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# A randomized trial of transcutaneous electric acupoint stimulation as adjunctive treatment for opioid detoxification

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## Abstract

This pilot study tested the effectiveness of transcutaneous electric acupoint stimulation (TEAS) as an adjunctive treatment for inpatients receiving opioid detoxification with buprenorphine-naloxone at a private psychiatric hospital. Participants (N = 48) were randomly assigned to active or sham TEAS and received three 30-minute treatments daily for 3-4 days. In active TEAS, current was set to maximal tolerable intensity (8-15 mA); in sham TEAS, it was set to 1 mA. By 2 weeks post-discharge, participants in active TEAS were less likely to have used any drugs (35% vs. 77%, $p < .05$). They also reported greater improvements in pain interference ($F = 4.52$, $p < .05$) and physical health ($F = 4.84$, $p < .01$) over time. TEAS is an acceptable, inexpensive adjunctive treatment that is feasible to implement on an inpatient unit and may be a beneficial adjunct to pharmacological treatments for opioid detoxification.

### Keywords

transcutaneous electric acupoint stimulation; opioid detoxification; opioid dependence; randomized clinical trial

## 1. Introduction

Opioid dependence is a major public health concern, with prescription opioid abuse rapidly becoming one of the biggest drug problems in the United States. In 2007, an estimated 1.4 million Americans abused oxycodone and 366,000 abused heroin (SAMSHA, 2008). In a nationally representative sample, 0.1% met full diagnostic criteria for opioid dependence within the past year (Compton, Thomas, Stinson, & Grant, 2007). The social, medical, and

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economic consequences of opioid dependence are profound, including lost productivity, crime and violence, disrupted relationships, HIV/AIDS and other diseases, and death (Hser, Hoffman, Grella, & Anglin, 2001; Institute of Medicine, 1997).

Physiological dependence on opioids can be severe, and withdrawal is characterized by acute symptoms, such as nausea, chills, sweating, muscle cramps, loss of appetite, irritability, and insomnia (APA, 2000). Pharmacological treatment is often used to ease withdrawal. Sublingual buprenorphine combined with naloxone (bup-nx) is an increasingly common treatment for opioid detoxification (Jones, 2004). Buprenorphine, a partial μ-opioid agonist and κ-opioid antagonist, blocks the effects of opioids and mitigates withdrawal symptoms (Walsh & Eissenberg, 2003). Unfortunately, relapse to drug use often occurs within 1 month of detoxification, with many individuals using drugs within days of discharge (Gossop, Stewart, Browne, & Marsden, 2002; Ling et al., 2005). Factors associated with relapse include withdrawal symptoms (Gossop, Green, Phillips, & Bradley, 1989; Soyka, Zingg, Koller, & Kuefner, 2008), craving (Bradley, Phillips, Green, & Gossop, 1989; Heinz et al., 2006), psychiatric distress (Hser, 2007; Llorente del Pozo, Fernandez Gomez, Gutierrez Fraile, & Vielva Perez, 1998), physical pain (Larson et al., 2007; Potter, Prather, & Weiss, 2008), and sleep disturbance (Burke et al., 2008).

In a 2003 review of clinical trials, the World Health Organization listed drug abuse as one of the many disorders for which acupuncture may have a therapeutic effect (Zhang, 2003). A number of randomized trials investigating auricular acupuncture for cocaine dependence have yielded disappointing results (Avants, Margolin, Holford, & Kosten, 2000; Killeen et al., 2002; Margolin, Avants, & Arnold, 2005; Margolin et al., 2002), bringing into question the effectiveness of traditional needle acupuncture as a stand-alone treatment for cocaine dependence. However, studies examining acupuncture for opioid dependence have been somewhat more promising. In the early 1970s, a report from Hong Kong suggested that opioid withdrawal could be successfully treated with a method of acupuncture that includes electrical stimulation (Wen & Cheung, 1973). In North America, only two randomized clinical trials of acupuncture for opioid dependence have been conducted, and both of these tested auricular acupuncture without stimulation among patients receiving outpatient treatment. The first study found that participants who received active compared to sham acupuncture remained in treatment for longer, but overall retention was very low (Washburn et al., 1993). The second study, conducted in a methadone clinic, found that participants who received active versus sham acupuncture did not differ on treatment attendance, withdrawal symptoms, or drug use (Wells et al., 1995). An alternative method of acupuncture, called transcutaneous electric acupoint stimulation (TEAS), uses skin electrodes to apply electrical stimulation to acupoints. In China, randomized clinical trials have found that patients who receive active compared to sham stimulation experience less severe heroin withdrawal symptoms during inpatient detoxification (Han, Wu, & Cui, 1994; Wu, Cui, & Han, 1995). In another study of Chinese patients receiving inpatient heroin detoxification with buprenorphine found that those who also received TEAS required a lower dosage of buprenorphine over the 14-day protocol (Wu, Cui, & Han, 1999). Similar results were found in a subsequent study of inpatients receiving heroin detoxification with methadone (Wu, Cui, & Han, 2001). Observational studies conducted in China have found that TEAS may also reduce the risk of relapse up to 12 months following detoxification when patients administer treatments at home as needed; however, control groups were not included (Han, Trachtenberg, & Lowinson, 2005; Han, Wu, & Cui, 2003). In sum, further research is warranted on the potential benefits of TEAS for opioid dependence among patients receiving treatment in the United States.

The purpose of this pilot study was to test the effectiveness of TEAS as an adjunctive treatment for patients receiving inpatient opioid detoxification with bup-nx. This trial was randomized, sham-controlled, and single-blind. Since all patients received bup-nx, we expected that both

groups would experience reductions in withdrawal symptoms and craving during detoxification. Our primary hypothesis was that participants receiving active TEAS, compared to those receiving sham TEAS, would maintain abstinence from drug use for longer following detoxification. Secondarily, we examined whether participants receiving active TEAS might also experience greater improvements in withdrawal symptoms, craving, physical pain, sleep quality, and health status during and following detoxification.

## 2. Materials and Methods

### 2.1. Participants

Participants were men and women 18-59 years of age who sought inpatient opioid detoxification at the Alcohol and Drug Abuse Treatment Program at McLean Hospital between August 21, 2007 and July 24, 2008. They had a diagnosis of opioid dependence and required medical management of opioid withdrawal (i.e., detoxification with bup-nx). Co-dependence on other substances did not exclude individuals unless immediate medical attention was required to manage withdrawal. For safety reasons, individuals with acute mania, psychosis, or suicidality or a history of seizure disorder or heart disease, including use of a pacemaker, were excluded. Female participants were required to have a negative pregnancy test.

Figure 1 outlines the flow of participants through the trial. Among 177 patients who were admitted to the unit with a diagnosis of opioid dependence, 98 (55%) were not eligible. An additional 4 were not approached due to temporary staff shortage. Among the remaining 75 participants, 63 (84%) were enrolled into the study, and 55 (87%) were randomized. An equal number of participants in each condition completed treatment (92% vs. 83%, $\chi^2(1) = 1.12$, $p = .29$). Reasons for discontinuation were: 3 withdrawals (2 unexpectedly required medical management of benzodiazepine withdrawal, 1 became ill with flu-like symptoms unrelated to TEAS) and 4 dropouts (3 refused the baseline assessment, 1 attributed severe withdrawal symptoms to TEAS (this individual was in the sham condition)). Thus, the final sample included 48 treatment completers. Of these, 35 completed at least one of the 2 follow-ups, with no difference between participants in active and sham TEAS (75% vs. 71%, $\chi^2(1) = .11$, $p = .75$).

### 2.2. Procedures

This was a single-blind, sham-controlled, randomized clinical trial in which participants received either active or sham TEAS. Each weekday morning, new admissions were reviewed for eligibility. The attending psychiatrist assessed individuals' competency to provide informed consent before research staff approached them about the study. Participants provided written informed consent and a one-way release allowing research staff to extract data from their medical record.

Participants were randomly assigned to one of the two treatment conditions, with participants blinded to their assignment. To maintain the blind, all participants enrolled in a given week were assigned to the same condition, with that condition assigned at random each week. When two or more participants were enrolled in the same week, treatments occurred in close proximity in terms of time and space on the inpatient unit. Moreover, patients often interacted throughout their hospitalization. If they had been assigned to different treatment conditions, this would have been apparent (one would have experienced strong sensation, typically producing a twitch, the other would have felt no stimulation), possibly breaking the blind. Because patients admitted to the unit on weekends were not recruited, this system ensured that there was no overlap of participants randomized to one condition on a given week and those randomized to another condition on the next week. The random sequence was generated by computer and assigned by a research staff member who was uninvolved in recruitment,

enrollment, or assessment. After the first participant of the week was enrolled, he revealed the assignment to the person responsible for administering treatments.

The first treatment was delivered after the first dose of bup-nx and as soon as possible after enrollment. Treatments were typically delivered in the morning (8-10 AM), late afternoon (3-5 PM), and evening (9-11 PM), with at least 4 hours between treatments. In addition to bup-nx and TEAS treatments, all participants received individual and group substance abuse counseling during their inpatient detoxification.

Participants completed assessments on the day of enrollment (baseline), immediately prior to discharge (discharge), and at 1- and 2-weeks post-discharge (1- and 2-week follow-ups, respectively). A short follow-up period was chosen because the effects of a 4-day TEAS protocol were believed to be short-lived following treatment cessation. Participants received $45 for each follow-up visit, plus a $20 bonus for completing both visits. Study procedures were approved by the institutional review board at McLean Hospital.

### 2.3. Intervention

Participants received three 30-minute TEAS treatments daily for up to 4 days while on the inpatient unit; 4 days was the mean, median, and modal length of stay for patients receiving opioid detoxification with bup-nx. The Han's Acupoint Nerve Stimulator (Hans International Inc, Beijing) was used to transcutaneously deliver TEAS via skin electrodes and electroconductive pads. No needles were used. As in prior studies (Han et al., 1994; Wu, 1999; Wu et al., 1995), the “hegu” and “neiguan” acupoints were stimulated. The first set of electrodes was placed on the dorsal and palmar surface of one hand between the first and second metacarpal bones. The second set of electrodes was placed on the dorsal and ventral surface of the other forearm across the median nerve. The frequency of stimulation alternated between 2 and 100 Hz at 3-second intervals. In active TEAS, the current was increased in 1 mA increments to maximal tolerable intensity (a strong but not painful sensation, typically producing a twitch). At “hegu” site, the level of stimulation ranged from 6 to 15 mA (M = 8.86, SD = 2.04). At the “neiguan” site, it ranged from 8 to 15 mA (M = 10.57, SD = 1.97). In sham TEAS, the level of stimulation was set at 1 mA, which was undetectable. Participants were told that the study was investigating different types of stimulation. During setup, the HANS device was held so that participants were unable to see the amount of stimulation administered. The HANS device is programmed so that it locks once the current level is set, with the frequency and intensity of stimulation blocked from view; it automatically shuts off after 30 minutes. Nevertheless, participants were monitored to ensure that they received the full treatment at the proper level of stimulation.

Dr. Ji-Sheng Han, developer of the HANS device, provided an in-depth training to Dr. Meade and Ms. Eldridge. They, in turn, trained study staff (research assistants and nurses) through didactics, demonstrations, and practice sessions. Staff were certified to administer treatments only after they demonstrated pre-specified competency in operating the apparatus, delivering both active and sham TEAS, and answering questions about the treatment.

### 2.4. Measures

**Substance use—**An abbreviated version of the Addiction Severity Index was administered at baseline to assess severity of problems in medical, occupational, drug, alcohol, legal, social, and psychiatric domains (McLellan et al., 1992). The timeline follow-back methodology was used to assess substance use in the 30 days prior to admission. At follow-up visits, participants reported day-by-day substance use since the previous interview. This data was recoded to yield three key variables: any use in the 2 weeks post-discharge (yes/no), number of days of drug use during those 2 weeks (frequency), and number of days to first drug use (if applicable).

Supervised urine samples were collected, typically at the beginning of each visit, to corroborate self-reports. Drug screens were coded quantitatively as positive or negative for drug metabolites of morphine, methadone, oxycodone, cocaine, methamphetamine, marijuana, amphetamine, and benzodiazepines.

**Secondary outcomes—**Opioid withdrawal was assessed using the Subjective Opiate Withdrawal Scale, a 21-item measure of the severity of current opioid withdrawal signs and symptoms (Handelsman et al., 1987). Scores range from 0 to 84; higher scores indicate greater symptoms. Opioid craving in the past 24 hours was assessed using a 3-item scale that utilizes a 10-point visual analog scale (Weiss et al., 1997). Scores range from 3 to 30; higher scores indicate greater craving. Physical pain in the past 24 hours was assessed using the Brief Pain Inventory, which has subscales for pain severity (4 items) and pain interference (7 items) (Cleeland & Ryan, 1994). Scores range from 0 to 10; higher scores indicate greater severity and interference. The Pittsburgh Sleep Quality Index, a 19-item questionnaire, was used to assess global sleep quality in the past week (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Scores range from 0 to 21; higher scores indicate poorer sleep quality. Physical and mental health status were assessed using the acute form of the Medical Outcomes Survey short-form survey, a 36-item questionnaire that assesses functional health and well-being in the past week (Keller et al., 1997). Scores range from 0 to 100; higher scoring indicate better health status (Ware, Kosinski, & Dewey, 2001).

### 2.5. Data analysis

The primary outcome was presence or absence of any drug use in the first 2 weeks post-discharge. This was based on self-reported TLFB data, corroborated by urine screen. That is, if participants self-reported any drug use during the follow-up period and/or had a positive urine screen at one or both of the follow-up visits, they were coded as having used drugs. Chi-square analysis was used to compare the rate of any drug use and any opioid use by treatment condition. T-tests were used to compare days of drug use and opioid use by treatment condition. Cox survival analysis was used to examine number of days to first drug use by treatment condition. The secondary outcomes were opioid withdrawal, opioid craving, pain severity and interference, sleep quality, and physical and mental health status. Mixed model analyses were used to examine treatment effects on changes from baseline to discharge, 1-week follow-up, and 2-week follow-up. This type of analysis appropriately accounts for the correlation among the 4 repeated measures of the secondary outcomes and allows for incompleteness due to missing data. Comparison of the treatment groups in terms of their patterns of change from baseline translate into treatment-by-time interaction effects.

## 3. Results

### 3.1. Participant characteristics

Table 1 describes participant characteristics by treatment condition. Overall, the sample included 33 men and 15 women ranging in age from 18 to 57 years. Most were Caucasian (88%), single (77%), and high school educated (94%). Despite randomization, participants in sham TEAS had 1.5 more years of education than those in active TEAS ($p < .05$). Half of the sample used heroin, and the rest used other opioids (e.g., oxycodone, methadone). In the 30 days prior to admission, participants reported an average of 24.0 days of opioid use. Participants in the two treatment conditions did not differ on principal drug used, days of substance use, severity of opioid dependence, or severity of problems in medical, occupational, drug, alcohol, legal, social, or psychiatric domains.

Follow-up data was available for 35 participants (73%), with no difference between treatment conditions. Participants who did not return lived farther from the hospital (M = 31.1 miles, SD

= 23.2) compared to those who did return (M = 21.1 miles, SD = 16.1), but this difference was not significant. Participants who did not return also had lower alcohol severity (M = .04, SD = .06 vs. M = .14, SD = .19; t(46) = -2.74, $p = .01$). They did not differ on any other demographic or substance abuse variables.

### 3.2. Intervention characteristics

Participants received an average of 9.1 TEAS treatments (SD = 1.33) and missed an average of 0.38 treatments (SD = .67), with no difference between treatment conditions. In four cases (< 1% of all treatments), participants in sham TEAS received an active "dose" of stimulation for one of their treatments. During one session, one participant reported pain and discontinued treatment after 10 minutes; the level of stimulation was subsequently decreased slightly, and this individual completed all remaining treatments.

All participants received a bup-nx taper. They received an average of 31.42 mg (SD = 6.16) across 9 doses (SD = 1.38) administered over 3 or 4 days. Many participants received ancillary medications for sleep (90%; e.g., diphenhydramine, zolpidem) and pain (33%; e.g., ibuprofen, acetaminophen). There were no differences between treatment conditions.

To evaluate the success of the blinding, participants were asked at follow-up to indicate whether or not they had received an "effective dose" of treatment. Participants in the active and sham conditions were equally likely to report yes versus no or unsure (56% vs. 50%; $\chi^2(2) = .36$, $p = .84$).

### 3.3. Drug use following discharge

As shown in Table 2, by 2 weeks post-discharge, participants in sham TEAS, compared to those in active TEAS, were more than twice as likely to have used any drugs (relative risk = 2.2; 77% vs. 35%; $p < .05$) and opioids (relative risk = 2.2; 29% vs. 65%; $p < .05$). If one were to assume that participants who did not return for follow-up had relapsed, participants in the sham condition were still significantly more likely to have used any drugs (relative risk = 1.54; 83% vs. 54%; $p < .05$) and opioids (relative risk = 1.50; 75% vs. 50%; $p < .05$). Participants in sham TEAS also used drugs and opioids on more days in the 2 weeks following discharge, but these differences were not statistically significant. Figure 2 shows that participants in sham TEAS, compared to those in active TEAS, were more likely to begin using drugs after fewer days following discharge. This difference was significant ($\chi^2(1) = 3.87$, $p < .05$), yielding a hazard ratio of 2.65.

### 3.4. Secondary outcomes

Table 3 presents the mean values for each secondary outcome by treatment condition at baseline, discharge, and 1- and 2-week follow-ups. It also summarizes the results of the mixed model analyses examining the effect of treatment on changes in secondary outcomes over time. There were significant treatment by time effects for pain interference ($p < .05$) and physical health ($p < .01$). These results indicate that participants in active TEAS, compared to those in sham TEAS, had greater decreases in pain interference between baseline and discharge (B = -1.33, SE = 0.65, t(43) = -2.03, $p < .05$) and 2-week follow-up (B = -2.52, SE = 0.83, t(38) = -3.05, $p < .01$). That is, participants in active TEAS had additional decreases of approximately 1.3 units on pain interference at discharge and an additional 2.5 unit decrease at 2-week follow-up. For physical health, treatment effects did not emerge until the 2-week follow-up (B = 5.51, SE = 2.40, t(28) = 2.30, $p < .05$). That is, participants in active TEAS had an additional 5.5 unit increase on physical health at 2-week follow-up. Because return to drug use could affect these outcomes, the analyses were rerun controlling for drug use; results did not change for pain interference (F = 4.63, $p < .05$) or physical health (F = 3.81, $p < .05$). There was no

significant treatment by time effect for opioid withdrawal, opioid craving, pain severity, sleep quality, or mental health.

## 4. Discussion

The results of this study suggest that TEAS, administered as an adjunctive treatment to bup-nx during inpatient detoxification, may contribute to improved outcomes in patients with opioid dependence. Following discharge from the hospital, participants who received active TEAS abstained from drugs for longer. They were more than two times less likely to have used drugs by the 2-week follow-up visit: only 35% of participants in the active condition had used drugs compared to 77% of those in the sham condition. While a brief course of TEAS is unlikely to have long-lasting effects, the results of this trial are encouraging. Further research should examine the possible benefits of longer-term TEAS offered after detoxification to reduce the risk of relapse.

Participants in the active TEAS condition reported significantly greater improvements in pain interference and overall physical health during follow-up. These improvements may have been a direct result of the TEAS, or may have occurred secondarily through drug abstinence. Prior studies have found that TEAS is an effective treatment for chronic pain (Ng, Leung, & Poon, 2003; Sator-Katzenschlager et al., 2004; Xue et al., 2004; Zheng et al., 2008) and contributes to improved physical health (Ghoname et al., 1999; Hamza et al., 2000; Sallam, McNearney, Doshi, & Chen, 2007). Many individuals with opioid dependence experience co-occurring pain (Potter et al., 2008), which is often a trigger for relapse (Larson et al., 2007). Thus, among patients undergoing opioid detoxification, TEAS may help mitigate the effects of physical pain and promote improvements in physical health, which in turn may help prevent relapse. Future research is needed to identify the mechanisms through which TEAS works.

While this study was not designed to test the mechanism of action of TEAS, prior research has found that it accelerates the production and release of neuropeptides in the central nervous system that interact with different opioid receptors to ease pain and withdrawal symptoms and produce other physiological effects (Han, 2004). Low frequency (2 Hz) TEAS accelerates the release of endomorphin, enkephalin, and β-endorphin that interact with μ- and δ-opioid receptors, whereas high frequency (100 Hz) TEAS accelerates the release of dynorphins that interact with κ-opioid receptors (Chen & Han, 1992; Han, Ding, & Fan, 1986; Han & Wang, 1992). Stimulation that alternates between 2 and 100 Hz produces the simultaneous release of all four opioid neuropeptides, resulting in maximal therapeutic effects (Chen & Han, 1992; Han et al., 1986; Han & Wang, 1992). Human studies have confirmed that alternating frequency of stimulation is most effective for the treatment of pain (Hamza, White, Ahmed, & Ghoname, 1999) and opioid withdrawal (Wu, 1999). Thus, activation of the endogenous opioid system by TEAS may help prevent rapid relapse to drug use following detoxification, but further research is needed to further delineate the mechanisms of action.

In contrast to previous studies (Han et al., 1994; Zeng, Lei, Lu, & Wang, 2005), TEAS did not yield greater improvements in opioid withdrawal symptoms or opioid craving during treatment. This null finding may be due to the co-occurring use of bup-nx, which is highly effective in reducing opioid withdrawal symptoms and craving (Ling et al., 2005; O'Connor et al., 1997; Oreskovich et al., 2005). As expected, participants in both TEAS conditions reported substantial improvements in withdrawal symptoms and craving during inpatient detoxification, possibly causing a floor effect. TEAS also did not have a significant effect on mental health or sleep quality. Previous research has found that TEAS can be effective in the treatment of depression (Han, Li, Luo, Zhao, & Li, 2004; Luo, Meng, Jia, & Zhao, 1998) and insomnia (Tsay, Cho, & Chen, 2004; Xiao & Liu, 2008). However, in these studies, treatments were administered over 2 to 6 weeks and stimulated different acupoints. Therefore, the duration of

treatment and choice of acupoints in the current study may not have been optimal for treating psychiatric symptoms or insomnia.

The results of this pilot study suggest that TEAS is an acceptable adjunctive treatment for patients seeking inpatient opioid detoxification. Most patients who were approached about the trial chose to enroll. The treatment was feasible to implement on a busy inpatient unit, and the TEAS sessions were well tolerated with minimal side effects. In clinical practice, patients could be taught to self-administer the TEAS treatments. In sum, TEAS is a simple and inexpensive treatment that may be a beneficial adjunct to pharmacological opioid detoxification.

This study has several limitations. First, the sample size was modest, possibly limiting power to detect treatment effects. The results of this study should be considered preliminary, and replication with larger samples is indicated. Nevertheless, we found significant effects for drug use, pain interference, and physical health. Second, all participants (sham and active TEAS) received bup-nx to ease withdrawal symptoms, which may have masked some of the effects of TEAS (e.g., withdrawal, craving). Third, the duration of treatment was brief, occurring over 3 to 4 days, and we expected the effects of TEAS to be short-lived. Therefore, we chose a 2-week follow-up period intended to assess acute effects. With a longer follow-up, it would have been more difficult to attribute group differences to the TEAS treatment. Further research is needed to determine the optimal duration of treatment and longer-term effects. Fourth, due to limited resources, only treatment completers were followed. Fortunately, there were few non-completers, with fewer in the active condition, so this is unlikely to have had a significant effect. Fifth, participants in the active condition had fewer years of education. While statistically significant, this difference was small and could be attributed to chance alone (given nearly 20 baseline comparisons); if anything, it would be expected to predict poorer outcomes among participants in the active condition. Finally, the results may not generalize to all opioid dependent individuals, including those seeking treatment in the public sector or other areas of the world. In sum, results should be replicated in studies with larger, more diverse samples and longer treatment protocols and follow-up periods.

This study also had a number of noteworthy strengths. It was a randomized, sham-controlled, single-blind trial. Participants in both TEAS conditions received the same treatment, differing only in the level of stimulation, so results cannot be attributed to increased attention. Furthermore, the sham treatment was believable, with participants in both conditions being equally likely to report that the treatment was effective. Finally, the acceptance rate was high, yielding a fairly representative sample of patients receiving inpatient opioid detoxification at McLean Hospital.

## 5. Conclusion

Opioid dependence is a chronic relapsing disorder, with relapse to drug use frequently occurring within a month of detoxification (Gossop et al., 2002; Ling et al., 2005). Indeed, over half of participants in this sample used drugs within 2 weeks of discharge. The need for improved treatments for opioid dependence is clear. The results of this study suggest that adjunctive TEAS may lead to improved physical health and protect against relapse. Ongoing research is needed to further explore the potential benefits of TEAS for opioid dependence.

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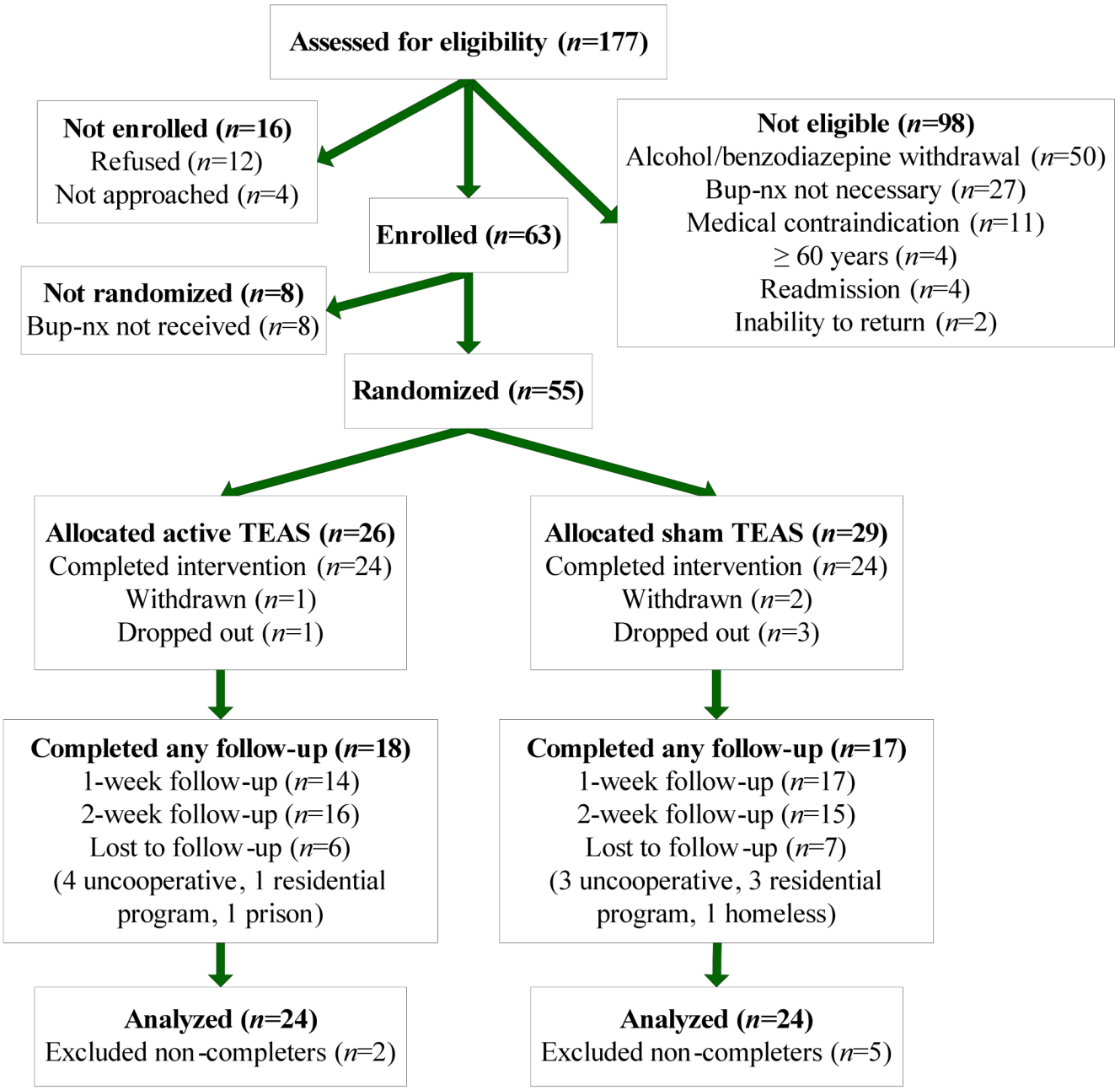


**Figure 1.**
Flow of participants through the trial

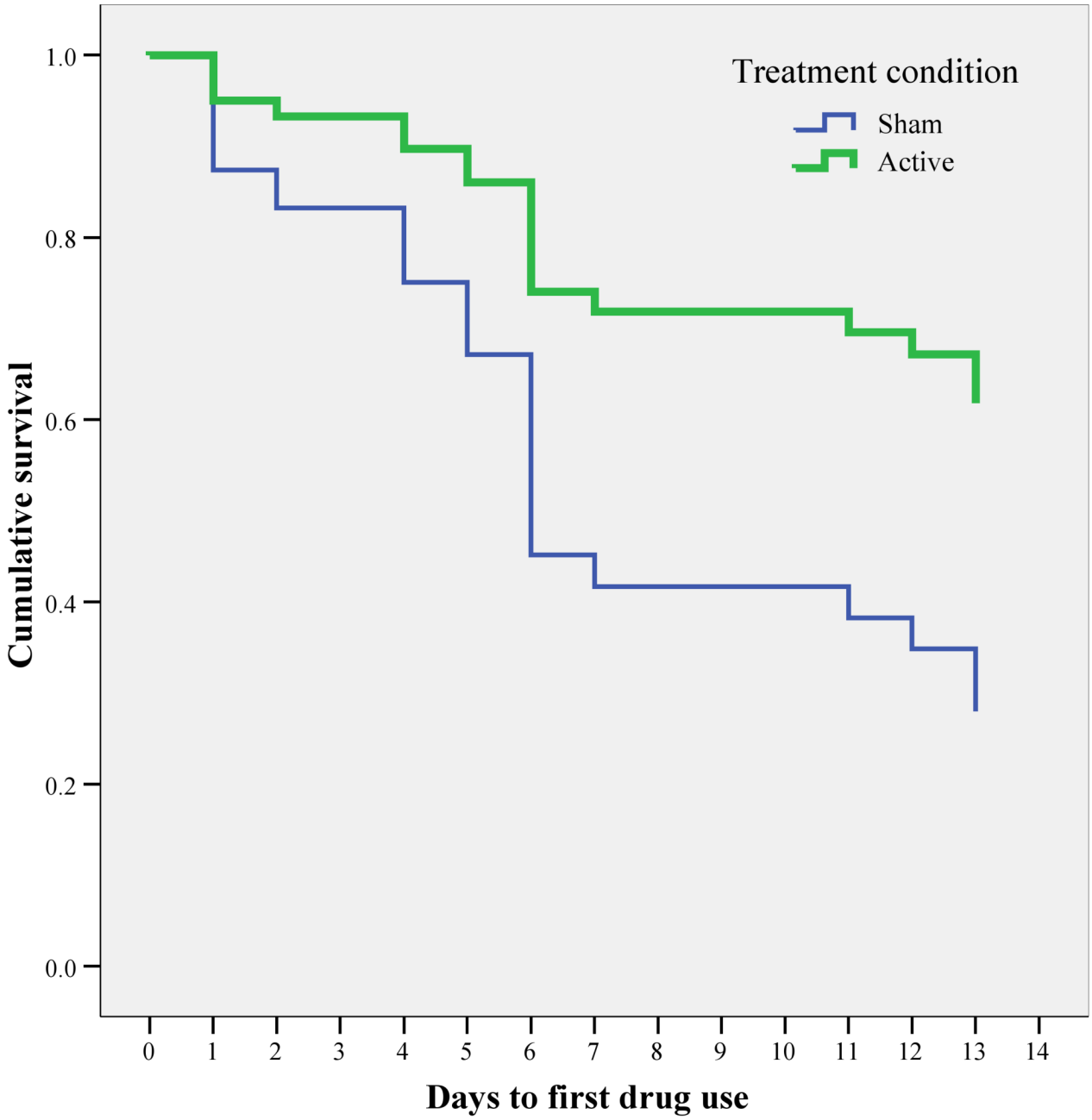


**Figure 2.**
Survival analysis showing days to first drug use by treatment condition
*Note*. $\chi^2(1) = 3.871$, $p = .049$; hazard ratio = 2.650 (95% confidence interval = 1.004 – 6.995).

## Table 1

Participant characteristics

| Characteristic | Active n = 24 | Sham n = 24 | Statistic | *p*-value |
|---|---|---|---|---|
| Age, years [M (SD)] | 27.67 (9.14) | 27.33 (9.02) | t(46) = -0.13 | 0.90 |
| Male [n (%)] | 16 (66.7%) | 17 (70.8%) | $\chi^2(1) = 0.10$ | 0.76 |
| Caucasian [n (%)] | 20 (83.3%) | 22 (91.7%) | $\chi^2(1) = 0.76$ | 0.38 |
| Education, years [M (SD)] | 13.08 (1.38) | 14.63 (1.79) | t(46) = 3.46 | 0.01 |
| Marital status [n (%)] | | | $\chi^2(2) = 0.23$ | 0.89 |
| Single | 19 (79.2%) | 18 (75%) | | |
| Married | 3 (12.5%) | 3 (12.5%) | | |
| Divorced/separated/widowed | 2 (8.3%) | 3 (12.5%) | | |
| Principal drug used [n (%)] | | | $\chi^2(1) = 0.00$ | 1.00 |
| Heroin | 12 (50%) | 12 (50%) | | |
| Other opioid | 12 (50%) | 12 (50%) | | |
| Severity of dependence [M (SD)] | 11.88 (2.53) | 11.71 (2.74) | t (46) = 0.22 | 0.83 |
| Days of use, past month [M (SD)] | | | | |
| Alcohol | 3.17 (5.44) | 4.08 (6.52) | t(46) = 0.53 | 0.60 |
| Any Drug | 24.21 (7.34) | 25.96 (6.58) | t(46) = 0.87 | 0.39 |
| Any Opioid | 23.50 (8.06) | 24.54 (7.98) | t(46) = 0.45 | 0.66 |
| Severity of problems [M (SD)] | | | | |
| Medical | 0.27 (0.36) | 0.25 (0.37) | t(46)= -0.19 | 0.85 |
| Occupational | 0.43 (0.18) | 0.44 (0.21) | t(46)= 0.26 | 0.79 |
| Drug | 0.33 (0.06) | 0.34 (0.07) | t(46)= 0.69 | 0.58 |
| Alcohol | 0.08 (0.13) | 0.14 (0.20) | t(46)= 1.22 | 0.23 |
| Legal | 0.15 (0.22) | 0.17 (0.18) | t(46)= 0.36 | 0.72 |
| Social | 0.30 (0.24) | 0.27 (0.23) | t(46)= -0.54 | 0.39 |
| Psychiatric | 0.45 (0.20) | 0.42 (0.19) | t(46)= -0.41 | 0.68 |
| Mood or anxiety disorder [n (%)] | 15 (62.5%) | 14 (58.3%) | $\chi^2(1) = 0.09$ | 0.77 |

## Table 2

Drug use outcomes at 2 weeks post-discharge [a]

| Drug use outcome [b] | Active n = 17 [c] | Sham n = 17 | Statistic | *p*-value |
|---|---|---|---|---|
| Any use (%) | | | | |
| Drugs | 35% | 77% | $\chi^2(1) = 5.85$ | .02 |
| Opioids | 29% | 65% | $\chi^2(1) = 4.25$ | .04 |
| Days of use [M (SD)] | | | | |
| Drugs | 2.13 (3.69) | 4.82 (5.26) | t(31) = 1.69 | .10 |
| Opioids | 1.69 (3.48) | 3.00 (1.69) | t(31) = 0.90 | .37 |

[a] Participants who completed at least one follow-up visit were included in this analysis.

[b] Drug use outcomes were based on self-report and corroborated by urine drug screens. Data from both follow-up visits were used.

[c] One participant in active TEAS did not provide drug use data and was not included in this analysis.

**Table 3**

Means and standard deviations for secondary outcomes by treatment condition over time

| Secondary outcome | Mean (standard deviation) | | | | Overall treatment by time effects (3 df tests) | |
|---|---|---|---|---|---|---|
| | Baseline | Discharge | 1- week follow-up | 2-week follow-up | F-value | *p*-value |
| Opioid withdrawal | | | | | 0.60 | .62 |
| Active | 28.17 (12.13) | 7.96 (7.30) | 9.57 (10.71) | 4.63 (6.10) | | |
| Sham | 24.56 (12.04) | 8.04 (7.19) | 8.59 (8.87) | 5.80 (3.93) | | |
| Opioid craving | | | | | 1.17 | .34 |
| Active | 21.22 (5.76) | 13.58 (7.98) | 13.64 (8.62) | 10.69 (7.15) | | |
| Sham | 20.25 (7.51) | 13.35 (7.55) | 13.67 (6.86) | 14.27 (6.95) | | |
| Pain severity | | | | | 1.64 | .20 |
| Active | 3.64 (2.15) | 2.51 (2.60) | 2.48 (2.22) | 1.77 (2.11) | | |
| Sham | 2.76 (2.50) | 2.60 (2.61) | 2.24 (2.60) | 1.30 (1.79) | | |
| Pain interference | | | | | 4.52 | .01 |
| Active | 3.77 (2.73) | 1.97 (2.24) | 2.11 (2.53) | 0.96 (1.59) | | |
| Sham | 2.56 (2.66) | 2.19 (2.36) | 1.97 (2.69) | 1.62 (2.55) | | |
| Sleep quality | | | | | 1.33 | .28 |
| Active | 12.71 (3.93) | 10.38 (4.02) | 9.79 (3.93) | 8.38 (4.57) | | |
| Sham | 12.17 (4.42) | 11.52 (4.59) | 11.65 (4.20) | 10.07 (3.90) | | |
| Physical health | | | | | 4.84 | .01 |
| Active | 59.14 (8.92) | 60.39 (7.16) | 63.43 (5.97) | 67.88 (5.16) | | |
| Sham | 60.02 (8.00) | 61.16 (7.94) | 62.15 (9.29) | 61.53 (8.53) | | |
| Mental health | | | | | 2.87 | .05 |
| Active | 36.24 (10.44) | 38.39 (8.57) | 40.14 (9.83) | 47.50 (9.54) | | |
| Sham | 35.38 (8.02) | 37.57 (5.43) | 41.00 (9.50) | 42.47 (10.64) | | |