Medication Assisted Treatment (MAT) 101

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State Opioid Treatment Authority

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Vermont Department of Health
Differing Roles of Medication in MAT

1. Intoxication/Overdose
2. Assist with Detoxification
3. Maintenance Medication
4. Prevent Relapse
5. Sequelae (e.g. Psychiatric, Medical, etc.)
Medication Strategies for Substance Use Disorders (SUD)

- Agonist (replacement/substitution)
- Antagonist (blocking)
- Aversive (punishment)
- Correction/treatment of underlying/associated concerns (depression/psychosis)
Substances for which MAT is currently available:

- Opioids
- Alcohol
- Benzodiazepines
- Tobacco

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SUD Treatment Basics

- Diagnostic Criteria
- Levels of Care (LOC)
- Determination of LOC
DSM 5: Substance Use Disorders

Maladaptive pattern of drug use for >12 months
- Tolerance
- Withdrawal
- More use than intended (loss of control)
- Unsuccessful efforts to quit
- Significant time spent in procurement, use, recovery
- Activities (occupational, social etc.) given up
- Continued use in the face of adverse health effects
- Recurrent interpersonal problems from use
- Use under dangerous conditions
- Craving
- Failure to live up to obligations
DSM 5: Substance Use Disorder

- 2-3- “Mild”
- 4-5- “Moderate”
- ≥6- “Severe”

Physiological dependence is neither necessary nor sufficient to diagnosis a use disorder
ASAM Levels of Care

.5 Early intervention

I. Outpatient (1-8 hours weekly)
II. IOP (9-18) hours weekly, PHP (usually 20+)

III. Residential treatment
   i. Social setting
   ii. Medically monitored
   iii. Medically managed

IV. Hospitalization

MAT can and is offered across LOC 1-4.
6 Placement Domains

- Acute Intoxication/withdrawal potential
- Medical co-morbidity
- Psychiatric/mental health co-morbidity
- Relapse/continued use potential
- Readiness for change
- Recovery environment

* Only Domains 1-3 considered for hospitalization

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ASAM defined goals of detoxification

1. “to provide a safe withdrawal from the drug(s) of dependence and enable the patient to become drug-free”
2. “to provide a withdrawal that is humane and thus protects the patient’s dignity”
3. “to prepare the patient for ongoing treatment of his or her dependence on alcohol or other drugs.”

ASAM 2004
Age of first use of opiates is generally older than age of first use of alcohol

Source: Alcohol and Drug Abuse Treatment Programs, admissions 2005-2011
However, People seek treatment for Opioids much sooner than with Alcohol.

**Elapsed Time (Years) Between Age of First Use and Age at Treatment Admission for Daily Users of Opiates and Alcohol**

- **Opiates**
  - Average Elapsed Time: 8.2 years
  - Number of Admits: 6776

- **Alcohol**
  - Average Elapsed Time: 24.8 years
  - Number of Admits: 6207

Source: Alcohol and Drug Abuse Treatment Programs, admissions 2005-2011
Alcohol withdrawal

- 500,000 episodes of withdrawal requiring medication annually in the USA
- 3% of individuals with chronic AUD have withdrawal associated seizures
  - 3% of them have status epilepticus
- Delirium Tremens estimated in 5% of patients with chronic AUD
  - older
  - concurrent illness
  - seek care after longer time since last drink

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Treatment of Acute Alcohol Withdrawal

Prior to the 1980’s, withdrawal was almost exclusively done inpatient.

Most alcohol withdrawal (roughly 80%) is now completed on an outpatient basis.
Treatment of Acute Alcohol Withdrawal

- Roughly 70% of outpatients complete outpatient detoxification
- In most studies roughly 50% continue with treatment following detox. (NIAAA) though retention is problematic
- Detoxification alone has no significant bearing on long-term treatment outcomes
Alcohol Withdrawal Syndrome Criteria

DIAGNOSTIC CRITERIA FOR ALCOHOL WITHDRAWAL

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.

B. Two (or more) of the following, developing within several hours to a few days after criterion
   1. Autonomic hyperactivity (e.g., sweating or pulse rate greater than 100 beats per minute)
   2. Increased hand tremor
   3. Insomnia
   4. Nausea or vomiting
   5. Transient visual, tactile, or auditory hallucinations or illusions
   6. Psychomotor agitation
   7. Anxiety

C. The symptoms in criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score Range</th>
<th>Symptom</th>
<th>Score Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting</td>
<td>0-7</td>
<td>Headache</td>
<td>(0-7)</td>
</tr>
<tr>
<td>Paroxysmal sweats</td>
<td>(0-7)</td>
<td>Auditory disturbances</td>
<td>(0-7)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>(0-7)</td>
<td>Visual disturbances</td>
<td>(0-7)</td>
</tr>
<tr>
<td>Agitation</td>
<td>(0-7)</td>
<td>Tactile disturbances</td>
<td>(0-7)</td>
</tr>
<tr>
<td>Tremor</td>
<td>(0-7)</td>
<td>Orientation and clouding sensorium</td>
<td>(0-4)</td>
</tr>
</tbody>
</table>
CIWA Ar continued

- Total score is simple addition of the item scores with maximum of 67
  - Score:<10 very mild withdrawal
  - 10-15 mild withdrawal
  - 16-20 modest withdrawal
  - >20 severe withdrawal

Note: medication treatment >8-10 but close monitoring prior
Medications for the treatment of alcohol withdrawal

- **Benzodiazepines:**
  - Treat psychomotor agitation
  - Prevent progression from minor withdrawal to more significant symptoms
  - Valium, Librium, Ativan most commonly recommended/used
  - Unless severe withdrawal medications given orally, IV if needed
  - Benzos usually sufficient, if not may need other meds in ICU along with open airways (protracted DT’s)
Gabapentin (Neurontin)

- FDA Approved for partial onset seizures, postherpetic neuralgia, and restless legs syndrome
- Good choice for use in patients who may be at risk of hepatic insufficiency (e.g., hepatitis, cirrhosis).
- Abuse potential less than benzodiazepines, though gabapentin is misused, particularly by individuals with OUD.
- Phenobarbital protocols also available for inpatient settings and in some ED’s.

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Alcohol Use Disorder

- Adults diagnosed with mental illnesses 4x more likely to have AUD (9.6% vs. 2.2%) per national survey on drug use and health (NSDUH)
- Roughly 18 million Americans have an AUD
- Number of alcohol related liver disease deaths: 15,183 (2009, CDC)
- Number of alcohol-induced deaths, excluding accidents and homicides: 24,518 (2009, CDC)
Implementing Alcohol Treatment Based on Clinical Presentation

- A mutually agreed-upon plan with the patient is a prerequisite to initiating treatment.
- Significant withdrawal symptomatology (i.e., CIWA-Ar score > 10) must be attended to.
- Psychosocial counseling provides a foundation for the intervention.
- Add pharmacotherapy for patients who have not succeeded in attempts to cut down or stop drinking.
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- Add pharmacotherapy for patients who have not succeeded in attempts to cut down or stop drinking.

Kranzler 2021  
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Medication Assisted Treatment Options for Alcohol

- Disulfiram (Antabuse) 1949
- Acomprasate (Campral) 2004
- Naltrexone (Revia) 1994
- Depot Formula Naltrexone (Vivitrol): 2006

Not FDA Approved but off label use
- Toprimate (Topimax)
- Gabapentin (neurontin)
  *** also for use in alcohol withdrawal avoiding medication changes
- Baclofen

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Disulfram (Antabuse)

- Mixing with EtOH causes adverse reactions of flushing, lightheadedness, palpitations and nausea
- Reactions can be severe and dangerous for some
- Does not promote abstinence without supervision to ensure adherence.
- May reduce harm by reducing drinking days among patients who relapse.
- Not suitable for use as a primary harm reduction strategy due to the adverse effects of the disulfiram-ethanol reaction.
- Studies find roughly 20% medication adherence rate

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Naltrexone (Oral and IM)

- Antagonist at opioid receptor sites
- FDA approved for alcohol and opioids
- Approved oral dose 50mg, safe used at 100mg
- Black box warning for acute hepatitis and liver failure. Active liver disease should be mutual decision between patient and provider
- Most studies showing med adherence (50% of days used in a month) suggest 40% adherence rates
- Can be episodically and/or alternative dosing strategies
- No ill effects or withdrawal if stopped and no risk of physical dependence
- IM version (Vivitrol): 30-day injection can make acute pain management more challenging but may increase adherence

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Rösner et al. 2010

Meta-analysis of 50 RCTs with 7,793 patients showed that oral naltrexone reduced:

- Risk of any heavy drinking to 83% of that in the placebo group
- Drinking days by about 4%
- Heavy drinking days by about 3%
# Naltrexone side effects

<table>
<thead>
<tr>
<th>Most Common</th>
<th>Less Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>Diarrhea, constipation, stomach pains, cramps</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Chest pain, joint/muscle pain</td>
</tr>
<tr>
<td>Headache</td>
<td>Rash</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Difficulty sleeping</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Excessive thirst, loss of appetite</td>
</tr>
<tr>
<td>Nervousness</td>
<td>Sweating</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Increased tears</td>
</tr>
<tr>
<td>Somnolence</td>
<td>Mild depression</td>
</tr>
<tr>
<td></td>
<td>Delayed ejaculation</td>
</tr>
</tbody>
</table>

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Acamprosate (Campral)

- 666 mg three times a day (TID)

- Adherence in large studies suggest 30%

- Requires several days of abstinence prior to initiation for effectiveness
Acamprosate (Campral)

Review of 24 RCT’s and 6915 patients showed that acamprosate significantly:

- **Reduced** the risk of any drinking to 86% of that in the placebo group
- Increased the cumulative abstinence duration by 10.94 days

Alternately:

3 Large US and Australian studies showed no benefit to using campral, alone or in combination with naltrexone
## Acomprosate side effects

### Common side effects
- Symptoms of anxiety
- Depression
- Xerostomia
- Pruritus of skin
- Dizziness
- Insomnia
- Hyperhidrosis
- Paresthesia
- Nausea
- Flatulence
- Diarrhea
- Accidental injury

### Serious side effects
- Mental/mood changes
- Signs of kidney problems
- Fainting
- Fast or pounding heartbeat
- Vision or hearing changes
- Increased thirst
- Abdominal pain that doesn’t go away
- Black stools
- Vomit that looks like coffee grounds
- Seizures

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Psychosocial Treatment and Mutual Aid

- Alcoholics/Narcotics Anonymous (AA/NA) (Consumer reports study, Seligman 1996)
- Motivational Interviewing
- CBT (Cognitive Behavioral Therapy)
- Contingency management
Psychosocial Treatment

- Intensive Outpatient Programming (IOP) has equal outcomes to residential treatment
- Intensity of support should match patient stage of change and intensity of use
- 90-day minimum duration of treatment, (not a specific setting) “to move the needle” for an individual with a significant substance use disorder
Opioids

- Agonist drugs: full opiate medications. The more you take, the more activity at the receptor sites (Mu)
  - Codeine
  - Hydrocodone
  - Oxycodone
  - Methadone
  - Morphine
  - Heroin

- Divided by synthetic vs. semi-synthetic vs. opiates (natural derivatives of poppy)

- Oxycodone not identified in standard opiate screening

- Fentanyl has highest affinity of full agonists to the Mu receptor making it potentially more lethal in overdose (requires larger dose of narcan to reverse respiratory suppression)

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Opioid Effects and Side Effects

- Analgesia - Pain relief
- Nausea
- Constipation
- Itching
- Vomiting
- Urinary retention
- Dry mouth
- Loss of menses in women

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Opioid Intoxication

- “Nodding out”
- “pinned” pupils
- Heavy, relaxed muscles and extremities
- Euphoria
- Slowed breathing and cardiac functioning
- Reduced sex drive
Heroin and other Opioids

- Most common “comorbid” conditions are other behavioral health issues: other substance use disorders, Anxiety, Depression and Personality Disorders
- Commonly associated with criminal justice populations
- For individuals who inject opioids: High rates of Hepatitis C, higher rates of HIV (though overall low in VT) and significant risks of overdose
- Recently abstinent individuals lose tolerance rapidly (particularly respiratory) and have even higher risk of OD (some studies have seen 40-129x the risk of general public) particularly in the first 2 weeks following release from incarceration

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Heroin and other Opioids

- Withdrawal, while painful, not inherently lethal—often equated to a bad stomach flu. However, it is reported that post acute withdrawal symptoms can last 9-12 months.
- Short term treatment interventions demonstrate little to no effectiveness.
- Less than 1 year of methadone maintenance shows no statistical long-term benefit.
- Short term Buprenorphine tapers associated with significant relapse rates (90%+).

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Opioid Withdrawal

- Sweats
- Diarrhea
- Nausea & Vomiting
- Aches and pains, particularly in back and stomach
- Goose flesh
- Cramps

- Irritation
- Agitation
- Anxiety
- Runny nose
- Yawning
- Insomnia
- Dilated pupils
- Depression and anxiety
## APPENDIX 1

**Clinical Opiate Withdrawal Scale**

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

<table>
<thead>
<tr>
<th>Patient's Name:</th>
<th>Date and Time <em><strong>/</strong></em>/___:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reason for this assessment:</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Resting Pulse Rate
- Measured after patient is sitting or lying for one minute
- 0 = pulse rate 80 or below
- 1 = pulse rate 81-100
- 2 = pulse rate 101-120
- 4 = pulse rate greater than 120

### GI Upset
- Over last 1/2 hour
- 0 = no GI symptoms
- 1 = stomach cramps
- 2 = nausea or loose stool
- 3 = vomiting or diarrhea
- 5 = multiple episodes of diarrhea or vomiting

### Sweating
- Over past 1/2 hour not accounted for by room temperature or patient activity
- 0 = no report of chills or flushing
- 1 = subjective report of chills or flushing
- 2 = flushed or observable moisture on face
- 3 = beads of sweat on brow or face
- 4 = sweat streaming off face

### Restlessness
- Observation during assessment
- 0 = able to sit still
- 1 = reports difficulty sitting still, but is able to do so
- 3 = frequent shifting or extraneous movements of legs/arms
- 5 = unable to sit still for more than a few seconds

### Pupil size
- Normal size for room light
- 0 = pupils normal size or normal for room light
- 1 = pupils larger than normal for room light
- 3 = pupils moderately dilated
- 5 = pupils so dilated that only the rim of the iris is visible

### Bone or Joint aches
- If patient has previously had pain, only the additional component attributed to opiate withdrawal is scored
- 0 = not present
- 1 = mild diffuse discomfort
- 2 = patient reports severe diffuse aching of joints/muscles
- 4 = patient is rubbing joints or muscles and is unable to sit still because of discomfort

### Anxiety or Irritability
- Observation during assessment
- 0 = none
- 1 = patient reports increasing irritability or anxiousness
- 2 = patient obviously irritable or anxious
- 4 = patient so irritable or anxious that participation in the assessment is difficult

### Gooseflesh skin
- Skin is smooth
- 0 = no gooseflesh
- 3 = pilosecretion of skin can be felt or hairs standing up on arms
- 5 = prominent pilarerection

### Runny nose or tearing
- Not accounted for by cold symptoms or allergies
- 0 = not present
- 1 = nasal stuffiness or unusually moist eyes
- 2 = nose running or tearing
- 4 = nose constantly running or tears streaming down cheeks

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**Score:**
- 5-12 = mild
- 13-24 = moderate
- 25-36 = moderately severe
- More than 36 = severe withdrawal

**Total Score:**
- The total score is the sum of all 11 items

Initials of person completing assessment:

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General Opioid Pharmacology

- Full agonists
  - Bind to the receptor and activate the receptor
  - Increasing doses of the drug produce increasing effects until a maximum effect is achieved (receptor is fully activated)
  - Most abused opioids are full agonists
Partial agonists

- Bind to the receptor and activate the receptor
- Increasing the dose does not lead to as great an effect as does increasing the dose of a full agonist - less of a maximal effect is achieved
General Opioid Pharmacology

- **Antagonists**
  - Bind to the receptor, but don’t activate the receptor
  - Block the receptor from being bound by a full agonist or partial agonist
  - Like putting gum in a lock...
Medication-Assisted Treatment

- Agonist Therapy: Methadone
  - LAAM: Long-acting form of methadone, rarely used due to cardiac side effects including Torsade de pointes

- Partial Agonist Therapy: Buprenorphine

- Antagonist Therapy: Naltrexone/Vivitrol
Methadone Maintenance Treatment

- 1960’s with FDA approval in 1973
- Specialized clinics (OTP’s/Hubs)
- Significant medication controls requiring daily observed ingestion until patient meets stability requirements
- Even upon stability, Federal take home schedule such that even patients stabilized for 365 days still must be seen for medication dosing 1x weekly
- Requires regular urine screens and counseling. Frequency and intensity is driven by patient stability
- “Low and Slow” initiation of meds not more than 30 mg initial dose
- Full agonist, can push dose to match intensity of patient use to develop “blockade” effect
- FDA approved in treatment of pregnancy
Buprenorphine: Data 2000

- Ceiling effect on medication, improves safety profile but limits dose effectiveness
- 2 formulations: mono and combination products (“Subutex” and Suboxone most common)
- Sublingual dosing: safe dosing form but only 50% bioavailability High affinity but low activity at Mu receptor
- Medication became available in late 2003 with sufficient supply to begin treatment in US.
- Solid side effect and safety profile but... not benign! 30x strength of oral morphine
Buprenorphine: Data 2000

- Causes euphoria in opioid naïve patients, can be lethal in OD for pediatrics and has limited response to Narcan reversal
- Partial agonist limits some people’s ability to stabilize on doses
- FDA approval up to 24mg, most common doses 16mg or less. 32 Max dose decided by expert panel consensus
- Prescriber limits on number of patients they can treat.. Max 275
- In Vermont—also dispensed in Hubs/OTPs
- Used in treatment of pregnancy, with some reductions in NAS (infant withdrawal syndrome) compared to Methadone but higher drop out rates by pregnant women
Buprenorphine products

- Oral/Sublingual (buprenorphine mono & Suboxone), Zubsolv
- Implant (Probuphine): 6 month
  - Expensive
  - Limited dose range of up to 8 mgs
  - Think Norplant
- Injection (Sublocade)
  - Decreased diversion
  - Up to 30 day dosing
  - 2 strengths
  - Can be removed up to 14 days after injection
  - Expensive
  - Engagement?
Antagonist Medications

Naltrexone: Relapse Prevention
- Indicated for both alcohol and opioid dependence
- High affinity at receptor but no activation of receptor site
- Requires 7-10 days abstinence prior to dosing for opiates
- Compliance is problematic
- Vivitrol: 30 day sustained release dose to assist in compliance the modal number of injections accepted is 1!

Naloxone/Narcan: OD Reversal
- Standing order and wide community availability in VT
- Used for reversal of opioid overdose syndrome, notably respiratory suppression
- Inactive ingredient in combination Buprenorphine product due to poor sublingual availability but higher IV availability
What we know about MAT for opioids: particularly Buprenorphine and Methadone

Generally, reduce or improve:

- Illicit opioid use
- Overdose
- IVDU/HIV related behaviors
- Criminal Justice Involvement
- Retention in Care

Adequate methadone dosing required for outcomes (most above 60mg)
Psychosocial Treatment and Mutual Aid

- Narcotics Anonymous (NA)
- Treatment without medications: Abstinence rates generally lower than 25% for opioid addiction
- Therapeutic communities suggested improvement in frequency of use and reduction in criminal behavior
Myth Busters

MAT is substituting one high for another...
A drug is a drug is a drug...
Everyone needs to start with detox in an inpatient/residential program
Everyone with AUD or OUD needs medication
No one with OUD/AUD needs medication
The goal of treatment is to get off MAT meds as soon as possible
Everyone who uses substances needs treatment or recovery supports
People can’t inject Buprenorphine because of Narcan in it...
Questions?????
Thank You!