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LINKAGE TO PRIMARY CARE FOR PERSONS FIRST RECEIVING INJECTABLE NALTREXONE DURING INPATIENT OPIOID DETOXIFICATION

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Abstract

Introduction—Opioid use disorders commonly require ongoing medication-assisted treatment to reduce relapse following discharge from inpatient detoxification programs. Naltrexone, an opioid antagonist, is an increasingly popular treatment option in its once-monthly injectable form (XR-NTX). The aim of this study was to examine the follow-up rates of persons who received an initial injection during inpatient detoxification and scheduled for receipt of a first outpatient injection in the primary care setting.

Methods—We reviewed the electronic health records of 62 consecutive opioid dependent adults who received an initial injection of XR-NTX during extended inpatient detoxification at Stanley Street Treatment and Resources (SSTAR) in Fall River, Massachusetts, from March 2013 to August 2015, and were referred to the adjacent SSTAR primary care health center for their second injection one month later. Demographic information, drug use and opioid treatment history, and aftercare planning were assessed.

Results—Participants averaged 32.4 (± 7.8) years of age, 90.3% were non-Latino Caucasian, 35.5% were homeless, 21.3% reported a drug overdose in the last year, and 53.2% had been in detoxification within the last year. Of the 62 participants referred to primary care, 34 (54.8%) followed up to receive their second XR-NTX injection. Twenty of these persons received at least a third XR-NTX injection. No demographic, treatment history, substance use behaviors, or aftercare plan variables were associated with receipt of a second injection ($p < .20$).

Conclusion—Predicting, and therefore improving, XR-NTX continuation during the transition from inpatient detoxification to primary care may be difficult in this population.

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Keywords

opiates; detoxification; naltrexone; care continuity

1.0 Introduction

The national epidemic of opioid use disorder (OUD) requires Medication-Assisted Treatment (MAT) to reduce relapse risk following discharge from inpatient detoxification programs where many opioid users first seek care (Connery, 2015). MAT options include full agonist (methadone), partial agonist (buprenorphine) and antagonist (naltrexone) agents to treat this growing public health concern (Volkow, Frieden, Hyde, & Cha, 2014). Naltrexone binds to the μ -opioid receptors, blocking the effects of opioids and has no abuse or overdose potential (Taylor, Raffa, & Pergolizzi, 2011), can be stopped without withdrawal effects, and unlike its agonist counterparts does not require special waiver or specific licenses to be prescribed or dispensed (Martin, Jasinski, & Mansky, 1973; Mello, Mendelson, Kuehnle, & Sellers, 1981; Walsh, Sullivan, Preston, Garner, & Bigelow, 1996). Furthermore, by administering a 30-day dose in a single injection, extended-release injectable naltrexone (XR-NTX) addresses patient adherence problems associated with daily oral naltrexone use (Johansson, Berglund, & Lindgren, 2006; Krupitsky, et al., 2011; Woody, 2014). In the initial United States randomized trial of community-recruited opioid users, the two-month treatment retention rate was 68% with opioid use outcomes superior to placebo (Comer, et al., 2006). The larger, pivotal Russian study showed efficacy in reducing opiate use compared to placebo (Krupitsky, et al., 2011). There is some evidence that persons with OUD who receive XR-NTX have similar or lower cost and less substance-related inpatient utilization than patients treated with other therapies (Hartung, et al., 2014).

Because the initiation of XR-NTX requires a 7–10 period of opioid abstinence prior to administration (Kleber, 2007), settings such as detoxification programs offer the opportunity to expand this form of MAT. Leslie, et al. found that those who received XR-NTX while in residential treatment were less likely to leave against medical advice (AMA) and more likely to engage in follow-up care post-discharge than those who did not receive XR-NTX (Leslie, et al., 2015).

In this first study of the transition from detoxification to primary care offices, where XR-NTX can be administered over the long-term, our aim was to examine the follow-up rates of persons who received their initial XR-NTX during detoxification, and to determine the factors associated with receipt of a first outpatient injection in the primary care setting.

2.0 Methods**2.1 Participants**

We reviewed the electronic health records of 62 consecutive persons with opioid use disorder who sought inpatient detoxification at Stanley Street Treatment and Resources (SSTAR) in Fall River, Massachusetts, who received an initial injection of XR-NTX while an inpatient there between March 2013 and August 2015, and were referred to the adjacent SSTAR primary care health center for follow-up care. SSTAR's detoxification program (an

ASAM 3.7 level unit) has 38 beds and is a 24-hour medically supervised treatment facility that provides evaluation and withdrawal management using a methadone taper protocol as well as individual and group counseling and case management. In the course of the standard 5-day detoxification, persons interested in XR-NTX speak with an MAT case manager about insurance coverage for XR-NTX, other MAT options, and aftercare planning. Persons who decide to receive XR-NTX must remain at SSTAR in a step-down residential care unit for ten days after their last methadone dose. On day 10, they receive an oral dose of naltrexone (25 mg), and if they show no withdrawal symptoms, they receive an additional 25 mg one hour later. If again there are no symptoms, XR-NTX (380 mg) is delivered 90 minutes later. After receipt of injection, patients can be discharged.

2.2 Measures

Demographic information, drug use and treatment history, and aftercare planning were assessed. Demographic sample descriptors included age, gender, race/ethnicity, marital status, employment (part or full-time vs. unemployed), living with a child under 14 years old, homelessness (any nights on street or in a shelter in the prior 90 days), years of education, and having previously been seen by a primary care physician at SSTAR. We assessed “What is your legal status?” with response options: none, on probation, on parole, on pretrial release. Drug use variables included years of opioid use, injection drug use in the 30 days prior to this detoxification, overdose and opioid detoxification in the past year, and any cocaine, alcohol, marijuana or benzodiazepine use in the prior 30 days. We assessed previous experience with MAT by obtaining the past history of prescribed buprenorphine or XR-NTX as well as involvement in methadone maintenance. Finally, we determined whether participants were discharged from SSTAR detoxification with aftercare plans for residential treatment or intensive outpatient treatment. This study was approved by the Butler Hospital Institutional Review Board.

2.3 Analytical Methods

Our primary outcome was the proportion of participants who received a second XR-NTX injection, and our analysis examined predictors of receipt. We also report the number of persons receiving more than 2 injections. We present descriptive statistics to summarize the sample characteristics and to describe differences based on treatment preferences. T-tests and χ^2 -tests are reported for between group differences. To evaluate the substantive magnitude of associations we calculated standardized effect sizes (Cohen, 1988) (Cohen’s *d* for continuous variables and *h* for dichotomous variables).

3.0 Results

Participants averaged 32.4 (± 7.8) years of age, 90.3% were non-Latino Caucasian. Almost all (58, 93.6%) participants reported heroin was the primary opiate; 4 (6.5%) reported other non-prescription opioids. Nearly one-quarter (24.2%) were involved in the legal system, 35.5% were homeless, 21.3% reported a drug overdose in the last year, and 53.2% had been in opioid detoxification within the last year (Table 1). No demographic, substance use behavior, treatment history, or aftercare plan variables were associated with receipt of a second injection ($p > .20$). Thirteen persons (21.0%), twenty (32.3%), and twenty-nine

(46.8%) received their first XR-NTX shot in 2013, 2014, and 2015, respectively, and second injection receipt was not significantly associated with detoxification year. Of the 62 participants referred to the SSTAR health center, 34 (54.8%) followed up with the health center to receive their second XR-NTX injection the next month. Twenty of these persons (32.2% of those given first injection) received at least a third XR-NTX injection, 14 (22.6%) had 4 or more injections, and 11 (17.7%) had 6 or more injections.

4.0 Discussion

In this cohort of persons with opioid use disorder who chose and received XR-NTX during inpatient detoxification, which required a prolonged stay to receive this initial injection, 54.8% successfully received a second injection in a primary care setting at the scheduled follow-up one month later. No variables were associated with continued XR-NTX treatment, which is in line with previous clinical trials (Krupitsky, et al., 2011; Nunes, et al., 2015).

Among treatment professionals, XR-NTX is a promising treatment for OUD because it has no abuse or diversion potential, no risk of physical dependence, does not require regulatory permission to prescribe, and has efficacy in patients across a range of demographic and severity characteristics (Bart, 2012; Krupitsky, et al., 2011; Nunes, et al., 2015). XR-NTX has been associated with few opioid-related and non-opioid related hospitalizations, and total healthcare costs 49% lower than methadone (Baser, Chalk, Fiellin, & Gastfriend, 2011; Hartung, et al., 2014), suggesting that despite its current high cost, its use is likely to expand. Indeed, there is growing interest in XR-NTX treatment among OUD populations, particularly among daily heroin users (Ahamad, et al., 2015). Leslie, et al. (2015) found that patients who received an initial injection of XR-NTX while in a residential setting had lower rates of AMA discharge and higher rates of transition to outpatient care than those who did not receive XR-NTX. Notably, in that study of persons leaving residential care, first appointment follow-up rates for continuing care in the first 10 days post-discharge were also low. Six-month retention in XR-NTX treatment here was very low (18%), lower than retention rates reported with buprenorphine maintenance (Cunningham, et al., 2008; Finch, Kamien, & Amass, 2007; Gryczynski, et al., 2014; Mattick, Breen, Kimber, & Davoli, 2014; Soeffing, Martin, Fingerhood, Jasinski, & Rastegar, 2009) that is typically begun in the outpatient setting and therefore does not require linkage between treatment providers.

Our study had several limitations. We recruited from only one detoxification program. Because we were interested in follow-up rates where primary care appointments could be scheduled at a facility known to participants, with insurance coverage guaranteed and a primary care appointment confirmed—eliminating some of the common structural barriers to linkage—we limited our assessment to persons referred to the health center at SSTAR and not to other PCP offices. Third, because this was a medical record review study, we did not assess opioid or other drug use, or other outcomes of interest such as psychosocial function, in the 30 days following the initial injection. Finally, we do not have information about the reasons participants did not follow-up for additional treatment.

5.0 Conclusions

Transition from inpatient to outpatient care is a challenge for all persons with chronic medical or psychiatric illness. Nonetheless, continuing treatment is critical to long-term opioid abstinence in persons initiating any form of treatment, and linkage between care sites—in this case from inpatient detoxification to primary care—is of great interest to providers. Evaluation of the reasons for XR-NTX drop-out will be important to developing and testing adjuvant psychosocial therapies—previously used with oral naltrexone treatment such as contingency management, motivational or CBT counseling, or involvement of supportive others—that may improve early linkage to primary care and longer term treatment success in persons with OUD (Nunes, Rothenberg, Sullivan, Carpenter, & Kleber, 2006). Although detoxification programs are ideal environments for the promotion of XR-NTX, questions remain as to the identification of individuals who can be successfully bridged to continuing XR-NTX in the primary care setting (Woody, 2014).

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Highlights

- XR-NTX begun during opioid detoxification can be continued in primary care settings
- 55% of XR-NTX recipients link to primary care for continued treatment
- We found no predictors of XR-NTX continuation in primary care

Table 1

Demographic Characteristics, Treatment History, and Substance Use Behaviors by Receipt of Second XR-NTX Injection

	Sample (n = 62)	Continued XR-NTX		t or χ^2 (p =)
		No (n = 27)	Yes (n = 35)	
Age	32.4 ($\pm$ 7.8)	33.5 ($\pm$ 8.8)	31.5 ($\pm$ 7.0)	1.00 (.322)
Gender (Male)	42 (67.7%)	21 (77.8%)	21 (60.0%)	2.20 (.138)
Ethnicity				
Non-Latino Caucasian	56 (90.3%)	24 (88.9%)	32 (90.3%)	
African-American	1 (1.6%)	1 (3.7%)	0 (0.0%)	1.33 (.514)
Latino	5 (8.1%)	2 (7.4%)	3 (8.6%)	
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Education	11.8 ($\pm$ 2.2)	12.0 ($\pm$ 2.1)	11.7 ($\pm$ 2.2)	0.40 (.694)
Marital Status				
Single	49 (79.0%)	22 (81.5%)	27 (77.1%)	
w Partner	7 (11.3%)	2 (7.4%)	5 (14.3%)	0.78 (.678)
Divorced	6 (9.7%)	3 (11.1%)	3 (8.6%)	
Probation/Parole	15 (24.2%)	6 (22.2%)	9 (25.7%)	0.10 (.750)
Child Under 14 (Yes)	6 (9.7%)	4 (14.8%)	2 (5.7%)	1.44 (.229)
Homeless (Yes)	22 (35.5%)	9 (33.3%)	13 (37.1%)	0.10 (.756)
Primary Care Physician	42 (67.7%)	18 (66.7%)	24 (68.6%)	0.03 (.874)
Years Opiate Use	9.5 ($\pm$ 6.8)	9.5 ($\pm$ 8.1)	9.5 ($\pm$ 5.8)	0.13 (.989)
IDU (Yes)	51 (82.3%)	22 (81.5%)	29 (82.7%)	0.02 (.888)
Overdose (Past Year)	13 (21.3%)	6 (23.1%)	7 (20.0%)	0.08 (.772)
Cocaine Use	18 (29.0%)	8 (29.6%)	10 (28.6%)	0.01 (.927)
Alcohol Use	25 (40.3%)	11 (40.7%)	14 (40.0%)	0.00 (.953)
Marijuana Use	14 (25.6%)	7 (25.9%)	7 (20.0%)	0.32 (.580)
Benzodiazepine Use	22 (35.5%)	8 (29.6%)	14 (40.0%)	0.72 (.397)
Methadone Ever	23 (37.1%)	10 (37.0%)	13 (37.1%)	0.00 (.993)
Buprenorphine Ever	21 (33.9%)	10 (37.0%)	11 (31.4%)	0.21 (.644)
XR-NTX Ever	5 (8.1%)	4 (14.8%)	1 (2.9%)	2.94 (.086)
Detox (Past Year)	33 (53.2%)	15 (55.6%)	18 (51.4%)	0.10 (.747)
Discharge to Residential	19 (30.7%)	8 (29.6%)	11 (31.4%)	0.02 (.879)
Referral to IOP	19 (30.7%)	7 (25.9%)	12 (34.3%)	0.50 (.479)