Integrating Buprenorphine Treatment into Your Practice: Treatment for Persons with Opioid Use Disorder and HCV

Maggie Lowenstein, MD, MPhil, MSHP
Assistant Professor, Division of General Internal Medicine, University of Pennsylvania School of Medicine
Mobile Addiction Treatment Physician, Prevention Point Philadelphia

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I have no conflicts of interest to disclose
Learning Objectives

- Review components of buprenorphine induction and maintenance visits for patients with opioid use disorder.
- Identify mechanisms to address common challenges encountered when managing patients on buprenorphine.
- Increase your comfort with patient-centered treatment for opioid use disorder.
Roadmap

- Background
- Initiating buprenorphine in office-based settings
- Maintenance and follow-up
- What happens when...
- Conclusions
Policy Changes Related to the X-waiver

- In April 2021, HHS issued new practices guidelines for prescribing buprenorphine for OUD eliminating the mandatory training requirement for DEA-registered healthcare providers (MD/DO or APP) who are treating 30 or fewer patients at a time.
- All providers still need to register for X-waiver.
- Need to complete training if prescribing to >30 patients.
HOW TO APPLY FOR AN X-WAIVER UNDER THE NEW BUPRENORPHINE PRACTICE GUIDELINES

1. **File a notice of intent here:** https://buprenorphine.samhsa.gov/forms/select-practitioner-type.php
2. **Enter your DEA number, your state license number, and select option for the 30-patient level**
3. **Under Section 8:**
   a. **APRN/PA:** Check SAMHSA's Providers Clinical Support System (PCSS) in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "practice guidelines" in the text box for the date.
   b. **Physician:** Select "Other" in "CERTIFICATION OF QUALIFYING CRITERIA," then enter "practice guidelines" in the text box for the city of the training. The training date should be the application date.
4. **Fill out the remaining information and submit**

"If you receive an error stating that you did not submit a form for CME you may disregard the notice and begin prescribing buprenorphine once you receive your x-waiver."
Background
What is Opioid Use Disorder (OUD)?

- OUD is a chronic disease that is highly influenced by psychosocial and behavioral contexts
- OUD defined by:
  1. Tolerance and withdrawal
  2. Negative Consequences (loss of control, health, work, relationships, legal, etc)

Source: DSM-5

Diagnostic Criteria for OUD

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use, despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use, despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance,* as defined by either of the following:
   A. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
   B. A markedly diminished effect with continued use of the same amount of an opioid.
Medications for OUD (MOUD) Review

Three FDA-approved MOUDs

• Methadone
• Buprenorphine
• Extended-release naltrexone

Source: Pew Charitable Trusts
Buprenorphine Basics

- Partial opioid agonist
- High binding affinity to opioid receptor
- Binding to opioid receptor prevents withdrawal, reduces craving
- Causes less respiratory depression than full agonist opioids

Source: NAABT.org
How do MOUDs work to reduce risk?

- MOUDs stabilize patients by:
  - Preventing withdrawal
  - Reducing cravings
  - Reducing the experience of opioids and the risks if a patient returns to use

- Provide opportunities to address the social and behavioral components of addiction
MOUDs Save Lives

Opioid agonist therapy reduces *all-cause* and *overdose* mortality by ~50%

Source: NASEM, 2019
Other Benefits of Opioid Agonist Therapy

- Increased retention in treatment
- Reduced risk of other opioid use and injection
- Reduced HIV and HCV diagnosis
- Improved social functioning
- Improved quality of life
- Improved maternal and fetal outcomes among pregnant women

Source: Mattick, 2014; NASEM, 2019
Medications and counseling

Used in conjunction with medications, counseling and other behavioral interventions:

• Target a broad range of problems and issues not addressed by the medications

• Studies on effectiveness are heterogeneous with mixed results

Source: Carroll and Weiss, 2017
Interim Buprenorphine vs Waiting List

Patients on buprenorphine waitlist randomized to starting buprenorphine with no additional intervention vs usual care

Source: Sigmon et al, NEJM, 2016
Brief Supportive Counseling in Office-Based Treatment

- Function and recovery goals
- Relationships and social supports
- Stress and triggers
- Empathic listening and non-judgmental discussion
Behavioral Interventions and MOUDs

Lack of availability or utilization of behavioral interventions is not a sufficient justification to withhold MOUDs

- National Academy of Sciences, Engineering and Medicine Report

**Teaching Point:** Offer, but do not require, traditional counseling services

Source: NASEM, 2019
Initiation of buprenorphine in office-based settings
Who is a candidate for buprenorphine treatment?

- Indications for buprenorphine: OUD or Opioid Dependence
- Contraindications:
  - Allergy to buprenorphine or naloxone (rare)
  - Use caution with LFTs >5x ULN
Who is a candidate for buprenorphine treatment?

- What about concurrent stimulant use?
  - MOUDS only treat OUD!
  - Risks relatively low with concurrent stimulant and buprenorphine use

Source: Martin, 2018
What about concurrent sedative use?

- Benzodiazepines + full opioid agonists increase overdose risk due to respiratory depression
- Most of the (rare) overdoses with buprenorphine occur in those who combined buprenorphine with large amounts of benzo or alcohol
- Newer data suggest that among those with AUD and benzo use, buprenorphine treatment is associated with fewer OD than off treatment
- Weigh risks and benefits

Sources: Xu, 2020; Xu, 2021; Schuman-Olivier, 2013; FDA, 2017
Who is a candidate for buprenorphine treatment?

- What about concurrent sedative use?

FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks

Source: FDA, 2017
Who is a candidate for buprenorphine treatment?

Health care professionals should take several actions and precautions and develop a treatment plan when buprenorphine or methadone is used in combination with benzodiazepines or other CNS depressants. These include:

- Educating patients about the serious risks of combined use, including overdose and death, that can occur with CNS depressants even when used as prescribed, as well as when used illicitly.
- Developing strategies to manage the use of prescribed or illicit benzodiazepines or other CNS depressants when starting MAT.
- Tapering the benzodiazepine or CNS depressant to discontinuation if possible.
- Verifying the diagnosis if a patient is receiving prescribed benzodiazepines or other CNS depressants for anxiety or insomnia, and considering other treatment options for these conditions.
- Recognizing that patients may require MAT medications indefinitely and their use should continue for as long as patients are benefiting and their use contributes to the intended treatment goals.
- Coordinating care to ensure other prescribers are aware of the patient’s buprenorphine or methadone treatment.
- Monitoring for illicit drug use, including urine or blood screening.

Source: FDA, 2017
What dose should I use?

Starting dose
- Traditional protocols 2-4 mg first dose
- Fentanyl era – beginning to do lower doses 1-2 mg
- Low dose (“microinduction”) – more on this in a minute

Daily dose
- No conversion from street drug or rx opioid use to buprenorphine dose
- Traditional protocols suggest doses of 8-12 mg on Day 1; may go higher in heavier use
- Clinical studies show that higher maintenance doses (12-16 mg, up to 32 mg) associated with improved treatment retention

Sources: Hser YI, 2014; Fareed, 2012
What formulation should I use?

- **Films vs Tablets**
  - Patient preference and insurance issues
  - Films usually preferred

- **Cutting films/tabs**
  - Technically drug distribution may not be uniform throughout
  - However, in practice we often suggest cutting in order to facilitate induction/dosing
  - Films easier to cut
Where should I initiate buprenorphine?

- Home vs office - “essentially equivalent”
- Home inductions safe and effective in multiple studies and contexts

Sources: Martin, 2018; Lee, 2014
How should I counsel my patient to take their medication?

- To maximize sublingual absorption
  - Do not eat, drink, or smoke for 20-30 minutes before and after
  - Recommend no talking, allowing saliva to pool and film/tab to fully dissolve
  - Don’t “chase” with food or drink
When do I tell my patient to start buprenorphine?

- Wait at least 12-24 hours after last full agonist use
- Mild to moderate withdrawal (COWS 8-12)
  - Patients will know what this looks like for them
  - Nausea, cramping, restlessness, tearing, running nose
  - Does NOT have to be severe withdrawal sx
- Increasing challenges with fentanyl - will discuss
Medications for Symptomatic Relief During Induction

- Ibuprofen or other NSAIDs – aches/pains
- Loperamide – diarrhea
- Clonidine – withdrawal symptoms
- Hydroxyzine – anxiety symptoms, withdrawal symptoms
- Trazodone – insomnia, depressive symptoms
What happens if my patient has precipitated withdrawal?

- **Mechanism**
- **Various approaches**
  - My approach: Increase the buprenorphine until opioid receptors saturated
    - Instruct patients to take 16 mg
    - Adjunctive medications
Low Dose ("Micro") Inductions

- Fentanyl and metabolites remain in body for many days, increasing risk of precipitated WD

Protracted renal clearance of fentanyl in persons with opioid use disorder

Andrew S. Huhn, J. Gregory Hobelmann, George A. Oyler, Eric C. Strain

* Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21238, USA
* Ashley Addiction Treatment, Home of Grace, MD 21409, USA
* Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD 21218, USA
Low Dose ("Micro") Inductions

- Can overcome this problem with cross-titration techniques that do not require patient to be in withdrawal
- This is also helpful for cross-titration from methadone and other full agonists to buprenorphine

Sample Protocol (Courtesy of Dr. Judy Chertok)

Prescribe 2mg strips x 17

Day 1: 0.5 mg (1/4 strip) once a day
Day 2: 0.5 mg (1/4 strip) twice a day
Day 3: 1 mg (1/2 strip) twice a day
Day 4: 2 mg (1 strip) twice a day
Day 5: 3 mg (1 1/2 strips) twice a day
Day 6: 4 mg (2 strips) twice a day
Day 7: 6 mg (3 strips) twice a day (stop other opioids)
Low Dose (“Micro”) Inductions

References:


Other Counseling

- Risk of concurrent substance use
- Safe storage
- Naloxone ALWAYS
Maintenance and Follow-up
How often do I need to follow-up?

- Weekly to monthly
  - Weekly:
    - New starts and dose titrations
    - Unstable in terms of ongoing opioid use, risky concurrent use (sedatives)
  - Monthly: Stable dose, no opioid or other substance use
What do I need to know (and document) at the visit?

- Adherence
- Withdrawal, cravings
- Side effects
- Other substance use
- Review: safe storage, risks of concurrent use, naloxone
- PMP Check
- UDS if collected
A word about urine drug screens

- Use as a tool to better support recovery and address return to use
- NOT to discharge from buprenorphine or compel to more intensive settings
- “Expected” vs. “unexpected” results
- Changes during COVID

Sources: ASAM COVID-19 Task Force, 2020; Martin, 2018
What happens when...
My patient uses opioids?

- Reassure patient (and yourself) that this is a normal part of the disease course.
  - Many will continue to use opioids, especially early on
  - Most people will resume use at some point

- Reinforce successes
  - Any positive change
  - “Think back to X months ago and tell me how this would have gone...”
My patient uses opioids?

**Treatment strategies**

- Keep engaged!
- Closer follow-up
- Address concurrent stressors or medical conditions
- Increase dose of buprenorphine if reporting cravings or withdrawal symptoms and not at max dose
- Consider long-acting injectable buprenorphine
- Consider referral to higher level of care, but caution in requiring this because often “higher level of care” = No care
My patient uses opioids?

Harm Reduction Strategies

• Goal is to reduce negative consequences – imperfect adherence still saves lives
• Review overdose prevention and naloxone
• Safer use strategies:
  • Don’t use alone
  • Clean injection site
  • Go slow, use a test dose
  • Don’t share syringes or other equipment (“works”)
  • Link to resources for syringes and fentanyl test strips
My patient wants to stop their buprenorphine?

- Buprenorphine should be prescribed “as long as it continues to benefit the patient”
  - Can be indefinitely

- Discuss reasons for stopping
  - What does it mean to be in recovery?
  - Is this coming from the patient or pressure elsewhere?
  - Are other chronic medical and psychiatric conditions well-controlled?
  - If tapering, slow and patient-centered
My patient has acute pain or surgery?

- DO treat pain on top of OUD
- DON’T stop buprenorphine

**Strategies**

- Maximize non-opioid analgesia
- Split buprenorphine into TID or QID dosing
- Consider raising the dose up to 32 mg
- **CAN** use short-acting full agonist opioids on top of buprenorphine in cases of severe pain
  - Consider oxycodone or hydromorphone (higher affinity)
  - May require higher doses

*Source: Buresh, 2020*
### My patient has acute pain or surgery?

<table>
<thead>
<tr>
<th>Pain Level</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very mild pain</td>
<td>Split methadone/buprenorphine TID</td>
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<tr>
<td>Mild pain</td>
<td>- Ibuprofen, acetaminophen, or topical analgesics</td>
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<tr>
<td></td>
<td>- Neuropathic pain: gabapentin, TCAs, SNRIs</td>
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<tr>
<td></td>
<td>- Spastic pain: tizanidine, baclofen, cyclobenzaprine (not carisoprodol)</td>
</tr>
<tr>
<td></td>
<td>- Anxiety/PTSD: sedating SSRIs or SNRIs</td>
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<tr>
<td></td>
<td>- Pregnancy: Nitrous oxide for labor pain, avoid ibuprofen, tizanidine, some SSRIs</td>
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<tr>
<td>Moderate-severe pain</td>
<td>- Neuraxial, regional, and local anesthesia</td>
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<tr>
<td></td>
<td>- Opioids: may need higher doses than patients without OUD due to tolerance—opioid requirements are lower if home methadone/buprenorphine is continued than if it is stopped</td>
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<tr>
<td></td>
<td>- Ketamine or dexmedetomidine</td>
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My patient may be diverting their buprenorphine?

- **What to worry about**
  - Typically, a sign of poor access to care
  - Among people who regularly use opioids, buprenorphine most commonly used to avoid/treat withdrawal

- **Best way to avoid diversion is to increase access to care.**

- **Discuss the issue and offer alternative**
  - Short prescriptions
  - Injectable buprenorphine
  - OTP or other higher level of care
  - Discharge with option to return
Conclusions
Summary

- MOUDs save lives!
- Buprenorphine maintenance is safe and effective in office-based settings for most patients
- Practices are shifting to be lower barrier, harm reduction oriented, and patient-centered
- You can do this in your practice!
Resources

SPECIAL ARTICLE

The Next Stage of Buprenorphine Care for Opioid Use Disorder
Stephen A. Martin, MD, EdM; Lisa M. Chiodi, PhD; Jordan D. Barre, MS, RN; and Amanda Wilson, MD

Primary Care and the Opioid-Overdose Crisis — Buprenorphine Myths and Realities
Sarah E. Wakeman, M.D., and Michael L. Bennett, M.D.

Sources: Martin 2018; Wakeman, 2018; NASEM, 2019: SAMHSA
HRSA-funded, free and confidential tele-consultation support to help end the epidemics

<table>
<thead>
<tr>
<th>Service</th>
<th>Contact Information</th>
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<tbody>
<tr>
<td>Substance Use Warline</td>
<td>(855) 300-3595</td>
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<tr>
<td>HIV/AIDS Warline</td>
<td>(800) 933-3413</td>
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<tr>
<td>Perinatal HIV Hotline</td>
<td>(888) 448-8765</td>
</tr>
<tr>
<td>PrEPline</td>
<td>(855) HIV-PrEP</td>
</tr>
<tr>
<td>Hepatitis C Warline</td>
<td>(844) HEP-INFO</td>
</tr>
<tr>
<td>PEPLine</td>
<td>(888) 448-4911</td>
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Clinical questions can also be submitted securely: nccc.ucsf.edu
THANK YOU AND QUESTIONS

Maggie Lowenstein, MD, MPhil, MSHP
margaw@upenn.edu
References


- FDA Drug Safety Communication, “FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks,” 2017


References Continued


- Providers Clinical Support System, 2014: Monitoring of Liver Function Tests and Hepatitis in Patients Receiving Buprenorphine (With or Without Naloxone)


