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Short communication

Reduced emergency department use among insured individuals receiving extended-release buprenorphine in a health system setting

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HIGHLIGHTS

- Proportion of individuals using ED services declined following XR-Bup initiation.
- Mean number of ED visits declined following XR-Bup initiation.
- Mean number of inpatient stays/days declined following XR-Bup initiation.

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ABSTRACT

Introduction: Extended-release buprenorphine (XR-Bup) is associated with reduced opioid use and opioid negative urine drug screens. Little is known about its use in outpatient addiction care provided within health systems.
Methods: Individuals prescribed XR-Bup were identified from electronic health records; chart abstraction was conducted. Primary outcome was all-cause emergency department (ED) use. Secondary outcomes included ED use or inpatient stays for mental health or substance use, ED use for any other cause, discontinuation reasons, and drug substitution. Statistical comparisons used nonparametric tests from related samples (McNemar's test and Wilcoxon matched pair tests) to test outcomes six months prior and 6 months following XR-Bup initiation.
Results: 152 individuals had an XR-Bup order, 126 received $\geq$1 injection. Among those consistently insured 6 months prior to and following XR-Bup initiation (n=99), the mean number of injections following initiation was 3.95; one-third received 6 doses in the 6 months. The proportion of individuals using ED services for all causes declined (41% prior vs. 28% following XR-Bup initiation, $p<.05$); similar results were found for secondary ED use outcomes. The proportion of individuals requiring inpatient treatment for mental health or substance use also declined (46% vs. 16%, $p<.01$). Common reasons for discontinuing XR-Bup included losing insurance (21%) or cost (11%). The most common non-prescribed substances used during treatment were opioids (n=31) and THC (n=20).
Conclusions: In this non-randomized retrospective observational study, use of XR-Bup was associated with reduced ED use 6 months following initiation. XR-Bup may help health systems reduce use of costly ED services.

1. Introduction

Medication for opioid use disorder (MOUD) with sublingual buprenorphine, methadone, or naltrexone is the standard of care for evidence-based pharmacotherapy for opioid use disorder (American Society of Addiction Medicine, 2020). Sublingual buprenorphine has proven to be efficacious (Degenhardt et al., 2023) and a preferred treatment for opioid use disorder (OUD) (Yarborough et al., 2016). It is associated with reduced opioid use, cravings, (Fudala et al., 2003), and reduced mortality (Sordo et al., 2017). Some evidence suggests methadone may retain more patients in treatment than buprenorphine (Nielsen et al., 2022), but the restrictive structure of monitored methadone administration at federally or state-regulated clinics creates a substantial barrier for some (Yarborough et al., 2016).

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Extended-release formulations are designed to overcome barriers or medication-related issues such as poor adherence, particularly among individuals with chronic conditions, and may be especially advantageous for high-risk populations (Brissos et al., 2014; Kim, 2021; Leighty and Ansara, 2019). In the case of OUD, poor adherence can lead to serious consequences including return to use of opioids, rehospitalization, overdose, and suicide. Extended-release medications reduce dosing frequency, provide a more consistent therapeutic effect by their prolonged duration of action, may have reduced side effects or improved tolerability, and may have improved effectiveness and safety (Siegel, 2005).

Extended-release buprenorphine (XR-Bup), requiring once monthly injections, offers convenience over daily sublingual buprenorphine or daily visits to a methadone clinic. Two XR-Bup products are now available in the U.S., Sublocade® and Brixadi®. The product used in the current study is available in 100 mg and 300 mg formulations delivered subcutaneously (typically abdominally) once monthly. The injection is designed to maintain consistent plasma levels of buprenorphine for one month and is typically readministered every 28–30 days. Clinical trials have shown that XR-Bup performs better than sublingual buprenorphine with better retention (Lofwall et al., 2018), fewer positive urine drug tests (Lofwall et al., 2018; Rutrick et al., 2023), and improved abstinence (Andorn et al., 2020; Haight et al., 2019; Rutrick et al., 2023). Improvements in patient-reported outcomes include improved physical component scores on the SF-36 (Ling et al., 2019), fewer withdrawal symptoms, lower pain, higher quality of life, and less depression (Ling et al., 2020a). Patient satisfaction with XR-Bup and self-reported longer-term abstinence have also been noted (Boyett et al., 2023; Ling et al., 2019, 2020b). To date, the only reported health care utilization outcome in the literature shows those receiving XR-Bup had fewer hospital days per person-year than those receiving placebo (Ling et al., 2019). Trials comparing acceptability and effectiveness of XR-Bup versus methadone are ongoing (Lowry et al., 2022; Marsden et al., 2022).

There is interest in moving the use of XR-Bup from clinical trials into large-scale clinical practice but reports on such efforts are lacking. It is difficult to discern from the literature whether this medication innovation is widely used, however the average cost per month of XR-Bup is considerably higher than other forms of medication treatment for OUD (Canadian Agency for Drugs and Technologies in Health, 2019), which is likely a substantial barrier. One recent study reported successful clinical outcomes from using XR-Bup in a specialty addiction medicine clinic within an academic medical setting. Results largely mirrored those of clinical trials, with improved retention and increased abstinence among those treated with XR-Bup (Heil et al., 2023). The current preliminary study was undertaken to 1) determine the feasibility and validity of identifying individuals receiving XR-Bup in a large health system, the feasibility of measuring outcomes associated with its use, and 3) to evaluate the hypothesis that XR-Bup reduces use of expensive emergency department (ED) and inpatient services. Secondary outcomes included reasons for discontinuing XR-Bup and whether there was evidence of drug substitution while being treated with XR-Bup.

2. Methods

Kaiser Permanente Northwest (KPNW), an integrated health system serving approximately 615,000 members in the Pacific northwest, offers primary care, outpatient specialty mental health care and addiction treatment services, and has 2 hospitals. KPNW members are covered through a variety of insurance options, including Medicaid (14%) and Medicare (19%). During the study period, sublingual buprenorphine was available, and XR-Bup was administered in a single addiction medicine outpatient clinic and inpatient settings. Limited XR-Bup was available to patients with state Medicaid insurance through certain external contracted providers and prior authorization was required. Methadone was provided by state- and federally licensed clinics; however, no individual in the current study had received methadone in the year before or after XR-Bup initiation. Extended-release injectable naltrexone was also available for treatment of OUD but was rarely used (data not collected). The Kaiser Permanente Northwest Institutional Review Board approved a waiver of consent to use electronic health records (EHR) to identify study subjects and ascertain prescribing, covariate, and outcomes data.

XR-Bup orders began in December 2020. Receipt of XR-Bup was defined as having an order and an associated visit with a coded drug injection (using Current Procedural Terminology [CPT] code 96372). The addiction medicine clinic also maintained a list of patients who had been ordered and/or received XR-Bup injections. Results from the data pull were confirmed by chart review (see below) and compared to the clinic list to validate that no individuals had been missed or misclassified.

Two team members reviewed the EHR of all identified patients. Using a standardized abstracting template, a method successfully employed in other projects (Yarborough et al., 2016), chart reviews captured vital information including: whether an injection followed an order, dates of all subsequent injections, clinical notes regarding side effects or self-reported negative or positive experiences, evidence of drug substitution in clinical notes or drug screen results, and reasons for discontinuing XR-Bup. The first ten cases were double coded to assure similarity in chart abstraction results; no major discrepancies were found, and remaining cases were abstracted.

Following chart abstraction, the research analyst identified outcomes in the EHR for all individuals with evidence of receiving $\geq$1 XR-Bup injection. Outcomes included ED use associated with a mental health or substance use diagnosis including overdose (secondary outcome), ED use for any other reason (secondary outcome), all-cause ED use (the primary outcome, a combination of the prior two), and inpatient treatment episodes for mental health or substance use issues (secondary outcome). See supplemental appendix for additional details.

Univariate frequencies were run from data collected by chart abstraction and EHR. Statistical analyses were completed using SPSS v.28. Outcomes were only assessed for individuals with evidence of insurance coverage 6 months prior to and 6 months following XR-Bup initiation. This was to ensure that all primary outcome data were available in the EHR, otherwise individuals not insured for the full period may have received ED or inpatient care outside of the health system possibly resulting in undercounting their prevalence. To compare individuals who received $\geq$1 injection with those who did not (Table 1), chi-square or Fisher's exact t-test were used to test for differences. Statistical comparison of the outcomes involved using nonparametric tests from related samples to account for autocorrelation and non-normal distributions — McNemar's test for categorical and Wilcoxon matched pair tests for continuous outcomes.

3. Results

152 individuals had an order for XR-Bup in the EHR between January 1, 2020 and February 13, 2023. Chart review determined that 26 individuals never received injectable XR-Bup; 126 received at least one injection (Fig. 1). The majority of the sample was male, white, had anxiety or depression diagnoses and had other comorbid substance use disorders beyond OUD. With regard to the demographic and diagnostic characteristics studied, individuals who did not complete at least one injection did not significantly differ from those who did. Past year engagement with addiction treatment also did not differ between the two groups with one exception: individuals who completed at least one injection of XR-Bup filled more prescriptions for sublingual buprenorphine than those who did not receive one injection (mean 5.0 versus 3.4; p=.03). See Table 1 for additional details.

Table 1
Demographic and clinical characteristics among all patients ordered extended-release buprenorphine, n=152.

	Order only (n=26)		1+ injection (n=126)		Total		P value
	N	%	N	%	N	%	
Sex/Gender							.65
–Male	17	65.4	71	56.3	88	57.9	
–Female	9	34.6	54	42.9	63	41.4	
–Other	0	0	1	0.8	1	0.7	
Race							.65
–White	22	84.6	107	84.9	129	84.9	
–Asian American	1	3.8	1	0.8	2	1.3	
–African American	0	0	3	2.4	3	2.0	
–Hispanic	1	3.8	7	5.6	8	5.3	
–More than 1 race	1	3.8	5	4.0	6	3.9	
–Other	0	0	2	1.6	2	1.3	
–Unknown	1	3.8	1	0.8	2	1.3	
Past 12-month history of mental health or substance use diagnoses at order date							
–Anxiety	17	65.4	92	73.0	109	71.7	.48
–ADHD	8	30.8	33	26.2	41	27.0	.63
–Bipolar	3	11.5	13	10.4	16	10.6	1.0
–Depression	16	61.5	77	61.1	93	61.2	1.0
–Psychosis	4	15.4	12	9.6	16	10.6	.48
–Personality disorder	1	3.8	12	9.6	13	8.6	.47
–PTSD	7	26.9	30	23.8	37	24.3	.80
–Schizophrenia	0	0	6	4.8	6	4.0	.59
–Other substance use disorder	18	69.2	80	63.5	98	64.5	.66
Past 12-month engagement with addiction medicine treatment							
Use of sublingual buprenorphine	23	88.5	119	95.2	142	94.1	.42
Engagement with outpatient addiction medicine services	25	96.2	123	98.4	148	98.0	.67
	Mean	SD	Mean	SD	Mean	SD	
Age, years	33.6	14.2	37.0	13.0	36.5	13.3	.23
Number of sublingual buprenorphine dispenses	3.4	3.6	5.3	4.2	5.0	4.1	.03
Number of outpatient addiction medicine service encounters	8.6	12.8	11.8	14.4	11.3	14.2	.30

[1]Sex assigned at birth or gender may be recorded in the electronic health record.

3.1. Primary and secondary outcomes (derived from electronic healthcare records)

Of the 126 individuals who received at least one XR-Bup injection and for whom outcomes were abstracted, 27 did not have insurance coverage during the full period of observation. Analyses of primary and secondary health care utilization outcomes were limited to the remaining 99 individuals. The mean number of XR-Bup doses in the six months following treatment initiation was 3.95; 33% received six doses in the first six months. The proportion of individuals using ED services for all causes declined following XR-Bup initiation (41% prior vs. 28% after, $p<.05$). The mean number of all-cause ED visits also declined following XR-Bup initiation from.63 (SD=1.32) to.30 (SD=.93; $p<.001$). The proportion visiting the ED for mental health or substance use related reasons declined following XR-Bup initiation (29% prior vs. 18% after, $p<.05$); the same was true for ED use for all other causes (27% prior vs.15% after, $p<.05$). Finally, the proportion of individuals requiring inpatient treatment for mental health or substance use-related reasons declined following XR-Bup initiation (46% prior vs. 16% after, $p<.001$). See Fig. 2. The number and length of inpatient stays over the six-month period prior to XR-Bup initiation was also calculated and compared with the number and length of inpatient stays after. The mean number of inpatient stays declined from 0.81 (SD=1.21) to 0.24 (SD=0.70; $p<.01$). The mean number of days in inpatient care declined from 4.42 (SD=7.28) to 1.61 (SD=5.03; $p<.01$).

3.2. Additional outcomes (derived from chart review)

Among individuals receiving at least one injection (n=126), 21% lost insurance coverage or access to coverage of XR-Bup during their treatment. Eleven percent had to discontinue due to cost (high copay amount or full out-of-pocket expense for Medicaid patients) and an additional 11% discontinued due to side effects. Smaller numbers of individuals wanted to return to sublingual buprenorphine use, had transportation issues, or did not feel that XR-Bup was having the desired effect (i.e., they experienced withdrawal symptoms and cravings too often).

Thirty-one individuals (25%) had an opioid positive urine drug test during treatment. Twenty tested positive for THC; many clinicians were aware of THC use during treatment and THC was fully legalized in the two-state KPNW service area. Thirteen individuals tested positive for amphetamines, and fewer than 5 individuals tested positive for cocaine, non-prescribed benzodiazepines, or barbiturates.

4. Discussion

No studies to date have reported health care utilization outcomes among a population receiving XR-Bup as part of non-academic, outpatient, health-system-based care. We found that individuals treated with XR-Bup had reduced health care utilization in the six months following treatment compared to the six months prior. All-cause ED use and the subset of ED use for mental health or substance use related treatment both declined significantly following treatment initiation. The proportion of individuals requiring inpatient treatment and the number of

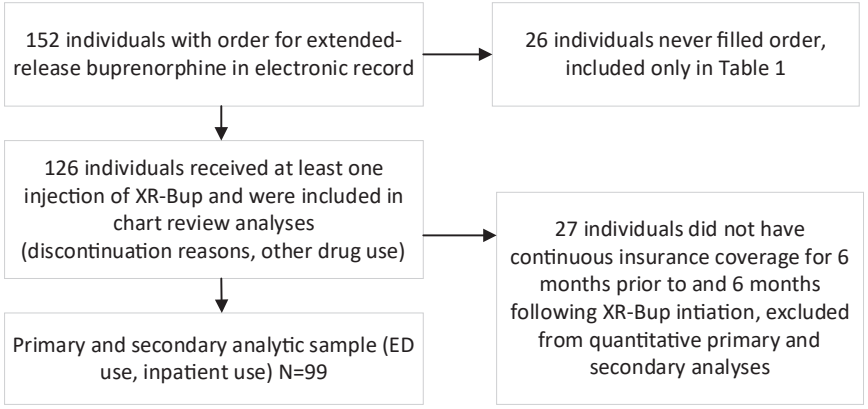

Fig. 1. Study flow diagram.

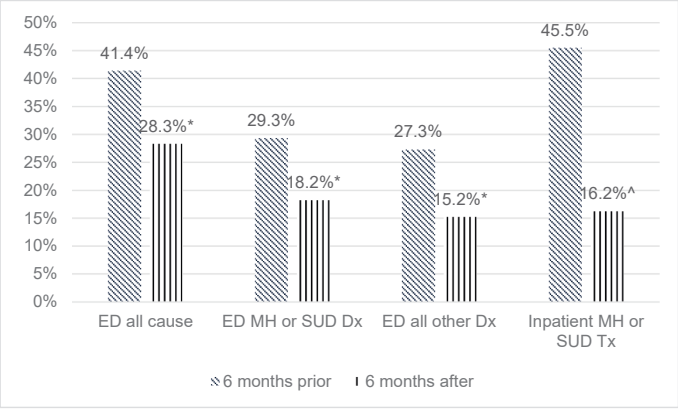

Fig. 2. Proportion experiencing each outcome 6 months prior to and 6 months following initiation of extended-release buprenorphine (n=99). *p<.05; ^p<.01. ED=emergency department; MH=mental health; SUD=substance use disorder; Dx=diagnosis; Tx=treatment.

inpatient treatment episodes and lengths of stay all declined as well. Common reasons for not continuing with treatment included cost and loss of insurance coverage. A portion of the sample engaged in opioid use while being treated. Most patients continued with XR-Bup treatment after testing positive for opioids as the health care system did not consider this a reason for discontinuation; rather, continuation of XR-Bup was seen as a harm reduction tool (to reduce risk of opioid-related overdose).

These results add to the positive findings from clinical trials and one addiction treatment clinic where XR-Bup outcomes were reported (Andorn et al., 2020; Haight et al., 2019; Lofwall et al., 2018; Rutrick et al., 2023). These findings suggest that routine use of XR-Bup may bring benefits to both patients and the healthcare system.

Several limitations to the current study should be noted. This was a non-randomized retrospective observational study. We cannot conclude that the outcomes observed were due to use of XR-Bup; they may be explained by clinical or other demographic circumstances or by other unmeasured confounders. The pre-post design used a within-group comparison rather than a comparison group engaged in sublingual buprenorphine or methadone treatment, or a placebo group as might be assessed in a comparative effectiveness clinical trial. The sample was predominantly white, and the distributions of race and ethnicity did not reflect the broader KPNW population; whether this is due to patient preferences or care disparities cannot be determined in this study. How the sample may differ from the broader population of individuals with opioid use disorder is unknown as the latter were not part of the study sample. Better understanding of who is and is not offered XR-Bup, is and is not a good candidate for this treatment, does and does not take advantage of it, and does and does not benefit from it are all important questions for future study. This study provides promising data to warrant a larger study designed to answer these and many more important research questions such as which patients are more likely to be offered XR-Bup and why, which patients benefit most from XR-Bup, and how to overcome access barriers such as cost.

5. Conclusions

In a non-randomized, pre-post, retrospective observational study, 99 patients who received XR-Bup had fewer all-cause ED visits after initiating XR-Bup compared to their pre-treatment average number of visits.

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Role of funding source

The funder had no role in the study design; data collection, analysis, or interpretation; writing; or decision to publish the results.

CRediT authorship contribution statement

Shannon L. Janoff: Writing – review & editing, Resources, Project administration, Investigation. **Erin M. Keast:** Writing – review & editing, Validation, Software, Data curation. **Bobbi Jo H. Yarborough:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization. **Scott P. Stumbo:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Michael C. Leo:** Writing – review & editing, Supervision, Methodology. **Sarah J. Leitz:** Writing – review & editing, Conceptualization.

Declaration of Competing Interest

Dr. Yarborough, Mr. Stumbo, Ms. Janoff, and Ms. Keast have received support managed through their institution from the Industry PMR Consortium, a consortium of companies working together to conduct postmarketing studies required by the Food and Drug Administration that assess risks related to opioid analgesic use. Drs. Leo and Leitz have no competing interests to declare.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dadr.2024.100233.

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