Official Title: Group Motivational Interviewing (GMI) For Homeless Veterans In VA Services

ClinicalTrials.gov ID: NCT02233738

Document Date: 1/8/2019

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A. SPECIFIC AIMS

Objectives: Study objectives are consistent with VA housing recommendations focusing on patient recovery, health services promotion, and treatment implementation evaluation. GMI will be compared to a control treatment condition (CT) on **(Specific Aim I; Five outcomes**: (Primary H1): treatment engagement; (Primary H1): substance use; (Secondary H2): psychosocial integration (e.g., social support, community participation); (Secondary H3) quality of life/psychiatric indices; and (Secondary H4): number of days engaging in structured/productive work activities in the 6-month follow up. **Specific Aim II** involves a process evaluation for documenting (A) formative (e.g., developmental), (B) process, and (C) summative outcomes; and **Specific Aim III** involves estimation of cost of intervention in terms of direct costs, indirect costs of staff, costs of capital and workload measures for future implementation and dissemination research.

B. BACKGROUND/SIGNIFICANCE

B1. Supportive housing for homeless Veterans is a national priority within VA. Veterans account for 13% (tens of thousands) of all homeless adults at any given point in time[19] and suffer unmet need for health/social services[20-21] and high mortality. Combining initiatives, $941 million was proposed for FY 2014 for VA homeless programs[23]. *Two cardinal VA housing programs collectively referred to as 'VA housing', are: Housing and Urban Development-Veterans Affairs Supported Housing (HUD-VASH, n= 56,850 slots) and Grant & Per Diem (GPD, n= 15,500 slots as of August, 2013).* HUD-VASH combines rental assistance for homeless Veterans with case management*; whereas GPD awards grants to community agencies for transitional housing programs that help Veterans regain social function and re-enter work and housing. Together, VA housing programs support over 150,000 homeless Veterans, reflecting massive expansion in the last 4 years.*

B2. Substance abuse is common among homeless Veterans. Over 60% of Veterans are admitted into VA housing with a SUD[9]. About 50% have both alcohol and drug use disorders. Some clients with severe alcohol dependence reduce drinking once housed[24], although most comparative studies have not found an overall beneficial impact of housing on the SUD itself[25-26]. *Despite a major expansion in clinical services, substance abuse overdose is the leading cause of death among formerly and currently homeless adults[4].* Substance use is a *risk factor* for recidivism to homelessness[27-29] and having a co-existing psychiatric disorder (e.g., PTSD) increases the risk of loss of housing by 85 percent[28]. The potential success of supportive housing for homeless Veterans in VA housing depends on effective treatment approaches that are respectful and impart autonomy.

B3. Veterans in VA housing are at high risk of continued impairment in health and social functioning. In one national study of 29,143 Veterans in VA housing, participants with a SUD reported greater psychopathology, engaged in more substance use over time, and showed more problems with alcohol and drugs at 6 months compared to VA housing participants without a substance use problem, indicating that active substance use impedes quality of life and functioning[3]. A significant number of Veterans in VA housing also report continued social isolation and show limited improvement in social integration despite being housed[30]. **Supportive *housing is not adequate by itself to address the mental health, psychosocial, and substance abuse treatment needs of Veterans in VA housing***[3].

B4. Housing First, adopted as VA's official approach to VA housing services, necessitates additional "wraparound" treatment services. Housing First (HF) is an evidence-based approach to supportive housing that emphasizes provision of subsidized housing as well as recovery support and case management services to the most vulnerable Veterans without preconditions of sobriety or involvement in treatment[31,32]. HF combines rapid housing with "wraparound" services, thereby addressing mental health and addiction treatment needs. Pathways to Housing[2] is an evidence-based HF model that uses Assertive Community Treatment (ACT) teams. ACT teams have been deployed on a pilot basis in 14 VA Medical Centers, and are well positioned to have a key role. However, alternatives to ACT also are needed because they are costly, not all clients require them[5,6], and case managers handling ratios of 25-36 clients per manager remains the default method of assuring clinical

support[7,8]. VA leadership mandates that support services should be "wrapped around the Veteran" to advance housing stabilization, quality of life, health outcomes, and long-lasting strides to recovery (Electronic communication sent October 15th, 2012 to all VHA VISN Directors on behalf of W. Schoenhard).

B5. The 'wraparound' treatment mandate highlights a potential void in optimizing SUD support in both types of VA housing. *With HUD-VASH, where harm reduction is a guiding philosophy and case managers are focused on logistics of housing, there is need for addiction interventions that respect client priorities, are relatively non-directive (consonant with harm reduction) and not staff-intensive. In GPD, current provision of SUD supportive care varies in relation to client needs and by program site. National leaders have expressed strong interest in diverse, non-resource intensive recovery support mechanisms (Personal Communication; GPD National Director J. Quarles, 11/7/2013). Given the uneven execution of SUD treatment support in both VA housing modes, our study offers a potentially valuable remedy to a pressing system need.*

B6. Addiction recovery supports for VA housing are required that operate on lean staffing models fully aligned with the philosophic emphasis of HF on consumer autonomy. There remains a need for SUD programs that are shorter in duration, efficient to deploy, easily layered onto existing VA housing services, require minimal staff to operate, and provide several paths of SUD assistance (e.g., lowered substance use, dual diagnosis recovery awareness, higher treatment engagement). **Our proposed study addresses this gap in VA services and will investigate the effectiveness, implementation, and process of an adaptation of motivational interviewing (MI) in a group format (i.e., GMI) that is provided in VA housing for Veterans with SUDs and comorbid psychiatric disorders.** GMI is based on MI; the latter possesses a significant evidence base for addictive disorders[11,33] and has well-established effectiveness in real world settings[34-35].

B7. Group motivational interviewing (GMI), an understudied intervention, may be a feasible/practical mode of treatment delivery and is consonant with HF. For years an effective group-based MI intervention for addictive disorders eluded investigators due to difficulties with translating key individual MI therapeutic components into a group format[36]. Only a few controlled trials examined MI in groups[13-14,37] and few clinicians are trained to provide MI in groups. As a consequence, MI is underutilized in practice despite its high potential to benefit dually diagnosed Veterans. Dr. Santa Ana developed and pilot tested a 4-session manualized GMI intervention addressing these translation issues prior to her CDA-2, (see Research Plan outlining innovative GMI components), referred to as 'Group Motivational Interviewing Treatment (GMI) for Individuals with Psychiatric and Comorbid Substance Use Problems[38]; also see treatment manual in Appendix). GMI is designed to foster important aspects of group therapy that offers advantages over individual treatment[12,36,39] (i.e. peer support, group cohesiveness), opportunities to share information, role modeling, peer feedback, altruism, and instillation of hope, while remaining consistent with the MI principles[11]. To date, only 2 controlled trials evaluated GMI for substance use and treatment engagement among dually diagnosed patients[13-14,37] with promising results (see section C). GMI is a useful intervention that is easily layered onto existing treatment for enhancing treatment engagement and reducing substance use among dually diagnosed Veterans. Given the recent adoption of HF as an approach in VA housing for homeless Veterans with SUDs, the delivery of MI for these individuals comes at a critical time for promoting their stabilization and quality of life.

B8. GMI concept description. In GMI, group members are introduced to a 'GMI culture' (**Phase I**) involving MI consistent group norms for maintaining MI Spirit[11] (e.g., avoid giving unsolicited advice). Second, the MI processes[11] and core MI microskills are facilitated through a set of group therapy dynamics (**Phase II**) that, according to Irvin Yalom[12], are most effective in group therapy. It is the *interplay between MI and these central organizing group dynamics that is the essence of GMI.* The schematic below shows the two primary GMI phases and the 10 dynamic aspects of group therapy and associated GMI strategies to accomplish the dynamic aspect: (See 'Project Logic Model' in Table 5 for Summative Intervention Impacts and Outcomes)

Phase I: GMI Normative Culture (group norms, MI therapist modeling, group MI practice)				
Phase II: Yalom's (1995) Group Dynamics and Associated GMI Activities				
Altruism -Brainstorming treatment obstacles/solutions -Dual diagnosis recovery: Three legged stool	**Group cohesiveness** -Normalizing ambivalence/emotions -Brainstorming treatment obstacles/solutions	**Universality** -A Hard Choice: Finding Your own pace -Values exploration -Interacting relationship between substance use and mental health	**Interpersonal Learning** -Personal strengths -Values clarification -Proactive behavior: good mental health/positive outcomes	**Guidance** -Establishing GMI culture -Brainstorming treatment obstacles/solutions -Decisional balance -Personal feedback

		-Therapist four open-ended questions	-Brainstorming treatment obstacles/solutions	-Proactive behavior: good mental health/positive outcomes
Identification -Proactive behavior: good mental health/positive outcomes	**Catharsis** -Normalizing ambivalence/emotions -Therapist four open-ended questions -Personalized feedback	**Self-Understanding** -Values Clarification -Decisional Balance -Dual Diagnosis recovery -Personalized feedback -Importance/confidence	**Instillation of Hope** -Normalizing ambivalence -Personal strengths -Importance/confidence -Personalized feedback -Brainstorming treatment obstacles/solutions	**Existential Factors** -Dual diagnosis recovery: 3-legged stool (staying sober, taking meds, attending treatment) -Values exploration -Personal strengths

B9. Significance to Veterans: Homeless Veterans with SUDs represent one of the largest and most chronic groups of psychiatric patients treated in the VA Healthcare System. With the ongoing execution of VA's "Plan to End Veteran Homelessness," Veterans entering housing require interventions that can be feasibly implemented with minimal reorganization of existing services. GMI is based on MI, an empirically valid treatment that aligns with Veteran-centered recovery models including Harm Reduction and more traditional treatment philosophies. The investment in GMI for VA housing may be minimal as it requires only a few staff to operate in relatively short time (e.g., 4 sessions, 90-min each) with modest (20 hours) staff training. It can be layered onto existing services with little interruption or reorganization of staff, and it has potential to be offered to larger numbers of Veterans with SUDs in VA housing who would otherwise not receive this intervention.

C. RESEARCH DESIGN AND METHODS

C1. Study Overview: GMI for Homeless Veterans in *VA housing*

The primary objective of this 4-year prospective, randomized, between groups, repeated measures effectiveness trial is to compare **(a)** GMI to a **(b)** control treatment condition (CT) *for dually diagnosed* Veterans *with SUDs in VA housing. The study intervention, GMI, will serve Veterans who attend a workshop addressing their substance abuse and mental health problems regardless of their level of commitment for undertaking behavioral change. This study is designed to recruit dually diagnosed Veterans in two primary VA housing programs, HUD-VASH and GPD. The programs share in common that they receive Veterans with substance use, and the dynamic of moving toward preserving housing even when lapse or relapse occurs. According to Jeffrey Quarles, National Director of VA GPD, GPD will be moving more "in-line" with VA Housing First over time (personal communication, Nov. 7, 2013). Thus, there is no a-priori reason to suggest that participants who volunteer to enroll in the study will experience differential benefits based on where they reside, and this study is not powered to test for such differences.* We will conduct a process evaluation to document formative (e.g., plan for intervention), process, and summative indicators. A logic model containing our plan for documenting aims, inputs, outputs, outcomes, and impacts is presented in Table 5 (below). Our third aim includes estimation of cost (direct and indirect costs, workload measures, costs of capital)[17-18]. Estimated costs of the intervention will be used in implementation and dissemination research. A racially/ethnically diverse sample of 186 Veterans with current alcohol/drug dependence or abuse will be recruited. Male and female Veterans with co-existing DSM-IV-TR Axis I disorders[40] (e.g., MDD, PTSD) will be eligible. Participants will be randomized using a variant of block randomization, where "recruitment week" is the unit of randomization; this will facilitate the process of forming "closed treatment groups" (e.g., approximately 6 members). Participants will be randomized to participate in 4 consecutive 90-minute GMI or CT sessions. *Timing for conducting GMI/CT and completion of assessments is as follows: Consent & Baseline interviews (**Week 1**) ➔ GMI or CT (4 sessions back-to-back; **Week 2**) ➔ one-month follow-up; **Week 4**) ➔ 3-month follow-up (**Week 12**) ➔ 6-month follow-up (**Week 24**).*

Table 1. Participant Characteristics		
Characteristic	**GMI (n = 59)**	**TAU (n = 59)**
Mean age (SD)	52.9	51.1

Gender		
Male	54 (92%)	54 (92%)
Female	5 (8%)	5 (8%)
Race		
Caucasian	27 (46%)	22 (37%)
African-American	32 (54%)	36 (61%)
Hispanic	0 (0%)	1 (2%)
Education		
≤ High School Grad	28 (48%)	24 (40%)
College	18 (30%)	28 (48%)
≥ College graduate	13 (22%)	7 (12%)

C2. Feasibility and Preliminary Data: Data and clinical research presented below provide a strong foundation for the current study.

C2a. Project 1: GMI resulted in higher treatment engagement and lower substance use compared to standard treatment[37]. We conducted a NIH-NIDA funded **Stage I-pilot** controlled trial comparing GMI (*N* = 50) to standard treatment (ST; *N* = 51) among 101 dually diagnosed psychiatric inpatients[37] randomized to two 120-minute GMI or ST sessions. Participants were those with at least one current SUD and a nonsubstance-related major Axis I disorder. All patients and collaterals were interviewed at 1 and 3-month follow-up. Three main outcomes of the pilot study showed that: 1) GMI reduced the number of inpatient hospital detoxification re-admissions after initial hospitalization compared to ST: GMI participants were re-admitted to inpatient detoxification fewer times (GMI: 6.8%; ST: 25.6%; p = .03) during the 3-month follow-up period[37]; 2) Participants in GMI attended more outpatient aftercare treatment sessions compared to participants in ST (M=5.7 [SD=6.7] vs. M=2.5 [1.9]; p=.001) and attended more 12-Step or AA/NA self-help sessions (M=21.7 [18.8] vs. M=6.8 [6.8]; p<.01) by 3-month follow-up; and 3) GMI was associated with reduced substance use: Participants in GMI drank less alcohol (measured in standard ethanol content units), compared to their counterparts in ST by 3-month follow-up (M=117.3 [182.8] vs. M=262.3 [312.9], p=.04), engaged in less binge drinking (M=4.6 [3.2] vs. M=13.9 [10.5], p=.001) and had fewer days of illicit drug use (M=5.2 [7.2] vs. M=13.0 [12.0]; p=.01) at 1-month follow-up. A smaller *proportion* of GMI participants reported binge drinking (34.1% in GMI vs. 55.8% in ST, p = .02) at the 3-month follow-up.

II. Project 2: GMI resulted in lower alcohol use, higher outpatient treatment attendance, and greater participant change talk compared to TAU[13-14]***.*** In her CDA-2 (CDA-2-016-08S) titled: 'Impact of Group Motivational Interviewing on Dually Diagnosed Veterans', Dr. Santa Ana compared GMI to treatment-as-usual (TAU) among 118 Veterans with current alcohol dependence or abuse, an accompanying drug abuse disorder, and a co-existing Axis I psychiatric disorder recruited through the Charleston VAMC Substance Abuse Treatment Center (SATC). Participants were randomized to GMI (n=59) or TAU (n=59). All participants were interviewed at 1 and 3-month follow-up. Patients attended four 75- minute sessions of GMI or TAU across 4 consecutive days. TAU was designed as a psycho-educational group (e.g., addiction as a chronic disease). Dr. Santa Ana modified her GMI protocol for application in the VA outpatient SATC, trained five clinicians to provide interventions, and provided consultation for continued therapist adherence/competence to the protocol. Participant characteristics and DSM-IV-TR substance use and comorbid Axis I diagnoses are listed in Tables 1 and 2. A study coordinator blind to study conditions evaluated participants at baseline and at a 1 and 3-month follow-up. Treatment utilization was assessed via CPRS. Researchers counted the number of outpatient substance abuse treatment encounters and individual mental health treatment appointments with mental health staff (e.g., case-managers, psychiatrists, psychologists) that occurred in the 3 months following the patient's consent (at the Charleston VAMC only). Substance use was assessed using the Time-Line Follow Back[41]. We measured daily and peak alcohol consumption in standard drinks at 3-month follow-up. Data analyses were conducted using ANCOVA with ZINB distribution. Although analyses remain ongoing, preliminary results for primary outcome variables reveal the following: **A)** Participants in GMI attended significantly more general outpatient mental health treatment sessions compared to TAU by 3-month follow up[13], b = .944 (.307), t = 3.079, p < .001; Cohen's d=.54. No baseline differences in treatment engagement were found.

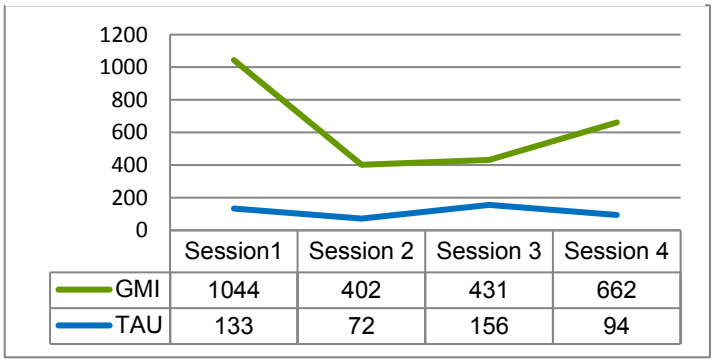
Table 2. DSM-IV-TR Substance Use	**GMI**	**TAU**
Alcohol Abuse/dependence	59 (100%)	59 (100%)
Opioid dependence	1 (16%)	3 (5%)
Sedative/hypnotic dependence	1 (2%)	0 (0%)
Cocaine abuse/dependence	16 (27%)	18 (31%)
Marijuana abuse/dependence	7 (12%)	8 (14%)
DSM-IV Comorbid Axis I Diagnoses		
Depressive Disorders	30 (51%)	30 (51%)
Bipolar I/II Disorders	4 (7%)	2 (3%)
Anxiety Disorders (PTSD, panic, GAD, social phobia)	30 (51%)	32 (54%)
Mood Disorders NOS	2 (3%)	0 (0%)
Substance Induced Mood Disorder	7 (12%)	3 (5%)

Schizophrenia/psychotic Disorder	1 (2%)	2 (3%)
Schizoaffective Disorder	1 (2%)	1 (2%)
Borderline Personality Disorder	1 (2%)	0 (0%)
Antisocial Personality Disorder	0 (0%)	1 (2%)
No co-existing Axis I Disorder	6 (10%)	8 (14%)

B) Participants in GMI relative to TAU consumed less alcohol in standard drinks, *b*=-155.3 (70.9), *t*=-2.19, *p*=.03; Cohen's *d*=.36) and drank fewer standard drinks in terms of their peak (highest) drinking day[14], *b*=-4.78 (2.03), *t*=-2.4, *p*=.02. No baseline differences between groups were found on alcohol consumption.

C) *Change talk mediates the effect of GMI and substance use outcome and is more prevalent in GMI compared to TAU[14]. Change talk is client language in favor of change and its enhancement is the primary goal of MI (e.g., "I want to quit drinking for my family")[42]. Change talk variables, such as "ability" language and its underlying dimensions (e.g., 'desire, reason, need, commitment, taking steps') underlie the efficacy of MI[43], such that stronger change talk predicts substance use[42]. Therapist adherence to MI increases change talk, which serves as a mediator between therapist behavior and lowering alcohol use consumption[44]. Studies on change talk indicate that it is the strongest indicator of mechanism of action in MI contributing to outcome[42]. GMI activities intentionally evoke change talk by design, although studies examining change talk in GMI have not been conducted. The presence of change talk in GMI provides evidence showing that similar mechanisms of action that are present in MI are also present in GMI.* Using a coding manual (adapted from the Motivational Interviewing Treatment Integrity (MITI) Code, version 3.1.1.)[45], t*wo trained raters blind to treatment condition coded 138 audio recorded GMI/TAU sessions for change talk [GMI=68; TAU=70], 8 on which they overlapped for establishing rater reliability. ICC's were excellent, ranging from lowest .92 to highest .99 across all six change talk categories. Using group clustered latent growth models examining between group frequency of change talk ratings, with the exception of 'commitment' [t=1.8; p=.07], all types of change talk ('desire' [t=4.9; p<.001], 'ability' [t=3.0; p=.002], 'reason' [t=5.1; p<.001], 'need' [t=3.8; p<.001], and 'taking steps' [t=5.1; p<.001]) was higher in GMI relative to TAU[14] and remained above TAU across all 4 sessions, as seen in Figure 3. To examine whether change talk predicts substance use outcome, we conducted a group clustered path mediation analysis. By 3-month follow up, 'Ability' change talk predicted less alcohol consumption (Estimate: -71.5; CI: -165.74, -2.0), while 'Need' change talk predicted greater alcohol consumption (Estimate: -104.9; CI: 28.0, 208.2), indicating that 'Ability' should be enhanced in GMI.* These data provide preliminary evidence that GMI enhances change talk and predicts substance use outcome among dually diagnosed Veterans. ***Note**: 19% (n=23; GMI=15/TAU=8) of Dr. Santa Ana's dually diagnosed sample (n=118) were homeless Veterans receiving VA housing services. 78% (n=18) completed all 4 treatment sessions (GMI=73%, n=11/TAU=88%, n=7); 91% (n=21) completed all study interviews (GMI= 87%, n=13/TAU=100%, n=8), showing evidence of feasibility among homeless Veterans.*

Figure 3. Overall between Group Change Talk across the Four Sessions



C3. Recruitment Plan and Feasibility of Recruitment

The VA housing program of the Charleston, SC VAMC will be the primary site of recruitment, including Myrtle Beach and Savannah. As there are no competing studies, we anticipate no difficulties with recruiting the needed participants within the 30 month recruitment period. Recruitment will occur through: 1) VA housing Referrals: study personnel will attend weekly *VA housing staff meetings* to discuss potentially eligible patients; 2) Invitation letters: Provided IRB approval, conducting VISTA queries (every 3 months) of Veterans with VA housing admissions and a DSM-V Axis I substance use disorder diagnosis. Letters of invitation describing the study and its eligibility requirements will be sent out *by study personnel* to patients so they who can return-mail their interest in participating; 3) General referrals: *We will recruit participants who have not formally entered SUD treatment from Tracks 1 and 2 'pre-treatment' groups of* the Charleston VAMC SATC outpatient program, and receive referrals from VA physicians and clinic staff, social workers, nurses, mental healthcare physicians, or patients themselves in response to study flyers. Approved recruitment flyers will be posted in prominent locations in the study clinics; 4) Interest (wait) list referrals: consisting of names and contact information of patients waiting to enroll in HUD-VASH. Wait list referrals are comparable to participants in HUD-VASH; the only exception being that they applied when vouchers were not available. *Only study personnel will recruit participants to prevent potential coercion by VA housing staff.*

Feasibility of Recruitment: This study requires 186 Veterans currently in VA housing or newly entering VA housing, but not yet housed. *We will recruit 50% (n = 93) of participants from HUD-VASH and the other 50% (n = 93) from GPD* within 30 months between Year 1, Month 7 and Year 3, Month 12 (see Gantt chart in Table 6 of Project Timeline). As of *10/2013* there are *385* vouchers (i.e., participants currently enrolled in HUD-VASH), 65 anticipated new vouchers for Fiscal Year 2014 (P. Bradford, personal communication, 10/2014), and 41 (x 2.5 years) patients on the interest list. Additionally there are ~104 new clients entering the system annually due to participant departure/turnover. *Taken together, at least 813 patients (385 + 65+ 41*2.5 years [103] +104*2.5 years [260] = 813) will be screenable over the course of 2.5 recruitment years. 50 to 60% of HUD-VASH participants have an SUD[9]. Taking the most conservative estimate of participants having any SUD (i.e., 50%) provides 407 participants eligible (813*.50 = 407); a figure well above the 186 participants needed for the study. 80% of residents in VA GPD have an SUD. In the GPD program, there are approximately 285 new (non-overlapping) admissions per year providing 570 participants eligible to participate (285*2.5 years = 713*.80 = 570). All combined, there are approximately 977 potentially eligible participants (407+570 = 977) during the 30 months of study recruitment, resulting in 32 new admissions, on average, per month.*

Attrition and Retention: This study's recruitment of 186 subjects (93 per trial arm) reflects a power calculation in which up to 30% could be lost to follow up. This conservative attrition estimate is well above the 13% study drop-out rate in Dr. Santa Ana's CDA-2. Additionally, it is consistent with average participant drop-out rates in the addiction field, and is well within NIDA recommended guidelines of at least 80% retention in research. This rate is conservative given that the majority of VA housing patients in the current protocol will already be "engaged" in ongoing VA services and these patients tend to remain in VA care.

Participant Payments: *All participants will receive subject fees based on an increasing incremental plan to enhance study retention: $25.00 for the baseline assessment*, *$25 for each of four treatment sessions, $25 for the Booster session, $50.00 for the one-month follow-up, $50.00 for the 3-month follow-up, and $50.00 for* the 6-month assessment for a combined possible total of $300.00. As participants in this study are likely to be unemployed, most will lack sufficient funds to obtain transportation to the group therapy site for the sessions.

C4. Participant Eligibility Criteria. *Participants will need to meet the following inclusion criteria: Veterans currently in HUD-VASH and GPD, newly entering the program but not yet housed, or Veterans on the HUD-VASH interest (wait) list, able to comprehend English, meeting DSM-V criteria for current substance use disorder, use of substances in past 30 days prior to date of consent, able to provide informed consent, functioning at an intellectual level sufficient to allow accurate completion of all assessment instruments, and willing to commit to 4 group therapy sessions, the booster session, and baseline, 1, 3, and 6 month follow-up assessments. We will record recruitment site from where participants were derived (HUD-VASH/GPD) as well as amount of time in VA housing to explore site effects (as covariate and effect-modifier) in the analytic phase. If there are differences based on these variables, they will become covariates and adjusted in the analysis.*

C5. Randomization Procedures. *Participants will be assigned to GMI or CT using a block randomization procedure successful in shortening the amount of time needed to fill a group. This procedure was successfully utilized in Dr. Santa Ana's CDA. In this procedure, a set of consecutively admitted participants will be assigned to the same treatment condition with 'recruitment week' being the unit of randomization (i.e., recruitment weeks themselves are randomized). A computer randomizes recruitment weeks; therefore, all participants entering the study in a treatment week enter the same treatment condition. Since session attrition occurs infrequently (i.e., some participants may elect to not attend a particular session for various reasons) and is typically no more than 1 to 2 absent individuals, we will recruit at least 6 participants per workshop to ensure that there will be enough attendees present.* Thus, we anticipate between 3 to 6 participants will attend any one session; providing a maximum of (up to) 62 workshops each containing four sessions for a maximum total of 31 workshops in GMI (124 sessions) and 31 workshops in CT (124 sessions). Once a Veteran is randomized he or she will be entered into the study and included in intent-to-treat analysis. *We will track session attendance. Should there be a difference on group member attendance between treatment conditions, we will account for within session correlations of outcome by including random effects corresponding to the clusters.*

C6. Description of Proposed Novel Intervention (see appendix for GMI treatment manual). GMI & CT group sessions will take place in various community locations (e.g., HUD-VASH apartment complexes/*GPD residential programs [e.g., Charleston Vets]).*

Group motivational Interviewing (GMI): Following randomization, participants will be scheduled with their study therapist (see therapist training in section C8) in a closed group. GMI participants will receive four structured,

back-to-back, 90-min sessions consistent with the central principles and spirit of MI[11]. GMI, which is based on a manualized protocol[38], is specifically designed for dually diagnosed Veterans. A focus of the intervention creates awareness of the relationship between the substance use and co-existing psychiatric disorder and the importance of treating both. The primary aim of GMI Session 1 is to introduce the guidelines of group behavior (e.g., the GMI normative culture), explore common emotions (e.g., anxiety, fear) associated with ambivalence to change, instill autonomy, evaluate pros/cons of substance use, and evaluate readiness/confidence to change. The primary aim of GMI Session 2 is to enhance discrepancy, a key element in building motivation for change. Participants are provided a sealed "Personalized Graphic Feedback Report" (PFR; An updated version will be engineered by Datstat Inc. and is discussed in the budget) based on the baseline assessment summarizing the participant's drinking and drug use patterns compared to the population, combined with 12 other feedback components (e.g., SUD consequences, liver enzymes). The primary aim of GMI Session 3 is to explore and clarify goals/values, increase self-efficacy, and engage members in a discussion on the interrelationship between their substance use and co-existing psychiatric disorder. The focus of this discussion relates positive (e.g., healthy) mental health and proactive behavior, such as engaging in a productive job or structured activity, fostering relationships with friends, family, and the community, taking medication, staying clean and sober, and going to treatment with positive outcome. The primary aim of GMI Session 4 is to enhance intrinsic motivation to go to treatment and engage in productive work or other structured activities, and introduce an activity to increase self-efficacy for continuing treatment and enhancing social activities.

C7. Description of Comparator/Control Conditions

Control Treatment Condition (CT): Participants in CT will attend four sessions equal in time and length to GMI (i.e., 90 minutes) and will involve the following topics: A popular 'box activity': participants will anonymously write evocative questions on slips of paper involving their personal concerns that are placed in a box and, when randomly selected, opened for group discussion (e.g., "How do I talk to my family about my alcohol problem?"), money management with feedback (2 sessions),psychoeducation about substance use, and cooking-home maintenance.

Session timing: We will aim to complete GMI and CT sessions over the course of one week (Tuesday – Friday) when feasible and practical. Our session timing aim is based on evidence from the PI's prior work, given her success with this approach in her pilot and CDA, whereas the efficacy of GMI delivered over a longer period of time is less certain. We plan to make every effort to complete group sessions on 4 consecutive days, as that approach was used in prior successful efforts. However, at times, we may encounter participants within a particular group who have limited availability to attend consecutive sessions within one week; thus, we will make reasonable efforts to reduce barriers to attend sessions (e.g., holding sessions every other day).

Description of Booster Session: Participants in both GMI and CT will be asked to attend a 1 hour booster session 2 months after they receive the intervention to maintain consistency with the treatment, reduce participant drop out (as there are no formal assessments being conducted at the second month) and to increase potential to motivate and enhance proactive behaviors among group members to engage in the therapeutic material discussed in both GMI and the TCC interventions.

C8. Treatment Fidelity to GMI.

Therapist Training and Supervision: Therapists for the project will be 2 part-time social workers serving Charleston, Myrtle Beach, and Savannah. Therapists will facilitate equal numbers of groups (e.g., maximum of 31 groups or 124 sessions each). Therapists will receive a 20-hour training facilitated by the PI, who is an expert trainer in Motivational Interviewing, over the course of three days, followed by a 4-week supervised training with non-study participants with the PI. Therapists will follow the GMI treatment manual and undergo weekly clinical supervision with the PI to maintain therapist adherence (for preventing protocol drift) and competence (for facilitating GMI skillfully). *Treatment Fidelity Checks: All treatment sessions will be audio-taped. 15% of these will be randomly selected and rated by trained independent raters to evaluate therapist adherence and competence and to ensure treatment discriminability between treatment conditions on the MI Global Scales (i.e., the combined global scores) and the MI Behavioral Frequency Counts (i.e., combined frequency of the behavioral categories) using the Motivational Interviewing Treatment Integrity (MITI) Code, version 3.1.1.[45]. Prior to seeing study participants, therapists will facilitate GMI sessions with patients not enrolled in the study and will be required to demonstrate adequate use of GMI consistent strategies, achieving MITI behavioral competency levels[45], during each session and for these strategies, demonstrate minimum competence on global scale ratings*

of 4 or higher in all 4 sessions to be certified before seeing study participants. Coding will occur at the beginning of year 3 and be completed by the end of year 3.

C9. Outcomes and Assessments

Measures used in this study include those for establishing eligibility and baseline descriptive information (e.g. demographics). *To reduce follow-up losses, participants will be asked to list the names/contact information of 2 family members (or close contacts).* We listed specific assessments in clusters associated with their specific aims and primary/ secondary hypotheses (H1 to H4) for ease of reference. Assessments will be administered at baseline, 1, 3 –and 6-month follow-up visits. A project coordinator trained in the administration of assessment interviews will conduct baseline assessments and a *full-time* research assistant blind to study condition (independent assessor) will administer follow-up assessments (see budget justification for more detailed role designations). After informed consent procedures, participants will complete a battery of assessments taking ~ 94 minutes at baseline and ~70 minutes at follow-ups.

C9a. Measures under Specific Aim I: Primary Hypothesis (H1); Substance Use and Treatment Engagement: are described in this section. Information regarding additional measures can be found in Table 4. The Timeline Follow-Back (TLFB)[41] obtains retrospective self-report of alcohol/drug use (e.g., cocaine, marijuana, stimulants, sedatives, opioids) frequency/quantity via estimates of daily drinking/drug use, # days spent drinking alcohol, and # binge drinking days by using a calendar and memory prompts to stimulate substance use recall. Alcohol consumption data will be converted into standard ethanol content (SEC) units (or standard drinks) equivalent to 0.5 oz of ethanol; Urine Drug Screen: samples will be tested with a RapidCHECK® Multi-Drug 10 Panel Test, which allows for the detection of THC/marijuana, cocaine, phencyclidine, opiates, methamphetamines, methadone, amphetamines, barbiturates, and benzodiazepines; Alcohol Breathalyzer Tests will be used to measure participant's blood alcohol concentration (BAC) at follow-ups. Samples >0.01 g/dl will be considered positive; Ethyl Glucuronide (EtG): is a conjugated alcohol metabolite formed by the enzymatic conjugation of glucuronic acid with alcohol in the liver and remains positive in urine for several days following cessation and can detect even small levels of drinking[46]. **(NOTE: Biologic data will not be made available in CPRS records or to VA housing staff)**. The Treatment Attendance Calendar (TAC; Based on the TLFB[41]) will be used to assess number of days treated for a substance abuse/mental health problem in the VA or any other outpatient aftercare setting and number of visits with a VA or outside physician for help related to a psychiatric or substance use problem. Researchers will count the number of outpatient substance abuse and mental health treatment encounters in Computerized Patient Record System (CPRS) medical records at the Charleston VAMC (e.g., with case-managers, psychiatrists, psychologists, social workers at the Charleston VAMC only); Twelve-Step Participation Questionnaire (TSPQ-21)[47] is a measure of involvement with 12-Step meetings (AA, NA) including self-help 'steps' that the patient worked and number of 12-Step meetings attended; Treatment Motivation Questionnaire (TMQ)[48] is a 29-item self-report that measures reasons for entering and remaining in treatment.

Table 4. Timeline of Assessment Instruments (18 items, not including informed consent; ~94 mins or less)

Instrument Name	Purpose/Domain	Time (min)	Rater	Assessment Time Point
A. Diagnostic/Screening Measures				
Informed Consent	*Obtain informed consent*	10 min	I	BL
1. Demographic form/*Homelessness History*	*Characterize sample*	2 min	I	BL
2. Structured Clinical Interview for DSM-5: SCID[49]	*DSM-I psychiatric disorders*	20 min	I	BL
B. MEASURES under SPECIFIC AIM I: Primary Hypothesis (H1): Substance Use				
3. Timeline Follow-Back (TLFB) [41]	*Assess substance use*	7 min	RA	BL, 1, 3, 6
4. Urine Drug Screen (UDS)	*Assess illicit drug use*	5 min	RA	BL, 1, 3, 6
5. Alcohol Breathalyzer	*Assess alcohol use*	2 min	RA	BL, 1, 3, 6
6. Ethyl Glucuronide (EtG) Alcohol Biomarker[46]	*Assess alcohol use*	5 min	RA	BL, 1, 3, 6
B1. SPECIFIC AIM I: Primary Hypothesis (H1): Substance Use Related Problems				
7. Addiction Severity Index-Lite (ASI-Lite)[50]	*Assess substance use severity*	15 min	RA	BL, 1, 3, 6
8. Short Inventory of Problems (SIP-R)[51]	*Assess substance use*	3 min	RA	BL, 1, 3, 6
B2. SPECIFIC AIM I: Primary Hypothesis (H1): Treatment Engagement				
9. Treatment Attendance Calendar (TAC)[41]	*Assess treatment attendance*	7 min	RA	BL, 1, 3, 6

10. 12-Step Participation Questionnaire[47]	*Assess 12-step attendance*	2 min	RA	BL, 1, 3, 6
11. Treatment Motivation Questionnaire (TMQ)[48]	*Assess treatment motivation*	2 min	RA	BL, 1, 3, 6
C. SPECIFIC AIM I: Secondary Hypothesis (H2): Psychosocial Integrative Activities				
12. Social Support Survey[52]	*Assess social support*	3 min	RA	BL, 1, 3, 6
13. Community Participation Survey[53]	*Assess community participation*	3 min	RA	BL, 1, 3, 6
D. SPECIFIC AIM I: Secondary Hypothesis (H3): Quality of Life				
14. SF-12 Health Survey[54]	*Assess changes in health*	5 min	RA	BL, 1, 3, 6
15. Quality of Life Scale (QOLS)[55]	*Assess quality of life*	4 min	RA	BL, 1, 3, 6
16. Brief Symptom Inventory-18 (BSI-18)[56]	*Assess psychiatric distress*	2 min	RA	BL, 1, 3, 6
17. Medical Symptom Validaty Test (MSVT)	*Assess Executive functioning*	5 min	RA	BL, 3
18. A/B Trailmaking Test	*Assess executive functioning*	10 min	RA	BL, 1, 3, 6
E. SPECIFIC AIM I: Secondary Hypothesis (H4): Structured/Productive Work Activities				
19.. Productive Work Activities Calendar (PWAC)[41]	*Assess work/volunteer*	4 min	RA	BL, 1, 3, 6
F. SPECIFIC AIM II: Process Measures				
20.. Charleston Psychiatric Outpatient Satisfaction Scale (CPOSS-	*Assess participant satisfaction*	2 min	RA	1
21.. Helping Alliance Questionnaire (HAQ-II)[58]	*Assess therapist alliance*	1 min	RA	1
22.. Group Cohesion Scale	*Assess group cohesion*	1 min	RA	1

I = Investigator (e.g., PI, Co-Is, Project Coordinator); RA = Research Assistant; BL = Baseline

C9b. *Process Evaluation: Measures under Specific Aim II & Analysis Plan for Formative, Process, and Summative Evaluation; (Specific AIM II):* *To conduct a process evaluation for documenting (A) Formative (e.g., developmental), (B) Process, and (C) Summative indicators[15-16] for: (1) identifying facilitators/ barriers to intervention delivery and plan for treatment (formative); (2) documenting and monitoring treatment implementation (process); and (3) assessing whether results of intervention met its stated goals (summative indicators).*

A) Formative Quantitative Process Evaluation Measures: 1) Participant Treatment *session dropout proportion (GMI/CT), scores on GMI session quiz (e.g., evaluates GMI learning to ensure that participants received the intervention as intended), and participant satisfaction (see table 5 below). GMI/CT treatment session attendance records will be maintained. We will compare process outcomes (e.g. treatment session attendance dropout proportion, participant satisfaction, and GMI learning) between intervention groups using the generalized linear mixed model (GLMM) framework, as described in section C12, with appropriate link functions corresponding to different data types. The binomial link function will be used for comparison of treatment session dropout proportion between GMI/CT (equivalent to logistic regression). GMI specific endpoints (e.g., group session attendance) will be described using standard descriptive analyses (e.g., proportions along with corresponding 95% CI). Reasons for treatment session dropout, missed sessions and protocol noncompliance will be obtained and described by frequency distributions and 95% CI.* ***2) Patient Satisfaction****: Charleston Psychiatric Outpatient Satisfaction Scale (CPOSS-VA; See Table 4, #18) is a 16-item measure with a Likert-scale response format based on a general measure of patient satisfaction. In a sample of Veterans, preliminary data showed excellent reliability (alpha = .96) and good convergent validity[56] that provides a second process measure.* ***3) Therapist adherence and competence (treatment fidelity) will be examined*** *with interclass correlation coefficients (ICC) using a random effects model[59] to provide: (1) an estimate of scale reliability within the sample of audio taped sessions with separate independent t-tests used to determine whether therapists successfully altered the treatment approach according to protocol and that the treatment conditions were discriminable from each other and; (2) that therapists adhered to manual guidelines and were delivered with adequate level of skill[45]. All audiotapes of the GMI/CT sessions will be rated by two independent raters to evaluate degree to which GMI was implemented as intended and could be discriminated from CT. A logic model[15-16] (based on the framework for containing our plan for documenting and evaluating formative, process (e.g., intervention fidelity, dose delivered/received, reach, context), and summative intervention aims, inputs, outputs, outcomes, and impacts is presented in Table 5 (below).* ***4) Patient Perceived Process Measure:*** *Helping Alliance Questionnaire (HAQ-II)[58] (See Table 4, #19) is a well-validated measure of therapeutic alliance, a construct that has been shown to predict outcomes for psychotherapy in substance use disorders.*

Table 5: PROJECT LOGIC MODEL PLAN

A. Formative Evaluation of the Intervention (adapted from Stetler and colleagues, 2006)

Specific Aim	Inputs	Outputs	Outcomes	Impacts

1) Identify facilitators/barriers to treatment implementation: Conduct Veteran and staff focus groups to discuss project and GMI/CT treatments	*Recruit focus group Veterans and staff, schedule focus groups, and develop focus group meeting agendas*	*Record, transcribe, & code focus group meeting discussions for themes*	*Interpretation of focus group themes, facilitators and barriers described, and findings prepared for publication*	*Refine & alter GMI/CT based on focus group info; share lessons learned*
*2) **Plan for Intervention Implementation**: assemble team, train therapists on GMI/CT, assess therapist adherence/competence; plan GMI/CT delivery*	*Hire study team, update GMI/CT interventions, design and schedule staff training*	*Conduct GMI/CT training, therapists conduct practice sessions with actual patients, conduct pre/post therapist training assessment*	*Study therapists trained to deliver GMI/CT; therapists practice sessions rated/coded as certified to deliver treatment*	*Study therapists provide GMI/CT to participants, participants recruited for the study*
B. Process Evaluation of Intervention Implementation (adapted from Saunders and colleagues 2005)				
Specific Aim	***Inputs***	***Outputs***	***Outcomes***	**Impacts**
*1) **Intervention Fidelity** Therapists deliver GMI/CT adherently and competently and follow a GMI treatment manual*	*Update/refine adherence/competence manual; PI listens to GMI/CT sessions and provides consultation to study therapists*	*Collect session recordings, study therapists improve protocol adherence based on PI feedback; two raters trained to code GMI/CT sessions.*	*GMI/CT delivered adherently/competently; ICC's calculated for therapist adherence/ competence; GMI/CT delivered as intended*	*Fidelity to GMI/CT; ICCs indicate GMI discriminable from CT*
*2) **Intervention dose delivered/received:** Participants attend full dose of intervention & received all study materials; participant knowledge enhanced*	*Create session attendance log; therapist session checklists provided; GMI/CT sessions recorded; GMI quiz provided to study participants*	*Participant session attendance, delivery of handouts, & utilization of therapist checklists documented; Raters code GMI/CT sessions for change talk; GMI quiz collected and scored*	*GMI/CT dropout is minimized; participants receive study materials as planned, therapists deliver GMI/CT as intended; raters rate change talk in GMI/CT; GMI quiz indicates participants understand GMI material*	*GMI/CT delivered as planned; Majority participants attend full dose of GMI/CT sessions; change talk in GMI > CT*
*3) **Reach (participation)** Study team successfully distributes knowledge of project to VA housing community; success in sufficient number of priority target audience being aware of & enrolling in the study*	*Consultations held with VA housing staff; study personnel track & maintain contact with study participants; number of participants inquiring/consenting to be in the study tracked.*	*Study personnel collaborate with VA housing staff to identify eligible participants & ensure participants are informed of the study, number of eligible patients who inquire, consent, or state knowledge of the study documented*	*Records indicate that eligible participants are successfully informed of the study; at least 80% of all eligible participants are aware of the study*	*VA housing staff reports that the project is a reliable resource for their patients; sufficient target participants are informed, invited, and recruited for the study*
*4) **Context:** Aspects of the study environment promote successful study implementation in terms of: communication with study team; and documentation of protocol process; obstacles to participant involvement are minimized*	*Study team completes weekly checklist of duties; arrives at project meetings with duties accomplished or proposed; and PI Works out any study complications or issues with study team*	*Study team meet in designated office for weekly study meetings; PI & PC talk daily by regarding project planning, directives, managing issues*	*PI assesses PC on a monthly basis (first six months) and then quarterly; assesses RA on a monthly basis (first six months) and then quarterly, C resolves contextual obstacles*	*Issues identified to ensure efficient operation of the project*
C. Summative Indicators of Intervention Implementation (Logic Model of Intervention)				
Specific Aim	***Inputs***	***Outputs***	***Outcomes***	**Impacts**
*1) **Participant outcome:** Participants resolve ambivalence in: Primary H1: Substance use/problems and Treatment engagement; Secondary H2: Productive work activities; H3: Social integration; H4: Quality of life; 2) **Link between Process & Outcome:** Satisfaction with GMI/CT, therapist alliance & change talk analyzed for relationship to H1 substance use and treatment engagement outcomes*	*Therapists are adherence/competent to GMI/CT; study personnel conduct standardized follow-up assessments; study personnel provide CPOSS-VA & HAQ-II to participants at end of GMI/CT*	*Therapists adherent to MI Spirit; MI processes; and MI microskills combined with GMI activities; CPOSS-VA; HAQ-II Assessments scored/ examined for completion*	*Participants engage in 'change talk' mediators: 'Desire, Ability, Reasons, Need, Commitment, Activation, Taking Steps' (DARN-CAT) & learn relationship between substance use and co-existing psychiatric disorder and importance of treating both*	*Measurable change in study outcomes based on follow-up assessments*

B. Qualitative Process Evaluation: 1) Stakeholder Perceptions of Treatment: *Using an exploratory constructivist grounded theory approach to qualitative evaluation[60], a total of 4 focus groups (2 in year 1 prior to data collection; 2 in year 4 at end of data collection) will be conducted with a sample of Veterans (n= 6); and a second focus group with therapists, housing staff and providers; to discuss perceptions, including perceived utility & satisfaction, difficulty, value/commitment, intervention attributes, and unintended consequences of GMI & CT. Focus groups will be recorded and transcribed, with identifiers removed. Coding and interpretation will examine themes related to treatment perception. This approach first uses open coding to generate categories from the data, then theoretical coding as conceptual connectors are identified between categories and their properties through constant comparison. This approach lends itself to axial coding as particular patterns emerge, such as common actions, events, assumptions, and relationships contributing to themes.*

2) Qualitative documentation of plan for intervention implementation*: Field notes will be collected regarding preparation of the study team for intervention delivery and fidelity of roll-out (**See Table 5:***

***'Intervention Fidelity'**). During study implementation, treatment, treatment fidelity, dose delivered/received, reach, and context will be* documented using checklists, activity logs, and coding sheets for maintaining careful records of each area.

***C) Summative Evaluation/Link to Process Measures:** In two exploratory process analyses, we will examine: 1) the association between patient satisfaction, therapist alliance, and MI therapist Spirit and H1 substance* use (e.g., quantity as measured by days, SECs) and treatment engagement (e.g., # sessions attended) *outcome variables. We will evaluate whether ratings on these 3 process measures are higher in GMI compared to CT and their association to outcome will be examined using GLMM; and 2) whether participant change talk mediates the effect of intervention and substance use outcome and whether it is more prevalent in GMI compared to CT using group clustered path mediation analysis.*

C9c. Cost Assessment. We will assess treatment cost following Rosenheck:[17] 1) Total cost of the salary/fringe will be determined for two part time licensed social workers *at GS level 9* for the time spent providing the intervention. Per-minute costs will be estimated using the annual salary based on the Federal General Schedule for salaries for the year 2014, with the addition of the cost-of-living adjustment (COLA) for a person federally employed in Charleston and the cost of benefits (base salary+COLA at (variable)% rate+35% for benefits); 2) Total cost of equipment and administrative supply costs will be calculated for each site: Charleston, Savannah, and Myrtle Beach and *will include digital audio recorders, easels, a color printer, etc. Supplies will include lamination services, urine drug screening, and lab services for Ethyl Glucuronide (EtG) Alcohol Biomarker test.* 3) Participant travel costs will be calculated for travel to the treatment site using modal cost per trip to represent the typical cost of participant travel for each year (using the mean cost provides too much weight to outlier costs). These travel costs will include the Federal government allowance per mile and the average number of miles the Veteran travels from home to VA once that Veteran has exceeded the threshold (currently 100 miles); 4) Participant per-session costs will be assessed using the number of participants in each treatment condition. A per-person cost for each treatment session will be calculated on the following variables: (A) personnel per session, (B) patient travel; 5) Total cost per participant will be estimated using the product of the per-session cost for the total treatment attendance for each person. All costs will be converted to 2014 dollars, depending on end of study data collection using the Consumer Price Index (http://www.bls.gov/data/inflation_calculator.htm) as of the last month in which study data is collected; 6) Cost per unit of service will be estimated by dividing costs by a measure of services delivered (e.g., the number of patient contacts per year and hours of direct participant care service provided per patient each year). A log will be kept specifying number of contacts and hours of direct care service provided; 7) Indirect costs will be assessed by gathering data on cost from VA accounting records for engineering, administration and maintenance departments and service lines; 8) Costs of capital[18] will be assessed by contacting local realty agents for the market value of the land on which the VAMC is located. Disaster insurance records will be examined to ascertain the cost of replacing the VAMC building.

C10. Data Management. Data will be compiled using codes in lieu of personal identifiers. Access to study data will be limited to research personnel. All paper-based assessments will be entered within 1 week after collection from the participant. As a result of double-data entry, two analyzable databases will be created. The validity of the databases will be checked by comparing the databases and macro programs will be written to check the data for logical consistency and values out of possible range. Quarterly database management and data integrity audits will be conducted. We will adhere to all data security procedures that are in place for our *COIN (the Charleston Health Equity and Rural Outreach Innovation Center [HEROIC]).* All data containing PHI will be stored on the *HEROIC* Server; no data with identifying information (PHI) is stored on individual hard drives. The server sits behind a secure firewall maintained by the VA.

C11. Sample Size Calculation and Power Analyses.

For sample size calculations, preliminary data from Santa Ana and colleagues[13-14] were used. In Santa Ana and colleagues[13], participants in GMI attended a significantly higher number of outpatient SUD treatment sessions compared to their counterparts in TAU. Using zero inflated negative binomial regression (ZINB) and accounting for group level nesting, at 3-month follow-up, participants in GMI attended significantly more outpatient mental health treatment sessions compared to TAU, b = .944 (.307), t = 3.079, p < .001; Cohen's d = .54. The efficacy of GMI relative to TAU for lowering substance was assessed among the same sample of dually diagnosed Veterans using ZINB[14]. At 3-month follow-up, participants in GMI consumed significantly less alcohol in standard drinks (b = -155.3 (70.9), t = -2.19, p = .03; Cohen's d = .36) and drank fewer standard drinks in terms of peak (highest) alcohol drinking day (b = -4.78 (2.03), t = -2.4, p = .02). No baseline differences between

groups were found on alcohol consumption. For comparing the longitudinal profile of the substance use outcomes (standard drinks/day, peak standard drinks/day, # drinking days, # binge drinking days) using repeated measures analysis assuming 3 measurement time points, level of significance α=0.05, two-tailed comparison, correlation between pairs of measurements within participants no larger than ρ=0.5, we estimate that 50 participants per group (total n=100) are needed to achieve a power of 89% to detect a difference of 0.5 standard drinks between GMI and CT. A sample size of 65 (n=130) will provide 83% power to detect a difference of 0.4 standard drinks between treatment conditions. The corresponding sample size requirements after adjusting for a 30% dropout rate are 142 (71 per group) and 186 (93 per group), respectively. To account for the "fraction of missing" information that must be imputed in the intent-to-treat (ITT) sample and the dilution effect of ITT analyses, we further inflate the sample size by 30% to achieve a final ITT sample size of 93 participants randomized to GMI and CT (total N = 186) to detect a difference of 0.4 standard drinks between treatment conditions[61]. For the global statistical test (GST), when the collection of outcomes (e.g., standard drinks/day, etc.) show consistent directionality with regard to improvement, GST will have higher power than that of tests of single outcomes[62].

C12. Overview of the statistical analysis plan.

Effectiveness analyses: all health services and participant outcomes (see section C9) will be obtained at three time points (month 1, 3 and 6-months post-randomization). These variables include: (a) Substance use outcomes (e.g., standard drinks/day (SEC), peak standard drinks/day, # drinking days, # binge drinking days, # illicit drug use days, etc.); (b) Treatment engagement (e.g. # of substance abuse/mental health treatment sessions attended, # AA sessions attended, # AA sponsor contacts; (c) Psychosocial adjustment (social support, community participation) and (d) Quality of life/psychiatric indices (QOLS, SF-12, BSI-18); (e) Engagement in structured/productive work activities (% of days each month engaged in work or volunteer activities); (c) Process measures (CPOSS-VA, HAQ) will be assessed at 1-month follow up.

Analysis sets. The ITT sample comprises all randomized participants. The per-protocol/completer sample comprises participants who are compliant with protocol requirements and for whom all required measurements have been made. Primary analyses will be carried out using the ITT analysis set.

C12a. Premature exits (study drop-outs) and missing data. We will employ longitudinal data methods (generalized linear mixed models [GLMM]), which allow for missing at random (MAR) data[63-64]. Analyses will be carried out separately for the ITT and per protocol samples to test sensitivity of conclusions to study drop-outs/non-adherence. For dichotomous outcomes, in additional "worst case" sensitivity analyses, we will assume that missing data are "failures" (non-successes), e.g. in calculating # of days not using alcohol, we will assume that missing entries in daily log regarding alcohol use are days in which alcohol was used. In addition, to understand the missing data and study drop-out process, we will fit a missing data model with a dichotomous outcome (1=missing, 0=not missing) using logistic regression. We will also use information on study drop-outs as one of the feasibility (process) outcome measures of the interventions being compared. To investigate potential limits on generalizability, we will compare characteristics of the non-completers/non-compliers with the completer/protocol adherent groups. These comparisons will be carried out for the total group and within treatment allocations. To describe potential bias due to missing observations, we will carefully document reasons for missing data. We will use this information to manage and correct for potential bias that could arise from informative study drop-out.

C12b. Measurement error: to account for measurement error we will put a structure into the R-side matrix of the GLMM. Given that deviating from the diagonal R matrix adds complexity to model fitting, we will try AR(1) and CS covariance structures to parsimoniously account for measurement error[65].

C12c. Multiple outcome variables. We acknowledge concern about inflation of Type I error. This concern must be balanced with the need to avoid overly conservative Type I (false positive) error rates that may result in excessively high Type II (false negative) error rates. As a standard method of balancing these concerns, we will use multivariate GLMM[64,66] to jointly model the correlated outcomes and study the relationship between the multiple outcomes and treatment. For each outcome (Yij), we consider the model, $E(Y_{ijk} | X_{ij}(t), Z_{ij}) = g^{-1}(X_{ij}(t)\beta_k + Z_i b_{ik})$, where g is a monotone link function, $b_{ik} \sim N(O, G_k)$ and Yij is the response for the ith subject at the jth time with ni (ni-1,…,10) repeated measurements, Xij and Zij represent vectors of fixed and random effect covariates, respectively, and G is the covariance matrix for bi. If bi is a vector of random intercept and slope, it indicates that there is natural heterogeneity among individuals in both their baseline level and changes in the expected outcomes over time[65,67]. In addition to the variability in the random effects, a diagonal R-side covariance matrix of the form 2In is included to account for random error. When the random error is suspected to have more measurement error than what is typically expected then we will use AR(1) R-side covariance matrix[68]. Additional

sensitivity analysis will be made to balance between model complexity and reduction in bias. We will use Poisson distribution with a log-link for count outcomes (e.g., # drinking/drug use days, # days SUD treatment, # days structured work activities), Binomial distribution with logit-link for binary outcomes (e.g. attended treatment/did not attend treatment) and Gaussian distribution with identity-link for continuous outcomes (e.g., standard drinks). When we suspect over-dispersion in the count models that is beyond what is assumed by the Poisson GLMM then we will use Negative Binomial distribution. To deal with zero inflation, we will use zero-inflated Poisson (ZIP) and negative binomial (ZINB) models. For multiple outcomes, we will use a joint model based on linking the GLMM models for each outcome type by assuming a joint statistical distribution for the random coefficients (intercept and slopes). Let Yijk be the response from the kth outcome for subject i at occasion or time j (i=1, …n; k=1, …K; j=1,2,…,ni). The GLMM can be given as, $E(Y_{ijk} | X_{ij}(t), Z_{ij}) = g^{-1}(X_{ij}(t)\beta_k + Z_i b_{ik})$, where $b_{ik} \sim N(O, G_k)$ and X_i and Z_i and Zi represent vectors of fixed and random effect covariates, respectively, and Gk is the covariance matrix for bik. We will use a random coefficient model with shared random intercept and random slope for each outcome. The resulting 'over all' covariance matrix (D) from this model will provide standard error estimates that account for correlation among the multiple outcomes. A key assumption for these models is conditional independence where the responses are independent given the random effects[65,67].These models can be fitted using Proc NLMIXED or GLIMMIX in SAS v9.3.

C12d. <u>Analysis plan for Clinical, Social, and Quality of Life outcomes (Specific AIM I; Hypotheses 1 through 4):</u> To evaluate the relative efficacy of (a) GMI and (b) CT on (a) <u>five health services outcomes</u> (i) substance use (ii) treatment engagement, (iii) psychosocial integration (e.g., social support, community participation), (iv) quality of life/psychiatric indices, and (v) # of days engaging in structured/productive work activities. The longitudinal trajectory of efficacy outcomes will be compared using the GLMM approach, which accommodates missing at random (MAR) data and a wide range of data types/distributional assumptions: counts (e.g., # AA sessions, # times talking with AA sponsor, # substance abuse treatment sessions attended); dichotomous (e.g., abstinent/not abstinent), proportions (proportion days not drinking alcohol or using illegal drugs), and ordinal (e.g. CPOSS-VA, QOLS). When the number of zeroes is in excess of what is normally expected from a poisson model, we will fit GLMM to accommodate zero-inflation. We will use negative binomial regression to deal with over dispersion. Logit link for dichotomous outcomes, log link for count outcomes will be considered. The basic modeling procedure involves using the longitudinal outcome measurements within each of the domains separately as the dependent (outcome) variable, with intervention group (fixed effect), time (random effect), and time by intervention as the primary independent variable*s*. In further multivariable modeling, additional covariables (as appropriate for a given dependent variable) will be added to the basic model to adjust for potential confounding effect of these variables. GLMM accommodates both fixed and time-varying covariates. For example, for the treatment engagement variable, the # of AA sessions measured monthly for 6 months will be an outcome variable, intervention group (GMI, CT), time, and time X intervention will be the primary independent variables in the basic (unadjusted) model, and psychiatric comorbidity (number and severity), age, race, and gender will be added in the subsequent (adjusted) model to adjust for the possible confounding effect of these variables. Unadjusted and covariate-adjusted least squares means for each outcome variable will be compared at the primary time point (month 1) and at intermediate secondary time points (months 3 and 6) using appropriate model contrasts and the Tukey-Kramer adjustment for multiple comparisons for the secondary time points. These contrast comparisons, along with corresponding 95% CI, will provide estimates of the difference in outcome means (effect sizes) for the hypothesized comparisons. For longitudinal dichotomous outcomes (e.g., maintenance of sobriety), we will compare unadjusted and covariate-adjusted proportions across the longitudinal trajectory (at 1, 3 and 6 months) for GMI and CT. For the end-of-active treatment time point, this analysis is equivalent to a logistic regression analysis.

C12e. <u>Analysis Plan for Cost Estimation of Intervention (Specific Aim III):</u>

Descriptive statistics will be used to describe the estimated cost of intervention for Veterans living at various distances from the VAMC where care is provided. Differences in mean VA costs for GMI vs. CT will be estimated. *We will employ GLMM as for the clinical outcomes, to estimate the independent association of Veteran demographic and clinical factors with cost as well as test for sensitivity of cost results across clinical outcomes and workload[63-64].* Research economists (if they have access to PHI) will evaluate VINCI health services utilization and cost data up to one year post intervention for all participants in the study. To be consistent with this time period as well as to provide greater methodological rigor to the study, we would like to evaluate a comparison group of Veterans similar to study participants in that they are deemed homeless or have used the homeless clinic.

C13. Dissemination/Implementation Plan

Given positive findings from this study, future dissemination/implementation efforts of GMI within VISN 7 may positively impact a substantial number of Veterans with SUDs in VA housing. Findings from this study will be of interest to administrators and VA mental health professionals in local (e.g., Charleston VAMC), regional, (e.g., VISN 7) and national offices, particularly the National Center on Homelessness among Veterans (NCHAV), VA housing services, Veterans Homelessness Prevention Demonstration Program (VHPD), Mental Illness Research, Education, and Clinical Centers (MIRECC), and Supportive Services for Veteran Families.

C.13a. A systematic plan of five dissemination activities to impact these agencies will involve:

1) Presentations, courses, seminars, invited grand rounds, and workshops describing project results and demonstrating GMI application in VA housing programs starting in Columbia, Alabama, Atlanta, Birmingham, and Tuscaloosa; **(2)** Synthesizing and summarizing data for distribution to relevant stakeholder groups (e.g., NCCHV, VA's within the VISN) using descriptive materials outlining the study and its objectives in the form of white papers and brochures. In-person and Live Meeting presentations will be conducted for NCCHV, HUD-VASH, GPD, MIRECC, and VHPD with the coordination and direction of Patricia Bradford, VISN 7 Network Homeless Coordinator of the VA Southeast Network, Keith Harris, Ph.D. National Director of VHA Clinical Operations of the Homeless Program Office; and Stefan Kertesz, MD, HUD-VASH research investigator at Birmingham VAMC. Other presentations and workshops will occur at scientific conferences (e.g., APA, ABCT, CPDD, VA Housing First meetings); **(3)** Publication of study results and brief executive summaries in professional and non-professional outlets (e.g., psychiatric, psychological, medical journals, VA newsletters). The PI will draft publication guidelines within the first three months of the study. An additional responsibility will be development of a standardized dissemination "package" when the primary manuscript is accepted for publication. Such a package might include a model cover letter or memo, a press release, and reprints of the primary manuscript and secondary manuscripts already published; **(4)** Contacting and informing the newly created VA Evidence Based Practice EBP representatives in order to 'get the word out' to practitioners. Nationwide, 3/8 support of a senior clinician at every VAMC has been designated by Central Office for this program. Representatives attend a national conference and work within their VA to enhance dissemination of evidence based clinical strategies; **(5)** A social marketing plan will be assembled by the PI and Patricia Bradford for launching the seven structured implementation activities below.

C.13b. A structured plan of seven implementation activities will involve: **(1)** Reviewing data from the study and discussing the implications of study findings among members of the project team (Drs. Santa Ana, Kertesz, Rosenheck, and Ms. Bradford) with reference to immediate relevance to the Housing First initiative. GMI may serve as a key tool and may become a permanent part of the dissemination package within VA housing, designated as an in initial 'wraparound' treatment service in the newly adopted Housing First initiative within VA; **(2)** In their VISN level roles, Dr. Santa Ana and Ms. Bradford will set up consultation with Dr. Keith Harris, National Director of VHA Clinical Operations of the Homeless Program Office, Mr. Jeffrey Quarles, National Director GPD, and Mr. Vince Kane, Director of NCCHV and for support with the aim of discussing dissemination throughout VISN 7 and to create a plan of promulgating directives and implementation activities for moving GMI forward; **(3)** As the Evidence-Based Training Program Coordinator in VISN 7 and based on the findings of her implementation research, Dr. Santa Ana will develop a set of standard operating procedures necessary for creating a successful GMI program, consisting of training tasks, intervention location, patient recruitment tasks, program/administrative support requirements, and treatment monitoring tasks; **(4)** SOP procedures will be disseminated with the assistance of Ms. Bradford, Dr. Harris, and Mr. Quarles in each HUD-VASH/GPD program, giving Dr. Santa Ana a VISN-wide impact with respect to training and GMI adoption; **(5)** Dr. Santa Ana will conduct a series of VISN 7 VA housing site visits starting in Columbia, Alabama, Atlanta, Birmingham, and Tuscaloosa to evaluate GMI implementation needs, conduct organizational readiness/attitude belief surveys and perceptions of the GMI program to diagnose potential obstacles as necessary, evaluate feasibility, and identify staff/MI leads to enhance program support (these data will be used in a QUERI SDP proposal-see below); **(6)** These five tasks will support a GMI VISN 7 initiative directed by Dr. Santa Ana that moves beyond Charleston so that a GMI VA housing program is operating in other locations within the VISN. This will involve a) Staff agreement/adoption; b) GMI staff training; c) identifying MI 'site' leads; and d) disseminating standard operating procedures; **(7)** A Service Directed Project (SDP) will be sought as a potential 'next step' through the Quality Enhancement Research Initiative (QUERI), after evidence for GMI is shown to be substantial, for providing implementation support for translating research into practice.

Table 6. PROJECT MANAGEMENT PLAN

	Task Description	PI	Project Staff	Co-I's
Study Design/Set up	Coordinate GMI/CT training	X	X	
	Coordinate IRB submission	X	X	
	Update/Refine GMI protocol/feedback report	X		SM
	Assemble study team	X		
	Coordinate study design	X	X	
	Assemble project documents (assessments)	X	X	
	Oversee patient recruitment, consent, retention	X	X	
	Implementation, Formative, Process, & Summative Evaluation	X	X	
	Statistical Analysis	X	X	CP, MG
Data Management & Programming	Set up project databases	X		MG, RR, LD
	Oversee/conduct data cleaning/data checks	X	X	
	Cost estimation	X	X	
	Track Formative, Process, and Summative Evaluation	X		RR, LD
	Update therapist fidelity protocol	X		CP
	Rate GMI/CT sessions	X	X	SM
	Oversee therapist adherence/competence data	X		SM
Dissemination	Oversee development of study materials	X		SM
	Oversee publication of study results in professional/ non-professional outlets	X		ALL-Co-I
	Oversee development of presentations (invited grand rounds, meetings, workshops) describing project results	X		ALL-Co-I
Project meetings	Lead	X		ALL-Co-I
Project budget	Ongoing budget review	X		

Table 7. PROJECT TIMELINE

Months	Year 1 *1-6*	Year 1 *7-12*	Year 2 *1-6*	Year 2 *7-12*	Year 3 *1-6*	Year 3 *7-12*	Year 4 *1-6*	Year 4 *7-12*
Submit IRB protocol for full review	X							
Datstat refines computerized GMI PFR/troubleshoot	X							
Update/refine GMI treatment manual	X							
Hire project coordinator and research assistant	X							
Hire study therapists	X							
Compile study assessments & process measures	X							
Co-I Bob Rosenheck meet for cost estimation	X	X-IP	X	X	X	X	X-IP	
Conduct Veteran &staff stakeholder focus groups	X						X	
Develop & conduct GMI Training for therapists	X							
Establish/conduct therapist fidelity monitoring	X	X	X	X	X	X		
Develop quantitative process assessments & monitoring	X		X		X		X	
Participant consenting/recruitment/enrollment		X	X	X	X	X		
Establish project database	X							
Conduct participant F/U assessments		X	X	X	X	X	X	
Conduct data entry and data checks		X	X	X	X	X	X	
Update GMI adherence/competence manual		X						
Train raters on therapist adherence/competence					X			
Raters rate therapy tapes using MITI					X	X		
Meet with economist for cost estimation	X	X	X	X	X	X	X	
Meet with statistician for analyses		X		X		X	X	X
Statistical analyses for main outcomes							X	X
Manuscript preparation/submission							X	X

*IP = In Person

PROTECTION OF HUMAN PARTICIPANTS

1. Risks to the Participants

A. Human Participants Involvement and Characteristics

The PI and Co-Is have all completed the University of Miami computer-based CITI Human Participants Research Education Course. One hundred eighty-six (186) ethnically/racially diverse male and female Veterans with current alcohol/drug dependence or abuse will be recruited over a 30-month period. Participants with a non-substance related major DSM-IV-TR Axis I disorder (e.g., major depressive disorder, bipolar disorder, anxiety disorder, schizophrenia, schizoaffective disorder, psychotic disorder) will be eligible.

Additional inclusion and exclusion criteria are described below.

Inclusion Criteria

1) Men and women Veterans currently in HUD-VASH or GPD, newly entering the program but not yet housed, or Veterans on the HUD-VASH interest (wait) list.

2) Able to comprehend English.

3) Meets DSM-V criteria for a current substance use disorder and have used substances in the 30 days prior to treatment entry. Participants on medications targeting their substance use must be stabilized on medications for at least 2 weeks before therapy initiation.

4) May meet criteria a mood, anxiety or other psychiatric disorder. Participants on maintenance medications for a mood or anxiety disorder must be stabilized on medications for at least 2 weeks before therapy initiation.

5) Able to adequately provide informed consent and function at an intellectual level sufficient to allow accurate completion of all assessment instruments.

6) Willing to commit to 4 group therapy sessions, baseline, 1, 3, and 6 month follow-up assessments.

Exclusion Criteria

1) Active suicidal or homicidal ideation with a plan as this is likely to require hospitalization or other interventions that could interfere with study participation.

2) Unstable psychiatric condition that is likely to require hospitalization or other interventions that would interfere with study participation.

3) Unstable medical condition or one that may require hospitalization during the course of the study.

B. Sources of Materials

1. Research material obtained from individual participants includes self-report questionnaires, structured interviews with study personnel, taped therapy sessions as well urine and breathalyzer samples.

2. The research material will be obtained specifically for research purposes. Written research material obtained will be stored in a locked file cabinet in an office that is locked when not in use. The master list of participants linking study numbers to any source identifying information will be in a separate locked file cabinet at the Charleston VAMC in the PI's office (Room A562a). Urine samples will be discarded after results are documented.

3. Therapy sessions will be digitally audio-recorded to be used for supervision and adherence monitoring. They will be transferred electronically and stored behind the VA firewall and accessible only to project staff.

C. Potential Risks

Risks to the patients include feeling distress being interviewed regarding substance use and other sensitive information, adverse events related to the study intervention (see adverse event definitions below) and risk of loss of confidentiality regarding the information obtained during the assessment and follow-ups and taped therapy sessions. Potential psychological risk of the treatment includes exacerbations of distress and increase in substance use during the assessment and/or treatment sessions.

2. Adequacy for Protection Against Risk and Harm to Participants

A. Recruitment and Informed Consent

Participants will be recruited from the Charleston (VAMC) HUD-VASH and GPD housing programs. Housing or project staff (Note: The PI, Dr. Santa Ana, works in the housing program and she is considered housing staff) will invite patients to inform them about the study and elicit interest. Interested potential participants will be screened for major inclusion/exclusion criteria including substance use and psychiatric/health/medication status. Prior to any study procedures being performed, the Institutional Review Board (IRB) approved informed consent will be obtained by research staff trained in informed consent procedures. Informed consent will be collected at the study research offices, in a private and interruption-free environment. Explanation of the informed consent document will include a detailed description of the study in easy to understand detail with the participant, along with statements regarding participants' rights to withdraw from the procedure at any time without consequences. The participant will be asked to read the document and if he or she has any questions, they will be answered prior to participant signature. Consent will be documented by the date and signature of the participant on an informed consent agreement and by the date and signature of the individual obtaining the consent. A HIPAA authorization form will also be signed, and copies of both documents will be provided to the participant. Potential participants may decide to discuss participation with their families and/or significant others prior to making a decision to sign consent.

B. Protection against Risk

All investigators and project personnel have completed a certified program of instruction in the protection of human participants in research, the University of Miami CITI course. These courses on the responsible conduct of research and the protection of human research participants will be completed on a regular basis, in compliance with MUSC institutional regulations. All research activity, informed consents and continuing reviews will be reviewed by MUSC's IRB in compliance with 45CFR46 before the research is started and continuing review will occur annually. The research staff will ensure that all information needed for the continuing review is at the IRB in accordance with IRB requirements.

We will take careful precautions to maintain confidentiality for all participants, using procedures we have used with similar previous studies. All data will be stored in a confidential manner (i.e., in locked files in the Study Coordinator's research office and behind the VA computerized firewall) so as to protect the confidentiality of participant information. Access to research records (paper and computerized) will be restricted to the project staff. Specifically, access to de-identified study data will be limited to named project investigators, the Study Coordinator and MUSC IRB or R&D audit personnel. Binders with study data will have a study number that will be kept locked separately from any source documents with identifying information. The master list of participants linking study numbers to any source identifying information will be kept in a separate locked file cabinet in the PI's office at the Charleston VAMC. When study results are published or presented, only aggregate reports of the results will be used and participants' identity will not be revealed. All analyses will be conducted on de-identified data only.

Therapy sessions will be digitally audio-recorded to be used for therapist supervision and adherence monitoring. They will be transferred electronically and stored behind the VA firewall and accessible only to project staff.

Exclusion criteria are crafted to exclude potential participants at higher risk for adverse effects, including those with co-occurring medical or psychiatric disorders where they may be more likely not to benefit from the intervention and/or to be hospitalized during the course of the study. The informed consent document specifically reviews potential psychological distress as a potential outcome of participation.

Measures to avoid potential risk associated with psychological distress/substance use include exposure to the intervention that includes non-judgmental therapist feedback, imparting autonomy (e.g., participants are free to decide what they want to do about their substance use), and reduction of substance use through enhancing participant motivational change talk. Additional measures include informing participants that they are free to terminate treatment sessions at any time. Risks associated with assessment include the possibility that participants might be upset by questions pertaining to their emotional functioning. Some participants might be offended by detailed questions about health status and impairment. Our past research suggests that data collection using many of these measures can be conducted without undue psychological distress or exacerbation

of symptoms among adult participants. This experience includes research with younger and older adult Veterans, victims of violence, and substance abusing individuals asking questions about similar topics with general population samples.

Social risks are present if another person or parties observe participants attending treatment or learn by other means of participants receiving treatment. Participants will not be overtly identified as research participants or participants for psychological intervention.

In the event participants experience extreme psychological distress secondary to participation, they will be encouraged to talk with the Principal Investigator (PI) or the Co-I's. In addition, they will have access to the VAMC treatment services. Any such adverse effects noted by any project personnel in response, or in potential response to any project intervention, assessment protocol, or study involvement will be immediately reported to the PI and Co-I's. Participants will also be given the PI's name and telephone number and the Study Coordinator's contact information. Moreover, if research or clinical staff believes that a participant is significantly distressed by participation, the PI will be notified and will contact the participant to assess distress and assure participant safety. If called by participants, the PI will attempt to address all participant concerns and if indicated, set up an alternate referral for counseling for those who desire it from outside the project.

If at any point during the assessment, treatment or follow-up period, participants are in need of medical management, psychiatric consultation or psychiatric hospitalization, they will be evaluated and if indicated, referred to a more intensive level of treatment. If a participant becomes suicidal, emergency psychiatric assessment will be arranged. The participant will be closely monitored clinically until they are no longer suicidal or an appropriate safety plan is in place. A procedure for clinical deterioration has been established based upon our experience with previous studies. Therapists will be instructed to use their best clinical judgment regarding emergencies and inform the PI, Co-I's or PC as soon as possible. In addition to relying on clinical judgment on the part of the treating therapists(s) who are experienced with this population, substance use, and psychiatric indices will also be monitored at follow-ups (TLFB, BSI) in order to detect any symptom worsening requiring further evaluation. Additionally, participants are advised to observe any signs of worsening substance use, depression and anxiety symptoms and to discuss these with their therapist or other project staff. If in the clinical judgment of the therapist in collaboration with the PI/Co-I's, it is determined that the participant symptoms are worsening at any point during study participation, appropriate referrals will be made. These decisions will be dealt with in training and supervision of project staff and will be monitored carefully.

Patients will be terminated from the study and referred for more intensive treatment if there are:

a. Increases in alcohol or drug use leading to the need for a more intensive level of care (i.e., medical detoxification, inpatient).

b. Active suicidal or homicidal ideation.

c. Inability to manage psychiatric symptoms within the inclusion/exclusion criteria of the study (i.e., need for the initiation of maintenance psychotropic medications; development of psychosis). If it is determined, based on clinical criteria, that a participant needs to be started on maintenance medications for anxiety, mood or psychotic symptoms during the course of the study, they will be discontinued from the treatment trial.

At the VAMC, there is a well-established protocol for emergency psychiatric evaluation, crisis intervention and/or psychiatric hospitalization for suicidal, homicidal, psychotic or other acutely distressed patients. Immediately on detection of these needs, the PC, RA, or research therapist will contact the PI or on-site Co-I's to review the patient's situation. If appropriate, PI or on-site Co-I's will personally evaluate the patient. During evenings or weekends, the PI/Co-I's will be on call for emergencies. At these times, acutely distressed patients will be instructed to go to the psychiatric emergency room for evaluation by a psychiatric resident. The PI/Co-I's will notify the resident in advance of the patient's situation. Acute psychiatric hospitalization is available for emergencies.

3. Potential Benefits of Proposed Research to Participants and Others/ Importance of Knowledge to be Gained

The benefit to participants is a potential reduction in substance use and related problems. In addition, they may benefit from the cognitive realization that, through their volunteer efforts, they are helping to advance the state of knowledge as it applies to mental health care for substance use disorders. The proposed study has the potential benefit of developing an effective intervention for substance use disorders delivered in group format. The study will help inform critical questions about rehabilitation options for individuals with substance use disorders. Such a finding would have the potential benefit of (1) improving long-term outcomes for Veterans with substance use disorders and (2) reducing functional impairment and related health care costs associated with substance use disorders in Veterans.

4. Inclusion of Women and Minorities

It is estimated the study sample will be approximately 46% African American (AA),15% other minorities, and 11% female, as this represents the proportion of AA, other minorities, and females in VA housing within the VISN, according to demographic records extracted by the VISN 7 Deputy Network Homeless Coordinator.

5. Inclusion of Children

Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. (VHA Handbook 1200.05, 3. i.). Individuals above the age of 18 will be admitted to the study. The intervention has not been tested in children less than 18 years of age. The reason children under the age of 18 will not be included in this study because the focus of this preliminary investigation is to determine the effectiveness of the intervention in adult men and women with substance use disorders.

6. Data Monitoring and Safety Plan

Data Management and Analysis: A data analysis plan is outlined in the Data Analysis section. Briefly, the primary outcomes are (Hypothesis 1): Substance use (e.g. standard drinks, peak standard drink day, # drinking days, drinks per drinking day, binge drinking days, # illicit drug use days, etc); and (b) Treatment engagement (e.g. number of substance abuse/mental health treatment sessions attended, # AA sessions attended, # AA sponsor contacts).

Secondary outcome measures will be: (c) Psychosocial adjustment (Hypothesis 2; social support, community participation); (d) Quality of life/psychiatric indices (Hypothesis 3; QOLS, SF-12, BSI-18); (e) Engagement in structured/productive work activities (Hypothesis 4; percent of days each month engaged in work or volunteer activities); and (c) Process measures (CPOSS, HAQ) will be assessed at post-treatment (1-month follow up).

The longitudinal trajectory of efficacy outcomes will be compared using the generalized linear mixed models (GLMM) approach. GLMM accommodates missing at random (MAR) data and a wide range of data types/distributional assumptions: counts (e.g., # AA sessions, # times talking with AA sponsor, # substance abuse treatment sessions attended); dichotomous (e.g., abstinent/not abstinent), proportions (proportion days not drinking alcohol or using illegal drugs), ordinal (e.g. CPOSS-VA, QOLS). When the number of zeroes is in excess of what is normally expected from a poisson model, we will fit GLMM that can accommodate zero-inflation. We will use negative binomial regression to deal with over dispersion. Unadjusted and least squares adjusted means from the GLMM contrast comparisons, along with corresponding 95% CI, will provide estimates of the difference in outcome means (effect sizes) for the hypothesized comparisons. For longitudinal dichotomous outcomes (e.g., maintenance of sobriety), we will compare unadjusted and covariate-adjusted proportions across the longitudinal trajectory (at 1, 3 and 6 months) for the intervention groups using GLMM for a binary outcome. For the end-of-active treatment time point, this analysis is equivalent to a logistic regression analysis.

Quality Assurance*:* Data quality will be monitored by random inspection of the completed forms by research staff and any irregularities or problems detected will be discussed with the PI. Therapists will receive standardized

training and adherence will be monitored using audiotapes and individual supervision. If therapy drift is observed the therapists will be re-trained.

DSM Plan and Administration: The research assistant and project coordinator will be responsible for data collection, entry and checking. The research staff will examine data for errors or gaps on the day of collection, and immediately make the correction. The PC will be responsible for conducting and supervising coding, entry, cleaning and processing of raw data. All paper-based assessments will be entered into a standard software package, using double data entry. Completed assessments will be entered within 1 week after the information has been collected from the participant. As a result of the double data entry, two analyzable databases will be created. The validity of the databases will be checked by comparing the databases, and macro programs will be written to check the data for logical consistency and values out of possible range. Quarterly database management and data integrity audits will be conducted.

The PI will be responsible for monitoring the study. The PI will regularly examine the outcomes database for missing data, unexpected distributions or responses, and outliers.

Regulatory Issues: All unexpected Adverse Events (AEs) will be reported to the MUSC Committee on Human Research within 48-business hours. Serious AEs (SAEs) will be reported within 24-business hours. Follow-up of all unexpected and serious AEs will also be reported. All AEs are reviewed weekly by the PI, bi-annually by the Data Safety Monitoring Board (DSMB) and yearly by the IRB. Any significant actions taken by the local IRB and protocol changes will be reported to the federal funding agency. AEs and SAEs occurring during the course of the trial will be collected, documented, and reported in accordance with protocol and IRB reporting requirements. All research staff involved with adverse event reporting will receive general and protocol specific AE/SAE training including identification, assessment and evaluation, and documentation and reporting. The research assistant, Study Coordinator, or Project Therapists will identify any potential AEs during the course of the study from participant self-report and administration of assessments and procedures. This information will be provided to the PI, Co-I's (MD, PhD), who will be responsible for AE/SAE assessment and evaluation including a determination of seriousness and study relatedness.

A. Adverse Events Reporting and Documentation

Adverse events will be monitored throughout the study and all events will be followed to resolution or stabilization. All serious adverse events will be collected and reported immediately to the IRB. If complete information is not available when the initial 24-hour SAE report is disseminated, follow-up information will be gathered to enable a complete assessment and outcome of the event. This information may include hospital discharge records, autopsy reports, clinic records, etc. The research staff will attach copies of source documents to the SAE report for review by IRB.

We will report adverse events to the MUSC IRB online as soon as possible, but no later than 10 working days after the investigator first learns of the event. The MUSC IRB AE reporting requirements are as follows: All deaths that occur during the study or 30 days post termination from the study are required to be reported as adverse events even if they are expected or unrelated. Other adverse events are reportable to the MUSC IRB if the AE is unexpected AND related or possibly related AND serious or more prevalent than expected. All three criteria must be met for an AE to be reported to the MUSC IRB. The IRB definition of unexpected is that the AE is not identified in nature, severity or frequency in the current protocol, informed consent, investigator brochure or with other current risk information. The definition of related is that there is a reasonable possibility that the adverse event may have been caused by the intervention. Reportable AEs are reviewed by the IRB Chair and reported to the IRB Board at the next meeting.

Serious Adverse Events: Each Adverse Event will be categorized as serious or not. Serious adverse events are defined as any fatal, life-threatening, permanently and/or substantially disabling condition; or one that is a congenital anomaly, requires an initial hospitalization or prolongs a hospitalization, or is an event which requires intervention to prevent permanent impairment or damage. The PI, Co-I (Ph.D., MD) should be consulted if questions arise as to whether an AE should be categorized as serious. Initial notification of an SAE to the IRB is

to be followed by submission of the Serious Adverse Event Form within 24 hours. Failure to comply with reporting requirements can result in serious negative consequences, including criminal and/or civil penalties.

Trial Safety: The potential risks and benefits and methods to minimize these risks are outlined above. Protocols for reported AEs and SAEs are outlined above. All unexpected AE and SAEs will be monitored until resolved. A detailed summary of all AEs will be prepared weekly by the research staff. At the weekly team meetings (or before if urgent), the research staff will report any premonitory symptoms of clinical deterioration.