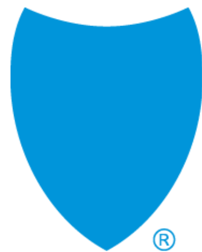

Medication Selection Considerations for Medication-assisted Treatment (MAT)

Learning objectives

- Identify the pros, cons, and barriers to widespread use of medication-assisted treatment (MAT)
- Discuss pharmacotherapy options for opioid use disorder
- 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

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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:

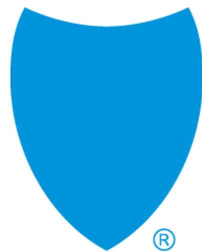
- ✓ Provider awareness
- ✓ NSI case management
- ✓ SafeMed LA collaboration
- ✓ Chronic pain management program
- ✓ Limit high doses and over-prescribing for acute pain and cough/cold
- ✓ Restrict ER opioids
- ✓ Inhibit stockpiling
- ✓ Prevent extended use for acute pain
- ✓ NSI provider education webinar 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

Opioid use disorder / medication-assisted treatment gap

- 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

Past year opioid abuse or dependence
OA-MAT capacity
Maximum potential buprenorphine capacity
OTP patients on methadone

Number of Individuals

2 500 000
2 000 000
1 500 000
1 000 000
500 000
0

2003 2004 2005 2006 2007 2008 2009 2010 2011 2012

Year

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

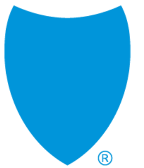
- Stigma associated with negative attitudes and beliefs from patient, family, and community
- Logistical challenges (e.g., daily appointments, transportation, occupation, childcare)
- Poor communication and coordination of care
- Regulatory restrictions on practice (e.g., patient management caps, methadone 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

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

* 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?

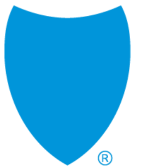
Buprenorphine therapy can result in replacing one addiction with another.

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**

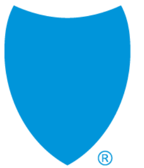
Outcomes of MAT agents

Methadone	Buprenorphine	Naltrexone
• ↑ patient treatment retention • ↓ illicit opioid use • ↓ risk of overdose-deaths • ↓ risk of HIV (including risk behaviors) and hepatitis C infection • ↓ risk of cellulitis	• ↑ patient treatment retention • ↓ illicit opioid use • ↓ treatment failure and mortality • ↓ number of opioid-positive drug tests • ↓ risk of HIV risk behaviors	• ↑ patient treatment retention • ↓ illicit opioid use • ↓ opioid craving • ↓ relapse (longer time to return to substance use, lower rate of return to use) • ↑ negative urine screens

Comparative effectiveness

Comparison	Effectiveness results
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

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

OUD medications overview continued…

Generic	Brand	Formulations	Dosing (target dose)
Methadone	• Methadose™ • Dolophine®	• Oral tablet • Oral solution	• 80 – 120mg PO QD
Buprenorphine Buprenorphine XR	• Subutex® • Probuphine® • Sublocade™	• Sublingual tablet • Subdermal implant • Subcutaneous injection	• 16mg PO QD • 80mg every 6 months • 100mg SQ monthly
Buprenorphine/ Naloxone	• Zubsolv® • Suboxone® • Bunavail®	• Sublingual tablet, • Sublingual film • Buccal film	• 11.4mg/29mg QD • 16mg/4mg QD • 8,4mg/1.4mg QD
Naltrexone	• Revia®	• Oral tablet	• 50mg QD
Naltrexone XR	• Vivitrol®	• Intramuscular injection	• 380mg IM monthly

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®)

Advantages	Disadvantages
• No ceiling effect • Longest track record • May be used during pregnancy	• 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®)

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

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®)

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

Examples for patient selection

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

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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