**Supplemental Materials for:**

**Variation in initiation, engagement, and retention on medications for opioid use disorder based on health insurance plan design**

**Supplemental Table 1: Out-of-pocket costs 34 and 180 days after initiating medication for opioid use disorder, among those initiating medication treatment**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | 34 day | | 180 day | |
|  | Median | IQR | Median | IQR |
| Among those initiating | $239 | ($73-$749) | $631 | ($245-$1854) |
| Buprenorphine | $187 | ($60-$520) | $516 | ($230-$1591) |
| Methadone | $110 | ($9-$320 | $363 | ($84-$920) |
| Oral NTX | $405 | ($124-$1235) | $897 | ($320-$2606) |
| XR-NTX | $750 | ($242-$1491) | $1,275 | ($515-$2300) |
| Cost sharing |  |  |  |  |
| Pharmacy deductible |  |  |  |  |
| <$1000 | $215 | ($70-$694) | $585 | ($242-$1697) |
| $1000+ | $419 | ($133-$1165) | $1,034 | ($347-$2609) |
| Medical deductible |  |  |  |  |
| <$1000 | $212 | ($70-$624) | $552 | ($225-$1316) |
| $1000+ | $251 | ($76-$875) | $730 | ($263-$2180) |
| Pharmacy copay |  |  |  |  |
| At or below | $249 | ($81-$773) | $631 | ($245-$1837) |
| Above | $204 | ($54-$670) | $632 | ($245-$1858) |
| Medical copay |  |  |  |  |
| At or below median cost | $238 | ($70-$730) | $610 | ($226-$1744) |
| Above median cost | $239 | ($80-$836) | $679 | ($310-$2229) |

**Supplemental Table 2: Logistic models predicting medication for opioid use disorder initiation, engagement, and retention stratified by medication type**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Buprenorphine | Methadone | Oral NTX | XR-NTX | Buprenorphine | Methadone | Oral NTX | XR-NTX |
|  | Initiation | Initiation | Initiation | Initiation | Engagement | Engagement | Engagement | Engagement |
|  | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Pharmacy deductible |  |  |  |  |  |  |  |  |
| <$1000 | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| $1000+ | 1.02 (0.78-1.34) | 1.18 (0.72-1.93) | 1.25 (0.90-1.74) | 1.26 (0.61-2.58) | 0.96 (0.52-1.77) | NC | 0.90 (0.44-1.81) | 2.91 (0.38-22.55) |
| Medical deductible |  |  |  |  |  |  |  |  |
| <$1000 | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| $1000+ | 0.89 (0.73-1.08) | 0.90 (0.62-1.31) | 0.88 (0.69-1.12) | 0.49 (0.31-0.79) | 1.51 (0.98-2.32) | 0.10 (0.01-1.42) | 0.92 (0.55-1.53) | 1.88 (0.47-7.51) |
| Pharmacy copay |  |  |  |  |  |  |  |  |
| Above median cost | 1.04 (0.84-1.29) | 1.21 (0.82-1.79) | 0.90 (0.69-1.18) | 1.30 (0.79-2.13) | 0.91 (0.57-1.45) | 4.14 (0.35-48.67) | 1.49 (0.84-2.62) | 1.25 (0.32-4.92) |
| at or below median | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Medical office copay |  |  |  |  |  |  |  |  |
| Above median cost | 0.89 (0.73-1.08) | 0.82 (0.56-1.20) | 1.31 (1.04-1.66) | 1.08 (0.67-1.75) | 0.98 (0.63-1.53) | 0.36 (0.08-1.63) | 1.06 (0.65-1.72) | 1.16 (0.29-4.60) |
| at or below median | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Current plan quarter |  |  |  |  |  |  |  |  |
| 1 | 1.18 (0.92-1.51) | 1.42 (0.89-2.25) | 1.00 (0.73-1.38) | 0.67 (0.39-1.15) | 1.54 (0.84-2.83) | NC | 0.77 (0.39-1.50) | 2.40 (0.45-12.68) |
| 2 | 1.04 (0.79-1.36) | 0.78 (0.45-1.34) | 1.12 (0.79-1.57) | 0.72 (0.40-1.31) | 0.71 (0.38-1.33) | NC | 0.62 (0.32-1.20) | 1.01 (0.19-5.50) |
| 3 | 0.74(0.54-1.01) | 0.63(0.34-1.17) | 1.45(1.04-2.04) | 0.45(0.22-0.92) | 0.74(0.37-1.45) | NC | 0.68(0.34-1.35) | 0.93(0.13-6.46) |
| 4 | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Sex |  |  |  |  |  |  |  |  |
| Male | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Female | 1.33 (1.11-1.58) | 1.22 (0.86-1.72) | 1.18 (0.94-1.47) | 0.60 (0.37-0.98) | 1.13 (0.77-1.67) | 0.35 (0.08-1.60) | 1.20 (0.76-1.88) | 0.95 (0.23-3.89) |
| Age |  |  |  |  |  |  |  |  |
| 16-24 | 0.97 (0.37-2.53) | NC | 1.17 (0.45-3.06) | 1.81 (0.22-14.55) | NC | NC | NC | NC |
| 25-64 | 1.92 (0.78-4.75) | NC | 1.13 (0.45-2.83) | 1.68 (0.22-12.65) | NC | 0.48 (0.08-3.12) | NC | NC |
| 65+ | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Region |  |  |  |  |  |  |  |  |
| Metropolitan | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Micropolitin | 0.80 (0.58-1.11) | 1.15 (0.66-1.98) | 1.00 (0.67-1.50) | 0.63 (0.23-1.76) | 1.03 (0.50-2.12) | NC | 1.07 (0.45-2.52) | 0.59 (0.03-10.59) |
| Small town | 0.70 (0.41-1.19) | 1.10 (0.48-2.53) | 1.08 (0.61-1.93) | 0.39 (0.05-2.84) | 4.84 (0.61-38.50) | NC | 0.67 (0.19-2.41) | NC |
| Rural | 0.98 (0.47-2.03) | 0.92 (0.22-3.81) | 1.19 (0.50-2.83) | 4.00 (1.36-11.76) | 1.13 (0.22-5.91) | 0.17 (0.01-3.10) | 1.27 (0.18-8.94) | 3.05 (0.23-40.36) |
| Missing | 2.16 (0.63-7.44) | 3.04 (0.39-23.63) | 1.13 (0.14-8.92) | NC | 0.88 (0.07-10.53) | NC | NC | NC |
| Clinical covariates |  |  |  |  |  |  |  |  |
| Concurrent substance use |  |  |  |  |  |  |  |  |
| Sedative | 1.05 (0.49-2.26) | NC | 0.91 (0.57-1.45) | 0.39 (0.12-1.27) | 0.21 (0.03-1.35) | NC | 0.71 (0.28-1.80) | NC |
| Cocaine | 1.11 (0.47-2.66) | NC | 1.00 (0.60-1.66) | 0.44 (0.12-1.68) | 1.25 (0.11-14.21) | NC | 1.81 (0.65-5.01) | NC |
| Cannabis | 0.62 (0.23-1.73) | 0.90 (0.12-6.72) | 0.93 (0.54-1.60) | 1.06 (0.38-2.95) | NC | NC | 1.51 (0.48-4.73) | NC |
| Amphetamine | 0.25 (0.06-1.04) | 0.77 (0.10-5.77) | 1.23 (0.75-2.03) | 0.13 (0.02-1.00) | NC | NC | 1.19 (0.44-3.24) | NC |
| Hallucinogen | NC | NC | 0.76 (0.21-2.76) | 6.33 (1.05-38.32) | 1.56 (0.35-6.90) | NC | 0.35 (0.02-7.06) | 2.72 (0.73-10.17) |
| Alcohol | 0.52 (0.31-0.88) | 0.16 (0.02-1.17) | 6.18 (4.77-8.00) | 12.61 (7.93-20.04) | NC | NC | 1.34 (0.80-2.23) | NC |
| Prior opioid overdose |  |  |  |  |  |  |  |  |
| Yes | 0.80 (0.11-6.16) | 5.04 (0.62-41.25) | 1.51 (0.43-5.27) | NC | NC | NC | 0.35 (0.02-5.25) | 0.74 (0.12-4.37) |
| No | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Injection-related infection |  |  |  |  |  |  |  |  |
| Yes | 1.29 (0.55-3.02) | NC | 0.51 (0.12-2.11) | 0.98 (0.12-7.82) | 1.41 (0.31-6.48) | NC | NC | 0.30 (0.04-2.17) |
| No | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Hepatitis C |  |  |  |  |  |  |  |  |
| Yes | 3.11 (1.64-5.88) | 3.77 (1.28-11.05) | 0.27 (0.04-2.00) | NC | 1.01 (0.52-1.93) | NC | NC | NC |
| No | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| Mental health |  |  |  |  |  |  |  |  |
| Depression | 0.79 (0.59-1.05) | 0.70 (0.36-1.39) | 1.22 (0.93-1.61) | 0.76 (0.43-1.36) | 0.78 (0.44-1.36) | NC | 1.10 (0.63-1.93) | NC |
| Anxiety | 1.08 (0.84-1.39) | 0.45 (0.23-0.88) | 1.22 (0.94-1.59) | 1.62 (0.97-2.70) | 0.91 (0.44-1.91) | 0.91 (0.44-1.91) | 1.25 (0.72-2.15) | 2.81 (0.10-75.51) |
| ADHD | 1.39 (0.99-1.95) | 0.80 (0.32-1.99) | 0.99 (0.66-1.50) | 0.77 (0.30-1.98) | 0.93 (0.25-3.51) | 0.93 (0.25-3.51) | 0.97 (0.40-2.35) | NC |
| PTSD | 1.04 (0.55-1.97) | NC | 1.18 (0.70-1.97) | 1.03 (0.30-3.58) | 1.57 (0.44-5.61) | 1.57 (0.44-5.61) | 1.75 (0.60-5.09) | 5.60 (1.18-26.61) |
| Bipolar | 0.64 (0.36-1.15) | 1.25 (0.44-3.49) | 1.11 (0.73-1.69) | 0.43 (0.13-1.43) | 1.02 (0.05-19.90) | 1.02 (0.05-19.90) | 0.54 (0.21-1.38) | 23.28 (1.03-526.30) |
| Psychoses | 0.49 (0.12-2.00) | 1.18 (0.16-8.93) | 0.39 (0.15-1.00) | 0.48 (0.06-3.89) | 0.80 (0.44-1.46) | 0.80 (0.44-1.46) | 1.07 (0.14-8.26) | 1.77 (0.10-31.08) |
| Modified Elixhauser |  |  |  |  |  |  |  |  |
| 0 | Reference | Reference | Reference | Reference | Reference | Reference | Reference | Reference |
| 1 | 0.63 (0.48-0.82) | 0.52 (0.30-0.93) | 1.02 (0.78-1.35) | 1.26 (0.75-2.13) | 0.99 (0.40-2.46) | 0.99 (0.40-2.46) | 1.65 (0.93-2.90) | 1.65 (0.93-2.90) |
| 2 | 0.51 (0.34-0.76) | 0.77 (0.38-1.56) | 0.54 (0.33-0.86) | 0.91 (0.40-2.10) | 0.48 (0.18-1.28) | 0.48 (0.18-1.28) | 1.05 (0.38-2.89) | 1.05 (0.38-2.89) |
| 3+ | 0.33 (0.21-0.52) | 0.23 (0.07-0.74) | 0.58 (0.38-0.89) | 0.36 (0.13-1.02) | 0.85 (0.14-4.99) | 0.85 (0.14-4.99) | 0.65 (0.25-1.72) | 0.65 (0.25-1.72) |
| NTX=naltrexone; XR-NTX=extended release injectable naltrexone  NC=not calculable due to small sample | | | | | | | | |

**Supplemental Table 3:** **Multivariable logistic regression models predicting medication for opioid use disorder initiation, engagement, and retention where each model uses the entire sample**

|  |  |  |
| --- | --- | --- |
|  | Engagement | Retention |
|  | OR (95% CI) | OR (95% CI) |
| Pharmacy deductible |  |  |
| <$1000 | Reference | Reference |
| $1000+ | 1.10 (0.87-1.39) | 0.90 (0.64-1.27) |
| Medical deductible |  |  |
| <$1000 | Reference | Reference |
| $1000+ | 0.90 (0.76-1.07) | 0.87 (0.69-1.09) |
| Pharmacy copay |  |  |
| Above median cost | 1.16 (0.96-1.39) | 1.19 (0.93-1.52) |
| at or below median | Reference | Reference |
| Medical office copay |  |  |
| Above median cost | 0.98 (0.82-1.16) | 0.88 (0.70-1.12) |
| at or below median | Reference | Reference |
| Current plan quarter |  |  |
| 1 | 1.49 (1.18-1.88) | 0.78 (0.53-1.14) |
| 2 | 1.06 (0.82-1.37) | 1.67 (1.21-2.31) |
| 3 | 0.97 (0.74-1.27) | 1.66 (1.26-2.19) |
| 4 | Reference | Reference |
| Sex |  |  |
| Male | Reference | Reference |
| Female | 1.19 (1.02-1.40) | 1.32 (1.07-1.64) |
| Age |  |  |
| 16-24 | 0.86 (0.36-2.04) | 0.54 (0.20-1.43) |
| 25-64 | 1.88 (0.82-4.30) | 1.26 (0.51-3.13) |
| 65+ | Reference | Reference |
| Region |  |  |
| Metropolitan | Reference | Reference |
| Micropolitan | 0.88 (0.66-1.17) | 0.97 (0.67-1.42) |
| Small town | 0.88 (0.57-1.35) | 1.25 (0.75-2.10) |
| Rural | 1.19 (0.67-2.13) | 1.67 (0.84-3.32) |
| Missing | 1.54 (0.46-5.14) | 2.26 (0.53-9.69) |
| Clinical covariates |  |  |
| Concurrent substance use |  |  |
| Sedative | 0.59 (0.34-1.02) | 0.66 (0.27-1.62) |
| Cocaine | 1.08 (0.64-1.83) | 1.79 (0.84-3.83) |
| Cannabis | 1.19 (0.70-2.03) | 1.10 (0.43-2.77) |
| Amphetamine | 0.78 (0.43-1.39) | 0.29 (0.07-1.21) |
| Hallucinogen | 1.06 (0.24-4.73) | 4.76 (0.94-24.19) |
| Alcohol | 2.38 (1.86-3.03) | 0.94 (0.60-1.48) |
| Prior opioid overdose |  |  |
| Yes | 0.66 (0.16-2.82) | NC |
| No | Reference | Reference |
| Injection-related infection |  |  |
| Yes | 0.94 (0.43-2.06) | 2.65 (1.30-5.40) |
| No | Reference | Reference |
| Hepatitis C |  |  |
| Yes | 1.96 (1.07-3.60) | 1.64 (0.70-3.86) |
| No | Reference | Reference |
| Mental health |  |  |
| Depression | 0.87 (0.68-1.09) | 0.62 (0.43-0.89) |
| Anxiety | 1.03 (0.83-1.27) | 1.11 (0.83-1.50) |
| ADHD | 1.09 (0.80-1.50) | 1.27 (0.83-1.95) |
| PTSD | 1.20 (0.75-1.93) | 0.53 (0.19-1.45) |
| Bipolar | 0.68 (0.44-1.06) | 0.66 (0.34-1.32) |
| Psychoses | 0.54 (0.22-1.36) | NC |
| Modified Elixhauser |  |  |
| 0 | Reference | Reference |
| 1 | 0.82 (0.67-1.02) | 0.66 (0.48-0.91) |
| 2 | 0.65 (0.47-0.91) | 0.85 (0.56-1.29) |
| 3+ | 0.34 (0.23-0.51) | 0.34 (0.19-0.61) |
| Initiation is not included in this table as this regression includes the entire sample in the base case analysis. In the base case, engagement is only modeled among those who initiate, and retention is only modeled among those who engage. In this supplemental analysis, engagement and retention are modeled for the entire sample. NC=not calculable due to small sample | | | |  |

**Protocol for Impact of Health Insurance Type and Transitions on Treatment for Opioid Use Disorder**

*Aims 3:* *Analyze the impact of insurance cost sharing in a large national sample of commercially insured individuals on MOUD initiation, engagement and retention.*

Version 1.2: September 1, 2020

**Abbreviations**

|  |  |
| --- | --- |
| ICD-9 or ICD-10 | International Statistical Classification of  Diseases and Related Health Problems,  revision 9 or 10 |
| OUD | Opioid use disorder |
| MOUD | Medication for opioid use disorder |

**Addendum History**

**Chronological description of changes:**

12/23/2019: Initial protocol finalized

07/06/2020: Included extended release buprenorphine as an outcome (not as a cohort definition)

09/01/2020: Expanded end of observation time from December 31, 2018 to July 31, 2019 due to availability of new data.

11/12/2020: Limited sample to commercially insured to capture all cost variables and clarified age brackets

**A. Introduction**

Mortality and morbidity due to opioids have reached epidemic proportions in the United

States. Massachusetts has been particularly affected, with opioid overdose deaths more than tripling from 656 to 2,155 in the five-year period from 2011 to 2016. Medications for opioid use disorder (MOUDs) are a proven treatment for opioid use disorder (OUD) and a critical tool in addressing the epidemic, yet remain underutilized. One barrier to treatment may be insurance, either through coverage restrictions or burdensome cost sharing. Emerging evidence, for example, has suggested that while expanding Medicaid increased treatment for OUD, transitioning into, out of, or between health insurance plans, otherwise known as churn, is negatively associated with access to health care services. Specifically, it is unclear whether insurance type, cost sharing, or transitions impact the receipt of MOUDs. This evidence is needed to support health insurance benefit design and policy initiatives that lead to improved access to and treatment with life-saving MOUD.

Our primary endpoint is receipt of MOUD and is operationalized as initiation, engagement, and retention.

**B. Study Objective**

Analyze the impact of insurance cost sharing in a large national sample of commercially insured individuals on MOUD initiation, engagement and retention.

* *Hypothesis a: Higher cost sharing will be associated with lower rates of initiation and engagement, longer time to initiation and engagement, and lower retention in MOUD.*
* *Hypothesis b: Higher cost sharing will be associated with lower fill rates for individuals prescribed buprenorphine or naltrexone.*

**C. Study Design**

**Data source**

For this objective we will use OptumLabs® Data Warehouse (OLDW), a large, national database with de-identified claims data on more than 125 million privately insured and Medicare Advantage enrollees in a large U.S. health plan. The database contains longitudinal health information, including inpatient, outpatient, and pharmacy claims, representing a diverse mixture of ages, ethnicities and geographical regions across the United States. Claims data are linked to clinical EHR data for approximately 15% of individuals.

**Timeframe**

October 1, 2015 - July 31, 2019

**Study population**

Basic inclusion criteria:

1. Incident OUD diagnosis.
2. > 16 years of age.
3. Contiguous Commercial or Medicare Advantage coverage in OLDW for 90 days before and after index date.
4. Available data on cost sharing.
5. *For hypothesis b*: at least one prescription for buprenorphine or naltrexone following OUD diagnosis.

Observation period

The **index date** will be the first data an individual is identified as OUD (see identification algorithm below). Individuals must be enrolled in the data at least 90 days prior to and following this index date. Consequently, the earliest possible index date is December 30 2015 (allowing for 90 days of enrollment prior to this) and the latest first diagnosis is July 31 2019 to allow for 90 days of follow-up after this date.

Defining opioid use disorder (OUD)

Individuals can be characterized as having OUD in two ways:

* Based on claim(s) for opioid **dependence**
  + ≥1 inpatient opioid dependence claim *or* ≥2 outpatient opioid dependence claims that occur within 90 days of each other (see appendix table A1 for corresponding ICD-10 codes)

**AND**

* + The above opioid dependence claim(s) does not occur during an episode of ongoing long-term opioid therapy, which may indicate physiologic opioid dependence rather than a use disorder. See definition of long-term prescribed opioid episode below.

OR

* Based on claim(s) for opioid **dependence**, **abuse**, or **use**
  + ≥1 claim for opioid dependence, abuse, or use (see appendix table A1 for corresponding ICD-10 codes)

**AND**

* + Has one of the following confirmatory diagnoses/events within 90 days (+/-) of the OUD diagnosis (see appendix table A2 for corresponding ICD-10 codes for each event):
    - Evidence of opioid overdose
    - Evidence of treatment with buprenorphine, methadone, or naltrexone (see definition below)
    - Evidence of an opioid-related detox or rehabilitation stay (see definition below)
    - Hepatitis C
    - Injection-related infectious episode

If an individual qualifies for OUD under both conditions, the Index Date will be the earliest of the dates available (either the earliest OUD diagnosis date or, if earlier, the date of the confirmatory diagnosis/event indicating OUD as specified above).

Defining ongoing long-term opioid therapy

We do not include individuals with a code for opioid dependence while receiving ongoing long-term opioid therapy (e.g., chronic pain patients) as the use of the opioid dependence may reflect physiologic dependence rather than a use disorder. We defined long-term opioid therapy based on the algorithm published by LaRochelle et al. in *Annals of Internal Medicine* (LaRochelle et al. 2016):

* Opioid episodes defined as consecutive dispensing with 60 or fewer days between the run-out date (fill date plus days supplied) and the fill date of the next dispensing.
* Long-term prescribed opioid episodes met three criteria:
  + ≥3 dispensing that were at least 21 days apart
  + Duration of at least 84 days (12 weeks)
  + At least 84 days supplied.

OUD may develop or be recognized during long-term opioid therapy and trigger discontinuation of opioid prescribing. As such, if the claim for opioid dependence occurs in the final 45 days of a long-term opioid therapy episode, it will not meet criteria for ongoing long-term opioid therapy. The claim for OUD will thus be considered evidence of OUD.

Defining injection-related infectious episode

We will use an indication of an injection-related infection two ways. First, it will be used to confirm OUD diagnosis as described above. Second, it will be used as a covariate to indicate OUD severity. See appendix table A2 for a full list of codes used to define injection-related infectious episodes. In short, we include the following classes of infections:

* Endocarditis
* Abscess/cellulitis
* Phlebitis
* Infectious arthritis
* Hepatitis C

Defining treatment for OUD

Inpatient treatment of OUD or use of medications for OUD are used to confirm OUD diagnosis.

*Inpatient detoxification or inpatient treatment for OUD (rehabilitation)*. These services were identified using a combination of revenue or procedure codes for inpatient stays that also included an ICD-10 diagnosis code for opioid use.

|  |  |
| --- | --- |
| **>1 of Following Revenue or ICD-10 Procedure Codes** | |
| Revenue | 0116, 0126, 0136, 0146, 0156, 0118, 0128, 0138, 0158, 1002† |
| ICD-10 | HZ\* |
| **PLUS > 1 of Following ICD-10 Diagnosis Codes** | |
| ICD-10 | F11\* |

*Medication for opioid use disorder (MOUD).* Includes FDA-approved treatment for OUD including buprenorphine, methadone, and naltrexone using pharmacy and medical claims as follows:

|  |  |  |
| --- | --- | --- |
| Medication | Pharmacy Claims | Medical Claims |
| Buprenorphine | *Include*: mono-formulated buprenorphine and buprenorphine/naloxone  *Exclude*: transdermal buprenorphine and buccal film (Belbuca) indicated for pain | HCPCS J0570, J0571, J0572, J0573, J0574, J0575, J0592 |
| Extended-release buprenorphine (for MOUD outcomes only) | *NDC:* 12496030001; 12496030002; 12496030005; 12496010001; 12496010002; 12496010005 | HCPCS Q9991, Q9992 |
| Methadone | N/A (methadone for OUD is dispensed in OTPs only, not identified via retail pharmacies) | HCPCS H0020 |
| Naltrexone | Oral or injectable | HCPCS J2315 |

**Study endpoints**

Primary study endpoints will be based on any of the MOUDs listed above. However, for sensitivity analyses, the type of MOUDs involved with initiation, engagement, and retention should be retained. For example, it is unclear how large a role methadone will play, or how generalizable commercially covered methadone is, so we will evaluate the counts of methadone usage.

*Initiation*: We define initiation as the presence of an NDC code for MOUD in the outpatient pharmacy claims or medical claims as identified above. We will examine both overall time to initiation and the proportion of those initiating within 14 days. We selected 14 days as it mirrors the time from diagnosis in used for NCQA measure Initiation and Engagement of Alcohol and Other Drug Abuse or Dependence Treatment (IET); however, we will also consider initiation within 30 days.

*Engagement*: We define engagement as receipt of MOUD a second time within 34 days after meeting criteria for initiation. We selected 34 days as it mirrors the time from diagnosis in used for NCQA measure Initiation and Engagement of Alcohol and Other Drug Abuse or Dependence Treatment (IET); however, we will also consider engagement within 60 days of initiation.

*Retention*: Time from initiation of buprenorphine or naltrexone until discontinuation where discontinuation is defined as a gap in treatment exceeding 14 days. We will ascertain treatment duration using the days’ supply variable in the outpatient pharmacy dataset. We will evaluate both retention overall, as well as retention in the 180 days following treatment.

**Key independent variables**

*Cost sharing*: Cost sharing is measured in two ways. First, the deductible associated with an individual’s healthcare plan is dichotomized as being high for deductibles over $1,000, or low. Second, pharmacy copays will be dichotomized as above or below the median tier 2 copay for the sample.

**Covariates**

Socio-demographic

* Gender
* Age: 16-24; 25-64; 65+
* National region of residence
* Insurance type: commercial

Medical/mental health

* Elixhauser comorbidity index (modified to exclude mental health and non-opioid substance use which are captured separately)
* Concurrent non-opioid substance use disorder
* Indicators of OUD severity
  + Opioid-related overdose
  + Injection-related infections
  + Hepatitis C
* Other mental health comorbidities
  + Depression
  + Anxiety
  + ADHD
  + PTSD
  + Bipolar disorder
  + Evidence of psychosis
* Hospitalizations

**Statistical analysis**

We will model initiation, engagement, and retention in two ways. First we will assess the probability of initiating and becoming engaged within 6 months, and the probability of being retained at the end of 6 months, of the index date identifying OUD. Each of these dichotomized outcomes will be modeled using logistic regression where the probability of initiating, engaging, and being retained at and within 6 months is a function of cost sharing and the covariates identified above. We will evaluate multicollinearity with the variance inflation factor and adjust our included covariates if significant collinearity exists. These analyses will require individuals in the cohort to have at least 6 months of follow-up in the data.

**Sensitivity analyses**

We will evaluate the effect of the definition of loss to follow up for the retention measure, which is a gap in treatment of 14 days or more in the base case by testing the effect of requiring a 30 or 60 day gap in treatment to be lost to follow up.

**Appendix Table A1.** Diagnosis codes to identify opioid dependence use, or abuse.

|  |  |
| --- | --- |
| **Opioid Dependence** | |
| ICD-10 | F11.2\* |
| **Opioid Use or Abuse** | |
| ICD-10 | F11.1\*, F11.9\* |

**Appendix Table A2.** Diagnosis codes to identify confirmatory events or diagnoses for algorithm to identify OUD.

|  |  |
| --- | --- |
| **Opioid Overdose** | |
| ICD-10 | T40.0X1, T40.0X2, T40.0X4, T40.0X5, T40.1X1, T40.1X2, T40.1X4, T40.2X1, T40.2X2, T40.2X4, T40.2X5, T40.3X1, T40.3X2, T40.3X4, T40.3X5, T40.4X1, T40.4X2, T40.4X4, T40.4X5 |
| **Hepatitis C** | |
| ICD-10 | B17.10, B17.11, B18.2, B19.20, B19.21, Z22.52 |
| Source | Schranz et al. 2019 |
| **Abscess and/or Cellulitis** | |
| ICD-10 | A48.0, G06.1, G06.2, L02.11, L02.413, L02.414, L02.415, L02.416, L02.419, L02.511, L02.512, L02.519, L02.611, L02.612, L02.619, L02.91, L03.011, L03.012, L03.019, L03.031, L03.032, L03.039, L03.113, L03.114, L03.115, L03.116, L03.119, L03.22, L03.90 |
| Notes: | Started with list of ICD-9 codes identified in Tookes et al. 2015, converted to ICD-10 codes and reviewed with Dr. Simeon Kimmel, Infectious Disease and Addiction clinician and researcher. We excluded furuncle and carbuncle. Focused on skin/soft tissue infections and limited cutaneous abscesses and cellulitis to common sites of injection, including neck, extremities, hands, fingers, feet. |
| **Infectious Arthritis** | |
| ICD-10 | M00.0\*, M00.2\*, M00.8\*, M00.9 |
| Notes: | Started with list of ICD-10 codes in Marks et al. 2019, and added M00.2\* (streptococcal arthritis) and M00.9 (pyogenic arthritis, unspecified) after review with Dr. Simeon Kimmel, Infectious Disease and Addiction Clinician. |
| **Infectious Endocarditis** | |
| ICD-10 | B37.6, I33.0, I33.9, I38, I39 |
| Notes: | Initial list generated by examining Felischauer et al 2017 and Schranz et al. 2019. After review with Dr. Simeon Kimmel, Infectious Disease and Addiction Clinician, we kept B37.6 (candida endocarditis) included in Schranz et al and not Fleischauer et al, and excluded A32.82 (listerial endocarditis) that was included in Schranz et al. only due to clinical relevance for injection druse associated endocarditis. |

**References**

Fleischauer AT, Ruhl L, Rhea S, Barnes E. Hospitalizations for endocarditis and associated health care costs among persons with diagnosed drug dependence. North Carolina, 2010-2015. MMWR Morb Mortal Wkly Rep. 2017;66(22):569–73.

Larochelle MR, Liebschutz JM, Zhang F, Ross-Degnan D, Wharam JF. Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose. *Annals Of Internal Medicine*. 2016;165(5):376-377. doi:10.7326/L16-0168

Schranz, A. J., Fleischauer, A., Chu, V. H., Wu, L. T., & Rosen, D. L. (2019). Trends in Drug Use-Associated Infective Endocarditis and Heart Valve Surgery, 2007 to 2017: A Study of Statewide Discharge Data. Annals of internal medicine, 170(1), 31–40. doi:10.7326/M18-2124

Tookes H, Diaz C, Li H, Khalid R, Doblecki-Lewis S. (2015). A Cost Analysis of Hospitalizations for Infections Related to Injection Drug Use at a County Safety-Net Hospital in Miami, Florida. PLoS ONE 10(6): e0129360. https://doi.org/10.1371/journal.pone.0129360