

Off-Label Use of Buprenorphine for Chronic pain

Laurel Rabson, MD

VA Interprofessional Advanced Fellowship for Addiction Treatment

William S. Middleton Memorial VA, Madison WI

National VA-
PBM/
MedSafe
Multisite MUE

- Off-Label Use of Buprenorphine for Pain Management Medication Use Evaluation
 - Fran Cunningham, PharmD, Director
 - Muriel Burk, PharmD, MUE Program Manager
 - Ken Bukowski, BS, Programmer
 - Asma Awad, PharmD, VAMedSAFE PGY2 Resident
 - Mitchell Nazario, PharmD, VA PBM Pain Management Expert

Background

- Buprenorphine (partial opioid agonist) safer compared to full opioid agonists (FOA)
- SL Buprenorphine (BUP) products are FDA approved for the management of OUD, but increasingly being used off-label for the management of chronic pain
- VA PBM published procedure and guidance for the off-label use of BUP for pain management in Oct 2017.
- Not much is known about off-label BUP use for the management of pain
- Purpose: To assess the extent, safety, and effectiveness of this off-label use, particularly in patients transitioned from potentially higher risk full opioid agonist therapy.

Advantages of Buprenorphine for Pain

- Ceiling Effect on Respiratory Depression
- Less Euphoria
- Less constipation
- Less opioid induced hyperalgesia effects
- Relatively fewer drug-drug interactions
- Safer in renal and hepatic impairment

Misconceptions about Buprenorphine

- **Partial mu opioid receptor agonist interpreted as partial/low efficacy for pain**
- **Lack of awareness that Buprenorphine can be prescribed for pain**
- **Multiple formulations of Bupe (some for pain, some for OUD)-confusion over what is legal**
- Lack of awareness of how to convert from FOA to Bupe and fear of precipitated withdrawal
- Naloxone containing formulations-viewed as blocker

Webster et al 2020

Study Design

- *Design:* Retrospective database extraction and chart review
- *Target Population:* Patients newly initiated on BUP SL tablets or film (Suboxone® or Subutex®) for off-label pain management with or without OUD.
- *Timeframe:* Prescriptions from January 1, 2018 – March 31, 2020 (27 months). Chart review should span 6 months prior and 6 months post initiation.
- Approved as a nonresearch QA/QI Project by Hines VA IRB

MUE Flowchart – Launched Nov 2020

Cohort Construction

- VA patients with index prescription for BUP SL tab or film
- Timeframe: Incident RX from January 1, 2018 – March 31, 2020 (27 months) (N=13,712)
- After excluding (database level): OUD Dx F11.2x AND once daily BUP dosing AND absence of pain dx codes 6 months post index (N=12,669)

Chart Review at 24 VAMCs (N=3336)

- Confirm eligibility
- Apply exclusions at chart level (i.e. exclude if on BUP for OUD ONLY/MAT therapy with NO documented pain benefit)
- Chart review \pm 6 months of index
- Complete online data collection form

Submit Data for Analysis

- Use data submission form on SharePoint
- VAMedSAFE Team will aggregate, analyze results

Madison Data- Included Veterans

- 72 Veterans
- 26/72 Included
- 22 Male/4 Female
- Average Age 55.5 years
- 2/26 SL Buprenorphine started for Pain Management Only
- 24/26 SL Buprenorphine started for Pain and Opioid Dependence/OUD
- 3/26 SL Buprenorphine started as part of plan to taper off FOAs
- 26/26 initiated and treated with SL Bupe within MH setting (most in Suboxone Clinic within Psychiatry)

Madison Data- Pain Management Prior to SL Buprenorphine

- 22/26 Veterans had history of prescribed opioid treatment prior Bupe(methadone/morphine/hydrocodone/oxycodone/tramadol): 3 had transitioned to illicit only (heroin/kratom/illicit oxy)
- Average Morphine Mg Equivalents (MME) for Veterans on prescribed opioids just prior Bupe 19/22 data available: 120 MME
- 25/26 veterans on non opioid analgesics prior to SL Buprenorphine (acetaminophen/NSAIDS/anticonvulsants/topicals/muscle relaxants/antidepressants)

Madison Data- Buprenorphine Details

- **Average # of days on Buprenorphine: 471**
- **17/26 Remain on Buprenorphine**
- **Adverse Effects from Bupe: 9/26 (GI/sedation/edema); No hospitalizations/overdoses/deaths/suicide attempts**
- 3/26 Continued on SL Bupe from Non VA Provider
- 1/26 Prior SL Buprenorphine experience
- 0/26 Prescriptions annotated for Pain Management Only.
- Average initial doses: 6.64 mg with range of 2-16 mg
- Average maintenance dose: 17.96 mg with range of 5-32 mg
- Reasons for d/c Bupe within 6 months: 4 for adverse effects, 1 insufficient pain control, 1 veteran choice

Madison Data -Pain Assessments

- Pain Assessed- Prior and During Bupe
- Documentation of pain limited (multiple validated pain scales considered)
- Most pain documentation descriptive
- During Bupe: 20/26 “improved” pain
2/26 “worse” pain
4/26 unable to determine






Madison Data-Utilization Outcomes

Before Buprenorphine

- SUD/Addiction Care: 11/26
- AV Telephone Calls: 9.45
- AV Hospitalizations: 0.538
- AV ER visits: 1.0
- AV Referrals: 1.84

Illicit Substance Use: 13/26 (included 10 illicit opioids)

During Buprenorphine

- SUD/Addiction Care: 20/26 
- AV Telephone Calls: 8.6 
- AV Hospitalizations: 0.192 
- AV ER visits: 0.69 
- AV Referrals: 1.19 

Illicit Substance Use: 6/26 (0 illicit opioids) 

Lived Experience

- Most Veterans had been on LTOT for years
- LTOT ends/changes with providers leaving/retiring/changing prescribing patterns, patient relocating/initiating care with VA, failed taper, + UDT results, other aberrant behaviors
- Weeks/months of inadequate pain control/destabilization
- Controlled Substance Advisory Board
- Stigma
- Specific comment from Veteran: “ The VA got me hooked on opioids- what are my other options?”

Madison Data- Insights/Limita- tions

INSIGHTS

- SL Buprenorphine for Chronic Pain alone is uncommon at Madison VA
- SL Buprenorphine for chronic pain + Opioid Dependence/ODD exclusively prescribed in Mental health setting
- Difficult to distinguish patients with suboptimal pain who are Opioid Dependent from patients with OUD
- SL Buprenorphine appears to be stabilizing for some veterans transitioning from LTOT with improved pain control/less illicit substance use/lower utilization of resources

LIMITATIONS:

- Small numbers, MH dx/outcomes not included, chart review subjective (pain eval), confounding factors (especially MH interventions/Addiction Care)

Next Steps

- Awaiting data from the national study (June 2021)
- Increasing education on Buprenorphine in Primary Care
New HHS Reg: [HHS Releases New Buprenorphine Practice Guidelines, Expanding Access to Treatment for Opioid Use Disorder | HHS.gov](#)
- Earlier recognition of high risk veterans -on high dose LTOT with concurrent psychiatric/SUD/ behavioral aberrancy- consider transition to SL Buprenorphine (via STORM reports or referral)
- Models: Opioid Reevaluation Clinic/High Risk Pain Management Clinic, embedding Addiction Medicine in Pain clinics