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A randomized pilot clinical trial to evaluate the efficacy of Community Reinforcement and Family Training for Treatment Retention (CRAFT-T) for improving outcomes for patients completing opioid detoxification*

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Abstract

Background—Detoxification with psychosocial counseling remains a standard opioid-use disorder treatment practice but is associated with poor outcomes. This study tested the efficacy of a newly-developed psychosocial intervention, Community Reinforcement Approach and Family Training for Treatment Retention (CRAFT-T), relative to psychosocial treatment as usual (TAU), for improving treatment outcomes.

Methods—A randomized, 14-week trial with follow-up visits at 6 and 9 months post-randomization conducted at two substance use disorder (SUD) treatment programs. Opioid-dependent adults (i.e., identified patient - IP) enrolled in a residential buprenorphine-detoxification program and their identified concerned significant other (CSO) were randomized to CRAFT-T (n=28 dyads) or TAU (n=24 dyads). CRAFT-T consisted of 2 sessions with the IP and CSO together and 10 with the CSO alone, over 14 weeks. TAU for the CSOs was primarily educational

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Contributors:

Dr. Brigham lead the design and implementation of the study in collaboration with Drs. Somoza and Slesnick. Mr. Lewis and Dr. Guo conducted the analyses and provided critical review of the manuscript. Dr. Brigham drafted the manuscript and Drs. Winhusen, Slesnick, and Somoza contributed to the interpretation of the findings and critically revised the manuscript for intellectual content. All authors have approved the final manuscript.

Conflict of Interest

The authors have no conflicts to declare.

and referral to self-help. All IPs received treatment as usually provided by the SUD program in which they were enrolled. The primary outcome was time to first IP drop from treatment lasting 30 days or more. Opioid and other drug use were key secondary outcomes.

Results—CRAFT-T resulted in a moderate but non-significant effect on treatment retention ($p = 0.058$, hazard ratio = 0.57). When the CSO was parental family, CRAFT-T had a large and significant effect on treatment retention ($p < 0.01$, hazard ratio = .040). CRAFT-T had a significant positive effect on IP opioid and other drug use ($p < 0.0001$).

Conclusion—CRAFT-T is a promising treatment for opioid use disorder but replication is needed to confirm these results.

Keywords

addiction; dependence; family; treatment

1. Introduction

In 2009, there were an estimated 2.3 million Americans with an opioid-dependence disorder (Substance Abuse and Mental Health Services Administration, 2010). Over four decades of research indicates that agonist maintenance therapy (AMT) utilizing methadone (a full opioid agonist) and, more recently, buprenorphine (a partial opioid agonist) is the most effective treatment for opioid dependence (Kleber, 2008; Kreek et al., 2010; Mattick et al., 2008). Social, economic and regulatory barriers limit access to AMT and consequently detoxification followed by psychosocial counseling, with accompanying high relapse rates, is the most common approach to opioid dependence treatment (Mattick et al., 2009; Mayet et al., 2005). Availability of buprenorphine has improved the effectiveness of opioid detoxification (Brigham et al., 2007; Ling et al., 2005) however, without AMT, treatment drop-out and relapse rates are high and potentially lethal (Strang et al., 2003). Interventions are needed to increase retention in treatment and prevent relapse.

Community Reinforcement and Family Training (CRAFT), developed by Robert Meyers, works with concerned significant others (CSOs) to motivate treatment-refusing persons with a substance use disorder to volunteer for treatment. CRAFT has demonstrated a robust effect in several randomized clinical trials (Kirby et al., 1999; Meyers et al., 1998, 2003; Miller et al., 1999).

Between April of 2009 and November of 2010 fifteen dyads, each consisting of an opioid dependent adult identified patient (IP) and their respective CSO, were enrolled in stages 1a and 1b of a therapy development study (Rounsaville, 2001) to modify CRAFT. The new manualized treatment, Community Reinforcement and Family Training for Treatment Retention (CRAFT-T), works with the CSOs of IPs already in treatment, to increase the IP's retention in treatment and recovery support. This report presents the results of a randomized clinical pilot evaluating CRAFT-T.

2. METHODS

2.1 Participants

We enrolled 104 participants into an intent to treat (ITT), 2-group randomized clinical trial at two Ohio locations: Site 1, in a metropolitan county, with 1.2 million residents, and Site 2, in a smaller county, with 178,000 residents. The study was IRB approved and sponsored by the National Institute on Drug Abuse. A detailed study protocol is available (Brigham et al., 2009).

Participants enrolled as dyads consisting of an IP and a CSO. IPs were approached during a detoxification program and, if interested, provided contact information for a CSO. CSOs and IPs were consented and screened separately. IPs were adults who: met DSM-IV-TR criteria for opioid dependence; planned to transfer from detoxification to outpatient; and had a CSO willing to participate. CSOs were relatives, spouses, or intimate partners, or planned to live with the IP following randomization. IPs and CSOs were ineligible if they had: a history of violence with each other; current suicide or homicide intent; a medical or psychiatric condition that would make participation difficult; or were court ordered to complete treatment.

2.2 Procedures

Participants were randomized to CRAFT-T or TAU using urn randomization balanced on site (1 or 2), race (Black or other), and CSO type (parent or other). The study treatment phase was 14 weeks during which there were 2 weekly research assessment visits for IPs and 12 for CSOs. The follow-up phase extended to 38 weeks with research visits for IPs and CSOs at weeks 14, 26, and 38. Randomization began in January of 2011 and follow-up was completed in June of 2012. Participants were compensated for research visits by gift cards (\$20 for baseline and screening, \$10 for each weekly treatment assessment, and \$20 each for the end of treatment assessment and two follow-ups).

2.2.1 Treatments

2.2.1.1 Treatment as usual (TAU) for IPs: All IPs received the usual services offered at the treatment program which began with a 13-day BUP taper detoxification (Brigham et al., 2007). At Site 1 the taper was initiated in a residential sub-acute medical detoxification setting followed by step-down to ambulatory detoxification. At Site 2 the entire taper was completed in an ambulatory setting. At both sites IPs transferred to outpatient treatment following detoxification.

2.2.1.2 Treatment as usual (TAU) for CSOs: The TAU for CSOs was minimal consisting of an invitation to attend a volunteer-facilitated support group and an informal referral to self-help (Al-Anon or Nar-Anon).

2.2.1.3 Community Reinforcement and Family Training for Treatment Retention

(CRAFT-T): This unilateral family intervention worked primarily with the CSO with the goal of influencing the IP's behavior. CRAFT-T used a cognitive behavioral approach to assist the CSO in using behavioral principles to increase the IP's treatment retention and

reduce their drug use. CRAFT-T departed from the CRAFT model in five important ways: it worked with the CSO's of IP's who were in treatment; CSOs were identified by the IP; it targeted retention in treatment; the IP participated in two initial sessions; and it targeted reduction of HIV risk behavior.

CRAFT-T consisted of twelve weekly one-hour sessions. The IP and CSO attended the first two sessions together and the remaining ten sessions were attended by the CSO alone. Two optional sessions were also available. The CRAFT-T manual was designed to supplement the book "*Motivating Substance Abusers to Enter Treatment*" (Smith and Meyers, 2004).

2.2.2 CRAFT-T Therapist, Training, and Fidelity—Four therapists were recruited. Two had master's degrees with less than one year of post-graduate experience and two were non-degreed licensed drug abuse counselors with over ten years of experience. Therapists attended a two-day training followed by training cases. Prior to the start of the trial eleven participant dyads were enrolled to serve as training cases. All therapist training case sessions were audio-recorded and rated for fidelity. Therapists were certified to see trial participants after ratings of two training cases reached a criterion threshold. During the treatment phase of the study all CRAFT-T sessions were audio-recorded and 25% were rated by the study PI [G.B.]. All therapists maintained acceptable fidelity with an overall compliance rating of 87%.

2.3 Measures

The primary outcome was days to the IP's first drop of 30 days or more from all treatment as recorded in the clinic's electronic health record. Secondary outcomes included days of opioid use and any drug use. A Timeline Follow-back (TLFB) procedure (Robinson et al., 2012; Sobell et al., 1988), was used to record the IP's day-to-day use of alcohol, opioids, cocaine, marijuana, benzodiazepines, methamphetamine, and other illicit drugs. Urine samples were collected at each of the IP's research visits (weeks 1, 2, 14, 26, and 38) and were analyzed for opioids, cocaine, marijuana, benzodiazepines, methamphetamine using the Redi Test rapid screen system from Redwood Toxicology Laboratory. The Structured Clinical Interview for DSM-IV (First et al., 1996) was used with the IP to obtain the opioid-dependence diagnosis.

2.4 Data Analysis

Baseline measures are summarized in Table 1. Each measure was tested for between-treatment-arm differences using the Pearson Chi Square, Fisher Exact, Wilcoxon Rank Sum or Student's t.

Each outcome analysis was performed twice: grouping participants by treatment arm, and then by CRAFT-T participants with parental family CSO (parent, aunt, grandparent or sibling) vs. all others. This second grouping resulted from previous indication of CSO relationship as a potential moderator (Meyers et al., 1998; Miller et al., 1999), and from the small, pilot study sample size which precluded all but the simplest regression models.

The primary outcome variable was treated as survival data and tested for group differences using Cox Proportional Hazard regressions. There were no missing data on the primary

outcome. Daily TLFB IP opioid and drug use indicators, were assessed using random intercept mixed-model logistic regressions testing for both group effects and group-by-time interaction effects over weeks 1–2 (IP study treatment), over weeks 3–14 (CSO treatment after IP study treatment), and finally over the remaining follow-up weeks. No attempt was made to account for multiple analyses or missing data (on the drug use outcomes).

Urine drug screens (UDS) were too sparse for meaningful between-group comparisons. Instead, the Cohen Kappa was used to compare the UDS opioid indicators to TLFB results compiled over three-day periods ending with respective UDS days.

3. RESULTS

3.1 Participants

A total of 136 potential participants were pre-screened, 108 consented and screened, and 104 (52 dyads) randomized (Supplementary Figure S1¹). For weeks 14, 28 and 38 respectively, follow-up rates were 52%, 56% and 62% for IP, and 62%, 54%, and 79% for CSO. No reported baseline characteristics indicated significant between-treatment differences. IP participants averaged 29 years old and were 79% male, 94% white, and 73% unemployed (Table 1.). Based on the Risk Assessment Battery (RAB) self-reports, the CSO's substance use appeared minimal (data not shown).

3.2 Study Treatment Exposure

IPs attended an average of 1.78 (median of 2) of their 2 scheduled CRAFT-T sessions. CSOs attended an average of 7.62 (median of 9.5) of their 12 scheduled study treatment sessions. Three CRAFT-T dyads dropped out before their first session. Of the two optional CSO sessions, 8 CSOs attended at least one session, and 2 attended both.

3.3 Primary Outcome

The primary outcome measure had 3 censored participants (2 for early withdrawal and one for outlasting the 38-day assessment period) and no missing data. CRAFT-T participants showed a longer time-to-dropout which approached significance with $p = 0.058$ and a hazard ratio of 0.57 indicating they were 57% as likely as TAU participants to dropout at any given point in time. CRAFT-T participants with parental-family CSOs showed a longer time-to-dropout with $p < 0.01$ and hazard ratio = 0.40 (Figure 1).

3.4 Daily Drug Use Outcomes

For both of the participant groupings, week 3–14 regressions and follow-up regressions demonstrated significant time-by-treatment interaction effects for both opioid and drug use TLFB indicators ($p < 0.0001$). The corresponding graphs in Figure 1 suggest divergence during weeks 3–14 favoring CRAFT-T and CRAFT-T-with-parental-family-CSO respectively, with differences diminishing during follow-up. A Cohen Kappa of 0.54 resulted from testing the TLFB opioid results for agreement with UDS results: disagreement balanced between positive and negative urines.

¹Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:...

4. DISCUSSION

The goal was to determine if adding CRAFT-T to opioid detoxification followed by outpatient, would improve treatment retention and drug use outcomes. The primary outcome was days to the IP's first drop of 30 days or more from treatment. Compared to TAU, CRAFT-T resulted in a moderate-sized effect that approached significance. We also evaluated the effect of type of CSO and found that when dyads with both CRAFT-T and CSOs from parental family were compared to all others, the effect on retention was large (Hazard Ratio = 0.4, Cohen's $d = 0.95$) and significant. This is consistent with previous CRAFT research by Meyers (1998) who found parents were significantly more effective than spouses. Retention in treatment is important as it is consistently associated with improved drug use outcomes (Mertens et al., 2012; Simpson et al., 1997).

We also examined effects on drug use and found that assignment to CRAFT-T resulted in significant reductions in both opioid and drug use days reported on the TLFB. While this observed effect on drug use is encouraging, the overall rates of relapse and drug use were high. These outcomes should be interpreted with caution due to the relatively low follow-up rates.

CSOs attended an average of 8 of the 12 planned sessions, which is low compared to previous CRAFT research. In CRAFT research the CSO initiates involvement. In CRAFT-T, IPs invite a specific CSO and the relationships often appeared strained with a sense that the CSO was being engaged with reluctance.

This study had numerous strengths: the ITT randomized trial design, a manual guided treatment, and no missing data on the primary outcome measure. Some limitations resulted from the small sample size: lack of generalizability, lack of power to evaluate therapist effects and to fully evaluate the effects of CSO relationship type, and possibly distorted estimates of effect sizes (Kraemer et al., 2006). CSO's utilization of CRAFT-T skills was not measured and therefore we cannot conclude that use of these skills caused the observed effects.

In conclusion, these preliminary results suggest that CRAFT-T is a promising intervention for improving treatment retention and drug use outcomes in adults with opioid use disorder.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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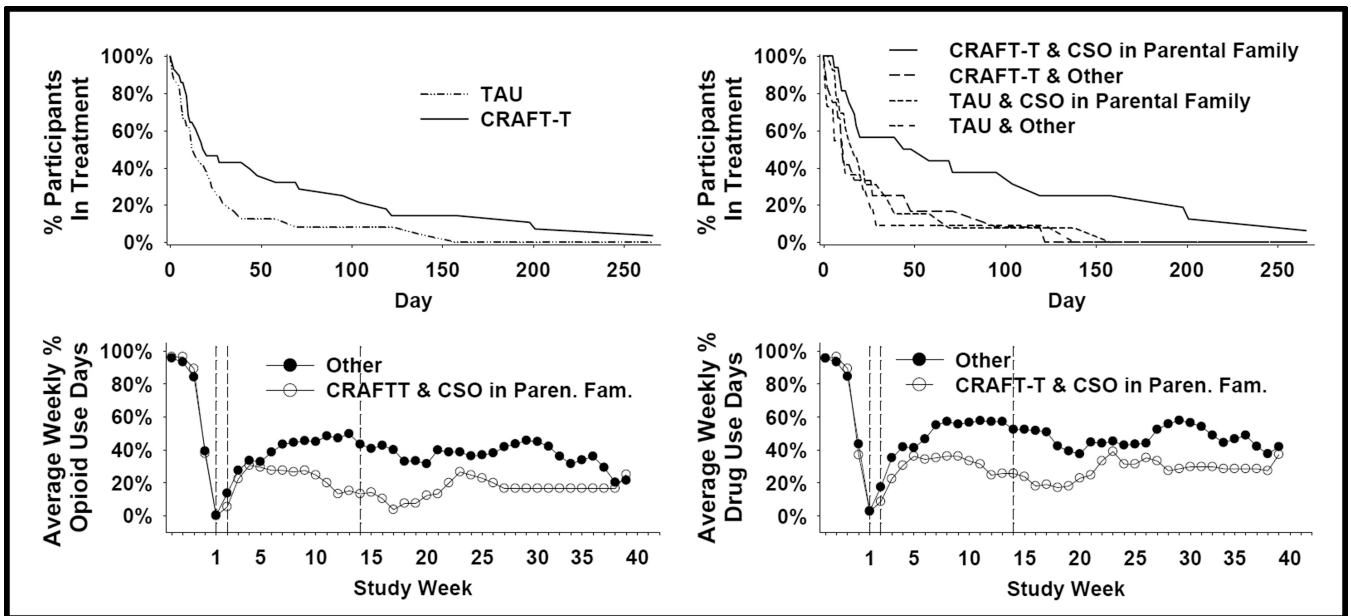


Figure 1.

(a,b) Survival curves for IP retention in drug abuse treatment are shown. Time point 0 is baseline and 1 – 250 are days in drug abuse treatment following randomization. (c,d) Comparison of treatments on TLFB reports of weekly percentage of opioid use and any drug use days are shown. Weeks 1 – 2 are treatment weeks in which both the CSO and IP attend CRAFTT sessions, 3 –14 are the weeks in which only the CSO attends CRAFT-T sessions, and weeks 15–40 are follow-up.

Table 1

Participant Comparison at Baseline by Treatment Group

	TAU (N=24)	CRAFT-T (N=28)	Total (N=52)
Site (n, %):			
Site 1	16, 66.7%	20, 71.4%	36, 69.2%
Site 2	8, 33.3%	8, 28.6%	16, 30.8%
IP:			
Age in yrs. (mean, std.dev.)	28.7, 6.7	29.5, 9.2	29.2, 8.1
Males (n, %)	18, 75.0%	23, 82.1%	41, 78.8%
Race (n,%):			
Black	1, 4.2%	1, 3.6%	2, 3.8%
White	22, 91.7%	27, 96.4%	49, 94.2%
Other	1, 4.2%	0, 0.0%	1, 1.9%
CSO:			
Age in yrs. (mean, std.dev.)	40.3, 14.8	28 44.3, 12.1	42.5, 13.4
Males (n, %)	5, 20.8%	4, 14.3%	9, 17.3%
Race (n,%):			
Black	2, 8.3%	1, 3.6%	3, 5.8%
White	21, 87.5%	26, 92.9%	47, 90.4%
Other	1, 4.2%	1, 3.6%	2, 3.8%
CSO Relation (n, %):			
Parent/Aunt/Grandparent	11, 45.8%	15, 53.6%	26, 50.0%
Spouse/Common Law	2, 8.3%	5, 17.9%	7, 13.5%
Girlfriend/Boyfriend/Fiancee	8, 33.3%	5, 17.9%	13, 25.0%
Sibling	2, 8.3%	1, 3.6%	3, 5.8%
Friend	1, 4.2%	2, 7.1%	3, 5.8%
CSO in Parental Family* (n, %)	13, 54.2%	16, 57.1%	29, 55.8%
IP Secondary SUD Diagnosis (n, %):			
None	19, 79.2%	23, 82.1%	42, 80.8%
Sedative-Hyp-Anx Abuse	1, 4.2%	0, 0.0%	1, 1.9%
Cannabis Abuse	0, 0.0%	2, 7.1%	2, 3.8%
Cannabis Dependence	1, 4.2%	1, 3.6%	2, 3.8%
Stimulant Dependence	0, 0.0%	1, 3.6%	1, 1.9%
Cocaine Abuse	1, 4.2%	0, 0.0%	1, 1.9%
Cocaine Dependence	1, 4.2%	1, 3.6%	2, 3.8%
Poly Drug Dependence	1, 4.2%	0, 0.0%	1, 1.9%

None of these variables showed significant between-treatment differences.

* CSO is parent, aunt, grandparent, or sibling