

Regular article

Using buprenorphine short-term taper to facilitate early treatment engagement

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Abstract

The U.S. Federal Food and Drug Administration approved buprenorphine for drug abuse treatment in 2002, and it became available for clinical use in early 2003. Maryhaven, a community treatment program, participated in a National Institute on Drug Abuse Clinical Trials Network trial evaluating buprenorphine–naloxone (BNX; Suboxone) short-term taper for medically managed opioid withdrawal and later adopted this treatment. In a retrospective review, the first 64 patients treated with a BNX taper were compared with two groups of patients treated with clonidine before and after the implementation of the BNX program. Significantly more patients (about 80%) receiving BNX continued in further treatment compared to about 30% of those receiving clonidine. Patient outcomes are discussed in the context of the critical need for treatment continuation following detoxification. Common questions of potential adopters of the BNX taper are presented and addressed. Overall, BNX was readily integrated into the existing treatment service. © 2007 Elsevier Inc. All rights reserved.

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1. Introduction

The 2004 National Survey on Drug Use and Health reports that approximately 3.1 million Americans aged ≥ 12 years have tried heroin at least once and approximately 166,000 reported use in the last month (Substance Abuse and Mental Health Services Administration, 2005). Opioid addiction is a chronic disorder that has been associated with increased criminal activity, illness, unemployment, and death (NIH Consensus Conference, 1998). It has been a particular source of concern because of its role in fueling the

HIV/AIDS epidemic (Centers for Disease Control and Prevention, 2002). Injection drug users, about half of whom inject opioids, are at risk for contracting or spreading HIV through the sharing of injection equipment (Office of Applied Studies, 2003). Methadone maintenance is an effective treatment for opioid addiction, but only about 20% of opioid-dependent individuals receive it (Ball & Ross, 1991; NIH Consensus Conference, 1998; Office of National Drug Control Policy, 2002; Strain, Bigelow, Liebson, & Stitzer, 1999). As a full opioid agonist, methadone has been highly regulated and its availability has been restricted, which may account, in part, for its limited use (NIH Consensus Conference, 1998; Bickel & Amass, 1995). Buprenorphine–naloxone (BNX; Suboxone), a partial μ -opioid agonist, has increased the availability of agonist treatment since it became available for use as an office-based therapy in 2003 (Drug Addiction Treatment Act, 2000; Bickel & Amass, 1995).

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Multisite randomized clinical trials conducted through the National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) (Hanson, Leshner, & Tai, 2002; O'Connor, 2001) have demonstrated that BNX offers substantial improvement over clonidine for short-term detoxification (Amass et al., 2004; Ling et al., 2005). Furthermore, efforts to integrate and adopt the short-term use of BNX in nontraditional settings, such as therapeutic communities, have reported improved treatment retention of opioid-dependent patients (Collins, Horton, Reinke, Amass, & Nunes, in press). Although the focus of BNX use in the United States is substitution treatment, many community treatment providers focus on short-term approaches to manage opioid withdrawal while attempting to engage these patients into addiction treatment. Maryhaven, an integrated addiction and mental health service in Columbus, OH, implemented the short-term taper use of BNX in its detoxification program following participation in trials of BNX (Amass et al., 2004). Maryhaven was motivated to participate in clinical trials and adoption efforts to improve treatment for the opioid-dependent population by the finding that, like other detoxification programs (Mark, Dilonardo, Chalk, & Coffey, 2002, 2003), only about 30% of these patients complete a detoxification program and continue with treatment. Maryhaven regularly receives inquiries from other community treatment providers, who are considering adoption of a BNX taper, with a range of questions, including: BNX dosing strategies, use of ancillary medications, BNX diversion concerns, risks of inducing sudden acute withdrawal, staffing patterns, and treatment outcomes in community settings. The current report addresses the questions of potential adopters by describing both the early BNX adoption experience and the relative effectiveness of the BNX taper compared to the standard clonidine detoxification program at one community treatment program (Lamb, Greenlick, & McCarty, 1998).

2. Materials and methods

This study, approved by the Institutional Review Board (Friends Research Institute), is a retrospective chart review of patients admitted to Maryhaven for residential opioid detoxification. All admission and discharge data were derived from a retrospective electronic records review, with an additional review of BNX patients' physical records for Clinical Opiate Withdrawal Scale (COWS; Wesson & Ling, 2003) scores and medication administration records for BNX and ancillary medications. Medical management meeting notes were reviewed, and both physicians and nurses were interviewed regarding their early adoption experiences and their interpretation of chart review data.

2.1. Clinical setting

Maryhaven is a freestanding, private, public benefit (nonprofit) corporation, which provides mental health and

addiction recovery services to individuals and families regardless of their ability to pay. Services include homeless shelter/engagement center, subacute medical detoxification, ambulatory detoxification, short-term residential treatment, halfway house, day treatment, and intensive outpatient and outpatient services. The target populations for the detoxification program are adults with substance dependence, as defined by *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria (American Psychiatric Association, 1994), and adults in need of detoxification, as defined by the Ohio Department of Alcohol and Drug Addiction Services Patient Placement Criteria (<http://www.odadas.state.oh.us/GD/Templates/Pages/ODADAS/ODADASPrimary.aspx?page=3&TopicRelationID=220>). The program has a capacity of 25 beds and admits more than 600 opioid-dependent individuals annually. The length of stay is determined by medical necessity and ranges from 24-hour observation to 21-day BNX taper treatment for the medical management of opioid withdrawal. Patients are encouraged to participate in the daily program schedule as tolerated, which includes education sessions, group counseling, individual counseling, and on-site 12 Step meetings. The primary goals of this program are patient evaluation, stabilization, and transition to ongoing treatment. All patients were informed of the increased risk of accidental overdose when returning to opioid use after even a brief period of abstinence.

2.2. Study patients

To receive either BNX or clonidine treatment, patients were required to meet specific admission criteria, including: opioid dependence, age of ≥ 18 years, and appropriateness for subacute medical management. To be eligible for BNX treatment, patients were required to meet additional specific criteria: nonpregnant and nonlactating; willing to commit to at least a 13-day taper and continued treatment; not in need of detoxification protocol for additional substances; a current daily dose of < 30 mg, if on methadone; and without allergy or sensitivity to buprenorphine or naloxone. Some patients who met the BNX criteria were not given BNX for the following reasons: did not want to wait for admission, declined participation in preadmission screening, were mistakenly not informed of the availability of BNX, or refused BNX.

Individuals seeking admission to the detoxification unit may have called ahead to schedule an admission appointment or may have applied for admission on a drop-in basis. When patients called to schedule an admission, they were given a brief telephone screening to determine their eligibility for detoxification services. This screening included demographic information, history of major medical problems, recent drug use history, and mental health and drug abuse treatment history (Hubbard, Craddock, Flynn, Anderson, & Etheridge, 1997). Patients applying for this

level of care were often under the influence of drugs at the time of call, so the screening was brief and focused on essential eligibility information. Upon drop-in or scheduled visit to the center, patients received a nursing assessment of current medical and mental status, and a multipanel urine drug test to determine whether they met admission criteria and whether they could be safely managed at a subacute medical level of care. Opioid-dependent patients were informed of the availability of the BNX treatment during the first contact. The determination of which treatment the patient should receive was made within 24 hours of admission.

2.3. Comparison groups

Effectiveness findings were derived from a comparison of three groups of participants: participants assigned to the BNX taper (BNX), participants assigned to standard detoxification after the BNX taper had been introduced (CLON), and participants admitted to inpatient detoxification in the months prior to the implementation of the BNX taper (PRE-BNX).

Four hundred forty-eight participants were included in one of the three groups. The first group, BNX, comprised the first 64 patients assigned to receive BNX short-term taper at Maryhaven; these patients were admitted between August 25, 2003, and January 31, 2004. The second group, CLON, included all opioid-dependent patients admitted during the same period (between August 25, 2003, and January 31, 2004) who were not assigned to receive BNX ($n = 227$) and thus were assigned to clonidine detoxification. The third group, PRE-BNX, comprised 157 consecutive admissions to detoxification for opioid dependence immediately preceding the implementation of BNX; these patients were admitted between June 10, 2003, and August 24, 2003. The inclusion of the PRE-BNX group helps to control for differences (that might be found between the BNX and the CLON groups) stemming from selection bias and from the effects of clonidine patients being treated at the same time as BNX patients (e.g., clonidine patients might note that BNX patients were withdrawing more comfortably, and this could be a source of frustration, leading to early termination).

2.4. Treatment protocols

2.4.1. BNX induction and taper schedule (treatment provided to the BNX group)

Patients dependent on short-acting opioids who demonstrated signs and symptoms of opioid withdrawal, as confirmed by a COWS score of at least 5, were inducted onto BNX in accordance with procedures previously published (Amass et al., 2004). The BNX taper differed from the taper previously described by Ling et al. (2005) in two important ways. First, to avoid the potential for inducing sudden acute withdrawal, a Day 0 was added in

which no BNX was administered and instead only supplemental medications (clonidine and propoxyphene/acetaminophen, 100–650 mg) were provided. Second, symptom-triggered dose titration drove the maximum doses delivered during the first few days up to a maximum of 32 mg, in accordance with published national clinical guidelines for BNX stabilization (Center for Substance Abuse Treatment, 2004). Patients received their initial 4-mg BNX dose (dose indicates the amount of buprenorphine) on their second day in treatment and were observed for signs of precipitated withdrawal. A second 4-mg dose was administered 1–2 hours later if no signs of precipitated withdrawal were present. Patients introduced to BNX were observed and assessed on an ongoing basis and received ancillary medications for breakthrough symptoms of withdrawal, as needed: lorazepam for anxiety, ibuprofen for arthralgia, trimethoprim/azithromycin for nausea, loperamide hydrochloride for unformed stool, and trazodone for insomnia. The nurses administering the medication directly observed all BNX dosings. The standard dose-escalation regimen, similar to that used in an earlier CTN trial, was 8 mg on Day 2, 16 mg on Day 3, with continued escalation, as needed, until symptoms were well controlled, followed by a gradual reduction to zero (Table 1). The dosing regimen could be modified by the physician based on clinical presentation and COWS scores.

For patients taking long-acting opioids, specifically illicit and prescribed methadone (< 30 mg/day), and for whom a methadone-positive urine screen had been obtained, a buprenorphine-alone tablet (Subutex) was sometimes used initially to avoid the possibility of precipitated withdrawals (Amass et al., 2000, 2001). These patients were then transferred directly to BNX on Day 2 of their BNX protocol. Opioid-dependent patients receiving BUP or BNX participated in all aspects of the usual detoxification program (see Section 2.1).

Table 1
Sample medication dosing for 13-day BUP-NX detoxification

Detoxification day	BNX dose
0	Darvocet N, 100 mg; clonidine, 0.1 mg, po, tid; lorazepam, 1 mg
1	4 mg plus 4 mg more if not contraindicated (Subutex for the first dose if long-acting)
2	8 mg
3	16 mg ^a
4	14 mg
5	12 mg
6	10 mg
7	8 mg
8–9	6 mg
10–11	4 mg
12–13	2 mg

^a Doses were initially adjusted as needed to manage withdrawal symptoms up to a maximum of 32 mg before eventually fixing the maximum dose at 16 mg.

Table 2
Demographic characteristics

Characteristics	BNX (n = 64)	CLON (n = 227)	PRE-BNX (n = 157)
Age (years) [M (SD)]	36.9 (11.1)	36 (10.5)	36 (9.8)
Sex (% male)	66.6	70.5	63.1
Race (%)			
African American	23.4	18.1	18.5
Caucasian	76.6	80.6	77.7
Unknown	0	1.3	3.8

2.4.2. Clonidine detoxification protocol (treatment provided to both the PRE-BNX and the CLON groups)

Patients who were not treated with BNX received a propoxyphene/acetaminophen (100–650 mg) and clonidine protocol for the medical management of opioid withdrawal. This treatment consists of residential administration of clonidine and propoxyphene/acetaminophen (100–650 mg; for up to 72 hours) supplemented with ancillary medications that were the same as reported above for the BNX protocol.

2.4.3. Measures

This study included a comparison of the three groups on two outcome measures: treatment completion and treatment continuation.

2.4.3.1. Treatment completion. Treatment completion was a dichotomous variable for which each participant was scored as completing or not completing treatment. To be scored as completing treatment, the participant must have completed the assigned medication protocol.

2.4.3.2. Treatment continuation. Treatment continuation was a dichotomous variable for which each participant was scored as continuing or not continuing treatment. To be scored as continuing treatment, the participant must have accepted a transfer to either outpatient or inpatient treatment and must have attended at least 1 day of that treatment.

Additional information, including BNX dosing information, COWS scores, and clinical impressions of the staff administering the BNX treatment, was collected for the BNX group.

2.5. Data analysis

Data were analyzed using SPSS Version 12.0.1 (SPSS, 2004). Chi-square analyses were conducted for categorical variables, and one-way analysis of variance (ANOVA) was conducted for the continuous variable, age, to determine whether there were baseline differences among the study groups. Chi-square analyses were used to compare the three groups on treatment completion and treatment continuation. Significant chi-squares were followed by chi-square analyses for each two-group combination (e.g.,

BNX vs. CLON; CLON vs. PRE-BNX, etc.) to determine which comparisons accounted for significant results. All statistical tests were conducted within the 5% Type I error rate (two-sided).

3. Results

3.1. Study sample

Data were collected on 448 opioid-dependent individuals, as represented by three groups (BNX, $n = 64$; CLON, $n = 227$; PRE-BNX, $n = 157$). Sample characteristics are given in Table 2. One-way ANOVA revealed no significant group differences for age, and chi-square analyses revealed no significant differences for race or sex among the study groups.

3.2. Group comparisons

3.2.1. Treatment completion

As can be seen in Fig. 1, the treatment completion rates for the BNX, CLON, and PRE-BNX groups were 84%, 56%, and 54%, respectively. The chi-square analysis comparing the three groups on treatment completion was significant ($p < .001$). Post hoc chi-square tests revealed that the BNX treatment completion rate was significantly greater than the completion rate for the CLON ($p < .001$) and PRE-BNX ($p < .001$) groups, whereas the treatment completion rates for the CLON and PRE-BNX groups did not differ significantly from each other.

3.2.2. Treatment continuation

As can be seen in Fig. 1, the treatment continuation rates for the BNX, CLON, and PRE-BNX groups were 83%, 32%, and 31%, respectively. The chi-square analysis comparing the three groups on treatment continuation was significant ($p < .001$). Post hoc chi-square tests revealed that the BNX treatment continuation rate was significantly

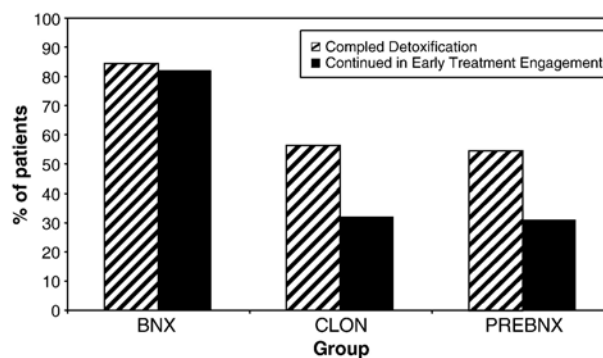


Fig. 1. Detoxification completion and early treatment engagement as functions of treatment group. Solid bars represent the percentage of patients completing detoxification; striped bars represent the percentage of patients attending at least 1 day of treatment following detoxification.

greater than the continuation rate for the CLON ($p < .001$) and PRE-BNX ($p < .001$) groups, whereas the treatment continuation rates for the CLON and PRE-BNX groups did not differ significantly from each other ($p > .05$).

3.3. BNX taper parameters and clinical impression

The chart review examined the amount and the duration of BNX received by each patient. The mean dose of BNX was 22.8 mg ($SD = 10.2$), which reflects the initial use of a dosing schedule that allowed a maximum dose of 32 mg. The mean duration of BNX dosing was 14.5 days ($SD = 6.9$). The chart review revealed that the use of higher BNX doses resulted in a longer time to taper down. A review of dose trends for the first 64 BNX patients demonstrates progression to the maximum dose, with successive admissions until, early on, nearly all patients were receiving ≥ 24 mg as a stabilizing dose. At higher dose ranges, the nursing staff reported receiving more frequent complaints of withdrawal-related discomfort upon the discontinuation of BNX. Admissions staff also began reporting refusals of BNX on admission, with patients stating that they had heard about the return of withdrawal symptoms following the discontinuation of BNX. Review of dosing practices with the medical team suggested that patients may have been exaggerating subjective complaints of withdrawal symptoms to achieve the maximum dose to divert some medication for use at a later date.

Ultimately, a combination of factors, including incidents of patients diverting the medication, complaints of returning withdrawal symptoms, and nursing reports of difficulty with discerning malingering from genuine need for additional medication, led the medical team to implement a fixed-dose taper with a maximum of 16 mg and with a stricter observation of BNX administration. The modified dosing taper, displayed in Table 1, used the same maximum dose as the schedule used in earlier trials (Amass et al., 2004; Ling et al., 2005). This change in maximum dose affected the last 9 of the 64 BNX patients included in this report. The stricter observation of administration involved the nurse observing the following: the patient placing the medication under their tongue, sitting for 10 minutes, drinking a cup of water, and then allowing the nurse to examine the content of one's mouth. The 16-mg maximum dose taper and the increased monitoring of administration reduced reports of medication diversion, minimized patient complaints of withdrawal on discontinuation, and reduced difficulties with evaluating patient malingering for higher doses.

4. Discussion

This retrospective chart review evaluated the relative effectiveness of the BNX taper compared to that of clonidine for detoxification. The results suggest that BNX, as compared to clonidine plus propoxyphene/acetaminophen (100–650 mg), produced significantly better outcomes

in both detoxification completion and engagement in postdetoxification treatment.

The finding that BNX significantly improved detoxification completion is consistent with findings from the NIDA CTN phase III multisite randomized effectiveness trials comparing BNX to clonidine for a 13-day taper detoxification for opioid dependence. These trials established that BNX short-term taper could be used safely and effectively by a wide range of community treatment providers (Amass et al., 2004). The primary findings were that 77% of inpatients assigned to BNX were present and drug-free on Day 13 versus 22% of those assigned to clonidine (Ling et al., 2005). The current study extends these findings by demonstrating that BNX improved the rate at which opioid-dependent individuals engaged in continued treatment.

Detoxification is a necessary step in engaging opioid-dependent patients in nonagonist-assisted addiction treatment; however, it is well established that detoxification alone is not an effective treatment for addiction (National Institute on Drug Abuse, 1999). Although detoxification can provide temporary reduction in the immediate risk of the direct consequences of opioid abuse, such as HIV infection and drug overdose, without ongoing addiction treatment, these benefits may be quickly reversed. BNX detoxification taper without ongoing treatment leads to rapid relapse (Fiellin, Kleber, Trumble-Hejduk, McLellan, & Kosten, 2004), and return to opioid use after even a brief period of abstinence may increase the risk for accidental drug overdose (Strang et al., 2003). Because detoxification is not a treatment for addiction and may even increase health risks for opioid-dependent individuals, the transition to continuing treatment is critical. Although the optimum dose and the duration of the BNX taper for opioid detoxification have not yet been established (Oreskovich et al., 2005), perhaps the most important measure for the success or the failure of this treatment is transition to ongoing addiction treatment.

Retention in treatment is linked to positive outcomes across a wide range of substance abuse problems (Brownell, Marlatt, & Lichtenstein, 1986; Hser, Grella, Hsieh, Anglin, & Brown, 1999; McLellan et al., 1985; 1994; Sees et al., 2000; Simpson, Joe, & Brown, 1997; Walker, Donovan, & Kivlahan, 1983). Realizing these benefits for opioid-dependent patients following detoxification is particularly challenging given that they have been found to have poor retention in abstinence-based treatment (Paraherakis, Charney, Palacios-Boix, & Gill, 2000). Numerous stakeholders in the quality improvement of substance abuse treatment programs have identified the transition to continued treatment as an important treatment performance measure. The Washington Circle Group, a multidisciplinary group of providers, researchers, managed care representatives, and public policy makers convened by the Center for Substance Abuse Treatment to establish performance measures and standards of accountability, has identified the linkage of detoxification with ongoing treatment as a

core performance measure for substance abuse treatment (Garnick et al., 2002; McCorry, Garnick, Bartlett, Cotter, & Chalk, 2000). The Center for Substance Abuse Treatment's (2006) recent treatment improvement protocol, *Detoxification and Substance Abuse Treatment*, specifies fostering patient readiness for and entry into substance abuse treatment as an essential part of detoxification. These efforts to improve the quality and the accountability of the health care system are in line with national initiatives aimed at improving substance abuse treatment by applying the recommendations of the Institute of Medicine (2001) report *Crossing the Quality Chasm: A New Health System for the 21st Century to Improving the Quality of Health Care for Mental and Substance-Use Conditions* (Institute of Medicine, 2006).

BNX detoxification prepares patients for continued treatment by relieving the symptoms of opioid withdrawal (Johnson, Strain, & Amass, 2003) and by improving subjective factors associated with treatment success, such as improved sense of well-being and self-efficacy (Ponizavsky, Greshpoon, Margolis, Cohen, & Rosca, in press). In this study, 49 of 54 patients (91%) who transitioned to ongoing treatment began treatment on or before the last day of BNX administration. This suggests that extending tapers to facilitate engagement in the next level of care is an important consideration in determining the optimum length of the BNX taper.

Lastly, capping the maximum dose of the BNX taper to 16 mg produced better results in terms of minimizing complaints of withdrawal, reducing medication diversion, and improving overall patient management. This observation is consistent with recent dose-escalation studies suggesting that there is a "ceiling" effect for BNX resulting in a lack of dose-proportional increases in effects for higher dose ranges (Ciraulo et al., 2006).

4.1. Limitations

The current report is based on a retrospective chart review in a clinical setting. In the absence of randomization, blinding, and other experimental controls, the observed differences between the groups may be due to factors other than the treatments administered, such as patient self-selection, staff expectations, patient expectations, and other nontreatment-specific factors. The BNX taper was also implemented as a program with a number of potentially important differences in addition to the medication (i.e., patients in the BNX group were required to consent to a longer treatment). It is not possible to distinguish which aspects of treatment contribute to the findings. However, previous BNX taper trials have matched these treatments on many of these nonspecific factors and found results similar to those of the current report (Ling et al., 2005). The consistency of current findings with previous well-controlled trials, combined with lack of differences in the clonidine groups before and after BNX was made available,

provides reasonable confidence in the conclusion that the treatment is effective.

Finally, unlike a prospective research protocol that has the ability to hold treatments constant over time and to ensure fidelity to protocols, the current report is a retrospective review of actual clinical practice. In this practice setting, clinicians modified the treatment in response to their own learning curve and in response to feedback from patients. Indeed, a range of dosing strategies was used within this brief implementation period. This program continues to change, and although the maximum 16-mg dosing schedule has been in place since January 1, 2004, the medical team has since begun using BNX in a range of approaches, including maintenance treatment and extended stabilization followed by taper. The current findings indicate that this treatment is robust and forgiving of inconsistencies in implementation, which are common in clinical practice.

5. Conclusions

This report provides outcomes from the adoption of an evidenced-based treatment within a community treatment program. We have attempted to address questions raised by providers regarding adoption of this treatment, including the following: What dose schedule should be used? Can a safety margin be added to prevent precipitated acute withdrawal? What level of medication monitoring is required when dosing heroine users in a residential setting? What results can be achieved in terms of detoxification completion and treatment continuation?

Even in the context of wide deviations from originally researched protocols, patients receiving the BNX taper had significantly better rates of detoxification completion and engagement in ongoing treatment. BNX was readily integrated into the existing treatment service and was well received by patients and staff. BNX's improvement of early treatment engagement following a short-term taper for medically managed opioid withdrawal is a critical step in improving patient outcomes. We recommend treatment continuation as a primary success criterion for determining the optimum BUP taper treatment dose and duration in research and treatment adoption efforts.

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now employed by Schering-Plough (the worldwide distributor of buprenorphine).

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