Brief Depression Intervention to Optimize Intensive Outpatient Methamphetamine Treatment among Gay and Bisexual Men who have Sex with Men

Sponsored by:

National Institutes of Mental Health (NIMH)
Grant # P30MH58107
to

Steven Shoptaw, Ph.D.
Professor, UCLA Departments of Family Medicine and Psychiatry and Biobehavioral Sciences
Vice Chair of Research, UCLA Department of Family Medicine
Center Director
UCLA, Center for HIV Identification, Prevention and Treatment Services

Jesse B. Fletcher, Ph.D.
Principal Investigator
Research Scientist
Friends Research Institute, Inc.

Cathy J. Reback, Ph.D.
CHIPTS Mentor
Senior Research Scientist
Friends Research Institute, Inc.
Core Director
UCLA, Center for HIV Identification, Prevention and Treatment Services

TABLE OF CONTENTS

SITE PARTICIPATING IN THE STUDY

Friends Community Center
A Division of Friends Research Institute, Inc.
6910 Santa Monica Blvd.
Los Angeles, CA 90038

INVESTIGATOR ROSTER

Principal Investigator
Jesse B. Fletcher, Ph.D.
Research Scientist
Friends Research Institute, Inc.
6910 Santa Monica Blvd.
Los Angeles, CA 90038
Phone: (323) 463-1601 x126
FAX: (323) 463-0126
E-Mail: jfletcher@friendsresearch.org

CHIPTS Mentor
Cathy J. Reback, Ph.D.
Senior Research Scientist
Friends Research Institute, Inc.
Executive Director, Friends Community Center
Core Director, Center for HIV Identification, Prevention and Treatment Services (CHIPTS)
6910 Santa Monica Blvd.
Los Angeles, CA 90038
Phone: (323) 463-1601
FAX: (323) 463-0126
E-Mail: reback@friendsresearch.org

STUDY AIMS

The objective of this study is to evaluate pilot data on the use of an evidence-informed depression intervention for optimizing treatment outcomes among gay and bisexual men enrolled in the *Getting Off* outpatient methamphetamine abuse treatment service program at Friends Community Center, a division of Friends Research Institute. MoodGym is a five module, once-weekly depression intervention that, like the *Getting Off* intervention, is based on the principles of Cognitive Behavioral Therapy (CBT). In addition to receiving weekly sessions, study participants will be assessed weekly for depression symptomology and, if appropriate, quarterly for ART/PrEP uptake and/or adherence. This study will examine the feasibility, acceptability, and potential utility of augmenting intensive outpatient methamphetamine treatment through the simultaneous application of an evidence-based depression intervention.

This study leverages insights on methamphetamine use, depression, and HIV sexual risk behavior to enhance a manualized outpatient treatment program for gay and bisexual men through the addition of an evidence-based depression intervention. Data from this study will clarify both the mediating and moderating influences of depression on the use/HIV risk link, may clarify the role of depression on HIV-related (i.e., PrEP or ART) medication adherence, and may suggest new avenues of inquiry into the behavioral and psychological links between addiction, depression, engagement in HIV sexual risk behaviors, and ART/PrEP uptake and adherence. Findings may also inform the process of recovery among gay and bisexual methamphetamine users, as evidence suggests depressive processes may play an important role.

The specific aims are:

1) **Specific Aim #1**: Test the feasibility and acceptability of applying among participants of the program.
    a. *$H1_a$: The Getting Off intervention will be both feasible to apply with, and acceptable for, participants of the program.*
2) **Specific Aim #2**: Estimate the effect of MoodGym on the HIV sexual risk behavior outcomes of participants.
    a. *$H2_a$: Increased attendance to MoodGym sessions will be associated with greater reductions in HIV sexual risk behavior.*
    b. *$H2_b$: Participants with higher comorbid depression scores will show greater reductions in HIV sexual risk behavior due to their attendance to sessions relative to participants with lower comorbid depression scores.*
    c. *$H2_c$: Relative to historical matched controls drawn from previous years of the program, participants receiving sessions will demonstrate greater reductions in HIV sexual risk behavior.*
3) **Secondary Aim**: Estimate the effect of MoodGym on the uptake/adherence to ART and PrEP among HIV-positive and HIV-negative participants, respectively.
    a. *$H3_a$: Increased attendance to sessions will be associated with lower comorbid depression scores which, in turn, will be associated with increased likelihood of ART medication uptake and/or adherence for HIV-*

positive participants as well as increased likelihood of PrEP uptake and/or adherence for HIV-negative participants.

INTRODUCTION

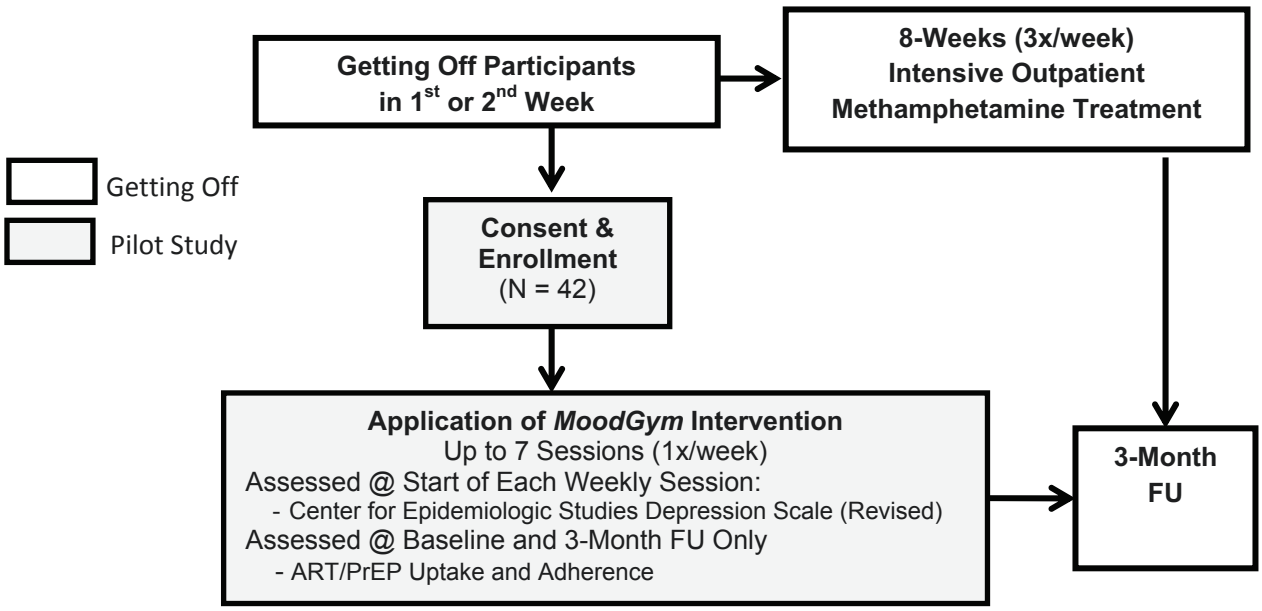
Background

Each year, 70% of new HIV infections in the United States occur with MSM,[1] and use is identified as a major driving force in the continued HIV/AIDS pandemic affecting MSM communities.[2] Though studies have consistently demonstrated associations between use and HIV transmission among MSM,[3,4] recent research has further illustrated that depression is likely an under-recognized mechanism in the /HIV link, statistically both mediating and moderating the link between use and engagement in sexual risk behaviors.[5] Further, depression is an obstacle to medication adherence for both HIV-positive and HIV-negative MSM; depression has been associated with reduced adherence to ART medication,[6,7] and MSM in the iPrex study with the highest levels of depression also demonstrated the lowest levels of PrEP adherence,[8] highlighting the important effects of depression on biobehavioral efforts to limit HIV transmission among MSM.

STUDY DESIGN

This study is a single-arm, non-randomized pilot study. Eligible participants are newly enrolled Getting Off service program participants who will be invited to participate in the study during their enrollment, and can enroll in the study at any time during their first two weeks of program participation (see Figure 1).

Figure 1: Study Design "Depression Intervention to Optimize Methamphetamine Treatment Outcomes among Gay and Bisexual Men"



Study activities will take place contemporaneously with participation in the service program (i.e., participants enroll during their first or second week of Getting Off, and

complete the 5 sessions over the remaining 6-7 weeks). If participants complete all five MoodGym modules prior to the 8-week endpoint, they will be offered the chance to revisit prior module(s); assessments and incentives will continue as scheduled. Getting Off program evaluation data from study participants will be matched and compared with historical program evaluation data to assess the impact of the MoodGym intervention on the Getting Off program outcomes through an observed treatment effects analysis.

MoodGym

MoodGym is a seven module computer-optimized, evidenced-based intervention for adults with depression and/or anxiety symptoms. Though MoodGym modules can be taken by participants without assistance, evidence suggests results may be improved by applying in a more structured setting. In this pilot study, MoodGym will be delivered with support and guidance from a trained Study Counselor. Each week participants will be asked to attend one one-hour individual appointment with the Study Counselor to complete a MoodGym module, for up to seven weeks.

Phone Call After One Missed Session of MoodGym

The SC will monitor participant attendance and conduct a phone call to any participant who does not attend a scheduled session, to reschedule.

SELECTION AND ENROLLMENT OF PARTICIPANTS

Inclusion Criteria

- A participant enrolled in the Getting Off service program at Friends Community Center; and,
- Within his first or second week in the program

Exclusion Criteria

- Not a participant in his first or second week of the Getting Off service program at Friends Community Center

STUDY PROCEDURES

Recruitment and Enrollment

Participants will be recruited from the Getting Off service program at Friends Community Center. Program participants will be invited to participate in the study at the time that they enroll in the program, and may enroll in the study at any time during their first or second week of program participation. Getting Off program staff will inform new participants about the research study. If the potential participant is interested in learning more about the study he will be directed to meet with the Study Counselor. Both the program staff and the SC will emphasize that participation in this study is voluntary and that participation in the program is not dependent on participation in this study. Interested participants will meet with the in a private room, then read the consent form, have questions answered by the, and sign the consent form if they wish to participate.

All in-person contact (recruitment, screening, consenting, MoodGym sessions, and administration of follow-up interviews) with participants will take place in a private room with a closed door at Friends Community Center. Any telephone calls made to

participants during the course of the study will be made from a private office with a closed door, so the phone conversation cannot be heard.

MoodGym Intervention

MoodGym is an Internet-based CBT program that uses fun, engaging, interactive content, alongside character-driven narratives, to help alleviate symptoms of depression and comorbid anxiety. The program also aims to improve the individual's functioning by promoting the development of skills and strategies to manage depression.

MoodGym consists of an introduction module, five structured intervention modules, and a workbook of assessments.

1. Getting Started
    a. An introduction to MoodGym, including CBT, the different characters and structure of the intervention content, and baseline mental health quizzes (e.g., depression, anxiety) that are scored in real time to help the participant understand their current level of mental health symptoms. This will be done during the first MoodGym session, given its brevity and relationship to the first module.
2. Feelings Module
    a. Understanding emotions, mood, and physical reactions of depression and anxiety, as well as the impact of your perspective on your personal feelings. Demonstrates links between events, thoughts, feelings, and behaviors.
3. Thoughts Module
    a. Addresses unwelcome, unhealthy, or intrusive thoughts, and demonstrates how some thoughts can help you overcome mental health symptoms. Discusses how to improve self-esteem by changing thought patterns.
4. Unwarping Module
    a. Introduces the idea of "warpy" thoughts, including false impressions that one must be perfect, that one can control all things, or that one is worthless if they are criticized.
5. Destressing Module
    a. Discusses means and strategies to reduce stress, which can have important impacts on depression and anxiety symptoms, and mental health more generally.
6. Relationships Module
    a. Discusses how relationships can both benefit or worsen one's mental health, and how to monitor and maintain healthy relationships.
7. Workbook
    a. Contains all quizzes and tests the participant encounters during each of the above sessions. If a participant would like to retest themselves on some dimension (e.g., depression, anxiety, warpy thoughts), they can revisit the assessment in the Workbook section, and receive an updated score in real time.

Each MoodGym session will last up to one hour and will begin with the brief CESD-R assessment, administered by the Study Counselor via the same computer as the MoodGym intervention, followed by one of the five online modules, which are self-contained and guide the participant through all intervention content. Online modules include quizzes, videos, characters, interactive activities, informational content, personal stories, workbook activities, and content summaries. Sessions can also include interactions with the Study Counselor, as much or as little as the participant chooses to initiate, including supportive feedback, guidance, help, and encouragement on activities.

Incentive Schedule

All incentives will be paid in gift cards, no cash will be given. The total amount a participant can earn for participating in the study is $70. Participants can earn $10 for each session they attend, up to seven session, at the conclusion of each session. After each gift card is dispensed, participants will be asked to sign a sheet, specific only to them, indicating they have received the incentive payout.

Timeline

Table 1. Proposed Timeline of Study Activities

	Year 1											
	Q1			*Q2*			*Q3*				*Q4*	
Month / **Study Activities**	1	2	3	4	5	6	7	8	9	10	11	12
Obtain IRB Approval	X	X	X									
Hire/Train Study Counselor		X	X									
Enroll 42 MA-Using MSM (6/mo)				X	X	X	X	X	X	X		
MoodGym Implementation				X	X	X	X	X	X	X	X	X
Data Cleaning & Analysis												X
Begin Publication & Dissemination												X

STATISTICAL CONSIDERATIONS

Assessments

1. Center for Epidemiologic Studies Depression Scale (Revised). The Center for Epidemiologic Studies Depression Scale (Revised) [CESD-R][9] is a widely used depression assessment which consistently shows strong psychometric properties and concurrent validity with clinical diagnostic instruments.[10] The CESD-R will be administered at the start of each session.

2. ART and PrEP Uptake and Adherence. Administered at baseline enrollment in the pilot study and 3-month follow-up only. The ART and PrEP Uptake and Adherence form briefly queries HIV-positive and HIV-negative participants as to whether they have begun and/or adhered to a prescribed ART or PrEP regimen in the past 3 months.

Statistical Analyses

Specific statistical analyses will be chosen based on the distributional properties of the variables being analyzed; sociodemographics or other variables found to significantly influence primary outcomes may be tested for inclusion as statistical controls and/or bases for contingency analyses. The outcome of primary analytical interest, i.e., engagement in HIV sexual risk behaviors, is most amenable to analyses employing the negative binomial or logistic link functions, for count and dichotomous operationalizations, respectively. Descriptive statistics will be provided for all variables, and inferential models related to Specific Aim 2 will assume three complementary but parallel analytical approaches. First ($H2_a$), an observed treatment effects dosage response analysis will test for observed associations between attendance to the weekly sessions and reductions in both the magnitude (negative binomial) and/or likelihood (logistic) of engagement in HIV sexual risk behaviors [note: sexual risk behavior data is gathered during standard *Getting Off* procedures]; analyses will be double-robustly estimated to ensure proper model specification.[11] Second ($H2_b$), the same model will be estimated, but will further include participants' CESD-R depression scores both as a main effect, as well as in a statistical interaction term with the number of sessions attended. Planning such a nested analysis allows for full specification of the effects of depression, both directly and in response to the intervention. Third ($H2_c$), participants' HIV sexual risk behavior outcomes will be statistically contrasted against those same outcomes from a group of historical matched controls sampled from the program (2009-2017) and matched using either caliper or nearest neighbor algorithm (based on method of best fit)[12] using participant age, race/ethnicity, HIV status, and the severity of their use. The proposed Secondary Aim will be tested using the Bernoulli family and logistic link function, where uptake or satisfactory (i.e., ≥ 85%) adherence to ART/PrEP during the course of the intervention will be coded a "1", "0" otherwise, and regressed on intervention exposure and/or CESD-R depression scores.

Missing Data

General Estimation Equation (GEE) analyses will test patterns of missing data in the follow-up assessments. Follow-up assessment data will be coded trichotomously (i.e., observed, intermittent missing, missing due to dropout) and regressed on arm assignment and relevant covariates (e.g., racial/ethnic identity, age) to ensure appropriate application of inferential logic. If a non-ignorable pattern of missing data is discovered (note: confirmed by Little's test of non-random missingness), sensitivity analyses will be conducted to ascertain which missing data management strategy (e.g., multiple partial imputation) should be applied.

DATA COLLECTION AND CONFIDENTIALITY

MoodGym Online Modules

The online modules do not report any sensitive data related to participants' mental health. All usage measures will be based on the recording of the modules completed by each participant during weekly sessions, and depression symptoms and trends are assessed via the weekly CESD-R assessments.

Study Counselor-Administered Assessments

The will briefly assess participants' depression symptoms (via the CESD-R) at the

beginning of each weekly session, and HIV-related medication uptake/adherence (via the ART and PrEP Uptake and Adherence form) at baseline and 3 month follow-up. In both cases, assessments will be administered via an online data entry form administered from the same computer the sessions are accessed. The online data entry form and short-term data hosting will be contracted using Qualtrics, a global data entry firm Friends Research Institute has ongoing multi-year contracts providing access to online survey creation and implementation software. The Qualtrics' system is HIPAA compliant and conforms to industry standard (e.g., ISO 27001 and FEDRAMP compliant) encryption and data security. Study data will be hosted on the Qualtrics cloud for the duration of the study, and will be removed at the completion of the data collection phase.

MONITORING AND ADVERSE EVENT REPORTING

Adverse event reporting will follow the WIRB policies. 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 events 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 study-related.

Distress Policy

In the instance of:

1) a participant presenting with a gun or other weapon, and/or threatening physical violence against staff, himself, or an identified other person;
2) a family member or friend of a participant informing a staff member that a participant is threatening to harm staff, himself, or an identified other person;

the Friends Community Center *Distress Protocol for Participants at Friends Community Center* is automatically triggered. Staff immediately contact a trained counselor or clinician to assess the situation and advise management. Staff are provided with a phone tree providing the names and contact information (including mobile phones and pagers) for six trained counselors/clinicians familiar with, and who have agreed to carry out, the Friends Community Center *Distress Protocol*. In the case of extreme immediate threat, staff are trained to remove themselves, immediately dial 911, and to ensure the safety of themselves, other staff, and participants above all else.

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 WIRB IRB. This information may come from the current study or findings from other studies. Any changes in the protocol or consent as a result of this information will be promptly reported to the WIRB and CHIPTS. The Principal Investigator will also report any irregularities in the conduct of the study such as: participant enrollment; obtaining informed consent; and, data collection and processing.

HUMAN PARTICIPANTS

Institutional Review Board (IRB) Review and Informed Consent

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

CRITERIA FOR PREMATURE STUDY DISCONTINUATION

The study may be discontinued at any time by CHIPTS, or other government agencies as part of their duties to ensure that research participants are protected.

REFERENCES

1. Centers for Disease Control and Prevention. *HIV Surveillance Report*, 2015; vol. 27. http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published November 2016. Accessed 03/16/2018.

2. Centers of Disease Control and Prevention (2016). *Gay and Bisexual Men's Health*. Atlanta, GA: National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. https://www.cdc.gov/msmhealth/substance-abuse.htm. Accessed 03/16/2018.

3. Halkitis, P. N., Levy, M. D., & Solomon, T. M. (2016). Temporal relations between methamphetamine use and HIV seroconversion in gay, bisexual, and other men who have sex with men. *Journal of health psychology*, 21(1), 93-99.

4. Hoenigl, M., Chaillon, A., Moore, D. J., Morris, S. R., Smith, D. M., & Little, S. J. (2016). Clear links between starting methamphetamine and increasing sexual risk behavior: a cohort study among men who have sex with men. *Journal of acquired immune deficiency syndromes* (1999), 71(5), 551.

5. Fletcher, J. B., & Reback, C. J. (2015). Depression mediates and moderates effects of methamphetamine use on sexual risk taking among treatment-seeking gay and bisexual men. *Health psychology*, 34(8), 865.

6. Grenard, J. L., Munjas, B. A., Adams, J. L., Suttorp, M., Maglione, M., McGlynn, E. A., & Gellad, W. F. (2011). Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. *Journal of general internal medicine*, 26(10), 1175-1182.

7. Yoo-Jeong, M., Waldrop-Valverde, D., McCoy, K., & Ownby, R. L. (2016). A Structural Equation Model of HIV-related Symptoms, Depressive Symptoms, and Medication Adherence. *Journal of HIV and AIDS*, 2(3).

8. Mehrotra, M. L., Glidden, D. V., McMahan, V., Amico, K. R., Hosek, S., Defechereux, P., ... & Schechter, M. (2016). The effect of depressive symptoms on adherence to daily oral PrEP in men who have sex with men and transgender women: a marginal structural model analysis of the iPrEx OLE study. *AIDS and Behavior*, 20(7), 1527-1534.

9. Eaton, W. W., Smith, C., Ybarra, M., Muntaner, C., & Tien, A. (2004). Center for Epidemiologic Studies Depression Scale: Review and Revision (CESD and CESD-R). In M. E. Maruish (Ed.), *The use of psychological testing for treatment planning and outcomes assessment: Instruments for adults* (pp. 363-377). Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers.

10. Van Dam, N. T., & Earleywine, M. (2011). Validation of the Center for Epidemiologic Studies Depression Scale—Revised (CESD-R): Pragmatic depression assessment in the general population. *Psychiatry research*, 186(1), 128-132.

11. Drukker, D. (2014). Double-Robust Treatment Effects. *Stata News*, 29(1), 3-5.

12. Austin, P. C. (2014). A comparison of 12 algorithms for matching on the propensity score. *Statistics in medicine*, 33(6), 1057-1069.