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Self-treatment: Illicit buprenorphine use by opioid-dependent treatment seekers

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Abstract

Outpatient-based opioid treatment (OBOT) with buprenorphine is an important treatment for people with opioid dependence. No quantitative empirical research has examined rationales for use of illicit buprenorphine by U.S. opioid-dependent treatment seekers. The current study sequentially screened OBOT admissions (n = 129) during a 6-month period in 2009. This study had two stages: (a) a cross-sectional epidemiological analysis of new intakes and existing patients already receiving a legal OBOT prescription (n = 78) and (b) a prospective longitudinal cohort design that followed 76% of the initial participants for 3 months of treatment (n = 42). The primary aims were to establish 2009 prevalence rates for illicit buprenorphine use among people seeking OBOT treatment, to use quantitative methods to investigate reasons for this illicit use, and to examine the effect of OBOT treatment on illicit buprenorphine use behavior. These data demonstrate a decrease in illicit use when opioid-dependent treatment seekers gain access to legal prescriptions. These data also suggest that the use of illicit buprenorphine rarely represents an attempt to attain euphoria. Rather, illicit use is associated with attempted self-treatment of symptoms of opioid dependence, pain, and depression.

Keywords: Buprenorphine; Illicit; Self-treatment; Pain; Depression

1. Introduction

> *"Ultimately, the risk of abuse of an opioid analgesic has to be judged against the therapeutic benefit it offers....Misusers do not appear to have come to harm from their use of buprenorphine" (Lewis, 1985, p. 364, 370).*

Despite years of clinical research and postmarketing data showing that misuse of buprenorphine does not result in the same harm as abuse of other opioids and confers less risk of serious side effects than does methadone (Bridge, Fudala, Herbert, & Leiderman, 2003), concern about the dangerous consequences of buprenorphine diversion is a recurrent topic in the popular media. Little published research is available to identify reasons for illicit buprenorphine use among opioid-dependent treatment seekers in the United States. Defining inappropriate use of buprenorphine has been a challenge, and currently no terminology consensus exists.

1.1. Self-treatment

Self-treatment refers to any attempt to provide an appropriate therapeutic strategy for oneself in the absence of professional advice or consent. During 1995, the Institute of Medicine argued for understanding the use of illicit methadone as self-treatment attempts to reduce the withdrawal symptoms and craving of heroin addiction (Lewis, 1999). Buprenorphine self-treatment could represent attempts to provide a therapeutic strategy in three broad categories: opioid dependence symptoms, negative affective

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states, and physical pain. More specifically, in our clinical experience, self-treatment with buprenorphine often represents a therapeutic strategy to address one of the following: to relieve opiate withdrawal symptoms, to prevent craving, to make a reasonable dose adjustment, to divide doses for perceived optimal coverage, to use extra buprenorphine as needed to prevent relapse during periods of stress, to control physical pain, or to reduce negative affective states (e.g., depression and anxiety). Clinicians, patients, and others can differentiate the intention behind these strategies from attempts to attain euphoria. No previous quantitative research has investigated the role self-treatment plays in illicit buprenorphine use for opioid dependence; this absence of research is notable especially because of the potential important relationship between buprenorphine use and treatment of comorbid pain and depression.

Self-medication is a familiar construct, embedded within the concept of self-treatment, in which people use illicit drugs to self-regulate their emotions, self-esteem, relationships, and self-care (Khantzian, 1997). Numerous clinicians have proposed that opioid-dependent patients often self-medicate dysphoric states associated with pain, anger, anxiety, restlessness, agitation, and/or depression (Khantzian & Albanese, 2008). Although this may represent legitimate attempts to ameliorate symptoms, in the long run, self-medication can be counterproductive.

A recent French experiment with buprenorphine treatment showed that prescriber, not patient, variables were responsible for doctor-shopping behaviors (Feroni et al., 2005). Similarly, in some cases, use of illicit buprenorphine might, to some degree, be an attempt at self-treatment, influenced by prescribers who are inattentive to individual variation in severity of opioid dependence or unaware of psychiatric and/or medical comorbidity.

1.2. Overview of research on buprenorphine misuse patterns

The use of buprenorphine as a treatment option for opiate dependence began in 1980 (Lewis & Walter, 1992; Mello & Mendelson, 1980). Since its introduction in France during 1996, sublingual buprenorphine (Subutex) has been available as a treatment of opioid dependence. Given the potential for abuse and diversion seen with this pure formulation (Obadia, Perrin, Feroni, Vlahov, & Moatti, 2001; Roux et al., 2008; Winstock, Lea, & Sheridan, 2008), Reckitt-Benckiser developed a combination sublingual formulation buprenorphine–naloxone (Suboxone) for distribution in the United States (Fudala & Johnson, 2006) by outpatient prescription with a waiver under the Drug Addiction Treatment Act of 2000 (Cicero & Inciardi, 2005).

A national study of buprenorphine abuse patterns, conducted between 2005 and 2007, revealed that the prevalence of clients in U.S. drug treatment programs who had used buprenorphine to get high during the past 30 days was between 20% and 25%, although these clients rarely endorsed buprenorphine as their primary drug. The peak prevalence of illicit buprenorphine use was 35% during mid-2006, before dropping back to approximately 20% during 2007; this level of use was lower than that of other widely available opioid medications, such as methadone, oxycodone, and hydrocodone (Cicero, Surratt, & Inciardi, 2007). In several countries, researchers investigated reasons for illicit use of straight buprenorphine, not combined with naloxone. A 2007 study of Swedish needle exchanges reported that 87% of heroin users reported intake of buprenorphine for withdrawal treatment or self-detoxification, whereas only 11% used buprenorphine to stimulate euphoria (Hakansson, Medvedeo, Andersson, & Berglund, 2007). A study of Australian community pharmacies revealed that 23.8% of buprenorphine-maintained participants reported diverting their sublingual dose during the preceding 12 months, and 9.1% of this cohort reported injecting buprenorphine to stimulate euphoria during the same time period (Winstock et al., 2008).

In contrast to these international studies, which look at different formulations of buprenorphine, OBOT treatment in the United States mainly uses buprenorphine prescribed as a combination sublingual tablet (Suboxone) and as part of treatment within primary care (Barry et al., 2007; Fiellin et al., 2006; Fiellin et al., 2008), mental health, or outpatient addiction treatment settings (Montoya et al., 2005).[1] Two recent qualitative, ethnographic studies from interviews with people who abused opioids in Baltimore and New England suggest that avoidance of withdrawal symptoms is the primary reason for use of diverted buprenorphine (Mitchell et al., 2009; Monte, Mandell, Wilford, Tennyson, & Boyer, 2009). We are aware of no U.S. research that has used quantitative methods to systematically examine the reasons for use of illicit buprenorphine in treatment-seeking opioid-dependent patients or the effects of OBOT treatment on illicit buprenorphine use behavior.

1.3. This study

This study seeks to extend epidemiological findings about the illicit use of buprenorphine within the United States, as well as to understand the problem of illicit use from the standpoint of the opioid-dependent treatment seeker. More specifically, in this study, we sought to investigate the use of illicit buprenorphine among opioid-dependent treatment-seeking patients and the effects of OBOT treatment on illicit buprenorphine use behavior. We developed an Illicit Buprenorphine Use Questionnaire (IBUQ), which operationally defined the use of illicit buprenorphine as any method of obtaining or using buprenorphine that is not legally permitted or authorized by a prescribing physician. We also developed a Buprenorphine Beliefs and Behaviors

[1] For the rest of this article, to use generic terminology, when referring to the use of buprenorphine–naloxone (Suboxone) in the United States, both licit and illicit, we will use the term *buprenorphine*.

Questionnaire (BBBQ) to assess patient beliefs and behaviors associated with their use of buprenorphine. We sought to establish rates of illicit buprenorphine use within a New England academic community addiction treatment center during 2009, including prevalence estimates of 90-day illicit use among opioid-dependent patients seeking OBOT treatment and among those already in OBOT treatment. We also sought to establish prevalence estimates for three primary reasons that opioid-dependent treatment seekers use buprenorphine: use to get high, use to prevent withdrawal, and use to reduce cravings.

1.4. Hypotheses

We formulated three primary hypotheses about the reasons for illicit buprenorphine use.

1.4.1. H1: effect of OBOT treatment on illicit use

The use of illicit buprenorphine among treatment-seeking patients will be higher for new intakes than existing patients who have access to prescribed buprenorphine. The rate of illicit buprenorphine use will decrease with time in treatment (i.e., those in standard treatment will not need to engage in self-treatment of their opioid dependence symptoms).

1.4.2. H2: self-treatment of pain and psychiatric symptoms

The use of illicit buprenorphine in treatment seekers will be related positively to participants' belief in its benefit for their symptoms of pain, depression, and/or anxiety.

1.4.3. H3: self-treatment of opiate dependence

Users of illicit buprenorphine will report that they are self-treating because they need more buprenorphine to prevent return to illicit opioid use.

1. Among those already in treatment (i.e., access to a legal prescription), users of illicit buprenorphine will feel they needed to use more than was prescribed.
2. Measured at 3-month follow-up, users of illicit buprenorphine will evidence a lower average prescribed dose than will licit users.
3. Measured at 3-month follow-up, users of illicit buprenorphine will have lower rates of opioid relapse (as defined by opiate or oxycodone positive urine) compared with licit users, representing effective self-treatment.

2. Materials and methods

This study consisted of two stages. Stage 1 was a cross-sectional epidemiological analysis of population variables, and Stage 2 was a prospective longitudinal cohort study with 3-month follow-up assessment of the first three quarters of the initial analyzed population. The purpose of Stage 2 was to identify longitudinal trends during the course of buprenorphine OBOT treatment. The Cambridge Health Alliance (CHA) institutional review board approved the conduct of this study, and all participants provided signed consents and were unpaid.

2.1. Participants

We screened 129 sequential admissions to an outpatient-based opioid treatment (OBOT) program for participation in this study. All participants met Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV-TR) criteria for opioid dependence. These clients were seeking outpatient treatment with buprenorphine.

To be eligible for the Stage 1 cross-sectional epidemiological study, clients had to (a) be 18 years or older with English proficiency, (b) be receiving buprenorphine treatment from psychiatrists or primary care physicians associated with the CHA OBOT network, and (c) agree to accept weekly psychosocial treatment (in the form of group or individual counseling), care management by an OBOT nurse care manager (RNCM), and at least monthly random urine toxicology screening. We excluded participants from this study if they were currently pregnant; currently evidencing psychotic illness, delirium, or intoxication at the time of interview; reported or currently qualified for a diagnosis of schizophrenia, schizoaffective disorder, or dementia; and reported a history of a manic episode (meeting DSM IV-TR criteria for Bipolar 1), history of traumatic brain injury, or history of recent suicide attempt during the past 3 months. One hundred eighteen (91%) of the OBOT clients screened as eligible for this study. Of those eligible, we excluded 19 (16%) based on the exclusion criteria noted earlier. Eighty-seven (88%) of those remaining after exclusion enrolled in the study. Of those who enrolled, 5 admitted that their intake interviews contained inaccuracies, and 4 had a limited pilot form of the assessment battery; consequently, we removed their data from the analysis. Fig. 1 summarizes the process associated with deriving the Stage 1 study sample. The following data in this report reflect those 78 participants who were enrolled and provided accurate and complete data.

For the participants included in the data analyses, their demographic characteristics were as follows: 39.7% were women; 70 (89.7%) were White; 1 (1.3%) was African American; 3 (3.8%) were Hispanic. Their mean age was 36.09 years (SD = 10.32 years). Seventy participants (89.7%) had completed at least 12 years of education, and 13 (16.7%) were employed. The typical (median) CHA OBOT participant is an opioid-dependent, unemployed 36-year-old, White man, with at least 12 years of education. Table 1 summarizes the Stage 1 sample characteristics.

For inclusion in the Stage 2 longitudinal prospective cohort, participants had to have been enrolled in Stage 1 and provided accurate data (n = 78). The first three quarters of these participants screened as eligible for the study (n = 59; see Section 2.3 for Stage 2 screening rationale). Of those eligible, 73% completed a 3-month follow-up evaluation

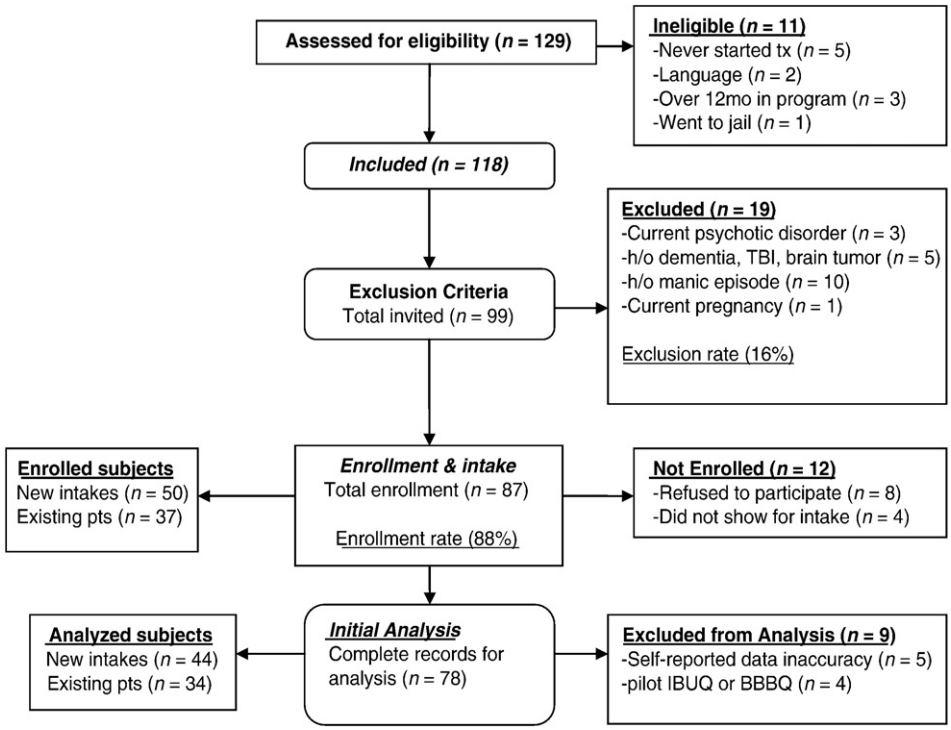

Fig. 1. Consort diagram for Stage 1 —epidemiological analysis.

(n = 43). One participant admitted that his follow-up interview contained inaccuracies, resulting in exclusion from the longitudinal analysis. Fig. 2 summarizes the process associated with deriving the Stage 2 study sample. The Stage 2 longitudinal data reflect those who provided accurate, complete follow-up data (n = 42).

Table 1
Baseline characteristics of participants in Stage 1 analysis

	New intakes (n = 44)	Existing patients (n = 34)	Overall (n = 78)
Age (years), $M \pm SD$	34.64 ± 9.63	37.97 ± 11.00	36.09 ± 10.32
Female	18 (40.9)	13 (38.2)	31 (39.7)
Married	5 (11.4)	6 (17.6)	11 (14.1)
Lives with child (<18 years old)	16 (36.4)	11 (32.4)	27 (34.6)
Salary employment	8 (18.2)	5 (14.7)	13 (16.7)
Education ≥ high school graduate	40 (90.9)	30 (88.2)	70 (89.7)
Gross year income ($), $M \pm SD$	10,952 ± 16,330	9,776 ± 10,952	10,448 ± 15,042
Homeless	0	2 (5.9)	2 (2.6)
Hispanic	0	3 (8.8)	3 (3.8)
Race			
White	44 (100)	28 (82.4)	70 (89.7)
African American	0	1 (2.9)	1 (1.3)
Other	0	5 (14.7)	5 (6.4)
Psychiatric severity			
History of psychotropic meds	31 (70.5)	21 (61.8)	52 (66.7)
History of hospitalization	14 (31.8)	11 (32.4)	25 (32.1)
Total BDI, $M \pm SD$ [a]	21.30 ± 9.23	12.03 ± 9.41	17.26 ± 10.34
Lifetime benzodiazepine use [b]	30 (68.2)	13 (38.2)	43 (55.1)
Addiction severity			
≥5 detoxification admissions	10 (22.7)	12 (35.3)	22 (28.2)
Years of opioid use	11.84 ± 8.96	13.76 ± 8.85	12.68 ± 8.90
No. comorbid SUDs	3.59 ± 1.35	3.12 ± 1.30	3.37 ± 1.34
Daily intravenous drug use (last 12 months)	11 (25.6)	4 (12.1)	15 (19.7)

Note. Values are presented as n (%), unless otherwise indicated.

[a] $t(76) = -4.36$, $p < .001$.

[b] $\chi^2(1, n = 78) = 6.95$, $p < .01$.

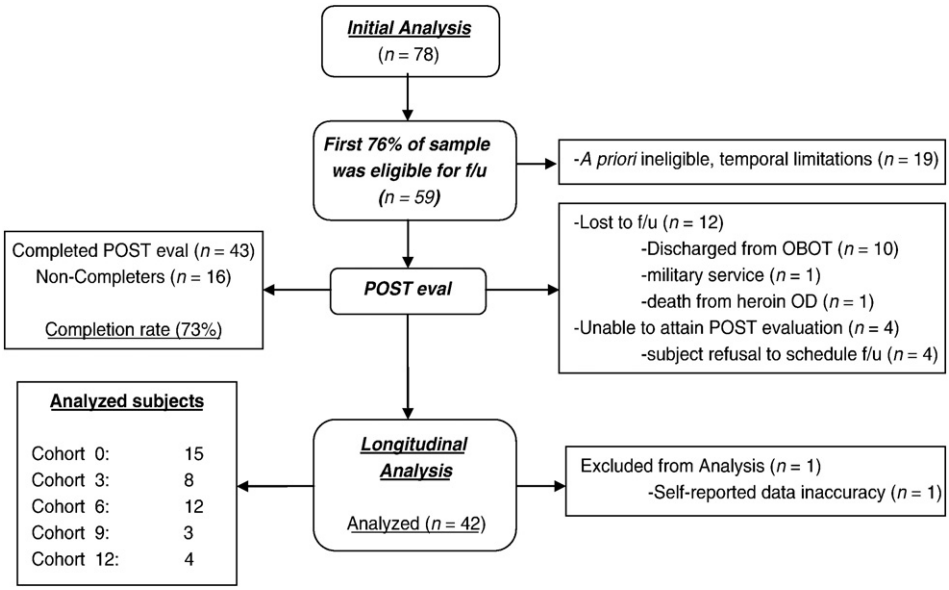

Fig. 2. Consort diagram for Stage 2—longitudinal analysis.

2.2. Materials

All participants completed a standardized assessment interview to obtain information about their demographics and history of licit and illicit substance use.

2.2.1. Buprenorphine Beliefs and Behaviors Questionnaire

This is a 10-item, self-report questionnaire about attitudes and behaviors related to buprenorphine use. Participants were asked to circle all items that were true about their use of buprenorphine in the past 90 days. Some examples of included items are the following: "I used Suboxone to get high," "I needed to use more Suboxone than I was prescribed," "I used Suboxone to save money," "I used Suboxone to reduce pain," and "I used Suboxone to treat my symptoms of depression."

2.2.2. Illicit Buprenorphine Use Questionnaire

This is a 5-item, self-report questionnaire related to the acquisition and/or use of illicit, nonprescription, "street" buprenorphine. Participants were asked to circle all items that were true about their use of buprenorphine in the past 90 days. One of the five items, "Had sex to obtain Buprenorphine," evidenced no variance (i.e., all responses were "no"), and therefore we excluded it from further analysis. The principal components analyses confirmed that the remaining four IBUQ items represented a single construct, accounting for 73.9% of the item variance, and Cronbach's reliability analyses demonstrated that the scale had high internal consistency ($\alpha = .88$). An example of an included item is "I bought illicit ('street') Suboxone." For data analysis in this study, we labeled participants who had a positive response on any IBUQ item as "users of illicit buprenorphine."

2.2.3. Reporting Accuracy Ruler

After completing the various clinical measures, interviewers showed participants a card with a horizontal, visual analog accuracy scale (0–100 mm), with 0 representing absolute inaccuracy and 100 representing absolute accuracy. Interviewers asked participants to "place a vertical mark representing the accuracy of the information you provided during this interview." The millimeter reflecting the point at which this mark intersected the ruler served as the measure of participant accuracy.

2.2.4. Beck Depression Inventory-II

This 21-item, multiple-choice self-report inventory is used widely for measuring the severity of depression (Johnson, Neal, Brems, & Fisher, 2006). The Beck Depression Inventory (BDI)-II was a 1996 revision of BDI developed in response to DSM-IV criteria for major depressive disorder. Each question has a set of at least four possible answer choices, ranging in intensity. For example, 0 means "I do not feel sad"; 1, "I feel sad"; 2, "I am sad all the time and I can't snap out of it"; and 3, "I am so sad or unhappy that I can't stand it."

2.2.5. Urine toxicology assessments

To participate in this study, participants had to complete urine toxicology on at least a monthly basis; however, 46% participated on a weekly basis and 78% on at least a semimonthly schedule. All participants completed urine toxicology through clinical laboratory assays, including enzyme-mediated immunoassay technique for general urine toxicology (Beckman Synchron, Beckman Coulter, Fullerton, CA) and specific rapid chromatographic immunoassays for buprenorphine and oxycodone levels (Bio-Rad, Hercules, CA).

2.3. Procedures

Investigators assigned participants a cohort number based on when during their OBOT treatment they had entered the study (i.e., at intake, 0; after the first 90 days, 3; after 180 days, 6; after 270 days, 9; or after 360 days, 12). We considered those enrolled at intake as new intakes and those in the other cohorts as existing patients. Participants had 1 month from the date of their scheduled quarterly assessment to be enrolled in the study.

To reduce bias, RNCMs, who were involved in participant recruitment and assessments, were blinded to the purpose of the study and were not involved in data analysis.

2.3.1. Stage 1 procedures and assessment battery

An OBOT RNCM completed an assessment interview with all participants to attain demographics, illicit substance use history, legal psychoactive substance history, and answers to the BBBQ and IBUQ. After completing the interview, participants completed the Reporting Accuracy Ruler (RAR). Next, participants completed the BDI-II.

2.3.2. Stage 2 follow-up assessments

The limitation of follow-up to the first three quarters of enrolled participants with high reporting accuracy was related to temporal and resource considerations; this limited sample offered adequate statistical power to assess for major longitudinal trends consistent with the exploratory nature of this investigation. This follow-up included members from each sequential cohort and involved completing regular urine toxicology. RNCMs conducted a repeat assessment interview using the complete battery, excluding the demographics, with those participants who were retained in treatment after 3 months.

2.4. Data analyses

After completing the Stage 1 assessment, we created a SPSS 17.0 database (SPSS Statistics for Windows 17.0, Rel. 17.0.0. 2008. Chicago: SPSS Inc.; Turner, Lessler, & Gfroerer, 1992). We conducted a review of missing or incomplete data on a regular basis. In the case of missing data related to demographics, substance use history, and the current prescribed buprenorphine dose, we imputed this information only when accurate and complete clinical documentation was available in the OBOT file. In the case of other aspects of the assessment battery, missing entries were assigned missing status and were excluded from analysis, although this was rare (including four missing entries on the demographic variable gross yearly income and one follow-up BDI-II that was not completed) and had negligible effects on aspects of data included in data analysis. We double entered a randomly selected 10% of the completed records; this procedure revealed greater than 99% data entry accuracy. We excluded the initial five pilot IBUQ cases and all participants with less than 90% self-reported data accuracy on RAR.

The PI (Z.S.O.), with the assistance of a statistician (S. N.), conducted the data analysis. For Stage 1, we obtained general sample descriptive statistics. For categorical and ratio measures, we employed Pearson chi-square, independent-samples t tests, and analysis of variance (ANOVA), respectively, to analyze differences between new intakes and existing patients, as well as to examine differences between users of illicit buprenorphine and licit users. For Stage 2, McNemar chi-square and repeated-measures t tests were used for categorical and ratio measures, respectively, to analyze longitudinal changes. Given the exploratory nature of this seminal study, we chose to maintain a liberal threshold to avoid Type 2 errors, selecting $p \leq .05$ as the threshold level for determining statistical significance. However, because there were multiple statistical tests, when possible, we applied a conservative (i.e., $p < .01$) threshold for determining statistical significance (Perneger, 1998).

3. Results

3.1. Prevalence

The 90-day prevalence of illicit buprenorphine use among this opioid-dependent treatment-seeking population was 49%. Whether used illicitly or with a prescription, 92% reported buprenorphine use to reduce cravings, 78% reported use to prevent withdrawal, and 3.8% reported use to get high. Illicit buprenorphine users ($n = 38$) differed from licit users in their endorsement of the following reported reasons for use: (a) prevent withdrawal symptoms, 90% versus 68%, $\chi^2(1, n = 78) = 5.52$, $p < .05$; (b) reduce pain, 47% versus 15%, $\chi^2(1, n = 78) = 9.59$, $p < .01$; (c) treat depression, 40% versus 20%, $\chi^2(1, n = 78) = 3.55$, $p = .05$; and (d) save money, 29% versus 8%, $\chi^2(1, n = 78) = 6.09$, $p < .05$. Although too few endorsed the reason for the difference to reach significance, all of the participants who reported buprenorphine use to get high were users of illicit buprenorphine. Table 2 summarizes these findings. No participants endorsed any other route of administration for buprenorphine except oral. Retention rates (signified by completion of 3-month assessment) were not significantly different between users of illicit buprenorphine (70%) and licit users (75%).

3.2. Population characteristics

More new intakes than existing patients reported lifetime benzodiazepine use, 30 (68.2%) versus 13 (38.2%), $\chi^2(1, n = 78) = 6.95$, $p < .01$, and the new intake cohort scored higher on the initial BDI than did the existing patients, 21.30 ± 9.23 vs. 12.03 ± 9.41, $t(76) = -4.36$, $p < .001$. The BDI difference is consistent with

Table 2
Reasons for use of buprenorphine

Beliefs about buprenorphine use	Illicit (n = 38)	Nonillicit (n = 40)	Total (n = 78)	p
To prevent cravings	37 (97)	35 (88)	72 (92)	NS
To prevent withdrawal	34 (89.5)	27 (67.5)	61 (78.2)	$\chi^2 = 5.52$, $p < .05$
To treat anxiety	16 (42.1)	13 (32.5)	29 (37.2)	NS
To reduce pain	18 (47.4)	6 (15.0)	24 (30.8)	$\chi^2 = 9.59$, $p < .01$
To treat depression	15 (39.5)	8 (20.0)	23 (29.5)	$\chi^2 = 3.55$, $p = .05$
To save money	11 (28.9)	3 (7.5)	14 (17.9)	$\chi^2 = 6.09$, $p < .05$
To get high	3 (7.9)	0 (0)	3 (3.3)	NS

Note. Values are presented as n (%), unless otherwise indicated.

reported evidence for pretreatment depressive symptoms associated with opioid dependence (Dean, Bell, Christie, & Mattick, 2004; Johnson et al., 2006). As summarized in Table 1, new intakes and existing patients did not differ on any other standard measures of psychiatric severity (history of psychotropic medication or history of hospitalization) or addiction severity (number of previous detoxification admissions, years of opioid use, number of comorbid substance use disorders [SUDs] or daily intravenous drug use [IVDU] in the past year).

3.3. H1: effect of OBOT treatment on illicit use

Sixty-one percent of new intakes and 32% of existing patients acknowledged using illicit buprenorphine during the past 90 days, $\chi^2(1, n = 78) = 6.46$, $p < .05$. Among completers of Stage 2 3-month follow-up assessment, using the IBUQ, illicit buprenorphine use during the past 90 days dropped by 70%, $\chi^2(1, n = 42) = 4.89$, $p < .05$. Fig. 3 demonstrates that most of those who stopped illicit buprenorphine use while in the OBOT treatment did so during their first 6 months of treatment.

3.4. H2: self-treatment of pain and psychiatric symptoms

As described earlier in the Results section, those participants who endorsed using illicit buprenorphine were more likely than were licit users to report using it to reduce pain or to treat symptoms of depression but no more likely to report using it to treat symptoms of anxiety, $\chi^2(1, n = 78) = 0.77$, $p = .38$. Because illicit use varied by whether participants were new intakes, we repeated these analyses for only the new intakes. Among new intakes, those who reported use of illicit buprenorphine were more likely than were licit users to report use for the reduction of pain, $\chi^2(1, n = 44) = 6.15$, $p < .05$. However, the difference between illicit and licit buprenorphine users to treat depression disappeared. To analyze the relationship between illicit use, beliefs about use of buprenorphine to treat depression, and depression severity, we conducted an ANOVA. There was a main effect of licit versus illicit buprenorphine use for depression severity but no main effect for beliefs and no interaction between the two. The mean total BDI score was higher for users of illicit buprenorphine (19.6 ± 9.6) than that for nonillicit users (15.1 ± 10.6), $F(1,77) = 4.66$, $p < .05$. Although the interaction was not statistically significant, users of illicit buprenorphine who also believed that buprenorphine helped treat depression reported the most severe depression on the BDI (21.5 ± 9.9).

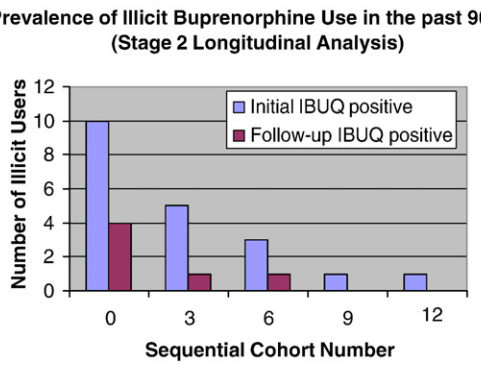

Fig. 3. Decline in prevalence of illicit users during treatment by cohort.

3.5. H3: self-treatment of opiate dependence

1. To assess the reasons for use of illicit buprenorphine among those participants who had legal access to prescriptions, we conducted a Pearson chi-square subgroup analysis among existing patients. This analysis showed that users of illicit buprenorphine were significantly more likely than were licit users to report needing more medication than prescribed, $\chi^2(1, n = 34) = 6.88$, $p < .05$. In addition, among existing patients, users of illicit buprenorphine were significantly more likely than were nonillicit users to report using buprenorphine to save money, $\chi^2(1, n = 34) = 6.08$, $p < .05$.
2. Among completers of Stage 2 three-month follow-up assessment, those who still remained users of illicit buprenorphine (i.e., positive response on IBUQ in past 90 days) at 3-month follow-up did not have a significantly different dose of prescribed buprenorphine than did the licit users, $t(40) = -0.76$, $p = .45$.
3. To assess if continued use of illicit buprenorphine was related to effective self-treatment attempts preventing opiate relapse during treatment, we also conducted an independent-samples t test, comparing the prevalence

of opiate and oxycodone positive urines between users of illicit buprenorphine and licit users during 3 months of completed treatment. Among those who completed a postevaluation after 3 months with a legal prescription, we did not find any significant difference between the mean percentage of opiate and oxycodone positive urines of those who reported illicit buprenorphine use (4% ± 10%) and the nonillicit users (2.5% ± 6%), $t(39) = 0.341$, $p = .735$. In addition, the prevalence of opioid relapse (as defined by opiate or oxycodone positive urine during the past 3 months) among both groups was nearly identical (17% licit, 16% illicit).

4. Discussion

The results of this study suggest that the demand for illicit buprenorphine is driven by people trying to avoid withdrawal and to reduce cravings; these results do not support the position that buprenorphine users are trying to attain euphoric effects. These results suggest that illicit buprenorphine use often represents an attempt at self-treatment. This activity can be distinguished from diversion of legally prescribed buprenorphine, which is considered a criminal activity.

4.1. Self-treatment of opioid dependence

As the results revealed, participant use of illicit buprenorphine decreases dramatically once engaged in legal OBOT treatment. This study establishes the past 90-day prevalence rate for illicit buprenorphine use among an opioid-dependent treatment-seeking population in New England as 61% among those newly seeking OBOT treatment and 32% among those already in OBOT treatment. Similarly, our longitudinal data suggest a 70% decrease in the number of illicit buprenorphine users during a 90-day period of OBOT treatment. Lack of easy access to OBOT treatment (i.e., a legal prescription) likely promotes illicit buprenorphine use. In addition, it is notable that users of illicit buprenorphine were more likely to report using buprenorphine to prevent withdrawal than were licit users. The predominate use of illicit buprenorphine for self-treatment can reduce concerns among providers, families, media and our larger U.S. society about the misuse of buprenorphine. If use of illicit buprenorphine among opioid-dependent treatment seekers mainly represents attempts at self-treatment, then it follows that the primary focus of clinical concerns should be to increase access to professional treatment and to adjust standard treatment to more adequately meet the complex needs of opioid-dependent patients rather than to prevent the use of illicit buprenorphine. This suggestion is especially relevant for those patients with comorbid chronic pain and depression.

4.2. Self-treatment of pain

To illustrate, this study evidences a strong positive relationship between the use of buprenorphine to reduce pain and the use of illicit buprenorphine. This association might reflect that patients with chronic pain feel that they need increased doses of buprenorphine to relieve their comorbid pain. This hypothesis is consistent with current off-label prescribing practices for chronic pain patients reported in the pain management literature, in the form of sublingual three- or four-times-a-day dosing (Heit & Gourlay, 2008) and as a transdermal formulation in Europe (Sittl, 2005). However, there are four other primary alternative possibilities: (a) Pain patients with opioid dependence, compared with heroin users without chronic pain, might have developed stronger connections with sources of illicit prescribed opioid medication (e.g., dealers who sell or family and friends who share); (b) people with chronic pain are at an increased risk of illicit use; (c) opioid-dependent patients with pain are more likely to test buprenorphine before officially seeking OBOT treatment; and finally, (d) reducing pain might merely be a marker for an inability to tolerate distress. Regardless, the strong relationship of illicit buprenorphine use with use for pain reduction suggests that a transdermal formulation of buprenorphine might offer a significant benefit for patients with comorbid opioid dependence and chronic pain.

4.3. Self-treatment of depression

From a self-treatment perspective, the small but statistically significant positive association between use of buprenorphine to treat symptoms of depression and illicit buprenorphine use suggests that patients with severe comorbid depression might experience subjective improvement in depressive symptoms from additional buprenorphine. Several studies demonstrating the efficacy of buprenorphine for treatment-resistant depression (Bodkin, Zornberg, Lukas, & Cole, 1995; Emrich, Vogt, & Herz, 1982), particularly among opioid-abusing patients (Kosten, Morgan, & Kosten, 1990), support this perspective. Although a recent trial did not demonstrate a greater antidepressant effect than that of methadone (Dean et al., 2004), buprenorphine seems to be more effective than methadone in reducing illicit opioid abuse in opioid-dependent patients affected by major depression (Callaway, 1996), possibly due to κ opioid receptor antagonism (Gerra et al., 2006; Mysels, 2009). Although this is a legitimate perspective to entertain, the reverse possibility that illicit buprenorphine use represents continued engagement in illicit activities that contribute to increased severity or persistence of negative affective states should also be considered.

4.4. Self-treatment during OBOT

We found that, once in OBOT treatment, most opioid-dependent treatment seekers no longer need to engage in

self-treatment of their opioid dependence symptoms. Those who continue using illicit buprenorphine despite receiving a legal prescription often report the subjective experience of needing more buprenorphine than one's physician will prescribe and the intention to save money.

No objective criteria distinguished the subjective experience of needing more buprenorphine than prescribed to treat underdosed opioid dependence. For example, those who used illicit buprenorphine were not any less likely to have documented relapse to oxycodone or heroin use on urine toxicology. We also did not find any relationship between the objective magnitude of buprenorphine dosing and illicit use; in fact, the users of illicit buprenorphine tended on average to have slightly higher dosages. This suggests that prescriber variables, like unwillingness to dose liberally, were not a major cause of illicit buprenorphine use among this limited sample. This finding might not be applicable to other clinical settings and should be tested in future studies that use multiple clinical sites.

An interesting finding, about which we did not hypothesize, is that illicit users were twice as likely to report using buprenorphine to save money. This economic incentive for illicit use is often observed in clinical situations when a preauthorization request or change in insurance status requires self-pay of an entire monthly prescription. In this common situation, instead of purchasing an entire monthly prescription, the patient chooses to return to their original source of illicit buprenorphine until the insurance conflict is resolved. An alternative explanation for the finding could also be that some users of illicit buprenorphine are not truly invested in recovery of opioid dependence, viewing their buprenorphine treatment as an inexpensive substitute to daily heroin and oxycodone abuse.

Despite our expectations, these data suggest that use of illicit buprenorphine occurs commonly in OBOT patients during treatment. As clinicians, we potentially fall victim to our assumptions, causing us to limit our investigation into patterns of illicit use after treatment commences. In our experience, these assumptions often have been based on preconceived notions about protective effects of socioeconomic status or a less virulent form of dependence when it arises during treatment of pain. These assumptions often continue, although accessing illicit sources of opioids and then hiding this illicit activity from one's closest confidantes are both central themes of opioid dependence. Importantly, clinician countertransference fear and denial (e.g., "If they lie about this, they could be lying about everything"; Shaffer, 1994) can prevent thorough continued investigation into illicit use patterns during treatment.

4.5. Limitations

This study is not without its limitations. This seminal investigation was limited by its short time for enrollment and follow-up. The Stage 1 epidemiological study design comparing patients at different stages of the treatment process should not be understood to suggest an actual longitudinal comparison; rather, new intakes and existing patients represent different people with possibilities of individual variation. However, given the similarity in demographics and core measures of addiction severity and psychiatric severity, we believe that useful comparisons can be made. We also think that the longitudinal approach taken in Stage 2 addresses the doubts raised by Stage 1 design concerns, reinforcing the observed OBOT Treatment × Time effect on decreased use of illicit buprenorphine. The difference in baseline depression is likely accountable to the effect of OBOT treatment on depressive symptoms. The difference in lifetime benzodiazepine use might represent an increase in anxiety symptoms among new intakes, but this is unlikely to affect the study's results because use of buprenorphine for anxiety was not significantly different in new intakes compared with existing patients. Finally, by making "use of illicit buprenorphine" a categorical variable, we limited our ability to assess the severity and frequency of illicit use. This is something that researchers can revise if this study is repeated in a larger, multisite sample. Finally, given the single research site in New England and a largely Caucasian population with low socioeconomic status, these findings might not generalize to other populations. This limitation can be resolved by replicating this study using a more diverse, multicenter approach like the National Institute on Drug Abuse Clinical Trials Network.

4.6. Conclusion

Multiple factors associated with attempts at self-treatment represent the major reasons for use of illicit buprenorphine in treatment seekers, whereas economic pressures play a minor role. Use of illicit buprenorphine by opioid-dependent treatment seekers is an important variable to assess at intake and during treatment.

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