Integrating Buprenorphine Treatment for Opioid Use Disorder in HIV Primary Care

Michael MacVeigh, MD
Kristen Meyers, BS, CADC1
May 10-12, 2017
Portland
Our Clinic Building
Portland
BRIDGETOWN
OREGON
Overview

Welcome Back and Overview of Bup TA training

Site Specific Updates

Opioid Crisis: Nationwide Overview

Stigma, Shame, and the Power of Language

Relapse Sensitive Environments and Retention in Care

Methods to Reduce Diversion

Higher Level of Care, Alternatives to OBOT, Tapering Off Bup

Mental Health and OUD

Pain and OUD
Metro Health Clinic
Bluegrass Care Clinic
Centro Ararat Clinic
Opioid Crisis Nationwide

Nationally, opioids were involved in more than 61 percent of deaths from overdoses in 2014
By HAЕYOUN PARK and MATTHEW BLOCH JAN. 19, 2016, New York Times

The C.D.C. says that 91 people in the United States die every day from opioid overdose.
By CHRISTINE HAUSER FEB. 13, 2017, New York Times

2015 Data Comparison
Overdose deaths: 52,404.
Car crashes deaths: 37,757
Gun deaths, including homicides and suicides: 36,252
NBC News, Dec 9 2016
Estimated Age-adjusted Death Rates for Drug Poisoning by County, United States: 1999

Estimated Age-adjusted Death Rate per 100,000:
- 0-2
- 2.1-4
- 4.1-6
- 6.1-8
- 8.1-10
- 10.1-12
- 12.1-14
- 14.1-16
- 16.1-18
- 18.1-20
- >20

Estimated Age-adjusted Death Rates for Drug Poisoning by County, United States: 2009

Year: 2009

Estimated Age-adjusted Death Rate per 100,000:
- 0-2
- 2.1-4
- 4.1-6
- 6.1-8
- 8.1-10
- 10.1-12
- 12.1-14
- 14.1-16
- 16.1-18
- 18.1-20
- >20

How the Epidemic of Drug Overdose Deaths Ripples Across America

By HAEYOUN PARK and MATTHEW BLOCH  JAN. 19, 2016

![Map of overdose deaths per 100,000](map-url)

2003  2004  2005  2006
2007  2008  2009  2010
2011  2012  2013  2014

[Map image with color coding for overdose deaths]
### Figure 26. Drug Poisoning Deaths Involving Selected Illicit Drugs, 2007-2014

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Prescription Drugs(^f)</td>
<td>19,601</td>
<td>20,044</td>
<td>20,848</td>
<td>22,134</td>
<td>22,810</td>
<td>22,114</td>
<td>22,767</td>
<td>25,760</td>
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<td>Cocaine</td>
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<td>Heroin</td>
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<td>3,278</td>
<td>3,036</td>
<td>4,397</td>
<td>5,927</td>
<td>8,257</td>
<td>10,574</td>
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</table>

Source: National Center for Health Statistics/Centers for Disease Control and Prevention

\(^f\) Prescription drug poisoning deaths include deaths from prescription opiates and benzodiazepines.
Opiate Crisis Nationwide

“Deaths from overdoses are reaching levels similar to the H.I.V. epidemic at its peak”

Robert Anderson, the C.D.C.’s chief of mortality statistics.
HIV and OUD: Who? What? are we treating?

29 year old male

1/18/2017: HIV Viral Load = <20

1/25/2016: Pain MGMT Profile:
+Amphetamines
+Methamphetamines
+Benzodiazepines
+Marijuana
+Opiates
+Morphine
HIV and OUD

32 year old male

11/15/2016: HIV Viral Load= 26

2/19/2017: Pain MGMT Profile:
+Alcohol Metabolites
+Amphetamines
+Methamphetamine
+Benzodiazepines
+Lorazepam
+Cocaine
+Opiates
+Morphine
HIV and OUD

36 year old female

02/13/2017: HIV Viral Load= <20

2/14/2017: Pain MGMT Profile:
+Alcohol Metabolites
HIV and OUD

50 year old male

12/16/2016: HIV Viral Load= <20

2/14/2017: Pain MGMT Profile:
+Marijuana Metabolites
HIV and OUD

41 year old male

02/08/2017: HIV Viral Load= <20

01/08/2017: Pain MGMT Profile: +Marijuana Metabolites
HIV and Stigma

NASTAD joins public health experts and leaders in affirming that there is now conclusive scientific evidence that a person living with HIV who is on antiretroviral therapy (ART) and is durably virally suppressed (defined as having a consistent viral load of less than <200 copies/ml) does not sexually transmit HIV. This statement accelerates our longstanding work to end the dual epidemics of HIV and HIV-related stigma and to dramatically reduce new HIV infections, and is supported by policies and public health practice grounded in science.

WHY IT’S IMPORTANT

The new evidence will help ameliorate decades of HIV-related stigma and discrimination by confirming that treatment is a powerful preventive intervention.
Stigma

Stigma is defined as a set of negative beliefs that a group or society holds about a topic or group of people. According to the World Health Organization (WHO), stigma is a major cause of discrimination and exclusion and it contributes to the abuse of human rights. When a person experiences stigma they are seen as less than because of their real or perceived health status.

Stigma in Methadone and Buprenorphine Maintenance Treatment
Edwin A. Salsitz, M.D., FASAM, PCSS-MAT MODULES
In a study across 14 countries of 18 of the most stigmatized issues, including being a criminal, illicit drug addiction was number 1, and alcohol addiction number 4.

John Kelly, PhD, Language, Substance Use Disorders, and Policy: They need to reach consensus on an “Addictionary”.
Proposed SUD Stigma statement

• Treatment of substance use disorder leads to reduction in morbidity and mortality in this population.

• Addiction-related stigma is a major barrier to access to, funding for, and acceptance of such treatment.

• Combating this stigma is critical to support our patients in their recovery and access to care.

• The dramatic increase in overdose and the SUD epidemic demonstrates a need for an approach similar to our success with HIV. The combination of successful therapies and stigma reduction have led to broader acceptance of HIV testing and care.

• Understanding and accepting the value of stigma reduction linked to addiction therapies is critical for both providers and patients.
Impact of Stigma on Treatment

According to the Substance Abuse and Mental Health Services Administration (SAMHSA), addiction affects approximately 23.5 million Americans every year, and roughly 11 percent receive treatment.

While there are many factors that contribute to this addiction-treatment gap, stigma is one of the largest.

https://vimeo.com/153845422
Stigma and Treatment

Common Myths:

• Why not taper off?
• Substituting one drug/addiction for another
• Methadone (and now Buprenorphine) is harmful
• You are not in recovery
• You should not get pregnant
• You are on methadone; no need for post-op pain meds
Shame

“A powerful, but unquestioned, conviction that in some important way one is flawed and incompetent as a human being... The self condemnation and self-loathing that shame precipitates are part and parcel of a pervasive, persistent, and destructive set of emotions that grips the sufferers with a crippling sense of terror and pessimism, preventing them from living harmoniously and confidently.” (Goldberg, 1991)
Shame is common among individuals with OUD and associated with use and relapse.

Within individuals with OUD, particular subgroups associated with shame include injection heroin users and pregnant women and mothers.

Shame should be a focus of OUD treatment.

The Role of Shame in Opioid Use Disorders
Ashley Braun-Gabelman, Ph.D,
PCSS-O MODULES
Words are important. If you want to care for something, you call it a flower; if you want to kill something, you call it a weed. Don Coyhis, Founder of White Bison
The power of language

Recovery Brands [https://vimeo.com/185592929](https://vimeo.com/185592929)
Stop Talking Dirty

<table>
<thead>
<tr>
<th>Dirty/Clean UDS</th>
<th>vs</th>
<th>Positive/Negative UDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>substance abuser</td>
<td>vs</td>
<td>substance use disorder</td>
</tr>
<tr>
<td>person <em>is</em> the problem</td>
<td>vs</td>
<td>person <em>has</em> a problem</td>
</tr>
</tbody>
</table>

In general, person first language is preferable (persons with/suffering from..)
Relapse Sensitive Environment

1891-1892 - Keeley League “Laws must realize a leading fact: Medical not penal treatment reforms the drunkard.”

Drugs and the Brain

Drugs and pathological gambling behaviors exert their initial effects by acting on the same reward circuitry in the brain that makes food and sex, for example, profoundly reinforcing.  

Drugs of abuse directly or indirectly target the brain’s reward system by flooding the circuit with dopamine. This reward system is involved in the reinforcement of behaviors and the production of memories. 

1 ASAM  http://www.asam.org/quality-practice/definition-of-addiction

2 NIH  https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain
Neurochemistry of substance use - simplified

Most drugs of abuse target the brain’s reward system by flooding it with dopamine.
<table>
<thead>
<tr>
<th>Substance</th>
<th>Action Description</th>
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<tbody>
<tr>
<td>Caffeine</td>
<td>Blocks reuptake -&gt; incr dopamine</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Strongly blocks dopamine reuptake : incr dopamine</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>Blocks reuptake &amp; increases dopamine release</td>
</tr>
<tr>
<td>Tobacco</td>
<td>Nicotinic receptors -&gt; incr dopamine release</td>
</tr>
<tr>
<td>Etoh</td>
<td>Effect on GABA -&gt; incr dopamine release</td>
</tr>
<tr>
<td>Opiates</td>
<td>Effect on GABA -&gt; incr dopamine release</td>
</tr>
<tr>
<td>Marijuana</td>
<td>Endocannabinoid binding leads to GABA effect -&gt; incr dopamine release</td>
</tr>
</tbody>
</table>
DRUGS OF ABUSE TARGET THE BRAIN’S PLEASURE CENTER

Brain reward (dopamine) pathways

These brain circuits are important for natural rewards such as food, music, and sex.

Drugs of abuse increase dopamine

Typically, dopamine increases in response to natural rewards such as food. When cocaine is taken, dopamine increases are exaggerated, and communication is altered.
Brain's Reward Center

- Cerebral cortex
- Nucleus accumbens
- Amygdala
- Hippocampus
Neurobiology - Circuitry of addiction/ Reward center

Activation of ventral tegmental area (midbrain) ->

Stimulation of the ventral striatum (espec nucleus accumbens : “pleasure center”) ->

Release of dopamine to the entire limbic system, especially:

- Hippocampus: memory formation
- Amygdala: emotion formation
- Ventral striatum: formation of habits (action w/o thought)

Also affects connections to prefrontal cortex and cerebellum.

**All these circuits become stronger and more efficient neural pathways as they are activated multiple times**
Relapse Sensitive Environment

What is it?

A systemic philosophy of care with the goal of maintaining an individual in addiction treatment to enhance the potential for sustained recovery.

This can be expanded to encompass an individual's definition of recovery with outcomes based on quality of life and not solely on abstinence.
Key Concepts for building a Relapse Sensitive Environments (cont)

- Supported by Disease Model
- Supported by Neuroscience which provides evidence on biological reasons for relapse
  - Treatment engagement, not punitive measures for return of biological-based symptoms
- Supports the SAMHSA definition of recovery which includes, health, wellness, and self determination
- Supports Quality of Life as an outcome rather than solely on negative urine drug screens
Key Concepts for building a Relapse Sensitive Environments

- The client is not in control of their alcohol and/or drug intake or its consequences
- Increase recovery supports after a relapse and don’t discharge
- Explore different measures of treatment success (like quality of life)
- Understanding that relapse is biological
- Long-term recovery is best supported by patience and support rather than punishment and abandonment
- Treatment for addictive disorders is not typically a “oneshot” type of intervention
Retention in Care

“All Treatments Work For Some People/Patients”

“No One Treatment Works for All People/Patients”

Alan I. Leshner, Ph.D Former Director NIDA
Factors Effecting Retention in Care

Patient characteristics, behavior, and other factors unrelated to treatment have been found to contribute relatively little to retention in MAT.

One comprehensive study found that retention was determined almost entirely by what happened during treatment, not before, although two factors, older age and less involvement with the criminal justice system, predicted longer retention (Magura et al. 1998, 1999). Another factor found to affect retention was motivation or readiness for treatment (Joe et al. 1998).
Fostering change

In any setting, research has shown these four factors are responsible and needed to effect change:

1. Empathy
2. Positive regard
3. Genuineness
4. Feedback

Change is a process...

Current State → Transition → Future State

Not an event.

Improving Retention, Outcomes and Supervision with PCOMS
Presented by George S. Braucht, LPC & CPCS
NAADAC Training Module
**Recommended steps to improve patient retention**

**Individualize medication dosages.** Adequate, individualized medication dosages are probably the most important factor in patient retention (Joseph et al. 2000).

**Clarify program goals and treatment plans.** Treatment providers should explain program goals and treatment plans to every patient. Inconsistent messages adversely affect patient retention, particularly when these messages are about the advisability of...

**Simplify the entry process.** Shortening intake results in better program retention (see chapter 4).

**Attend to patients' financial needs.** Patients’ inability to pay may limit both treatment entry and retention, especially in States where MAT is not covered by Medicaid, State funds, or private insurance.

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Approaches to Providing Comprehensive Care and Maximizing Patient Retention.

2005 SAMHSA (Treatment Improvement Protocol (TIP) Series, No. 43.) Chapter 8.
Recommended steps to improve patient retention (cont.)

Reduce the attendance burden. Attendance requirements can exert powerful effects on retention. Rhoades and colleagues (1998) found that patients who were required to visit an OTP less frequently were less likely to dropout of treatment and no more likely to use other drugs than patients on a daily attendance schedule.

Provide useful treatment services as early as possible. Patients were more likely to stay in treatment when they were motivated strongly and engaged earlier in useful activities (Simpson, D.D., et al. 1997b).

Enhance staff-patient interactions. Good staff attitudes and interactions with patients have been associated with higher retention. In one study, patients’ frequent contact with staff members and the involvement and visibility of OTP administrators increased patient retention (Magura et al. 1999).

Improve staff knowledge and attitudes about MAT. OTP staff members should understand MAT and appreciate the wealth of science supporting it, and they should be aware of recommended treatment practices so that they can interact effectively and constructively with patients. Bell (2000)

Approaches to Providing Comprehensive Care and Maximizing Patient Retention. 2005 SAMHSA (Treatment Improvement Protocol (TIP) Series, No. 43.) Chapter 8.
Local example of Bup treatment

Allied Methadone Clinic:
• Must attend daily for 90 days
• Build up to 1, 2, then 4 take outs per week.
• Build up to weekly take outs
• Build up to monthly take outs
• Take outs pulled if positive UDS
• All take outs require stable home environment, etc
Helpful Methods to Reduce Diversion

• Know your patient
  – Thorough assessment and history
  – Risk of other SUD

• Use of controlled-substance agreements
  – Buprenorphine specific

• Thoughtful dose management

• Compliance monitoring
  – e.g. pill counts and urine screens
  – regulatory and legal measures
Urine Drug Screens

• UDT is a test we do for the patient’s care, not to the patient

• UDT results should increase not decrease communication with the patient

• UDT does not diagnose
  – SUD
  – Physical dependence
  – Impairment or Diversion
Urine Drug Screens (cont)

- Specimen collection

- Characteristics of urine
  - Appearance - Color of a urine specimen is related to the concentration of its constituents
  - Temperature - 4 minutes of voiding should fall within the range of 90°F to 100°F with a volume of 30 ml. or more
  - pH - Range of 4.5 to 8.0
  - creatinine concentration: normal human urine has a greater than 20 mg/dL
Urine Samples - clues
“Trust, but verify”

• UDS-check creatinine levels

• Naloxone levels should be low

• Metabolite levels should be positive meaning that the patient is actually taking the medication and it is being metabolized (norbuprenorphine present)

• Specific gravity - clue to water/watered down sample

• Temp dots - helpful re recent sample.
PDMP

Stateline States Require Opioid Prescribers to Check for ‘Doctor Shopping’ Christine Vesta May 09, 2016
Higher Levels of Care (BUP)

Office Based vs Outpatient Program (APG)

Inpatient Treatment while on BUP (KK case)
Case Review APG - OBOT vs OTP

32 yo male with borderline personality disorder, chronic anxiety, chronic pain, polysubstance use, with multiple ED/clinic visits and doc shopping for any and all altering substances (benzos, opiates, stimulants and other psychoactive meds).

Successful HIV suppression and prior Hep C cure. Unpredictable clinic attendance, frequent ED visits, and confrontational behavior. Several hospitalizations with dual dx program with early d/c or AMA. Ongoing polysubstance use and provider concern due to benzos.
Case Review APG - OBOT vs OTP

Outside consultation via ECHO led to recs of:

Preferred:
• Inpatient tapering of Buprenorphine due to inability to control outpatient management
  – potentially taper his buprenorphine and initiate naltrexone at Cedar Hills
  – Depot naltrexone may be a better option for his MAT

Second Option:
• Local detox followed by outpatient OTP of depot naltrexone

Third Option:
• Outpatient Treatment Program for MAT: to include Bup taper and depot naltrexone

Least desirable option:
• Continue with OBOT prescribing; limit duration of the prescriptions to 3-5 days to help reduce risk of diversion and abuse. the pregabalin should stop since it is likely either being abused or diverted.
• Continue aggressive monitoring
Case Review KK - Inpt while on Bup

43 yo male w/longstanding hx of polysubstance abuse with heroin, meth (both IDU), MJ, and intermittent Etoh. Entered medical care after prolonged ICU stay for severe PCP with untreated HIV.

Successful HIV therapy once engaged in both HIV and buprenorphine therapies. However, constant struggle with meth. He weaned off suboxone per his preference, but then relapsed in midst of housing crisis and accelerated meth use. Re-induced on suboxone successfully, but meth use out-of-control.
• Utilizing both case manager, patient navigator, weekly and sometimes biweekly visits, and constant encouragement - he ultimately chose to pursue inpatient treatment for his methamphetamine use.

Issues:
• Finding a program that would accept his Bup rx and his insurance
• Logistics of intake, med supply, trust issues between staff at facility and patient, facility’s general approach of total control, discomfort with his medical condition (was off HIV meds at time: “what if..?”)
Alternatives to BUP

Methadone (RP)

Naltrexone (data we have and recs)
## Medication Efficacy For Opioid Use Disorder

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<tr>
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<th>Treatment Program Retention</th>
<th>Opioid Misuse</th>
<th>Criminal Activity</th>
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<tr>
<td>Methadone</td>
<td>↑ (n=3)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>↓ (n=6)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>No Effect (n=3)&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td>Buprenorphine</td>
<td>↑ (n=4)&lt;sup&gt;b&lt;/sup&gt;</td>
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<tr>
<td>PO NTX</td>
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<tr>
<td>XR NTX</td>
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<td>↓ (n= 3)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>No data</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mattick RP, et al. Cochrane Database Syst Rev 2011;  
<sup>c</sup>Minozzi S, et al. Cochrane Database Syst Rev 2011;  
<sup>d</sup>Krupitsky E et al. Lancet. 2011; Comer SD et al. Arch Gen Psychiatry 2006; Lee et al. NEJM 2016
Switching from Bup to naltrexone

Taken together, published clinical practice recommends induction to full dose naltrexone 5–7 days after buprenorphine discontinuation [48].
Depot Naltrexone to BUP switch

Came up in past via emails regarding patients receiving naltrexone in jail upon discharge and then presenting with interest in buprenorphine.

I would still recommend:
One would anticipate that naltrexone would block the suboxone and it would be best to wait for the end of a month after naltrexone injection before expecting a response. By then - (if no opiate use) could just start (Bup)
If relapse - back to the withdrawal sx's before induction
Also - a good place for rapid UDS before starting...
Meanwhile…

what our patients might be doing

I just received my vivitrol shot while having a heroin habit. Obviously went into severe p.w. not my 1st time by the way.. usually 5 days it'd be till I could return to construction work. Sleep a few more days. Anyways this time I tried IV suboxone because I had to be better for work. Did a full day of full blown precipitated withdrawal. Then injected 8mg suboxone. And here's what happened. .. I didn't get high ... and after about 30min started to not feel sick. So it out competes the naltreoxe side and the bupe kicks in…

Meanwhile…

Another patient perspective:

I took 10mg naltrexone 25 hours ago. It sent my into severe PWD so I took a 8mg suboxone 2 hours afterwards thinking it would overpower the naltrexone. The sub didn't do much at all, presumably because it's binding affinity is weaker than naltrex so it couldn't break through.

Fast forward to now and I've got some dope. Yesterday, the suboxone was rendered infective because of the naltrexone I had taken a few hours before. Does that mean I can ignore the bupe's blocking timeframe since it never had a chance to bind to my receptors (bc of naltrexone)? Or did the bupe slide into my receptors after the naltrexone came off, despite originally being inactive?

Essentially, I'm trying to understand if I should follow the blockade timeline of 8mg bupe or of 10mg naltrexone to determine when I can expect this dope to get me high. Cheers!

EDIT: Whoa, now I'm nodding off. Crushed a bundle earlier today. Then another bundle about an hour ago. I guess I broke through the blockade.
Tapering off Bup

Can be patient or provider initiated

Can be rapid or slow (slow recommended)

Patients frequently report concerns when they are at the lower doses
# Planned Taper

Enter your current steady* buprenorphine dose: **16.00** mgs./day

*The steady buprenorphine dose is calculated using the prior 10 days' doses. [use this form](http://www.helpmegetoffdrugs.com/taper)

Enter a different starting date: **04/20/2017**

[Submit](#)

[Print this table](#)

## 60 Day Taper - Requiring Total of 166 mgs.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Day</th>
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<tbody>
<tr>
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<td>12.00mgs.</td>
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<tr>
<td>Friday, April 21, 2017</td>
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<tr>
<td>Tuesday, May 02, 2017</td>
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<tr>
<td>Wednesday, May 03, 2017</td>
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<td>4.00mgs.</td>
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[http://www.helpmegetoffdrugs.com/taper](http://www.helpmegetoffdrugs.com/taper)
## Planned Taper

<table>
<thead>
<tr>
<th>8mgs.</th>
<th>4mgs.</th>
<th>2mgs.</th>
<th>Coin</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1mg.</td>
<td>0.5mgs.</td>
<td>0.25mgs.</td>
<td>0.13mgs.</td>
</tr>
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</table>
Timeline of w/d

Patients have described the following general timeline for suboxone withdrawal symptoms:

• 72 hours: Physical symptoms at their worst
  – Nausea and vomiting
  – Muscle/body aches
  – Insomnia or drowsiness
  – Indigestion
  – Anxiety, depression, and irritability
  – Cravings
  – Fever or chills
  – Sweating
  – Headache
  – Difficulty concentrating

• 1 week: Bodily aches and pains, insomnia, and mood swings

• 2 weeks: Depression

• 1 month: Cravings and depression
Severity of Opioid-Withdrawal Symptoms after Abrupt Discontinuation of Equivalent Doses of Heroin, Buprenorphine, and Methadone.

Buprenorphine withdrawal is
- less intense than heroin withdrawal
- less intense and briefer than methadone withdrawal
MH Tx - is there some magic?

We were unable to find any data that specific diagnoses are better treated by specific drugs in the setting of OUD or specifically in patients on buprenorphine. That being said, there are lots of studies documenting higher rates of many MH diagnoses in this population.

The essence of the literature is that treatment of the psychiatric condition should proceed as it would without OUD, with tailoring to the specific patient re drug tolerance, effectiveness and preferences. Obviously, the use of sedatives would be of greater concern, especially benzos.

NO. There is no magic.
Depression

- **Pharmacotherapy:**
  Selective serotonin reuptake inhibitors (SSRIs): (e.g. fluoxetine, sertraline) o “First line” due to safety profile, generally well tolerated, affect the hepatic P450 system thus pay attention to potential for drug-drug interactions.
  Serotonin and norepinephrine reuptake inhibitors (SNRIs) (e.g. venlafaxine, duloxetine): Monitor blood pressure, particularly with venlafaxine
  Tricyclic antidepressants (TCAs): Contraindicated in those with cardiac conduction delays, fatal in overdose.
  Some positive evidence for treating depression in those on methadone maintenance (Nunes et al 1998; Woody et al 1975; Titievksy 1982)
  Monoamine oxidase inhibitors (MAO-I): Required dietary restrictions, wash out period required when switching from irreversible MAO-I to another antidepressant
  Other: bupropion (norepinephrine and dopamine reuptake inhibitor), mirtazapine (alpha 2 adrenergic blocker), trazodone/nefazodone (5HT2 antagonists)

- **Psychotherapy:** Evidence-based psychotherapies for depression include: Cognitive Behavioral Therapy (CBT) and Interpersonal Psychotherapy (ITP) (Butler AC 2006; Van Hees ML 2013)
PTSD

**Psychotherapy:** Evidence-based psychotherapies for PTSD include Cognitive Behavioral Therapy (CBT), including exposure-based CBT. CBT for PTSD involves a combination of psychoeducation, relaxation and anxiety management techniques, cognitive techniques, imagined and in vivo exposure to trauma-related stimuli, and relapse prevention (Gabbard et al. 2007).

**Pharmacotherapy:**

Meta-analyses and several randomized controlled trials published generally support the superiority of SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) over placebo for non-combat-related PTSD. The data for SSRIs and combat-related PTSD is more mixed; the most recent (2004) APA guidelines recommended SSRIs as first-line. Tricyclic antidepressants and monoamine oxidase inhibitors showed improvement in intrusive and depressive symptoms, but SSRIs are considered first-line in part due to safety profiles. Mirtazapine and nefazodone have also been shown to be superior to placebo in treating PTSD. Prazosin has been found to be effective for PTSD-related nightmares and sleep disturbance. Other medications with some indication, often in uncontrolled reports, include: carbamazepine, beta-blockers, lithium, clonidine, benzodiazepines, to name a few.

Adjunctive treatment with a second-generation antipsychotics in patients who have partially responded to an SSRI or an SNRI have also been shown to be effective (Gabbard et al. 2007; Brady et al. in Nunes et al. 2010)
Comorbidity of Adult ADHD and SUD in Adults: Epidemiologic Data

National Comorbidity Survey Replication (N=3199)

Prevalence of ADHD, %

Among Respondents With SUD: 10.8%
Among Respondents Without SUD: 3.8%

Prevalence of SUD, %

Among Respondents With ADHD: 15.2%
Among Respondents Without ADHD: 5.6%

Kessler et al. 2006.
ADHD

• Nonpharmacological interventions which encompass a wide-range of interventions including behavior therapy, academic interventions, family therapy, care coordination have been well studied in children but not adults (Murphy 2005)

• Pharmacologic interventions can be broken down into stimulants and non-stimulants:
  • Stimulants have demonstrated efficacy in numerous double-blind, placebo controlled trials. Considered first-line treatments. Examples include: methylphenidate and related compounds: dexamethylphenidate, and longer-acting methylphenidate agents (e.g. Concerta, Metadate CD, Ritalin LA) and dextroamphetamine and mixed amphetamine salts and longer acting related compounds (e.g. Vyvanse, Adderall XR)
  • Non-stimulants: atomoxetine (Strattera) is the first/only non-stimulant medication FDA approved for treatment of ADHD in adults. Other medications demonstrating some efficacy include: bupropion, alpha agonists (guanfacine, clonidine—both FDA approved for treatment of ADHD in children and adolescents), modafanil, TCAs, MAOIs
ADHD continued

No data in ADHD-OUD to guide treatment however, based on studies with ADHD-SUD:

• Atomoxetine: First-line treatment, particularly shown helpful for abstinent alcohol-dependent individuals, those with tic disorder. High drop-out rate when given to cocaine abusers with ADHD (Levin et al. 2009)
• Bupropion (“Off-Label” – not FDA approved for ADHD) Efficacy in smoking cessation Useful in comorbid mood disorders Open studies show improved ADHD/SUD/Mood outcome
ADHD - additional concerns

Stimulants: Use in substance-abusing patients is complex and controversial

- Use extended-release formulations of stimulants (e.g., OROS MPH, d-MPH XR, MAST XR, of MPH SR)
- Monitor closely - both ADHD symptoms and pattern of alcohol/drug use
- If severe SUD may refer for intensive intervention prior to starting medication
  - May need to avoid stimulants if they have current abuse/dependence on prescription stimulants or high risk of diversion of medication (i.e., sold medication in past)
- Non-pharmacologic approaches adjunctively: For SUD: Group and individual psychotherapy (e.g. cognitive-behavioral therapy); Self-help; Family therapy for adolescents and young adults For ADHD: Cognitive-behavioral therapy, organizational coaches
Pain issues and Buprenorphine

2 fairly different settings:

1. Patients with chronic pain issues and on treatment with buprenorphine for OUD

1. Patients on buprenorphine for OUD and in need of acute pain management (especially post-surgical/trauma)
Buprenorphine as analgesic

- Small studies in Europe and Asia demonstrate analgesic efficacy of SL formulation (0.2-0.8 mg q 6-8 h) in opioid naïve post-operative pain

- CNS and respiratory depression ceiling effect

- Analgesic ceiling effect is UNCERTAIN
  - Differing data on analgesic ceiling effect in animal models
  - No published data indicating an analgesic ceiling in humans

Edge WG et al. Anaesthesia. 1979
Sublingual Bup and Chronic Pain

- Systematic review • 10 trials involving 1,190 patients • Due to heterogeneity of studies, pooling results and metaanalysis not possible
- All studies reported effectiveness in treating chronic pain
- Majority of studies were observational and low quality

- Current evidence insufficient to determine effectiveness of SL buprenorphine for treatment of chronic pain
Cotes J, Montgomery L. Pain Medicine 2014

Recall - buprenorphine is available in a transdermal formulation specifically for the treatment of chronic pain and that formulation does NOT require a waiver. BUT - it CANNOT be used to treat OUD ( per licensure).
Buprenorphine maintenance theoretical concerns for acute pain

Buprenorphine (a partial mu agonist) may
- antagonize the effects of previously administered opioids or
- block the effects of subsequent administered opioids

However…Experimental mouse and rat pain models:
Combination of buprenorphine and full opioid agonists (morphine, oxycodone, hydromorphone, fentanyl, etc) resulted in additive or synergistic effects

- Receptor occupancy by buprenorphine does not appear to cause impairment of mu-opioid receptor accessibility

Acute Pain Management Options

1. Continue buprenorphine (lower dose) and titrate short-acting opioid analgesic
2. D/C buprenorphine, use opioid analgesic, then re-induce
3. Divide buprenorphine to every 6-8 hours
4. Use supplemental doses of buprenorphine*
5. If inpatient some are using # 1 (above) or:
   • d/c buprenorphine
   • start methadone 20-40mg (or other extended-release, long-acting opioid)
   • use short-acting, immediate-release opioid analgesics
   • then re-induce w/ buprenorphine when acute pain resolves

Alford DP. Handbook of Office-Based Buprenorphine Treatment of Opioid Dependence. 2010
Looking Forward

- NP, PA Can Prescribe-CARA Act
- Addiction Medicine Officially Recognized as a Medical Subspecialty
- Probuphine: Injectable, Long-Acting Bup, once a month, clinical trial under way!
- ECHO (Extension for Community Healthcare Outcomes)
- MAT BH Consultant positions
- Peer Recovery Mentors
- Hospital based addiction medicine consultation
- Other clinic based groups (art therapy, harm reduction groups)
- Coordination with outside agencies (12-step, housing, Bup friendly tx programs)
- Other Ideas?
Resources