, and they reside in substandard living conditions, eat non-nutritious meals during brief work breaks, and have little or no access to Russian health care if sick or injured.[20] Also, some unknown number, having entered Russia illegally, constantly hides from authorities. Moreover, if diagnosed with HIV they face deportation and restriction from re-entry.[21] These factors, along with the psychosocial stress and separation from family and friends, can coalesce to produce emotional distress including depression and feelings of loneliness that encourage risky behavior.[22]

1.2. HIV risk behavior among Moscow Tajik migrants occurs in a country that has an exceedingly high and still rising HIV rate.[23] While globally new infections declined by an estimated 16% from 2010 to 2017,[24] in Eastern Europe and Central Asia the number of new infections grew by an estimated 30%. The Russian Federation accounts for 70% of HIV cases in this region and accounted for 75% of new HIV infections in the region in 2017.[11] Most HIV infections in the region are among people who inject drugs (PWID) and their sexual partners,[25] yet harm reduction service coverage is low. A recent study of PWID in St. Petersburg reported an HIV incidence rate of 9.3 per 100 person years.[26] In the Russian Federation in particular, insufficient access to sterile injecting equipment and the unavailability of opioid substitution therapy (OST) are significant roadblocks to reducing HIV infections among people who inject drugs.[12, 27] Tajik migrants form a potential bridge for HIV to move from high-prevalence Russia to low prevalence Tajikistan, which currently has a centralized epidemic primarily among PWID. HIV prevalence among PWID in Tajikistan is estimated at 13.5% compared to 25.6% in the Russian Federation.[25]

1.3. HIV risk behavior among Tajik labor migrants who inject drugs in Russia is alarmingly high. In our first survey of 106 Tajik migrant men who inject drugs (MWID),[7] 105 (99%) of the sample reported using heroin in Tajikistan before relocating to Moscow; 94% reported injecting drugs at least once a week; and 83% reported having shared needles or syringes in the last 30 days. Sharing unclean "works" appears to be a normative practice. As one of our sample participants explained, "We use the same syringe and

needle every time. We share our equipment; we are one circle of friends." Meanwhile, although knowledge that HIV can spread sexually was well-known (93%), 66% of the MWID that we sampled didn't know it could be transmitted through unclean needles. One participant who rejects this notion remarked, ""If it is transmitted through sex, then how can there be a link between HIV and drug use? There isn't any link." Only 9 participants reported injecting with a non-Tajik (nearly all Russian women). Condom use was low with 74% of the MWID with regular sexual partners reporting never using them even when buying sex. Risky alcohol consumption was common, with 23% engaging in possible hazardous use according to the WHO Alcohol Use Disorders Identification Test.[28]

1.4. Hepatitis C virus (HCV) transmission is also driven largely by the sharing of injection equipment. Rates of HCV infection among PWID in Tajikistan indicate high levels of risk behavior. Estimates of HCV prevalence among PWID in Tajikistan range from 23 to 67% infected.[29, 30] A study conducted in the capital city Dushanbe reported that HCV infection among PWID was significantly associated with living/working outside Tajikistan in the past 10 years, as well as daily injection of narcotics, while being female and always using a sterile needle were inversely associated with HCV infection.[31]

1.5. The MASLIHAT Intervention and our research efforts build synergistically on 3 theoretical models. Like the SHIELD model, MASLIHAT's approach to intervention draws on social-cognitive- behavioral theory,[32] which suggests that individuals will adopt new norms and practices that reduce their HIV risk by learning how and why they should do so and by observing role models to follow.[33] Social network theory[34] guides our belief that as one or two influential members of a social network change, others do so as well. A key to promoting safer behavior lies in embedding members within networks as a catalyst to change. We also draw on Yang's Theory of Migration,[22] which posits that successfully changing risk behavior requires modifying the psycho-social conditions and life circumstance that help to generate it. The intervention model is depicted in Figure 1. We expect MASLIHAT training to improve participant HIV knowledge, risk awareness, knowledge of prevention strategies and prevention self-efficacy. We also expect to see improved psychosocial well-being evidenced by decreased depression and loneliness as a result of the life course strategies that the model promotes. Participants will disseminate their knowledge to their injection network, resulting in improved behavioral norms, safer sex, drug use, and alcohol use among both participants and network member. Both our study and the MASILIHAT model build on the premise that peer educators will endorse and promote safer HIV prevention norms and reduce their own HIV risk behavior due to active participation in the MASLIHAT intervention as will their network members through targeted interaction with the peer educators. In doing so, the intervention will yield positive changes in risky drug and sexual behavior at both the individual and social network levels for Tajik migrants both in their host country and their home country upon returning.

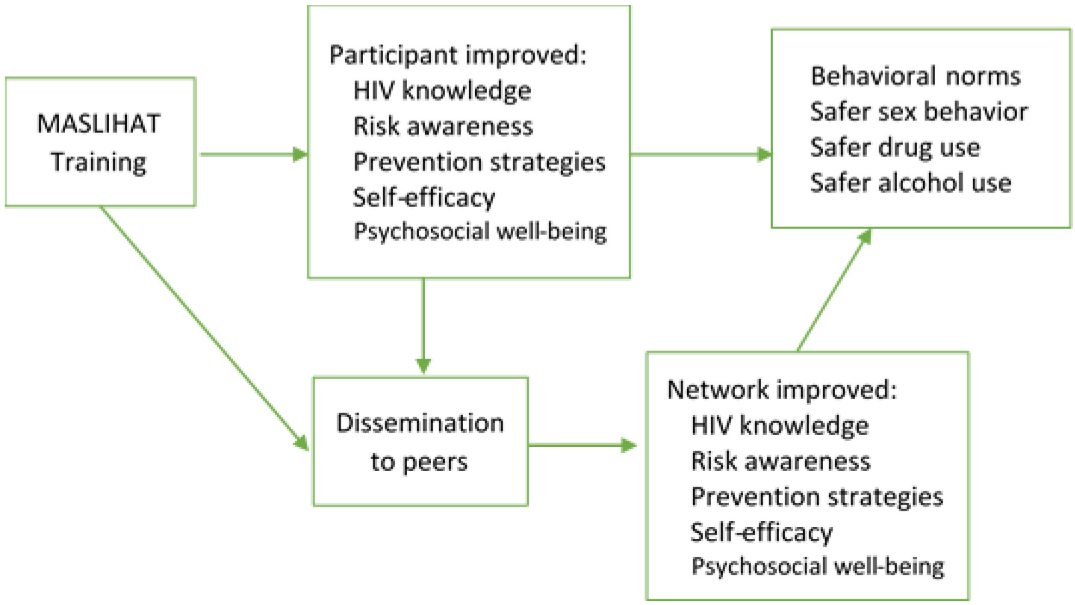


Figure 1. Intervention model

1.6. The MASLIHAT intervention that we developed addresses all 3 risk behaviors common to Tajik migrant MWID: risky drug, alcohol, and sexual practices as experienced within the psychosocial context of temporary labor migration. The word "maslihat" in Parsi denotes, "group respect and decision-making in resolving a problem." Our model builds on a socio- cultural adaption of the successful prevention model, "Self- Help in Eliminating Life-Threatening Diseases (SHIELD)." [35] Developed by Dr. Latkin (consultant) and his colleagues, the CDC designates SHIELD as a best practice, evidenced-based HIV prevention intervention in the U.S. Clinical trial findings showed that when compared to their counterparts in a control group at 6-month follow-up, injection drug users who received the SHIELD intervention reported significantly greater reductions in needle sharing, less frequent injecting, and greater increases in condom use with casual sexual partners. The prevention model was built on research that we conducted on HIV risk among male Tajik migrants who inject drugs in Moscow.[7] We found that like the general population of Tajik migrants studied by Bakhromov and Weine,[36] those migrants who also inject drugs face the same social, cultural and health challenges as their counterparts plus the added burden of stigma and the double jeopardy of social marginalization within both Russian society and Moscow's Tajik communities due to their drug use. While some Tajiks migrants who inject drugs maintain close social ties with family and friends in Moscow, others withdraw.

1.7. MASLIHAT is a small-group, interactive intervention that relies on peer networks to reduce drug, alcohol, and sexual risk behaviors among temporary migrant workers who inject drugs. Migrants in the host country who are current or former MWID are trained as peer educators to promote positive HIV risk-reduction norms and behavioral change through role modeling and sharing what they learned during MASLIHAT training sessions with their at-risk network members, especially other MWID. The intervention includes 5 HIV knowledge and skill-building sessions that involve goal setting, role playing,

demonstrations, homework (practicing peer education skills), and group discussions. These sessions teach participants techniques for personal risk reduction and the communication and outreach skills needed to encourage others at HIV risk to adopt them as well. As migrants often confront special challenges based on social marginalization and economic disadvantage as a population within the host country, MASLIHAT sessions also address lifestyle, health, and safety issues.

1.8. MASLIHAT fits well with the prevention needs of Tajik MWID living in diaspora: 1) It is delivered by migrants to migrants, and not dependent on support from a host national health care system that denies them access to services; 2) Using current and former MWID to recruit and teach other MWID can reach migrant drug-using populations that are hidden or hard-to–reach; 3) It addresses risk reduction at both the individual and network levels; and 4) It requires little resource investment to implement. Staff at existing diaspora service organizations or former peer educators can serve as facilitators, and its 5 sessions can be delivered at any location with sufficient meeting space, including socio-geographic "hot spots" where risky behavior occurs.

1.9. In addition to reducing HIV among Tajik labor migrants who are MWID, MASLIHAT is expected through increased HIV knowledge and normative change to help decrease HIV transmission in Tajikistan when Tajik men return home to their spouses and sex partners. Earlier research has shown that Tajik migrant males seldom use condoms with their partners in Tajikistan despite high-risk behavior while away from home.[37] Also, Tajikistan is a key transit point in the Northern Route of opium trafficking from its southern neighbor, Afghanistan, which produces more than 90% of the world's opium.[38] Until recently, injection drug use was the main mode of HIV transmission in Tajikistan, accounting for over half of all cases[39]. However, recent reports indicate that the HIV epidemic has become more generalized. In 2016, heterosexual transmission accounted for 65% of cases[40]. Notably, according to a 2015 survey by the Tajik Center for AIDS Prevention and Control, over 50% of HIV-infected women reported that their sexual partners were labor migrants. MASLIHAT peer educators and network members who adopt safer HIV norms and practices while in Russia are likely to continue and disseminate them to their counterparts in Tajikistan when they return home. In doing so, they can help to block the bridge of transmission from a high prevalence to low prevalence country.[41]

1.10. MASLIHAT meets the grave need globally for HIV intervention for labor migrants in general. To date, only a few interventions for migrants have been developed or tested despite their grave vulnerability to HIV. Yet the need for interventions is pressing.[42] The MASLIHAT approach and intervention can be adapted for use with other migrant populations at risk for HIV and hepatitis C through injection drug use, including migrant workers and other immigrants who inject drugs in Central Europe[43], Southeast Asia[3, 44], China[22], South Africa[45], and the United States.[41, 46-52] While a number studies have been conducted on HIV risk among temporary workers in the U.S., especially Caribbean and Mexican seasonal laborers,[53-60] few studies have addressed HIV risk acquired through injection drug use or its prevention.[46, 61] With the recent increase in injection drug use in the U.S. and its heavy economic reliance on foreign labor, if shown to be successful with Tajiks in Moscow, the MASLIHAT intervention also holds promise in preventing HIV transmission among similar populations in the U.S.

1.11. Preliminary Studies

1.11.(a). Background Research. In research conducted through a Senior Fellowship from the International AIDS Society and NIDA to Dr. Bakhromov under the mentorship of Dr. Levy, focus group discussions were conducted with 24 Tajik male migrants who regularly inject drugs.[7] The focus group results suggest that Tajik migrant MWID are at double jeopardy for social marginalization from both Russian society as migrants and also from their own Tajik migrant communities as MWID. Newly arrived Tajik MWID quickly make connections with others who can facilitate access to drugs; and using drugs together and sharing equipment offer the men a sense of camaraderie and community often missing from other aspects of their lives in Moscow. As part of the study, in-depth interviews conducted with 106 Tajik migrant MWID revealed that 83% of the men reported sharing an unclean needle in the last 30 days, only 26% had ever used condoms with a partner in Russia, 25% of the men engaged in hazardous drinking as defined by the WHO Audit-C Scale, and more than half (66%) were unaware that HIV could be spread through unsafe injection drug use. This research formed the impetus and laid the groundwork for developing the MASLIHAT HIV/AIDS prevention intervention for this highly vulnerable population.

1.11.(b). Development and pilot test of MASLIHAT (R21DA039068, Levy/Mackesy-Amiti, PI). In this study we developed, manualized, and pilot tested the MASLIHAT intervention. We presented the proposed intervention to community leaders and solicited their input, and then pre-tested the intervention with a small group of participants and conducted focus groups to collect feedback. After finalizing the intervention manual and assessment instruments, and training facilitators, we pilot tested the intervention with 30 participants who were trained as peer educators (PEs). Prior to the training, each participant recruited two network members to participate in the assessments. Assessments were conducted with the 30 participants and 60 network members at baseline, and 6 weeks, 3 months, and 6 months after the index participant completed the peer educator training. We also collected qualitative feedback from PEs after the training. Nearly all PEs completed the entire sequence of five MASLIHAT sessions; three participants each missed one session, and two participants were removed from a session due to intoxication. There was no loss to follow-up among PEs, and 95% of network members had complete follow-up. Three network members had left Moscow.

We tested the effects of time and participant type on each outcome using GEE and mixed effects regression. HIV knowledge increased significantly from baseline to 6-weeks for both PEs and network members (B=4.84, 95% CI 4.15-5.54), with significant reductions in frequent alcohol use (31% to 2.3%), casual sex without a condom (33% to 1%), and syringe sharing (52% to 0%). Neither group reported consistently cleaning their syringes at baseline, but all did sometimes at 6 weeks, and 87% always at 6 months. PEs reported a high level of satisfaction with the sessions deliver by facilitators, and felt that the content was culturally relevant for Tajik migrants who inject drugs.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The primary risk is associated with potential loss of confidentiality.

- It is possible that study participants who are actively injecting drugs may become known to Russian authorities or other Tajiks who were unaware of their drug use. If it becomes known that the participant is attending a program for people who inject drugs, this has potential legal and social consequences for the participant.
- Unintentional disclosure of HIV-positive status may have serious consequences due to stigma.

The study's structured interviews will ask participants to report on sensitive behavioral and health information that might embarrass them, make them uncomfortable, or cause difficulties in their relations with others should what they disclose become known.

Participants who are undocumented may face risks in traveling to the PRIZMA Research Center, as police may stop them to check their documents.

HIV and HCV confirmatory testing for those who screen positive requires a blood draw which has the risk of slight discomfort from the needle stick.

COVID-19 risks:

Group activities and face-to-face interviews pose a potential risk of COVID-19 transmission.

2.3.2 KNOWN POTENTIAL BENEFITS

There are no direct benefits to study participants related to their enrollment in the proposed research. They may, however, benefit from the health and risk prevention information and written materials that they receive as intervention participants concerning HIV risk-reduction or healthier living. Network members may potentially benefit from health-related information disseminated by intervention participants. All participants will also have the opportunity to receive free HIV/HCV counseling and testing, and linkage to care through the diaspora organization.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Sampling procedures, data collection and other research protocols for this study were selected or designed in full recognition of the special ethical challenges of protecting the rights and safety of people who inject drugs and labor migrants (some of whom may be in Moscow illegally) as particularly vulnerable research populations. The risks of participation are minimal and no greater than the risks normally encountered by participants.

Labor migration is one of the major contributors to the global HIV/AIDS epidemic, including among Tajik males who travel to Russia for work. Here they engage in risky drug injection practices, hazardous drinking, and high- risk sexual behaviors. This study is designed to test the efficacy of the MASLIHAT intervention, which is based on an adaption of the SHIELD model, and takes a peer education, social network approach to reducing risky drug, alcohol, and sexual behavior among male Tajik migrants who inject drugs while living in Moscow. If successful, it will help to reduce HIV transmission among members of a highly vulnerable population and their sexual and needle partners. It also will help to curb the transmission of HIV across country borders.

Protections Against Risk

(1) Investigator IRB certification and training: All US investigators and Tajik research staff, including interviewers and MAHLIHAT and TANSIHAT session facilitators, will complete Human Subjects Research training through online CITI training. In addition, the PI and Co-Investigators will extensively train field and research staff in the use of all of the data collection instruments. Field staff also will attend a session providing them with an overview to understanding drug use, HIV risk behaviors, diverse sexualities, and related areas. This training will provide field staff with the tools to carry out interviews in a non-judgmental way and to use a variety of culturally appropriate terms and phrases as probes when a respondent does not understand a question. Although all U.S. investigators are IRB-trained in compliance with HIPPA regulations, these regulations do not apply legally to patients or study participants in Russia. Moscow staff will be exempt from this training.

IRB Approvals: The study will obtain IRB approval from 3 sources:

- The University of Illinois at Chicago (FWA 00000083)
- PRIZMA Research Center (FWA00017140).
- Autonomous NGO "Scientific and Educational Center "Most v budushee" (Bridge to the future) IRB#1 (00010190) in Russia

(2) Referral for medical or psychological treatment as the result of study participation if needed: The project team works closely with the Tajik Union in Moscow as an NGO that advocates and represents the interests of Tajiks in the Russian diaspora including their legal problems related to drug use or other illegal activities. The Union will arrange referral of services for participants who (if any) experience legal problems related to drug use or undue psychological stress due to their participation in the study. Participants who report recent thoughts of self-harm or suicidal ideation during an interview will be referred to the Union for assistance in accessing mental health services.

(3) HIV/HCV rapid testing will be voluntary and sharing results with the research will be optional.

Participants who receive a positive confirmatory test will be referred to the Tajik Union for assistance in accessing follow-up services in Moscow through the Volunteer Doctors Association or linkage to care in Tajikistan.

(4) Procedures for Research Team Management of AEs, SAEs and Other Study Risks: All research staff and session facilitators will be trained in how to recognize and appropriately respond to both an adverse event (AE) and a serious adverse event (SAE) should one should occur as part of the study. Staff members will be instructed that such events or incidents must be reported immediately to the Moscow site coordinator and documented using a specially prepared project form, and then reported within 24 hours to Drs. Mackesy-Amiti and Bakhromov. They, in turn, will inform the NIH funding agency and also the IRBs of the University of Illinois at Chicago (FWA00000083), PRIZMA Research Center (FWA00017140), and the Scientific and Educational Center in Moscow (IRB #00010190). Further action will be taken under the advisory guidance of the three IRBs and NIH. (See also below for further details on actions to be taken with a possible breach of confidentiality.)

(5) At subway stops where on-duty Moscow police are known to stop and check the documents of passengers with non-Slavic (Russian) appearance, group facilitators will accompany intervention participants to and from the station to the PRIZMA office for the group sessions.

(6) Strategies to protect privacy and confidentiality:

a. Intervention sessions will be held at the PRIZMA Satellite Office. The PRIZMA office conducts a variety of activities unrelated to injection drug use; visiting the office will not place participants at risk of being identified as a drug user.

b. Interviews will be held at the PRIZMA Satellite Office or a location selected by the participant that is sufficiently private that his answers cannot be overheard.

c. To protect the confidentiality of data, questionnaires will not include personal identifiers. A research ID number will be assigned to each participant. A project tracking database in REDCap will record participants' names and project-assigned anonymous ID numbers for follow-up purposes. The log will be used to contact participants for follow-up interviews. It also will be used by Mr. Jonbekov to assure that participants' anonymous ID numbers are entered consistently across interview data points, and during coding to link the anonymous ID number of each intervention participant with the anonymous number of each of their 2 network recruits in examining network diffusion. No names or personal identifiers, however, will ever appear on the study's questionnaires, in the project data set, or other project material. The tracking data will be destroyed when primary data analysis has been completed.

d. Test results will be stored in a secure REDCap database separate from interviews and other study data. Participants will be assigned a testing code number that is separate from their research ID number used to identify interviews. A list of matching identifiers will be kept in REDCap. Only the PI, the Moscow site PI, the Moscow Project Coordinator, and the data coordinator will have access to this list.

e. When study participants are referred to the Tajik Union for assistance with legal, health, or mental health issues, no personal information will be disclosed to Union staff, including information regarding their substance use or HIV or hepatitis C status.

f. All publications resulting from the study will appear without participant names or information that would identify them.

g. NIH Certificate of Confidentiality: We will not apply for an NIH Certificate of Confidentiality that protects against disclosure of personally identifiable information in the U.S. as this legal document has no legal status in Russia or Tajikistan.

h. Protection of Data: Data collected on tablets with the Qualtrics offline mobile app will be uploaded to the secure web-based platform whenever a network connection is available. Process data will be entered into a secure REDCap database hosted at UIC. Participant tracking data will be stored in in a locked file at the PRIZMA Moscow office to which only the Moscow Site PI (Bakhromov), Moscow Project Coordinator (Jonbekov) and the senior interviewer/data coordinator (TBA) will have access. Test results will be stored in a secure REDCap database to which only the investigators and key personnel with a valid user ID will have access. Test results will be recorded with different identifiers than interview data, and a list of matching interview and test result identifiers will be kept in REDCap. Data collected on laptop computers or tablets will be deleted after being transferred to the central repository. Laptops will have whole drive encryption enabled and will be kept in a locked storage cabinet when not in use. Data will not be stored on removable devices.

Completed audio recordings will be kept with only code numbers (no names or other identifiers) in secure Box Health Data folder and destroyed six months after being transcribed.

Data transfers to UIC will include only de-identified data and will be carried out by Dr. Bakhromov or Mr. Jonbekov using the UIC Box service. This is the university-approved method for secure file sharing outside of the university network. The PI will set up a secure folder with restricted access for file transfers.

i. Should any breach of confidentiality occur five steps will be taken. First, the participant will be informed as to the nature of the breach, and its possible ramifications. Second, the Investigators will immediately notify the IRBs of the University of Illinois at Chicago (FWA00000083), PRIZMA Research Center (FWA00017140), and the Scientific and Educational Center in Moscow (IRB #00010190) and the project's NIH funding agency. Third, the Investigators will review existing confidentiality safeguards to determine why and how the breach occurred. Fourth, the PIs will halt client intake until such time that the IRBs can review existing procedures as to their quality and completeness. Finally, appropriate steps will be taken as determined by the 3 IRBs and approved by NIH. The participant also will be referred if needed to the Tajik Union for legal support and/or referral to appropriate service providers or other relevant organizations. The Union has agreed to accept this role.

(7) COVID-19 mitigation procedures

a. Masks will be required during group activities and face-to-face interviews.
b. Physical distancing will be employed during group activities and face-to-face interviews
c. Equipment (e.g. tablet computers) will be disinfected between uses

Other safety procedures include participant temperature checks before entry into the intervention or interview room, hand sanitizer will be supplied at intervals within the project area, the intervention and interview rooms will be disinfected after each use, interviews will be scheduled with sufficient time between participants to allow for disinfectant of contact areas, staff will have a check-list of safety procedures to follow with each eligibility screening, intervention session, and interview.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Primary			
Assess the efficacy of the MASLIHAT intervention compared to the TANSIHAT control condition for reducing injection equipment sharing, condomless sex, and heavy alcohol use among intervention participants and among their network members.	Reduce the proportion of men sharing syringes or other injection equipment in the past 3 months to 10% or less; reduce the proportion of men engaging in condomless sex in the past 3 months to 10% or less. Reduce the proportion of men engaging in heavy	Behavioral outcomes are predictive of HIV and hepatitis C infection. Sharing of syringes and other injection equipment is a significant risk factor for HIV and HCV, and condomless sex is a significant risk factor for HIV. Heavy alcohol use increases the	MASLIHAT is a peer education network intervention based on social cognitive theory which suggests that individuals will adopt new norms and practices that reduce their HIV risk by learning how and why they should do so and by observing role

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
	alcohol use in the past 3 months to 10% or less.	likelihood of risky behavior that leads to infection acquisition, and increases the risk of liver disease associated with HCV.	models to follow. We also draw on Yang's Theory of Migration, which posits that successfully changing risk behavior requires modifying the psycho-social conditions and life circumstance that help to generate it. By transforming their own HIV norms and behavior, and encouraging others at risk to do so too, migrant peer educators can initiate positive changes at the individual and social network levels in both their host country and their home country when they return.
Secondary			
Assess the efficacy of the MASLIHAT intervention compared to the TANSIHAT control condition for reducing the incidence of HIV and hepatitis C infection among intervention participants and among their network members.	Reduce the 12-month incidence of HIV and HCV by 50% compared to the control group.	The risk of HIV and HCV infection will be reduced by changes in individual and peer network behavior.	
Tertiary/Exploratory			
Assess network penetration and diffusion among networks of MASLIHAT participants.	80% of MASLIHAT participant network members report conversations about syringe cleaning, condom use, etc.	The MASLIHAT intervention teaches participants to engage in peer education activities	

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS	PUTATIVE MECHANISMS OF ACTION
Assess changes in and mediating effects of HIV knowledge, risk awareness, behavioral norms, and self-efficacy among MASLIHAT participants and their network members compared to the TANSIHAT control condition.			HIV knowledge, risk awareness, behavioral norms, and self-efficacy are theoretical mediators for intervention effects.
Assess the mediating and moderating effects of depression and loneliness among MASLIHAT participants and their network members compared to the TANSIHAT control condition.			Depression and loneliness are indicators of psycho-social well-being that potentially mediates or moderates intervention effects.

4 STUDY DESIGN

4.1 OVERALL DESIGN

This phase 2 cluster-randomized parallel groups trial will test the efficacy of the MASLIHAT intervention model on reducing risky drug, alcohol, and sexual behaviors among male Tajik labor migrants who inject drugs while working in Moscow in comparison with a control condition. This study will be conducted at the Moscow satellite site of PRIZMA Research and Training Center directed by Dr. Bakhromov. We include only men because few Tajik labor migrants are women, and moreover injection drug use among Tajik women is rare. However, the intervention presumably will benefit the female sex partners of participants when the men return to Tajikistan. Recruitment will be conducted by outreach at twelve distinct sites, including diaspora organizations, bazaars, and worksites.

We will use cluster randomization, with each recruitment site being randomized to one arm of the study. The Tajik Diaspora Union, under the leadership of Dr. Davlatov (consultant), will assist with referrals. In both study arms, the recruited men (index participants) will be required to recruit two eligible MWID peers for interviews prior to being interviewed themselves. After peer-recruited network members are enrolled and interviewed, the index participant will participate in the MASLIHAT training as peer educators or the control group activities depending on their recruitment site. All participants

and network members will then be followed and re-interviewed at 3-month intervals for one year to assess changes in risky drug, alcohol, and sexual behaviors due to intervention participation and through diffusion to network members. We will also collect data from voluntary HIV and HCV testing conducted at 6 months (HCV) and at 12 months (HIV and HCV) post-intervention.

In the MASLIHAT intervention, we will train Tajik migrant MWID as peer educators who will deliver the intervention to their network members both during the five-week training and after completion. We will assess changes in drug, alcohol, and sexual risk behavior at 3, 6, 9 and 12 months post-intervention. **We hypothesize that the MASLIHAT intervention participants and their network members will experience a greater reduction in risk behavior compared to those in the control condition.**

We will examine mechanisms of behavior change among MASLIHAT participants, including purported mediators and potential moderators. We will assess changes in HIV knowledge, risk awareness, prevention self-efficacy, psychosocial well-being, and behavioral norms among participants and network members, and test associations with injection drug use (IDU) social network interactions and mediation of behavior change outcomes. **We hypothesize that the MASLIHAT intervention will influence behavior of both peer educators and network members by increasing knowledge and awareness of HIV transmission risks, modifying behavioral norms, and improving self-efficacy.**

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

We will use a cluster-randomized design to prevent control group contamination due to the nature of the intervention. Because the intervention is designed to reach the participant's social network through peer education activities, individual randomization to condition is not feasible.

The Targeted Application of Network and Social Intervention on Health Assistance for Tajiks (TANSIHAT) program will serve as the control condition. TANSIHAT was adapted from the Healthy Lifestyles for Labor Migrants intervention designed by Drs. Bakhromov and Stevan Weine to serve as a control condition in testing an HIV prevention model delivered to Tajik migrants. We expanded the program contents to include TB risk and prevention and organized it to be parallel to MASLIHAT in the number and length of sessions. This program provides relevant health information for Tajik migrant workers and encourages participants to share the information with other migrants, but it does not address HIV/STI risk and prevention, condom use, or drug use. It does address heavy alcohol use which will affect our ability to detect effects on drinking behavior.

4.3 JUSTIFICATION FOR INTERVENTION

MASLIHAT is a small-group, interactive intervention that relies on peer networks to reduce drug, alcohol, and sexual risk behaviors among temporary migrant workers who inject drugs. It is based on a successful evidence-based peer-education approach for people who inject drugs in the U.S. (SHIELD), and adapted for migrant workers. Migrants in the host country who are current or former MWID are trained as peer educators to promote positive HIV risk-reduction norms and behavioral change through role modeling and sharing what they learned during MASLIHAT training sessions with their at-risk network members, especially other MWID. MASLIHAT fits well with the prevention needs of Tajik MWID living in

diaspora: 1) It is delivered by migrants to migrants, and not dependent on support from a host national health care system that denies them access to services; 2) Using current and former MWID to recruit and teach other MWID can reach migrant drug-using populations that are hidden or hard-to–reach; 3) It addresses risk reduction at both the individual and network levels; and 4) It requires little resource investment to implement. Staff at existing diaspora service organizations or former peer educators can serve as facilitators, and its 5 sessions can be delivered at any location with sufficient meeting space, including socio-geographic "hot spots" where risky behavior occurs. Pilot testing showed excellent acceptability and very promising results on risk behavior reduction.

The minimum acceptable participation for evaluation is 80% of participants attend all 5 sessions and 90% of participants attend at least 4 sessions. In pilot testing, all participants successfully recruited the required 2 network members and 83% completed the entire sequence of 5 MASLIHAT sessions; none missed more than one session.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the baseline assessment, at least 4 intervention sessions, and the 6-month and 12-month follow-up assessments, and baseline and 12-month HIV and HCV testing.

The end of the study is defined as completion of the 12-month follow-up assessment and HIV/HCV testing shown in the Schedule of Activities (SoA), **Section 1.3**.

5 STUDY POPULATION

Study participants will include 1) 5 participants for pilot testing of instruments, 2) 140 index participants who receive the MASLIHAT or TANSIHAT control intervention, and 3) 280 network members of intervention participants.

5.1 INCLUSION CRITERIA

Participants for pilot testing will be Tajik men who currently inject or formerly injected drugs and who have experience as a migrant worker in Russia.

To be eligible as an index participant (MASLIHAT peer educator or control group member), prospective participants must meet the following criteria:

1. Male Tajik migrant age 18 or older
2. Show evidence of recent injection drug use (track marks)
3. Intend to reside in Moscow for the next 12 months
4. Agree to attend 5 weekly intervention sessions at PRIZMA
5. Agree to recruit 2 Tajik MWID network members to participate in interviews

6. Give informed consent

To be eligible for participation, network members must meet the following criteria:

1. Male Tajik migrant age 18 or older
2. Injected drugs at least once in the last 30 days (verified by inspection of track marks)
3. Someone whom the index participant sees at least once a week
4. Intend to reside in Moscow for the next 12 months
5. Give informed consent

5.2 EXCLUSION CRITERIA

Index participants will be excluded from participation in this study if:

1. they do not successfully recruit 2 network members within the allotted time frame, or
2. they do not attend the first intervention session

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently entered in the study. This may occur if an index participant does not successfully recruit two network members within the allotted time period, or he does not attend the first intervention session. An index participant who does not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria may be considered for rescreening if the second group for the cluster has not yet been filled. Only index participants who identified more than 2 potential network recruits during screening will be allowed to replace network recruits who failed screening. Rescreened participants will be assigned the same participant number as for the initial screening.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

The study will enroll a total of 420 male Tajik migrant MWID including 140 index participants (MASLIHAT or control intervention) and 280 IDU network members. Based on pilot study experience, since recruitment materials will specify the requirements for participation, nearly all men who present for screening will meet the criteria for enrollment. We anticipate screening up to 150 MWID for participation as index participants, and up to 300 MWID for participation as network members.

Timing for recruitment. Recruitment of index participants (70 MASLIHAT peer educators and 70 control group participants) will take place throughout the intervention/baseline data collection period (18 months) through referrals from the Tajik diaspora organizations and recruitment at the 6 worksites and 4 bazaar sites until sample requirements for 140 index participants are met. Network member recruitment (n=280) will occur through referral by the index participants. As with the pilot study, only

index participants who successfully recruit two eligible network members will participate in the interventions. Recruitment will be conducted intensively at two sites at a time, one assigned to the intervention and the other to the control. We will recruit from these sites until we have filled two groups of 5 to 7 eligible participants (each having successfully recruited 2 network members). Groups will be closed to new members after the first session. When we have filled 2 groups for each site in the pair, the recruitment team will move on to the next pair of sites. We will run four intervention groups each quarter (2 MASLIHAT and 2 TANSIHAT) over a period of 18 months (20 groups total).

Sample composition. The sample will be entirely composed of Tajik male labor migrants working in Moscow. No women are included in the research, as few women travel to Moscow for work. Also the study focuses on injection drug use which is practiced primarily by Tajik males. All study participants are Tajik nationals working in Moscow. Most are likely to be ethnic Tajiks, but members of Tajik ethnic minority groups (Uzbeks, Pamiris, Tatars, and Belarusians) also will be eligible to participate. Children under 18 will not be included in the research, as Tajik migrant workers are required by law to complete secondary school. In addition, injection drug use among children under 18 in Tajikistan is extremely unlikely. Through NGO referrals and worksite/bazaar recruitment, we will be able to sample migrant MWID originating from all five regions of Tajikistan.

Recruiting intervention participants. Recruitment of intervention participants will be conducted by outreach at twelve sites including 2 diaspora organizations, 4 bazaars, and 6 other worksites located near metro stations in districts with substantial migrant settlement. We will recruit 10 to 14 Tajik migrant men who inject drugs (MWID) at each of these sites to participate in the MASLIHAT (n=70) or control (n=70) intervention. Participants will be assigned to condition based on recruitment site. Recruitment sites will be pair matched and randomly assigned to a study arm, with one site of each pair assigned to MASLIHAT (see Section 6.3 for details). Recruiters will be blinded to site assignment. Recruitment materials (flyers, cards) will include a code to identify the recruitment site. When a potential participant contacts the research staff for pre-screening, he will be asked for this code.

Recruiting from diaspora organizations. The Moscow site PI (Dr. Bakhromov) and the Chair of the Tajik Union (Dr. Davlotov) will meet with leaders of the NUR and Selart Tajik diaspora organizations to explain the study and discuss the recruitment plan. Diaspora organization staff will inform men about the study and the requirements for participation, and distribute a handout that includes contact information. They will encourage visitors to refer men they know who appear to meet the study's eligibility criteria to contact PRIZMA for screening and possible participation.

Recruiting from worksites. Most Tajik male migrants in Moscow work either in bazaars or in construction. The PRIZMA research team has experience in recruiting Tajik migrants from worksites for participation in research. We have selected four bazaars and six other worksites near metro stations as recruitment sites. Workers at the bazaars are organized in brigades, each consisting of 5 to 15 workers. The number of brigades within bazaars varies from 5 to 150. Dr. Bakhromov and Dr. Davlatov will meet with diaspora organization leaders to make connections with Tajik brigade leaders and worksite managers. They will meet with the brigade leaders and worksite managers to explain the purpose of the study and make plans for distribution of study information. The brigade leaders and worksite managers will distribute cards with study information, eligibility criteria, and contact details to Tajik migrants.

Recruiting network members. Men who call the PRIZMA center will be screened for eligibility by the project coordinator and given an appointment for the enrollment visit. At the enrollment visit the project coordinator will explain the study requirements and confirm eligibility. Eligibility will be confirmed by inspecting for injection marks, or if marks are not visible, asking the subject about the injection process using a series of questions designed to identify PWID (SATHCAP injection screener). After completing the

informed consent process and confirming their willingness to recruit two other Tajik migrant MWID for interviewing, index participants will be given two coupons to recruit network members who meet the study criteria for interviews. Network members must meet the same criteria as intervention participants but also: 1) have injected drugs at least once in the last 30 days; and 2) be someone whom the index participant sees at least once a week. When network members present for enrollment, the project coordinator will verify network member eligibility and confirm the identity of the index participant who made the referral.

Retention. Participants will be enrolled only if they expect to remain in Moscow for the next 12 months, and they will be asked to notify the PRIZMA office if they are returning to Tajikistan prior to the study completion. Participant tracking and participant retention will build on successful strategies used by the investigators in achieving high follow-up rates with PWID or migrant populations in prior studies. One challenge of studying migrants is that they can disappear without warning due to legal difficulties or an unexpected reason to return to home. Many are without permanent residence. We will use a series of strategies to retain participants over time. Key contact information (work, residence, friends/family, regular "hang-outs") will be collected at intake for follow-up interviewing and updated at each follow-up contact. Participants will be contacted by phone or other preferred arrangements prior to each MASLIHAT session or interview as a reminder. If a participant cannot be reached by phone or other contact methods after missing an appointment, the Moscow Project Coordinator will visit the person's last known address or locations where he typically frequents, and inquire with his recruiter or network members.

Compensation: Participants will receive the customary compensation in Moscow of $20.00 for each interview completed. Intervention participants will also receive transit passes to attend the group sessions at the PRIZMA Research Center.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

MASLIHAT Intervention. MASLIHAT's 5 sessions are based on the SHIELD model and the social cognitive theory that drives it.[35] Drawing on Yang's theory of migration,[22] we also added issues and risk-reduction strategies to address the challenges of migrant life that contribute to high-risk behavior. We expect MASLIHAT to produce positive change in peer educators' and network members' condom use, needle hygiene, and safer alcohol use. Primary outcome measures are syringe sharing in the past 3 months, and vaginal or anal sex without a condom in the past 3 months. Other measures include syringe cleaning methods, and the Alcohol Use Disorder Identification Test (AUDIT) to assess alcohol consumption and alcohol-related problems at each time point. In addition to risk behavior, we will assess theoretical mediators including HIV knowledge, risk awareness, behavioral norms, self-efficacy, depression, and loneliness.

The intervention consists of five 2-hour sessions delivered to participants recruited as peer educators who meet as a group once a week for five weeks. Light refreshments are provided. The content of the 5 sessions, which are specified in detail in the MASLIHAT facilitators' manual, focus on: 1) An introduction

to MASLIHAT and its goals; general risks and safety for Tajik migrant workers; living a healthy life style, resources & organizations serving Tajik migrants; 2) HIV 101; peer communication skills; 3) HIV/STI risk/prevention thorough safer sex; alcohol use and HIV risk; 4) HIV risk/prevention related to injection drug use; and 5) Maintaining a healthier life style; sustaining peer outreach. Homework assignments and case studies in each session help to script peer educator messages to deliver to network peers.

Control Condition. The Healthy Lifestyle for Labor Migrants program was designed by Drs. Bakhromov and Stevan Weine to serve as a control condition in testing an HIV prevention model delivered to Tajik migrants traveling from Dushanbe to Moscow by train.[36] Since few migrants in the last 5 years have traveled to Russia by rail as air travel is so much faster, neither the train intervention or the TANSIHAT program are currently being delivered. Fully manualized, the original Healthy Lifestyle program consists of three modules that provide information about general risks to health, healthy nutrition, personal hygiene, fitness, and stress management. This program provides relevant health information for Tajik migrant workers (including prevention of cardiovascular disease, the most common cause of death in Tajikistan), and encourages participants to share the information with other migrants, but it does not address HIV/STI risk and prevention, condom use, or drug use.

We have designed additional content and organized the program to consist of five sessions to parallel the MASLIHAT intervention in terms of time commitment. Additions include information on workplace safety and an added emphasis on strategies for avoiding respiratory infections (TB, COVID19) as these are important health issues in Russia among labor migrants. The content of the 5 sessions, which are specified in detail in the Healthy Lifestyle facilitators' manual, focus on: 1) understanding health risks facing Tajik migrants in Moscow; 2) healthy nutrition and personal hygiene; 3) fitness and stress management; 4) workplace safety; and 5) prevention of respiratory infections.

6.1.2 ADMINISTRATION AND/OR DOSING

The MASLIHAT and TANSIHAT interventions will be delivered in 5 weekly small group sessions led by a trained facilitator. Sessions will take place at the PRIZMA Research Center. MASLIHAT sessions include group discussions and interactive role-playing activities to practice the communication and outreach skills. MASLIHAT treatment dosage effects for peer educators will be measured by: (1) total number of sessions attended, and (2) specific sessions attended.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Facilitator qualifications and training. Four facilitators will be hired and trained by Drs. Bakhromov, Levy, and Latkin to co-lead the MASLIHAT sessions using the Facilitators' Guide developed in the pilot study and the control group sessions using the TANSIHAT manual. To qualify, each facilitator must be a Tajik migrant with experience in conducting group sessions. We also will screen for facilitators who are non-judgmental and well respected within the Moscow Tajik migrant community. Two facilitators will be trained to deliver the MASLIHAT sessions, and two will be trained to deliver TANSIHAT. Facilitator

training will include a refresher on basic group facilitation skills (e.g. communication skills, etc.), as well as training on the intervention background, structure, and content. Facilitator training will begin with Dr. Bakhromov and Mr. Jonbekov presenting the entire program to the trainees so that they can become familiar with the content and observe the role of the facilitator. Next, facilitator trainees will receive 3 days of training led by Drs. Levy and Latkin, and guided by the MASLIHAT or TANSIHAT Manual in how to facilitate the intervention sessions. Finally, trainees will receive practice in delivering the intervention with a small group of MWID (day 5).

Day 1: Introduction and MASLIHAT / TANSIHAT presentation
Day 2: Basic group facilitation skills and practice; Session 1 training and practice
Day 3: MASLIHAT / TANSIHAT sessions 2 & 3 training and practice
Day 4: MASLIHAT / TANSIHAT sessions 4 & 5 training and practice
Day 5: MASLIHAT / TANSIHAT live practice

Fidelity to the MASLIHAT and Healthy Lifestyle Models. Our process evaluation is designed to check whether or not the interventions are being delivered and implemented with fidelity to the two models. Five methods will be used. 1) The MASLIHAT and Healthy Lifestyle facilitators' manuals will provide a detailed guide as to the content and procedures for each specific session. 2) Facilitators will be rigorously trained in how to use the manuals and deliver each of the 5 sessions. 3) Dr. Bakhromov and/or the Project Coordinator (Jonbekov) will observe and summarize in writing their perception of the facilitators' and sessions' fidelity to the particular model at the end of each session and provide further training or guidance if needed. All sessions will be audio recorded. Dr. Bakhromov will audit the recordings, and randomly selected sessions will be translated and transcribed for independent review by the U.S. investigators. 4) Each facilitator will fill out a project-prepared assessment form recording his perception of where each session succeeded and/or deviated from what was planned and strategies devised by facilitators and project staff to enhance fidelity if appropriate. 5) As part of its members' duties, the CAB will meet annually to review the study's progress and to assess its fidelity in delivering the interventions.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

The 12 recruitment sites will be pair matched and randomly assigned to a study arm. One of each pair will be assigned to MASLIHAT and the other to the control condition. Dr. Bakhromov will create the matched pairs based on site characteristics, and randomization will be determined by the PI using a random number generator. A random number will be generated for each site, and within each matched pair, the site with the smaller number will be assigned to MASLIHAT. To minimize bias during recruitment, site assignments will be masked from project staff engaged in recruitment. The PI will inform the Moscow project coordinator of the site assignment as needed for group scheduling, after the first cohort of participants has been filled for the site. Participants will be informed of their assignment at the time of scheduling the group sessions. Dr. Bakhromov will also have access to this information as needed, after recruitment activities are underway. Interviewers will be blinded to site assignment, and the same interview instrument will be used for MASLIHAT and control condition participants. Session facilitators, who may become aware of the recruitment sites from which participants originated, will be instructed during training not to reveal this information to interviewers. Intentional or unintentional breaking of the blind is to be reported to the PI.

The randomization codes will be kept in a password-protected file accessible to the PI, co-investigators, the project coordinator, and the data manager. When preparing data for analysis, the data manager will

blind code recruitment site and study arm. Masking will be removed for reporting interim results to the DSMB.

In addition, we will adopt a position of clinical equipoise. Intervention facilitators and interviewers will be informed that we are testing two different interventions, but neither is assumed to be superior to the other. Facilitators will be assigned to one or the other, while interviewers will be blinded to participant condition. Data collection will be conducted by interviewers who are not involved in intervention delivery. Interviews will be standardized using a computer-assisted instrument, and sensitive sections will be self-administered.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

Session facilitators will record participant attendance and submit attendance records to the project coordinator. Session facilitators will also record instances when a participant is removed or leaves, e.g. due to intoxication or disruptive behavior.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

A subject may be discontinued from the MASLIHAT or TANSIHAT intervention group by the session facilitator or project coordinator if he is repeatedly disruptive or engages in hostile or aggressive behavior toward staff or other participants. When a subject discontinues from the group sessions but not from the study, remaining study procedures will be completed as indicated by the study protocol. The reason(s) for discontinuing the participant from the intervention will be recorded. The participant will be included in all future scheduled assessments, even though participation in the intervention was discontinued.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time.
The investigator will discontinue a participant from the study for the following reasons:

- Failing to attend the first group session
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant

The reason for participant discontinuation or withdrawal from the study will be recorded on the Withdrawal Case Report Form (CRF). Subjects who sign the informed consent form but do not receive the study intervention may be replaced. Subjects who sign the informed consent form and receive the MASLIHAT or Control (Healthy Lifestyle) intervention and subsequently withdraw, or are discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he fails to return for two consecutive scheduled visits and study staff are unable to contact the participant after at least 3 attempts. A participant who contacts research staff following an absence will be allowed to rejoin the study.

The following actions must be taken if a participant fails to return to the research center for a scheduled study visit:

- Project staff will attempt to contact the participant, reschedule the missed visit within 2 weeks, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study
- Before a participant is deemed lost to follow-up, project staff will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a visit to the participant's last known residential address). These contact attempts will be documented in the participant's study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Eligibility pre-screening. Potential index and network participants will call the PRIZMA Research Center for preliminary screening. The project coordinator will explain the study requirements and schedule an appointment for the enrollment visit (index participant) or enrollment and baseline interview (network member).

Screening & Enrollment. Participant screening, enrollment, and informed consent will take place in a private room at the PRIZMA office. A trained interviewer will interview each potential subject for the intervention conditions or as network members to identify those who meet the criteria to participate. Injection drug use will be confirmed by the presence of injection marks (tracks), or if marks are not visible, asking the subject about the injection process using a series of questions designed to identify PWID. The interviewers will then explain the purpose and activities of the study to eligible subjects and obtain informed consent from those who indicate their willingness to participate. Contact information also will be collected from the enrollees for follow-up purposes and the participants will be given contact information for the study coordinator should they have further questions.

Index participants. Project staff will confirm the participant's willingness to recruit two other Tajik migrant MWID for interviewing. Participants will complete a brief social network survey to enumerate their IDU network, and they will be given two coupons to recruit network members who meet the study criteria for interviews. Coupons will be valid for 30 days. Index participants will return to complete the baseline interview after network participants have enrolled.

Network participants. Project staff will check the participant's recruitment coupon and confirm his relationship to the index person who recruited him before continuing to administer the baseline interview.

Interviews: Intervention participants and network members will complete computer-assisted personal interviews (CAPI) at baseline (prior to first intervention session), and at 3, 6, 9, and 12 months post-intervention. All baseline and 12-month interviews will be conducted in a private room at the PRIZMA office; intermediate follow-up interviews may be conducted at the PRIZMA office or at a location selected by the subject. Trained interviewers will administer the 60 to 90-minute questionnaire, using a computer-assisted personal interview (CAPI) system (Qualtrics) to record responses. For the more sensitive questions such as sexual behavior and STIs, the interviewer will instruct the participant to enter his responses. The CAPI system will ensure proper administration of skip sequences. For quality control purposes, 20% of interviews will be randomly selected to be audiotaped, and half of these audiotapes will be reviewed by Dr. Bakhromov or Mr. Jonbekov for quality assurance. Using electronic data capture and requiring timely data uploads will allow the data manager to monitor research progress and conduct quality control checks. The questionnaires were developed and tested with members of the population using cognitive interviewing (CI).[62] Translations were validated using "back translation" with a member of the study population.

Self-report Measures

Background measures. The baseline interview includes measures of basic sociodemographic variables (education, marital status, migration history, religion), community involvement/social activities, and health (general health, STIs). The follow-up interviews also collect self-reported STIs since last interview.

Outcome measures. Primary outcome measures are syringe sharing in the past 3 months, and vaginal or anal sex without a condom in the past 3 months. Other measures include syringe cleaning methods, and the Alcohol Use Disorder Identification Test (AUDIT)[63] to asses alcohol consumption and alcohol-related problems at each time point.

Theoretical mediators. In addition to risk behavior, the questionnaire will assess theoretical mediators including HIV knowledge, risk awareness, behavioral norms, self-efficacy, depression, and loneliness. HIV knowledge is assessed with 16 true/false items; risk awareness is assessed with questions such as "How likely are you to get HIV?" and "How much do worry about HIV?" Behavioral norms[64-66] will be assessed with questions such as "How many of your friends who shoot drugs use a needle after someone else, without bleaching or cleaning?" (descriptive norms), and "How many of your friends would disapprove if you shared a needle with a stranger?" (injunctive norms). Responses are given on a 5-point scale from 1 (none) to 5 (all). Self-efficacy for safer drug injection will be measured with six items adapted from the CIDUS-III study[67] (e.g., ''I can avoid sharing a needle even if I am dope sick or in withdrawal''), rated on a four-point scale from ''strongly agree'' to ''strongly disagree''. Depression will be measured using the Centers for Epidemiological Studies Depression Scale -- Revised (CESD-R) [68], and loneliness will be measured using the UCLA Loneliness Scale[69].

Network penetration & diffusion. Diffusion of MASLIHAT messaging/norms at the network level will be assessed using measures successfully used by SHIELD and other public opinion leadership interventions such as asking network members as to how many (if any) MASLIHAT peer educators they know, whether anyone within their drug using network talked with them about HIV since they were last interviewed, and whether they talked about specific topics (e.g. condom use, syringe cleaning, HIV testing).

Peer educator personal development. Measures of peer educator personal development (in addition to knowledge and behavior change) will be administered at baseline and at 12-month follow-up, including self-esteem, self-efficacy, and substance use self-stigma. The 10 items of the Rosenberg Self-Esteem Scale[70, 71] assess a person's overall evaluation of his or her worthiness as a human being, including subscales of self-competence and self-liking. Items are rated on a 4-point scale from 1 (strongly disagree) to 4 (strongly agree). The New General Self-Efficacy Scale[72] includes 8 items to measure general self-efficacy (e.g. "I will be able to achieve most of the goals that I set for myself.") rated on a Likert scale from strongly disagree to strongly agree. Internalized stigma of substance use will be assessed with 6 items adapted from a measure of HIV stigma[73], rated on a 5-point Likert-type scale, e.g. "I feel ashamed of being a person who uses drugs".

Intervention engagement

Session facilitators will record participant attendance, note homework completion, and rate participant engagement at each session.

HIV/HCV counseling and testing.

Intervention participants and network members will be referred to the Moscow HIV Prevention Center (MHPC) for voluntary HIV/HCV rapid and confirmatory testing and counseling following the baseline interview, and later at the 6-month (HCV) and 12-month (HIV and HCV) follow-up. We chose to not require HIV testing as a condition of study enrollment as its impact on study recruitment and participation are unknown. Participants will be informed that their results will be shared with the research study unless they choose to opt out. We will explain the measures we will employ to maintain the confidentiality of the results.

We will give each participant a card with a code number on which test results will be reported. The testing code number will be separate from the research ID number used to identify interviews, and will

consist of a group number and an individual code. The list matching testing codes with research IDs will be kept in a secure REDCap database separate from locator data and interview data. Participants who object to having their test results linked to their personal interview data will be given the option of blacking out the individual code number, keeping only the group number. This will allow us to track results by intervention group even if the results cannot be linked to individuals.

OraSure OraQuick® ADVANCE HIV-1/2 (oral fluid) and OraQuick® HCV (finger stick) rapid antibody tests and confirmatory tests for positive results (HIV immunoassay and HCV RNA PCR) will be administered to participants by Moscow HIV Prevention Center (MHPC) staff. Test results will be collected from MHPC by PRIZMA staff. Missing test results will be flagged for follow-up by the project coordinator.

8.2 SAFETY ASSESSMENTS

N/A

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

Adverse Events (AEs) are defined in this study as “any unfavorable and unintended diagnosis, symptom, sign, syndrome or disease which either occurs during the study, having been absent at baseline, or, if present at baseline, appears to worsen.” An AE may or may not have a causal relationship with the treatment.

Potential AEs:

- violation of confidentiality
- discomfort due to assessment procedures
- embarrassment in disclosing sensitive personal information
- disclosure of information about current and/or intended physical harm to persons
- dissatisfaction with the assessment procedures
- dissatisfaction with the intervention activities
- COVID-19 infection

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Serious Adverse Events (SAEs) are defined as “any medical occurrence that results in death; is life-threatening; requires inpatient hospitalization or prolongation of existing hospitalization; creates persistent or significant disability/incapacity, or a congenital anomaly/birth defects.” No medical treatment or administering of drugs are a part of this research or its study design, but study participants may be vulnerable to other potential SAEs as shown below.

Potential SAEs:

- death

- life threatening injury or condition
- hospitalization
- persistent or significant disability/incapacity
- adverse attention, action or other negative consequences for a participant that are imposed by Russian authorities as the result of having become knowledgeable of his drug use as a consequence of participation in the study
- other conditions which in the judgment of the investigators represent significant hazards

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by an appropriately-trained scientist based on temporal relationship and his/her expert judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

OR

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study procedures administration and cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the

study procedures should be clinically plausible. The event must be pharmacologically or phenomenologically definitive.

- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study procedures, is unlikely to be attributed to concurrent disease or other drugs or chemicals, and follows a clinically reasonable response on withdrawal.
- **Potentially Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of study procedures). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study procedures administration makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after administration of the study procedures) and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study procedures administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.]

8.3.3.3 EXPECTEDNESS

An AE will be considered unexpected if the nature, severity, or frequency of the event is not expected based on (a) information contained in the protocol, informed consent document, or other research materials; and (b) the characteristics of the subjects, including underlying diseases, behaviors, or traits.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant, or upon review by a study monitor.

All AEs, not otherwise precluded per the protocol, will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, assessment of severity, relationship to study procedures, and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

The project coordinator will record events with start dates occurring any time after informed consent is obtained until the last day of study participation.

8.3.5 ADVERSE EVENT REPORTING

All research staff and session facilitators will be trained in how to recognize and appropriately respond to an adverse event (AE) should one should occur as part of the study. Staff members will be instructed that such events or incidents must be reported promptly to the Moscow site coordinator and documented using a specially prepared project form, and then reported by the site coordinator (Jonbek) within 24 hours to Drs. Mackesy-Amiti, Levy, and Bakhromov. They, in turn, will inform NIDA and also the IRBs of the University of Illinois at Chicago (IRB #00009693), the Scientific and Educational Center in Moscow (IRB #00010190) and PRIZMA Research Center (IRB00009927). Further action will be taken under the advisory guidance of the IRBs and NIDA.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

As with AEs, staff members will be instructed any SAE event or incident must be reported promptly to the Moscow site coordinator and documented using a specially prepared project form and then reported within 24 hours by the site coordinator (Jonbek) to Drs. Mackesy-Amiti, Levy, and Bakhromov. In consultation with the PI, Dr. Bakhromov will be responsible for conducting an investigation of a SAE. The PI will report the results of such investigation to the NIDA PO within 3 days and to the UIC, Moscow, and PRIZMA IRBs no later than 5 working days after the investigator first learns of the event. Further action will be taken under the advisory guidance of the IRBs and NIDA.

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

The project coordinator will monitor session attendance and follow-up interview participation, and record any instances of arrest or deportation whether or not associated with study participation. Incarceration of a research participant will be reported to the UIC IRB.

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("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); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The Moscow site investigator will report unanticipated problems (UPs) to the IRB of the PRIZMA Research Center (FWA00017140), to the Scientific and Educational Center in Moscow IRB#1 (00010190), and to the principal investigator (PI). The PI will submit the report to the IRB of the University of Illinois at Chicago (IRB #00009693). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to NIDA and to the three IRBs within 3 days of the investigator becoming aware of the event
- Any other UP will be reported to the three IRBs and to NIDA within 10 days of the investigator becoming aware of the problem
- The UIC Office for the Protection of Research Subjects (OPRS) will promptly report to applicable institutional officials, funding sources, agency heads and regulatory agencies determinations by the IRB that an event represents a reportable unanticipated problem involving risks to subjects or others as determined by the IRB. The letter from the OPRS Director will be sent to the Office for Human Research Protections (OHRP) within 10 working days of the convened IRB's determination.

In the event a situation requires extended time to investigate or resolve, a preliminary report will be sent and followed by a final report. In no event will a preliminary report to institutional officials, the supporting agency head, or OHRP be delayed beyond 30 days of the OPRS/IRB receiving notice of a reportable event.

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

- Primary Endpoints:

We hypothesize that, compared to MWID who receive a health education control intervention, those who receive the MASLIHAT peer education intervention will have reduced frequency of syringe and other injection equipment sharing, and reduced frequency of vaginal and anal intercourse without a condom 12 months following the intervention. Alternatively, our null hypothesis is that there will be no difference in the effects of MASLIHAT and the health education control intervention on injection and sexual risk behavior of intervention participants 12 months following the intervention.

We hypothesize that, compared to IDU network members of MWID who receive a health education control intervention, IDU network members of MWID who receive the MASLIHAT peer education intervention will have reduced frequency of syringe and other injection equipment sharing, and reduced frequency of vaginal and anal intercourse without a condom 12 months following the intervention. Alternatively, our null hypothesis is that there will be no difference in the effects of MASLIHAT and the health education control intervention on injection and sexual risk behavior of IDU network members 12 months following the intervention.

- Secondary Endpoint(s):

We hypothesize that, compared to MWID who receive a health education control intervention, those who receive the MASLIHAT peer education intervention will have lower incidence of HIV infection and lower incidence of hepatitis C infection 12 months following the intervention. Alternatively, our null hypothesis is that there will be no difference in the effects of MASLIHAT and the health education control intervention on the incidence of HIV or HCV among intervention participants 12 months following the intervention.

We hypothesize that, compared to IDU network members of MWID who receive a health education control intervention, IDU network members of MWID who receive the MASLIHAT peer education intervention will have lower incidence of HIV infection and lower incidence of hepatitis C infection 12

months following the intervention. Alternatively, our null hypothesis is that there will be no difference in the effects of MASLIHAT and the health education control intervention on the incidence of HIV or HCV among IDU network members 12 months following the intervention.

Statistical Analysis Plan (SAP): A formal SAP will be prepared prior to the first interim analysis of 3-month follow-up outcomes.

9.2 SAMPLE SIZE DETERMINATION

We estimated power allowing up to 10% attrition among intervention participants and up to 15% attrition among network members. Power calculations were computed using PASS software and considering effects observed in the pilot study.

We expect to see large reductions in syringe sharing and condomless sex in the MASLIHAT intervention group, and little change in these behaviors in the control group. In the pilot study, syringe sharing decreased from 52% at baseline to 0% at six months, and condomless sex decreased from 35% at baseline to 1% at six months. For binary outcomes, we computed Mixed Models Tests for Two Proportions in a 3-Level Hierarchical Design (Level-3 Randomization), with an intracluster correlation of 0.05 and alpha=.01. We computed power for outcomes ranging from 0.30 to 0.50 for the control group, and 0.05 to 0.15 for the MASLIHAT intervention group, and with 10, 20 or 30 subjects per cluster, representing intervention participants, network members, and the complete sample. We will have at least 80% power to detect predicted changes in condomless sex, and over 90% power to detect predicted changes in syringe sharing. In the larger sample, we will have adequate power to detect effects even if they are not as large as anticipated.

The intervention also targets alcohol use and in the pilot study, days of alcohol use in the past month decreased from 5 to 2, with b/SE = -6.52, yielding a Cohen's d effect size of -0.69. We estimated power by computing Mixed Models Tests for the Slope Difference in a 3-Level Hierarchical Design with Fixed Slopes (Level-3 Randomization), with subject icc=0.30 and alpha=0.01, for a standardized mean difference (SMD) of 0.50 to 0.70, with cluster sizes of 10, 20. and 30. For the intervention participants, we will have at least 80% power to detect a SMD=0.70; for network members we will have at least 80% power to detect a SMD=0.50, and for the complete sample we will have at least 80% power to detect a SMD=0.41.

For HIV and hepatitis C virus (HCV) outcomes, we computed detectable effects for a one-sided Test for the Difference between Two Poisson Rates in a Cluster-Randomized Design, given our sample with k=30 subjects per cluster, coefficient of variation (CV) = 0.50 for the control group and CV=1 for the intervention group, alpha=0.05, and power=0.80. Assuming a base rate HIV incidence of 10% for the control group, we will have at least 80% power to detect an event rate ratio of 0.11, corresponding to an incidence rate of 1% in the treatment group. For HCV, we must assume that a fair number of the sample will be infected as baseline and therefore excluded from the analysis. Assuming 15 subjects per cluster and HCV base rate incidence of 40%, we will have at least 80% power to detect an event rate ratio of 0.21, corresponding to an incidence rate of 8.6% in the treatment group.

9.3 POPULATIONS FOR ANALYSES

All participants who complete the baseline interview will be included in the analyses in accordance with intention to treat (ITT) analysis.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Descriptive analyses of the study sample will include percentages for categorical variables and means and standard deviations for continuous measures. Chi-square tests and t-tests will be computed to compare study arms on baseline sociodemographic measures. We will compare follow-up between conditions using GEE logistic regression. Results will be reported as odds ratios with 95% confidence intervals and exact p-values for 2-tailed tests.

We will examine the distributions of outcome measures to ascertain whether there is sufficient variability to analyze frequency measures as ordinal. Response categories with a small number of responses will be collapsed for analysis. We will analyze missing data patterns to assess the extent of missing data, and to determine if there is evidence of non-ignorable missingness (i.e. missing not at random, MNAR).

We will conduct repeated measures linear, logistic, and modified Poisson regressions using mixed effects models with random intercepts for subject and recruitment site to test the effect of intervention condition on changes in mediator and outcome variables. In the event of missing data in more than 5% of cases, or unbalanced loss-to-follow-up, analyses will be conducted in Mplus using full-information maximum likelihood methods. We will include the interaction of time and participant type (intervention participant vs. network member) to test for differential effects. Following analysis of the main outcomes we will conduct analyses to explore hypothesized mediation and moderation effects.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

Relative frequency of syringe sharing, equipment sharing, and vaginal or anal sex without a condom in the past 3 months will be measured at each time point on a 7-point Likert-type scale (Never, Rarely, Less than half the time, About half the time, More than half the time, Most of the time, Always). We will analyze ordinal outcomes, and we will also dichotomize responses to analyze binary (none/any) outcomes.

We will conduct repeated measures mixed effects regressions with random intercepts for subject and recruitment site to test the effect of intervention condition on changes in the outcome variables. We will use ordinal logistic regression for ordinal outcomes and modified Poisson regression for binary outcomes. We will conduct a test of the proportional odds assumption with a likelihood ratio test comparing the proportional odds model with a non-proportional odds model.[74] We will include the interaction of time and participant type (intervention participant vs. network member) to test for differential effects. If the interaction term suggests differential effects ($p<.10$), we will stratify analyses by participant type. Sociodemographic characteristics (age, education, time in Moscow) will be included as covariates in the analysis if they are related to the outcome at baseline or if they vary significantly across conditions. All participants with at least one follow-up interview will be included in the analysis.

Dosage: If there is variability in attendance, we will estimate repeated measures mixed effect models predicting outcomes with session attendance and the interaction between time, intervention condition, and session attendance as predictors. A significant interaction effect will indicate that the effect of the intervention is moderated by session attendance.

Social Network Diffusion. Additional analyses among network members will examine associations between exposure to intervention concepts (i.e. conversations about health, drugs/alcohol HIV) and changes in outcomes over time.

The results of mixed effects ordinal logit models will be reported as odds ratios with 95% confidence intervals, and exact p-values. Predicted probabilities will be computed from the logit model. The results of mixed effects modified Poisson regressions will be reported as relative risk ratios with 95% confidence intervals, and exact p-values. We will also report intra-class correlations for the subject and site (cluster) levels.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

Secondary outcomes are HIV and HCV incidence over 12 months. Participants who are HIV antibody positive at baseline will be excluded from the analysis. Participants who are HCV RNA positive at baseline and at 6-months (i.e. chronic infection) will be excluded from the analysis. HCV infection will be operationalized as a positive antibody test following a negative antibody test, or for persons who are AB+ at baseline, a positive HCV RNA test following a negative HCV RNA test. We will conduct a missing data analysis to check for differences between participants with and without test results. If more than 5% of the data are missing we will employ full-information maximum likelihood methods using Mplus.

We will compare incidence rates of HIV and HCV infection between the two intervention conditions among intervention participants, and among network members, with GEE modified Poisson regression to estimate relative risks, adjusted for clustering by recruitment site.[75] We will estimate the effect of intervention condition, adjusting for covariates including age, education, duration of injection, and length of time in Russia if they are related to the outcome at baseline or if they vary significantly across conditions. The results will be reported as relative risk ratios with 95% confidence intervals, and exact p-values.

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

We will compare Intervention groups on sociodemographic characteristics of age, ethnicity, region, education, religion, and duration of time in Moscow. We will compare groups on baseline behaviors including alcohol use, drug use, duration and frequency of injection drug use, network characteristics, and injection risk behaviors. We will compute t-tests for continuous measures and chi-square tests for

categorical measures. We will compare the prevalence of HIV and HCV between groups, and we will use Poisson regression to compute relative risks adjusted for sociodemographic and behavioral variables that differ between groups.

9.4.6 PLANNED INTERIM ANALYSES

Interim analysis of behavioral outcomes will be conducted at each follow-up point. We do not plan to halt the study based on interim results. If early results indicate strong effects we will continue the study to assess whether the effects persist, and if early results indicate no effects we will continue the study to assess potential delayed effects. In addition, we will continue the study to assess secondary biological outcomes at the final follow-up.

The analysis will be conducted by the PI with data blind-coded by the data manager. The analysis will be reviewed by the co-investigators and the DSMB.

9.4.7 SUB-GROUP ANALYSES

The population for the study intervention is homogeneous (Tajik migrant males who inject drugs), therefore we do not plan any sub-group analyses.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will not be tabulated.

9.4.9 EXPLORATORY ANALYSES

We will conduct analyses to explore hypothesized mediation and moderation effects. We will test whether changes in HIV knowledge, risk awareness, risk reduction self-efficacy, behavioral norms, and social network interactions mediate changes in risk behavior. We will test whether psychosocial well-being (depression, loneliness) moderates intervention effects on risk behavior.

Mediation: We will investigate the effects of intervention condition on theoretical mediators, and test whether changes in proposed mediating variables predict changes in behavior. We will use multilevel structural equation modeling in Mplus to assess mediation effects, with the predictor (intervention condition) at the cluster level (level-2), and mediators and outcomes at the individual level (level-1), using 6-month outcomes and 3-month mediators. This method involves separation of observed variables into latent between and within-cluster components that are modeled separately but simultaneously, producing a theoretically unbiased estimate of the indirect effect.[76, 77]

Peer educator development: We will conduct analyses to test the effects of peer educator training on participant self-esteem, self-efficacy, and substance use self-stigma.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

All subjects will be asked to give informed consent before enrolling in the study. Verbal consent will be obtained for eligibility screening.

The following recruitment and consent materials are submitted with this protocol:

1. Recruitment flyer
2. Recruitment script
3. Script for verbal consent to eligibility screening
4. Consent form

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The consent process will be conducted by interviewers with human subjects training. The interviewer will inform prospective participants who responded to recruitment flyers that they will be asked to answer a few questions to determine whether or not they are eligible to participate in the research study. The interviewer will complete an eligibility screening report in REDCap to document each screening.

To obtain informed consent, the interviewer will provide each eligible subject with study information in writing (in Tajik language), and explain what participation as an intervention participant or network member will entail, explain the compensation for time and travel related to participation, and also review issues of confidentiality and data safety. Prospective participants will be told that:

- Participation is entirely voluntary and that they can decline or end participation in the study at any time or decline to answer any question during an interview that they prefer not to answer without penalty;
- The study's structured interviews will ask them to report on sensitive behavioral and health information that might embarrass them, make them uncomfortable, or cause difficulties in their relations with others should what they disclose become known.
- It is possible that those who are actively injecting drugs may become known to Russian authorities or other Tajiks who were unaware of their drug use. This knowledge may carry negative consequences.

We will request a waiver of documentation of informed consent due to the sensitive nature of the subject population. The interviewer will question the subject to assess understanding of the research requirements and subject rights. Persons will not be enrolled in the study if they do not demonstrate the

cognitive ability to provide informed consent, as assessed by asking them to describe key elements of the study as they review these elements during the informed consent process.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigators, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to the study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)
- Data that are not sufficiently complete and/or evaluable

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the data and safety monitors, and the National Institute on Drug Abuse. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party.

The Data and Safety Monitoring Board, authorized representatives of the funding agency (NIDA), and representatives of the Institutional Review Board (IRB), may inspect all documents and records required to be maintained by the investigator. The clinical study site will permit access to such records.

Privacy

All research activities will be conducted in as private a setting as possible. Intervention sessions will be held at the PRIZMA Satellite Office. The PRIZMA office conducts a variety of activities unrelated to injection drug use; visiting the office will not place participants at risk of being identified as a drug user. Interviews will be held at the PRIZMA Satellite Office or a location selected by the participant that is sufficiently private that his answers cannot be overheard. When study participants are referred to the Tajik Union for assistance with legal, health, or mental health issues, no personal information will be disclosed to Union staff, including information regarding their substance use or HIV or hepatitis C status.

Confidentiality of Participant Data

Participant screening, enrollment, and tracking data will be collected and stored using the UIC REDCap database. REDCap is a secure web application specifically geared to support online and offline data

capture for research studies and operations. Participant records will be identified with a confidential research ID number that is linked to contact information needed for follow-up.

The participant contact information will be stored in a separate secure database in REDCap with its own permission settings for internal use during the study. Only the Moscow Site PI (Bakhromov), Moscow Project Coordinator (Jonbekov) and the senior interviewer/data coordinator (TBA) will have access.

HIV and HCV testing data will be collected from the Moscow HIV Prevention Center and entered into REDCap in a separate database with its own permissions settings. Testing data will be identified with a testing ID number different from the research ID. A list of matching identifiers will be kept in a secure REDCap database. This double coding will provide higher protection for sensitive testing data. Only the PI, co-investigators, the Moscow Project Coordinator, and the UIC data manager will have access to the master list.

Study participant interview data will be collected using the UIC Qualtrics secure web-based platform. Interview data will contain no identifying information. Interview records will be identified only by the coded research ID number. The offline data collection app on tablet computers will be used to ensure continuous access to the study instrument. Data collected offline will be uploaded to the secure web-based platform whenever a network connection is available and then deleted from the tablet. The data manager at UIC will download data from the Qualtrics server to an encrypted and password-protected hard drive, and a backup copy will be stored on a secure local server. As each stage of the study is completed (baseline, 3/6/9/12-month follow-up), interview data will be deleted from the Qualtrics server and tablet computers.

Digital audio files will identified only with code numbers. Data transfers to UIC will include only de-identified data and will be carried out by Dr. Bakhromov or Mr. Jonbekov using the UIC Box service. This is the university-approved method for secure file sharing outside of the university network. The PI will set up a secure Box Health Data folder with restricted access for file transfers. Audio files will be deleted six months after being transcribed.

Data collected on laptop computers or tablets will be deleted after being transferred to the central repository. Laptops will have whole drive encryption enabled and will be kept in a locked storage cabinet when not in use. Data will not be stored on removable devices.

When data collection is completed, all study databases will be de-identified and archived. The data and metadata will be formatted using the Data Documentation Initiative (DDI) specifications and shared by depositing the de-identified data set and associated documentation in a digital repository within 12 months of the completion of the study. Access to the data will be restricted and will require a data sharing agreement.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

N/A

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Independent Safety Monitor**
Mary E. Mackesy-Amiti, Ph.D. *Research Associate Professor*	*Nabila El Bassel, Ph.D.* *University Professor of Social Work*
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Dr. El Bassel is chair of the Data and Safety Monitoring Board (DSMB) for this study.

Overall Structure of the Study Team

School of Public Health (SPH), University of Illinois at Chicago (UIC): UIC SPH will be the administrative and data coordinating site for this study. Dr. Mackesy-Amiti (PI) will be responsible for supervising administration of the study, coordinating data management, conducting data analysis, and writing reports and manuscripts with Dr. Levy who maintains a nearby office in SPH. Ms. Oakley will perform administrative tasks including budget monitoring and fiscal reporting, processing travel reimbursements, and coordinating the subcontract. Other staff include a data manager and a graduate research assistant.

PRIZMA Research Center: PRIZMA is a leading NGO research and training center with headquarters in Dushanbe, Tajikistan and a satellite office in Moscow. All activities involving participants will be conducted at the Moscow site. Dr. Makhbatshosho Bakhromov (Co-investigator) will be responsible for overseeing all aspects of the research in Moscow including the hiring and training of facilitators, participant recruitment, implementation of the intervention, and data collection. Reporting directly to Dr. Bakhromov, Mr. Jonbek Jonbekov will be the Project Coordinator responsible for directing project activities. Other staff will include group facilitators, interviewers, and a data coordinator. HIV/HCV testing and counseling will be conducted nearby at the Moscow HIV Prevention Center.

Communication between U.S. and foreign site: Due to current travel restrictions U.S. investigators will not visit the Moscow site until deemed safe and approved by the UIC IRB that monitors research travel safety related to covid-19. Plans for the Moscow site PI to meet with the U.S. investigators in Chicago once a year are also on hold until IRB approved. We will have virtual meetings by videoconference (e.g. Zoom) at least monthly to discuss study plans and progress. During enrollment and follow-up phases, the Moscow site project coordinator will provide weekly updates to the PI by email on number of participants enrolled, interviewed, and attended intervention. All participant screening, enrollment, and tracking data will be entered into a REDCap database, and participant interviews will be conducted using the Qualtrics web-based survey platform. The data manager at UIC will monitor data collection in these systems.

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Board (DSMB) composed of individuals with the appropriate expertise, including injection drug use, HIV and hepatitis C infection and prevention, migrant populations, and biostatistics. Members of the DSMB will be independent from the study conduct and free of conflict of interest. The DSMB will meet at least annually to assess safety and efficacy data from each arm of the study. The DSMB will operate under the rules of an approved charter that will be written and reviewed at the organizational meeting of the DSMB. At this time, each data element that the DSMB needs to assess will be clearly defined. The Chair of the DSMB will summarize the outcome of each DSMB session and provide it to the PI for action if needed. The results also will be reported in the study's annual report to NIDA and the National Institutes of Health.

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2.1, Interventionist Training and Tracking**.

Electronic data collection — REDCap and Qualtrics data collection processes will include automated and manual consistency checks.

Source documents and the electronic data --- Testing data will be initially captured on source documents (see **Section 10.1.9, Data Handling and Record Keeping**) and will ultimately be entered into the study database. To ensure accuracy site staff will compare a representative sample of source data against the database.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Quality management procedures will be detailed in the Manual of Procedures (MOP). Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff at the PRIZMA Moscow Satellite site under the supervision of Dr. Bakhromov. The site investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

Paper documentation will include pilot participant screening forms and interview notes, intervention attendance records, CRFs for AEs and UPs, and testing records obtained from the Moscow HIV Prevention Center. Paper forms for eligibility screening and enrollment will be available as a backup method. All paper source documents will be completed in a neat, legible manner to ensure accurate interpretation of data. Paper documents will be stored in a locked filing cabinet in a locked office at the PRIZMA Moscow office.

With the exception of pilot data, all data collected on paper will be entered into REDCap, a HIPPA-compliant data capture system provided by the Center for Clinical and Translational Science (CCTS) at UIC. Data entry will be completed within 7 days of collection. All other participant tracking data will be entered directly into the REDCap system. The REDCap data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. It also includes logging and audit trails on all data interactions.

Interview data will be collected using the UIC Qualtrics survey application. The offline data collection app will be installed on tablet computers to ensure continuous accessibility. Survey data will be deleted from the tablet after being uploaded to the Qualtrics server.

UIC staff will be responsible for conducting regularly scheduled reviews of the data, checking data quality and consistency, and reconciling discrepancies. The data manager will generate biweekly reports to be reviewed by the PI.

Digital audio recordings of intervention sessions will be transferred to UIC by uploading to a protected Health Data folder on the UIC Box file sharing service. Original digital audio files will be deleted after transfer. Selected session recordings will be sent to CETRA Language Solutions for translation and transcription. Transcripts will be stored by the PI on an encrypted password-protected hard drive.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 1 year after the submission of the Federal Financial Report (FFR).

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or MOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1

- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation, or within 10 working days of the scheduled protocol-required activity. All deviations will be addressed in study source documents, reported to the PI and to the NIDA Program Official. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 1 year after the completion of the primary endpoint by contacting Dryad Digital Repository. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Institute on Drug Abuse has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
CRF	Case Report Form
DSMB	Data Safety Monitoring Board
FFR	Federal Financial Report
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
IRB	Institutional Review Board
ITT	Intention-To-Treat
MOP	Manual of Procedures
NCT	National Clinical Trial
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOA	Schedule of Activities
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale

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