A Preliminary Randomized Controlled Trial of a Distress Tolerance Treatment for Opioid Dependent Persons Initiating Buprenorphine

Michael D. Stein[a,b], **Debra S. Herman**[a,b], **Ethan Moitra**[a,b], **Jacki Hecht**[b], **Rosalie Lopez**[b], **Bradley J Anderson**[b], and **Richard A. Brown**[a,b]

[a]Alpert Medical School of Brown University, Department of Medicine, Providence, RI

[b]Butler Hospital, Providence, RI

Abstract

Background—Buprenorphine opioid agonist treatment (OAT) has established efficacy for treating opioid dependency but early relapse rates are high and are often associated with withdrawal-related or emotional distress.

Methods—To determine whether a novel distress tolerance (DT) intervention during buprenorphine initiation decreases opioid relapse, we conducted a preliminary randomized controlled trial with opioid-dependent outpatients. Participants received buprenorphine-naloxone induction and 3-months of maintenance buprenorphine plus seven, 50-minute manualized, individual sessions (DT vs. Health Education (HE) control) over a 28-day period, linked to clinician medication dosing visits, and beginning 2 days prior to buprenorphine induction. Primary outcomes included use of illicit opioids (positive defined as any self-reported use in the prior 28 days or detected by urine toxicology) and treatment drop out.

Corresponding Author: Michael D. Stein, Professor of Medicine, Health Services, Policy Practice, Alpert School of Medicine at Brown University, Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906, USA, Telephone: (401) 455-6646, FAX: (401) 455-6685, Michael_Stein@brown.edu.

Results—Among 49 participants, the mean age was 41 years, 65.3% were male. Persons randomized to DT had lower rates of opioid use at all three monthly assessments, and at 3-months, 72% of HE participants were opioid positive compared with 62.5% of DT participants. Rates of dropout were 24% and 25% in the HE and DT arms, respectively.

Conclusions—This distress tolerance treatment produced a small, but not statistically significant reduction in opioid use during the first three months of treatment although no differences were found in drop-out rates between conditions. If replicated in a larger study, DT could offer clinicians a useful behavioral treatment to complement the effects of buprenorphine. Trial registered at clinicaltrials.org. Trial number NCT01556087.

Keywords

Buprenorphine; distress; relapse; opioid

1. INTRODUCTION

The nonmedical use of opioids, including prescription pain relievers and heroin, is a growing public health concern. In 2011, an estimated 2.2 million Americans met DSM-IV (APA, 1994) criteria for opioid abuse or dependence (Substance Abuse and Mental Health Services Administration, 2012). Buprenorphine, an opioid agonist treatment (OAT) that has been prescribed to more than a million individuals in the U.S. since it became available in 2003 (Boothby and Doering, 2007). Offered as an office-based maintenance treatment alternative to methadone, buprenorphine has demonstrated efficacy in reducing cravings, ameliorating withdrawal discomfort, and increasing periods of abstinence. In regard to treatment effectiveness (variously defined as reducing street crime, illicit drug use, HIV risk, or improving vocational development and psychological functioning), buprenorphine has long-term positive outcomes (Mattick et al., 2008). However, buprenorphine treatment drop-out rates are high, with observational studies reporting 50-65% retention rates at 6 months, and the great majority of attrition occurring during the *first three months* of treatment (Cunningham et al., 2008; Finch et al., 2007; Fudala et al., 2003; Lee et al., 2009; Magura et al., 2007; Mintzer et al., 2007; Soeffing et al., 2009; Stein et al., 2005).

Lapse to opioid use soon after initiation of buprenorphine is common and a strong predictor of poor treatment retention and return to chronic opioid use. Evidence from our group suggests that a significant proportion of persons initiating buprenorphine will lapse within the first week of treatment and those with a positive opioid toxicology by week four are at five times higher risk for continuing opioid use during treatment, treatment drop-out, and relapse (Stein et al., 2010). In subsequent work, we demonstrated that opioid craving, particularly during the first two weeks of buprenorphine treatment, similarly portends worse treatment outcome (Tsui et al., 2014). Thus, convergent evidence indicates that early craving and lapses to opioid use are both frequent and highly predictive of continued opioid use during buprenorphine treatment and of subsequent relapse (Stein et al., 2005, 2010).

Reasons for early attrition from buprenorphine treatment include inadequate dosing of buprenorphine, a desire to continue illicit drug use, social pressures due to a partner's or friend's drug use, and barriers to ongoing medication receipt such as cost and difficulty

keeping medical appointments (Gryczynski et al., 2014; Mattick et al., 2008; Stein et al., 2005). However, these factors do not account for all instances of relapse. Early illicit opioid lapse despite motivation for abstinence and pharmacologic treatment of acute withdrawal with buprenorphine implicates the substantial role that early events or situations play in increasing craving and motivating drug-seeking behavior (Goldstein and Volkow, 2002; Lubman et al., 2004; Robinson and Berridge, 2001). Indeed, early recovery situations and events that are associated with emotional distress, including the sensation of inadequate opioid substitution and prolonged withdrawal symptoms, continued exposure to environmental drug cues, stresses of everyday life (e.g. financial, familial), or concurrent mood disorder symptoms, reliably induce craving among treated opioid users (Hyman et al., 2007). Indeed, negative affect is well-established as a primary precipitant of early lapse and features prominently in current models of addiction maintenance and relapse (e.g., Baker et al., 2004; Hendershot et al., 2011; Witkiewitz and Marlatt, 2004), which have informed the development of behavioral treatments unrelated to opioid agonist treatment. Skills for the management and reduction of negative affect (e.g., stress management techniques, avoidance of triggers) are primary elements of these treatments. Meta-analyses indicate that cognitive-behavioral intervention for the treatment for substance use disorder is efficacious (Magill and Ray, 2009). However, recent trials evaluating cognitive-behavioral treatment (Fiellin et al., 2013; Ling et al., 2013) and additional drug counseling (Weiss et al., 2014) have not shown significant benefit over physician management for patients taking buprenorphine (Amato et al., 2011). But earlier studies have not initiated behavioral treatment prior to buprenorphine initiation in preparation for the increased challenge of opioid withdrawal and the risk of early lapse.

Research in the area of nicotine dependence has revealed that it is not solely the severity or intensity of distress, but also one's ability to tolerate both physical and psychological distress (i.e., distress tolerance) occurring in the context of withdrawal and early abstinence that predicts whether one succumbs to a lapse (Brandon et al., 2003; Brown et al., 2002, 2009; Quinn et al., 1996). In these studies, distress tolerance was measured as duration of persistence on psychological and physical challenge tasks that served as analogs for the types of stresses experienced during nicotine withdrawal.

Like nicotine withdrawal and craving, acute opioid withdrawal, which is required as part of standard clinical care in the hours prior to initiating buprenorphine, and craving in the days and weeks after the initiation of buprenorphine, produce uncomfortable interoceptive symptoms such as bone and muscle aches, restlessness, and nausea. Such experiential discomfort, to a greater or lesser degree, demands the use of distress tolerance skills in order to be successful in maintaining abstinence. Evidence suggests that opioid users are overly sensitive to the discomfort associated with anxiety symptoms (Lejuez et al., 2006; Tull et al., 2007). It seems likely then, that for those opioid users initiating buprenorphine treatment who have a low threshold for tolerating distress, and/or difficulty controlling, avoiding, or suppressing the experience of distress, ongoing illicit drug use may serve as a way to manage discomfort. These illicit substance-based efforts to avoid or escape distress are maintained by negatively reinforcing effects such as the reduction of urges or negative affect, even as euphoria is blocked by the agonist properties of buprenorphine.

Supporting this hypothesis, we have recently extended findings from research on nicotine dependence to opioid dependence. The pattern of lower persistence times on the PASAT (Paced Auditory Serial Addiction Task; Diehr et al., 1998; Holdwick and Wingenfeld, 1999) showed that the probability of opioid lapse was greatest soon after initiating buprenorphine, stabilized over subsequent weeks, and was highest among those with low persistence scores (Strong et al., 2012). Given that inability or reduced ability to tolerate distress interferes with efforts to establish longer-term opioid-free behavior change (Strong et al., 2012), individuals who are initiating buprenorphine treatment may benefit from learning new skills or strategies to tolerate these withdrawal symptoms, cravings, and negative affect during early abstinence.

In the current study, we present an adaptation of a distress tolerance treatment (DT), originally developed for smokers (Brown et al., 2008, 2013), that was tailored for opioid dependent individuals initiating buprenorphine treatment. This treatment combines behavioral exposure to opioid craving with training in skills based in Acceptance and Commitment Therapy (Hayes, 2006) to promote maintenance of abstinence. By teaching buprenorphine initiators to minimize avoidance or efforts to escape this discomfort, treatment is meant to strengthen their ability to remain opioid abstinent. We have reported on the development piloting of a novel DT treatment for buprenorphine initiators previously (Brown et al., 2014). Based on feedback from this open trial work, we have created a treatment that we now test in a preliminary randomized trial comparing the distress tolerance treatment (DT) to a health education (HE) comparison condition.

2. METHODS

2.1 Participants

Participants were recruited via advertisements (newspaper, bus). Inclusion criteria were age 18-65, seeking buprenorphine treatment, and planning to remain on buprenorphine for at least 3 months. Individuals were excluded for: current participation in methadone maintenance treatment; 15 or more days of benzodiazepine or cocaine use in the last month; daily alcohol use or binges weekly or more; medically necessary opioid treatment for chronic pain; surgery in the next 3 months; current suicidality; neuropsychological dysfunction; justice system involvement that might interfere with participation; bipolar or psychotic disorder; or pregnancy.

Between April, 2013 and October, 2013, 278 individuals were screened after calling the study line. Of these, 194 did not meet eligibility criteria for the following reasons: 65 reported bipolar symptoms or disorder, 52 had a history of psychotic symptoms, 28 had high levels of benzodiazepine, cocaine, or binge alcohol use, 21 had suicidal ideation, 17 were leaving the area in the next 3 months, and 11 were receiving methadone. Of the 84 eligible persons invited for an interview, 31 did not show up and 53 completed a baseline interview. Four were ruled ineligible (3 due to buprenorphine use and negative opioid toxicology and one due to heavy alcohol). Of the remaining 49 persons, 25 were assigned to health education (HE) and 24 to DT condition using permuted block (block sizes of 4 or 6) randomization generated by an off-site statistician.

2.2 Standard Buprenorphine Care

The office-based buprenorphine-naloxone (hereafter buprenorphine) treatment protocol included an induction day (Day 0), 12 weeks of buprenorphine maintenance treatment, and four additional weeks of buprenorphine taper. At the induction visit, under supervision, four milligrams of buprenorphine (with 1 mg of naloxone, provided as Suboxone tablets) was given sublingually to participants while they were experiencing mild-moderate opioid withdrawal (Wesson and Ling, 2003). Additional buprenorphine was taken home for use later in the day (Lee, et al., 2009) and the next day, with a total dose of 16 milligrams per day. The participant was scheduled to return two days later and given enough buprenorphine to last until the next visit five days later. Physician follow-up visits, paired with blinded assessments, were scheduled for days 7 and 14 after induction and at weeks 4, 6, 8 and 12 (the final study outcome assessment). At each physician visit, participants were given enough buprenorphine to use 16 mg per day until the subsequent appointment. After 12 weeks, the four-week buprenorphine taper began for participants unable to find a long-term provider. Participants planning to continue with another buprenorphine provider were maintained at 16mg, rather than tapering, until they transferred care at week 16. At each visit beginning at induction, brief physician management (PM) counseling was provided by either of the two study clinicians (Fiellin et al., 2006, 2002). Additionally, phone numbers for self-help groups (all off-site) were offered. Twelve-step involvement was recommended but not mandated.

2.3 DT Treatment

The DT treatment (Brown et al., 2014) was drawn from exposure-based and acceptance-based (ACT; Hayes et al., 1999) treatment approaches and adapted from our DT smoking cessation treatment (Brown et al., 2008). In order for an exposure treatment to be maximally effective, individuals must fully engage in exposure without attempts to use distraction or engage in avoidance strategies. Patients need to demonstrate a willingness to remain in this uncomfortable state as they work toward their desired goal of quitting opioids. To this end, ACT strategies were incorporated into the treatment, as ACT places a central focus on acceptance. ACT (Hayes et al., 1999) is designed to produce acceptance behaviors aimed at private events that have interfered with behaving consistently with one's life values. Acceptance may be defined as actively engaging in the process of experiencing thoughts and feelings without attempting to avoid or change these experiences (Hayes et al., 1999), as well as the behavior of approaching psychologically aversive internal stimuli while behaving adaptively (Gifford, 1994; Gifford and Hayes, 1997).

The DT treatment included seven, 40-50-minute, manualized, individual sessions over a 28-day period, with sessions occurring 1-2 days prior to buprenorphine induction, on induction day (Day 0), on the day after induction, and on days 5, 7, 14, and 28 after induction. Thus, we front-loaded the DT sessions such that the majority occurred prior to buprenorphine initiation and during the first weeks of treatment when the risk of lapse is highest (Stein et al., 2010; Tsui et al., 2014). For pragmatic reasons, and to reduce participant burden, we linked all DT and HE sessions to physician visits.

2.3.1 Sessions 1 and 2 (Day −2 and Day 0 – Buprenorphine Induction)—These first two sessions occurred prior to buprenorphine induction, the first two days prior to induction and the second just hours before induction when the participant was just starting to experience withdrawal symptoms. In Session 1, the initial discussion focused on *life values and goals*, which allowed a therapeutic alliance to develop and lay the framework for the subsequent sessions. The participant's list of values was written on an index card ("values card") so that participants could have a tangible reminder of values that might motivate distress tolerance. After therapists presented the theoretical model of drug use (physical addiction, learned habit, comfort regulation) they introduced the concept of a trigger and the distinction between external (e.g., drug cues, interpersonal conflict) vs. internal (e.g., affective, cognitive, physiological) triggers and personalized for each participant, which lay the framework for later discussions. In Session 2, because participants were experiencing sensations of opioid withdrawal in preparation for buprenorphine induction, the focus was on *exposure to withdrawal discomfort*, and included meditation exercises, the introduction of the concept of acceptance as a strategy for managing internal triggers, and included the ACT metaphor *Man in the Hole* (Hayes et al., 1999), which compares efforts to control discomfort to trying to dig one's way out of a hole as a way to highlight the futility of managing discomfort through continued illicit drug use.

2.3.2 Sessions 3, 4, and 5 (Days 1, 4, and 7)—These sessions during the first week of buprenorphine treatment involved the use of *self-management skills* for external triggers, (avoiding, altering, delaying or substituting triggers), and *acceptance and exposure* for internal triggers (through exercises and metaphors). For example, to illustrate the difficulty in controlling or avoiding thoughts, participants were asked what would happen if they were told, "Don't think about a jelly donut." They were asked to consider how avoiding this thought would be similar to trying to avoid thoughts about drug use. Through the *Quicksand* metaphor (Luoma et al., 2007), therapists illustrated how efforts to control or avoid internal experience may actually have the opposite effect, resulting in opioid use and difficulty abstaining.

Willingness was introduced using the *Two Scales* metaphor (Hayes et al., 1999) – the two scales referring to 1) intensity of discomfort and 2) degree of willingness to experience discomfort without trying to change, avoid, or escape it. It was suggested to participants that although they may try to control the discomfort scale, willingness is the only scale they actually have control over and therefore they should shift their focus to keeping the willingness scale set to maximum (willingness). As part of this component, participants explored their tendency to place limits on acceptance; for example, by making deals or bargains with themselves that they would be willing to endure discomfort only to a certain point, beyond which time they would lapse to drug use (e.g., "If I have a really bad day, then it's ok to use.").

Finally, participants used exercises designed to facilitate values clarification and engagement in values-consistent behavior. For example, they imagined themselves in 6 weeks, 3 months, 6 months, and a year as drug-free. We also used an exercise that was adapted from a eulogy exercise (Hayes et al., 1999). In this exercise, participants imagined being contacted 10 years in the future by a publisher who wanted to write their life story,

including interviews with the people closest to them. They envisioned what they would ideally want these people to say about how they lived their life.

2.3.3 Sessions 6 and 7 (Days 14 and 28)—The last two sessions occurred two weeks and four weeks after buprenorphine induction. The focus was on providing additional pportunities for exposure and practice of acceptance, willingness, and guiding the participant to create plans to: maintain a commitment to effective changes, develop and maintain social support, prepare relapse prevention strategies, and taper off buprenorphine or transition their care.

All DT sessions began with an interventionist-led five-minute mindfulness meditation exercise to foster present-moment awareness and acceptance-based skills. Each of the 7 sessions closed with the question "What's one thing you can take away from this lesson that might be helpful to you?" to better understand which concepts, metaphors and skills participants found most relevant and to help them consolidate plans for moving forward. As participants left each session, we encouraged them to review their values cards, and commit to at least one action that would help them get one step closer to living a life that is consistent with their expressed values and goals.

2.4 Health Education Control Condition

We used a Health Education (HE) intervention as a control condition. The seven, 20-30-minute individual information and education sessions were identical in their timing to the DT condition. The seven sessions covered: 1) nutrition, 2) sleep hygiene, 3) building immunity (e.g., how to avoid colds/flu), 4) relaxation strategies (e.g., progressive muscle relaxation, deep breathing etc.), 5) injury/disease prevention (e.g., seat belts), 6) the value of exercise/cardiac health, and 7) alternative medicine (e.g. acupuncture, massage). These sessions were purely didactic and consisted of health education, followed by discussion.

2.5 Therapist Training and Treatment Fidelity

The two therapists, a masters level R.N. and a post-doctoral clinical psychologist who had previous experience with ACT treatment, but had not worked with opioid dependent persons, met with Drs. Herman and Brown weekly to review audiotaped sessions and therapist adherence to the DT and HE manuals. We created manual adherence scales that included all the main elements of each section of the manual, such as the theory behind the treatment, metaphors used, and skill-building exercises, or, for the HE sessions, elements related to each of the didactic information points. Each point of adherence could be rated as Fully Adherent, Partially Adherent, or Not Adherent.

Two clinical psychologists independent of this study each rated a set of audiotaped sessions (12% of DT sessions, 8% of HE sessions) using the study Adherence Measure. DT sessions received consistent ratings 77.3% of the time with average rater ICC = .78. HE sessions received consistent ratings 87.5% of the time with average rater ICC = .74. For the DT sessions, therapists were fully adherent 96.2% of the time, and partially adherent 3.8% of the time. Therapists were fully adherent to the HE sessions 100% of the time, with no evidence of DT elements present. Participants assigned to DT participated in an average of 5.6

sessions, those assigned to HE participated in an average of 6.2 sessions. The average length of the DT sessions was 46 minutes, and of the HE sessions was 24 minutes. Both therapists conducted the DT and HE interventions.

2.6 Measures

Sample descriptors included age, gender, race or ethnicity, ever prescribed buprenorphine (yes/no). The Timeline Followback (TLFB) method (Fals-Stewart et al., 2000) was used at each assessment to assess self-reported drug consumption since the previous assessment. Urine toxicologic testing for opioids including morphine, heroin, oxycodone, and methadone was done at each assessment and physician visit.

2.7 Analytical Methods

We present descriptive statistics to summarize the characteristics of the cohort and compare intervention arms. Because this is a pilot project with a small sample size we have chosen to present measures of effect size and 95% confidence interval estimates. For our primary outcome (any self-reported illicit opioid use in the last 28 days or urine toxicology positive for opioids at each monthly assessment), we present counts and percentages. We also present the between group difference in percent (calculated as the percentage in the HE arm – the percentage in the DT arm) and the 95% confidence interval estimate for that difference. Additionally, we report the population averaged odds-ratio, estimated by GEE, comparing DT to HE across time (Hardin and Hilbe, 2002). The GEE model included baseline frequency of self-reported illicit opioid use and time as covariates. Statistical comparisons of self-reported frequency of illicit opioid use during follow-up were problematic (see results). We describe these continuous distributions in detail and report descriptive statistics by intervention arm and assessment period.

When planning this pilot study we anticipated floor effects. Specifically, we expected a relatively high proportion of participants in both study arms would have substantial improvements with respect to opioid outcomes as a result of initiating buprenorphine treatment. Thus, a priori we determined that a 10% difference in opioid positive outcomes at follow-up would represent a clinically meaningful improvement.

3. RESULTS

Participants averaged 41.1 (± 11.3) years of age, 32 (65.3%) were male, and 42 (85.7%) were non-Latino White (Table 1). Fourteen (28.6%) reported they had ever received prescribed buprenorphine. The mean rate of illicit opioid use in the 30 days prior to baseline was 25.2 (± 7.1) days. Background characteristics were similar across groups although the HE arm tended to have a higher percentage of non-Latino Whites (92.0%) than the DT arm (79.2%).

A total of 12 participants (24.5%) dropped out of treatment; rates of dropout were 24% and 25% in the HE and DT arms, respectively (Table 1). Five subjects (2 randomized to HE and 3 randomized to DT) had dropped out of the treatment protocol by week 1, 5 additional subjects (2 randomized to HE and 3 randomized to DT) had dropped out prior to the 1-month follow-up, and 2 more (both in the HE arm) dropped out prior to receiving their last

buprenorphine prescription. Ten subjects were opioid abstinent (defined as no positive or missed toxicology tests at months 1-, 2-, or 3-months, and no self-reported illicit opioid use on the TLFB during the 3-month follow-up). Six (25.0%) participants randomized to DT and 4 (16.0%) of participants randomized to HE were opioid abstinent.

Concordance between self-reported opioid use and urine toxicology results during follow-up was good. Of 52 positive toxicology tests, only 1 subject failed to self-report illicit opioid use during the corresponding assessment period. Participants self-reported opioid use on 18 occasions which were not confirmed by toxicology screens; this was not unexpected given the 30-day self-reporting period and the shorter time frame for opioid use captured by toxicologic testing.

Table 2 gives between group differences with respect to any opioid use a 1-, 2-, and 3-month assessments. The intent-to-treat analysis assumes all persons who dropped out of treatment were using opioids. Persons randomized to DT had lower rates of opioid use at all three follow-ups, though between group differences were substantively small. At 2-months the difference was 56.0% (HE) compared to 50.0% (DT), and at 3-months 72% of persons randomized to HE were opioid positive compared with 62.5% of persons randomized to DT. The as-treated analysis gives results that are generally consistent with the intent-to-treat analysis (Table 2). The estimated population-averaged OR, adjusted for month and baseline frequency of opioid use, was 0.68 (95%CI 0.25; 1.84) for the intent-to-treat analysis and 0.59 (0.20; 1.68) for the as-treated analysis.

In Table 3 we give the categorical distribution of self-reported opioid use frequency by intervention arm and follow-up assessment. As expected, in both study arms, mean and median frequency of self-reported illicit opioid use was much lower during follow-up than at baseline. The distributions are extremely skewed with the modal response category at the lower limit of 0. Most participants who report any use report using illicit opioids on only 1-2 days during any assessment period. At all 3-time points, between group differences in mean frequency of use are lower in DT arm than in the HE arm.

4. DISCUSSION

We tested the preliminary efficacy of a distress tolerance intervention to reduce ongoing illicit opioid use among person initiating buprenorphine treatment and found a small improvement in opioid use during the first three months of treatment compared to a health education control condition. This DT treatment incorporates elements from exposure-based and acceptance-based treatment approaches and participants demonstrated good treatment attendance by associating the behavioral intervention sessions with buprenorphine dosing visits.

Accumulating evidence indicates that ACT is an efficacious treatment approach across a variety of clinical problem areas, such as affective disorders (Zettle, 1984; Zettle and Hayes, 1986; Zettle and Rains, 1989) and anxiety disorders, including obsessive-compulsive disorders, agoraphobia (Hayes, 1987; Hayes et al., 1990), stress in the workplace (Bond and Bunce, 2000), and social anxiety (Block, 2002). Although a number of studies have shown

promising results for smoking cessation (Bricker et al., 2010; Brown et al., 2008, 2011, 2013; Gifford et al., 2004; Hernandez-Lopez et al., 2009), very limited research has examined the use of ACT for the treatment of other substance use disorders such as opioid dependence (Hayes et al., 2004; Stotts et al., 2012, 2009). We chose to focus on buprenorphine initiators because this growing population is at high risk for treatment drop-out and drug relapse, and seeks addiction treatment in primary care settings, which are increasingly involving behavioral health specialists and counselors (Butler et al., 2008), and offer the opportunity to begin a behavioral intervention prior to an induction date. Given that inability or reduced ability to tolerate distress interferes with efforts to establish longer-term opioid-free behavior change (Strong et al., 2012), we hypothesized that persons initiating buprenorphine treatment might benefit from learning new skills or strategies to tolerate the discomfort of withdrawal symptoms, cravings, and negative affect during early abstinence.

Although the rate of illicit opioid use was lower at the 1, 2 and 3 month assessments, there was no difference by treatment assignment in persons leaving treatment, a signal of relapse to drug use. The DT treatment had a modest positive effect on illicit opioid use. Readers should note that sample size was small and 95% confidence interval estimates were large and failed to exclude 0. We offer several explanations for this result. First, much of the distress of withdrawal, necessary at the time of buprenorphine initiation but transient, was ameliorated by the medication itself. Opioid replacement may have lessened the effect of a behavioral intervention; we chose a buprenorphine dose (16 mg) associated with rates of retention higher than rates seen in studies of 8 mg (Mattick et al., 2008). Still, fixed buprenorphine dosing is a study limitation; symptom-based dosing may lead to higher average daily doses greater than 16mg and perhaps better outcomes (Weiss et al., 2014). Over one-third of participants were fully abstinent over the 3-month follow-up; most others reported only infrequent used of illicit opioids (to be positive at the monthly assessment a participant had to report *any* use during the month or have a positive toxicology). In addition, persons assigned to HE received the structure associated with multiple medical visits and counseling sessions, which may have further mitigated finding strong effects of the DT treatment. Second, the intervention, based in metaphor, was linguistically abstract, and we believe this intervention could improve with the use of more concrete ways to use acceptance-based techniques. .Still, the low level of illicit opioid use through all three months of treatment suggests the power of external triggers. As devised, our DT intervention may not have provided tools to develop alternative strategies to combat these triggers. We interpret the lack of statistically significant differences in our primary outcomes cautiously as our study was likely underpowered (Kraemer et al., 2006). Our focus instead, was on testing preliminary efficacy of DT *and* to determine if a larger-scale, fully powered trial, would be worthwhile in this population.

We achieved approximately a 10% difference in opioid use by the three-month assessment, the a priori target for meaningful group difference. It remains possible that we could have seen a greater effect beyond three months when our intervention's focus on the identification of personal values might engender a greater willingness to persist in choosing not to use opioids when provoked by craving or negative affect. Abstinence-oriented approaches for the treatment of opioid dependence that complement buprenorphine, such as our DT

treatment, will be necessary to optimize outcomes. If a 10% difference in opioid use is considered to have important clinical and public health meaning, our DT intervention may be worthy of testing in a large clinical trial.

Acknowledgments

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Highlights

- Distress Tolerance (DT) participants had high rates of session attendance, demonstrating feasibility

- DT participants had lower rates of opioid use at all follow-up assessments vs health education (HE)

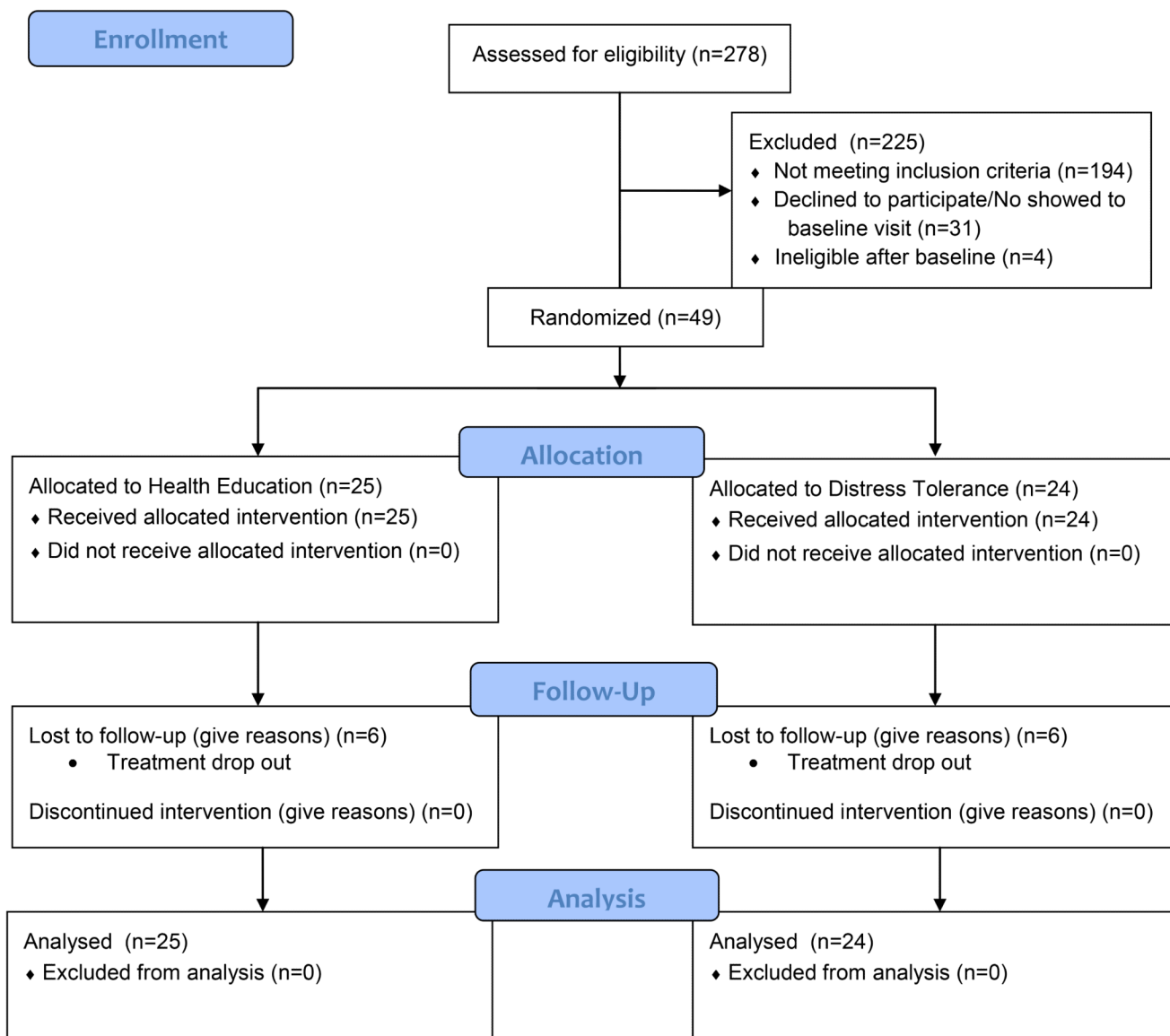- Rates of buprenorphine dropout were 24% and 25% in the HE and DT arms, respectively

Figure 1.
Participant Flow Diagram

Table 1

Participant Characteristics by Intervention Arm.

	Cohort (n=49)	HE (n=25)	DT (n=24)	Diff (95% CI)[a]
Age	41.1 (± 11.3)	40.6 (± 12.0)	41.7 (± 10.8)	−1.1 (−7.6; 5.5)
Gender (Male)	32 (65.3%)	16 (64.0%)	16 (66.7%)	2.7 (−29.3; 24.0)
Non-Latino White (Yes)	42 (85.7%)	23 (92.0%)	19 (79.2%)	12.8 (−6.5; 32.3)
Ever Prescribed Buprenorphine (Yes)	14 (28.6%)	6 (24.0%)	8 (33.3%)	−9.3 (−34.6; 15.9)
Days / 30 Non RX Opioid Use[b]	25.2 (± 7.1)	24.6 (± 8.7)	26.0 (± 5.0)	−1.4 (−5.5; 2.7)
Dropped Out of Treatment (Yes)	12 (24.0%)	6 (24.0%)	6 (25.0%)	−1.0 (−25.1; 23.1)
Opioid Abstinent at 3 months (Yes)	10 (20.4%)	4 (16.0%)	6 (25.0%)	9.0 (−13.5; 31.5)

[a]Between group difference in mean or % and 95% confidence interval estimate.

[b]Days / 30 days participants reported using opioids on the baseline time-line follow-back.

Table 2

Any Opioid Use[a] by Intervention Group and Month of Follow-Up.

	INTENT TO TREAT[b]			AS TREATED[c]		
Opioid + at	HE (n = 25)	DT (n = 24)	Diff (95% CI)[d]	HE (n =[e])	DT (n =[f])	Diff (95% CI)[c]
Month 1	15 (60.0%)	14 (58.3%)	1.7 (−25.9; 29.2)	11 (52.4%)	8 (44.4%)	7.9 (−23.4; 39.3)
Month 2	14 (56.0%)	12 (50.0%)	6.0 (−21.9; 33.9)	8 (42.1%)	6 (33.3%)	8.8 (−22.3; 39.9)
Month 3	18 (72.0%)	15 (62.5%)	9.5 (−16.7; 35.7)	10 (58.8%)	9 (50.0%)	8.8 (−24.1; 41.7)

[a] Any self-reported opioid use or positive urine toxicology test at 1-, 2-, or 3-month assessments.

[b] Assumes dropouts were opioid positive.

[c] Observed data from participants in the study protocol.

[d] Between group difference in % testing opioid+ and 95% confidence interval estimate for the between group difference.

[e] The number of available observations were 21, 19, and 17 at 1-, 2-, and 3-month assessments, respectively.

[f] The number of available observations was 18 at all follow-ups.

Table 3

Distribution of Self-Reported Illicit Opioid Use by Intervention Group and Month of Follow-Up.

DAYS USED	MONTH 1		MONTH 2		MONTH 3	
	HE (n = 21)	DT (n = 18)	HE (n = 19)	DT (n = 18)	HE (n = 17)	DT (n = 18)
None	10 (47.6%)	11 (61.1%)	12 (63.2%)	14 (77.8%)	10 (58.8%)	10 (55.6%)
1-2 Days	6 (28.6%)	6 (33.3%)	5 (26.3%)	4 (22.2%)	5 (29.4%)	7 (38.9%)
3-5 Days	4 (19.0%)	1 (5.6%)	1 (4.3%)	0 (0.0%)	0 (0.0%)	1 (5.6%)
6-10 Days	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
11-20 Days	1 (4.8%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (5.9%)	0 (0.0%)
> 20 Days	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)
Mean (± SD)	1.67	0.67	1.68	0.39	2.29	0.72
SD	2.83	1.24	4.57	0.78	5.25	1.07
Median	1.0	0.0	0.0	0.0	0.0	0.0