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Buprenorphine Initiation and Linkage to Outpatient Buprenorphine do not Reduce Frequency of Injection Opiate Use Following Hospitalization

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Abstract

Background—Buprenorphine has established effectiveness for outpatient treatment of opioid use disorder. Our previously published STOP (Suboxone Transition to Opiate Program) trial showed that buprenorphine induction, stabilization, and linkage to outpatient treatment in opioid-dependent inpatients (injection and non-injection drug users) decreased illicit opioid use over 6 months. The present study was a planned subgroup analysis of injection opiate users from STOP.

Objective—To determine if inpatient buprenorphine initiation and linkage to outpatient buprenorphine reduce injection opiate users' frequency of injection opiate use (IOU).

Methods—Inpatient injection opiate users at a safety-net hospital were randomized to buprenorphine linkage (induction, stabilization, bridge prescription, and facilitated referral to outpatient treatment) or detoxification (5-day inpatient buprenorphine taper). Conditional fixed-effects Poisson regression was used to estimate the effects of intervention on 30-day (self-report) at 1, 3, and 6 months, measured using 30-day timeline follow-back. The secondary outcome was linkage effectiveness, measured as % presenting to initial outpatient buprenorphine visits after hospital discharge.

Results—Analysis was limited to persons (n = 62 randomized to detoxification and n = 51 to linkage) with baseline IOU. There were no significant differences in age, ethnicity, or baseline IOU frequency. At follow-up, linkage patients (70.6%) were significantly more likely ($p < 0.001$) to present to initial buprenorphine visits than detoxification patients (9.7%). However, there was no significant between group difference in the rate of IOU at 1-(IRR = 0.73, p = 0.32), 3- (IRR = 1.20, p = 0.54), or 6-month (IRR = 0.73, p = 0.23) follow-ups. Using person–day analysis, participants self-reported IOU on 5.8% of follow-up days in which they used prescription

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buprenorphine and 37.5% of non-buprenorphine days. Using a generalized estimating equation, the estimated odds of IOU was 4.57 times higher ($p < 0.001$) on non-buprenorphine days.

Conclusions—Despite STOP's success in linking patients who inject opiates to outpatient buprenorphine, the intervention did not significantly decrease their IOU frequency. Injection opiate users will require a more intensive protocol to sustain outpatient buprenorphine treatment and decrease injection with its attendant risks.

Keywords

Buprenorphine; Hospitalization; Injection drug use; Opioid use disorder; Transitions of care

1. Introduction

An unfortunate reality of the current “opioid epidemic” (CDC, 2011) is that injection opiate use (IOU) is on the rise. In 2013, an estimated 517,000 persons reported past-year heroin abuse or dependence, representing an increase of almost 150% since 2007 (Substance Abuse and Mental Health Services Administration, 2014). The majority of patients who use heroin report injection as their primary route of intake (SAMHSA, Center for Behavioral Health Statistics and Quality, 2012). In addition to the risks of overdose-related death and disability (Jones, 2013; SAMHSA, Drug Abuse Warning Network, 2013), injection of opiates exposes users to the viruses HIV, Hepatitis C, and Hepatitis B, as well as to serious bacterial infections of the skin, heart, bones, and other organs (Stein, 1999).

Buprenorphine is known to be an effective treatment for opioid use disorder (Kakko, Svanborg, Kreek, & Heilig, 2003; Ling et al., 2005; Umbricht et al., 2003) and, unlike methadone, which can only be prescribed in federally-licensed methadone centers, buprenorphine can be prescribed by physicians in primary care and behavioral health settings. Moreover, treatment with buprenorphine has been found to reduce risks for both HIV (MacArthur et al., 2012) and Hepatitis C (Tsui, Evans, Lum PJ, Hahn, & Page, 2014) in patients who inject opioids. However, the majority of persons with opioid use disorder (OUD) are not actively seeking treatment (SAMHSA, 2012).

In an effort to engage “non-treatment-seeking” individuals in opioid agonist treatment, attention to hospitalized patients with OUD is growing. Observational studies have examined the feasibility of linking these highly vulnerable patients to outpatient treatment (Aszalos, McDuff Weintraub, Montoya, & Schwartz, 1999; Shanahan, Beers, Alford, Brigandi, & Samet, 2010; Sittambalam, Vij, & Ferguson, 2014; Suzuki et al., 2015) and measured their long term retention (Caldiero, Parran, Adelman, & Piche, 2006). However, these studies did not evaluate whether in-hospital induction, stabilization, and linkage to outpatient treatment actually reduced opioid use. Nor did they differentiate among patients who injected versus did not inject opioids.

Stratification of intervention effect by injection status carries potential clinical importance because injection (vs. non-injection) of opioids is associated with more severe OUD. Compared to non-injectors, patients who inject tend to have lower levels of education (Darke et al., 2007), longer durations of OUD, and increased likelihood of unemployment,

homelessness (Neaigus et al., 2001), arrest, and incarceration (Young & Havens, 2012). Furthermore, studies in outpatient settings with treatment-seeking individuals have shown that opioid injection (vs. non-injection) is a risk factor for failure of medication-assisted treatment (Hillhouse, Canamar, & Ling, 2013; Potter et al., 2013).

Our recent STOP (Suboxone Transition to Opiate Program) randomized clinical trial (RCT) showed promise in benefiting the high-risk group of hospitalized patients with OUDs (Liebschutz et al., 2014). Specifically, we found that in-hospital buprenorphine induction, stabilization, and linkage to outpatient care in this population (both injection opiate users and non-injection opioid users) resulted in 72% entry into outpatient treatment and decreased odds (0.6 aOR) of illicit opioid use over 6 months compared to hospital detoxification without linkage (Liebschutz et al., 2014). Given the high prevalence of IOU in our original study (81.3% of our 139 participants reported injection of opiates at baseline), the greater risk for medical and infectious complications, and the greater severity of drug use disorders among those who inject, we planned a subgroup analysis of STOP. The objective of this analysis was to determine if buprenorphine initiation during hospitalization and linkage to outpatient-based buprenorphine treatment after discharge reduces injection opiate users' number of injection days compared to an in-hospital buprenorphine detoxification.

2. Methods

2.1. Study design and participants

Full details of the STOP RCT have been described elsewhere (Liebschutz et al., 2014). In brief, from August 1, 2009, through October 31, 2012, a total of 663 opioid-dependent inpatients (both injection opiate users and non-injection opioid users) on the general medical wards of an urban safety-net hospital were identified. The city in which the hospital resides offers several outpatient buprenorphine programs; at the time of the study the average wait time between a patient's contact with a program and induction of buprenorphine was 2–6 weeks (LaBelle, 2015).

Of the original 663 patients identified, 322 did not meet eligibility criteria because of active legal problems, benzodiazepine use disorder, alcohol use disorder, chronic pain, severe medical or behavioral issues, lack of opioid dependence, current enrollment in buprenorphine or methadone maintenance treatment, receipt of methadone during current hospitalization, a language barrier, or inability to receive primary care at the affiliated hospital. Of the eligible patients, 202 declined participation, while 139 patients (both injection opiate users and non-injection opioid users) completed the baseline interview and were assigned to the detoxification (n = 67) or linkage (n = 72) group of the parent study.

The present subgroup analysis of the original STOP study compares the injection opiate users (any self-reported opiate injection in the 30 days prior to enrollment) in the detoxification (n = 62; 92.5% of the STOP sample) group with those in the linkage (n = 51; 70.8% of the STOP sample) group. It should be noted that 100% of our participants reported injection of heroin. Boston Medical Center and Butler Hospital institutional review boards approved this study, and all participants provided written informed consent.

2.1.1. Detoxification group—The detoxification group received a five-day buprenorphine/naloxone taper protocol (all doses reported represent a 4:1 ratio of buprenorphine:naloxone; 8 mg on days 1 and 2, 6 mg on day 3, 4 mg on day 4, 2 mg on day 5, and then no additional buprenorphine/naloxone). At discharge, research staff offered a list of local OUD treatment centers to which patients could self-refer.

2.1.2. Linkage group—The linkage group received induction with buprenorphine/naloxone and dose stabilization (8 mg on day 1, 12 mg on day 2, and 16 mg from day 3 until hospital discharge). Prior to discharge, research staff facilitated linkage to the hospital-associated primary care buprenorphine clinic. The buprenorphine clinic staff contacted the participant, conducted its usual admission process, and scheduled the initial nurse intake visit within 7 days of hospital discharge. A buprenorphine-licensed physician clinically assessed each patient during the inpatient stay and, upon discharge, prescribed sufficient buprenorphine, 16 mg/day, to last until the buprenorphine clinic intake appointment. After intake, the buprenorphine clinic staff determined all ongoing treatment (Liebschutz et al., 2014).

The hospital-based OBAT clinic to which linkage participants were referred utilizes a collaborative care model, in which buprenorphine-waivered primary care physicians work in conjunction with nurse care managers (NCMs),a nurse program director, and a program coordinator (Alford et al., 2011; LaBelle, Han, Bergeron, & Samet, 2016). The NCMs are central to the model and perform the majority of the patient education, support, day-to-day communication, as well as collection of urine toxicology screenings, all according to federal guidelines (Center for Substance Abuse Treatment, 2004; LaBelle et al., 2016). The NCM and the buprenorphine prescribers jointly make medication management decisions. According to the clinic protocol, buprenorphine doses rarely exceed 16 mg (LaBelle, 2015).

2.2. Outcome measures

The primary outcome for this analysis was the number of days in which opiates were injected over the prior 30 days, assessed at 1, 3, and 6 months post-hospitalization. These rates were based on patients' self-report in interviews administered by a research assistant and calculated using a standard 30-day timeline follow-back (TLFB) method (Sobell, 1996). The secondary outcome was effectiveness of the linkage as measured by the proportion of participants in each group who presented to an initial visit at the hospital-based outpatient buprenorphine clinic after hospital discharge. This was obtained by review of documentation in the electronic health record at the referral buprenorphine outpatient treatment site.

2.3. Statistical analysis

We report descriptive statistics to characterize the cohort and compare intervention arms. T-tests and χ^2-tests were used to compare detoxification and linkage arms with respect to baseline characteristics. Measured characteristics included age, gender, ethnicity, housing status (homeless vs. no), psychiatric comorbidity (self-reported psychiatric diagnosis vs. no, asked, “Has a professional clinician ever diagnosed you with major depression, panic attacks, bipolar disorder, schizophrenia, an anxiety disorder, or PTSD?”), previous opioid agonist treatment program (past buprenorphine or methadone vs. no), baseline frequency of

opioid agonist use (calculated as the percent of self-reported days using buprenorphine and/ormethadone, either bought off the street or as part of a program the patient has since left, over the previous 30 days) and baseline frequency of IOU (calculated as the percent of self-reported injection days over the previous 30 days).

The outcome variable was operationalized as days of IOU per 30 TLFB days. We analyzed intervention effects as a count variable using conditional fixed effects Poisson regression; this method compares within-subject change over time and controls for all time-invariant between-subject differences (Allison, 2009; Cameron & Trivedi, 1998). In this model the intervention effect was estimated as the treatment-by-time interaction.

Prior to estimating intervention effects, we used a likelihood ratio χ^2 difference test (LR^2) to compare a model treating time as linear to one treating time as categorical, with each assessment represented as a separate dummy indicator. An unconditional growth model operationalizing time as a categorical variable fit the observed data significantly better than a linear growth model ($LR^2 = 26.85$, df = 2, p = 0.001). Because the response distributions were over-dispersed and not well approximated by any exponential family distribution, we used bootstrap resampling with 5000 replications to estimate standard errors and 95% confidence interval estimates. To facilitate interpretation, we report both the linear-additive coefficient and the incidence rate ratio. Separate coefficients are reported for each intervention arm to clarify the treatment-by-time interaction.

As an auxiliary analysis, we used a generalized estimating equation (GEE) model to conduct a person-day evaluation of the association between prescription buprenorphine use and IOU during follow-up.

2.3.1. Loss to follow-up—Because missing data were a concern for the stability of the findings, we report two additional analyses to evaluate the potential sensitivity of our primary analysis to subject attrition. First, we used multiple imputation as implemented in Stata 12.1 (StataCorp, 2014) to generate 20 complete panels. The negative binomial model was used when generating the imputations; variables used in the imputation model were age, gender, ethnicity, homelessness, recent cocaine use, baseline frequency of opioid use, treatment group, and participant identification (cluster variable defining the panel). Second, we used last observation carried forward, which provides a plausible upper bound on treatment differences under the assumption that participants have returned to prior levels of IOU, but is biased toward rejecting the null hypothesis.

3. Results

3.1. Demographics

Participants (n = 113) averaged 39.5 (±11.9) years of age; 78 (69.0%) were male, 55 (48.7%) were non-Latino Caucasian, 26 (23.0%) were African American, 23 (20.4%) were Latino, and 9 (8.0%) were of other ethnicities (Table 1). Thirty-nine (34.5%) had recently spent a night on the street or in a shelter and 65 (57.5%) reported ever having been diagnosed with a psychiatric disorder. The mean baseline rate of IOU was 20.3 (±9.59) days and the mean baseline rate of opiate agonist use (buprenorphine or methadone) was 1.41

(±2.59) days. About 46.9%, 31.0%, 62.0%, and 37.2% of the participants reported recent (past 30-days) use of alcohol, benzodiazepines, cocaine, and cannabis, respectively. Recent use of amphetamines (3.5%), barbiturates (2.7%) and hallucinogens (2.0%) was relatively uncommon.

With the exception of cannabis use at baseline and observation rate at 6-months, differences between treatment arms did not approach statistical significance on any of the characteristics evaluated in Table 1. Follow-up rates for completing study assessments were 63.7%, 58.4%, and 56.7% at 1-, 3-, and 6-months, respectively; 83.2% were assessed at 1 or more follow-ups. Participants randomized to linkage tended to have higher follow-up rates at all assessments: At 1-month, 68.6% of participants randomized to linkage and 59.7% of participants randomized to detoxification were assessed (p = 0.325). At 3-months, 60.8% of participants randomized to linkage and 56.5% of participants randomized to detoxification were assessed (p = 0.642). At 6-months, 66.7% of participants randomized to linkage and 48.4% of participants randomized to detoxification were assessed (p = 0.051).

3.2. Injection opiate use during follow-up

Table 2 gives results for the fixed-effects Poisson regression model estimating intervention effects. The coefficients in the first section of the table (change in detoxification arm) give the change in the rate of IOU for persons randomized to detoxification. Relative to baseline, the rate of IOU decreased significantly at all 3 time points for those in detoxification. Similarly, as can be seen in the second section (change in linkage arm), relative to baseline, the rate of IOU decreased significantly at all 3 time points for those in linkage. Finally, the third section of the table (treatment by time interaction), shows the difference in change rates between persons randomized to detoxification and linkage. Those in linkage had larger reductions in the rate of IOU at 1- (IRR = 0.73, 95% CI 0.40; 1.35, p = 0.32) and 6-months (IRR = 0.73, 95% CI 0.39; 1.40, p = 0.23), but a smaller reduction (IRR = 1.20, 95% CI 0.67; 2.16, p = 0.54) at 3-months; none of these between-group comparisons was statistically significant.

Analysis using 20 complete imputed data sets (n = 113) produced results generally consistent with the as-treated analysis reported in Table 2. The IRRs were 0.59 (95% CI 0.17; 2.06, p = 0.40), 0.77 (95% CI 0.19; 3.07, p = 0.71), and 0.55 (95%CI 0.21; 1.92, p = 0.41). At all 3 time points, the confidence interval estimates for the IRRs estimating the effects of intervention were not statistically significant. Using last observation carried forward analysis, the IRR estimating the effect of intervention at 1 month was 0.79 (95%CI 0.57; 1.08, p = 0.14), at 3-months it was 0.93 (95% CI 0.66; 1.31, p = 0.68), and at 6-months it was 0.87 (95% CI 0.60; 1.29, p = 0.45).

3.3. Entry into outpatient treatment during follow-up

At 1-month follow-up, patients in the linkage group (70.6%) were significantly (p = 0.001) more likely to present to an initial visit at a buprenorphine program than those in detoxification group (9.7%). At 6-months, 3.2% of persons randomized to detoxification and 13.7% of persons in linkage remained engaged with a buprenorphine program (p = 0.08).

3.4. Self-reported buprenorphine during follow-up

Using a person–day analysis, participants self-reported IOU on 5.8% of follow-up days in which they also reported prescription buprenorphine use and 37.5% of days in which they did not report prescription buprenorphineuse. Using GEE, the odds of IOU were estimated to be 4.57 times higher on days when prescription buprenorphine was not used ($p < 0.001$). Overall, however, participants reported using prescribed buprenorphine on only 30.2% of follow-up days, with attrition in use over time in both groups. The overall mean rates (days/30 observed TLFB days) of reported buprenorphine use were 14.4 (±11.9), 11.2 (±12.5), and 8.0 (± (11.9) at 1-, 3-, and 6-months, respectively. At 6 months, the mean rates of reported buprenorphine use were 8.5 (±12.4) in the linkage arm and 7.5 (±11.42) in the detoxification arm ($p = 0.72$).

When examining month 1 specifically, the mean rates of reported buprenorphine use were 22.4 (±10.0) in the linkage arm and 7.0 (±8.0) in the detoxification arm ($p < 0.001$). Yet during this month, the mean 30-day IOU rate was not significantly different between groups, 13.2 (±7.5) in the detoxification arm and 11.9 (±7.89) in linkage ($p = 0.47$).

4. Discussion

In our subgroup analysis of hospitalized patients who inject opiates, patients who received buprenorphine induction, stabilization, and facilitated linkage to outpatient buprenorphine treatment were significantly more likely to present to an initial outpatient buprenorphine visit than patients who received inpatient buprenorphine detoxification. The linkage rates we report here are very similar to those reported in our earlier study that included non-injectors (Liebschutz et al., 2014). However, the linkage group did not report significant improvement in IOU frequency during 6 months of follow-up compared to the detoxification group. The 6-month retention rate in our subgroup analysis (13.7%) is especially discouraging when compared to the overall rate at our hospital-affiliated buprenorphine clinic (65%) at 6 months (Weinstein & Sisson, 2016).

Although these results may be driven by a small number of participants, we attribute this lack of treatment effect to a combination of rapid attrition from buprenorphine treatment and unexpectedly high rates of continued injection during treatment in the linkage group. In contrast to the encouraging results of our original STOP study, which demonstrated a 40% reduction in overall opioid use following hospital discharge, this planned subgroup analysis of IOU outcomes among those who injected at baseline was disappointing.

Why would hospitalized opioid-dependent patients who inject be more treatment resistant than those who do not inject? Although our study is the first of its kind in hospitalized patients with OUD, studies in other settings have shown that patients who inject are less likely than those who do not inject to succeed in medication-assisted treatment programs (Fiellin et al., 2008; Hillhouse et al., 2013; Potter et al., 2013). The factors that lead patients who inject to misuse opioids during treatment and/or drop out of treatment are complex, and may include their lack of stable social situation (Potter et al., 2013), their loss of the injection ritual (McBride, Pates, Arnold, & Ball, 2001), their greater use of other substances (e.g. cocaine, benzodiazepines) that precipitate drop-out or treatment program discharge

(Hillhouse et al., 2013; Wu, Woody, Yang, & Blazer, 2011), and a greater neurochemical dependence on opioids (Gossop, Griffiths, Powis, & Strang, 1992), suggesting a more severe substance use disorder compared to their non-injecting counterparts.

What types of interventions could improve clinical care to better maintain persons who inject opiates in medication-assisted treatment? It seems intuitive that counseling techniques might be effective. However, multiple studies evaluating the potential benefit of adding various behavioral strategies to medication-assisted therapy have proven negative. A Cochrane systematic review of clinical trials comparing any psychosocial intervention plus any opioid agonist to any opioid agonist alone did not find a significant benefit of psychosocial interventions (Amato, Minozzi, Davoli, & Vecchi, 2011). In a 2013 RCT of 202 patients with opioid use disorder, Ling and colleagues found that, when added to outpatient buprenorphine treatment, neither contingency management nor cognitive behavioral therapy nor a combination of the two showed a statistically significant decrease in opiate-positive urine toxicology screens compared to treatment with buprenorphine alone (Ling, Hillhouse, Ang, Jenkins, & Fahey, 2013).

It has also been suggested that residential-based rehabilitation programs might be more effective than outpatient programs in helping people who have more severe substance use disorders maintain abstinence. Randomized studies have not been performed to test residential versus outpatient buprenorphine programs, but the observational studies that exist do not show a clear benefit. Burdon, Dang, Prendergast, Messina, and Farabee (2007) evaluated 4165 parolees who participated in residential-only versus outpatient-only substance use treatment programs for opioids, alcohol, stimulants, cocaine, or “other” following release from prison and concluded that, at 12-month follow-up, participants benefited equally from outpatient and residential programs, regardless of the severity of their substance use disorder (Burdon et al., 2007). Similarly, Hser, Evans, Huang, and Anglin (2004) found that, among 1939 participants at one of 13 residential or outpatient substance use programs for opioids, alcohol, cocaine, amphetamines, or marijuana in California, the intensity of and satisfaction with services provided, but not residential versus outpatient status, were correlated with improved treatment outcomes at 9 months (Hser et al., 2004).

Although studies of psychosocial interventions and residential treatment have not shown clear benefit in improving outcomes, studies of increased dose of opioid agonist have shown more promising results. In a secondary analysis of 1267 participants enrolled in nine opioid treatment programs between 2006 and 2009 and randomized to receive 24 weeks of either buprenorphine or methadone, program retention increased linearly with higher doses of buprenorphine, with 60% program completion in participants taking 30–32 mg of buprenorphine compared to 46% for buprenorphine patients as a whole (Hser et al., 2014). By contrast, participants in our intervention group were titrated up to 16 mg/day of buprenorphine during their hospital stays. Subsequently, our patients' doses were adjusted by buprenorphine-waivered doctors in our hospital-affiliated primary care practice, where the doses above 16 mg per day are rare (LaBelle, 2015).

Another possible adjustment in protocol that could lead to sustained treatment of high-needs injection opiate users would be a change from buprenorphine to methadone. Unfortunately,

requiring daily in-person dosing at federally licensed methadone clinics could present additional barriers to treatment for some patients. The study described above by Hser and colleagues, conducted in the years just following introduction of buprenorphine (2006–2009), provides some evidence that retention rates are higher in methadone compared to buprenorphine clinics (Hser et al., 2014). In that study, the treatment completion rate was 74% among patients randomized to methadone versus 46% among patients randomized to buprenorphine (Hser et al., 2014). Moreover, a 2014 Cochrane systematic review of 31 RCTs of buprenorphine versus placebo or methadone for management of OUD explored the relationship between dose of opioid agonist and both treatment retention and opiate-negative urine. It concluded that, when prescribed in flexible doses <16 mg, buprenorphine is inferior to methadone in retaining people in treatment but equal in its ability to reduce illicit opioid use among those retained. However, when buprenorphine doses ≥16 mg were used, buprenorphine and methadone therapies were equally effective in both treatment retention and suppression of illicit opioids (Mattick, Breen, Kimber, & Davoli, 2014). The Cochrane review did not perform subgroup analysis of participants who injected versus those who did not inject opioids. Future investigations of opioid agonists should include RCTs that specifically examine buprenorphine at various doses versus methadone at various doses and should also include subgroup analyses of injection versus non-injection opioid users.

Our study should be interpreted in the context of certain limitations. First, our study population was small. As such, we were not able to measure more sensitive outcomes such as frequency of opiate injection per day; it is possible that those participants who continued to inject might have reduced their frequency per day and thereby decreased their overall risk for infectious and other medical complications. Second, we used participants' self-report of their IOU. Third, we relied on imputation techniques to account for the missing data that is commonplace when assessing difficult-to-reach populations over time. Finally, ours was a single-site study conducted at a large, urban medical center for an underserved population—it is unclear how generalizable our results would be to other settings.

Like other studies conducted in outpatient (Alford et al., 2011; Fiellin et al., 2008; Kakko et al., 2003; Mattick et al., 2014; Soyka, Zingg, Koller, & Kuefner, 2008) and emergency department (Berg et al., 2007; D'Onofrio et al., 2015) settings, our study supports buprenorphine induction as a means of initially engaging patients in treatment. Our findings also uphold the efficacy of the medication itself—our participants were significantly less likely to inject opiates on days they used buprenorphine. Furthermore, our study demonstrates successful linkage to treatment for a group that had not previously been examined and that is at high risk for opiate-related illness and overdose.

5. Conclusion

Despite the robust efficacy of the linkage protocol in facilitating entry of hospitalized, injection opiate users into initial outpatient buprenorphine treatment, the STOP intervention did not significantly decrease the frequency of IOU over the 6 months following hospital discharge. Most hospitalized injection opiate users are not actively seeking treatment for substance misuse and are likely to have especially complex medical and social needs. They may require a more intensive treatment protocol than do non-injection misusers of opioids,

consisting possibly of higher doses of buprenorphine or a change in regimen to methadone maintenance. Further research is needed to determine how to engage these highly vulnerable patients in sustained addiction treatment beyond the initial linkage.

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Table 1

Baseline characteristics by intervention.

	Total (n = 113)	Detox (n = 62)	Linkage (n = 51)	t or χ^2 (p =)
Mean age (yrs)	39.5 (±11.9)	38.7 (±11.4)	40.5 (±12.5)	−0.78 (0.440)
n % male	78 (69.0%)	45 (72.6%)	33 (64.7%)	0.81 (0.368)
n (%) ethnicity				
Caucasian	55 (48.7%)	28 (45.2%)	27 (52.9%)	3.66 (0.301)
African-American	26 (23.0%)	12 (19.4%)	14 (27.5%)	
Latino	23 (20.4%)	16 (25.8%)	7 (13.7%)	
Other	9 (8.0%)	6 (9.7%)	3 (5.9%)	
Homeless (yes)	39 (34.5%)	22 (35.5%)	17 (33.3%)	0.06 (0.811)
Psychological diagnosis (yes)	65 (57.5%)	37 (59.7%)	28 (54.9%)	0.26 (0.609)
Methadone Trt. (ever)	59 (52.2%)	32 (51.6%)	27 (52.9%)	0.02 (0.888)
Buprenorphine Trt. (ever)	27 (23.9%)	12 (19.4%)	15 (29.4%)	1.56 (0.212)
Mean rate (days IOU/30)	20.3 (±9.59)	20.4 (±9.26)	20.2 (±10.1)	0.10 (0.920)
Mean % days IOU	1.41 (±2.37)	1.37 (±2.78)	1.5 (±2.36)	−0.16 (0.871)
Past 30-day use of other substances (%)				
Alcohol	53 (46.9%)	32 (51.6%)	21 (41.2%)	1.22 (0.269)
Benzodiazepines	35 (31.0%)	21 (33.9%)	14 (27.5%)	0.54 (0.463)
Cannabis	42 (37.2%)	28 (45.2%)	14 (27.5%)	3.76 (0.053)
Cocaine	70 (62.0%)	43 (69.4%)	27 (52.9%)	3.20 (0.074)
Observed at 1-month	72 (63.7%)	37 (59.7%)	35 (68.6%)	0.97 (0.325)
Observed at 3-months	66 (58.4%)	35 (56.5%)	31 (60.8%)	0.22 (0.642)
Observed at 6-months	64 (56.7%)	30 (48.4%)	34 (66.7%)	3.81 (0.051)

Table 2

Conditional fixed-effects Poisson regression model estimating intervention effects at 1-, 3-, and 6-month follow-ups (n = 94[*]).

	Change in detox arm[a]			Change in linkage arm[b]			Treatment by time interaction[c]		
Time	**b[d]**	**IRR[e] (95% CI)[f]**	**z (p =)[f]**	**b[d]**	**IRR[e] (95% CI)[f]**	**z (p =)[f]**	**b[d]**	**IRR[e] (95% CI)[f]**	**z (p =)[f]**
Month 1	−0.87	0.42 (0.29; 0.60)	−4.67 (<0.001)	−1.17	0.31 (0.19; 0.50)	−4.79 (<0.001)	−0.31	0.73 (0.40; 1.35)	−0.99 (0.33)
Month 3	−0.80	0.45 (0.29; 0.70)	−3.51 (<0.001)	−0.62	0.54 (0.37; 0.78)	−3.24 (0.001)	0.19	1.20 (0.67; 2.16)	0.62 (0.54)
Month 6	−0.61	0.54 (0.34; 0.87)	−2.56 (0.010)	−0.92	0.40 (0.26; 0.62)	−4.14 (<0.001)	−0.31	0.73 (0.39; 1.40)	−0.95 (0.23)

[a] Estimated change in detox arm, baseline to each follow-up assessment.

[b] Estimated change in linkage arm, baseline to each follow-up assessment. Coefficients are redundant but presented to facilitate interpretation of the treatment by time interaction.

[c] Effect of intervention. Estimated between group difference in change in from baseline to follow-up.

[d] Linear and additive Poisson regression coefficients.

[e] Incidence rate ratios ($\exp^b$) giving the factor change in the expected number of days.

[f] Confidence interval estimates and standard errors were estimated by bootstrap with 5000 resamplings with 5000 tests of significance based on robust standard errors. Model based robust standard errors generated consistent results concerning statistical inference.

[*] 94 of the 113 participants were available for at least one of the 1-, 3-, or 6-month follow-up assessments.