NIDA CTN Protocol 0031

Stimulant Abuser Groups to Engage in 12-Step (STAGE-12): Evaluation of a Combined Individual-Group Intervention to Reduce Stimulant and Other Drug Use by Increasing 12-Step Involvement

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1.0 LIST OF ABBREVIATIONS

AA	Alcoholics Anonymous
AE	Adverse Event
ASI	Addiction Severity Index
CA	Cocaine Anonymous
CBT	Cognitive-Behavioral Therapy
CMA	Crystal Meth Anonymous
CoC	Certificate of Confidentiality
CRF	Case Report Form
CSAT	Center for Substance Abuse Treatment
CSS	Clinician and Supervisor Survey
CT	Cognitive Therapy
CTN	Clinical Trials Network
CTP	Community Treatment Program
DVA	Department of Veterans Affairs
DSMB	Data and Safety Monitoring Board
FWA	Federal-Wide Assurance
GCP	Good Clinical Practice
GDC	Group Drug Counseling
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Conference on Harmonization
IDC	Individual Drug Counseling
IOP	Intensive Outpatient Program
IRB	Institutional Review Board
ITT	Intent to Treat
MATCH	Matching Alcoholism Treatment to Client Heterogeneity
MET	Motivational Enhancement Therapy
NA	Narcotics Anonymous
NCCTS	NIDA Cocaine Collaborative Treatment Study
NIDA	National Institute on Drug Abuse
OPT	Outpatient Psychosocial Treatment
PI	Principal Investigator
RA	Research Assistant

SAE	Serious Adverse Event
SE	Supportive-Expressive Therapy
SECA	Systematic Encouragement and Community Access
SEQ-P	Self-efficacy Questionnaire – Patient version
SOCRATES	Stages of Change Readiness and Treatment Eagerness Scale
STAGE-12	Stimulant Abuser Groups to Engage in 12-Step
SUD	Substance Use Disorders
SUSS	Short Understanding of Substance Abuse Scale
TAU	Treatment-as-Usual
TSF	Twelve-Step Facilitation Therapy
TSR	Treatment Services Review
SHAQ	Self-Help Activities Questionnaire

2.0 STUDY SYNOPSIS

STUDY OBJECTIVES: The primary objective of this protocol is to evaluate the degree to which a combined group and individual 12-Step facilitative intervention, Stimulant Abuser Groups to Engage in 12-Step (STAGE-12), improves substance-related outcomes compared to treatment as usual (TAU) without STAGE-12 among stimulant abusers. For this protocol, STAGE-12 will be integrated into treatment as usual. The primary objective is to evaluate reduction in percent of days of stimulant use as measured by self-report. Secondary objectives include evaluating reduction in percent days of use of other substances, the degree to which STAGE-12 increases involvement in 12-step activities and attendance at 12-step meetings, and the extent to which such 12-step involvement and meeting attendance mediate substance use outcomes.

STUDY DESIGN: This is a randomized, 2-group design comparing STAGE-12 integrated into TAU (STAGE-12) to TAU without STAGE-12 (TAU) for stimulant abusers receiving formal substance abuse treatment in participating community-based treatment programs (CTPs). For the purposes of this study, the STAGE-12 sessions will replace 8 sessions (3 individual and 5 group sessions) from TAU during the course of the intervention period, which may range from 5 up to 8 weeks. Eligible, consented stimulant abusers entering treatment at participating CTPs will be assigned randomly within site through a centralized randomization procedure to STAGE-12 or TAU and will be stratified by participants' court-mandated for treatment versus not court-mandated. Assessments will be conducted as indicated in Table 1 at baseline, weeks 2, 4, and 8. Follow-up assessment will occur at 3 and 6 months after randomization.

STUDY POPULATION: A total of approximately 400 stimulant users seeking formal treatment, recruited from approximately 10 CTPs, will be randomized to STAGE-12 or TAU. Each CTP will enroll approximately 40-50 participants, with a target of 20-25 per CTP in each treatment condition. Eligible CTPs and counselors will be assessed to characterize their general treatment philosophy/orientation.

ELIGIBILITY CRITERIA: Participants will be individuals 18 years of age or older who are seeking outpatient treatment for stimulant abuse or dependence, have used stimulants over the previous 60 days, have a current diagnosis of stimulant abuse or dependence, and are willing to participate in the protocol (e.g., to be randomized to treatment, be contacted for follow-up assessment, to have their sessions audio-taped). Individuals who are not sufficiently medically or psychiatrically stable to participate in outpatient treatment will be excluded. Individuals who have pending legal actions that would inhibit their participation in the study, or who, in the clinical judgment of CTP staff, are in need of detoxification from opiates will also be ineligible.

TREATMENTS: The STAGE-12 intervention will consist of a combination of five group and three individual sessions. The five group sessions will be taken from the Project MATCH Twelve Step Facilitation manual as modified for use with drug abusers (Baker 1998; Carroll, Nich et al. 1998) and adapted for delivery in a group format (Brown, Seraganian et al. 2002; Brown, Seraganian et al. 2002). The group sessions will be augmented by three individual sessions derived from the introductory and termination sessions from the TSF manual and incorporating elements of the brief intensive 12-step referral procedure developed by Timko and colleagues (Timko, DeBenedetti et al. 2006). The group and individual sessions focus on increasing both understanding 12-step principles and attending 12-step meetings and engaging in 12-step activities. The Twelve-Step Facilitation (TSF)-based group sessions utilize those sessions defined as "core" topics. These focus on the principles of Steps 1–3, such as surrender and acceptance, as well as changing one's lifestyle and getting active in 12-step programs. The individual sessions focus on and reinforce the theme of getting active in 12-step and facilitate this by arranging for participants to connect with

volunteers from a local 12-step group who will take them to a meeting and serve as a temporary sponsor. The group and individual sessions thus complement each other. The STAGE-12 group sessions emphasize the need to gain an understanding and acceptance of the concepts and principles of 12-step philosophy. Correspondingly, the intensive referral intervention emphasizes and facilitates getting actively involved, through behaviors such as attending 12-step meetings, reading 12-step literature, and getting a sponsor. Participants assigned to the TAU condition will be offered the treatment typically provided by the CTP, which may include more passive procedures for referring clients to 12-step meetings. Counselors selected to deliver the STAGE-12 intervention will be chosen randomly from a pool of eligible counselors within CTPs who volunteer to participate.

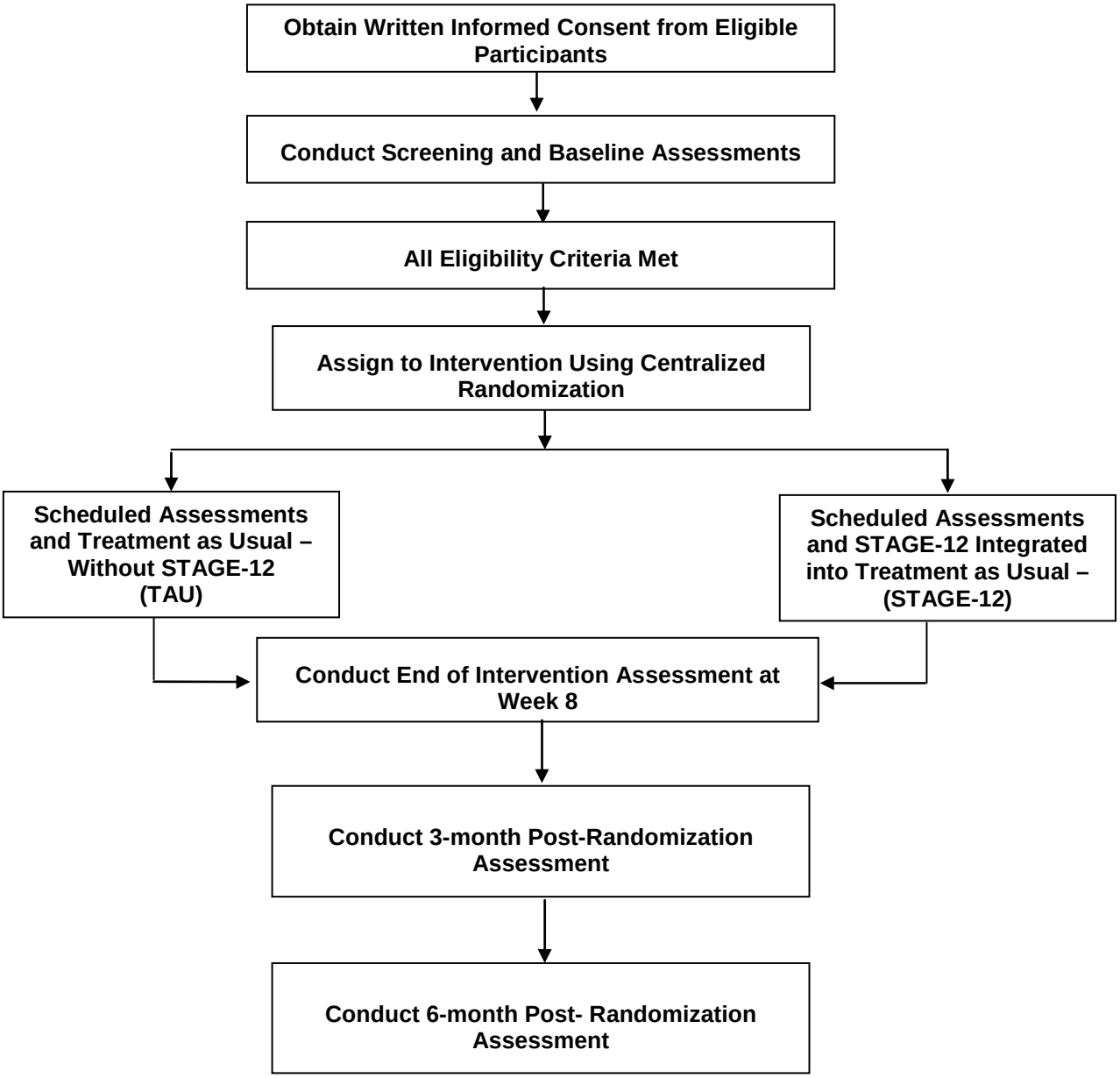
SAFETY ASSESSMENT: All participants will provide informed consent prior to their involvement in the protocol. There will be ongoing monitoring of adverse events, with participants having an opportunity at each research visit point to indicate whether they have experienced any adverse events.

OUTCOME ASSESSMENTS: The primary outcome measure will be percent of days of stimulant use based on a substance use calendar. Secondary substance use outcome measures will include percent of days of use of drugs other than stimulants, urine toxicology results, and ASI Alcohol and Drug Composite scores. Additional secondary outcomes will include measures of involvement in 12-step activities (e.g. reading 12-step literature, helping set up for a meeting, getting a sponsor), 12-step meeting attendance, and 12-step beliefs. These primary and secondary measures will be collected as indicated in Table 1.

ANALYSIS: The primary and secondary outcome variables will be analyzed using appropriate statistical methods for an intent-to-treat (ITT) population.

REGULATORY ISSUES: The trial will be conducted in compliance with protocol, ICH Good Clinical Practice (GCP) guidelines, and applicable regulatory requirements.

Figure 1: STAGE-12 Protocol Study Schema



3.0 BACKGROUND AND SIGNIFICANCE

3.1 Role of 12-Step Self-Help Groups in Substance Abuse Treatment and Recovery

Twelve-step and mutual/self-help groups represent an important, readily available, and pervasive resource in substance abuse recovery, whether associated with formal treatment or not (Room and Greenfield 1993; Humphreys 1999; Kelly 2003). Substance abusers can become involved with 12-step groups before entering professional treatment, as part of their professional treatment, as aftercare following professional treatment, or instead of professional treatment (Fuller and Hiller-Sturmhofel 1999). These groups, which include Alcoholics Anonymous (AA), Narcotics Anonymous (NA), Cocaine Anonymous (CA), Crystal Meth Anonymous (CMA) and a number of others, are highly accessible and are available at no cost in communities throughout the world. For some substance abusers, these meetings are the only resource ever used to resolve a drinking or drug problem (Room and Greenfield 1993; Hasin and Grant 1995; Kaskutas, Weisner et al. 1997). The 12-Step philosophy has had a strong influence on the evolution of formal alcoholism treatment in the United States, primarily in the form of the Minnesota Model (Alford, Koehler et al. 1991; McElrath 1997; Stinchfield and Owen 1998). Although initiated with alcohol as its primary focus, this philosophy has also been integrated into the treatment of drug dependence, as in the Group Drug Counseling (GDC) and Individual Drug Counseling (IDC) approaches developed for treatment of cocaine addicts (Crits-Christoph, Siqueland et al. 1997; Crits-Christoph, Siqueland et al. 1999; Daley, Mercer et al. 1999; Mercer and Woody 1999). Participation in 12-step groups is also a recommended component in the Matrix Model used in the treatment of both cocaine and methamphetamine dependence (Shoptaw, Rawson et al. 1994; Rawson, Shoptaw et al. 1995; Obert, McCann et al. 2000). Many residential and outpatient substance abuse treatment programs include 12-step meetings on-site and encourage clients to become involved in community-based 12-step meetings and activities (Fuller and Hiller-Sturmhofel 1999).

The 12-step philosophy refers to a particular view of the recovery process. It emphasizes the importance of accepting addiction as a disease that can be arrested but never eliminated, enhancing individual maturity and spiritual growth, minimizing self-centeredness, and providing help to other addicted individuals (e.g., sharing recovery stories in group meetings, sponsoring new members) (Humphreys, Wing et al. 2004). Self-help groups based on this philosophy outline 12 consecutive activities, or steps, that substance abusers should achieve during the recovery process. These steps specify that substance abusers must admit their powerlessness over alcohol and drugs, take a moral inventory of themselves, admit the nature of their wrongs, make a list of individuals whom they have harmed, and make amends to those people. Involvement in such groups is meant to provide participants with support for remaining substance free, a social network (the “fellowship”) with which to affiliate, and a set of 12 guiding principles (the “steps”) to be followed in the recovery process (Kaskutas, Bond et al. 2002). Caldwell and Cutter (Caldwell and Cutter 1998) described the general guidelines for recovery based on this philosophy as the “12-step‘six pack:” don’t drink or use drugs, go to meetings, ask for help, get a sponsor, join a group, and get active.

3.2 Effectiveness / Efficacy of 12-Step Self-Help Groups

There has been an increased focus on 12-step self-help groups by clinicians, policy makers, and researchers over the recent past. Humphreys (Humphreys 1999) suggests that fiscal factors and

developments in clinical research have contributed to this increased attention. First, given recent cutbacks in funding for professional substance abuse treatment, 12-step groups are seen as an inexpensive and readily available complement to formal treatment and as a source of support following treatment (Etheridge, Craddock et al. 1999; Fiorentine 1999; Humphreys 1999; Humphreys 2003). Secondly, until recently there have been few well-controlled studies supporting the clinical effectiveness of 12-step approaches (Tonigan, Toscova et al. 1996). However, more recent efficacy and effectiveness trials provide support for the effectiveness of 12-step oriented approaches (Donovan 1999). Generally, these studies have found a positive relationship between 12-step involvement and improvement on substance use outcomes for both alcoholics and drug abusers, even over extended periods of time ranging up to 16 years (Emrick, Tonigan et al. 1993; Montgomery, Miller et al. 1995; Timko, Finney et al. 1995; Morgenstern, Labouvie et al. 1997; Project Match Research Group 1997; Watson et al., 1997; Ouimette, Moos et al. 1998; Fiorentine and Hillhouse 2000; Fiorentine and Hillhouse 2000; Weiss, Griffin et al. 2000; McKay, Merikle et al. 2001; Tonigan 2001; Kaskutas, Bond et al. 2002; Morgenstern, Bux et al. 2003; Moos and Moos 2004; Kaskutas, Ammon et al. 2005; Moos and Moos 2005; Moos and Moos 2006).

While the positive relationship between 12-step involvement and clinical outcomes is encouraging, it is not possible to infer a causal relationship from correlational findings. Three recent studies, using cross-lagged analyses of longitudinal data or structural equation modeling, have begun to elucidate the nature of this relationship. Connors, Tonigan, Miller, and the Project MATCH Research Group (Connors, Tonigan et al. 2001) found that a construct of intake symptomatology (i.e., severity of alcohol dependence, alcohol involvement, psychiatric severity, and readiness to change) predicted AA involvement (which included both meeting attendance and activities) during the first 6 months following treatment. Further, AA involvement during the first 6 months post-treatment predicted drinking outcomes during months 7-12. Drinking outcomes, however, were not predicted by intake symptomatology. This latter result helped rule out a competing hypothesis that the relationship between AA involvement and clinical outcome might rather be due to a more global construct of “good prognosis.”

McKellar, Stewart, and Humphreys (McKellar, Stewart et al. 2003) examined the predictive utility of a latent variable, AA involvement, in a structural equation model (SEM). Latent variables in SEM are hypothetical constructs that are defined by directly measured indicator variables. Four indicators defined the AA Involvement latent variable. These indicator variables, each rated on a 5-point scale with respect to the immediately preceding 3-month time frame, were: (1) number of AA meetings attended, (2) frequency of reading AA books and/or pamphlets, (3) frequency of talking to one’s AA sponsor, and (4) and the number of AA friends. The AA Involvement construct, assessed in the first year post treatment, predicted reduced drinking and alcohol-related problems in year 2. However, the level of drinking and alcohol-related problems in year 1 did not predict 12-step attendance or involvement in year 2. Two studies (Connors, Tonigan et al. 2001; McKellar, Stewart et al. 2003) controlled for levels of readiness to change, thus removing differential motivation across subjects as an explanatory factor.

Weiss et al. (Weiss, Griffin et al. 2001; Weiss, Griffin et al. 2005), in a cross-lagged analysis, found that self-help meeting attendance by individuals being treated for cocaine dependence did not predict subsequent drug use. However, active involvement in self-help activities (as opposed to meeting attendance) in a given month predicted fewer days of cocaine use in the next month. Moreover, patients who increased their involvement in self-help activities during the first three months of treatment had significantly fewer days of subsequent cocaine use and lower scores on the Addiction Severity Index (ASI) Drug Use Composite in the subsequent 3 months. Further, the best outcomes were found among those individuals who both received the 12-step oriented Individual Drug Counseling (IDC) and increased their 12-step participation in months 1-3, while

patients who neither received IDC nor increased their participation had the worst outcomes. Individuals who received IDC but did not increase their participation and those who did not receive IDC but did increase their participation had outcomes that were intermediate between these other two groups. Thus, the combined effects of being involved in a treatment approach that emphasizes 12-step involvement plus actual engagement in self-help activities was associated with the best outcomes, better than those found with either of these alone.

The conclusion drawn by McKellar, et al. (McKellar, Stewart et al. 2003) applies equally well to the results of Connors, et al. (Connors, Tonigan et al. 2001), and Weiss, et al. (Weiss, Griffin et al. 2001; Weiss, Griffin et al. 2005): "The current study increases confidence in the effectiveness of AA (and other 12-step self-help groups) by using multi-wave longitudinal data and by accounting for potential third variable influences such as motivation and psychopathology" (p. 307). These data provide increasingly supportive evidence for the hypothesis that 12-step involvement "works;" that is; increased 12-step meeting attendance and/or involvement appear to lead to a decrease in subsequent alcohol and drug use. Attendance at 12-step meetings, whether independent of formal treatment or as an adjunct to treatment, has also been found to be associated with reductions in health care costs, particularly those related to subsequent substance abuse treatment (Humphreys and Moos 1996; Humphreys and Moos 2001). Further, treatment approaches or interventions that are meant to increase engagement appear to be effective in doing so and, thus, contributing to positive substance use outcomes through their impact on increasing 12-step activities and attendance (Carroll, Nich et al. 1998; Humphreys 1999; Morgenstern, Bux et al. 2003; Weiss, Griffin et al. 2005).

3.3 12-Step Meeting Attendance and Engagement in 12-Step Activities

McKellar, et al. (McKellar, Stewart et al. 2003) questioned whether measures of meeting attendance alone would predict the same substance use outcomes and to the same extent as involvement in 12-step practices and activities (e.g., reading 12-step literature, getting a sponsor, "working" the steps, or helping set up meetings). These two variables, though related, appear to have different relationships with subsequent substance use (Weiss, Griffin et al. 2005). Involvement, rather than attendance, appears to be the better predictor of substance use outcomes: the greater the level of involvement in 12-step activities, the better the outcome. This has been found for both alcoholics (Gilbert 1991; Montgomery, Miller et al. 1995; Caldwell and Cutter 1998) and cocaine abusers (Weiss, Griffin et al. 2000; Weiss, Griffin et al. 2001; Weiss, Griffin et al. 2005). As Emrick, et al. (Emrick, Tonigan et al. 1993) concluded, "mere attendance at meetings may, in fact, be a fairly weak indicator of commitment" (p.63). Tonigan, Connors, and Miller (Tonigan, Connors et al. 1996) note that measures of 12-step attendance are likely to overestimate the extent of 12-step engagement: More people are attending than are getting involved in the program. However, regular attendance may be a precursor for involvement for many. Caldwell and Cutter (Caldwell and Cutter 1998) found that individuals who attend AA daily in early recovery are more likely to embrace both the program and fellowship dimensions of AA, and that those who have dropped out or who attend meetings infrequently or erratically tend to be less accepting of all aspects of AA. This latter group also appears to do less well than those who have frequent and consistent attendance (Morgenstern, Kahler et al. 1996; Weiss, Griffin et al. 2000; Moos and Moos 2004; Kaskutas, Ammon et al. 2005; Moos and Moos 2005). Fiorentine (Fiorentine 1999) found that weekly or more frequent meeting attendance was associated with drug and alcohol abstinence among clients at outpatient drug treatment programs. Similarly, Moos (Moos and Moos 2004) found that more frequent participation in AA (e.g., attending two or more meetings per week) during the first year after seeking help was associated with a higher likelihood of subsequent abstinence at 1- and 8-year follow-ups. Furthermore, the timing of this attendance was crucial. Early involvement

was important; individuals who delayed participation for a year or more and then eventually entered AA had outcomes that were no better than those of individuals who never entered AA. Continued attendance and the duration of involvement in 12-step activities over time were also important and were predictive of a broader range of substance use and psychosocial outcomes than was attendance. Finally, participation in AA had a positive influence on alcohol-related outcomes over and above the effects attributable to professional treatment, which is consistent with the findings of Fiorentine and Hillhouse (Fiorentine and Hillhouse 2000) with drug abusers.

A clinical implication of these findings is that it is important not only to get substance abusers to attend 12-step meetings, but to do so early after they have sought treatment and to encourage consistent attendance over time. It is also important to have substance abusers become actively involved in the 12-step process beyond meeting attendance. However, interventions that are effective in increasing attendance may be insufficient to ensure active involvement. Caldwell and Cutter (Caldwell and Cutter 1998) suggest that individuals who are attending AA but are having difficulty embracing key aspects of the program may need professional assistance that focuses more on 12-step practices and tenets and less on meeting attendance.

3.4 Low Rates of 12-Step Attendance and Involvement Following Treatment As Usual

Despite the potential benefits associated with 12-step involvement and attendance, from 60-70% of substance abusers have never attended a 12-step meeting. Harris, et al. (Harris, Best et al. 2003) found that while about 75% of alcoholics entering residential treatment reported that they had attended AA meetings previously, only 16% indicated that they had ever worked on any of the 12 Steps. Of the 150 patients who were interviewed, only 38% reported a positive attitude toward AA. Although drug abusers appear to hold a somewhat more positive attitude toward 12-step groups than do alcoholics (Best, Harris et al. 2001), Rawson, et al. (Rawson, Obert et al. 1991) found that long-term regular involvement in 12-step groups and activities was initiated by fewer than 30% of cocaine abusers receiving outpatient treatment. The rate of 12-step attendance was only somewhat higher, 40%, among those discharged from a 28-day inpatient cocaine treatment program. This low rate occurred despite what was described as “strong encouragement” to attend from each of the treatment programs involved and the availability of 12-step meetings on site (Rawson, Obert et al. 1991). Similarly, Weiss, et al. (Weiss, Griffin et al. 1996) found that only 34% of clients enrolling in the NIDA Collaborative Cocaine Treatment Study (CCTS) had attended a 12-step meeting in the week prior to their beginning treatment. This pretreatment participation was prognostic of early success in achieving abstinence in this outpatient trial. Of self-help attenders who actively participated, 55% initiated abstinence within the next month, compared with 40% of non-attenders and 38% of non-participating attenders. Over the follow-up period, only a third of the clients (33.6%) were classified as consistently high meeting attenders, while 47.9% were classified as consistently low attenders, and 18.5% had a decreasing attendance pattern across time. A similar pattern was found for involvement in 12-step activities: 35.4% of subjects were classified in the high participation group, with 47.5% in the low and 17.0% in the decreasing participation groups. Low and inconsistent involvement was associated with poorer outcomes (Weiss, Griffin et al. 1996; Weiss, Griffin et al. 2000; Weiss, Griffin et al. 2005). The five clinical sites participating in the CCTS evidenced a high degree of variability in meeting attendance by the sixth month of the trial, ranging from 20% to 69% of clients attending meetings. This occurred despite all sites having used the manual-guided Group Drug Counseling (Daley, Mercer et al. 1999), which recommended and emphasized self-help meeting attendance, as their standard “treatment as usual” (TAU). Variability in the recommended or required frequency of attendance was also noted in the TAU of

those community-based treatment programs (CTPs) involved in the multi-site methamphetamine treatment trial (Galloway, Marinelli-Casey et al. 2000). All eight of the participating programs are described as "encouraging" 12-step involvement. Four of the eight CTPs "recommended" 12-step attendance. The remaining four CTPs required attendance, including once per week for 4 to 8 weeks, once per week for 12 weeks, 6 meetings total over 12 to 16 weeks, and 3 meetings per week for 18 months. However, there is no data available from this study documenting actual levels of participation in 12-step meetings by the methamphetamine abusers being treated in these programs.

Fiorentine (Fiorentine 1999) examined 12-step involvement among individuals receiving outpatient drug treatment. The sample was composed primarily of poly-substance abusers; stimulants constituted a major portion of the drugs used by this group (primary drugs used in the year preceding treatment included crack cocaine - 57%, cocaine - 20%, and methamphetamine-16%). Higher levels of post-treatment attendance at 12-step meetings were associated with higher rates of abstinence from both drugs and alcohol. A set of 12-step attendance patterns similar to those of Weiss, et al. was also found. The relationship of the pattern of attendance between the 6-month and 24-month follow-ups to abstinence was of note. Forty percent of individuals were categorized as "persistors" (continued active participation); they generally maintained a high rate of abstinence. Those who never attended 12-step meetings during this intervening period (26%) had a marked decrease in their abstinence rates. Those who dropped out of 12-step participation during this time period (26%) also showed a decline in abstinence rates, which fell between the rates of the other two groups. Those who initiated 12-step attendance during this period (9%) did not show an increase in their abstinence rates between months 6 and 24. Another important finding was that there was an additive effect of involvement in formal drug treatment and self-help group participation; those who participated concurrently in both drug treatment and 12-step programs had higher rates of abstinence than those who participated only in treatment or in 12-step programs (Fiorentine and Hillhouse 2000).

These findings concerning the patterns of 12-step participation and substance use outcomes are consistent with those of Moos and Moos (Moos and Moos 2004). They found that individuals with alcohol use disorders who participated in AA for 4 months or longer in the first year after seeking help had better 1-year and 8-year alcohol-related outcomes than individuals who did not participate in AA. Individuals who continued in AA in Years 2–8, provided their participation was sustained, had better 8-year outcomes than did individuals who did not continue to participate or who participated for a shorter interval. Consistent with Fioretine's finding about those initiating 12-step involvements between months 6 and 24, Moos and Moos found that individuals who delayed participation in AA had no better outcomes than those who never participated. Consistent with this, Kelly and Moos (Kelly and Moos 2003) found that individuals who initiated 12-step behaviors during the course of treatment were significantly less likely to drop out during the subsequent year.

These findings suggest that early engagement during and/or shortly after treatment and sustained involvement in 12-step groups contribute positively to substance use outcomes. They have prompted clinical researchers to recommend that treatment programs emphasize the importance of self-help groups and encourage 12-step group attendance and participation (Caldwell 1999; Humphreys 1999; Fiorentine and Hillhouse 2000; Weiss, Griffin et al. 2000; Humphreys 2003). However, such low rates of attendance during or after TAU are found despite the fact that most treatment programs incorporate a 12-step philosophy and that professional staff report a high rate of referral to 12-step meetings (Humphreys 1997). However, as Caldwell (Caldwell 1999) notes, referral by professionals is not always introduced to clients in a manner that fosters acceptance of 12-step groups. This is of concern since substance abusers appear less likely to become involved in 12-step activities if left to do so on their own than if more active encouragement and referral are

provided in treatment (Sisson and Mallams 1981; Humphreys 1999; Weiss, Griffin et al. 2000; Timko, DeBenedetti, et al. 2006). Even if substance abusers initially attend meetings, there typically are high rates of attrition, which may prevent individuals from receiving the maximum benefit from 12-step involvement (Godlaski, Leukefeld et al. 1997). Kelly and Moos (Kelly and Moos 2003), for example, found that approximately 40% of a cohort of nearly 3,000 individuals who had attended 12-step meetings in the 90 days prior to or during treatment had dropped out over the following year. Caldwell and Cutter (Caldwell and Cutter 1998) suggest that early attrition from attending meetings may, in part, be due to individuals' inability to embrace or utilize other aspects of the 12-step program.

These findings raise questions about the effect that TAU, delivered in community-based treatment programs (CTPs), has on 12-step attendance and involvement. There is evidence that standard care can have a positive impact. Davis et al. (Davis, Campbell et al. 2002) compared alcoholics who were randomly assigned to either an outpatient treatment program that was based on a 12-step Minnesota Model or to a control condition in which they received minimal treatment (in lieu of no-treatment control). Those receiving the standard outpatient treatment doubled their 12-step meeting attendance from 4.33 meetings during the 3 months prior to treatment to 8.17 meetings over the 6-month post-treatment follow-up. However, the absolute rate of attendance, just over 1 meeting per month, still leaves considerable room for improvement. No change from baseline occurred across the 6 months of follow-up for those in the minimal treatment condition (2.44 meetings versus 2.31 meetings).

In a naturalistic study of inpatient substance abuse treatment within the Department of Veterans Affairs (DVA), programs were categorized into one of three groups based on their underlying philosophy and treatment practices (Swindle, Peterson et al. 1995): 12-step, cognitive-behavioral, and eclectic (eclectic programs blended 12-step and cognitive-behavioral philosophies and practices). Patients in the 12-step and eclectic treatment programs had higher rates of subsequent participation in 12-step self-help groups than did patients treated in cognitive-behavioral programs (Humphreys, Huebsch et al. 1999). Of potentially greater importance, the three treatment approaches had comparable substance use and psychosocial outcomes at a 1-year follow-up, except that individuals treated in the 12-step oriented programs had significantly higher rates of substance abstinence at the follow-up than did those in the cognitive-behavioral programs (Ouimette, Finney et al. 1997), a finding consistent with Project MATCH (Project Match Research Group 1997; Donovan 1999). There was no treatment-by-client attribute matches found (Ouimette, Finney et al. 1999). Furthermore, the theoretical orientation of the treatment program moderated the outcome of self-help group participation: the greater a program's emphasis on 12-step approaches, the stronger the positive relationship between 12-step participation and better substance use outcomes. Also, 12-step oriented programs and those having a higher percentage of staff in recovery were more likely to make referrals to 12-step groups than were cognitive-behavioral or eclectic programs (Humphreys 1997). Thus, it appears possible to enhance the attendance at and effectiveness of 12-step self-help groups, particularly when involved in a formal treatment program that has a strong 12-step orientation (Humphreys, Huebsch et al. 1999; Fiorentine and Hillhouse 2000; Fiorentine and Hillhouse 2000). This finding is consistent with that of Weiss, et al. (Weiss, Griffin et al. 2005) in the NIDA Collaborative Cocaine Treatment Study in which the combined effects of being involved in a treatment that emphasized 12-step involvement plus actual engagement in self-help activities was associated with the best outcomes.

3.5 Efficacy of Interventions Targeting Increased 12-Step Involvement

3.5.1 Single Site or Small Scale Clinical Trials

Results of single-site trials have been equivocal with respect to the relative efficacy of interventions targeting 12-step engagement compared to other types of treatment such as cognitive-behavioral therapy with respect to substance use outcomes. Maude-Griffin, et al. (Maude-Griffin et al., 1998) compared the relative efficacy of manually guided cognitive-behavioral therapy (CBT) and a TSF intervention, modeled after Project MATCH and the work of Nowinski and Baker (Nowinski and Baker 1992; Nowinski, Baker et al. 1992), in treating crack cocaine addicts. The goals of the 12-step treatment were to introduce group members to the 12 steps of AA and Cocaine Anonymous, to encourage working the first 4 steps, and to encourage 12-step meeting attendance in the community. Clients in both conditions attended 3 group sessions and one individual session weekly for 12 weeks. Clients in the CBT had better outcomes as measured by the percent achieving 4 consecutive weeks of abstinence from cocaine during the active treatment phase and 30-day point prevalence at the end of treatment and at a 14-week post-treatment follow-up. Wells, et al. (Wells, Peterson et al. 1994), compared cognitive-behavioral relapse prevention and a 12-step oriented intervention delivered in a group format in treating cocaine abuse. The latter group consisted of a "recovery support group" (Ehrlich and McGeehan 1985) based on the 12-steps of AA. It was designed to represent the 12-step philosophy often employed in treatment programs and focused on the first three of the 12 steps (acceptance, higher power, and surrender). The 12-step group included discussions about these steps, the cocaine recovery cycle, overcoming denial, getting social support, addiction as a disease, codependency, identifying symptoms of relapse, and staying motivated. Both groups, which were manually guided, were scheduled for 17 2-hour group sessions over a 24-week period. Clients in both conditions evidenced substantial and significant reductions in substance use. The two groups were comparable, with no differences between conditions, with respect to cocaine, marijuana, or alcohol use either during the treatment period or at a 6-month follow-up.

Brown and colleagues (Brown, Seraganian et al. 2002; Brown, Seraganian et al. 2002) randomly assigned substance abusers from three community-based treatment programs to either structured cognitive-behavioral relapse prevention or a 12-step facilitation aftercare condition. Both interventions were delivered in a closed-group therapy format, consisting of 10 weekly 90-minute group sessions. The 12-step condition followed the TSF manual developed in Project MATCH and adapted for group delivery. Both interventions were associated with substantial and significant reductions in alcohol and drug use at a 6-month follow-up. The two conditions were comparable, however, with no differences found between the two conditions on any of the substance use outcomes (days of use, ASI Alcohol and Drug Composite Scores, days to first lapse, and days to first relapse). Significant treatment-by-client attribute interaction effects were found. Women, individuals with a multiple substance abuse profile (primarily combined cocaine and alcohol), and those with higher levels of psychiatric severity had better substance use outcomes when treated in the TSF condition than in the relapse prevention condition. Given the findings that the outcomes of TSF were equal to or better than those seen with relapse prevention, Brown et al. (Brown, Seraganian et al. 2002) concluded that the adoption of a well-supervised and structured TSF-inspired aftercare program seems a reasonable strategy for most clients.

Carroll, et al. (Carroll, Nich et al. 1998) compared individually delivered TSF and CBT, either with or without adjunctive disulfiram, to an individual clinical management condition in the treatment of individuals dependent on both cocaine and alcohol. The clinical management condition was meant to provide non-specific, common factors of a psychotherapeutic relationship, including a supportive doctor-patient relationship, education, empathy and the instillation of hope, without providing active

ingredients specific to either CBT or TSF. The TSF intervention followed a manual adapted from Project MATCH for use with cocaine dependent clients (Baker 1998). The results indicated that TSF treatment was effective in promoting patients' involvement with self-help groups over the 12-week treatment period. Self-help involvement during treatment was significantly higher for patients assigned to TSF (13.8 days mean days of self-help group attendance) compared to those assigned to CBT (1.1 days, $F = 11.8$, $p < 0.001$) or patients assigned to clinical management (5.4 days; $F = 5.2$, $p < 0.05$). Furthermore, 58% of all participants reported attending at least one AA or self-help meeting over the follow-up period, with a mean of 3.9 days per month in which a self-help meeting was attended. The mean total days of self-help attendance during the 1-year follow-up was higher for participants who had been assigned to TSF compared with participants assigned to clinical management or CBT, but not significantly so (48.7 days vs. 33.2 days vs. 24.2 days, respectively). Both TSF and CBT were associated with substantial and significant reductions in alcohol and cocaine use over the course of the 12-week treatment period compared to the clinical management condition; the substance use outcomes for TSF and CBT were comparable. At a 1-year follow-up the differences between the clinical management condition and either the TSF or CBT were no longer significant, and TSF and CBT had comparable outcomes (Carroll, Nich et al. 2000). Carroll and colleagues (Carroll, Nich et al. 1998; Carroll, Nich et al. 2000) also found that participants who attended any self-help groups, regardless of treatment condition, had significantly better cocaine outcomes during follow-up than those who did not.

With the exception of the study by Maude-Griffin, et al. (Maude-Griffin et al., 1998), the results from these trials indicate that interventions designed to facilitate involvement in 12-step groups, whether delivered as individual or group therapies, result in significant and substantial reductions substance use comparable to and not different from the outcomes of more established, evidenced based treatments such as CBT and relapse prevention.

3.5.2 Large Multisite Clinical Trials

Two large-scale multisite clinical trials support the conclusions of Fiorentine and Hillhouse (Fiorentine and Hillhouse 2000; Fiorentine and Hillhouse 2000), Humpheys (Humphreys, Huebsch et al. 1999), Weiss, et al (Weiss, Griffin et al. 2005), Carroll, et al. (Carroll, Nich et al. 1998; Carroll, Nich et al. 2000), and the results from the naturalistic study of treatment program philosophies within the Department of Veterans Affairs (DVA) inpatient programs (Ouimette, Finney et al. 1997; Humphreys, Huebsch et al. 1999) that it is possible to enhance the attendance at and involvement in 12-step self-help groups particularly when involved in a formal treatment program that has a strong 12-step orientation, and, in doing so, improve outcomes. Project MATCH (Project MATCH Research Group 1993; Project Match Research Group 1997) evaluated three manually guided, individually delivered treatments for alcohol dependence: Cognitive-Behavioral Therapy (CBT), brief Motivational Enhancement Therapy (MET), and Twelve Step Facilitation Therapy (TSF) (Donovan, Kadden et al. 1994; Donovan, Carroll et al. 2003). The content of TSF therapy was designed to be consistent with AA and other 12-step groups and with treatment programs based on the Minnesota Model (Nowinski and Baker 1992; Nowinski, Baker et al. 1992). The primary goal of TSF is to promote abstinence by facilitating the client's: (1) "acceptance," which includes the realization that drug dependence is a chronic, progressive disease over which one has no control, that life has become unmanageable because of drugs, that willpower is insufficient to overcome the problem, and that abstinence is the only alternative; (2) "surrender," which involves giving oneself over to a higher power, accepting the fellowship of other recovering alcoholics, and following the recovery activities laid out by the 12-Step program; and (3) active involvement in 12-Step meetings and related activities.

TSF has demonstrated efficacy with both alcoholics and cocaine abusers (Project Match Research Group 1997; Carroll, Nich et al. 1998; Carroll, Nich et al. 2000). Participants in all three Project MATCH therapies demonstrated significant and relatively comparable reductions in the number of drinks per drinking day and increases in the percent days abstinent. In a result consistent with that of the naturalistic DVA study (Ouimette, Finney et al. 1997), those Project MATCH participants who received TSF had significantly higher rates of continuous abstinence when compared to the other two treatments at a 1-year follow-up, while being comparable to MET and CBT on the other drinking-related outcomes. This differential benefit for the TSF group appears to have been related to differences in the treatments' ability to engage clients in 12-step activities. MATCH participants had not been attending AA actively prior to their entry into the trial. Three-fourths (75.1%) of participants in the outpatient arm reported no AA attendance in the 90 days before study enrollment. Those who did report attendance had attended a meeting on only 2.66 days out of the 90-day window (an average of about 1 meeting per month). Consistent with the trend found by Carroll, et al. (Carroll, Nich et al. 2000) with cocaine abusers, outpatients in Project MATCH who received TSF as their primary treatment had significantly higher rates of 12-step attendance overall during the year following treatment compared to the CBT and MET therapies. In contrast, outpatients in CBT showed no increase in AA attendance across the 3-months of treatment or the subsequent follow-up. Outpatients in MET demonstrated a small increase in attendance during the 3-month treatment phase. Over half of the CBT (55%) and MET (52%) outpatients had no AA attendance over the entire 15-month treatment and follow-up period, while only 19% of those in TSF failed to attend an AA meeting over this same period. Participants in the outpatient TSF also reported significantly more involvement in 12-step activities than those in either CBT or MET. AA participation, in turn, positively predicted the frequency of abstinent days in the post treatment period (Connors, Tonigan et al. 2001). An examination of the putative active ingredients of TSF (Longabaugh, Donovan et al. 2005) indicated that TSF had features unique from CBT and MET. Compared to these other two interventions, TSF resulted in a greater awareness of a higher power, endorsement of total abstinence, and engagement in AA practices. Two of these active ingredients, emphasis on abstinence and commitment to AA practices, were predictive of greater abstinence, and commitment to AA practices mediated or explained why TSF clients reported significantly higher abstinence rates 6 months after treatment relative to CBT and MET.

In the National Institute on Drug Abuse Cocaine Collaborative Treatment Study (NCCTS) (Crits-Christoph, Siqueland et al. 1997; Crits-Christoph, Siqueland et al. 1999) all clients received Group Drug Counseling (GDC) (Daley, Mercer et al. 1999) as a "base" therapy or TAU. GDC educated patients about addiction and recovery and strongly encouraged 12-step involvement. Outpatients were randomly assigned to receive GDC alone or in combination with Cognitive Therapy (CT), Supportive-Expressive Therapy (SE), or Individual Drug Counseling (IDC) (Mercer and Woody 1999). The IDC was based on 12-step philosophy, emphasized the disease concept of addiction, advocated healthy behavioral and lifestyle changes, and strongly encouraged and reiterated the importance of self-help group attendance. The SE and CT therapies were generally supportive of self-help meetings, but neither treatment strongly encouraged self-help attendance. Individual treatment was scheduled twice a week for the first 12 weeks and weekly during weeks 13 - 24, for a maximum of 36 sessions. GDC sessions were scheduled weekly for 24 weeks for a maximum of 24 sessions. Overall, clients in all treatment conditions reduced their cocaine use significantly; however, those in the combined GDC-IDC condition, combining group plus individual 12-step oriented approaches, reduced their cocaine use significantly more and did so more rapidly than those in the other conditions (Crits-Christoph, Siqueland et al. 1999).

Weiss and colleagues (Weiss, Griffin et al. 2000) examined the 12-step involvement among clients in the four treatments of the NCCTS. Overall, the combined GDC-IDC condition had the highest rates of 12-step attendance and involvement. The incremental benefit of adding Individual Drug

Counseling to Group Drug Counseling was notable. Clients in the GDC-only condition reported, on average, that they attended at least one 12-step meeting in just over a third of the weeks (37.9%) during the 6-month treatment phase of the trial. This compared to nearly half (47.7%) of the weeks attended by those in the GDC-IDC condition. Those treated in the combined GDC-IDC condition also were the most likely to report both frequent attendance at 12-step groups and involvement in 12-step activities. The difference across groups in frequent attendance was most pronounced during month 6 of the treatment phase: 63.6% of clients in the combined GDC-IDC condition compared to only 38.5%, 34.8% and 21.9% for the GDC-only, GDC-CT, and the GDC-SE groups, respectively. Similarly, the percentage of frequent involvement in 12-step activities was 59.1% for the combined GDC-IDC group compared to 30.8%, 30.4%, and 18.8%, in the GDC-alone, GDC-CT, and GDC-SE conditions, respectively. Finally, 47% of GDC-IDC participants had consistently high attendance and high involvement, compared to only 31.2% of those who received GDC alone. Thus, there appear to be potential incremental benefits of combining individual- and group-based 12-step facilitative approaches with cocaine dependent individuals.

3.6 Treatment as Usual and Twelve Step Facilitation Are Not the Same

Many programs and counselors present themselves as "already doing" TSF. The fact that a program or a counselor indicates that treatment is guided by 12-step philosophy does not necessarily mean that 12-step practices, let alone 12-step facilitation practices, are actually being employed. TSF therapy is quite different from 12-step referral methods typically found in substance abuse programs. As Carroll, et al. (Carroll, Nich et al. 2000) noted in describing TSF as employed in their study with cocaine abusers:

> It should be noted that because we evaluated a closely supervised, manual-guided, individual version of TSF, our TSF treatment is probably quite different from that currently used by many clinicians. It is not clear whether or how much additional training and supervision would be required for clinicians' in general clinical settings to deliver TSF as it was implemented here. It should also be emphasized that TSF is formal treatment that seeks to foster an enduring relationship by the patient with self-help; it should not be concluded that merely referring a patient to a self-help group would be associated with similar outcomes. Indeed, studies evaluating referral to self-help compared with formal treatment have suggested that merely referring substance-dependent patients to self-help groups is often insufficient. It should also be noted that TSF, like the other treatments evaluated in this efficacy study, was delivered by therapists who were selected for their expertise in delivering this treatment and who were trained and closely supervised throughout the trial. Thus, future 'effectiveness' studies are needed to evaluate whether these findings extend to other types of therapists. (pp. 1345-1346)

The Department of Veterans Affairs (DVA) – Center on Substance Abuse Treatment (CSAT) Workgroup on Substance Abuse Self-Help Organizations (Humphreys, Wing et al. 2004) pointed out that many people mistakenly believe that all substance abuse treatment programs in the United States are based on the 12-step philosophy and that all clinicians in them are already promoting self-help groups. However, the Workgroup indicated that this belief is not supported by research. There are few "pure" 12-step treatment programs or practitioners. Rather, most are likely to incorporate an eclectic perspective, blending 12-step, cognitive-behavioral, and other philosophies and techniques. Even practitioners who describe themselves as "12-step oriented" typically consider only a subset of 12-step processes important for clients. Thus, even having TAU with a 12-step program philosophy and counselors that encourage 12-step involvement may not be

sufficient to increase 12-step involvement and activities; a systematic, manually guided 12-step facilitative intervention and TAU are not equivalent.

The Workgroup's point is exemplified by two recent studies that examined community-based TAU. First, Morgenstern, et al. (Morgenstern, Blanchard et al. 2001) characterized the TAU in community-based intensive outpatient treatment programs (IOP) in which they were conducting clinical research. The programs were described as having a 12-step orientation, a focus on overcoming denial, an emphasis on facilitating involvement with self-help groups, the provision of education about the disease of addiction, and an emphasis on the need for abstinence. All of these are viewed as 12-step-oriented treatment components. However, based on monitoring of program content, only one of these treatment elements, encouraging involvement with self-help groups, was observed to be occurring. And even this was not to a high degree (a mean score of 2.85 +/- 1.8 on a 5-point Likert scale (1 = not at all, to 5 = extensively). Other 12-step activities, including discussing the disease concept of addiction, encouraging 12-step recovery, invoking the concepts of spirituality and higher power, and exploring the client's denial, were even less frequently employed. Second, Galloway, et al. (Galloway, Marinelli-Casey et al. 2000) found a high degree of variability in the extent to which attendance at 12-step meetings was required as part of TAU by community-based programs involved in the CSAT-funded multi-site trial of treatment for methamphetamine abuse. As noted previously above, of the 8 community-based programs participating in the project, only half required any participation. Of those sites requiring participation, the expectation for attendance ranged from once per week for 4 - 8 weeks to 3 times per week for 18 months.

One of the recommendations of the DVA-CSAT Workgroup (Organizations 2003; Humphreys, Wing et al. 2004) is that community-based treatment programs, even those that label and represent themselves as "12-step oriented," should evaluate whether their current program practices actively support involvement in 12-step self-help groups. Further, they also should examine the methods employed by their counselors in this regard. Typically, they noted, when counselors do attempt to support 12-step self-help group involvement in TAU, they rarely use empirically supported methods. When clinicians use empirically validated techniques to support mutual help group involvement, it is far more likely to occur (Humphreys 1999).

3.7 Briefer 12-Step Interventions to Fit Current Clinical Constraints: Issues of Sustainability

The DVA-CSAT Workgroup (Humphreys, Wing et al. 2004) has recommended that clinicians use such empirically validated approaches as TSF derived from Project MATCH when seeking to foster self-help group involvement. However, both Humphreys (Humphreys 1999) and the DVA-CSAT Workgroup (Humphreys, Wing et al. 2004) have suggested that it would not only be appropriate to investigate the effectiveness of 12-step facilitative interventions further, but also to consider briefer interventions that may fit better within existing clinical practice and reimbursement models than do previously employed TSF interventions. TSF as developed in Project MATCH and adapted for use with cocaine abusers is a formal individual psychotherapy approach that is not without costs to incorporate into clinical programs (Cisler, Holder et al. 1998; Donovan, Carroll et al. 2003), unlike attendance at self-help groups in the community. Such concerns contributed to Humphreys' (Humphreys 1999) argument that in order to make 12-step facilitative interventions more useful in practice, researchers and clinicians should develop and evaluate briefer forms of such interventions.

One potential approach that has been evaluated recently is motivational enhancement therapy targeting 12-step involvement. However, Kahler and colleagues (Kahler, Read et al. 2004) found no differences between the standard brief advice to attend AA (which reflected standard practice) and the motivational enhancement condition with respect to either 12-step group attendance or drinking outcomes over the subsequent 6-month follow-up period. A significant interaction was found between the type of intervention received and prior experience in 12-step groups. The motivational enhancement approach was more effective for individuals with relatively little prior self-help involvement while the brief advice was better for those who have more 12-step experience.

3.7.1 Intensive Referral and the "Buddy System"

Another alternative that is more directly related to the 12-step recovery model than is motivational enhancement therapy involves the use of 12-step members serving as the "bridge" between formal treatment and individuals' entrance into the 12-step program. It has been a common practice in many treatment programs to use AA or NA members who serve as volunteers in a "buddy system" or as temporary sponsors (Blondell, Looney et al. 2001; Collins and Barth 1979; Chappel and DuPont 1999). Patients who have engaged in 12-step activities through the efforts of such volunteers have credited the peer intervention as being the most important factor that motivated them to seek help for their substance use disorder. Blondell, et al. (Blondell, Looney et al. 2001) pointed out that when recovering alcoholics and drug addicts provide help to a substance-abusing patient, they are furthering their own 12-step work and that such interventions are relatively simple, practical, involve little or no costs, and pose little patient risk.

One particular form of this type of intervention recommended by Humphreys (Humphreys 1999) and Miller (Baker 1998; Owen, Slaymaker et al. 2003) for further study is "systematic encouragement and community access" (SECA), an intensive referral procedure developed by Sisson and Mallams (Sisson and Mallams 1981). In one of the first studies to evaluate such a volunteer buddy system, alcoholic outpatients were randomly assigned to a "simple" or "enhanced" referral procedure. In the simple condition, consistent with TAU in many programs today, a therapist suggested that the patient attend AA or Al-Anon and provided a printed list of meeting times and locations. In the enhanced condition, the therapist supplemented the aforementioned intervention with an in-session telephone call to a current member of AA or Al- Anon, who talked to the patient briefly and arranged to attend a meeting with him or her. The 12-step group member contacted the patient with a reminder telephone call the night before the meeting, drove the patient to the meeting, and let the patient's therapist know on the following day whether the patient had attended. During the month following the intervention, 100 percent of patients in the enhanced referral condition attended at least one meeting (average 2.3 meetings), compared with none of the patients in the simple referral condition. Although the study was based on a small sample (n = 20) and followed patients for only 1 month, the results suggest that such a fairly brief intervention can have a significant impact.

Timko and colleagues (Timko, DeBenedetti et al. 2006) have recently completed a larger (n = 345) and more thorough evaluation of a manualized intensive 12-step referral procedure in a two-site randomized trial with individuals entering outpatient substance abuse treatment. Clients in outpatient substance abuse treatment were randomized to receive either 3 sessions of standard referral or intensive referral to 12-step meetings over a 1- month period. In the first session of the standard referral condition, the counselor gave the client a schedule of AA and NA meetings in the local area and encouraged the patient to attend 12-step self-help group meetings; subsequent sessions focused on relapse prevention and general educational issues around substance abuse and treatment. The first session of the intensive referral condition also provided the individual with information about available local 12-step self-help meetings. Counselors also provided and reviewed with the clients a pamphlet explaining the 12-step philosophy, the structure and

terminology of 12-step groups, common concerns about participation, and encouraged clients to set goals for attending self- help, working the first Steps, joining a home group, and getting a sponsor. The counselor and client also called a self- help group volunteer during the session and the volunteer arranged to meet the patient before an AA or NA meeting so that they could attend the meeting together. The counselor and client agreed on which meeting would be attended before the next session. The client was to keep a journal to record the 12-step meetings attended (dates, times, places) and, briefly, their personal reactions to, and thoughts about, the meetings (or their reasons for not attending). The focus of the second session depended on whether the client had attended a self- help meeting during the intervening time. If so, the counselor reviewed the client's journal, discussed their reactions to the meetings, provided a list of available individuals who might serve as a sponsor, encouraged the client to ask one of these individuals to serve as a temporary sponsor, and agreed on another meeting to be attended. For those who had not attended a meeting, the focus was on barriers to attendance. As in the first session, a call was made to a 12-step group member to arrange a meeting with the client at an AA or NA meeting. The third session focused on whether the client had attended a meeting or not and had made arrangements for a temporary sponsor. If the person had not yet attended a meeting, a call was once again made to a 12-step volunteer to arrange a meeting with the client at a self- help meeting.

Individuals assigned to the intensive and standard referral conditions did not differ on measures of 12-step meeting attendance over a 6-month follow-up period; however, those in the intensive referral condition demonstrated greater engagement in 12-step activities (doing service work, having experienced a spiritual awakening, and overall involvement). Those in the intensive referral condition also had significantly greater reductions on the alcohol and drug use composite scores of the Addiction Severity Index and had significantly higher rates of abstinence from drugs, although not alcohol, than individuals who received the standard referral.

3.7.2 12-Step Interventions Delivered in Group Format

One approach that may be more sustainable with respect to both clinical service delivery and reimbursement models than individually administered TSF is the provision of 12-step facilitative interventions in a group setting. Group formats represent the modal form of delivery of substance abuse treatment services (Stinchfield, Owen et al. 1994; Brook and Spitz 2002; Weiss, Jaffee et al. 2004; Flores and Georgi 2005). Treatment programs choose group treatment because of its cost-efficiency and perceived effectiveness at engaging patients and bringing about abstinence or reduced drug use. Further, groups may involve a number of "curative factors" that facilitate behavior change and the acquisition and maintenance of abstinence. Such factors include knowing that one is not alone, giving and receiving support, instilling hope, learning from others' experiences and from interacting with others; learning to communicate feelings and needs more effectively, making sense of one's own experience through interaction with similar others, and confronting problematic behaviors, such as denial, manipulativeness and grandiosity (Stinchfield, Owen et al. 1994; Flores and Georgi 2005). However, for a number of logistical, methodological, and statistical reasons, addiction researchers have not focused on evaluating group treatment to the extent that it has been studied in other areas of behavioral health (National Institute on Drug Abuse 2003). This constitutes a major gap between substance abuse research and practice (Lamb, Greenlick et al. 1998) that has been difficult to address, across both the field in general and within the Clinical Trials Network (CTN). The CTN CTP Caucus has identified research on group therapies as one important priority within the category of "research building on treatment as usual." Kaskutas and Oberste (Kaskutas and Oberste 2002) suggest that group approaches may be more appropriate than individual therapy for the delivery of 12-step interventions, since an individualized format neither offers the potential curative benefits of group approaches nor prepares clients for the group context and process that they will encounter in 12-step groups in the community. The mechanisms

of change associated with group therapy may well be operative in such 12-step groups (Kassel and Wagner 1993).

The results of controlled trials of group therapy with substance abusers, in general, have been equivocal (Weiss, Jaffee et al. 2004). However as noted above, the results of Wells and colleagues (Wells, Peterson et al. 1994) and Brown and colleagues (Brown, Seraganian et al. 2002; Brown, Seraganian et al. 2002) indicated that 12-step oriented interventions delivered in a group format were comparable to more well-established, empirically supported relapse prevention groups with respect to substance use outcomes. Further, Brown et al found treatment matching effects, for gender, substance abuse patterns, and psychiatric severity that favored treatment in the 12-step facilitation group. These findings suggest the viability of group-based approaches to 12-step facilitative interventions. Further, the results of the NIDA Collaborative Cocaine Treatment Study suggest that group based 12-step approaches may be enhanced further by the addition of individual sessions that reinforce and augment the 12-step emphasis provided in groups. As Crits-Christoph and colleagues (Crits-Christoph, Siqueland et al. 1999) concluded, a manual-guided combination of intensive individual drug counseling and group drug counseling has promise for the treatment of cocaine dependence, as compared with professional psychotherapy. However, this conclusion needs to be considered in light of the findings of Maude-Griffith et al. (Maude-Griffin et al., 1998) that showed a combined group plus individual cognitive-behavioral intervention resulted in better substance use outcomes than a combined group plus individual 12-step intervention.

A combination of individual plus group counseling is a common method of delivering care in outpatient treatment, particularly intensive outpatient care (Center for Substance Abuse Treatment 1994). Thus, such a format would be compatible with current clinical service delivery practices. This is the method endorsed by the CTPs within the CTN in a recent survey (CTN0031 Protocol Development Executive Committee 2006). As part of the protocol planning process, non-residential psychosocial CTPs within the CTN were asked to indicate the type of treatment delivery that they would be most likely to use to adopt and integrate a 12-step facilitative intervention into their programs. They were asked to rank-order three alternatives: individual therapy delivery alone, group alone, or group plus individual. From the 67 responding CTPs, combined group plus individual treatment was ranked first (i.e., most likely to be used or preferred) by 59.4% of the CTPs, group alone was ranked first by 39.1%, and individual treatment delivery was ranked first by only 1.6%CTPs. Combined group plus individual treatment may also provide fiscal advantages to clinics due to differential reimbursement rates when compared to either group or individual sessions alone. For example, a counselor seeing 4 clients for individual sessions plus conducting one 1.5 hour group session with 6 patients is estimated to generate approximately 50% more revenue than the same counselor conducting individual sessions with 6 clients (Daley 2006).

A potential practical disadvantage of 12-step facilitative interventions delivered in a group format (Wells, Peterson et al. 1994; Daley, Mercer et al. 1999) or a combination of group and individual (Maude-Griffin et al., 1998; Crits-Christoph, Siqueland et al. 1999) is the length of the intervention. It may be difficult for many programs to accommodate or sustain such lengthy interventions in the current climate of briefer treatment episodes. Furthermore, there is a concern about the impact of the length of an intervention and client attrition. As noted previously, Wells, et al. (Wells, Peterson et al. 1994) conducted 17 group sessions over 24 weeks; treatment began with 2 weeks of twice-weekly sessions, followed by ten weekly sessions and three review sessions held at 4-week intervals. However, participants in the 12-step group condition only attended an average of 6.14 sessions (which did not differ significantly from the 7.4 sessions in the relapse prevention group condition). Participants in Maude-Griffith, et al. (Maude-Griffin 1998) were scheduled to attend 3 group sessions and 1 individual session weekly for 12 weeks. However, as they noted, their participants proved difficult to retain in treatment. There were no differences between the 12-step

facilitation and cognitive-behavioral conditions with respect to attendance. On average, participants attended 14 group sessions (out of 36 possible) and 5 individual sessions (out of 12 possible) across both treatment conditions. Attendance at group and individual sessions was highly and significantly correlated. Individuals in the NCCTS were scheduled to attend individual sessions twice a week for the first 12 weeks and weekly during weeks 13 - 24 (a maximum of 36 sessions), with 24 group counseling sessions scheduled weekly over 24 weeks. Only 23% of the patients completed the intervention; 35% had dropped out by one month and 55% by 3 months.

The major implication of these attrition rates is that a majority of participants may not receive the prescribed dose of sessions if the intervention is too lengthy. It should be noted that the individual-, group-, and combined 12-step facilitative interventions reviewed have served as freestanding outpatient or aftercare services. That is, they were the only treatment that individuals received. Such freestanding interventions might have required a greater length and intensity than would be necessary for interventions that are integrated into the standard treatment as usual offered in community-based treatment programs. Thus, a briefer 12-step facilitative intervention, combining group and individual components and integrated into treatment as usual, would fit the realistic clinical and fiscal constraints of community-based programs.

3.8 Summary and Rationale

William Miller, serving as a discussant for a symposium on AA involvement and change mechanisms (Baker 1998; Owen, Slaymaker et al. 2003), provided the following conclusions about the current status and future direction of research and clinical practice in this area (p.531):

> AA cannot be ignored in understanding treatment outcomes. At the very least, studies should carefully inquire about AA involvement, to examine its relationship to treatments and outcomes.
>
> It is possible to facilitate AA attendance. Without question, there are counseling procedures that significantly increase AA attendance, at least during and often after treatment. ***TSF therapy clearly did this in Project MATCH. Systematic encouragement can significantly increase attendance [emphasis added]***.
>
> Treatment is the time to initiate AA attendance. If AA attendance is not initiated during the period of treatment, it is quite unlikely to happen. Treatment, then, is a good time to encourage sampling of the program and meetings of AA.
>
> Attendance is not involvement. When frequency of AA meeting attendance is measured separately from behavioral indicators of involvement in the program and fellowship of AA, the two measures are moderately correlated. In fact, among more frequent AA attenders during Project MATCH treatment, AA attendance declined over the course of follow-up while AA involvement remained steady or increased. This suggests a gradual process of internalization of the AA program and surely indicates that conclusions cannot be drawn from attendance alone.
>
> AA involvement predicts better outcomes. Longitudinal studies usually, although not always, find that AA involvement after treatment is associated with higher rates of abstinence regardless of the kind of treatment received. When AA attendance and AA involvement are both measured, the latter tends to be the stronger predictor of outcome.

Miller's conclusions about AA, as well as the empirical findings on which they are based, have helped shape the present protocol that will focus on a broader range of 12-step groups. It will evaluate the impact on stimulant and other substance use of a combined group and individual

treatment approach for stimulant abusers. Specifically, the present approach is based on the TSF therapy from Project MATCH as modified for use with drug abusers (Baker 1998) and as delivered in a group format (Brown, Seraganian et al. 2002; Brown, Seraganian et al. 2002). These group sessions will be augmented further by three individual sessions, two of which are drawn from the TSF manual, into which are integrated action-oriented interventions derived from the intensive referral procedure of Timko, et al. (Timko, DeBenedetti et al., 2006) as a means of increasing involvement in 12-step activities and meeting attendance. This combined group plus individual approach has been named STAGE-12 (STimulant Abuser Groups to Engage in 12-Step). The study will examine the extent to which this approach, integrated into treatment as usual, will lead to significantly greater reductions in stimulant use compared to treatment as usual (TAU). It will also examine the extent to which STAGE-12 increases involvement and meeting attendance over and above that of clients receiving TAU. The extent to which increases in 12-step involvement and attendance mediate reductions in subsequent substance use also will be examined.

Twelve-step programs serve as cost-effective resources that complement, support, and extend the cognitive and behavioral changes made in treatment (McCrady 1994). However, given the low rates of involvement in and high rates of attrition from 12-step programs, it is necessary to evaluate methods to help substance abusers and treatment programs take full advantage of self-help groups (Humphreys 1999). Implementation of systematic, structured, and manual-guided 12-step programs, integrated within treatment, represents one such method to increase engagement and retention in professional treatment. The proposed project responds to a topic identified by the CTN's CTP Caucus and CTP staff (Forman, Bovasso et al. 2001) as a high priority for investigation in the CTN, namely facilitating12-step involvement. If successful, this structured, manual-guided intervention would augment the more general 12-step orientation characterizing many community-based providers and promote better treatment outcomes.

4.0 STUDY OBJECTIVES

4.1 Primary Objective

To evaluate the degree to which a brief, combined group-plus-individually delivered 12-step facilitative intervention (STAGE-12), integrated into treatment as usual, reduces the percent of days of stimulant drug use for participants with stimulant abuse or dependence disorders compared to treatment as usual (TAU).

4.2 Secondary Objectives

- To evaluate the degree to which STAGE-12, integrated into treatment as usual, reduces the percent of days of use of non-stimulant drugs for participants with stimulant abuse or dependence disorders compared to TAU.
- To evaluate the degree to which STAGE-12, integrated into treatment as usual, increases involvement in 12-step activities, meeting attendance, and acceptance of 12-step beliefs and values, compared to TAU.
- To examine client attitudes and beliefs as mediators of 12-step meeting attendance and involvement.
- To examine 12-step meeting attendance and involvement as mediators of substance use outcomes.
- To examine the relative differences in 12-step meeting attendance and involvement and substance use outcomes of different client subtypes (e.g., ethnic/racial groups, gender, drug of choice, psychiatric severity, readiness to change).

5.0 STUDY DESIGN AND STUDY PROCEDURES

5.1 Overview of Study Design

This is a randomized, two-group, intent-to-treat study evaluating the effectiveness of a combined group-plus-individual intervention, Stimulant Abuser Groups to Engage in 12-Step (STAGE-12), on stimulant use outcomes. The STAGE-12 intervention is integrated into treatment as usual by replacing 8 (5 group and 3 individual) treatment sessions, in the site-specific treatment as usual, over a maximum of 8 weeks. The STAGE-12 intervention is meant to facilitate involvement in 12-step activities and attendance at 12-step self-help meetings. The comparison group will be treatment as usual without STAGE-12 (TAU). TAU will consist of the standard therapy offered by the site(s) over the 8-week period. The study consists of three phases: the screening/baseline phase, the treatment phase, and the follow-up phase. A diagram of the study schema is presented above in Figure 1 in Section 2.

5.1.1 Screening/Baseline Phase

Study participants will be recruited from individuals with stimulant abuse or dependence disorders that are seeking admission or are being enrolled into outpatient substance abuse treatment, including regular outpatient, intensive outpatient, day hospital, or partial hospital programs, at participating CTPs.

The study research staff will explain the protocol to the prospective participants and obtain informed consent and HIPAA authorization (if applicable). Those who complete the consent process will proceed to the screening/baseline phase of the study. The inclusion and exclusion criteria for the participants are given in section 5.3.3.1 below. Further, information collected during this phase will also be used in the randomization process (section 5.1.2.2) to assign those individuals who meet study inclusion criteria to one of the two treatment conditions. The randomization procedure is meant to balance the treatment conditions within CTPs.

5.1.2 Randomization

5.1.2.1 Counselor Randomization

All counselors within a CTP who are interested in potentially participating in the protocol must provide informed consent and sign consent forms. Those who complete the battery of clinician measures, meet the basic eligibility criteria, and volunteer to participate in the trial will serve as a pool within each CTP from which a minimum of two counselors will be chosen randomly to provide the STAGE-12 intervention. A computerized randomization application managed by the Data and Statistics Coordinating Center (DSC) will be used to select the STAGE-12 counselors from this pool. Given that a condition for inclusion in the pool of potential study counselors is completion of the counselor assessments, it will be possible to compare those randomly chosen to serve as STAGE-12 counselors with those who were not chosen on a number of demographic, experience, counseling skills, and therapeutic orientation variables. Those not chosen to serve as STAGE-12 counselors will continue with standard clinic care and will not provide additional data for the study.

5.1.2.2 Participant Randomization

Participants will be randomized after completing the initial eligibility screen, baseline data collection, and a check to be sure that they are still attending outpatient treatment in the participating CTP. Participants will be randomized to one of the two treatment conditions (TAU or STAGE-12) after

completion of baseline assessments. The randomization process will be conducted in a centralized process through the Data and Statistics Center (DSC). Randomization will be stratified by site and by participants court-mandated to treatment vs. participants not court mandated to treatment.

5.1.3 Treatment Phase

The second phase of the study (the "treatment phase") begins after a participant has successfully completed the baseline assessments and has been randomized to one of the two treatment conditions. Counselors from the participating CTP will deliver the treatments: TAU at the participating CTP or STAGE-12. All research participants will receive treatment as usual at the participating CTP, which provides at least 2 sessions per week during the intervention phase. STAGE-12 will consist of 3 individual sessions lasting approximately 45-75 minutes each plus 5 group sessions, each lasting approximately 90 minutes. The STAGE-12 sessions will replace 8 TAU sessions for those participants randomized to this treatment arm. The comparison condition will be TAU without the integrated STAGE-12 sessions.

The group component of the STAGE-12 intervention will be guided by procedures developed by Brown and colleagues (Brown, Seraganian et al., 2002; Brown, Seraganian et al. 2002) for the delivery of TSF in a group format. The three individual sessions will include the introductory and termination sessions from the TSF manual and will integrate the procedures developed by Timko (Timko, DeBenedetti et al. 2006) for the delivery of the intensive referral intervention. A number of within-treatment process variables will be assessed during this active intervention phase, including an assessment of counselors' adherence to the intervention guidelines.

For the purposes of assessments, the "end of treatment" will be standardized across conditions by setting it relative to the completion of the active treatment phase, at 8 weeks post-randomization.

5.1.4 Follow-Up Phase

The third phase of the study involves follow-up assessments of participants. Participants will be followed during visit windows at 3-months and 6-months post-randomization.

5.1.5 Discontinuation, Termination and Participant Replacement

5.1.5.1 Therapy Discontinuation

Participants must be discontinued from the treatment portion of the study if they experience significant physical or psychiatric conditions such that, in the judgment of the site Principal Investigator (PI) and/or the Lead Investigator, continuation in the clinical arm of the trial is contraindicated. Other reasons for considering possible discontinuation include non-compliance with research protocol requirements or a serious adverse event (SAE) that places the participant at risk should he or she continue in the study therapy. Participants who experience deterioration of their clinical status that temporarily results in more intensive level of care (e.g., detoxification, inpatient treatment) may return to the treatment protocol (within 8 weeks of randomization) following stabilization. Individuals who are discontinued from the treatment will be encouraged to complete all follow-up assessments.

5.1.5.2 Study Termination Criteria

Participants are free to withdraw their consent from further participation in the study at any time without cause and without penalty from the CTP where they are receiving their drug abuse treatment. Participants may be involuntarily terminated from all study activities if the site staff, with possible consultation with the Lead Investigator, deems that further participation will be harmful to the participant or for reasons consistent with CTP discharge policies on violence, drug sale, etc.

Once randomized, the clinical deterioration, substance use, and the potential need for more intensive care will be captured in assessments and in the Treatment Services Review (TSR). Reasons for refusal or withdrawal will be documented.

5.1.5.3 Replacement of Participants

In this intent-to-treat design, all randomized participants will be followed for all possible assessment points. Participants who are randomized to the STAGE-12 intervention but do not attend the initial individual session will not be replaced. Consistent with the intent-to-treat design, attempts will be made to follow these non-attenders in the follow-up assessments and they will be included in the intent-to-treat analyses.

5.2 Number of Sites and Participants

A target of approximately 400 participants from approximately 10 CTPs will be recruited. The goal is to have a sufficient number of interested and qualified CTPs available so that replacement of a CTP can be made in the event of program closure or withdrawal. Each CTP will have approximately 40-50 participants with 20-25 participants in each condition. The overall sample size and number of subjects per participating CTP may be adjusted based on the outcome of a blinded variance check to be conducted after approximately 200 subjects have been randomized (see Section 10.7). An attempt will be made to recruit approximately 50% female participants. In addition, efforts will be made to recruit a sample of study participants that reflects the proportion of minorities in the community where the site is located. Potential participants must satisfy study inclusion and exclusion criteria, listed in section 5.3.3.1

5.3 CTP, Counselor, and Participant Selection

5.3.1 CTP Selection

5.3.1.1 CTP Characteristics

CTPs participating in this protocol should:

- Provide psychosocial (non-opiate replacement) outpatient ambulatory care of sufficient treatment intensity to allow for STAGE-12 group and individual sessions to replace 3 individual and 5 group sessions of TAU each week, for at least 5 weeks during the 8-week intervention phase.
- Have adequate numbers of stimulant-abusing clients seeking outpatient treatment to meet target recruitment goals.
- Have adequate space to accommodate research assistants (RA) and study protocol procedures including on-site urine drug screen (UDS) collection and testing.
- Have a pool of potential counselors from which a minimum of 2 counselors for the STAGE-12 treatment condition can be chosen, willing to:
    - Participate in this protocol,
    - Be randomly chosen from a pool of eligible counselors to deliver the STAGE-12 intervention,
    - Attend a face-to-face training for STAGE-12 and provide recordings of their sessions to be rated for competence and adherence to the intervention,

- Have at least one clinical supervisor chosen to willingly participate in the protocol, face-to-face training, complete an additional training of trainers and have supervision reviewed by a protocol supervisor.

5.3.1.2 Rationale for CTP Selection

The current study is focused on an outpatient intervention and therefore CTPs must provide that level of care to participate in the study. The STAGE-12 intervention is designed to be integrated into the existing outpatient treatment and therefore the CTPs must provide outpatient treatment that meets at least two times per week to allow for the two conditions (TAU and STAGE-12) to be balanced on the amount of treatment available to participants each week. The site selection process will assess the CTPs' treatment frequency, as well as treatment models and client census.

An additional criterion for CTP involvement is based on both the duration of the outpatient program and the minimum number of treatment sessions per week. The STAGE-12 treatment is designed for delivery in a period from 5 up to 8 weeks duration. The CTP must have outpatient programs designed for treatment duration from 5 up to 8 weeks to allow for the two groups to be matched on length of treatment available and to allow for the integration of the study intervention into existing outpatient treatment groups. This time frame for delivery of the STAGE-12 intervention is supported by data on the number of sessions attended by clients in outpatient treatment trials.

The current study will utilize a rolling, or open, admission group process. This will require CTPs to have a sufficient number of new admissions with primary or secondary stimulant use disorders each week to keep both study conditions populated. In addition, participants will need to meet certain study inclusion/exclusion criteria to be enrolled in the study. These inclusion/exclusion criteria represent an additional burden on recruitment and therefore it is expected that only outpatient programs with a high static capacity and a high volume of admissions will be able to meet the study recruitment criteria. Interested CTPs will be evaluated on available participants, staff and facilities to be considered for inclusion as a site in the current study.

Counselors and supervisors will be voluntary participants in the current study. Counselors and supervisors will be required to provide informed consent to be eligible for the study. Each site will require a minimum of two counselors and one supervisor to provide the STAGE-12 intervention and a sufficient number of non-study counselors to maintain the existing TAU services. In addition, CTPs must ensure that the staff participation is fully voluntary; therefore counselors' willingness to participate and their performance in the study will not affect their employment status in any way.

A clinical supervisor will be needed to ensure that counselors are implementing the intervention with an adequate degree of fidelity. The clinical supervisor will fill in for the counselor in the event that the counselor is unavailable. During these periods when the clinical supervisor is seeing participants, he/she will receive supervision from the Lead Node trainer.

The counselor and supervisor trainings require that they attend face-to-face trainings. CTPs will be required to ensure that staff participating in the study will be provided with support to dedicate the necessary effort to complete these trainings and the required training cases in the period of time allowed by the protocol implementation schedule.

5.3.2 Counselor Selection

Counselors will be recruited from participating CTP staff. The educational background, credentials, and experience of the clinical staff implementing the intervention will vary among CTPs. The term "counselor" as used in the present protocol does not imply a particular educational background or

credentialing. Rather, it is used as a shorthand term to refer to the clinical staff members administering the treatments.

5.3.2.1 Counselor Informed Consent

Counselors who volunteer to participate in this study and to be randomly selected to provide the STAGE-12 intervention will be asked to provide informed consent to indicate their willingness to participate. As part of the informed consent process, potential counselors will also be informed about their need to complete brief questionnaires and have their sessions recorded and reviewed by clinical supervisors.

5.3.2.2 Counselor Inclusion/Exclusion Criteria

Counselors and supervisors will be eligible for the protocol who:

- Are credentialed to provide these services in their respective regions,
- Are willing to participate in this study (and sign the informed consent form), complete the counselor assessments, learn and implement a manual guided STAGE-12 intervention and conform to any restrictions placed on TAU during the course of the study,
- Are willing to be randomly chosen to provide the STAGE-12 intervention,
- Are willing to have their sessions recorded and reviewed by a national expert, a supervisor, and/or independent rater; to participate in regular supervision sessions; and to complete process/adherence ratings for the duration of the protocol,
- Are approved by the CTP's administrative/supervisory staff as appropriate for the study (e.g., reliable, competent, likely to be with the CTP for the duration of the study),
- Have a working familiarity with 12 step recovery principles and the self-help groups that utilize them.

Counselors and supervisors will be excluded who:

- Are unfamiliar with or negative toward a 12-step orientation to treatment.

All counselors who sign informed consent, meet the criteria above and are interested in participating in this protocol will be part of the pool of counselors from which two will be selected to provide the STAGE-12 intervention. Note that while specific training in the manual-driven TSF or Intensive Referral therapies excludes a counselor from the study, both counselors and supervisors will be required to have working familiarity with 12 step recovery principles and the 12-step recovery self help fellowships (AA, CA and/or NA). The counselor training for the STAGE-12 treatment is designed to work with counselors who are already familiar with the 12-step approach to recovery.

5.3.3 Participant Selection

5.3.3.1 Inclusion/Exclusion Criteria

Individuals will be eligible for the protocol who:

- Are 18 years of age or older
- Have been admitted to outpatient treatment at a participating CTP which has met the CTP inclusion criteria and have at least 5-8 weeks of outpatient treatment available with an intensity of 5-15 hours of treatment per week.
- Are able to provide consent for study procedures

- Are willing to provide information about their drug and alcohol use
- Have used cocaine, methamphetamine, amphetamine or other stimulant drugs within the past 60 days, or have been incarcerated within the past 60 days and had used stimulants during the 30 days prior to their incarceration
- Meet DSM-IV diagnostic criteria for current (within the last 6 months) abuse or dependence of cocaine, methamphetamine, amphetamine or other stimulant drugs as a primary or secondary drug of abuse
- Are willing to be randomly assigned to either STAGE-12 or treatment-as-usual and plan to be available for 6 months following randomization
- Are willing to be recorded during group and individual sessions

Individuals will be excluded who:

- Are in need of detoxification for opiate withdrawal (as judged by CTP clinical staff)
- Are seeking detoxification only, methadone maintenance treatment or residential/ inpatient treatment
- Have a medical or psychiatric condition that would, in the opinion of the clinic staff, make participation in this study hazardous
- Have been incarcerated more than 60 days within that past 90 days prior to baseline assessments
- Have pending legal action that would inhibit participation in the study
- Have previously enrolled in the study having met all eligibility criteria

5.4 Outcome Measures and Assessments

In selecting assessment measures and the timing of their administration, an attempt was made to balance the amount of assessment involved from baseline through the active intervention period and the follow-up points against the desire for adequate coverage of relevant assessment domains (Gastfriend, Donovan et al. 2005). Concerns exist about both assessment burden for participants and potential assessment reactivity (Clifford and Maisto 2000; Epstein, Drapkin et al. 2005); that is, the frequency and duration of the assessments may serve an unintended therapeutic effect that may reduce the differences across conditions. The Protocol Development Team is aware of and sensitive to both the potential relationship between increased client burden and participant attrition and potential “assessment effects.” These concerns were taken into account in deciding the measures chosen for the client.

A listing of the measures, description of the domains covered by each, and the times at which they will be administered is found in Table 1.

Table 1: STAGE-12 Schedule of Assessments

Instrument/ Assessment	Est Time to Administer	Computer Administer (Participants)	Baseline Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8/ End of Treatment	3 mo post-randomization	6 mo post-randomization
Informed Consent													
Informed Consent	15-30 min		X										
Administrative Forms													
Incl./Exclus-ion	5-10 min		**X**										
Randomiza-tion	5 min		**X**										
Visit Form*	2 min			**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**		
Visit Form (Research)	2 min		**X**		**X (Stage 12 only)**		**X**				**X**	**X**	**X**
Participant Assessment Instruments													
Demographic, Diagnostic, Medical, and Psychosocial Background Measures													
CTN Demo-graphic Form	5 min		X										
DSM-IV Checklist	20 min		X										
Medical History	5-10 min		X										
Substance Use Measures													
Substance Use Calendar (SUC)**	10-30 min		X (past 90 days)				X				X	X	X
Addiction Severity Index – Lite (ASL) (with AUDIT-C)	45 min at baseline; 15 min at followup		X									X	X
Alcohol Breathalyzer	2 min		X				X				X	X	X
Urine Drug Screen	5 min		X				X				X	X	X
Fagerstrom Nicotine Dependence	5 min		X								X	X	X

Instrument/ Assessment	Est Time to Administer	Computer Administer (Participants)	Baseline Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8/ End of Treatment	3 mo post-randomization	6 mo post-randomization
Secondary Outcomes: 12-Step Involvement and Attendance Measures													
Self-help Activities Question-naire (SHAQ)	5 min	X	X				X				X	X	X
Predictors and Mediators: 12-Step Measures													
12-Step Experiences and Expecta-tions (TSEE)	**3 min**	X	X										
Survey of Readiness for Alcoholics Anonymous Participation (SYRAAP)	**5 min**	X	X								X		
Short Understanding of Substance Abuse Scale (SUSS)	**5 min**	X	X										
Spiritual Involvement and Beliefs Scale – Revised (SIBS-R)	**5 min**	X	X								X		
Predictors and Mediators: Substance-Related Measures													
Drug Taking Confidence Questionnaire – 8 (DTCQ – 8)	**3 min**	X	X								X		
Self-Efficacy Questionnaire – Patient (SEQ-P)	**3 min**	X	X								X		
Stages of Change Readiness & Treatment Eagerness Scale (SOCRATES)	**5 min**	X	X								X		

Instrument/ Assessment	Est Time to Administer	Computer Administer (Participants)	Baseline Week 0	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8/ End of Treatment	3 mo post-randomization	6 mo post-randomization
Treatment Process Measures													
Helping Alliance Questionnaire (HAQ-II)	**5 min**	X			**X (Stage 12 only)**						**X (Stage 12 only)**		
Treatment Services Review (TSR) – 30 day abbreviated version	**10 min**		X				X				X	X	X
Participant Satisfaction Survey (PSS)	**5 min**	X									**X (Stage 12 only)**		
Administrative Forms													
Adverse Events	**10-15 min**			To be collected at any time after randomization									
Serious Adverse Events	**10-15 min**			To be collected at any time after randomization									
Substance Use Events	**10-15 min**						X				X	X	X
Protocol Violations	To be collected at any time during the study.												
Study Termination	To be collected at any time treatment dropout occurs during the study or 6-months post-randomization (whichever occurs first). If the participant terminates from the study prior to Week 8, a concerted attempt will be made to obtain all of the measures collected for study week 8.												
Treatment Tracking Form***	**10-15 min**			X	X	X	X	X	X	X	X		

* Three individual and 5 group sessions must be completed within eight weeks.

** Substance Use Calendar will only collect data up to the previous follow-up visit. Because of data collection windows the exact number of days will vary by participant.

*** Treatment Tracking Form is not administered to participants. Information is gathered through clinic treatment records.

Counselor Measures			
Instrument/Assessment	**Time to Administer (in minutes)**	**Prior to Randomization**	**End of protocol participation**
Counselor Informed Consent	**~15**	**X**	
Short Understanding of Substance Abuse Scale (SUSS)	**5**	**X**	
Clinician and Supervisor Survey (CSS)	**15**	**X**	
Addiction Counseling Self-Efficacy Scale (ACSES)	**5**	**X**	
Attitudes towards 12-Step Groups (ATSG)	**5**	**X**	
STAGE-12 Integration Goal Commitment	**5**	**X**	
Counselor/ Administrator Perceptions of Impact of Protocol Participation	**5**		**X**

5.4.1 Screening, Diagnostic and Descriptive Measures

The screening, diagnostic and descriptive measures will be used to help determine eligibility and gather information to assist with retention and future analysis.

5.4.1.1 Locator Questionnaire

A locator form, including home address, will be completed at baseline and kept confidential in the participant's records. Data collected on the Basic Data and Locator Questionnaire will be used to facilitate contact with the participants during the research and follow-up. Participants will be asked to provide locator information including their contact information and the contact information of friends or relatives who can reach the participant if the participant cannot be reached directly.

5.4.1.2 CTN Demographic Form

The CTN Demographic Form collects information about age, gender, race, and ethnicity. This will be completed for all participants and potential counselors at baseline.

5.4.1.3 The DSM-IV Checklist

Substance use disorder diagnoses will be derived from the psychoactive substance abuse disorder sections of the DSM-IV Criteria Checklist (DSM-IV Checklist) (Hudziak, Helzer et al., 1993). The DSM-IV Checklist is a semi-structured interview that provides current diagnoses for substance use disorders (SUD) based on DSM-IV diagnostic criteria. It has been shown to be an efficient method for screening and diagnosis for major psychiatric disorders while amassing a database that can be used for later clinical and research activities. This form will be administered at baseline.

5.4.1.4 Medical History

A brief medical history checklist will be collected for all study participants at baseline. The information will be used to establish a baseline for adverse events reporting during the course of the study.

5.4.2 Primary Outcome Measures

The primary objective of this study is to examine the degree to which the STAGE-12 intervention integrated into treatment as usual (TAU) reduces the percent of days of stimulant drug use, particularly cocaine, methamphetamine, and amphetamine compared to TAU alone. As such, the primary outcome will be measured by participant self-report of stimulant use (cocaine, methamphetamine, and amphetamine) from baseline through the 6-month follow-up period, as assessed by the Substance Use Calendar. The primary measures will be collected as indicated in Table 1. Information regarding substances other than stimulants will be collected for secondary analysis.

5.4.2.1 Substance Use Calendar

Self-reports of substance use will be assessed at each research visit via the Substance Use Calendar (SUC). Similar to the Timeline Follow-back procedure, the SUC is a calendar-based assessment in which individuals are asked to indicate whether they used cocaine, amphetamines, methamphetamines, opiates, alcohol, cannabis, or benzodiazepines on each day of the assessment period. The calendar is marked with both general (e.g., weekend days, holidays) and personal (e.g., birthday, anniversary, pay days) to help anchor the period and facilitate recall. The measure thus assesses substance use on a daily basis and allows flexible, continuous evaluation of substance use. The number of days used, either of any of the drugs or of each of them, is the variable derived from the SUC. Substance abusers' reports about their drug consumption using this method have been found to have high retest reliability, convergent and discriminate validity with other measures,

agreement with collateral informants' reports of patients' substance use, and agreement with results from urine assays (Fals-Stewart, O'Farrell, et al., 2000).

Secondary analyses will be conducted using percent of days of non-stimulant drug use and percent of days of use of any of the assessed drugs (stimulants and non-stimulants) as outcome variables. Days of 12-step meeting attendance will also be assessed using the Substance Use Calendar and will serve as one of the 12-step secondary outcome measures. Secondary measures will be collected as indicated in Table 1.

5.4.3 Secondary Outcome Measures

Secondary outcomes will be measured using the assessments listed below, as well as additional data collected on the Substance Use Calendar (section 5.4.2.1 above). While substance use is the ultimate outcome of interest, the STAGE-12 intervention specifically targets increasing participants' attendance at meetings and engagement in 12-step activities. As such, indices of meeting attendance and involvement in 12-step activities will serve as secondary outcomes. Also, as has more frequently been done in prior research, it is possible to view 12-step variables as "proximal outcomes" that may mediate the effectiveness of treatments on drug use (Morgenstern, Frey et al. 1996; Finney, Noyes et al. 1998; Finney, Moos et al. 1999; Allen 2000). Exploratory analyses of the 12-step outcomes as proximal, mediating variables in relation to substance use following the intervention will also be included.

5.4.3.1 Substance Use Indices

5.4.3.1.1 Urine Drug Screen

Although the Substance Use Calendar that will be used to assess days of drug use has demonstrated reliability and validity when compared against both collateral reports of drug use and urine toxicology results (Ehrman and Robbins 1994; Fals-Stewart, O'Farrell et al. 2000), and there is considerable evidence supporting the validity of self-reported substance abuse by drug users (Brown, Kranzler et al. 1992; Darke 1998), there continue to be concerns about the veracity of such self-reports (Magura and Kang 1996). Therefore, urine will be tested for the presence of cocaine, opiates, cannabis, benzodiazepines, methamphetamines, and amphetamines. Urine samples will be collected at the baseline interview, weeks 4 and 8 during the active intervention phase, and at each of the follow-up assessments.

Zanis et al (Zanis et al.1994) indicated that their results suggest that self-reports of drug use are more inclusive estimates of use than even weekly urinalysis. However, they as well as others (e.g., Fals-Stewart, et al., 2000; Del Boca and Noll, 2000) indicate that such self-reports were collected in the context of a setting in which urine results were also being collected and recommend continued use of urine collection. However, they do not necessarily advocate that urine results be viewed as a "gold standard." Rather, they point to the fact that one of the important conditions for obtaining valid self-reports of substance use is informing participants that their self-reports will be validated against an objective standard such as urines. This may enhance the accuracy of the participants' self-reports via a *bogus pipeline* effect (Jones and Sigall, 1970). Such effects occur when research participants provide information under conditions where they are led to believe that objective, external validation of their responses is available. The possibility that inaccuracies can be detected is hypothesized to increase the validity of verbal report data (Del Boca and Noll, 2000). This hypothesis was supported by the results of Hamid and colleagues (Harnid, Deren et al.1999), who found that the agreement between self-reported drug use and urine test results was significantly higher when the urine collection occurred prior to the self-report associated with timing of urine testing. Thus, urine screens will be conducted prior to the Substance Use Calendar to maximize the validity of the self-reports.

However, because of limitations in the use of urine toxicology as a "gold standard" and the lack of a standardized method of using urine results to adjust continuous measures of substance abuse such as percent days of use (Del Boca and Noll, 2000), urine results will not be used to attempt to make adjustments to self -reports.

The 8-oz urine collection cups that will be used in this study will have temperature strips on them to determine if the sample is within the allowable range of temperature. Observed urine collection is not required in this protocol.

5.4.3.1.2 Breathalyzer

A Breathalyzer will be administered at the baseline interview, at weeks 4 and 8 during the active intervention phase, and at each of the follow-up assessments to collect information on alcohol use, and to ensure that participants are not intoxicated during the completion of the assessment measures.

5.4.3.1.3 Addiction Severity Index – Lite, CTN Version

The ASI, developed by McLellan et al. (McLellan, Kushner et al. 1992) is a standardized, multidimensional, semi-structured interview that provides clinical information important for formulating treatment plans as well as problem severity profiles in six domains commonly affected in substance abusers. The domains covered are substance abuse (alcohol and drug), medical, psychiatric, legal, family/social and employment/support. Individuals are asked to indicate the number of days that they have experienced certain behaviors, emotions, or circumstances. A modified, shortened version of the ASI (CTN-ASI Lite) has been developed for use in the CTN; it includes only those questions used to derive the composite scores along with some demographic information. This version will be administered at baseline. The follow-up version of the CTN-ASI Lite uses a subset of the items in each of the domains; it will be administered at the 3 and 6-month follow-ups.

A potential limitation of the ASI is that it does not adequately assess drinking behavior. We incorporated the first three items of the Alcohol Use Disorder Identification Test (AUDIT; Saunders, Aasland, Babor, & de la Fuente, 1993) into the beginning of the ASI Alcohol and Drug Use Section. The AUDIT has been used increasingly as a highly effective, sensitive screening and case-finding instrument with a variety of respondent populations (Reinert & Allen, 2007), including drug abusers (Skipsey, Burleson, & Kranzler, 1997). The AUDIT assesses three main areas: alcohol consumption/hazardous drinking, alcohol-related problems/harmful drinking and alcohol dependence symptoms. Skipsey, et al. (Skipsey, Burleson, & Kranzler 1997) recommend the AUDIT for identifying individuals with a drug use disorder who consume alcohol at hazardous and harmful levels. The first three items of the AUDIT, comprising the AUDIT-C, assess alcohol consumption. The items ask individuals about how often they drink alcoholic beverages, how many drinks they consume on a typical day, and the incidence of heavy drinking. The 3-item AUDIT-C has been shown in a number of studies to be as accurate, sensitive, and specific in identifying hazardous or harmful drinking as the longer 10-item AUDIT (Reinert & Allen, 2007). Recent versions of the AUDIT-C (Dawson, et al., 2005a, 2005b) have modified the definition of heavy drinking from 6 or more drinks per occasion on the World Health Organization's version to 5 or more drinks per day for men and 4 or more drinks per day for women based on the U.S. definition of a standard drink and to be consistent with the National Institute on Alcohol Abuse and Alcoholism's guidelines and criteria (2007). These latter definitions of heavy drinking will be used in the present study.

The number of days of drug use, days of alcohol use, and the Drug and Alcohol Use Composite scores will serve as substance-use-related secondary outcome measures. The alcohol and drug use sections from the ASI-Lite will provide self-reported substance use during the 30-day window preceding the assessment and the Alcohol and Drug Use Composite scores will provide indices of

severity that allow the measurement of change across treatment or time. The Psychiatric Severity Composite will be used as a predictor variable. In addition to evaluating the impact of the intervention on substance use and 12-step engagement, the ASI-Lite will be used to assess the impact on more general psychosocial function through the Medical, Employment, Legal, Family/Social, and Psychiatric Status indices of the measure.

5.4.3.1.4 Fagerstrom Test for Nicotine Dependence

Fagerstrom Test for Nicotine Dependence (FTND) The FTND is a 6-item self-report questionnaire that assesses dependence on nicotine (Heatherton et al., 1991; Kozlowski et al., 1994). This instrument has acceptable internal consistency (.61) and its items form a homogeneous set in factor analysis. The scale correlates significantly with biological measures of smoking consumption. One of its items provides a measure of number of cigarettes smoked per day. The FTND will be completed during the baseline assessment, at study week 8, and at the 3- and 6-month follow-up visits.

5.4.3.2 12-Step Indices

5.4.3.2.1 Validity of Self-Reports of 12-Step Involvement and Meeting Attendance

There is often concern about the veracity of self-reported drug use behavior among substance abusers. These concerns might also be extended to the validity of self-reports of 12-step meeting attendance and activities. Tonigan, Connors, and Miller (Tonigan, Connors et al. 2003) have reported a relatively high correspondence between client and collateral reports of meeting attendance. As part of a 3-month post-treatment follow-up assessment in Project MATCH, outpatients were asked about their attendance at AA meetings. Collateral informants were also asked to estimate the exact percentage of days during the 90-day follow-up window that the client had attended AA meetings. The correlation between the client and collateral reports was .84. This was an increase from a correlation of .67 found for the outpatients and their collaterals at intake. Based on these results, and their previous finding that their measure of AA attendance had a high degree of test-retest reliability over a two day period (r = .92) (Tonigan, Miller et al. 1997), Tonigan, et al. (Tonigan, Connors et al. 2003) concluded that client self-reports of AA attendance are highly reliable and reasonably valid. Based on the work of Tonigan, we have chosen to continue with self-reports of 12-step activities and meeting attendance without external verification.

5.4.3.2.2 Self-Help Activities Questionnaire (SHAQ)

The SHAQ is a self-report instrument which will be administered at all research visits, that was developed for use in the NIDA Cocaine Collaborative Treatment Study. It assesses the frequency of attendance at a number of self-help groups (both 12-step – e.g., AA, NA, CA, CMA and non-12-step – e.g., Rational Recovery, Secular Organization for Sobriety) and the degree of participation in self-help activities in each of these groups (Weiss, Griffin et al. 1996). At each assessment, participants are asked to indicate whether they have an AA/NA/CA sponsor. They are also asked how many days in a given time period that they attended Speaker meetings and Step meetings (e.g., attendance measures), how many days that they have attended meetings in which they have had duties (e.g., setting up, making coffee), spoken at meetings, met with sponsors or other group members outside of the meetings, phoned or have been phoned by sponsors or other group members, read 12-step recovery literature, and worked on any of the steps (e.g., measures of participation). The original time frame was a week, so that subjects indicated the frequency of these behaviors from 0 to 7. Measures of internal consistency reliability were high (Cronbach alpha ranging from .78 to .85) for AA, NA, and CA items. Factor analyses resulted in three primary factors: “work performed at meetings,”

"interpersonal work performed outside of meetings," and "work performed alone and outside of meetings." The measure has been used to describe self-help related behaviors (Weiss, Griffin et al. 1996), to evaluate differential changes in these behaviors as a function of the type of treatment received (Weiss, Griffin et al. 2000), and to compare the relationship between 12-step attendance and participation with subsequent drug use outcomes (Weiss, Griffin et al., 2005).

Two modifications have been made in the measure. First, the time frame has been increased beyond one week up to a month. Dr. Weiss, the scale's developer, has been using a 30-day window in his ongoing research (Weiss, personal communication, 2003). The reasons for this modification include reducing the potential of an "assessment reactivity effect" and making the assessment time window comparable to that of the other measures in the protocol. The assessment window is 30-days at baseline, weeks 4 and 8, and the follow-up visits. A second modification is to ask participants how helpful they feel these behaviors have been to them during the assessment period.

5.4.3.2.3 Survey of Readiness for Alcoholics Anonymous Participation (SYRAAP)

A potential contributor to individuals choosing not to attend 12-step meetings or engage in 12-step activities is their ambivalence about the 12-step approach and groups. Kingree and colleagues (Kingree, Simpson, Thompson, McCrady, Tonigan, & Lautenschlager, 2006; Kingree, Simpson, Thompson, McCrady, & Tonigan, 2007) have recently developed and validated a brief, 15-item measure that assesses issues related to ambivalence and readiness to engage in 12-step activities. The Survey of Readiness for Alcoholics Anonymous Participation (SYRAAP) consists of three 5-item subscales, each item is rated on a 5-point Likert scale (1 = strongly disagree, 5 = strongly agree). These measure individuals' perceptions about the severity of their substance use problems (e.g., "My substance use has hurt some other people"), the perceived benefits of their involvement in 12-step groups (e.g., "Going to AA gives me courage to change"), and the perceived barriers to participating in 12-step groups (e.g., "Going to AA can be embarrassing to me"). Internal reliability was excellent for Perceived Benefits (.92), good for the 15-item composite (.85), good for Perceived Severity (.81), and fair for Perceived Barriers (.71). Concurrent validity was demonstrated by positive correlations of the Perceived Severity, Perceived Benefits, and total composite score with recent AA participation, while the Perceived Barriers scale was negatively correlated with recent AA participation (Kingree, et al., 2006). Predictive validity was demonstrated by baseline scores on the SYRAAP being associated with higher levels of AA participation at 3- and 6-month post treatment assessments (Kingree, et al., 2007). The wording of items will be modified to specify 12-step involvement in addition to AA. The SYRAAP will be administered at baseline.

5.4.3.2.4 Twelve-Step Experiences and Expectations (TSEE)

The TSEE is a brief measure of participants' prior experiences with 12-step groups developed for use in this protocol. Individuals are asked to indicate whether they have ever attended 12-step groups (AA, NA, CA, and CMA) or other substance-related self-help groups (Secular Organizations for Sobriety [SOS], Rational Recovery [RR]). If they have, they are asked to estimate the number of meetings they have attended in total and over the past 3 months, and to rate how helpful they feel that the meetings have been. They are also asked how likely they are to get involved in a 12-step group during this treatment episode and how helpful they anticipate such involvement will be. The TSEE will be administered at baseline.

5.4.3.3 Spiritual Involvement and Beliefs Scale - Revised (SIBS-R)

Twelve-step programs are often described as "spiritual fellowships," and spirituality is thought to be an important component in the recovery process facilitated by involvement in 12-step programs (Galanter, 2006; Miller, 2003). Although spirituality is difficult to define and is thought to be

multidimensional (Cook, 2004; Miller, 1998), broadly speaking, the role of spirituality in recovery from substance use disorders relates to the promotion of individuals' achieving a meaningful life (Galanter, 2006). This often occurs through a process of spiritual awakening. The Spiritual Involvement and Beliefs Scale (SIBS) (Hatch, Burg, Naberhaus, & Hellmich, 1998) will be used to assess this component of 12-step involvement. This self-report measure, as originally developed, consisted of 26 items. It demonstrated high levels of internal consistency (alpha = .92) and test-retest reliability (.92), and a four-factor structure. Subsequent scale refinement has led to a revised and shortened scale of 22 items that maintain the high level of reliability and the four-factor structure (Hatch, personal communication, 2006). The factors assess core spirituality (connection, meaning, faith, involvement, and experience), spiritual/existential perspective, personal application/humility, and acceptance/insight (i.e. insight into futility of focusing attention on things that cannot be changed). This 22-item version will be used. The SIBS-R will be administered at baseline and the End of Treatment/week 8 visit.

5.4.3.4 Substance-Related Measures: Predictors and Mediators

5.4.3.4.1 Short Understanding of Substance Abuse Scale (SUSS)

Humphreys and colleagues (Humphreys, Greenbaum et al. 1996) developed the Short Understanding of Substance Abuse Scale (SUSS) as a modified version of the Understanding of Alcoholism Scale. The latter scale was developed originally by Moyers and Miller (Moyers and Miller 1993) to assess alcoholics' beliefs about the etiology and treatment of alcoholism. Two changes were made. First, the scale was shortened from 50 items to 20 items. Second, the wording of the items, as well the inclusion of some new items, has been broadened to focus on both alcohol and drug use. Three factor analytically derived subscales have been identified: disease model, psychosocial model, and eclectic orientation. These subscales had Chronbach alpha coefficients of internal consistency of .78, .85, and .61 respectively. A difference between the original and modified short SUSS is that Humphreys, et al. (Humphreys, Greenbaum et al. 1996) had the measure filled out by treatment staff members, while Moyers and Miller (Moyers and Miller 1993) had the original completed by clients in treatment. The SUSS will be administered to both participants and participating counselors. This scale will be collected at baseline.

5.4.3.4.2 Self-Efficacy Measures

While 12-step facilitation interventions have been found to increase 12-step related attitudes and behaviors, they have also been found to increase more general skills and perceptions of self, such as self-efficacy expectancies and substance-focused coping skills (Finney, Noyes et al. 1998). We will assess two aspects of self-efficacy using two brief measures, both of which will be collected at baseline and at the End of Treatment/week 8 visit.

5.4.3.4.2.1 Drug Taking Confidence Questionnaire (DTCQ-8)

The first is the 8-item Drug Taking Confidence Questionnaire (DTCQ-8; Sklar & Turner, 1999). This measure, derived from a longer 50-item version, provides a global index of coping self-efficacy across eight situational areas associated with relapse: unpleasant emotions, physical discomfort, pleasant emotions, testing personal control, urges and temptations to use, conflict with others, social pressure to use and pleasant times with others. The 8 items on the DTCQ-8 were selected, based on regression and factor analyses, as the best exemplar of the eight high-risk relapse areas. Individuals rate their degree of confidence that they could resist the urge to use their primary or secondary problem drug across these eight high-risk relapse situations. High levels of efficacy as measured by the DTCQ-8 are associated with greater confidence that one is able to refrain from using, less difficulty in quitting use, greater motivation for and commitment to quit using.

5.4.3.4.2.2 Self-Efficacy Questionnaire – Patient Version (SEQ-P)

A second element of perceived self-efficacy is the degree of confidence the individual has that he or she will be able to remain drug-free and/or sober over a specified period of time (e.g., 3 months). The patient version of the Self-Efficacy Questionnaire (SEQ-P) developed by Goldbeck, et al. (Goldbeck, Myatt et al. 1997) consists of five items in which the individual rates his or her degree of confidence in remaining abstinent over the next 3 months, the expected difficulty in being able to do so, the amount of help that might be needed to do so, the strength of one's desire to do so, and the degree to which one believes that it would be possible to use drugs once or twice without starting to use heavily again. Goldbeck, et al (1997) found that the level of self-efficacy as measured by the SEQ-P at the end of treatment was predictive of abstinence status at 3-month follow-up.

5.4.3.4.3 Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES)

The SOCRATES (Miller and Tonigan 1996) is a 20-item self-report measure of clients' readiness to change their substance use behaviors. It will be administered at the baseline and End of Treatment/week 8 visits. Originally, the 40-item scale had five subscales based on Prochaska and DiClemente's Stages of Change model of addictive behaviors. The SOCRATES was developed and its psychometric properties determined in Project MATCH. Isenhardt (Isenhart 1994) has used a modified version of the SOCRATES that includes references to drug use with a broader range of substance abusers; this is the version that will be employed. The current version has three subscales: Taking steps, Recognition of a problem, and Ambivalence. The instrument is intended to assess which of these stages the individual is in at the time of the assessment. Psychometric properties of the SOCRATES are good to excellent. Cronbach's alpha for the three scales ranged from .88 to .96, while test-retest reliability ranged from .83 to .99. The final three-factor solution seems stable. Inclusion of a measure of readiness to change is important in light of the findings by Laudet (Laudet 2003). Major obstacles to participation in 12-step programs centered on motivation and readiness for change and on perceived need for help, rather than on aspects of the 12-step program often cited as points of resistance (e.g., religious aspect and emphasis on powerlessness).

5.4.3.5 Process measures

5.4.3.5.1 Helping Alliance Questionnaire- Revised (HAQ-II)

The client version of the HAQ-II (Luborsky, et al., 1996), which was developed on a sample of cocaine dependent individuals, is a self-report measure that assesses the extent to which the individual experiences the therapist and the therapy as helpful. It consists of 19 items that are rated on a 6-point Likert scale (1 = strongly disagree to 6 = strongly agree) that address two types of helping alliance: perceived helpfulness (e.g., the individual's experience of the therapist as providing or being capable of providing the help that is needed) and collaboration or bonding (e.g., the individual's experience of treatment as a process of working together with the therapist toward the goals of treatment). This measure is administered to participants randomized to STAGE-12 only and will be assessed at the week-2 and End of Treatment/week 8 study visits.

5.4.3.5.2 Treatment Services Review (TSR)

The TSR (McLellan, Alterman et al. 1992) is a measure of the type and extent of the treatment services that a client reports receiving over a given time period. These time periods have included 7-day, 14-day, and 30-day assessment time frames. An abbreviated TSR will be used in part to capture all treatment sessions attended by participants, and to determine the content of "treatment as usual"

and the comparability of services received across treatment conditions. This abbreviated version will assess those services most likely to be provided within the context of participating CTPs; these include the General, Medical, Alcohol and Drug, and Psychological Services sections. The TSR has been used in a similar way to compare services received in inpatient, day hospital, intensive outpatient, and outpatient programs (Alterman, O'Brien et al. 1994; Alterman, Snider et al. 1996; McLellan, Hagan et al. 1997). The TSR will be administered at baseline, 4 weeks, End of Treatment/week 8 and the follow-up visits.

5.4.3.5.3 Participant Satisfaction Survey (PSS)

The Participant Satisfaction Survey (PSS) evaluates both global aspects of satisfaction with the STAGE-12 intervention and the perceived helpfulness of more specific aspects of the intervention. The general satisfaction items for this measure were modeled after those used in other brief measures of client satisfaction (e.g., Attkisson and Greenfield 1994; Attkisson and Greenfield 1999), particularly those used to assess participant satisfaction in Project MATCH (Donovan, Kadden et al. 2002) which also served as the source for the items used in the CTN protocol on motivational enhancement therapy with pregnant substance abusers (CTN0013). There are eight items in this section. Two items ask about the participants' current condition and the change in their status since beginning treatment. The remaining six items ask participants to rate their overall satisfaction with the STAGE-12 intervention, the number of STAGE-12 individual and group counseling sessions, their STAGE-12 counselor, the extent to which the STAGE-12 intervention met their needs, and the extent to which they would return to the STAGE-12 program if they were to seek treatment in the future. The second section of the survey asks participants to rate how helpful they felt specific components of the STAGE-12 intervention were. These included their STAGE-12 counselor, the group meetings and individual counseling sessions, gaining a better understanding of 12-step programs and principles, assignments or "recovery tasks" to do between sessions, encouragement to attend 12-step meetings, arranging for an outside 12-step member to help get the participant to a meeting, and attending a 12-step meetings in the community. This is administered to participants randomized to STAGE-12 only and will be administered at the End of Treatment/week 8 visit.

5.4.3.5.4 Treatment Attendance

Clinic treatment attendance form both STAGE-12 and TAU participants will be monitored with the treatment tracking form. This information will provide an additional measure of participant treatment, augmenting the Treatment Services Review and providing a more continuous measure of the number of sessions and hours received during the first eight weeks of study participation.

5.4.3.6 Counselor Measures

5.4.3.6.1 Short Understanding of Substance Abuse Scale (SUSS)

As noted previously in section 5.4.3.4.1, the SUSS (Humphreys, Greenbaum et al. 1996) will be administered to counselors as well as to clients.

5.4.3.6.2 Clinician and Supervisor Survey (CSS)

This self-report survey (Ball, Bachrach et al. 2002) obtains information on: a) counselor demographics; b) levels of experience, education, and credentials; c) personal recovery; d) counseling orientation; e) and beliefs about treatment, clients, and the recovery process. For counseling orientation, clinicians are asked to rate on a 5-point Likert scale the extent to which each

of seven common addiction counseling approaches describes their typical approach. The approaches listed include: 12-step/disease concept, relapse prevention/cognitive-behavioral therapy, reality therapy, motivational interviewing, Rogerian/client centered, Gestalt/experiential, and psychodynamic/interpersonal therapy. Items dealing with treatment beliefs and those specific to motivational interviewing, which was the primary focus in the study by Ball and colleagues, will not be asked since they are not relevant to the current protocol.

5.4.3.6.3 Addiction Counseling Self-Efficacy Scale (ACSES)

The ACSES (Murdock, Wendler et al. 2005) is a self-report measure of counselors' perception of their skillfulness in five areas involved in working with substance abusers. These include (a) specific addiction counseling skills, (b) assessment, treatment planning, and referral skills, (c) co-occurring disorders skills, (c) group counseling skills, and (d) basic counseling skills. Counselors rate their degree of confidence on each item on a scale from 1 = not at all confident to 5 = highly confident. The scales have a high degree of internal consistency (alphas = .87 to .92). For the present study, we propose using the 8-item specific addiction counseling skills, the 5-item group counseling skills, and the 4-item basic counseling skills scales since these have applicability to the skills particularly relevant to the intervention.

5.4.3.6.4 Attitudes towards 12-Step Groups (ATSG)

Laudet and colleagues (Laudet, 2003; Laudette & White, 2005) have developed a brief 12-item measure from a much larger pool of items assessing clinicians' attitudes toward 12-step groups. Responses are rated on Likert scales. The first 3 items assess the perceived helpfulness and importance of such groups in the treatment and recovery process. The remaining 9 items define three factor-analytically derived subscales dealing with controversial aspects of 12-step groups. These factors deal with issues of religion and powerlessness, risks of participation, and untrained leadership. Laudet and White (2005) found that counselors who hold more positive attitudes toward 12-step groups were much more likely to refer clients to 12-step groups. Conversely, counselors who expressed greater concern about the emphasis on religion and powerlessness reported referring fewer clients to 12-step groups.

5.4.3.6.5 Goal Commitment to Integrating STAGE-12 into Standard Care

Hollenbeck and colleagues (Hollenbeck, Williams, & Klein, 1989) developed a measure of goal commitment in the context of complex tasks. It consists of 9-items that examine an individual's commitment to a specified goal. For the purpose of the present protocol, the focus is specified as the goal of integrating the STAGE-12 intervention into their CTP's program (e.g., "I am strongly committed to pursuing the goal of integrating the 12-Step Program into our practice"; "I am willing to put forth a great deal of effort beyond what I'd normally do to achieve the 12-Step integration goal"). This variable may mediate adherence to the intervention manual and also may predict subsequent programmatic adoption of the STAGE-12 intervention. The measure will be administered to counselors prior to study implementation. This measure will also be integrated with the Drug and Alcohol Treatment Program Inventory, which will be completed by CTP Clinical Directors.

5.4.3.6.6 Counselor/Administrator Perceptions of Impact of Protocol Participation

Recently Knudsen, Ducharme, and Roman (2007) have investigated the impact of research protocol participation in the NIDA Clinical Trials Network on staff retention/turnover depending on whether this

participation was viewed as burdensome/stressful or rewarding. They have used a 15-item, 5-point Likert scale measure to assess these perceptions. This scale will be administered to participating counselors and the Clinical Director upon completion of providing the STAGE-12 intervention to participants within the CTP at the end of the trial. Its purpose is to evaluate clinicians' experience of their protocol participation and a potential predictor of subsequent CTP adoption of STAGE-12.

5.4.3.6.7 Computer Administered Assessment Instruments

A number of the participant assessment instruments will be administered via computer, with the individual completing the measures on the computer himself/herself rather than being administered as interviews and entered onto computer screens by the research staff. Research staff will provide the individuals with an overview of the computer, the assessment instrument computer screen, and instructions on how to enter responses and to move from item to item within a given instrument and to the next instrument in the computerized assessment battery. Research staff will be available and can assist the individual as needed and/or requested.

5.4.4 Safety Assessments

5.4.4.1 Adverse Events

Adverse events will be captured as defined in Section 7, beginning at the first visit after randomization.

5.4.4.2 Substance Use Events

Those events meeting the criteria of being related to drug use and are expected and prevalent in the study population will be captured on the Substance Use Events form. These events will include admission for detoxification, symptoms associated with withdrawal, worsening of drug use, and cravings. This assessment will be collected at 4 weeks, End of Treatment/week 8 and the follow-up visits.

5.5 Participant Reimbursement

Participants will be reimbursed for their transportation, inconvenience, and time for non-treatment assessment visits. The format and distribution schedule will be determined by the participating CTP and the local Institutional Review Board (IRB), with the approval of the Lead Investigator.

6.0 TREATMENTS

6.1 Treatment as Usual

Study participants will be enrolled in the currently employed outpatient psychosocial treatment (OPT) in the participating CTPs. The TAU in participating CTPs will likely reflect varying theoretical orientations and treatment philosophies. Many CTPs may reflect a 12-step treatment philosophy and provide encouragement of clients to become involved in 12-step activities. However, it is likely that this effort typically is not applied in a structured or systematic manner. As Carroll, et al. (Carroll, Nich et al. 2000) noted, the structured method of 12-step facilitative interventions is quite distinct from what most CTPs employ. Although discussions about 12-step meetings between staff and patients will take place as they would otherwise, CTP counselors providing TAU will not provide participants the components of the STAGE-12 intervention (either the TSF-based groups or Intensive Referral), including project-prepared handouts, reading material, or journal (and so are not encouraged to write down their plans and reactions regarding 12-step meeting attendance). Participants in TAU also will not be connected to a community-based 12-Step volunteer nor will they receive a list of potential sponsors. These preclusions are consistent with those included in the standard referral/TAU against which Timko's intensive referral condition was evaluated.

Treatment as usual (TAU) will consist of 5 –15 hours of weekly outpatient therapy, as is typically provided by the CTP. Information will be collected from the Clinical Directors of participating sites to document the nature of treatment delivered in TAU. As part of this information, the Clinical Directors will be asked to complete relevant portions of Drug and Alcohol Program Treatment Inventory (DAPTI; Swindle, Peterson, et al., 1995). The DAPTI assesses treatment goals and activities specific to a number of treatment orientations and has been used to classify programs within the Veterans Administration system as being primarily 12-step oriented, cognitive-behaviorally oriented, or an eclectic mix of these two (Ouimette, et al., 1997, 1998, 1999). This description of typical therapy at the CTP will be collected prior to site initiation, and changes will be communicated to the study team as necessary. Treatment may include regular outpatient, intensive outpatient, day and evening programs, and/or partial hospitalization and provide sufficient treatment intensity to allow group and individual sessions comparable to the 1.5 to 2.5 hours replaced each week in the TAU by STAGE-12 sessions for at least 5 weeks during the 8-week intervention phase.

6.2 Stimulant Abuser Groups to Engage in 12-Step (STAGE-12)

6.2.1 Overview of STAGE-12 Intervention

Section 3.7.2 described the rationale for delivering a 12-step intervention in a group format and integrating individual sessions to enhance adherence to treatment and maximize outcome. The STAGE-12 intervention includes five, approximately 90-minute, group sessions adapted from the Twelve-Step Facilitation Therapy for Drug Abuse and Dependence developed by Baker and colleagues at Yale (Baker 1998; Carroll, Nich et al. 1998). These group sessions will be supplemented by three, approximately 45-75 minute, individual sessions, including the introductory and termination sessions from the TSF manual, and incorporating the intensive referral protocol developed by Timko and colleagues (2006). The STAGE-12 intervention will be delivered over a period from 5 to 8 weeks in duration, during which 8 sessions of the TAU program provided at the CTP will be replaced with the STAGE-12 sessions. In addition to the STAGE-12 sessions, participants randomized to this group will participate in additional TAU sessions as determined by the standard therapy at the CTP. Group sessions for STAGE-12 will focus primarily on helping participants better understand and incorporate the core principles of 12-Step approaches while also

encouraging involvement, while the intensive referral / SECA sessions will focus primarily on facilitating participants' entry into, and active participation in, 12-Step groups. It is felt that combining these two interventions, each of which has demonstrated efficacy, will lead to an increased effect. It is also consistent with the suggestion of Caldwell and Cutter (Caldwell & Cutter 1998) that interventions that are effective in increasing attendance may be insufficient to ensure active involvement and that individuals also may need professional assistance that focuses more on 12-step practices and tenets and less on meeting attendance. Intensive referral focuses on getting individuals to attend, while the group-based TSF sessions focus on assisting individuals to understand the rationale of the 12-step approach.

6.2.2 Group Component Sessions

Sessions are based on the adaptation of TSF content for delivery in a group format by Brown and colleagues (Brown, Seraganian et al, 2002). The primary goal of TSF is to promote abstinence from substances by facilitating the client's acceptance and surrender of his/her addiction, and encouraging active involvement in 12-Step meetings and related activities. The four core topics plus one session from the elective topics from the TSF intervention will be used. These were chosen since they were viewed by the developers of the TSF intervention as core or as those sessions thought to be essential for all participants to receive. The main role of the counselor is to provide education, facilitate group discussions of session topics, and be supportive and encouraging to participants. General session outlines and content are found in Table 2.

Table 2: Group Sessions

1. **Acceptance (Step 1), session #1**: This session will include a review of previous assignments and participant experiences. Step work will begin in this session. Recovery assignments will be provided for review at the next session.

2. **People, places, & things (habits & routines), session #2**: This session begins with a review of previous recovery assignments and patient experiences. A review of lifestyle changes will be the focus of this session. Recovery assignments will be provided for review at the next session.

3. **Surrender (Steps 2 & 3), session #3**: This session will involve reviewing previous recovery assignments and participant experiences. Step work will be continued and recovery tasks for the upcoming week will be assigned.

4. **Getting active in 12-Step programs, session #4**: This session will include a review of previous recovery assignments and patient experiences. The focus of this session will be on abstinence vs. sobriety with a recovery program and the details of meeting involvement. Recovery tasks for the upcoming week will be assigned

5. **Emotions, Session #5:** This session will involve reviewing previous recovery assignments and participant experiences. The focus of this session will be to help the individual identify emotions that are most often associated with slips. Recovery tasks for the upcoming week will be assigned.

The five group sessions follow a similar format beginning with a "check-in" in which members introduce themselves, report on their homework related to AA, NA, CA, or CMA participation, and any strong desires or cravings to use drugs or alcohol. The remainder of the session focuses on an interactive discussion of the content of the sessions, a summary of key "take-home" messages, and the assignment of homework between sessions. There is no set order in which participants are required to attend sessions; that is, session content is independent and there is no prerequisite of attending one session before the next. This allows for rolling admission to groups. When surveyed about their preference of closed-admission, cohort-based groups versus open, rolling admission groups, CTPs overwhelmingly (95.4%) endorsed the use of rolling admission.

Rolling admission will be used in the group sessions, so that a minimum membership may be maintained in each session. Participants assigned to the STAGE-12 intervention will be able to join the group at any session, following attendance at their first individual therapy session. In order to facilitate the rolling admissions to groups, two of the core sessions from the TSF for Drug Abuse and Dependence manual will be delivered as individual sessions. These include the introduction/assessment session and the termination session. The content of these sessions does not lend itself to rolling admissions and seems appropriate to be delivered individually. Each group will have a minimum of 2 and a maximum of 15 participants per session.

6.2.3 Individual Component Sessions

Three individual sessions will be used to augment the group sessions. The individual sessions will incorporate the intensive referral/SECA model of Timko and colleagues (Timko, DeBenedetti et al., 2006) and are provided to complement the TSF group sessions. All three sessions focus on facilitating the client's use of 12-step recovery programs in the community, emphasizing active participation in 12-step activities as a primary means to recovery. The participant is encouraged to attend 12-step meetings, to turn to the 12-step program to gain support in changing old habits that maintain substance use, and to increase social involvement with other 12-step members. An aspect of the intervention noted by participants in Timko's study was the positive experience of personal contact with a 12-step group volunteer who served as both a role model and an additional source of support. Participants will begin their involvement in STAGE-12 with the introductory individual session, which will allow an orientation to the overall intervention and the sequence of the group sessions into which they will enter, thus facilitating the rolling admission process. The first individual session, incorporating the TSF introductory component and the call to a 12-step group member to arrange for their becoming involved with the participant, is likely to require more time than the other two sessions, which have considerably less content to cover. The general individual session content is found in Table 3.

Table 3: Individual Sessions

1. **First Individual Session**: The first session will involve activities such as establishing rapport and introducing the 12-step view of substance use and dependence. The session will include discussion on the patient's history and future goals for sobriety and 12-Step participation. The counselor provides the participant with 12-step group information. During this session, the counselor and participant call a self-help group volunteer who will meet the participant before the first meeting so they can attend the meeting together. Recovery assignments to be reviewed at the next session will be assigned.
2. **Second Individual Session**: The second session content will vary, depending on whether the participant has attended a 12-step meeting since the first session. If so, the participant's reactions to the meeting will be discussed and homework will be reviewed. If not, the session will focus on perceived and actual barriers to attendance and a 12-step meeting volunteer will again be contacted.
3. **Third Individual Session**: The third session will involve reviewing recovery assignments and participant experiences. The session will be focused on reviewing views of addiction and 12 step programs now as opposed to prior to treatment. It will either focus on finding a sponsor if a meeting was attended since the last session or setting up a meeting with a 12-step group volunteer if a meeting was not attended. Barriers to participation will be reviewed. Goals and plans for the future will be discussed.

An important component of STAGE-12 intervention is the work done outside of sessions. Both group and individual sessions have "homework" that the participant is asked to complete between sessions and be ready to share in the group or with the counselor. There are four elements to this homework. The first is literature (e.g., AA's Big Book, NA's Basic Text) that clients are asked to read. This material is meant to complement the topics discussed during the weekly sessions. The second is "recovery tasks," which the participant is asked to do, such as contacting a sponsor, taking on service work at a meeting, etc. The third is strong encouragement from the counselor to attend several different kinds of 12-step meetings per week. The final element is keeping a journal. The journal

documents 12-step group attendance and participation, reactions to the meetings and other assigned recovery tasks, or, if the client did not attend a meeting, what factors served as barriers to attendance. They are also asked to keep track of when, where, and with whom they experienced urges to use drugs or actual slips, how they handled these, and what they could do in the future (e.g., calling a 12-step friend, going to a meeting, going to a 12-step group social activity, calling one's sponsor). The journal entries are reviewed at the beginning of each individual session, while the other activities are reviewed during the check-in at group session. These activities provide additional material for the weekly sessions.

6.2.4 Non-Participant STAGE-12 Group Members

STAGE-12 group sessions may be populated with non-participant group members. These individuals are clients in treatment who were not enrolled in the study due to various reasons: beginning treatment prior to the beginning of study recruitment, being ineligible for study participation, or being initially uninterested in the study. CTP clients not interested in participating in the study may subsequently seek an alternative to groups offered at the clinic as part of treatment as usual and may decide to attend STAGE-12 groups. Because these clients are involved in an experimental intervention, they must also provide informed consent or provide verbal consent with an approved information sheet. They must also be made aware of the risks and benefits of group participation. A separate consent form or information sheet is provided for non-study participants.

Non-participant group members are involved primarily to guarantee that group size does not fall below the minimum of 2 participants. To ensure that STAGE-12 groups run continuously throughout the study, each group session may include up to 6 non-participants.

These are their key characteristics:

- Non-participant group members are not considered either STAGE-12 or TAU participants in the study. Essentially, they are "auditing" the STAGE-12 group sessions similar to how students audit a college course: they are not truly "enrolled" in the class but they could gain a benefit from the experience.
- Non-participant group members are consented with a separate consent form or information sheet. They are involved in STAGE-12 group sessions only; they are not involved with STAGE-12 individual sessions.
- Non-participant group members do not have to meet eligibility requirements or meet diagnosis for stimulant abuse or dependence.
- Non-participant group members are not randomized and do not complete research visits or study assessments. No data are collected on individual non-participant group members, though the number of non-participant group members attending each session will be collected.
- Non-participant group members are not compensated for their participation.
- Non-participant group members meet with research staff only for the consent process and to determine the next available group session to attend.
- Non-participant group members may be audio-recorded during the group sessions but the recordings are protected during the study and deleted after procedures have ended, according to local IRB practices. This information is included in the consent form or information sheet.

6.3 Treatment Measures

6.3.1 Quality Control of Treatments Administered

Quality control for the STAGE-12 intervention will be conducted via ongoing review of recordings of group and individual sessions. Adherence scales will be used both for the group and the individual interventions.

Group session adherence scale: Counselor adherence to the structure and content of the protocol in delivery of TSF content of the group sessions will be evaluated following the procedures described by Baker (Baker 1998). Both counselors and supervisors complete parallel adherence rating forms after each session conducted or viewed. The forms consist of Likert-type items covering a range of key TSF interventions (review of recovery tasks, exploration of the patient's use of denial, encouragement to make use of 12-Step programs, etc.). The counselor version of the form is based the TSF Therapist Checklist (Carroll, Nich et al., 1998), and asks the counselor to rate what TSF strategies and interventions were implemented in a given session, and how much the intervention was used. This form has a variety of purposes. First, it is intended to remind the counselor, at each session, of the key ingredients of TSF. Second, it is intended to foster a greater adherence to the manual through self-monitoring of adherence. Third, it can organize and provide the basis for supervision, as the counselor can more readily note and explore with the supervisor the strategies and interventions s/he has trouble implementing with a given participant.

The supervisor version of the form based on the TSF Rating Scale (Carroll, Nich et al., 1998) differs from the counselor version by adding a skillfulness rating for each item. Thus for each intervention, both *quantity* and *quality* are rated. This form is an essential part of training, as it provides structured feedback to the counselor and forms the basis of supervision. It also provides a method of determining whether a counselor in training is ready to be certified to deliver the treatment. When used with ongoing supervision, it enables the supervisor to monitor and correct counselor drift in implementation of the treatment.

Individual session adherence scale: The three individual sessions will be rated using checklists developed for use with the intensive referral procedures. The forms consists of a series of specific activities that counselors are expected to include in each session. For sessions 2 and 3, the specified activities differ depending on whether or not the participant attended a 12-step meeting or not. The counselor indicates which of the elements of the intensive referral strategies and interventions were implemented in a given session. Supervisors can similarly complete the checklist based on their review of session tapes.

6.3.2 Other Procedures to Minimize Potential Biases and Contamination in Administration of Therapies

The threat of cross-contamination is potentially problematic. We will instruct and encourage participants in the STAGE-12 intervention not to share information about the specifics of their treatment with individuals outside of those who are in the intervention group. However, there is no guarantee participants will not discuss their treatment, especially if their treatment raises issues that are then brought into other groups. Likewise, there are concerns about possible cross-contamination coming from program staff (i.e. a counselor learns some of the elements of the STAGE-12 intervention and communicates to other counselors who begin to incorporate elements into other TAU groups). These issues will be addressed in protocol-specific training. Overall, because the STAGE-12 treatment is unique and has many structured sessions and elements, we believe that it is unlikely

participants or staff in the TAU, or those not involved directly with the trial, will be contaminated by casual contact.

6.4 Counselors/Staffing

Two counselors and one supervisor will be selected at each CTP to provide the STAGE-12 intervention. The counselors will each provide the STAGE-12 intervention based on meeting scheduling and caseload, and may also cover TAU sessions as assigned by the CTP. The supervisor will provide fidelity monitoring to the intervention and provide back-up support for group sessions in the event a counselor is unavailable for a scheduled session. All other staff at the CTP will provide the standard treatment.

7.0 REPORTING AND MONITORING

7.1 Statement of Compliance

This trial will be conducted in compliance with the appropriate protocol, current Good Clinical Practice (GCP), the principles of the Declaration of Helsinki, and all other applicable regulatory requirements. Participating sites must obtain written approval of the study protocol, consent form, other supporting documents, and any advertising for participant recruitment from their local institutional review board (IRB) in order to participate in the study. Prior to study initiation, the protocol and the informed consent documents will be reviewed and approved by an appropriate Ethics Review Committee (ERC) or IRB. Any amendments to the protocol or consent materials must be approved before they are implemented.

7.2 Regulatory Files

The regulatory files should contain all required regulatory documents, study-specific documents, and all important communications. Regulatory files will be checked at each participating site for the regulatory documents compliance prior to study initiation, throughout the study, as well as at the study closure.

7.3 Informed Consent

The informed consent form is a means of providing information regarding the trial to a prospective participant and allows for an informed decision about participation in the study. All participants (or legally acceptable representative) must read, sign, and date a consent form prior to undergoing any study-specific procedures and participating in the study. In order to ensure that potential study participants understand the research study, a comprehension “quiz” may be administered to potential participants prior to the informed consent being signed. If the potential participant misses an item on the quiz, the research staff will re-review that information to ensure understanding of study procedures and may have the person re-take the consent quiz prior to signing the informed consent document. The content of the quiz may be modified per local IRB requirements.

The informed consent form must be updated or revised whenever important new safety information is available, or whenever the protocol is amended in a way that may affect a participants’ participation in the trial. A copy of the informed consent will be given to a prospective participant to review during the consent process and to keep for reference. The participant will be informed that their participation is voluntary and they may withdraw from the study at any time, for any reason without penalty.

Study counselors randomized to provide interventions will also require informed consent in order to participate in the study. As with participants, each potential study counselor will be given a current copy of the counselor informed consent form. For both study participants and counselors, all aspects of the study will be explained in appropriate language and all of the candidate’s questions will be answered. Individuals who refuse to participate or who withdraw from the study will be treated without prejudice. Study sites will be responsible for maintaining signed consent forms as source documents for quality assurance review and regulatory compliance.

7.4 Health Insurance Portability and Accountability Act (HIPAA)

Study sites may be required by their institutions to obtain authorization from participants for use of protected health information. Sites will be responsible for communicating with their IRBs or Privacy Boards and obtaining the appropriate approvals or waivers to be in regulatory compliance.

7.5 Investigator Assurances

Each community treatment program site (CTP) must file (or have previously filed) a Federal Wide Assurance (FWA) with the DHHS Office for Human Research Protection setting forth the commitment of the organization to establish appropriate policies and procedures for the protection of human research subjects, with documentation sent to NIDA or its designee. Research covered by these regulations cannot proceed in any manner prior to NIDA receipt of certification that the research has been reviewed and approved by the IRB provided for in the assurance (45 CFR 46.103(b) and (f)). Prior to initiating the study, the principal investigator at each study site will sign a protocol signature page, providing assurances that the study will be performed according to the standards stipulated therein.

7.6 Financial Disclosure

All investigators will comply with the requirements of 42 CFR Part 50, Subpart F to ensure that the design, conduct, and reporting of the research will not be biased by any conflicting financial interest. Everyone with decision-making responsibilities regarding the protocol will have an up-to-date signed financial disclosure form on file with the sponsor.

7.7 Monitoring

Investigators will host periodic visits by NIDA contract monitors who will ensure all study procedures are conducted and that study data are generated, documented and reported in compliance with the protocol, GCP, and applicable regulations. These monitors will audit, at mutually agreed upon times, regulatory documents, case report forms (CRFs), and corresponding source documents for each participant.

Qualified node personnel will provide site management for each site during the trial. This will take place as specified by the local protocol team or node PI and will occur as often as needed to help prevent, detect, and correct problems at the study sites. Node staff will verify that study procedures are properly followed and that site staffs are trained and able to conduct the protocol appropriately. If the node staff's review of study documentation indicates that additional training of study personnel is needed, node staff will undertake or arrange for that training.

7.8 Data and Safety Monitoring Board

An independent CTN DSMB will examine accumulating data to assure protection of participants' safety while the study's scientific goals are being met. The CTN DSMB is responsible for conducting periodic reviews of accumulating safety and efficacy data. It will determine whether there is support for continuation of the trial, or evidence that study procedures should be changed, or if the trial should be halted, for reasons relating to the safety of the study participants, the efficacy of the treatment under study, or inadequate trial performance (e.g., poor recruitment).

7.9 Protocol Violations Reporting and Management

A protocol deviation is any departure from procedures and requirements outlined in the protocol. Protocol departures may occur on two levels, deviation versus violation. The difference between a protocol deviation and violation has to do with the seriousness of the event and the corrective action required. A protocol deviation is considered an action (or inaction) that by itself is not likely to affect the scientific soundness of the investigation or seriously affect the safety, rights, or welfare of a study participant. Protocol violations are departures that may compromise the participant safety, participant rights, inclusion/exclusion criteria or study data and could be cause for corrective actions if not rectified or prevented from re-occurrence. Protocol violations will be monitored at each site for (1) significance, (2) frequency, and (3) impact on the study objectives, to ensure that site performance does not compromise the integrity of the trial. The decision about whether a departure from the protocol will be designated as a protocol deviation or a protocol violation will be made by the protocol's Lead Investigator in conjunction with the Clinical Coordinating Center. The consequences will be specified and participating sites should be informed.

All protocol violations will be recorded in the Electronic Data Capture (EDC) system via the Protocol Violations CRF. Additionally, each site is responsible for tracking and reporting to the local IRB as required. Protocol deviations will be noted by participating sites and reported to local IRBs as required.

The Clinical Coordinating Center and the Data and Statistics Center must be contacted immediately if an unqualified/ ineligible participant is randomized into the study.

7.10 Confidentiality

By signing the protocol signature page the investigator affirms that information furnished to the investigator by NIDA will be maintained in confidence and such information will be divulged to the IRB, Ethical Review Committee, or similar expert committee; affiliated institution; and employees only under an appropriate understanding of confidentiality with such board or committee, affiliated institution and employees. The lead investigator will obtain a federal Certificate of Confidentiality (CoC), protecting participants against disclosure of sensitive information (e.g., drug use), and will distribute it to all sites when received. The NIH office that issues the CoC will be advised of changes in the CoC application information. Participating CTP sites will be notified if CoC revision is necessary.

Participant records will be held confidential by the use of study codes for identifying participants on CRFs, secure storage of any documents that have participant identifiers, and secure computing procedures for entering and transferring electronic data.

7.11 Adverse Events (AE)

The Lead Investigator (LI) will appoint a Study Clinician (MD, PhD, or PI) for this study, who will review or provide consultation for each Serious Adverse Event (SAE) as needed. These reviews will include an assessment of the possible relatedness of the event to the study intervention or other study procedures. The Study Clinician will also provide advice for decisions to exclude, refer, or withdraw participants as required. In addition, NIDA will assign a Safety Monitor to this protocol to independently review the safety data, present it to the DSMB for periodic review, and provide PIs a Safety Letter when necessary. The study staff will be trained to monitor adverse events and Serious Adverse Events.

Each of the CTPs has established practices for managing medical and psychiatric emergencies, and the study staff will be trained to utilize these procedures. Treatment providers at each CTP will be responsible for monitoring participants for possible clinical deterioration or other problems, and for recommending appropriate responses.

While counselors are consented and randomly assigned to the STAGE-12 intervention, no adverse event reports will be collected on them in this protocol.

7.12 Definition of Adverse Event and Serious Adverse Event

Adverse Event: An adverse event (AE) is defined as any reaction, side effect, or untoward event that occurs during the course of the clinical trial, whether or not the event is considered study-related or clinically significant. A new illness, symptom, sign or worsening of a pre-existing condition or abnormality is considered an AE. A thorough history during the eligibility assessment phase should record any chronic, acute, or intermittent preexisting or current illnesses, diseases, symptoms, or laboratory signs of the participant to avoid reporting false AEs and to assist in the assessment of worsening in intensity or severity of these conditions that would indicate an AE. Stable chronic conditions, such as arthritis, which are present prior to clinical trial entry and do not worsen are not considered AEs. All AEs must be recorded on the AE form. The AE form is also used to record follow-up information for unresolved events reported on previous visits. A study investigator will classify each AE, as serious or non-serious, and follow appropriate reporting procedures.

For the purpose of this study, the following events will not be classified as AEs but will be documented as described below:

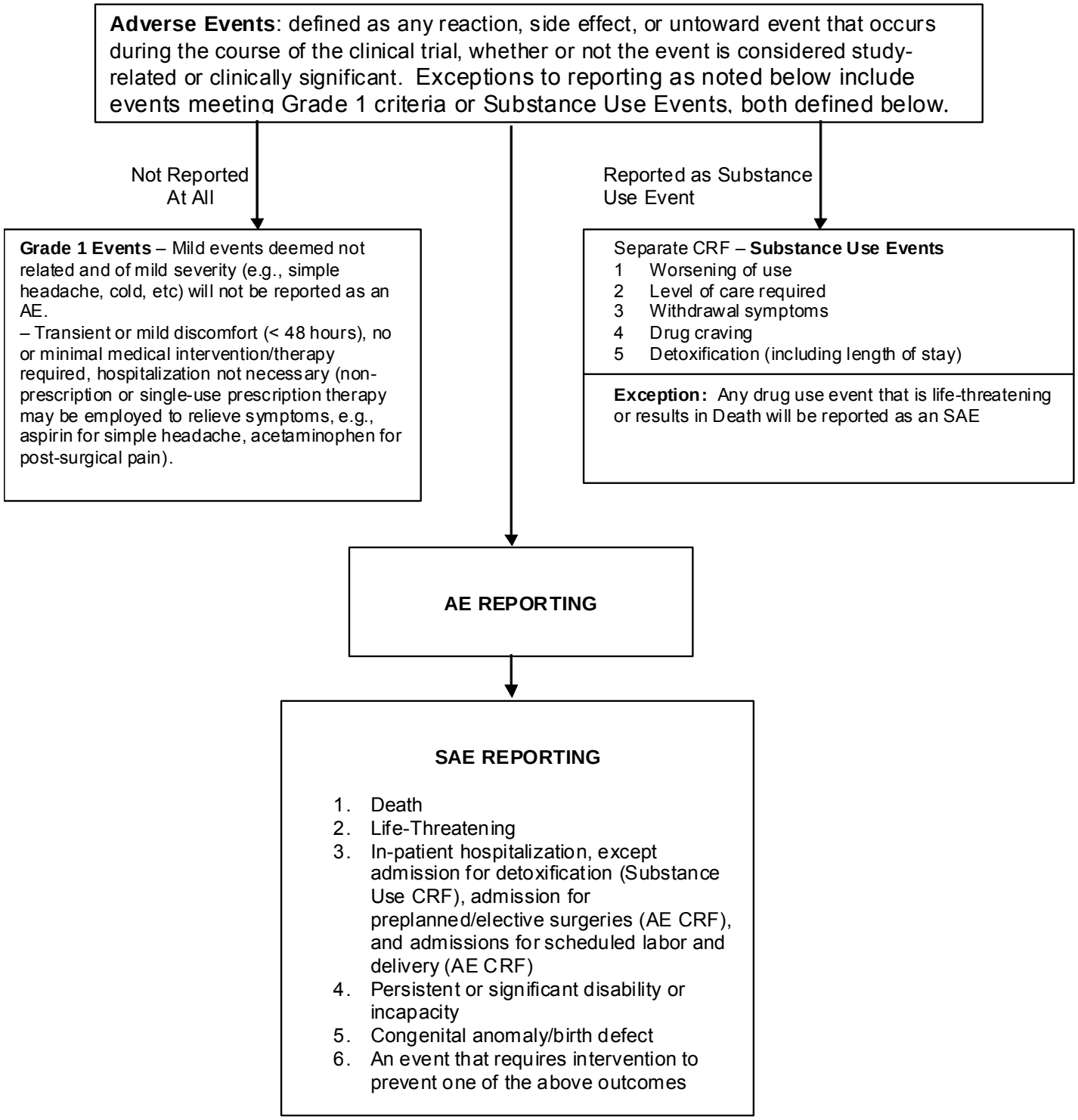
Any physical event deemed not related and of mild severity (e.g., headache, cold, etc; as determined by the site PI according to severity and relatedness criteria defined in section 7.13) will be captured in source documentation but not reported in the study database.

Symptoms associated with withdrawal will be captured on the Substance Use Events CRF.

Worsening of substance abuse symptoms (relapse) will be captured on the Substance Use Events CRF.

Figure 2 illustrates the safety reporting process for the study.

Figure 2
Safety Reporting



Serious Adverse Event (SAE): A serious adverse event is defined as any untoward physical or psychological occurrence during the study that suggests a significant hazard, side effect, or precaution will be defined as an SAE. This includes, but may not be limited to any of the following events:

- Death: A death occurring during the study or which comes to the attention of the investigator during the protocol-defined follow-up after the completion of therapy, whether or not considered treatment-related, must be reported.
- Life threatening: Any adverse therapy experience that places the participant or participants, in the view of the investigator, at immediate risk of death from the reaction as it occurred (i.e., it does not include a reaction that had it occurred in a more serious form, might have caused death).
- In-patient hospitalization or prolongation of existing hospitalization.
- Persistent or significant disability or incapacity.
- Congenital anomaly/birth defect.
- An event that required intervention to prevent one of the above outcomes.

For the purpose of this study, the following will not be considered SAEs:

- Admission to a hospital or freestanding residential facility for drug detoxification; the event will be captured on the Substance Use Event CRF (See Figure 2).
- Admission to a hospital/surgery center for preplanned/elective surgeries; the event will be captured as an AE and documented on the AE form.
- Admission to a hospital for scheduled labor and delivery; the event will be captured as an AE and documented on the AE form.

Eliciting and Monitoring Adverse Events: Appropriate research staff will elicit participant reporting of AEs/SAEs. Adverse events (medical and/or psychiatric) assessment will initiate with participant randomization and will continue through 30 days post last study visit. The research staff will obtain as much information as possible about the AE/SAE to complete the AE/SAE forms and will consult with designated staff as warranted. SAEs will be reported as indicated below in Section 7.14. A study investigator will review AEs for seriousness, severity, and relatedness weekly. Appropriate site staff will review all adverse event (AE) documentation and verify accuracy of assessments during each counselor visit with the participant to ensure that all AEs are appropriately reported and to identify any unreported SAEs. AEs/SAEs will be followed until resolution or stabilization or study end, and any serious and study-related AEs will be followed until resolution or stabilization even beyond the end of the study. Each participating site's Protocol PI is responsible for study oversight, including ensuring human research subject protection by designating appropriately qualified, trained research staff and medical clinicians to assess, report, and monitor adverse events.

Protocol monitors from the CCC and local node staff will review the study sites and study data on a regular basis and will promptly report any previously unreported safety issues and ensure that the SAEs are being followed appropriately by the research staff. The node staff or CCC monitor will ensure that any unreported or unidentified SAEs discovered during visits are promptly reported by the site to NIDA, the Study EC Chair's site, the Node or Protocol PI or designee, and the IRB per local IRB requirements and will be reported on the monitoring report. Staff education, re-training or appropriate corrective action plan will be implemented at the participating site when unreported or unidentified AEs or SAEs are discovered, to ensure future identification and timely reporting by the site. The NIDA CTN DSMB will also review data related to safety monitoring for this trial periodically at regularly scheduled meetings.

7.13 Assessment of Severity and Relatedness

A study investigator will review each AE for seriousness, relatedness, and severity. A study investigator will review all AEs and SAEs for severity and relatedness during each counselor visit with the participant, and will consult with other research personnel as needed. The severity of the experience refers to the intensity of the event. The relatedness of the event refers to causality of the event to the study. Relatedness requires an assessment of temporal relationships, underlying diseases or other causative factors, medication challenge/re-challenge and plausibility.

Severity: Severity grades are assigned by the study site to indicate the severity of adverse experiences. Adverse events severity grade definitions are provided below:

Grade 1	Mild	Transient or mild discomfort (< 48 hours), no or minimal medical intervention/therapy required, hospitalization not necessary (non-prescription or single-use prescription therapy may be employed to relieve symptoms, e.g., aspirin for simple headache, acetaminophen for post-surgical pain)
Grade 2	Moderate	Mild to moderate limitation in activity some assistance may be needed; no or minimal intervention/therapy required, hospitalization possible.
Grade 3	Severe	Marked limitation in activity, some assistance usually required; medical intervention/ therapy required hospitalization possible.
Grade 4	Life-threatening	Extreme limitation in activity, significant assistance required; significant medical/ therapy intervention required, hospitalization or hospice care probable
Grade 5	Death	

Relatedness: Relationship to therapy is defined as:

- Definitely related: An adverse event that follows a temporal sequence from administration of the test product and/or procedure; follows a known response pattern to the test article and/or procedure; and, when appropriate to the protocol, is confirmed by improvement after stopping the test product (positive dechallenge) and by reappearance of the reaction after repeat exposure (positive rechallenge); and cannot be reasonably explained by known characteristics of the participant's clinical state or by other therapies.
- Probably related: An adverse event that follows a reasonable temporal sequence from administration of the test product and/or procedure; follows a known response pattern to the test product and/or procedure, is confirmed by improvement after dechallenge; and cannot be reasonably explained by the known characteristics of the participant's clinical state or other therapies.
- Possibly related: An adverse event that follows a reasonable temporal sequence from administration of the test product and/or procedure and follows a known response pattern to the test product and/or procedure, but could have been produced by the participant's clinical state or by other therapies.

- Unrelated: An adverse event that does not follow a reasonable temporal sequence after administration of the test product and/or procedure; and most likely is explained by the participant's clinical disease state or by other therapies. In addition, a negative dechallenge and/or rechallenge to the test article and/or procedure would support an unrelated relationship.

7.14 Reporting and Management Procedures of AE/SAEs

Standard reporting, within 7 days of the site becoming aware of the event, is required for reportable adverse events. Expedited reporting (within 24 hours of their occurrence and/or site's knowledge of the event) is required for serious adverse events (including death and life-threatening events). A participating site must alert the Study EC Chair and the NIDA-assigned Safety Monitor of SAEs within 24 hours of learning of the event. The SAE form and summary and any other relevant documentation should also be submitted with the initial report if adequate information is available at the time of the initial report to evaluate the event and provide a complete report.

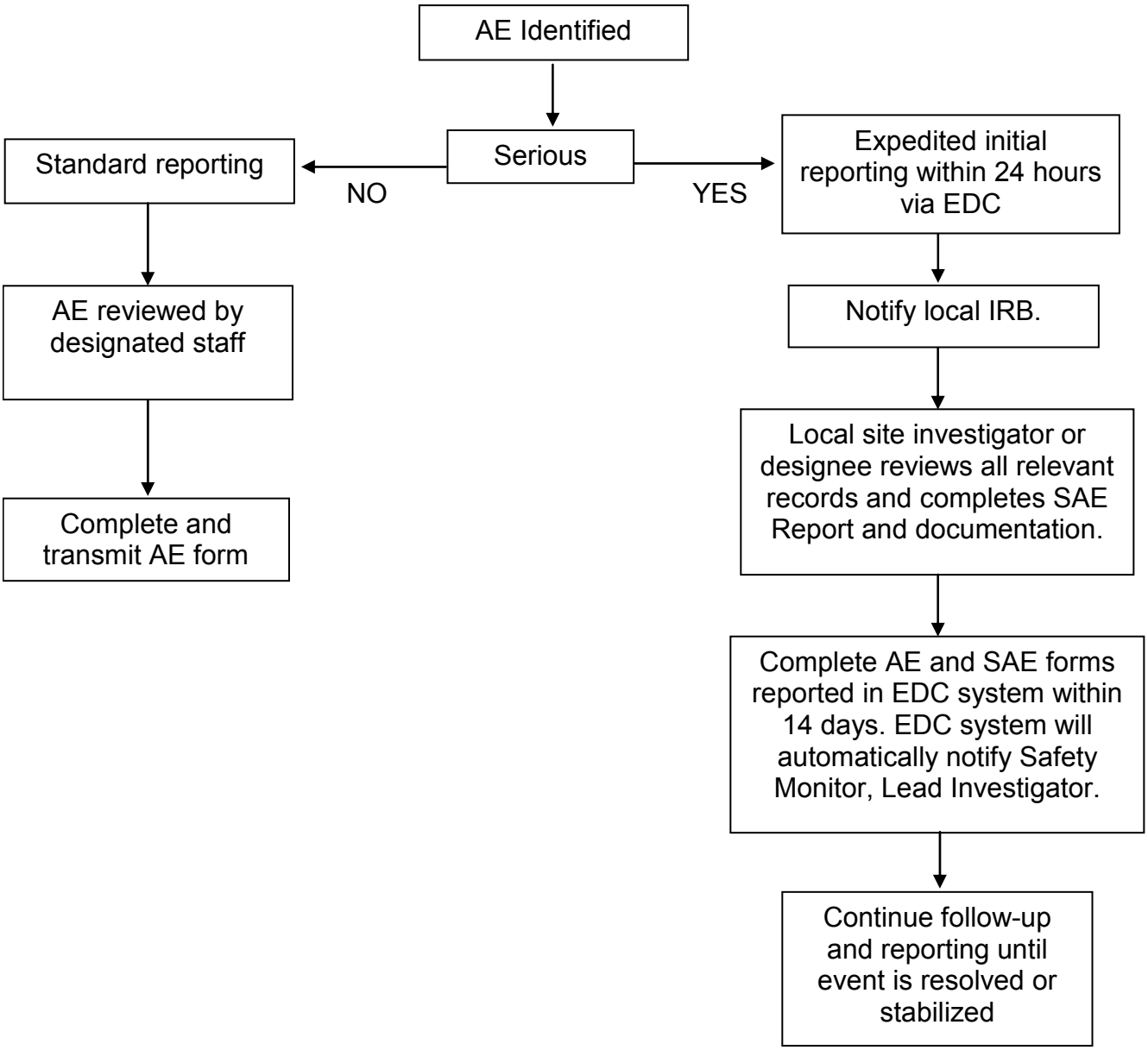
Additional information may need to be gathered to evaluate the SAE and to complete the AE and SAE forms. This process may include obtaining hospital discharge reports, physician records, autopsy records or any other type records or information necessary to provide a complete and clear picture of the SAE and events preceding and following the event. Within 14 days of learning of the event, an SAE form and related documents must be completed and sent to the Study EC Chair and the NIDA-assigned Safety Monitor. If the SAE is not resolved or stabilized at this time or if new information becomes available after the SAE form and summary is submitted, an updated SAE report must be submitted as soon as possible, but at least within 14 days after the site learns the information.

The Site Principal Investigator (PI) must apply his/her clinical judgment to determine whether or not an adverse event is of sufficient severity to require that the participant be removed from treatment. The Site PI may consult with the Study EC and the Safety Monitor as needed. If necessary, an Investigator may suspend any trial treatments and institute the necessary medical therapy to protect a participant from any immediate danger. Subsequent review by the Medical Monitor, DSMB, ethics review committee or IRB, the sponsor, or the FDA or relevant local regulatory authorities may also suspend further trial treatment at a site. The study sponsor and DSMB retain the authority to suspend additional enrollment and treatments for the entire study as applicable. A participant may also voluntarily withdraw from treatment due to what he/she perceives as an intolerable adverse event or for any other reason. If voluntary withdrawal is requested, the participant should be asked to continue (at least limited) scheduled evaluations, complete an end-of-study evaluation and be given appropriate care under medical supervision until the symptoms of any adverse event resolve or their condition becomes stable.

A NIDA-assigned Safety Monitor is responsible for reviewing all serious adverse event reports. The monitor will also report events to the sponsor and the Data and Safety Monitoring Board (DSMB). The DSMB will receive summary reports of all adverse events annually, at a minimum.

Serious adverse events will be followed until resolved or considered stable, with reporting to the NIDA assigned Safety Monitor through the follow-up period. The site must actively seek information about the SAE as appropriate until the SAE is resolved or stabilized or until the participant is lost to follow-up and terminated from the study. The Study EC Chair, or the NIDA- assigned Safety Monitor may also request additional and updated information. Details regarding remarkable adverse events, their treatment and resolution, should be summarized by the Investigator in writing upon request for review by the NIDA-assigned Safety Monitor, local ethics Committee/IRBs or regulatory authorities.

Figure 3: SAE Reporting Procedure Flowchart



8.0 DATA MANAGEMENT

8.1 Design and Development

This protocol will utilize a centralized Data and Statistics Center (DSC). The DSC will be responsible for development of the electronic case report forms (eCRFs), development and validation of the clinical study database, ensuring data integrity, and training site and participating node staff on applicable data management procedures. A web-based distributed data entry model will be implemented. This system will be developed to ensure that guidelines and regulations surrounding the use of computerized systems used in clinical trials are upheld. The remainder of this section provides an overview of the data management plan associated with this protocol.

8.2 Data Collection Forms

The data collection process consists of direct data entry at the study sites into the EDC system(s) provided by the DSC. This process excludes the SUC which will be captured on a calendar prior to entry. The DSC will provide the sites with a final set of guided source documents and instructions. The guided source documents will be distributed electronically to the participating CTPs. These documents are used to collect data in the event the database is unavailable. Data entry of the eCRFs should be completed according to the instructions provided and project specific training. The investigator is responsible for maintaining accurate, complete and up-to-date records, and for ensuring the completion of the eCRFs for each research participant. The DSC is not responsible for maintaining any source documentation related to the study, including any films, tracings, computer discs or tapes.

8.3 Data Acquisition and Entry

Data entry into electronic CRFs shall be performed by authorized individuals. Selected eCRFs may also require the investigator's written signature or electronic signature, as appropriate. Electronic CRFs will be monitored for completeness, accuracy, and attention to detail during the study.

8.4 Site Responsibilities

The data management responsibilities of each individual CTP will be specified by the DSC.

8.5 Data Center Responsibilities

The DSC will 1) develop a data management plan and will conduct data management activities, 2) provide final eCRFs for the collection of all data required by the study, 3) develop data dictionaries for each eCRF that will comprehensively define each data element, 4) conduct ongoing data monitoring activities on study data from all participating CTPs, 5) monitor any preliminary analysis data clean up activities, and 6) rigorously monitor final study data clean up.

8.6 Data Editing

Completed data will be entered into the DSC automated data acquisition and management system. If incomplete or inaccurate data are found, a data clarification request will be generated and distributed to sites for a response. Sites will resolve data inconsistencies and errors and enter all corrections and changes into the DSC automated data acquisition and management system.

8.7 Data Transfer

Data will be transmitted by the DSC to the NIDA central data repository as requested by NIDA. The DSC will conduct final data quality assurance checks and "lock" the study database from further modification. The final analysis dataset will be returned to NIDA, as requested, for storage and archive.

8.8 Training

The training plan for CTP staff includes provisions for training on assessments, eCRF completion guidelines, data management procedures, and the use of computerized systems.

8.9 Data QA

To address the issue of data entry quality, a random sample of eCRFs will be selected from each CTP for a source-to-database audit according to the DSC's Internal Audit SOP. The random selection process should occur as a regular part of the data management process, but the frequency of sampling can remain flexible during data capture. The results of the audits should be made available to the study executive group at any time during the study, and a final summary report will be required as part of the pre-lock procedures. An acceptable quality level will be established as a part of the data management plan.

9.0 COUNSELOR SELECTION, TRAINING, AND SUPERVISION

9.1 Introduction:

This study will utilize a centralized training of counselors and a training-of-trainers/supervisors model.

9.2 Counselor/Supervisor Selection

Study counselors and supervisors will be chosen from the participating CTPs. The educational background, credentials, and experience of the clinical staff implementing the intervention will vary between CTPs. All counselors and supervisors will be assessed during the recruitment process on their 12-step knowledge and familiarity with using a 12-step model during treatment. Potential counselors for the study will be identified by the Site PI in conjunction with CTP supervisors. After informed consent process and successfully completing a screening session, a select number of counselors will be chosen randomly from the available pool to serve as STAGE-12 counselors, and participate in a national training program. All training sessions conducted by trainees for selection and certification will be recorded. At least one counselor and one supervisor from each participating CTP will attend this training.

9.3 STAGE-12 Counselor Training

The STAGE-12 training will be completed prior to study initiation. Counselors will be briefed about the general study aim of the merits of 12-step facilitation in substance abuse settings. Counselors hired after training will be trained at their local site with consultation from the Lead Node training group.

Appropriate training for the STAGE-12 intervention requires completion of a didactic seminar and supervised training cases, as required. The STAGE-12 training will include a didactic seminar, presented in a face-to-face training by experts in TSF and Intensive Referral. The training seminar will include a review of basic 12-step principles, topic-by-topic review of the STAGE-12 manual, several role play and practice exercises, discussion of case examples, and rehearsing strategies for difficult or challenging cases.

9.4 Certification and Additional Training for Supervisors

In addition to the therapy training, treatment supervisors will attend an extra training session. This component will focus on providing supervision and using the adherence scales to rate recorded sessions. Those ratings will be compared to ratings made by a Lead Node expert trainer in the study intervention.

Ongoing Supervision of Counselor: During the study, STAGE-12 counselors will receive regularly scheduled individual supervision that will include review and discussion of randomly selected, recorded sessions. Supervisors will rate the sessions for adherence prior to the individual meeting with the counselor.

Ongoing Supervision of Supervisors: In order to ensure ongoing supervisor competency, supervisors will have conference calls with experts in the intervention to answer questions that arise about the treatment and supervision. Supervisors will also submit adherence ratings for expert review. The Lead Node will co-rate 20% of the sessions to assure supervisor fidelity.

10.0 STATISTICAL ANALYTIC PLAN

10.1 Objectives of the analysis

The primary objective of this study is to examine the degree to which 12-Step Facilitation Therapy (STAGE-12) integrated into treatment as usual (TAU) reduces days of stimulant use compared to TAU alone.

10.2 Randomization

Participants will be randomized to one of the two treatment conditions. Randomization will be stratified by site and by whether the participant was court-mandated for treatment vs. not court-mandated. The randomization process will be conducted in a centralized process through the Data and Statistical Center (DSC).

10.3 Primary Outcomes

10.3.1 Hierarchical linear model

The primary outcome variable will be percent of days of stimulant use over the assessment window, based on Substance Use Calendar alone and assessed at baseline, weeks 4 and 8/end of treatment, 3 months and 6 months. This measure will be analyzed using hierarchical linear models. Specifically, the trajectory over time for an individual patient will be described by the Level-1 model

(1) $$Y_{ijk} = X_i\varphi + \beta_{0ij} + \beta_{ij}t_{ik} + \varepsilon_{ijk}, \qquad k=1,\ldots, n_i$$

where Y_{ijk} and ε_{ijk} are percent of days of stimulant use and error term of participant i at site j at post-baseline assessment k, β_{0ij} is the baseline percent of stimulant use, β_{ij} is the slope for participant i, t_{ik} is the number of weeks at post-baseline assessment k, n_i is the number of post-baseline assessments for participant i, which can differ between the participants reflecting attrition; X_i is a baseline variable describing whether participant i was court mandated for treatment (X_i = 1) vs. not court-mandated for treatment (X_i = 0).

The Level-2 model describes the slope for participant i as a function of the treatment arm:

(2) $$\beta_{ij} = \alpha_{0j} + \alpha_1 I(\text{STAGE-12}) + b_{ij}$$

Here α_{0j} is the intercept for participants at the jth treatment site, α_1 is the effect of the STAGE-12 treatment, I(STAGE-12) is a 0-1 STAGE-12 treatment indicator and b_{ij} is a subject-specific random error term.

The Level-2 model also describes the baseline outcome measure for participant i:

$$\beta_{0ij} = \alpha_{00j} + b_{0ij}$$

Here α_{00j} is the intercept for participants at the jth treatment site and b_{0ij} is a subject-specific random error term.

The assumptions of the model are: a) $\mathbf{e_{ij}} = (\varepsilon_{ij1},\ldots,\varepsilon_{ijn_i})^T$ are independent $N(0,\Sigma_i)$ where Σ_i depends in i only through its dimension, b) b_{ij} are independent $N(0, \sigma_b^2)$, uncorrelated with ε_{ijk}, c) b_{0ij} are independent $N(0, \sigma_0^2)$, uncorrelated with b_{ij} and ε_{ijk}

The primary analysis will evaluate the hypotheses H_0: $\alpha_1 = 0$ vs. H_1: $\alpha_1 \neq 0$ and rejection of the null hypothesis with $\alpha_1 < 0$ would indicate that STAGE-12 treatment reduces percent of days of substance use compared to TAU.

10.3.2 Subject-specific vs. population-averaged model

We chose to employ a subject-specific model as it allows to model explicitly different sources of variability and makes it easier to specify the covariance structure. Under the identity link with Gaussian errors, the model coefficients have both a subject-specific and a population-averaged interpretation. Further, if interdependence between the participants attending the same group therapy sessions has to be incorporated into the model, this could be easily done using a subject-specific model.

10.4 Secondary Outcomes

Key secondary endpoints are listed below in order of priority. No adjustment for multiplicity of the comparisons will be made and any statistically significant findings will be treated as exploratory.

1. Substances use other than stimulants (including alcohol) derived from Substance Use Calendar
2. 12-step meeting attendance derived from Substance Use Calendar
3. 12-step meeting attendance derived from Self-Help Activities Questionnaire
4. Involvement in 12-step activities derived from Self-Help Activities Questionnaire
5. Urine drug screen
6. Alcohol and Drug Use Composite Scores derived from the ASI

Other secondary endpoints should be considered as exploratory.

The following data analytic methods will be used to test hypotheses related to these secondary endpoints.

a. Hierarchical linear modeling will be used to assess the following endpoints:

1. % of days of non-stimulant use over assessment window (via Substance Use Calendar)
2. % of days of 12-step meeting attendance
3. Involvement in 12-step activities
4. ASI Drug and Alcohol composite Scores
5. Spirituality derived from the Spiritual Involvement and Beliefs Scale
6. Perceived barriers to 12-step involvement derived from the Survey of Readiness for Alcoholics Anonymous Participation

b. The proportional mean model will be used to assess these endpoints:

1. Positive drug screen from urinalysis

10.4.1 Substance Use Outcomes

10.4.1.1 Objective

To evaluate the degree to which a brief, combined group-plus-individually delivered 12-step facilitative intervention, integrated into treatment as usual, reduces the percent of days of use of non-stimulant drugs for participants with stimulant abuse or dependence disorders compared to TAU

10.4.1.1.1 Hypothesis

STAGE-12 will result in less non-stimulant substance use, as indicated by percent days of use on the Substance Use calendar, than TAU.

The outcome variable will be percent of days of non-stimulant use over the assessment window, based on Substance Use Calendar alone and assessed at baseline, weeks 4, 8/end of treatment, 3 months and 6 months. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_{NS} denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_{NS} =0 vs. H_1: $\alpha_{NS} \neq 0$ will be evaluated and rejection of the null hypothesis with $\alpha_1 < 0$ would indicate that STAGE-12 treatment reduces percent of days of substance use compared to TAU.

10.4.1.1.2 Hypothesis

STAGE-12 will result in fewer positive drug screens/urinalyses than TAU.

The outcome variable will be positive drug screen (yes/no) measured at baseline, weeks 4, 8/end of treatment, 3 months and 6 months. The data will be analyzed using the proportional mean model for recurrent events (Lin et al., 2000):

$$\mu_Z(t) = E\{N_i(t) \mid Z_i\} = \exp(\lambda_D Z_i)\mu_0(t),$$

where Z_i = 0 if the participant belongs to TAU group and Z_i = 1 if the participant belongs to STAGE-12 group; $N_i(t)$ is the total number of positive drug screen results for participant i at the time of assessment t; λ_D is the effect of the STAGE-12 treatment. The advantage of the proportional mean model is that it does not assume the nature of the influence of prior events on the future recurrence. The following statistical hypotheses will be assessed: H_0: λ_D =0 vs. H_1: $\lambda_D \neq 0$. Rejection of the null hypothesis with $\lambda_D < 0$ would indicate that STAGE-12 treatment results in fewer positive drug screens than TAU. The analysis will be performed using PROC PHREG with TIE=DISCRETE option for handling ties event times and COV(AGGREGATE) option to request the robust sandwich covariate matrix estimate.

10.4.1.1.3 Hypothesis

STAGE-12 will result in lower scores on the ASI Drug and Alcohol Composite Scores than TAU.

The outcome variable will be ASI Drug and Alcohol Composite Scores assessed at baseline, week 8/end of treatment, 3 months and 6 months. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_S denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_S =0 vs. H_1: $\alpha_S \neq 0$ will be evaluated and rejection of the null hypothesis with $\alpha_S < 0$ would indicate that STAGE-12 treatment results in lower ASI Drug and Alcohol Composite Scores than TAU.

10.4.2 12-Step Outcomes

10.4.2.1 Objective

To evaluate the degree to which a brief, combined group-plus-individually delivered 12-step facilitative intervention, integrated into treatment as usual, increases involvement in 12-step activities, meeting attendance, and acceptance of 12-step beliefs and values, compared to TAU.

10.4.2.1.1 Hypothesis

STAGE-12 will result in greater 12-step attendance (attend more meetings) than TAU

The outcome variable will be percent of days (frequency) of the 12-step meeting attendance in the SUC over the assessment window, measured at baseline, weeks 4, 8/end of treatment, 3 months and 6 months. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_{AA} denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_{AA} =0 vs. H_1: α_{AA} ≠0 will be evaluated and rejection of the null hypothesis with $\alpha_{AA} > 0$ would indicate that STAGE-12 treatment results in greater levels of 12-step meeting attendance than TAU.

10.4.2.1.2 Hypothesis

STAGE-12 will result in greater levels of 12-step activities than TAU.

The outcome variable will be percent of days (frequency) of the behaviors addressed in the SHAQ over the assessment window, measured at baseline, weeks 4, 8/end of treatment, 3 months and 6 months. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_{ACT} denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_{ACT} =0 vs. H_1: α_{ACT} ≠0 will be evaluated and rejection of the null hypothesis with $\alpha_{ACT} > 0$ would indicate that STAGE-12 treatment results in greater levels of 12-step activities than TAU.

10.4.2.1.3 Hypothesis

STAGE-12 will result in a greater increase on measures of spirituality than TAU.

The outcome variable will be a measure of spirituality as assessed by the Spiritual Involvement and Beliefs Scale at baseline and week 8/end of treatment. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_{SP} denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_{SP} =0 vs. H_1: α_{SP} ≠0 will be evaluated and rejection of the null hypothesis with $\alpha_{SP} > 0$ would indicate that STAGE-12 treatment results a greater increase on measures of spirituality than TAU.

10.4.2.1.4 Hypothesis

STAGE-12 will result in a greater reduction in 12-step perceived barriers to 12-step involvement than TAU.

The outcome variable will be a measure of perceived barriers to 12-step involvement as assessed by the Perceived Barriers subscale of the Survey of Readiness at baseline and week 8/end of treatment. The data will be analyzed using a hierarchical linear model similar to the model for the primary outcome. Let α_{PBAR} denote the effect of the STAGE-12 treatment in the Level-2 model. The hypotheses H_0: α_{PBAR} =0 vs. H_1: α_{PBAR} ≠0 will be evaluated and rejection of the null hypothesis with

$\alpha_{PBAR} < 0$ would indicate that STAGE-12 treatment results a greater reduction on measures of 12-step ambivalence than TAU.

10.4.3 Mediation

10.4.3.1 Objective

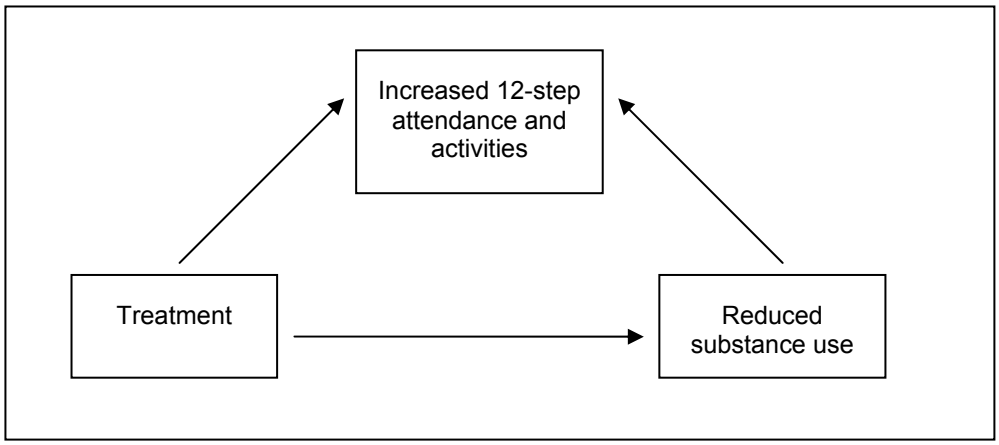
To examine 12-step meeting attendance and involvement as mediators of substance use outcomes.

10.4.3.1.1 Hypothesis

Reductions in substance use, regardless of treatment condition, are mediated by increases in 12-step attendance and 12-step activities.

The outcome variable will be percent of days of substance use over the assessment window, based on Substance Use Calendar alone and assessed at baseline, weeks 4, 8/end of treatment, 3 months and 6 months. The hypothesis will be investigated by adding an interaction term time*Mediator to the hierarchical linear model for the primary outcome, where Mediator denotes the factor of interest (12-step attendance or 12-step activities). Let γ_M denote the model coefficient associated with the time*Mediator term. The hypothesis H_0: $\gamma_M = 0$ vs. H_1: $\gamma_M \neq 0$ will be evaluated and rejection of the null hypothesis with $\gamma_M < 0$ would indicate that increases in 12-step attendance (12-step activities) result in reduction in substance use, regardless of treatment condition.

Objective: To examine client attitudes and beliefs as mediators of 12-step meeting attendance and involvement.



10.4.3.1.2 Hypothesis

Increases in 12-step meeting attendance and involvement, regardless of treatment condition, are mediated by increases in spirituality.

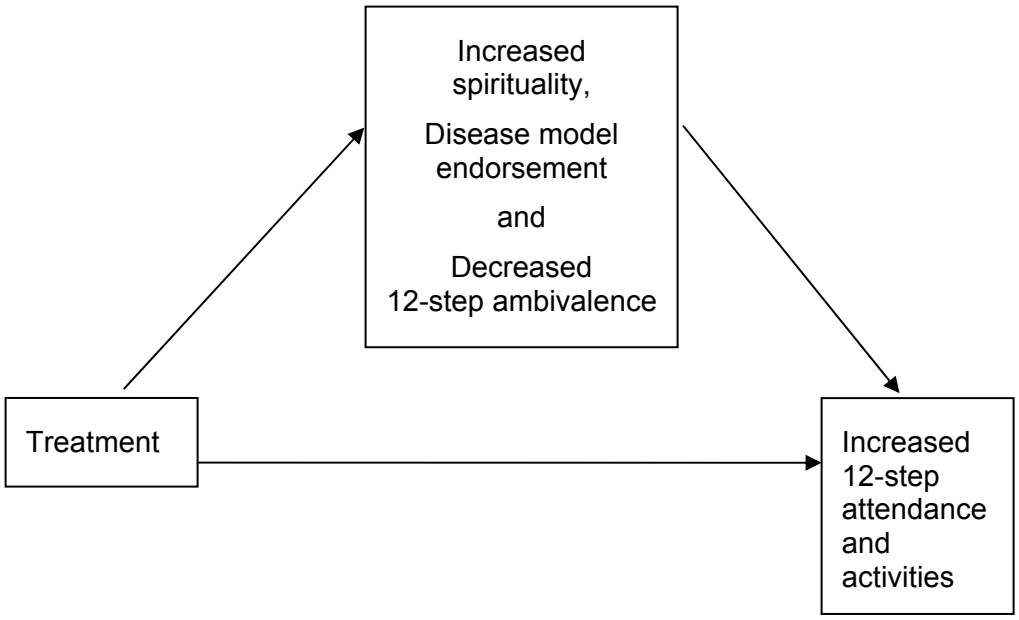
10.4.3.1.3 Hypothesis

Increases in 12-step meeting attendance and involvement, regardless of treatment condition, are mediated by decreases in 12-step ambivalence.

10.4.3.1.4 Hypothesis

Increases in 12-step meeting attendance and involvement, regardless of treatment condition, are mediated by increases in disease model endorsement.

The outcome variable will be percent of days (frequency) of the behaviors addressed in the SUC, SHAQ, and ITSI over the assessment window, measured baseline, weeks 4, 8/end of treatment, 3 months and 6 months. Each of the above hypotheses will be investigated by adding an interaction term time*Mediator to the hierarchical linear model, where Mediator denotes the factor of interest. Let γ_M denote the model coefficient associated with the time*Mediator term. The hypothesis H_0: $\gamma_M = 0$ vs. H_1: $\gamma_M \neq 0$ will be evaluated.



10.4.4 Exploratory hypotheses examining different client subtypes within STAGE-12

10.4.4.1 Objective

To examine the relative differences in 12-step meeting attendance and involvement and substance use outcomes of different client subtypes (e.g., ethnic/racial groups, gender, drug of choice, psychiatric severity, readiness to change).

10.4.4.1.1 Hypothesis

Individuals identified as ethnic minorities will be less likely to attend 12-step meetings and engage in 12-step activities than are Caucasian individuals.

10.4.4.1.2 Hypothesis

Men are more likely to attend 12-step meetings and engage in 12-step activities than are women.

10.4.4.1.3 Hypothesis

Individuals with higher levels of psychiatric severity, as assessed by the Addiction Severity Index, are less likely to attend 12-step meetings and engage in 12-step activities than are those with lower levels of psychiatric severity.

10.4.4.1.4 Hypothesis

Participants with different types of drug dependency (cocaine vs. methamphetamine) will differ with respect to their 12-step meeting attendance and engagement in 12-step activities.

10.4.4.1.5 Hypothesis

Individuals with higher levels of readiness to change their substance use behaviors are more likely to attend 12-step meetings and engage in 12-step activities than are those with lower levels of readiness to change.

The outcome variable will be 12-step meetings meeting attendance (yes/no). For each of the hypotheses listed above the data will be analyzed using the proportional mean model for recurrent events similar to the model for mean number of positive drug screens in 10.4.1.1.2. In this model, variable Z_i will be an indicator of a particular group of interest (e.g., ethnic minorities vs. Caucasian in the analysis for 1.3.4.1)

10.5 Missing Data

Missing data are very common in drug abuse research, with the amount of missingness increasing as the length of follow-up increases. The maximum likelihood methodology that will be employed for the estimation in the hierarchical model allows observations with arbitrary pattern of missingness to be used in estimation. However, unbiasedness of the resulting estimates is only guaranteed when the observations are missing completely at random. When observations are not missing completely at random, pattern mixture models (Little and Rubin, 1987) can be used to compare the outcomes across the various patterns of missing data. In pattern mixture analysis, participants are grouped according to their missingness pattern and such grouping identifies an indicator variable that can then be used in the analysis. The impact of the treatment arm on the missingness pattern is of greatest importance. However, such analysis can be confounded when participants in a particular missingness pattern group belong to one treatment arm only. This is especially likely to happen when there are multiple visits and therefore potentially many missingness patterns.

10.6 Sample Size and Power Calculations

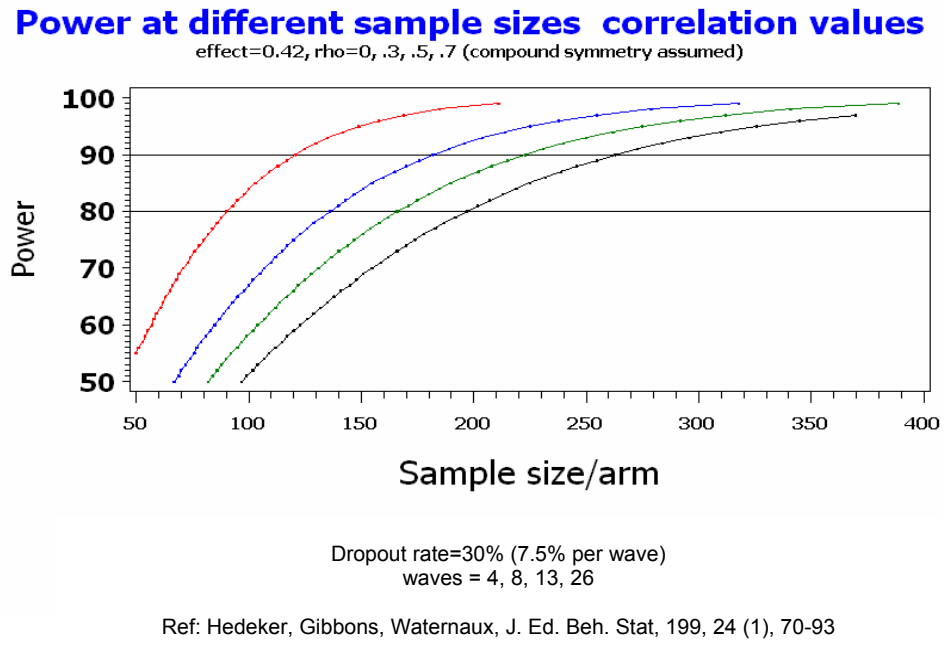
The sample size required for detecting a time by group interaction is estimated using the formulas due to Hedeker et al. (Hedeker, Gibbons, Waternaux, 1999). The following assumptions are employed. Four replicate, continuous, approximately normally distributed outcome (Percent of Days of Drug Use) measurements are to be obtained at 4, 8, 13 and 26 weeks (the baseline value is to be entered as a covariate). A two-sided type-I error rate (alpha) is set at 0.05 and power (1-beta) is assumed as 80%.

The expected effect size was determined by incorporating information from two sources. First, in the Brown, Serganian, et al. (2002) study of group-based TSF versus an active comparison therapy (relapse prevention [RP]), the standard deviation for "days of use in previous 90 days" was 24 days in the TSF group and 17.7 days in the RP group, giving a pooled estimate of the standard deviation of 21.3 days, or 23.7% of days of substance use over the 6-month assessment window. Second, clinicians and program directors from multiple CTPs in the CTN were asked about what they viewed as a potentially clinically meaningful difference between their TAU and an experimental treatment such as TSF. They indicated that a 10% difference, on average, in percent days of use between TAU and a new therapy would be clinically meaningful. A 10% difference divided by a standard deviation of 23.7% gives a standardized effect size of 10/23.7 = 0.42. Effects of this magnitude are in the 'small' to 'medium' range in the power analysis literature (Cohen, 1983). Based on or anticipated ability to track, follow, and assess participants at the follow-up points, a total retention rate of 70% for the duration of the trial was assumed, with the dropout rate occurring evenly over the 4 post baseline points is assumed; however, it should be noted that the follow-up rates in the Brown, Serganian, et al. (2002) was only about 50% at the 6-month follow-up. Compound symmetry with a correlation parameter of 0.5 is also assumed; however, there is no information available on the correlation pattern between observations.

Given this, we looked at a range of potential sample sizes based upon these initial assumptions, as well as additional assumptions in which the attrition rates and correlation parameters varied from the original assumptions. The table below shows potential sample sizes for effect size of 0.4, with attrition rates of either 30% or 50%, and the correlation parameters (rho) ranging from 0.3 to 0.7.

Effect Size	Attrition Rate	rho	Sample Size/Condition
0.4	0.3	0.3	139
0.4	0.3	0.5	165
0.4	0.3	0.7	191
0.4	0.5	0.3	181
0.4	0.5	0.5	213
0.4	0.5	0.7	245

Similarly, the graph below presents potential sample sizes and levels of power based on an effect size of 0.42 with differing levels of rho.



Dropout rate=30% (7.5% per wave)
waves = 4, 8, 13, 26

Ref: Hedeker, Gibbons, Waternaux, J. Ed. Beh. Stat, 199, 24 (1), 70-93

Based on these projections, we propose equal sample sizes of approximately 200 in each of two arms (TAU and STAGE-12). Based on the above table, this would provide power of 80%, rho of 0.5, both more originally assumed, while accommodating a potentially higher attrition rate than used in the original assumptions. And, based on the graph above, using the effect size of 0.42, rho = .5, and an attrition rate of 30%, this would provide power of approximately 85%. Thus, the trial is adequately powered to detect a small to moderate change in the difference in the change over time between the two groups in average level of drug use. As described below, a blinded variance check of the primary endpoint will be conducted relatively early in the trial to allow a more accurate estimate of this parameter to determine the adequacy of the projected sample size.

10.7 Interim Analysis

In coordination with the Data and Statistics Center, a blinded interim variance check of the primary outcome measure will be conducted to assess the adequacy of the projected study sample size since this parameter is being estimated from limited data. The analysis will be conducted when approximately 200 participants (about 100 per arm) have been enrolled and have been assessed at the 3-month follow-up point. A subset of these participants for whom 6-months post-randomization data are available will be examined to determine the consistency in the variance of the primary endpoint across time.

A DSMB will monitor the trial's progress. No interim analyses other than the blinded variance check are proposed for the trial. An interim analysis could still be performed to assess efficacy, futility or safety if requested by the DSMB or NIDA. Trial monitoring guidelines for early stopping considerations of benefit are based on an O'Brien-Fleming boundary (O'Brien and Fleming, 1979) using a 2-sided 0.05-level upper boundary. The monitoring guidance for early stopping considerations for lack of benefit or for futility will be based upon an approach of conditional probability (Turnbull and Jennison, 2000). Additional safety interim looks will be performed (without formal testing being performed) as per the DSMB's request.

SIGNATURES

SPONSOR'S REPRESENTATIVE

Typed Name	Signature	Date
CCTN Designee		

INVESTIGATOR (S)

- I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol and will only make changes in the protocol after notifying the sponsor except when necessary to protect the safety, rights, or welfare of participants.
- I will ensure that the requirements relating to obtaining informed consent and institutional review board (IRB) review and approval in 45 CFR 46 are met.
- I agree to report to the sponsor adverse experiences that occur in the course of the investigation, and to provide annual reports and a final report in accordance with 45 CFR 46.
- I agree to maintain adequate and accurate records and to make those records available for inspection in accordance with 45 CFR 46.
- I will ensure that an IRB that complies with the requirements of 45 CFR 46 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human participants or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human participants.
- I agree to personally conduct or supervise this investigation and to ensure that all associates, colleagues, and employees assisting in the conduct of this study are informed about their obligations in meeting these commitments.
- I agree to comply with all the applicable federal, state and local regulations regarding the obligations of clinical investigators as required by DHHS, the state and the IRB.

Typed Name	Signature	Date
Principal Investigator		
Sub-Investigator		
Sub-Investigator		

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