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Drug Use Evaluation: Indications for Sublingual Buprenorphine

Research Question 1:

1. Since removal of the prior authorization (PA) criteria for medication assisted treatment (MAT), has there been a change in off-label prescribing and use for sublingual buprenorphine?

Conclusions:

- The number of patients prescribed sublingual buprenorphine over the 6-month study period increased by over 20% (from 364 patients to 472 patients after removal of the PA) indicating increased prescribing for sublingual buprenorphine. During this same timeframe the average monthly fee-for-service enrollment increased by about 5% from 2019 to 2020.
- Since removal of the PA for sublingual buprenorphine, the proportion of patients with a diagnosis of opioid use disorder (OUD) were similar before and after the PA removal (89% vs. 87%, respectively). Similar rates were observed for the subgroup of patients prescribed combination buprenorphine/naloxone.
- In a subgroup of patients with paid claims for sublingual buprenorphine monotherapy, the proportion of patients without a diagnosis of OUD increased after removal of the PA from 6.5% to 20.6%. However, this group still represents a small proportion of the overall population with claims for sublingual buprenorphine (4.4%).

Recommendations:

- No policy changes recommended.

Background

Numerous studies have demonstrated that use of MAT improved outcomes in patients with OUD. Recent guidelines updated in 2021 from the VA/DOD recommend use of combination buprenorphine/naloxone or methadone for treatment in patients with opioid use disorder (strong recommendation; high quality evidence).[1] Buprenorphine/naloxone is recommended in most situations because it discourages intravenous use and decreases risk of diversion.[1] However, any buprenorphine formulation has benefit over no treatment in patients with OUD, and there is insufficient evidence to recommend any specific buprenorphine formulation or route of administration over another based on available evidence for efficacy or safety.[1] These guidelines recommend that clinicians consider multiple factors in selecting the appropriate therapy including a patient's values and preferences, clinical history, and pharmacoeconomics.[1]

Currently available formulations of buprenorphine for treatment of OUD include subcutaneous injections, sublingual tablets, and sublingual films. Buprenorphine formulations which are indicated for treatment of severe pain include buccal film, transdermal patches, and intramuscular or intravenous injections. In FFS, various buprenorphine formulations are categorized by their FDA-approved indication. Therefore, transdermal patches and buccal films are

categorized as long-acting opioids and subject to clinical criteria for opioids. Subcutaneous injections and sublingual formulations are categorized as MAT for OUD and are available without PA. The focus of this policy evaluation is on sublingual formulations of buprenorphine and buprenorphine/naloxone.

In 2020, to reduce administrative barriers and improve access to MAT, Oregon legislation prohibited use of PA during the first 30 days of medication-assisted treatment for both opioid- and alcohol-related substance use disorders.[2] In accordance, the Fee-for-Service (FFS) policy was updated to remove PA for all MAT for treatment of OUD.[2] Since then, other Nationwide regulatory changes have been implemented in an effort to increase access to MAT for OUD. For example, in April 2021, the United States Department of Health and Human Services (HHS) and Substance Abuse and Mental Health Services Administration (SAMHSA) released updated practice guidelines which removed training requirements for providers treating up to 30 patients with buprenorphine for OUD.[3,4] Previously, providers had to complete this training before they were able to obtain a waiver to prescribe buprenorphine for OUD.[3] Training is still required for practitioners prescribing buprenorphine for more than 30 patients.[4]

While use of buprenorphine products for OUD is supported by high quality evidence, long-term use of opioids for pain is not without risk. Quantity limits of 24mg/day were maintained for sublingual buprenorphine to limit use of high doses for off-label conditions. While buprenorphine is a partial opioid agonist, it is associated with many of the same effects and risk factors as a full opioid agonist. Warnings and precautions for sublingual buprenorphine/naloxone and sublingual buprenorphine include withdrawal symptoms upon abrupt discontinuation, risk of hepatic injury, and risk of overdose in opioid naïve patients, and respiratory depression especially in conjunction with other respiratory depressants or in patients with underlying respiratory insufficiency.[5] Similar to other opioids, buprenorphine also has a warnings for addiction, abuse and misuse.[5] In January 2022, the FDA also released a safety warning regarding dental problems associated with use of sublingual and buccal formulations of buprenorphine.[6] Dental problems have included tooth decay, cavities, abscesses and infections, and loss of teeth. This warning was based on case reports from medical literature and data from the FDA Adverse Event Reporting System (FAERS) database which identified 305 cases of dental adverse events through December 31, 2018. In many cases, more than one tooth was involved (n=113) and dental problems were observed in individuals with and without a prior history of dental problems.[6] The most common treatment for these dental problems was removal of the affected tooth (n=71).[6] Labeling for these products was updated to recommend that providers screen patients for oral disease prior to initiation of therapy, refer patients for a baseline dental screening as soon as possible after initiation of therapy, recommend routine dental visits, and educate the patient regarding appropriate medication administration and oral health to minimize risk of these adverse events.[6]

The goal of this policy evaluation is to evaluate changes in access for MAT since removal of the PA criteria and to evaluate the proportion of patients who may be prescribed off-label use of MAT for non-OUD diagnoses such as chronic pain.

Methods:

Patients were identified for inclusion in the study based on paid FFS claims for sublingual buprenorphine (First Databank HICL sequence numbers [HSNs] 001762 or 024846; route: sublingual). The evaluation window for buprenorphine claims was from 1/1/2019 to 6/30/2019 for the control group and from 1/1/2020 to 6/30/2020 for the intervention group. Cohorts were assigned to the control or intervention groups based on the first paid FFS claim (the index event [IE]). For each patient, the baseline period was defined based as the 6 months prior to the IE (exclusive of the IE).

Inclusion Criteria:

1. At least one FFS paid claim for sublingual buprenorphine during the evaluation window for buprenorphine claims

Exclusion Criteria:

1. Patients not assigned to either the control or intervention groups

2. Primary insurance coverage (i.e., third party liability [TPL]) at any time during the baseline period
3. Patients with Medicare Part D coverage or limited or no Medicaid drug benefit at any time during the baseline or follow-up periods. Claims data for these patients may be incomplete. Patients were identified based on the following benefit packages:

Category	Benefit Package	Description
Medicare Part D coverage	BMM	Qualified Medicare Beneficiary + Oregon Health Plan with Limited Drug
	BMD	Oregon Health Plan with Limited Drug
	MED	Qualified Medicare Beneficiary
Limited or no Medicaid drug benefit	MND	Transplant package
	CWM	Citizenship Waived Emergency Medical
	SMF	Special Low-Income Medicare Beneficiary Only
	SMB	Special Low-Income Medicare Beneficiary Only

4. Non-continuous Medicaid eligibility during the baseline period
5. Patients included in both the control and intervention groups.

Outcomes evaluated in this analysis included diagnosis of OUD defined based on ICD-10 codes on medical claims during the baseline period or on the index date.

Results:

Demographics of patients with paid claims for sublingual buprenorphine are shown in **Table 1.** The number of patients prescribed sublingual buprenorphine over the 6-month study period increased by over 20% (from 364 patients to 472 patients after removal of the PA). Total enrollment in fee-for-service has increased over time which may account for some changes in prescribing. In the study period before removal of the PA, the average monthly fee-for-service enrollment was 86,368 patients. This had increased to an average of 90,817 patients in the study period after removal of the PA (5.2% increase).

Almost 50% of patients were female and almost 60% were young adults (≤35 years of age). The largest racial groups identified in the study were patients identifying as White (36-38%) and patients identifying as American Indian/Alaskan Native (16-29%). There were a larger proportion of American Indian/Alaskan Native patients in 2020 (after PA removal) compared to 2019 (before removal of the PA).

The Elixhauser Comorbidity Index was used to estimate disease burden in the population. The index is a weighted measure based on relevant diagnoses submitted on medical claims during the baseline period. The presence or absence of diagnoses are identified in medical claims and categorized into 29 comorbidity variables. Each category is assigned a weighted score from -7 to +12. Lower scores indicate lower disease burden whereas higher scores are indicative of higher disease burden. The index is reported as 2 separate measures which can be used to predict risk of in-hospital mortality (the "M" index) and risk for 30-day readmission (the "R" index).[7] Indices were similar for both groups indicating similar disease burden in the population over time. The most common diagnoses contributing to the Elixhauser comorbidity index were drug abuse (88-89%), depression (19-20%), and alcohol abuse (15%).

The majority of patients with paid claims for sublingual buprenorphine had a diagnosis of OUD in the prior 6 months (**Table 2**) with similar rates before and after removal of the PA (89% vs. 87%). Most patients prescribed sublingual buprenorphine formulations had paid claims for the combination therapy with buprenorphine/naloxone. In this subgroup, the proportion of patients with a diagnosis of OUD was similar before and after removal of the PA. In the subgroup of patients with paid claims for sublingual buprenorphine monotherapy, the proportion of patients without a diagnosis of OUD increased after removal of the PA criteria (from 6.5% to 20.6%). However, these patients still represent a small proportion of the overall population (4.4%).

Table 1. Demographics for paid FFS pharmacy claims

	Before		After	
	364	%	472	%
Female	173	47.5%	230	48.7%
Age – mean (range)	35	(2-63)	35	(17-63)
<18	1	0.3%	2	0.4%
18-35	215	59.1%	273	57.8%
36-64	148	40.7%	197	41.7%
>=65	0	0.0%	0	0.0%
Race				
White	138	37.9%	170	36.0%
Unknown	160	44.0%	148	31.4%
American Indian/Alaskan Native (HNA)	60	16.5%	136	28.8%
Other	6	1.6%	18	3.8%
*Average Elixhauser Score "M"	-6.79		-6.88	
*Average Elixhauser Score "R"	20.58		20.63	

*Weighted index based on diagnoses on medical claims in the baseline period.

Table 2. Patients with OUD diagnoses (F11x) and buprenorphine claims

	Before		After	
All IE	364		472	
OUD diagnosis in baseline period	324	89.0%	411	87.1%
No OUD diagnosis in baseline period	40	11.0%	61	12.9%
Buprenorphine/naloxone IE	333		370	
OUD diagnosis in baseline period	295	88.6%	330	89.2%
No OUD diagnosis in baseline period	38	11.4%	40	10.8%
Buprenorphine IE	31		102	
OUD diagnosis in baseline period	29	93.5%	81	79.4%
No OUD diagnosis in baseline period	2	6.5%	21	20.6%

Limitations

- Diagnostic data is based on claims history which may be incomplete or not accurately reflect true patient diagnoses. Social stigma associated with OUD diagnoses (from patients or providers) may result in incomplete or missing diagnoses billed on medical claims. Diagnostic data was evaluated only over a 6-month period, and diagnoses for patients on stable maintenance therapy may be missed if they had infrequent provider visits.
- A significant proportion of patients identified with paid FFS claims for sublingual buprenorphine were ineligible for inclusion in study due to required inclusion criteria. More than half of patients identified with a sublingual buprenorphine claim (53%) were ineligible because they had potentially incomplete claims data due to other primary insurance or were not eligible for Medicaid for the required 6-month baseline period. This study assumes that included patients are still representative of the entire Medicaid population.
- The post-study period from January to June 2020 included a significant period of time when provider offices were closed due to the COVID-19 public health emergency. From March 19, 2020 to April 27, 2020 non-emergency healthcare offices were closed in Oregon to preserve supplies of personal protective equipment (PPE). After this date, healthcare offices could open depending on sufficient supply of PPE. Phased opening for businesses, schools and other organizations began in May 2020. It is unclear how this closure may impact data collected in this study. Diagnoses collected for patients in 2020 may be incomplete if they were unable to see a provider during this period leading to a potential decline in OUD diagnoses in the study period. Similarly, it is unclear how this may have impacted number of patients with paid claims for prescriptions. Patients unable to access MAT via in-person provider visits may have transitioned to dispensing via pharmacies leading to increased pharmacy utilization in the period after the PA removal.
- This analysis does not evaluate use of MAT when administered in a clinical setting. MAT may be billed using a variety of mechanisms (both pharmacy and medical), but only pharmacy claims were included in this analysis.
- Removal of the PA criteria for preferred MAT products allowed increased access to MAT in the FFS population. However, ongoing national and state-wide efforts may have also enhanced access to or referral for treatment of OUD and may account for the increasing utilization of MAT. For example, factors which may impact utilization of MAT include changes in opioid prescribing patters, increased awareness and diagnoses of OUD, efforts to increase the number of prescribing providers for buprenorphine, and availability of medical clinics for treatment of OUD.

References:

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Appendix 1: Key Inclusion Criteria

	Key question #1: Diagnoses
Population	Patients with continuous Medicaid eligibility in the 6 months prior to the index event (the first sublingual buprenorphine claim in the treatment period)
Intervention	Initiation of sublingual buprenorphine (index event; see associated HSNs in methods)
Comparator	Patients with sublingual buprenorphine claims from 1/1/2019-6/30/2019 vs patients with sublingual buprenorphine from 1/1/2020-6/30/2020 (before vs. after removal of PA criteria)
Outcomes	Proportion of patients with sublingual buprenorphine use and an opioid use disorder diagnosis
Setting	Fee-for-Service