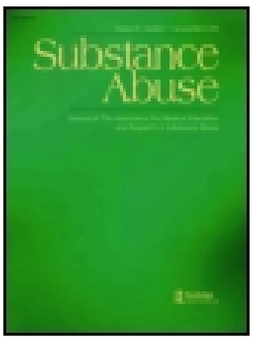

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COMMENTARY

Demystifying buprenorphine misuse: Has fear of diversion gotten in the way of addressing the opioid crisis?

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ABSTRACT

Buprenorphine is considered one of the most effective treatments for opioid use disorder and significantly reduces risk of overdose death. However, concerns about its diversion and misuse have often taken center stage in public discourse and in the design of practices and policies regarding its use. This has been to the detriment of many vulnerable patient populations, especially those involved in the criminal justice system. Policies that restrict access to buprenorphine in criminal justice and other settings due to concerns of diversion do not accurately reflect the relative risks and safety profile associated with it, creating unnecessary barriers that drive an illicit market of this much-needed medication. Although proper regulation of all controlled medications should be a priority, in most instances the benefits of buprenorphine highly outweigh its risks. In the midst of a national crisis, efforts should be focused on expanding, and not restricting, access to this life-saving treatment.

KEYWORDS

Addiction; buprenorphine; criminal justice; diversion; opioid; substance use

A public health crisis

The opioid crisis in the United States has reached epidemic proportions, with 2.1 million individuals estimated to have an opioid use disorder (OUD).[1] In 2017 alone, there were over 72,000 overdose deaths in the United States, 68% of which involved an opioid.[2] States in all regions of the United States have suffered, with 52 jurisdictions in 45 states reporting an average increase in opioid overdoses of 30% between 2016 and 2017.[3] In the midst of this national emergency, we are fortunate to have medications that have proven to be effective in the treatment of OUD and are considered a key strategy for combating the opioid crisis. Buprenorphine, approved by the Food and Drug Administration (FDA) in 2002, is considered to be one of the highest standard of care for OUD.[4] The most common form used to treat OUD is buprenorphine-naloxone, which is an abuse-deterrent formulation that prevents the drug from being easily injected and is therefore less prone to abuse.[5] Both national and international data have demonstrated consistently that buprenorphine treatment is safe and is associated with a decrease in opioid overdose deaths.[6–8] In the 40 countries where buprenorphine is prescribed for OUD, hundreds of thousands of individuals have been able to stop using illicit opioids, regain stability, and resume leading more productive lives.[9]

Since its approval, the availability of buprenorphine has expanded significantly across the United States. Particularly appealing is the fact that buprenorphine, unlike methadone, can be prescribed by licensed physicians with a waiver from the Drug Enforcement Agency as a take-home medication. This saves patients the need to attend a treatment program daily, thereby allowing them to more easily fulfill other responsibilities. It also allows OUD treatment to be integrated into other health care settings, since buprenorphine can be prescribed by trained general practitioners.[10] Still, there remains a wide gap in access to buprenorphine among those who need it: One study reported that 96% of states have rates of OUD that exceed their buprenorphine treatment capacities.[11] Even when patients do have access to buprenorphine providers, engagement and retention in treatment is a constant challenge.[12] Multiple factors contribute to the lack of continuous access to buprenorphine, ranging from insurance regulations, to a dearth of physicians trained to prescribe the medication, to stigma regarding the use of medications in treating addiction.[13,14] However, critical barriers to treatment that are seldom discussed in the discourse about the opioid epidemic are the strict restrictions commonly placed on buprenorphine due to concerns of its diversion and misuse.

The fear of diversion

As buprenorphine has become more widely available, concerns about its diversion and misuse have often taken center stage. It is rare to find a media article about buprenorphine that does not mention diversion or misuse, and articles with titles such as "*Addicted to a treatment for addiction*" and

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"*Addiction treatment with a dark side*" have fueled the public's association of this medication with abuse and danger.[15,16] And yet, compared with most opioids, buprenorphine has a very high safety profile: It is a partial opioid agonist, meaning that it activates the brain's opioid receptors to a much lesser extent than full agonists such as heroin and prescription opioids.[17] Buprenorphine does not cause respiratory depression and has a "ceiling effect," meaning that the effects of the medication reach a plateau and do not increase with higher dosages, rendering it significantly less prone to abuse and overdose than other opioids.[18]

It is not only the media that is preoccupied with diversion. Buprenorphine is already a highly controlled substance, and physicians must undergo training and receive a DATA2000 waiver in order to prescribe it.[10] Even upon receiving a waiver, physicians are limited to treating 30, 100, or 275 patients at a time, depending on individual authorization from the Center for Substance Abuse Treatment.[10,19] In response to concerns of diversion and misuse, some medical systems have placed additional limits on providers' abilities to prescribe buprenorphine. Currently, 12 states limit the total duration of time for which an individual can be treated with buprenorphine throughout their lifetime. This is particularly harmful, as OUD is a relapsing and remitting chronic disease: when not in treatment, patients face increased likelihoods of overdose and death.[20] Other medical systems have requirements for prior authorization before filling a buprenorphine prescription, quantity limits, and complex network requirements, many of which stem from concerns about diversion.[21] Some facilities also have "fail first" or "step therapy" criteria, which require documentation that other therapy modalities have been attempted and were ineffective before buprenorphine is prescribed.[21]

Concerns about diversion also contribute to many providers' unwillingness to become certified to prescribe buprenorphine in the first place. In the United States, only 4% of primary care physicians have received the DATA 2000 waiver.[10] One study reported that 26% of physicians who had not applied for the waiver expressed that potential diversion issues were their primary reservation; however, after receiving the education and training required to obtain the waiver, the number of physicians citing diversion concerns dropped to 10% ($P = .002$).[22] Adding to these concerns is that most funding and regulatory organizations for buprenorphine services require protocols to minimize diversion as a principal condition of providing care.

A particularly vulnerable population

Patients who may be most harshly affected by the focus on diversion are those involved in the criminal justice system. More than half of state prisoners and nearly two thirds of jail inmates are estimated to have a substance use disorder.[23] This population also experiences the greatest risk of overdose death—a 129-fold increase in the first 2 weeks after release from incarceration compared with the general population.[24–27] And yet, those with criminal justice involvement are least likely to receive medication-assisted treatment: According to a 2016 survey conducted by Pew Charitable Trusts, fewer than 40 of the nation's 5000 jails and prisons (less than 1%) offer any access to medication-assisted treatment, and among those that do, most serve only small subsets of those who are in need or are used for detoxification purposes, not for ongoing treatment.[28,29] In addition, a recent national study demonstrated that less than 5% of those referred to specialty treatment by a criminal justice source receive medication-assisted treatment.[30]

Much of the lack of medication-assisted treatment, and of buprenorphine in particular, in criminal justice settings is attributed to concerns about diversion and misuse. Criminal justice staff, including wardens and prison directors, frequently express negative attitudes about such medications, with risk of diversion often cited as a primary reason for opposing providing it in their facilities.[28,31–34] Resistance to medication-assisted treatment due to concerns of diversion has also been documented in other criminal justice settings, including parole, probation, and drug courts.[28,35] Although these concerns are often cited to defend practices that prevent access to buprenorphine in criminal justice facilities, there is little evidence about true rates of diversion in these settings. Such low utilization of buprenorphine persists despite evidence that justice-involved persons who are allowed access to uninterrupted medication-assisted treatment are less likely to reoffend, more likely to continue treatment, and less likely to overdose.[36–40]

Diversion as self-medication

Numerous studies have found that the majority of diverted buprenorphine is actually used to self-medicate for detoxification or to reduce withdrawal symptoms, rather than to "abuse" the drug or experience euphoria. Across multiple studies, few individuals report using buprenorphine as their primary drug of choice.[41,42] One study found that most persons who had obtained nonprescription buprenorphine reported doing so to treat withdrawal symptoms (74%), to stop using other opioids (66%), and because they couldn't afford proper treatment (64%).[43] Another study reported that 91% of respondents used illicit buprenorphine to manage withdrawal symptoms, of whom 40% were waiting for treatment at the time of use.[44] Another found that nearly 60% of participants who had shared buprenorphine did so to help friends or partners who were in withdrawal.[45] In a qualitative study, illicit buprenorphine users explained that buying buprenorphine on the street was often more practical than finding a prescribing doctor or having to pay insurance fees associated with the medication.[41] Thus, using the potential for diversion as the primary reason for not providing evidence-based treatment is not only counter to public health efforts but also may actually exacerbate the illicit use of these medications. Indeed, there is evidence demonstrating that illicit buprenorphine use decreases when treatment seekers are able to obtain legal prescriptions.[43,46,47]

It is important to recognize that diverted buprenorphine may even benefit those who are not ready for structured treatment or who are not prepared to stop using illicit

substances, a prerequisite for many programs. For some, illicit buprenorphine use may provide a gateway to treatment: Research has found that illicit buprenorphine users were more interested in and more likely to initiate treatment but generally reported being unsure about where to go to obtain it legally.[48] Individuals with prior experience using buprenorphine, either prescribed or nonprescribed, have also been found to fare better in the treatment induction process and have better treatment retention rates than those who are buprenorphine naïve.[49,50] One study found that patients with prior experience using nonprescribed buprenorphine had significantly higher odds of remaining in treatment for at least 6 months, with qualitative data identifying that those with prior experience had a higher perceived effectiveness of buprenorphine based on their history of nonprescribed use.[51] Another study demonstrated that those with a history of nonprescribed buprenorphine use prior to entering a treatment program had higher rates of abstinence from other illicit substances after 6 months of treatment.[52]

Although diversion and illicit use of buprenorphine are not desired outcomes, weighing the relative risks and benefits of buprenorphine when generating policies and practices related to its accessibility is critical. Risks attendant to diversion exist but are relatively small compared with the risk created when treatment access is restricted. For example, although emergency department visits involving nonprescribed buprenorphine– and buprenorphine-related deaths have been reported, they are often limited to individuals who combine it with contraindicated substances such as benzodiazepines.[6,53] Buprenorphine deaths are also significantly rarer than those involving methadone or other prescription opioid medications.[54] One study reported a 6-fold lower rate of poison center calls related to buprenorphine than methadone.[55] Another study of outcomes associated with nonprescribed use of buprenorphine and methadone reported 26 deaths among those using methadone, compared with zero deaths among those using buprenorphine, in addition to much lower rates of hospitalization and other negative medical outcomes among the latter group.[56] The Center for Behavioral Health Statistics and Quality has consistently found that emergency department visits related to buprenorphine are the lowest among all commonly used opioids.[53] Increasing access to legal, low-threshold buprenorphine treatment that is accompanied by counseling on safe use of the medication will further reduce any associated adverse risks.

A more humane approach to buprenorphine

Throughout buprenorphine's relatively short history, much of our national conversation has focused on a fear of diversion, oftentimes to the detriment of those who need it most. As long as there remains a major gap between demand for and access to low-threshold and readily accessible treatment, medication diversion and misuse will continue to exist. Taking seriously the urgent need to devise and deliver solutions to the nation's opioid epidemic requires that policies focus on creating systems that balance appropriate restrictions with adequate accessibility. Such policies should more accurately reflect both reality and science, rather than allowing amplified concerns to shape policy and practice. As in all areas of medicine, we must make efforts to ensure that buprenorphine is properly used, and we should expect responsible prescribing practices and medication use from both clinicians and patients. Appropriate steps can and should be taken to minimize misuse of buprenorphine, and most providers already utilize many of these strategies, including drug tests, pill counts, and prescription drug monitoring programs (PDMPs).[57] As new formulations of buprenorphine such as depot injections and implants become more widely available, these can also be used as alternative ways of assuring medication adherence.[58] Although these measures are important, they should be implemented without imposing additional restrictions on vulnerable individuals seeking treatment.[59]

Moving forward, our focus must be on expanding access to treatment. As research has repeatedly demonstrated, making buprenorphine more readily available to those who need it will help minimize the presence of the illicit market.[20,44,54,60,61] It is critical to increase outreach to those who are currently using nonprescribed buprenorphine to self-treat and encourage them to engage in comprehensive treatment programs rather than criminalizing them.[9] It is also necessary to minimize barriers that prevent individuals from accessing treatment and remaining in care, such as rigid program criteria and overly complex admission processes. This means expanding low-threshold buprenorphine programs—those with minimal requirements for entering and remaining in care—and those that are focused on harm reduction rather than on abstinence. Minimizing requirements for buprenorphine treatment can help attract patients who may otherwise choose to obtain illicit buprenorphine rather than enrolling in a program with conditions that they are unable to fulfill. This means that requirements such as mandatory attendance at behavioral therapy sessions or abstention from all illicit substance use must be relaxed to truly reach those who are most difficult to engage. Utilizing a flexible approach prioritizes the public health goal of minimizing harmful behaviors and outcomes, such as risky use and overdose, while working on incremental progress to address the challenging nature of OUD.[62]

Establishing continua of care is an important way to reach those who are most vulnerable and transition them as appropriate when they become more comfortable engaging with formal treatment settings, beginning with the lowest threshold possible. This first step should be dedicated to connecting individuals to licit buprenorphine through willing providers, educating them on the risks of overdose, and ensuring that they are able to access basic resources such as health insurance and personal identification cards. Mobile treatment sites, for example, have demonstrated success in expanding access to harm reduction and treatment services for those who are disconnected from the health care system and have been shown to enroll greater proportions of certain minority groups compared with fixed treatment sites.[63–68] Programs that increase accessibility of services and

medications through legal channels directly in the local community can minimize the time and resources that people need to expend in order to obtain it. Once individuals demonstrate that they are responding and adhering well to medications, they can be transitioned to a more structured substance use clinic setting where they will have opportunities to engage in support groups, behavioral therapy, basic skills training, and assistance with job placement. Finally, an ultimate goal for many may be transitioning to primary care settings that incorporate a wider range of health services in addition to chronic OUD management. Movement between the levels in such a continuum must be responsive to the needs of the individual, as each person's journey with OUD varies widely.

We must also continue to improve quality of care in the treatment of both OUD itself and the complex behavioral issues related to addiction that might contribute to buprenorphine misuse and diversion. These efforts are most likely to succeed through flexible, compassionate care; frequent visits with properly trained health care providers; and the provision of additional supports such as psychosocial services. Using educational interventions for physicians through Continuing Medical Education (CME) activities increases the number of available providers trained in best practices to properly monitor and guide patients in using these medications safely, which will improve treatment quality.[69–71] Additionally, increasing the 30-patient buprenorphine prescribing limit and the physician supervision requirements currently imposed on nurse practitioners and physician assistants in many states would alleviate some of the dearth of licensed providers willing to work in low-threshold treatment programs, particularly in resource-poor areas.[72–74]

Our priority as a public health community and society is to save lives, and the effectiveness of buprenorphine treatment has been demonstrated time and again. Sustaining negative attitudes toward medication-assisted treatment and devising policies that are based on mistrust of persons with OUD alienates these individuals and discourage them from seeking proper care. Let us not allow the historical stigma of substance use disorders and their treatment to get in the way of addressing today's public health crisis, saving lives, and helping people achieve the health, recovery, and stability they deserve.

Author contributions

M.D., N.K., D.A., and M.F. contributed to the conceptualization of the manuscript. M.D. and N.K. contributed to writing the manuscript. M.D., N.K., D.A., and M.F. were involved in revision.

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