Buprenorphine 101

Laura G. Kehoe, MD, MPH, FASAM
Medical Director, MGH Substance Use Disorder Bridge Clinic
Assistant Professor of Medicine
Harvard Medical School
Mu Opioid Receptor Pharmacodynamics

Full MU Agonist:
- Methadone
- Heroin
- Morphine
- Oxycodone

Partial MU Agonist:
- Buprenorphine

Full MU Antagonist:
- Naltrexone
- Naloxone

*Naltrexone has the highest receptor AFFINITY, then buprenorphine, then methadone
Pharmacology of Treatments
Heroin acts on the opioid receptor, causing:

- Pain relief
- Euphoria
- Constipation
- Slow breathing
1) Buprenorphine is a partial agonist

- Pain relief
- Euphoria
- Constipation
- Slow breathing

Buprenorphine
2) Buprenorphine has a very high affinity for the opioid receptor.
Goal of Medications for Addiction Treatment

- Relieve withdrawal symptoms
- Block effects of other opioids
- Reduce cravings
- Restore normal reward pathway
High affinity + Partial agonism = Potential for precipitated withdrawal
Heroin

Buprenorphine
Precipitated withdrawal

Administering buprenorphine while full agonists are present leads to ANTAGONIST effects
Good Candidate

- Preference and motivation for office-based opioid treatment
- No unstable severe alcohol/benzodiazepine use disorder
- Self-endorsing a diagnosis of opioid use disorder with evidence for physiologic dependence
- No unstable psychiatric issues (i.e. +SI/Hi)
Initiating Buprenorphine

• Must be in mild to moderate withdrawal before taking initial dose

• This can be done in-office or at home

• Many patients have taken buprenorphine before—patients can be our guide
Initiation for Patients Not Currently Using Opioids

- Consider if good evidence of history of opioid use disorder and high risk for relapse
- Start lower dose and increase more slowly
  - 2 mg reasonable starting dose
- Examples:
  - Recently released from prison
  - Leaving a sober house or halfway house
Total possible analogues – (bad guy tweaks)
red x purple x green x blue = 6 x 3 x 16 x 8 = 2,304

LSS observations:
of known: 22/34 = 65% of potential: 22/2,304 = 0.95%
A Guide for Patients Beginning Buprenorphine Treatment at Home

Before you begin you want to feel very sick from your withdrawal symptoms

It should be at least...

- 12 hours since you used heroin/fentanyl
- 12 hours since snorted pain pills (Oxycontin)
- 16 hours since you swallowed pain pills
- 48-72 hours since you used methadone

You should feel at least three of these symptoms...

- Restlessness
- Heavy yawning
- Enlarged pupils
- Runny nose
- Body aches
- Tremors/twitching
- Chills or sweating
- Anxious or irritable
- Goose pimples
- Stomach cramps, nausea, vomiting or diarrhea

Once you are ready, follow these instructions to start the medication

**DAY 1:**
8-12mg of buprenorphine

Most people feel better the first day after 8-12mg. (Dosing depends on how early on the first day you started)

**Step 1.**
Take the first dose

- 4mg

**Step 2.**
Wait 45 minutes
- If still sick? Take next dose
- 4mg

**Step 3.**
Wait 6 hours
- Still uncomfortable? Take last dose
- Stop

Most people feel better after two doses = 8mg
- Stop after this dose
- Do not exceed 12mg on Day 1

**DAY 2:**
up to 16mg of buprenorphine

Take up to a 16mg dose

Most people feel better with up to a 16mg dose

Repeat this dose until your next follow-up appointment

If you develop worsening symptoms while starting buprenorphine before your scheduled outpatient appointment return to the emergency department

*Note: This is a modified version of a NIDA guidance document*
KEEP CALM AND LISTEN TO YOUR PATIENTS
Need to Break Down Barriers to Care

“Patients don’t fail treatment, treatment fails people”
Patient Reflection

Don't hate the Addict
Hate the disease
Don't hate the person
Hate the behavior
If it is hard to watch
Imagine how hard it is
to be living it
Myths

• Short term treatment is ok
• No one should ever be Rx above 16 mg daily
• Everyone must engage in therapy if Rx buprenorphine
• Buprenorphine is absolutely contraindicated if using other substances
• Everyone must be moved to a higher level of care if using other substances or not engaging
• Teaching about or encouraging safe injection practice, may trigger more use

Gjersin L 2013, Feillen DA 2013, Dugosh 2010
People Die Waiting for Treatment

Buprenorphine Maintenance
- 75% retained in treatment
- 75% abstinent by toxicology

Detoxification + Counseling
- 0% retained in treatment
- 20% died

Control
- p=0.0001

Kakko et al. Lancet. 2003 Feb 22;361(9358):662-8

Short Term Treatment Ineffective and Dangerous
Overdose Risk Elevated Post Detox

6/16/16

Had my first overdose after 20 years of IV drug use. I can describe my thoughts and feelings, after being saved by Narcan, in one word alone... grateful. This medication/drug is saving lives. Thank God, God bless. Keep the faith.

Nick

6/17/16

Today is my Birthday and I have received the best present ever... another chance at life. So grateful for my family, so grateful for my health, so grateful for this program. And a grateful heart will never relapse.
Interim Buprenorphine Improves Outcomes

Individuals using SEPs report barriers to accessing buprenorphine treatment.

Those using illicit buprenorphine describe interest in treatment but barriers to access.

Experiencing barriers associated with preference to receive care in harm reduction agency.

Barriers include:
- Inability to pay
- Unsure of where to obtain care
- Lack of transportation
- Having been treated poorly at the clinic
- Wanting to avoid being seen at the clinic
- Distrusting doctors
- Lack of child care

Meeting People “Where They Are” Can Happen Anywhere

- Emergency Department
- Inpatient
- Primary Care
- Psychiatry
- OB/GYN
- Syringe Exchange Programs
- Formal Addiction Treatment Programs
Treating Hospitalized Patients

• Initiating methadone in hospital:
  – 82% present for follow-up addiction care

• Initiating buprenorphine vs detox:
  – Bupe: 72.2% enter into treatment after discharge
  – Detox: 11.9% enter treatment after discharge

Good Retention in Low Threshold Models

• Low threshold methadone:
  – 88% retention at 30 days, 64% at 1 year
  – Significant reduction in heroin & cocaine
  – Increased stable living conditions

• Low threshold buprenorphine:
  – Patients retention similar to “standard” bup
  – 68%, 63%, 56%, 42% retained at 3, 6, 9, 12 mo

ED Initiated Treatment

- 78% vs 37% engaged in buprenorphine treatment
- Fewer days of self-reported opioid use
Evidence Based Treatment

“Access to medication – assisted treatment can mean [the] difference between life or death.”

Michael Botticelli, October 23, 2014
Director, White House Office of National Drug Control Policy
High level of evidence found to support effectiveness of buprenorphine in improving treatment retention and decreasing illicit opioid use.

When dosed appropriately, buprenorphine is as effective as methadone in suppressing illicit opioid use, but may not be as effective in treatment retention.

Inconclusive evidence on buprenorphine’s impact on non-opioid drugs.

Growing evidence that higher doses (>16mg) are more efficacious than lower doses.

Effective for heroin users as well as prescription opioid users.

Both buprenorphine and methadone improve pregnancy related outcomes.
Treatment Effective in Primary Care

No difference in self reported opioid use, opioid abstinence, study completion, or cocaine abstinence between the 2 groups

What About Polysubstance Use?

Participants Who used Cocaine had:
• Reduced self-reported opioid use from 94% to 27%
• 6-month treatment retention of 59%
• No significant difference in retention or opioid use compared to those who didn’t use cocaine

# Changes in FDA Recommendations

## What about Benzodiazepines?

<table>
<thead>
<tr>
<th>08/2016</th>
<th>09/2017</th>
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<tr>
<td>- Boxed Warning for combined use of opioid medicines with benzodiazepines or other CNS Depressants (e.g. Alcohol)</td>
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<td>- Risks of slowed or difficult breathing; Sedation; Death</td>
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<td>- Buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS).</td>
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<td>- The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks.</td>
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<td>- Careful medication management by health care professionals can reduce these risks.</td>
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“Based on our additional review, the U.S. Food and Drug Administration (FDA) is advising that the opioid addiction medications **buprenorphine and methadone should not be withheld from patients taking benzodiazepines** or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, **the harm caused by untreated opioid addiction can outweigh these risks.**”

FDA Drug Safety Communication, 9/20/17
What’s the OD risk on Buprenorphine?

• Very low
• Hard to overdose on buprenorphine
• Partial agonist, ceiling effect, risk respiratory depression low
• OD Deaths from buprenorphine low
  • most combined with high dose IV benzos
  • children who got into it

Ling 2002, JSAT
Early Use During Treatment Expected

![Graph showing estimated days of opioid use by the types of treatment based on Model 4 (N = 795)‡‡.](image)

**Figure 4** Estimated days of opioid use by the types of treatment based on model 4 (n = 795)‡‡. BUP: buprenorphine; MET: methadone.

‡‡The number of participants in each type of treatment varied in each month and is therefore not indicated in the figure; on average over the follow-up period, each month there were about 14.2% of the participants in BUP treatment, 38.5% in MET treatment, and 46.9% in neither BUP nor MET treatment.
Relapse

- Reframe as a learning experience
- Deconstruct the relapse, not your patient
- Emphasize you want to continue seeing patient
- Be positive and hopeful
- Remind your patients that treatment works

*Emphasize hope if they can’t see it*
Celebrating Progress is Crucial
Abstinence is Not the Only Marker of Recovery

[The FDA] intended “to correct a misconception that patients must achieve total abstinence in order for MAT to be considered effective.”

Alex Azar, Health and Human Services Secretary
Feb 25, 2018
Reducing Negative Consequences

• Congruent with other chronic disease management
• Critical to management of other chronic disease management
• Safer substance use
• Safer injection or use practices
• Intranasal Naloxone for overdose prevention
• Immediate access to pharmacotherapy
What About Diversion?

- Happens
  - Poor access to care
  - Sub-therapeutic dosing
  - Helping others
  - Can be a way to help get people into care
- Best way to decrease diversion is to increase access to care
- Short Rx and closer interval fu
- Open communication

Johnson Int J Drug Pol 2014
Launonen Int J Drug Pol 2015
Monico JSAT 2015
What is a Higher Level of Care?

- Closer interval follow up, shorter Rx, dose change
- Comprehensive care
- Small achievable goals
- Reduction of harmful consequences
- Recall other chronic diseases and their management if patient not responding

“HIGHER level of care” can mean NO level of care
Buprenorphine Wrap Up

- Immediate Access, engagement as priority
- Schedule III can be called in, faxed, Rx admin while await PA
- Tox screen as guide, not weapon
- Assess and assure therapeutic dosing
- Shorter Rx, close fu, open communication, competing priorities vs. DC
- Advocate to induce, stabilize and maintain, not detox
- Remission takes time, be flexible; reducing harm underscores medical care
Wherever you go, go with all your heart.

Thank you for not kicking me off.
Thank You!

lgkehoe@mgh.harvard.edu