Impact of Medications for Opioid Use Disorder on Infectious Disease Management

256

Jamie Lo, PhD MPH[1]; Anusorn Thanataveerat, DrPH[2]; Amanda Manfredo, PharmD[2]; Jennifer Falk, DPM, MS[2]; Ni Zeng, PhD[2]; Stephanie Wall, MPH[2]; Taylor Ryan, MHI[2]; William Pratt, MS[2]; Sami El-Dalati, MD[3]; Sabrina Gaiazov, MPH[1]

[1]Indivior Inc, North Chesterfield, Virginia; [2]Veradigm Inc., Raleigh, NC; [3]University of Kentucky College of Medicine, Internal Medicine, Lexington, Kentucky

Introduction

- Opioid use disorder (OUD) significantly impacts overall health, leading to increased morbidity with the exacerbation of other severe health conditions.[1]
- Injection opioid misuse is associated with the spread of infectious diseases (IDs) such as hepatitis C virus, human immunodeficiency virus (HIV), and skin and soft tissue infections.[1] This is likely due to needle sharing, unsafe injection practices, or other risky behaviors associated with illicit drug use.[2,3]
- Medications for opioid use disorder (MOUD) such as buprenorphine, methadone, and extended-release naltrexone are effective treatments for OUD and can significantly reduce ID risk or improve outcomes.[4]
- Despite MOUD availability, treatment success is largely dependent on patient engagement and treatment adherence.[5] Only a few published studies have analyzed the effects of longer-term MOUD adherence on ID-related outcomes.[6,7]

Objectives

This study compared the effect of transmucosal and extended-release buprenorphine on acute ID incidence and ID-specific healthcare resource utilization (HCRU).

Methods

Retrospective observational cohort study

- Veradigm® outpatient electronic health records (EHR) linked to a claims database between January 2016–June 2024 were used to identify patients treated with either transmucosal buprenorphine (BUP-TM) or extended-release buprenorphine (BUP-XR; Sublocade®) for ≥90 consecutive days in the US. The index date was defined as the first qualifying buprenorphine claim in the selection window of July 2018–December 2023.
- To approximate new treatment episodes, BUP-XR patients could have up to 14 days of BUP-TM (induction) immediately prior to starting BUP-XR, but were excluded if they had any longer use of BUP-TM (>14 days) or any other MOUD during the 90-day BUP-XR treatment period. Patients included in the BUP-XR cohort were allowed ≤45-day gaps between MOUD doses.
- Both unweighted analyses and analyses adjusted using inverse probability of treatment weighting (IPTW) were conducted to assess the impact of BUP-TM compared to BUP-XR on acute ID incidence rates and ID-specific HCRU 6 months following treatment initiation, employing a Difference-in-Difference approach.

Results

Unweighted baseline characteristics are presented in **Table 1**.

Table 1. Baseline Demographics and Clinical Characteristics of Interest

Characteristic	BUP-XR n=467	BUP-TM n=118,112
Age at index, years, Mean (SD)	38.5 (10.8)	40.3 (11.9)
Sex, N (%)		
Male	277 (59.3)	58,847 (49.8)
Female	190 (40.7)	59,265 (50.2)
Race, N (%)		
White	297 (63.6)	73,464 (62.2)
Black	27 (5.8)	7,136 (6.0)
Asian	9 (1.9)	1,956 (1.7)
Other	50 (10.7)	10,476 (8.9)
Unknown/Not Reported	84 (18.0)	25,080 (21.2)
Geographic Region, N (%)		
Northeast	153 (32.8)	24,659 (20.9)
Midwest	104 (22.3)	24,884 (21.1)
South	117 (25.1)	43,341 (36.7)
West	84 (18.0)	22,278 (18.9)
Unknown/Not Reported	9 (1.9)	2,950 (2.5)
Payer Type, N (%)		
Commercial	107 (22.9)	28,310 (24.0)
Medicaid	337 (72.2)	80,203 (67.9)
Medicare	22 (4.7)	9,512 (8.1)
Other/Unknown	1 (0.2)	87 (0.1)
Clinical Conditions, N (%)		
Skin conditions	66 (14.1)	11,539 (9.8)
Bone and joint infections	1 (0.2)	800 (0.7)
HIV/AIDS	5 (1.1)	1,034 (0.9)
Hepatitis B and C	55 (11.8)	9,058 (7.7)
Sexually transmitted infections	10 (2.1)	2,437 (2.1)

- Unweighted ID-related HCRU analyses revealed BUP-XR patients had significant reductions in inpatient (81%; 95% CI: 18%–96%) and outpatient (55%; 95% CI: 24%–74%) skin infection visits compared to BUP-TM.
- Unweighted ID-related HCRU analyses also showed that outpatient visits for the treatment of hepatitis B and C (63%; 11%–138%) and bone/joint infections (823%; 17%–7192%) were higher for BUP-XR vs. BUP-TM patients, suggesting improved chronic care treatment.
- After adjusting for IPTW, there was a significant reduction in sexually transmitted infection (STI) outpatient visits (77%; 95% CI: 43%–91%) among BUP-XR vs. BUP-TM patients (**Table 3**).

- Compared to the BUP-TM cohort during the 6 months following treatment initiation, the BUP-XR cohort had (**Table 2**):
  - 37% lower incidence (95% CI: 12%–55%) of acute skin infections (e.g., cellulitis) in unweighted analyses
  - 62% lower incidence (95% CI: 26%–81%) of bacteremia in IPTW-weighted acute ID incidence analyses

Table 2. Incidence Rate of Acute Infectious Disease (per 1,000 PYs)

	BUP-XR (Main) Cohort Unweighted: n=467 Weighted: n=437				BUP-TM Cohort Unweighted: n=118,112 Weighted: n=118,104				Additional effect of BUP-XR (Main) vs. BUP-TM on ID outcomes*	
Infectious Disease of Interest	6M Baseline Period		6M Follow-Up Period		6M Baseline Period		6M Follow-Up Period			
	IR	95% CI	IR	95% CI	IR	95% CI	IR	95% CI	exp (treatment* period)	95% CI
Skin Conditions										
Unweighted	411	336.60 - 502.18	240	184.57 - 311.64	293	288.49 - 297.22	271	266.93 - 275.33	**0.63**	**0.45 - 0.88**
Weighted	292	228.87 - 373.64	253	194.52 - 329.42	293	288.96 - 297.70	271	267.05 - 275.46	0.94	0.65 - 1.34
Acute Hepatitis C										
Unweighted	4	0.60 - 30.40	9	2.14 - 34.25	8	7.11 - 8.53	11	10.26 - 11.96	1.41	0.13 - 15.56
Weighted	2	0.05 - 44.69	3	0.23 - 34.31	8	7.13 - 8.55	11	10.27 - 11.97	1.26	0.02 - 83.16
STIs										
Unweighted	69	41.98 - 111.85	86	55.26 - 132.76	53	51.39 - 55.11	69	66.82 - 71.05	0.97	0.50 - 1.87
Weighted	121	82.46 - 176.81	105	69.70 - 157.97	53	51.39 - 55.11	69	66.83 - 71.06	0.67	0.38 - 1.18
Bone and Joint Infections										
Unweighted	4	0.60 - 30.40	17	6.43 - 45.64	26	24.29 - 26.87	21	19.78 - 22.11	4.89	0.55 - 43.78
Weighted	2	0.14 - 36.57	27	11.94 - 60.25	26	24.31 - 26.89	21	19.79 - 22.12	14.37	0.80 - 258.69
Bacteremia Infections										
Unweighted	120	82.80 - 173.67	60	35.51 - 101.24	94	91.89 - 96.84	90	87.19 - 92.02	0.53	0.28 - 1.00
Weighted	147	104.11 - 207.79	53	29.51 - 93.73	94	91.88 - 96.84	90	87.17 - 92.00	**0.38**	**0.19 - 0.74**

* This term quantifies the additional impact of BUP-XR following the intervention, relative to the effect of BUP-TM, by capturing the difference in acute ID incidence outcomes between the two groups from the pre- to post-index period. For example, the exp(treatment*period) of 0.6 suggests that the BUP-XR cohort experiences a 40% lower rate of acute ID than the BUP-TM cohort.

Table 3. Healthcare Resource Utilization Outcomes (IPTW weighted analyses)

		BUP-XR Cohort n=437		BUP-TM Cohort n=118,104		Additional effect of BUP-XR (Main) vs. BUP-TM on HCRU outcomes	
HCRU Type	Service Type	6M Baseline Period	6M Follow-Up Period	6M Baseline Period	6M Follow-Up Period	exp (treatment* period)	95% CI
All-cause HCRU, Mean (SD)	Inpatient services	0.33 (0.7)	0.10 (0.4)	0.32 (0.9)	0.22 (0.8)	**0.44**	**0.31 - 0.62**
	ED services	0.69 (1.3)	0.42 (0.8)	1.00 (2.1)	0.78 (1.7)	**0.78**	**0.65 - 0.94**
	Outpatient services	8.06 (10.6)	12.37 (13.4)	11.94 (18.1)	23.08 (21.8)	**0.79**	**0.76 - 0.83**
Skin Condition-specific HCRU, Mean (SD)	Inpatient services	0.02 (0.1)	0.01 (0.1)	0.02 (0.2)	0.01 (0.1)	1.02	0.34 - 3.10
	ED services	0.04 (0.2)	0.04 (0.2)	0.04 (0.3)	0.04 (0.2)	1.17	0.61 - 2.24
	Outpatient services	0.07 (0.4)	0.06 (0.3)	0.06 (0.5)	0.06 (0.6)	0.90	0.53 - 1.54
Hepatitis B&C-specific HCRU, Mean (SD)	Inpatient services	0.01(0.1)	0.00 (0.0)	0.00 (0.1)	0.00 (0.1)	0.07	0.001 - 3.88
	ED services	0.00 (0.0)	0.00 (0.0)	0.00 (0.03)	0.00 (0.03)	0.00	N/A
	Outpatient services	0.06 (0.3)	0.16 (0.6)	0.05 (0.4)	0.10 (0.6)	1.46	0.92 - 2.32
STIs-specific HCRU, Mean (SD)	Inpatient services	0.01 (0.1)	0.00 (0.0)	0.00 (0.02)	0.00 (0.02)	0.00	N/A
	ED services	0.01 (0.1)	0.00 (0.0)	0.00 (0.04)	0.00 (0.04)	0.00	N/A
	Outpatient services	0.05 (0.4)	0.01 (0.1)	0.01 (0.1)	0.01 (0.1)	**0.23**	**0.10 - 0.57**

* This term quantifies the additional impact of BUP-XR following the intervention, relative to the effect of BUP-TM, by capturing the difference in HCRU outcomes between the two groups from the pre- to post-index period.

Conclusions

- BUP-XR treatment was associated with larger reductions in acute skin infections and bacteremia incidence, as well as STI-related outpatient visits compared to BUP-TM, suggesting a potential benefit for BUP-XR in mitigating acute ID complications.
- Increased hepatitis B, hepatitis C, and bone-joint infection outpatient visits among BUP-XR patients may reflect improved chronic ID management through regular clinical follow-ups.

Limitations

- The use of retrospective EHR and claims data introduces potential biases and the data source itself has inherent gaps.
- Treatment was not randomized, and there may be inherent differences between patients who received BUP-XR vs. those on BUP-TM (e.g., clinical severity, social support, or provider practice style) that were not captured.
- Patients' interactions with the healthcare system were only partially observed. By relying on a single EHR-claims network, care events that occurred outside of that network were likely missed; therefore, outcomes may be underestimated.
- Laboratory data were notably incomplete, limiting the ability to confirm diagnoses or monitor disease markers.
- The BUP-XR cohort was relatively small; therefore, the study was underpowered to detect anything but fairly large differences between cohorts.
- Findings cannot be generalized to all patients, especially to those who are not in continuous and consistent care (inclusion criteria: ≥90 consecutive days of treatment).
- The primary analysis did not censor or exclude any BUP-TM induction phase; thus, some early follow-up time for BUP-XR patients includes days on BUP-TM, which could bias estimates toward the null if BUP-XR's full benefits manifest only after induction, leading to an underestimation of the positive impact of BUP-XR.

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Abbreviations

6M: 6 months; BUP-TM: transmucosal buprenorphine; BUP-XR: extended-release buprenorphine; CI: confidence interval; ED: emergency department; EHR: electronic health records; Exp: exponential function (Euler's constant); HCRU: healthcare resource utilization; HIV: human immunodeficiency virus; ID: infectious disease; IPTW: inverse probability of treatment weighting; IR: incidence rate; OUD: opioid use disorder; MOUD: medication for opioid use disorder; N/A: not applicable; STI: sexually transmitted infection; SD: standard deviation; PY: person-year.

Disclosures

This study was funded by Indivior Inc. Authors JL and SG were employees of Indivior Inc at the time the research was conducted. Authors AT, AM, JF, SW, and TR are full-time employees of Veradigm® which was contracted by Indivior Inc. Author WP was an employee of Veradigm® at the time the research was conducted. Author SED did not receive compensation for this work.

Acknowledgments

The authors thank Maher Abdel-Sattar, PharmD, MS, FAMCP (Indivior Inc.) for supporting content development and presenting the poster findings. The authors also thank William Mullen, MPH, PA-C (Indivior Inc.) and Meghan Thompson, PharmD, PhD (former employee of Indivior Inc.) for their review of the poster content.

Presented at the Academy of Managed Care Pharmacy (AMCP) Nexus 2025, October 27–30, National Harbor, MD