Improving Prescribing

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Before We Jump In

• Introductions

• What are your top questions about integrating medications for opioid use disorder into your behavioral health programs?
Treatment Goals

• Range of treatment goals

Minimization of harms from ongoing use

Sustained recovery with abstinence from all substances

• Treatment Options; Federations of State Medical Boards 2013

• Buprenorphine / Methadone / Naltrexone
• Simple detoxification and no other treatment
• Counseling and/or peer support without MAT
• Referral to short or long term residential treatment
Treatment Retention and Decreased Illicit Opioid Use on MAT

- Buprenorphine promotes retention, and those who remain in treatment become more likely over time to abstain from other opioids

Kakko et al., 2003
Soeffing et al., 2009
Benefits of MAT: Decreased Mortality

Death rates:

- General population
- Medication-assisted treatment

Standardized Mortality Ratio

Dupouy et al., 2017
Evans et al., 2015
Sordo et al., 2017
Core Components of Addiction Treatment

*Medications
*Support
*Counseling

*When appropriate

Source: https://www.samhsa.gov/treatment
Psychosocial Treatment

- Employment
- No criminal activity
- Stable home
- Medical and psychiatric treatment

Good functioning

Slide Credit: Roger D. Weiss, MD
Psychosocial Treatment

- 12-step
- Cognitive and/or Behavioral Psychotherapies
- Motivational Enhancement Therapy
- Community Reinforcement
- Contingency Management
- Multisystemic Therapy
- Multidimensional Family Therapy
Addiction Treatment Intensities

Psychosocial Treatment

- Many patients do well with medications for opioid use disorder alone, but we’re not good at predicting who will and who won’t do well
- Limited resources for behavioral treatment
- Some patients don’t want counseling
- Understanding the importance of early treatment response may help our decision-making

Medication First Model

1. People with OUD receive pharmacotherapy treatment as quickly as possible, prior to lengthy assessments or treatment planning sessions;

2. Maintenance pharmacotherapy is delivered without arbitrary tapering or time limits;

3. Individualized psychosocial services are continually offered but not required as a condition of pharmacotherapy;

4. Pharmacotherapy is discontinued only if it is worsening the person’s condition.

• Medication first does not mean Medication only

http://MissouriOpioidSTR.org/treatmentFor
In Opioid Use Disorder: Adding psychosocial support does not change the effectiveness of retention in treatment and opiate use during treatment.

Amato L, Minozzi S, Davoli M, Vecchi S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD004147. DOI: 10.1002/14651858.CD004147.pub4
Challenge #1 – How to Start

- How to start buprenorphine?
  - Instruct the patient to stop using opioids, wait until they’re in withdrawal, then have them take sublingual buprenorphine and up-titrated until they’re not longer in withdrawal.
Challenge #1 – How to Start

• How to start buprenorphine?
  • Usual dose:
    • 2mg/0.5mg or
    • 4mg/1mg q2H
  • Can go up to a recommended max dose of 8mg-12mg on day 1 and 16mg on day 2; not every patient needs these doses.
Challenge #1 – How to Start

- Patient handouts and education available
Example of a Handout:

How to Start Buprenorphine/naloxone at Home (Suboxone Induction)

Get into some withdrawal before starting buprenorphine
- Heroin, oxycodone (Percocet), hydrocodone (Norco), morphine: don’t use for 8-18 hours
- Extended Release Oxycodone/morphine (Oxycontin, MS-Contin): don’t take any for 24-36 hours
- Methadone: don’t use for at least 72 hours, be down to 20-30mg (maybe longer, ask your provider)
  Waiting longer is better. If you take buprenorphine too soon, you can feel worse. You should feel better once starti

You need at least 3 of the following feelings before taking your first buprenorphine dose*:

- Yawning
- Enlarged pupils
- Joint and bone aches
- Shaking or twitches
- Watery eyes/Runny Nose
- Nausea, vomiting or Diarrhea
- Sweating or chills
- Restless/Can’t sit still
- Anxiety, irritable, fast heart beat
- Bumpy skin (Gooseflesh)
- Lost Appetite, Stomach cramps
**Buprenorphine Home Start Instructions** (hydrocodone, short-acting oxycodone, heroin, etc)

Prescribe buprenorphine/naloxone 8/2mg tablets or films #14, PRN withdrawal meds are typically not needed but optional

**Day One/First Dose:** Don’t use for 8-18 hours. When you feel bad*, put 4 mg (1/2 tablet or film) under your tongue and keep it there until it dissolves (about 20 minutes). You should feel better soon. *If you swallow buprenorphine tablets they will not work.*

**Second Dose:** At 2 hours after your first dose, see how you feel.

If you feel fine, don’t take any more. If you still have withdrawal, take another 4 mg dose.

**Do not take more than 8 mg (1 tab or film) of buprenorphine on Day One.**

**Day Two:** Take one full tablet or film under the tongue. Wait 2 hours. If you still feel bad, take another 1/2 (daily dose is 12mg). If feeling ok, don’t take more (8mg/day).

Two hours later, you may take a second 1/2 if you still feel bad (daily dose is 16mg).

**Day Three and until your next visit**

Take Dose from Day two: 1 to 2 tab/film(s) under the tongue as a single dose first thing every morning.
Buprenorphine Implants and LAI

- Trade Names:
  - Probuphine
  - Sublocade
Buprenorphine Implants and LAI

- Requires sublingual buprenorphine lead-in
- Probuphine:
  - Achieved and sustained prolonged clinical stability on transmucosal buprenorphine
  - On 8 mg per day or less of Subutex or Suboxone or its equivalent for three months
- Sublocade:
  - Five day transmucosal lead-in
  - Equivalent of 8 to 24 mg of buprenorphine daily
What About Methadone?
Methadone treatment efficacy

n=727, Hubbard et al. 1997

- Heroin use: Pretreatment 89%, Posttreatment 28%
- Cocaine use: Pretreatment 42%, Posttreatment 22%
What About Methadone?

• If a patient is coming off methadone, they need to wait longer before taking buprenorphine
### What About Methadone?

#### Adjunctive medications

<table>
<thead>
<tr>
<th>Withdrawal Symptoms</th>
<th>Adjunctive Medications</th>
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<tbody>
<tr>
<td>Anxiety/restlessness</td>
<td>▪ a-2 Adrenergic agonists (e.g. clonidine)</td>
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<td>Insomnia</td>
<td>▪ Sedating antidepressants (e.g. trazodone)</td>
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<td>Musculo-skeletal pain</td>
<td>▪ Acetaminophen, Ibuprofen</td>
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<td>GI Distress (nausea, vomiting, diarrhea)</td>
<td>▪ Oral hydration</td>
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<td>▪ Antispasmotics (e.g. dicyclomine)</td>
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<td>▪ Antiemetics (e.g. ondansetron)</td>
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<td>▪ Anti-diarrheals (e.g. loperamide)</td>
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What About Pregnant Patients?

- Same process, but use buprenorphine (monotherapy) instead of buprenorphine / naloxone
- Caution the patient about pre-term labor from opioid withdrawal
Home Vs. Office Starts
What About Patients In Controlled Settings?

- Start with 2mg/0.5mg daily, then 4mg/1mg daily, then 6mg/2mg daily and up titrate as tolerated
Naltrexone: LAI vs. Oral

- **Adherence** is key to naltrexone being effective
- Behavioral Naltrexone Therapy (BNT)
  - Voucher Incentives (CM)
  - Motivational and Cognitive Behavioral therapies
  - Involve a significant other (for monitoring medication adherence)
There may also be a higher proportion of opioid, cocaine, benzodiazepine, cannabinoids, amphetamine - free patients. Comer et.al., 2011
Oral Naltrexone

- Comparing naltrexone versus placebo or no pharmacological treatments, no statistically significant difference were noted.

Oral Naltrexone for OUD

Outcome: Treatment Retention

### Oral Naltrexone for OUD

#### Outcome: Treatment Retention

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Naltrexone LAI – How to Start

• How to start naltrexone long acting injection?
  • *Window period* is biggest factor
  • *Doesn’t* require oral lead-in
  • *Doesn’t* require recent LFTs
Window period

- 7 days from heroin and other short acting opioids (i.e. oxycodone / hydrocodone)
- 10 days from extended release opioids (oxycodone-CR, or morphine sulfate-CR)
- 14 days from buprenorphine or methadone
Naltrexone Long Acting Injection

- **Window Period** - how to be sure?
  - Toxicology information is the usual standard
  - History
  - Collateral
  - CURES
  - *Naloxone challenge administered in the office*
Naltrexone Long Acting Injection

• **Monitoring?**
  
  • Liver monitoring only absolutely required if there are signs of liver disease (jaundice, abdominal pain, nausea, vomiting)
  
  • Generally good practice to obtain quarterly LFTs, but **do not withhold naltrexone** if liver function testing has not yet been obtained if patient is without signs or symptoms of active liver disease
Naltrexone Long Acting Injection

![Graph showing the concentration of Naltrexone over time for VIVITROL 380 mg IM injection and Oral naltrexone 50 mg.]
Naltrexone Long Acting Injection

https://www.youtube.com/watch?v=IZBaDClWSwg
Naltrexone Long Acting Injection
Naltrexone Long Acting Injection
Which Medication to Select?
Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial

Ease of induction is a limitation of naltrexone and an advantage of buprenorphine.

Once successfully inducted to either naltrexone LAI or buprenorphine / naloxone similar outcomes:

• relapse-free survival
• overall relapse
• retention in treatment
• negative urine samples
• days of opioid abstinence
• self-reported cravings

How To Guide Patient Medication Selection
Payer Questions

• Medi-Cal covers with no TAR / PA:
  • Buprenorphine/Naloxone tablets (generic)
  • Buprenorphine/Naloxone film (Suboxone®)
  • Buprenorphine/Naloxone tablets (Zubsolv®)
  • Buprenorphine tablets (generic)
Payer Questions

• Medi-Cal covers with no TAR / PA:
  • Oral Naltrexone

• Medi-Cal covers with a TAR / PA:
  • Naltrexone Long Acting Injection
  • Buprenorphine Implants
  • Buprenorphine Long Acting Injection
Integrating MAT Into Psychosocial Treatment

- Behavioral Naltrexone Therapy (BNT)
How Long to Continue Treatment?

proportion of days when buprenorphine was taken

14% fewer ED visits
18% fewer admissions

months since starting treatment

Lo-Ciganic et al., 2016
How Long to Continue Treatment?

Fiellin et al., 2014
What Else?
Questions / Feedback

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Interested in more? Come to the:

• CA Integrated Care Conference
  https://dmh.lacounty.gov/event/16th-statewide-integrated-care-conference

• ASAM Annual Meeting: https://www.asam.org

• CSAM Annual Meeting: https://csam-asam.org/page/AnnualConference

• AAAP Annual Meeting: https://www.aaap.org