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Buprenorphine Prescribing: To Expand or Not to Expand

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Abstract

As a result of the prescription opioid epidemic in the United States, there has been an increasing need for effective treatment interventions, both pharmacologic and non-pharmacologic.

Buprenorphine has emerged as a critical component of the treatment of opioid use disorder, yet its adoption has not been without some concerns. This article first reviews the pharmacology, clinical use, and US legislative action related to buprenorphine, followed by a discussion of the misuse and diversion of buprenorphine in the United States as well as internationally. We then explore the impact of buprenorphine abuse as well as discussing strategies for its reduction, including changes in policy, prescription and pharmacy monitoring, and continuing medical education for guiding and improving clinical practice.

Keywords

buprenorphine; prescription opioids; abuse; diversion; regulation; policy

THE PRESCRIPTION OPIOID EPIDEMIC

Emerging over the past 15 years, the prescription opioid epidemic in the United States has been characterized by a striking increase in the use and misuse of, and dependence upon, prescription opioid medications as well as associated medical and societal consequences. According to the US Center for Disease Control (CDC), sales of prescription opioids increased fourfold from 1999 to 2010, which was equivalent to 710 mg per person in the United States in 2010; similarly, mortality from opioid overdoses in 2008 was almost

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quadruple the rate observed in 1999.¹ Estimated emergency department visits from nonmedical use of opioid analgesics increased 111%, from 143,500 visits in 2004 to 271,700 visits in 2008.² In the meantime, the admission rate into specialty treatment for opioid use disorders in 2009 was almost 6 times the rate in 1999. The term “specialty treatment” refers to treatment received at a substance rehabilitation program (inpatient or outpatient), hospital (inpatient services only), and mental health centers, excluding treatment received in an emergency department, private office, self-help group, or prison.¹ According to data in the 2012 and 2013 National Surveys on Drug Use and Health (NSDUH) sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), there were an estimated 4.5 million current (past month) nonmedical users of prescription pain relievers,³ and opioids were second only to cannabis in their rate of illicit use, which is far above the prevalence of other illicit substances.⁴

STRATEGIES TO CURB THE EPIDEMIC

In response to this epidemic of nonmedical use of opioids, various pharmacological and non-pharmacological strategies have been implemented to curb its further progression. From a pharmacological standpoint, numerous abuse-deterrent formulations of opioid pain medications have been developed. For example, the reformulation of extended-release oxycodone, which reduced the ability of illicit users to crush the medication and use it by nasal insufflation or intravenous (IV) routes, led to a significant and immediate decline in the misuse of oxycodone, particularly when compared to that seen with the original formulation.⁵⁻⁸ However, some concern remains that this strategy alone simply shifts misuse and abuse to other more easily crushed or altered opioids.^{5,8} From a non-pharmacological standpoint, regulation and health policy have been shown to be influential in reducing morbidity and mortality from opioid diversion.^{9,10} Opioid diversion can be broadly understood as the movement of prescription opioid medications from licit, health-related channels to illicit forms of distribution or use; it includes such behaviors as “doctor-shopping” and sale on the black market. As a means of addressing this type of activity, prescription monitoring programs (PMPs) work well in facilitating prescribing practices that increase patient safety while also tracking the use of opioids by individuals. PMPs have been associated with lower prescription volume¹¹ and reductions in poison center intentional exposures and opioid treatment admissions,¹² as well as overdose mortality from prescriptions opioids.⁹ However, not all studies have found an association between PMPs and decreased rates of opioid abuse.^{13,14}

In addition, studies indicate that responsible clinical practices in pain management and risk stratification have demonstrated efficacy in preventing diversion and abuse of prescription opioids.¹⁵⁻¹⁷ Furthermore, because leftover medications represent a significant source for abused prescription opioids¹⁸ and there is widespread unsafe storage and disposal of unused prescription opioids, particularly those initially prescribed from emergency departments,¹⁹ efforts have been made to increase and make more widely available take-back programs for unused prescription medications.²⁰

In the midst of this epidemic of opioid misuse and abuse, buprenorphine has garnered a great deal of attention as a cornerstone deterrence strategy because it stands out as an effective

treatment for opioid use disorder, targeting and reducing demand for opioids rather than focusing solely on their supply and availability. The use of buprenorphine has not been completely devoid of controversy, however. Because of reports concerning limited access to buprenorphine therapy, proposals have been made to increase the prescribing of buprenorphine, yet some concerns have also been raised about the abuse and diversion of buprenorphine, creating conflicting attitudes about more liberal regulation. Recently proposed legislation, such as the *Recovery Enhancement for Addiction Treatment Act* of 2014 (see more detailed discussion below), reflects the potentially more liberal approach to both regulation and application that we will explore in this article. First, we will briefly discuss buprenorphine and its efficacy in treating opioid dependence. We will then review the status of buprenorphine abuse and misuse in the United States and other parts of the world. Finally, we conclude with a discussion of how to balance the benefits and risks of buprenorphine prescribing in an effort to further reduce harms of opioid misuse.

OVERVIEW OF BUPRENORPHINE

Buprenorphine, a high affinity partial agonist at the μ -opioid receptor, is associated with reduced abuse potential (ie, less subjective euphoria, physiological dependence, and reduced withdrawal severity) as well as a favorable safety profile (ie, reduced risk of overdose and respiratory depression) due to its pharmacologic ceiling effect.²¹ Currently, the most commonly prescribed buprenorphine formulation for opioid dependence treatment is the combined formulation of buprenorphine and naloxone, an opioid receptor antagonist, at a ratio of 4:1. Naloxone is added in order to further decrease the intravenous abuse potential of buprenorphine, since it has minimal absorption when taken orally but becomes pharmacologically active and can precipitate withdrawal when taken intravenously.

While methadone has been a mainstay of treatment for opioid use disorder since the 1960s, buprenorphine may have some advantages over methadone as agonist therapy. According to data from 2003 to 2009 provided by the American Association of Poison Control Centers, non-medical use of buprenorphine is associated with considerably better medical outcomes than methadone in terms of hospitalization rates (32.2% vs. 67.4%), admission to intensive care units (15% vs 50%), and mortality (0 vs. 1.6%).²² However, the associated risk of substance abuse is correlated with routes of use, and the risk associated with buprenorphine may have increased since 2009 due to new buprenorphine abuse patterns and routes of administration, particularly intranasal abuse of crushed buprenorphine tablets.

Numerous studies have demonstrated the efficacy of buprenorphine in clinical treatment with various populations. Buprenorphine was demonstrated to be an effective medication for maintenance treatment in heroin dependence in a meta-analysis done by Cochrane collaborations, which summarized data from 31 randomized control trials of good quality.²³ Real world studies have also demonstrated effectiveness similar to that found in clinical trials. In a population with comorbid cocaine use disorder and mood disorder, Haddad et al found that buprenorphine had treatment retention rates and rates of opioid-free urine tests similar to rates in clinical trials in primary opiate dependent subjects.²⁴ A German non-interventional, post-marketing surveillance study also demonstrated high effectiveness and safety in office-based routine care with buprenorphine.²⁵ Access to buprenorphine therapy

has been associated with reductions in heroin mortality of more than 50% in France and 37% in Baltimore, Maryland.^{26,27} In addition, buprenorphine therapy may decrease emergency department utilization and improve overall quality of life^{28,29} and psychosocial functioning.^{28,30-33}

DATA 2000 AND CURRENT PRESCRIBING STATUS OF BUPRENORPHINE

In 2000, the U.S. Congress passed the Drug Abuse Treatment Act of 2000 (DATA 2000), which permitted qualified physicians to obtain a waiver to treat opioid addiction with schedule III to V narcotic medications. Physicians must meet several criteria to prescribe, including completion of no less than 8 hours of certified training concerning opioid dependence. The waiver allows office-based opiate maintenance treatment of opioid use disorders outside the traditional setting of the methadone maintenance program or clinic. Buprenorphine is the first, and currently only, medication meeting DATA 2000 requirements, after its approval and classification as a Schedule III controlled substance by the U.S. Food and Drug Administration in October, 2002. Treatment with buprenorphine is initially limited to 30 patients per physician, and the capacity can be increased to 100 patients after 1 year by submitting an additional waiver request.

Since its approval in 2002, the utilization of buprenorphine therapy has gradually, but significantly increased. The number of buprenorphine/naloxone tablets sold increased from 8 million in 2005 to over 145 million in 2009.³⁴ Medical use of buprenorphine increased from 70,332 grams/100,000 population in 2004 to 1,700,414 grams/100,000 population in 2011, a 2,318% increase;³⁵ yet buprenorphine remains in great demand and some studies suggest limiting access to this agent could contribute to diversion and misuse.^{34,36} In addition, despite this increase in buprenorphine prescribing, a significant geographic maldistribution of physicians with a waiver to prescribe it exists, with the majority of these prescribers located in urban areas and an estimated 53% of counties in the United States not having a single physician with a DEA DATA waiver.³⁷

To increase access to buprenorphine treatment for opioid dependence, there is a proposal that requests that DATA 2000 be amended to allow qualified advanced nurse practitioners and physician assistants to prescribe buprenorphine.³⁸ The bill, entitled the Recovery Enhancement for Addiction Treatment or TREAT Act, would also raise the cap of patient numbers from 100 to unlimited after 1 year.³⁹ This legislation has not yet been passed and support for it is not unanimous. There is legitimate concern about abuse and diversion associated with increased accessibility and wider availability, especially with less restrictive control of buprenorphine prescribing practices and prescribers. In the meantime, advocates point to the relative safety and effectiveness of buprenorphine, overall evident benefits for public health, and the actual limited access to buprenorphine in the context of the current opioid abuse epidemic. In fact, supporters of the legislation argue that diversion and misuse could be due to limited access to buprenorphine therapy and suboptimal dosing, particularly since there are reports suggesting that patients misuse buprenorphine to self-medicate their withdrawal symptoms.^{36,40,41} For example, in a report from France, the authors suggested that suboptimal dosage of buprenorphine was a risk factor for use by the intravenous route.⁴⁰ In addition, in a review by Larance et al⁴¹ focusing on the availability, diversion, and

injection of pharmaceutical opioids in south Asia, low dose buprenorphine was reported to be the most commonly misused opioid among a variety of prescription opioids.

Although there is some disagreement in the literature concerning both (a) the methods by which buprenorphine access can be increased, and (b) whether low- or high-dose buprenorphine is associated with the greater risk of misuse, it is clear that there is a demonstrated need to further expand these services and to monitor both low- and high-dose users of the medication.

MISUSE, ABUSE, AND DIVERSION OF BUPRENORPHINE

The efficacy and effectiveness of buprenorphine are evident, as reviewed earlier. However, it is critical also to review the misuse, abuse, and diversion of buprenorphine in the United States and some other countries in the world.

The Abuse Potential of Buprenorphine

Several controlled laboratory studies have examined the abuse liability of buprenorphine and buprenorphine/naloxone through different routes of administration in both dependent and non-dependent subjects. Comer et al⁴² demonstrated that buprenorphine/naloxone has intravenous abuse potential in intravenous heroin abusers maintained on buprenorphine, although the potential is lower than with buprenorphine alone. Jones et al⁴³ found that intranasal buprenorphine was reinforcing, although it had less effect than intravenous buprenorphine. In addition, in non-dependent opioid abusers, the addition of naloxone did not significantly alter the subjective, hydromorphone-like effects of buprenorphine when taken through sublingual and intramuscular routes. This finding is consistent with earlier studies that suggested that the addition of the naloxone antagonist to buprenorphine does not significantly alter the agonist effects of buprenorphine.⁴⁴ Taken together, studies such as these demonstrate that the use of buprenorphine does result in a physiologic and subjective response consistent with other μ -opioid receptor agonists.

Buprenorphine Misuse, Abuse, and Diversion in Other Countries

Although a review of the many cases of buprenorphine diversion worldwide is outside the scope of this article, discussion of buprenorphine misuse in three countries—Finland, France, and Sweden—will provide cultural context and demonstrate the global impact of this phenomenon (for a complete review, see the Yokell et al discussion of buprenorphine prescribing in countries all over the world, which includes history, policy regulations, and outcomes⁴⁵).

Despite the laboratory evidence reviewed in the preceding section that confirmed the expected lower euphoric effects and reduced abuse potential of buprenorphine and buprenorphine/naloxone, in the real world, abuse of these agents has been reported in many countries. For example, by 2002, the mono-formulation of buprenorphine had replaced heroin as the most commonly abused substance among treatment-seekers in Finland.⁴⁶⁻⁴⁸ As a result, buprenorphine/naloxone was replaced with the mono-formulation. Despite this change, in one study population, 68% of participants reported intravenous use of buprenorphine/naloxone on one occasion, and 66% of those individuals tried a second time,

or even continued with regular use, despite the majority of them reporting a “bad experience” with intravenous use of buprenorphine/naloxone compared with buprenorphine alone.⁴⁸

In France, buprenorphine has been very successful with a significant public health benefit of reducing mortality from opioid overdose by 79% from 1995 to 1999 after major expansion of buprenorphine access.^{26,49} However, there is also evidence of increased buprenorphine abuse and diversion. In a 2008 survey of 5542 subjects recruited from specialized addictions treatment centers, over 30% reported abuse of high dosage buprenorphine, and buprenorphine and methadone were the 2 prescription drugs with the highest self-reported misuse.⁵⁰ In a French study by Fatseas et al, 11% of outpatients in treatment reported misuse of buprenorphine via the intravenous route, and 10% to 20% of this population were suspected of “doctor-shopping” behaviors.⁴⁹ In addition, the authors found that between 1996 and 2000, a total of 137 buprenorphine-related deaths in France were reported, with intravenous buprenorphine injection and concomitant use of large doses of alcohol and sedatives associated with the highest overdose risk.⁴⁹

In Sweden, a significant reduction (20%–30%) from 1998 to 2006 in opiate-related mortality and inpatient care was correlated with a less restrictive policy on access to and continuation on opioid agonist treatment; increased use of “take-away doses” of methadone and buprenorphine (prescribed doses of methadone or buprenorphine that do not have to be taken at an opioid agonist treatment program (directly observed therapy), but are instead taken as outpatient medications); and a reduction in discharge from treatment due to misuse of these opioids. However, a significant increase in mortality specifically related to buprenorphine and methadone also occurred.⁵¹

Impact of Buprenorphine Abuse

After reviewing data on the misuse and abuse of buprenorphine, one may wonder about the potential pattern of and harm associated with buprenorphine abuse. The largest amount of literature on this topic concerns Finland due to its epidemic of buprenorphine abuse. A 12-year follow-up study in Finland demonstrated that the annual proportion of clients seeking treatment for buprenorphine abuse increased from 3.0% in 1998 to 38.4% in 2008.⁴⁷ Daily abuse (73.8%) and intravenous administration (80.6%) were common. Buprenorphine clients in Finland resembled “street users” in other countries in terms of socioeconomic status.⁴⁷ In another study, 25% of all lethal intoxications in people who abused drugs in Finland in 2007 involved buprenorphine.⁵² Lethal buprenorphine intoxications were typically associated with concurrent use of benzodiazepines and alcohol (82% and 58% of buprenorphine poisonings in Finland from 2000 to 2008, respectively).⁵³ The mortality rate in clients seeking treatment for buprenorphine abuse was three times higher than the national average, a finding similar to that reported in clients seeking treatment for abuse of other substances. Of note, survival rates among clients who were dependent on heroin did not differ from rates among clients who abused buprenorphine, an observation ultimately attributed to the high proportion of intravenous use in both groups. Drug-related deaths were the most common cause of mortality among buprenorphine clients, although it is unknown if these were related to use of buprenorphine or abuse of other drugs.⁵⁴ Ultimately, although laboratory studies and

reports based on routine clinical practice suggest that buprenorphine has less abuse potential than heroin, its epidemic intravenous abuse can certainly cause damage similar to that associated with heroin use disorder.

Current Misuse and Diversion of Buprenorphine in the United States

Reports on misuse and diversion of buprenorphine in the United States can be chronologically divided into 2 phases. Reports from the early stage were primarily positive and expressed minimal concern about abuse and harm, while more recent literature reveals greater concerns and the emergence of intravenous abuse of buprenorphine.

A report in 2005 found that buprenorphine abuse was no greater than that observed with tramadol and was much less than that seen with methadone and oxycodone in the first 2 years after the medication became commercially available.⁵⁵ Another study conducted in Baltimore, Maryland from 2004 to 2007 had similar findings and provided additional details.⁵⁶ [Mitchell SG, Kelly SM, Brown BS, Reisinger HS, Peterson JA, Ruhf A, Agar MH, O'Grady KE, Schwartz RP. Uses of diverted methadone and buprenorphine by opioid-addicted individuals in Baltimore, Maryland. *Am J Addict* 2009; 18: 346-55. The Baltimore study found that street methadone was more widely used than street buprenorphine and both drugs were largely used as self-medication for detoxification and withdrawal symptoms. The use of low dosage buprenorphine was reported, and no injection use was reported. However, only 13.8% of the opioid abusing population reported a history of buprenorphine treatment, so exposure to buprenorphine at that time was low.

Only a few years later, studies seemed to indicate the beginnings of a reversal in this trend. In a survey of injection drug users in 2008 ($N=602$), the percentage of misuse and diversion seemed higher, with 23% obtaining buprenorphine from the street and 13% from a friend. The prevalence of use of buprenorphine obtained from the street in the previous 3 months was 9% overall, and the majority of respondents reported that they used it to manage withdrawal and/or to wait for treatment.³⁶ In a national post-marketing surveillance program, measures of buprenorphine diversion and abuse from 2005 to 2009 were consistent with these findings. The number of exposures to buprenorphine/naloxone reported to poison control centers increased over 400%, rising from 765 in 2006 to 3212 in 2009. Over the same period of time, the number of emergency department visits due to abuse/misuse of buprenorphine rose even more dramatically, increasing from 5025 in 2006 to 70,637 in 2009. In addition, reported diversion in applicants to specialized substance abuse treatment programs increased from 27% in 2005 to 46% in 2009.³⁴ According to hospital emergency department data from the Drug Abuse Warning Network (DAWN), the misuse of buprenorphine increased from 4,440 emergency department visits in 2006 to 21,483 in 2011, a 384% increase.³⁵ Strikingly, in both studies, despite the increased misuse and diversion of buprenorphine and the rise in emergency department visits, the increases were still well below the increased percentage of diversion and emergency department visits related to other prescription opioids.

More recent literature points to misuse for recreational purposes as well as to stave off withdrawal symptoms. A study of 503 buprenorphine users in an Appalachian community revealed that 70.1% reportedly used buprenorphine to “get high” in their lifetimes and

46.5% used diverted buprenorphine over the 6-month follow-up period. Among these buprenorphine users, 50.6% were sporadic users and 9.6% were daily users. The most common sources from which buprenorphine was obtained were dealers (58.7%) and friends (31.6%).⁵⁷ Moreover, a recent national survey combined with qualitative interviews found that misuse of buprenorphine had increased substantially in the previous 5 years, particularly among those who had used heroin during the past month. In these cases, buprenorphine serves as a substitute for other drugs, for example, heroin, when the desired drug is not available.⁵⁸ Alarming, this study also found over one-third of buprenorphine misusers had used by intravenous route in the month before treatment. Importantly, buprenorphine/naloxone tablets and film had been used for injection. In addition, participants reported using a number of simple and easy methods by which they believed buprenorphine could be separated from naloxone.⁵⁸ Altogether, since 2002, the utilization of buprenorphine as therapy for opioid use disorder has increased significantly; however, we have also witnessed a significant increase in misuse and diversion rates. The relatively recent emergence of intravenous abuse of buprenorphine is also especially concerning.

DISCUSSION

Buprenorphine is an effective treatment for opioid use disorder; however, with increased access and availability, its abuse and diversion may be inevitable. This real-world, almost paradoxical, phenomenon demonstrates the complexity inherent in the treatment of addictive disorders—a medication intended to treat substance use disorder that has its own abuse potential, upon gaining popularity and increased availability, will inevitably be explored by drug abusers for reward and reinforcement purposes. Given these concerns, limitation of buprenorphine prescribing already exists in some medical systems. For example, in a recent article, Clark and Baxter⁵⁹ reported that by 2013, Medicaid programs in all states covered buprenorphine; however, almost all of them required prior authorization, and 11 states imposed lifetime limits on the duration of buprenorphine therapy, which ranged from 12 to 36 months. However, we should not limit or impede the use and expansion of buprenorphine therapy simply due to its abuse potential, particularly since buprenorphine has strong biological and clinical evidence to support its application and utilization in daily clinical practice. Furthermore, with limited studies examining the optimal duration of buprenorphine maintenance therapy and/or failure to recognize the chronic, relapsing nature of substance use disorders, placing limits on the availability of buprenorphine treatment may increase, rather than reduce, harms. Alternative strategies may guard against misuse as well as lead to cost savings for state programs. Novel approaches, such as dose-based prior authorization policies, can help decrease the risk of diversion that may occur with high dosage prescribing of more than 16 mg/day without decreasing access for compliant patients.

Overall, appropriate caution is necessary to prevent increasing abuse and diversion of buprenorphine. A harm reduction approach would advocate vigorously for the expansion of buprenorphine treatment due to its evident public health benefits in reducing mortality rates associated with opioid abuse as well as the prevalence of HIV. However, we should also be careful to avoid aggressive widespread prescribing, given the potential to create another epidemic, as seen in Finland. Attitudes among professional who treat addiction, who tend to be more cautious regarding unconditional expansion of buprenorphine therapy, provide some

guidance about potential strategies for proceeding. Many professional agree with expanding prescribing power to include qualified nurse practitioners and physician assistants, if these professionals are familiar with treating substance use disorders. Lifting the cap on the number of patients that can be treated by a clinician could also be quite beneficial. It is important to note that physicians with higher caseloads and new classes of prescribers would need additional support to fully comply with guidelines for counseling and to guard against simply prescribing the medication.

In summary, the question is not whether or not to expand buprenorphine prescribing. It is *how* to expand buprenorphine prescribing safely and effectively. However, with this in mind, some data raise concerns about the safety of current prescribing practices. The U.S. Substance Abuse and Mental Health Services Administration (SAMSHA) has published specific guidelines on buprenorphine prescribing, which include induction protocols, prescribing dosage, provider capacity to provide or refer to addiction counseling, and monitoring measures, including urine drug tests and pill counts.²¹ However, current compliance with these guidelines seems poor. Lofwall et al⁶⁰ showed that only 50% of doctors routinely induct patients while in opioid withdrawal, while the other patients have been given buprenorphine while displaying no symptoms of active opioid withdrawal. Another study surveyed physicians on the steps taken to prevent abuse and diversion. Respondents reported that the 3 most commonly employed strategies were (a) limit 30-day prescriptions to complying patients (72.4%), (b) prescribe only the lowest effective daily dose (60.6%), and (c) require regular urine screening or other drug screening (59.3%).⁶¹ Ideally, the employment of these practices should approach 100% compliance. In both studies, the authors suggested that continuing medical education targeting improved office-based opioid therapy practice would help enhance clinical practice and quality of care. Of note, longer experience prescribing buprenorphine and concern about diversion were also associated with better compliance with guidelines.

In this regard, policies and regulations promoting safe practice are especially beneficial. Because of the complexity of buprenorphine prescribing, including the induction process, focus on the monitoring process (utilization of urine drug screens, pill counts, use of state-level prescription monitoring programs, and the need for counseling) and additional effort by physicians to ensure a safe practice are necessary. Thus, a higher financial incentive coupled with mandatory enforcement of essential components of safe practice should go along with promoting the expansion of therapy to ensure quality of care. We know that simply getting more physicians certified to prescribe does not necessarily lead to increased prescribing,⁶² since the average number of patients for certified prescribers is only 26 out of a theoretical limit of 100, and 25% of physicians with a waiver have *never* prescribed the medication.⁶³ In addition, recent estimates indicate the average state has only 8 waived physicians per 100,000 residents.⁶⁴

People may argue that in France, which has the most relaxed prescribing practice internationally with no limit on numbers of patients treated and no specific physician qualifications, the benefits seem to have exceeded the harm. Indeed, all primary care physicians in France have been able to prescribe buprenorphine without special training or license/certification since 1995. According to a 2007 report, approximately 20% of all

physicians in France were prescribing buprenorphine to treat more than half of the estimated 180,000 problem heroin users in the country.⁴⁹ However, despite the lack of requirements, physicians involved in prescribing buprenorphine often had extra training in addiction medicine and were involved in community-based treatment networks. In addition, pharmacy involvement was found to play a very important role in their success. Community pharmacies supervise buprenorphine dosing, which ranges in frequency from daily dosing to weekly dosing, and with a maximum of 4 weeks of take-home doses permitted by prescribing physicians. Lack of urine monitoring of drug use and the lack of supervised dispensing in pharmacies have been shown to represent risk factors for diversion and misuse; in contrast, there are improved outcomes with observed and supervised initial daily dosing, rather than allowing take-home medication after the initial treatment contact of 1 to 2 days, which is a more standard practice in the United States.²¹

Opportunities for pharmacy involvement already exist in the United States. Lofwall et al⁶⁵ surveyed 179 pharmacies in 2009, and 74% were willing to participate in dispensing buprenorphine and 22.3% were unwilling to do so. In fact, 5 pharmacies reported already performing pill counts for buprenorphine. Of note, the top 3 reasons for disinterest were not stocking buprenorphine and/or no buprenorphine customers, too busy/insufficient staff, and concern about patient's destructive behaviors. Involvement of pharmacies could represent a valuable partnership approach, and this type of monitoring could potentially ensure a safer practice and identify misuse and diversion issues early in the treatment process.

Other ways to address the diversion and abuse issue can also be considered. It may be helpful to identify high risk populations, such as intravenous heroin users, who are particularly vulnerable to intravenous buprenorphine abuse.⁶⁶ An electronic medicine dispenser has been introduced to decrease the likelihood of diversion of take-home medications, because the device will not allow obtaining more than a single dose daily. This electronic device may indeed have some curbing effects and ensure more safety with unsupervised medication dispensing and intake.⁶⁷ However, the device alone would not address the root problem, nor could it be the main approach to address the issue of diversion.

Addictive disorders are chronic, complex disorders with high rates of relapse and comorbidity with psychiatric diseases as well as a need for psychosocial support. A significant addictive potential also exists for opioid treatment medications (ie, buprenorphine and methadone). The treatment of these patients requires safe medication prescribing and comprehensive mental health care and counseling services. We are fortunate to have buprenorphine, an effective medication for the treatment of opioid use disorder; yet any single approach will only have partial benefits. The efforts and regulations to expand buprenorphine therapy deserve support; however, simultaneously, we need to ensure safe practice and develop other measures, including financial incentives for physicians and pharmacies, and mandatory enforcement of urine monitoring and counseling compliance, particularly in high risk populations, such as former intravenous drug users.

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