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A randomized controlled trial of treatments for co-occurring substance use disorders and post-traumatic stress disorder

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ABSTRACT

Background and Aims Post-traumatic stress disorder (PTSD) is common among people with substance use disorders, and the comorbidity is associated with negative outcomes. We report on a randomized controlled trial comparing the effect of integrated cognitive–behavioral therapy (ICBT) plus standard care, individual addiction counseling plus standard care and standard care alone on substance use and PTSD symptoms. **Design** Three-group, multi-site randomized controlled trial. **Setting** Seven addiction treatment programs in Vermont and New Hampshire, USA. **Participants/Cases** Recruitment took place between December 2010 and January 2013. In this single-blind study, 221 participants were randomized to one of three conditions: ICBT plus standard care (SC) ($n = 73$), individual addiction counseling (IAC) plus SC ($n = 75$) or SC only ($n = 73$). One hundred and seventy-two patients were assessed at 6-month follow-up (58 ICBT; 61 IAC; 53 SC). Intervention and comparators: ICBT is a manual-guided therapy focused on PTSD and substance use symptom reduction with three main components: patient education, mindful relaxation and flexible thinking. IAC is a manual-guided therapy focused exclusively on substance use and recovery with modules organized in a stage-based approach: treatment initiation, early abstinence, maintaining abstinence and recovery. SC are intensive out-patient program services that include 9–12 hours of face-to-face contact per week over 2–4 days of group and individual therapies plus medication management. **Measurements** Primary outcomes were PTSD severity and substance use severity at 6 months. Secondary outcomes were therapy retention. **Findings** PTSD symptoms reduced in all conditions with no difference between them. In analyses of covariance, ICBT produced more favorable outcomes on toxicology than IAC or SC [comparison with IAC, parameter estimate: 1.10; confidence interval (CI) = 0.17–2.04; comparison with SC, parameter estimate: 1.13; CI = 0.18–2.08] and had a greater reduction in reported drug use than SC (parameter estimate: –9.92; CI = –18.14 to –1.70). ICBT patients had better therapy continuation versus IAC ($P<0.001$). There were no unexpected or study-related adverse events. **Conclusions** Integrated cognitive behavioral therapy may improve drug-related outcomes in post-traumatic stress disorder sufferers with substance use disorder more than drug-focused counseling, but probably not by reducing post-traumatic stress disorder symptoms to a greater extent.

Keywords Co-occurring disorders, evidence-based treatment, integrated cognitive behavioral therapy (ICBT), integrated treatments, PTSD, substance use.

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INTRODUCTION

Co-occurring substance use disorders and post-traumatic stress disorder (PTSD) are common in the general population [1–5], and even more prevalent in treatment settings [6–18]. Comorbidity is associated with negative treatment and life outcomes [6,12,19–26]. Several integrated behavioral therapies have been developed recently to address both substance use and PTSD within a unified approach [27–30].

Integrated cognitive–behavioral therapy (ICBT) for co-occurring substance use and PTSD has been studied within a stage-based framework [31–33]. Across three trials, ICBT

demonstrated patient safety and acceptability, was feasible to deploy in routine care settings, had positive PTSD and substance use outcomes and therapy retention was excellent [28,29,34].

ICBT focuses on substance use, PTSD and the interaction of the disorders using a cognitive–behavioral, coping skills-based approach. ICBT is not exposure-based, but draws on the efficacy of cognitive restructuring therapies for PTSD [35–37]. The favorable patient retention in ICBT, plus the ease of community therapist delivery in previous randomized controlled trials (RCTs), suggested its promise for effectiveness and for successful community translation.

This is a report on a NIH Phase III clinical trial [38]. Participants were randomized to either: (a) ICBT plus standard care (SC: intensive out-patient programming and other services as usual); (b) an individual addiction counseling (IAC) plus SC; or (c) SC only. To enhance the external validity of findings, study therapists were employees of the agencies that participated in the study.

The trial addresses the following questions:

1 What are the substance use outcome advantages to adding ICBT or IAC to SC services, and between ICBT versus IAC?
2 What are the PTSD outcome advantages to adding ICBT or IAC to SC services, and between ICBT versus IAC?
3 How do the therapy continuation rates of ICBT and IAC compare?

METHODS

Design

This is a three-group, repeated-measure, parallel-group, RCT design. This was a single-blind study in that patients, but not assessors, were informed of the treatment condition. Randomization blocks of nine were used to maintain equal group size. Participants were re-assessed at 3 and 6 months post-baseline. Intervals were intended to match the three study condition time-lines. The plan was for the 3-month assessment to serve as the post-intervention evaluation and the 6-month assessment as the post-treatment follow-up. In reality, the majority (79.6%) of participants had not completed ICBT or IAC by 3 months. Therefore, the 6-month assessment was the default measure of post-treatment effects. Outcomes assessed were PTSD severity, substance use and severity and therapy continuation.

Participants and sampling

Eligibility criteria included: (1) newly admitted patients meeting current diagnostic criteria for both PTSD and substance use disorder; (2) intention to enter the intensive out-patient program; (3) no current legal or impending relocation factors that could jeopardize timely protocol completion; and (4) patients provided informed consent. Patients with acute psychotic symptoms or a suicide attempt in the past 30 days were excluded. The randomization sequence was generated by the study biostatistician and concealed from the researchers conducting study assessments. After confirming that a participant met study inclusion criteria, the assessor would contact the research coordinator for assignment to study arm. Participants were compensated $60 for the baseline assessment and $80 for the 6-month follow-up assessments. Recruitment occurred from December 2010 to January 2013.

Settings

The study was conducted with seven addiction treatment agencies in Vermont and New Hampshire, United States, all serving a large proportion of uninsured or publicly funded patients. Sites received financial incentives to offset their cost for staff time in collecting data and serving as study therapists.

Study therapists

The study therapists ($n = 23$) were addiction counselors employed by the treatment programs. Each participating counselor was trained to deliver both ICBT and IAC.

Study interventions

ICBT is a manual-guided therapy focused on PTSD and substance use symptom reduction. It includes three main components: (1) patient education, (2) mindful relaxation: centering and breathing techniques to manage acute negative affect and cravings and (3) flexible thinking: a cognitive restructuring technique targeting the interactions of cognitions, emotions and behaviors. ICBT addresses PTSD symptoms, substance use and the patient's experience of the interaction of these components. It is delivered in weekly 45–50-minute individual sessions during an 8–12-week time-frame. Typically, eight sessions are necessary to cover all eight therapy modules, but based on pace and patient response, up to 12 sessions are sometimes needed [28,29].

IAC is a manual-guided therapy focused exclusively on substance use and recovery. It does not address PTSD directly. Modules are organized in a stage-based approach: treatment initiation, early abstinence, maintaining abstinence and recovery. It is delivered in weekly 45–50-minute individual sessions during an 8–12-week time-frame. IAC is a combined adaptation of individual drug counseling (IDC) from the NIDA Cocaine Collaborative Study and Twelve-Step facilitation (TSF) from the NIAAA Project Match [39,40]. Eight sessions are needed to cover the required therapy modules; however, some patients require more sessions to complete the material.

SC consists of intensive out-patient program services, which include 9–12 hours per week during 2–4 days of group and individual therapies, and medication management. The intensive out-patient phase occurs typically during a 6–8-week period, followed by a weekly continuing care group for 12 weeks. Three of seven of the study sites also offered trauma-focused group sessions using Seeking Safety materials.

Measures

Patient demographics

Patient age, sex, race, ethnicity and marital status were obtained via chart review and the self-administered Addiction Severity Index (ASI-SA) [41–43].

Diagnoses

MINI International Neuropsychiatric Interview. version 6.0 (MINI). A structured diagnostic interview to assess for DSM-IV disorders, validated with other standardized diagnostic interviews and used to document substance use and psychiatric disorders [44–46].

PTSD severity

PTSD checklist—civilian (PCL-C). This is a self-report measure for PTSD, used to establish potential eligibility on current PTSD diagnostic criteria [47].

The clinician-administered PTSD scale (CAPS) is a structured interview for diagnosing PTSD and its severity; a current PTSD diagnosis determined study eligibility. The CAPS total score was the primary PTSD outcome, and is a composite of the frequency and intensity of re-experiencing, hyperarousal and avoidance symptom clusters [48–50].

Substance use and severity

Toxicology. Urine drug screen and alcohol breathalyzer data were collected. Positive urine drug or alcohol breath samples indicate active substance use, and are used as the primary outcome measure of active substance use.

Addiction Severity Index—drug severity score (ASI-drug). Used to derive the ASI-drug severity score [41–43], it is the primary outcome measure of drug problem severity and provides a composite score of consequences of drug use [51,52].

Addiction Severity Index—alcohol severity score (ASI-alcohol). Used to derive the ASI-Alcohol severity score [41–43], it is the primary outcome measure of alcohol problem severity and provides a composite score of consequences of alcohol use [51,52].

Time-line follow-back interview (TLFB). Used to gather data on the frequency and amount of substance use during the past 90 days or, if in a controlled environment during this time-frame, during the period prior to confinement. TLFB-drug and TLFB-alcohol data were collected [53,54].

Recent treatment survey (RTS). A modified version of the treatment services review used to track services received within and outside the program [55,56].

Adherence and competence ratings

ICBT adherence and competence rating scale. A 13-item seven-point rating scale on therapist adherence (1 = not at all to 7 = extensively) and competence (1 = very poor to 7 = excellent) in ICBT. Items are rated for the specific module(s) covered in the session. Based on previous research, we set the cut-off for 'adequate' adherence and competence at scores of 4 and above.

IAC adherence and competence rating scale. A two-item seven-point rating scale on therapist adherence (1 = not at all to 7 = extensively) and competence (1 = very poor to 7 = excellent) in IAC. The cut-off for 'adequate' adherence and competence are scores of 4 and above.

Therapy continuation

ICBT and IAC clinicians completed the clinician checklist after each session, which included the date, the session number and modules completed; ICBT and IAC therapy attendance was treated as a continuous variable.

Procedure

Newly admitted patients completed the PCL-C at admission. They were pre-eligible with a total PCL-C score of 44 or greater. Program site coordinators approached patients about the study and, if interested, scheduled an informed consent and assessment session with a research assistant.

Patients were assessed for DSM-IV diagnoses (MINI), PTSD (CAPS) and substance use (toxicology, ASI and TLFB). If verified as eligible, they were randomized to one of the three study arms using a 1 : 1 : 1 randomization ratio. Both ICBT and IAC were planned for delivery once per week during 8–12 weeks by a program-based counselor who served as a designated study therapist. SC was conducted by program staff members, including study therapists. Therapists were supervised in ICBT and IAC by a research clinical supervisor within a format of weekly encounters, alternating between on-site group and individual telephone sessions. All therapy sessions were audio-recorded. Therapist-blind raters sampled 25% of each patient's audio-recordings and rated for fidelity using the ICBT and IAC adherence and competence rating scales.

Primary outcome measures were repeated at 3 and 6 months post-baseline. The collection of data, analyses and reporting of findings were approved by the Dartmouth institutional review board (IRB). This study was conducted

in strict accordance with all human subject protections and good clinical practice (e.g. Helsinki Declaration, Belmont Principles and Nuremberg Code).

Outcome measures

The primary outcome measures were CAPS, toxicology, ASI-drug, ASI-alcohol and TLFB. All primary outcomes were collected at baseline, 3 and 6 months post-baseline. The secondary outcome was therapy retention (ICBT and IAC).

A priori statistical power analyses ensured that the sample size was sufficient to detect meaningful differences on primary outcomes. We set the following parameters based on previous research: alpha = 0.05; two-tailed test of significance, desired power = 0.80, unstructured covariance matrix, two time-points (baseline, follow-up), correlation = 0.40 between repeated assessments and attrition at 30% from baseline to follow-up. With an $n = 222$ (74 per group), the study has 80% power to detect a medium effect size of 0.55 for group (treatment types) difference on primary outcomes.

Data analyses

Baseline equivalence across the three arms was examined using χ^2 (categorical variables) and analysis of variance (ANOVA) (continuous variables) statistics. Because the ICBT and IAC therapy participants had not typically completed the course of treatment by 3 months, we had to use only the 6-month assessment as a combined post-treatment and follow-up measure. The reason the therapy extended beyond the planned 3 months included transportation difficulties, residential treatments and incarcerations, medical hospitalizations and other interruptions to the anticipated time-line. A generalized linear model was used to evaluate potential difference by treatment type on primary outcomes at the 6-month end-point, controlling from baseline [unconditional model analogous to analysis of covariance (ANCOVA)], and also for key covariates: study site and PTSD severity (conditional model analogous to adjusted ANCOVA).

By the end of 6 months, the total sample of 221 had dropped to 172. Because we conducted a 6-month end-point analysis with baseline as a covariate more current analytical methods, such as the mixed-effects model or the generalized estimating equation (GEE) model, were not effective for handling dropouts. To ensure that the groups were still balanced with respect to baseline characteristics, we tested group difference (with $n = 172$) and dropouts ($n = 49$), and found one group difference: age. Thus, age was included as a covariate in the model. Age was not significant, and therefore has no substantial impact on the primary outcome analyses. Subsequently, for parsimony, we did not include age as a covariate in the final model.

The effect size was calculated based on ANCOVA [57]. Because toxicology is a categorical variable, the effect size was estimated by taking the proportion of positive toxicology drug screens at the 6-month follow-up, converting to an arcsin value, and then calculating the difference between groups [57]. Therapy continuation was examined using χ^2 tests. All data were analyzed using IBM SPSS version 21 [58] and SAS version 9.3 [59].

RESULTS

Characteristics of participants

Fig. 1 depicts the Consolidated Standards of Reporting Trials (CONSORT) diagram. Of 361 patients who were pre-eligible, 284 were confirmed as meeting criteria for current PTSD, substance use, and were able to commit to 6 months of study participation. Fifty-three were excluded because they never engaged in SC. Ten were excluded for reasons including protocol deviations (therapist delivered the incorrect study intervention, therapists not using a study manual, and patients did not have a qualifying traumatic event for PTSD diagnosis). Two hundred and twenty-one participants were randomized and included in the intent-to-treat analyses. For the within-treatment assessment period an 85.1% follow-up rate was achieved, and for the post-treatment (6-month) follow-up a 77.8% rate was obtained. The rates of completed follow-up data obtained did not differ significantly across the three study arms. No unexpected or study-related adverse events occurred in any of the three treatment conditions.

Participants were predominantly white and not Hispanic. The average age was mid-30s and largely female. With respect to trauma-related and PTSD factors, childhood sexual assault and adult physical assault were common. The average CAPS total score was 77.35. It is notable that a score of 45 or more is considered diagnostic of PTSD and a score of 65 or more is considered 'severe PTSD'. In terms of substance use disorder types, alcohol and opioid use disorders were the most prevalent. More detailed information on the types of psychiatric and substance use disorders can be found in Table 1.

Primary outcome analyses

Table 2 depicts intent-to-treat analyses of primary outcomes by treatment type using the generalized linear model. There were two models: (1) group (treatment type) difference at 6-month end-point analysis with baseline outcome as covariate, and (2) group (treatment type) difference at 6-month end-point analysis with baseline outcome, PTSD severity and study site as covariates. PTSD symptom severity declined across all three treatment

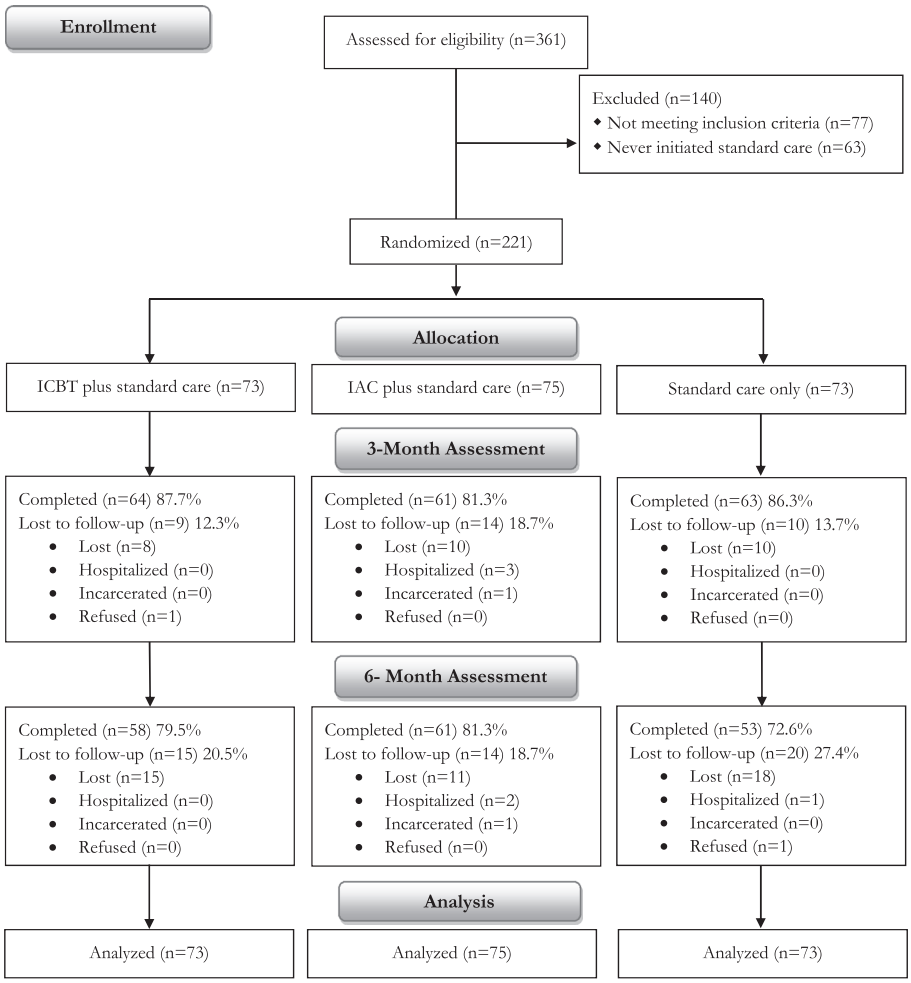

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) diagram of randomized controlled trial (RCT) of treatments for co-occurring substance use disorders and post-traumatic stress disorder (PTSD)

conditions over time. The primary outcome measure of toxicology (positive urine drug screen) differentiated ICBT from the other two treatment groups ($P<0.05$) using both the ANCOVA adjusted for baseline outcome as well as the ANCOVA adjusted for baseline plus the other covariates (PTSD severity and site). Parameter estimate and confidence interval (CI) for ANCOVA were used to compare ICBT versus IAC and ICBT versus SC. Significant specific group differences were found between ICBT and IAC on toxicology (1.10; CI = 0.17–2.04). In the ICBT versus SC only comparison, toxicology (1.13; CI = 0.18–2.08) and TLFB-drug (–9.92; CI = –18.14 to –1.70) were also significant. The effect sizes for all outcome comparisons between ICBT and either IAC or SC conditions are also presented in Table 2.

To underscore, the substance use outcomes (positive urine drug screen/TLFB-drug) resulted in significant treatment type differences. For toxicology, ICBT was superior to the both IAC and SC conditions. The rates of positive urine drug screens for IAC and SC rose from baseline to 6-month assessment, whereas the toxicology results of ICBT patients were stable. Examining TLFB drug use, ICBT patients had greater reductions in days of drug use (past 90 days) than SC only conditions. We found no significant differences between ICBT and IAC on the ASI or TLFB. Fig. 2 portrays the primary outcome data in a visual format.

Therapy continuation

As depicted in Fig. 3, although early attendance favors ICBT, there were no significant differences in engagement rates up to session 8 but as the therapies progressed, of those who did engage, significantly more ICBT patients continued treatment.

Through the quality monitoring process, we observed that both ICBT and IAC therapies were delivered above the adequate adherence and competence levels (≥4 on the ICBT and IAC adherence and competence rating scales): adherence: ICBT M = 6.18 (standard deviation = 0.90) and IAC M = 6.49 (standard deviation = 0.79) and competence: ICBT M = 5.67

Table 1 Patient demographics and baseline diagnoses, substance use and post-traumatic stress disorder (PTSD) characteristics ($n = 221$).

	ICBT + SC (*n* = 73)	*IAC + SC* (*n* = 75)	*SC only* (*n* = 73)	*Overall* (*n* = 221)	*F-value* χ^2
Demographics					
Age mean (SD)	36.22 (10.1)	35.82 (11.8)	33.86 (9.1)	35.30 (10.42)	1.07
Gender (male)	28 (38.4%)	31 (41.3%)	31 (42.5%)	90 (40.7%)	0.27
Race (Caucasian/white)	67 (91.8%)	73 (97.3%)	71 (97.3%)	211(95.5%)	6.76
Ethnicity (not Hispanic or Latino)	72 (98.6%)	75 (100.0%)	70 (95.9%)	217 (98.2%)	3.63
Psychiatric disorders and PTSD					
Psychiatric disorder type					
Post-traumatic stress	73 (100.0%)	75 (100.0%)	73 (100.0%)	221 (100.0%)	
Major depression (current)	41 (56.2%)	49 (65.3%)	44 (61.1%)	134 (60.6%)	1.31
Generalized anxiety	32 (43.8%)	32 (42.7%)	31 (43.1%)	95 (43.0%)	0.03
Panic with agoraphobia	20 (27.4%)	19 (25.3%)	24 (33.3%)	62 (28.1%)	0.72
Social anxiety	21 (28.8%)	19 (25.3%)	20 (27.8%)	61 (27.6%)	0.29
Major depression (recurrent)	9 (12.3%)	14 (18.7%)	14 (19.4%)	37 (16.7%)	1.53
Panic	15 (20.5%)	10 (13.3%)	9 (12.5%)	34 (15.4%)	2.84
Obsessive–compulsive	10 (13.7%)	11 (14.7%)	12 (16.7%)	33 (14.9%)	0.22
Agoraphobia	10 (13.7%)	9 (12.0%)	9 (12.5%)	29 (13.1%)	0.13
Dysthymia	13 (17.8%)	6 (8.0%)	8 (11.1%)	27 (12.2%)	3.48
Bipolar type disorders	6 (8.2%)	11 (14.9%)	7 (9.6%)	24 (10.9%)	1.87
n of psychiatric disorders, mean (SD)	3.71 (1.59)	3.62 (1.70)	3.82 (1.73)	3.72 (1.67)	19.34
CAPS total score, mean (SD)	76.71 (18.1)	78.79 (21.4)	76.51 (20.8)	77.35 (20.1)	0.29
Substance use					
Positive urine drug screen, *n* (%)	16 (21.9%)	14 (18.7%)	16 (22.2%)	46 (20.9%)	0.35
Substance use disorder type					
Prescription opioids	37 (50.7%)	34 (45.3%)	42 (57.5%)	113 (51.1%)	2.21
Cocaine	32 (43.8%)	30 (40.0%)	38 (52.1%)	100 (45.2%)	2.26
Cannabis	30 (41.1%)	28 (37.3%)	32 (43.8%)	90 (40.7%)	0.65
Heroin	22 (30.1%)	22 (29.3%)	27 (37.0%)	71 (32.1%)	1.19
Sedatives	14 (19.2%)	17 (22.7%)	18 (24.7%)	49 (22.2%)	0.65
Amphetamines	10 (13.7%)	12 (16.0%)	17 (23.3%)	39 (17.6%)	2.52
Hallucinogens	8 (11.0%)	2 (2.7%)	5 (6.8%)	15 (6.8%)	4.02
Other	6 (11.0%)	8 (10.7%)	7 (9.6%)	21 (9.5%)	0.26
Alcohol	45 (61.6%)	48 (64.0%)	42 (57.5%)	135 (61.1%)	0.67
n of substance use disorders, mean (SD)	2.81 (1.88)	2.75 (1.78)	3.22 (2.09)	2.92 (1.92)	14.02
ASI composite scores					
Drug (SD)	0.13 (0.09)	0.14 (0.11)	0.15 (0.09)	.14 (0.10)	0.55
Alcohol (SD)	0.21 (0.22)	0.21 (0.19)	0.17 (0.19)	.20 (0.20)	1.29
Time-line follow-back					
Mean number of days using drugs (SD)	21.27 (25.1)	20.13 (26.2)	31.64 (29.1)	24.31 (27.2)	4.10
Mean number of days drinking (SD)	18.04 (23.1)	13.67 (19.8)	13.82 (20.6)	15.16 (21.2)	1.01

ICBT = integrated cognitive behavioral therapy; IAC = individual addiction counseling; SC = standard care; SD = standard deviation; CAPS = clinician-administered PTSD scale; ASI = Addiction Severity Index.

(standard deviation = 1.21) and IAC M = 5.95 (standard deviation = 1.19). IAC was delivered with slightly greater adherence overall ($t = -1.99$, d.f. = 116, $P<0.05$), but there was no difference in overall competence ratings.

DISCUSSION

Summary of findings

PTSD symptom severity declined significantly over time regardless of treatment approach. With respect to ICBT as an integrated behavioral therapy for comorbid PTSD symptoms, this is arguably a negative finding. However, this finding is consistent with other RCTs of therapies for co-occurring PTSD and substance use disorder interventions (Seeking Safety) [24,60,61] but not with previous ICBT research or recent reports of another integrated approach [Concurrent treatment of PTSD and Substance Use Disorders using Prolonged Exposure (COPE)] [28,29,62]. Even without the added complexity of comorbid substance use, a recent meta-analysis of PTSD treatments (medication and psychosocial) found that active comparators had significant and positive effects [63]. In the ICBT, IAC and

Table 2 Intent-to-treat analyses of primary outcomes by treatment type ($n = 221$).

	ICBT + SC		*IAC + SC*		*Standard care (SC)*				*Parameter Estimate and Confidence Interval or ANCOVA*[c]				*Effect size estimates*	
Variable name	*Baseline (n = 73)*	*6 months (n = 58)*	*Baseline (n = 75)*	*6 months (n = 61)*	*Baseline (n = 73)*	*6 months (n = 53)*	*Adjusted ANCOVA (baseline)*[a]	*Adjusted ANCOVA (baseline and covariates*[b]	*ICBT vs. IAC*[†]	*95% CI*	*ICBT vs. SC*[†]	*95% CI*	*ICBT vs. IAC*[†]	*ICBT vs. SC*[†]
Primary outcomes														
PTSD, mean (SD)														
CAPS total	76.71 (18.13)	46.81 (24.81)	78.79 (21.36)	49.62 (25.71)	76.51 (20.83)	52.60 (26.46)	1.61	1.46	−0.64	−9.08 – 7.79	−4.95	−13.65 – 3.74	−0.12	−0.24
Substance use														
Positive toxicology *n* (%)	16 (21.9%)	10 (18.5%)	14 (18.7%)	20 (37.7%)	15 (20.8%)	19 (38.8%)	6.31*	6.73*	1.10	0.17 – 2.04	1.13	0.18 – 2.08	−0.43	−0.45
ASI-drug, mean (SD)	0.13 (0.09)	0.08 (0.08)	0.14 (0.11)	0.09 (0.09)	0.15 (0.09)	0.09 (0.09)	0.47	0.42	−0.00	−0.03 – 0.03	−0.01	−0.04 – 0.02	−0.13	−0.13
ASI-alcohol, mean (SD)	0.21 (0.22)	0.15 (0.19)	0.21 (0.19)	0.15 (0.17)	0.17 (0.19)	0.11 (0.15)	0.65	0.81	−0.01	−0.07 – 0.05	0.01	−0.04 – 0.07	0.00	0.25
TLFB-drug, mean (SD)	21.27 (25.09)	7.76 (18.76)	20.13 (26.16)	9.49 (20.11)	31.64 (29.15)	18.30 (28.73)	6.15*	6.22*	−1.93	−9.87 – 6.02	−9.92	−18.14 – −1.70	−0.09	−0.45
TLFB-alcohol, mean (SD)	18.04 (23.11)	4.95 (12.25)	13.67 (19.84)	3.82 (11.34)	13.82 (20.57)	4.92 (16.10)	0.30	0.23	0.57	−4.05 – 5.18	−0.58	−5.36 – 4.20	0.10	0.00

*$P<0.05$.

[a]Wald χ^2 test for overall group difference analysis of covariance (ANCOVA) (adjusted for baseline score).

[b]Wald χ^2 test for overall group difference ANCOVA [adjusted for both baseline and covariates; post-traumatic stress disorder (PTSD) severity and site].

[c]Parameter estimate and confidence interval for ANCOVA adjusting for both baseline outcome and covariates.

[†]SC is the reference group for ICBT versus SC; IAC is the reference group for ICBT versus IAC. CAPS = clinician-administered PTSD scale; SD = standard deviation; SC = standard care; IAC = individual addiction counseling; ICBT = integrated cognitive behavioral therapy.

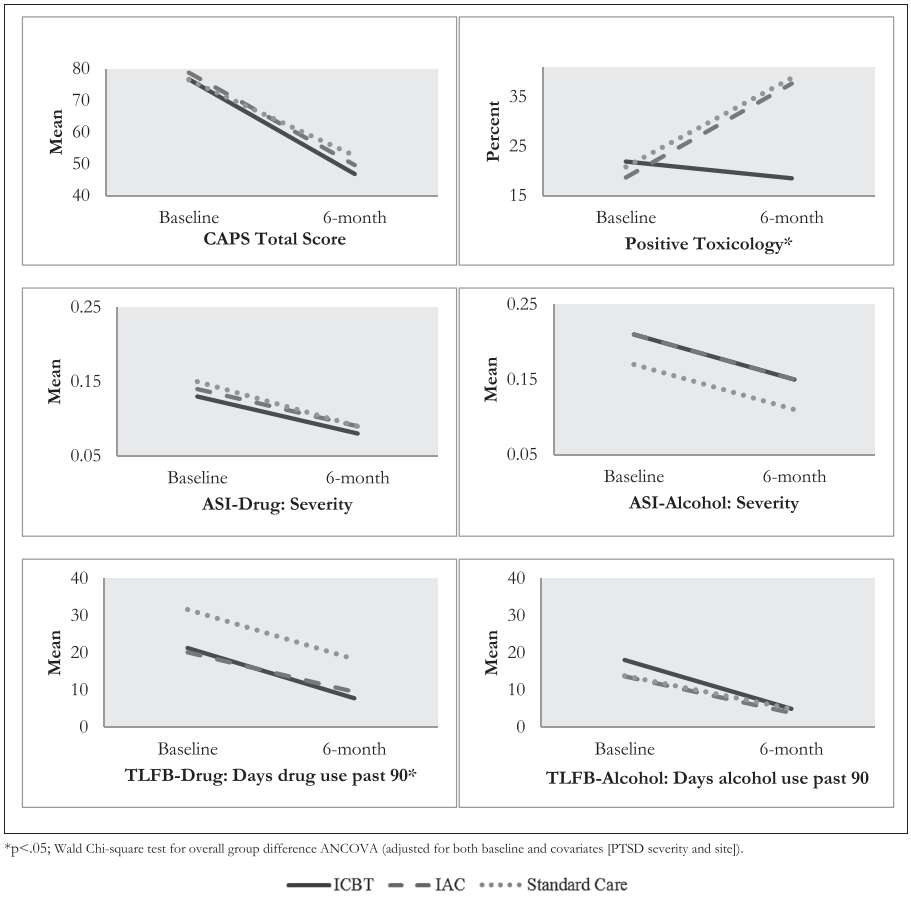

Figure 2 Intent-to-treat analyses of primary outcomes by treatment type ($n = 221$). ASI = Addiction Severity Index; CAPS = clinician administered PTSD scale

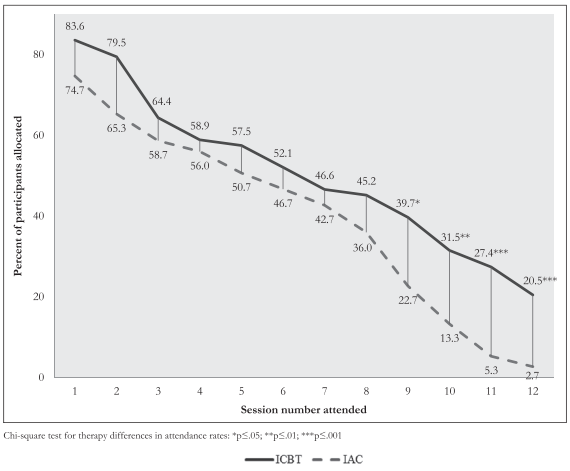

Figure 3 Study therapy continuation: integrated cognitive behavioral therapy (ICBT) and individual addiction counseling (IAC) session attendance (ICBT $n = 61$, IAC $n = 56$)

SC arms, PTSD severity scores decreased 30, 29 and 24 points, respectively, from baseline to 6-month follow-up. A reduction of 15 points is clinically significant.

ICBT demonstrated superiority in maintenance of reduced positive urine drug screens (effect size versus IAC = –0.43 versus SC = –0.45; $P<0.05$). On substance use outcomes related to frequency of use, ICBT was also superior to SC for drug use ($P<0.05$). Standard intensive outpatient services and IAC each primarily target substance use. In contrast, ICBT addresses both PTSD and substance use. Therefore, based on purported mechanisms of action and the findings from our previous clinical trials, we had hypothesized no difference on substance use outcomes across the three study arms. Surprisingly, in the present study we found that ICBT had generally more superior substance use outcomes than expected.

Treatment initiation and engagement slightly favored ICBT, but therapy continuation revealed ICBT's significant advantage. Community counselors were also able to deliver ICBT with acceptable adherence and competence. Both these findings would appear to auger well for ICBT's potential translation to routine practice settings.

Limitations

We planned for a 3-month time-line for ICBT and IAC delivery (i.e. 8–12 weekly individual sessions). We proposed to link the 3- and 6-month assessments to the SC arm, envisioning the 3-month evaluation as 'post-treatment' for ICBT and IAC and the 6-month evaluation as a

'3-month post-treatment follow-up'. This design was used in our previous trials, and we expected the same execution in this study. This was not the case. More than two-thirds of participants receiving the study therapies were still in the active phase of therapy at the 3-month assessment. The 6-month assessment served as the default combined post-treatment and follow-up measure. The reasons for the extended duration of the study therapies ranged from cancelled and missed appointments by patients and therapists to interruptions by patient incarcerations, hospitalizations and residential rehabilitations. Unfortunately, the study lacked a true measure of extended post-treatment follow-up. The absence of a true post-treatment and longer-term follow-up evaluation significantly mitigates interpretation of study findings.

In addition, the extensive amount and type of treatments received across all three study arms, including Seeking Safety groups in four of the study sites, created considerable 'noise' through which to discern positive effects. None the less, the goal of the study was to determine the advantage to adding ICBT to SC above and beyond what community patients might typically receive.

CONCLUSIONS

This is a report of a RCT to evaluate the effectiveness of an ICBT plus SC for co-occurring PTSD and substance use disorders compared with an IAC plus SC or with SC alone. Sampled from community addiction treatment programs, 221 patients were randomized to one of the three arms and therapies were delivered by counselors working in the agencies. Contrary to hypothesis, ICBT demonstrated no clear advantage over the other treatments at 6 months on PTSD symptom severity. However, ICBT demonstrated superior outcomes on drug use, as measured by positive urine drug screens and frequency of reported drug use. Consistent with prior studies of ICBT, patient acceptance (therapy continuation) and ease of therapist delivery were favorable. Study limitations, particularly the absence of a longer-term follow-up, attenuate interpretation. Future ICBT research, such as comparative effectiveness trials with the prominent therapies for this comorbidity, Seeking Safety and/or COPE, would seem warranted.

Declaration of interests

None.

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