CME

Models for Implementing Buprenorphine Treatment in the VHA

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Although proven as a cost-effective treatment in VHA settings, buprenorphine currently is underutilized by VA practitioners. These authors review the drug's advantages and describe how some VA programs are employing it successfully.

CONTINUING MEDICAL EDUCATION

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GOAL

To encourage buprenorphine treatment for opioid dependence at VHA facilities by describing why and how the treatment is used within the system.

LEARNING OBJECTIVES

After reading the article and taking the test, participants should be able to:

1. Describe the history of buprenorphine treatment within the VHA.
2. Discuss the barriers to use of buprenorphine treatment within the VHA.
3. Explain the models by which some VHA facilities have incorporated buprenorphine treatment into their practice.

INTENDED AUDIENCE

This CME activity is designed for physicians and other clinicians treating patients in the federal health care system.

ACCREDITATION

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The estimated time to complete this activity is one hour.

CME PEER REVIEW

This article has been peer reviewed and approved for CME credit by David M. Kaufman, MD, professor of neurology and psychiatry at Albert Einstein College of Medicine and Montefiore Medical Center, both in Bronx, NY. Review date: April 2009.

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Opioid dependence is a major problem for the American population in general and the VHA patient popula-

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tion in particular. This chronic, relapsing medical disorder affects up to two million individuals in the United States, 26,818 of whom are enrolled in the VHA.[1–4] When untreated or treated ineffectively, opioid dependence contributes to premature mortality and increased utilization of health care and social services.[5]

For VHA providers, buprenorphine treatment can be a useful tool in the fight against opioid dependence. Buprenorphine, a partial opioid agonist, has proved to be a safe and effective treatment for the disorder in nonspecialized outpatient settings, including VHA environments.[6–8] It has a major advantage over other opioid agonist treatments (OATs), which only can be offered through licensed OAT programs, in that providers can dispense it in office-based settings.[9–11] Buprenorphine treatment also has been shown to be cost-effective for the VHA.[12]

Despite these advantages, as well as the VHA's efforts to encourage buprenorphine treatment within the system, VHA providers may not perceive a need for the treatment of opioid dependence. In addition, they may perceive a lack of resources to handle office-based opioid dependence therapy, believe that opioid dependence treatment is inappropriate outside of licensed OAT programs, or simply choose not to treat opioid dependence.[13]

In order to help encourage the use of buprenorphine treatment within the VHA, this article will expand on the advantages this treatment has over other OATs in the VHA, describe the system's efforts to promote the treatment, and address some of the possible concerns providers may have with using buprenorphine. In addition, to disseminate the various buprenorphine treatment models, we will describe how three VA facilities have incorporated buprenorphine into their different treatment settings.

ADVANTAGES OF BUPRENORPHINE OVER OTHER OATs

Buprenorphine has several properties that provide a more favorable pharmacologic profile than methadone, the conventional treatment for opioid dependence. While methadone is a full opioid agonist, buprenorphine's status as a partial agonist reduces overdose potential, opioid craving, and withdrawal symptoms while maintaining an extremely high affinity for the opioid receptor—which discourages concomitant drug use. Adding naloxone (a full opioid antagonist) to buprenorphine in a combination sublingual tablet deters users from injecting the drug, thus reducing the potential for overdose, abuse, and diversion.[14,15]

In October 2002, Congress made an amendment to the Drug Addiction Treatment Act of 2000 (DATA) that allowed qualified physicians to prescribe and dispense sublingual buprenorphine and buprenorphine/naloxone tablets (hereafter collectively termed "buprenorphine") in office-based practices (Table 1).[9–11,16] Appropriately qualified physicians can begin prescribing buprenorphine in office-based practice after applying for and receiving a waiver from the Drug Enforcement Agency. Such physicians can receive support in managing opioid dependence from nurse practitioners and physician assistants (PAs) but cannot delegate drug prescribing responsibilities to these other providers. By contrast, methadone is not approved for use outside of licensed OAT programs.[17] Allowing buprenorphine to be dispensed through office-based practices provides a new treatment option for providers who have not prescribed OAT, and it may serve a new cohort of patients with opioid dependence who did not previously access treatment.[18]

Within the VHA, OAT programs have several drawbacks that do not apply to office-based buprenorphine treatment. One is that the VHA has fewer than 40 licensed OAT programs, which can treat only a finite number of patients. Thus, VHA providers often refer patients with opioid dependence to licensed OAT programs outside of the system for pharmacologic treatment[19]—a problematic solution in that some patients may feel uncomfortable receiving OAT in a non-VHA setting and that it can disrupt coordination and integration of care within the VHA. In addition, patients and health care providers may hesitate to take advantage of licensed OAT programs due to stigma associated with the programs and the programs' admission requirements, daily dosing, and prescribed nonpharmacologic therapies.

Recent data indicate that buprenorphine treatment can be provided within the confines of primary care practice with minimal accessory services. Through weekly dosing patterns in outpatient academic general practices, the therapy has reduced opioid use and increased retention rates effectively.[6] Because the VHA often has extensive support services (including nursing, laboratory, counseling, and pharmacy services) located near primary care practices, it is in an ideal position to provide OAT in primary care or other outpatient environments.

Cost savings is another advantage that buprenorphine treatment can offer to the VHA. Although the drug is more expensive than methadone initially, it reduces regulatory burdens, the need for resource-intensive OAT programs, infrastructure support, and salary costs. In prior research, VHA investigators concluded

Table 1. Definition of physician qualified to prescribe and dispense buprenorphine in office-based setting, according to the amended Drug Addiction Treatment Act of 2000 [a,16]

1. Physicians must meet one or more of the following training requirements:
   - Hold a subspecialty board certification in addiction psychiatry from the American Board of Medical Specialties
   - Hold an addiction certification from the American Society of Addiction Medicine
   - Hold a subspecialty board certification in addiction medicine from the American Osteopathic Association
   - Have completed not less than 8 hours of authorized training on the treatment or management of opioid-dependent patients
   - Have participated as an investigator in one or more clinical trials leading to the approval of a narcotic drug in schedule III, IV, or V for maintenance of detoxification treatment
   - Have such other training or experience as the state medical licensing board[b] considers to demonstrate the ability of the physician to treat and manage opioid-dependent patients
   - Have such other training or experience as the HHS secretary considers to demonstrate the ability of the physician to treat or manage opioid-dependent patients
2. Have the capacity to provide or to refer patients for necessary ancillary services, such as psychosocial therapy
3. Agree to treat no more than 30 patients at any one time[c]

[a]Physicians are deemed qualified if they satisfy conditions 1 through 3. [b]Of the state in which the physician will provide maintenance or detoxification treatment. [c]After one year of holding the waiver, physician may apply for waiver allowing treatment of no more than 100 patients.

that sublingual buprenorphine use is ultimately cost-effective at the current costs accrued by the VHA—especially if its adoption does not lead to a net decline in methadone use through licensed OAT programs.[12]

IMPLEMENTING THE TREATMENT

In the United States

Approximately 1,113 U.S. physicians received a waiver to prescribe buprenorphine in the first year after the DATA amendment. By the first quarter of 2005, approximately 4,700 waivered physicians used the drug to treat 104,640 patients. These providers' early experiences indicated that buprenorphine is effective and results in high levels of overall patient and provider satisfaction.[20,21] By 2008, an estimated 16,232 physicians had been trained in buprenorphine treatment, with approximately 90% of these physicians requesting waivers to prescribe buprenorphine and 81% receiving the waivers.[22,23] Approximately 585,000 patients had been treated with buprenorphine, and approximately 4.1 million total prescriptions for the drug had been written. As many as 70% of patients treated with buprenorphine had received maintenance treatment, as opposed to detoxification treatment.[22]

In the VHA

In 2003, the VHA responded to the DATA amendment by establishing national nonformulary guidelines for buprenorphine use in office-based practices.[24] Although the medication approval requirements of local and regional VHA pharmacy and therapeutic committees had to be met before dispensing the drug, these guidelines permitted waivered physicians to prescribe sublingual buprenorphine tablets through a nonformulary approval process. In 2006, the VHA approved buprenorphine for formulary status and published criteria for its use (Table 2).[16,25] These criteria are consistent with non-VHA guidelines for buprenorphine use.

Despite the current system-wide availability of buprenorphine treatment and a cost that is considerably less than that incurred by patients in other health care systems, VHA utilization of buprenorphine has been limited. When buprenorphine had nonformulary status in the VHA from fiscal year 2003 through fiscal year 2005, the number of VHA patients who received it increased only from 53 to 739.[19] In 2005, up to 5,100 patients in the VHA could potentially have received buprenorphine treatment if each waivered physician in the system had treated 30 patients (the highest number allowed at that time). This number represents almost 19% of all VHA patients diagnosed with opioid dependence, but it is about twice the number of patients currently receiving VHA care for opioid dependence. Furthermore, there was variability in

Table 2. Provider and patient criteria for buprenorphine use in the VHA[16]

Provider criteria[a]

The provider must:

- Be a qualifying physician[b]
- Meet all SAMHSA[c] and DEA[d] notification and registration requirements for the Opioid Treatment Waiver Program[e]
- Have experience in addiction medicine or addiction psychiatry (or, if inexperienced in addiction medicine, treat patients in consultation with a provider in the Physician Clinical Support System mentoring program[f])

Patient criteria

Sublingual buprenorphine is indicated for OAT[g] of opioid dependence,[h] including medically supervised withdrawal, in:

- New patients not currently receiving OAT who meet at least one of the following three criteria:
  - —Do not have timely access to a VA-supported OAT center
  - —Do not meet regulatory criteria for treatment in an OAT program
  - —Will have difficulty adhering to scheduled visits at a VA-supported OAT program (e.g., because of restrictive clinic hours)
- Appropriately selected patients receiving stable methadone maintenance who have difficulty adhering to scheduled visits at a VA-supported OAT center or may not need close supervision. Opioid treatment programs should determine the criteria for appropriate selection of these patients, and the criteria should take into consideration such factors as the patient's psychosocial adjustment, lifestyle stability, job stability, level of physiologic opioid dependence, and need for higher doses of methadone (e.g., ≥ 80 mg daily)
- Patients who have a documented severe, uncontrollable adverse effect or true hypersensitivity to methadone

[a]The provider must satisfy all three bullet points. [b]As defined by the amended Drug Addiction Treatment Act of 2000. [c]SAMHSA = Substance Abuse and Mental Health Services Administration. [d]DEA = Drug Enforcement Agency. [e]Available at http://www.dpt.samhsa.gov. [f]Available at http://www.pcssmentor.org. [g]OAT = opioid agonist treatment. [h]Diagnosed according to *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition criteria.

the implementation of buprenorphine across VHA facilities and VISNs. For example, by October 2005, two VISNs accounted for over one third of all outpatient buprenorphine prescriptions in the VHA, and six VISNs had filled no such prescriptions.[19]

VHA EFFORTS TO REACH MORE PATIENTS

The incomplete implementation of buprenorphine in the VHA and its facilities underscored a need for assistance in establishing buprenorphine use at individual sites. In response, the VHA's Substance Use Disorders—Quality Enhancement Research Initiative (SUD-QUERI) acted in 2006 to establish a Buprenorphine Work Group that was charged with implementing and evaluating buprenorphine use in the VHA. In fiscal year 2007, the VA Central Office provided funding to 15 VHA facilities—all of which had a high prevalence of opioid dependence diagnoses, underuse of buprenorphine, and no access to a licensed OAT program—to help them initiate buprenorphine treatment for opioid-dependent patients. One VHA facility declined this funding. Since the distribution of funds, the 14 sites that accepted funding have requested assistance in establishing clinics and using buprenorphine.

In March 2007, the Buprenorphine Work Group established a VHA Buprenorphine Consultation Service to assist VHA sites in establishing and maintaining buprenorphine treatment. This service, which consists of clinical experts in buprenorphine care and a program coordinator, works closely with faculty and staff of the VHA's Program Evaluation and Resource Center and the VHA's Center of Excellence in Substance Abuse Treatment and Education. It provides consultation through e-mail and a telephone helpline, and it arranges visits to existing facilities that use buprenorphine treatment. It has implemented several targeted strategies to assist in buprenorphine care within patient settings, including the development of a resource guide for clinicians and a monthly newsletter.

The service's telephone helpline steadily has increased contacts with VHA facilities interested in establish-

ing buprenorphine care. Over its first year of existence, from March 2007 to February 2008, it received 167 contacts from funded sites and 115 contacts from nonfunded sites, and it initiated hundreds of additional contacts. The helpline has received many inquiries, with providers at various sites requesting assistance in developing policies and procedures for their clinics and asking for examples of consent and treatment agreement forms used in buprenorphine treatment. Most callers request a resource guide and literature on buprenorphine treatment in an office-based setting, and some simply need guidance in finding patients. Many callers seek models of buprenorphine treatment specific to their particular clinical environment (M.K., unpublished data, 2008).

To expand implementation of buprenorphine treatment in the VHA, the VHA Mental Health Service Line sponsored two eight-hour VHA Employee Education System Buprenorphine Training Programs in Denver, CO and Washington, DC. These programs enabled physicians to apply for a waiver to prescribe buprenorphine. As was reportedly the case with other buprenorphine training programs described in the literature,[26,27] all of the participants reported that the eight-hour programs were worthwhile and compared favorably to other CME activities. All reported that they had accomplished the program objectives fully, felt competent to apply these objectives in the setting of opioid dependence treatment, and would be able to use their new knowledge in their regular work assignments. Despite the programs' initial popularity, however, only a few of the 18 VHA physicians who attended received the waiver and only two of them were prescribing buprenorphine nine months later.[28]

ADDRESSING POSSIBLE PROVIDER BARRIERS

A number of barriers at the provider level may be preventing more robust use of buprenorphine treatment in the VHA. For instance, negative clinician attitudes toward treatment of opioid dependence in outpatient settings may be inhibiting more widespread implementation of the treatment.[26] Studies suggest, however, that physicians and pharmacists, in general, are satisfied with the use of buprenorphine in practice.[29,30] Another possibility is that primary care providers do not treat a high proportion of patients who are opioid dependent or consider routine substance abuse treatment to be within their scope of practice.

One strategy to increase buprenorphine use may be to target physicians who treat a large proportion of opioid-dependent patients within specialty settings.

One strategy to increase buprenorphine use may be to target physicians who treat a large proportion of opioid-dependent patients within specialty settings. Recent studies indicate that specialty environments may be locations where office-based OAT is particularly useful. For example, buprenorphine may be an ideal therapy to initiate in clinics that are designed to treat patients with comorbid HIV and hepatitis C virus infection but that also have a high proportion of patients with opioid dependence.[31–34]

Some providers and administrators may be averse to prescribing buprenorphine due to concerns about diversion or abuse of the medication. Buprenorphine has had minimal diversion in the United States, however, compared with methadone and oxycodone—both of which are prescribed widely for pain by clinicians working in outpatient settings.[35]

The relative cost of buprenorphine compared to methadone may have been a significant barrier to buprenorphine's nonformulary use, and perceptions of cost may continue to be a barrier now that buprenorphine has formulary status. The average daily cost of methadone (60 to 80 mg/day) in the VHA is $0.36 to $0.48 (A.J.G., J.T., unpublished data, 2009). Before buprenorphine was added to the VHA formulary, typical doses of buprenorphine (12 to 16 mg/day) cost between $9.48 and $10.10 within the system.[25] Since the medication was added to the formulary, a 16 mg dose of buprenorphine alone costs $8.63 and a 16 mg dose of buprenorphine/naloxone costs $6.86 in the VHA (A.J.G, J.T., unpublished data, 2009). As previously discussed, however, research has shown buprenorphine to be cost-effective in the long run.

Regional differences in the use of buprenorphine certainly exist in non-VHA settings, but these differences may be amplified in VHA settings.[21] Institutional change may be more challenging for such a large health care system as the VHA, particularly when it attempts to adopt potentially

controversial treatments such as office-based substance abuse treatment. Although an individual practitioner outside the VHA simply can decide to be trained in buprenorphine treatment, receive the waiver to prescribe the drug, and prescribe it, VHA practitioners must maneuver through multiple policy and institutional barriers. Nonetheless, many VHA facilities are providing buprenorphine treatment successfully to their patients.

MODELS FOR BUPRENORPHINE TREATMENT

Currently, four models for buprenorphine treatment are being used within the VHA. One model (not discussed here) is delivered through inpatient consultative services. The other three are offered on an outpatient basis and include the licensed OAT program/office-based model, the substance use disorder (SUD) program model, and the outpatient primary care clinic model.

Licensed OAT program model

At the VA Puget Sound Health Care system in Seattle, WA, buprenorphine treatment is provided through a clinic-based track (licensed OAT program) or an office-based track (general addiction clinic). Patients who are unstable (indicated by the ongoing abuse of multiple substances, homelessness, or psychiatric symptoms) and meet the criteria for buprenorphine therapy first receive their treatment through the OAT program's clinic-based track. The clinic where buprenorphine is dispensed adheres to the same federal and local guidelines as the existing methadone treatment program regarding take-home medication, urine sample frequency, dosing times with observed ingestion, and counseling frequency. Patients who are stable (indicated by employment, stable relationships, and lack of multiple substance abuse) or who live far from the VA medical center and who meet criteria for buprenorphine therapy may be started in the office-based track.

Patients can advance from the clinic-based to the office-based track, and they can be "demoted" from the office-based to the clinic-based track if their treatment adherence and stability is not satisfactory. In order for patients to advance from clinic-based to office-based treatment, they must be clinically stable, adhere to treatment requirements, and abstain from alcohol and illicit drugs other than cannabis for at least 90 days. Additional criteria include stable psychiatric symptoms, stable living environment and relationships, and stable employment or disability funding.

The office-based treatment begins with an eight-week "introduction" phase in which the patient is required to come into the office every week to pick up medication, provide a urine sample, and visit with the physician if needed. The patient also must attend four brief, weekly, one-on-one meetings with a care coordinator to complete the psychosocial assessment and treatment plan. Beginning in this introduction phase and continuing throughout treatment, the patient is required to attend a monthly therapy group with other patients receiving the same office-based buprenorphine treatment.

The second phase of the office-based treatment is the eight-week "intermediate" phase, in which the patient is required to come into the office every other week to pick up medication, provide a urine sample, and meet with the physician if needed. During this phase, the patient is required to call the pharmacy one week prior to the appointment to order medication and to attend the monthly group.

The treatment's third phase is the "stable" phase, during which the patient visits the office once per month to provide a urine sample, attend the monthly group, and see the physician if needed. As long as patients meet the program's criteria, they can remain in the stable phase and take buprenorphine indefinitely. Alternatively, buprenorphine treatment can be tapered off completely if the patient asks to cease treatment and if such a step is deemed medically appropriate. Patients who have tapered off the drug are strongly encouraged—but not required—to continue attending the monthly groups regularly.

During any of the phases of the office-based treatment, if a patient fails to provide a urine sample, provides a sample that tests positive, or misses appointments, he or she is given a letter of warning. If the patient continues to demonstrate instability, he or she is placed on concern status and treatment is reintensified by increasing the frequency of visits to supply buprenorphine, requiring weekly meetings with a care coordinator, and mandating weekly urine sample submissions. If a patient on concern status demonstrates stability for eight weeks, he or she is eligible for promotion back to intermediate or stable status. If a patient continues to demonstrate instability while on concern status, however, he or she is transferred to the clinic-based treatment track for a minimum of 90 days. If such a patient continues to demonstrate instability, providers intensify the treatment by reducing medication supplies and requiring the patient to provide weekly urine samples, attend counseling sessions one to two times per week, and follow all other stringent federal and local guidelines. If the patient cannot follow these requirements, providers offer methadone treatment to the patient.

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SUD program model

The New Mexico VA Health Care System (NMVAHCS) provides buprenorphine in the context of a large SUD program within the behavioral health care line that includes a residential treatment unit, a mini-intensive outpatient program, and many other counseling and therapy options.[36] The direct staff of the buprenorphine clinic are an addiction psychiatrist, an addiction psychiatry fellow, a clinical pharmacist, a clinical nurse specialist (CNS), and a PA. In addition, several other waivered physicians provide coverage for the primary prescriber—and, recently, several physicians in the NMVAHCS's community-based outpatient clinics (CBOCs) obtained their waivers, expanding rural buprenorphine treatment. Consultations from providers in the emergency department, primary and specialty care medical clinics, CBOCs, and medical and surgical units are obtained through the electronic consultation package for SUD referrals.

The CNS or PA usually performs the initial assessment in an outpatient setting, but assessments are performed in the emergency department or main hospital when clinically indicated. An evaluation of current and prior substance abuse; psychiatric history, diagnoses, and treatment; medical illnesses and medications; social support; and patients' motivations and treatment preferences are obtained. The first visit also establishes a therapeutic alliance between patient and provider and is used to provide the patient with extensive oral and written education regarding buprenorphine, clinic rules and responsibilities, and protocol for induction. If no recent physical examination or required laboratory tests have been performed, they are ordered, along with a urine drug test. The addiction psychiatrist then reviews the full assessment; if the patient is thought to be an appropriate candidate for buprenorphine therapy, induction is arranged to take place, usually within a few days.

Inductions are performed several times each week, with one team member taking primary responsibility for overseeing the process and another providing backup. The addiction psychiatrist supervises each induction, which usually is completed in two days; rarely, a third day is needed for complicated cases. Formal informed consent is obtained for all buprenorphine treatment, and induction dosing is facilitated through use of the Clinical Opiate Withdrawal Scale (COWS).[37] At the end of induction, patients have a second educational session, this time with the clinical pharmacist, who has a doctor of pharmacy degree and focuses on drug interactions, adverse effects, and emergencies that may require opioid analgesia.

The patient returns one week later and enters the stabilization phase, during which he or she participates in a weekly counseling option that was agreed upon during the initial assessment. Counseling options available through the SUD program include residential treatment, a mini-intensive treatment program, a seeking safety group, dual diagnosis groups, relapse prevention, and individual therapy. Any comorbid psychiatric and medical conditions that may have been difficult to diagnose clearly and treat effectively during active opioid use and induction are further assessed and treated. Patients requiring social and vocational support also make contact with specialized on-site providers to ensure that all aspects of relapse prevention are addressed. Patients are provided with and asked to carry a medical alert card that explains the effects of taking opioids and buprenorphine simultaneously. During stabilization, patients also are required to attend weekly or biweekly appointments with the CNS or PA, during which urine drug tests are performed.

Although detoxification also is offered at the NMVAHCS, the vast majority of patients receiving opioid dependence treatment at the facility are taking maintenance therapy. Maintenance therapy is the most appropriate for patients who have abused opioids for decades and have made many unsuccessful attempts to abstain without medication. Many patients have expressed the view that maintenance therapy is the most effective at improving their mental and physical health, family relationships, and social situations. In order to consolidate recovery, providers recommend to most patients that they

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continue to take buprenorphine for at least three months before they consider tapering off the medication. When patients elect to stop buprenorphine treatment, their dosage is tapered by no more than 2 mg/week over several weeks or months. This approach allows plenty of opportunity to monitor patients closely for signs of relapse and minimize symptoms of withdrawal.

Patients who elect maintenance therapy are seen every one to three months, depending on their time in sobriety, clinical stability, comorbidities, social support, and location (rural locations often preclude more frequent visits). They are seen by a physician, a PA, or a CNS as clinically indicated. When indicated, random urine drug tests are used. Positive results are addressed therapeutically, with intensification of psychosocial interventions, more aggressive treatment of psychiatric conditions and chronic pain, and, at times, an increase in buprenorphine dosage. Since the buprenorphine clinic's inception, however, average doses have decreased steadily to 16 mg or less for the majority of patients. Loss of prescriptions, early refills, and other signs of misuse or abuse of buprenorphine also are evaluated and managed on an individual basis. Prescribing medication on a weekly basis and more frequent interactions with clinicians are the standard methods of managing maintenance therapy.

So far, no patients have been dismissed from the NMVAHCS program for diversion or aberrant use, and only a handful have been referred to methadone programs because buprenorphine therapy did not adequately address the severity of their dependence or comorbid chronic pain. The facility has seen an influx of patients who have developed a dependence to prescription opioids and other comorbid SUDs and, thus, require treatment of both pain and addiction. The program also is in the process of developing a specialized counseling group that will address issues specific to patients treated with buprenorphine.

Outpatient primary care clinic model

The VA Pittsburgh Healthcare System (VAPHS) provides buprenorphine within several environments, including an OAT program, a specialty Substance Abuse Assessment Team clinic, and outpatient primary care and psychiatric clinics. Patients are referred for buprenorphine treatment by several sources, including a consultation package in the electronic record system, CBOCs, primary care providers, and self-referrals through direct telephone calls to the facility. A PA (who has training in and experience with buprenorphine treatment) collaborates with the three primary care physicians who have waivers to prescribe buprenorphine at the VAPHS, two of whom treat patients and one of whom serves as backup for coverage concerns. The physicians and PA each typically see 10 to 16 patients per half day in the primary care or substance abuse clinic for buprenorphine treatment.

Providers generally prescribe buprenorphine as a maintenance medication (as opposed to a detoxification medication) in a three-phased approach: induction, maintenance, and withdrawal. During the initial assessment, providers evaluate the patient's substance abuse history, obtain a urine drug test and baseline laboratory tests, and educate the patient about buprenorphine and other treatment options. It is rare for the patient to receive the medication during this initial assessment. Rather, the provider establishes rapport with the patient, confirms an opioid dependence diagnosis, discusses the various nonpharmacologic and pharmacologic treatment options, and encourages nonpharmacologic treatment. If the provider and patient agree that buprenorphine is the best treatment option, the patient is scheduled to return to the clinic for induction.

The second visit usually is brief and functions mainly to ensure, by subjective and objective assessments using COWS, that the patient is experiencing opioid withdrawal. The patient is given several days' worth of buprenorphine and returns for assessment of treatment response. During this induction phase, dose adjustments are made on an individual basis, with providers assessing cravings and illicit use. Patients often have positive urine drug test results during induction. Although this traditionally has been seen as a reason to terminate therapy, the harm-reduction approach associated with buprenorphine therapy regards it as a reason to press on. The induction phase may last for several weeks and is completed when the patient is taking a stable buprenorphine dose.

Once a stable does is achieved, the maintenance phase begins. During this phase, medical, environmental, and social support is emphasized. The patient is required to make an office visit once per week for several weeks to pick up a prescription and submit a urine sample. Urine drug tests are performed and analyzed at the VAPHS laboratory. The tests detect qualitative amphetamines, barbiturates, cocaine, methadone, and other opiates (except oxycodone or fentanyl), propoxyphene, alcohol, and marijuana. Gas chromatography/mass spectrometry testing is available through an outside laboratory to confirm positive drug tests, including use of oxycodone and fentanyl, and it also can confirm the presence of buprenorphine. A pro-

vider observes the urine sample collection if a patient provides a sample that is cold or otherwise suspect.

When a patient adheres consistently to buprenorphine treatment policies and administration, receives negative results for several urine drug tests in a row, and demonstrates the ability to keep regular appointments, visits are scheduled one month apart and the patient is given a month's supply of medication. Positive urine drug test results are handled on a case-by-case basis. Self-reported opioid use often is treated differently than use that is denied by the patient but confirmed by urine drug test. Although there is no automatic discharge of patients per any protocol, patients have been discharged for continued opiate positivity, ongoing co-occurring substance use (including alcohol), and threatening or unruly behavior in the clinic (which is extremely rare). After a patient has a positive urine drug test result, a urine sample is collected at every visit until several consecutive samples have tested negative for illicit drugs. A urine test to confirm the presence of buprenorphine is performed once a patient is in the maintenance phase or suspected of diversion. To reduce diversion, a patient's daily buprenorphine dose is provided in as few tablets as possible, with most patients receiving one or two 8-mg tablets per day.

The third phase of treatment, the withdrawal phase, usually occurs when the patient asks to reduce or end office-based OAT. Most patients maintain their buprenorphine treatment for months before potentially entering this phase. During withdrawal, the buprenorphine dose is reduced gradually by about 2 mg/week until the patient is taking a stable dose of 2 mg/day. Patients may choose to continue taking this low dose, but the provider may elect to increase the dose if patients report abuse urges or have problems with illicit use. During the last few doses of buprenorphine, patients may opt to receive symptomatic treatment (with clonidine or ibuprofen) if they experience any withdrawal symptoms.

THE BIG PICTURE

Future work should establish the best models of offering buprenorphine therapy and examine the efficacy and cost-effectiveness of the different delivery models. In the meantime, the VHA continues to supply facilities with resources to encourage and assist providers in offering buprenorphine treatment. Making buprenorphine treatment more widespread throughout the VHA would allow for many more patients to receive opioid dependence treatment that is integrated with their medical care. Patients who live in areas where no VHA methadone treatment program is available, in particular, would benefit from increased provider utilization of buprenorphine. ●

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

REFERENCES

1. Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Dept of Health and Human Services. *Results from the 2007 National Survey on Drug Use and Health: National Findings*. Rockville, MD: Dept of Health and Human Services; 2008. NSDUH series H-34, DHHS publication SMA 08-4343.
2. Raisch DW, Fye CL, Boardman KD, Sather MR. Opioid dependence treatment, including buprenorphine/naloxone. *Ann Pharmacother*. 2002;36(2):312–321.
3. McKellar JD, Saweikis M. *Health Services for VA Substance Use Disorder Patients: Comparison of Utilization in Fiscal Years 2004, 2003, and 1998*. Palo Alto, CA: Program Evaluation and Resource Center; Center for Health Care Evaluation, VA Palo Alto Health Care System; 2005.
4. Dalton A, Saweikis M, McKellar JD. *Health Services for VA Substance Use Disorder Patients: Comparison of Utilization in Fiscal Years 2005, 2004, 2003, and 2002*. Menlo Park, CA: Program Evaluation and Resource Center; Center for Health Care Evaluation, VA Palo Alto Health Care System; 2006.
5. Mark TL, Woody GE, Juday T, Kleber HD. The economic costs of heroin addiction in the United States. *Drug Alcohol Depend*. 2001;61(2):195–206.
6. Fiellin DA, Pantalon MV, Chawarski MC, et al. Counseling plus buprenorphine-naloxone maintenance therapy for opioid dependence. *N Engl J Med*. 2006;355(4):365–374.
7. Fudala PJ, Bridge TP, Herbert S, et al; Buprenorphine/Naloxone Collaborative Study Group. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *N Engl J Med*. 2003;349(10):949–958.
8. Stein MD, Cioe P, Friedmann PD. Buprenorphine retention in primary care. *J Gen Intern Med*. 2005;20(11):1038–1041.
9. Fiellin DA, O'Connor PG. Office-based treatment of opioid dependent patients. *N Engl J Med*. 2002;347(11):817–823.
10. O'Connor PG, Fiellin DA. Pharmacologic treatment of heroin-dependent patients. *Ann Intern Med*. 2000;133(1):40–54.
11. Fiellin DA, Rosenheck RA, Kosten TR. Office-based treatment for opioid dependence: Reaching new patient populations. *Am J Psychiatry*. 2001;158(8):1200–1204.
12. Barnett PG, Zaric GS, Brandeau ML. The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States. *Addiction*. 2001;96(9):1267–1278.
13. Saxon AJ, McCarty D. Challenges in the adoption of new pharmacotherapeutics for addiction to alcohol and other drugs. *Pharmacol Ther*. 2005;108(1):119–128.
14. Cicero TJ, Inciardi JA. Potential for abuse of buprenorphine in office-based treatment of opioid dependence. *N Engl J Med*. 2005;353(17):1863–1865.
15. Fudala PJ, Johnson RE. Development of opioid formulations with limited diversion and abuse potential. *Drug Alcohol Depend*. 2006;83(suppl 1):S40–S47.

16. Goodman F, Gordon A, Kivlahan D, et al. *Criteria for Use of Buprenorphine/Naloxone and Buprenorphine Sublingual Tablets*. VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel, Dept of Veterans Affairs; June 2007. http://www.pbm.va.gov/Clinical%20Guidance/Criteria%20For%20Use/Buprenorphine,%20Criteria%20for%20Formulary%20Use.pdf. Accessed April 16, 2009.
17. Krantz MJ, Mehler PS. Treating opioid dependence. Growing implications for primary care. *Arch Intern Med*. 2004;164(3):277–288.
18. Sullivan LE, Chawarski M, O'Connor PG, Schottenfeld RS, Fiellin DA. The practice of office-based buprenorphine treatment of opioid dependence: Is it associated with new patients entering into treatment? *Drug Alcohol Depend*. 2005;79(1):113–116.
19. Gordon AJ, Trafton JA, Saxon AJ, et al. Implementation of buprenorphine in the Veterans Health Administration: Results of the first 3 years. *Drug Alcohol Depend*. 2007;90(2–3):292–296.
20. Kissin W, McLeod C, Sonnefeld J, Stanton A. Experiences of a national sample of qualified addiction specialists who have and have not prescribed buprenorphine for opioid dependence. *J Addict Dis*. 2006;25(4):91–103.
21. Stanton A, McLeod C, Luckey B, Kissin WB, Sonnefeld LJ; for Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, Dept of Health and Human Services. SAMHSA/CSAT evaluation of the buprenorphine waiver program. Expanding treatment of opioid dependence: Initial physician and patient experiences with the adoption of buprenorphine. Paper presented at: Annual Medical-Scientific Conference of the American Society of Addiction Medicine; May 5, 2006; San Diego, CA. http://buprenorphine.samhsa.gov/ASAM_06_Final_Results.pdf. Accessed December 5, 2006.
22. Kleber HD. Differential patterns of buprenorphine use in the U.S. Paper presented at: American Psychiatric Association 2008 Annual Meeting; May 5, 2008; Washington, DC.
23. Renner JA. Education status report: Successes & challenges. Paper presented at: Buprenorphine Summit; February 21, 2008; Washington, DC. http://buprenorphine.samhsa.gov/presentations/Renner.pdf. Accessed March 17, 2008.
24. Goodman F, Gordon A, Kivlahan D, et al. *Criteria for Non-formulary Use of Buprenorphine Sublingual Tablets for Opioid Dependence*. Washington, DC: VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel, Dept of Veterans Affairs; June 2003.
25. Goodman F, Gordon A, Kivlahan D, et al. *Criteria for Use of Buprenophine/Naloxone and Buprenorphine Sublingual Tablets*. Washington, DC: VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory Panel, Dept of Veterans Affairs; November 2005.
26. Wong JG, Holmboe ES, Jara GB, Martin J, Becker WC, Fiellin DA. Faculty development in small-group teaching skills associated with a training course on office-based treatment of opioid dependence. *Subst Abus*. 2004;25(4):35–40.
27. Gunderson EW, Fiellin DA, Levin FR, Sullivan LE, Kleber HD. Evaluation of a combined online and in person training in the use of buprenorphine. *Subst Abus*. 2006;27(3):39–45.
28. Gordon AJ, Liberto J, Granda S, Salmon-Cox S, Andree T, McNicholas L. Outcomes of DATA 2000 certification trainings for the provision of buprenorphine treatment in the Veterans Health Administration. *Am J Addict*. 2008;17(6):459–462.
29. Raisch DW, Fudala PJ, Saxon AJ, et al. Pharmacists' and technicians' perceptions and attitudes toward dispensing buprenorphine/naloxone to patients with opioid dependence. *J Am Pharm Assoc*. 2005;45(1):23–32.
30. Becker WC, Fiellin DA. Provider satisfaction with office-based treatment of opioid dependence: A systematic review. *Subst Abus*. 2006;26(1):15–22.
31. Sullivan LE, Fiellin DA. Buprenorphine: Its role in preventing HIV transmission and improving the care of HIV-infected patients with opioid dependence. *Clin Infect Dis*. 2005;41(6):891–896.
32. Sullivan LE, Fiellin DA. Hepatitis C and HIV infections: Implications for clinical care in injection drug users. *Am J Addict*. 2004;13(1):1–20.
33. Sullivan LE, Bruce RD, Haltiwanger D, et al. Initial strategies for integrating buprenorphine into HIV care settings in the United States. *Clin Infect Dis*. 2006;43(suppl 4):S191–S196.
34. Sullivan LE, Barry D, Moore BA, et al. A trial of integrated buprenorphine/naloxone and HIV clinical care. *Clin Infect Dis*. 2006;43(suppl 4):S184–S190.
35. Cicero TJ, Inciardi JA, Muñoz A. Trends in abuse of Oxycontin and other opioid analgesics in the United States: 2002–2004. *J Pain*. 2005;6(10):662–672.
36. Geppert CM, Toney GB, Siracusano D, Thorius M. Outpatient buprenorphine treatment for opioid dependence. *Fed Pract*. 2005;22(7):9–10, 18–20, 23–26, 32–34, 40.
37. Wesson DR, Ling W. The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*. 2003;35(2):253–259.

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pharmacotherapy for type 2 diabetes: A retrospective cohort study of adults with employer-sponsored health insurance. *Clin Ther*. 2005;27(7):1064–1073.
22. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(5):487–497.
23. Choo PW, Rand CS, Inui TS, et al. Validation of patient reports, automated pharmacy records, and pill counts with electronic monitoring of adherence to antihypertensive therapy. *Med Care*. 1999;37(9):846–857.
24. Wagner GJ, Rabkin JG. Measuring medication adherence: Are missed doses reported more accurately than perfect adherence? *AIDS Care*. 2000;12(4):405–408.
25. Farmer KC. Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clin Ther*. 1999;21(6):1074–1090.
26. Siegel D, Lopez J, Meier J. Antihypertensive medication adherence in the Department of Veterans Affairs. *Am J Med*. 2007;120(1):26–32.
27. Walker EA, Molitch M, Kramer MK, et al. Adherence to preventive medications: Predictors and outcomes in the Diabetes Prevention Program. *Diabetes Care*. 2006;29(9):1997–2002.
28. Peyrot M, Rubin RR, Lauritzen T, Snoek FJ, Matthews DR, Skovlund SE. Psychosocial problems and barriers to improved diabetes management: Results of the Cross-National Diabetes Attitudes, Wishes and Needs (DAWN) Study. *Diabet Med*. 2005;22(10):1379–1385.
29. Serour M, Alqhenaei H, Al-Saqabi S, Mustafa AR, Ben-Nakhi A. Cultural factors and patients' adherence to lifestyle measures. *Br J Gen Pract*. 2007;57(537):291–295.
30. Garay-Sevilla ME, Nava LE, Malacara JM, et al. Adherence to treatment and social support in patients with non-insulin dependent diabetes mellitus. *J Diabetes Complications*. 1995;9(2):81–86.
31. Galasso P, Amend A, Melkus GD, Nelson GT. Barriers to medical nutrition therapy in black women with type 2 diabetes mellitus. *Diabetes Educ*. 2005;31(5):719–725.
32. Krein SL, Heisler M, Piette JD, Makki F, Kerr EA. The effect of chronic pain on diabetes patients' self-management. *Diabetes Care*. 2005,28(1):65–70.
33. Paes AH, Bakker A, Soe-Agnie C. Impact of dosage frequency on patient compliance. *Diabetes Care*. 1997;20(10):1512–1517.
34. Donnan PT, MacDonald TM, Morris AD. Adherence to prescribed oral hypoglycaemic medication in a population of patients with type 2 diabetes: A retrospective cohort study. *Diabet Med*. 2002;19(4):279–284.
35. Chao J, Nau DP, Aikens JE. Patient-reported perceptions of side effects of antihyperglycemic medication and adherence to medication regimens in persons with diabetes mellitus. *Clin Ther*. 2007;29(1);177–180.
36. Mateo JF, Gil-Guillén VF, Mateo E, Orozco D, Carboyo JA, Merino J. Multifactorial approach and adherence to prescribed oral medications in patients with type 2 diabetes. *Int J Clin Pract*. 2006;60(4):422–428.
37. Shrank WH, Hoang T, Ettner SL, et al. The implications of choice: Prescribing generic or preferred pharmaceuticals improves medication adherence for chronic conditions. *Arch Intern Med*. 2006; 166(3):332–337.
38. Martinus R, Corban R, Wackerhage H, Atkins S, Singh J. Effect of psychological intervention on exercise adherence in type 2 diabetic subjects. *Ann N Y Acad Sci*. 2006;1084:350–360.
39. Grant RW, Devita NG, Singer DE, Meigs JB. Improving adherence and reducing medication discrepancies in patients with diabetes. *Ann Pharmacother*. 2003;37(7–8):962–969.
40. Vermeire E, Wens J, Van Royen P, Biot Y, Hearnshaw H, Lindenmeyer A. Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. *Cochrane Database Syst Rev*. 2005;(2):CD003638.