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Understanding the use of diverted buprenorphine

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ABSTRACT

Background: Buprenorphine is approved in many countries for the treatment of opioid use disorder (OUD), but problems with diversion and abuse exist. There is a need to understand how and why patients use diverted buprenorphine, and whether barriers to access contribute to illicit use.

Methods: Adults >18 years with DSM-IV criteria for substance use disorder and primarily using an opioid completed the online Survey of Key Informants’ Patients (SKIP) between August and September 2016. The survey included closed- and open-ended questions regarding reasons for buprenorphine use with and without a prescription, sources of buprenorphine, route of administration, and barriers to treatment.

Results: Of 303 respondents, 175 (58%) reported a history of diverted buprenorphine use, 65 (37%) of whom reported never receiving a prescription. The most common reasons for illicit buprenorphine use were consistent with therapeutic use: to prevent withdrawal (79%), maintain abstinence (67%), or self-wean off drugs (53%). Approximately one-half (52%) reported using buprenorphine to get high or alter mood, but few (4%) indicated that it was their drug of choice. Among respondents who had used diverted buprenorphine, 33% reported that they had issues finding a doctor or obtaining buprenorphine on their own. Most (81%) of these participants indicated they would prefer using prescribed buprenorphine, if available.

Conclusions: Although 58% of survey respondents reported a history of using diverted buprenorphine, the most frequently cited reasons for non-prescription use were consistent with therapeutic use. Diversion was partially driven by barriers to access, and an unmet need for OUD treatment persists.

1. Introduction

Buprenorphine is a μ-opioid receptor partial agonist (Bloms-Funke et al., 2000) approved by the US Food and Drug Administration (FDA) for the treatment of opioid use disorder (OUD). At low doses, buprenorphine has effects similar to μ-opioid full agonists; at high doses there is a ceiling on its agonist activity (Walsh et al., 1994). As higher doses are reached, partial agonists function as antagonists—occupying receptors without activating them (or partially activating them)—while simultaneously displacing or blocking full agonists from binding the receptors (Greenwald et al., 2003). The partial agonist profile of buprenorphine coupled with its high affinity for the μ-opioid receptor may contribute to a favorable safety profile over μ-opioid receptor full agonists, particularly with respect to respiratory depression and fatal overdose.2 The pharmacology also suggests that buprenorphine may have less abuse liability compared with μ-opioid full agonists (Walsh et al., 1994) supported by the fact that when available, μ-opioid full agonists are preferred for illicit use over buprenorphine formulations.
withdrawal symptoms, as a substitute to get high when more preferred drugs were unavailable, and/or because other OUD treatment was unaffordable (Bazazi et al., 2011; Cicero et al., 2014). Several international studies also indicate that many of those who use diverted buprenorphine do so to prevent withdrawal or to stop using other opioids (Yokell et al., 2011). Barriers to access through medical channels might contribute to this diversion, (Lofwall and Havens, 2012) and treatment program costs and lack of prescribing physicians may deter users from seeking licensed buprenorphine medical treatment (Bazazi et al., 2011).

In the US, prescription waivers can be obtained by healthcare providers for Schedule III, IV, and V medications approved by the FDA to treat OUD. These waivers, made available through the Drug Addiction Treatment Act of 2000 (DATA 2000)Drug Addiction Treatment Act, 2000Drug Addiction Treatment Act of 2000 (DATA 2000), were intended to integrate addiction treatment into medical offices and other appropriate settings (Drug Addiction Treatment Act (DATA) of 2000). Initially, DATA-waived physicians could prescribe buprenorphine to 30 total patients; in 2007, the limit was raised to 100 for physicians with at least one year of experience. In 2016, the Comprehensive Addiction and Recovery Act (CARA) further raised the limit to 275 patients and extended waiver privileges to qualified nurse practitioners and physician assistants, with patient limits as allowed by state law (Comprehensive Addiction and Recovery Act (CARA) of 2016). However, there are still a limited number of physicians in the US with DATA waivers. Moreover, only 44-66% of these physicians prescribe buprenorphine, and most do not prescribe to their maximum patient limit (Hutchinson et al., 2014; Kissin et al., 2006; Kunins et al., 2013; McCarty et al., 2004; Walley et al., 2008). This unused capacity may be related to physician reluctance to add office-based opioid treatment due to lack of time, payment (insufficient reimbursement) and pharmacy issues; concerns about medication diversion and resistance from staff or colleagues; increased administrative and clinical resources (e.g., nursing support); deficits in knowledge about opioid treatment; lack of belief in agonist treatment; and/or fear of taking on increased medicolegal risks (Huhn and Dunn, 2017; Walley et al., 2008). More than half of DATA-waivered physicians who are not prescribing to capacity report that nothing would increase their willingness to prescribe more buprenorphine (Huhn and Dunn, 2017) suggesting that numbers of waivers are unlikely to increase unless healthcare professionals are provided with resources and information to sufficiently address their concerns.

To better inform policies and practices that affect the availability of buprenorphine for OUD treatment, more information is needed about the reasons for its abuse, misuse, and diversion. The purpose of this study was to examine motivations for use of diverted buprenorphine products and explore the role of unmet need for treatment.

2. Methods

2.1. Study sample

Data were from the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System, a comprehensive series of programs that collect and analyze post-marketing data on the misuse and diversion of prescription opioid analgesics and heroin (Cicero et al., 2007a; Dart et al., 2015).

The Survey of Key Informants’ Patients (SKIP) Program comprises treatment centers (Key Informants) that recruit patients entering treatment for OUD to complete an anonymous survey on opioid misuse patterns and related behaviors. Survey participants must be 18 years or older and meet Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for substance abuse or dependence with a primary drug that is an opioid (prescription or heroin).

The Researchers and Participants Interacting Directly (RAPID) Program consists of a subset of participants from the ongoing nationwide SKIP Program. These participants indicated by a mail-in postcard (provided with the SKIP survey) that they were willing to give up their anonymity and, following completion of a registration that includes written consent, participate in the RAPID program. RAPID participants complete online surveys (hosted by SurveyMonkey) that included: (1) direct, quantitative questions based on SKIP analyses and prior literature on the topic; and (2) open-ended, qualitative essay-style questions used to explain, in greater detail, participants’ responses to quantitative questions. From 2008-3q18, there were a total of 21,087 SKIP participants, who were given a postcard to return if they were interested in future follow-up studies. A total of 10,445 postcards were received from interested SKIP participants. Of these, 3885 were eligible to be contacted for the RAPID program (after excluding those with no email, a working email, illegible/incomplete postcards, duplicates, etc.).

A total of 654 eligible respondents were registered and consented with the RAPID program and were sent the RAPID survey for this study.

Data for the current study were collected from a five-part RAPID survey that ran from August 15, 2016 to September 19, 2016 and asked a series of questions concerning: (1) use of buprenorphine prescribed by a physician to treat opioid addiction; (2) use of diverted buprenorphine (i.e., buprenorphine without a prescription); (3) barriers to buprenorphine access; (4) buprenorphine formulation preferences among those with a history of using buprenorphine, with or without a prescription; and (5) demographics and characteristics of respondents. This survey focused on use of buprenorphine (with and without a prescription), reasons for diverted buprenorphine use, sources of diverted buprenorphine, routes of administration, and barriers to treatment in the past year and lifetime of the respondent. Participants in the RAPID program were compensated with a $20 Wal-Mart gift card. All protocols were approved by the WUSTL Institutional Review Board (IRB).

2.2. Statistical analysis

Each survey response was reviewed by the authors for completeness and consistency. Descriptive statistics were used to summarize survey responses. No inferential testing was completed. Data analysis was completed using IBM SPSS Statistics v.22 for quantitative data and NVivo v.10 for qualitative data.

3. Results

3.1. Survey respondents

Of 303 patients who responded to the RAPID survey, 53 (18%) used buprenorphine exclusively through a physician’s prescription (Fig. 1). A total of 175 respondents had a history of diverted buprenorphine use, 65 (37%) of whom never received a prescription. Seventy-five respondents reported no buprenorphine use.

The majority of respondents were female (55%), aged 25–44 years (72%), and Caucasian/White (90%) (Table 1). Respondents tended to be from rural/suburban communities (57%) and at least partly employed (full-time, 56%; part-time, 15%). A variety of health insurance sources were reported, including private (30%), Medicaid/Medicare (34%), VA/Military (3%), and dependent (9%). Nearly one-quarter (24%) reported having no/other insurance coverage.

3.2. Use of buprenorphine prescribed by a physician

More than one-half (54%) of survey respondents reported a lifetime history of receiving a buprenorphine prescription for OUD. Among participants who responded to specific questions about aberrant behaviors, 38% reported failure to remain completely abstinent while on buprenorphine and 32% reported not taking buprenorphine only as prescribed. One-third (33%) admitted they had given away, sold, or traded some/all of their buprenorphine prescriptions.

Among the 63% of respondents who had ceased buprenorphine use and who answered why they stopped receiving their most recent buprenorphine prescription, the most common reasons cited were that...
they chose to stop seeing their doctor or lost the ability to visit or pay for doctor’s visits or prescriptions (Fig. 2). Doctor and patient agreement on treatment program completion was endorsed by 19% of respondents, while 12% reported their doctor stopped prescribing, despite the respondent feeling his/her treatment program was not over.

Over one-quarter of respondents provided open-ended responses for why their buprenorphine prescription became inactive. Example responses included the respondent deciding to “go to treatment,” switching to methadone therapy, incarceration, and viewing buprenorphine as a “crutch.”

3.3. Use of buprenorphine without a physician prescription

Among respondents who used diverted buprenorphine (N = 175), 68% reported using single-ingredient buprenorphine tablets, 66% used combination tablets (buprenorphine/naloxone), and 75% used combination film. Three of the four most common reasons for diverted buprenorphine use were for the intended purposes of the medication, including to avoid/ease withdrawals, to maintain abstinence from other drugs, and to try weaning oneself off drugs (Fig. 3). While a majority of respondents used buprenorphine to get high or to alter their mood, less than 5% reported buprenorphine as their drug of choice for getting high or thought that buprenorphine provided a better high than other drugs.

Non-prescription buprenorphine was mostly obtained through a dealer/street dealer, a friend/relative, or a doctor’s prescription (Fig. 4A). Open-ended responses indicated that methadone clinics and rehabilitation facilities were also additional venues for obtaining the drug. Among users of illicitly obtained buprenorphine, most reported using the drug at least once a day (Fig. 4B), and the most common route was dissolution under the tongue (Fig. 4C). Snorting, swallowing whole, and injecting drug were each endorsed by approximately 25% of respondents.

Qualitative follow-up responses indicated that routes of administration other than dissolving under the tongue were used commonly to heighten or accelerate a high. Respondents stated, “I injected them so they would hit me faster,” “I injected them to get high, that was my method of choice for any drug,” and “I would snort or inject it if I needed to get high or ease withdrawal quicker.” Users would favor specific formulations depending on their purpose of use. One buprenorphine oral film user would “dissolve and snort to get high, dissolve under tongue when low quantity/trying to wean off or avoid withdrawals.”

3.4. Barriers to buprenorphine access

Survey respondents were asked questions regarding difficulty in obtaining buprenorphine prescriptions, and whether changes in restrictions would affect their interest and/or usage of buprenorphine. Regardless of prior history of buprenorphine use (with or without a prescription), lack of access to doctors who could legally prescribe buprenorphine and high out-of-pocket costs were widely endorsed as barriers to access.

Problems finding a doctor or obtaining a buprenorphine...
prescription were reported by respondents who had used diverted buprenorphine (33%) as well as by respondents who did have a prescription (38%). Open-ended responses included: “hard to find and expensive”; “it’s difficult to find a doctor that is taking patients. Or have to wait a year for a new patient appointment”; “costly to see a doctor who would prescribe it even with insurance”; “hard to get into program, long waiting lists”; and “it usually comes down to money [since] some doctors are cash only to get into their SUBOXONE® program.”

Most (81%) of respondents with any history of using diverted buprenorphine indicated that easier access to a doctor who could prescribe buprenorphine would encourage them to get a prescription rather than seeking buprenorphine on their own. One respondent stated that a prescription “…would make the process of obtaining the drug safer and easier. There would [be] no illegal street deals to get the drugs and insurance would help me to obtain it for cheaper.” Another stated that “If it wasn’t so hard to get legally there would most likely be more people taking it and getting cleaned up than people taking drugs.” Among all users who ever used buprenorphine (with a prescription or diverted use), 43% indicated they would use buprenorphine more often if it was easier to find and more accessible by prescription or through other sources.
4. Discussion

This survey of 303 patients formerly in treatment for OUD was conducted to estimate how many had ever used diverted buprenorphine and explore why this illicit use occurred. Diverted buprenorphine was prevalent, with 58% of respondents having used diverted buprenorphine. Even among a population of patients seeking treatment for OUD who might be at risk for the abuse or non-medical use of
buprenorphine, reasons for use of diverted buprenorphine were largely for indicated therapeutic purposes such as managing withdrawal symptoms or maintaining abstinence. Buprenorphine diversion was often driven by issues surrounding barriers to access, and 81% of respondents who used diverted buprenorphine indicated they would be more encouraged to obtain buprenorphine from a doctor if access improved.

Open-ended responses by participants revealed three main barriers to buprenorphine access: difficulty in accessing physicians, high cost, and social stigma. Prescribing physicians were “hard to find” and respondents were often put on long waiting lists while experiencing withdrawal symptoms that discouraged obtaining buprenorphine legally. In an analysis by Jones et al. (2015) examining opioid treatment need and capacity in the US, 96% of states had opioid abuse or dependence rates higher than their buprenorphine treatment capacity. In 2012, only 27.5% of DATA-waived physicians in the United States were certified for the 100-patient limit, despite the fact that 82.3% of opioid treatment programs were at ≥80% capacity (Jones et al., 2015). As of January 2018, based on Substance Abuse and Mental Health Services Administration (SAMHSA) updates, 20% of DATA-waived physicians were certified for the 100-patient limit and only 8% were certified for the newer 275-patient limit.

Expense was another commonly cited issue associated with finding a prescribing physician. Respondents reported many physicians were cash only, and despite insurance coverage, some found the cost of buprenorphine therapy to be prohibitive. A conjoint analysis found a patient’s method of payment was the second largest factor in a physicians’ decision to start buprenorphine therapy in a new patient, second only to co-occurring substance use (Knudsen et al., 2018). Physicians had a clear preference for cash-paying patients, and an unwillingness to accept patients paying with Medicaid. Cash may reduce administrative burdens associated with Medicaid reimbursement; however, the reasons for a cash preference within physicians is not well understood. Given the expansion of Medicaid under the Affordable Care Act (ACA), additional patients seeking treatment for OUD may gain access to healthcare (McLellan and Woodworth, 2014). If physicians prescribing buprenorphine are unwilling to accept Medicaid, growth through the ACA in access to prescribing physicians may be weakened.

It is still unclear how the costs of obtaining buprenorphine through a doctor’s prescription compare to the costs of obtaining buprenorphine on the street. While some respondents stated obtaining buprenorphine legally would lower costs for individual dosages due to insurance coverage, the cost of the doctor’s visit and/or the limited number of insurance policies accepted may be prohibitive. The introduction of generic buprenorphine in 2009 reduced the price of certain formulations, and a 2009 self-administered survey in Providence, RI found that among 100 opioid users, the majority found buprenorphine/naloxone to be less expensive than an equivalent amount of heroin or other prescription opioid (Bazazi et al., 2011). Results from the same survey indicated that 73% of respondents found obtaining buprenorphine/naloxone to be easy or very easy. With easy access to cost-effective buprenorphine formulations readily available on the street, users may have less incentive to obtain buprenorphine through a doctor’s prescription.

Lastly, the social stigma associated with seeking treatment for OUD may have prevented some respondents from seeking care. Respondents frequently expressed that buprenorphine is a “crutch” or that buprenorphine is simply a substitute for other opioid addictions. Stigma in the arena of addiction can contribute to social isolation, undermine long-term recovery, and reduce help-seeking behaviors (White, 2012). Reducing social barriers to buprenorphine use may encourage additional patients to seek treatment for OUD.

A fine line exists between abusing buprenorphine and using diverted buprenorphine for therapeutic purposes, and it is worth noting that decreasing barriers to access may also increase diversion for non-therapeutic purposes (Cicero et al., 2007a,b). Buprenorphine inherently carries a risk for abuse because the mechanism used to prevent withdrawal is similar in nature to the mechanisms underlying euphoric effects (Donaher and Welsh, 2006) and users have reported different ways of manipulating these products to produce better highs and separate buprenorphine from naloxone to generate “pure buprenorphine” for injection (Cicero et al., 2014). In the current survey, 52% of respondents who used diverted buprenorphine reported having used a buprenorphine product to get high or alter mood, with snorting and injection endorsed as common routes of illicit use. However, few respondents indicated that buprenorphine was their drug of choice to get high. Additional research is needed to better elucidate the dynamic between treatment benefits and potential abuse with all OUD medications.

Concern about abuse and diversion is a major barrier affecting availability of buprenorphine to individuals who need treatment for OUD. One leading reason why prescribers do not seek a buprenorphine prescription waiver is the concern about diversion (Huhn and Dunn, 2017). While there are valid reasons for prescribers and policymakers to be concerned about the potential harm of diverted buprenorphine use, including local injection site reactions and systemic diseases associated with injections, overdose (commonly associated with concurrent use of sedatives such as benzodiazepines and/or alcohol) (Hakkinen et al., 2012; Tracqui et al., 1998), and unintended exposure to children (Martin and Rocque, 2011; Pedapati and Bateman, 2011), increased understanding of the motivations for use of diverted buprenorphine and the role of unmet treatment needs is important for reducing physicians’ reluctance to prescribe buprenorphine in the midst of an opioid crisis.

Limitations applicable to survey data also apply to this study. This sample of respondents may not be representative of all opioid users, as it reflects a convenience sample of unknown sampling frame. Relative to the SKIP participants, the RAPID sample included lower numbers of younger and non-white participants (Supplemental Table 1), populations that may demonstrate different patterns of use than what was found. These populations may require extra attention for participation in follow-up studies, which we hope to focus on as our research continues. The voluntary, self-administered, online nature of this survey leads to response bias and does not provide a way to probe respondents further. Moreover, the survey respondents were individuals seeking medication-assisted treatment for OUD and as such, the results presented here may not reflect those of the population of buprenorphine abusers who have never sought or received legitimate OUD treatment. Despite these weaknesses, this study sample was drawn from a known drug user population at a higher risk for using drugs illicitly for reasons outside therapeutic intentions. Underreporting of buprenorphine abuse is unlikely, as this sample of respondents are in recovery and are likely seeking opportunities to provide information on opioid use and abuse. The survey also allowed for the inclusion of open-ended responses, which mitigated the inability to further probe respondents on their answers.

While the focus of this study was on a US sample, buprenorphine abuse and diversion are of global concern. Results from this study were consistent with a limited number of international studies that indicate that diverted buprenorphine is often used to prevent withdrawal and stop use of other opioids (Yokell et al., 2011), and may be due to lack of access to treatment (Johnson and Richert, 2015). More research is necessary to understand motivations for use of diverted buprenorphine internationally, given the extent of use of diverted buprenorphine in the countries in which buprenorphine is available for the treatment of opioid use disorder.

5. Conclusions

The findings of this study suggest that those who use diverted buprenorphine prefer obtaining it through a valid prescription. It is important to find ways to increase access by reducing barriers such as cost, unavailability of prescribers, and social stigma. Although increased
buprenorphine availability has potential to increase diversion, the majority of buprenorphine use in this high-risk population was for the intended therapeutic purpose of easing and preventing withdrawal, suggesting that improved prescriber access might provide more potential benefit than harm.

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Contributors
All authors participated in analyzing and interpreting the data, and in drafting and reviewing the manuscript. All meet ICMJE criteria for authorship and have read and approved the final version of the manuscript.

Conflict of interest
All authors completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Chicloat is employed by Indivior, Inc., manufacturer of SUBUTEX®, SUBOXONE®, and SUBLOCADE®. Dr. Cicero serves as a consultant on the scientific advisory board of the non-profit Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) System. Mr. Ellis reports no conflict of interest.

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Appendix A. Supplementary data
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