Healthcare Resource Utilization Associated with Extended-Release Naltrexone Compared with Other Treatments in Publicly Insured Patients with Opioid Use Disorder

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BACKGROUND AND OBJECTIVE

- Opioid use disorder (OUD) is a chronic, relapsing disease associated with significant economic, humanistic, and public health impact.[1]
- Approximately 2.1 million people in the United States (US) had an OUD diagnosis in 2017,[2] and an estimated 12% of adults ≥18 years covered by Medicaid have a substance use disorder diagnosis, suggesting a potentially heavy disease burden to families and the healthcare system.[3]
- The US Food and Drug Administration approved medications for OUD include buprenorphine with or without naloxone (BUP), methadone (MET), and extended-release injectable naltrexone (XR-NTX) which is approved for the prevention of relapse to opioid dependence. Current treatment guidelines encourage the use of non-pharmacological treatment (NPT) in combination with medication.[1]
- Despite the availability of these treatment options, <20% of individuals with OUD receive treatment annually. For example, of the 1.3 million patients in substance use treatment facilities, <2% received XR-NTX in 2017.[4]
- In a published study of commercially insured patients with OUD, patients in the XR-NTX cohort had the greatest percentage reduction in hospital admissions and emergency department (ED) visits between the baseline and follow-up period compared to BUP, MET, and NPT cohorts.[5]
- To our knowledge, no study has assessed these outcomes for OUD treatments among Medicaid beneficiaries.
- The objective of this study was to describe healthcare resource utilization (HRU) associated with XR-NTX versus alternative treatments for OUD among publicly insured patients.

METHODS

Study Design and Data Source: A retrospective, observational cohort study was conducted using the MarketScan® Multi-State Medicaid Database. Data from 01/01/2010 through 12/21/2017 were utilized.[6]

Study Sample

Inclusion Criteria

- ≥ 2 claims for XR-NTX, BUP or MET, or ≥3 claims for NPT within a period of 45 days between 01/01/2011-12/31/2016 (the date of first claim served as the index date. Patients were first screened for XR-NTX claims before other treatment claims. Only oral BUP was approved during the study period.);
- ≥ 1 medical claim with a diagnosis of OUD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM], 304.0; ICD-10, F11.2) in the 12 months prior to or on the index date;
- ≥ 18 years of age as of the index date;
- Continuous enrollment with medical and pharmacy benefits for ≥12 months prior to (the baseline period) and after (the follow-up period) the index date.

Exclusion Criteria

- Use of pharmacological treatment (namely, BUP, MET, or oral naltrexone) for OUD in the month prior to the index date for the BUP, MET, and NPT only cohorts. This exclusion criterion was not applied to the XR-NTX cohort because patients are required to undergo withdrawal (detoxification) from opioids prior to initiating treatment with XR-NTX, and agonist medications are often used for withdrawal management;
- Claims for >1 of the treatments of interest (namely, XR-NTX, BUP, or MET) on the index date;
- Patients eligible for Medicare.

Study Outcomes

- Baseline demographic characteristics were measured on the index date and included age, gender and race.
- Clinical characteristics were evaluated during the baseline period and included Elixhauser Comorbidity Score and individual comorbidities such as alcohol dependence, anxiety disorder, bipolar disorder, and depression.
- All-cause HRU outcomes were measured during the 12-month baseline and follow-up periods, respectively, including: inpatient admissions, inpatient days among those with inpatient admissions, ED visits, outpatient visits, and outpatient pharmacy fills.
- Adherence to the index treatment was defined as proportion of days covered (PDC) and calculated as the sum of days covered by the prescription divided by the number of days during the follow-up period.

Statistical Analyses

- Baseline characteristics and outcomes were summarized using descriptive statistics (means and standard deviations [SD] for continuous variables; counts and percentages for categorical variables).
- HRU outcomes are presented as means (SD) and difference [95% Confidence Interval (CI)] between baseline and follow-up within each treatment cohort using paired t-tests.
- Mean differences in HRU were compared across treatment cohorts using generalized linear regression, adjusting for baseline characteristics.
- PDC between XR-NTX, BUP, and MET was compared using paired t-tests.
- P-values less than 0.05 were considered statistically significant.

RESULTS

Study Sample

- A total of 80,375 patients were included: 6,451 on XR-NTX, 39,646 on BUP, 12,985 on MET, and 21,293 on NPT.

Baseline Characteristics (Table 1)

- Patients in the XR-NTX cohort were younger than those in the BUP and MET cohorts and comparable to those in the NPT cohort in terms of age.
- The majority of patients in each cohort were female and White.
- The XR-NTX cohort had higher baseline Elixhauser comorbidity scores versus other cohorts.
- Alcohol dependence, anxiety disorder, bipolar disorder, and depression were more prevalent in the XR-NTX cohort compared to the BUP, MET, and NPT cohorts.

TABLE 1: Baseline Demographic and Clinical Characteristics

Characteristics	XR-NTX (n=6,451)	BUP (n=39,646)	MET (n=12,985)	NPT (n=21,293)
Age (years), mean (SD)	33.5 (8.9)	34.0 (9.1)*	36.7 (11.0)*	33.4 (9.8)
Gender, female, n (%)	3,374 (52.3)	24,139 (60.9)*	8,177 (63.0)*	11,420 (53.6)
Race, n (%)				
White	5,234 (81.1)	33,047 (83.4)*	10,431 (80.3)	17,299 (81.2)
Black	387 (6.0)	1,813 (4.6)*	1,792 (13.8)*	2,100 (9.86)*
Hispanic	78 (1.2)	792 (2.0)*	203 (1.6)	357 (1.7)*
Other	213 (3.3)	1,144 (2.9)	290 (2.2)*	690 (3.2)
Unknown/Missing	539 (8.4)	2,850 (7.2)*	269 (2.1)*	847 (4.0)*
Elixhauser Comorbidity Score, mean (SD)	2.90 (2.1)	2.27 (1.9)*	2.01 (1.9)*	2.04 (2.1)*
Comorbidities, n (%)				
Alcohol Dependence	1,528 (23.7)	2,909 (7.3)*	524 (4.0)*	2,891 (13.6)*
Anxiety Disorder	2,811 (43.6)	13,962 (35.2)*	2,602 (20.0)*	5,632 (26.4)*
Bipolar Disorder	1,344 (20.8)	5,265 (13.9)*	1,286 (9.9)*	2,800 (13.1)*
Depression	2,790 (43.2)	12,132 (30.6)*	2,676 (20.6)*	5,875 (27.6)*

Abbreviations: BUP, Buprenorphine; MET, Methadone; NPT, Non-pharmacological therapy; SD, Standard deviation; XR-NTX, Extended-release Naltrexone.
*p<0.05; Reference category: XR-NTX

HRU Estimates During Baseline (Figure 1)

- Patients in the XR-NTX cohort had more inpatient admissions and pharmacy fills compared to the other cohorts during the 12-month baseline period (Figures 1A & 1D).
- The XR-NTX cohort was comparable to the BUP cohort in terms of ED visits during baseline but had more ED visits during baseline than the MET and NPT cohorts (Figure 1B).
- Patients in the XR-NTX cohort also had more baseline outpatient visits compared to the BUP and NPT cohorts (Figure 1C).

Change in HRU Between Baseline and Follow-up (Figures 1 & 2)

- The percentage reduction in inpatient admissions between baseline and follow-up was greatest for the XR-NTX cohort (Figure 1A).
- While outpatient visits and pharmacy fills increased for all cohorts, XR-NTX cohort showed the smallest percentage increase (Figures 1C & 1D).
- Baseline to follow-up changes in all HRU outcomes in the BUP cohort were significantly different from the XR-NTX cohort after adjusting for baseline covariates (p<0.05; Figure 2). Baseline to follow-up changes in ED visits, outpatient visits, and pharmacy fills in the MET cohort and changes in outpatient visits in the NPT cohort were significantly different from the XR-NTX cohort after adjusting for baseline covariates (p<0.05; Figure 2).

Treatment Adherence (Table 2)

- Treatment adherence as measured by PDC and the proportion of patients who were adherent to treatment (defined as PDC ≥ 0.80) were lower for XR-NTX compared to the BUP and MET cohorts.

TABLE 2: Treatment Adherence During the Follow-Up Period

Treatment Adherence	XR-NTX (n=6,451)	BUP (n=39,646)	MET (n=12,985)
PDC, mean (SD)	0.44 (0.26)	0.56* (0.35)	0.48* (0.35)
Patients adherent to treatment (PDC≥0.8), n (%)	886 (13.73)	14,967 (37.75)	3,718 (28.63)

Abbreviations: BUP, Buprenorphine; MET, Methadone; NPT, Non-pharmacological therapy; PDC, Proportion of Days Covered; XR-NTX, Extended-release Naltrexone.
*p<0.05; Reference category: XR-NTX.

FIGURE 1: Percentage Change in Healthcare Resource Utilization from Baseline to Follow-up Within Each Treatment Cohort

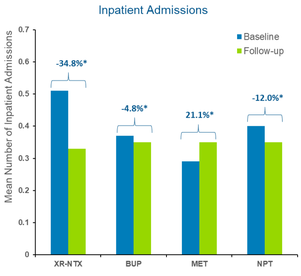


Figure 1A: Inpatient Admissions

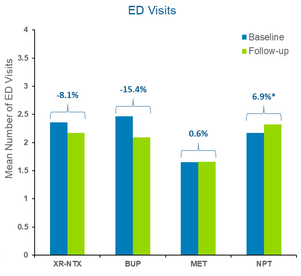


Figure 1B: ED Visits

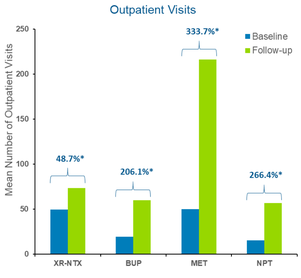


Figure 1C: Outpatient Visits

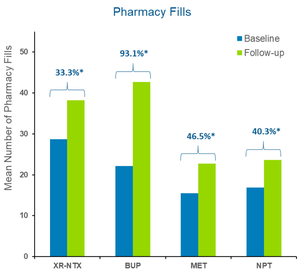
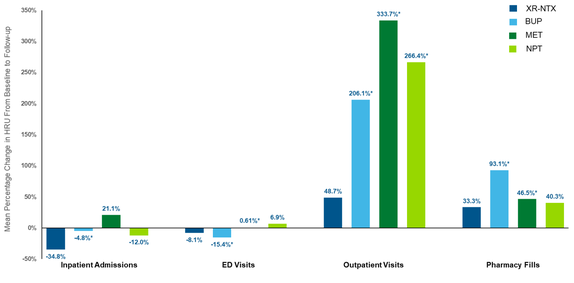


Figure 1D: Pharmacy Fills

Abbreviations: BUP, Buprenorphine; ED, Emergency Department; MET, Methadone; NPT, Non-pharmacological therapy; XR-NTX, Extended-release Naltrexone.
*p<0.05 for mean percentage change from baseline to follow-up within each treatment cohort by each HRU outcome.

FIGURE 2: Comparison of Percentage Change in Healthcare Resource Utilization from Baseline to Follow-Up in BUP, MET and NPT cohorts with XR-NTX cohort



Abbreviations: BUP, Buprenorphine; ED, Emergency Department; MET, Methadone; NPT, Non-pharmacological therapy; XR-NTX, Extended-release Naltrexone. Reference category: XR-NTX.
*Denotes significant difference when compared with XR-NTX cohort at p<0.05. p-values were based on generalized linear models (GLM) with a log-link function and gamma distribution after controlling for baseline covariates.

LIMITATIONS

- With claims data, the diagnosis and procedure codes used to identify the study cohorts and define the outcomes are subject to data coding variation and data entry errors.
- Filled prescription claims for a self-administered treatment do not indicate if the treatment was actually taken as prescribed.
- Patients were assigned to the treatment cohorts based on outpatient claims and any treatments received during inpatient stays were not captured.
- Given that this study was restricted to patients with ≥2 claims for XR-NTX, BUP or MET, or ≥3 claims for NPT, the findings may not be generalizable to all patients receiving these treatments.

CONCLUSIONS

- To date, this study is the first to analyze the real-world HRU associated with XR-NTX versus other treatments for OUD in the Medicaid population.
- The XR-NTX cohort had higher baseline comorbidities and HRU compared to the BUP, MET, and NPT cohorts.
- Despite higher baseline comorbidities, the XR-NTX cohort had the largest decrease in inpatient admissions and smallest increase in outpatient visits and pharmacy fills between the baseline and follow-up periods compared to the other treatment cohorts.
- This highlights the potential economic value of XR-NTX for publicly insured patients with OUD.

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Disclosures
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BH, JL, JF, and AKO are paid employees of Alkermes, Inc. AP was a paid employee of Alkermes, Inc. at the time of study; JLM is a paid employee of Stratevi who received funding from Alkermes, Inc. for conducting this study. XN was a paid employee of Stratevi at the time of the study.

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