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Scope of, Motivations for, and Outcomes Associated with Buprenorphine Diversion in the United States: A Scoping Review

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Abstract

Background: Expanding access to medications to treat opioid use disorder (OUD), such as buprenorphine, is an evidence-based response to the mounting drug overdose crisis. However, concerns about buprenorphine diversion persist and contribute to limited access.

Methods: To inform decisions about expanding access, a scoping review was conducted on publications describing the scope of, motivations for, and outcomes associated with diverted buprenorphine in the U.S.

Results: In the 57 included studies, definitions for diversion were inconsistent. Most studied use of illicitly-obtained buprenorphine. Across studies, the scope of buprenorphine diversion ranged from 0% to 100%, varying by sample type and recall period. Among samples of people receiving buprenorphine for OUD treatment, diversion peaked at 4.8%. Motivations for using diverted buprenorphine were self-treatment, management of drug use, to get high, and when drug of choice was unavailable. Associated outcomes examined trended toward positive or neutral, including improved attitudes toward and retention in MOUD.

Conclusions: Despite inconsistent definitions of diversion, studies reported a low scope of diversion among people receiving MOUD, with inability to access treatment as a motivating factor for *using* diverted buprenorphine, and increased retention in MOUD as an outcome associated with use of diverted buprenorphine. Future research should explore reasons for diverted buprenorphine

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use in the context of expanded treatment availability to address persistent barriers to evidence-based treatment for OUD.

Keywords

Buprenorphine; diversion; drug treatment; medications for opioid use disorder; drug policy; scoping review

Introduction

The ongoing overdose crisis in the United States (U.S.) continues to challenge prevention efforts, including those for people experiencing substance use disorders (SUD). Increasing access to effective treatments for opioid use disorder (OUD), including methadone and buprenorphine, is a key national overdose prevention strategy (Becerra, 2021; Saloner et al., 2018; Kinlock et al., 2007; Mattick et al., 2014). Despite improvements in access to these medications for OUD (MOUD), an unmet treatment need persists, demonstrated by a national study finding that less than 20% of people with OUD have used any opioid-specific treatment (Haffajee et al., 2019; Weimer et al., 2021; Wu et al., 2016). This unmet treatment need hinders national overdose prevention efforts. Because these medications are opioids, hesitation among some public safety (e.g., criminal justice and law enforcement) and health care professionals to expand access often comes from concerns about diversion—the unauthorized rerouting or misappropriation of prescription medication to someone other than for whom it was intended, including sharing or selling a prescribed medication (Doernberg et al., 2019; Haffajee et al., 2018; Macy, 2016). Considering a 16% increase in the national number of overdose deaths from 2021 to 2022 (Ahmad et al., 2021), there is an urgent need to understand the risk of diversion as it pertains to MOUD expansion (Wakeman et al., 2020).

Buprenorphine classification as a Schedule III narcotic

Buprenorphine has a unique and complex pharmacological profile. As a partial agonist, buprenorphine produces pain relieving effects while its respiratory depression effects are more moderate than full-agonists like heroin and methadone and reach a plateau, thereby lowering overdose risk (Pergolizzi et al., 2010). Limited formulations of buprenorphine have been used to treat chronic pain in the U.S. since 1985 (Campbell & Lovell, 2012). In 2002, two buprenorphine products (i.e., Suboxone[®] and Subutex[®]) were additionally approved by the Food and Drug Administration (FDA) as OUD treatment. Considering its accepted medical uses, buprenorphine has a Schedule III classification by the Drug Enforcement Administration (DEA), meaning it has a moderate to low risk profile.

DATA 2000 and expanded access to buprenorphine

In 2000, the Drug Addiction Treatment Act (DATA) was passed, permitting qualifying physicians to apply for a waiver, allowing for office-based provision of buprenorphine and making it the first and only MOUD to be prescribed or dispensed in physicians' offices, rather than designated opioid treatment clinics. In response to increasing numbers of people with OUD in need of MOUD, the *Comprehensive Addiction and Recovery Act* (CARA) of 2016 and the *Substance Use Disorder Prevention that Promotes Opioid Recovery*

and Treatment for Patients and Communities (SUPPORT) Act of 2018 provided increased access to buprenorphine. To mitigate the impact of COVID-19 in early 2020, the in-person examination requirement to prescribe buprenorphine was waived and treatment via telehealth began (Davis & Samuels, 2021). In 2021, the U.S. Department of Health and Human Services (HHS) published new *Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder*, intending to reduce barriers to buprenorphine treatment (Becerra, 2021).

Buprenorphine diversion

Concerns that buprenorphine diversion is highly prevalent, is caused by desires to get high, and leads to morbidity contribute to limited access to buprenorphine as a MOUD (Andraka-Christou et al., 2019; Andraka-Christou & Capone, 2018; Cooper et al., 2020; Doernberg et al., 2019). Despite these concerns, reviews validating these problems have either not been conducted or have substantial limitations. Related to prevalence, a national study assessed buprenorphine diversion using law enforcement and other agency case files and showed statistically significant increases in diversion cases between 2007 and 2019 (Buttram et al., 2021). However, the study's focus on reported investigations might not be an accurate measure because it does not measure actual diversion by prescribers, dispensers, or patients.

To better understand factors driving buprenorphine diversion, one study showed that attempting and failing to access buprenorphine treatment motivated diverted buprenorphine use (Lofwall & Havens, 2012). Chilcoat et al. (2019) systematic review of motives for buprenorphine misuse, abuse, and diversion found that motives are commonly related to a desire to manage withdrawal or help abstain from using other opioids and concluded that diversion is primarily driven by restricted access to the medication. This is the most robust review on the topic to date, but has several limitations, including the study was funded by a buprenorphine product manufacturer (Indivior), raising questions about the validity of its findings and conclusions, as conflicts of interest are associated with biased presentations of findings (Friedman & Richter, 2004).

Lofwall and Walsh (2014) examined harms in their narrative review of buprenorphine diversion and misuse, concluding that buprenorphine misuse has resulted in some deaths, most often when concomitant use of benzodiazepines or alcohol occurred, although they are fewer compared to deaths involving other opioid prescriptions. Because their review included international research and focused on negative outcomes of diversion, its utility in informing domestic drug treatment policies is limited.

Scoping review purpose

Given the limitations of the existing literature, questions remain regarding the breadth of the problem (measured by use of diverted buprenorphine as well as diversion of prescribed buprenorphine), consequences of, and motivations for diversion. Recent momentum to expand access to MOUD in the U.S. could be further propelled by additional evidence. This scoping review aims to add to this evidence by applying a standardized methodology to summarize the ways buprenorphine diversion (including scope of, motivations for, and

outcomes of use) has been studied among *people using buprenorphine* in the U.S. We contextualize existing studies and their implications to inform expansion of buprenorphine availability.

Methods

Systematic reviews typically use strict inclusion criteria to examine causal relationships or intervention effectiveness while scoping reviews examine a wider range of literature to explore the evidence on a topic (Munn et al., 2018). We followed the PRISMA extension for scoping reviews guidelines to: 1) identify the research question, 2) identify relevant studies, 3) select studies, 4) chart the data, and 5) collate, summarize, and report the results (Appendix 1). These procedures were guided by our research question: What is the evidence on the scope of, motivations for, and outcomes of buprenorphine diversion among people who use buprenorphine in the U.S.? The research question was not pre-registered and a review protocol for this scoping review does not exist; results should be considered exploratory.

Search strategy

The following search string was used based on consultation with a public health librarian and keywords within our research question: (*Buprenorphine AND (divers* OR misuse OR abuse OR use* OR overuse OR illicit) OR ((Buprenorphine OR buprenex OR prefin OR Subutex OR temgesic OR suboxone OR sublocade) AND (divers* OR misuse OR abuse OR use* OR overuse OR illicit)). Articles published after the year 2000 were included to coincide with implementation of DATA.(Campbell & Lovell, 2012) The literature search for this review was run on February 11, 2021 in the following databases: Medline, Embase, PsycINFO, CINHALL, and Scopus.

Study selection

Our search returned 5,976 articles (Figure 1). To be included, articles had to meet the following inclusion criteria: 1) published in English, 2) conducted inside the U.S., 3) non-experimental research design to examine how diversion manifests outside of a research environment, 4) primary research (i.e., no reviews, reports, or other articles not presenting original, peer-reviewed research), 5) sample includes people currently or formerly using buprenorphine, and 6) provides evidence on scope of, motivation for, and/or outcomes of buprenorphine diversion. After conducting title and abstract reviews, 288 articles remained. These studies were uploaded into Covidence (<https://www.covidence.org>), an application for organizing reviews. For each article, two coauthors independently reviewed the full text. Where disagreements about inclusion occurred, a third coauthor weighed in and all three coauthors discussed until consensus was met.

Data charting and review

The following elements were extracted from the included articles: study aim, study design, data collection dates, location, sample description, sample size, definition of buprenorphine diversion, whether the study reports on scope of, motivation for, and outcomes of diversion, and the corresponding findings. Scope was operationalized as the prevalence of diversion

among the sample. Therefore, five articles were excluded from the scope syntheses where the sample consisted entirely of people who reported diversion, but these articles contributed evidence on motivations and outcomes (Carlson et al., 2020; Gryczynski et al., 2013; Gwin Mitchell et al., 2009; Kavanaugh & McLean, 2020; McLean & Kavanaugh, 2019). To be considered a motivation for or outcome of diversion, articles must establish temporality where motivation occurs before diversion and outcomes occur during the same recall period or after diversion. Some of the qualitative data extracted (e.g., sample description, definition, motivation, and outcome) were grouped according to inductively-derived categories and coded accordingly for synthesis purposes. The summary characteristics of included articles (Table 1) are presented in mutually exclusive categories defined by the authors of this review. As this was a scoping review, a quality assessment was not included (Tricco et al., 2018).

Results

Fifty-seven articles published between 2007 and 2021 met criteria for this scoping review (Appendix 2). Here, we report on 1) the summary characteristics of articles included in the review and the evidence on the 2) scope of diversion, 3) motivation for diversion, and 4) outcomes of diversion.

Summary characteristics of included articles

Most of the included studies (66.7%) involved data collection beginning prior to buprenorphine expansion provided by the 2016 CARA Act. Twenty-eight studies used a cross-sectional design, 15 were qualitative, eight were prospective cohorts, four were retrospective cohorts, and two employed mixed methods designs (Table 1).

Fifty-two studies (91.2%) sampled people who use drugs (PWUD); of these, 26 studied people with OUD, and nine studied people receiving MOUD. General samples of people who may or may not use drugs included pregnant women (Alexander et al., 2020), undergraduate students (Dart et al., 2014), individuals on probation and parole (Wish et al., 2012), and patients of pain management physicians (Guo et al., 2013). Two of the qualitative studies involved online discussion forum participants, one for people who use illicit drugs (Daniulaityte et al., 2015) and another specifically for people who use buprenorphine (Brown & Altice, 2014). Across the 42 quantitative studies included, sample sizes ranged from 12 to 45,695.

No consistent definition of diversion was found. Most (61.4%) studies defined buprenorphine diversion according to how the drug is obtained (e.g., “without a prescription”, “non-prescribed”, “from a friend or dealer”, “street-obtained”, “using, selling or sharing through extra-medical channels”). Nine articles defined buprenorphine diversion based on the purpose for use (e.g., for “non-medical” purposes, to use “not as prescribed,” or “to get high”), and four studies defined diversion by both source and purpose. Nine studies measured diversion based on drug screening results that were inconsistent with prescription status (i.e., testing positive for buprenorphine without a prescription, or drug screen did not detect expected amounts of prescribed buprenorphine). Finally, nine of the articles

did not explicitly define diversion; instead, the authors used phrases such as “diverted buprenorphine” or “illicit use of buprenorphine.”

Five of the studies examined illicit supplying of buprenorphine by participants while the remaining 52 examined diverted buprenorphine use (use without a prescription).

Evidence on scope of diversion

Of the 57 articles, 44 provided evidence on the scope of diversion (Table 2). The prevalence ranged from 0% of patients enrolled in buprenorphine treatment (DiPaula & Park, 2011; Tofighi et al., 2021) who used diverted buprenorphine to 100% of people with OUD who were not receiving MOUD using diverted buprenorphine (Monte et al., 2009; Tofighi et al., 2019), all in small (i.e., less than 100) studies with samples.

Variations in scope existed by type of sample and recall period. Sample description categories are mutually exclusive. The two cross-sectional studies with large samples (i.e., over 500) from the general population found that 5.9% of pregnant women reported current use of diverted buprenorphine and 1.4% of undergraduate students reported use in the past 3 months (Alexander et al., 2020; Dart et al., 2014). The remaining 42 articles reporting on scope sampled PWUD. Twenty-seven of these sampled PWUD who did not report OUD or current use of MOUD. In these studies, scope varied from 3.6% of people who inject drugs using diverted buprenorphine in the past month (Zhao et al., 2020) to 95.8% of long-term, drug-free, residential recovery participants doing so in the past 6 months (Walker et al., 2018), both in large, cross-sectional studies. PWUD with OUD provided evidence on the scope of diversion in 16 studies, with eight of these studies specifically sampling people initiating MOUD or supervised detoxification (Cicero et al., 2007; 2014; Cunningham et al., 2013; Hood et al., 2020; Monico et al., 2015; Schuman-Olivier et al., 2010; Smith et al., 2020; Tofighi et al., 2019). These rates ranged from 18.7% of a large sample of people with OUD initiating corrections-based treatment using diverted buprenorphine in the past month (Smith et al., 2020) to 100% of lifetime diversion in two small samples, one comprised of people admitted for inpatient detoxification (Tofighi et al., 2019) and one among non-treatment seeking individuals who reported diverting buprenorphine to others (Monte et al., 2009). Finally, four articles reported on scope of current diversion to others among people small or medium (i.e., 100–500 people) receiving MOUD in cohort studies, which ranged from 0% to 4.8% (Bachhuber et al., 2018; DiPaula & Park, 2011; Suzuki et al., 2017; Tofighi et al., 2021).

Evidence on motivation for diversion

Twenty-six articles provided evidence on motivations for using diverted buprenorphine (Table 3). Motivations fell into five categories: 1) to avoid withdrawal symptoms, 2) for self-treatment of OUD (as opposed to formal treatment), 3) to get high 4) for management of drug use and effects, and 4) when experiencing an inability or difficulty procuring drug of choice in order to prevent withdrawal symptoms (studies rarely reported motivations as mutually exclusive categories; Table 3).

Avoidance of withdrawal symptoms was presented as motivation in 20 articles. Treatment of OUD, with the goal of abstaining from other opioids, was offered as motivation in

18 articles where participants described buprenorphine diversion when unable to access treatment due to unavailability in their area, cost, waiting lists, or inability to adhere to requirements like daily dosing (Daniulaityte et al., 2012; Genberg et al., 2013; McLean & Kavanaugh, 2019; Monte et al., 2009; Silverstein et al., 2020; Smith et al., 2020; Sohler et al., 2013). A desire to avoid formal treatment also motivated study participants to use non-prescribed buprenorphine due to a negative previous experience, previous incorrect dosing (Daniulaityte et al., 2015; Schuman-Olivier et al., 2010), perceived stigma around disclosing their drug use, (Daniulaityte et al., 2012) or distrust of treatment providers (Brown & Altice, 2014). Some respondents reported self-efficacy to use buprenorphine to wean themselves off other opioids (Brown & Altice, 2014; Cicero et al., 2014).

“To get high” was a motivation for buprenorphine diversion in 13 studies where participants described preferring buprenorphine as their drug of choice, (Cicero et al., 2014) receiving a better high from it than other drugs (Cicero et al., 2018), and using it to boost their high from another drug (Walker et al., 2018; Wish et al., 2012). In seven of these studies, ‘to get high’ was the least commonly cited motivation (Carroll et al., 2018; Cicero et al., 2014; Daniulaityte et al., 2019; Genberg et al., 2013; Silverstein et al., 2019; Tsui et al., 2018), and two of these studies were conducted among incarcerated populations who were unable to procure other opioids (Monico et al., 2021; Wish et al., 2012).

In 12 articles, study participants disclosed using non-prescribed buprenorphine to manage their drug use and related effects. Drug use and related effects were managed in an effort to maintain themselves during work or social events (Cicero et al., 2018), avoid harms associated with illicit opioid use (Allen & Harocopos, 2016), take a break from other opioid use, or reduce opioid tolerance (Bazazi et al., 2011; Carroll et al., 2018; McLean & Kavanaugh, 2019). Managing other effects of opioid use such as relief from pain, anxiety, and depression were other reasons cited (Cicero et al., 2014; Schuman-Olivier et al., 2010).

Finally, in 11 articles, an inability or difficulty to procure the drug of choice drove buprenorphine diversion, operationalized as: buprenorphine was cheaper or easier to find than the drug of choice, trusted source of drugs was unavailable, diverting (reselling) buprenorphine funded procurement of a drug of choice (Allen & Harocopos, 2016; Carroll et al., 2018; Cicero et al., 2014; Daniulaityte et al., 2012; Monte et al., 2009).

Evidence on outcomes associated with buprenorphine diversion

Eighteen included articles provided evidence on the outcomes associated with use of diverted buprenorphine, which fell into six categories: 1) non-fatal overdose, 2) illicit opioid use, 3) drug treatment use, 4) attitudes about drug treatment, 5) involvement in the justice system, and 6) physical health. Findings from quantitative studies are listed in Table 4.

Two studies, both among individuals with OUD who reported non-prescribed buprenorphine use in the past six months, found statistically significant associations between buprenorphine diversion and reduced odds of non-fatal drug overdose. In one, more frequent buprenorphine use reduced the odds of non-fatal overdose (AOR 0.81; 95% CI 0.66, 0.98). (Carlson et al., 2020) In the other, people who used non-prescription buprenorphine on a near-daily

basis had a lower prevalence of overdose compared to people who used non-prescribed buprenorphine sporadically ($p = 0.023$) (Daniulaityte et al., 2019).

Findings on illicit use of non-buprenorphine opioids were mixed. One study showed a significant relationship between greater frequency of non-prescribed buprenorphine use and a lower frequency of heroin/fentanyl use ($\beta = -0.076$; 95% CI $-0.098, -0.053$) (Carlson et al., 2020). Additionally, in a qualitative study, participants reported that diverting buprenorphine helped them reduce their heroin consumption (Gwin Mitchell et al., 2009). Conversely, a study of syringe exchange program (SEP) attendees found no difference in current opioid use among individuals with a history of illicit buprenorphine use, compared to buprenorphine-naïve participants (AOR 0.47; 95% CI 0.07, 3.46) (Cunningham et al., 2013). Finally, a study among PWID found that non-medical buprenorphine use was associated with increased odds of non-medical methadone use (AOR 3.12; 95% CI 1.31, 7.47), both within the past 30 days (Zhao et al., 2020).

Three quantitative studies provided evidence on retention on treatment using MOUD in the past six months as an outcome associated with using diverted buprenorphine. There was no difference between individuals with and without a history of illicit buprenorphine use who attended a SEP (Cunningham et al., 2013). However, higher odds of retention were identified among individuals who diverted buprenorphine in a cohort ($p < 0.001$) (Hood et al., 2020) and a mixed-methods study (AOR 2.09; 95% CI 1.23, 3.65) (Monico et al., 2015). In qualitative studies, participants reported that positive experiences with diverted buprenorphine use made them aware of, more receptive to, or more prepared for drug treatment (Fox et al., 2015; Gryczynski et al., 2013; Gwin Mitchell et al., 2009; Monico et al., 2015; 2021; Silverstein et al., 2019; Tofighi et al., 2019).

Additionally, several articles examined attitudes toward drug treatment following diversion. Greater proportions of participants with diverted buprenorphine use, versus without, expressed interest in initiating treatment, (Fox et al., 2014) were willing to receive treatment in the future (Kenney et al., 2018), and considered drug treatment to be extremely or considerably important, compared to not, slightly, or moderately important (Smith et al., 2020). Qualitative studies described the impact of diverted buprenorphine use on physical health. In two studies, participants reported that use alleviated withdrawal symptoms (Fox et al., 2015; Gwin Mitchell et al., 2009). Similarly, participants in one qualitative study reported that buprenorphine diversion made them feel 'normal' or 'well' (Gwin Mitchell et al., 2009) while it resulted in achieving an unintentional high, feeling withdrawal symptoms, and losing consciousness for participants in three qualitative studies (Allen & Harocopos, 2016; Fox et al., 2015; McLean & Kavanaugh, 2019).

Finally, two studies examined involvement in the justice system as an outcome associated with diverted buprenorphine use and found no significant differences (Daniulaityte et al., 2019; Surratt et al., 2018).

Discussion

This scoping review offers a current, methodologically rigorous review of literature on three key elements of buprenorphine diversion—scope, motivations, and outcomes in the U.S. The review builds upon an existing body of literature, including earlier narrative reviews, which focused on one or more of the elements summarized in our review. Importantly, studies reported a low scope of diversion, less than 5%, among people receiving MOUD, with inability to access treatment as a motivating factor for *using* diverted buprenorphine, and a positive outcome of increased retention in treatment using MOUD associated with use of diverted buprenorphine. Taken together and consistent with previous review studies, our findings suggest that continued expansion of access to buprenorphine as a treatment for OUD could decrease buprenorphine diversion (Lofwall & Havens, 2012; Schuman-Olivier et al., 2010). First, because diversion is hardly observed among people receiving MOUD and second, because it could decrease the demand for diverted buprenorphine by increasing the number of people receiving MOUD through the healthcare system (Bachhuber et al., 2018; DiPaula & Park, 2011; Suzuki et al., 2017; Tofighi et al., 2021). Aligning with previous studies, our findings apply to correctional settings, where concerns about diversion are prominent, by suggesting that opioid misuse could be reduced if jails and prisons made MOUD more available (Gryczynski et al., 2021).

Issues presented by inconsistent definitions of diversion

The study highlights the importance of purposeful sampling and data collection methods, including clear definitions of diversion. Among the included studies, *diversion* is inconsistently defined and studied, highlighting the complexity of studying and interpreting its scope. The term diversion is used throughout the literature to mean both the illegal channeling of medication to those for whom the product was not prescribed *and* use of non-prescribed buprenorphine. The two-pronged (supply and demand) definition complicates people's understanding of the phenomenon. Diversion encompasses an economy of supply driven by those redirecting prescribed buprenorphine to others and demand driven by people who obtain buprenorphine illicitly for a variety of reasons. Of the studies reviewed, a majority defined the problem from the perspective of the person receiving diverted buprenorphine. In those studies, the percentage of those *obtaining* buprenorphine illicitly ranges from just 1.4% of undergraduate students to 100% among those with OUD not enrolled in MOUD treatment (Dart et al., 2014; Monte et al., 2009; Tofighi et al., 2019).

Only five studies looked at diversion from the *supply* side, that is among patients with OUD receiving MOUD and diverting to others, for which the highest reported rate of diversion was 4.7% (Suzuki et al., 2017). This low rate could reflect the difficulty in accurately measuring patient diversion. In MOUD clinics, determining whether a patient is diverting is a complex gestalt of drug testing results, discussion with patients, discussion with counseling or other health care team members, and patterns of behavior in a particular patient. Further, three of the five studies used drug screening to assess diversion; drug screening alone as a measure of diversion can be problematic. The complex nature of buprenorphine metabolism and kinetics can partially explain this difficulty. Dose, time of ingestion, body weight, and genetic polymorphisms all contribute to presence and quantity

of buprenorphine and buprenorphine metabolites in samples such as urine (Jamshidi et al., 2021). To date, there is no agreement as to what quantitative buprenorphine or metabolite level constitutes someone who is taking less buprenorphine than prescribed and therefore at risk for diverting buprenorphine. Furthermore, when objective evidence of diversion is lacking, prescribers may be hesitant to accuse patients of diversion in fear of compromising their therapeutic relationship.

Diversion highest among those without licit access

Despite inconsistencies in measuring buprenorphine diversion, our review does highlight patterns across categories of samples. Specifically, use of diverted buprenorphine was highest among people with OUD not receiving MOUD, 100% in two samples of people with OUD who were not being treated with MOUD at the time of assessment (Monte et al., 2009; Tofighi et al., 2019). This finding supports the conclusions of Chilcoat et al. (2019) and suggests that efforts to cull diversion could be focused on further increasing, rather than limiting access to MOUD (Lofwall & Havens, 2012).

Self-treatment as a prevalent motivation for buprenorphine diversion

In our scoping review, all 26 of the studies examining motivation for use of illicitly-obtained buprenorphine identified at least one of the following motivations: “to avoid withdrawal symptoms”, “treatment of OUD”, “management of drug use and its effects”, and “unable or difficult to obtain drug of choice.” Each of these motivations could be summarized as attempting self-treatment, suggesting that use of illicitly-obtained buprenorphine is driven by either a desire or need to engage in an alternative to formal treatment. Further, each of these motivations is related to a goal of avoiding withdrawal symptoms, which could be precipitated by several circumstances, including 1) managing ongoing substance use (i.e., to avoid feeling high for a period or achieve intermittent periods of abstinence from another drug), 2) a deliberate effort to permanently stop using opioids (i.e., self-treatment), or 3) an inability to access a drug of choice (possibly from a trusted source). Future studies that identify avoiding withdrawal symptoms as motivation for buprenorphine diversion could seek to uncover the underlying reason for experiencing withdrawal to discern whether the drug is being used to manage ongoing drug use or to support long-term treatment and recovery from drug use. Additionally, future reviews could expand on our identification of motivations by examining their weight to identify the strongest motivators.

Outcomes associated with buprenorphine diversion not concerning

While not definitive, outcomes associated with using diverted buprenorphine trend toward positive outcomes. One study found higher rates of non-medical methadone use in patients who used non-medical buprenorphine which is concerning because of methadone’s higher risk profile, but the ultimate significance is unclear (Modesto-Lowe et al., 2010). Limited evidence of harms resulting from diverted buprenorphine use was found but a greater understanding of negative experiences with self-treatment or self-management might inform strategies to increase people’s willingness to engage in medically-directed treatment. This review did not specifically examine rates of fatal or non-fatal overdoses involving buprenorphine because of its well-established low risk compared to other full agonist opioids (Boothby & Doering, 2007). Overwhelmingly, studies included in this review

suggested positive outcomes were associated with buprenorphine diversion such as lower rates of non-fatal opioid overdose, more positive attitudes toward MOUD treatment, and similar rates of retention in MOUD treatment. Use of other illicit opioids and involvement in the justice system did not differ significantly between individuals who used diverted buprenorphine versus those who did not use diverted buprenorphine, based on included studies. To this end, some U.S. jurisdictions have decriminalized possession of diverted buprenorphine, seeing it as potential harm reduction and overdose prevention strategy and a way to decriminalize OUD, reduce stigma toward MOUD, and compensate for a gap in MOUD treatment capacity (Buttram et al., 2021; del Pozo et al., 2020). Findings from this review could be used to identify datapoints to evaluate the effects of these policy changes from both public health and criminal justice perspectives.

Limitations

There are limitations of this scoping review. Per the methodology of scoping reviews, we erred on the side of sensitivity over specificity to include all literature on the topic of buprenorphine diversion. However, studies that contradict our findings may exist and many included recruited convenience samples or small sample sizes. To examine this topic further, we recommend a systematic review or meta-analysis of high-quality studies with consistent generalizability for each of the sub-topics included in this review (i.e., scope, motivations, and outcomes). Next, due to the exploratory nature of scoping reviews, our study erred on the side of sensitivity over specificity. Although we intended to limit inclusion criteria to articles that specified diversion, we had to include articles examining buprenorphine misuse, as diversion was described but not necessarily named. This scoping review was only intended to identify motivations, not measure their relative pervasiveness as was done in a previous review (Chilcoat et al., 2019). Therefore, conclusions cannot be drawn about the relative impact of the identified motivations on diversion rates. Finally, in our assessment of the evidence on outcomes associated with diversion, we included studies where both diversion and the outcome were measured in the same recall period. While the literature supports categorization of these variables as outcomes (Lofwall & Walsh, 2014), it is possible that the observed outcomes could have been predictors or correlates of outcomes rather than outcomes themselves.

Conclusions

This review suggests that the scope of diversion among those formally receiving MOUD is between 0% and 5%. Further, the motivations for use of illicitly-obtained buprenorphine related to treatment and management of drug use, along with the finding that those with OUD who are using illicitly-obtained buprenorphine may be more inclined to enter formal treatment at some point in the future, indicate that increased availability of buprenorphine treatment could effectively *reduce* demand for diverted buprenorphine. One caveat is that expanded prescribing ability does not necessarily mean that all barriers to formal treatment will be addressed. Due to issues such as cost and stigma, illicitly-obtained buprenorphine could remain a preferred mode of treatment or management for some people with OUD unless and until these barriers are addressed. Thus, future research should focus on addressing barriers to treatment.

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Appendix 1.: Preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR) checklist.

Section	Item	Prisma-ScR checklist item	Reported on page #
Title			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	4
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	4–5
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	5
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	5
Information sources	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	5
Selection of sources of evidence	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	5
Data charting process	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	6
Critical appraisal of individual sources of evidence	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	N/A
Summary measures	13	Not applicable for scoping reviews.	N/A
Synthesis of results	14	Describe the methods of handling and summarizing the data that were charted.	6
Risk of bias across studies	15	Not applicable for scoping reviews.	N/A

Section	Item	Prisma-ScR checklist item	Reported on page #
	16	Not applicable for scoping reviews.	N/A
RESULTS			
Selection of sources of evidence	17	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Figure 1
Characteristics of sources of evidence	18	For each source of evidence, present characteristics for which data were charted and provide the citations.	6–7
Critical appraisal within sources of evidence	19	If done, present data on critical appraisal of included sources of evidence (see item 12).	N/A
Results of individual sources of evidence	20	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	4–6
Synthesis of results	21	Summarize and/or present the charting results as they relate to the review questions and objectives.	Tables 1–4
Risk of bias across studies	22	Not applicable for scoping reviews.	N/A
Additional analyses	23	Not applicable for scoping reviews.	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	11
Limitations	25	Discuss the limitations of the scoping review process.	13–14
Conclusions	26	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	14
FuNDING			
Funding	27	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	14

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Appendix 2.: Full list of 57 included studies

First author, date	Data collection period (years)	Study design	Sample type	Sample Size	Reports on scope	Reports on motivations	Reports on outcomes
Alexander, 2020	2016–2018	Cross sectional	General population	898	Yes	No	No
Allen, 2016	2013–2015	Qualitative	PWUD	42	No	Yes	Yes
Applewhite, 2020	2018	Cross sectional	PWUD	103	Yes	No	No
Bachhuber, 2018	2011–2014	Retrospective cohort	PWUD	124	Yes	No	No
Bazazi, 2011	2009	Cross sectional	PWUD	100	Yes	Yes	No
Brown, 2014	2010–2012	Qualitative	Online discussion post forums	121 discussion board threads	No	Yes	No

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First author, date	Data collection period (years)	Study design	Sample type	Sample Size	Reports on scope	Reports on motivations	Reports on outcomes
Butler, 2018	2015	Cross sectional	PWUD	45695	Yes	No	No
Buttram, 2020	2018–2019	Cross sectional	PWUD	324	Yes	No	No
Carlson, 2020	2017–2018	Cross sectional	PWUD	356	Yes	Yes	Yes
Carroll, 2018	2016	Cross sectional	PWUD	128	Yes	Yes	No
Cicero, 2007	2005–2007	Cross sectional	People with OUD	799	Yes	No	No
Cicero, 2014	2008–2013	Cross sectional	People with OUD	10568	Yes	Yes	No
Cicero, 2018	2016	Cross sectional	People with OUD	303	Yes	Yes	No
Cunningham, 2013	2004–2009	Prospective cohort	People with OUD	87	Yes	No	Yes
Daniulaityte, 2012	2009–2010	Mixed Methods	PWUD	396	Yes	Yes	No
Daniulaityte, 2015	2005–2013	Qualitative	Online discussion post forums	404 posts	No	Yes	No
Daniulaityte, 2019	2017–2018	Cross sectional	People with OUD	356	No	Yes	Yes
Dart, 2014	2009–2011	Cross sectional	General population	13514	Yes	No	No
DiPaula, 2011	2012–2013	Prospective cohort	People with OUD	12	Yes	No	No
Fox, 2014	2011	Cross sectional	PWUD	102	Yes	No	Yes
Fox, 2014	2013	Cross sectional	PWUD	138	Yes	No	No
Fox, 2015	2012–2013	Qualitative	People on MOUD	21	Yes	No	Yes
Genberg, 2013	2008	Cross sectional	PWUD	602	Yes	Yes	No
Gryczynski, 2013	Not Listed	Qualitative	People with OUD	80	Yes	Yes	Yes
Guo, 2013	2008–2011	Cross sectional	General population	20929	Yes	No	Yes
Gwin Mitchell, 2009	2004–2007	Qualitative	PWUD	22	Yes	Yes	Yes
Hood, 2020	2017	Prospective cohort	People on MOUD	146	Yes	No	Yes
Kavanaugh, 2020	2018	Qualitative	PWUD	40	Yes	Yes	No
Kenney, 2018	2017	Cross sectional	People with OUD	338	Yes	Yes	Yes
Khosla, 2011	2005–2006	Cross sectional	PWUD	1320	Yes	No	No
Ling, 2019	2015–2018	Prospective cohort	People on MOUD	533	Yes	No	No

First author, date	Data collection period (years)	Study design	Sample type	Sample Size	Reports on scope	Reports on motivations	Reports on outcomes
Manubay, 2015	Not Listed	Cross sectional	People with OUD	205	Yes	No	No
McLean, 2019	2018	Qualitative	PWUD	20	Yes	Yes	Yes
Mitchell, 2015	Not Listed	Prospective cohort	People with OUD	300	Yes	No	No
Monico, 2015	Not Listed	Mixed Methods	People on MOUD	300	Yes	Yes	Yes
Monico, 2021	Not Listed	Qualitative	People with OUD	26	Yes	Yes	Yes
Monte, 2009	2007–2018	Cross sectional	PWUD	49	Yes	Yes	Yes
Otachi, 2020	2018–2019	Cross sectional	PWUD	324	Yes	No	Yes
Park, 2018	2016	Cross sectional	PWUD	203	Yes	No	Yes
Schuman-Olivier, 2010	2009	Cross sectional	People on MOUD	129	Yes	Yes	Yes
Silverstein, 2019	2018–2019	Qualitative	People with OUD	63	No	Yes	Yes
Silverstein, 2020	2017–2018	Qualitative	People on MOUD	65	No	Yes	Yes
Smith, 2007	2003–2005	Cross sectional	PWUD	103 million calls	Yes	No	No
Smith, 2019	2017	Cross sectional	People with OUD	478	Yes	Yes	No
Smith, 2020	2016–2018	Cross sectional	People with OUD	12007	Yes	Yes	Yes
Sohler, 2013	2010	Qualitative	PWUD	38	No	Yes	No
Surratt, 2018	2012–2015	Prospective cohort	People with OUD	172	Yes	No	Yes
Suzuki, 2017	2013–2014	Retrospective cohort	People on MOUD	168	Yes	No	No
Tofighi, 2014	2012–2013	Cross sectional	People on MOUD	91	Yes	No	No
Tofighi, 2019	2018	Qualitative	People with OUD	23	Yes	No	Yes
Tofighi, 2021	2020	Retrospective cohort study	People on MOUD	78	Yes	No	No
Tsui, 2018	2015	Cross sectional	PWUD	487	Yes	Yes	No
Walker, 2018	2015–2016	Cross sectional	People with OUD	896	Yes	Yes	Yes
Walley, 2019	2013–2015	Retrospective cohort	PWUD	2916	Yes	No	No
Wiegand, 2016	2011–2013	Retrospective cohort	PWUD	unknown	Yes	No	No
Wish, 2012	2010	Qualitative	General population	15	No	Yes	No
Zhao, 2020	2011–2013	Cross sectional	PWUD	777	Yes	No	Yes

Abbreviations: MOUD = medications for opioid use disorder; OUD = opioid use disorder; PWUD = people who use drugs

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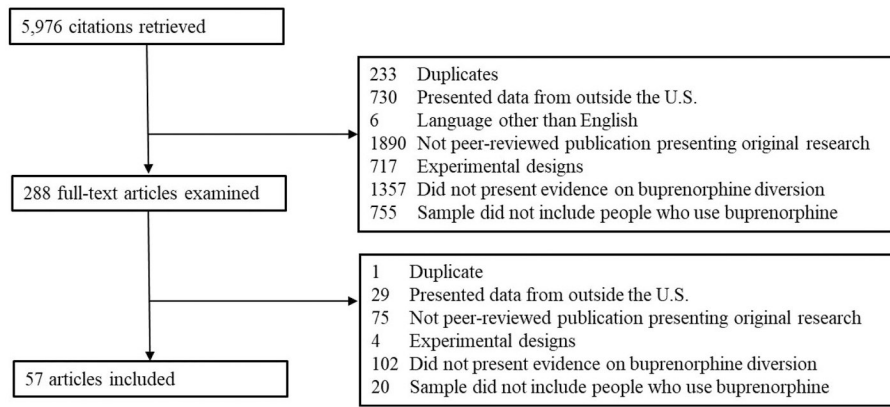


Figure 1. PRISMA diagram for the scoping review on the scope of, motivations for, and outcomes of buprenorphine diversion in the United States.

Table 1.

Summary characteristics of articles included in the scoping Review on the scope of, motivations for, and outcomes of buprenorphine diversion in the united States (N = 57).

Article Characteristics	Number of studies (%)
When data collection began	
Before 2016	38 (66.7)
2016 or later	19 (33.3)
Study Design	
Cross sectional	28 (49.1)
Qualitative	15 (26.3)
Prospective cohort	8 (14.0)
Retrospective cohort	4 (7.0)
Mixed methods	2 (3.5)
Sample Population	
General population	4 (7.0)
Pregnant women	1 (1.8)
undergraduate students	1 (1.8)
People on probation or parole	1 (1.8)
Pain management patients	1 (1.8)
People who use drugs	52 (91.2)
People with OUD	26 (45.6)
People Receiving MOUD	9 (15.8)
Online discussion forum posts	2 (3.5) *
Quantitative Sample Sizes (N = 42)	
<100	4 (9.5)
100–499	24 (42.1)
500–999	6 (14.3)
1000–5000	3 (7.1)
>10,000	5 (11.9)
How “diversion” is defined/assessed in data collection	
Based on source (Without a prescription/non-prescribed; from the street, a friend or dealer; “not prescribed to you”; “street buprenorphine” or “street-purchased buprenorphine”; “using, selling or sharing through extra-medical channels”)	35 (61.4)
Based on intended use (for non-medical/non-therapeutic use, not as prescribed, to relax, get high, or come down; “in a non-treatment context”)	9 (15.8)
Drug screen inconsistent with prescription status	9 (15.8)
Not defined other than “diverted buprenorphine”, “obtained illicitly”, “illicit use of buprenorphine”, or “illicit buprenorphine”	9 (15.8)

* One of the studies using web-based discussion boards specifically focused on people who use drugs.

Table 2.

Sample type and recall period for studies reporting scope of buprenorphine diversion in the united States, in ascending order by scope.

First author, date	Sample type	Scope (%)	Recall period
DiPaula, 2011	People receiving MOUD	0.0	Current
Tofighi et al., 2021	People receiving MOUD	0.0	Current
Dart et al., 2014	General population	1.4	Past 3 months
Bachhuber et al., 2018	People receiving MOUD	1.6	Current
Zhao et al., 2020	PWUD	3.6	Past month
Suzuki et al., 2017	People receiving MOUD	4.8	Current
Khosla, 2011	PWUD	5.8	Past 6 months
Alexander et al., 2020	General population	5.9	Current
Walley, 2009	PWUD	5.9	Current
Applewhite et al., 2020	PWUD	6.8	Current
Butler et al., 2018	PWUD	7.7	Past month
Daniulaityte et al., 2012	PWUD	7.8	Lifetime
Genberg et al., 2013	PWUD	9.0	Past 3 months
Smith et al., 2020a	People with OUD	18.7	Past month
Fox et al., 2015	People with OUD	19.0	Lifetime
Otachi et al., 2020	PWUD	20.8	Past 3 months
Smith et al., 2020b	PWUD	21.8	Past month
Fox et al., 2014b	PWUD	22.0	Lifetime
Smith et al., 2020b	PWUD	26.2	Past 12 months
Park et al., 2018	PWUD	26.6	Past 6 months
Mitchell et al., 2015	People with OUD	28.0	Current
Cicero et al., 2014	People with OUD	30.0	Past month
Ling et al., 2019	People with OUD	31.6	Lifetime
Butler, 2018	PWUD	32.2	Past month
Cicero et al., 2007	People with OUD	33.0	Past month
Hood et al., 2020	People with OUD	33.0	Current
Cunningham et al., 2013	People with OUD	34.5	Lifetime
Alexander et al., 2020	PWUD	37.0	Current
Carroll et al., 2018	PWUD	38.0	Past 2 months
Manubay et al., 2015	People with OUD	40.5	Lifetime
Bazazi et al., 2011	PWUD	41.0	Past month
Guo et al., 2013	PWUD	41.9	Current
Tsui et al., 2018	PWUD	45.0	Lifetime
Monico et al., 2015	People with OUD	45.3	Past month
Lofwall & Havens, 2012	PWUD	46.5	Past 6 months
Surratt et al., 2018	People with OUD	47.0	Past month
Buttram and Surratt, 2020	PWUD	48.9	Past 3 months
Schuman-Oliver, et. al., 2010	People with OUD	49.0	Past 3 months

First author, date	Sample type	Scope (%)	Recall period
Smith et al., 2019	PWUD	52.1	Past 12 months
Kenney et al., 2017	People with OUD	53.5	Lifetime
Fox et al., 2014a	PWUD	55.9	Lifetime
Lofwall & Havens, 2012	PWUD	70.1	Lifetime
Carroll et al., 2018	PWUD	73.0	Lifetime
Bazazi et al., 2011	PWUD	76.0	Lifetime
Kenney et al., 2018	People with OUD	78.1	Past month
Walker et al., 2018	PWUD	92.9	Lifetime
Walker et al., 2018	PWUD	95.8	Past 6 months
Monte et al., 2009	People with OUD	100.0	Lifetime
Tofighi et al., 2019	People with OUD	100.0	Lifetime

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Table 3. Motivations for buprenorphine diversion in the united States, by category, and total number of articles presenting evidence for each category¹.

First author, date	Avoid withdrawal symptoms	Self-treatment of OUD	To get high	Management of drug use and effects	Unable or difficult to procure drug of choice
Allen & Harocopos, 2016	X	X		X	X
Bazazi et al., 2011	X	X	X	X	X
Brown & Altice, 2014		X		X	
Carlson et al., 2020	X				
Carroll et al., 2018	X	X	X	X	X
Cicero et al., 2014	X	X	X	X	X
Cicero et al., 2018	X	X	X	X	X
Daniulaityte et al., 2012	X	X	X	X	X
Daniulaityte et al., 2015	X			X	
Daniulaityte et al., 2019	X		X		
Genberg et al., 2013	X	X	X		
Gryczynski et al., 2013	X	X			
Mitchell et al., 2009	X	X		X	
Kavanaugh & McLean, 2020	X	X	X	X	X
McLean & Kavanaugh, 2019	X	X			
Monico et al., 2015	X	X			
Monico et al., 2021			X	X	X
Monte et al., 2009	X				X
Schuman-Olivier et al., 2010		X			
Silverstein et al., 2019	X	X	X		X
Silverstein et al., 2020		X			
Smith et al., 2020		X			
Sohler et al., 2013	X	X		X	
Tsui et al., 2018	X		X		
Walker et al., 2018			X		
Wish et al., 2012	X		X		X
Total number of studies	20	18	13	12	11

¹Studies rarely reported mutually exclusive motivations.

Table 4. Outcomes of buprenorphine diversion in the united States, provided by quantitative studies.

Outcome	Indicator	Measure	First author, date
Non-fatal overdose	Non-fatal overdose, past 6 months	AOR 0.81 (95% CI 0.66, 0.98)	Carlson et al., 2020 ^a
	Non-fatal-overdose, past 6 months	p = 0.023	Daniulaityte et al., 2019 ^b
Illicit opioid use	Frequency of heroin/fentanyl use, past 6 months	Beta -0.076 (95% CI -0.098, -0.053)	Carlson et al., 2020 ^a
	Current opioid use	AOR 0.47 (95% CI 0.07, 3.46)	Cunningham et al., 2013
	Nonmedical methadone use, past 30 days	AOR 3.12 (95% CI 1.31, 7.47)	Zhao et al., 2020
	Retention in MOUD, past 6 months	AOR 2.92 (95% CI 0.95, 8.91)	Cunningham et al., 2013
Treatment use	Retention in MOUD, past 6 months	p < 0.001	Hood et al., 2020
	Retention in MOUD, past 6 months	AOR 2.09 (95% CI 1.23, 3.65)	Monico et al., 2015
	Interest in initiating buprenorphine treatment	p = 0.03	Fox et al., 2014
Attitudes about drug treatment	Willingness to receive buprenorphine treatment in the future	p = 0.025	Kenney et al., 2018
	Consider drug treatment to be extremely or considerably important (versus not, slightly, or moderately)	p = 0.001	Smith et al., 2020
Involvement in justice system	Arrest within 3 months of release from incarceration	AOR 1.01 (0.99, 1.02)	Surratt et al., 2018 ^c
	Incarceration, past 6 months	p = 0.901	Daniulaityte et al., 2019 ^b

Unless otherwise noted, reference group is no diverted buprenorphine use.

^a Association with frequency of non-prescribed buprenorphine use.

^b Compares intense non-prescribed buprenorphine use to low non-prescribed buprenorphine use.

^c Association with days of illicit buprenorphine use.