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Buprenorphine treatment formulations: Preferences among persons in opioid withdrawal management☆

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ABSTRACT

Background: In the current study, we examined factors predicting willingness to receive buprenorphine treatment and preferences for various buprenorphine formulations (oral, injection, implant) among persons in opioid withdrawal management.

Methods: Participants were three hundred thirty-eight persons entering brief inpatient opioid withdrawal management programs at two sites. We used *t*-tests and Pearson $\chi 2$ – tests of independence to compare participants willing and unwilling to be prescribed buprenorphine in the future. Among persons willing to receive buprenorphine, we used multinomial logistic regression to estimate the adjusted effects of potential correlates of type of buprenorphine formulation preferred.

Results: Participants averaged 33.9 (± 9.5) years of age, 70.4% were male, 82.8% were White, and 11.0% were Latino/a. In all, 55.6% of participants had been prescribed buprenorphine in the past, and 54.7% were willing to use prescribed buprenorphine in the future. Those reporting past month illicit buprenorphine use and prior overdose were more willing to use prescribed buprenorphine. Of these (n = 180), most preferred daily buprenorphine formulations (tablet or film) (48.6%) over a weekly or monthly injection (23.1%) or bi-annual implant (28.3%).

Conclusions: Past buprenorphine prescription does not predict future willingness to restart. Among those willing to use buprenorphine, newer formulations of buprenorphine appealed to more than half of the participants.

1. Introduction

Opioid overdose rates continue to rise to unprecedented levels in the United States (Center for Behavioral Health Statistics and Quality, 2016; Morbidity and Mortality Weekly Report, 2017). A primary treatment challenge of controlling the opioid epidemic is that addiction to heroin and other opioids are chronic relapsing disorders. Although opioid withdrawal management programs serve a substantial proportion of individuals with OUD, comprising over one-quarter of all treatment service admissions for heroin or other opiates nationally (Center for Behavioral Health Statistics and Quality, 2016), opioid withdrawal management in itself is largely ineffective in preventing relapse (e.g., Gossop, Stewart, Browne, & Marsden, 2002).

For individuals completing withdrawal management, transitioning to opioid agonist treatment (OAT; e.g., methadone, buprenorphine, buprenorphine-naloxone) may be a particularly effective treatment protocol for maintaining long-term abstinence (see Connery, 2015 for review; Volkow, Frieden, Hyde, & Cha, 2014). Yet patients completing opioid withdrawal management often do not transition to OAT, fail to adhere to treatment protocol, or drop out of treatment once enrolled (see Connery, 2015 for review). Challenges to OAT effectiveness include structural barriers (e.g., time, transportation required to receive medication; Uebelacker, Bailey, Herman, Anderson, & Stein, 2016), lack of commitment to take at-home oral medication (Substance Abuse and Mental Health Services Administration, 2008), unwillingness to use certain formulations (e.g., unpleasant taste of sublingual formulation, Awgu, Magura, & Rosenblum, 2010; slow dissolution of tablet, Strain, Harrison, & Bigelow, 2011), and non-adherence, which is associated

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with an exponential likelihood for relapse (Tkacz, Severt, Cacciola, & Ruetsch, 2012). In an effort to enhance adherence and retention, and to curb diversion researchers have developed new formulations of OAT. However, it is not yet known how amenable persons with opioid use disorders may be to various formulations or what their preferences may be.

Relative to methadone, buprenorphine, a partial agonist approved to treat opioid use disorder as an office-based treatment in 2002 (Substance Abuse and Mental Health Services Administration, 2005), is similarly effective in reducing withdrawal and craving (Gowing, Ali, & White, 2009), but has a more desirable safety profile (Bell, Butler, Lawrance, Batey, & Salmelainen, 2009; Hser, Evans, Huang, & Anglin, 2004) and exhibits lower abuse liability (Johanson, Arfken, di Menza, & Schuster, 2012; Johnson, Strain, & Amass, 2003). Still, oral buprenorphine, which requires daily self-administration of tablets or film, is associated with non-adherence (e.g., not taking prescribed pills; Fareed et al., 2014), diversion (Alho, Sinclair, Vuori, & Holopainen, 2007; Moratti, Kashanpour, Lombardelli, & Maisto, 2010), and higher dropout rates than methadone (Bell, Trinh, Butler, Randall, & Rubin, 2009; Mattick, Kimber, Breen, & Davoli, 2008), often in the early phases of treatment (Hser et al., 2004). Longer-acting formulations of buprenorphine could hold promise for increasing treatment retention. The FDA recently approved a monthly buprenorphine injection (Sublocade) for opioid use disorder (Food and Drug Administration, 2017) and a second depot injectable formulation with 1 week and 4 week dosing is under review. Probuphine, an implantable buprenorphine that provides six months of internal dosing without the need for in-office visits, has demonstrated efficacy in several trials (Ling et al., 2010; Rosenthal et al., 2013; White et al., 2009).

Little is known about persons' willingness to begin buprenorphine treatment or their preferences for these new formulations of the medication. In prior work (Stein et al., 2012), demographics (age, gender, race) did not predict buprenorphine preference (vs. methadone) treatment, although females, older persons, and whites were more likely to initiate OAT. In other work, prior heroin injection was associated with higher interest in injectable OAT (Ahamad et al., 2015). Cunningham, Roose, Starrels, Giovanniello, and Sohler (2013) found that patients with prior buprenorphine experience—whether illicit or prescribed—exhibited better buprenorphine treatment retention than buprenorphine-naïve patients, but it is not known how this prior experience impacts one's willingness to begin a future course of buprenorphine treatment.

Our prior work (Bailey, Herman, & Stein, 2013; Uebelacker et al., 2016) showed that 63% to 78% of patients in opioid withdrawal management reported a desire for OAT following withdrawal, with more people favoring buprenorphine than methadone maintenance (Uebelacker et al., 2016). In the current analysis, years later in the opioid epidemic, we hypothesized first that a majority of persons entering a short-term withdrawal management program would be willing to receive buprenorphine treatment in the future. Based on existing literature, we hypothesized that injection drug use (IDU) and prior illicit or prescribed buprenorphine use would be related to greater willingness to receive buprenorphine. We also hypothesized that oral buprenorphine would remain the preferred choice of formulation among persons willing to receive buprenorphine treatment and wanted to identify the factors associated with formulation preferences so as to inform OAT services.

2. Methods

2.1. Recruitment

Between April and September 2017, we recruited consecutive persons seeking inpatient opioid withdrawal management at two sites—Stanley Street Treatment and Resources, Inc. (SSTAR) in Fall River, Massachusetts and Butler Hospital in Providence, Rhode Island—to participate in a one-time survey research study. SSTAR's program provides evaluation and withdrawal management using a methadone taper protocol, individual and group counseling, and aftercare case management. On average, admitted patients stay 4.9 days and are offered rapid linkage with outpatient buprenorphine and methadone maintenance care, assisted by case managers at the withdrawal management unit. The Alcohol and Drug Inpatient (ADI) Unit at Butler Hospital also provides detoxification under medical supervision, using clonidine, benzodiazepines and anti-emetics for symptom mitigation but no opioid agonists. The average length of stay at ADI is 5.3 days. During their stay, patients attend group therapy and are assigned a case manager to establish counseling and medical care upon discharge.

Of persons seeking care at SSTAR or Butler, 284 and 102, respectively, met Butler Hospital's Institutional Review Board-approved study eligibility criteria: 18 years or older, English speaking, and ability to provide informed consent. Twenty persons at SSTAR and twenty-eight persons at Butler refused study participation or were discharged before staff could interview them. The remaining 264 (SSTAR) and 74 (Butler) persons completed a non-incentivized, face-to-face interview administered by non-treating research staff. Interviews lasted approximately 15 min.

2.2. Measures

In addition to age, sex, race/ethnicity, years of education, past year IDU, and past month heroin use, the following variables were assessed.

2.2.1. Employment status

Respondents were asked if they were currently working. Those reporting that they worked full-time (> 35 h) or part-time (< 35 h) were coded as employed. Respondents reporting being currently unemployed, receiving disability, or being a full- or part-time student were coded as unemployed.

2.2.2. Homelessness

Respondents were asked where they had slept/spent their nights in the past three months. Respondents spending any nights on the street or in a shelter were coded as homeless and all others not homeless.

2.2.3. History of overdose

Respondents were asked if they had ever overdosed. We defined overdose (on any drug) as “you were unarousable (couldn't be woken) with shaking or calling your name because of the drugs you consumed.”

2.2.4. Illicit buprenorphine use

Respondents were asked, “In the past 30 days, how many days did you use buprenorphine (Suboxone) without a prescription?”

2.2.5. Prescribed buprenorphine use

Respondents responded “yes” or “no” to ever having been prescribed buprenorphine.

2.2.6. Prescribed methadone use

Respondents responded “yes” or “no” to ever having been enrolled in a methadone maintenance program.

2.2.7. Prescribed extended release naltrexone (Vivitrol) use

Respondents were asked if they had ever been prescribed Vivitrol. Respondents were provided the following explanation: “Vivitrol is a medication-assisted treatment. It's an injection (shot) of naltrexone that the patient receives once per month. Vivitrol works by blocking the ‘high’ one might experience from opiate use.”

2.2.8. Willingness to receive buprenorphine

Respondents were asked if they would “be willing to be prescribed buprenorphine or Suboxone in the future?” Answer options were “yes”