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Prior Experience with Non-Prescribed Buprenorphine: Role in Treatment Entry and Retention

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ABSTRACT

Buprenorphine availability continues to expand as an effective treatment for opioid dependence, but increases in availability have also been accompanied by increases in non-prescribed use of the medication. Utilizing data from a randomized clinical trial, this mixed-method study examines associations between use of non-prescribed buprenorphine and subsequent treatment entry and retention. Quantitative analyses ($N = 300$ African American buprenorphine patients) found that patients with prior use of non-prescribed buprenorphine had significantly higher odds of remaining in treatment through 6 months than patients who were naïve to the medication upon treatment entry. Qualitative data, collected from a subsample of participants ($n = 20$), identified three thematic explanations for this phenomenon: 1) perceived effectiveness of the medication; 2) cost of obtaining prescription buprenorphine compared to purchasing non-prescribed medication; and 3) convenience of obtaining the medication via daily-dosing or by prescription compared to non-prescribed buprenorphine. These findings suggest a dynamic relationship between non-prescribed buprenorphine use and treatment that indicates potential directions for future research into positive and negative consequences of buprenorphine diversion.

1. Introduction

Buprenorphine is an effective treatment for opioid dependence (Amass et al., 2004; Gibson, Doran, Bell, Ryan, & Lintzeris, 2003; Johnson, Jaffe, & Fudala, 1992; Mattick, Kimber, Breen, & Davoli, 2008) whose use has seen rapid expansion in the U.S. over the last decade, including a four-fold rise in the distribution of buprenorphine units to pharmacies, and a five-fold rise in individuals receiving buprenorphine prescriptions from physicians (Lofwall & Walsh, 2014). This increase in the number of opioid-dependent individuals engaged in treatment has been associated with public health benefits such as reductions in heroin overdose deaths (Auriacombe, Fatseas, Dubernet, Daulouede, & Tignol, 2004; Schwartz et al., 2013), safer injection practices and lower rates of high-risk HIV activity (Kumar et al., 2000; Sullivan et al., 2008), and decreases in the amount of heroin and other non-prescribed opioids used by patients (Mattick et al., 2008; Woody et al., 2008).

However, the increase in availability of buprenorphine treatment has been accompanied by increased buprenorphine diversion (Bazazi, Yokell, Fu, Rich, & Zaller, 2011; Genberg et al., 2013; Lee, Klein-Schwartz, Welsh, & Doyon, 2013; Schuman-Olivier et al., 2010; Soyka, 2014; Yokell, Zaller, Green, & Rich, 2011), and related medical problems associated with its misuse (Auriacombe et al., 2004; Cicero, Surratt, & Inciardi, 2007; Daniulaityte, Falck, & Carlson, 2012; Ho, Ho, & Mak, 2009). Prior research identified that many opioid-dependent individuals who use diverted or "street buprenorphine" do so primarily for the purpose of self-medicating their withdrawal symptoms, and not to "get high" (Bazazi et al., 2011; Genberg et al., 2013; Hakansson, Medvedeo, Andersson, & Berglund, 2007; Mitchell et al., 2009; Monte, Mandell, Wilford, Tennyson, & Boyer, 2009; Schuman-Olivier et al., 2010). Other reasons cited for both diversion and misuse among buprenorphine patients include: peer pressure; helping a friend or family member who is going through opioid withdrawal; making money; habitual using behaviors; perceived under-dosing of the medication; and relieving negative emotional states, such as pain, anxiety, or depression (Lofwall & Walsh, 2014).

The use of non-prescribed buprenorphine can lead to complications, such as negative drug interactions, pediatric exposure, and death (Boyer, McCance-Katz, & Marcus, 2010; Lofwall & Walsh, 2014; Martin & Rocque, 2011; Pedapati & Bateman, 2011). However, some research suggests that there may also be associated benefits, including improved buprenorphine treatment retention for patients who have used non-prescribed buprenorphine prior to entering treatment (Cunningham, Roose, Starrels, Giovanniello, & Sohler, 2013; Yokell et al., 2011). One study found that patients who used non-prescribed buprenorphine

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prior to opioid-agonist treatment entry had improved rates of treatment retention after 12 months and abstinence from other illicit drugs after 6 months (Alford et al., 2011). Additionally, patients with prescribed and non-prescribed buprenorphine use prior to entering opioid-agonist treatment also exhibited fewer induction complications compared to buprenorphine-naïve patients (Whitley et al., 2010).

Understanding how prior non-prescribed buprenorphine use shapes current treatment choices and experiences has important clinical and public health implications. This mixed-methods analysis examines prior experience with non-prescribed (i.e., "diverted") buprenorphine among African-American men and women receiving buprenorphine treatment, and its impact on both treatment entry and treatment retention issues. These data were not previously reported in the parent study publications (Mitchell et al., 2013).

2. Methods

2.1. Parent study

This mixed-methods study is a secondary analysis from a randomized clinical trial of counseling intensity conducted with 300 African American buprenorphine patients in two outpatient programs in Baltimore, Maryland. At the time of the study, subsidized buprenorphine was available through public funding in the outpatient treatment program system in Maryland. In these programs, buprenorphine was generally administered directly to patients during the first day of treatment, and in rare cases, patients received their initial dose on the second day of intake. Once patients were stabilized on a maintenance dose, they were able to receive an increasing amount of buprenorphine for self-administration outside the program (i.e., at home). These participants were covered by insurance with little or no co-payment for buprenorphine. The parent study found no significant differences in treatment retention, drug use, or functioning between standard outpatient and intensive outpatient levels of care (Mitchell et al., 2013).

Participants in the parent study completed structured, face-to-face interviews with a trained research interviewer at baseline, 3-, and 6-month follow-up. The 6-month follow-up rate was 93%. Based on searches of public databases, a number of participants lost-to-follow-up were found to be incarcerated. The parent study was approved by the Friends Research Institute's Institutional Review Board (IRB) and the Sheppard Pratt IRB (parent organization of one of the study sites) for the protection of human subjects. All participants provided informed consent. A Federal Certificate of Confidentiality was obtained for the study.

2.1.1. Participants

2.1.1.1. Quantitative sample. Participants in the parent study were African American adults newly-admitted to buprenorphine treatment at one of the participating treatment programs ($N = 300$). The quantitative sample's mean age was 46 years ($SD = 6.45$), and 38% were female. Of the total sample, 51% reported having been in buprenorphine treatment, and 40% reported having been in methadone treatment, prior to the current treatment episode.

2.1.1.2. Qualitative interview sample. Semi-structured qualitative interviews were conducted with a subsample of 20 trial participants at the 3-month follow-up time-point using a purposive sampling strategy to ensure representation based on assigned study condition, demographics, and treatment retention status. Interviews were digitally recorded, professionally transcribed, and checked for accuracy.

2.1.2. Measurement of prior buprenorphine experience

As part of the baseline assessment, all 300 trial participants completed a study-specific questionnaire that included several items about prior use of buprenorphine, including specific questions about prior buprenorphine treatment ("*Have you been in buprenorphine treatment before?*"); lifetime use of non-prescribed buprenorphine ("*Have you ever taken buprenorphine that was not prescribed to you* [for example, that you bought on the street or that someone gave to you]?"); extent of exposure to non-prescribed buprenorphine ("*How many different times have you taken buprenorphine that was not prescribed to you?" [response options: once or twice, 3–5 times, 6–10 times, 11–15 times, or more than 15 times]*); and, recent use of non-prescribed buprenorphine just prior to treatment entry ("*Have you taken buprenorphine that was not prescribed to you [for example, that you bought on the street or that someone gave to you] in the last 30 days?)*. Treatment retention at 6 months (either in the original program or at another provider) was assessed using a combination of self-report and clinic records, with the few participants who were lost to follow-up classified as being "out-of-treatment."

2.1.3. Semi-structured interviews

Semi-structured interviews were conducted with patients to elucidate an understanding of patients' reasons for entering treatment, experiences while in treatment, and perspectives toward incorporating buprenorphine into their recovery. Patients were asked about their previous use of prescribed and non-prescribed buprenorphine ("*Have you tried buprenorphine before entering the program at* [Treatment Center]*? If so, where* (e.g., in a clinic, private doc, on the street)?"), drawing subsequent thematic conclusions directly from these patient narratives.

2.2. Analysis

2.2.1. Quantitative analysis

Prior use of non-prescribed buprenorphine and prior buprenorphine treatment experience were characterized using descriptive statistics and cross-tabulations, with association tested by the likelihood ratio χ^2 test of independence. We then fit a series of logistic regression models to examine the association between prior use of non-prescribed buprenorphine (no vs. yes) and treatment retention at 6 months (in treatment vs. out of treatment). The binary variable of prior non-prescribed buprenorphine use was selected as the predictor of interest due to its ease of interpretation and its alignment with prior buprenorphine treatment experience, which was also asked as a binary variable in a lifetime time frame.

The relationship between prior non-prescribed buprenorphine and 6-month treatment retention was first examined using an unadjusted logistic regression model. To disentangle experiences with prescribed versus non-prescribed buprenorphine and their respective ability to prospectively predict treatment retention, a second model was fit that also included the second binary predictor variable of prior buprenorphine treatment. A final model was fit with both of these predictors, as well as additional controls for a small number of common potential confounds. These control variables included patient demographic characteristics of gender and age, clinic site (because of the potential for retention differences across sites and differential access to non-prescribed buprenorphine in the neighborhoods from which the sites' respective patient populations were drawn), and co-occurring cocaine use at baseline (because of its known negative association with retention in buprenorphine treatment; Gryczynski et al., 2013).

2.2.2. Qualitative analysis

The narrative text of the qualitative data was coded and analyzed through an inductive process, allowing themes and support to emerge directly from the interview data. An initial coding process was conducted to synthesize thematic and conceptual areas largely targeted by the interview guide. A subsequent coding phase allowed qualitative researchers to identify relationships between the codes generated during the initial coding process and develop emergent themes related to patients' previous experiences with non-prescribed buprenorphine and their reasons for entering buprenorphine treatment. These emergent themes were discussed among the qualitative researchers, and