

AN INVESTIGATION OF EARLY RESPONSE AS A MEDIATOR IN GROUP  
PSYCHOTHERAPY FOR WOMEN WITH POST-TRAUMATIC STRESS DISORDER AND  
SUBSTANCE USE DISORDERS  
A DISSERTATION  
SUBMITTED TO THE FACULTY  
OF  
THE GRADUATE SCHOOL OF APPLIED AND PROFESSIONAL PSYCHOLOGY  
OF  
RUTGERS,  
THE STATE UNIVERSITY OF NEW JERSEY  
BY  
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IN PARTIAL FULFILLMENT OF THE  
REQUIREMENTS FOR THE DEGREE  
OF  
DOCTOR OF PSYCHOLOGY

NEW BRUNSWICK, NEW JERSEY

October 2013

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## ABSTRACT

The depression, substance abuse, and bulimia psychotherapy literature has demonstrated that symptom improvement within the first 4-8 weeks of treatment bears a predictive relationship with long-term outcomes and that this information can be used for treatment planning purposes. However, little is known about the mechanisms through which early response is related to therapeutic change. Theoretical arguments maintain that early improvement reflects the effects of nonspecific factors and may mediate the oft-observed relationship between common factors, such as therapeutic alliance, and post-treatment outcomes. Early response to psychotherapy has not been studied among individuals with PTSD. Utilizing data from the Clinical Trials Network - Women and Trauma Study, the present study assessed the predictive validity of early treatment response among 353 women diagnosed with PTSD and substance use disorders. Participants were randomized to receive 12 sessions of Seeking Safety group psychotherapy or Women's Health Education over 6 weeks. It was hypothesized that early response mediated the relationship between helping alliance and subsequent trauma and substance abuse outcomes, and that subjects in Seeking Safety improved more rapidly. ROC curves were used to assess the validity of early response and to generate clinical cutoff values predicting an individual's likelihood of non-response during follow-up. Latent growth curve methodology was utilized to test the proposed mediation model. While subjects demonstrated early improvement in trauma symptoms, there was no early improvement in substance abuse symptoms. Trauma symptom severity and cumulative abstinence at the fourth week of treatment predicted response status up to one year following treatment with a fair to excellent degree of accuracy. The rates of early improvement in trauma symptoms showed near-significant differences between the two treatment groups ( $p = .06$ ), suggesting that trauma symptoms improved more quickly among

subjects in Seeking Safety. Early symptom improvement was not found to be a viable mediator of helping alliance and outcomes. Results diverged from previous findings regarding early response to substance abuse treatment, which may be attributable to study limitations. The current study is unique in that it supports the predictive validity of early improvement in PTSD symptoms among women with comorbid PTSD and addiction.

### **Acknowledgements**

I would like to thank my family and friends for their love and support throughout this process. I would like to especially thank Erin and Vanessa.

I also wish to thank my chair, Dr. Denise Hien, for her knowledge, support, encouragement, and humor in the dissertation process and during my time working at the Trauma and Addiction Project (TAP). To my readers, Dr. James Langenbucher and Dr. Thomas Hildebrandt, whose invaluable guidance and expertise helped me continually improve my dissertation.

Finally, I wish to thank the staff of TAP and colleagues at Columbia University who provided guidance in developing my dissertation topic and practical support, including Lisa Cohen, Lesia Ruglass, Aimee Campbell, and Mei-Chen Hu.

## TABLE OF CONTENTS

CHAPTER	PAGE
I. Background.....	1
II. Literature Review.....	6
Post-traumatic Stress Disorder and Substance Use Disorders.....	6
Seeking Safety and manualized trauma-focused treatments.....	13
Early Response and generation of cut off values.....	19
Therapeutic Alliance.....	22
Therapeutic Alliance and Outcomes.....	22
Therapeutic Alliance and Group Psychotherapy .....	28
Therapeutic Alliance and PTSD .....	30
Therapeutic Alliance and Substance Use Disorders .....	33
III. Hypotheses.....	34
III. Method .....	39
Study Background.....	39
Procedures.....	40
Participants.....	41
Measures .....	42
Analyses.....	44
IV. Results.....	46

V. Discussion .....	59
VI. References .....	67

## LIST OF TABLES

Table 1. Baseline sociodemographic and clinical characteristics of subject .....	52
Table 2. Summary of area under the curve estimates for prediction of non-response on the Clinician Administered PTSD Scale (CAPS) by PSS-SR score during Weeks 1-6 of active treatment .....	53
Table 3. Summary of area under the curve estimates for prediction of non-response on the PSS-SR by PSS-SR score during Weeks 1-6 of active treatment.....	53
Table 4. Coordinates of the curve: Cutoff thresholds on the PSS-SR during Week 4 of active treatment in prediction of treatment nonresponse on the CAPS at follow-up .....	53
Table 5. Summary of area under the curve estimates for prediction of response on the Addiction Severity Index (ASI) by SUI score during Weeks 1-6 of active treatment .....	53
Table 6. Coordinates of the curve: Percent days abstinent during Week 4 of active treatment in prediction of substance abuse nonresponse according to the ASI at follow-up .....	54
Table 7. Effects of covariates on in-treatment change in PSS-SR latent growth variables during treatment weeks 4-6 .....	54



## LIST OF FIGURES

Figure 1. Receiver Operator Characteristic Curves: Prediction of non-response at 1-week, 3 months, 6 months, and 12 months post-treatment according to the clinician administered PTSD scale (CAPS) by PSS-SR scores during weeks 1-6 of active treatment .....	55
Figure 2 Receiver Operator Characteristic Curves: Prediction of non-response at 1 week, 3 months, 6 months, and 12 months post-treatment according to the PSS-SR by PSS-SR scores during weeks 1-6 of active treatment .....	56
Figure 3 Receiver Operator Characteristic Curves: Prediction of response on Addiction Severity Index (ASI) at 1-week, 3 months, 6 months, and 12 months as predicted by days of use (SUI) during active treatment.....	57
Figure 4. Latent Growth Curve of PSS-SR scores $\times$ time $\times$ treatment condition: The conditional mean slopes of PSS-SR scores from Weeks 4-6 in Seeking Safety and Women's Health Education. ....	58

## **Background**

In treating persons suffering from the lingering psychological impact of interpersonal trauma, the most influential clinical observations have held that establishing safety is the first task of therapeutic work. In establishing safety, the therapist encourages the person to bring about physical and emotional safety in his or her personal life, as one cannot effectively confront threatening experiences in the past while still actively in harm's way. Safety also denotes a foundation of trust in the therapeutic relationship, in that to risk the vulnerability that working through traumatic memory entails, the person must feel sufficiently emotionally safe with the therapist and hold at least rudimentary hope that he or she will reap benefit from therapy.

In her seminal work on trauma, Herman (1992) identified a felt sense of safety on the part of the patient with the therapist, the establishment of safety in the patient's life, and the strengthening of one's emotional and interpersonal resources as the central tasks of the first phase of trauma therapy. Over the past 20 years, the increase in the number of manualized and evidence-based treatments for post-traumatic stress disorder have expressly incorporated safety as a foundational aspect of treatment, or at minimum include a discussion of a strong therapeutic alliance as prerequisite to the manual's implementation. Seeking Safety, a manualized group treatment specifically created for women with comorbid trauma and addiction contains modules that explicitly address safety, and imparts skills and concepts directing patients in caring for their physical safety, health, cultivating safe relationships, eliminating self-harm behaviors and substance abuse, and accessing resources (Najavits, 2002). Given that individuals with post-traumatic stress disorder frequently meet criteria for comorbid substance use

disorders, addressing addiction through the development of safe, alternative means of coping with distress is an integral principle of Seeking Safety.

Accomplishing stabilization in this first phase may hinge upon the strength of the therapeutic alliance, considered a common factor of therapeutic action across various therapeutic modalities. A strong therapeutic alliance may enable the patient to feel sufficiently safe with the therapist and to experience treatment as containing. A large portion of psychotherapy outcomes literature for individuals with PTSD supports the notion that a strong, positive alliance contributes to successful reduction of symptoms.

A less frequently studied common factor, early response, has been shown to be a viable predictor of post-treatment outcomes among various psychiatric populations, however has not been explored in psychotherapy for individuals with PTSD to date. Early response has traditionally been defined as improvement detected between weeks 4-6 of treatment and originates in the pharmacological literature (Lambert, 2005). A patient's response within the first one to two months of treatment has been shown to reliably predict his or her likelihood of improvement over long-term follow up. It has been suggested that early responders engage differently in therapy, utilizing a sequential problem-solving approach to therapeutic tasks; patients' early response in treatment has been shown to precede an increase in their ratings of the alliance with their therapists (Tang & DeRubeis, 1999a). Early response enables clinicians to predict, with a reasonable degree of accuracy, the patients who are unlikely to respond to a given treatment, thus offering a means of guiding decisions as to whether to offer additional or alternative treatments (Hildebrandt, McCrady, Epstein, Cook, & Jensen, 2010). Given the contemporaneous treatment landscape, in which there is increasing demand for time-

limited, cost-efficient mental health treatments, early response offers a potential algorithm for determining the allocation of treatment resources.

Early response has also been found to predict outcomes among patients with heterogeneous diagnoses (Haas, Hill, Lambert, & Morell, 2002; Lutz & Stultz, 2007; Stultz & Lutz, 2007). Early response in the treatment of individuals with PTSD - and in the large subset of individuals with comorbid PTSD and addiction - is an area warranting investigation. Individuals with this comorbidity tend to have more severe psychiatric, medical, and economic problems than those with either diagnosis alone, making empirical research on treatment with this notoriously difficult to treat population especially relevant. The opportunities for treating individuals with PTSD and substance use tend to be brief, given the economic and logistical constraints frequently preventing this patient population from attending regularly and fully engaging with treatment (Greenfield, Brooks, Gordon, Green, Kropp, & McHugh, et al. 2007). Empirical investigation into the validity and utility of early treatment response in this population is relevant because it offers a means of reliably determining patients' treatment needs in a relatively brief period of time. This concept is useful in clinics and hospitals in which there are long wait lists, limited treatment resources are limited, and in working with a population in which treatment opportunities are typically short-term and tenuous.

There are multiple ways to define early treatment response. For the purposes of a trauma and substance use-disordered population, establishing cutoff values on commonly used PTSD and substance abuse measures, is a reliable means of determining whether early response has occurred. In the treatment of substance abuse, quantifying days of

abstinence or reductions in the amount and frequency of use are other methods of defining early response.

The present dissertation utilizes the dataset of a larger project funded by the National Institute of Drug Abuse entitled *The Women and Trauma Study* (NIDA - NCT0078156 <http://clinicaltrials.gov/ct2/show/NCT00078156?term=NCT00078156&rank=1>). The *Women and Trauma Study* was a multi-site trial investigating the efficacy of Seeking Safety, a manualized group therapy for women with co-morbid Post-traumatic Stress Disorder (PTSD) and Substance Use Disorders, in reducing PTSD symptoms and substance use in women receiving standard substance abuse treatment. Subjects were recruited over a 21-month period from 2004 – 2005 across seven sites nation-wide. N=353 women were randomized to receive either 12 sessions of Seeking Safety, a cognitive behavioral group treatment for substance-use disorders and posttraumatic stress disorder, or 12 sessions of the comparison treatment, Women's Health Education, a psychoeducational group treatment focusing on health and the body. Treatment was twice per week for a total of six weeks. PTSD symptoms and substance use were assessed weekly during treatment, and follow-up assessments were given at 1-week, 3-months, 6-months, and 12-months post treatment. The study's primary outcome measures assessed PTSD and substance use, as measured by the Clinician-Administered PTSD Scale (CAPS), the Post-traumatic Symptom Severity – Self Report (PSS-SR), the Substance Use Inventory (SUI), and the Addiction Severity Index-Lite (ASI-Lite).

The hypothesized process through which Seeking Safety facilitates clinically meaningful reductions in PTSD symptoms has not been fully explored. Potential change

mechanisms include the trauma-specific psychoeducational, behavioral, and cognitive techniques of Seeking Safety, by which patient learning and the integration of new skills fosters symptom reduction. The skills learned include interpersonal skills, coping and emotional regulation skills, and practical skills on seeking community resources. However, it is equally plausible that non-specific or common factors are the dominant causal change mechanisms in Seeking Safety group treatment. One of the most extensively studied non-specific factors, helping alliance, was measured in the Women and Trauma Study. The format and content of Seeking Safety ostensibly provides more opportunities for the therapist and patient to build a strong alliance than Women's Health Education.

The current dissertation seeks to (1) investigate whether the concept of early response was valid within the context of this dataset, as virtually no research has been done on early response in psychotherapy treatments for PTSD or in PTSD and substance abuse comorbidity; (2) determine clinical cutoffs on the PSS-SR for the prediction of nonresponse to trauma treatment, and (3) explore early treatment response as a potential mediator through which therapeutic alliance effects trauma outcomes. The present study is unique in that it examines early response in the context of PTSD and substance abuse comorbidity, as well as in Seeking Safety group psychotherapy treatment.

The findings of the *Women and Trauma Study* have been previously published (Hien et al.; 2009; Hien et al., 2010; Pinto, Campbell, Hien, Yu, & Gorroochurn, 2011). Participants in Seeking Safety with severe alcohol use at baseline demonstrated significantly greater improvement in substance use at follow-up than heavy drinkers in the comparison condition, however this was only the case for those whose PTSD

symptoms significantly improved. Subsequent analyses demonstrated that improvement in PTSD symptom severity preceded reductions in substance use. A re-analysis of the original findings using statistical techniques for analyzing rolling-group treatment designs revealed a significant interaction between the effects of treatment group and latent attendance class membership on alcohol use outcomes. Those in the Seeking Safety condition with an inconsistent attendance pattern (a 50 – 80% likelihood of attendance) demonstrated significantly greater reductions in alcohol use at follow-up than those in the Women’s Health Education condition with similarly inconsistent attendance. Similar but non-significant trends were found for cocaine use.

Ruglass et al. (2012) found that helping alliance measured at Week 2 predicted PTSD outcomes as measured by the CAPS at one week post-treatment and higher retention in both conditions over the course of treatment.

### **Literature Review**

The present review will include an overview of: (1) PTSD and substance use comorbidity in women, (2) Seeking Safety, (3) early response, (4) existing research on therapeutic alliance and outcomes across a variety of disorders, with a particular emphasis on PTSD and substance abuse.

### **PTSD and Substance Use Disorders**

It has long been observed that PTSD and substance use disorders frequently co-occur, with an estimated 30% - 60% of individuals in substance abuse treatment carrying a PTSD diagnosis (Brady, Back, & Coffey, 2004). The National Comorbidity Survey estimated that individuals with PTSD are 2-4 times more likely to meet criteria for a

substance use disorder than those without PTSD (Kessler, Sonuga-Barke, Bromet, Hughes, & Nelson, 1995). Subsequent large-scale epidemiological surveys similarly have found that nearly half of all individuals with PTSD also meet criteria for substance use disorder (46.4%) and slightly more than one-fifth meet criteria for substance dependence (22.3%) (Pietrzak, Goldstein, Southwick, & Grant, 2011); treatment-seeking patients with PTSD have been estimated to have up to a 14-fold likelihood of having a substance use disorder when compared with patients without PTSD (Ford, Russo, & Malmgren, 2007). Those with both disorders are more likely to demonstrate more severe symptoms, poorer treatment adherence, poorer treatment outcomes, higher rates of suicide attempts and self-harm, higher rates of chronic health problems, and poorer social functioning than those with PTSD or a substance use disorder alone (Driessen et al., 2008; Harned, Najavits, & Weiss, 2006; McCauley, Killeen, Gros, Brady, & Back, 2012; Norman, Tate, Anderson & Brown, 2007; Sacks, McKendrick, & Banks, 2008).

Concurrent trauma and addiction disproportionately affects women (Back, Sonne, Zuniga, Randall, & Brady, 2003). Among men and women with alcohol dependence, women were more than twice as likely to have lifetime PTSD, with respective rates of 10.3% to 26.2% (Back et al., 2003; Kessler et al., 1995). More recent studies have demonstrated that women tend to have a higher rate of PTSD than men in substance abuse treatment settings. Within substance abuse programs, 77-81% of women report having been exposed to trauma and abuse, as compared to 54-69% of men. (Grella, 2003; Liebschutz, Sacks, McKendrick, & Banks, 2008; Savetsky, Saitz, Horton, Lloyd-Travaglini, & Samet, 2002).



Women who abuse substances report a substantially higher prevalence of exposure to violence than women in the general population (Sacks, McKendrick, & Banks, 2008), raising the possibility that the risky lifestyle that often accompanies substance abuse places these women at greater risk of exposure to traumatic events and may account for their high rates of PTSD. However, women who abuse substances report high rates of childhood trauma and abuse, indicating that their exposure to trauma precedes the onset of their substance use (Banyard, Williams, & Siegal, 2003; Sacks, McKendrick, & Banks, 2008). Women exposed to trauma early in life demonstrate high rates of re-victimization, substance abuse, and high-risk behaviors in adulthood (Goodman, Rosenberg, Mueser, & Drake, 1997).

In an effort to explain the oft-seen comorbidity between trauma and substance abuse and to identify viable treatment approaches, three explanatory models have been developed. The largest, most consistent body of empirical support exists for the *self-medication hypothesis*, which suggests that trauma symptoms precede the onset of excessive substance use and that a traumatized individual's relationship with substances evolves out of an ongoing need to medicate emotional arousal and other trauma-related symptoms (Khantzian, 1999; Reed, Anthony, & Breslau, 2007). Three prior treatment studies have demonstrated a temporal relationship between PTSD symptoms and subsequent improvements in substance use. In a study of 353 women with PTSD and SUD comorbidity, Hien et al. (2009) sought to determine the temporal sequence of improvement in PTSD symptoms and substance use during 6 weeks of active treatment among women in outpatient substance abuse treatment. Using a continuous Markov model fit onto four possible response categories - nonresponse, substance use response,

PTSD response, and combined PTSD and substance use response - they found that only patients with PTSD response early in treatment were likely to reduce their substance use or attain abstinence by the end of the active treatment phase. Patients in the nonresponse and substance abuse response categories did not show improvement in PTSD symptoms. Over the course of one year post-treatment, improvements in PTSD symptoms from baseline to follow up predicted long-term improvements in substance use. Ouimette, Reed, Wade, & Tirone (2010) followed 35 men and women with PTSD and SUD comorbidity and tracked their symptoms on a weekly basis for 26 weeks. They found that worsening PTSD symptoms were followed by increases in substance use. Back, Brady, Sonne, & Verduin (2006) investigated the temporal relationship between improvements in PTSD and alcohol dependence symptoms among 94 outpatients over the course of a 12-week treatment program. They likewise demonstrated that improvements in PTSD symptoms were followed by decreases in subjects' alcohol consumption and dependence symptoms. Support for the reverse relationship was not found, in that reductions in drinking were not associated with subsequent reductions in PTSD symptoms.

Further research in support of the self-medication hypothesis has found pairings between an individual's PTSD symptom profile and their substance of choice, suggesting that one may prefer a given substance because it counteracts a particular set of symptoms. For example, alcohol dependent individuals were found to have more severe hyperarousal symptoms than those with cocaine dependence (Saladin, Brady, Dansky & Kilpatrick, 1995). Back, Sonne, Killeen, Dansky, & Brady (2003) found that women with alcohol dependence and PTSD had more severe clinician-rated hyperarousal, avoidance, and overall PTSD severity than women with cocaine dependence and PTSD, while those with

cocaine dependence had more social and functional impairment from their trauma symptoms. Worsening PTSD symptoms during treatment has been found to be a powerful predictor of relapse following the completion of substance abuse treatment (Clark, 2001).

Coffey et al. (2002) found that subjects reported increased cravings in response to initial exposure to idiosyncratic trauma cues in an experimental setting. Likewise, Saladin et al. (2003) found that subjects' severity of PTSD symptoms predicted the magnitude of cravings.

Similar to the self-medication hypothesis, the *chemical dissociation hypothesis* describes substance use as chemically induced dissociation, thus allowing a person to avoid emotions related to traumatic material. The role of dissociation in the relationship between PTSD and addiction is complex and has only recently begun to be empirically explored. It has been shown that among individuals with PTSD and substance use disorders, those with high levels of dissociation have more severe symptomatology, are more likely to be female, have earlier onset as opposed to later traumas, and abuse drugs as opposed to alcohol (Najavits & Walsh, 2012).

Competing hypotheses addressing the etiology of PTSD and SUD comorbidity posit that in the majority of cases, individuals with pre-existing substance use disorders are at greater risk for developing PTSD. The *high-risk hypothesis* states that individuals who abuse substances are more likely to be exposed to traumatic events - particularly interpersonal violence – on account of the high-risk behaviors and social dangers associated with chronic drug and alcohol use (Chilcoat & Breslau, 1998). The *susceptibility hypothesis* ascribes the high prevalence rates to a shared neurobiological

vulnerability, considering the effects of chronic substance abuse on the central nervous system to be a risk factor rendering these individuals more likely to develop PTSD upon exposure to a traumatic event (Jacobsen, Southwick, & Kosten, 2001; Sharkansky, Brief, Peirce, Meehan, & Mannix, 1999; Stewart, Conrod, Samoluk, Pihl, & Dongier, 2000).

Patients with PTSD and substance abuse often exhibit distinct attendance patterns and high dropout rates from treatment, likely due to the myriad economic and social barriers preventing patients from attending consistently and to the nature of PTSD itself (Schottenbauer, Glass, Arnkoff, Tendick, & Hafter Gray, 2008). High rates of dropout and nonresponse to treatment are characteristic of patients receiving manualized PTSD treatments. Among Prolonged Exposure, EMDR, and relaxation for PTSD, dropout rates have been as high as 54% and non-response rates have exceeded 50% on certain measures (Bradley et al., 2005; Schottenbauer et al., 2008). Those with PTSD are more prone to drop out of treatment prematurely. However, co-occurring depression may impact retention in treatment among those with PTSD, as findings suggest that depressed individuals tend to stay longer in treatment (Ghee, Johnson, Burlew, & Boulding, 2009).

A common experience in working with individuals with complex PTSD is for patients to attend treatment inconsistently and yet maintain ongoing contact with providers (i.e. over the phone; disappearing and resurfacing). The pattern of contact may reflect the disturbed attachment often seen in those with complex PTSD (Herman, 1992; Hien, Cohen, Miele, Litt, & Capstick, 2004; Hien et al., 2010). Indeed, individuals with histories of multiple traumas are more likely to have disorganized or insecure attachment styles as compared to those without such histories; furthermore, these styles may inform the health and stability of relationships in adulthood. PTSD is further characterized by

avoidance, in which the traumatized person avoids distressing thoughts, feelings, and contact with trauma reminders, and may avoid attending therapy sessions as a result.

The attendance and retention patterns commonly observed in individuals with PTSD may express the ramifications of trauma on the attachment system and the avoidance of trauma-related material characteristic of PTSD. High dropout rates observed among women with PTSD and substance abuse may be attributed to economic and logistic barriers, such as difficulties obtaining and affording childcare, accessing transportation to treatment, competing medical appointments for multiple medical complaints, and complications involving housing and public assistance (Hien et al., 2004). Patient-level characteristics such as severity of alcohol use have been found to be related to dropout from manualized PTSD treatments (Schottenbauer et al., 2008).

Aside from patient-level characteristics, the high dropout rate observed in cognitive behavioral PTSD treatments as compared to supportive treatments for PTSD (apx. 22% to 11%, respectively) may be because the agenda that manuals impose on therapists hinders their ability to be fully responsive to the patient's needs and thus interferes with alliance formation (Hembree et al., 2003).

Individuals in substance abuse treatment demonstrate high rates of dropout, reaching as high as 50% within the first month (Greenfield et al., 2007). Several patient-level characteristics have been shown to predict retention among women with addictions. Economic stability and extent of social support appear to be important factors influencing whether women remain in treatment. Higher income and being married have been identified as predictive factors for completing treatment, whereas being unemployed, lack of support, and high levels of anger have been shown to predict dropout among female

substance users. Among female-only samples, identified predictors of substance treatment completion include having fewer children, high levels of personal stability, less involvement with child protective services, and fewer family problems. Severity of psychiatric and medical symptoms and substance abuse was related to retention rate among N=203 women in residential treatment, in which those with greater number and severity of problems had lower retention rates (Greenfield et al., 2007).

### **Seeking Safety and Other Evidence-based Treatments for Trauma and Substance Abuse**

As the research and clinical interest in trauma has expanded over the past 40 years from an almost exclusive focus on veterans to include study of the impact of interpersonal violence on women, existing trauma treatments have been applied to this population and targeted treatments have been developed (Cloitre, Stovall-McClough, Miranda, & Chemtob, 2004; Triffleman, Carroll, & Kellogg, 1999). Trauma-focused treatments focus on exposure to traumatic memory and on developing meaning and coherence out of this memory (van Dam, Vedel, Ehring, & Emmelkamp, 2012). Trauma-focused treatments that have gained empirical support include Cognitive Processing Therapy (CPT) (Resick & Schnicke, 1992), Prolonged Exposure (PE) (Foa, Hembree, Rothbaum, & Olasov, 2007), Eye Movement Desensitization and Reprocessing (EMDR) (Shapiro, 1995), and Skills Training for Affective and Interpersonal Regulation (STAIR) (Cloitre, Cohen, Koenen, & Han, 2002). CPT and PE were developed to treat women with histories of rape, while STAIR was initially developed to address the treatment needs of individuals with histories of childhood abuse and emphasizes safety through the development of coping skills and resource-building (Cloitre, Cohen, Koenen, & Han,

2002). Evidence-based treatments for substance abuse include Relapse Prevention and coping skills training (Marlatt & Gordon, 1985), Contingency Management (Higgins, Silverman, & Heil, 2008), and behavioral couples therapy (van Dam et al., 2012).

Integrated treatments for comorbid PTSD and substance use disorders have been developed and studied in recent years. As compared to treatments intended to target PTSD alone, combined treatments for PTSD and SUD tend to be longer, conducted in group format, and emphasize stabilization and coping rather than exposure as a means of addressing trauma symptoms. More recently, four different therapy models integrating exposure with standard relapse prevention or Seeking Safety have been developed (Najavits & Hien, 2013). Studies on integrated treatments to date have been comprised of individuals with more severe psychiatric symptoms and psychosocial stressors compared to studies addressing PTSD alone, in which studies on combined treatments tended to have samples consisting of individuals with histories of complex trauma, ongoing psychosocial stressors, polysubstance abuse, history of legal problems and imprisonment, and homelessness (Najavits & Hien, 2013).

Overall, effects sizes of integrated treatment programs' reductions on PTSD and SUD symptoms ranged from .60-.88 (Torchalla, Nosen, Rostam, & Allen, 2012). After potential sources of bias were accounted for, they determined a marginally greater efficacy of integrated treatment programs over non-integrated treatment programs in reducing symptoms. However, when taken as a whole, meta-analytic studies suggest that while patients benefit from combined PTSD-SUD treatments, no conclusions can be drawn supporting the superiority of these treatments to those focusing on one disorder alone. Van Dam et al. (2012) reviewed 17 studies on integrated treatments for PTSD and

SUD's; 6 of these had a trauma-focused component, whereas 4 did not. They concluded that while there is no firm evidence suggesting that combined PTSD-SUD treatments are more effective than SUD-only treatment, there is some support suggesting that certain subgroups of patients benefit from a trauma-focused approach. Differential treatment effects have also been shown for those who abuse alcohol but not other types of substances (Torchalla et al., 2012).

Similarly, in their review and meta-analysis of treatment literature on combined trauma and addiction programs, Torchalla et al. (2012) concluded that integrated programs reduce PTSD and substance abuse symptoms overall, however do not appear to be more effective at doing so than non-integrated treatment programs. Methodological limitations account for this lack of clarity. Of the 17 studies reviewed, they designated only five as being high quality, of which only one was a true RCT. Limitations of the studies included small sample sizes, lack of actual difference between integrated and non-integrated treatments due to contamination, lack of equivalent control groups, and the use of assessors who were not blinded. Across studies, subjects attended only portion of integrated treatment sessions, consequently a "full dose" of this type of treatment was not received.

Of the 35 studies on combined PTSD-treatments to date, Seeking Safety was utilized in 22 of these. Seeking Safety, a manualized group treatment for women with trauma and substance abuse comorbidity, is based on cognitive-behavioral, interpersonal, and community resource-building principles. It consists of 25 sessions and may be conducted in group or individual format. The content of the sessions focuses on the development of adaptive coping skills and patients' abilities to access community



resources. Across sessions, Seeking Safety treatment describes substance abuse as a maladaptive means of coping with trauma symptoms and emphasizes the development of alternative ways of coping (Najavits et al., 2008).

Four randomized clinical trials on Seeking Safety have been conducted; Seeking Safety has been the only type of treatment shown to have positive effects on outcomes when compared to a comparison treatment (Boden et al., 2012; Hien et al., 2009; Najavits, Gallop, & Weiss, 2006; Najavits & Hien, 2013; Zlotnick, Johnson, & Najavits, 2009). The majority of studies support the effectiveness of Seeking Safety in treating PTSD and substance use symptoms in various populations, including veterans, women, adolescents, incarcerated individuals, and those in substance abuse treatment settings (Cook, Walser, Kane, Ruzek, & Woody, 2006; Lynch, Heath, Mathews, & Cepeda, 2011; Najavits, Weiss, Shaw, & Muenz, 1998; Norman, Wilkins, Tapert, Lang, & Najavits, 2010; Zlotnick, Johnson, & Najavits, 2009; Zlotnick, Najavits, Rohsenow, & Johnson, 2003). However, small sample sizes, poor follow-up rates, and pre-experimental designs lacking a control group posed significant threats to validity in several of these studies. Seeking Safety is considered an effective treatment according to the criteria set forth by Chambless and Holland (1998). It has been demonstrated to produce better outcomes than no intervention, and has been shown to be more effective than treatment-as-usual (TAU) or when added as an adjunctive treatment to treatment as usual among adults (Gatz et al., 2007; Hien, Cohen, Miele, Litt, & Capstick, 2004) and adolescent females (Najavits, Gallop, & Weiss, 2006). Whether or not Seeking Safety is *superior* to other interventions has not yet been clearly established, as findings have been mixed (Searcy & Lipps, 2012).

In their study of 98 male veterans with PTSD symptoms in an outpatient VA substance use disorders clinic, Boden et al. (2012) compared Seeking Safety with Treatment As Usual in a randomized controlled effectiveness trial. Authors aimed to investigate whether integrating Seeking Safety into a standard VA substance abuse treatment program had an additive or enhancing effect. Seeking Safety was delivered in 24 sessions in group and individual format. Although assignment to the experimental group or TAU was random, it was stratified based on whether subjects had a romantic partner, had participated in the wars in Iraq or Afghanistan, and use of illicit drugs. Latent growth curve methodology was employed to evaluate several potential mediators, including changes in active coping skills from pre to post treatment, change in PTSD symptoms, attendance, and patient satisfaction. Over the course of 6 months post-treatment follow up, participation in Seeking Safety was significantly associated with better drug use outcomes, however alcohol use and PTSD severity decreased equally under both conditions. Notably, Seeking Safety was associated with increased attendance rate, patient satisfaction, and use of active coping. A study limitation was that the extent of subjects' PTSD symptomatology was not equivalent in the experimental and control groups, in that patients in Seeking Safety were diagnosed with partial or full PTSD, whereas some in the TAU group carried a partial or full PTSD diagnosis and some did not.

The findings of Zlotnick, Johnson, & Najavits (2009) did not support the superiority of Seeking Safety to treatment as usual among 49 incarcerated women with an SUD and full or sub-threshold PTSD receiving intensive substance abuse treatment. The Seeking Safety treatment consisted of group treatment during incarceration and

individual treatment after subjects were released, while TAU consisted of 180-240 hours of individual and group treatment over 4 to 8 weeks. The group receiving Seeking Safety in addition to TAU demonstrated no significant difference from the group receiving TAU alone on improvement of PTSD, substance abuse, psychopathology, or legal problems. However, nonsignificant trends were found suggesting that participants who received Seeking Safety showed greater improvements on clinician-rated PTSD symptoms and continued improvement in post-treatment psychopathology ratings than those who received TAU; trends also indicated that participants receiving TAU showed greater post-treatment reductions in alcohol use than those receiving Seeking Safety. The ambiguous findings in this study may be attributed to its notable limitations, including small sample size resulting in the inability to account for group-level effects, possible cross-contamination between the two treatment groups, and the community resources aspect of Seeking Safety treatment having been dropped from the protocol.

Seeking Safety appears to positively impact retention (Boden et al., 2012). Among substance dependent women, Seeking Safety has been found to increase retention when added to standard treatment (Gatz et al., 2007), even when as little as 6 sessions were added as an adjunctive treatment (Ghee, Johnson, Burlew, & Boulding, 2009). However, in their study utilizing the Women and Trauma Study dataset, Ruglass et al. (2012) found no difference in retention among women receiving Seeking Safety versus a control group treatment. Rather, they found differences in retention based on patient-rated helping alliance.

Potential mediators and mechanisms of change in Seeking Safety treatment that have been posited include learned coping skills, improved interpersonal functioning,

patient satisfaction with treatment, and improved ongoing access to community resources (Boden et al., 2012; Norman et al., 2010). Because Seeking Safety is based on CBT, case management, and interpersonal principles, the potential means by which it evokes change are likely multi-determined, consisting of both theory-driven and non-specific psychotherapy process factors.

### **Early Response and Clinical cut-offs**

The depression, substance abuse, and bulimia literature has shown that early treatment response consistently predicts post-treatment improvement and is positively related to better immediate and long-term outcomes (Bradford et al., 2011; Doyle, Le Grange, Loeb, Doyle, & Crosby, 2010; Fennel & Teasdale, 1987; Hildebrandt, McCrady, Epstein, Cook, & Jensen, 2010). A notable exception is an investigation by Van et al. (2008), which did not demonstrate a clear relationship between early improvement and sustained symptom reduction among depressed outpatients, however did find a predictive relationship between lack of improvement in symptoms and nonresponse at the end of treatment.

Early response typically refers to a clinically meaningful decrease in symptoms or change in functioning by the fourth to the sixth week of treatment (Bradford et al., 2011; Ceperich & Ingersoll, 2011; Craighead, Sheets, Bjornsson, & Arnarson, 2005), while early response detected as early as the fourth session (Doyle, Le Grange, Loeb, Doyle, & Crosby, 2010) has been shown to predict subsequent improvement. Early responders have been found to engage in therapy differently than late responders, which may account for these findings (Fennel & Teasdale, 1987). This information is useful for determining an individual's likelihood of ultimately responding once treatment has begun and aids in

decision-making as to the appropriateness of continuing with a given treatment (Lambert, 2005; Lutz et al., 2006; Lutz, Stultz, Martinovich, Leon, & Saunders, 2009).

Lutz, Stultz, and Kock (2009) examined distinct patterns of early change in depression severity during treatment among 162 outpatients diagnosed with major depression randomly assigned to receive CBT, IPT, and psychopharmacological treatment with clinical management. Latent growth curve analyses demonstrated that patients' rate of change during the first eight weeks of treatment was a stronger predictor of depression outcomes at the end of treatment than treatment modality. All patients with moderate to severe depression who demonstrated rapid, early improvement showed complete remission of their depression at follow-up; nearly all early responders sustained these gains one and a half years later. Stulz, Lutz, Leach, Lucock, and Barkham (2007) found that among 192 outpatients with heterogeneous diagnoses, those who demonstrated rapid, early improvements on measures of depression and anxiety continued to sustain these gains at termination. Individuals in this subgroup demonstrated dramatic symptom improvement from one session to the next, although they typically attended fewer sessions than fourteen psychotherapy sessions. A subgroup of patients who did not show early improvement remained nonresponders at the end of treatment, although the majority of these patients attended over thirty psychotherapy sessions. A possible limitation of this finding is that the measures used may not have adequately reflected changes that occurred over the course of therapy for the nonresponder subgroup.

To date, the early response literature on PTSD is comprised of a study on the efficacy of sertraline as compared to placebo in preventing relapse of PTSD symptoms (Davidson et al., 2001); no articles on early response in psychotherapy treatments for

PTSD have yet been reported. Davidson et al. (2001) found that among 96 PTSD patients randomly assigned to sertraline or placebo, early response in the first four weeks of treatment was associated with a significantly lower risk for subsequent reemergence of PTSD symptoms among patients receiving either sertraline or placebo. The ability of early response to predict a sustained treatment response was greater among those taking sertraline.

Early response phenomena have been demonstrated in clinical trials utilizing substance abuse interventions in women. Hildebrandt, McCrady, Epstein, Cook, and Jensen (2010) investigated early non-response in a trial comparing two alcohol-focused treatments among 102 females with alcohol use disorders. They found that among women randomized to individual behavior therapy, extent of drinking at the end of treatment and at one year follow-up was predicted by subjects' cumulative days of abstinence by the fourth week of treatment. Notably, early response was not found to be a viable predictor of long-term outcomes in the comparison treatment, a behavioral intervention for couples. Hildebrandt et al. (2010) is one of the few studies to investigate the prediction of non-response to treatment. They argue that this approach is more clinically useful than predicting treatment response because it enables clinicians switch patients to a different treatment early on they are expected to not respond. Ceperich and Ingersoll (2011) investigated an intervention to reduce binge drinking in 207 college-age women, and found that early response to the intervention at one month significantly predicted reduced risk of risky alcohol consumption as well as high-risk sexual behaviors.

With the aim of prediction of those who will ultimately respond or not respond to treatment, developing cut-off scores in commonly used measures is a way that clinicians may determine a patient's likelihood of response or non-response (Hildebrandt et al., 2010). Predictive cutoffs of well-validated trauma measures has enabled such cutoffs to be generated in PTSD research. Coffey, Gudmundsdottir, Beck, Palyo, and Miller (2007), in which they used ROC curves to determine cutoff values in the PSS-SR and IES in detecting PTSD among motor vehicle accident survivors, finding that a cutoff of 14 on the PSS-SR yielded optimal sensitivity and specificity in correctly identifying PTSD cases. ROC methodology has also been used to generate clinical cutoffs on the CAPS in accurate prediction of PTSD diagnosis among a sample of individuals exposed to neighborhood violence (Pupo et al., 2011). In substance abuse research, response is typically defined in terms of abstinence or the attainment of moderate drinking (Hildebrandt et al., 2010).

### **Therapeutic Alliance**

**Therapeutic alliance and treatment outcomes.** Therapeutic alliance, also called the helping alliance and working alliance, broadly refers to the collaboration and mutuality between the patient and therapist, and is considered to be a common factor across psychotherapy modalities (Horvath & Bedi, 2002). Therapeutic alliance is now understood as an a-theoretical construct (Paivio & Patterson, 1999), however originated in psychodynamic psychotherapy process literature (Gelso & Samstag, 2008). An ongoing tension exists within contemporary psychotherapy research between those who conceive of alliance as a primary therapeutic change mechanism (Luborsky & Luborsky,

2006) versus those who view alliance as an ancillary supportive factor that allows for active therapeutic techniques to be implemented, yet does not itself evoke change (Craighead, Sheets, Bjornsson, & Arnarson, 2005; Tang & DeRubeis, 1999a). Craighead, Sheets, Bjornsson, & Arnarson (2005) found that improvement occurred before cognitive behavioral techniques were administered across several studies of cognitive behavioral treatment for depression. Authors concluded that the rapid treatment response - which occurred before several specific CBT techniques could be implemented – support non-specific therapy factors to be a “prominent causal force” in cognitive therapy.

Alliance has been conceptualized as consisting of the agreement between the patient and therapist on the goals and tasks of treatment and the strength of the emotional bond between the two. Quantitative definitions of alliance have identified two factors: a “working bond” and a “liking bond” (Gelso & Samstag, 2008). This description depicts alliance as independent of theoretical orientation and the presenting problem, however the picture may be more complex. While alliance has been shown to predict positive outcomes across various therapeutic modalities, including cognitive, behavioral, brief dynamic, gestalt, and psychopharmacological studies (Gaston, Thompson, Gallagher, Cournoyer, & Gagnon, 1998; Marmar, Gaston, Gallagher, & Thompson, 1989), there is some variation in the alliance-outcome relationship among psychiatric disorders. A positive relationship has been consistently found for depression (Gaston et al., 1998; Weiss, Gaston, Propst, Wisebord, & Zicherman, 1997), anxiety disorders, personality disorders, PTSD, bipolar disorder (Strauss & Johnson, 2006), and schizophrenia (Johnson, Penn, Bauer, Meyer, & Evans, 2008). However less consistent support exists for the therapeutic alliance as a predictor of outcome in the substance abuse literature



(Meyer, Barrowclough, & Donnell, 2005). Furthermore, the dynamics particular to PTSD may have unique implications for alliance formation and the strength of the therapeutic relationship.

Alliance is a process variable that changes over the course of treatment, and may vary depending upon patient characteristics and therapeutic events such as alliance rupture and repair (Muran et al., 2009; Paivio & Patterson, 1999). Alliance typically increases over the course of treatment (Ramnero & Ost, 2007).

Alliance may be assessed at multiple time points over the course of treatment and from various perspectives. Alliance measured at the early, middle, and later phases of treatment has been shown to predict post-treatment symptom improvement, however alliance measured early in treatment has consistently been shown to be the most powerful predictor of outcomes (Barber, Connelly, Crits-Christoph & Siqueland, 2009; Krupnick et al., 1996). Patient-rated alliance has been found to be a stronger predictor of outcomes across studies than other vantage points, such as therapist-rated and observer-rated alliance. Joyce, Piper, & Ogrodniczuk (2007) determined that patient-rated alliance was predictive of outcomes, whereas therapist-rated alliance was not. Piper, Ogrodniczuk, Lamarche, Hilscher, & Joyce (2005) found that in time-limited group therapy only patient-rated alliance (both early alliance in the first four sessions and the change across sessions) was linearly related to improved outcomes. No predictive relationship was found for therapist-rated alliance and outcomes, however significant interaction effects were detected. These findings have been corroborated by two meta-analyses in which patients' assessments of the therapeutic relationship showed larger associations with outcomes than did clinicians' ratings of the relationship (Horvath & Bedi, 2002; Horvath

& Symonds, 1991; Strauss & Johnson, 2006). Although comparably fewer, some studies have nevertheless shown therapist-rated alliance to be a stronger predictor of outcomes than patient-rated alliance (Belding, Iguchi, Morral, & McLellan, 1997) and equally as strong a predictor as patient-rated alliance (Conners, Carroll, DiClemente, Longabaugh, & Donovan, 1997).

Patient-, therapist-, and group-level characteristics may predict patients' levels of alliance early in treatment. There are multiple factors that may predict patient-rated alliance. Client characteristics explained 17% of the variance in group alliance in an investigation by Johnson, Penn, Bauer, Meyer, and Evans (2008). The quality and extent of social support in patients' lives has emerged as a consistent predictor of early alliance. Higher early alliance has been found to be associated with higher levels of social support and satisfaction with social relationships; clients' depressive symptoms and poor social support may interfere with early alliance development with the therapist. In light of these findings, one of the mechanisms by which the therapeutic alliance may effect outcomes is through improvements in clients' social support systems outside therapy (Strauss & Johnson, 2006). Patients' capacity for insight has been identified as a predictor of therapeutic alliance regardless of the therapeutic modality (Johnson et al., 2008). Within a group setting, characteristics of other group members may influence an individual patient's alliance rating. In Project MATCH, a study investigating treatments for individuals with alcohol use disorders utilizing data from 707 outpatients and 480 aftercare patients, patients' level of motivational readiness to change was the strongest predictor of patient-rated alliance (Conners et al., 2000).

Several decades of research on therapeutic alliance has yielded a substantial body of support for a modest but consistent relationship between a strong, positive alliance and improvement post-treatment (Gaston et al., 1991; Horvath & Bedi, 2002; Horvath & Symonds, 1991; Joyce et al., 2007). Meta-analytic findings demonstrate a significant association between alliance and treatment outcome with effect sizes ranging from .22 - .26 (Horvath & Symonds, 1991; Martin, Garske, & Davis, 2000); it has been reported that a significant association between alliance and outcomes exists in 66 – 70% of studies (Horvath & Bedi, 2002).

Beyond a correlational relationship, alliance has been shown to predict and mediate symptom improvement. It has been estimated that the patient-therapist relationship contributes 10 – 20% to outcomes in therapy (Aveline, 2005). The strength of the therapeutic alliance significantly predicted outcomes in CBT treatment for alcohol (Conners, Carroll, DiClemente, Longabaugh, & Donovan, 1997), depression (Marmar, Gaston, Gallagher, & Thompson, 1989; Safran & Wallner, 1991; Stiles, Agnew-Davies, Hardy, Barkham, & Shapiro, 1998) and OCD (Hoogduin, de Haan, & Schapp, 1989). Alliance was found to mediate the relationship between patients' expectancies of therapy and outcomes in individual (Joyce et al., 2003; Meyer et al., 2002) and group therapy (Abouguendia, Joyce, Piper, & Ogrodniczuk, 2004) for depression. Patients who expect treatment to be effective may be more engaged and foster a stronger alliance, thus bringing about a marked reduction in symptoms (Watson & Geller, 2005).

Although a large body of research supports a significant association between alliance and outcomes, other findings have called the validity of this relationship into question. Several studies have not found a significant relationship between alliance and

psychiatric outcome in supportive and insight-based (Belding et al., 1997; Woody & Adessky, 2002) and cognitive behavioral therapies (Krupnick et al., 1994; Ramnero & Ost, 2007), however these discrepant findings can be explained by methodological limitations including small sample sizes, limited variability in alliance ratings, and questionable validity of alliance measures used.

It is logical to assume that patients who perceive a strong alliance with the therapist early in treatment are more likely to attend sessions consistently and actively engage in therapeutic work. Empirical support exists for an association between positive alliance and subsequent treatment attendance, however this relationship has not been consistently demonstrated across studies (Belding et al., 1997). Therapeutic Alliance has been shown to predict fewer dropouts, better attendance, and increased adherence to treatment in patients with PTSD, substance use disorders, depression, schizophrenia, as well as other disorders in both individual and group psychotherapy (Arnow et al., 2007; Connors et al., 1997; Johnson et al., 2008; Keller, Zoellner, & Feeley, 2010). Among individuals with alcoholism, both patient and therapist-related alliance have been shown to predict the number of weeks of treatment attended (Connors et al., 1997). Schizophrenic individuals enrolled in group therapy with stronger therapeutic alliance ratings missed fewer therapy sessions, complied more with treatment tasks, and were rated as more engaged (Johnson et al., 2008). Within a brief, 12-week individual treatment for depression, weak alliance at Session 2 predicted dropout (Arnow et al., 2007). Najavits, Weiss, Shaw, and Muenz (1998) found that therapist-rated alliance early in treatment predicted retention among women with PTSD and substance use disorders receiving Seeking Safety treatment.

**Therapeutic alliance in group psychotherapy.** The concept of therapeutic alliance within a group context is distinct from alliance within a therapy dyad because the influence of the group must be taken into account. Individual and group therapy likely have related change mechanisms, however several hypothesized change mechanisms in group therapy do not occur in individual therapy, such as group cohesion and the experience of universality with other members (Johnson et al., 2008; Kivlighan, Coleman, & Anderson, 2000).

Working alliance is distinct from group cohesion (Joyce, Piper, & Ogrodniczuk, 2007; van Andel, Erdman, Karsdorp, Appels, & Trijsburg, 2003). Whereas alliance is generally understood to refer to the relationship between the patient and the therapist, cohesion refers to the relationships between group members or the relationship between members and the therapeutic work. Alliance has been found to be a stronger predictor of outcome than group cohesion in a short-term group therapy treatment for borderline personality disorder (Marziali, Monroe-Blum, & McCleary, 1997), however it should be noted that this study was limited by a small sample size and high level of patient dropout. Van Andel, Erdman, Karsdorp, Appels, & Trijsburg (2003) demonstrated that group cohesion and helping alliance were distinct, non-overlapping constructs that each independently contributed to symptom improvement in a group of cardiac outpatients. Authors measured group cohesion and helping alliance at sessions 5 and 10 in a cognitive behavioral group treatment aiming to reduce depression, hostility, exhaustion, and depression in cardiac outpatients.

Johnson, Penn, Bauer, Meyer, and Evans (2008) is one of the rare studies that measured client-rated group alliance, a concept that refers to the patient's alliance with

the group as a whole and conceptually overlaps with group cohesion. In an RCT comparing 12 sessions of manualized CBT and supportive group therapies for 63 schizophrenic outpatients, authors found that stronger group alliance at the mid-point of treatment was associated with more positive outcome.

Alliance has been shown to be a significant predictor of outcomes in group therapy (Piper, Ogrodniczuk, Lamarche, Hilscher, & Joyce, 2005). Therapeutic alliance was found to mediate the relationship between expectations and symptom improvement in interpretive and supportive group therapies for complicated grief (Abouguendia et al., 2004). However, other studies have found a lack of relationship between working alliance in a group context and post-treatment outcomes (Woody & Addessky, 2002). Woody and Addessky (2002) investigated the relationship between working alliance, group cohesion, and homework completion among 53 patients with social phobia in cognitive-behavioral group therapy treatment. They found a linear growth in patients' Working Alliance as measured by the Working Alliance Inventory (WAI) over the course of treatment, however no significant relationship was ultimately detected between alliance development, post-treatment improvement, or homework completion over the course of treatment. Authors suggested that an alliance – outcomes relationship was not detected because outcomes data was only collected at the termination of treatment and not at later follow-up time points.

Although an alliance-outcome relationship has been observed in individual and group therapy studies, a major criticism is that these studies neglected to account for early symptom improvement in treatment, which may contribute to the establishment of a helping alliance and better predict subsequent treatment progress (DeRubeis & Feeley,

1990). For the majority of alliance studies that did not take early symptom change into account, the validity of their findings may be called into question based on this consideration. Therapeutic alliance has been found to predict outcomes even while controlling for early symptom improvement (Barber, Connolly, Crits-Cristoph, Gladis, & Siqueland, 2009), however other studies have found that early treatment response predicted post-treatment symptom improvement as well as subsequent strength of alliance (Belding, Iguchi, Morral, & McLellan, 1997), suggesting that early symptom improvement may make patients more willing to engage in a collaborative relationship with the therapist, and strong alliance may indicate that a treatment is going well but does not in itself predict outcomes (Joyce, Piper, & Ogrodniczuk, 2007).

**Therapeutic alliance and PTSD.** Individuals with histories of chronic trauma are more likely to exhibit complex PTSD syndromes. *Complex PTSD* conjointly refers to individuals who have experienced multiple as opposed to single-incident traumas and to trauma-related syndromes such as Disorders of Extreme Stress Not Otherwise Specified (DESNOS), which encompasses diffuse profiles of dissociative symptoms, emotion regulation difficulties, somatization, alexithymia, social dysfunction, hostility, and anxiety often seen in individuals with histories of recurring interpersonal trauma beginning in childhood or adolescence (van der Kolk, Pelcovitz, Roth, & Mandel, 1996). Women with childhood sexual abuse histories are more likely to manifest symptoms of Disorders of Extreme Stress Not Otherwise Specified (DESNOS) in adulthood than those without such a history (Zlotnick, Zakriski, Shea, & Costello, 1996).

Individuals with histories of early interpersonal trauma have more severe profiles than those who have experienced adulthood trauma. Women with histories of childhood

sexual abuse report more difficulties with drug abuse, alcoholism, and suicidality in adulthood, tend to have more dissociative symptoms, report greater overall psychiatric symptomatology than women without such histories; women with histories of physical and/or sexual abuse in childhood are more likely to be sexually victimized in adulthood (Back et al., 2003; Briere, 1992; van der Kolk et al., 1996).

Therapeutic alliance is considered a primary vehicle of change in treating PTSD (APA, 2004). Recovery from trauma is thought to occur via a relationship in which the survivor is able to re-establish trust in others and gain a sense of basic safety (Herman, 1992). Interpersonal trauma may have profound effects on an individual's ability to engage in and maintain relationships. The therapeutic relationship is an integral component of the trauma recovery process, however PTSD populations often have difficulty forming a positive alliance and treatment retention with this population is notoriously problematic (Davies & Frawley, 1994).

The formation and trajectory of the therapeutic alliance over the course of treatment may be different for women with histories of multiple traumas, usually beginning in childhood, as opposed to other populations. It has often been observed that individuals with complex trauma have greater difficulty forming a strong therapeutic relationship due to the negative impact of trauma on trust and the ability to form healthy, emotionally intimate relationships (Davies & Frawley, 1994; Herman, 1992; Price, Hilsenroth, Petretic-Jackson, & Bonge, 2001). Several studies have demonstrated that women with histories of extensive interpersonal trauma are able to form strong alliances with therapists (Hien et al., 2010; Keller, Zoellner, & Feeny, 2010). For example, Cloitre, Stovall-McClough, Miranda, and Chemtob (2004) found that among 34 women



with PTSD and a history of early trauma receiving STAIR manualized treatment, the strength of the therapeutic alliance during the first stage of treatment predicted PTSD symptom improvement during the second stage of treatment. Furthermore, affect regulation was found to mediate the relationship between alliance and reduction in PTSD symptoms.

It may be difficult for women with histories of repeated interpersonal trauma to form strong alliances due to the long-observed impact of trauma on individuals' sense of self, perceptions of others, and relational schemas. Clinical and theoretical observations have made a link between a history of child abuse and impaired interpersonal functioning in adulthood. According to a developmental trauma perspective, the long-term impact of childhood trauma may include impaired development in empathic capacities and mentalization that may interfere with forming healthy, reciprocal relationships later in life (Allen, Fonagy & Bateman, 2008; Herman, 1992).

Women with histories of childhood interpersonal trauma have an increased likelihood of revictimization in adulthood, involvement in abusive partnerships, engaging in risky sexual behavior, and poorer social support than non-traumatized individuals (Cohen, Hien, Litt, & Miele). Individuals with a history of childhood sexual abuse often demonstrate difficulties in forming and maintaining intimate relationships (Davies & Frawley, 1994; Herman, 1992). The interpersonal difficulties that many individuals with a history of repeated abuse experience outside of therapy may translate into weak alliance with a therapist (Keller, Zoellner, & Feely, 2010).

Difficulties with forming an alliance observed in trauma populations may be attributed to patient-characteristics, therapist-characteristics, and environmental

characteristics above and beyond the presence of a trauma history. In their study of predictors of alliance in adults receiving emotionally-focused psychotherapy for the long-term effects of child abuse (N=33), Paivio & Patterson (1999) concluded that client-characteristics contributed to the strength of patient-rated alliance at both the early and late stages of treatment. Severity of early abuse was associated with poor alliance early in treatment. However, alliance improved over time for patients without an Axis II disorder.

In their study on alliance in a population of individuals with child abuse histories, Paivio and Patterson (1999) found that severity of early abuse in childhood was related to difficulties forming a positive alliance early in treatment as a nonsignificant trend. Eltz, Shirk, and Sarlin (1995) found a significant association between poor helping alliance from the patient's perspective, more severe early maltreatment, and poorer outcomes with adolescents in an inpatient setting.

**Therapeutic alliance and substance use disorders.** The relationship between Therapeutic Alliance and outcomes in treating individuals with Substance use disorders has yielded mixed findings; as such, no clear relationship exists between alliance and outcomes in the substance abuse literature (Meyer, Barrowclough, & Donnall, 2005). Several studies have found no association between helping alliance and substance abuse outcomes for individuals in substance abuse treatment programs (Belding et al., 1997; Carroll, Nich, & Rounsaville, 1997).

The development of alliance and its impact on outcomes may differ between substance abuse counseling and psychotherapy. Tunis, Delucchi, Schwartz, Banys, and Sees (1995) found a significant correlation between alliance measured late in treatment in a 180-day opioid detoxification program and later decrease in substance use, suggesting

that alliance may take a longer time to build in standard substance abuse treatment than in psychotherapy.

Some studies have found a positive relationship between helping alliance and substance abuse outcomes (Connors et al., 1997; Luborsky, McLellan, Woody, O'Brien, & Auerbach, 1985; Tunis et al., 1995). In their study of therapeutic alliance among N=1,726 outpatients with alcohol use disorders, Connors et al. (1997) hypothesized a linear relationship between patient and therapist-rated alliance, treatment attendance, and positive drinking outcomes both during and after treatment. Treatment lasted for 12 weeks, and alliance ratings using the WAI were taken at session 2 for both patients and therapists. Therapeutic alliance scores accounted for 3.5% of the variance in patient drinking outcomes.

Luborsky et al. (1985), and a re-analysis of their data by Gerstley, McLellan, Alterman, and Woody (1989), found large correlations between the Helping Alliance measured after Session 3 with drug use at 7-months in a methadone maintenance treatment setting. However, both studies' findings are limited by their use of the HAQ-I, the validity of which has been called into question on the grounds that it measures symptom improvement rather than the strength of the patient-therapist relationship.

## **Hypotheses**

### **Rationale**

1. Subjects' trauma and substance use severity at the fourth week of treatment will accurately predict non-response status at follow-up in both treatment conditions.

In an investigation by Hildebrandt et al. (2010), subjects' percent days abstinent by the fourth week of alcohol-focused treatment predicted continued drinking at the end of treatment and at 18 months after treatment had ended. In the present study, it is anticipated that early improvement in substance use, as measured by subjects' cumulative days of abstinence at treatment week 4, will accurately predict continued use of drugs or alcohol at all four follow-up time points.

Previous research suggests that rapid, early treatment response between the fourth and eighth week of treatment predicts subsequent improvement among individuals with depression, anxiety, and heterogeneous diagnoses receiving various types of treatments (Lutz, Stulz, & Kock, 2009; Stulz et al., 2007). This research base supports the expectation that subjects' trauma scores by the fourth week of treatment will accurately predict response status at follow up.

2. Participants in Seeking Safety will demonstrate significantly larger, more rapid reduction in PSS-SR scores by weeks 4-6 than those in Women's Health Education. Hien et al. (2009) found that individuals in Seeking Safety demonstrated significantly more rapid reductions in mean PSS-SR than those in the Women's Health Education group after 1 week post-treatment. Ruglass et al. (2012) found that the Seeking Safety condition had higher overall levels of alliance than the comparison condition, and that higher Helping Alliance at Week 2 significantly predicted greater reduction in PTSD symptoms as measured by the CAPS at one week post-treatment in both treatment conditions.

The development of emotion regulation skills has been found to mediate the relationship between alliance and outcome in a PTSD treatment for female child sexual abuse survivors (Cloitre et al., 2004).

Seeking Safety aims to impart affect-regulation and cognitive coping skills; the format of sessions increases the likelihood that patients will share emotionally-laden material with the group, experience trauma-related affects, and receive support from the therapist.

Thus, the women receiving Seeking Safety are more likely to have developed a stronger emotional connection with the therapist. Given the emphasis in Seeking Safety on affect regulation skills, we would expect that Seeking Safety would be more effective in fostering helping alliance and in reducing trauma symptoms. Given that improvement in trauma symptoms has been shown to precede improvement in substance use, we would expect to detect more rapid improvement in trauma symptoms than substance use symptoms (Back, Brady, Sonne, & Verduin, 2006; Hien et al., 2010).

3. Early response will mediate the relationship between therapeutic alliance and PTSD and substance abuse outcomes post-treatment.

Research on therapeutic change has demonstrated that a subgroup of patients have a sudden, early response to cognitive behavioral treatments for depression, substance abuse, and bulimia. Cognitive behavioral theoreticians have pointed out that this phenomenon cannot be explained as a therapeutic ‘placebo’ effect because the later treatment gains associated with early response are usually sustained. Were early response merely a reflection of a placebo effect, we would expect patients’ psychological symptoms to return over time (Rachman, 1999). Thus early response may be a marker of true underlying change mechanisms at work in the therapies studied within this body of research.

Previous research has suggested that early response bears a causal relationship to “nonspecific” mechanisms of therapeutic change, such as the therapeutic alliance (Haas,

2002; Lambert, 2005). It is recommended that investigations of therapeutic change focus on the role of early mediators of the treatment effect (Wilson, 1999). In understanding the relationship between therapeutic alliance and response to trauma-focused treatment, it is plausible that a strong initial therapeutic relationship facilitates early improvement in symptoms. Early response patients then assimilate the information, skills, and experiences acquired treatment in such a way that their trauma symptoms ultimately decrease. Thus early response is a potential mediator of the relationship between therapeutic alliance and subsequent trauma outcomes.

### **Statement of Hypotheses**

1. Severity of trauma symptoms and extent of abstinence by the fourth week of treatment will predict response status during all four follow-up time points with acceptable degree of accuracy.

Receiver Operator Characteristic (ROC) Curves will be calculated to define the optimal thresholds for response to PSS-SR and cumulative abstinence as assessed by the SUI in the prediction of associated outcomes.

- 2.a. There will be a treatment group effect, in that participants in Seeking Safety will demonstrate a significantly larger, more rapid reduction in PSS-SR scores from weeks 4-6 than those in Women's Health Education.

To address Hypothesis 2.a., separate latent growth curve models for Seeking Safety and Women's Health Education will be estimated to establish the validity of early response within each treatment group. Helping alliance will be examined as a covariate in the latent growth curve models. Additional covariates will include the change in PSS-SR

scores from Baseline to week 2 of treatment, and substance use score at baseline. The dependent variables will be the mean slope factors of PSS-SR scores between weeks 4-6 of treatment and the PSS-SR intercept factor at week 4. To address Hypothesis 2.a., the slopes of the two curves will be compared to assess for a significant difference between treatment groups.

2.b. There will be a treatment group effect, in that participants in Seeking Safety will demonstrate a significantly larger, more rapid increase in cumulative percent days abstinent from weeks 4-6 than those in Women's Health Education.

To address Hypothesis 2.b., separate latent growth curve models for Seeking Safety and Women's Health Education will be estimated to establish the validity of early response within each treatment group. Helping alliance will be examined as a covariate in the latent growth curve models. Additional covariates will include early acquired abstinence from Baseline to week 2 of treatment and substance use score at baseline. The dependent variables will be the mean slope factors of cumulative percent days abstinent between weeks 4-6 of treatment and the cumulative percent days abstinent intercept factor at week 4. To address Hypothesis 2.b., the slopes of the two curves will be compared to assess for a significant difference between treatment groups.

3.a. Early Response to treatment will mediate the relationship between patient-rated Helping Alliance and post-treatment trauma symptoms.

A latent growth curve mediation analysis will be conducted. The independent variables will include HAQ-P-II scores at week 2, treatment group, change in PSS-SR scores from Baseline to week 2 of treatment, and substance use score at baseline. The mean intercept factor of PSS-SR scores at week 4 and the mean slope factors of PSS-SR scores at week 4-6 will be modeled as a mediator of the effect on the dependent variable,

the mean CAPS slope factor at 1-week, 3 months, 6 months, and 12 months post-treatment.

3.b. Early Response to treatment will mediate the relationship between patient-rated Helping Alliance and post-treatment substance abuse symptoms.

A latent growth curve mediation analysis will be conducted. The independent variables will include HAQ-P-II scores at week 2, treatment group, reduction in substance abuse from Baseline to week 2 of treatment, and substance use score at baseline. The mean intercept factor of cumulative percent days abstinent at week 4 and the mean slope factors of cumulative percent days abstinent at week 4-6 will be modeled as a mediator of the effect on the dependent variable, the mean ASI slope factor at 1-week, 3 months, 6 months, and 12 months post-treatment.

## **Method**

### **Study Background**

The present study utilizes the dataset of a larger project funded by the National Institute of Drug Abuse entitled *The Women and Trauma Study* (NIDA - NCT0078156 <http://clinicaltrials.gov/ct2/show/NCT00078156?term=NCT00078156&rank=1>). The *Women and Trauma Study* was a multi-site trial investigating the efficacy of Seeking Safety, a manualized group therapy for women with co-morbid Post-traumatic Stress Disorder (PTSD) and Substance Use Disorders, in reducing PTSD symptoms and substance use in women receiving standard substance abuse treatment. This study utilized a randomized, controlled, repeated-measures design. Research was conducted across seven substance abuse treatment sites nationwide. The sites consisted of five urban and two suburban settings in the United States located in the West (n=1), Midwest (n=1),



Northeast (n=2) and Southeast (n=3). The Institutional Review Board of the leading institutional site and all treatment sites approved of the larger study. All subjects provided written informed consent and signed HIPAA forms.

### **Procedure**

Recruitment took place over a 21-month period from 2004-2005. The study was advertised in brochures, fliers, and local newspaper ads, and through referrals to counselors at the local substance abuse treatment site. Individuals were first screened over the phone, and if eligible, were invited to come in for further screening. Before participating in the in-person baseline screening, subjects provided written informed consent and HIPAA consent forms.

Eligible subjects were required to meet the following inclusion criteria during an extensive screening process: Subjects had to have been exposed to at least one traumatic stressor in their lifetime and met criteria for PTSD or sub-threshold PTSD as measured by the Clinician-Administered PTSD Scale, had to have used alcohol or an illicit substance within the past 6 months and have a current diagnosis of drug or alcohol dependence as measured by the SCID-I, and had to be capable of giving informed consent. Eligible participants were required to participate in outpatient treatment at the substance abuse treatment program to be considered for the study. Women were excluded if they had an advanced stage medical disease, impaired cognition (as assessed by the Mini-mental State Examination score <21), if they met criteria for bipolar disorder or had a history of a schizophrenia-spectrum illness as measured by the SCID-I, a history of active psychosis in the past 2 months, if they posed a significant risk for suicidal or homicidal behavior as measured by the PRISM, or current involvement in litigation

related to PTSD. Subjects were excluded if they did not speak English or if they refused to be audiotaped and videotaped (Hien et al., 2009).

After the baseline assessment, subjects were randomized to either Seeking Safety or Women's Health Education. Each of the seven sites delivered both treatment conditions, and groups were held twice per week for six weeks while continuing with Treatment as Usual at their outpatient substance abuse program at the site. The group treatments were 75-90 minutes in length, and had an open admission, rolling design. The groups ran so long as two or more members were present, and three or more women needed to be enrolled for a group to exist.

81.9% (n=289) of participants attended at least one treatment session, and 56.4% (n=199) attended at least six treatment sessions, with an average of 6.2 sessions in the Seeking Safety group completed and an average of 6.0 sessions in the Women's Health Education group completed.

### **Participants**

The participants of the *Women and Trauma Study* consisted of women between the ages of 18 – 65 enrolled in substance abuse treatment programs at seven sites across the United States. The average age of the sample was 39.2 years. 46% were Caucasian, and one-third were African American. Almost 18% were married, 41.1% lived with a partner, half were divorced or separated, and 37% were never married. 55% of subjects were unemployed.

80.4% of subjects met full threshold for PTSD, and 19.6% met subthreshold criteria for PTSD. Subjects were diagnosed with cocaine (70.5%), alcohol (56.1%), marijuana (27.2%) and opioid dependence (25.6%).

## Measures

*Addiction Severity Index – Lite (ASI)*. (McLellan, Cacciola, & Zanis, 1997). The ASI-Lite is clinician-administered measure based on the Addiction Severity Index (ASI) (McLellan, Luborsky, Woody, & O'Brien, 1980), a commonly used measure with excellent psychometric properties. The ASI assessed past and current functioning in multiple domains, including substance use, psychiatric, medical, interpersonal, and occupational functioning/ legal history. To expedite administration, the ASI was shortened to the ASI-Lite, an abbreviated version containing 160 items. The ASI-Lite generates domain-specific and overall composite scores. The psychometric properties of the ASI-Lite have not been evaluated.

*Clinician-Administered PTSD Scale (CAPS)*. The CAPS is a 17-item structured clinical interview intended to aid in the diagnosis of post-traumatic stress disorder. CAPS items correspond to DSM-IV PTSD Criterion A through E. An established rating system guides the clinician in assessing the frequency and severity of symptoms, rated on a 5-point (0-4) Likert Scale. The CAPS provides a continuous score reflecting trauma severity (Weathers, Keane, & Davidson, 2001).

The CAPS has been used as a diagnostic tool in more than 200 studies on post-traumatic stress disorder to date. Considered a gold standard diagnostic instrument, it has been demonstrated to have excellent reliability, discriminant validity, and convergent validity. In their review of investigations on the psychometric properties of the CAPS conducted from 1991 to 2001, Weathers, Keane, and Davidson (2001) report internal consistency alpha ratings ranging from .80 to .90 for all 17 CAPS items and interrater reliability scores consistently above .80. Findings suggest excellent convergent validity

of the CAPS, in which agreement with a clinically-based PTSD diagnosis was determined to be above .80 in all studies surveyed, with the majority reporting values above .90 and kappa values greater than .70. Correlations with self-report PTSD measures, including the IES, PCL, Mississippi Scale, and the DTS were frequently in the .80 to .90 range.

*Helping Alliance Questionnaire (HAQ-II-C/T)*. The HAQ-II is a 19-item self-report scale that seeks to measure the components of the therapeutic alliance as defined by Bordin (1994), consisting of agreement on goals, tasks, and the emotional bond between the patient and therapist. In this study, the revised Helping Alliance Questionnaire (Luborsky et al., 1996) was completed by each participant at weeks 2 and 6 (and in some cases was permitted to be completed at week 3 and 1-week post treatment, respectively) and by counselors for any week that they had a participant in treatment week 2 or 6.

The HAQ-II was developed after significant threats to validity were noted in the original instrument, the HAQ-I (Luborsky et al., 1986). Items on the original HAQ were worded positively and in such a way as to measure early symptom improvement rather than alliance. Six items were removed from the original and fourteen new items were added in developing the HAQ-II. The validity of the HAQ-II has been investigated and found to have sound psychometric properties (Le Bloc'h et al., 2006; Luborsky et al., 1996).

The HAQ-II was validated in a population of 246 cocaine dependent outpatients and found to have very good internal consistency and test-retest reliability; furthermore, no association was found between helping alliance scores and pre-treatment psychiatric

severity. The HAQ-II was found to have good convergent validity with the California Psychotherapy Alliance Scale (CALPAS) (Luborsky et al., 1996).

*Post Traumatic Stress Disorder Symptom Scale-Self Report (PSS-SR)* is a 17-item self-report inventory that assesses the frequency and severity of PTSD symptoms corresponding to DSM-IV diagnostic criteria (Foa, Riggs, Dancu, & Rothbaum, 1993). The PSS-SR was administered to a sample of 118 female sexual and non-sexual assault victims, and found to have good internal consistency and concurrent validity and high test-retest reliability. Furthermore, when used to diagnose PTSD, the self-report version of the PSS-SR was found to be more conservative than the interviewer-administered version (Foa, Cashman, Jaycox, & Perry, 1997). In the present study, the PSS-SR was filled out every other session by participants at Weeks 1-6.

*Substance Use Inventory (SUI)* consists of a series of self-report questions about quantity (i.e. in dollars spent per day), frequency (i.e. in days), and craving intensity of various substances used over the past week. This method adapts the Time-Line Followback Assessment Method for alcohol use first used by Sobell et al. (1980). The SUI assesses use of opiates, cocaine, alcohol, marijuana, amphetamines, sedatives, PCP, and prescription medications. The SUI was filled out every other session by participants at Weeks 1-6. (*Women & Trauma study Protocol*).

### **Analyses**

Receiver Operator Characteristic (ROC) analyses (Wickens, 2002) describing the prediction of nonresponse were utilized to assess the validity of early response in post-traumatic stress disorder and substance abuse as measured by the post-traumatic symptom scale – self report (PSS-SR) and the substance use inventory (SUI). ROC

analyses were conducted using SPSS for Windows, version 20.0 with non-parametric standard errors. ROC analyses have been used in prior research on early response (Coffey et al., 2007; Hildebrandt et al., 2010; Pupo et al., 2011). Per Wickens (2002), .8 is considered good and .9 is considered excellent when estimating the Area Under the Curve using a single continuous measure.

Individuals with a diagnosis of full or subthreshold PTSD at follow up according to the CAPS were designated non-responders, whereas those without PTSD were designated responders. Missing data for the ROC analyses were filled in using last observation carried forward for all for whom at least minimal PSS-SR, CAPS, SUI, and ASI data was available.

To address Hypotheses 2 and 3, data was examined for missing data and potential violations of assumptions. Descriptive statistics including means, variances, and covariances were calculated for all identified variables for the sample of N=223 participants for whom complete data was available. Data parameters were identified and estimated using a maximum likelihood estimator. Patterns of missing data were examined and met all missing at random assumptions. MPLUS 7.0 software was used to test the fit of the growth trajectory models.

Latent Growth Curve (LGC) analysis is a method to model change and provides a means of identifying predictors of non-linear change over time (Duncan, Duncan, & Strycker, 1999). The Structural Equation Modeling approach (SEM) to latent growth curve analysis was described by McArdle and Epstein (1987), Meredith and Tisak (1990); Muthén (1991), and Willett and Sayer (1994). LGC models have been used in prior research on Seeking Safety group treatment in veterans (Boden et al., 2012) and in

other research on rapid, early response in psychotherapy (Lutz et al. 2009; Stulz et al. 2007).

Longitudinal growth models which encompass the SEM approach to latent growth curve analysis are able to model changes in group over time in a variable of interest while accounting for individual- and group level clustering of observations (Morgan-Lopez & Fals-Stewart, 2007). In the current study, patients' level of Helping Alliance during the second week of treatment, treatment group, early change in trauma scores, and baseline substance use are the hypothesized covariates effecting the proposed mediator, early response (the latent slope factors of the PSS-SR), accounting for trauma outcomes at follow up. Thus, the latent slope factor of post-treatment trauma symptoms, as measured by the CAPS, will be the dependent variable of interest (Duncan, Duncan, & Strycker, 1999).

## **Results**

### *Hypothesis 1 - Early response and generation of cutoff values for prediction of nonresponse*

In order to assess the predictive accuracy of early response in both treatment groups, the relation between PTSD diagnosis on the Post-Traumatic Symptom Scale – Self Report (PSS-SR) and the Clinician Administered PTSD Scale (CAPS) was examined using ROC curves. Additionally, the ROC curves were used to identify cutoff scores for a PTSD diagnosis on the PSS-SR in which sensitivity and specificity were both maximized. In plotting sensitivity against 1-specificity, the score that generates the largest Area Under the Curve (AUC) is considered the most accurate predictor. The AUC

values at four follow-up time points ranged from .708 to .747 suggesting that the PSS-SR at Weeks 4, 5, and 6 of active treatment identified non-responders with a fair degree of accuracy (Table 2). Figure 1 represents the ROC curve for values of the PSS-SR when a diagnosis of PTSD according to the CAPS was used as a dichotomous outcome variable (PTSD responder vs. PTSD nonresponder).

On the PSS-SR, a cutoff score of 14 was used to classify individual response status at follow-up (Coffey, Beck, Palyo, & Miller, 2007; Sin et al., 2012). Using a cutoff of 14 on the PSS-SR, ROC curves were generated featuring the relationship between PSS-SR score during weeks 1 through 6 of active treatment and PSS-SR score at the four follow up time points. The AUC values for the PSS-SR ranged from .751 - .854 during Weeks 4, 5, and 6, denoting an acceptable level of accuracy in identifying treatment nonresponders at follow up (Table 3). Figure 2 represents the ROC curve for values of the PSS-SR when a diagnosis of PTSD according to the PSS-SR was used as a dichotomous outcome variable (PTSD responder vs. nonresponder).

Tables 2 and 3 feature area under the curve estimates for the prediction of nonresponse by trauma scores (PSS-SR) at Week 1 through Week 6. For 1-week, 3-months, and 6-months post-treatment, significant prediction of non-response in both treatment groups emerged by the 4<sup>th</sup> week of treatment. For 12-month post-treatment follow up outcomes on the CAPS, only PSS-SR scores at Weeks 5 and 6 of active treatment were marginally significant predictors of nonresponse.

Table 4 lists the sensitivity, specificity, and tau for the optimal cutoff score on the PSS-SR by Week 4 of treatment. Individuals whose PSS-SR score falls at or above this



cutoff value by Week 4 of treatment are likely to continue to meet criteria for PTSD up to one year after treatment has ended.

In order to assess the predictive accuracy of cumulative abstinence during treatment, the relation between the percent of cumulative days of abstinence at each treatment week as measured by the Substance Use Inventory (SUI) and substance use outcomes on the Addiction Severity Index (ASI) were examined using ROC curves. Treatment response was defined as abstinence at follow-up, while nonresponse was defined as having had one or more days of drug or alcohol use in the past 30 days. Refer to Table 5 and Figure 3 for further detail. Table 6 lists the sensitivity, specificity, and tau for cumulative percent days abstinent by Week 4 of treatment. Individuals who do not achieve a designated minimum of cumulative days abstinent by Week 4 of treatment are highly likely to continue to use drugs and alcohol over the year following treatment.

## *Hypothesis 2*

### *Multiple Group Model – Trauma outcomes*

The third model which was fit is a multiple group model in which the effects of three covariates, HAQ at Week 2, change in PSS-SR from baseline to Week 2, and baseline substance use (square root transformed) were used to predict the intercept and slope growth factors of Early Response (PSS-SR Week 4 – PSS-SR Week 6) in both groups simultaneously (Table 7). As in the previous two models the goodness of fit statistics were acceptable, i.e., the model chi-square was statistically insignificant ( $p =$

.83), the RMSEA (=0) and the CFI statistic was (1.0). In this model, the analytic focus was on testing whether the PSS-SR growth factors, i.e., the intercept and slope, differed significantly across the two treatment groups. A Wald test was used to test whether the set of two growth parameters, again the PSS-SR intercept and slope, differed significantly in the Seeking Safety and the Women's Health Education subgroups.

The Wald test was statistically insignificant ( $p = 0.17$ ) indicating the two growth parameters, taken as set, did not differ significantly in the two treatment conditions. Separate between-group tests of the PSS-SR intercept and the PSS-SR slope finds that the conditional intercepts did not differ significantly at week 4 (69.13 vs. 66.01,  $p = .398$ ). However, the conditional mean slopes of change in the PSS-SR from week 4 to week 6 approached a significant difference in the two treatment groups (-3.19 vs. -0.52,  $p = .062$ ), suggesting that the rate of improvement in the PSS-SR scores in the Seeking Safety group was faster than that observed in the Women's Education group (Figure 4).

#### *Multiple Group Model – Substance Abuse outcomes*

A multiple group model was fit in which the effects of three covariates, HAQ at Week 2, early improvement in substance use from baseline to Week 2, and baseline substance use (square root transformed) were used to predict the intercept and slope growth factors of Percent Days Abstinent at Week 4 – Week 6 in both Seeking Safety and Women's Health Education subgroups simultaneously. In this model, the analytic focus was on testing whether the percent days abstinent growth factors, i.e., the intercept and slope, differed significantly across the two treatment groups. Although goodness of fit statistics were acceptable, the percent days abstinent values from Week 4 – Week 6 were highly correlated. In both treatment groups, the change in slope of cumulative percent

days abstinent from Week 4 – Week 6 was not significant, suggesting that early response did not occur for substance abuse outcomes.

*Hypothesis 3 - Multiple Group Mediation Model for Trauma outcomes*

This multiple group model examined the impact of three covariates, HAQ at Week 2, the change in PSS-SR from baseline to Week 2, and baseline substance use (square root transformed) on the slope growth factor of the mediator, Early Response (PSS-SR week 4 – PSS-SR week 6).

The model assessed the indirect effects of the three covariates, HAQ at Week 2, baseline substance use, and early change in PSS-SR from baseline to week 2 on the slope of the dependent variable, post-treatment trauma score (CAPS at 1-week, 3 months, 6 months, and 12 months), via the proposed mediator (the slope of the PSS-SR from weeks 4-6). The model converged. For the multiple group model, the chi-square test of model fit was acceptable ( $p = 0.21$ ) as were the RMSEA ( $= 0.028$ ) and CFI goodness of fit indices ( $= 0.984$ ).

In both the Seeking Safety and Women's Health Education subgroups, the effects via the mediator, Early Response, on the slope of the CAPS were not significant, and there were no significant indirect effects of the three covariates on the slope of the CAPS at follow up. The longitudinal mediation hypothesis was not supported by the data.

In the Seeking Safety subgroup, the effect of early improvement in trauma symptoms from baseline to Week 2 on the slope of the PSS-SR was significant ( $b = -0.16$ ,  $p = .043$ ). This negative association demonstrated that subjects with greater improvement in trauma scores, as measured by a greater decline in PSS-SR scores, had a

faster rate of change on the PSS-SR from treatment weeks 4-6 as compared to those with less early improvement.

For the Women's Health Education subgroup, none of the three covariates had a significant effect on the slope of the PSS-SR from weeks 4-6. There was a significant effect of HAQ at Week 2 on the CAPS intercept ( $b = -3.77$ ,  $p = .012$ ), indicating that individuals with higher alliance scores had lower CAPS scores at follow up. There was a significant effect of baseline substance use on the PSS-SR intercept ( $b = -7.77$ ,  $p = .036$ ), indicating that individuals with heavier baseline use showed more marked early improvement in trauma symptoms than those who were abstinent at baseline.

TABLE 1. *Baseline Sociodemographic and Clinical Characteristics of Women Randomly Assigned to Receive 12 Sessions of Either Trauma-Focused or Health Education Group Treatment for Comorbid PTSD and Substance Use*

Variable	Total (N=353) (N=177)		Trauma-focused (N=176)		Health Education	
	N	%	N	%	N	%
Race/ ethnicity						
African American	120	34.0	58	33.0	62	35.0
Caucasian	161	45.6	83	47.2	78	44.1
Latina	23	6.5	7	4.0	16	9.0
Multiracial	47	13.3	27	15.3	20	11.3
Other	2	0.6	1	0.6	1	0.6
Marital Status						
Married	62	17.6	26	14.8	36	20.3
Single	130	36.8	66	37.5	64	36.2
Divorced/ separated	161	45.6	84	47.7	77	43.5
	Mean	SD	Mean	SD	Mean	SD
Age (years)	39.2	9.3	39.3	9.5	39.0	9.1
Education (years)	12.5	2.4	12.7	2.3	12.4	2.6
Employment						
Employed	40.2		40.3		40.1	
Unemployed	55.0		54.6		55.4	
Student/ Retired/ Disabled	4.8		5.1		4.5	
Current Abuse or Dependence Diagnosis						
Cocaine	70.5		72.7		68.2	
Stimulants	7.7		8.5		6.8	
Opiates	25.6		25.6		25.6	
Marijuana	27.2		27.8		26.6	
Alcohol	56.1		59.7		52.5	
PTSD Diagnosis (% Meeting Full Criteria)	80.4		76.7		84.2	
Lifetime Traumatic Experiences						
Child Physical Abuse	58.7		61.1		56.3	
Adult Physical Abuse	84.8		83.4		86.2	
Child Sexual Abuse	70.1		73.6		66.7	
Adult Sexual Abuse	67.6		65.1		70.1	
Transportation Accident	72.7		72.2		73.3	
Life-threatening illness	39.8		41.5		38.1	
Exposed to violent death	19.3		16.5		22.2	
Substance Use (past 30 days)						
Alcohol	4.2	7.7	4.7	8.1	3.7	7.2
Cocaine	4.2	8.1	4.4	8.1	4.1	8.1
Marijuana	2.7	7.1	2.9	7.1	2.5	7.0
Opiates	1.3	4.6	1.2	4.2	1.3	4.9
Sedatives	1.1	4.3	1.2	4.3	1.0	4.2
Stimulants	0.5	3.3	0.6	3.8	0.3	2.8
Heroin	0.2	1.7	0.2	2.3	0.1	0.7
Barbiturates	0.1	0.8	0.1	1.2	0.03	0.3
Inhalants	0.02	0.2	0.04	0.3		
Hallucinogens	0.01	0.2	0.02	0.2		
Substance Use (past 7 days)	1.6	2.5	1.7	2.6	1.6	2.5
Clinician-Administered PTSD Scale	62.9	19.4	61.6	19.4	64.2	19.4
PTSD Symptom Scale - Self Report	45.5	15.3	45.4	15.3	45.6	15.3

TABLE 2. *Summary of area under the curve estimates for prediction of non-response on the Clinician Administered PTSD Scale (CAPS) by PSS-SR score during Weeks 1-6 of active treatment.*

Treatment Week	1-Week Post-treatment AUC (SE)	3-Month AUC (SE)	6-Month AUC (SE)	12-Month AUC (SE)
PSS-SR Week 1	.634 (.031)	.670 (.029)	.658 (.029)	.617 (.030)
PSS-SR Week 2	.678 (.031)	.691 (.029)	.684 (.028)	.656 (.029)
PSS-SR Week 3	.693 (.030)	.702 (.029)	.706 (.028)	.654 (.029)
PSS-SR Week 4	.728 (.029)	.741 (.027)	.736 (.026)	.693 (.028)
PSS-SR Week 5	.718 (.029)	.740 (.027)	.747 (.026)	.712 (.027)
PSS-SR Week 6	.728 (.028)	.736 (.027)	.737 (.026)	.708 (.028)

TABLE 3. *Summary of area under the curve estimates for prediction of non-response on the PSS-SR by PSS-SR score during Weeks 1-6 of active treatment.*

Treatment Week	1-Week Post-treatment AUC (SE)	3-Month AUC (SE)	6-Month AUC (SE)	12-Month AUC (SE)
PSS-SR Week 1	.761 (.027)	.781 (.025)	.697 (.028)	.690 (.028)
PSS-SR Week 2	.797 (.026)	.799 (.025)	.732 (.027)	.735 (.027)
PSS-SR Week 3	.811 (.026)	.784 (.026)	.744 (.027)	.728 (.027)
PSS-SR Week 4	.838 (.024)	.812 (.024)	.783 (.025)	.751 (.026)
PSS-SR Week 5	.839 (.023)	.811 (.024)	.775 (.025)	.763 (.026)
PSS-SR Week 6	.854 (.022)	.820 (.024)	.777 (.025)	.770 (.025)

TABLE 4. *Coordinates of the curve: Cutoff threshold on the PSS-SR during Week 4 of active treatment in prediction of treatment nonresponse on the CAPS at follow-up*

Follow-up timepoint	$\tau$	Sensitivity	Specificity
1 week post tx	17	.740	.651
3 months	22	.623	.785
6 months	22	.636	.751
12 months	23	.568	.746

TABLE 5. *Summary of area under the curve estimates for prediction of response on the Addiction Severity Index (ASI) by SUI score during Weeks 1-6 of active treatment.*

Treatment Week	1-Week Post-treatment AUC (SE)	3-Month AUC (SE)	6-Month AUC (SE)	12-Month AUC (SE)
SUI Week 1	.786 (.027)	.756 (.028)	.714 (.029)	.678 (.030)
SUI Week 2	.805 (.026)	.778 (.027)	.727 (.028)	.694 (.029)
SUI Week 3	.817 (.025)	.793 (.026)	.738 (.028)	.698 (.029)
SUI Week 4	.835 (.024)	.801 (.026)	.753 (.027)	.710 (.029)
SUI Week 5	.838 (.024)	.803 (.026)	.755 (.027)	.712 (.029)
SUI Week 6	.833 (.024)	.797 (.026)	.750 (.027)	.705 (.029)

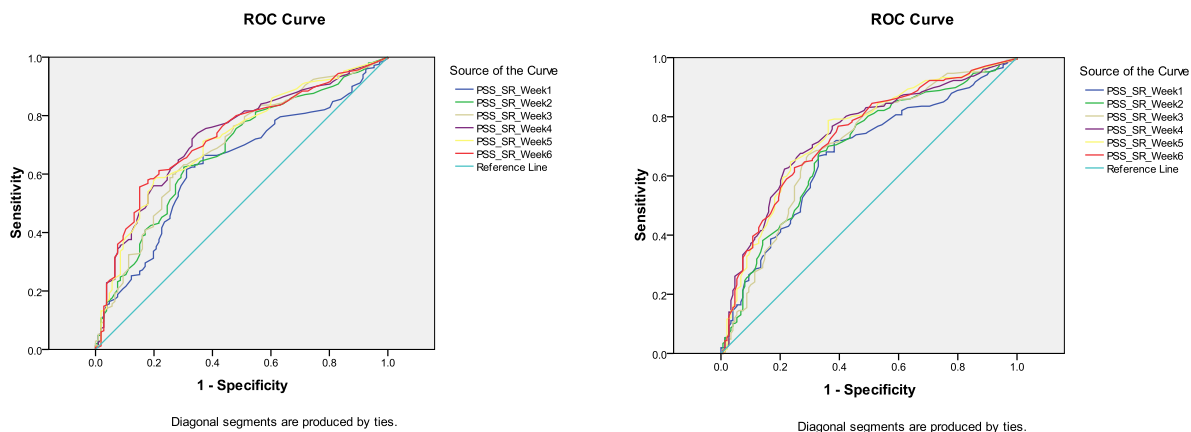
TABLE 6. *Coordinates of the curve: Percent days abstinent during Week 4 of active treatment in prediction of substance abuse nonresponse according to the ASI at follow-up*

Follow-up timepoint	$\tau$	Sensitivity	Specificity
1 week post tx	81% (23 days)	.721	.903
3 months	78.9% (22 days)	.651	.927
6 months	73.8% (21 days)	.575	.901
12 months	69.1% (19 days)	.530	.853

TABLE 7. *Effects of covariates on in-treatment change in PSS-SR latent growth variables during treatment weeks 4-6 (N=353).*

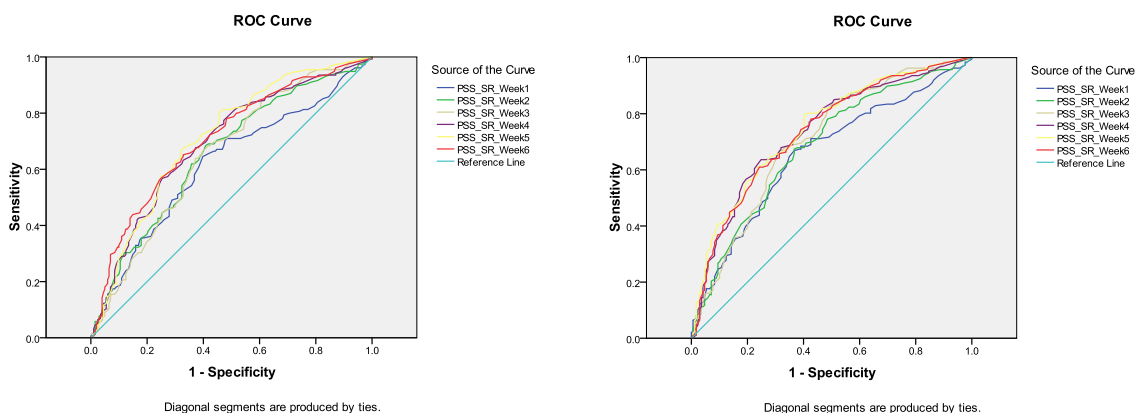
Covariates	Seeking Safety (N=176)				Women's Health Education (N=177)			
	Intercept (SE)	p	Slope (SE)	p	Intercept (SE)	p	Slope (SE)	p
HAQ-II-P	4.52(8.1)	.58	-3.47(3.3)	.30	8.47(5.23)	.11	3.5(2.3)	.13
Early change in PTSD severity	.25(.15)	.09	-.16(.06)	.01	.28(.08)	0	-.03(.05)	.48
Baseline substance use	1.69(1.69)	.32	.55(.61)	.36	-2.83(1.27)	.03	.64(.47)	.18

## Receiver Operator Characteristic Curves for Post-Treatment Non-Response to Seeking Safety and Women's Health Education



Prediction of nonresponse at 1-week post-treatment treatment

Prediction of nonresponse at 3 months post-treatment



Prediction of nonresponse at 6 months post-treatment treatment

Prediction of nonresponse at 12 months post-treatment

FIGURE 1. Panels depicted above summarize prediction of non-response at 1-week, 3 months, 6 months, and 12 months post-treatment according to the clinician administered PTSD scale (CAPS) by PSS-SR scores during weeks 1-6 of active treatment.



## Receiver Operator Characteristic Curves for Post-Treatment Non-Response to Seeking Safety and Women's Health Education

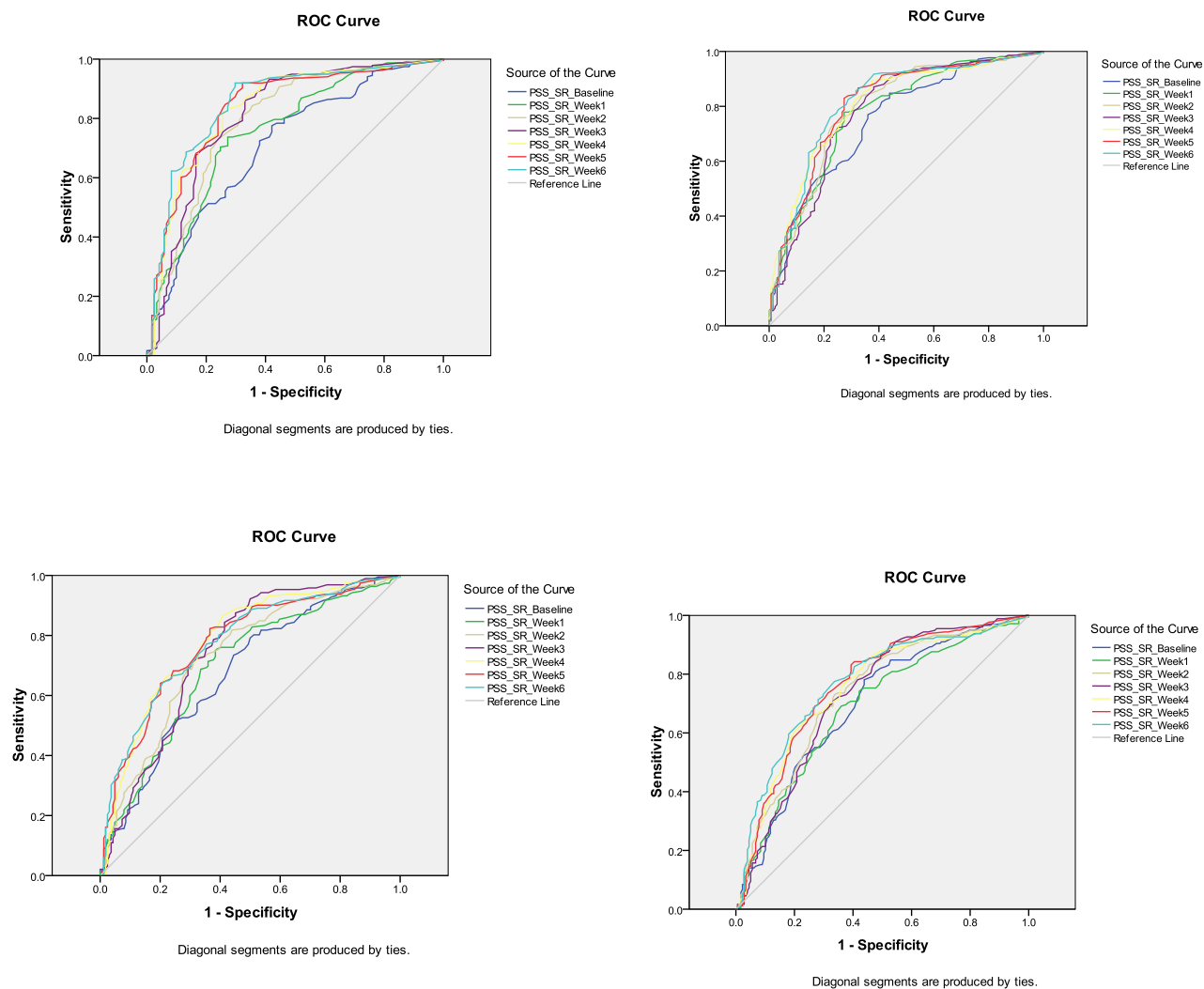


FIGURE 2. Panels depicted above summarize prediction of non-response at 1 week, 3 months, 6 months, and 12 months post-treatment according to the PSS-SR by PSS-SR scores during weeks 1-6 of active treatment.

# Receiver Operator Characteristic Curves for Post-Treatment Substance Abuse Non-Response to Seeking Safety and Women's Health Education

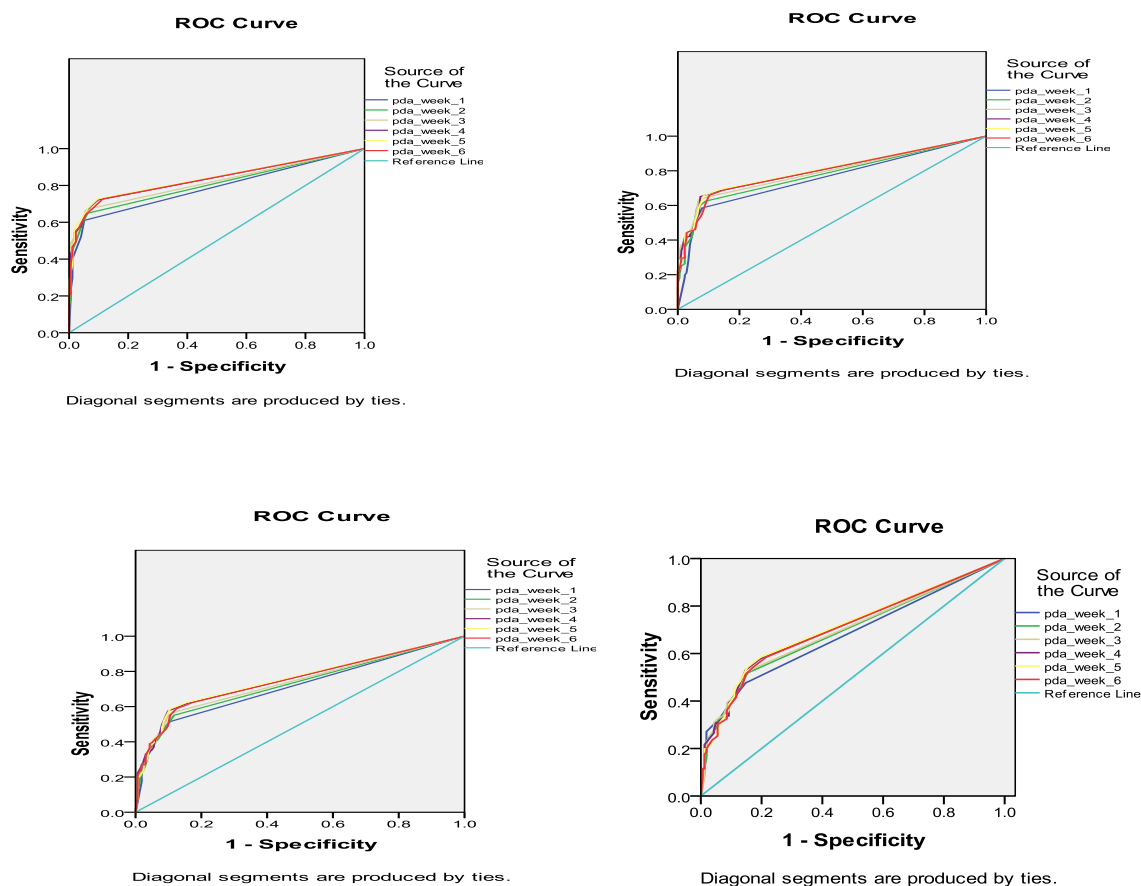


FIGURE 3. Panels depicted above summarize prediction of response on Addiction Severity Index (ASI) at 1-week, 3 months, 6 months, and 12 months as predicted by days of use (SUI) during active treatment.

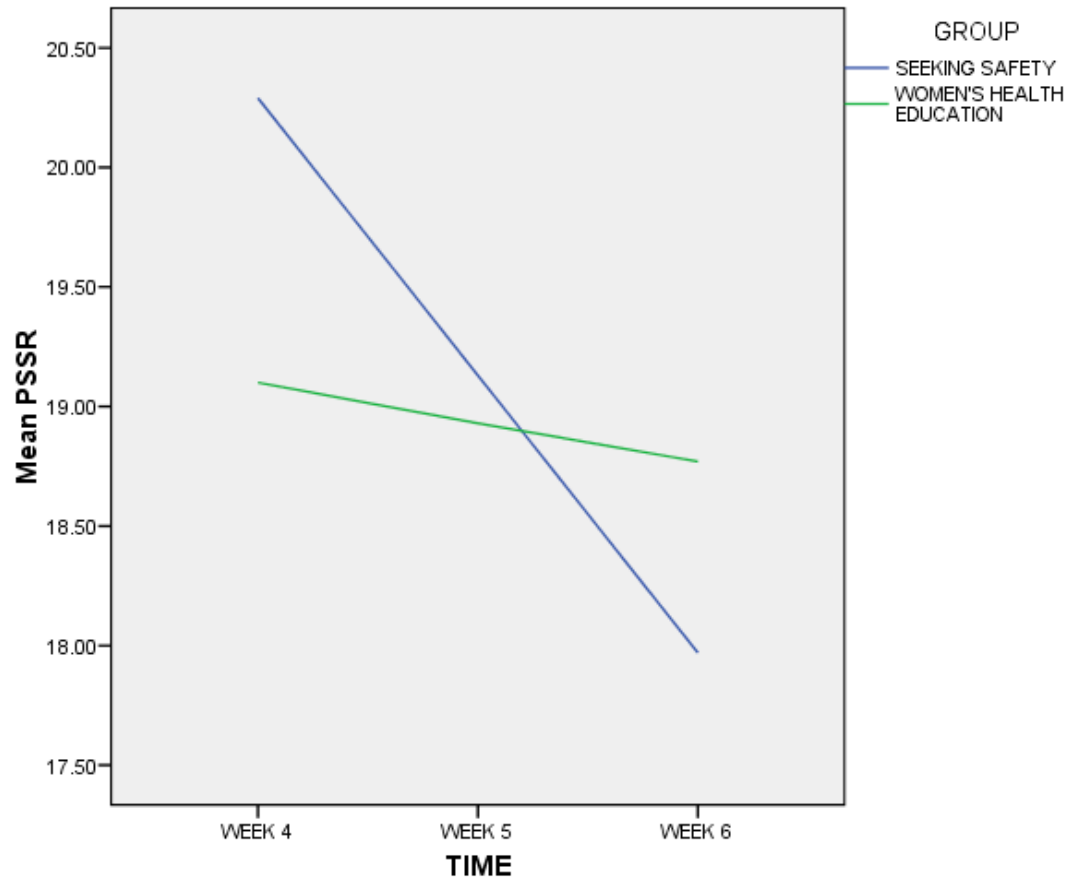


FIGURE 4. PSS-SR scores  $\times$  Time  $\times$  Treatment Condition. The conditional mean slopes of PSS-SR scores from Weeks 4-6 were marginally significantly different between the two treatment groups (-3.17 vs. -0.45,  $p = .06$ ), suggesting that trauma symptoms improved at a faster rate in the Seeking Safety group than observed in the Women's Health Education group. The conditional intercepts did not differ significantly at week 4 (69.312 vs. 66.059,  $p = .37$ ).

## **Discussion**

The *Women and Trauma Study* was a multi-site trial investigating the efficacy of Seeking Safety, a manualized group therapy for women with co-morbid Post-traumatic Stress Disorder (PTSD) and Substance Use Disorders, in reducing PTSD symptoms and substance use in women receiving outpatient substance abuse treatment. 353 women were randomized to receive either 12 sessions of Seeking Safety or 12 sessions of a comparison treatment, Women's Health Education. Treatment was twice per week for a total of six weeks. PTSD symptoms and substance use were assessed weekly during treatment and follow-up assessments were given at 1-week, 3-months, 6-months, and 12-months post treatment.

The current dissertation investigated (1) whether the concept of early response is valid within PTSD and substance use comorbidity, as virtually no research has been done on PTSD and early treatment response to date, (2) potential PSS-SR and cumulative abstinence cut off values for the prediction of treatment non-response, (3) whether subjects' trauma and substance abuse symptoms improved more rapidly in the Seeking Safety condition than in the Women's Health Education condition, and (4) whether early treatment response mediated the effect of helping alliance on post-treatment trauma and substance abuse outcomes.

### **Early Response and the Prediction of Trauma and Substance Abuse Non-response**

Trauma and substance abuse symptom severity at the fourth through the sixth week of treatment predicted response status in the months following treatment with a fair to excellent degree of accuracy. Area Under the Curve estimates depicting trauma outcomes at 1 week, 3 months, 6 months, and 12 months generally ranged from fair to

good (.71 to .83), indicating among those who improved, therapeutic changes were sustained over time. Those whose scored 22 or above on the PSS-SR at the fourth week of treatment were likely to continue meeting diagnostic criteria for PTSD at 3 months and 6 months post-treatment, while those who scored a 23 or above were likely to be non-responders at 12 months post-treatment. Subjects' substance abuse severity scores at the fourth through the sixth week of treatment, defined as cumulative percent days abstinent, predicted substance abuse response status with good accuracy. Area Under the Curve estimates depicting substance abuse outcomes at post-treatment, 3 months, 6 months, and 12 months ranged from fair to good (.71 to .84) with most AUC estimates falling in the .8's range. This suggests that those who did not achieve sobriety in the year following treatment could be accurately predicted by their cumulative days of abstinence by the fourth week of treatment. Those who achieved less than 78.9% cumulative abstinence (22 days) by the fourth week of treatment were likely to continue to use drugs or alcohol 3 months later. Those who achieved less than 73.8% (21 days) and 69.1% (19 days) cumulative abstinence by the fourth week were likely to continue to drink or use at 6 months and 12 months following treatment, respectively.

These findings are consistent with extant literature on early response, which identifies the fourth through the eighth treatment week as the period yielding the most accurate predictive information. In the present study, the severity of trauma and substance abuse symptoms at Week 4 was the earliest point at which subsequent response status could be accurately predicted (Wilson, 1999). The trauma findings are consistent with those of Bradford et al. (2011), who found that among 76 older adults diagnosed with GAD being treated with 10 sessions of cognitive behavioral therapy, improvement at one

month of treatment predicted sustained reduction in anxiety symptoms at 1 month, 3 months, and 1 year follow up. Utilizing hierarchical linear modeling, they also found that subjects' extent of early improvement predicted the slope of improvement in anxiety symptoms over the year following treatment. Findings are also consistent with early response studies among depressed and anxious outpatients, in which rapid, early improvement predicted post-treatment outcomes (Lutz, Stulz, & Kock, 2009; Stulz, Lutz, Leach, Lucock, & Barkham, 2007).

Although levels of cumulative abstinence by the fourth week of treatment provided accurate prediction of subsequent outcomes, early improvement in substance abuse did not occur in this sample. This finding is not consistent with previous investigations of early improvement among individuals in substance abuse treatment (Brensilver, Heinzerling, Swanson, & Shoptaw, 2012; Ceperich & Ingersoll, 2011). However, Hildebrandt et al. (2010) found that while early response, defined as cumulative percent days abstinent, occurred in an individual behavioral alcohol intervention, it was not valid in a behavioral couples alcohol intervention. It is possible that early response to substance abuse treatment is likely to occur in individual psychotherapy, however not within group or couples interventions. While prior studies have demonstrated the validity of early improvement in substance use symptoms, none have included patients with PTSD in their samples. Given that patients with comorbid PTSD and addiction have more severe psychiatric symptoms, it may take longer for this population to attain abstinence.

The majority of participants in the Women and Trauma study were in early recovery and largely abstinent at baseline; this limiting factor may have precluded the

detection of early substance abuse response. Among those who were actively using at baseline, improvement in trauma symptoms preceded reductions in substance use for virtually all subjects; thus observable reduction in use likely occurred later in the study (Hien et al., 2009).

### **Rapid, early improvement in Seeking Safety vs. Women's Health Education**

The slopes of the latent growth curves examining helping alliance as a predictor of early improvement in trauma scores showed near-significant differences between the two treatment groups ( $b = -2.73$ ,  $p = .06$ ), suggesting that trauma symptoms improved at a faster rate among subjects in the Seeking Safety condition. That this trend did not achieve significance may be accounted for by the limited variability in HAQ scores at Week 2, in which most subjects assigned high ratings to their alliance with group therapists. Missing data may also account for lack of detection of an unequivocally significant effect, given that Week 2 HAQ data was available for only 223 participants.

The trend suggesting rapid, early response in trauma observed among those in the Seeking Safety treatment condition may be attributed to the trauma-specific content of Seeking Safety, which ostensibly provides a more effective treatment. While helping alliance did not significantly contribute to the prediction of the slope of improvement in trauma symptoms during treatment and post-treatment, it was a significant predictor of the CAPS intercept at follow up. This is consistent with the findings of Ruglass et al. (2012), who found that helping alliance was related to post-treatment improvements in CAPS scores among  $N = 223$  Women and Trauma study participants.

The current findings partially corroborate those of Hien et al. (2010), who investigated  $N = 353$  Women and Trauma Study participants. Hien et al. (2010) found

that Seeking Safety was significantly more effective in reducing PTSD symptoms than Women's Health Education both during treatment and at post-treatment follow up for women with baseline alcohol misuse. Among subjects with no alcohol misuse at baseline, trauma symptoms improved equally in both treatment conditions. While the current findings suggest that sharper, more dramatic symptom improvement occurred in the Seeking Safety group, baseline substance use did not significantly contribute to the prediction of outcomes. Baseline substance use may not have emerged as a significant predictor because all substances were considered unitarily, whereas Hien et al. (2010) parsed out alcohol use from other substance use. Various classes of substances may differentially impact the symptom profiles and course of recovery of individuals with PTSD (Back et al., 2003). Inaccurate measurement of substance use may account for the lack of a significant treatment effect.

#### **No support for mediation model**

Early response to substance abuse treatment did not occur in this sample; as a result, a mediation model for substance abuse outcomes could not be tested. Early improvement in trauma symptoms was not found to be a significant mediator of the relationship between therapeutic alliance and trauma outcomes. These results diverged from previous findings and theoretical expectations of the relationship between therapeutic alliance and early response. It has been proposed that nonspecific factors, particularly therapeutic alliance, cause early symptom improvement among a subgroup of patients. Early response often occurs before theory-specific techniques have been introduced into treatment, leading some researchers to conclude that early improvement reflects the effects of common factors (Haas, 2002; Lambert, 2005). Haas (2002) argued



that early response mediates the relationship between nonspecific factors and subsequent psychotherapy outcomes. Tang and DeRubeis (1999b) demonstrated a relationship between therapeutic alliance and early response, in which sessions in which patients demonstrated sudden reductions in symptoms were immediately followed by improvements in their ratings of the alliance with their therapists. They posited that the patient develops more trust in the therapist and engages more in therapy following early improvement. The lack of meaningful findings for a mediating role of early response may be explained by an incorrect causal order, in which early response may actually precede improvements in alliance, and not vice versa. A limitation of the present study was that therapeutic alliance was only measured at Weeks 2 and 6, limiting the ability to track session-by-session changes in alliance; thus the immediate effect of early response on helping alliance could not be assessed.

Other potential covariates involved in the prediction of early response were not explored in the present study. In seeking to explain early improvement in patients receiving cognitive behavioral therapies, Wilson (1999) argued that theory-specific interventions such as self-monitoring and homework assignments are likely viable mediators of early treatment response. This raises interesting possibilities with regards to the present study, in which technical interventions unique to Seeking Safety, such as community resource-seeking, may have been worth exploring as potential covariates.

### **Study Limitations**

The lack of variability in HAQ and baseline substance abuse scores may account for the lack of support for the proposed mediation model. The large amount of missing data may also have precluded a significant effect from being detected. Additional

limitations include the possibility that group-level factors and missing data were not adequately accounted for in the chosen model (Tasca et al., 2010). Analyses employed traditional latent growth models that assume group membership was unchanging over time, when in fact the membership of the groups was continually changing. Traditional latent growth models also assume that data was Missing-At-Random (MAR), whereas this assumption may not have been accurate (Morgan-Lopez & Fals-Stewart, 2007). It may have been beneficial to use an alternative method, such as latent class pattern mixture modeling, which models differences in treatment effects across latent attendance classes and the point at which the subject entered treatment, and does not utilize the Missing-At-Random assumption.

### **Treatment Implications for Women with PTSD and Addiction**

The demonstrated validity of early response among a sample of women with comorbid PTSD and addiction has potential clinical applications. Tracking patients' response during treatment may be important for predicting their likelihood of symptom relief and attainment of sobriety. The ability to identify patients unlikely to respond to treatment provides a means of planning individual treatment and allocating treatment resources. Women with comorbid trauma and addiction typically demonstrate poor retention rates, thus it is preferable if progress can be assessed early in treatment, given that the window of opportunity for treatment with this population is usually brief. Early response provides a means of assessing whether to give more intensive or targeted treatment, and could provide a cost-efficient means of assigning services to women with comorbid trauma and addiction (Hien, Litt, Cohen, Miele, & Campbell, 2009).

The present finding supports the utility of early response for a PTSD population. It is notable that early response was found to be valid among individuals with PTSD, given that early response assumes a linear course of symptom improvement over time. This finding counters the commonly-held belief among clinicians that the course of symptom improvement among PTSD patients is variable. Many clinicians assume that a patient undergoing treatment for PTSD may “get worse before getting better” because treatment often encourages patients to confront traumatic memories and trauma reminders, requiring them to tolerate an increased level of anxiety. However, only minimal empirical evidence exists to support the notion that recovery from PTSD takes a fluctuating course. Among a variety of exposure-based and CBT therapies for PTSD, a minority of patient’s symptoms temporary worsened during active treatment (Foa, Zoeller, Feeny, Hembree, & Alvarez-Conrad, 2002). Cahill, Foa, Hembree, Marshall, & Nacash (2006) point out that minimal empirical evidence for this treatment course among PTSD patients exists, and that indeed the majority of trauma patients’ course of improvement appears to take a linear course of improvement. Seeking Safety group treatment focused on learning coping skills and not on directly confronting traumatic material, and so a temporary worsening of symptoms would not be expected within Seeking Safety treatment.

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