Medication Treatment for Opioid Use Disorder

Developed collaboratively by teams at: University of Washington, Boston Medical Center, Western New York Collaborative, and University of New Mexico
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Learning Objectives

• Understand how opioids work.
• Learn what medications are available for treatment and the benefits and limitations of each.
• How to prevent overdoses.
How do Opioids Work?

• Bind to several different types of receptors in the brain, spinal cord and GI tract
• The main receptor for euphoria and for slowing breathing is the “mu” opioid receptor
• Affected areas regulate pain, mood, digestion, heart beat, blood pressure, and respirations
Tolerance & Physical Dependence

Acute use

Chronic use

Withdrawal

Normal

Tolerance & Physical Dependence

Medication Treatment

Adapted from Alford, Boston University, 2012
Medications for Opioid Use Disorder

Goals:
• Alleviate physical withdrawal and craving
• Opioid blockade (blunt the euphoric effect of other opioids)
• Reduce or eliminate risky substance use
• Normalize deranged brain changes and physiology

Options:
• Methadone (full opioid agonist)
• Buprenorphine (partial opioid agonist)
• Naltrexone (opioid antagonist)
Economics of Treatment

• Substance use disorders cost the US > $600 billion annually
• Every dollar invested in substance use treatment programs yields a return between $4 - $7 in reduced crime and criminal justice costs
• When savings related to healthcare are included, total savings can exceed costs by a ratio of 1 to 12
• The average cost for 1 year of methadone treatment is $4,700/person, whereas 1 year of imprisonment is $24,000/person

Pharmacotherapy for opioid use disorder: Methadone

How it works

• Full mu opioid receptor agonist
• Very long-acting; dose is titrated every 3-4 days
• Once daily dosing for substance use disorder; TID dosing for pain.

Who can prescribe for treatment of substance use disorder?

• Only designated Opioid Treatment Programs (OTP)
• Illegal to prescribe methadone for substance use disorder in general practice
Pharmacotherapy for opioid use disorder: Methadone

Benefits

• Daily, observed dosing
• Highly structured environment
• Multi-disciplinary approach
• High potency
• Well studied: proven to improve survival, increase employment, decrease hepatitis and HIV infections, decrease criminal activity, and to be cost-effective
• Best treatment retention rates in studies
Pharmacotherapy for opioid use disorder: **Methadone**

**Limitations**

- Still carries risk of overdose
- Potential medication interactions
- Slow titration results in longer time to stabilize on dose
- Poor access
- Risk of QT prolongation (Torsades de Pointes)
- Environment may be a trigger for relapse
- Stigma
MYTHS

Bad for your baby
Always sedated
Can’t drive
Can’t nurse your baby
Gets in the bones
Rots your teeth
Still addicted

FACTS

Highly effective
Improves pregnancy outcomes
Reduces relapse
Normalize physiology

One of the WHO list of 100 essential meds that should be available worldwide

Methadone...
Decreases risk of HIV and Hepatitis C infection
Pharmacotherapy for opioid use disorder: Buprenorphine

How it works

- Partial mu opioid agonist
- High receptor affinity
- Formulated with naloxone – misuse deterrent
- Sublingual tablets and films, and newer injectable & implant

Who can prescribe

- Physicians who have DATA-2000 waiver (DEA-X) – requires 8 hour training course
- New as of spring 2017, NPs and PAs who have taken 24 hours of approved training
Pharmacotherapy for opioid use disorder: Buprenorphine

Benefits
- Lower risk of overdose and sedation
- Minimal QT prolongation
- Minimal medication interactions; but beware of benzos

Treatment can be integrated in primary care:
- Reduces stigma
- Provide medical and behavioral care, prevention
- Important tool when problems arise during chronic opioid therapy
- Home induction safe and effective

Important: very effective for pain when dose is divided TID-QID
Pharmacotherapy for opioid use disorder: Buprenorphine

Limitations

• Risk of diversion
• Possible lower retention rates compared to methadone
• Limited access due to reluctance to prescribe

Barriers in primary care include:

• Urgency of scheduling
• Induction visit and frequent early follow up
• Urine testing and prescription logistics
• Linkages to psychosocial services
• Fear of DEA visit

Highly gratifying form of treatment!
Why is overdose potential low with buprenorphine?

- Opioid Effects
  - Respiratory suppression, death
  - Partial Agonist: Buprenorphine
  - Antagonist: Naltrexone
  - Agonist: Methadone, Heroin, etc.

Log dose

Opioid Effects
Trial of buprenorphine

- 40 people addicted to heroin
- Buprenorphine 16 mg/day vs taper + placebo
- All received indiv counseling + therapy groups
- Followed for 1 year

<table>
<thead>
<tr>
<th></th>
<th>Buprenorphine</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>Retained at 1 yr</td>
<td>70%</td>
<td>0</td>
</tr>
<tr>
<td>% died</td>
<td>0</td>
<td>20%</td>
</tr>
</tbody>
</table>

Kakko et al, Lancet 2003
How effective is buprenorphine for treatment of opioid use disorder?

<table>
<thead>
<tr>
<th>Author, Journal</th>
<th>Year</th>
<th>“n”</th>
<th>Setting</th>
<th>% retained in treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fudala, NEJM</td>
<td>2003</td>
<td>461</td>
<td>Multicenter trial</td>
<td>57% @ 6 months</td>
</tr>
<tr>
<td>Alford, JGIM</td>
<td>2006</td>
<td>85</td>
<td>Acad med ctr/ community clinic; ½ patients homeless; nurse care manager</td>
<td>81% @ 12 month</td>
</tr>
<tr>
<td>Mintzer, Ann Fam Med</td>
<td>2007</td>
<td>99</td>
<td>4 primary care practices</td>
<td>54% @ 6 months</td>
</tr>
<tr>
<td>Soeffing, J Subst Abuse</td>
<td>2009</td>
<td>255</td>
<td>Urban academic health center</td>
<td>57% @ 12 months</td>
</tr>
<tr>
<td>Haddad, Drug Alc Dep</td>
<td>2013</td>
<td>266</td>
<td>Community health center network</td>
<td>57% @ 6 months</td>
</tr>
</tbody>
</table>
New: Long-acting buprenorphine prescribing

- Obtain through specialty pharmacy
- Patient must first be stabilized ≥ 7 days on SL bup
- Recommended dose is 300 mg subcut injection into abdomen monthly for two months, and then 100 mg per month
- Injection should only be done by clinical staff
- Very dangerous if injected intravenously (forms solid mass)
Long-acting injectable buprenorphine

• 39 adult patients with OUD who were not treatment-seeking
• Stabilized on 4-24 mg buprenorphine
• Then given a 300 mg injection of RBP-6000 (Sublocade®), which was repeated 4 weeks later
• Tested opioid-blocking effect by having subjects report how much they “liked” hydromorphone (0, 6, or 18 mg, which is approximately equal to 135 mg morphine)

After two doses of injectable buprenorphine, blocking levels of buprenorphine maintained for at least 12 weeks
Pharmacotherapy for opioid use disorder: **Naltrexone**

**How it works**
- Opioid antagonist
- Causes acute withdrawal in opioid-dependent patients
- Two formulations available:
  - Oral 50 mg PO daily—not effective
  - Extended-release injectable (Vivitrol) 380 mg IM monthly

**Who can prescribe**
- Any prescriber
- Insurance coverage for injectable may vary
- Special injection technique
Norwegian naltrexone study by Tanum

- 159 adult patients with OUD detoxed in inpatient or jail setting
- Randomized after detox to injectable naltrexone or SL bup/nx 4-24 mg
- Followed for 12 weeks, endpoints included trial completion, UDS results, self-reported use of heroin
- Naltrexone non-inferior to bup on retention, UDS results, and use of heroin

Tanum, JAMA Psychiatry, 2017
US Naltrexone study by Lee

• 8 sites enrolled 570 adults with OUD
• Randomly assigned to naltrexone injection or SL bup/nx in inpatient setting
• Patients assigned to naltrexone were more likely to leave during initiation/detox
• 94% of bup-assigned patients were successfully inducted, vs 74% of naltrexone patients
• For patients who stayed and stabilized on meds, treatment results (retention, UDS, craving, overdose) were similar with bup/nx and naltrexone

Lee, Lancet, 2017
Pharmacotherapy for opioid use disorder: **Naltrexone**

**Benefits**

- No withdrawal if stopped
- Also effective in alcohol use disorder treatment
- Medication itself does not cause respiratory depression or sedation
- Not a controlled substance, no restrictions on prescribing
- Retention appears similar to buprenorphine if successful initiation is achieved
Pharmacotherapy for opioid use disorder: **Naltrexone**

**Limitations**

- Must abstain for opioids for 3-10 days prior to first dose
- No pain relief, and no effect from opioids
- Non-opioid approaches to pain management
- Long-term studies still lacking
Overdose prevention

• Naloxone (“Narcan”) reverses opioid overdose
• Overdose education and naloxone are an effective harm reduction strategy
• For those at high risk of overdose and their friends or family
• Populations: syringe exchange, exit from jail, in drug treatment, high risk prescribed opioids
• PrescribetoPrevent.org
• Should be provided to every patient who is being treated for opioid use disorder
Emerging models for Medication Treatment for OUD

• Massachusetts Nurse Care Manager Model
  • Full time RN and Program Manager can screen and assess, perform induction and follow closely
  • Prescriber time leveraged
  • Regular team meetings aid in decision-making
  • Allows primary care practices to involve multiple prescribers
  • RN can follow 100-125 patients

• Hub and Spoke Model (Vermont)
  • Centralized screening, assessment, stabilization
  • Transfer to primary care sites for ongoing treatment
Summary: Medications for Opioid Use Disorder

• Maintenance medications are an **essential component** of evidence-based treatment for opioid use disorder
• Strongest long-term data to support methadone and buprenorphine
• Naltrexone also highly effective, but can only be initiated in patients who are not currently physically dependent on opioids
• Primary care teams play an important role in treatment of opioid use disorders and prevention of overdose
References

HRSA Opioids Crisis Webpage

The ASAM National Practice Guideline for the use of medications in the treatment of addiction involving opioid use


Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders. Lee JD¹, Friedmann PD¹, Kinlock TW¹, Nunes EV¹, Boney TY¹, Hoskinson RA Jr¹, Wilson D¹, McDonald R¹, Rotrosen J¹, Gourevitch MN¹, Gordon M¹, Fishman M¹, Chen DT¹, Bonnie RJ¹, Cornish JW¹, Murphy SM¹, O'Brien CP¹. N Engl J Med. 2016 Mar 31;374(13):1232-42. doi: 10.1056/NEJMoia1505409.


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