Getting Off: A Theory-based mHealth Intervention for Methamphetamine-using MSM

Lay Title: *Getting Off* App

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GLOSSERY OF TERMS

ACASI	audio computer assisted self-interview
AIDS	acquired immunodeficiency syndrome
APP	mobile smartphone application
ART	antiretroviral therapy
CAB	community advisory board
CAI	condomless anal intercourse
CBT	cognitive behavioral therapy
CDC	Centers for Disease Control and Prevention
DBS	dried blood spot
DSM-5	Diagnostic and Statistical Manual of Mental Disorders-version 5
FCC	Friends Community Center
FRI	Friends Research Institute, Inc.
GPS	global positioning system
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
IRB	institutional review board
MA	methamphetamine
mHealth	mobile health
MSM	men who have sex with men
MTL	Molecular Testing Labs
NIH	National Institutes of Health
PEP	post-exposure prophylaxis
PrEP	pre-exposure prophylaxis
RA	research assistant
RCT	randomized controlled trial

SAE	serious adverse event
SOC	stages of change
STI	sexually transmitted infection

SCHEMA

Getting Off:
A Theory-based mHealth Intervention for Methamphetamine-using MSM

Lay Title: *Getting Off* App

DESIGN	*Getting Off* App is a randomized controlled trial (RCT) to assess the impact of *Getting Off*, a culturally competent Cognitive Behavioral Therapy-based app for reducing methamphetamine use, HIV sexual risk behaviors, and increase advancement along the HIV Prevention or Care Continuum, with the desired outcome of significant reductions in methamphetamine use and HIV sexual risk behaviors as well as increased odds of advancement along the HIV Prevention or Care Continuum among men who have sex with men (MSM), aged 18-65, who report using methamphetamine within the past year. Over the course of 30-days, participants are asked to complete 24 intervention sessions in the *Getting Off* app derived from an existing, manualized, group-based intervention with established efficacy. The study will implement a two-arm RCT to determine intervention effects through comparison of participants who are given immediate access to the *Getting Off* app (Immediate Delivery [ID]) and participants who are given access to the *Getting Off* app after a delayed 30-day period (Delayed Delivery [DD]).
DURATION	30 days
SAMPLE SIZE	300 participants (n=150: Immediate Delivery / n=150: Delayed Delivery)
POPULATION	MSM who are between the ages of 18 and 65 years of age, who have used methamphetamine within the past 365 days, who have their own Android or iOS running smartphone with a current data plan, and who are able and willing to provide informed consent and comply with study requirements.

1.0 STUDY OBJECTIVES

1.1 Specific Aims

1.1.1 Specific Aim 1a: Conduct a RCT to evaluate reductions of methamphetamine use and HIV sexual risk behaviors, and increased advancement along the HIV Prevention or Care Continuum using a two-arm RCT to determine intervention effects through comparison of the Immediate Delivery [ID] (n=150) and Delayed Delivery [DD] (n=150) arms.

1.1.2 Specific Aim 1b: Evaluate reductions in methamphetamine use and HIV sexual risk behaviors, and increased advancement along the HIV Prevention or Care Continuum using an observed treatment effects analysis powered for prospective sub-group analyses to compare longitudinal pre/post data from the pooled ID and DD arms (n=300);

1.1.3 Specific Aim 1c: Evaluate reductions in methamphetamine use and HIV sexual risk behaviors, and increased advancement along the HIV Prevention or Care Continuum using a two-arm historical matched comparison design to evaluate the outcomes of the *Getting Off* app (ID+DD; n=300) relative to a matched sample of participants having previously attended the brick-and-mortar group-based *Getting Off* intervention (n~600; total n=900).

1.2 Secondary Aim

1.2.1 Secondary Aim 1: Determine the impact of structural- (e.g., housing insecurity, food scarcity, educational attainment, access to healthcare) and individual-level (e.g., homophobia, stigma, and discrimination) factors as moderators of intervention outcomes.

2.0 INTRODUCTION

2.1 Rationale

Methamphetamine use among MSM is associated with increased rates of HIV prevalence and transmission, as well as substandard advancement along the HIV Prevention and Care Continua. Methamphetamine use among MSM is deeply integrated into socio-sexual networks including the use of smartphone apps and websites to find sexual partners. Given the growth of mobile health technology, it is no longer necessary or reasonable to limit methamphetamine treatment options to physical sites, clustered in urban areas, and administered using generic, non-tailored content. The project builds upon the established efficacy of our manualized methamphetamine-use treatment intervention, "*Getting Off*: A Behavioral Treatment Intervention for Gay and Bisexual Male Methamphetamine Users," and the highly promising findings from the successful Stage I proof-of-concept study, to complete translation of *Getting Off* into a cross-platform (iOS and Android) app and assess the app's efficacy *and* non-inferiority in a scientifically rigorous randomized trial. The *Getting Off* app, like the group-based intervention before it, will use the principles of Cognitive Behavioral Theory and Stages of Change to help MSM reduce or eliminate methamphetamine use and HIV sexual risk behaviors, and increase advancement along the HIV Prevention or Care Continuum (including uptake of HIV testing, pre-, and post-exposure prophylaxis [PEP/PrEP] and PrEP adherence and persistence for those who are HIV negative; ART uptake and adherence for those who are HIV positive).

2.2 Background

2.2.1 Methamphetamine Use and HIV among MSM

MSM have elevated rates of methamphetamine use relative to non-MSM,[1-3] as methamphetamine use is deeply integrated into the sexual identities and sexual behaviors of MSM in the United States,[3-6] and permeates the venues most often associated with high-risk sexual behaviors among MSM.[7-9] Use of methamphetamine by MSM before or during sex is associated with decreased behavioral inhibition and increased engagement in HIV risk behaviors,[10-12] including condomless anal intercourse (CAI)[13-16] with serodiscordant sexual partners.[17-19] HIV prevalence is significantly higher among MSM who use methamphetamine,[19-21] and increases in concert with the intensity of methamphetamine use.[22] Methamphetamine use has thus been identified by the CDC as a driving force of the HIV epidemic among MSM in the United States.[12] Methamphetamine use is associated with poor antiretroviral therapy (ART) adherence and outcomes[23-24] and reduced adherence to HIV post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) among HIV-positive/-negative MSM, respectively.[25] In combination, the HIV Prevention and Care Continua address the National HIV/AIDS Strategy to reduce incidence and optimize care outcomes. Providing methamphetamine treatment to MSM is a public health imperative for addressing HIV/AIDS in the 21st century.

2.2.2 Methamphetamine Use and HIV Sexual Risk in MSM-targeted Digital Spaces

MSM use smartphones for sexual partner selection, sexual health information, and sexual identity expression at a higher rate than non-MSM,[26-31] and use smartphone applications ("apps") to facilitate GPS-based sexual partner selection (e.g., Scruff, Grindr, Jack'd);[32-34] such behaviors increase odds of both methamphetamine use and HIV sexual risk behavior.[35] Young MSM report using such apps daily,[27,29,36] and young, racial minority MSM are simultaneously both the group most at-risk for methamphetamine use and HIV infection as well as the group most likely to use smartphones.[28-30,36] MSM living in rural areas rely on Internet resources and GPS-enabled smartphones for locating sexual partners.[37] High rates of smartphone usage by young racial/ethnic minority and rural MSM dovetail cleanly with the current methamphetamine treatment and HIV risk reduction deficits evidenced in the United States health care system.[28]

2.2.3 Public Health Significance of a Methamphetamine Use Intervention App for High-risk MSM

The *Getting Off* app could broadly disseminate culturally competent methamphetamine use and HIV risk reduction content to large numbers of demographically and geographically diverse users who otherwise could not access such services, particularly racial/ethnic minority MSM and MSM living in rural areas. [28,45-46] Psychosocial factors (e.g., stigma) are the primary barriers discouraging MSM from accessing methamphetamine treatment,[47-48] obstacles obviated through technology-based delivery. The ability to access treatment from a smartphone would eliminate embarrassment, homophobic prejudice, and/or any stigma associated with methamphetamine use and/or HIV sexual risk behaviors.[48-49] Providing theory-driven, MSM-specific methamphetamine treatment, which integrates HIV risk reduction programming, reminders about HIV testing/PrEP/PEP, and information about HIV care (including ART reminders), will address a range of HIV-related health deficits and address key priorities set by the NIH HIV/AIDS research priorities and the National HIV/AIDS Strategy. Furthermore, the overall public health benefits could be tremendous as methamphetamine use has also been associated with major physical harm,[50] dental disease,[51] psychological harm,[13,44,52] and neurological damage.[53] The broader scientific community would benefit substantially from the knowledge that

methamphetamine use and HIV sexual risk behaviors can successfully be reduced via remote intervention, and clinical practice could face a potential paradigm shift towards mobile content delivery for difficult-to-reach and/or stigmatized populations.

Given the growth of mobile technology, it is no longer reasonable to limit methamphetamine treatment options to physical sites, clustered in urban areas, and administered using generic, non-tailored content. Only 1% of app-using MSM express a preference to participate in programming delivered in-person; 70% prefer content delivered via smartphone.[26] The *Getting Off* intervention is particularly well-situated for translation into a mobile app-driven format, as it has been adapted to be carried out in community settings with peer counselors and does not require delivery via Masters' level/experienced Cognitive Behavioral Therapy (CBT) counselors.

2.2.4 Preliminary Studies: Developing and Evaluating the Group-based, Manual-driven Intervention

Getting Off began as a MSM-specific, manual-driven intervention based on the theoretical principles and techniques of CBT, as originally incorporated in the Matrix Model.[54] The original 48-session, 16-week intervention was rigorously evaluated in two randomized controlled trials (RCT).[38-41] In the first study, *Getting Off* was shown to significantly reduce HIV sexual risks compared to a mainstream CBT arm; all arms produced significantly more methamphetamine-negative urine samples compared to the control arm.[40] In the second study, *Getting Off* sustained greater reductions in methamphetamine use compared to a gay social support therapy control arm.[41] In the third study, *Getting Off* was tailored to a 24-session, 8-week intervention and modified for implementation within the limited resources and capacity of community-based organizations while retaining significant reductions in methamphetamine use and HIV sexual risk.[38,42] Since 2007, the tailored *Getting Off* intervention has been sustained as a service program with public health funding and has been adopted by multiple community sites and public health facilities nationally and internationally. The evolution of *Getting Off* towards greater scalability responds to the mHealth opportunity to advance treatment options into the digital sphere.

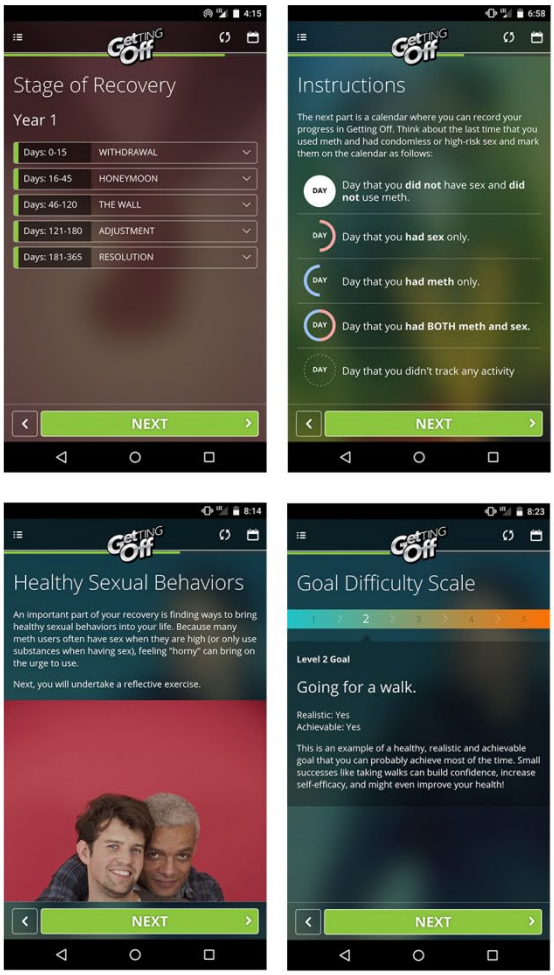
2.2.5 Preliminary Studies: Summary of Stage I Findings

During the proof-of-concept study, three focus groups (N=23) provided feedback from treatment-savvy participants who completed a minimum of 18/24 sessions (75%) of the group-based *Getting Off* intervention. Based on focus group input, one-third of the manual intervention (8/24 sessions) was developed into an app format. Focus group participants provided very constructive feedback regarding their treatment experiences, offering valuable guidance for app development on session selection, adaptation of content, and app design. Participants emphasized the importance of interactivity and had specific suggestions about adapting manualized exercises to fit with and fully exploit the capabilities of mobile smartphone technology. Sample screenshots from the app are shown below.

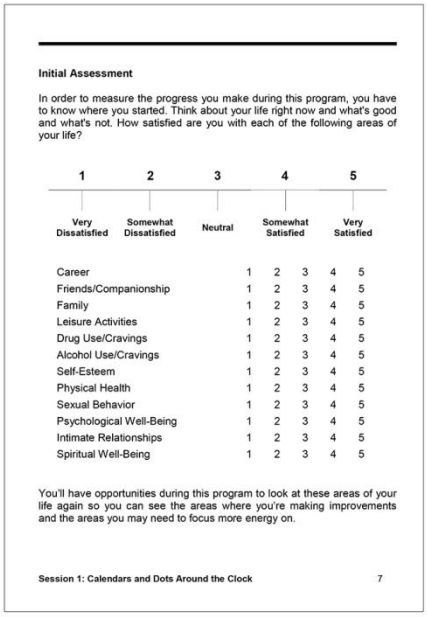
The initial eight sessions were developed using an iterative development process with close communication between Investigators and the technology team. A cross-platform app was developed that included the following content, features, and functionality: 1) HIV and methamphetamine health, prevention, and risk behavior information, including a risk calculator; 2) behavioral self-assessments; 3) multimedia health promotion and educational information; 4) mobile-optimized interface; 5) avatar creation and personalization; 6) culturally competent (i.e., gay-specific content, themes, and pictures), user-friendly, and attractive interface; and, 7) passcode protected platform and HIPAA compliant data collection and storage.

Personalized Avatar

Screenshots



Initial Assessment Translated from the Manual to the App



Initial Assessment

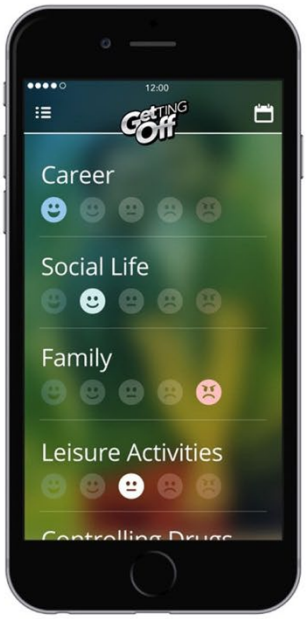
In order to measure the progress you make during this program, you have to know where you started. Think about your life right now and what's good and what's not. How satisfied are you with each of the following areas of your life?

1	2	3	4	5
Very Dissatisfied	Somewhat Dissatisfied	Neutral	Somewhat Satisfied	Very Satisfied

Career	1	2	3	4	5
Friends/Companionship	1	2	3	4	5
Family	1	2	3	4	5
Leisure Activities	1	2	3	4	5
Drug Use/Cravings	1	2	3	4	5
Alcohol Use/Cravings	1	2	3	4	5
Self-Esteem	1	2	3	4	5
Physical Health	1	2	3	4	5
Sexual Behavior	1	2	3	4	5
Psychological Well-Being	1	2	3	4	5
Intimate Relationships	1	2	3	4	5
Spiritual Well-Being	1	2	3	4	5

You'll have opportunities during this program to look at these areas of your life again so you can see the areas where you're making improvements and the areas you may need to focus more energy on.

Session 1: Calendars and Dots Around the Clock 7



Top left: Each user can personalize his avatar by choosing facial structure, skin tone, hair, facial hair, clothing, and background. Bottom left: An example of the translation from manual to app. Right: Screenshots showing how the *Getting Off* app provides information on the stages of recovery from methamphetamine use, a risk calculator for methamphetamine use and high-risk sexual behaviors, a reflective exercise on disassociating sexual behaviors from methamphetamine use, and a goal-setting exercise to increase self-efficacy.

A feasibility pilot test was conducted on the original eight sessions. Participants (N=15) in the feasibility pilot test were 40% Caucasian/White, 33% African American/Black, and 27% Hispanic/Latino; 73% identified as gay and 27% identified as bisexual. Ages ranged from 25-55 years (Mean=43; SD=9); 67% were HIV positive. Most (87%) met criteria for DSM-5 methamphetamine use disorder (60% severe). In the past 30 days, 80% reported methamphetamine use, 67% reported sex with a casual male partner (Mean=1.7; SD=0.9), and 25% reported sex with an anonymous male partner (Mean=2.5; SD=2.4). Pilot test participants were identified as similar to prospective app users; 53% (n=8) were out-of-treatment, current methamphetamine users and 47% (n=7) were methamphetamine users who had recently sought treatment for their methamphetamine use with no more than six months of recovery. Backend app user data indicated that average progression rates (i.e., how much of a session the participant completed) ranged from 62% (Recall) to 91% (Redefine), and the median completion rate for every session was 100% across all 15 participants. Twelve (80%) participants finished all sessions and completed both the initial and closing self-assessments; on average these participants reported improvements in self-esteem, social life, family life, drug

use, and alcohol use. Follow-up interviews (n=14; 93%) indicated mean participant satisfaction rating was high (8.5/10).

2.2.6 Preliminary Studies: Lessons Learned

Three components addressed feasibility: 1) Physical location versus computer delivery: Could the *Getting Off* intervention, written to be delivered in a treatment clinic, be successfully delivered through an app?, 2) Clinical versus self-directed: Could the *Getting Off* intervention, originally designed to be delivered by a counselor, be self-directed? and, 3) Group versus individualized: Could the *Getting Off* intervention, originally designed for a group format, be individualized? Findings demonstrated proof-of-concept for the *Getting Off* app. *Getting Off* was easily delivered as a mHealth intervention; participants were engaged, were able to understand the CBT concepts, and thoroughly navigated through the sessions. Overall, satisfaction was very high. Areas for improvement that were identified: increased interactivity between the user and the avatar; an accumulation of points that could be used to "purchase" items to personalize and enhance the avatar (e.g., a computer, clothes, a dog); reduce text in certain sessions; and, increased gamification.

2.2.7 Stage II Application Development in Response to Stage I Findings

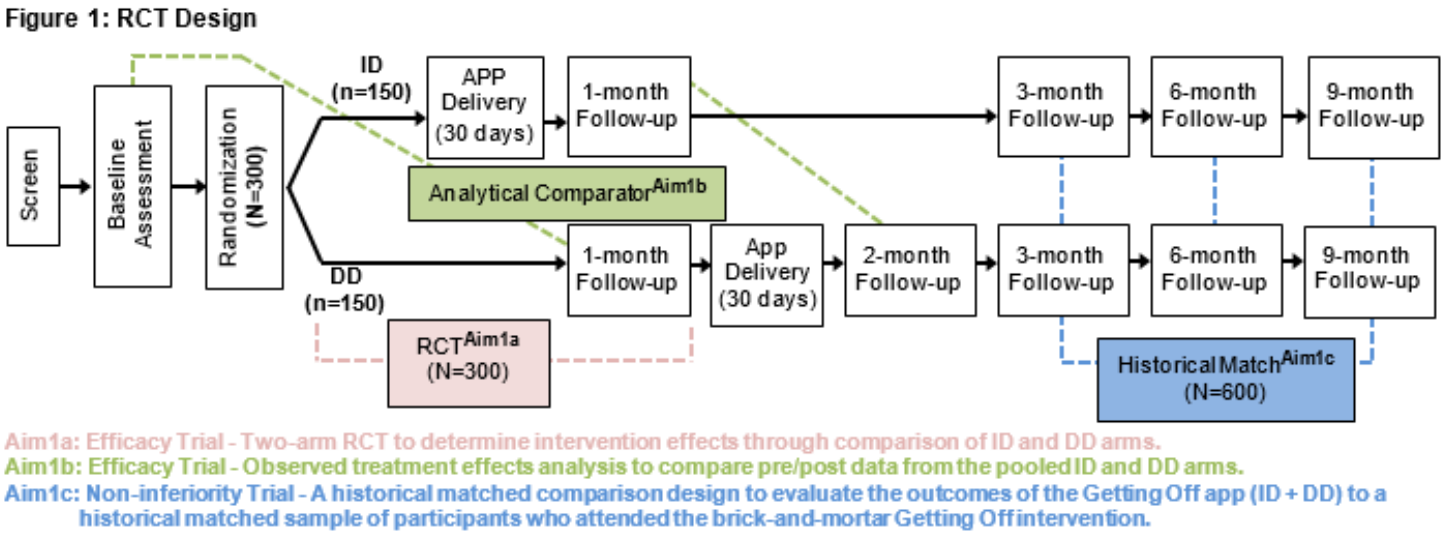
The Stage II development of the cross-platform *Getting Off* app will be based on focus groups and a beta usability pilot test; user feedback from the Stage I feasibility pilot test; current literature on app preferences among MSM; as well as state-of-the-art technology. To be reflective of the needs of MSM methamphetamine users, refinement of the first eight sessions and development of the remaining 16 sessions will focus on increased interactivity; personalization of avatar functionality; gamification in the form of earnable points (particularly but not limited to the "purchase" of items for the avatar); reduced text and increased images; the ability to view peer testimonials; links to Internet sites (particularly for local resources related to methamphetamine treatment, HIV/STI testing, PrEP/PEP, HIV care); increased information on PrEP/PEP; and, a self-administrated risk calculator. The app will be an interactive presentation of the *Getting Off* manual. Health content, behavioral self-assessments, "homework" assignments, and multimedia content will be integrated in a walk-through (i.e., step-by-step) manner where the consumer will be presented dynamic content, all under the guidance of a culturally competent, user-friendly, attractive interface.

3.0 STUDY DESIGN

3.1 Overview

Getting Off App is a randomized controlled trial to assess the impact of *Getting Off*, a culturally competent Cognitive Behavioral Therapy-based app for reducing methamphetamine use, HIV sexual risk behaviors, and increase advancement along the HIV Prevention or Care Continuum, with the desired outcome of significant reductions in methamphetamine use and HIV sexual risk behaviors as well as increased odds of advancement along the HIV Prevention or Care Continuum among MSM, aged 18-65, who report using methamphetamine within the past year. The design of *Getting Off* App is illustrated in Figure 1.

Figure 1: *Getting Off* App Study Design



Following screening, informed consent and baseline assessments, participants will be randomized into one of two arms: Arm A: Immediate access to the Getting Off app (Immediate Delivery [ID]); or, Arm B: Participants will have access to the Getting Off app after a delayed 30-day period (Delayed Delivery [DD]). Participants in both arms will receive the same Getting Off app and participants in both arms will be given 30-days to complete the 24 sessions; it is expected to take far less time to progress through the self-directed app than the group-based intervention. The randomized two-arm repeated measures design will assess participants at 1-, 2- (DD arm only), 3-, 6-, and 9-months post-randomization to determine longitudinal intervention effects, observed treatment effects, and a historical comparison with a matched sample of participants who have attended the brick-and-mortar group-based Getting Off intervention (see Figure 1). The study will use an "intent-to-treat" design; participants will be assessed regardless of participation or retention.

4.0 STUDY SITE

FCC, the community site for Friends Research Institute (FRI) and clinical site for the study, is in the MSM sex work district on the border of Hollywood and West Hollywood. The location allows easy (walking distance and public transportation) access to methamphetamine-using MSM who congregate in the area. FCC provides a full spectrum of HIV and substance abuse prevention service programs for out-of-treatment substance users and outpatient treatment for treatment-seeking MSM methamphetamine users. Most FCC program participants are current substance users, many are sex workers, persons of color, and homeless or living in a transitional living situation. The *Getting Off* service program has been operating at FCC since 2007. The RCT will be conducted at the study site, with the option to have the follow-ups conducted through a virtual platform. All participants will be required to visit the study site for their baseline assessment and enrollment.

5.0 PARTICIPANTS

5.1 Inclusion Criteria

5.1.1 Self-identified MSM;

5.1.2 Methamphetamine use within the past 365 days;

5.1.3 Between 18 and 65 years of age;

5.1.4 Resident of Los Angeles County;

5.1.5 Has an iPhone 7 or later running iOS 10.0 or higher, or has an Android smartphone with a minimum 3 GB RAM running Android 6.0 or higher operating system, with a current data plan;

5.1.6 Willing to download an experimental app; and has at least 2 GB of available storage memory on their smartphone;

5.1.7 Willing and able to receive and self-administer at-home HIV/STI test kits or have the test kits completed in-person at the study site;

5.1.8 Willing to provide informed consent; and

5.1.9 Willing to comply with study requirements.

5.2 Exclusion Criteria

5.2.1 Does not identify as a MSM;

5.2.2 Has not used methamphetamine within the past 365 days;

5.2.3 Under 18 years or over 65 years of age;

5.2.4 Is not a resident of Los Angeles County;

5.2.3 Does not have an iPhone 7 or higher running iOS 10.0 or higher, or an Android smartphone with a minimum 3 GB RAM running Android 6.0 or higher operating system; or does not have an active data plan;

5.2.4 Unwilling to download an experimental app; or does not have at least 2 GB of available storage memory on their smartphone;

5.2.5 Unwilling or unable to receive and self-administer at-home HIV/STI test kits or have the test kits completed in-person at the study site;

5.2.5 Unwilling to provide informed consent; and

5.2.6 Unwilling to comply with study requirements.

6.0 PROJECT PROCEDURES

6.1 Recruitment

Four recruitment strategies are being utilized to ensure enrollment targets are met and a diversity of participants are enrolled. Furthermore, the diversity in recruitment strategies will foster a range in the sociodemographic profiles. All potential participants who inquire about the study are scheduled for an intake within 24-48 hours.

6.1.1 Online recruitment

Both website- and app-based online recruitment will be utilized. Banner ads/digital flyers will be placed on gay websites, apps, and social media sites that specifically target MSM such as Adam4Adam, Jack'd, Grindr, Craigslist.org. FCC has established relationships with online venues that cater to MSM, which will enable a successful and robust Internet-based recruitment strategy.

6.1.2 Street- and Venue-based Outreach

The Research Coordinator and Research Assistant (RA) will utilize a semi-structured time-space sampling methodology to conduct street- and venue-based outreach identified through the Community Advisory Board (CAB) and ongoing community mapping as locations where methamphetamine-using MSM congregate (e.g., parks, street corners, cruising locations, sex clubs, bathhouses, churches, shelters, food lines, social services agencies).

6.1.3. Poster Advertisement

Posters that introduce the study will be posted throughout FCC and at local community-based organizations to inform potential participants that they can contact the RA for further information regarding the research study.

6.1.4 Long-chain Referral Sampling

Current study participants will be asked to recruit potential new participants. Current participants will receive $2 when they bring a potential participant to the site and $18 if an eligible participant enrolls.

6.2 Informed Consent Procedures

During the enrollment session, the Research Coordinator or RA describes the study in detail to the potential participant. If the potential participant is deemed eligible and is interested in participating, he is administered the Informed Consent Form. Participants must pass an informed consent quiz verifying his full understanding of study procedures (e.g., length of study participation, incentive schedule). Participants will be informed of procedures for ensuring their confidentiality, including the issuance of a Certificate of Confidentiality by the federal government; the use of numbers and codes rather than participants' names; and the maintenance of a cloud-based HIPAA compliant (secure and encrypted) commercial data website (Qualtrics.com). Participants will be given the contact numbers of both the Principal Investigator and Western IRB to answer questions about the study or one's rights as a human subject.

6.3 Enrollment Procedures

After the Informed Consent Form for the study has been read, any questions have been answered, the informed consent quiz has been passed, and the participant has electronically signed the consent form, a Research Coordinator or RA will deliver the baseline assessment, which takes approximately 60-90 minutes. To maximize accurate disclosure of high-risk and sensitive behaviors, data is collected via an audio computer-assisted self-interview (ACASI). Studies have demonstrated that disclosure rates of perceived stigmatized behaviors are increased through ACASI assessments. After the ACASI is completed, participants will be instructed to download the *Getting Off* app on to their smartphone. Once access to the app is granted (determined by randomization), participants will have 30-days to complete the 24 sessions.

6.4 Random Assignment

Following informed consent and completion of the baseline assessment, participants will be randomized to either the ID or DD arm through a computerized variable-balanced block randomization procedure. Recent work with MSM with substance use disorder (predominantly methamphetamine) at FCC revealed treatment outcomes to be associated with participant substance use histories and sociodemographics. A variable-balanced procedure will thus provide multivariate balance among the characteristics known or expected to influence outcomes. The randomization procedure will balance across age (<34, ≥34), race/ethnicity (Caucasian/White, all other race/ethnicities), HIV serostatus (+, -), and SOC (contemplation/preparation, action/maintenance).

6.5 Incentive Schedule

Incentives are comprised of 1) incentives for baseline assessment ($40 gift card); 2) incentives for completing follow-up assessments [$50 gift card for completing the 1-month follow-up assessment, the 2-month follow-up assessment (DD arm only), the 3-month follow-up assessment, the 6-month follow-up assessment, and the 9-month follow-up assessment]; 3) incentives for self-administering and returning the at-home HIV/STI test kits within 45 days of receipt [$50 gift card for returning after the 3-month assessment, after the 6-month assessment, and after the 9-month assessment] and 4) a $2 gift card when an active participant brings a potential participant to the site to screen for eligibility, and an additional $18 gift card if the potential participant is eligible and enrolls (maximum of three eligible and enrolled participants per active participant). Participants randomized into the ID arm can thus earn a maximum of $450 in gift cards. Participants randomized into the DD arm can earn a maximum of $500 in gift cards.

All participants may earn up to $50 in gift cards each time they provide all requested biological marker samples or test results at the follow-ups, if conducted at-home and returned within 45 days of receiving the kit. HIV-positive participants may earn a $20 gift card for returning a complete at-home test kit for Chlamydia, N. gonorrhea and Syphilis. If the DBS sample is insufficient for processing the Syphilis test, participants will be asked to provide results of a recent (within 3 months) Syphilis test from their medical provider, or to come to the study site for an in-person blood draw. HIV-positive participants may earn the additional $30 gift card (totaling $50 in gift cards) for providing recent (within 3 months) HIV viral load test results from their medical provider, or by coming to the study site for a blood draw. HIV-negative participants may earn the full $50 gift card for returning a complete at-home test kit for Chlamydia, N. gonorrhea, Syphilis and HIV. Including, an additional DBS card for PrEP (TDF/FTC or TAF/FTC), if

appropriate. If the DBS sample(s) is insufficient, only a $20 gift card will be dispersed, and the participant will be asked to provide results of a recent Syphilis and TDF/FTC or TAF/FTC adherence test (both within 3 months) from their medical provider, or to come to the study site for an in-person blood draw to earn the additional $30 gift card (totaling $50 in gift cards).

6.6 Assessments

6.6.1 Assessments Overview

Behavioral assessments will be conducted at baseline and follow-ups. Follow-up assessments will be conducted at 1-, 2- (for those randomized to the DD condition only), 3-, 6-, and 9-months post-randomization to measure methamphetamine use, HIV sexual risk behaviors, and advancement along the HIV Prevention or Care Continuum.

6.6.2 Behavioral Assessments

6.6.2.1 DSM-5 Methamphetamine Use Disorder contains the DSM-5 diagnostic items necessary to make a determination of mild, moderate, or severe methamphetamine use disorder. This information will determine the app's utility for consumers at various levels of methamphetamine use. DSM-5 diagnostic criteria for other substance use disorders will also be collected. Administered at baseline only.

6.6.2.2 University of Rhode Island Change Assessment (URICA) is a brief, self-administered inventory used to assess the participant's current position regarding readiness for change (e.g., precontemplation, contemplation, action). Administered at all time points.

6.6.2.3 Admission/Follow-up Form collects demographic information, housing status, food security, educational attainment, alcohol and other drug use history, family and social history, legal status, HIV status, location on the HIV Prevention or Care Continuum, experiences with stigma and/or discrimination, and general and mental health status. The full form will be administered at baseline, an abbreviated version at all follow-up time points.

6.6.2.4 Substance Use Frequency is a brief assessment, developed by Dr. Cathy Reback (Principal Investigator) that assesses substance use, injection drug use, and injection protocols in the past 30 days. Administered at all time points.

6.6.2.5 Behavioral Questionnaire – Amphetamine (BQA)-Abbreviated Version gathers information on HIV-related drug and sexual risk behaviors, assesses self-efficacy for sexual behavior change, and collects detailed information on discrete sexual behaviors (with primary or non-primary partners and whether or not the behavior occurred under the influence of methamphetamine and/or other substances), as well as episodic data about participants' most recent sexual encounters. Administered at baseline, and an abbreviated version is administered at all follow-up time points.

6.6.2.6 PrEP Uptake and Adherence is a brief assessment, developed by Dr. Cathy Reback (Principal Investigator), that gathers information of PrEP readiness, initiation and adherence to access advancement along the HIV Prevention Continuum. Administered at all time points.

6.6.2.7 ART/HIV Care is a brief assessment, developed by Dr. Cathy Reback (Principal Investigator), that gathers information of HIV care and ART medication adherence to access advancement along the HIV Care Continuum. Administered at all time points.

6.6.3. Biomarker Assessments

6.6.3.1 HIV-antibody Test. HIV-negative and status unknown participants will receive a fingerstick DBS test at 3-month intervals, as recommended by the CDC for high-risk individuals. Participants who show documentation of HIV-positive serostatus are not given a HIV-antibody test. If the test is reactive, then the participant will be presumed positive for HIV antibodies and referred for additional evaluation and treatment. If the DBS sample is rejected by the lab or if the quantity of blood is insufficient, participants will be asked to come to the study site to have the test performed via fingerstick blood test using the INSTI HIV 1/HIV 2 antibody test, or to provide a copy of recent results (within 3 months) from their medical provider. Conducted at baseline and at the 3-, 6-, and 9-month follow-up time points (if previously tested HIV-negative or status is unknown).

6.6.3.2 STI Testing. Participants will be tested for urinary N. gonorrhea and Chlamydia, pharyngeal and rectal swabs will be taken for N. gonorrhea and Chlamydia, and syphilis will be tested by fingerstick DBS. Positive STI results will be reported per state guidelines and will be immediately referred to care. If the DBS sample is rejected by the lab or if the quantity of blood is insufficient, participants will be asked to come to the study site to have the test performed via intravenous blood draw or to provide a copy of recent results (within 3 months) from their medical provider. Conducted at baseline and at the 3-, 6-, and 9-month follow-up time points.

6.6.3.3 Virologic Control for HIV-positive Participants. As indicated by an undetectable HIV-1 level via intravenous blood draw, which has a threshold for undetectability = <30 copies/mL will be performed by Foundation Laboratory. Viral load testing through Foundation Laboratory may be bypassed if participants can provide recent (within 3 months) lab results from their medical provider. Conducted at baseline and at the 3-, 6-, and 9-month follow-up time points.

6.6.3.4 Dried Blood Spot (DBS) for HIV-negative Participants who Report PrEP Uptake. A blood sample will be collected and a DBS analysis for intra-erythrocytic TFV-DP will be performed by Molecular Testing Labs. Conducted at baseline and at the 3-, 6-, and 9-month follow-up time points.

6.6.4. Follow-up Locator Questionnaire

6.6.4.1. Health Study Locator Questionnaire. The locator form was originally developed by UCLA Integrated Substance Abuse Programs (ISAP) investigators for the Methamphetamine Treatment Project to facilitate contact with the participant during intervention and follow-up and has been modified by the Principal Investigators for MSM. The form asks participants to give consent for follow-up and to provide names, addresses, email and Internet site profiles, particularly social network sites, and phone numbers of relatives and friends who can reach the participant in emergencies. Information is also collected on where (libraries, clubs, bars) and with whom the participant associates (i.e., social network), and a physical description, including tattoos, scars, and birthmarks.

7.0 TIMELINE

The timeline and research procedures are presented in Table 1.

Table 1. Timeline and Activities

Timeline of Research Procedures	Aim	Year 1 7/15/18-4/30/19				Year 2 5/1/19-4/30/20				Year 3 5/1/20-4/30/21				Year 4 5/1/21-4/30/22				Year 5 5/1/22-4/30/23			
Month:		N/A	Aug, Sep, Oct	Nov, Dec, Jan	Feb, Mar, Apr	May, Jun, Jul	Aug, Sep, Oct	Nov, Dec, Jan	Feb, Mar, Apr	May, Jun, Jul	Aug, Sep, Oct	Nov, Dec, Jan	Feb, Mar, Apr	May, Jun, Jul	Aug, Sep, Oct	Nov, Dec, Jan	Feb, Mar, Apr	May, Jun, Jul	Aug, Sep, Oct	Nov, Dec, Jan	Feb, Mar, Apr
Milestones:																					
Develop study materials & protocol	n/a		x																		
Obtain IRB/regulatory approval	n/a		x																		
Obtain CoC	n/a		x																		
The Formative Stage																					
Convene Community Advisory Board	1 & 2			x		x		x		x		x		x		x		x		x	
Conduct focus groups	2			x																	
App development (sessions 1-24)	1 & 2				x	x	x	x	x	x	x										
Alpha phase (post-development bug testing)	2											x									
Beta phase (usability pilot study)	2												x								
App refinement	2												x								
Hire and train Research Assistant	n/a													x							
The RCT Stage																					
Recruit & enroll ~25-30 participants/mo (N=300)	3												x	x	x	x	x				
1-, 2-, 3-, 6-, 9-month f/u assessments	3												x	x	x	x	x	x	x	x	
Data cleaning & analysis	3												x	x	x	x	x	x	x	x	x
Report and manuscript preparation	n/a																	x	x	x	x
Dissemination of findings	n/a																	x	x	x	x

8.0 STATISTICAL ANALYSES

8.1 General Analytical Approach

All primary outcomes are operationalized and assessed in at least two discrete ways, increasing accuracy of measurements, reducing concerns of fully missing data, and allowing for post-hoc comparisons of concurrent validity across assessment modalities (see Table 2 for all outcome operationalizations). Descriptive statistics will be calculated and provided for all outcomes, with specific metrics chosen based on the distributional properties of each variable (e.g., counts and percentages for nominal variables; means and standard deviations for parametric continuous variables; ranges and medians for non-parametric continuous variables). Diagnostic (i.e., DSM-5), psychosocial (e.g., URICA), barriers and facilitators (e.g., housing insecurity, lack of transportation), and/or sociodemographic variables will be tested for significant association with study outcomes (i.e., advancement through the HIV Prevention or Care Continuum, methamphetamine use, HIV sexual risk behaviors), with specific tests of association chosen based on the distributional properties of the outcome variables in question. All variables demonstrating significant statistical association with one or more of the study outcomes will be included as statistical covariates in all multivariate outcome analyses associated with Specific Aims 1a-1c, and will additionally be included in exploratory sub-group analyses to test for moderating effects on treatment response and/or contingent effects among subsets of participants. Primary outcome analyses for Specific Aims 1a, 1b, and 1c will be carried out using mixed effects Generalized Linear Model (GLM) equations.

8.2 Advancement through the HIV Prevention or Care Continuum

Advancement through the HIV Prevention or Care Continuum will be assessed at all time points throughout the study, and will be operationalized dichotomously (i.e., yes/no achievement of one of the steps on either the HIV Prevention or Care Continuum; e.g., viral suppression), and

as a counted variable (e.g., consecutive DBS results indicating successful PrEP adherence). Power calculations related to advancement through either continuum will assume a 30% probability of achievement of at least one of the steps on either the HIV Prevention or Care Continuum (equivalent to ~1:2 odds of advancement). Methamphetamine use outcomes will be assessed repeatedly (i.e., at all time points) and will be operationalized dichotomously (e.g., methamphetamine-metabolite-free urine sample), as a counted variable (i.e., number of methamphetamine-metabolite-free urine samples provided), and as a continuous variable (i.e., Treatment Effectiveness Score [total number of methamphetamine-metabolite-free sample divided by total samples possible]). Power calculations related to methamphetamine use outcomes assume an 80% probability of methamphetamine use during the pre-intervention period for participants in the DD arm (equivalent to 4:1 odds of use).

8.3 HIV Sexual Risk Behavior

HIV sexual risk behavior outcomes will be assessed at all time points throughout the study, and will be operationalized dichotomously (e.g., incident STI via biomarker testing), as a counted variable (e.g., number of days/times engaged in CAI in the past 30 days), and as a continuous variable (e.g., a HIV risk severity index generated from multiple factor-analyzed items). Power calculations for engagement in HIV sexual risk behaviors assume a 65% probability of engagement during the pre-intervention period for participants in the DD arm (equivalent to ~2:1 odds of engagement). Multivariable inferential analyses of dichotomous outcomes will take the form of GLMs employing the Bernoulli family and logit link function; counted outcomes will be analyzed with GLMs employing the Poisson-log or negative binomial link functions as distributional patterns dictate (note: if data evidence an over-representation of zeros or an overdispersion of variance, zero-inflated Poisson and/or negative binomial analyses may be substituted); continuous outcomes will be analyzed using GLMs employing the identity link and Gaussian family functions and assume a single covariate unless otherwise stated (note: iteratively reweighted, bootstrapped, or jack-knifed estimation procedures may be used in Gaussian models if sensitivity analyses indicate undue influence from outliers). Mixed effects GLM models are considered the best linear unbiased estimators for repeated measures data employing non-parametric and/or limited dependent variables. All power calculations are premised on tests of association across two time points (e.g., baseline with app completion; app completion with brick-and-mortar program completion), providing the most conservative estimate of minimum detectable effect (MDE) size estimations; all power calculations assume $\alpha \leq 0.05$ (two-tailed), and $1 - \beta = 0.80$.

Table 2: Instruments, Targets, Variable Operationalizations, and Minimum Detectable Effects

Table 2: Instruments, Targets, Variable Operationalizations, and Minimum Detectable Effects (1 - β = 0.80; α = 0.05, two-tailed)

		Variable Operationalizations			Power-- Minimum Detectable Effects		
Instrument	**Target**	Dichotomous (Di)	Count (Cu)	Continuous (Co)	Model 1— RCT (Aim 1a; n=150/n=150)	Model 2— Tx Effects (Aim 1b; N = 300)	Model 3— Matched Comparison (Aim 1c; N = 300/N ~ 600)
DSM-5 (MA)	Diagnosis of MA Use Disorder	Presence/Absence of MA Use Disorder	# of Diagnostic Criteria Endorsed	*N/A*	Potential Statistical Controls; Exploratory Sub-Group Analyses		
URICA	Stage of Change/ Readiness for Change	Above/Below "Action" Stage	N/A	URICA Score(s)	Potential Statistical Controls; Exploratory Sub-Group Analyses		
Admissions & Follow-up Form	Sociodemographics; HIV Status and Tx History, Barriers & Facilitators	Sexual Identity; HIV Status; Linked/Unlinked; Housing Insecurity	Prior Drug Treatment Episodes; Symptomology	Age; Income	Potential Statistical Controls; HIV-Related Sub-Group Analyses; Barrier/Facilitator Moderator Analyses		
	HIV Prevention or Care Continuum[a]	HIV Test; PrEP Uptake; Advance along HIV Prevention or Care Continuum	# of HIV Prevention or Care Continua Steps Completed	N/A	**Di:** OR = 1.97; **Cu:** IRR = 1.51; **Co:** f^2 = 0.03	**Di:** OR = 1.61; **Cu:** IRR = 1.35	**Di:** OR = 1.52; **Cu:** IRR = 1.30; **Co:** f^2 = 0.01
Biomarker Tests (UA, VL, DBS, HIV/STI)	MA Use, HIV Prevention/Care Continuum Outcomes, Sexual Risk Behavior	Incident STI /Incident HIV	Log reductions in HIV VL; DBS Analysis of PrEP	Treatment Effectiveness Score	**Variable**	**Variable**	**Variable**
Substance Use Freq.	MA Use	Use/Non-use	Days of Use	N/A	**Di:** OR = 0.48; **Cu:** IRR = 0.85; **Co:** f^2 = 0.03	**Di:** OR = 0.59; **Cu**: IRR = 0.89; **Co:** f^2 = 0.01	**Di:** OR = 0.62; **Cu:** IRR = 0.90; **Co:** f^2 = 0.01
BQA	HIV Sexual Risk Behavior	CAI[b]	# CAI[b] Episodes	HIV Sexual Risk Scale	**Di:** OR = 0.52; **Cu:** IRR = 0.78; **Co:** f^2 = 0.03	**Di:** OR = 0.63; **Cu:** IRR = 0.85; **Co:** f^2 = 0.01	**Di:** OR = 0.66; **Cu:** IRR = 0.87; **Co:** f^2 = 0.01
Locator	Contact Information						

[a]HIV Prevention Continuum (HIV testing and PrEP/PEP uptake) and HIV Care Continuum (link, ART adherence, virological suppression).

[b]CAI: Condomless Anal Intercourse includes both receptive and insertive anal intercourse, and will be assessed by partner type (e.g., main, casual, exchange)

9.0 ANALYTIC APPROACH

9.1 Specific Aim 1a Analysis

Aim 1a, which begins the efficacy trial, is a two-arm, non-blinded RCT whereby half of all participants are randomly assigned to receive the Getting Off app immediately (ID arm; n=150; equivalent to an “active intervention” arm) and half are randomly assigned to receive the app after a 30-day delay (DD arm; n=150; equivalent to a “control” arm). The proposed analytical model allows for causal analysis of intervention effects. Power Calculations for Specific Aim 1a: estimated RCT MDEs for HIV Prevention or Care Continuum outcomes related to Specific Aim 1a are: 1) dichotomous (Di)—Odds Ratio (OR) = 1.97; 2) counted (Cu)—Incidence Rate Ratio (IRR) = 1.51; 3) continuous (Co)—f2 = 0.03; for methamphetamine use outcomes: 1) Di—OR = 0.48; 2) Cu—IRR = 0.85; 3) Co—f2 = 0.05; for HIV sexual risk behaviors outcomes: 1) Di—OR = 0.52; 2) Cu—IRR = 0.78; 3) Co—f2 = 0.05.

9.2 Specific Aim 1b Analysis

Aim 1b completes the efficacy trial by doubling the size of the analytical sample and allowing for highly accurate specification of observed treatment effects; it is a single-arm, pooled (i.e., ID+DD) observed treatment effects analysis whereby data points from the ID arm are paired with their analytical comparators from the DD arm (i.e., ID enrollment data with DD 1-month post-enrollment data; ID 1-month post-enrollment data with DD 2-months post-enrollment data);

the proposed analytical model provides increased analytical power for HIV subgroup and/or contingency analyses, given the greater number of persons receiving the intervention relative to the proposed RCT model (i.e., N=300 receiving the app). Power Calculations for Specific Aim 1b: estimated pre-/post-test observed treatment effect MDEs for HIV Prevention or Care Continuum outcomes related to Specific Aim 3b are: 1) Di—OR = 1.61; 2) Cu—IRR= 1.35; for methamphetamine use outcomes: 1) Di—OR = 0.59; 2) Cu—IRR = 0.89; 3) Co—f2 = 0.01; for HIV sexual risk outcomes: 1) Di—OR = 0.63; 2) Cu—IRR = 0.85; 3) Co—f2 = 0.01.

9.2 Specific Aim 1c Analysis

Aim 1c provides a non-inferiority trial against the group-based, brick-and-mortar intervention upon which the app is based, and will be a historical matched comparison analysis whereby pooled data from the proposed study (i.e., ID+DD, N=300) is contrasted against historical data from participants who have attended the brick-and-mortar Getting Off intervention after 2012 (N~600; matched according to age, race/ethnicity, and HIV status [see Random Assignment]). The proposed analytical model allows for non-inferiority analyses comparing the relative efficacies of brick-and-mortar vs. mHealth delivered intervention content. Power Calculations for Specific Aim 1c: estimated historical matched comparison MDEs for HIV Prevention or Care Continuum outcomes related to Specific Aim 3c are: 1) Di—OR = 1.52; 2) Cu—IRR = 1.30; 3) Co—f2 = 0.01; for methamphetaminue use outcomes: 1) Di—OR = 0.62; 2) Cu—IRR = 0.90; 3) Co—f2 = 0.01; for HIV sexual risk outcomes: 1) Di—OR = 0.66; 2) Cu—IRR = 0.87; 3) Co—f2 = 0.01.

10.0 DATA COLLECTION AND CONFIDENTIALITY

Data are collected for the purposes of this study; no other use will be made of the data. All assessment data will be collected via an ACASI administered by the Qualtrics system. All materials will be stored in Qualtrics' commercial cloud-based databases that are HIPAA compliant (secure and encrypted), which means all personal identifiers and any information that can be combined by any reasonable person to identify unique individuals will be stripped from the research record. Research materials are directly obtained from participants. Identification necessary to follow these individuals will be collected in order to maintain high follow-up rates necessary to answer the scientific aspects of the study.

The study consent form will inform participants of confidentiality guidelines. Strict confidentiality will be maintained; records that have personal identifiers (i.e., follow-up locator information) will be stored in a separate encrypted file from the assessment. Only the research team assigned to the follow-up of the participants will have access to non-anonymous records, and only for the purpose of contacting participants with reminders of their follow-up assessment. All research data are maintained in databases. No presentation or publication of the study results will refer to participants individually. Manuscripts published regarding this work will be based on the accumulated database. Additionally, the federal Certificate of Confidentiality, issued to all NIH-funded grants, protects subjects' records against subpoena. Exceptions to confidentiality for participants is any information that would lead to suspicion of child abuse, suspected abuse or neglect of elderly individuals, or dependent or vulnerable adults, or threat of imminent action on suicidal or homicidal ideation, which must be reported to the appropriate authorities. Participants will be informed of these exceptions during the informed consent process. In addition, representatives from the IRB will have limited access to the research record (e.g., to monitor the integrity of the research record).

10.1 Monitoring and Adverse Event Reporting

Adverse event reporting will follow the FRI policy. Serious adverse events (SAEs) include any of the following outcomes for the participant: 1) death; 2) acute life-threatening incidents; 3) hospitalization or the prolongation of a hospitalization; or 4) persistent or significant disability. SAEs may be communicated to the Principal Investigator by participants or staff, or may be observed directly by the Principal Investigator. SAEs will be reported regardless of whether they are considered project-related.

10.1.1 Regulatory Updates. The Principal Investigator will report any information related to unanticipated risks or new information that may change the risk-benefit ratio to the Western IRB. This information may come from the current project or findings from other projects or studies. Any changes in the protocol or consent as a result of this information will be promptly reported to the Western IRB. The Principal Investigator will also report any irregularities in the conduct of the project such as participant enrollment, obtaining informed consent, and data collection and processing.

10.1.2 Criteria for Premature Project Discontinuation. A participant may request to be self-withdrawn from study participation. A participant may be withdrawn from study participation by the Principal Investigator should a psychological condition make the risk to benefit balance of study participation unfavorable for the participant. The project may be discontinued at any time by NIH, or other government agencies as part of their duties to ensure that participants are protected.

10.2 Institutional Review Board Review and Informed Consent

This protocol, the informed consent document and any subsequent modifications will be reviewed and approved by the Western IRB, which is responsible for oversight of the study. An electronically signed consent form will be obtained from each participant. The consent form will describe the purpose of the project, the procedures to be followed, and the risks and benefits of participation. A copy of the consent form will be emailed to the participant, and this fact will be documented in the participant's record.

REFERENCES

1. Reback CJ, Fletcher JB, Shoptaw S, Grella CE. (2013). Methamphetamine and other substance use trends among street-recruited men who have sex with men, from 2008 to 2011. *Drug Alcohol Depend,* 133(1):262-5.
2. Halkitis P, Levy M, Moreira A, Ferrusi C. (2014). Crystal methamphetamine use and HIV transmission among gay and bisexual men. *Curr Addict Rep*, 1(3):206-13.
3. Goldstein ND, Burstyn I, LeVasseur MT, Welles SL. (2016). Drug use among men by sexual behavior, race and ethnicity: prevalence estimates from a nationally representative US sample. *Int J Drug Policy,* 36: 148-150
4. Reback CJ. (1997). *The social construction of a gay drug: methamphetamine use among gay and bisexual males in Los Angeles*. City of Los Angeles, AIDS Coordinator's Office. Friends Community Center. Available at: http://www.friendscommunitycenter.org/documents/Social_Construction_of_a_Gay_Drug.pdf. Accessed March 6, 2016.
5. Hoenigl M, Chaillon A, Moore DJ, Morris SR, Smith DM, Little SJ. (2015). Clear links between starting methamphetamine and increasing sexual risk behavior: a cohort study among men who have sex with men. *J Acquir Immune Defic Syndr* (1999).
6. Benotsch EG, Lance SP, Nettles CD, Koester S. (2012). Attitudes toward methamphetamine use and HIV risk behavior in men who have sex with men. *Am J Addict*, 21(s1):S35-S42.
7. Grov C. (2012). HIV risk and substance use in men who have sex with men surveyed in bathhouses, bars/clubs, and on Craigslist. org: venue of recruitment matters. *AIDS Behav*, 16(4):807-17.
8. Semple SJ, Strathdee SA, Zians J, Patterson TL. (2010). Social and behavioral characteristics of HIV-positive MSM who trade sex for methamphetamine. *Am J Drug Alcohol Abuse*, 36(6):325-31.
9. Garofalo R, Mustanski BS, McKirnan DJ, Herrick A, Donenberg GR. (2007). Methamphetamine and young men who have sex with men: understanding patterns and correlates of use and the association with HIV-related sexual risk. *Arch Pediatr Adolesc Med*, 161(6):591-6.
10. Semple SJ, Patterson TL, Grant I. (2004). A comparison of injection and non-injection methamphetamine-using HIV positive men who have sex with men. *Drug Alcohol Depend*, 76(2):203-12. doi:10.1016/j.drugalcdep.2004.05.003
11. Centers of Disease Control and Prevention [CDC] (2007). *Methamphetamine Use and Risk for HIV/AIDS*. Atlanta, GA: Department of Health and Human Services.
12. Centers of Disease Control and Prevention [CDC] (2013). *HIV and Substance Use in the United States*. Atlanta, GA: Centers for Disease Control and Prevention.
13. Fletcher JB, Reback CJ. (2015). Depression mediates and moderates effects of methamphetamine use on sexual risk taking among treatment-seeking gay and bisexual men. *Health Psychol*, 34(8):865.
14. Friedman MR, Wei C, Klem ML, Silvestre AJ, Markovic N, Stall R. (2014). HIV Infection and sexual risk among men who have sex with men and women (MSMW): A systematic review and meta-analysis. *PLoS ONE*, 9(1):e87139.
15. Bowers JR, Branson CM, Fletcher JB, Reback CJ. (2012). Predictors of HIV sexual risk behavior among men who have sex with men, men who have sex with men and women, and transgender women. *Int J Sex Health*, 24(4):290-302.
16. Boone MR, Cook SH, Wilson P. (2013). Substance use and sexual risk behavior in HIV-positive men who have sex with men: an episode-level analysis. *AIDS Behav*, 17(5):1883-7.
17. Colfax G, Coates TJ, Husnik MJ, Huang Y, Buchbinder S, Koblin B, ... & Vittinghoff E. (2005). Longitudinal patterns of methamphetamine, popper (amyl nitrite), and cocaine use and high-risk sexual behavior among a cohort of San Francisco men who have sex with men. *J Urban Health*, 82:i62-i70.

18. Schwarcz S, Scheer S, McFarland W, Katz M, Valleroy L, Chen S, Catania J. (2007). Prevalence of HIV infection and predictors of high-transmission sexual risk behaviors among men who have sex with men. *Am J Public Health*, 97(6):1067-75.
19. Beyrer C, Baral SD, Van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL, Brookmeyer R. (2012). Global epidemiology of HIV infection in men who have sex with men. *Lancet*, 380(9839):367-77.
20. Beyrer C, Sullivan P, Sanchez J, Baral SD, Collins C, Wirtz AL, ... & Mayer K. (2013). The increase in global HIV epidemics in MSM. *AIDS*, 27(17):2665-78.
21. Ostrow DG, Plankey MW, Cox C, Li X, Shoptaw S, Jacobson LP, Stall RC. (2009). Specific sex-drug combinations contribute to the majority of recent HIV seroconversions among MSM in the MACS. *J Acquir Immune Defic Syndr (1999)*, 51(3):349.
22. Shoptaw S, Reback CJ. (2006). Associations between methamphetamine use and HIV infection among men who have sex with men: a model for guiding public policy. *J Urban Health,* 83(6):1151-7. doi:10.1007/s11524-006-9119-5. PMCID: PMC3261283
23. Carrico AW, Shoptaw S, Cox C, Stall R, Li X, Ostrow DG, ... & Plankey MW. (2014). Stimulant use and progression to AIDS or mortality after the initiation of highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* (1999), 67(5):508-13.
24. Horvath KJ, Carrico AW, Simoni J, Boyer EW, Amico KR, Petroll AE. (2013). Engagement in HIV medical care and technology use among stimulant-using and nonstimulant-using men who have sex with men. *AIDS Res Treat*, *2013*.
25. Landovitz RJ, Fletcher JB, Shoptaw S, Reback CJ. (2015, January). Contingency management facilitates the use of postexposure prophylaxis among stimulant-using men who have sex with men. *Open Forum Infect Dis*, (Vol. 2, No. 1, p. ofu114). Oxford University Press.
26. Holloway IW, Rice E, Gibbs J, Winetrobe H, Dunlap S, Rhoades H. (2014). Acceptability of smartphone application-based HIV prevention among young men who have sex with men. *AIDS Behav*, 18(2):285-96.
27. LeGrand S, Muessig KE, Pike EC, Baltierra N, Hightow-Weidman LB. (2014). If you build it will they come? Addressing social isolation within a technology-based HIV intervention for young black men who have sex with men. *AIDS Care*, 26(9):1194-200.
28. Levy ME, Watson CC, Wilton L, Criss V, Kuo I, Glick S N, ... & Magnus M. (2015). Acceptability of a mobile smartphone application intervention to improve access to HIV prevention and care services for Black men who have sex with men in the District of Columbia. *Digit Cult Educ*, 7(2):169.
29. Muessig KE, Pike EC, LeGrand S, Hightow-Weidman LB. (2013). Mobile phone applications for the care and prevention of HIV and other sexually transmitted diseases: a review. *J Med Internet Res*, 15(1):e1.
30. Muessig KE, Nekkanti M, Bauermeister J, Bull S, Hightow-Weidman LB. (2015). A systematic review of recent smartphone, Internet and Web 2.0 interventions to address the HIV continuum of care. *Curr HIV/AIDS Rep*, 12(1):173-90.
31. Mustanski B, Greene GJ, Ryan D, Whitton SW. (2015). Feasibility, acceptability, and initial efficacy of an online sexual health promotion program for LGBT youth: The Queer Sex Ed intervention. *J Sex Res*, 52(2):220-30.
32. Goedel WC, Duncan DT. (2015). Geosocial-networking app usage patterns of gay, bisexual, and other men who have sex with men: Survey among users of Grindr, a mobile dating app. *JMIR Public Health Surveill*, 1(1):e4.
33. Phillips G, Magnus M, Kuo I, Rawls A, Peterson J, Jia Y, ... & Greenberg AE. (2014). Use of geosocial networking (GSN) mobile phone applications to find men for sex by men who have sex with men (MSM) in Washington, DC. *AIDS Behav*, 18(9):1630-7.
34. Sarbu MI, Georgescu SR. (2015). Gay-Related smartphone applications: potential and risk-a review of the medical literature in the field. *Journal of Mind and Medical Sciences*, 1(1):11-8.

35. Landovitz RJ, Tseng CH, Weissman M, Haymer M, Mendenhall B, Rogers K, ... & Shoptaw S. (2013). Epidemiology, sexual risk behavior, and HIV prevention practices of men who have sex with men using GRINDR in Los Angeles, California. *J Urban Health*, 90(4):729-39.
36. Aliabadi N, Carballo-Dieguez A, Bakken S, Rojas M, Brown III W, Carry M, ... & Schnall R. (2015). Using the Information-motivation-behavioral skills model to guide the development of an HIV prevention smartphone application for high-risk MSM. *AIDS Educ Prev*, 27(6):522-37.
37. Greenwood GL, White EW, Page-Shafer K, Bein E, Osmond DH, Paul J, & Stall RD. (2001). Correlates of heavy substance use among young gay and bisexual men: The San Francisco Young Men's Health Study. *Drug Alcohol Depend*, 61(2):105-12. doi:10.1016/S0376-8716(00)00129-0.
38. Reback CJ, Shoptaw S. (2014). Development of an evidence-based, gay-specific cognitive behavioral therapy intervention for methamphetamine-abusing gay and bisexual men. *Addict Behav*, 39(8):1286-91. doi: 10.1016/j.addbeh.2011.11.029.
39. Reback CJ, Larkins S, Shoptaw S. (2004). Changes in the meaning of sexual risk behaviors among gay and bisexual male methamphetamine abusers before and after drug treatment. *AIDS Behav*, 8(1):87-98. doi:10.1023/B:AIBE.0000017528.39338.75.
40. Shoptaw S, Reback CJ, Peck JA, Larkins S, Freese TE, Rawson RA. (2005). *Getting Off: a behavioral treatment intervention for gay and bisexual male methamphetamine users*. Los Angeles, CA: Friends Research Institute, Inc.
41. Shoptaw S, Reback CJ, Larkins S, Wang PC, Rotheram-Fuller E, Dang J, Yang X. (2008). Outcomes using two tailored behavioral treatments for substance abuse in urban gay and bisexual men. *J Subst Abuse Treat,* 35(3):285-93. doi:10.1016/j.jsat.2007.11.004.
42. Reback CJ, Veniegas R, Shoptaw S. (2014). Getting Off: The development of a model program for gay and bisexual male methamphetamine users. *J Homosex,* 61: 540-554. doi: 10.1080/00918369.2014.865459
43. Shoptaw S, Reback CJ, Peck J A, Yang X, Rotheram-Fuller E, Larkins S, ... & Hucks-Ortiz C. (2005). Behavioral treatment approaches for methamphetamine dependence and HIV-related sexual risk behaviors among urban gay and bisexual men. *Drug Alcohol Depend*, 78(2):125-34. doi:10.1016/j.drugalcdep.2004.10.004.
44. Peck JA, Reback CJ, Yang X, Rotheram-Fuller E, Shoptaw S. (2005). Sustained reductions in drug use and depression symptoms from treatment for drug abuse in methamphetamine-dependent gay and bisexual men. *J Urban Health*, 82:100-8. doi:10.1093/jurban/jti029.
45. Centers of Disease Control and Prevention [CDC] (2015). *HIV among Gay and Bisexual Men*. Atlanta, GA: CDC.
46. Sullivan PS, Carballo-Diéguez A, Coates T, Goodreau SM, McGowan I, Sanders EJ, ... & Sanchez J. (2012). Successes and challenges of HIV prevention in men who have sex with men. *Lancet*, 380(9839):388-99.
47. Cumming C, Troeung L, Young JT, Kelty E, & Preen DB. (2016). Barriers to accessing methamphetamine treatment: A systematic review and meta-analysis. *Drug Alcohol Depend*, 168:263-73.
48. Parsons JT, Vial AC, Starks TJ, Golub SA. (2013). Recruiting drug using men who have sex with men in behavioral intervention trials: a comparison of internet and field-based strategies. *AIDS Behav*. 17(2):688-99.
49. Catalani C, Philbrick W, Fraser H, Mechael P, Israelski DM. (2013). mHealth for HIV treatment & prevention: a systematic review of the literature. *Open AIDS J*, 7:17-41.
50. Panenka WJ, Procyshyn RM, Lecomte T, MacEwan GW, Flynn SW, Honer WG, & Barr AM. (2013). Methamphetamine use: A comprehensive review of molecular, preclinical and clinical findings. *Drug Alcohol Depend*, 129(3):167-179.
51. Shetty V, Mooney LJ, Zigler CM, Belin TR, Murphy D, & Rawson R. (2010). The relationship between methamphetamine use and increased dental disease. *J Am Dent Assoc*, 141(3):307-318.

52. McKetin R, Lubman DI, Lee NM, Ross JE, Slade TN. (2011). Major depression among methamphetamine users entering drug treatment programs. *Med J Aust*, 195(3):S51-S5.
53. Northrop NA, Yamamoto BK. (2015). Methamphetamine effects on blood-brain barrier structure and function. *Front Neurosci*, 9:69.
54. Obert J L, McCann MJ, Marinelli-Casey P, Weiner A, Minsky S, Brethen P, Rawson R. (2000). The Matrix model of outpatient stimulant abuse treatment: history and description. *J Psychoactive Drugs*, 32(2):157-64. doi:10.1080/02791072.2000.10400224.