Medication Assisted Treatment (MAT) 101

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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

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

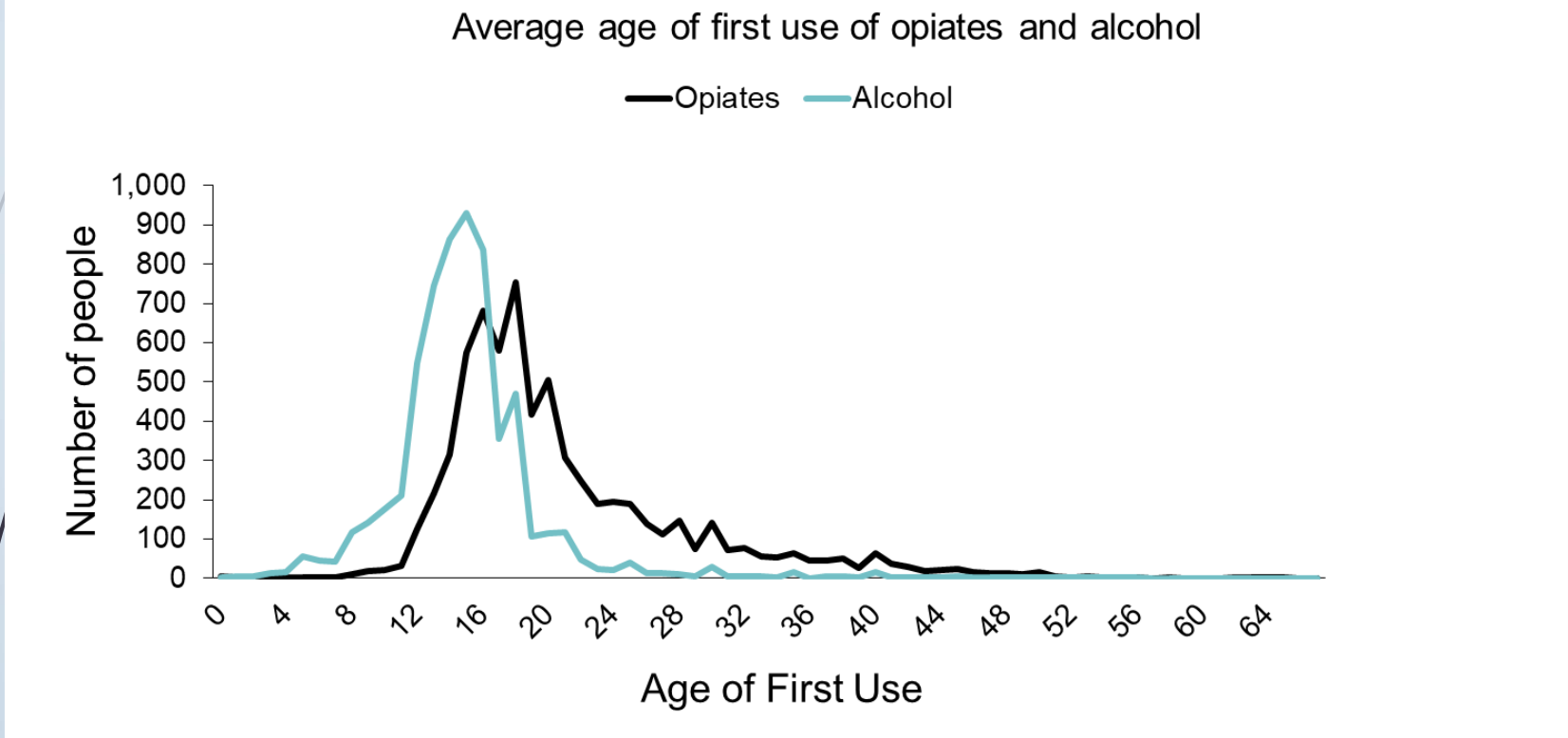
- Acute Intoxication/withdrawal potential
- Medical co-morbidity
- Psychiatric/mental health co-morbidity
- Relapse/continued use potential
- Readiness for change
- Recovery environment

* Only Domains 1-3 considered for hospitalization

ASAM defined goals of detoxification

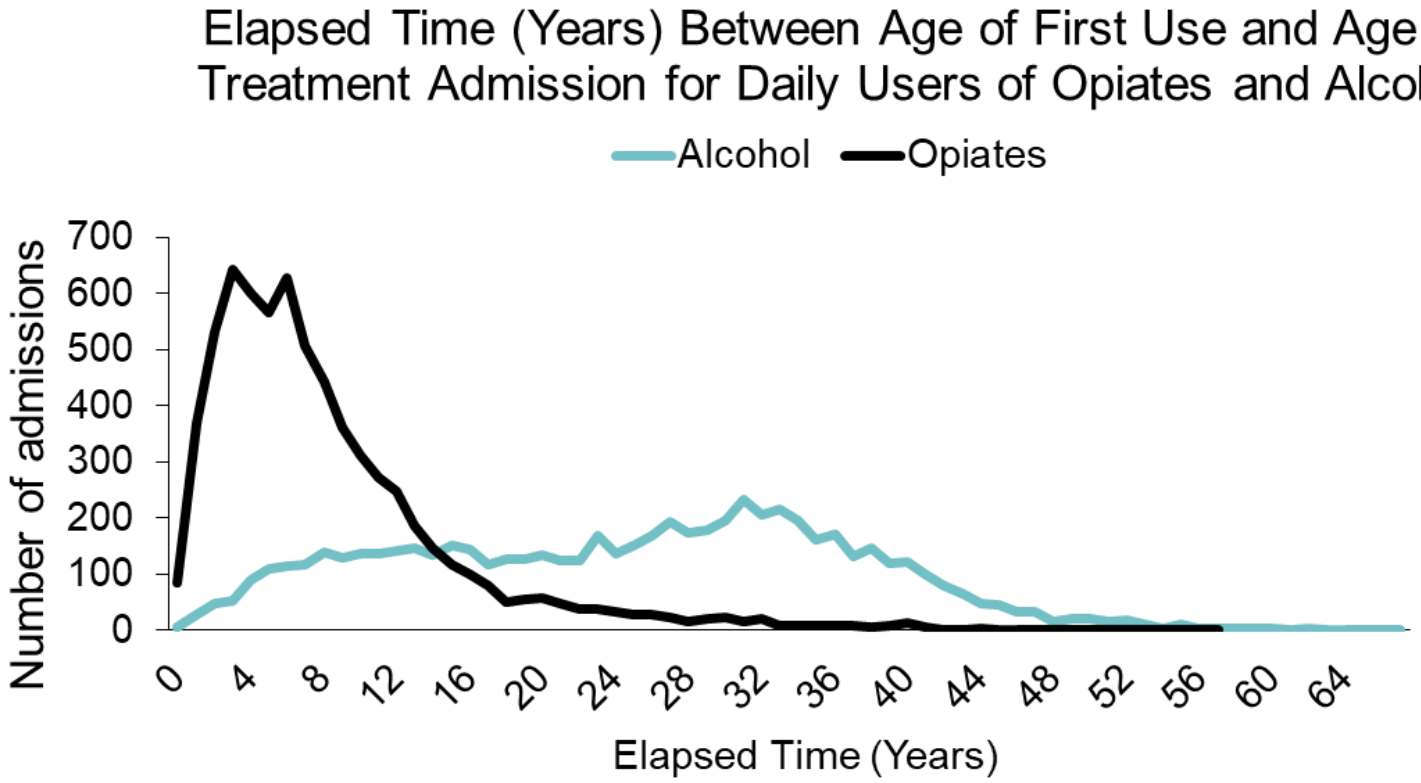
- (1) “to provide a safe withdrawal from the drug(s) of dependence and enable the patient to become drug-free”
- (2) “to provide a withdrawal that is humane and thus protects the patient’s dignity”
- (3) “to prepare the patient for ongoing treatment of his or her dependence on alcohol or other drugs.”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



	Opiates	Alcohol
Average Elapsed Time	8.2	24.8
Number of Admits	6776	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

Treatment of Acute Alcohol Withdrawal

Prior to the1980's, withdrawal was almost exclusively done inpatient

Most alcohol withdrawal (roughly 80%) is now completed on 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**
    8. **Grand mal seizures.**
- 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.

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed., text revision. Washington, D.C.: American Psychiatric Association, 2000:216.

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

Nausea and vomiting 0-7	Headache (0-7)
Paroxysmal sweats (0-7)	Auditory disturbances (0-7)
Anxiety (0-7)	Visual distrurbances (0-7)
Agitation (0-7)	Tactile disturbances (0-7)
Tremor (0-7)	Orientation and clouding sensorium (0-4)

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 in inpatient settings and in some ED's.

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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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

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

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

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

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

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

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

Opioid Effects and Side Effects

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

Opioid Intoxication

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

Heroin and other Opioids

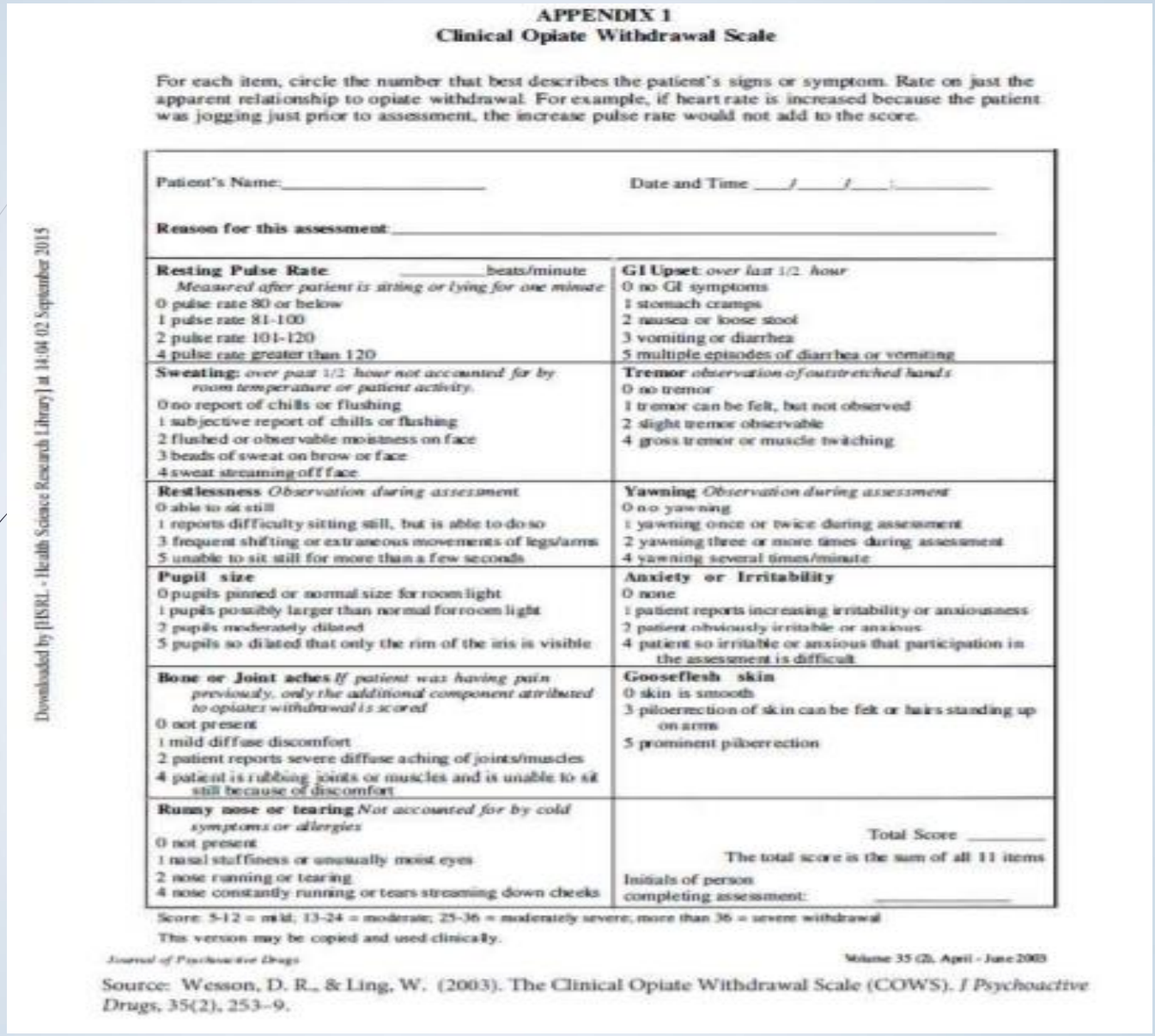
- Most common “comorbid” conditions are other behavioral health issues: other substance use disorders, Anxiety, Depression and Personality Disorders
- Commonly associated with criminal justice populations
- For individuals who inject opioids: High rates of Hepatitis C, higher rates of HIV (though overall 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

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%+)

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.

Patient's Name:_____ Date and Time ____/____/____:_____

Reason for this assessment:_____

Resting Pulse Rate: _____beats/minute *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 moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
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	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 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
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates 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	**Gooseflesh skin** 0 skin is smooth 3 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
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	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

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

This version may be copied and used clinically.

Journal of Psychoactive Drugs Volume 35 (2), April - June 2003

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs*, 35(2), 253–9.

Vermont Department of Health

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


www.auto-types.com

General Opioid Pharmacology

- 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


U-HAUL
ONE-WAY & IN-TOWN MOVES
Mom's Attic
U-HAUL
RIGHT EQUIPMENT / LOWEST COST
America's
Moving Adventure
UTAH
Dinosaur
National
Monument
Gentle-Ride Van

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!