

## Adverse events in an integrated trauma-focused intervention for women in community substance abuse treatment

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### Abstract

A substantial number of women who enter substance abuse treatment have a history of trauma and meet criteria for posttraumatic stress disorder (PTSD). Fear regarding the extent to which PTSD treatment can evoke negative consequences remains a research question. This study explored adverse events related to the implementation of an integrated treatment for women with trauma and substance use disorder (Seeking Safety) compared with a nontrauma-focused intervention (Women's Health Education). Three hundred fifty-three women enrolled in community substance abuse treatment were randomized to 1 of the 2 study groups and monitored weekly for adverse events. There were no differences between the two intervention groups in the number of women reporting study-related adverse events (28 [9.6%] for the Seeking Safety group and 21 [7.2%] for the Women's Health Education group). Implementing PTSD treatment in substance abuse treatment programs appears to be safe, with minimal impact on intervention-related adverse psychiatric and substance abuse symptoms. More research is needed on the efficacy of such interventions to improve outcomes of PTSD and substance use. © 2008 Elsevier Inc. All rights reserved.

**Keywords:** Seeking safety; PTSD; Substance abuse; Adverse event

### 1. Introduction

Integrated PTSD and substance abuse disorder (SUD) treatments are increasingly being implemented in community substance abuse treatment programs (Brady, Danksy, Back, Foa, & Carroll, 2001; Finkelstein et al., 2004; Hien, Cohen, Miele, Litt, & Capstick, 2004; Najavits, Weiss, Shaw, & Muenz, 1998). There is a general consensus in the

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literature that despite concerns over adverse reactions or negative experiences attributed to treatment, patients who do engage in nonpsychopharmacological interventions see significant improvements in PTSD symptoms (Seedat, Stein, & Carey, 2005). Despite this consensus, there remains an ongoing concern within the treatment community that integrated treatment for PTSD poses a potential risk for increasing the patient's adverse psychiatric symptoms (Hien et al., 2004). This concern is also present in the nonintegrated treatment (i.e. cognitive processing and exposure therapy) literature. Few studies have focused on this topic. However, across PTSD treatment studies the following developments have been found in some degree: worsening of psychiatric symptoms among some individuals that is not generally indicative of poorer long-term outcomes (Foa, Zoellner, Feeny, Hembree, & Alvarez-Conrad, 2002; Tarrier et al., 1999) and individual differences leading to variations in treatment response (Hembree, Street, Riggs, & Foa, 2004; Morrissey et al., 2005; Speckens, Ehlers, Hackmann, & Clark, 2006; Tarrier et al., 1999). These developments make clear that further investigation is needed.

PTSD symptoms have been found to increase during behavioral intervention in a small number of studies. For example, Foa et al. (2002) found that greater number of women in a prolonged exposure condition experienced increased symptoms of anxiety and depression following imaginal exposure than did women in an imaginal exposure plus cognitive-restructuring condition. However, short-term increases in symptoms did not lead to worse PTSD symptoms at the conclusion of treatment. Similarly, Tarrier et al. (1999) found that deterioration during treatment was not reflected in follow-up data. Few studies, however, have actually reported impacts of cognitive-behavioral treatments, and the full extent of negative impacts on treatment outcomes is not known.

Similarly, there is some indication that certain individual-level variables may influence responsiveness to PTSD treatment or integrated treatment. Speckens et al. (2006) found that initial PTSD symptom severity (but not initial anxiety, depression, dissociation, or self-blame) was associated with the degree of change in intrusive memories following imaginal reliving in the context of a cognitive-behavioral treatment. Tarrier et al. (1999) found that patients who deteriorated were rated as less motivated by their therapists than were patients who improved. These studies suggest that certain individuals may be more likely to improve, and others were likely to show some deterioration. However, there are few empirical studies to guide practice in this area, and there has not been a theoretical model proposed to guide research into important individual differences.

It is important to note in the adverse event and trauma literature that populations who are screened as high risk or are considered the most severe cases are often excluded from study participation. This may limit the generalizability of findings regarding patient reaction to trauma treatment (nonintegrated or integrated). Study participants who have

been identified as having high risk for suicidality (Back, Brady, Sonne, & Verduin, 2006; Speckens et al., 2006) alcohol or drug dependence (Speckens et al., 2006), serious depression or bipolar disorder (Back et al., 2006; Speckens et al., 2006), or psychosis (Talbot et al., 1999) are often excluded. Although such exclusions are often appropriate to maximize patients' ability to benefit from treatment and minimize risk, they do result in more restricted samples than those typically entering community treatment programs.

In addition to exclusion criteria limiting the generalizability of patient adverse reactions to trauma treatment, the finding of poor treatment retention contributes to our lack of knowledge regarding adverse events. One study by Talbot et al. (1999) cited attrition as possibly tied to an iatrogenic effect of being in the Women's Safety Group. Of the 26 women who dropped out of the study, they noted that 18 of those women left for reasons unrelated to study participation. The remaining 6 women noted that the content of the material was too difficult as the reason for their withdrawal from the program. There is some evidence that worsening of symptoms during treatment is associated with poorer attendance (Tarrier et al., 1999) and that lack of symptom improvement is associated with failure to complete treatment (Back et al., 2006). However, a review of cognitive-behavioral PTSD treatment studies found no evidence of differential dropout for particular forms of treatment (i.e., exposure vs. cognitive vs. stress inoculation vs. eye movement desensitization and reprocessing treatments; Hembree et al., 2003). Further research is needed to determine how poor study retention is related to patient adverse reactions to integrated trauma treatment. Thus far there has been little focus on this relationship.

For high-risk patients with PTSD or comorbid SUD and PTSD, some form of cognitive-behavioral or integrated treatment remains the primary option (Seedat et al., 2005). Gathering and reporting information on the occurrence and impact of symptom worsening on treatment retention and outcomes will provide useful information to practitioners and guide the development and refinement of treatments.

This study evaluated data from the Clinical Trials Network's women-with-trauma and SUD study to determine the occurrence and impact of adverse events throughout a nonexposure-integrated treatment for women with trauma and SUD. Specifically, study-related adverse events were compared between the experimental and a control intervention that did not address PTSD. The nature of the adverse events as well as their relatedness to the study interventions, retention, substance use, and PTSD symptoms were addressed.

## 2. Materials and Methods

### 2.1. Participants

Participants included 353 women enrolled in seven outpatient community-based treatment agencies for SUDs

recruited into a multisite clinical trial of psychosocial treatments for PTSD. Recruitment occurred over a 21-month period in 2004 and 2005. Data reported are from the adverse event assessment collected during baseline, weekly throughout the 6-week intervention phase, and 1 week postintervention. To be eligible, participants needed to have had at least one traumatic event in their lifetime and to have met *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* criteria for either full or subthreshold PTSD. For subthreshold PTSD, participants had to fulfill *DSM-IV* criteria A (exposure to a traumatic stressor), B (re-experiencing symptoms), either C (avoidance and numbing symptoms) or D (symptoms of increased arousal), as well as E (symptom duration of at least 1 month) and F (significant distress or impairment of functioning). Other inclusion criteria were (a) between 18 and 65 years of age; (b) have used alcohol or an illicit substance within the past 6 months and have a current diagnosis of drug or alcohol abuse or dependence; and (c) capable of giving informed consent. Women were excluded from participation if they had (a) advanced stage medical disease (e.g., AIDS, TB) as indicated by global physical deterioration; (b) impaired mental cognition as indicated by a mini-mental status examination (Folstein, Folstein, & McHugh, 1975) score <21; (c) significant risk of suicidal/homicidal intent, behavior, or history as assessed by the Psychiatric Research Interview for Substance and Mental Disorders (Hasin et al., 1996); (d) significant history of schizophrenia-spectrum diagnosis; (e) a history of active (past 2 months) psychosis; (f) involvement in litigation related to PTSD; or (g) refused to be videotaped or audiotaped.

## 2.2. Community treatment programs

Seven community-based treatment programs participated in the study. All participating programs offered a combination of outpatient individual and group treatment components, reflecting varying orientations and philosophies of addiction treatment. All but one of the sites had mixed gender programs, and most did not have trauma-specific treatment available at the time of the study. All study participants were enrolled in one of the psychosocial outpatient substance abuse treatment programs and received usual care at the time of their randomization. Each study participant was required to attend treatment as usual during the study's 6-week intervention phase. If participants dropped from treatment prior to completing the intervention phase, they were removed from the treatment portion of the study but continued with follow-up assessments.

## 2.3. Procedures

### 2.3.1. Design

This study used a randomized, controlled design to assess the effectiveness of Seeking Safety Treatment (Najavits et al., 1998) plus standard substance abuse treatment (SS+SST)

in comparison to a control treatment, Women's Health Education, plus standard substance abuse treatment (WHE+SST). Prior to study implementation, all sites received study and informed consent approval from their perspective institutional review boards. All procedures were followed in accordance with the standards of the committee on human experimentation of the institutions in which the experiments were done. Participants signed one informed consent for screening to determine preliminary eligibility. If eligible, they signed another informed consent for baseline assessment and study participation. Independent assessors who were blind to study condition performed all baseline and follow-up assessments. After baseline assessment, eligible participants were randomly assigned to 1 of the 2 treatment conditions. Each intervention consisted of an initial individual session with the therapist to discuss randomization, intervention format, and group rules, followed by 12 twice-weekly group sessions over approximately 6 weeks. Groups had an open, rolling enrollment format, lasted approximately 75 to 90 minutes, and ran as long as at least 3 women were enrolled in that particular treatment arm. Due to the criteria of 3 women needed to conduct the group, many women took longer than 6 weeks to complete the interventions. Some women were assessed but never actually exposed to the intervention. In addition to within treatment weekly self-report questionnaires, follow-up assessments were conducted at 1-week, and 3, 6, and 12 months posttreatment. For the current study only the baseline, weekly questionnaires and the 1-week follow-up were used in the data analysis.

### 2.3.2. Seeking Safety

(Najavits et al., 1998) is a short-term, manualized cognitive-behavioral treatment specifically designed to address both trauma and substance abuse in either group or individual settings. Sessions are structured and include basic education on SUD and PTSD, action skills to prevent drug use and control PTSD symptoms, cognitive restructuring with particular attention to maladaptive thoughts associated with SUD and PTSD, and a focus on relationship issues and developing effective communication skills to build a healthy support network. Session topics are meaningfully connected to patient reports of unsafe behavior and coping skills. Twelve out of the 24 manualized sessions, which represented the core sessions, were used in this study (Najavits, personal communication, 2003).

### 2.3.3. Women's Health Education

(Tross, 1998) is a nonspecific short-term manualized treatment that provided the comparison arm of this study. Sessions focus on such topics as understanding the female body, human sexual behavior, pregnancy and childbirth, sexually transmitted diseases, HIV, and AIDS, but did not address trauma or PTSD. The treatment uses minilecture, video, story telling, text readings, and discussion techniques to provide the health information.

## 2.4. Measures

### 2.4.1. PTSD

PTSD was assessed via the Clinician-Administered PTSD Scale (CAPS) which measures frequency and intensity of signs and symptoms of PTSD in the past 30 days and overall symptom severity over time and is used as a measure of *DSM-IV* PTSD diagnosis for eligibility and treatment outcome (Blake, Weather, Nagy, Kaloupek, & Klauminzer, 1990). The CAPS was administered at the initial screening visit, and if participants met criteria for PTSD or subthreshold PTSD, they proceeded to the baseline assessment. The CAPS was also administered at 1 week postintervention.

An adverse event (AE) questionnaire was administered by research staff at baseline after administration of the CAPS interview, weekly during the intervention phase, and at 1 week postintervention. Participants were asked about the occurrence of any new AEs or change in severity of any existing AEs since their last AE assessment. Information concerning possible AEs was also identified through counselors who delivered the study interventions, research staff, and documentation in the source records or case report forms, including substance use and PTSD measures administered weekly during the treatment phase. For the purposes of this report, baseline, intervention phase, and 1-week postintervention data are presented. AEs collected during the intervention phase and at 1 week postintervention more accurately reflected the impact of the interventions on participant responses. AEs collected at baseline more accurately reflected the potential impact of the CAPS screening interview on participant responses.

All symptoms that occurred more frequently than anticipated, were more severe than expected, and/or represented an increase from baseline were reported as AEs and documented on an AE Log Form. Expected AEs were those symptoms most likely to occur in this population: increased PTSD symptoms, increased depression symptoms, and increased or more severe alcohol or substance use. A study-related designation was given to an AE that was completely or partially a result of participation in the study or one in which the study could not be ruled out as an implicating factor. Study-relatedness was verified through conversation with the participant, information from case report forms and source documents, including hospital records when available, and through consultation with a study clinician. An AE was also evaluated for severity (mild, moderate, and severe) and seriousness. A serious AE (SAE) is defined as any fatal, life-threatening, permanently and/or substantially disabling condition or one that is a congenital anomaly, requires an initial hospitalization or prolonged hospitalization, or is an event which requires intervention to prevent permanent impairment or damage. AEs that were expected, study related or serious, were documented more comprehensively on an AE Form. SAEs were further detailed on a SAE Form and SAE narrative completed by the study clinician. Every attempt was made to follow all SAEs, regardless of study

relatedness, to resolution. The present analysis will focus on the occurrence of new onset study-related AEs.

Adverse events were also monitored by reviewing two weekly self-report questionnaires, the Substance Use Inventory (SUI) and the Posttraumatic Stress Disorder Symptom Scale-Self Report (PSS-SR). The SUI consists of a series of questions about quantity and frequency of substance use adapted from the Time Line Follow-Back method (Sobell et al., 1980). The PSS-SR assesses the frequency and intensity of PTSD symptoms (Foa, Riggs, Dancu, & Rothbaum, 1993).

### 2.4.2. Substance Use

Substance abuse and dependence diagnostic data were collected via the alcohol and drug modules of the Composite International Diagnostic Interview (CIDI), a fully structured, interviewer-administered measure used to determine lifetime and current substance disorder diagnoses for alcohol, marijuana, stimulants, opioids, cocaine, and sedatives (Cottler & Compton, 1993). The CIDI was administered at screening to determine eligibility. Additional alcohol and substance use data such as past 30-day use were collected on the Addiction Severity Index (ASI), a standardized, multidimensional, semistructured interview that provides clinical information important for formulating treatment plans and constructing problem severity profiles in six domains: medical, employment/support, legal, alcohol and drug use, family/social, and psychiatric (McLellan et al., 1992). The ASI was administered at baseline and 1 week postintervention.

### 2.4.3. Sociodemographics

Basic demographic data, including age, ethnicity, and race were collected at the screening assessment and additional sociodemographic data including marital status, education, and employment pattern (prior 3 years) were obtained from the ASI.

A study termination form was completed for all participants regardless of their study completion or discontinuation status. Length of time in treatment and number of sessions attended were obtained from this form. In addition, whenever possible, reason for early termination was recorded on this form.

## 2.5. Data analysis

Demographic and diagnostic characteristics at baseline, proportions of patients experiencing new study-related adverse events within the treatment, and severity of new study-related AEs were compared across two treatment groups with chi-square tests for categorical variables and *t* tests for continuous variables. The Wilcoxon rank test was used to compare the number of new study-related adverse events per patient between the two treatment arms. The association between the number of sessions attended and the number of new study-related adverse events within treatment was estimated and tested by fitting a log-linear model for the number of patient study-related AEs with the number of sessions and treatment as predictors. The effect of the

Table 1  
Demographic and psychosocial characteristics

Variables	Total N = 353	Seeking Safety 176	Women's health 177	p value
Age	38.7 (9.3)	38.8 (9.5)	38.6 (9.1)	.8
Ethnicity				.2
African American	120 (34%)	58 (33%)	62 (35%)	N/A
Caucasian	161 (46%)	83 (47%)	78 (44%)	N/A
Latina	23 (6.5%)	7 (4%)	16 (9%)	N/A
American Indian	1 (0.3%)	1 (0.6%)		N/A
Other	1 (0.3%)		1 (0.6%)	N/A
Multiracial	47 (13%)	27 (15%)	20 (11%)	N/A
Marital status				.4
Married	62 (18%)	26 (15%)	36 (20%)	N/A
Single	130 (37%)	66 (38%)	64 (36%)	N/A
Divorced/Separated	161 (46%)	84 (48%)	77 (43%)	N/A
Education	13.5 (2.4)	12.7 (2.3)	12.4 (2.6)	N/A
Employment				1.0
Employed	142 (40%)	71 (40%)	71 (40%)	N/A
Unemployed	194 (55%)	96 (55%)	98 (55%)	N/A
Student/Retired/ Disabled	17 (5%)	9 (5%)	8 (5%)	N/A
Substance use diagnosis (current dependence)				
Cocaine	249 (70%)	128 (73%)	121 (68%)	.3
Stimulants	27 (8%)	15 (9%)	12 (7%)	.4
Opiates	90 (26%)	45 (26%)	45 (26%)	.6
Marijuana	96 (27%)	49 (28%)	47 (27%)	.4
Alcohol	198 (56%)	105 (60%)	93 (53%)	.4
# of days used in the past month				
Amphetamine	0.5 (3.3)	0.6 (3.8)	0.3 (2.7)	.4
Heroin	0.2 (1.7)	0.2 (2.3)	0.1 (0.7)	.6
Other opiate	1.3 (4.6)	1.2 (4.2)	1.3 (4.9)	.9
Alcohol	2.9 (6.6)	3.3 (7.0)	2.4 (6.1)	.2
Marijuana	2.7 (7.1)	2.9 (7.1)	2.4 (7.1)	.6
Cocaine	4.2 (8.1)	4.4 (8.1)	4.1 (8.1)	.7
Total CAPS severity	62.9 (19.4)	61.6 (19.4)	64.2 (19.4)	.2

N/A = not applicable.

number of study-related AEs within treatment on patients' substance use and PTSD symptoms (CAPS scores) at postintervention were examined using similar models (linear model for CAPS scores) with the number of study-related AEs and treatment as predictors adjusted for the baseline measure of the corresponding outcome. PROC GENMOD in

SAS 9.1.3 was used to conduct the analyses. All tests were two tailed and performed at the significance level  $\alpha = .05$ .

### 3. Results

Table 1 displays demographic and psychosocial characteristics for the 353 randomized participants and for participants in each treatment group. Demographic data, baseline past 30-day substance use, substance use diagnoses, and baseline PTSD severity scores were not significantly different between groups. The average age of the sample was  $38.7 \pm 9.3$  years. Forty-six percent were Caucasian, 34% were African American, 13% were multiracial, and 7% were Latino. Less than 20% were married, and more than half (55%) were unemployed. The average score for the CAPS was  $62.9 \pm 19.4$  which was in the moderately severe range.

#### 3.1. AEs reported prior to study intervention

Of the 353 randomized women, 62 (18%) dropped out of the study prior to receiving any intervention. Of these 62 women, 13 (21%) dropped out due to any AEs, 9 (15%) due to study-related AEs, and only 3 patients due to clinical deterioration as evaluated by the study clinician. There was no other information on reasons for dropping out of the study for the other women. There were no between-group differences in the proportion of women who dropped out of treatment ( $p = .5$ ) prior to the initiation of the interventions. Nineteen women experienced 26 new study-related AEs following the screening assessment prior to the initiation of the intervention. Of the 26 study-related AEs, 24 were mild to moderate in severity, and 2 were severe. The percentage of women experiencing postscreening study-related AEs was not different between the two treatment groups ( $p = .6$ ).

#### 3.2. AEs reported during study intervention

Table 2 displays the total new onset AEs, SAEs, and study-related AEs occurring during the intervention phase.

Table 2  
AEs experienced during treatment

Variable	Total	Seeking safety	Women's health	p value	
Any AEs	Total #	190	79	111	N/A
	# of distinct participants	110 (38%)	51 (36%)	59 (39%)	.4
	Average #	1.73	1.55	1.88	.2
SAEs	Total #	35	12	23	N/A
	# of distinct participants	27 (9%)	10 (7%)	17 (11%)	.2
	Average #	1.3	1.2	1.35	.6
Study-related AEs	Total #	83	42	41	N/A
	# of distinct participants	49 (17%)	28 (20%)	21 (14%)	.3
	Average #	1.69	1.5	1.95	.3
Study-related AE severity	Mild	22 (27%)	14 (33%)	8 (19%)	.2
	Moderate	60 (62%)	28 (67%)	32 (78%)	N/A
	Severe	1 (1%)	0	1 (2%)	N/A

N/A = not applicable.

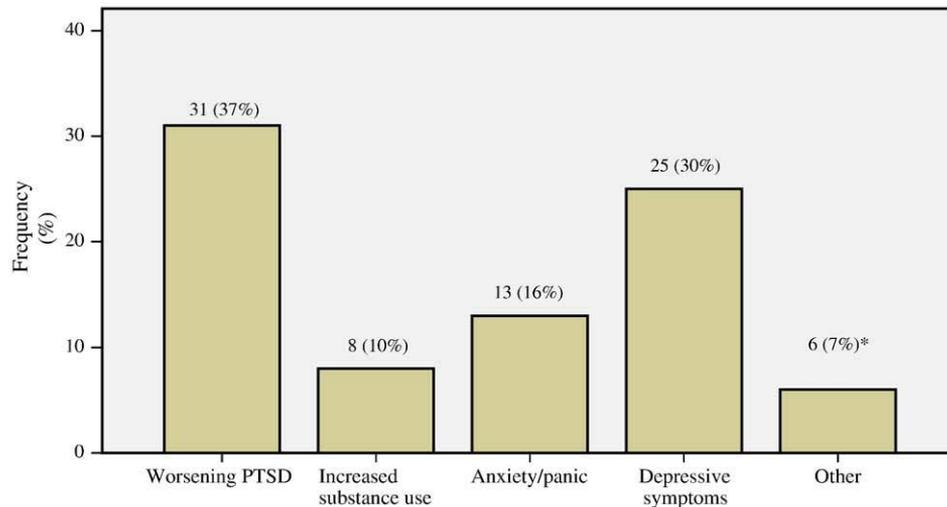


Fig. 1. Study-related AE descriptions.

Forty-nine women reported 83 new study-related AEs. Only one of these AEs was evaluated as being severe. The percentage of women experiencing study-related AEs was not different between the two treatment groups (20% for SS vs. 14% for WHE;  $p = .3$ ). There were 27 women who experienced 35 SAEs, most of which were non-study-related medical problems. There was no relationship between number of study-related AEs experienced and length of time to complete treatment ( $\chi^2 = .88$ ,  $df = 1$ ,  $p = .3$ ). Fig. 1 displays the type of study-related AEs experienced by the participants. Nearly 70% of study-related AEs involved worsening of PTSD symptoms or increase in depression. Only 8 women (3%) experienced 8 (10%) AEs that involved an increase in substance use. Other AEs included increase in self-destructive thoughts, marital conflict, worsening of eating disorder, and night sweats. There were no between-group differences in serious and non-study-related AEs.

There was a significant effect of the number of attended intervention sessions on the number of new study-related AEs. The more sessions a participant attended, the more study-related AEs experienced ( $\chi^2 = 6.67$ ,  $df = 1$ ,  $p = .01$ ). However, this was not different between the two treatment groups ( $\chi^2 = .01$ ,  $df = 1$ ,  $p = .9$ ).

Fewer study-related AEs were seen in women who used more cocaine ( $p \leq .002$ ) and alcohol ( $p \leq .003$ ) in the 30 days prior to baseline and had higher total CAPS scores and subscale C and D CAPS scores at baseline ( $p \leq .0001$ ).

### 3.3. AEs-reported poststudy intervention

For all participants, past 30-day cocaine use measured at postintervention was associated with fewer reported study-related AEs ( $p = .03$ ). There was a statistically significant interaction between intervention and the number of study-related AEs during the treatment related to participants' past 30-day use of opiate ( $p = .03$ ) and past 30-day use of marijuana ( $p = .04$ ) reported at postintervention. Within the

WHE group, women who experienced more study-related AEs during treatment reported less past 30-day opiate use and greater past 30-day use of marijuana at postintervention, whereas those associations in SS group were not significant. It should be noted that past 30-day opiate and marijuana use was low at postintervention, and AEs involving increase in substance abuse during treatment was also low. Finally, there was no relationship between study-related AEs and CAPS total and subscale scores at 1 week postintervention.

## 4. Discussion

This randomized, multisite clinical trial offers a unique opportunity to examine adverse events in women attending integrated outpatient treatment for PTSD and SUDs. The population in this study represents women of diverse race, socioeconomic status, educational background, geographic location, substance use diagnosis, and psychiatric symptom severity.

Women enrolled in the Seeking Safety intervention, a trauma-focused treatment, did not experience any more treatment-related AEs than did women receiving the health education control. This suggests that addressing trauma-related issues concomitantly with substance abuse treatment was well tolerated by study participants. It is important to note that Seeking Safety is a cognitive-behavioral treatment that intentionally avoids discussion or imagery related to the traumatic events themselves. Instead, the focus is on understanding the connection between trauma symptoms and SUD and on developing coping skills. Thus, the present data do not address the tolerability of exposure-based treatments for substance-dependent populations. Also of note, the absence of adverse events is not indicative of treatment efficacy, but rather clinicians are more informed about implementing such trauma-focused interventions without triggering more harm.

Only 17% of the women in the study experienced study-related AEs, which were primarily increases in PTSD, depression, and other anxiety symptoms. Fluctuations in psychiatric symptoms reflect the normal process of recovery during treatment (Bourne, 1995; Lipschitz, 1988). It was expected that some increases in PTSD symptoms would occur because participants were exposed to previous avoided anxiety-provoking stimuli (e.g., questioning regarding traumas during research evaluations and exposure to trauma-focused treatment). Avoidance is one of the major hallmarks of anxiety disorders such as PTSD; people avoid what they fear (Bourne, 1995; Lipschitz, 1988). The diagnosis of PTSD requires a minimum of three avoidance/numbing (cluster C) symptoms. It seemed likely that women who agree to participate in the study, complete numerous comprehensive assessments, and attend randomly assigned SS or WHE groups, would no longer be able to avoid issues relating to the traumatic event(s). Thus, the very act of participating likely would increase symptoms.

The finding that women with higher CAPS scores at baseline had fewer AEs during the intervention was probably related to these women being more symptomatic at baseline and, thus, not having as low a threshold for emergence of new AEs during the study.

There were only eight reported incidents of increased substance use during the intervention phase. This suggests that study participants, in general, did not use substances to cope with increases in PTSD or depression symptoms experienced during treatment. Conversely, the negative association between postintervention past 30-day cocaine use and reports of study-related AEs may lend further evidence that for those few participants who continued to use higher levels of substances, anxiety and depression symptoms may have been masked and avoidance behaviors may have been perpetuated, resulting in fewer reported AEs.

In both SS and WHE groups, the more treatment sessions that were attended, the more study-related AEs were reported. Understandably, women attending more sessions have more opportunities to report such events. In addition, women who attended more regularly were more likely to complete the weekly assessments. On the weekly self-report measures, participants were specifically asked whether they had experienced any AEs in the past week. It is possible that direct questioning during the assessments resulted in reporting of symptoms that are an artifact of the research process; that is, the frequency and magnitude of the assessments associated with a research study may elicit reporting of symptoms that would not ordinarily be shared in a nonresearch community treatment setting. However, the fact that there was no difference between the two treatment groups suggests that women are quite able to tolerate the Seeking Safety treatment.

Prior to the initiation of treatment, 62 women (18%) who had been randomized dropped out of the study, although only 9 (15%) of these women cited study-related AEs as the reason. This is similar to the 22% of randomly assigned

participants who dropped out prior to receiving any SS sessions in a previously reported study (Hien et al., 2004). Early attrition is also common in substance abuse treatment programs (Baekeland & Lundwall, 1975; Jacobson, 2004) as well as treatment outcome research (Brady et al., 2001; Crits-Christoph et al., 1999).

#### 4.1. Limitations

There were some limitations to this study, which examined treatment of trauma-related symptoms in community substance abuse treatment. A diagnosis of PTSD or subthreshold PTSD was required for inclusion. Level of symptom frequency and severity may not reflect symptom levels ordinarily found in community treatment populations. Therefore, results may not generalize to populations without co-occurring PTSD and substance use diagnoses. Because SS was a nonexposure-based intervention, findings cannot be generalized to the population of women receiving exposure-type interventions.

As previously mentioned, the participants completed frequent and lengthy assessments that would not have been administered to a nonresearch treatment group. Thus, it is possible that these findings may not reflect actual levels of treatment-related AEs that may occur in community substance abuse treatment settings, where assessments would be less comprehensive and less frequent. In addition, some increases in symptoms may be due to a combination of factors, including receiving multiple treatment services or experiencing negative life events unrelated to treatment. A study clinician considered all factors, including the participant's self-report, when determining study-relatedness.

Finally, although research personnel were trained on administration of the AE questionnaire, variability in presentation could have elicited variations in responses and reporting. However, there is no reason to suspect that this variability was in any way systematically biased.

#### 4.2. Conclusion

This is the first large-scale multisite trial conducted in community treatment programs across the country to explore the occurrence of AEs related to implementing a trauma-focused group for women with SUDs and trauma. The relatively low frequency of AEs occurring throughout the study and no differences in AE reporting between the trauma focused and the control group provide more evidence to the safety and feasibility of implementing such integrated interventions in substance abuse treatment programs. Allaying safety concerns associated with integrated treatments for trauma and SUDs may also increase clinician acceptability and readiness to disseminate such interventions. Although the low rates of AEs observed here are reassuring regarding safety and tolerability, the present data do not address the relative efficacy of the interventions tested. The relative efficacy of these interventions is the subject of a separate

report (Hien, 2007). Cognitive–behavioral interventions for PTSD have evidence for efficacy from samples of patients without substance problems (Bradley, Greene, Russ, Dutra, & Westen, 2005), but more such research is needed among substance-dependent populations, where PTSD is prevalent and associated with worse prognosis (Brady, Killeen, Saladen, Dansky, & Becker, 1994; Read, Brown, & Kahler, 2004). The relative safety observed here should help to encourage such further research efforts.

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