Drug and Alcohol Dependence Reports 4 (2022) 100090

Contents lists available at ScienceDirect

Drug and Alcohol Dependence Reports

journal homepage: www.elsevier.com/locate/dadr

The introduction of a novel formulation of buprenorphine into organized health systems☆,☆☆

William Mullen[a,*], Michaela Hedberg[a], Brian Gadbois[b], Christian Heidbreder[a]

[a] Indivior, Inc., Richmond, VA, USA
[b] BoardPrep Recovery, Tampa, FL, USA

ARTICLE INFO

Keywords:
Opioid use disorder
Medication-assisted treatment
Medication for opioid use disorder
Buprenorphine, BUP-XR

ABSTRACT

Background: Effective medications for opioid use disorder (MOUD) are underutilized. This exploratory study used real-world data to analyze US distribution patterns of buprenorphine extended-release (BUP-XR) within organized health systems (OHS), including the Veterans Health Administration (VHA), Indian Health Service (IHS), criminal justice system (CJS), and integrated delivery networks (IDNs).

Methods: National BUP-XR distribution data within each OHS were available from WNS Global Services and were evaluated from July 2019 through July 2020. BUP-XR distribution data by OHS subtype (VHA, IHS, CJS, IDN) and state were aggregated and reported.

Results: The total distribution of BUP-XR increased from 6,721 units in the second half of 2019 (H2'19) to 12,925 in the first half of 2020 (H1'20). OHS distribution increased from H2'19 to H1'20 in every subtype but was primarily driven by IDN distribution growth. IDNs accounted for 73% of total units in H2'19 and continued to grow in H1'20. In H1'20, IDNs accounted for 78%, VHA for 12%, CJS for 6%, and IHS for 4%. IDN distribution for BUP-XR increased from 4,911 to 10,100 units, showing the highest growth rate of 106% within all OHS subtypes. The states with the highest total BUP-XR distribution over the 12-month period were Massachusetts (4,534), Pennsylvania (3,773), and California (1,866).

Conclusions: Overall distribution of BUP-XR, as a treatment option for OUD, is increasing; however, access to MOUD varies greatly across OHS subtypes and geography. Identifying and overcoming barriers to appropriate MOUD use is critical in addressing the opioid crisis.

1. Introduction

The epidemic of opioid misuse, abuse, and addiction that took root in the United States in the 1990s continues to the present day (2021). In 2020, an estimated 9.5 million Americans aged 12 or older misused opioids, 2.7 million met criteria for opioid use disorder (OUD), and only 798,000 received treatment for opioid misuse, including 278,000 with a past-year OUD diagnosis (2021). The predicted provisional number of opioid overdose deaths in the US increased to 71,238 in the 12-month period ending in December 2021, up from 57,834 in 2020 (CDC, 2022).

Despite growing evidence supporting the benefits of medications for OUD (MOUD; i.e., buprenorphine, methadone, and naltrexone), these treatments are underutilized (National Institute on Drug Abuse, 2018; National Academies of Sciences, 2019; National Institute on Drug Abuse 2021). Primary barriers to accessing MOUD include lack of patient demand, time constraints in practice, insurance and other reimbursements, resistance from staff, limited institutional support, and poor access to behavioral health services (Jones and McCance-Katz, 2019). Additionally, supply barriers include an inadequate number of providers certified to prescribe buprenorphine, as well as providers not utilizing their certification or prescribing substantially lower than the authorized waiver patient limit (Huhn and Dunn, 2017; Jones and McCance-Katz, 2019). Among the underlying issues, some physicians have a negative perception of buprenorphine stemming from potential diversion concerns (Huhn and Dunn, 2017; National Academies of Sciences, 2019). This lack of access results in a substantial treatment gap—in 2020 only 11.2% of people aged 12 or older with a past-year OUD received MOUD in the past year for opioid misuse (2021).

Long-acting injectable (LAI) formulations of MOUD have recently become available in the United States. Buprenorphine extended-release

☆ **Funding:** This work was supported by Indivior, Inc., North Chesterfield, VA, USA.
☆☆ **Role of the sponsor:** This research and manuscript were funded by Indivior, Inc., North Chesterfield, VA, USA.
* **Corresponding author at:** Associate Director for Real World Evidence, Indivior, Inc. 10710 Midlothian Turnpike, North Chesterfield, Virginia, USA.
E-mail addresses: William.mullen1@indivior.com (W. Mullen), michaela.hedberg@Indivior.com (M. Hedberg), brian.gadbois@boardpreprecovery.com (B. Gadbois), Christian.Heidbreder@indivior.com (C. Heidbreder).

https://doi.org/10.1016/j.dadr.2022.100090
Received 7 March 2022; Received in revised form 28 July 2022; Accepted 29 July 2022

(BUP-XR; also referred to as RBP-6000 or SUBLOCADE® [Indivior, Inc., North Chesterfield, VA]) is a monthly subcutaneous injection of buprenorphine that was approved by the FDA in November 2017 to treat adults with moderate to severe OUD. The BUP-XR development program leveraged knowledge of the relationship between buprenorphine plasma levels, whole brain mu-opioid receptor occupancy (MOR), and the key clinical pharmacodynamic effects of withdrawal suppression and opioid blockade, based on sublingual dosing studies. Population pharmacokinetics analyses (Laffont et al., 2016; Nasser et al., 2014) and an opioid blockade study (Nasser et al., 2016) showed that the minimum threshold plasma concentration of buprenorphine needed to effectively block the subjective drug-liking effects of a full opioid agonist such as hydromorphone was 2 ng/mL, which translated into at least 70% MOR occupancy in the brain for the entire 1-month period. In pivotal Phase III trials, with two active dose regimens (300/300 mg [6×300 mg] and 300/100 mg [2×300 mg then 4×100 mg]), BUP-XR was shown to produce significantly higher percentage abstinence and treatment success versus placebo (Haight et al., 2019). BUP-XR was also shown to be safe and well tolerated compared with participants who received individual counseling and placebo. Participants who received BUP-XR for up to 12 months experienced improvement in health-related quality of life, health status, treatment effectiveness as assessed by the four domains (substance use, health, lifestyle, community) of the Treatment Effectiveness Assessment tool and high medication satisfaction (Ling et al., 2019). These improvements were sustained over the study period, suggesting that BUP-XR facilitates long-term engagement of life activities that reflect recovery (Ling et al., 2020). A recent 12-month prospective open-label trial in Australia also showed that retention following BUP-XR treatment at 24 and 48 weeks was 86% and 75%, respectively (Farrell et al., 2022). The odds of use of all illicit substances except for cannabis use decreased significantly with time retained in treatment. Significant increases in employment, quality of life and treatment satisfaction were also observed together with a significant decline in pain and a significant reduction in the odds of moderate-severe depression for every 4 weeks retained in treatment.

BUP-XR is available only through the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) program (2020), which manages known or potential risks associated with BUP-XR and is required by the FDA to ensure that its benefits outweigh the risks (US Food and Drug Administration, 2020; Buprenorphine [package insert] 2021). Common side effects of buprenorphine include gastrointestinal (constipation, nausea, vomiting), headache, and tiredness (2021a). In addition to the buprenorphine side effects mentioned previously for buprenorphine, common side effects of BUP-XR also include injection site pain, injection site itching, and erythema (Indivior, 2021). BUP-XR must be administered by a healthcare professional to treat adults with moderate to severe OUD and have received treatment with a buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days. BUP-XR is received via a “closed distribution system,” whereby the healthcare provider or entity orders and administers treatment (inSupport, 2021b). This process mitigates risk of diversion, which has been reported with other formulations where patients can order medication from an outpatient pharmacy and self-administer unsupervised (inSupport, 2021a).

In fact, a survey including 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, showed that 58% of survey participants reported a history of diverted buprenorphine use (Cicero et al., 2018). 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%). Most (81%) of these participants indicated they would prefer using prescribed buprenorphine, if available. These findings were confirmed by a narrative review examining the rates and motives for use of illicit buprenorphine in the United States (Chilcoat et al., 2019). Findings from the 17 included studies suggested the majority of study participants using illicit buprenorphine did so to manage opioid withdrawal symptoms or achieve/maintain abstinence from other opioids.

Organized health systems (OHS) are entities with certification from the US Drug Enforcement Administration (DEA) to receive BUP-XR and can include the Veterans Health Administration (VHA), Indian Health Service (IHS), criminal justice system (CJS), and integrated delivery networks (IDNs) (2021b). All OHS pharmacies or providers must undergo REMS certification to receive BUP-XR from a specialty distributor (2021a, b).

IDNs are considered an important and growing part of the US healthcare system (Martin, 2018). IDNs are groups of different, but affiliated, types of healthcare facilities, such as a hospital with a linked outpatient clinic. There are estimated to be more than 1,000 IDNs across the United States, varying in size (large IDNs own 80 or more facilities) and location (Martin, 2018).

This analysis was conducted to assess the national distribution patterns of BUP-XR across OHS subtypes and to evaluate the specific areas within OHS where BUP-XR is being ordered for the OUD patient population. Knowledge of distribution patterns can help to identify systemic and geographic barriers to MOUD access and to formulate possible solutions.

2. Methods

2.1. Data Source

National BUP-XR distribution data within OHS were available from WNS Global Services, Indivior’s contracted data aggregator. All data were de-identified and did not contain protected health information. Data were obtained from REMS-certified partners.

2.2. Outcomes

BUP-XR distribution is reported as unit volume and by the 4 OHS subtypes: VHA, IHS, CJS, and IDNs. BUP-XR distribution within each OHS subtype was also aggregated and evaluated for each US state. Outcomes were evaluated over a 12-month period, July 2019 through July 2020.

3. Results

The total distribution of BUP-XR increased from 6,721 units in H2’19 to 12,925 in H1’20. OHS distribution from H2’19 to H1’20 increased in every subtype but was primarily driven by distribution growth in IDNs (**Fig. 1**). IDNs accounted for 73% of total units in H2’19 and continued to grow in H1’20. In H1’20, IDNs accounted for 78% (10,100 units), VHA for 12% (1,564 units), CJS for 6% (732 units), and IHS for 4% (529 units) (**Fig. 2**). IDN distribution for BUP-XR increased from 4,911 units to 10,100 units, showing the highest growth rate of 106% within all OHS (**Fig. 3**).

VHA distribution of BUP-XR increased from 965 units in H2’19 to 1,564 units in H1’20, which equates to 62% growth over the previous year. IHS distribution of BUP-XR increased from 396 to 529 units (34% growth) and CJS distribution of BUP-XR increased from 449 units to 732 units (63% growth) (**Fig. 4**).

The states with the highest total distribution of BUP-XR over the 12-month period were Massachusetts, Pennsylvania, and California (**Supplementary Fig. S1**). The top states for CJS distributions were New Hampshire (479 units), New Jersey (421 units), and Kentucky (98 units); IHS distributions: California (369 units), Alaska (277 units), and Oregon (92 units); IDN distributions: Massachusetts (4,502 units), Pennsylvania (3,626 units), and California (1,283 units); and VHA distributions: Florida (520 units), Washington (296 units), and California (214 units) (**Fig. 5**).

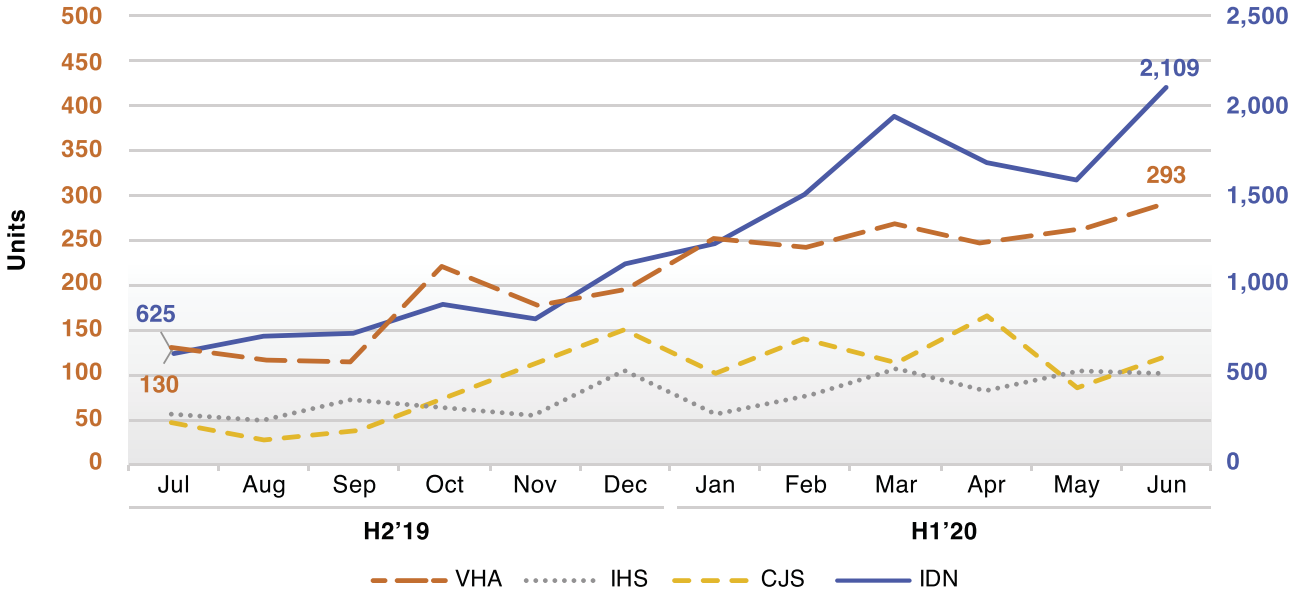

Fig. 1. Trend of monthly BUP-XR distribution by OHS subtype, H2'19 to H1'20. CJS, criminal justice systems; IDN, integrated delivery network; IHS, Indian Health Services; OHS, organized health systems; VHA, Veterans Health Administration.

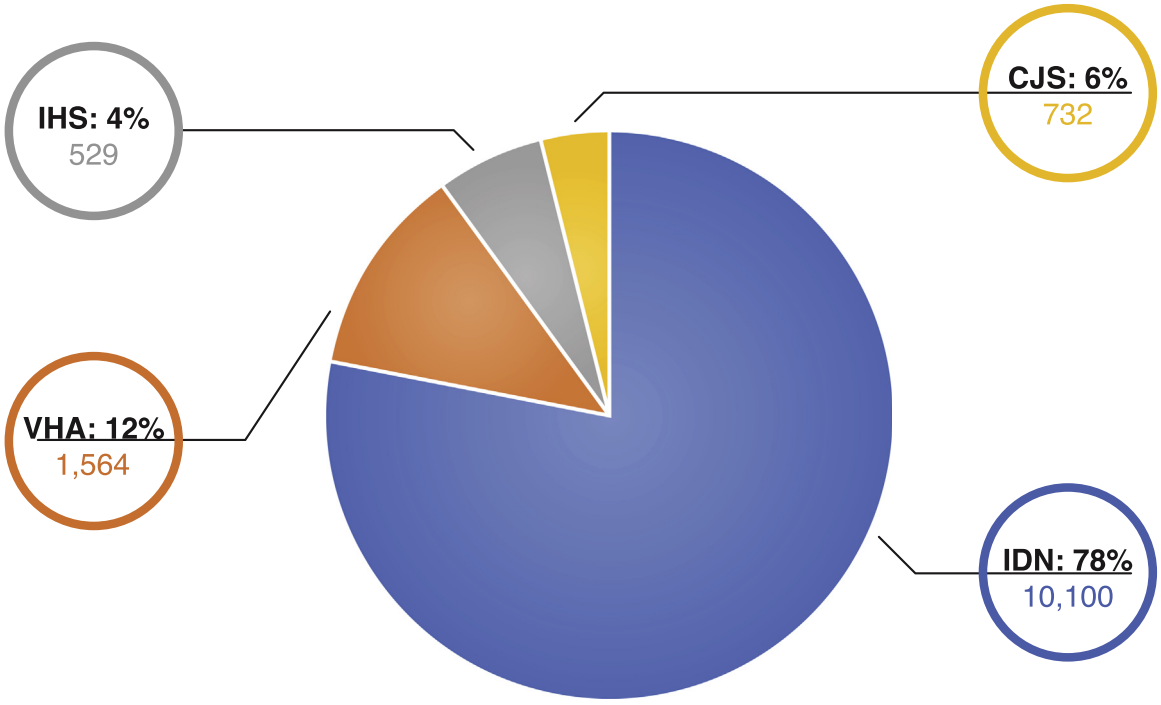

Fig. 2. Proportion of total BUP-XR distribution by OHS subtype, H1'20. CJS, Criminal Justice Systems; IDN, Integrated Delivery Network; IHS, Indian Health Services; OHS, organized health systems; VHA, Veterans Health Administration.

4. Discussion

Overall, the distribution of BUP-XR as a treatment option for patients with OUD is increasing within the OHS but occurring at different rates across subtypes. However, numerous barriers remain within each OHS subtype that impede access to MOUD, despite evidence for their effectiveness in reducing morbidity and mortality from OUD, increasing treatment retention, and improving the well-being of patients with OUD (National Academies of Sciences, 2019).

The results of our study show that IDNs contributed a significant percentage of the overall national distribution of BUP-XR and demonstrated higher BUP-XR growth over time compared with other OHS subtypes (Clarivate, 2020). This growth may be attributable to the proliferation of IDNs as a preferred service model in regional healthcare, along with increased federal and state efforts to find innovative ways to implement MOUD payment and delivery system reforms into existing integrated care models (2020; Townley and Dorr, 2017). In 2015, the Centers for Medicare & Medicaid Services (CMS) released guidance encouraging states to leverage section 1115 of the Social Security Act, through which demonstration waivers are used to incentivize states to integrate OUD treatment, by offering flexibility and federal funding for costs that CMS might not otherwise match (Townley and Dorr, 2017).

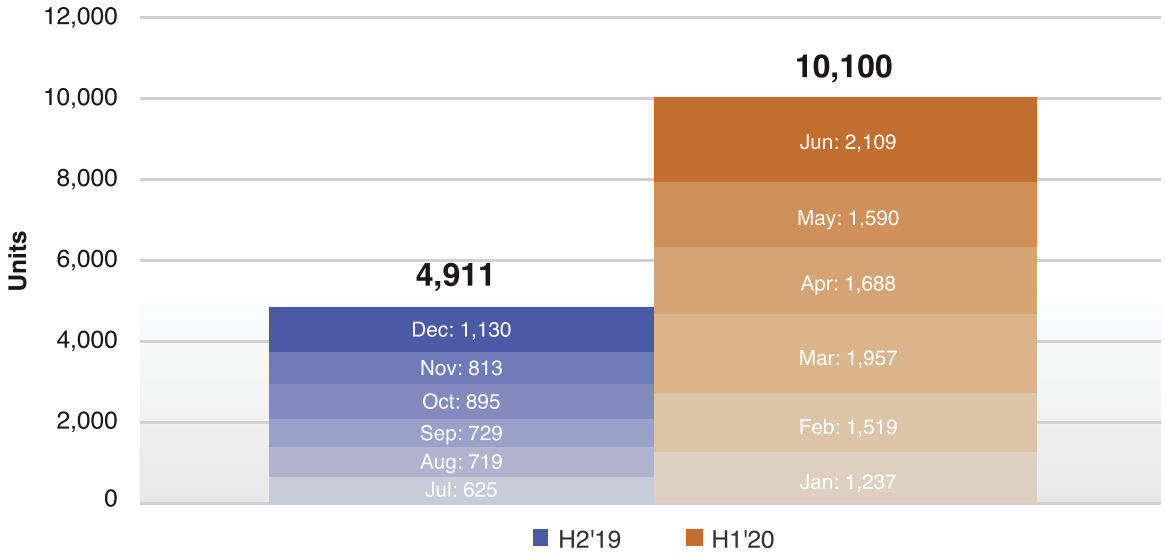

Fig. 3. Cumulative BUP-XR distribution from IDN subtype: H2'19 vs. H1'20. IDN, integrated delivery network.

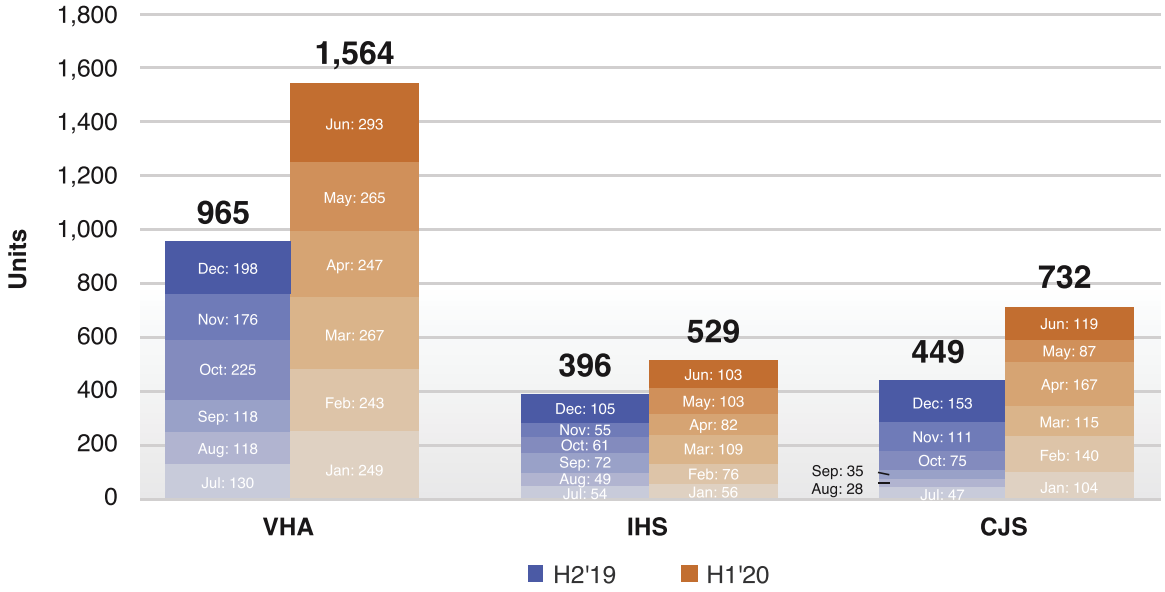

Fig. 4. Cumulative BUP-XR distribution from VHA, IHS, and CJS: H2'10 vs H1'20. CJS, criminal justice systems; IHS, Indian Health Services; OHS, organized health systems; VHA, Veterans Health Administration.

Utilizing these waivers, states such as New Hampshire have created regional IDNs to increase the adoption of MOUD and promote integrated services and continuum of care for individuals with OUD (Hinde et al., 2017; New Hampshire Department of Health and Human Services, 2016; Townley and Dorr, 2017). Despite such efforts to increase MOUD access, IDNs continue to encounter barriers for distribution. While access to BUP-XR is better for patients with OUD in IDNs than in other OHS subtypes, it is still limited. Policies are often made without in-depth knowledge of the complexities, intricacies, and challenges faced at the regional and local levels (LexisNexis Risk Solutions, 2016). There are also inpatient versus outpatient formulary rules, use of specialty pharmacy versus specialty distributors issues, and staffing challenges, as policies are based on an outpatient oral model and not administration by a healthcare provider, as is required for BUP-XR. In addition, DEA assignment is specific to the address of the license and is not transferrable to other locations within the IDN (Code of Federal Regulations, 2021).

The VHA is reported to be the largest healthcare delivery network and direct provider of substance use disorder treatment in the United States (Wyse et al., 2018). It comprises 1,293 facilities, including 171 medical centers and more than 1,000 outpatient clinics, for approximately 9 million veterans (US Department of Veterans Affairs, 2021).

Our findings also suggest that relatively few VHA patients receive BUP-XR, despite efforts in facilitating the extensive provision of MOUD and policies requiring it to be available (Gordon et al., 2020) and despite encouraging results supporting the use of BUP-XR as a useful treatment option for complex treatment-resistant veterans with significant medical and psychosocial co-morbidities (Cotton et al., 2021). System-level barriers that may reduce the prescribing of MOUD within the VHA include differences in policies and protocols compared with other local and state healthcare institutions—VHA systems operate locally but are under federal as opposed to state guidelines (Priest et al., 2020). To facilitate the sharing of best practices and increase education, the VHA has invested in several nationwide initiatives to help improve access to MOUD, such as the Buprenorphine in the VA Initiative, the Medication Addiction Treatment Initiative, and the Stepped Care for Opioid Use Disorder Train the Trainer Initiative (Gordon et al., 2020). States with

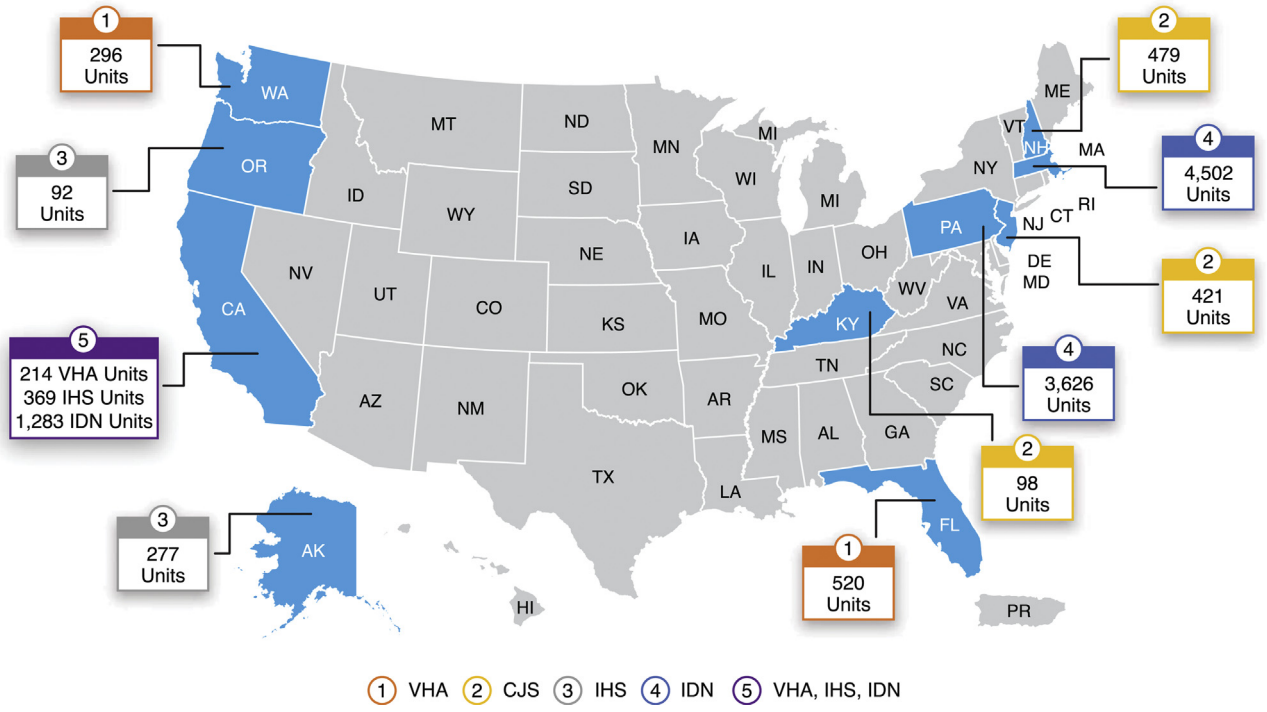

Fig. 5. National OHS distribution. CJS, criminal justice systems; IDN, integrated delivery network; IHS, Indian health services; OHS, organized health systems; VHA, Veterans Health Administration.

the highest BUP-XR distribution within the VHA may be the result of more progressive institutions that have readily adopted new programs and policies to treat their OUD population.

In a pilot study across two VHA outpatient clinics, 26 clinically complex patients at high risk for hospitalization and mortality received at least one BUP-XR injection (Cotton et al., 2021). Treatment retention was robust, 81% received more than six injections and 77% were maintained on the 300 mg dosage strength. Treatment was also associated with reduction in Emergency Department (ED) visits (-48%), hospitalizations (-39%), days of hospitalization (-41%), non-prescribed opioid use, and homelessness.

The CJS comprises different types of correctional facilities, and in 2018, it supervised an estimated 6.4 million persons incarcerated in federal or state prison, in custody in local jails, or in community-based corrections such as parole and probation (Maruschak and Minton, 2020). CJS facilities are required to provide health services to incarcerated individuals but the level of care provided varies significantly across states and types (Gates et al., 2014).

A pilot proof-of-concept study (Lee et al., 2021) also compared treatment retention following release from jail among adults receiving daily sublingual buprenorphine-naloxone vs. those receiving BUP-XR and showed that subjects in the BUP-XR arm had fewer jail medical visits compared with daily sublingual medication administration. Furthermore, community buprenorphine treatment retention at week 8 post-release was 69.2% in the BUP-XR group vs. 34.6% in the sublingual buprenorphine-naloxone group, and rates of opioid-negative urine tests were 55.3% in the BUP-XR group vs. 38.4% in the sublingual buprenorphine-naloxone group.

Another recent series of qualitative interviews conducted among adult participants with OUD who were recently released from NYC jails and maintained on BUP-XR after switching from daily sublingual buprenorphine/naloxone also suggested that BUP-XR treatment during jail-to-community reentry was perceived by participants as a favorable treatment approach to reduce their risk of opioid reuse, illicit activities, stigma associated with daily receipt of MOUD, and COVID-19 exposure (Cheng et al., 2022).

Based on our national distribution data, the CJS continues to see steady adoption of LAIs for OUD, although overall MOUD uptake has been slow to be incorporated into routine practice in this OHS subtype. This may be due to policies concerning controlled substances in prisons, as some states' licensing, credentialing, and regulations pose impediments to the efficient and effective use of LAIs for OUD, deterring facilities from becoming providers. In addition, many facilities do not have the staff, capacity, or incentive to register as certified providers (Substance Abuse and Mental Health Services Administration, 2019; Substance Abuse and Mental Health Services Administration, 2021). Furthermore, there is often a lack of trained personnel, little knowledge about MOUD and, in some cases, resistance to utilize MOUD due to negative perceptions of 'substituting one drug for another,' leading to stigma or concerns about security and liability (National Academies of Sciences, 2019; Substance Abuse and Mental Health Services Administration, 2019). In addition, this special population does not qualify for Medicaid, as eligibility is terminated during incarceration, limiting ongoing treatment (National Academies of Sciences, 2019; Substance Abuse and Mental Health Services Administration, 2019). Finally, CJS programs may incorrectly assume that they cannot afford to provide LAIs for OUD due to the costs of medication, staffing, training, additional certifications, and storage requirements (Substance Abuse and Mental Health Services Administration, 2019). These and other misperceptions about the function of MOUD and its side effects lead to underutilization.

CJS programs and facilities could greatly benefit from modifying their policies, procedures, and training to ensure LAIs for OUD are administered according to regulations so as to minimize diversion (Substance Abuse and Mental Health Services Administration, 2019). Such strategies could include educating and providing ongoing training for staff, monitoring the dispensing of medications, and ensuring the safe, secure storage of medications (Substance Abuse and Mental Health Services Administration, 2019). To overcome financial barriers, CJS programs and facilities may consider using federal and state grant funding to expand the use of evidence-based treatments such as BUP-XR in criminal justice settings (Substance Abuse and Mental Health Services Administration, 2019).

The IHS administers direct healthcare services through a system of 12 area offices, 170 IHS and tribally operated service units, and 41 Urban Indian Organizations. As of January 2020, the IHS provided healthcare services to approximately 2.6 million American Indians and Alaska Natives who belong to 574 federally recognized tribes in 37 states (Indian Health Service, 2020).

With only 34% growth in our study, the IHS shows the slowest adoption of LAIs for the treatment of OUD. This OHS subtype serves primarily American Indians and Alaska Natives, a population that is particularly vulnerable to OUD, due to unique individual, familial, cultural, community, and structural risk factors and drivers (Soto et al., 2019). In 2018, national death rates due to OUD were the second highest in this population after White, non-Hispanic people in the United States (Wilson et al., 2020). Thus, there remains considerable need for increased attention to barriers to adoption by IHS to expand and better integrate treatment services for people with OUD. Barriers identified in these assessments have included stigma and shame in seeking treatment and services, limited funding and cost, insufficient or lack of insurance coverage, unstable housing, fragmented service delivery, geographical isolation, and lack of residential treatment facilities for substance use disorders (Soto et al., 2019). Practice-based evidence programs that provide recovery support and continuity of treatment and recovery care, and mitigate geographic and transportation barriers through grassroot efforts such as The Wellbriety Movement, Tribal MAT programs in Tribal Health Programs (THPs), and telehealth technology services like Tele-MAT, can be adapted to meet the needs of these communities (Soto et al., 2019).

The geographic variation we observed in LAI distribution may relate to state populations, which, in turn, affect BUP-XR utilization. Our data show that in areas with low population density, fewer units are being dispensed overall. This is not surprising since many rural areas also lack buprenorphine-waivered providers (Madras et al., 2020). In states with larger populations, more units were being dispensed overall. The lower adoption rates seen in rural areas, could be due to barriers such as stigma, shortages of providers, limited healthcare infrastructure, and only a few treatment programs offer all forms of MOUD (Madras et al., 2020).

There are also general barriers that affect all OHS types, add to existing impediments to uptake, and impact how quickly facilities can adopt LAIs for OUD. For example, the many regulations (federal, state, and local) related to procurement of BUP-XR necessitate that institutions create new policies, procedures, and protocols for LAI, as current policies often only consider oral medications, outpatient pharmacy prescriptions, and patient self-medication (2021a).

Within OHS systems, logistics are a critical part of specialty medication distribution. BUP-XR is a schedule III controlled substance and is subject to regulation by the DEA, including storage and security requirements (2021b). In addition, it can only be procured for patients from either specialty pharmacies or specialty distributors (2021a). Healthcare settings (including prescriber offices) and pharmacies that purchase from a specialty distributor must be certified prior to purchasing, dispensing, and storing BUP-XR (2021a). In addition, if dispensing for a specific patient, a prescription is required through a certified provider from a specialty pharmacy (2021a). Most institutions acquire BUP-XR through specialty distributors but some purchase from specialty pharmacies (2021a).

Specialty pharmacies and specialty distributors each pose unique barriers to access and administration of BUP-XR medication. By purchasing BUP-XR from specialty pharmacies, providers are not required to provide payment for the medication up front; however, if purchased for a specific patient, it cannot be administered to a different patient if the patient misses their dose (2021a; 2021b). In contrast, when purchasing BUP-XR from specialty distributors, providers must enroll and participate in the BUP-XR buy-and-bill program and provide payment upon ordering (2021a; 2020). In addition, the medication that is purchased is not designated to a specific patient, and providers must be REMS certified (2021a; 2021a).

As distributors of BUP-XR, specialty pharmacies are responsible for the administrative processing of the prescription; however, processing delays can impede access (2020). Other barriers include ensuring staff is available to receive delivery of medication, particularly in smaller practices or in rural locations (2020). Also, although buy-and-bill distribution allows providers to keep medications in stock, some providers prefer not to use this method because of the potential financial risk (2020). Smaller practices may not have the infrastructure or resources to handle the administrative responsibilities of this program, nor the ability to purchase medications up front. Problematically, if patients do not use the medications before they expire or reimbursement does not cover the full cost, providers risk financial loss (2020).

Federal regulations require that schedule III substances be stored in a securely locked cabinet to safeguard against theft and diversion (2021b; 2021). As BUP-XR moves through the distribution process, its storage and inventory are controlled and secured at every step. The closed system distribution process provides accountability to meet DEA regulations and mitigate diversion. There are also additional requirements for the storage and handling of BUP-XR. BUP-XR requires refrigeration, once removed it be stored in its original packaging at room temperature for up to 7 days before administration. If left at room temperature for longer than 7 days, it should be discarded (2021b).

Managing reimbursement is also increasingly complex, leading to additional delays or barriers to treatment access. Prescriptions are not always filled by specialty pharmacies until payer reimbursement, especially if manually processed, which can lead to delays in the dispensing of medication (2020). In addition, patients might not be financially able to cover the cost of treatment (Hinde et al., 2017; Madras et al., 2020).

The monthly dosing of BUP-XR may also require a different, more flexible approach to how treatment and care are structured, as periodic assessment to determine the effectiveness of the treatment and overall patient progress is necessary (2021b). This could result in providers scheduling additional appointments for re-evaluation and follow-up, as OUD is a chronic illness and there is no maximum recommended duration of maintenance treatment (2021b). Once steady state is achieved, both doses of BUP-XR maintain plasma levels above 2 ng/mL and with repeated dosing can maintain such levels for weeks, which can be advantageous in case a dose is missed, distinguishing BUP-XR from oral or sublingual formulations (Jones et al., 2021). Conversely, it could be argued that LAIs such as BUP-XR may reduce patient interactions with healthcare systems, which could help OHS keep healthcare workers and patients safe from unnecessary exposures in healthcare facilities—an issue brought to light during the COVID-19 pandemic.

It is important to acknowledge the changes made to health administration policies enacted to address the COVID-19. (Ahmad et al., 2022; Livingston et al., 2021) In response to the pandemic, the federal government loosened MOUD guidelines to not only mitigate risk of exposure to COVID-19, but also prevent disruption to OUD treatment. These new MOUD delivery approaches brought on by the COVID-19 pandemic aimed to offset disruption to MOUD treatment, expand treatment options, and reduce the need for in-person visits, enabling people with OUD to access care where and when they needed it. There are calls to make the healthcare policies enacted during the pandemic permanent, to ensure increased access and remove existing barriers to care (Livingston et al., 2021).

5. Limitations

A limitation of our study is that we were not able to evaluate whether BUP-XR distribution to an OHS entity correlates with clinical utilization and administration of the medication. The objective of our study only allowed us to capture a descriptive snapshot of the current US distribution landscape of BUP-XR in OHS. Further research is needed to investigate whether a relationship between BUP-XR distribution and utilization and administration exists.

6. Conclusions

Removing system-level, provider-level, and local-level barriers to quality treatment and integrating OUD treatment into routine care and other settings, are critical steps to ensuring access to evidence-based MOUD and represent a cornerstone of the opioid crisis response in the United States. The distribution patterns seen in our study illustrate and underscore the importance of OHS in bridging the gap in access to BUP-XR within the OUD treatment ecosystem.

Author contributions

Gadbois participated in the analysis or interpretation of data, drafted the publication and/or revised it critically for important intellectual content (Discussion section), and approved the version of the manuscript to be submitted for publication.

Heidbreder participated in the conception and design of the work being described in the publication, participated in the analysis or interpretation of data, drafted the publication and/or revised it critically for important intellectual content (Introduction, Methods, Results, and Discussion sections), and approved the version of the manuscript to be submitted for publication.

Mullen participated in the conception and design of the work being described in the publication, drafted the publication and/or revised it critically for important intellectual content (Introduction, Methods, Results, and Discussion sections), and approved the version of the manuscript to be submitted for publication.

Hedberg participated in the analysis or interpretation of data, drafted the publication and/or revised it critically for important intellectual content (Introduction, Results, and Discussion sections), and approved this version of the manuscript with minor revisions requested (no changes to data, results, or conclusions).

All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding

This work was supported by Indivior, Inc., North Chesterfield, VA, USA.

Declaration of Competing Interest

Mullen, Hedberg, and Heidbreder are employees of Indivior, Inc. Gadbois is an employee of the Department of Veterans Affairs and is paid by Indivior, Inc., to speak about SUBLOCADE.

Acknowledgments

Medical writing assistance and editorial support were provided to the authors by Peloton Advantage LLC, an OPEN Health company, Parsippany, NJ, and funded by Indivior, Inc.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2022.100090.

References

Ahmad, F.B., Rossen, L.M., Sutton, P., 2022. Provisional drug overdose death counts. https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm. (Accessed February 24, 2022.

Buprenorphine [package insert]. 2021. Roxane Laboratories, Inc., Columbus, OH.

CDC, 2022. U.S. Overdose Deaths In 2021 Increased Half as Much as in 2020 – But Are Still Up 15%. https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2022/202205.htm. (Accessed June 7, 2022.

Cheng, A., Badolato, R., Segoshi, A., McDonald, R., Malone, M., Vasudevan, K., Badiei, B., Sugarman, A., Macdonald, R., Mangat, J., Giftos, J., Lee, J.D., Tofighi, B., 2022. Perceptions and experiences toward extended-release buprenorphine among persons leaving jail with opioid use disorders before and during COVID-19: an in-depth qualitative study. Addict. Sci. Clin. Practice 17 (1), 4.

Chilcoat, H.D., Amick, H.R., Sherwood, M.R., Dunn, K.E., 2019. Buprenorphine in the United States: Motives for abuse, misuse, and diversion. J Subst Abuse Treat 104, 148–157.

Cicero, T.J., Ellis, M.S., Chilcoat, H.D., 2018. Understanding the use of diverted buprenorphine. Drug Alcohol Depend 193, 117–123.

Clarivate, 2020. Integrated delivery networks and their growing influence on regional healthcare in the US. https://decisionresourcesgroup.com/solutions/integrated-delivery-networks-and-their-growing-influence-on-regional-healthcare-in-the-us/. (Accessed November 4, 2020.

Code of Federal Regulations, 2021. 1301.75 Physical security controls for practitioners. https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=2342a2bc713ed03b682f5866f93384e0&mc=true&n=pt21.9.1301&r=PART&ty=HTML#se21.9.1301_175. (Accessed June 21, 2021.

Cotton, A.J., Lo, K., Kurtz, F.B., Waldbauer, L., 2021. Extended-release buprenorphine outcomes among treatment resistant veterans. The American journal of drug and alcohol abuse Nov 15 Online Ahead of Print.

Farrell, M., Shahbazi, J., Byrne, M., Grebely, J., Lintzeris, N., Chambers, M., Larance, B., Ali, R., Nielsen, S., Dunlop, A., Dore, G.J., McDonough, M., Montebello, M., Nicholas, T., Weiss, R., Rodgers, C., Cook, J., Degenhardt, L., 2022. Outcomes of a single-arm implementation trial of extended-release subcutaneous buprenorphine depot injections in people with opioid dependence. Int. J. Drug Policy 100, 103492.

Gates, A., Artiga, S., Rudowitz, R., 2014. Health Coverage and Care for the Adult Criminal JusticeInvolved Population. https://www.kff.org/uninsured/issue-brief/health-coverage-and-care-for-the-adult-criminal-justice-involved-population/. (Accessed July 8, 2021.

Gordon, A.J., Drexler, K., Hawkins, E.J., Burden, J., Codell, N.K., Mhatre-Owens, A., Dungan, M.T., Hagedorn, H., 2020. Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) initiative: expanding ACCESS to medication treatment for opioid use disorder within Veterans Health Administration facilities. Subst. Abuse 41 (3), 275–282.

Haight, B.R., Learned, S.M., Laffont, C.M., Fudala, P.J., Zhao, Y., Garofalo, A.S., Greenwald, M.K., Nadipelli, V.R., Ling, W., Heidbreder, C., 2019. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 393 (10173), 778–790.

Hinde, J., Hayes, J., Mark, T., Bernstein, S., Karon, S.L., 2017. State and Local Policy Levers For Increasing Treatment And Recovery Capacity To Address The Opioid Epidemic: Final report. US Department of Health & Human Services, Washington, DC.

Huhn, A.S., Dunn, K.E., 2017. Why aren't physicians prescribing more buprenorphine? J. Subst. Abuse Treat. 78, 1–7.

Indian Health Service, 2020. Indian Health Services profile fact sheet. https://www.ihs.gov/newsroom/factsheets/ihsprofile/. (Accessed July 8, 2021.

Indivior, 2021. Sublocade risk evaluation and mitigation strategy (REMS). https://www.sublocaderems.com/. (Accessed June 22, 2021).

inSupport, 2021a. SUBLOCADE (buprenorphine extended-release) buy-and-bill pathway. https://www.insupport.com/pdf/insupport-buy-and-bill-channel-flashcard-branded.pdf. (Accessed June 21, 2021.

inSupport, 2021b. SUBLOCADE (buprenorphine extended-release) specialty pharmacy pathway. https://www.insupport.com/pdf/insupport-specialty-pharmacy-channel-flashcard-branded.pdf. (Accessed June 21, 2021.

Jones, A.K., Ngaimisi, E., Gopalakrishnan, M., Young, M.A., Laffont, C.M., 2021. Population pharmacokinetics of a monthly buprenorphine depot injection for the treatment of opioid use disorder: a combined analysis of Phase II and Phase III Trials. Clin. Pharmacokinet 60 (4), 527–540.

Jones, C.M., McCance-Katz, E.F., 2019. Characteristics and prescribing practices of clinicians recently waivered to prescribe buprenorphine for the treatment of opioid use disorder. Addiction 114 (3), 471–482.

Laffont, C.M., Gomeni, R., Heidbreder, C., Jones 3rd, J.P., Nasser, A.F., 2016. Population Pharmacokinetic Modeling After Repeated Administrations of RBP-6000, a new, subcutaneously injectable, long-acting, sustained-release formulation of buprenorphine, for the treatment of opioid use disorder. J. Clin. Pharmacol. 56 (7), 806–815.

Lee, J.D., Malone, M., McDonald, R., Cheng, A., Vasudevan, K., Tofighi, B., Garment, A., Porter, B., Goldfeld, K.S., Matteo, M., Mangat, J., Katyal, M., Giftos, J., MacDonald, R., 2021. Comparison of treatment retention of adults with opioid addiction managed with extended-release buprenorphine vs daily sublingual buprenorphine-naloxone at time of release from jail. JAMA network open 4 (9), e2123032.

LexisNexis Risk Solutions, 2016. White Paper: the ABCs of IDNs: the new keys to commercial success for life sciences organizations.

Ling, W., Nadipelli, V.R., Solem, C.T., Farabee, D., Ronquest, N.A., Perrochet, B., Learned, S.M., Deshpande, C.G., Heidbreder, C., 2019. Measuring recovery in opioid use disorder: clinical utility and psychometric properties of the Treatment Effectiveness Assessment. Subst. Abuse Rehabil. 10, 13–21.

Ling, W., Nadipelli, V.R., Solem, C.T., Ronquest, N.A., Yeh, Y.C., Learned, S.M., Mehra, V., Heidbreder, C., 2020. Effects of monthly buprenorphine extended-release injections on patient-centered outcomes: a long-term study. J. Subst. Abuse Treat 110, 1–8.

Livingston, N.A., Ameral, V., Banducci, A.N., Weisberg, R.B., 2021. Unprecedented need and recommendations for harnessing data to guide future policy and practice for opioid use disorder treatment following COVID-19. J. Subst. Abuse Treat. 122, 108222.

Madras, B.K., Ahmad, N.J., Wen, J., Sharfstein, J., 2020. Improving access to evidence-based medical treatment for opioid use disorder: strategies to address key barriers within the treatment system. https://nam.edu/improving-access-to-evidence-based-

medical-treatment-for-opioid-use-disorder-strategies-to-address-key-barriers-within-the-treatment-system/. (Accessed June 21, 2021.

Martin, R., 2018. White paper: integrated delivery networks. https://www.iqvia.com/locations/united-states/library/white-papers/integrated-delivery-networks. (Accessed March 8, 2021.

Maruschak, L.M., Minton, T.D., 2020. Correctional populations in the United States, 2017-2018. https://bjs.ojp.gov/library/publications/correctional-populations-united-states-2017-2018. (Accessed July 8, 2021.

Nasser, A.F., Greenwald, M.K., Vince, B., Fudala, P.J., Twumasi-Ankrah, P., Liu, Y., Jones 3rd, J.P., Heidbreder, C., 2016. Sustained-release buprenorphine (RBP-6000) blocks the effects of opioid challenge with hydromorphone in subjects with opioid use disorder. J. Clin. Psychopharmacol. 36 (1), 18–26.

Nasser, A.F., Heidbreder, C., Gomeni, R., Fudala, P.J., Zheng, B., Greenwald, M.K., 2014. A population pharmacokinetic and pharmacodynamic modelling approach to support the clinical development of RBP-6000, a new, subcutaneously injectable, long-acting, sustained-release formulation of buprenorphine, for the treatment of opioid dependence. Clin. Pharmacokinet. 53 (9), 813–824.

National Academies of Sciences, E., and Medicine, 2019. Medications for Opioid Use Disorder Save Lives.

National Institute on Drug Abuse, 2018. Medications to Treat Opioid Use Disorder Research Report. National Institute on Drug Abuse, Bethesda, MD.

National Institute on Drug Abuse, 2021. Opioid Overdose Crisis.

New Hampshire Department of Health and Human Services, 2016. Building Capacity For Transformation: New Hampshire's DSRIP waiver program.

Priest, K.C., McCarty, D., Lovejoy, T.I., 2020. Expanding access to medications for opioid use disorder: program and policy approaches from outside the Veterans Health Administration. J. Gen. Intern. Med. 35 (Suppl 3), 886–890.

Soto, C., West, A., Unger, J., Miller, K., Zeledon, I., Telles, V.M., Henderson, B., Nguyen, V., Begay, C., Martinez, D., Franklin, R., Johnson, C., Dickerson, D., Antony, V., Domaguin, D., Schweigman, K., Moerner, L., 2019. Addressing the Opioid Crisis In American Indian & Alaska Native Communities In California: A Statewide Needs Assessment. University of Southern California.

Substance Abuse and Mental Health Services Administration, 2019. Use of medication-assisted treatment for opioid use disorder in criminal justice settings. National Mental Health and Substance Use Policy Laboratory. Substance Abuse and Mental Health Services Administration, Rockville, MD.

Substance Abuse and Mental Health Services Administration, 2021. 2020 NSDUH annual national report. https://www.samhsa.gov/data/report/2020-nsduh-annual-national-report. (Accessed November 9, 2021.

Townley, C., Dorr, H., 2017. Integrating substance use disorder treatment and primary care. https://www.nashp.org/wp-content/uploads/2017/02/Primary-Care-Integration-Brief.pdf. (Accessed June 21, 2021.

US Department of Veterans Affairs, 2021. Veterans Health Administration.

US Food and Drug Administration, 2020. Risk Evaluation and Mitigation Strategy (REMS) Document SUBLOCADE (buprenorphine extended-release) REMS Program.

Wilson, N., Kariisa, M., Seth, P., Smith, H.I., L., D.N., 2020. Drug and opioid-involved overdose deaths—United States, 2017–2018. MMWR Morb. Mortal. Wkly. Rep. 69 (11), 290.

Wyse, J.J., Gordon, A.J., Dobscha, S.K., Morasco, B.J., Tiffany, E., Drexler, K., Sandbrink, F., Lovejoy, T.I., 2018. Medications for opioid use disorder in the Department of Veterans Affairs (VA) health care system: historical perspective, lessons learned, and next steps. Substance Abuse 39 (2), 139–144.