Tailored Response to Psychiatric Comorbidity to Improve HIV Care Engagement in the United States (TRACE)

STUDY PROTOCOL

DATE: February 6th, 2023

I. STUDY OVERVIEW

Few protocols address treating patients with multiple mental health disorders in patients living with HIV. These psychiatric conditions are major barriers to HIV treatment engagement and success. This study hopes to address this gap in research by adapting the Common Elements Treatment Approach (CETA) for the particular needs of adults receiving HIV care in the US and pilot-test the adapted intervention to assess its acceptability and effectiveness to improve the mental health of patients with multiple psychiatric condition and increase their HIV care engagement.

II. OBJECTIVES

The long-term goal of our research program is to develop and disseminate effective, resource-efficient strategies to address psychiatric comorbidities as barriers to HIV care engagement and treatment success. The overall objective of this proposal is to adapt CETA for the particular needs of adults receiving HIV care in the US and pilot-test the adapted intervention to assess acceptability, feasibility, fidelity, and preliminary indications of impact. Our hypotheses are that the adapted CETA intervention will be acceptable to patients and providers, will prove feasible to integrate in a busy HIV primary care setting, will be delivered with fidelity, and will demonstrate preliminary indications of impact in improving HIV (primary) and mental health (secondary) outcomes. To achieve our objective, our specific aims are to:

Aim 1. Adapt the proven CETA protocol to (1) integrate content addressing ART adherence and HIV care engagement and (2) be optimized for delivery by staff such as LCSWs to patients with HIV in the US.

Aim 2. Pilot the adapted CETA protocol in a small two-arm individually randomized trial.

Aim 3. Assess the feasibility, acceptability, and fidelity of delivery of the adapted CETA protocol as well as preliminary indicators of its impact in improving both HIV (primary) and mental health (secondary) outcomes.

The CETA approach has the potential to make an important contribution to addressing the overlap between common mental health disorders and barriers to HIV treatment success. This proposal will generate critical evidence to guide the design of a full-scale RCT to test the effectiveness of the adapted CETA protocol in improving both HIV treatment and mental health outcomes for this vulnerable population. This clinical site for this study is the 1917 Clinic at University of Alabama at Birmingham (UAB).

III. STUDY ACTIVITIES

a) CETA MANUAL ADAPTATION

Aim 1: Our team has an established manual for CETA, and procedures for adapting the CETA manual for specific settings and contexts. We will follow the ADAPT-ITT model to adapt the CETA protocol for our population and outcomes. In the third of eight steps in the model, entitled Adaptation, we will add a session to CETA for all participants explicitly targeting HIV medication adherence and care engagement, based on the evidence-based single-session LifeSteps intervention. Then we will

modify the existing CETA sessions so as to integrate HIV-specific examples and content).

The second stage of adaptation will formally involve feedback from both potential clients and counselors. We will present the modified CETA protocol to three groups each including 4-5 individuals: one of male patients with HIV, one of female patients with HIV, and one of LCSWs and other behavioral health providers from the clinic - the cadre who would deliver CETA. We will solicit their feedback through recorded discussion and written surveys.

b) STUDY POPULATION

The target population for the pilot trial and the eventual full trial will be patients with elevated symptoms of depression, anxiety, post-traumatic stress, and/or substance use, who are also at risk for suboptimal HIV care engagement. 60 participants will be enrolled.

Inclusion Criteria

1. Age >= 18 years.
2. Patient receiving HIV care at UAB 1917 Clinic.
3. Elevated symptoms of depression, anxiety, post-traumatic stress, or substance use disorder: At least one of the following:
    i. Patient Health Questionnaire-9 score >= 10;
    ii. Generalized Anxiety Disorder 7-Item Scale score >= 10;
    iii. . Post-Traumatic Stress Symptoms Checklist for DSM-5 score >= 33;
    iv. ASSIST score >=11 for alcohol or >=4 for any other substance
4. At risk for suboptimal HIV care engagement: At least one of the following:

i. Engaged in HIV care for the first time within the past 6 months;

ii. Have an HIV RNA viral load >1,000 copies/mL within the past 6 months;

iii. . Antiretroviral regimen was changed due to treatment failure within the past 6 months;

iv. No-showed to an HIV primary care appointment within the past year.

5. Willing to provide written informed consent.

Exclusion Criteria

1. Do not speak or understand English
2. Unable to attend counseling sessions
3. Unwilling to provide informed consent

Participants will be recruited via e-mail solicitation to clinic providers (NPs, MDs), counselors and social workers, as well as referrals

c) PRE-SCREENING (phone)

Potential participants will be prescreened over the phone using our prescreening phone script If the individual passes the telephone prescreen, he or she will be scheduled for a screening and enrollment visit via phone. The date and time of the pre-screening visit along with the participant contact information and preferred method of contact will be recorded on the Prescreening Log. If the participant is eligible for enrollment, a Screening and Enrollment Visit will be scheduled and recorded on a Screening and Enrollment Visit form. A separate excel log will collect data from the screening and enrollment visit form for tracking purposes.

d) SCREENING AND ENROLLMENT

The Screening and Enrollment Visit will be scheduled based on the patient and research staff's availability and be recorded on a Screening and Enrollment Visit log. Participants will receive a reminder call at about a week and 48 hours prior to the scheduled screening and enrollment visit. The following scales will be administered to the patient to confirm eligibility. If symptoms are elevated in any one of the following, proceed to do the verbal informed consent and complete the baseline questionnaire. If the participant isn't eligible, thank them for their time and pay them $25.

a. Depression: PHQ-9
b. Anxiety: GAD-7
c. PTS: Trauma Questionnaire + PCL-5
d. Alcohol/Drugs: WHO ASSIST

Informed Consent Procedures

Informed consent will be administered by staff trained in accordance to the University of Alabama at Birmingham Institutional Review Board guidelines for obtaining informed consent. The staff member obtaining consent must verify the following: protocol name, version number, dates for use, and institution. The Study team member will also ensure that the most recent informed consent is being used for the study. Initial informed consent must be completed and documented before any other study related procedures are done.

Comprehension will be assessed by asking the participant to summarize the study activities or some general open ended questions will be asked like what can you tell me

about this study, can you tell me about how long the study may last, etc. The consent process is estimated to take around 15-20 minutes. The staff member will document the verbal consent on the verbal consent form.

Baseline Assessment

If a participant is ineligible based on screening assessment, they will be given a $25 incentive and thanked for their time, and they will not be considered to have been enrolled in the study at any point. If a participant is eligible, the baseline assessment will then be completed. Completion of Baseline assessment will be recorded in excel logs.

RANDOMIZATION

Our team will utilize a 1:1 ratio for allocation to the CETA intervention and Enhanced Usual Care (UC) conditions. Importantly, the PIs and outcomes assessor will be blinded to intervention vs. comparison allocation. Participants in the intervention and comparison conditions will have full access to all available clinical services at their respective sites.

e) INTERVENTION

Participants randomized to the adapted CETA arm will initiate CETA with the trained counselor. The number of CETA sessions will depend on the patient's presentation, but, including the new LifeSteps session, will range from 7-13 weekly in-person 1-hour sessions.

f) COMPARISON CONDITION

The comparison group will receive "treatment as usual" as described above. The comparison group will also be provided with the intervention manual, however, no additional treatment will be provided to participants allocated to the control group.

Assessments

Type	Name	Time Frame	Description
Primary	Feasibility of recruitment	Duration of recruitment phase (9 months)	Number of patients approached in order to accrue the final sample
Primary	Client acceptability	9 months post-baseline	Client Satisfaction Questionnaire-8
Primary	Fidelity	At end of study	Supervisor rating of each counselor's overall fidelity to each core component that the counselor routinely employed, averaged into a single overall fidelity score
Secondary	Suppressed HIV RNA viral load	4 months post-baseline	HIV RNA viral load <200 copies/mL
Secondary	Suppressed HIV RNA viral load	9 months post-baseline	HIV RNA viral load <200 copies/mL
Secondary	HIV appointment attendance	From baseline to 12 months post-baseline	Kept visit proportion: Total number of kept visits divided by total number of missed plus kept visits
Secondary	Depressive symptoms	4 months post-baseline	PHQ-9
Secondary	Anxiety symptoms	4 months post-baseline	GAD-7
Secondary	Post-traumatic stress symptoms	4 months post-baseline	PCL-5
Secondary	Substance use symptoms	4 months post-baseline	ASSIST

The ***primary outcomes*** of the pilot trial will be the feasibility, acceptability, and fidelity of delivery of the adapted CETA protocol. ***Secondary outcomes*** will include preliminary indicators of impact of the adapted CETA protocol in improving HIV-related

outcomes (eventual R01 primary outcomes) and mental health outcomes (eventual R01 secondary outcomes).

Feasibility will be evaluated by examining the recruitment rate (number of patients approached in order to accrue the final sample), reasons for non-participation, proportion of CETA sessions attended, reasons for non-attendance, and total counselor time per session and per patient including preparation, documentation, and supervision.

Acceptability among CETA participants will be assessed via the Client Satisfaction Questionnaire (CSQ)-8 at treatment exit. Acceptability among providers will be assessed using a version of the CSQ-8 modified to elicit provider rather than client satisfaction. These semi-structured interviews will also include open-ended questions about providers' experiences with and perceptions of the usefulness of the adapted CETA protocol. Providers interviewed will include CETA counselors, other behavioral health providers in the clinic, and HIV providers treating patients in the CETA protocol. A total of 10 providers will be interviewed prior to study launch, at study midpoint, and after study completion.

Fidelity will be defined as the counselors' *adherence* to each session's content and their *competence* in delivering that session content. This assessment will be completed by the clinical supervisor once for each counselor after all counseling sessions have concluded. The primary fidelity measure will be the supervisor's rating of the extent to which the counselor was doing each CETA core component with high fidelity, averaged across all core components that the counselor did regularly.

HIV-related outcomes (the primary outcomes for the eventual full-scale trial) will be defined as (a) suppressed HIV RNA viral load at 4 and 9 months and (b) HIV appointment adherence between baseline and 12 months. Viral load will be captured from clinical records when possible; if no viral load is scheduled at the requisite time point for the study, then the study will order and pay for a viral load test. Suppressed viral load will be defined as a value <200 copies/mL. HIV appointment attendance will be defined using the HRSA attendance measure (primary) and the kept-visit proportion (secondary). *Mental health outcomes* (the secondary outcomes for the eventual full-scale trial) will be defined as depressive, anxiety, post-traumatic stress, and substance use symptom severity measured at 4 months and 9 months. Depressive symptom severity will be measured using the Patient Health Questionnaire-9 (PHQ-9), anxiety symptom severity by the GAD-7, post-traumatic stress symptoms by the PTSD Checklist for DSM-5 (PCL-5), and substance use using the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). We will consider both the simple severity level at follow-up as well as the percentage reduction in symptoms from baseline. We will also create a measure of global symptom improvement which will be the average of the percentage reduction in symptoms from baseline across all of the domains which were elevated at baseline (which could be 1-4 domains depending on the participant's initial presentation).

Assessments will be conducted 4 and 9 months after study enrollment. Participants will receive up to 3 reminder calls at about a week and 48 hours prior to the next outcome assessment.

RETENTION PROCEDURES

However, consistent with standard clinical practice at UAB, participants will be eligible for gas vouchers or bus tickets to facilitate counseling session attendance.

g) FIDELITY AND SUPERVISION

Supervision will take place weekly, led by Dr. Darnell. Supervision will include a brief review of all sessions held since the last supervision as well as detailed discussion and feedback on at least one audio-recorded session per week. Sessions will be audio recorded with clients' permission and will be shared via a secure shared drive. Remote supervision will be facilitated by use of the Evidence-Based Practices Toolkit (www.ebptoolkit.com), a secure web-based platform that allows tracking and supervision of a growing number of evidence-based interventions; CETA has been built into the EBP Toolkit already. Counselors log each session including key metrics (symptom severity scores), and supervisors and counselors can then review cases together.

Fidelity monitoring will include methods successfully used in previous CETA RCTs. Both clinician adherence (completion of required treatment components) and competence (degree of skill) in delivering CETA will be monitored and systematically rated by Dr. Darnell. Dr. Darnell will review clinician documentation of sessions through the EBP Toolkit to monitor adherence and observe a subset of recorded CETA sessions representing the full range of CETA components to rate both clinician adherence and competence. Any observations of low adherence or competence will result in additional clinician training. Dr. Darnell will also review cases with clinicians and provide feedback on adherence and competence during weekly supervision.

h) TRACKING OF STUDY PATIENTS

Study staff will use Qualtrics to capture baseline, 4 and 9 month assessments, as well as viral loads, CETA therapy attendance, HIV care and mental health visits. Study staff will use excel logs to capture prescreening, enrollment, randomization, timeline/window of outcome assessments, status of assessments, reminder call status for assessments. All study staff will be trained in Human Subjects Protections, and this data will be handled in accordance with UAB electronic storage and data transfer guidelines.

The program manager at the University of North Carolina-Chapel Hill will provide oversight of data quality and will conduct monthly audits.

i) MANAGEMENT AND INTEGRATION OF UAB AND UCSD SITES

Study PI Dr. Brian Pence will conduct regular video conference communication with the UAB staff. Additionally, there will be monthly study team meetings with staff across UAB, UNC-Chapel Hill, Harvard, and the University of Washington. The purpose of these weekly meetings will be to track progress with study milestones, troubleshoot issues that may arise, and discuss any adverse events.

j) SUMMARY OF COMPENSATION

Intervention and Control groups

Screening/Enrollment (Baseline) visit	$50
4, and 9 month assessments	$50 each

Participants in the CETA arm will not receive compensation for attending CETA counseling sessions, but will be eligible for gas vouchers or bus tickets to facilitate attendance at counseling sessions, as is standard practice at UAB for all patients.

IV. DATA COLLECTION AND MANAGEMENT

All study documentation will be kept in locked file cabinets in in study personnel's offices at UAB. The Qualtrics database can only be accessed by TRACE personnel using UAB and UNC-Chapel Hill computers or encrypted laptops.

V. DATA ANALYSIS

Analyses of primary feasibility, acceptability, and fidelity outcomes will focus on reporting summary statistics with confidence intervals. Analyses of secondary health outcomes will be intent-to-treat analyses between arms comparing each of the secondary outcomes using a generalized linear regression model with link and error distribution appropriate for the specific outcome (i.e., log link and binomial error distribution for binary outcomes; identity link and normal error distribution for continuous outcomes). Intent-to-treat results will be reported as risk or mean differences with two-sided confidence intervals and P values, setting the Type I error probability to 5%.

VI. SAFETY PROTOCOL

The study safety protocol is to be used if a participant indicates thoughts of self-harm during the screening or follow-up study assessments.

VII. PROTECTION OF HUMAN SUBJECTS

Our team has devised a comprehensive plan for ensuring protection of human subjects throughout the course of the proposed study. We will utilize an English-language consent form with common phrasing that describes that no special privileges or considerations will be conferred as a result of study participation, and that access to medical care will not be affected by the potential participant's decision to enroll in the

study. The procedures listed in the following sections detail procedures that have been approved and utilized during recent years of clinical and behavioral trials at each site for collaborative research that utilizes sensitive information from participants. Our team will make every effort to protect all participants' confidential and private information in order to minimize possible study-associated risks.

All findings related to this research will be available and provided to study participants in accordance with standard practices. Clinical and measurement data used for research studies will be released only in de-identified fashion.

In addition, all study personnel are required to renew Human Subjects trainings annually, or in accordance with their site regulatory mandates.

VIII. KEY PERSONNEL AND ROLES

Principal Investigators:

Brian Pence	Principal Investigator	University of North Carolina-Chapel Hill
Bradley Gaynes	Co-Investigator	University of North Carolina-Chapel Hill
Doyanne Darnell	Co-Investigator	University of Washington
Michael Mugavero	Co-Investigator	University of Alabama at Birmingham
Christina Psaros	Co-Investigator	Harvard Medical School
Shannon Dorsey	Consultant	University of Washington

Research Team:

Bernadette Johnson	Program Director	University of Alabama at Birmingham
Mariel Parman	Coordinator	University of Alabama at Birmingham
LaKendra Grimes	CETA Counselor	University of Alabama at Birmingham
Savannah Henderson	CETA Counselor	University of Alabama at Birmingham
Minu Ranna-Stewart	CETA Counseling Supervisor	University of Washington

Tess Filipowicz	Graduate Assistant/Data Manager	University of North Carolina-Chapel Hill