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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 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.

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

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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