# Office-Based Treatment for Opioid Dependence: Reaching New Patient Populations

**David A. Fiellin, M.D.**

**Robert A. Rosenheck, M.D.**

**Thomas R. Kosten, M.D.**

Heroin addiction is a costly and personally destructive public health problem that is often portrayed in the nonprofessional media as a problem primarily facing the lower socioeconomic segment of the U.S. population. Epidemiologic studies, however, show that opioid addiction affects 810,000 people each year, representing all segments of American society, as well as their families and communities, with annual costs estimated at $21 billion (1).

The most effective treatment for this disorder is opioid maintenance with medications such as methadone or levo-alpha-acetyl methadol (2). In this treatment, legal, long-acting, medically managed medications replace illegal drugs and block both the painful withdrawal syndrome and craving as well as the subjective drug high that motivate continued use (3). This treatment, however, has been significantly restricted by limited public funding, local opposition to the establishment of new clinics, state licensing restrictions, and stringent federal regulations designed to prevent the medication from being diverted from its medical use and resold as a substance of abuse on the street. These regulations restrict the delivery of these medications to specialized methadone clinics that are often located in undesirable neighborhoods, are inconvenient to reach, and require almost daily attendance. For these reasons, only about 15% of the total heroin-dependent population participates in methadone or levo-alpha-acetyl methadol treatment, although studies clearly demonstrate that this therapy is more effective than drug-free outpatient care in promoting sustained abstinence (4–6). Although progress has been made in developing more cost-effective methods for outpatient detoxification, this approach has limited long-term usefulness because of frequent relapses after detoxification, even in well-motivated patients with good social supports (7–10).

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## Office-Based Treatment

Fortunately, in the past few years, treatment with buprenorphine, a new maintenance medication with unique pharmacological properties that make it especially suitable for office-based practice, has evolved and may soon provide an important alternative to the traditional methadone clinic. Buprenorphine is a partial agonist at the μ opioid receptor, which means that it has less potential for the adverse effects (e.g., abuse, respiratory depression, and overdose) that are associated with full opioid agonists like methadone (11–13). Owing to its unique pharmacologic properties, which reduce its potential for diversion, buprenorphine is undergoing evaluation by the Food and Drug Administration (FDA) for provision in less stigmatized locations, most important, in office-based medical practices (14). This practice would be permitted under the Drug Addiction Treatment Act of 2000, which allows qualifying physicians to prescribe schedule III, IV, and V narcotic medications or combinations of such medications for the treatment of opioid dependence. This act stipulates that physicians use medications that have been approved by the FDA for maintenance and detoxification treatment of opioid dependence.

Buprenorphine has three major advantages over the currently available alternatives. First, because it is a partial opioid agonist, the associated withdrawal syndrome is milder than with methadone or levo-alpha-acetyl methadol, and eventual tapering of the medication may be easier to accomplish. Second, because it is long lasting, dosing can be limited to 2–3-day intervals, necessitating less frequent clinic visits, even without take-home doses. Third, it can be combined with the opioid antagonist naloxone and taken sublingually. Although it is harmless if taken as prescribed, when the combined buprenorphine-naloxone preparation is injected into an opioid-dependent person, it precipitates immediate and painful withdrawal and thus is not likely to be diverted for abuse. Because the risk of diversion is sharply reduced by the combined buprenorphine-naloxone preparation, it has great potential for use in office practice. This is an important development with potentially far-reaching consequences.

We present a case report that details the experience of a patient who entered and reentered the treatment system multiple times through detoxification and outpatient drug-free programs. The case illustrates the complex pattern of relapse and treatment reentry experienced by opioid-dependent patients and demonstrates the potential of buprenorphine for providing an alternative strategy to stabilize patients with an opioid-based medication in an office setting. This approach appears to be more acceptable

to patients and may also be more cost-effective for treating their substance abuse and psychiatric and medical problems, because the additional cost of buprenorphine may be offset by savings from other health care costs.

Although the patient discussed here is not an exceptionally high service user with extensive use of public-sector resources, he had used modest amounts of substance abuse and medical care services of various types over the 5-year period before initiating treatment with buprenorphine, a period during which his opioid addiction was poorly contained. The patient consistently refused the methadone treatment modality because of the extensive travel required by his job. This case report illustrates the existence of clinical subgroups of opioid-dependent patients who would have not attended a methadone maintenance program previously but who found buprenorphine to be a welcome and acceptable approach toward coping with heroin addiction. Although this case represents an unknown proportion of the hundreds of thousands of heroin-dependent patients not currently receiving opioid maintenance therapy, clinical experience suggests that this type of patient is not uncommon and that his health care costs before the initiation of office-based buprenorphine treatment may have been substantial. We thus hope in this report to provide a concrete case study of both the clinical and potential economic advantages of this promising new treatment.

## Case Report

Mr. A was a 34-year-old Caucasian man who began "chipping" intranasal heroin (less than daily use) about 5 years ago. He had used cocaine for 5 years before that and went from intranasal use on weekends to steadily increasing binges of smoking cocaine over a 3-year period. He used alcohol extensively to control the paranoia and withdrawal that he experienced during these binges, although he did not become dependent on it and never required medical detoxification. He stopped most of his alcohol abuse when others noted the frequency of alcohol on his breath as well as his frank intoxication. Instead, he began using heroin and cocaine together because the combination of smoked cocaine and snorted heroin provided relatively long-lasting euphoria, with a markedly attenuated crash after he stopped a cocaine binge. These reasons for adding heroin to cocaine abuse are relatively common among those who abuse both drugs and particularly among those who begin by using cocaine. He did not initially seek treatment on his own, but his family had become increasingly concerned about him.

Mr. A had inherited the family business, a food marketing chain, after his father died when he was 28 years old, about 1 year before he sought treatment. This job required frequent travel for periods of 1 or 2 days on business. Both his older brother, an attorney, and his mother were increasingly concerned that he was not successfully managing the daily operations of the business and was falling into debt. They met with his wife, who was herself concerned about his temper outbursts at home with their two young children, as well as about his inability to get the funds for building an addition on their house; she was beginning to consider filing for divorce. As a result of a family confrontation, Mr. A resolved to change his "high-pressure" work life and appeared to slow down. He resisted getting professional help for his substance use, but his family felt that he had responded to their concerns by changing his behavior.

Lack of money, however, still appeared to be a major problem, and one of his store managers reported to his brother that Mr. A appeared to spend several hours locked in his office and unavailable. When this brother asked whether Mr. A had been like this at work in the past, the manager stated that the situation seemed more serious. In the past Mr. A had become irritable and would sometimes disappear for several hours, but he usually came back full of energy. Now Mr. A was appearing sleepy and uninterested. This sedation was a sign of opioid intoxication at work, whereas the irritability probably reflected both opioid withdrawal as well as cocaine-induced paranoia, which appeared when he used cocaine alone, without either heroin or substantial amounts of alcohol.

The family insisted that Mr. A seek professional medical help and threatened that his mother would take over control of the family business if he did not. They indicated that his lawyer brother had drawn up the required documents. Mr. A resisted but finally agreed to see the family's primary care physician. He reported fatigue, occasional insomnia, weight loss, and occasional palpitations. The physician noted an unremarkable physical examination and proceeded to rule out thyroid disorders, HIV, and hepatitis as the cause of Mr. A's complaints. The results of routine screening tests for these disorders were normal, and the physician ascribed Mr. A's complaints to stress and a possible anxiety disorder and recommended counseling, which Mr. A resisted. Mr. A then had a serious auto accident that appeared to be related to a seizure. In the emergency room, a urine toxicology screen was positive for cocaine and opioids. After this crisis he agreed to seek psychiatric help. The precipitant for seeking treatment was an emergency room screening for illicit drugs, emphasizing the importance of screenings after serious accidents.

In the initial assessment interviews, at age 29, Mr. A appeared concerned and open. He acknowledged that his father's death the previous year had been a great loss to him and that his cocaine use had escalated during his father's illness and death from lung cancer. Both Mr. A and his father were tobacco smokers. Mr. A had stopped smoking briefly after his father's illness was diagnosed, but he soon relapsed and continued to smoke. Mr. A admitted using heroin with cocaine and stated that he snorted and smoked these drugs. He never used intravenous opioids, he claimed, and was aware of the risk of AIDS with intravenous drug use. Because his heroin use was intermittent, he had no signs of opioid withdrawal, and he had clear problems with alcohol, we agreed that in addition to weekly individual psychotherapy he would begin taking naltrexone twice weekly at 150 mg. At this dose he would be blocked from the use of heroin, and naltrexone would also reduce the potential for relapse to alcohol abuse.

In therapy it appeared that Mr. A's grieving for his father had been seriously aborted by his drug use, and therapy was intended to focus, in part, on this aborted grief in addition to tracking his substance use with

breathalyzers for alcohol use and regular urine monitoring for heroin and cocaine. In addition, his sister and brother were seen monthly by a different therapist, while Mr. A went to couples counseling weekly with his spouse. Finally, he was to attend at least weekly Alcoholics Anonymous meetings. The weekly therapy lasted for 4 months, and Mr. A was compliant; he was observed taking naltrexone twice weekly: once at the individual sessions when a urine toxicology screen was also obtained and once at the weekly couples therapy session. After 4 months he declared himself "cured" and left the couple's therapy and agreed to monthly individual contact but no further medication. After 2 monthly contacts, he terminated his visits.

Six months later, almost on the 1-year anniversary of our initial contact, he returned to the emergency room with a heroin overdose. The overdose was sufficient to require naloxone reversal but was not serious enough to require hospital admission. Mr. A had no suicidal intent and refused hospitalization. Since he did not meet utilization review criteria for emergency hospitalization and because his insurance carrier was also denying coverage, he was referred to substance abuse day treatment starting the next morning, and he was held overnight in the emergency room. During that night he did not sleep and experienced the opioid withdrawal symptoms of sweating, rhinorrhea, and abdominal cramping. His initial response to naloxone was a clear sign of opioid overdose but not necessarily opioid dependence. His persistent withdrawal symptoms, well beyond the 30–45 minutes that naloxone would last, were consistent with opioid dependence.

When he was interviewed, Mr. A indicated that he had stopped most of his cocaine use but that he was smoking or using heroin intranasally daily. When confronted in the emergency room about the heroin dependence he had developed, he stated that he believed that as long as he did not "shoot" heroin he could not become dependent on it. Nevertheless, it was clear that Mr. A needed some treatment for withdrawal symptoms; clonidine therapy was discussed. A day program was available that used clonidine plus naltrexone to complete detoxification during a 5-day program. Mr. A agreed to participate in this day program for a week, followed by an intensive evening outpatient program for a month. During this evening program, he intended to return to work part-time during the day.

The day program began with a rapid 3-day clonidine-naltrexone detoxification that was more difficult than Mr. A had anticipated. Participants were to arrive before 9:00 a.m.; he came directly from the emergency room accompanied by his mother. During the next 3 days, he underwent rapid detoxification with clonidine and naltrexone. Although he medically tolerated it well, he complained of sleeplessness and anxiety that lasted for a week. After 6 days he was stable while taking naltrexone and having no detectable opioid withdrawal symptoms, although he continued to complain of disrupted sleep lasting about 6 hours per night. His daytime sedation had subsided, however. We considered this a successful medical detoxification and resumed giving him naltrexone, 150 mg twice a week.

After this difficult period of outpatient detoxification, standard outpatient care with urine monitoring, weekly individual and couples treatment, and weekly Alcoholics Anonymous group visits were reinstituted. Mr. A participated for 6 months with good compliance in using naltrexone and had no positive illicit drug urine screens, but he again left treatment, resisting continued follow-up. During the next 3 years, he had two inpatient detoxifications for heroin use but would not enter a methadone maintenance program. He remained working at his family business and was successful in many areas. His heroin use was daily, and he sought inpatient detoxification when his intranasal habit became too expensive and interfered with his work schedule. This is an example of failed outpatient drug-free treatment that is frequently seen in this chronic, relapsing disorder and emphasizes the need to consider sustained opioid maintenance treatment.

Mr. A again was seen for treatment and again had been heroin dependent for several months, having been using heroin in the year since his most recent inpatient detoxification. He specifically came to the research program that used buprenorphine in office-based treatment in a psychiatric setting. This type of care was quite appealing to him in contrast to methadone maintenance, with its many rules and restrictions.

Mr. A had mild abdominal cramping and insomnia on his first day of induction to buprenorphine therapy, but overall he felt much better by the second dose. He continued his heroin use but discontinued it after 1 week of treatment. His induction involved a starting dose of 4 mg of sublingual buprenorphine on days 1 (Monday) and 2, 8 mg on days 3 and 4, and 16 mg on day 5 to last until Monday (day 8). All the buprenorphine doses were given under direct observation and were moved to a regular schedule of Monday (12 mg), Wednesday (12 mg), and Friday (20 mg). Mr. A reported that the reduced requirements for clinic attendance with buprenorphine allowed him to continue to perform his usual job without interruptions. In addition to weekly brief counseling sessions, he attended three Narcotics Anonymous meetings in the first week and continued with these meetings at least once a week throughout treatment. His weekly counseling visits focused on job- and family-related issues, while once-weekly urine toxicology screens verified his abstinence. These urine screens were obtained on a random schedule each week on one of the three days that Mr. A was medicated. His abstinence was interrupted by abuse of prescription drugs for 1 week, causing mild euphoria, but he continued to pursue treatment and became abstinent after reinduction of buprenorphine. At the end of the 12-week maintenance period, Mr. A attempted to transfer to opioid-antagonist therapy with naltrexone but was unable to remain abstinent from opioids for the required 4 days after his last dose of buprenorphine. He ultimately returned for continued maintenance with buprenorphine.

Long-term continuation treatment with buprenorphine, with intermittent office visits, may be a future possibility for this type of patient and an alternative to a formal narcotic treatment program. In summary, induction of buprenorphine did not require detoxification and could be managed with a three-times-a-week dosing schedule after the first week. With buprenorphine, it also was easier to keep Mr. A in treatment and to get him back even after a brief relapse early in the initial 3 months. In the future, direct observation of dosing should not be required, and in

clinical practice, prescriptions can be given for the patient to self-administer this medication either daily or three times a week, with weekly or less frequent visits to the prescribing physician. This flexibility may be particularly well suited to patients such as this with extensive social supports and stability.

## Discussion

This case illustrates office-based buprenorphine treatment in a primarily psychiatric office setting. The patient had an extensive series of treatments for opioid dependence during a 5-year period, including inpatient and outpatient detoxifications and outpatient maintenance with naltrexone with the addition of professional individual and couples counseling. In spite of this extensive intervention in treating a patient with good social supports, economic opportunity, and vocational skills, multiple detoxifications and drug-free outpatient care were not successful. Mr. A specifically resisted methadone maintenance therapy, but he responded to an alternative office-based psychiatric intervention. This type of intervention may become more available for opioid dependence in the near future and offers great promise for appropriately selected patients. It may not only be more acceptable to these relatively high-functioning patients, but it may prove to be more cost-effective than detoxification or the alternative of methadone maintenance in narcotic treatment programs.

Buprenorphine has the potential to transform and substantially expand the availability of opioid maintenance treatment because it will encourage a shift in the locus of care from heavily regulated clinics to conventional office-based medical practices. Greater numbers of opioid-dependent patients will potentially take advantage of an effective treatment, and as this case illustrates, patients who would have been reluctant to seek help from traditional methadone clinics will be willing to seek help. Currently in use in France and the United Kingdom, buprenorphine is able to suppress heroin self-administration and is substantially more effective than placebo in decreasing illicit opioid use (15, 16). Head-to-head clinical trials comparing buprenorphine treatment to methadone maintenance have had somewhat variable results demonstrating similar (17, 18), improved (19), and reduced (20) efficacy in promoting abstinence from opioids, but a meta-analysis of its efficacy supported equivalence between buprenorphine doses of 8–12 mg/day and 60 mg/day of methadone (21).

Clinicians selecting appropriate patients for office-based buprenorphine treatment should consider a range of issues. First, does the patient understand the opioid properties of buprenorphine, and can he be expected to be reasonably compliant? Compliance includes resisting abuse or diversion of this medication, which will become a greater issue as prescriptions are given to patients for self administration rather than the observed dispensing used with our patient. Second, is the patient psychiatrically stable, and can he or she be expected to follow safety procedures in the self-administration of this opioid? A particular concern is the abuse of benzodiazepines. Fatal overdose with buprenorphine alone is unlikely, but fatalities have occurred in combination with benzodiazepines (22). Other medications, such as nifedipine, imipramine, and HIV protease inhibitors, can have metabolic interactions with buprenorphine because of its metabolism by the cytochrome P450 system (3). A recent study (23) indicated that highly active antiretroviral therapy for AIDS appears to have no adverse interactions in patients maintained with buprenorphine, however. This factor may be critical for medically complex patients with AIDS and heroin dependence. Third, are the psychosocial circumstances of the patient stable and supportive? The current case report clearly illustrates many aspects of such a family environment. Fourth, can the provider's office provide the backup and needed resources? For example, coverage for vacations or other periods must include physicians who are comfortable treating opioid-dependent patients and working with buprenorphine maintenance. In the current report, a medical group was available and had extensive experience with methadone maintenance and buprenorphine, as well as various types of opioid detoxification.

Because of their extensive experience in the treatment of drug addiction, current methadone clinics are also likely to offer buprenorphine treatment as an alternative to methadone for both new patients and for long-term stabilized patients. Buprenorphine is not likely to be any more or less effective than methadone but should increase the number of opioid-dependent patients who receive opioid maintenance treatment because of its greater accessibility and acceptability.

Buprenorphine therapy in office practice was successful for this patient. Before his treatment with buprenorphine, he had made limited or no use of methadone maintenance and had consumed extensive health resources with repeated detoxifications. To the extent that opioid maintenance becomes more available and/or acceptable to high-cost patients such as this, net cost savings and clinical benefit could be substantial. Mark et al. concluded a recent review (1) by saying that available data are insufficient to make any predictions about the societal impact of expanding the availability of opioid-maintenance therapy. The case we presented, however, illustrates many of the concrete benefits offered by this treatment, and issues we have identified may serve as a framework for the more comprehensive evaluation of cost-effectiveness issues in the future.

Received Aug. 31, 2000; revision received April 20, 2001; accepted April 25, 2001. From the VISN 1 Mental Illness Research, Education, and Clinical Center, New Haven, Conn.; the Departments of Internal Medicine and Psychiatry, Yale University School of Medicine; and the VA Connecticut Healthcare System, West Haven, Conn. Address reprint requests to Dr. Fiellin, Yale University School of Medicine, 333 Cedar St., P.O. Box 208025, New Haven, CT 06520-8025; david.fiellin@yale.edu (e-mail).

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