Understanding and Managing Patients with Opioid Addiction

-A Workshop for Clinicians-

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Disclosures

• The presenter has no conflicts of interest to disclose
Learning Objectives

At the end of this presentation, participants will be able to:

• Understand the historical progression of opioids throughout the years.

• Appreciate the challenges in working with patients with OUD.

• Describe and be able to apply various treatment approaches tailored based on individual characteristics.
The Magnitude of the Opioid Epidemic

- Estimated cost of the OPIOID EPIDEMIC was $504 BILLION in 2015.²
- An estimated 1.4M AMERICANS have OUD related to opioid painkillers; 438K have heroin-related OUD.²
- Opioid overdose caused 49,860 DEATHS nationwide in 2019—this exceeded the # caused by motor vehicle crashes.⁴⁵
- 1.6 MILLION people in the U.S., ages 12 and older, had OUD involving PRESCRIPTION OPIOIDS, HEROIN, or both in 2019.¹⁶
- OPIOID ADDICTION is linked with high rates of ILLEGAL ACTIVITY and INCARCERATION.⁸²⁹
- OPIOID-RELATED EMERGENCY DEPARTMENT visits more than tripled from 2005 to 2017.²²²³
- OPIOID-RELATED inpatient hospital stays INCREASED 119% nationally from 2005 to 2017.²⁶²⁷
Overdose deaths

New Hampshire

Number of Overdose Deaths by Year

- 2011: 201
- 2012: 163
- 2013: 198
- 2014: 342
- 2015: 444
- 2016: 486
- 2017: 490
- 2018: 471
- 2019: 415
- 2020: 402*
How did we get here?
3400 B.C. - 300 A.D.

• 3400 B.C. - Opium poppy is cultivated in Mesopotamia – “Joy plant” (euphoric effects)

• 460-357 B.C. - Hippocrates “father of medicine” advocates for opium’s usefulness as a in treating “diseases of women”, etc.

• 330 B.C - Arabs, Greeks and Romans use it as a sedative, analgesic

• 220-264 A.D. - Chinese surgeon uses opium preparations for his patients before surgery
1300 - 1799 A.D.

- 1606 - Ships bring Indian opium back to England.
- 1680 - Thomas Sydenham “father of English medicine”
  - Sydenham's Laudanum (opium, sherry wine and herbs)
- 1700 - Dutch introduce the pipe.
- 1729 - Chinese emperor prohibits smoking of opium and its sale, except under license for medicinal use. Trade and cultivation illegal.
- 1750 - British East India Company assumes control of opium-growth in India
1800s

• 1806 - German chemist isolates morphine.
  – Becomes “mainstay” of medical treatment, used to treat pain, anxiety, respiratory problems, etc.
  – Used as pain killer during the Civil War

• 1819 - Experimentations with opium as recreational use is common

• 1827 - E. Merck & Company begins commercial manufacturing of morphine
1800s - continued

- 1843 – Hypodermic needle leads to IV morphine
  - Instantaneous and potent effects

- 1874 - San Francisco bans smoking opium
1800s - continued

• 1878 - Britain passes Opium Act
  – Opium sales is restricted to registered Chinese opium smokers and Indian opium eaters

• 1895 - Bayer Company dilutes morphine to diacetylmorphine "heroin"
  – Cough suppressant, “non-addictive” morphine substitute.
Early 1900s

• 1902 – NY campaign provides free heroin and cocaine by mail to morphine addicts.

• 1906 - Physicians experiment with treatments for heroin addiction (belladonna, cocaine, morphine/heroin taper).

• 1913 - Bayer stops heroin production

• 1914 - Harrison Narcotics Tax Act

• 1916 - German chemists synthesize oxycodone ("analgesic effects with less dependence").
1920s & 1930s

• 1923 – **Legal narcotics sales are banned**
  – Those addicted turn to **illegal street dealers**

• 1925 - A thriving black market opens up in New York's Chinatown and the term “**junkie**” is coined.

• 1930s – An increase in drug-related **crime** is reported throughout the country.
U.S. approaches

- 1935 – “Narcotic Farms” (detox treatment facilities) open in TX and KY.
  - Admissions from prison / court ordered or voluntary.
  - Length of stay 6mo-10years with 2:1 patient:staff ratio.
  - Social, medical, psychological, and psychiatric services.
  - Follow-up studies:
    - relapse rate of 93% in 1,881 former patients over a 1- 4.5-year
    - relapse rate of 97% in 453 former patients over follow-up periods of 6 months -5 years
China - Maoist Methods Wipe-out Addiction

• 1/3 of the population is addicted to opium

• 1949 – New government, Maoist revolutionaries used mass line to take on addiction, the enemy.
  – No punishment for those that stepped forward, support, detox provided
  – People were destroying opium businesses

• 1952 – no more “addicts”, no more pushers, no more cultivation, no more drugs smuggled in.
1973 - Drug Enforcement Agency (DEA) was created by Executive Order

1974 – Narcotic Addict Treatment Act

- Enables the use of an opioid medication to treat opioid addiction as “maintenance treatment.”
- Requires separate DEA registration by physicians and separate federally funded facilities
Methadone Maintenance programs

• Methadone synthesized in 1930s
• Rockefeller Foundation developed a system of dosing methadone to prevent heroin use

• At doses 80-120mg/day:
  • relieves narcotic craving
  • blocks euphoria associated with heroin
  • improves social function
  • lowers HepC, HIV
• Programs expanded nationally.
The 1980’s and 1990’s

- 1980 – Naltrexone is FDA approved
- 1980s – Opioids for terminal cancer pain
  - Tolerance to sedation, improved quality of life, low risk of addiction
- 1990 – In lobbying for pain management physicians explore the use of opioids for non-terminal cases
  - specialty clinics: similar results as above, low rates of addiction(0.2%)
- 1994 – Pharmaceutical companies thrive
LAAM Development

• Levo-alpha acetyl methadol (LAAM) approved by FDA in 1993
• Whereas methadone suppressed opioid withdrawal symptoms for 24 hours or longer, LAAM achieved this effect for 48 to 72 hours or longer.
• Discontinued in early 2000s due to cardiac side effects
2000 – 2009

• Prescriptions and dosages / prescription increase
  – Pain becomes a vital sign
  – ED visits rise

• 2000 - Drug Addiction Treatment Act

• Buprenorphine-Naloxone (Suboxone) gets FDA approval in 2002
The Portugal Experiment

• 1974 - Carnation revolution
  – Newfound freedom leads to recreational drug use.
  – Initial response: criminal justice system

• 1999 – High percentage of population addicted to heroin; AIDS highest in Europe

• 2001 – decriminalization of possession and use.
  – Commission for the Dissuasion of Drug Addiction
    • Recommends treatment or a minor fine
The Portugal Experiment - continued

- Initial increase in drug use, then decline
- Decline in HIV infections
- Decrease in imprisonment for drug-related charges
- Surge in visits to health clinics for addiction and disease treatment
Heroin-Assisted Treatment in the UK

• 2009 – conclusion of a 4-year study using daily IV heroin, as part of a treatment program aimed at gradually getting individuals off heroin.
  – Sites supervised by physicians and individuals receive counseling.
  – Drug use and drug-related crime among participants reduced.
Canadian supervised injection sites

- “Insite” – first in N. America
- Risk mitigation
- Less overdoses, more engage in HepC and HIV treatment
Failures in Drug Addiction and Treatment

• Malaysia and Singapore mandates the death penalty for drug traffickers.
  – Testing positive for drugs - automatically sentenced to a year of compulsory treatment.
  – Users don’t seek help
• Vietnam subjects drug users to “rehabilitation” - forced labor and near starvation.
• Saudi Arabia: anyone caught using drugs and traffickers can be executed by hanging
Dealing with the Drug Problem in America

Oregon decriminalized possession in 2021 – no evidence for increased crime or treatment
2010 – Today

- Pharmaceutical manufacturers develop product formulations with abuse-deterrent properties:
  - Physical / chemical barriers to crushing, dissolving, etc.
  - Agonist / antagonist combination
  - Prodrug form
  - Aversion techniques if deviation from dose / route
  - Delivery systems such as patches, implants
- FDA increases training to prescribers
- States implemented prescription drug monitoring programs
- DEA removes requirement for X waiver (2023)

*Both 19th century epidemic and today’s begun with overprescribing. With FDA involvement, prescribing decreases however heroin picks up. Today’s illegal trafficking are much more able to step in as government cracks down*
Where do we stand now?

• “National emergency”
• Drug overdoses are the leading causes of death in Americans <50 years of age
• In 2015 >60% overdoses involve opioids
• Deaths due to prescribed starting to decline while illicit and synthetic (most) climb

CDC data: Drugs involved in US overdose deaths; 2000 - 2016
Synthetic Opioids

• 2016: Deaths from fentanyl up 540% in 3 years

• Fentanyl – fast acting and potent opioid (50–100x more potent than morphine)

• sufentanil, alfentanil, lofentanil, remifentanil, carfentanil followed

• Increase in street heroin being cut with these
Why are synthetic opioids driving the overdose rates?

- Purposefully seeking highly lipophilic opioid agonist
- Rapid crossing of the blood-brain barrier
- Rapid distribution to the peripheral tissue and a slow return to the central compartment
- Low Community Awareness
- People who use drugs may not be aware they are using fentanyl
- Most people buying heroin were not intentionally seeking fentanyl
- Street-level sellers may not know their drug products contain fentanyl
- Therefore individuals who are not aware that they are using fentanyl are at increased risk of overdose
- This suggests the need to educate users on risk reduction practices, such as not using alone, taking turns when using, avoiding mixing drugs, and having naloxone on hand
Pharmaceutical fentanyl is not the driver, NOT “big pharma”
Forms of Fentanyl

Purest fentanyl comes from China; may be diluted and trafficked through Mexico.

Pill presses are used to produce counterfeit pills that look like alprazolam.
Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs

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**Fig. 4.** Range of literature $K_i$ values for opioid drugs in MOR inhibition assays.
Roadmap to treat OUD

- Intoxication
- Withdrawal
- Detoxification
- Maintenance Treatment
  - No pharmacological agents
  - Opioid agonist therapy
  - Opioid antagonist therapy
- Pharmacotherapy for Co-Occurring Disorders
Intoxication

- Life threatening—especially among individuals with limited tolerance to opioids
- Euphoria
- Pupillary constriction
- Slowed respiratory rate
- Drowsiness
- Slurred speech, and Inattention
- The best predictor of opioid toxicity is a respiratory rate
Withdrawal clinical features

• Psychological: Anxiety, Insomnia, yawning, dysphoric mood
• Cardiac: hypertension, diaphoresis, tachycardia
• GI: Nausea, vomiting, diarrhea, cramping, Increased bowel sounds
• Gen: Restlessness, irritability, lacrimation, rhinorrhea
• Musc: Myalgia, arthralgia.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of Withdrawal (hours)</th>
<th>Peak Effects (hours)</th>
<th>Most Symptoms are Over</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heroin</td>
<td>8-12</td>
<td>36-72</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Morphine</td>
<td>8-12</td>
<td>36-72</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>8-12</td>
<td>36-72</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4-5</td>
<td>36-72</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>3-5</td>
<td>8-12</td>
<td>4-5 days</td>
</tr>
<tr>
<td>Methadone</td>
<td>36-72</td>
<td>96-144</td>
<td>14-21 days</td>
</tr>
<tr>
<td>Reason for this assessment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Resting Pulse Rate:** | **GI Upset:** over past 1/2 hour
| _______ beats/minute | 0 no GI symptoms
| Measured after patient is sitting or lying for one minute | 1 stomach cramps
| 0 pulse rate 80 or below | 2 nausea or loose stool
| 1 pulse rate 81-100 | 3 vomiting or diarrhea
| 2 pulse rate 101-120 | 5 multiple episodes of diarrhea or vomiting
| 4 pulse rate greater than 120 | |
| **Sweating:** over past 1/2 hour not accounted for by room temperature or patient activity. | **Tremor** observation of outstretched hands
| 0 no report of chills or flushing | 0 no tremor
| 1 subjective report of chills or flushing | 1 tremor can be felt, but not observed
| 2 flushed or observable moistness on face | 2 slight tremor observable
| 3 beads of sweat on brow or face | 4 gross tremor or muscle twitching
| 4 sweat streaming off face | |
| **Restlessness** Observation during assessment | **Yawning** Observation during assessment
| 0 able to sit still | 0 no yawning
| 1 reports difficulty sitting still, but is able to do so | 1 yawning once or twice during assessment
| 3 frequent shifting or extraneous movements of legs/arms | 2 yawning three or more times during assessment
| 5 unable to sit still for more than a few seconds | 4 yawning several times/minute
| **Pupil size** | **Anxiety or Irritability**
| 0 pupils pinned or normal size for room light | 0 none
| 1 pupils possibly larger than normal for room light | 1 patient reports increasing irritability or anxiousness
| 2 pupils moderately dilated | 2 patient obviously irritable or anxious
| 5 pupils so dilated that only the rim of the iris is visible | 4 patient so irritable or anxious that participation in the assessment is difficult
| **Bone or Joint aches** If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored | **Gooseflesh skin**
| 0 not present | 0 skin is smooth
| 1 mild diffuse discomfort | 3 piloerection of skin can be felt or hairs standing up on arms
| 2 patient reports severe diffuse aching of joints/muscles | 5 prominent piloerection
| 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort | |
| **Runny nose or tearing** Not accounted for by cold symptoms or allergies | **Total Score** _______
| 0 not present | The total score is the sum of all 11 items
| 1 nasal stuffiness or unusually moist eyes | **Initials of person**
| 2 nose running or tearing | completing assessment: _______
| 4 nose constantly running or tears streaming down cheeks | Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal
Goals of Detox

1. Eliminate acute physiological dependence from chronic opioid use
2. Diminish the pain and discomfort of opioid withdrawal
3. Provide a safe environment for remaining abstinent during acute withdrawal
4. Identify and treat any concurrent medical problems
5. Refer patient for treatment to prevent relapse* and to address family, work, and legal problems

*Should include maintenance medication assisted treatment as within one month of discharge from detoxification without maintenance medication treatment, 80%-90% of patients have relapsed, with first week post treatment being highest likelihood of overdose and death (Smyth et al., 2010, Weiss et al., 2011).
Detox Approaches

• The symptom-driven approach targets individual symptoms of opioid withdrawal.
  – Alpha-adrenergic agonists (e.g. clonidine) are the primary medications utilized in this approach; targeting the autonomic hyperactivity and associated anxiety seen in opioid withdrawal.

• The initial dose of clonidine should be a test dose of 0.1mg. Withhold clonidine for systolic blood pressure less than 90 or diastolic less than 50.

• Clonidine does not address withdrawal symptoms, such as insomnia, muscle aches, or drug cravings.

• A clonidine patch is not recommended in the early phase of detoxification when dose titration may vary depending on the individual’s symptoms.

• During the physical withdrawal period, besides monitoring vital signs, electrolytes are closely evaluated for dehydration and replaced if needed.
Ancillary Medications: Non-Opioid Detoxification Agents

- **Alpha-2 agonists** (e.g. clonidine)
  - Reduce sympathetic hyperactivity by feedback inhibition of presynaptic neurons (sweating, increased HR, etc)
  - Clonidine 0.1mg PO up to every 4 hours; encourage the patient to start lower; monitor blood pressure, lightheadedness, dizziness, sedation
- **Benzodiazepines** (e.g. clonazepam)
  - For insomnia, anxiety, muscle spasm
  - Clonazepam 1mg PO up to twice daily; can start with 0.5mg; monitor for sedation, misuse
- **Pain relievers** (acetaminophen OR ibuprofen)
  - For muscle and bone pain
  - Acetaminophen 500mg PO Q6H (based on baseline liver function tests)
  - Ibuprofen 400-800mg PO Q8H
- **Anti-emetics** (ondansetron OR prochlorperazine)
  - For nausea
  - Ondansetron 4-8mg PO Q8H
  - Prochlorperazine 5-10mg PO Q8H
  - Monitor for sedation, abnormal movements
- **Anti-diarrheal agents** (e.g. loperamide)
  - Loperamide 2-4mg PO Q6H (max up to 16mg/day)
- **Hypnotic agents** (e.g. zolpidem, trazodone)
  - Zolpidem 5-10 PO QHS
  - Trazodone 50-100mg PO QHS
  - Monitor for excess sedation, misuse

Example dosing and medication; discretion up to physician and can target elements of COWS
The Chronic Disease Model

• Sobriety is the primary goal
• Personalized diagnosis and treatment planning tailored to the individual and family
• Active therapeutic stance
• Anticipate lapses & relapses,
• Medications for relapse / craving
• Effective behavioral interventions ( CBT )
• Learn to work with A.A. / N.A and community services
• Treat co-morbid psychiatric disorders
• Avoid prescription tranquilizers
Pharmacotherapies

**The Impact of MAT on Survival Probability**

- **MAT Group** shows a higher survival probability compared to the **Control Group**.

**The Impact of Buprenorphine, Methadone, and Naltrexone on Staying in OUD Treatment**

- **MAT Group** has a higher retention rate over time compared to the **Control Group**.

*Source: NIH 2021*

*Individuals engaged in MAT have better survival outcomes.*

*Individuals engaged in MAT are more likely to remain in treatment.*
# Medications for Opioid Use Disorder

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand names</td>
<td>Dolophine, Methadose</td>
<td>Suboxone, Subutex, Zubsolv</td>
<td>ReVia, Vivitrol</td>
</tr>
<tr>
<td>Class</td>
<td>Agonist-full</td>
<td>Partial agonist</td>
<td>Antagonist</td>
</tr>
<tr>
<td>Use, effects</td>
<td>Once daily orally to reduce cravings and withdrawal</td>
<td>Sublingual daily to reduce cravings and withdrawal</td>
<td>Oral daily or monthly injection to block opioid effect</td>
</tr>
<tr>
<td>Pros</td>
<td>Gold standard, structured format, witnessed dosing, 40 years experience</td>
<td>Doctor’s office, by prescription, more available, less stigma</td>
<td>Non-addicting, no physical dependence, once monthly dosing (IM)</td>
</tr>
<tr>
<td>Cons</td>
<td>Official OTP only: limited availability; daily dosing; full agonist: overdose possible; P450 drug: drug</td>
<td>Abuse, diversion liability; difficult to arrange psychosocial support</td>
<td>Poor compliance; 7 day abstinence required; overdose risk high</td>
</tr>
<tr>
<td>Cost drug+tx/mo from <em>Cepac</em> 2014</td>
<td>$15 + $480 = $495</td>
<td>$210 + $300 = $510</td>
<td>$1200 + $125 = $1325</td>
</tr>
</tbody>
</table>
Opiate Potency of Methadone and Buprenorphine

Partial Agonist “Ceiling Effect”
- Limited euphoria
- Reduced risk for overdose

Full Agonist (Methadone)

Partial Agonist (Buprenorphine)

Antagonist (Naloxone)

Log Dose of Opioid

% Efficacy
Treatment Retention

Risk Ratio for Retention for Each Medication against Control

Compared with Control

- Buprenorphine: Risk Ratio (95% Crl) 2.15 (1.76, 2.69)
- Methadone: Risk Ratio (95% Crl) 2.62 (2.09, 3.33)
- Naltrexone: Risk Ratio (95% Crl) 1.54 (1.26, 1.90)
- SROM: Risk Ratio (95% Crl) 2.52 (1.62, 3.94)
Initiating treatment

• OUD diagnosis
• Workup, PDMP
• Level of care
• Treatment setting
  – Outpatient / Inpatient / ED / telemedicine / rural area
• *Identifying MOUD of choice*
  – Buprenorphine
  – Methadone
  – Naltrexone
<table>
<thead>
<tr>
<th>DAY</th>
<th>Indications for dose increase. Need 2 of 3 categories days 1-10.</th>
<th>Conditions</th>
<th>METHADONE DOSE using COWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Must show mild signs of withdrawal with COWS score ≥ 7. If no signs of w/d, contact physician</td>
<td>No psychomotor impairment, nurse may do Sobriety Test.</td>
<td>Initial Dose Maximal</td>
</tr>
<tr>
<td>2</td>
<td>COWS ≥ 7 Prior night used opioids Intense opioid craving</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Prior day total. May increase, based on COWS, if following conditions met: Can give up to 5mg for COWS greater than or equal to 7 and less than 12; up to 10mg if greater than or equal to 12.</td>
</tr>
<tr>
<td>3-5</td>
<td>COWS ≥ 7 Prior night used opioids Intense opioid craving</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Prior day total. May give increase, based on COWS, if conditions met.</td>
</tr>
<tr>
<td>6-10</td>
<td>COWS ≥ 7 Prior night used opioids Intense opioid craving</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>If stable at 50mg, then hold. Or increase as for day 3 to max 60 mg</td>
</tr>
<tr>
<td>11-15</td>
<td>Did dose provide opioid blockade?</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Adjust dose based on COWS scoring and blockade.</td>
</tr>
<tr>
<td>16-20</td>
<td>Did dose provide opioid blockade?</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Adjust dose based on COWS scoring and blockade.</td>
</tr>
<tr>
<td>21-25</td>
<td>Did dose provide opioid blockade?</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Adjust dose based on COWS scoring and blockade.</td>
</tr>
<tr>
<td>26-31</td>
<td>Did dose provide opioid blockade?</td>
<td>No sedation at prior day’s peak dose No psychomotor impairment</td>
<td>Adjust dose based on COWS scoring and blockade.</td>
</tr>
</tbody>
</table>
Naltrexone Induction Challenge -- The "washout" Period

- Two phases of treatment: 1) detoxification, 2) naltrexone induction
- Current FDA-sanctioned method involves 7-10 days "washout" period between the two phases: last dose of opioid and first dose of NTX
# Fentanyl

## Outpatient LDB induction protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>0.5 mg x1 (1/4th of 2mg strip)</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.5 mg twice/day</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 3</td>
<td>1 mg twice/day (Half of 2mg strip)</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 4</td>
<td>2 mg twice/day (4mg total)</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 5</td>
<td>2 mg x TID, Or (6mg total)</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 6</td>
<td>4 mg twice/day or 8mg daily (8mg total)</td>
<td>Continue full opioid agonists</td>
</tr>
<tr>
<td>Day 7</td>
<td>12mg and above</td>
<td>Discontinue full opioid agonists</td>
</tr>
</tbody>
</table>

Modified/adapted from Terasaki 2019, Robins 2021, Randhawa 2020
Maintenance

- Frequency of visits
- Supports
- Urine toxicology screens
- Dosing challenges
- Formulations
Individuals abusing high doses of opioids may require higher concentrations for opioid blockade*.

μ-Opioid Receptor Occupancy

0% 100%

- Reinforcing Effect
- Analgesic Effect
- Withdrawal Suppression
- Opioid Blockade

50-60% μORO (BUP ≥ 1 ng/mL)
≥ 70-80% μORO (BUP ≥ 2-3 ng/mL)

Non-injection Users

Injecting Users

Probability of Abstinence (% [95% CI])

Buprenorphine Plasma Concentration (ng/mL)
‘Probuphine’

- 6 month implantable, SC
- Limited reinsertions
- Limited daily dose delivery of ~8mg
- Stability required
- REMS program
- $$
Buprenorphine Extended-Release ‘Sublocade’

- 11/30/2017 FDA approved, available Q2 2018
- Monthly depot dosing, SC
- Two initial monthly 300mg then maintenance 300mg or 100mg monthly
- Initial 300mg -- [plasma] 2ng/mL
  - Subsequent 100mg steady state -- [plasma] 3.21ng/mL
  - Subsequent 300mg steady state -- [plasma] 6.54ng/mL
Special considerations

- Benzodiazepines
- Stimulants
- Cannabis
- Pain
- Pregnancy
- Harm reduction approaches
Naloxone

• Effective at reversing opioid-related overdoses however long-term survival rates are low
  – Review of >12,000 emergency Naloxone doses given during a 2 year period:
    • 93% survived an overdose
    • But only 84% of those were still alive a year later (Massachusetts ambulance study between 2013 and 2015)

• Multiple doses required when synthetics involved; sometimes ineffective

• Who is at risk? Previous overdoses; recently discharged from detox or prison / initiating or ending treatment; recreational users; co-prescribing CNS suppressants
Telemedicine

• RHA
• Regulations for starting vs maintaining Bup
• Payer and federal / state regulator requirements esp. urine tox.
• Billing

<table>
<thead>
<tr>
<th>Table 2. Adjuncts &amp; alternatives to point-of-care urine toxicology testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical interview and functional assessment</td>
</tr>
<tr>
<td>Urine toxicology testing at an outside, more accessible lab, with results transmitted to clinician</td>
</tr>
<tr>
<td>Supervised home testing (e.g., patient displays results via video visit)</td>
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<tr>
<td>Remote pill counts via video</td>
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<tr>
<td>Routine use of state prescription drug monitoring program</td>
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<tr>
<td>Collateral information from family and friends</td>
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</tbody>
</table>
In Conclusion...

• Balancing medicinal properties of opioids with euphoric effects has always been a struggle

• Non-punitive approaches have best outcomes

• Synthetic opioids present a huge problem for individuals, providers, and regulatory agencies

• MOUD is effective however there are challenges

• Clinicians need to individualize treatment and keep up to date with protocols, guidelines and emerging formulations
Thank you!