Outpatient Buprenorphine Treatment for Opioid Dependence

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Office-based pharmacotherapy for opioid dependence holds the potential to close critical gaps in access to care. These VA clinicians explain how to establish a buprenorphine clinic in an existing SUD program.

Due to their prevalence and severity, substance use disorders (SUDs) are among the most significant public health challenges facing the VHA.[1] Within the broad category of SUDs, opioid and alcohol dependence have been identified as the most pressing concerns among veterans (V.A. Waldorf, PhD, written communication, 2003).

In the case of opioid dependence (which, according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*, encompasses functional impairment and problematic behavior as well as the presence of physical withdrawal or tolerance[2]), the issue of treatment has been fraught for many years with controversy and obstacles. While studies have linked methadone maintenance therapy with high success rates,[3] many patients who might benefit from such therapy do not receive it—either because of a lack of local availability of methadone programs or due to a variety of social and logistic factors that make patients wary or unwilling to try methadone treatment.[3,4]

Recent legal and clinical developments in SUD treatment have presented an opportunity to expand access to and enhance acceptability of pharmacologic treatments for opioid dependence. Among the most significant of these was the FDA's 2002 approval of two sublingual formulations of buprenorphine, a partial agonist of μ-opioid receptors, for the office-based treatment of opioid dependence.[5] While conceptually similar to methadone maintenance therapy, buprenorphine treatment is considered to have less potential for abuse, which has facilitated its approval for office-based therapy.

Nevertheless, early reports indicate that few VA SUD programs have incorporated buprenorphine treatment. Why not? Because the treatment faces some of the same obstacles that have plagued SUD therapy historically: a lack of confidence among physicians, despite training, to treat opioid addiction; the difficulty of facilitating psychosocial treatment and negotiating with pharmacies; stigmatization of opioid replacement therapy in general; and a lack of adequate financial and human resource ex-

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penditures needed for effective care.[6]

With the aim of helping other facilities overcome some of these challenges, we describe herein an outpatient buprenorphine treatment clinic that was implemented at the New Mexico VA Health Care System (NMVAHCS), Albuquerque in April 2004. After reviewing the background on opioid treatment in general and buprenorphine treatment in particular, we discuss the development and operation of the clinic. We detail specific exigencies and practical problems encountered during major aspects of the planning and implementation processes—including the training of providers, securing of pharmacy approval and cooperation, organization of the clinic, screening of patients, and initiation and maintenance of treatment. In addition, we share some preliminary observations on the clinic's success, which is due in large part to the collaborative relationship between pharmacy and behavioral health care (clinicians working in the areas of psychiatry, psychology, social work, nursing, and medicine).

TREATING OPIOID DEPENDENCE IN THE VHA

Major changes in VA health care delivery since 1995 have shifted the focus of SUD treatment dramatically from the inpatient setting to the residential and outpatient settings,[7] to the degree that 96% of VA patients with SUDs now receive outpatient care.[8] This shift places a greater emphasis on outpatient modalities of treating opioid dependence, including those centered on pharmacotherapy—the most common of which is methadone maintenance. Studies have shown that opioid agonist therapies (OATs), such as methadone maintenance, can improve treatment retention, which in turn can decrease the use of health care and social services.[4,9]

In 1999, the VHA was providing treatment for opioid dependence to approximately 30,000 veterans—which represents less than 20% of all veterans with this diagnosis.[5] This may be explained, at least in part, by the fact that many veterans nationwide historically have obtained mental health and SUD services from the community rather than the VHA.[10] As community systems face their own financial and service crises, however, it's likely that these veterans will turn to the VHA in increasing numbers.

Given the VA's shift to outpatient care and the anticipation of more and more veterans seeking treatment for opioid dependence from the VHA in coming years, it's reasonable to assume that the need for outpatient programs for opioid dependence will only intensify. Unfortunately, under the present circumstances, the availability of specialized services, such as OAT programs, is problematic.[4] Many VISNs that serve populations with high rates of heroin use—such as VISN 18, which includes New Mexico and other western states—have no OAT programs of their own and insufficient community facilities to meet the demand for services.[11]

Even in areas where methadone treatment programs are available, veterans may not take advantage of them because of an associated stigma, lack of transportation, financial problems, or difficulty adhering to a rigid clinic schedule.[12] There is also considerable variance among programs in terms of their adherence to treatment guidelines, which is related substantially to efficacy and treatment retention.[13] And when patients drop out or ask to discontinue methadone treatment, even after successful detoxification, studies have shown they have a very high rate of relapse.[14]

THE ROLE OF BUPRENORPHINE

The use of buprenorphine offers a possible alternative to OAT therapy for veterans with opioid dependence. Classified as a C-III narcotic, buprenorphine is available for use in treating opioid dependence in the form of two sublingual agents: one composed of buprenorphine alone and the other containing buprenorphine and naloxone in a four to one ratio (Table 1).[15] The sublingual route is used because oral forms of buprenorphine are destroyed quickly through first-pass

Table 1. Product information for sublingual buprenorphine formulations

Generic name	Trade name	Tablet appearance	Available strengths*
Buprenorphine	Subutex†	White, oval	2 mg, 8 mg
Buprenorphine /naloxone	Suboxone†	Orange, hexagonal	2 mg/0.5 mg, 8 mg/2 mg

*All formulations of various strengths are supplied in bottles of 30 tablets each. †Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA.

Continued on page 18

Continued from page 10

metabolism. The purpose of the combination drug is to deter intravenous abuse of buprenorphine: Naloxone is an opioid antagonist that can precipitate opioid withdrawal if used intravenously but is not pharmacologically active in the sublingual form at the doses used.[16]

Buprenorphine has three advantages compared to methadone that make it ideal for the outpatient treatment of patients with opioid dependence. First, it has a lower abuse potential—because it is a partial rather than a full μ-opioid receptor agonist and because naloxone is used in the combination product.[17] Second, it is less dangerous in overdose because of a ceiling effect that limits respiratory depression.[18] Third, as a partial agonist it induces less physical dependence and thus a milder withdrawal syndrome than the full agonist methadone.[17] A caveat is that, at high doses, buprenorphine can act as an antagonist and precipitate withdrawal with heavy narcotic users even in the sublingual formulation. At optimal doses, however, adverse effects (which include sedation, constipation, and elevation of liver enzymes) tend to be mild.[19]

A meta-analysis by Barnett and colleagues from the VA's Health Economics Resource Center found that buprenorphine may be as effective as methadone in maintenance treatment for opioid dependence.[3] The researchers reviewed data from five randomized, controlled trials comparing buprenorphine and methadone[20–24] and found that: the relative risk of treatment failure for patients taking buprenorphine was 1.26 that of patients taking methadone, patients treated with buprenorphine were retained in their SUD treatment programs 85% as long as those treated with methadone, and buprenorphine patients had 8.3% more positive urine samples. The report concluded that these modest differences probably were not clinically significant and that buprenorphine was as effective as methadone during treatment.

It's important to note that there was substantial variation in outcomes between the studies analyzed, which was attributed to differences in dosages, patient exclusion criteria, and provision of psychosocial treatment.[3] This reinforces the need for more clinical efficacy studies to determine appropriate patient selection criteria that lead to a favorable buprenorphine response, optimal dosing levels, and protocols for medication administration in conjunction with psychosocial treatment.[3,22,25]

The FDA approval of buprenorphine to treat opioid dependence marked a major shift in the treatment of addiction in that it allowed the drug to be dispensed in an office setting without the cumbersome federal regulations that apply to methadone and other similar programs.[26,27] Instead, physicians who hold certain certifications in addiction subspecialties or who complete a rigorous training course receive a waiver from the Drug Enforcement Agency allowing them to prescribe buprenorphine.

Prior to this approval, another study by the VA Health Economics Resource Center examined the potential cost-effectiveness of this type of office-based treatment with buprenorphine, using a dynamic model to capture the effects of adding it to the current OAT system.[28] The study found that, at a price of less than $5 per dose, buprenorphine would have a comparable cost-effectiveness to other medical treatments for opioid dependence. At $15 per dose, the cost-effectiveness would persist provided the availability of buprenorphine didn't take patients away from existing methadone programs.

The analysis also found that the use of buprenorphine in a variety of scenarios, including those involving patient populations with a high prevalence of HIV infection, would result in a favorable incremental cost per quality-of-life–adjusted year.[5,28] While these researchers found buprenorphine to be less cost-effective than methadone overall, a VA National Pharmacy Benefits Management drug monograph on buprenorphine released in June 2003 concluded that its office-based administration is much more feasible institutionally and clinically, given the regulatory requirements and practical inconvenience involved in OAT.[5]

DEVELOPING THE BUPRENORPHINE CLINIC

Recent data from the NMVAHCS SUD program indicate that 4.6% of veterans receiving care at this facility have a lifetime diagnosis of opioid dependence, as do 14.2% of those enrolled in the mini-intensive outpatient treatment program (a psychoeducational group intervention for veterans with SUDs that is staffed by a multidisciplinary instructional team and meets six hours a day, three days a week for four weeks). Yet, prior to the establishment of the buprenorphine clinic, the NMVAHCS had no on-site OAT program authorized to dispense methadone or levo-alpha-acetyl-methadol, and no VA-based methadone maintenance programs were available elsewhere in our VISN. The recognition of this unmet need spurred our initial efforts

to organize the buprenorphine clinic and helped generate support for the clinic among facility administrators and the pharmacy and therapeutics (P&T) committee.

When planning the clinic, an integral source of information was a VA toolkit released in 2002.[29] This toolkit contains instructions for the clinical use of buprenorphine, including regulatory guidance, criteria for nonformulary use, induction protocols for withdrawal, and maintenance of patients switching to buprenorphine from either short- or long-acting opioids. Since it was derived from an analysis of medical literature on buprenorphine, the toolkit is evidence-based and, as such, should enhance patient safety and improve clinical effectiveness. In our experience, this toolkit was key in the development of effective assessment and administration procedures, and we continue to use it to help standardize protocols, which in turn enhances the generalizability of data from our clinic to other facilities.[5,30]

P&T committee approval

Obtaining approval of buprenorphine treatment from the P&T committee can present difficulties, as several VHA SUD programs have reported (A.J. Gordon, Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, written communication, December 2, 2003). The lack of other VA pharmacologic programs to treat opioid dependence in our region certainly lent weight to the claim that there was a need for a buprenorphine clinic. Also instrumental in our success was the fact that we worked closely with our facility's pharmacy leadership from the planning stages of the clinic. The primary author presented to the P&T committee chair and the chief of pharmacy a package of materials about the use of buprenorphine that included several VHA documents.[5,30–32] After several subsequent face-to-face and e-mail discussions to clarify questions, the P&T committee granted their approval of the clinic in 2003.

Provider training

The primary author, an addiction psychiatrist who has completed consultation-liaison and ethics fellowships, qualified for the buprenorphine waiver as soon as she was eligible (in 2003). Since then, two other physicians have qualified. Qualification can be achieved through several avenues, and detailed information about waivers for prescribing buprenorphine is available on the Substance Abuse and Mental Health Services Administration (SAMHSA) Center for Substance Abuse Treatment web site (www.buprenorphine.samhsa.gov/bwns/waiver_qualifications.html). Since each physician who qualifies for a waiver can treat a maximum of 30 patients, it's important for buprenorphine clinics to have at least two qualified physicians. In addition to expanding the total capacity of the clinic, additional qualified physicians can cover for sick and annual leave and unexpected absences.

In preparation for our buprenorphine clinic, a clinical pharmacist provided an inservice training session on buprenorphine to the nursing staff. Topics covered in this session included:

- the role of the buprenorphine monotherapy and combination products in the treatment of opioid dependence, including the purpose of naloxone in the combination product;
- a brief description of the pharmacology and pharmacokinetics of buprenorphine and the implications for treatment;
- the dosage and administration of both formulations;
- storage, dispensing, and drug accountability information;
- the clinic protocol for induction and maintenance phases of treatment; and
- patients rights and responsibilities regarding enrollment in the buprenorphine clinic.

Although FDA regulations allow only physicians to prescribe buprenorphine, a physician assistant (PA) with a Masters degree in counseling and a psychiatric clinical nurse specialist (CNS) agreed to work under the attending addiction psychiatrist at the clinic, assisting with all ancillary services. These individuals received both didactic training prior to the start of the clinic and hands-on experience with the attending physician once the clinic began operating.

Patient qualification criteria

The consensus of our clinic was that patients should be accepted into the buprenorphine clinic only after assessment in our facility's SUD program—not enrolled directly from the medical or surgical services. In addition to SAMHSA and VA criteria for the use of buprenorphine, we developed our own screening and selection criteria for clinic admission (Table 2).

Before the buprenorphine clinic became operational, the staff of the NMVAHCS SUD program kept a list of potential clinic candidates who were taking methadone or had been diagnosed with opioid dependence. Those who requested detoxification were treated with clonidine, adjunctive supportive

medications, and psychosocial therapy and were educated about the impending availability of buprenorphine. One month before the clinic was scheduled to open, patients who had expressed interest were contacted.

Since the clinic's inception, new patients have been recruited through a process of motivation, education, and assessment by SUD program staff. This process begins when prospective patients are given a copy of the SAMHSA pamphlet, *Introducing Office-Based Treatment of Opioid Addiction*,[33] which is kept on hand by all staff members. The staff members assess the appropriateness of candidates for buprenorphine therapy and refer them to the attending physician, who makes the final decision regarding clinic enrollment. The SUD staff members also ensure that each candidate is participating in group therapy, individual therapy, or some combination of the two. In the context of our SUD program, this may include cognitive-behavioral therapy, motivational enhancement, family or couples therapy, 12-step–modeled interventions, a dual diagnosis group, or relapse prevention.

Because there have been a number of deaths in France when benzodiazepines were combined with buprenorphine, patients taking high doses of benzodiazepines who otherwise qualify for the outpatient buprenorphine program are provided with a tapering schedule. In the French reports, most of the deaths were due to the intravenous use of both drugs, and higher buprenorphine doses may have been used than are customary in the United States.[34,35] Clinically, in patients taking modest doses of benzodiazepines, we have used buprenorphine to treat posttraumatic stress disorder or other psychiatric conditions only when the patients agree to close observation and we feel their clinical condition would deteriorate substantially if the anxiolytic were stopped.

CLINIC OPERATION

Buprenorphine treatment generally is comprised of three phases: induction, stabilization, and maintenance. Induction, which usually lasts two to three days, involves starting the medication during the early phase of withdrawal from opioids. Stabilization encompasses the period during which doses are adjusted in response to adverse effects (such as sedation) or any continuing use of or cravings for illicit opioids. Maintenance refers to the phase in which patients have reached an optimal dose and illicit drug use is in remission or substantially reduced. In practice, there is considerable overlap between the stabilization and maintenance phases.

Buprenorphine also has been used for "detoxification" or withdrawal from opioids under medical supervision. Our clinic offers opioid detoxification with buprenorphine over a one- to three-month period. Although the optimal length of buprenorphine-assisted detoxification has not been established, early evidence indicates that, as with methadone-assisted detoxification, longer treatment periods produce more favorable results than do shorter ones.[36–38]

Initially, we offered buprenorphine induction every week on Tuesday and Wednesday. After the first month, however, we decided to hold induction clinic hours monthly rather than weekly because of the large time investment required for safe and effective procedures, as well as the intensive case load of our SUD staff. Rather than trying to observe, counsel, and manage patients beginning buprenorphine treatment in between other appointments and clinical du-

Table 2. Patient screening criteria used by the buprenorphine clinic at the New Mexico VA Health Care System

Inclusion criteria for outpatient buprenorphine treatment
- Opioid dependence or opioid abuse with strong likelihood of becoming dependent without treatment
- Stable psychiatric illness
- Absence of end-stage liver, cardiac, or renal disease
- Remission of other substance use disorders
- Willingness and ability to participate in psychosocial treatment
- Adequate social support
- Stable environment

Contraindications to outpatient buprenorphine treatment
- Use of benzodiazepines (potential for lethal interaction)
- Decompensated liver disease
- Use of more than 40 mg of methadone at the time of proposed clinic enrollment
- History of opioid dependence controlled only with more than 60 mg of methadone (unlikely to be successful)

Continued on page 23

Continued from page 20

ties, staff now reserve a three-day block for induction into the buprenorphine clinic each month, dedicating this time to providing the highest quality services for all prospective clinic patients.

New patient appointments are scheduled in one-hour time slots and follow-up appointments are scheduled in 30-minute intervals. Confidential patient information is safeguarded, with files kept in locked cabinets and electronic medical records protected by passwords. Full names are not used to call patients from the waiting room. We have found that waiting patients feel a sense of community with one another and frequently express support and discuss progress even without knowing each other's identity or reason for visiting.

Induction

Patients who express interest in the buprenorphine clinic during a given month are provided education and counseling regarding buprenorphine treatment and then scheduled to come early in the morning on the last Tuesday of the month. At the end of the week prior to induction, the clinic PA or CNS calls each patient and reminds him or her to refrain from using illicit opioids or taking prescription maintenance therapy far enough in advance to ensure that he or she will come to the clinic in an early withdrawal phase. This is key to minimizing discomfort and maximizing therapeutic benefit. The length of time each patient must abstain varies depending on the half-life of the drug being used and may be as short as four hours for heroin or as long as 24 hours for higher doses of methadone.

Prior to scheduling the induction appointment, we instruct all patients taking methadone to taper their dose slowly, over a course of several months, to no more than 40 mg.[39] Although patients can be induced or detoxified from higher methadone doses, such an approach is not recommended generally.[36]

At the first induction visit, patients are given a copy of the FDA patient information leaflet about buprenorphine[40] and asked to read it and discuss the contents with the clinic staff. For patients who can't read English well, the PA explains the contents of the leaflet and answers any questions. Patients are asked to sign and date the leaflet, which serves as their consent to treatment, and a copy of the signed leaflet is placed in the chart.

The PA or CNS then administers the Clinical Opioid Withdrawal Scale (COWS),[41] checks the patient's vital signs, takes a urine specimen, and performs a physical examination if the patient has not had one within the previous month. Serum chemistries, particularly liver function tests, are reviewed prior to clinic enrollment, and any pertinent tests not available are ordered at the first visit. Patients then track their substance use over the past six months by completing a timeline follow-back grid, a tool that consists of a calendar on which the individual indicates how many substances he or she used.[42] A tracking sheet designed for our clinic is initiated, which lists the date and time of each buprenorphine administration during the induction period, scores for all administrations of the COWS, and the medication dosages given for all phases of buprenorphine treatment. The attending physician then completes a substance abuse assessment, which focuses on the patient's medical, psychiatric, and social history. (Prior to this first visit, a specially designed electronic note is used and background information is prepared in order to facilitate intake.)

Following these assessments, patients are given a dose of the buprenorphine monotherapy product, 2 to 4 mg depending on withdrawal scores. Patients who are not experiencing withdrawal at their first visit are asked to continue to abstain from opioid use and return when symptoms manifest. Each patient is observed taking the sublingual medication to prevent possible diversion. We learned early on to have a supply of bottled water available to offer patients as the sublingual tablet is quite bitter and must be allowed to dissolve for five to 10 minutes. Every patient is observed in an adjacent waiting room for an allergic drug reaction for 45 to 60 minutes following the first dose. Patients then are asked to return in approximately three hours for reassessment. For the remainder of that day, patients are evaluated every three to four hours and dosed according to COWS scores, with additional 2- to 4-mg doses given as indicated, up to a maximum total dose of 8 mg for the first day.

At the end of the first day, the PA or the attending physician prescribes medication as needed for withdrawal symptoms and adverse effects—commonly, clonidine for primary withdrawal symptoms, an antiemetic for nausea and vomiting, an antispasmodic for abdominal cramping, ibuprofen for joint pain, or trazodone for sleep. Patients are instructed to return the following morning, at which time they are reassessed.

If the COWS score indicates continued withdrawal symptoms on

the second morning, the patient is given the total buprenorphine dose from the previous day and asked to come back in two to four hours. Again, additional doses of 2 to 4 mg are given at these intervals until the patient is no longer in withdrawal or the maximum total dose for the second day (16 mg) is reached. Although this intensive induction schedule may seem inconvenient, patients generally prefer it to being confined in an inpatient unit or waiting in long lines at a methadone clinic. Still, we have found it necessary to arrange for both accommodations and reimbursement of travel expenses for many of our patients who must travel long distances to reach our clinic.

Stabilization and maintenance

On the third morning, patients who are without withdrawal symptoms are converted to buprenorphine plus naloxone at the final buprenorphine dose that relieved their symptoms. (Those who are still experiencing withdrawal continue with induction until their symptoms are controlled and are then converted.) Patients are prescribed a week's supply of buprenorphine plus naloxone to start with, and a follow-up appointment is made for a week later.

Unlike buprenorphine alone, which is stocked in the clinic according to the VA's rules for controlled substance ward stock, the combination product is dispensed from the outpatient pharmacy following the same procedures that apply to other C-III prescriptions, except that only certified prescribers may write orders for buprenorphine plus naloxone. Before patients collect their supply of the combination product from the pharmacy at the beginning of the stabilization phase, the clinical pharmacist conducts an extensive counseling session on its use within the buprenorphine clinic.

Patient-specific counseling is necessary because of the wide range of patients enrolled in the buprenorphine clinic. The veterans we treat have varying backgrounds and capacities for understanding information regarding their medication. It is important that the medication counseling be at a cognitive level appropriate for each patient. Regardless of the individual situation, however, the counseling must reinforce a few major points that could have a significant impact on patient treatment and well-being, including the necessity for sublingual administration, the need to inform all other health care providers that they are being treated with buprenorphine, and the potential implications of not giving this information—particularly in a medical emergency situation. The clinical pharmacist also discusses the potential for drug interactions and their possible significance, the need to safeguard the medication from diversion, what to do if the medication supply is lost or damaged, and the effects of using other opioids while taking buprenorphine. At the conclusion of the counseling session, the clinical pharmacist reviews the patients' rights and responsibilities with the patient and places a signed copy of these rules in the chart (Figure).

One of the important practical lessons we have learned is to administer the total daily dose of buprenorphine alone to the patient before they leave the clinic on the day of conversion in order to prevent them from experiencing withdrawal while waiting for their medication to be filled at the pharmacy or for any outstanding laboratory results to come in. Patients also are instructed on how to contact our staff if they have problems in between visits.

Each follow-up visit includes screening of urine samples and, for the first month, a repeat administration of the COWS. If patients abstain from illicit drug use, attend psychosocial treatment, and experience no adverse effects, their initial weekly follow-up visits are extended to every two weeks and then to once a month.[43] Patients who continue to use opioids or other illicit drugs (such as cocaine), as detected by self-report or urine screening; fail to attend psychosocial treatment regularly; or have adverse effects are seen weekly until the problem has been addressed sufficiently and treatment stabilized. Since buprenorphine can cause elevation of liver enzymes and our population has a high prevalence of hepatitis C virus (HCV) infection and past alcohol abuse, liver function tests are performed at the end of one month of treatment and every three months thereafter.[44]

During the maintenance phase, patients have the option of switching from daily to every other day or every third day dosing, which requires doubling or tripling the baseline dose. These regimens have shown similar efficacy to once-a-day dosing and were preferred in several studies.[45,46] None of our patients have chosen this option to date, however, because they feel the daily ritual of taking the medication helps reinforce sobriety and they're not confident they could take the number of tablets required at one time for every other day or every third day dosing.

Since our patients currently must be seen in the clinic at least monthly, no refills for buprenorphine plus naloxone are authorized, though there are no legal constraints prohibiting the authorization of such refills. If the supply of medication is damaged or lost, the patient must contact one of the clinic prescribers to obtain a replacement supply.

Other facilities considering implementation of a buprenorphine clinic should be sure that the pharmacy keeps adequate supplies of buprenorphine alone and buprenorphine plus naloxone in stock. Patients cannot miss doses of buprenorphine without risk of withdrawal, and it may be difficult to find another pharmacy from which to "borrow" a supply since it is likely that only a small number of pharmacies stock buprenorphine regularly. Both buprenorphine products are available through the federal prime vendor and can be ordered with all other C-III–V controlled substances.

I agree to the following requirements as a condition of receiving buprenorphine from the VA Substance Abuse Treatment Program:

- Random toxicology screens and laboratory testing will be done.
- Failure to attend regular psychosocial treatment will result in discontinuation of medication.
- Any diversion (selling of drugs or prescriptions or intravenous use of medications or giving medications to other persons) will result in discharge from clinic and referral to a local methadone program.
- Toxicology screens positive for other substances will be managed on a case-by-case basis and will usually result in a higher intensity of psychosocial and/or medication treatment.
- Loss of prescriptions will be handled on a case-by-case basis, but a pattern of such misuse will result in buprenorphine being administered only under supervision of clinic personnel.
- Once a patient reaches a stable level of medications, the patient may receive every 2- to 3-day dosing.
- Patients on stable dosing may be seen on a weekly or monthly basis and receive take-home prescriptions for self-administration.
- Violence toward the treatment team will result in discontinuation of medication.
- Patients who have a medical or psychiatric decompensation or become suicidal or homicidal may require inpatient admission. Every effort will be made to continue buprenorphine if the patient is on maintenance therapy.

Patient Name_____ Date_____

Figure. Patient rights and responsibilities form developed for the buprenorphine clinic at the New Mexico VA Health Care System.

PRELIMINARY OBSERVATIONS

Between April and December 2004, 24 patients completed the induction and stabilization phases of outpatient buprenorphine treatment (Table 3). Of those, 18 (75%) were still active in the maintenance phase of treatment as of December 2004 (Table 4). These early results are encouraging.

The average age of the 24 patients was 52.4 years (range, 42 to 66 years). A total of 23 (96%) were male, 14 (58%) were Hispanic, nine (38%) were Caucasian, and one (4%) was Native American. The average maintenance dose of buprenorphine among active patients was 17.56 mg, for an average medication cost of $10.48 per day.

At the end of our data collection period, half of the patients had abstained from illicit opioids since induction. A small number of patients tested positive for marijuana during treatment. Although this use is discouraged, we have been reluctant to discontinue patients who test positive for marijuana due to the overall positive effects of buprenorphine therapy.

We have successfully treated patients dependent on a variety of opioids, including heroin, methadone, and long- or short-acting prescription opioids. We have found that patients switching from methadone to buprenorphine may require more dose adjustments during the stabilization phase compared with those taking illicit or prescription opioids. We suspect this may be due to the prolonged half-life of methadone compared with shorter-acting opioids. Unless patients express a strong wish for rapid buprenorphine-assisted detoxification, we recommend stabilization and maintenance on buprenorphine plus naloxone after induction for at least a month. Those who then want to stop buprenorphine are placed on a gradual tapering schedule of approximately 2 mg a week or less, depending on withdrawal symptoms.

Adverse effects have been minimal, with mild hypotension and headache being the most common. No patients have required medical treatment or dosage alteration for adverse effects—including those taking low doses of benzodiazepines, antipsychotic drugs, and antidepressant drugs. Patients, as well as providers, have noted a marked improvement in clarity of thinking and sense of well-being—particu-

Table 3. Characteristics of the 24 patients who completed induction and stabilization at the New Mexico VA Health Care System outpatient buprenorphine clinic between April and December 2004

Patient	Comorbidities	Drug use prior to induction*
1	HCV,† PTSD,‡ cervical stenosis	Heroin use, 10 years; morphine sulfate, four years (30 mg/day at induction)
2	HCV, cocaine dependence, alcohol dependence	Opiate dependence, 23 years; prescription opioid use; methadone 40 mg/day at induction
3	HCV, trigeminal neuralgia, migraine headache	Heroin use, 36 years ($400/week for 10 years preceding induction)
4	CAD,§ hypertension, type 1 diabetes, alcohol and cocaine dependence	Heroin or methadone use, 30 years; methadone 30 mg/day at induction
5	HCV, history of head trauma, PTSD, chronic pain	Heroin use, 25 years ($80/day at induction)
6	Bipolar disorder, HCV, degenerative disc disease, seizure disorder, amphetamine abuse	Prescription opioids, 10 years; methadone 40 mg/day at induction
7	HCV, emphysema, PTSD	Heroin use, 35 years ($60–$80/day at induction)
8	GERD,‖ chronic pain	Heroin use, seven years; methadone 40 mg/day at induction
9	HCV, anxious neurosis, hyperthyroidism, peripheral neuropathy	Heroin or methadone use, 22 years; methadone 40 mg/day at induction
10	PTSD, seizure disorder, chronic pain	Heroin use, 35 years ($40–$60/day at induction); diazepam (20 mg/day at induction)
11	HCV, chronic pain	Heroin use, 33 years ($30/day at induction)
12	HCV, GERD, osteoarthritis	Heroin use, 35 years ($60–$80/day at induction); sporadic cocaine abuse
13	HCV, cirrhosis, PTSD, depression with psychotic features	Heroin or methadone use, 40 years; methadone 40 mg/day at induction
14	HCV, PTSD, depression with psychotic features, chronic pain	Heroin use, 30 years ($20/day at induction); intermittent methadone maintenance
15	HCV, thrombocytopenia, depression, chronic pain	Heroin use, eight years continuous, sporadic prior to that; methadone 40 mg/day at induction

Continued on page 32

Continued from page 26

Table 3. (continued) Characteristics of the 24 patients who completed induction and stabilization at the New Mexico VA Health Care System outpatient buprenorphine clinic between April and December 2004

Patient	Comorbidities	Drug use prior to induction*
16	HCV, thrombocytopenia, depression, alcohol dependence in remission, chronic pain, BPH¶	Heroin or methadone use, 25–30 years; methadone 20 mg/day at induction
17	HCV, PTSD, chronic pain	Heroin use, 33 years ($20/day at induction); intermittent methadone use
18	HCV, antisocial PD,# benzodiazepine dependence, intermittent cocaine abuse	Heroin use, 10 years ($20/day at induction)
19	HCV	Heroin use, 25 years; methadone 50 mg/day plus heroin at induction
20	HCV, alcohol dependence in remission, depression, chronic pain	Heroin or methadone use, 23 years; methadone 40 mg/day at induction
21	HCV, PTSD, alcohol dependence in remission	Heroin use, 36 years (0.25 g/day at induction)
22	HCV, PTSD, chronic pain	Heavy prescription opioid use, four years (12–15 tablets hydrocodone and 10 capsules propoxyphene daily at induction)
23	HCV, alcohol dependence, cocaine abuse, chronic pain, anxiety, depression, OCD**	Heroin use, 33 years ($25/day at induction)
24	HCV, depression, mitral valve disorder, COPD††	Heroin or methadone use, 36 years; methadone 35 mg/day at induction

*Due to discrepancies in purity, measurement, and strength of heroin, self-reported frequency and amount are noted. †HCV = hepatitis C virus. ‡PTSD = posttraumatic stress disorder. §CAD = coronary artery disease. ||GERD = gastroesophageal reflux disorder. ¶BPH = benign prostatic hypertrophy. #PD = personality disorder. **OCD = obsessive compulsive disorder. ††COPD = chronic obstructive pulmonary disease.

larly patients who were previously taking methadone. This could be due to the fact that buprenorphine is a partial rather than a full agonist and that its interactions at opioid receptors are more complex than those of methadone.[47]

Psychosocially, patients have compared buprenorphine treatment favorably to prior, often failed experiences at methadone clinics where they felt stigmatized. Several of our patients live in remote areas that made access to even community OAT programs impossible and have traveled distances greater than 300 miles to attend our clinic. Patients with unstable living conditions, such as those who are homeless, have been the most likely to drop out of treatment.

Studies show that nearly 80% of patients who abuse opioids may meet criteria for another SUD, and up to 50% have an additional Axis I or II psychiatric diagnosis.[48,49] A significant aspect of our clinic

Table 4. Preliminary results for the 24 patients who completed induction and stabilization at the New Mexico VA Health Care System outpatient buprenorphine clinic between April and December 2004

Patient	Induction/maintenance dose	Continued or recurrent illicit drug use	Current treatment status
1	6 mg/16 mg	None	Active; dose tapered to 4 mg/day
2	20 mg/20 mg	Two relapses	Inactive (treatment dropout)
3	32 mg/32 mg	Two relapses; three episodes of illicit use	Active
4	14 mg/14 mg	One episode of illicit use; one missed appointment	Active
5	32 mg/32 mg	One episode of illicit use	Lost to follow-up
6	18 mg/18 mg	None	Active
7	18 mg/20 mg	One episode of illicit use	Active
8	12 mg/12 mg	None	Inactive (incarcerated)
9	12 mg/14 mg	One relapse	Active; repeat induction at 8 mg
10	30 mg/28 mg	None	Active
11	20 mg/22 mg	Tested positive for marijuana	Active
12	14 mg/14 mg	None	Lost to follow-up
13	20 mg/22 mg	None	Active
14	14 mg/14 mg	Two episodes of illicit use	Lost to follow-up
15	10 mg/10 mg	One episode of illicit use	Active
16	10 mg/10 mg	One relapse; two episodes of illicit use	Active; repeat induction at 6 mg
17	12 mg/14 mg	Two episodes of illicit use	Active
18	14 mg/14 mg	Tested positive for marijuana	Active
19	24 mg/24 mg	None	Inactive (entered naloxone detoxification program)
20	12 mg/16 mg	None	Active
21	12 mg/20 mg	Tested positive for marijuana	Active
22	14 mg/18 mg	None	Active
23	18 mg/18 mg	None	Active
24	10 mg/10 mg	None	Active

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is that we do not exclude these patients. Indeed, most of our clinic patients have multiple medical and psychiatric comorbidities, which require careful evaluation and ongoing psychiatric and medical monitoring. These patients also must be screened for drug interactions, particularly those who are taking medications metabolized through cytochrome P450 3A4, the main route of buprenorphine metabolism.[50]

The SAMHSA buprenorphine curriculum states that one of the purposes of office-based treatment of opioid dependence is to "mainstream the treatment of opioid dependence by coordinating it with treatment for other medical conditions."[36] For example, HCV infection is one of the most prevalent comorbidities in patients with SUDs, since intravenous drug use is the major risk factor for acquiring the disease. HCV infection also has a higher prevalence rate in veterans than in the general population and has been identified as a major focus of VHA care.[51–54] Studies with methadone maintenance therapy have established that this treatment can reduce the incidence of infectious diseases such as HCV, and it is logical to assume that the same result would apply to buprenorphine treatment.[4,12,55] Patients with HCV infection who are actively using opioids often are barred from antiviral treatment, whereas those undergoing buprenorphine treatment (like those receiving methadone maintenance) may be acceptable candidates and have beneficial results from therapy.[56]

At our clinic, we work closely with other behavioral health and primary care providers to address problems that arise during the course of buprenorphine treatment, such as the emergence of depression that had been masked by substance use or the need to reduce antiglycemic medication once patients with diabetes have begun to care for themselves better.[57] Moreover, the trust we have established with our veteran patients has enabled us to reconnect many who have not seen a health care professional in decades with the health care system.

THE BENEFIT OF EXPERIENCE

Recent reviews and government reports have highlighted substantial decreases in funding for SUD treatment, especially residential or inpatient programs, resulting in many veterans being unable to obtain adequate treatment for addiction.[8,58] As the first FDA-approved medication for office-based treatment of opioid addiction, buprenorphine has the potential to expand access to SUD treatment for a substantial proportion of these veterans. Research suggests that outpatient buprenorphine treatment is an option that can be both clinically efficacious and cost-effective when incorporated into VHA SUD programs.

While fewer legal processes are required for establishment of an office-based buprenorphine treatment program, implementation still may be complicated by several factors, such as negative attitudes about opioid replacement therapy among administrators, providers, and patients and the intensive scheduling requirements for the induction period of treatment. By detailing our experience and sharing the strategies we have used to overcome these barriers, we have attempted to encourage and aid other federal facilities and health care professionals who are planning or implementing outpatient buprenorphine treatment. Although we are still in the data collection phase of empiric evaluation, our preliminary results appear promising and we have noted a high level of patient, staff, and administration satisfaction with the use of buprenorphine. ●

The opinions expressed herein are those of the authors and do not necessarily reflect those of Federal Practitioner, *Quadrant HealthCom Inc., the U.S. government, or any of its agencies. This article may discuss unlabeled or investigational use of certain drugs. Please review complete prescribing information for specific drugs or drug combinations—including indications, contraindications, warnings, and adverse effects—before administering pharmacologic therapy to patients.*

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Continued on page 40

Continued from page 34

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