

Regular article

Using buprenorphine to facilitate entry into residential therapeutic community rehabilitation

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Abstract

For opioid-dependent patients, the need for detoxification has been a barrier to entry into long-term residential treatment. This report describes a retrospective observational cohort study with the first 38 opioid-dependent patients entering First Step, a 14-day buprenorphine–naloxone (Suboxone) detoxification regimen integrated into a long-term residential therapeutic community (TC) program. Eighty-nine percent (34 of 38) of First Step patients completed a 14-day buprenorphine taper protocol, 50% (19 of 38) completed an initial 3- to 4-week stay, and 39% (15 of 38) completed at least 3 months of residential treatment at the TC. Retention did not differ significantly in a demographically matched concurrently admitted control group without impending opioid withdrawal, in which 65% (24 of 37) completed an initial 3- to 4-week stay ($p = .20$) and 57% (21 of 37) completed at least 3 months of treatment ($p = .14$). Withdrawal symptoms were mild, and there were no instances of precipitated withdrawal. The findings suggest the potential for buprenorphine to serve as a bridge, improving the viability of long-term residential treatment for managing opioid dependence. © 2007 Elsevier Inc. All rights reserved.

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1. Introduction

Opioid addiction is a serious public health problem that results in profound personal and social costs, including disability, criminal activity, death from drug overdose, and increased risk of transmission of HIV and other blood-borne diseases. Agonist maintenance treatment with methadone is well established as effective and has been a mainstay of treatment for opioid dependence for nearly four decades. However, this treatment option has primarily been restricted to specially licensed clinics and has not been widely

embraced by providers of long-term “drug-free”-oriented residential treatment.

Opioid-dependent patients seeking treatment in long-term residential settings typically have to negotiate with opioid withdrawal syndrome, and this has served as a major barrier to entry and retention in drug-free programs. High early attrition and subsequent relapse rates have been seen, which are likely due to a less effective management of opioid withdrawal syndrome and failure to recognize that opioid addiction is a chronic relapsing disease. Only about 40–50% of patients completed 2–3 months of residential treatment and even fewer (20–30%) completed a 6-month stay (DeLeon & Schwartz, 1984; Simpson, Joe et al., 1997). Moreover, data on outcome following short-term inpatient detoxification have been poor, generally showing that less than 30% of patients completed detoxification and transferred to ongoing, long-term, drug-free treatment

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(Mark, Dilonardo, Chalk, & Coffey, 2002, 2003; McCusker, Bigelow, Luippold, Zorn, & Lewis, 1995). Reasons likely include inadequate regimens for medical withdrawal that discharge clients too soon while they are still symptomatic with opioid withdrawal symptoms, low motivation on the part of recently detoxified patients, a fragmented treatment system with stand-alone elements that are poorly linked to facilitate successful transfers, and an inadequate understanding of the dynamics of the early engagement and transitioning of clients into longer term treatment.

Long-term residential treatment programs, such as therapeutic community (TC) programs, provide a particularly attractive alternative for patients who have failed to succeed in agonist-based outpatient treatment or who need greater structure/distance from environments that promote their substance use. Large-scale studies of treatment outcome, such as the Drug Abuse Reporting Program (DARP) (Simpson & Sells, 1982), Treatment Outcome Prospective Study (TOPS) (Hubbard et al., 1989), and Drug Abuse Treatment Outcome Study (Hubbard, Craddock, Flynn, Anderson, & Etheridge, 1997), suggested that long-term residential treatment, as well as related outcomes such as reduced crime and improved employment, is effective in reducing drug abuse. Furthermore, time spent on treatment was associated with better long-term outcome (Condelli & Hubbard, 2003; Hubbard et al., 1997; Simpson, 1981; Simpson, Brown, & Joe, 1997).

The Phoenix House of New York is a TC offering long-term drug-free residential treatment that has provided services to opioid-dependent patients for more than 38 years. Historically, new opioid-dependent clients requiring medical withdrawal were referred to local inpatient detoxification programs for methadone tapering regimens. Fewer than half returned to begin residential treatment. Of those who did return, anecdotal reports from the program staff and on-site medical staff suggested that continued withdrawal symptoms were common and that rates of early dropout from residential treatment and subsequent relapse were high. A better model was needed, but existing federal and state regulations forbade community-based detoxification.

In 1997, the New York State enacted *Part 816 Chemical Dependence Crisis Service Regulations*, which allowed for the creation of community-based detoxification. In 2000, the landmark legislation *Drug Addiction Treatment Act of 2000 (DATA 2000)* was passed. *DATA 2000* permits qualified physicians to prescribe Schedule III–V medications approved by the U.S. Food and Drug Administration for the treatment of opioid dependence in their offices or community-based treatment settings (Boatwright, 2002). In 2002, sublingual buprenorphine (Subutex) and buprenorphine–naloxone (Suboxone) tablets were approved in the United States for treating opioid dependence and became available for clinical use as of early 2003. Buprenorphine is a partial μ -opioid agonist with a long duration of action due to its slow dissociation from the receptor. It has been shown to be an effective medication for ameliorating the symptoms

of opioid withdrawal and for the maintenance treatment of opioid dependence (Fudala et al., 2003; Gowing, Ali, & White, 2004; Johnson, Strain, & Amass, 2003). Buprenorphine is well suited for use in community treatment settings because it is generally easy to administer and manage, is effective for the treatment of opioid withdrawal symptoms, is nonsedating (thereby facilitating participation in group and community activities), and does not possess the stigma or regulatory burden associated with other agonists such as methadone (Amass et al., 2004).

A multicenter study of short-term buprenorphine–naloxone for medical withdrawal from opioids showed that buprenorphine–naloxone could be safely and effectively implemented across a range of residential and outpatient settings (Amass et al., 2004) and resulted in superior outcomes relative to the sympatholytic nonopioid agent, clonidine (Ling et al., 2005). Phoenix House participated in this trial, and the resulting positive experience suggested to the medical and clinical staff that a short-term on-site buprenorphine–naloxone regimen for medical withdrawal was safe and feasible, and held great promise as a tool to improve the early engagement and retention of opioid-dependent patients in long-term residential treatment. Phoenix House therefore established the First Step program for opioid-dependent patients entering the TC, in which an on-site, short-term, flexible regimen of buprenorphine–naloxone is provided and fully integrated into the initial phases of long-term residential treatment. This report describes the initial outcomes with this novel program, which is designed to utilize buprenorphine–naloxone as a bridge to ongoing participation in long-term residential treatment for opioid-dependent patients.

2. Materials and methods

This was a retrospective chart review conducted on the clinical charts of a consecutive series of the first 38 opioid-dependent patients admitted to a newly developed buprenorphine detoxification service (First Step) situated within a long-term residential TC and on a sample of matched concurrent patients without impending opioid withdrawal. The protocol for chart review was approved by the Institutional Review Boards of Phoenix House and the New York State Psychiatric Institute.

2.1. Clinical setting

Phoenix House is a traditional residential TC that admits patients with drug or alcohol dependence for long-term residential treatment of 1–2 years' duration. During the admissions evaluation process, patients are assessed for severity of addiction and appropriateness for residential treatment. The ability to participate safely in all community and group activities is a primary consideration. Patients are excluded and referred to more specialized or higher levels of

care if they present with psychiatric or medical problems requiring acute or emergency management. Patients are first admitted to a 60-bed induction unit for a stay of approximately 1 month, during which they are stabilized and introduced to a TC milieu. Patients who complete treatment at the induction unit are referred to one of a variety of long-term residences for the duration of their 1- to 2-year treatment at Phoenix House. The majority of patients admitted to the induction unit are poor, unemployed, minority men from New York City with a history of current or prior criminal justice involvement. The most common drugs of choice are cocaine, heroin, and alcohol. Significant medical and psychiatric comorbidities are common (Levin, Evans, & Kleber, 1998; Levin et al., 2004). To address client needs, Phoenix House has developed a comprehensive array of on-site health care, legal, educational, family, and vocational services. Within the campus of the induction unit, there is a primary care medical clinic, where patients' medical, dental, optometry, and psychiatric needs are evaluated and managed.

Prior to the introduction of the First Step program described below, patients presenting to Phoenix House for the treatment of opioid dependence and patients on impending withdrawal were referred elsewhere for medical withdrawal, usually to hospital-based inpatient detoxification units in the New York City area, which generally performed a brief methadone taper and discharged patients after 3–5 days. With the introduction of the First Step program, such patients, who otherwise met the eligibility criteria summarized above, were offered admission directly to the induction unit.

2.2. Procedures: the first step program

As noted above, First Step was developed after Phoenix House participated in a clinical trial of buprenorphine–naloxone through the National Institute on Drug Abuse (NIDA) Clinical Trials Network (CTN) (Amass et al., 2004; Ling et al., 2005). Lessons learned during participation were directly incorporated into the model. First Step clinical protocols were adopted from the CTN trial, including the use of the Clinical Opiate Withdrawal Scale (COWS) (Wesson & Ling, 2003) as a clinical tool to assess opioid withdrawal, the use of multipanel urine test screening, and the dosing schedules for buprenorphine–naloxone induction and tapering. Similar exclusion criteria were also adopted, including the exclusion of pregnant women and patients with acute medical, psychiatric, or medical and psychiatric conditions requiring hospital admission, although, in general, patients entering treatment in Phoenix House often had nonemergent medical or psychiatric problems that were managed in-house, including mild to moderate alcohol withdrawal.

Candidates for admission were prescreened by phone using a short questionnaire administered by program staff. Urine toxicology for the metabolites of opioids, methadone, benzodiazepines, barbiturates, cocaine, and cannabinoids

was obtained and reported either during prescreening or upon arrival at the facility. Acceptance into First Step required the approval of both the physician staff and the Admissions Department manager, ensuring appropriate placement into both residential and medically supervised withdrawal programs. After completing standardized Admissions Office procedures, candidates were transported with a staff escort via contracted car service to the Long Island City induction facility where they received a thorough search of their property and a shower before being delivered to the medical clinic.

Initial medical assessments were performed at the on-site medical clinic by an internist and a registered nurse, both of whom trained for and participated in an earlier NIDA CTN study. Medical intake included opioid withdrawal screening using COWS and, when indicated, alcohol withdrawal screening using the Clinical Institute for Withdrawal Assessment (CIWA) (Stuppaek et al., 1994), confirmation of multipanel urine testing results, pregnancy urine testing, breathalyzer testing, vital signs, and standardized history and physical examination performed by the staff physician. Asymptomatic patients considered at risk for withdrawal were admitted to the service for 24 hours of observation.

Mild to moderate alcohol withdrawal was managed using tapering doses of clonazepam (Klonopin). The admission of patients with positive urine screens for benzodiazepines but who were not thought to be at risk for withdrawal was also allowed. CIWA scales were incorporated into the admission and daily screening procedures when indicated.

First Step psychosocial programming was designed as a fully integrated outpatient enhancement to usual residential treatment. Morning group sessions were facilitated by TC program staff and incorporated TC orientation curriculum and drug- and health-related information. Sessions were supportive and informational, serving to facilitate peer-to-peer interactions, early engagement, and group cohesion. Patients who completed a buprenorphine taper but were still living on the induction unit regularly attend and participate. Individual counseling was available as needed by the licensed staff, all of whom were members of the induction staff and reported to the induction facility director, who was responsible for the administration of the residential program. Integration was further facilitated by cross-department case conferencing.

2.2.1. Buprenorphine–naloxone induction and taper schedule

Patients dependent on short-acting opioids, and demonstrating signs and symptoms of opioid withdrawal as confirmed by a COWS score of at least 5 were inducted directly onto buprenorphine–naloxone in accordance with previously published procedures (Amass et al., 2004). Patients received their initial 4 mg of buprenorphine–naloxone dose (expressed as milligrams of buprenorphine) 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. All first-day admissions were assessed once again prior to bedtime and received additional buprenorphine dosing or ancillary over-the-counter medication (e.g., ibuprofen, diphenhydramine) as needed. All buprenorphine dosings were directly observed. The standard dosing regimen, similar to that used in the earlier CTN trial, was 8 mg on Day 2, 16 mg on Day 3, and a gradual reduction to 0 by Day 14. 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 (less than 40 mg of daily use), and for whom a methadone-positive urine screen had been obtained, the buprenorphine-alone tablet (Subutex) was sometimes used initially to avoid the possibility of precipitated withdrawal due to naloxone in accordance with earlier recommendations (Amass, Kamien, & Mikulich, 2000, 2001). Such patients were then transferred directly to buprenorphine–naloxone. All other dosing procedures were as described above.

After initial dosing, patients were escorted to the residential program located on the campus in an adjacent building and continued with orientation activities. First Step patients were expected to participate in all aspects of usual TC activities. Special consideration for additional bed rest and reduced activities was granted when needed. Each morning between 9:30 a.m. and 11:00 a.m., all First Step participants were escorted to a designated group room in the medical clinic complex where they engaged in supportive group activities while they waited for daily medical assessments and buprenorphine dosing.

2.3. Data collection

2.3.1. First Step patients

Clinical charts were reviewed retrospectively on the consecutive series of the first 38 opioid-dependent patients admitted to First Step during its first 4 months of operation (May to September 2003) and a sample of matched concurrent patients without impending opioid withdrawal. Data extracted included the demographic and clinical features of patients on admission, parameters of their treatment with buprenorphine (dose and duration, ancillary medications), opioid withdrawal scores (COWS), and days retained on residential treatment. Patients still retained on treatment as of February 2004 were considered censored at that point for the purpose of survival analysis. Categorical measures of retention included whether the patient: (a) completed the 14-day buprenorphine detoxification; (b) completed at least 2 days of residential treatment after the last dose of buprenorphine–naloxone; (c) completed treatment at the induction unit (approximately 3–4 weeks) and was successfully transferred to a long-term residential unit; and (d) completed at least 3 months of residential

treatment at Phoenix House (induction unit and subsequent long-term residence).

2.3.2. Matched comparison group

A comparison group of patients without impending opioid withdrawal admitted to Phoenix House during the same time frame was also drawn for chart review and matched to First Step index patients. For each patient admitted to First Step, a case was drawn matched for: (1) age within 3 years of the index patient; (2) gender; (3) legal status (mandated vs. voluntary); (4) ethnicity; and (5) admission within 1 month of the index client. If no match could be found immediately for a given index case, the ranges for age and admission date were expanded until a match was identified. In a few instances, it was not possible to find a perfect match and, in one instance, the same comparison patient was used as match for two First Step patients. The purpose was to be able to compare clinical outcomes for First Step patients, in terms of retention in treatment, to those for a group of patients typically admitted to Phoenix House, who were matched on other basic demographic prognostic factors. Most of these patients had cocaine dependence as their primary drug problem. Matching on the primary drug problem was not possible because opioid-dependent patients in need of withdrawal were not admitted to Phoenix House prior to the inception of First Step, and, subsequently, all such patients were admitted to First Step.

2.4. Data analysis

Differences between First Step and control patients on baseline demographic and clinical features were carried out with chi-square or *t* tests. Categorical outcome measures (completion of treatment at the induction unit and successful transfer to long-term residence, and completion of at least 3 months of long-term residential treatment) were compared between groups with chi-square test. Days retained on treatment were compared between groups using Kaplan–Meier survival curves and log-rank test. Within the First Step group, baseline demographic and clinical variables

Table 1
Baseline demographic characteristics of opioid-dependent patients entering the First Step buprenorphine induction and concurrent nonopioid-dependent controls^a

| Characteristics | First step patients (<i>n</i> = 38) | Concurrent controls (<i>n</i> = 37) |
|---|--------------------------------------|--------------------------------------|
| Age in years [<i>M</i> (range)] | 37.8 (23–57) | 38.2 (21–58) |
| Gender [<i>n</i> (%)] | | |
| Female | 7 (18) | 6 (16) |
| Ethnicity [<i>n</i> (%)] | | |
| African American | 15 (39) | 16 (43) |
| Hispanic | 16 (42) | 14 (38) |
| Caucasian | 6 (16) | 6 (16) |
| Asian | 1 (3) | 1 (3) |
| Legal status (mandated) [<i>n</i> (%)] | 5 (13) | 8 (22) |

^a None of the differences is statistically significant.

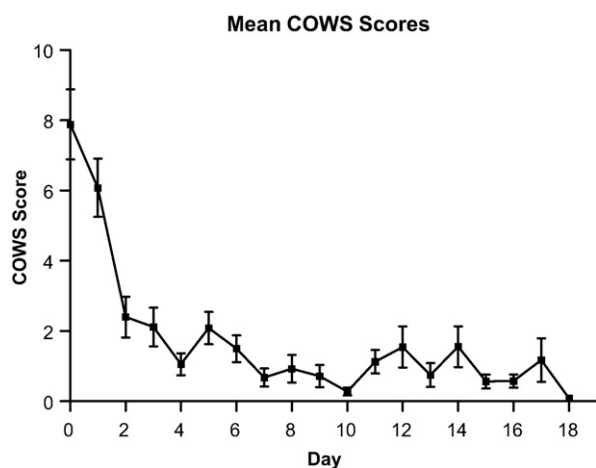


Fig. 1. Opioid withdrawal symptom severity (COWS) scores ($M \pm SE$) over the course of buprenorphine induction and 14-day taper among 38 opioid-dependent patients in a residential treatment program with integrated buprenorphine detoxification (First Step program).

were examined as predictors of long-term retention in treatment (with completion of at least 3 months of treatment as the dichotomous dependent variable) with chi-square or t tests. All tests were two-tailed, and α was set at $p < .05$.

3. Results

3.1. Sample description

Table 1 displays the demographic features of the First Step group ($n = 38$) and the matched concurrent control group ($n = 37$) that were used for matching. Opioid-dependent patients entering treatment in First Step had a wide age range (from young adult to middle age) and were predominantly male and of ethnic minority (African American and Hispanic), typical of samples seeking residential treatment at Phoenix House. Most were seeking treatment voluntarily, as opposed to being mandated by the courts. First Step patients were mostly unemployed (100%) and single (92%), and only 26% had completed high school. The matching procedure was successful, with close concordance between the First Step and concurrent controls.

First Step patients had been using heroin for an average of 13.3 years (range, 1–34 years) and were currently using an average of 8.3 bags/day (range, 2–20): 22 (58%) by intranasal route, 15 (39%) by intravenous route, and 1 (3%) by smoke inhalation. In addition, on admission, 8 (21%) had urine positive for methadone. Other substances used immediately prior to admission, as indicated by urine toxicology or self-report, included cocaine (47%), alcohol (56%), benzodiazepines (16%), and cannabis (16%). More than half of First Step patients had a history of significant medical problems (66%), including hepatitis C (18%), asthma or bronchitis (8%), hypertension (8%), migraine (5%), and one case each of arthritis, gastritis, paraplegia,

seizure disorder, HIV, and history of endocarditis, pulmonary embolism, or gastrointestinal bleeding.

3.2. Buprenorphine–naloxone treatment

Eighty-nine percent (34 of 38) of First Step patients completed the 14-day buprenorphine induction and taper. The mean number of days of buprenorphine administration was 11.6 (range, 2–20), with a mean maximum daily dose of 13.7 mg (range, 4–16). All patients tolerated the taper well (see Fig. 1). The mean COWS score on admission was 7.89 ($SD = 6.06$), indicative of a moderate level of withdrawal symptoms emerging prior to the initiation of buprenorphine–naloxone, and was rapidly relieved for most patients, with COWS scores dropping rapidly then remaining low throughout the taper (see Fig. 1). Three patients required adjunctive treatment with clonazepam for alcohol-related withdrawal symptoms. No episodes of precipitated withdrawal were observed.

3.3. Retention in long-term residential treatment

Seventy-six percent (29 of 38) of First Step patients remained in the residential treatment program 2 days after the completion of the buprenorphine taper. Among First Step patients, 50% (19 of 38) completed treatment at the induction unit (3–4 weeks) and were transferred to long-term treatment residences, compared to 65% (24 of 37) among concurrent controls, $\chi^2(df = 1) = 1.69$, $p = .20$. Among First Step patients, 39% (15 of 38) completed at least 3 months of long-term residential treatment, compared to 57% (21 of 37) among concurrent controls, $\chi^2(df = 1) = 2.24$, $p = .14$. Fig. 2 displays Kaplan–Meier survival curves for retention in long-term residential treatment (induction unit and subsequent long-term residence) for the First Step group versus the concurrent control group. As can be seen, retention was somewhat better overall among controls than

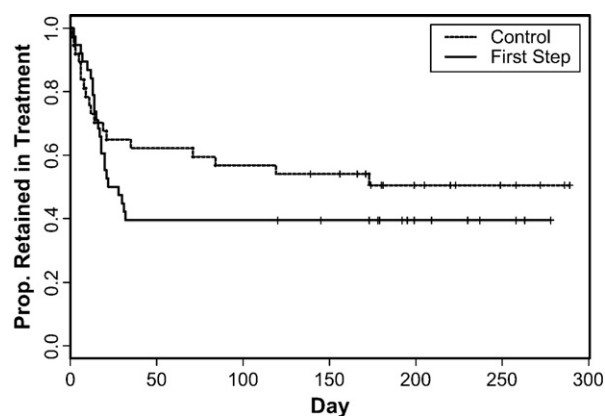


Fig. 2. Kaplan–Meier survival curves showing the proportion of patients retained in long-term residential treatment over time: opioid-dependent patients in the First Step program with initially integrated 14-day buprenorphine taper ($n = 38$) compared to concurrent controls ($n = 37$) without opioid dependence (log-rank test = 0.8, $p = .36$).

Table 2

Demographic and clinical predictors of long-term retention in residential treatment among opioid-dependent patients ($n = 38$) treated initially with the buprenorphine–naloxone taper^a

| Predictors | Retained for more than 3 months ($n = 15$) | Dropped out before 3 months ($n = 23$) | Test statistic ^b | p |
|---|--|--|-----------------------------|-----|
| Demographics | | | | |
| Age (years) [M (SD)] | 38.2 (9.4) | 37.5 (6.8) | 0.275 | .79 |
| Female (%) | 20 (3/15) | 17 (4/23) | 0.04 | .84 |
| African American (%) | 27 (4/15) | 48 (11/23) | 2.96 | .40 |
| Hispanic (%) | 44 (7/16) | 56 (9/16) | | |
| Caucasian (%) | 50 (3/6) | 50 (3/6) | | |
| Asian (%) | 100 (1/1) | 0 (0/1) | | |
| Education (years) [M (SD)] | 11.1 (1.3) | 10.3 (1.4) | 1.86 | .07 |
| Legal pressure (%) ^c | 20 (3/15) | 35 (8/23) | 0.97 | .33 |
| Medical problems (%) ^d | 47 (7/15) | 70 (16/23) | 1.99 | .16 |
| Heroin use | | | | |
| Route (intravenous or smoke inhalation) (%) | 53 (8/15) | 35 (8/23) | 1.28 | |
| Years of use [M (SD)] | 13.4 (10.2) | 13.2 (10.0) | 0.07 | .95 |
| Current use (bags/day) [M (SD)] | 9.81 (5.48) | 7.09 (4.44) | 1.48 | .16 |
| Number of past detoxifications [M (SD)] | 2.13 (2.39) | 1.91 (1.88) | 0.32 | .76 |
| Number of past treatments [M (SD)] | 1.60 (1.92) | 0.74 (1.01) | 1.81 | .08 |
| Other-drug use | | | | |
| Methadone-positive urine (%) | 36 (5/14) | 25 (5/20) | 0.46 | .50 |
| Current alcohol use (%) | 27 (4/15) | 30 (7/23) | 0.06 | .81 |
| Urine positive for other drugs (%) ^e | 50 (7/14) | 85 (17/20) | 4.86 | .04 |
| Course of detoxification | | | | |
| Initial COWS score [M (SD)] | 8.00 (6.83) | 7.78 (5.74) | 0.10 | .92 |
| Required adjunctive medication ^f (%) | 13 (2/15) | 48 (11/23) | 4.80 | .04 |

^a Values are expressed as M (SD) or % (number of cases with predictor/total in retention category).

^b t Statistic for continuous predictors, or chi-square test for categorical predictors.

^c Court-mandated (five cases), parole (two cases), or alternative to incarceration (four cases).

^d The most common were hepatitis C (eight cases), asthma/bronchitis (five cases), hypertension (three cases), HIV (two cases), migraines (two cases), or ulcer/gastritis (two cases).

^e Cocaine (19 cases), benzodiazepines (6 cases), or cannabis (5 cases).

^f Clonazepam (three cases), diphenhydramine (nine cases), ibuprofen (five cases), or Atarax (one case).

among First Step patients, although the difference was not significant (log-rank test = 0.80, $p = .36$). Most of the attrition in both groups occurred during the first 40 days of treatment, after which retention stabilized.

3.4. Predictors of retention among buprenorphine-treated patients

Table 2 displays the baseline demographic and clinical features of patients in the First Step program who were retained for at least 3 months in long-term residential treatment versus those who dropped out before 3 months. No demographic variables, other than years of education (at a trend level, $p < .07$), predicted retention. Interestingly, none of the measures of opioid dependence severity (such as years of use, route of use or bags per day, or initial COWS score) predicted retention, and retention was equally likely among patients with methadone-positive urine on admission. Patients who dropped out were more likely to have had other-drug use prior to admission (cocaine, benzodiazepines, or cannabis), in addition to opioids ($p < .04$), as indicated by urine toxicology on admission, and were more likely to have been prescribed adjunctive medications [clonazepam (Klonopin), diphenhydramine (Benadryl), ibuprofen (Motrin), and hydroxyzine (Atarax)] ($p < .04$).

4. Discussion

Short-term buprenorphine–naloxone for medical withdrawal of opioid-dependent patients entering residential treatment at a TC was a useful adjunct to ongoing care that maintained rates of engagement and early retention in residential treatment comparable to those observed for a matched cohort of nonopioid-dependent patients. Most such opioid-dependent patients would not have been admitted to the TC before the buprenorphine–naloxone program addendum was established.

Ninety percent of opioid-dependent patients enrolled completed the 2-week buprenorphine–naloxone taper. This completion rate was comparable to those reported in the multisite trial of buprenorphine–naloxone on which the taper regimen was modeled (Amass et al., 2004; Ling et al., 2005) despite the enrollment of patients with more severe histories of medical and psychiatric comorbidity. The flexible procedures used in this study for both daily buprenorphine–naloxone and ancillary medication dosing, as well as the ability to adjust the length of the taper regimen, may have promoted retention. The findings underscore the suitability of buprenorphine suitability for opioid-dependent patients seen in community treatment settings.

Logistically, augmenting programming within the TC to include the use of buprenorphine–naloxone proved uncomplicated to manage. Daily dosing was easily integrated into the usual schedule of the treatment program. Similarly, there were no significant safety issues or medical complications encountered during the use of buprenorphine–naloxone for dose induction or medical withdrawal, and withdrawal symptoms were minimal, consistent with earlier findings with this taper regimen (Amass et al., 2004; Ling et al., 2005) and other reports of short-term buprenorphine tablet dosing regimens (Breen et al., 2003; Gibson, Doran, Bell, Ryan, & Lintzeris, 2003; Lintzeris, Bammer, Rushworth, Jolley, & Whelan, 2003; Lintzeris, Bell, Bammer, Jolley & Rushworth, 2002).

Of note, some patients in this series were using benzodiazepines prior to admission (16%; 6 of 38), and a few (8%; 3 of 38) required oral benzodiazepines for concomitant treatment of impending alcohol or benzodiazepine withdrawal. These patients tolerated the buprenorphine–naloxone combination uneventfully. Concern about the risk of fatal overdose resulting from the misuse of buprenorphine combined with intravenous benzodiazepines had been raised previously based on deaths following the introduction of buprenorphine in France (Pirnay et al., 2004). Because of this concern, patients using benzodiazepine had been excluded from participation in a prior clinical trial of buprenorphine–naloxone conducted in the CTN (Amass et al., 2004; Ling et al., 2005). The present findings are consistent with general clinical experience and suggest that the combined use of prescribed doses of benzodiazepines with sublingual buprenorphine is safe. Management of patients in a residential treatment setting would likely reduce the risk of misuse of the type of medication, which might engender overdose risk.

The First Step protocol inducted all patients taking opioids directly onto buprenorphine–naloxone without incident, consistent with prior reports (Amass et al., 2004) and with the general field experience in the United States with the use of buprenorphine–naloxone as part of office-based practice. There were no instances of precipitated withdrawal, even for clients who had been taking lower doses of the long-acting agonist methadone, and the presence of methadone in urine on admission was not associated with dropout. For some of the methadone-positive patients, the buprenorphine-only tablet formulation (Subutex) was used for dose induction with these patients before transfer to the combined buprenorphine–naloxone formulation, consistent with earlier recommendations (Amass et al., 2000, 2001), although the study was not designed to examine whether this contributed to retention. The use of long-acting agonists such as methadone prior to induction onto buprenorphine had been associated with precipitated withdrawal (Levin, Fischman, Connerney, & Foltin, 1997), and patients with a methadone-positive urine were excluded from participation in a prior clinical trial of buprenorphine–naloxone conducted in the CTN (Amass

et al., 2004; Ling et al., 2005). The present findings are consistent with other studies (Glasper, Reed, deWet, Gossop, & Bearn, 2005; Levin et al., 1997) suggesting that induction onto buprenorphine among patients using methadone is safe as long as the methadone dose is low (less than 30–40 mg/day), and withdrawal symptoms have clearly emerged prior to the first dose of buprenorphine.

Following treatment with buprenorphine–naloxone, about half of patients completed 1 month of residential treatment, and 39% completed at least 3 months of residential treatment. This rate of early treatment retention in long-term residential programming was within the same range as that observed in the comparison group of demographically matched patients entering treatment concurrently for other drug problems. The earlier multisite trial of short-term buprenorphine–naloxone included a number of residential treatment programs among its performance sites (Amass et al., 2004; Ling et al., 2005), although retention in long-term residential treatment was not reported as an outcome measure. This study therefore represents an extension of the earlier work and suggests that this approach could be widely implemented as a bridge to early engagement in long-term residential treatment for opioid-dependent patients. The current findings with buprenorphine–naloxone also corroborate Australian studies using buprenorphine for medical withdrawal, where at least 50% of patients who were inducted onto buprenorphine continued in postwithdrawal treatment, usually buprenorphine maintenance (Gibson et al., 2003; Lintzeris et al., 2002). Taken together, the data underscore the utility of short-term treatment approaches with buprenorphine to serve as an initial bridge to continuance of care.

Substantial attrition still occurred after completion of the 14-day buprenorphine–naloxone taper. Although subtle subacute withdrawal symptoms could have promoted later dropout, the low withdrawal scores suggest other factors at work that promote attrition. The findings raise the question as to whether an additional period of pharmacological stabilization (e.g., 2–3 months of buprenorphine before initiating a dose taper) might facilitate patients becoming more fully integrated into residential treatment. The length of stay in residential treatment (in particular, retention of 6 months or more) has been associated with improved long-term outcomes (Condelli & Hubbard, 2003; Hubbard, Craddock, & Anderson, 2003). A longer period of stabilization with agonist therapy might therefore permit a larger proportion of patients to be retained into the 3- to 6-month range, which has been associated with better outcomes. This notion is also supported by the findings noted above from Australian studies, where patients who initiated a short-term buprenorphine regimen had immediate access to ongoing agonist maintenance treatment. Half or more of patients in these studies remained in buprenorphine maintenance when assessed 1 month (Lintzeris et al., 2002) or 3 months (Gibson et al., 2003) after receiving the initial short-term intervention.

Two factors predicted greater attrition during residential treatment: prescription of adjunctive medications, and urine screens indicating nonopioid drug use prior to admission. The prescription of adjunctive medications (mainly clonazepam, ibuprofen, or diphenhydramine) likely reflected greater withdrawal discomfort. Future work should seek ways to further minimize withdrawal symptoms and reduce their impact on attrition. This could include the use of a broader dose range of, and/or longer periods of exposure to, buprenorphine. The use of drugs other than opioids (e.g., cocaine, benzodiazepines, or cannabinoids) may have reflected a greater overall severity of drug dependence or perhaps an impact of other withdrawal syndromes. For example, serious benzodiazepine withdrawal was not observed in our series, but even mild benzodiazepine withdrawal could have complicated the clinical picture. Thus, other-drug use might have indicated a need for a more intensive psychosocial support or, again, a greater attention to withdrawal symptoms or longer periods of pharmacological support with buprenorphine. Certainly, in studies of polysubstance abusers receiving opioid maintenance treatment with high-dose buprenorphine-only (Kakko, Dybrandt, Kreek, & Heilig, 2003) and buprenorphine–naloxone (Fudala et al., 2003) tablets for up to 1 year, the use of both opioid and nonopioid drugs declined substantially.

4.1. Limitations and future directions

The present findings must be interpreted cautiously given the limitations of this retrospective observational cohort design. A concurrent control group with acute opioid dependence requiring detoxification but was managed in the traditional way by referral to a hospital for inpatient detoxification prior to admission to Phoenix House was not available because, once the First Step program had begun operation, all opioid-dependent patients requiring detoxification were admitted directly to First Step. In the 5 months prior to the inception of the First Step program (December 2002 to April 2003), only 18 opioid-dependent patients requiring detoxification were screened and referred to inpatient detoxification units, of whom only 9 (50%) returned to be admitted to Phoenix House and 6 (33%) completed 3 months or more treatment. That 38 such patients were admitted during the first 5 months after the opening of First Step suggests that the First Step program enabled Phoenix House to substantially increase its recruitment of acute opioid-dependent patients. This suggests the potential positive impact of programs like First Step on service delivery, but also the difficulty of constructing a comparable historical control.

Future studies should be conducted using either prospective case–control designs or, preferably, randomized controlled trials in which outcome is compared between a model such as First Step and standard inpatient detoxification followed by admission to residential treatment, or between the former and longer durations of stabilization on

buprenorphine prior to taper or buprenorphine maintenance therapy. Such studies should also include formal cost-effectiveness analyses to examine whether strategies that avoid expensive inpatient detoxification would result in significant cost savings. For example, the First Step buprenorphine–naloxone program described in this report was carried out on an ambulatory basis, and the mean cumulative dose of buprenorphine–naloxone was 85 mg for a 14-day regimen, adding a total medication cost of approximately US\$50 per patient to services. By contrast, hospital-based inpatient detoxification costs are on the order of several thousand dollars per day.

In summary, the currently widespread model of hospital-based inpatient detoxification for opioid dependence has shown poor outcomes in terms of promoting participation in continued treatment and long-term abstinence, prompting a call by the Substance Abuse and Mental Health Services Administration (SAMHSA) to improve linkages between detoxification and substance abuse treatment (Mark et al., 2002). In this study, the First Step model resulted in rates of medical withdrawal completion and successful continuation into residential treatment that were comparable to those in a nonopioid-dependent sample, demonstrating a much needed improvement in early engagement and linkage to ongoing treatment for this difficult-to-engage patient population. These findings suggest that buprenorphine's availability for use in multiple treatment settings and buprenorphine's ability may serve as a bridge to continued care and may expand the viability of long-term residential treatment approaches for managing opioid dependence.

In the field of addictions treatment, new innovations springing from basic and clinical research have often failed to achieve widespread adoption among practitioners in the field as a whole (Institute of Medicine, 1998). This observation inspired the conception and launch of the NIDA CTN. The development of the First Step program within a community-based treatment organization, subsequent to participation in a CTN-sponsored clinical trial, suggests that research participation may serve as a powerful vehicle for the dissemination of new evidence-based techniques into clinical practice.

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