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The Impact of Addiction Medications on Treatment Outcomes for Persons With Co-Occurring PTSD and Opioid Use Disorders

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Abstract

Background and Objectives—Previous research has been inconclusive about whether adding psychosocial treatment to medication assisted treatment (MAT) improves outcomes for patients with co-occurring psychiatric and opioid use disorders. This study evaluated the impact of MAT and psychosocial therapies on treatment outcomes for patients with co-occurring opioid use disorders and PTSD.

Methods—Patients meeting criteria for PTSD and substance use disorders were randomly assigned to one of three treatment conditions: Standard Care (SC) alone, Integrated Cognitive Behavioral Therapy (ICBT) plus SC, or Individual Addiction Counseling (IAC) plus SC. Substance use and psychiatric symptoms were assessed at baseline and 6 months. Only patients with opioid use disorders were included in the present analyses ($n = 126$). Two-way ANOVAS and logistic regression analyses were used to examine associations between treatment conditions and MAT, for substance use and psychiatric outcomes.

Results—MAT patients receiving ICBT had significantly decreased odds of a positive urine drug screen, compared to non-MAT patients receiving SC alone (OR = .07, 95% CI = .01, .81, $p = .03$). For PTSD symptoms, a significant MAT by psychosocial treatment condition interaction demonstrated that MAT patients had comparable declines in PTSD symptoms regardless of psychosocial treatment type ($F(2, 88) = 4.74$, $p = .011$). Non-MAT patients in ICBT had significantly larger reductions in PTSD.

Conclusions and Scientific Significance—For patients with co-occurring opioid use disorders and PTSD, MAT plus ICBT is associated with more significant improvement in substance use. For non-MAT patients, ICBT is most beneficial for PTSD symptoms.

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

INTRODUCTION

An estimated 2.5 million Americans meet criteria for opioid use disorders (OUDs).¹ Medication assisted treatments (MAT), including methadone, buprenorphine, and naltrexone, are FDA-approved medications for the treatment of opioid addiction.^{2,3} Compared to psychosocial treatment only, MAT is associated with improved retention and decreased relapse rates.² Unfortunately, co-occurring psychiatric disorders are highly prevalent among patients with OUDs. Over one-third (37.9%) of treatment-seeking patients with OUDs also have a current psychiatric disorder.⁴ Without targeted treatment for their psychiatric symptoms, patients with co-occurring opioid use and psychiatric disorders have higher rates of continued substance use and overdose, poorer occupational functioning, and decreased quality of life.^{5–8}

Although MAT is considered efficacious for treating opioid dependence, the impact of co-occurring psychiatric disorders on treatment outcomes is equivocal. MAT patients with co-occurring disorders have more severe psychiatric, medical, and legal problems at intake^{8–10} and post-treatment, and are at higher risk for relapse and treatment noncompliance.^{8,10–12} Though MAT patients with co-occurring disorders are more severe at intake^{8,9} and have more severe psychiatric problems after release,^{9,11} some studies have found these patients to have equivalent or better substance use outcomes,⁹ including longer treatment retention^{13,14} and lower relapse rates.¹⁰ Researchers have hypothesized that increased psychiatric severity may motivate patients to seek and remain in treatment.⁹ These conflicting findings could be related to the provision of treatments targeting psychiatric disorders in addition to MAT.

While additional psychosocial treatment does not consistently improve psychiatric outcomes for MAT patients overall,^{15–17} targeted treatment for psychiatric symptoms may improve outcomes specifically for patients with co-occurring disorders.^{17,18} Unfortunately, the common practice of referring patients offsite to psychiatric treatment at neighboring mental health agencies results in low rates of treatment linkage and engagement.¹⁹ Therefore, integrated treatments that address both substance use and psychiatric disorders in the same setting and during the same treatment episode may be optimal.

Posttraumatic stress disorder (PTSD) is particularly prevalent among individuals with OUDs.²⁰ Compared to patients with other substance use disorders, patients with OUDs have a 42% increase in the odds of probable PTSD.²⁰ Even though 14–53% of MAT patients meet criteria for a current PTSD diagnosis,^{9,11,21} the impact of PTSD on MAT outcomes is uncertain. It is unclear whether PTSD increases or decreases the rate of illicit substance use among MAT patients.^{10,11} The receipt of additional psychosocial therapy may also mediate outcomes for patients with PTSD. Few studies on patients with PTSD and OUDs have provided information on psychosocial treatments offered in combination with MAT.^{10,11,22} Because integrated treatments are potentially efficacious,²³ research examining the impact of integrated treatment plus MAT may provide important information for treating patients with co-occurring disorders.

This study capitalizes on data from a large randomized controlled trial (RCT) comparing an integrated treatment for PTSD and substance use disorders with an addiction only treatment,

and with standard addiction care alone.²⁴ The goal of the current study, a secondary analysis of the RCT, is to evaluate the impact of MAT and integrated therapy on outcomes for patients with co-occurring OUDs and PTSD. We examined substance use and psychiatric outcomes for patients with opioid use disorders who received either MAT or addiction-focused treatment, addiction treatment only, MAT plus integrated treatment, or integrated treatment only. Our hypothesis was that the combination of MAT and integrated treatment would be the most effective condition for substance use and psychiatric outcomes.

METHODS

Procedure

A secondary analysis was conducted using data obtained from an RCT of integrated psychosocial treatment.²⁴ Adult patients entering treatment at seven community addiction treatment agencies were screened at intake for PTSD using the PTSD Checklist (PCL-C).²⁵ Consenting patients scoring 44 or above on the PCL-C completed a baseline study assessment. Those meeting diagnostic criteria for PTSD were randomized to one of three treatment conditions (see below). Assessments were conducted at baseline and 6 months. Study design, maintenance, and consent procedures were all monitored and approved by the Trustees of Dartmouth College Committee for the Protection of Human Subjects (CPHS). All research was conducted in accordance with human subjects' protections.

Participants and Sampling

Patients from community addiction treatment programs in Vermont and New Hampshire were enrolled between December 1, 2010 and January 31, 2013. Three-hundred sixty-one participants scored a 44 or greater on the PCL-C and completed a baseline assessment. Seventy-seven of these participants did not meet inclusion criteria, primarily due to failure to meet diagnostic criteria for a current PTSD diagnosis. Sixty-three participants were excluded after failing to initiate standard care. Two-hundred twenty-one participants were randomized. To determine the effect of MAT on treatment outcomes, patients without a current opioid use disorder were excluded from the sample. One-hundred twenty-six (57.0%) randomized participants met criteria for current opioid use disorders.

Study Interventions

Every enrolled patient received standard care (SC). SC consisted of intensive outpatient (IOP) treatment and continuing care at an addiction treatment program. The SC programs were all state-funded and offered care at the American Society of Addiction Medicine criteria for Level II Intensive Outpatient services (9–12 hours per week), and Level I Outpatient services (at least 1 hour per month).²⁶ SC included individual and group psychotherapy, as well as the possible provision of MAT and psychotropic medications. Each program varied on their delivery of mental health services, medications, instrumental support, and staff training. Some programs offered MAT on site, while other programs referred patients to nearby MAT providers.

Patients were randomized to one of three treatment conditions: Integrated Cognitive Behavioral Therapy (ICBT) plus SC, Individual Addiction Counseling (IAC) plus SC, or SC

alone. ICBT is an 8–12 week manual-guided individual therapy designed to address co-occurring PTSD and substance use.^{27,28} IAC is an 8–12 week manual-guided individual therapy focused on substance use problems, adapted from the Twelve Step Facilitation manual from the National Institute on Alcohol Abuse and Alcoholism Project MATCH Study and the Individual Drug Counseling manual from the National Institute on Drug Abuse Cocaine Collaborative Study.^{27,29,30} Both therapies were provided by licensed alcohol and drug counselors employed by the addiction treatment programs. Patients receiving ICBT or IAC were scheduled to complete one 60 minute individual session each week, in addition to SC programming.

Measures

Demographics and Baseline Characteristics—Information on patient demographics was collected using the Self-Administered Addiction Severity Index (ASI) and through systematic chart reviews.³¹ At baseline, the M.I.N.I. International Neuropsychiatric Interview-Version 6.0 (MINI) was used to assess patients for DSM-IV disorders.³²

Substance Use—At all research assessments, urine drug screens were used to confirm active substance use. The One Step Multi-Drug Screen Test Card with Integrated iCup tested for recent cannabis, cocaine, benzodiazepine, amphetamine, methamphetamine, and opiate use. Secondary substance use outcomes included the frequency and severity of substance use, which were assessed using the ASI and the Timeline Follow Back (TLFB) method. The TLFB is a structured interview eliciting self-report substance information for the past 90 days.³³

PTSD and Psychiatric Symptom Severity—At each assessment, a researcher administered the Clinician Administered PTSD Scale (CAPS). The CAPS is a structured diagnostic interview for PTSD.³⁴ To meet criteria for a current PTSD diagnosis, the CAPS total score must equal 44 or greater, and a patient must report re-experiencing, avoidance/numbing, and hyperarousal symptoms. CAPS total scores between 44 and 64 indicate moderate PTSD. Any CAPS score of 65 or greater is considered severe. As a secondary outcome, psychiatric problem severity was examined using the ASI psychiatric severity score.

Use of Addiction and Psychotropic Medications—Information on current methadone, buprenorphine, naltrexone, or naloxone prescriptions were obtained from systematic reviews of treatment program patient charts conducted at each assessment. Prescription of psychotropic and other medications were also recorded. For additional verification, patients were asked to self-report all MAT and psychotropic medication usage.

Treatment Utilization—At each site, a coordinator tracked all substance use and mental health treatment services received by each patient throughout the 6-month follow-up window. This information was collected and transmitted monthly to the research team through a secure server. Clinicians also tracked participant attendance at all ICBT and IAC sessions and relayed this information to the research team after each treatment session.

ANALYSIS

T-tests and chi-square tests were used to examine baseline differences in clinical and demographic characteristics of MAT and non-MAT patients. For all continuous variables, change scores were calculated by subtracting initial scores from 6-month scores. Two-way analysis of variance (ANOVA) was used to investigate the influence of MAT and integrated therapy on treatment outcomes. Significant main effects of treatment condition (ICBT, IAC, or SC) or MAT prescription were investigated using the Tukey post hoc test. For continuous variables, linear regression was used to adjust for age, gender, treatment site, and intravenous (IV) drug use. Logistic regression analysis models were used to study the effects of integrated psychosocial treatment and MAT on positive urine toxicology screens and IOP completion rates. Because no patients receiving both MAT and ICBT had positive toxicology screens at 6 months, one positive toxicology screen was added to this group to facilitate data analysis. The logistic regression model controlled for age, sex, IV drug use, treatment site, and rates of positive urine drug screens at baseline. To compare combinations of MAT and treatment condition, SC with no MAT was used as the reference group because this most closely resembled standard addiction treatment. For any significant interactions between treatment condition and MAT, estimated marginal means were used to obtain post hoc pairwise comparisons. All analyses were conducted using Stata, version 12.³⁵

RESULTS

Participant Characteristics and MAT Prescription

Baseline demographic, substance use, and psychiatric characteristics of patients are shown in Table 1. The majority of patients were female and Caucasian. Most met criteria for multiple substance use disorders, in addition to an OUD. Fifty-one (40.5%) participants had been in a residential program for substance use in the month prior to baseline. Participants attending residential programs remained in the hospital for an average of 17.0 days (sd = 10.1). The average CAPS score was in the severe range (>65).³⁴ Besides PTSD, patients met criteria for 3.71 (sd = 1.71) current psychiatric disorders on average, most commonly mood and anxiety disorders. Only 9.52% (12) patients met criteria for current PTSD only. Approximately 72.2% (91) of patients were prescribed psychotropic medications, including antidepressants, sleeping medications, non-benzodiazepine anxiolytics, benzodiazepines, and mood stabilizers.

During the 6-month follow-up period, 61.9% (78) of study participants with OUDs were prescribed MAT. Buprenorphine was the most common medication prescribed, followed by methadone (Table 1). Only three participants were prescribed naltrexone, while none were prescribed naloxone. Patients on methadone were prescribed an average of 81.0 mg per day (sd = 111.7), while patients on buprenorphine were prescribed an average of 11.7 mg per day (sd = 5.14). No dosage data was available for naltrexone prescriptions. There were no significant differences in buprenorphine dosage by treatment type ($F(2, 26) = 3.08, p = .07$). Because few patients were prescribed methadone, we were unable to test for significant differences in dosage by treatment condition. The proportion of patients prescribed methadone did not differ by psychosocial treatment condition ($p = .39$, Fisher's exact test (FET)). Overall, MAT and non-MAT patients had similar baseline demographic, substance

use, and psychiatric characteristics. Patients prescribed MAT were significantly more likely to be IV drug users than patients not prescribed MAT. Additionally, patients receiving MAT were more likely to meet criteria for social anxiety and obsessive compulsive disorder (OCD) (Table 1).

Substance Use Outcomes

Across the entire sample, there was no overall decrease in the rate of positive urine drug screens from baseline to 6-months ($p = .43$, FET). Using a multivariate logistic model, we examined the odds of a positive drug screen at 6-months, controlling for rates of baseline positive drug screens, age, gender, treatment site, and IV drug use. Compared to non-MAT patients receiving SC, MAT patients in the ICBT treatment condition had a 93.0% decrease in the odds of a positive drug screen (OR = .07, 95% CI = .01, .82, $p = .03$). No significant differences in the odds of a positive drug screen were detected when comparing all other treatment combinations with SC plus no MAT. As shown in Figure 1, MAT patients in SC only had a 50.7% (95% CI = 26.2%, 75.2%) predicted probability of a positive drug screen, and non-MAT patients receiving SC alone had a 40.3% (95% CI = 12.0%, 68.5%) probability of a positive drug screen. Non-MAT patients in ICBT had a 50.1% (95% CI = 12.2%, 68.5%) predicted probability of a positive drug screen, but only a 5.09% (95% CI = 0.01%, 14.8%) probability of a positive drug screen when prescribed MAT. Despite these differences, the overall interaction between MAT and treatment condition was not statistically significant ($\chi^2(5) = 7.50$, $p = .19$).

As shown in Table 2, average self-reported days of substance use ($t(88) = 11.11$, $p < .001$) and ASI drug use severity ($t(86) = 6.66$, $p < .001$) decreased significantly from baseline to 6 months. ASI alcohol severity decreased also, though not significantly ($t(83) = 1.70$, $p = .09$). Two-way ANOVAS and multiple linear regression analyses revealed no significant main effects ($p > .05$). Therefore, MAT prescription status and treatment condition were not associated with self-reported days of substance use or ASI substance use severity scores. In addition, no significant interactions between treatment condition and MAT were detected for the self-reported substance use outcomes (Table 2) or the multiple linear regression models.

PTSD and Psychiatric Outcomes

Average CAPS score decreased significantly from baseline to 6-months ($t(88) = 10.62$, $p < .001$). No main effects were found for MAT or treatment condition for the ANOVA (Table 2) or the multiple linear regression model (MAT: $\beta = 1.65$, 95% CI = -9.73, 13.04, $p = .77$; Treatment Condition: $\beta = 1.06$, 95% CI = -5.51, 7.63, $p = .75$). A significant MAT-by-psychosocial treatment condition interaction was detected ($F(2, 88) = 4.74$, $p = .011$). For MAT patients, pairwise comparisons of estimated marginal means showed no significant differences in mean CAPS change scores for ICBT ($M = 22.3$, $SE = 4.98$), IAC ($M = 36.8$, $SE = 5.97$), or SC alone ($M = 25.8$, $SE = 5.63$) (Fig. 2). Non-MAT patients randomized to ICBT had significantly larger decreases in CAPS total score than patients randomized to IAC ($p = .02$) or SC alone ($p = .02$). While non-MAT patients receiving ICBT had an average decrease of 47.6 points ($SE = 8.44$) on the CAPS total score, non-MAT patients getting IAC or SC alone had significantly smaller decreases ($M = 21.5$, $SE = 7.20$ and $M = 21.9$, $SE = 6.62$, respectively). Although the overall interaction term in the adjusted linear

regression model missed statistically significant ($F(5, 79) = 2.19, p = .06$), pairwise comparisons again showed that the combination of medication plus ICBT resulted in significantly larger declines in CAPS scores than the no MAT plus SC condition ($\beta = 24.40$, 95% CI = 3.33, 45.47, $p = .02$).

The ASI psychiatric severity score also decreased significantly across all treatment conditions ($t(79) = 7.85, p < .001$). ANOVA results revealed a main effect for MAT ($F(1, 79) = 4.57, p = .04$). Non-MAT patients had a greater reduction in ASI psychiatric severity ($M = .25, SE = .04$) than MAT patients ($M = .15, SE = .03$). This main effect was diminished after adjusting the analysis for age, gender, treatment site, and IV drug use ($\beta = -.09$, 95% CI = $-.19, .01, p = .07$). There was no significant main effect for treatment condition and no significant interaction between treatment condition and MAT in the ANOVA (Table 2) or multiple linear regression model (Treatment Condition: ($\beta = .03$, 95% CI = $-.03, .09, p = .28$); Interaction: ($F(5, 70) = .90, p = .49$)).

Treatment Utilization

As shown in Table 2, most patients attended IOP and other group sessions. Patients attended an average of 5.54 ($sd = 4.57$) ICBT sessions and 4.66 ($sd = 3.95$) IAC sessions. ICBT patients missed an average of 1.05 ($sd = .96$) sessions due to patient cancellations, therapist cancellations, and unexplained no-shows, while IAC patients missed an average of .91 ($sd = .91$) sessions. IOP, group, individual and ICBT/IAC session treatment utilization did not differ by MAT prescription or psychosocial treatment (Table 2). As expected MAT patients attended significantly more medication-related appointments than non-MAT patients ($F(1, 125) = 8.38, p = .005$).

DISCUSSION

Relative to psychosocial treatments, this study assessed the impact of an integrated behavioral therapy plus MAT for individuals with co-occurring OUDs and PTSD. Close to two-thirds (61.9%) of enrolled patients with OUDs were prescribed MAT during the study. This high rate of MAT prescription in Vermont is surprising because access to MAT is particularly poor in rural areas.³⁶ In addition, unlike other states, rates of MAT prescription in Vermont were comparable to the rate of psychotropic medication prescription.³⁷ At baseline, MAT and non-MAT patients had similar characteristics overall, though rates of IV drug use, OCD, and social anxiety were higher among MAT patients. Providers may have been more likely to refer individuals with a history of IV drug use to MAT, as IV drug use is associated with greater severity and increased risk for medical comorbidities.³

Self-reported substance use severity and frequency improved regardless of MAT prescription or treatment condition, although rates of positive urine drug screens did not change significantly from baseline to 6-months. Results showed that MAT and individual psychosocial therapies were not more effective than standard care in reducing self-reported days of use or substance use severity. In contrast, results of the urine drug screens demonstrated that the combination of MAT plus ICBT was associated with the lowest probability of a positive urine drug screen at 6-months. Rates of positive urine drugs screens were relatively low at baseline, perhaps due to high rates of residential program attendance

prior to the baseline assessment. At 6-months, MAT plus ICBT reduced the odds of a positive drug screen more than SC only. MAT patients receiving ICBT had only a 5% probability of a positive drug screen. MAT and non-MAT patients randomized to the other treatment conditions had 30–50% probabilities of positive drug screens. These results are comparable to a recent study showing improved substance use outcomes with prolonged exposure therapy plus naltrexone for patients with co-occurring alcohol dependence and PTSD.³⁸ Together, these studies provide support for delivering integrated psychosocial treatments in combination with addiction medications for patients with co-occurring substance use disorders and PTSD. The high level of psychiatric severity among patients in this study demonstrates that targeted psychiatric treatments may be especially important as an adjunct to MAT for patients with severe psychiatric symptoms.⁶

Contrary to our hypothesis, ICBT plus MAT was not more effective for reducing PTSD symptoms or general psychiatric severity. Among MAT patients, PTSD symptoms decreased comparably, regardless of assignment to SC, IAC, or ICBT. For non-MAT patients, ICBT was associated with the greatest reductions in PTSD symptoms. It is unclear why integrated treatment had a different effect on psychiatric outcomes versus substance use for MAT patients. One reason may be the effect of agonists or partial agonists on anxiety and PTSD symptoms. Individuals with PTSD often use opioids to numb their symptoms, and both methadone and buprenorphine have anxiolytic properties.^{3,20} It is possible that MAT could impact the potential benefits of psychosocial treatment by continuing this effect. Although ICBT is not exposure-based, the program encourages patients to process traumatic events while learning skills to work through their PTSD symptoms. Full and partial opioid agonists might prevent patients from fully processing events and symptoms if these medications contributed to numbing and avoidance. While patients in this study were not prescribed particularly high dosages of medications on average, the moderate doses taken by patients may still have impacted the processing of traumatic experiences.

Several limitations attenuate the interpretation of these findings. This study relied on chart reviews and patient self-report to gather data on MAT usage. Because many patients received MAT from physicians outside these addiction treatment programs, limited information on dosage was available for these patients. Additionally, we were unable to access information on duration of exposure to MAT. We were also unable to verify MAT treatment compliance with the state prescription monitoring system or with confirmatory toxicology screens. Patients could have misreported MAT utilization, which would impact the validity of our results. Patient charts complied with state guidelines, but medication information may have been incomplete or outdated. No data on missed IOP sessions were recorded, so we were unable to assess IOP adherence rates. Lack of randomization to MAT also increased the risk for selection bias. In the tradeoff between external and internal validity, this study's methodology was designed to be generalizable and externally valid. Unfortunately, several issues were therefore unable to be controlled experimentally, which adds significant noise to the study. Future studies of MAT and co-occurring treatment should randomize patients to receive MAT and integrated therapy. Additionally, duration of exposure to MAT should be tracked. Sample sizes in each of the three groups were also small, which reduced the study's power to detect true group differences. Improving treatment retention rates is also important. Because most ICBT participants did not complete

the entire therapy program, this study might be underestimating the effects of ICBT. In addition, patients in this study were predominately Caucasian, which limits inference to other ethnic groups.

CONCLUSIONS

This study found that Integrated Cognitive Behavioral Therapy (ICBT) plus MAT was more effective than standard care in reducing the probability of positive drug screens for patients with co-occurring PTSD and opioid use disorders. The combination of ICBT and MAT was not as effective for PTSD symptoms. For non-MAT patients, ICBT was more effective than non-integrated approaches in decreasing PTSD symptoms. PTSD symptom reduction was comparable for MAT patients regardless of psychosocial treatment condition. These findings demonstrate that ICBT provided in combination with MAT may improve substance use outcomes for patients with PTSD. The provision of ICBT may be particularly useful in reducing PTSD and psychiatric severity among patients who prefer behavioral treatment or cannot access MAT, such as in rural areas.

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FIG. 1.

Predicted probabilities and 95% confidence intervals of positive drug toxicology screen by medication assisted treatment (MAT) prescription status and treatment type. (MAT, medication assisted treatment; ICBT, integrated cognitive behavioral therapy; IAC, individual addiction counseling; SC, standard care.)

FIG. 2. Changes in clinician administered PTSD Scale (CAPS) total scores from baseline to 6 months by medication assisted treatment (MAT) prescription and psychosocial treatment type. (MAT, medication assisted treatment; ICBT, integrated cognitive behavioral therapy; IAC, individual addiction counseling; SC, standard care.)

TABLE 1

Patient demographics, posttraumatic stress disorder (PTSD), and substance use characteristics of participants prescribed and not prescribed medication assisted treatment (MAT) for opioid dependence at baseline

	MAT (n = 78)	No MAT (n = 48)	Overall (n = 126)	t/ χ^2 value ^a
Demographics				
Age, Mean (sd)	31.10 (8.03)	33.90 (10.03)	32.17 (8.91)	3.76
Gender (Male), n (%)	28 (35.9%)	20 (41.7%)	48 (38.1%)	.42
Race (Caucasian/White), n (%)	75 (96.2%)	47 (97.9%)	122 (96.8%)	3.48
Ethnicity (Not Hispanic or Latino), n (%)	76 (97.4%)	48 (100%)	124 (98.4%)	1.25
Substance use				
Positive urine drug screen, n (%)	19 (24.4%)	10 (21.3%)	29 (23.2%)	.16
Intravenous Drug Use, n (%)	46 (59.0%)	15 (31.3%)	61 (48.4%)	9.14 **
Substance use disorder type, n (%)				
Prescription Opioids	70 (89.7%)	43 (89.6%)	113 (89.7%)	0
Heroin	47 (60.3%)	24 (50.0%)	71 (56.3%)	1.27
Cocaine	52 (66.7%)	30 (62.5%)	82 (65.1%)	.23
Cannabis	37 (47.4%)	31 (64.6%)	68 (54.0%)	3.52
Alcohol	41 (52.6%)	25 (52.1%)	66 (52.4%)	0
Sedatives	25 (32.1%)	15 (31.3%)	40 (31.7%)	.01
Amphetamines	19 (24.4%)	12 (25.0%)	31 (24.6%)	.01
Hallucinogens	10 (12.8%)	4 (8.3%)	14 (11.1%)	.61
Other	3 (3.8%)	0 (.00%)	3 (2.4%)	1.89
Number of substance use disorders, Mean (sd)	4.08 (1.72)	3.98 (1.69)	4.04 (1.70)	.01
Timeline follow back, Mean (sd)				
Number of days drinking	13.11 (21.80)	11.23 (18.71)	12.40 (20.62)	1.28
Number of days using drugs	35.22 (27.31)	34.54 (27.92)	34.96 (27.43)	1
ASI composite scores, Mean (sd)				
Alcohol	.14 (.19)	.16 (.16)	.15 (.18)	1.33
Drug	.18 (.08)	.18 (.08)	.18 (.08)	.23
Psychiatric disorders and PTSD				
Psychiatric disorder type, n (%)				
Posttraumatic stress	78 (100%)	48 (100%)	126 (100%)	—
Major depression (current)	43 (55.1%)	26 (54.2%)	69 (54.8%)	.01
Generalized anxiety	29 (37.2%)	19 (39.6%)	48 (38.1%)	.07
Panic with agoraphobia	21 (26.9%)	14 (29.2%)	35 (27.8%)	.07
Social anxiety	28 (35.9%)	9 (18.8%)	37 (29.4%)	4.21 *
Major depression (recurrent)	9 (11.5%)	6 (12.5%)	15 (11.9%)	.03
Panic	15 (19.2%)	7 (14.6%)	22 (17.5%)	.44
Obsessive compulsive disorder	17 (21.8%)	4 (8.3%)	21 (16.7%)	3.88 *
Agoraphobia	12 (15.4%)	4 (8.3%)	16 (12.7%)	1.33

	MAT (<i>n</i> = 78)	No MAT (<i>n</i> = 48)	Overall (<i>n</i> = 126)	<i>t/χ² value^a</i>
Manic episode (current)	4 (5.1%)	3 (6.3%)	7 (5.6%)	.07
Hypomanic episode (current)	1 (1.3%)	1 (2.1%)	2 (1.6%)	.12
Psychotic mood (lifetime)	4 (5.1%)	2 (4.2%)	6 (4.8%)	.06
Psychotic mood (current)	3 (3.8%)	2 (4.2%)	5 (4.0%)	.01
Number of psychiatric disorders, Mean (sd)	3.86 (1.73)	3.48 (1.68)	3.71 (1.71)	.56
Meeting criteria for >1 psychiatric disorder, <i>n</i> (%)	43 (89.6%)	71 (91.0%)	114 (90.5%)	.79
CAPS Total Score, Mean (sd)	78.65 (20.56)	78.65 (20.73)	78.65 (20.54)	.19
Number of traumatic life events, Mean(sd)	6.18 (3.48)	5.71 (2.91)	6.00 (3.27)	.39
Prescribed medications				
Medication assisted treatment (MAT), <i>n</i> (%)				
Methadone	12 (15.4%)	—	12 (9.5%)	—
Buprenorphine	62 (79.5%)	—	62 (49.2%)	—
Naltrexone	3 (3.8%)	—	3 (2.4%)	—
Missing	1 (1.3%)	—	1 (.8%)	—
Psychotropic medication, <i>n</i> (%)	58 (73.4%)	33 (70.2%)	91 (72.2%)	.7
Antidepressants	45 (53.9%)	29 (60.4%)	71 (56.4%)	.52
Sleep medications	37 (47.4%)	18 (37.5%)	55 (43.7%)	1.19
Non-benzodiazepine anxiolytics	21 (26.9%)	10 (20.8%)	31 (24.6%)	.59
Benzodiazepines	11 (14.1%)	5 (10.4%)	16 (12.7%)	.36
Mood stabilizers	10 (12.8%)	4 (8.33%)	14 (11.1%)	.61

MAT, medication assisted treatment; ASI, addiction severity index; CAPS, clinician administered PTSD scale.

^aDifferences between groups were tested as follows: means by t-tests, proportions by chi-square tests;

*
p .05;

**
p .01.

TABLE 2

Changes in substance use and psychiatric symptoms from baseline to 6 months by medication assisted treatment (MAT) and psychosocial treatment group

Substance use	MAT (n = 78)				No MAT (n = 48)				F value ^d	
	ICBT (n = 28)	IAC (n = 22)	SC (n = 28)	ICBT (n = 13)	IAC (n = 16)	SC (n = 19)	Interaction	Main effects		
Positive urine drug screens n (%) ^{a,b}										
Baseline	5 (17.9%)	5 (22.70%)	9 (32.10%)	5 (38.50%)	3 (18.80%)	2 (11.10%)	—	—		
6 Months	0 (.00%)	5 (38.50%)	8 (47.10%)	4 (57.10%)	4 (36.40%)	5 (38.50%)	—	—		
Mean days drinking M (sd)										
Baseline	12.64 (19.58)	14.32 (24.80)	12.64 (22.17)	14.23 (24.77)	10.69 (17.11)	9.63 (15.88)	.63	MAT: .09, TxType: 1.07		
6 Months	3.70 (9.69)	4.25 (15.68)	9.06 (23.27)	1.75 (3.81)	3.45 (9.91)	7.00 (16.93)				
Mean days using drugs M (sd)										
Baseline	26.96 (24.68)	36.59 (29.73)	42.53 (26.53)	44.08 (29.52)	27.87 (25.95)	33.63 (28.05)	.66	MAT: .00, TxType: .17		
6 Months	5.22 (10.99)	11.25 (22.03)	21.28 (30.32)	13.13 (28.66)	13.00 (20.99)	19.85 (29.82)				
ASI Alcohol Composite Score M (sd)										
Baseline	.11 (.17)	.18 (.21)	.12 (.21)	.19 (.19)	.16 (.16)	.15 (.13)	.75	MAT: .01, TxType: .68		
6 Months	.08 (.15)	.11 (.16)	.13 (.22)	.14 (.13)	.11 (.11)	.11 (.11)				
ASI drug composite score M (sd)										
Baseline	.16 (.07)	.21 (.08)	.18 (.09)	.20 (.08)	.19 (.09)	.16 (.06)	.53	MAT: .32, TxType: 1.48		
6 Months	.09 (.06)	.13 (.11)	.13 (.11)	.13 (.13)	.11 (.07)	.08 (.07)				
Psychiatric disorders and PTSD										
CAPS total score M (sd)										
Baseline	77.50 (17.88)	81.91 (22.93)	77.25 (21.57)	80.92 (19.96)	80.63 (23.41)	75.42 (19.54)	4.74**	MAT: .15, TxType: 1.45		
6 Months	53.30 (22.62)	50.44 (27.92)	51.28 (26.68)	28.13 (20.79)	54.73 (21.98)	56.69 (27.52)				
ASI Psychiatric Composite M (sd)										
Baseline	.54 (.15)	.60 (.15)	.52 (.12)	.56 (.12)	.61 (.17)	.57 (.15)	.7	MAT: 4.57*, TxType: 1.20		
Treatment services received										
ICBT or IAC Sessions M (sd)	5.64 (4.61)	5.23 (4.01)	—	5.31 (4.64)	3.88 (3.86)	—	.25	MAT: .69, TxType: .83		
IOP sessions M (sd)	19.54 (14.58)	15.82 (10.83)	16.14 (12.57)	16.92 (9.29)	14.56 (10.59)	14.26 (5.50)	.39	MAT: .19, TxType: .70		
Group sessions M (sd)	6.07 (9.85)	7.91 (9.43)	6.54 (8.42)	4.23 (7.05)	4.69 (10.70)	5.74 (6.04)	.19	MAT: 1.42, TxType: .18		
Medication sessions M (sd)	.86 (2.05)	2.18 (2.56)	1.71 (2.77)	.00 (.00)	1.13 (2.22)	.21 (.71)	.25	MAT: 8.38**, TxType: 3.04*		

Substance use	MAT (n = 78)			No MAT (n = 48)			F value ^d	
	ICBT (n = 28)	IAC (n = 22)	SC (n = 28)	ICBT (n = 13)	IAC (n = 16)	SC (n = 19)	Interaction	Main effects
Individual sessions M (sd)	2.61 (5.63)	2.73 (3.49)	2.57 (3.95)	1.08 (2.29)	1.56 (3.60)	4.16 (4.31)	1.71	MAT: .23, TxType: 1.52

MAT, medication assisted treatment; ICBT, integrated cognitive behavioral therapy; IAC, individual addiction counseling; SC, standard care; ASI, addiction severity index; CAPS, clinician administered PTSD scale; IOP, intensive outpatient program.

^aSee Figure 1;

^bTested for cannabis, cocaine, benzodiazepines, amphetamine, methamphetamine, and opioid use;

^cChange scores calculated by subtracting baseline from 6-month scores;

* *p* .05;

** *p* .01.