Medication Selection Considerations for Medication-assisted Treatment (MAT)
Learning objectives

1. Identify the pros, cons, and barriers to widespread use of medication-assisted treatment (MAT)
2. Discuss pharmacotherapy options for opioid use disorder
3. Describe considerations for treatment selection for MAT options
Welcome from Blue Shield of California

Salina Wong, PharmD
Director, Clinical Pharmacy Programs
Pharmacy Services
Blue Shield of California
Blue Shield’s Narcotic Safety Initiative (NSI)

Reduce opioid use by 50% among Blue Shield members with non-cancer pain by the end of 2018

Reduce # of members on chronic high doses

Prevent progression from acute to chronic use

Reduce # of prescriptions and refills for those newly starting opioids

Through evidence-based interventions including:

- Provider awareness
- NSI case management
- SafeMed LA collaboration
- Chronic pain management program
- Limit high doses and over-prescribing for acute pain and cough/cold
- Restrict ER opioids
- Inhibit stockpiling
- Prevent extended use for acute pain
- NSI provider education webinar series
- Increase access to medication assisted therapy (MAT)

Achieved a 56% reduction by year-end 2018
Introducing our Blue Shield of California presenters

Stephen Jung, PharmD, BCPS
Principal Pharmacist, Pharmacy and Therapeutics

Tamara Tran, PharmD
Principal Pharmacist, Pharmacy and Therapeutics
Medication Selection Considerations for Medication-assisted Treatment (MAT)

Stephen Jung, PharmD
Tamara Tran, PharmD
Medication-assisted treatment (MAT)

MAT is the use of medications with counseling and behavioral therapies to treat substance use disorders (SUD) and prevent opioid overdose.

MAT provides a “whole patient” approach to the treatment of SUD.
An estimated 2.1 million people in the United States have opioid use disorder (OUD) related to prescription opioids, heroin, or both.

There is a gap between people who need OUD treatment and the capacity to treat them with OUD.

In 2012, this gap was estimated at nearly 1 million people, with 80% of opioid treatment programs (OTPs) operating at 80% capacity.

Fewer than half of private-sector treatment programs offer medications for OUD, and of the patients in those programs who might benefit, only one third will receive it.
Trends in OUD and MAT capacity
Pros of MAT therapy

- Curtails both cravings and withdrawal symptoms
- Stabilizes abnormal brain activity
- Is safe when used appropriately
- Helps prevent relapse
- Provides improved recovery outcomes vs. treatment without medication
Cons of MAT therapy

• Limited or no access to programs in many areas
• Is highly stigmatized
• Some MAT treatments:
  • Require waivers for prescribing privileges
  • Have a difficult induction (e.g., risk for respiratory depression, withdrawal symptoms)
  • Have *REMS programs for risk of misuse, diversion, and overdose

* Risk Evaluation and Mitigation Strategy (REMS): Drug safety program that the U.S. Food and Drug Administration (FDA) requires for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.
Barriers to widespread use of MAT

- Stigma associated with negative attitudes and beliefs from patient, family, and community
- Logistical challenges (e.g., daily appointments, transportation, occupation, childcare)
- Poor communication and coordination of care
- Regulatory restrictions on practice (e.g., patient management caps, methadone clinics)
- Lack of:
  - Patient awareness and/or demand
  - Consistent access to and coverage for MAT
  - Trained providers and treatment centers
  - Access to services (including behavioral health)
### Regulations and availability of MAT agents

<table>
<thead>
<tr>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Schedule II</td>
<td>• Schedule III</td>
<td>• Not scheduled</td>
</tr>
<tr>
<td>• Federally certified, accredited opioid treatment programs (OTPs)</td>
<td>• Physicians, NPs, and PAs who have a federal waiver (DATA*, CARA†)</td>
<td>• Any prescriber</td>
</tr>
<tr>
<td></td>
<td>• REMS certification for Probuphine implant and Sublocade™ injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• OTPs</td>
<td></td>
</tr>
</tbody>
</table>

*Drug Addiction Treatment Act
†Comprehensive Addition and Recovery Act
True or False?
True or False?

Buprenorphine therapy can be more difficult for the physician and more dangerous for the patient than other chronic disease treatments.
FALSE!

Buprenorphine therapy can be more difficult for the physician and more dangerous for the patient than other chronic disease treatments.

- Buprenorphine treatment is simpler than many other routine treatments in primary care (e.g., insulin titration, anti-coagulation, full-agonist opioids for pain) but physicians receive little training in it.

- A typical visit includes:
  - Assessment of medication adherence
  - Examination of disease control (cravings and use)
  - Titration of dosage
  - Ordering of laboratory tests
True or False?

Buprenorphine therapy can result in replacing one addiction with another.
False!

Buprenorphine therapy can result in replacing one addiction with another.

- Addiction is defined as compulsively using a drug despite harm.
- Taking prescribed medication to manage a chronic illness does not meet that definition.
Evidence for medication-assisted treatment (MAT)
Evidence for medication-assisted treatments

- Strong evidence supporting the effectiveness of MAT for OUD
  - Methadone, naltrexone, and buprenorphine have all been found to be more effective in reducing illicit opioid use than no medication in randomized clinical trials
  - Methadone and buprenorphine have also been associated with reduced risk of overdose death
## Outcomes of MAT agents

<table>
<thead>
<tr>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ↑ patient treatment retention</td>
<td>• ↑ patient treatment retention</td>
<td>• ↑ patient treatment retention</td>
</tr>
<tr>
<td>• ↓ illicit opioid use</td>
<td>• ↓ illicit opioid use</td>
<td>• ↓ illicit opioid use</td>
</tr>
<tr>
<td>• ↓ risk of overdose-deaths</td>
<td>• ↓ treatment failure and mortality</td>
<td>• ↓ opioid craving</td>
</tr>
<tr>
<td>• ↓ risk of HIV (including risk behaviors) and hepatitis C infection</td>
<td>• ↓ number of opioid-positive drug tests</td>
<td>• ↓ relapse (longer time to return to substance use, lower rate of return to use)</td>
</tr>
<tr>
<td>• ↓ risk of cellulitis</td>
<td>• ↓ risk of HIV risk behaviors</td>
<td>• ↑ negative urine screens</td>
</tr>
</tbody>
</table>
## Comparative effectiveness

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Effectiveness results</th>
</tr>
</thead>
</table>
| Methadone vs. Buprenorphine       | • Equally effective at reducing opioid use  
• Methadone as maintenance therapy appears to be associated with higher rates of treatment retention compared to buprenorphine                                                                                     |
| Buprenorphine vs. Naltrexone      | • Similarly effective in treating opioid use disorder (following detoxification for naltrexone)                                                                                                                                 |
| Naltrexone vs. Buprenorphine or Methadone | • Buprenorphine is superior to naltrexone in treatment retention and heroin abstinence rates  
• No head-to-head studies comparing naltrexone vs. methadone                                                                                                           |
Considerations for MAT selection
Treatment selections

- Currently, no empirical data indicate which patients will respond better to which OUD medications.

- Individualize decisions to patients’ medical, psychiatric, substance use histories, and their preferences:
  - Prior response to a medication
  - Medication’s side effect profile
  - Use of other substances
  - Occupation – for patients in safety-sensitive occupations, consider naltrexone
  - Pregnancy status
  - Physical dependence on opioids
  - Patient’s preferences
# OUD medications overview

<table>
<thead>
<tr>
<th></th>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of action</strong></td>
<td>Opioid receptor agonist</td>
<td>Opioid receptor partial agonist</td>
<td>Opioid receptor antagonist</td>
</tr>
<tr>
<td><strong>Prescriber requirements</strong></td>
<td>OTP physicians only</td>
<td>Waiver required (for non-OTP provider)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Sites of care</strong></td>
<td>OTPs only</td>
<td>Office/clinic or OTP</td>
<td>Office/clinic</td>
</tr>
<tr>
<td><strong>Misuse/diversion potential</strong></td>
<td>Low (OTPs); moderate (take-home doses)</td>
<td>Low (OTPs); moderate (take-home doses)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Respiratory depression</strong></td>
<td>Rare</td>
<td>Very rare</td>
<td>None</td>
</tr>
<tr>
<td><strong>Withdrawal symptoms</strong></td>
<td>• None when starting</td>
<td>• Can occur when starting</td>
<td>• Severe when starting (if period of abstinence is inadequate)</td>
</tr>
<tr>
<td></td>
<td>• Present when d/c</td>
<td>• Present when d/c</td>
<td>• None when d/c</td>
</tr>
</tbody>
</table>

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### OUD medications overview continued...

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Formulations</th>
<th>Dosing (target dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methadone</td>
<td>Methadose™</td>
<td>Oral tablet</td>
<td>80 – 120mg PO QD</td>
</tr>
<tr>
<td></td>
<td>Dolophine®</td>
<td>Oral solution</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Subutex®</td>
<td>Sublingual tablet</td>
<td>16mg PO QD</td>
</tr>
<tr>
<td>Buprenorphine XR</td>
<td>Probuphine®</td>
<td>Subdermal implant</td>
<td>80mg every 6 months</td>
</tr>
<tr>
<td></td>
<td>Sublocade™</td>
<td>Subcutaneous injection</td>
<td>100mg SQ monthly</td>
</tr>
<tr>
<td>Buprenorphine/Naloxone</td>
<td>Zubsolv®</td>
<td>Sublingual tablet,</td>
<td>11.4mg/29mg QD</td>
</tr>
<tr>
<td></td>
<td>Suboxone®</td>
<td>Sublingual film</td>
<td>16mg/4mg QD</td>
</tr>
<tr>
<td></td>
<td>Bunavail®</td>
<td>Buccal film</td>
<td>8.4mg/1.4mg QD</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Revia®</td>
<td>Oral tablet</td>
<td>50mg QD</td>
</tr>
<tr>
<td>Naltrexone XR</td>
<td>Vivitrol®</td>
<td>Intramuscular injection</td>
<td>380mg IM monthly</td>
</tr>
</tbody>
</table>
Methadone (Methadose™, Dolophine®)

• Suitable for patients with:
  • Higher opioid tolerance
  • Longer histories of use
  • Unstable living situations

• Potential risks and adverse events: constipation, sweating, and heart arrhythmias

• Can be used for induction therapy or for maintenance treatment

• OTPs can provide daily onsite administration or at-home self-administration for stable patients
**Methadone** (Methadose™, Dolophine®)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No ceiling effect</td>
<td>• Schedule II</td>
</tr>
<tr>
<td>• Longest track record</td>
<td>• Requires daily visits to OTP clinics</td>
</tr>
<tr>
<td>• May be used during pregnancy</td>
<td>• REMS program for misuse/abuse, overdose potential, respiratory depression, and QT prolongation</td>
</tr>
<tr>
<td></td>
<td>• Significant drug interactions</td>
</tr>
</tbody>
</table>

Advantages

- No ceiling effect
- Longest track record
- May be used during pregnancy

Disadvantages

- Schedule II
- Requires daily visits to OTP clinics
- REMS program for misuse/abuse, overdose potential, respiratory depression, and QT prolongation
- Significant drug interactions
Buprenorphine (Bunavail®, Probuphine®, Sublocade™, Suboxone®, Subutex®, Zubsolv®)

• Suitable first-line treatment option for patients with:
  • Mild-to-moderate levels of dependence
  • Greater life stability who require less treatment oversight

• Inclusion of naloxone deters diversion and abuse, but should be avoided in pregnancy

• May be used for induction, stabilization, or for maintenance treatment

• Physicians, NPs, and PAs need a waiver (or "X" license) to prescribe
**Buprenorphine** (Bunavail®, Probuphine®, Sublocade™, Suboxone®, Subutex®, Zubsolv®)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inclusion of naloxone deters diversion and abuse</td>
<td>• Schedule III</td>
</tr>
<tr>
<td>• Fewer drug interactions</td>
<td>• Potential for misuse and diversion still exists</td>
</tr>
<tr>
<td>• Safer due to its ceiling effect (lower risk of respiratory depression)</td>
<td>• Risk of precipitated withdrawal with injection</td>
</tr>
<tr>
<td>• Less sedating</td>
<td>• REMS due to misuse/abuse and overdose potential, serious safety concerns</td>
</tr>
<tr>
<td></td>
<td>• Reports of hepatitis</td>
</tr>
<tr>
<td></td>
<td>• Products containing naloxone should be avoided in pregnancy</td>
</tr>
</tbody>
</table>
Naltrexone (Revia®, Vivitrol®)

• May be an effective first-line treatment option for individuals with short histories of opioid use who access treatment early

• Used as a maintenance agent in patients who have undergone opioid management withdrawal and are not receiving opioid replacement therapy with methadone or Suboxone

• Injections are more effective than tablets
# Naltrexone (Revia®, Vivitrol®)

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No risk of abuse/misuse or dependence</td>
<td>• Little effect on opioid cravings</td>
</tr>
<tr>
<td>• No withdrawal when discontinued</td>
<td>• Increase risk for addiction relapse</td>
</tr>
<tr>
<td>• No sedating effects</td>
<td>• Must be opioid-free for 7-10 days before starting naltrexone to prevent precipitation of opioid withdrawal</td>
</tr>
<tr>
<td>• No daily dosing <em>(injectable formulation only)</em></td>
<td>• Poor patient adherence</td>
</tr>
<tr>
<td>• No special regulatory requirements</td>
<td>• Limited efficacy/safety in pregnant women</td>
</tr>
<tr>
<td></td>
<td>• Reports of hepatitis</td>
</tr>
</tbody>
</table>
## Examples for patient selection

<table>
<thead>
<tr>
<th>Methadone</th>
<th>Buprenorphine</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Previous response to methadone</td>
<td>• Previous response to buprenorphine</td>
<td>• Resistance to taking opioid agonists</td>
</tr>
<tr>
<td>• Pregnant women</td>
<td>• Pregnant women (for SL generic tablet)</td>
<td>• Opioid abstinent for at least one week</td>
</tr>
<tr>
<td>• Need higher level of outpatient structure</td>
<td>• Stable patients (best candidates for Probuphine)</td>
<td>• Poor prior history of opioid agonist therapy</td>
</tr>
<tr>
<td>• Need supervision for medication adherence</td>
<td></td>
<td>• Hectic schedule making daily OTP visits impossible</td>
</tr>
</tbody>
</table>
Conclusions

• There is strong evidence that shows MAT for OUD reduces illicit opioid use and overdose deaths, and improves treatment retention

• Despite this evidence, barriers to MAT utilization remain including stigma, lack of access, lack of clinician training, and logistical challenges

• As there is no “one size fits all” approach, providers should discuss the advantages and disadvantages of various MAT options with their patients
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