Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-1119

Drug Use Evaluation: Therapy Duration for Sublingual Buprenorphine

Research Question:

1. Since removal of the prior authorization (PA) criteria for medication-assisted treatment (MAT) for opioid use disorder (OUD) in Fee for Service (FFS), has there been a change in duration of treatment?

Conclusions:

- In FFS patients who were treatment-naïve to MAT for OUD, removal of the PA criteria had no impact on time to treatment discontinuation. Data are significantly limited by time patients remain in FFS and the proportion of patients who transition into coordinated care organizations (CCOs) after initiation of therapy. A larger population may be needed to discern statistical differences between groups.

Recommendations:

- No policy changes recommended.

Background

Despite current guidelines which recommend MAT as a first-line treatment, many patients do not continue long-term pharmacological therapy for OUD. Clinically relevant, long-term outcomes for patients with OUD include prevention of relapse, overdose, and death. Untreated OUD may also be associated with increased risk of sexually transmitted infections, decreased functional status, and criminal involvement.[1] However, because these outcomes are often difficult to evaluate in randomized controlled trials or claims-based studies, duration of therapy is often used as a surrogate marker of treatment success. Studies evaluating impact of MAT on treatment retention in adolescents have demonstrated that pharmacologic treatment of OUD may lead to a more than 4-times greater likelihood of abstinence with extended courses (2 to 3 months) of buprenorphine compared to short courses (14 to 28 days; low strength of evidence).[1] Similarly, retention in treatment has been associated with decreased mortality.[2] There is no recommended maximum time limit for maintenance therapy, and long-term treatment (in some cases lifelong therapy) is recommended for many patients due to high rates of relapse and increased risk of overdose after treatment discontinuation. However, estimates of treatment retention at 3 months vary widely (ranging from 19 to 94%), and remain low in many populations.[2] In a previous analysis of the Oregon FFS Medicaid population in 2017, it was estimated that only 44% of patients had prescriptions for continuous therapy with MAT for more than 120 days.[3] Because of limitations in claims data, it is unclear how directly this estimate correlates with actual patient adherence.

Many factors may contribute to lack of long-term treatment. Factors could include administrative barriers to access, coverage policies, stigma associated with MAT, costs and logistical issues with obtaining and maintaining treatment (e.g., availability of providers and pharmacies to prescribe and dispense therapy), untreated or undertreated comorbid conditions, fragmented systems of care, or involuntary referrals for treatment (e.g., drug court settings).[2] Several observational studies have evaluated risk factors for treatment discontinuation specifically for Medicaid patients.[4,5] In Medicaid patients with an OUD diagnosis and claims for MAT from 2013 to 2015 (n=17,329), risk factors associated with discontinuation of MAT within the first 6 months of treatment included lower

initial buprenorphine dose, younger age, non-white race, capitated insurance, comorbid substance use disorder, comorbid hepatitis C, opioid overdose history, or any inpatient care.[5]

Beginning 1/1/2020, Oregon legislation was enacted which prohibited use of PA during the first 30 days of MAT for both opioid- and alcohol-related substance use disorders. The primary goal of this legislation was to remove any coverage policies which may be creating administrative barriers for patients initiating care. In accordance, the FFS policy was updated to remove PA for all products to treat OUD (even beyond 30 days). Quantity limits of buprenorphine 24 mg per day were maintained to limit use of high doses for off-label conditions.

The goal of this policy evaluation is to evaluate whether removal of PA impacted duration of therapy for medication assisted treatment for OUD.

Methods:

Patients were identified for inclusion in the study based on paid FFS claims for sublingual buprenorphine (identified using 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 on the 30 days 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 or follow up periods
3. Patients with Medicare Part D coverage or limited or no Medicaid drug benefit at any time during the at any time during the baseline period. 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 with a prior history of MAT use defined as patients meeting any of the following criteria:
    - Patients with claims for MAT in (based on all FFS or CCO medical or pharmacy paid claims) in the baseline period. See **Appendix 1**, **Table A1** and **Table A2** for codes associated with MAT for opioid use disorder; OR
    - Patients with IE submitted with at least 1 refill; OR
    - Patients without any billed medical claims between their Medicaid enrollment date and the IE.
6. Patients included in both the control and intervention groups.

Outcomes evaluated in this analysis included duration of buprenorphine therapy. Because individuals were eligible for varying durations after the IE, a survival analysis curve was used to estimate duration of therapy. Kaplan-Meier curves were performed using SAS® Analytics Software.

- The primary outcome was time to treatment discontinuation defined as the number of days from the IE to the first gap of at least 14 continuous days between the end of coverage of one pharmacy claim and the beginning of coverage of the next pharmacy claim (treatment discontinuation). MAT for OUD may be billed using a variety of mechanisms (both pharmacy and medical), but only pharmacy claims were used to estimate covered days over the treatment period as days' supply is not available on medical claims. Duration of buprenorphine treatment was defined using pharmacy claims, and days covered by a claim were calculated by adding the days' supply submitted on the claim to the date of service. This outcome was evaluated in the 6 months following the IE.
- Patients were censored from the analysis if any of the following circumstances occurred before treatment discontinuation. Time to censoring was calculated using the same method described above by adding the days' supply submitted on the most recent paid claim to the date of service.
    - Enrollment in a CCO (CCOA or CCOB with coverage for physical health drugs)
    - Lost Medicaid eligibility
    - Enrollment in Medicare
    - Coverage by other primary insurance

Results:

Demographics of patients with paid claims for sublingual buprenorphine are shown in **Table 1.** The majority of patients (60-63%) were young adults and 44-47% of patients identified as female. The largest racial groups identified in the study were patients identifying as White (34-35%) and patients identifying as American Indian/Alaskan Native (22-31%). There were a larger proportion of American Indian/Alaskan Native patients in 2020 (after PA removal) compared to 2019 (before removal of the PA).

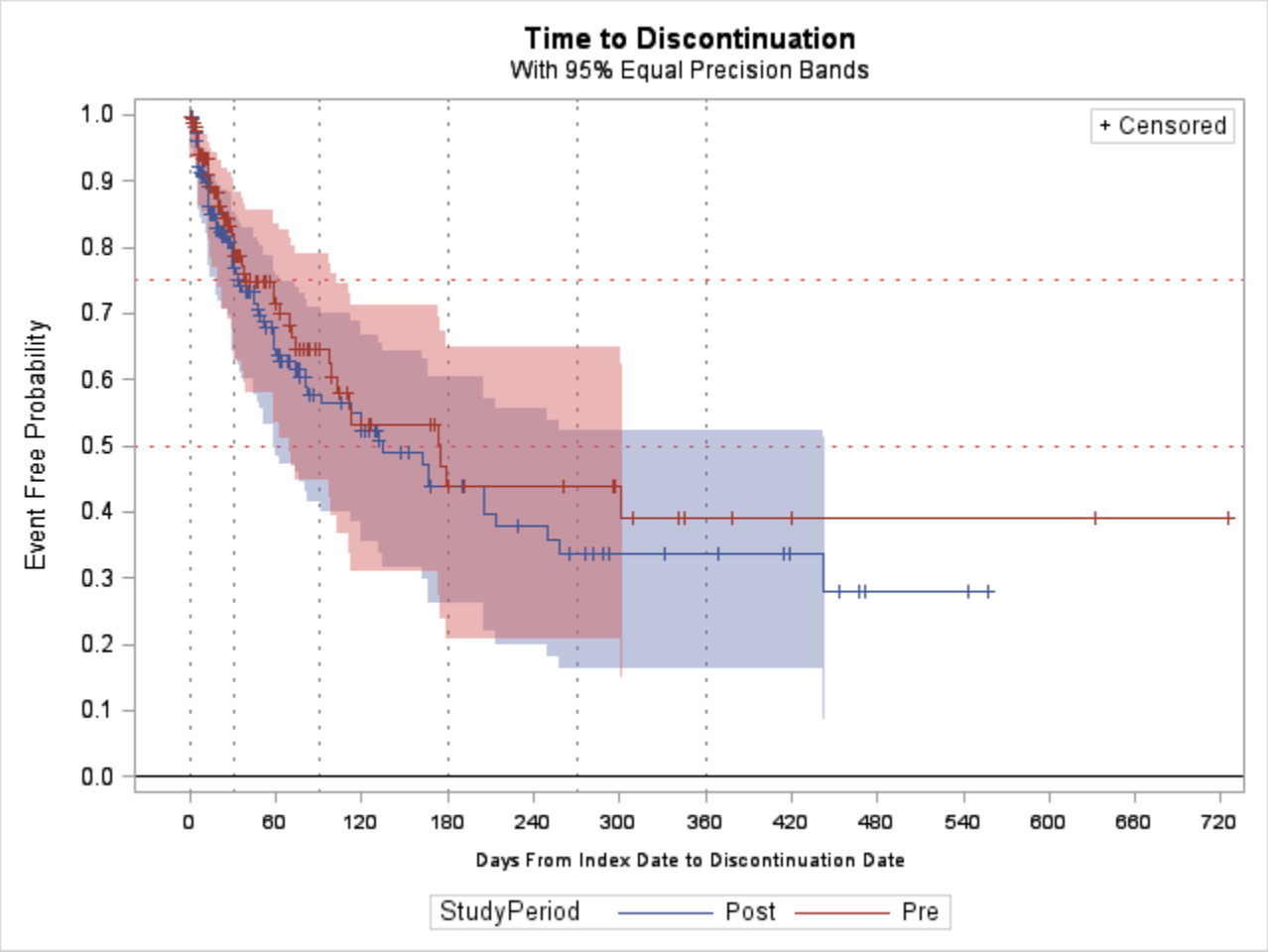
The Elixhauser Comorbidity Index, used to estimate disease burden in the population, was similar for both groups. The index is a weighted measure based on relevant diagnoses submitted on medical claims during the baseline period. The presence or absence of diagnoses are identified in medical claims and 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 predict risk of in-hospital mortality (the "M" index) and risk for 30-day readmission (the "R" index).[6] Given the short baseline period for this dataset (30 days prior to the IE), information on diagnoses may be incomplete. The most common diagnoses contributing to the Elixhauser Comorbidity Index included drug abuse (87-88%), alcohol abuse 11-12%), and depression (7-10%).

Table 1. Demographics for paid FFS pharmacy claims

	Before		After	
	297	%	395	%
Female	139	46.8%	173	43.8%
Age – mean (range)	34	(2-62)	35	(18-63)
<18	1	0.3%	0	0.0%
18-35	187	63.0%	237	60.0%
36-64	109	36.7%	158	40.0%
>=65	0	0.0%	0	0.0%
Race				
White	100	33.7%	138	34.9%
Unknown	123	41.4%	118	29.9%
American Indian/Alaskan Native (HNA)	65	21.9%	123	31.1%
Other	9	3.0%	16	4.1%
Average Elixhauser Score "M"	-6.91		-6.83	
Average Elixhauser Score "R"	17.45		17.31	

*Weighted index based on diagnoses on medical claims in the baseline period.
"M" score - in-hospital mortality index
"R" score - 30-day re-admission index

Figure 1. Kaplan-Meier Curve for Time to Treatment Discontinuation. Shading represents 95% confidence intervals.



Overall, there was no difference in time to treatment discontinuation before and after removal of PA criteria for MAT. The median time to treatment discontinuation was 175 days before removal of the PA criteria and 135 days after removal of the PA criteria. The analysis was significantly limited by the number of patients censored from the analysis prior to experiencing a treatment outcome. The primary reason for censoring was enrollment in a CCO (40-44%). Another 10% of patients lost Medicaid eligibility prior to treatment discontinuation.

Table 2. Reasons for censoring before buprenorphine treatment discontinuation

	Before		After	
	297	%	**395**	%
Enrollment in a CCO (CCOA or CCOB)	131	44.1%	157	39.7%
Lost Medicaid eligibility	31	10.4%	36	9.1%
Enrollment in Medicare	0	0.0%	0	0.0%
Coverage by other primary insurance	0	0.0%	0	0.0%

Limitations:

- Because many patients prescribed sublingual buprenorphine were new to Medicaid, the baseline period for assessment of diagnoses was limited to 30 days. However, a short baseline period significantly limits the number of medical claims that can be used to identify diagnoses and data used to estimate the Elixhauser Comorbidity Index is likely incomplete. Similarly diagnostic data based on claims may be inaccurate or not reflective of a patient's true diagnoses, especially for conditions associated with significant social stigma such as OUD.
- Medicaid includes a significant proportion of patients who are only transiently enrolled in FFS. Often patients are quickly enrolled into a CCO upon eligibility for Medicaid and remain in FFS for only a few months. In order to accurately capture data from this population in the analysis, a baseline period of only 30 days was required. However, this limitation led to several assumptions when identifying patients who may be treatment-naïve. Patients were assumed to be treatment-experienced if they met the following criteria: 1) had prior claims for MAT paid by Medicaid; 2) the pharmacy indicated that the first paid claim was a refill; or 3) the member did not have any paid medical claims between their enrollment date and the first paid claim for sublingual buprenorphine (with the assumption that members new to Medicaid but already on MAT would not have a recent provider visit). However, there are limitations to this definition, and it is possible that members who were actually treatment experienced may have been included. For example, patients who are new to Medicaid, but have frequent provider visits could have been included as a treatment-naïve patient when they may have been on MAT for some time.
- A significant proportion of patients were excluded because they had potentially incomplete claims data due to other primary insurance, were treatment experienced, or were not eligible for Medicaid for the required 30-day baseline period. Table 3 describes how individual exclusion criteria influenced number of patients eligible for inclusion in the study. After all exclusion criteria, about 30% of all patients with claims for sublingual buprenorphine were included in the study. This study assumes that included patients would still be representative of most treatment-naïve patients prescribed MAT in Medicaid.

Table 3. Population of included patients

	Before		After	
Number of included patients	#	%	#	%
With paid buprenorphine claim from 1/1/2019-6/30/2019 (pre) or from 1/1/2020-6/30/2020 (post)	**968**		**1,214**	
And after exclusion of limited benefit packages, Medicare, TPL in baseline period	843	87.1%	1,042	85.8%
And after continuous Medicaid enrollment requirement in the 30 days before the IE	730	75.4%	925	76.2%
And after treatment naïve restriction	323	33.4%	420	34.6%
And after removal of duplicate patients in control/experimental periods	299	30.9%	396	32.6%
And after removal of patients enrolled in a CCO-A at time of IE	297	30.7%	395	32.5%

- The COVID-19 public health emergency is also an external confounding factor which is not controlled for in this study. 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 much impact these closures may have had on duration of therapy for patients. For example, patients may have been reluctant to visit their pharmacy to fill medications during closures and may have had difficulty obtaining refills if provider offices were closed.
- 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.
- This analysis was not limited to patients with a diagnosis of OUD. Patients may be prescribed sublingual buprenorphine for other indications and uses.
- There are also several limitations associated with use of a survival analysis to measure outcomes:
    - One assumption of a survival analysis is that the probability of treatment discontinuation is the same for subjects remaining in the analysis as those that are censored from the analysis. Because of this assumption, time to treatment discontinuation after the first censored patient is just an estimate. As more patients are censored, the reliability of this estimate decreases. Just under 50% of patients were censored from the analysis prior to treatment discontinuation (primarily because they were enrolled in a CCO) which is a significant limitation of this analysis.
    - Another assumption of survival analyses is that the probability of treatment discontinuation is the same for subjects starting treatment early in the study period compared to later in the study period. However, ongoing national and state-wide efforts have increased awareness and access to therapies for OUD over time, and it is unclear how this may impact duration of therapy for our population. For example, efforts to increase the number of prescribing providers for buprenorphine, availability of medical clinics for treatment of OUD, and enhanced coverage of supportive therapies may increase retention in treatment over time.
    - A third assumption of a survival analysis is that treatment discontinuation occurs at a specified time. For example, if a patient fills a 30-day prescription for buprenorphine without subsequent treatment, treatment discontinuation would be defined as the date 30 days after the prescription was filled, when in reality, treatment discontinuation could have occurred at any time in the prior 30 days.

References:

1. Steele DW, Becker SJ, Danko KJ, Balk EM, Saldanha IJ, Adam GP, Bagley SM, Friedman C, Spirito A, Scott K, Ntzani EE, Saeed I, Smith B, Popp J, Trikalinos TA. Interventions for Substance Use Disorders in Adolescents: A Systematic Review. Comparative Effectiveness Review No. 225. (Prepared by the Brown Evidence-based Practice Center under Contract No. 290-2015-00002-I.) AHRQ Publication No. 20-EHC014. Rockville, MD: Agency for Healthcare Research and Quality. May 2020. Posted final reports are located on the Effective Health Care Program search page. DOI: https://doi.org/10.23970/AHRQEPCCER225.
2. Chan B GE, Arkhipova-Jenkins I, Gilbert J, Hilgart J, Fiordalisi C, Hubbard K, Brandt I, Stoeger E, Paynter R, Korthuis PT, Guise J-M. . Retention Strategies for Medications for Addiction Treatment in Adults With Opioid Use Disorder: A Rapid Evidence Review. (Prepared by the Scientific Resource Center under Contract No. HHSA 290-2017- 00003C). AHRQ Publication No. 20-EHC012. Rockville, MD: Agency for Healthcare Research and Quality. July 2020. Errata August 2020. Posted final reports are located on the Effective Health Care Program search page. DOI: https://doi.org/10.23970/AHRQEPCRAPIDMAT.
3. OSU Drug Use Research and Management Program. Policy Evaluation: Substance Use Disorders. January 2019. https://www.orpdl.org/durm/meetings/meetingdocs/2019_01_24/archives/2019_01_24_SubstanceUseDisorder_DUE.pdf. Accessed March 18, 2022.
4. Lo-Ciganic WH, Donohue JM, Kim JY, et al. Adherence trajectories of buprenorphine therapy among pregnant women in a large state Medicaid program in the United States. *Pharmacoepidemiology and drug safety.* 2019;28(1):80-89.
5. Samples H, Williams AR, Olfson M, Crystal S. Risk factors for discontinuation of buprenorphine treatment for opioid use disorders in a multi-state sample of Medicaid enrollees. *J Subst Abuse Treat.* 2018;95:9-17.
6. Moore BJ, White S, Washington R, Coenen N, Elixhauser A. Identifying Increased Risk of Readmission and In-hospital Mortality Using Hospital Administrative Data: The AHRQ Elixhauser Comorbidity Index. *Medical care.* 2017;55(7).

Appendix 1: Drug Coding

Table A1. Drug codes for MAT pharmacy claims

PDL Class	GSN	Form	Generic	PDL	Route
Substance Use Disorders, Opioid & Alcohol	060935	SUS ER REC	naltrexone microspheres	Y	IM
Substance Use Disorders, Opioid & Alcohol	029312	TAB SUBL	buprenorphine HCl	V	SL
Substance Use Disorders, Opioid & Alcohol	029313	TAB SUBL	buprenorphine HCl	V	SL
Substance Use Disorders, Opioid & Alcohol	077999	SOLER SYR	buprenorphine	Y	SQ
Substance Use Disorders, Opioid & Alcohol	078000	SOLER SYR	buprenorphine	Y	SQ
Substance Use Disorders, Opioid & Alcohol	051640	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	051641	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	066635	FILM	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	066636	FILM	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	070259	FILM	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	070262	FILM	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	071189	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	071190	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	073424	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	073425	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	074685	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL
Substance Use Disorders, Opioid & Alcohol	076981	TAB SUBL	buprenorphine HCl/naloxone HCl	Y	SL

Table A2. Drug codes for MAT medical claims

Code	Description
J3490, J3590,	Generic drug codes; Include only if associated with any of the pharmacy drug codes for MAT (see Table A1) or with methadone (GSNs 004237 004238; 004239; 004240; 004242; 023767)
H0033,	Oral Med Adm Direct Observe
T1502,	Medication Admin Visit
96372	Ther/Proph/Diag Inj Sc/Im; Include only if associated with any of the pharmacy drug codes for MAT (see Table A1) or with methadone (GSNs 004237 004238; 004239; 004240; 004242; 023767)
G2067	Medication Assisted Treatment, Methadone; Weekly Bundle Including Dispensing And/Or Administration,
G2068	Medication Assisted Treatment, Buprenorphine (Oral); Weekly Bundle Including Dispensing And/Or Admin
G2069	Medication Assisted Treatment, Buprenorphine (Injectable); Weekly Bundle Including Dispensing And/Or
G2070	Medication Assisted Treatment, Buprenorphine (Implant Insertion); Weekly Bundle Including Dispensing
G2071	Medication Assisted Treatment, Buprenorphine (Implant Removal); Weekly Bundle Including Dispensing A
G2072	Medication Assisted Treatment, Buprenorphine (Implant Insertion And Removal); Weekly Bundle Includin
G2073	Medication Assisted Treatment, Naltrexone; Weekly Bundle Including Dispensing And/Or Administration,
G2075	Medication Assisted Treatment, Medication Not Otherwise Specified; Weekly Bundle Including Dispensin
G2078	Take-Home Supply Of Methadone; Up To 7 Additional Day Supply (Provision Of The Services By A Medicar

G2079	Take-Home Supply Of Buprenorphine (Oral); Up To 7 Additional Day Supply (Provision Of The Services B
G2213	Initiation Of Medication For The Treatment Of Opioid Use Disorder In The Emergency Department Settin
G6053	methadone
H0020	Alcohol And/Or Drug Services; Methadone Administration And/Or Service (Provision Of The Drug By A Li
J0570	Buprenorphine Implant, 74.2 Mg
J0571	Buprenorphine, Oral, 1 Mg
J0572	Buprenorphine/Naloxone, Oral, Less Than Or Equal To 3 Mg Buprenorphine
J0573	Buprenorphine/Naloxone, Oral, Greater Than 3 Mg, But Less Than Or Equal To 6 Mg Buprenorphine
J0574	Buprenorphine/Naloxone, Oral, Greater Than 6 Mg, But Less Than Or Equal To 10 Mg Buprenorphine
J0575	Buprenorphine/Naloxone, Oral, Greater Than 10 Mg Buprenorphine
J0592	Injection, Buprenorphine Hydrochloride, 0.1 Mg
J1230	Injection, Methadone Hcl, Up To 10 Mg
J2310	Injection, Naloxone Hydrochloride, Per 1 Mg
J2315	Injection, Naltrexone, Depot Form, 1 Mg
Q9991	Injection, Buprenorphine Extended-Release (Sublocade), Less Than Or Equal To 100 Mg
Q9992	Injection, Buprenorphine Extended-Release (Sublocade), Greater Than 100 Mg
S0109	Methadone, Oral, 5 Mg

Table A3. Key Inclusion Criteria

	Key question #2: Duration
Population	new start patients with continuous Medicaid eligibility at least 30 days prior to the IE
Intervention	Initiation of buprenorphine SL (index event)
Comparator	Patients initiating buprenorphine SL from 1/1/2019-6/30/2019 vs Patients initiating buprenorphine SL from 1/1/2020-6/30/2020 (before vs. after removal of PA criteria)
Outcomes	Duration of buprenorphine therapy
Setting	FFS