Implementing Technology and
Medication Assisted Treatment
and Team Training in Rural Colorado

Behavioral Health Provider Training

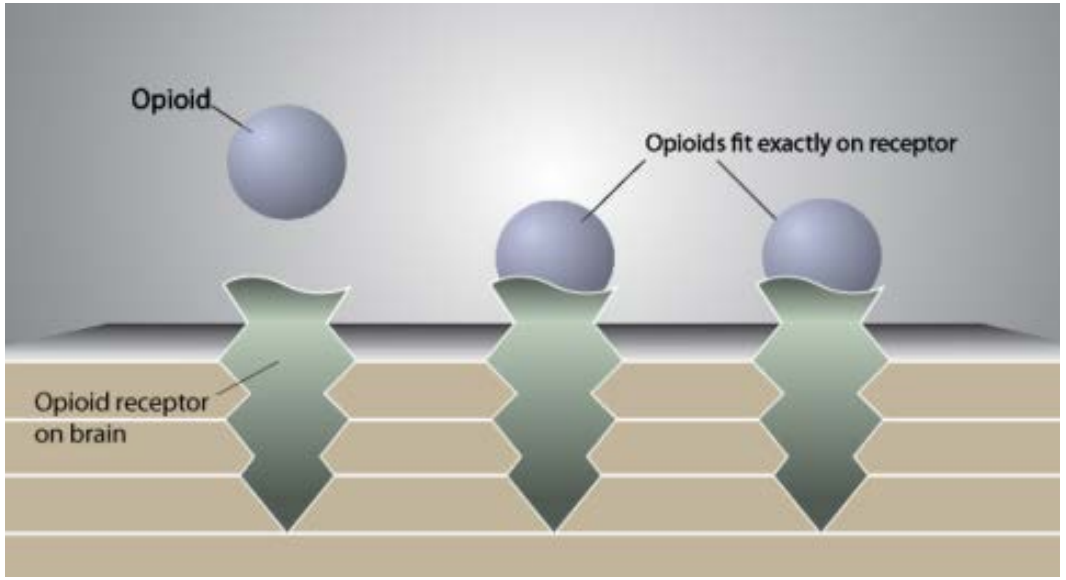
Module 3: Pharmacology of Buprenorphine and Other Drugs

What are opioids?

- Drugs that bind to the opioid receptors
  - Mu, Kappa, and Delta
- Can be produced naturally by plants or derivatives of naturally-occurring compounds (“opiates”)
  - Morphine, codeine
  - Heroin: 10x more potent than morphine
- Can be synthetic or semisynthetic drugs (“opioids”)
  - Methadone
  - Fentanyl: 100x more potent than morphine

Mu Receptor Mediates Opioid Effects

- Euphoria, sedation, relaxation, pain and anxiety relief, sleepiness
- Chemical opioids stimulate the receptor much more powerfully than the body's natural (endogenous) opioids



Agonist (here, the opioid) – activates the receptor

Antagonist – blocks the receptor

All chemical opioids may cause physical dependence and addiction.

Clinical Applications of Opioids

- In clinical settings as analgesics.
- Highly reinforcing. High potential for abuse.

Opioid Tolerance and Physical Dependence

Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure.

Tolerance:

Increased dosage needed to produce specific effect.
Develops readily for central nervous system and respiratory depression.

Physical Dependence:

Signs and symptoms of withdrawal by abruptly stopping the opioid, rapid dose reduction, or administration of antagonist

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Opioid Withdrawal: Diagnosis (DSM-5)

A) Cessation or reduction of opioid use that was substantial and protracted OR after administration of an opioid antagonist following a period of opioid use.

B) Three of the following:

- Dysphoric mood
- Nausea or vomiting
- Muscle aches
- Insomnia
- Diarrhea
- Yawning
- Fever
- Lacrimation or rhinorrhea
- Pupillary dilation, piloerection, or sweating

C) Impaired functioning not explained by another condition.

D) Duration and severity of opioid withdrawal are dependent on individual's drug of abuse and degree of dependence.

Opioid Withdrawal: using the Clinical Opiate Withdrawal Scale (COWS)

Clinical Opiate Withdrawal Scale (COWS)

Flowsheet for measuring symptoms over a period of time during buprenorphine induction.

For each item, write in 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 increased pulse rate would not add to the score.

Patient Name: _____ Date: _____

Buprenorphine Induction: _____

Enter scores at time zero, 30 minutes after first dose, 2 hours after first dose, etc.	Times of Observation:			
Resting Pulse Rate: Record Beats per 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				
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				
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				

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Opioid Withdrawal: Types

Spontaneous: Physically dependent individual suddenly stops or significantly decreases opioid usage.

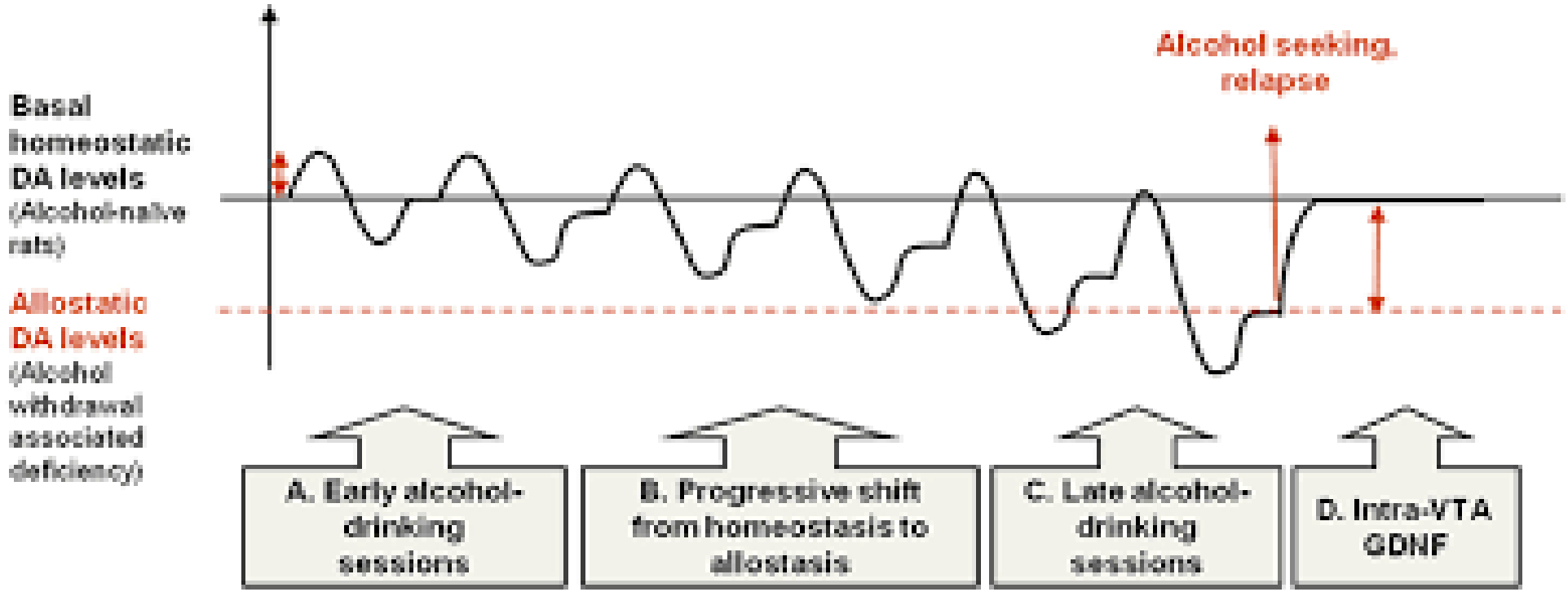
Precipitated: More intense than spontaneous and has much faster onset.

- Full agonist (e.g., heroin) displaced from receptors by antagonist (e.g., naloxone).

Protracted: Withdrawal symptoms or other symptoms continue past the time expected for acute withdrawal, and sometimes last for months or years.

Medically supervised: Withdrawal through tapering

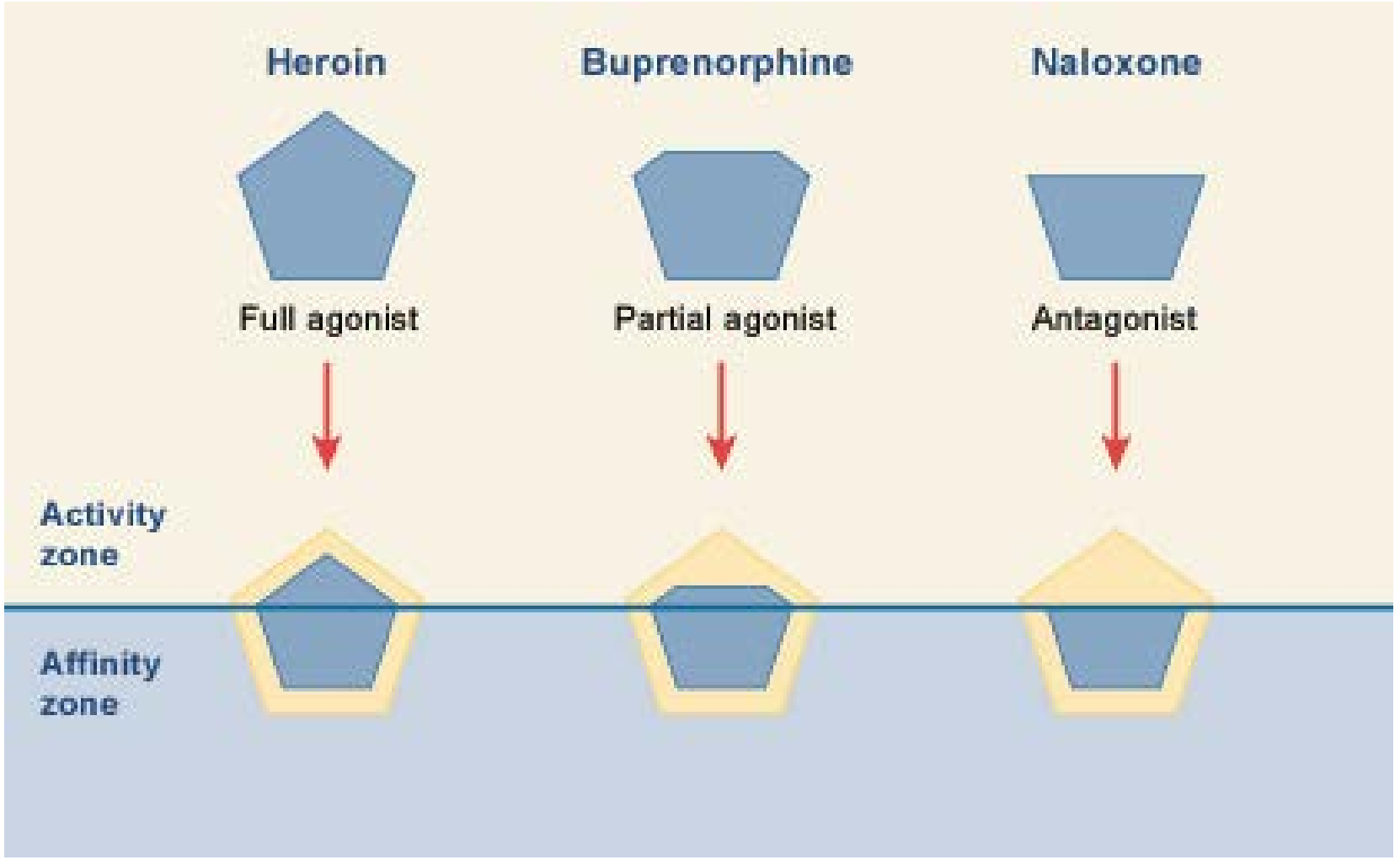
How Addiction Hijacks the Brain



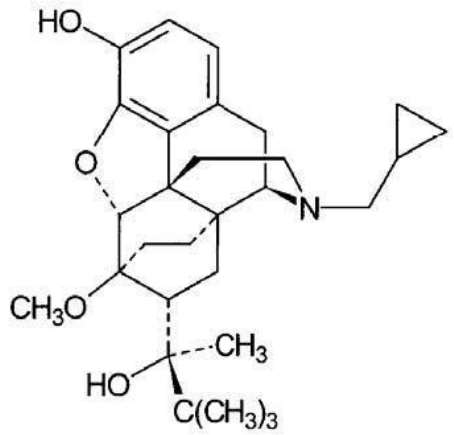
How does buprenorphine work?

Activity
What does it do?
Activate (agonist) vs. block (antagonist)

Affinity
How tightly it binds to the mu receptor.



Buprenorphine



- Partial mu-opioid agonist
- Metabolism
  - In liver with N-dealkylation by cytochrome P450 3A4 enzyme system into an active metabolite norbuprenorphine
    - Norbuprenorphine undergoes further glucuronidation
  - Elimination
    - Excreted in feces (70%) and urine (30%)
    - Mean elimination half-life = 37 hours
  - Commercial screening urine drug test for parent compound and metabolite
  - Does NOT show as opiate positive on standard drug screen

How Buprenorphine Is Supplied?

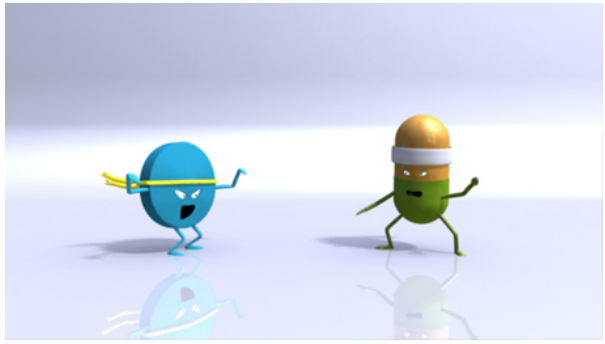
- Buprenorphine single ingredient or combined with naloxone.
- The following formulations are available:
  - Buprenorphine/naloxone (Suboxone®) for treatment of OUD
  - Monotherapy buprenorphine for treatment of OUD, including implant form
  - Formulations of buprenorphine for treating pain (Buprenex®, Butrans®, Belbuca ™)

Common Buprenorphine Side Effects

- Safe when used as indicated
- Side effects are rare, usually minor, and similar to side effects of other opioids.
  - Headaches
  - Pain
  - Nausea and vomiting
  - Constipation
  - Insomnia
  - Sweating
  - Numb mouth and painful tongue
  - Withdrawal syndrome (consider whether precipitated)

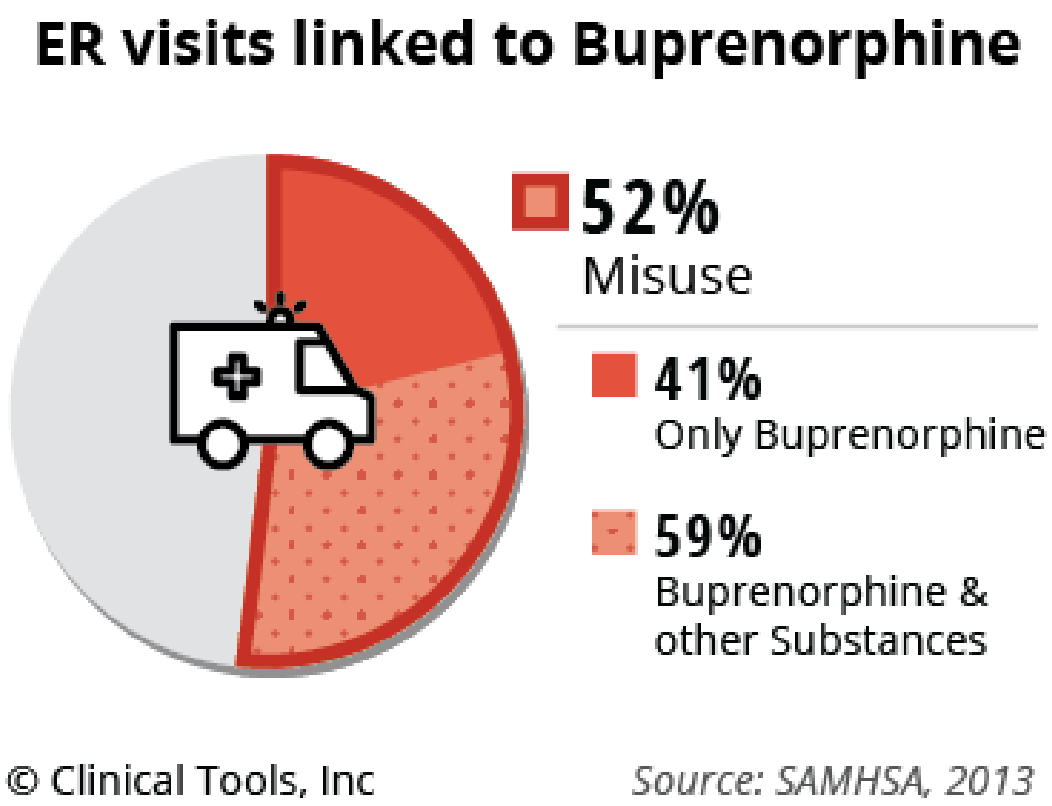
Drug Interactions

- Known interactions with buprenorphine or buprenorphine/naloxone combination include the following drug classes:
  - Benzodiazepines (e.g., Xanax, Valium)
  - Other CNS depressants (e.g., Ambien, Lunesta)
  - CYP3A4 inducers and inhibitors (e.g., Ketoconazole, Rifampicin)
  - Non-benzodiazepine muscle relaxants (e.g., metaxalone)
  - Anticholinergics (e.g., Cogentin)
  - Psychostimulants (e.g., Adderall)



Low Buprenorphine Overdose Risk

- Safe and efficacious in primary care setting
- Ceiling effect and poor bioavailability => low risk of overdose (accidental or intentional)
- Overdose and abuse possible due to opioid agonist effect



Naloxone

- Opioid agonist with stronger affinity to opioid receptors than opioids
  - Administration displaces opioids off receptors
- Naloxone is available for friends and loved ones of people with opioid dependence
  - 200 participating pharmacies in Colorado
  - Part of harm reductions efforts in the state

Module 3 Summary

- Tolerance: neurological adaptation in which sensitivity of opioid receptors decreases, requiring increasingly larger doses for the same drug effects.
- Opioid withdrawal: severe flu-like state, with duration and severity depending on drug of abuse and degree of physical dependence.
- Drug interacts with benzodiazepines, sedative hypnotics, cytochrome P450 3A4 drugs, antiretroviral agents, anti-seizure medications, and other opioids.
- Buprenorphine works!
- BH providers understand buprenorphine treatment.

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Mr. Brown

35 year old male with extensive history of heroin and other drugs. He was diagnosed with HIV a year ago, which he likely contracted due to unsafe needle use. Since his diagnosis he has continued to use heroin, though he has not injected. His medical provider is urging him to stop using heroin because it can interfere with his HIV treatment. He has previous inpatient detoxifications, which have ultimately failed.

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Module 4: OUD Detection and Diagnosis

Module Overview

- Screening and assessment of patients for OUD
- Importance of patient engagement

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Motivational Interviewing (MI)

Why Use MI?

- Facilitate connecting with patients for effective screening and diagnosis
- Motivate patients to obtain treatment and make changes
- Effective in medical settings and associated with improved health outcomes

How is MI different from everything else?

- Recognizes the expertise of the patient on his/her own motivations
- Guides patient to examine and resolve ambivalence about problem

Four Steps of MI

1) Building rapport with the patient
2) Focusing on the topic
3) Evoking or eliciting thoughts/emotions about the topic
4) Planning for change

Ms. Lopez

40 year old female with a history of generalized anxiety diagnosed with arthritis 5 years ago. She was started on opioids after failing NSAIDs. Throughout the years her daily dose has increased significantly and she is now taking hydrocodone and oxycodone. She has noticed that she feels ill whenever she does not take her medication and has even found herself stealing prescription opioids from her best friends medicine cabinet. She is concerned about her use and has been self-medicating with buprenorphine to reduce her use of hydrocodone and oxycodone.

SMART Goals

Intention: What is it that patient wants to achieve?

Specific

Who? What? When? Where?

Measurable

How much? How often? How many?

Attainable

Is it achievable?

Relevant

Is it important to what patient wants to achieve?

Time-based

By when?

Screening for OUD

Screening Instruments

- Use of an evidence-based screening tool can detect substance use problems more accurately than clinical judgment
- Even providers and practices experienced in diagnosing and treating substance use disorders can benefit from the use of formal screening instruments.

CAGE-AID

Cut down

Have you ever felt you ought to cut down on your drinking or drug use?

Annoyed

Have people annoyed you by criticizing your drinking or drug use?

Guilty

Have you ever felt bad or guilty about your drinking or drug use?

Eye-opener

Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover?

Scoring: Of the 4 items, a "yes" answer to one item indicates a possible substance use disorder and a need for further testing.

NIDA Quick Screen

In the *past year*, how many times have you used the following?					
Drug Type	Never	Once or Twice	Monthly	Weekly	Daily or almost Daily
Alcohol: Men: > 5 drinks/day Women: > 4 drinks/day					
Tobacco products					
Misused prescription drugs					
Illegal drugs					

Other Screening Instruments

Two-Item Conjoint Screening (TICS)

Both alcohol and drug use. Detects current substance use, NOT a history of use. Questions can be integrated into a standard clinical interview.

NIDA-Modified Alcohol, Smoking, and Substance Involvement Screening Test (NMASSIST)

Further assess drug use after a positive NIDA Quick Screen.

Drug Abuse Screening Test-10 (DAST-10)

Short version of the Drug Abuse Screening Test often used as a screening and diagnostic tool in primary care.

AUDIT

Brief alcohol screen often used in primary care.

Current Opioid Misuse Measure (COMM)

Identify patients with chronic pain taking opioids who have indicators of current aberrant drug-related behaviors.

Screening Adolescents: Practice Tips

- Phrase questions so they are perceived as least threatening
- Try making gentle assumptions
  - "How often do you drink alcohol?"
- Address positive responses immediately, with further assessment, intervention, and discussion of possible referral or treatment, if indicated, rather than postponing to later in the appointment.

Pharmacologic Treatment with Adolescents

- Pharmacologic therapy is recommended for adolescents with severe OUD.
- Buprenorphine is considered first line treatment. Most methadone clinics cannot admit patients under 18 years old.
- Optimal length of time for medication treatment is not known.

Teen Confidentiality

- Teens presenting with parents: Confidentiality is clinical decision of what should be shared with parents in context of parents already being aware of “big picture”
- Teens presenting without parents: Can consent at 15 in Colorado, though this does not guarantee confidentiality.
- Teens who refuse to involve parents: Explore reasons for excluding parents and reinforce help-seeking behavior, continue to discuss ways of “breaking the news” to parents

Screening Adolescents: CRAFFT

Car – Have you ever ridden in a car driven by someone (including yourself) who was "high" or had been using alcohol or drugs?

Relax – Do you ever use alcohol or drugs to relax, feel better about yourself, or fit in?

Alone – Do you ever use alcohol or drugs while you are by yourself or alone?

Forget— Do you ever forget things you did while using alcohol or drugs?

Family/Friend – Do your family or friends ever tell you that you should cut down on your drinking or drug use?

Trouble – Have you ever gotten into trouble while you were using alcohol or drugs?

Interpretation: Two or more positive items indicate the need for further assessment.

Adolescent Risk Factors

- ADHD, conduct disorder, and sensation-seeking behavior
- Homelessness in youth and running away associated with greater risk of injected opioid use
- Red flags:
  - Marked change in physical health
  - Deteriorating performance in school or job
  - Dramatic change in personality, dress, or friends
  - Involvement in serious delinquency or crimes
  - HIV high-risk activities
  - Serious psychological problems

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Signs and Symptoms of OUD

Physical Signs and Symptoms of Opioid Misuse

- GI problems
- Low blood pressure
- Decreased respiration rate
- Confusion
- Constipation
- Pupillary constriction
- Suppression of cough reflex
- Dry mouth and nose
- Decreased libido and/or sexual dysfunction
- Irregular menses
- Irritation of nose lining
- Perforated nasal septum
- Abscesses, cellulitis, or dermatitis at injection sites
- Skin necrosis
- Tourniquet pigmentation

Psychosocial Signs and Symptoms of OUD

Cravings	Added criterion in DSM-5 diagnosis of OUD. In asking about craving, include thinking a lot about using, dreams about using, having thought of using opioids on your mind a lot.
Behavioral	Agitation, anxiety, anger, irritability, depression, insomnia, mood swings, weight changes
Family	Marital problems (e.g., separation, divorce), abuse or violence, children's behavioral problems, family members' anxiety and depression
Social	Loss of long-standing friendships, spending time with other drug abusers, social isolation, loss of interest in regular activities
Work/School	Missing work or school, poor performance, frequent job changes or relocations
Legal	Arrests, DUIs, theft, drug dealing. Legal problems are no longer diagnostic criterion.
Financial	Recent large debt, borrowing money from friends/relatives, selling possessions

Opioid Use Disorder Criteria (DSM-5)

- ❑ Opioids taken in larger amounts or longer period than intended
- ❑ Persistent desire or unsuccessful efforts to cut down or control opioid use
- ❑ Great deal of time spent in activities necessary to obtain, use, or recover from effects of opioids
- ❑ Craving/strong desire or urge to use (new to DSM-5)
- ❑ Recurrent use resulting in failure to fulfill major role obligations at work, school, or home

Opioid Use Disorder Criteria (DSM-5)

- ❑ Continued use despite persistent or recurrent social or interpersonal problems caused by or exacerbated by effects of opioids
- ❑ Important social, occupational, or recreational activities give up or reduced due to use
- ❑ Recurrent use in physically hazardous situations
- ❑ Use continued despite persistent or recurrent physical or psychological problem likely to have been caused or exacerbated by opioids
- ❑ Tolerance
- ❑ Withdrawal

Do not apply if used appropriately under medical supervision

Treatment for those not regularly using opioids

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- Some high-risk, opioid-abusing patients who do not meet diagnostic criteria, may be good candidates for buprenorphine maintenance.
- Certain patients who are not currently abusing opioid may also qualify for office-based opioid treatment.
  - Inmate with a good prior treatment record with buprenorphine ("institutional abstinence") may be maintained on buprenorphine following release, if relapse is likely. ***Educate that opioid tolerance is now relatively lower, in order to reduce their risk of overdose.***

Assess Patients for Office Based Treatment

- Once you identify OUD in a patient:
  - ❑ Assess patient attitudes
  - ❑ Motivate patients for change
  - ❑ Determine appropriate interventions
  - ❑ Determine duration, pattern, and severity of opioid use disorder
  - ❑ Determine level of tolerance
  - ❑ Gather history of previous attempts to use agonist therapy
  - ❑ Gather history of previous attempts to quit
  - ❑ Assess current opioid use and withdrawal status
  - ❑ Determine history of withdrawal
- Refer to a MAT prescriber/provider/program in your community

Co-Occurring Conditions

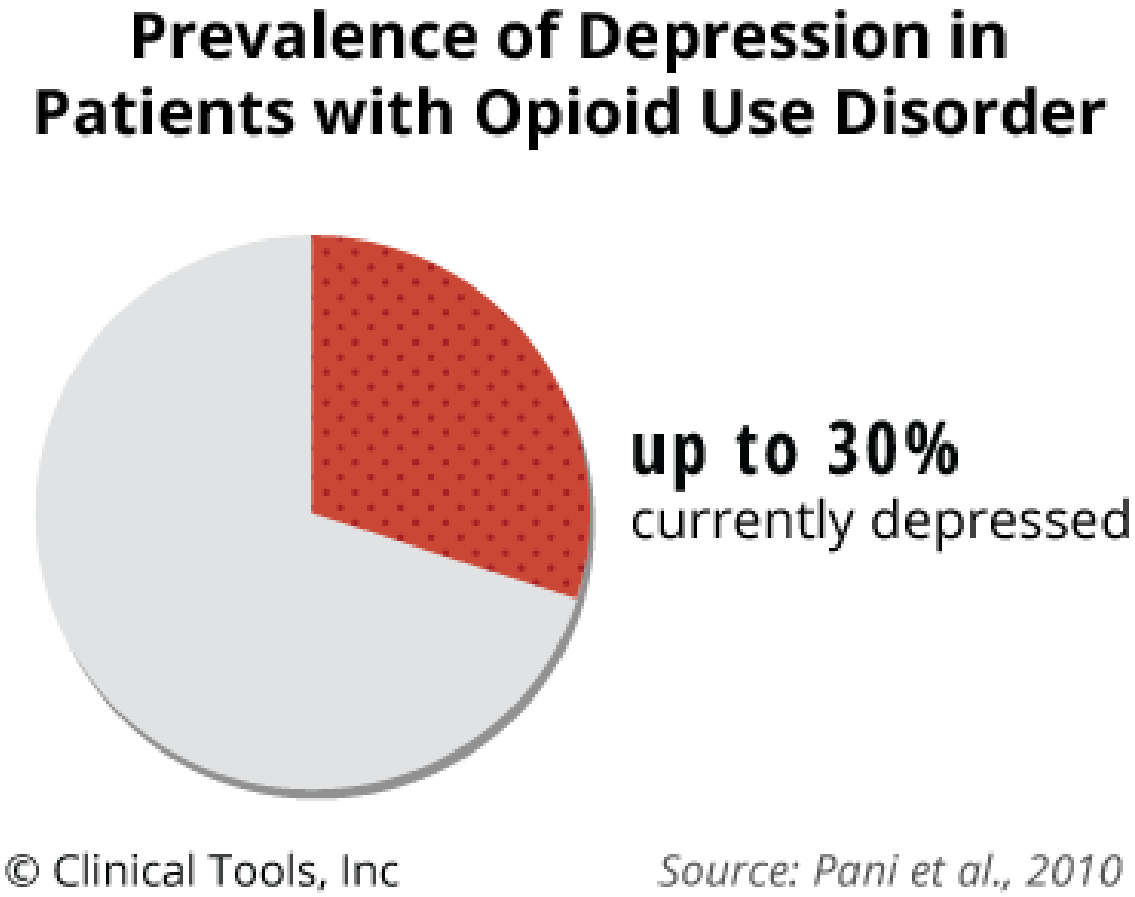
Increased Risk of Mental Illness

- Dual diagnosis of OUD with other forms of mental illness is common.
- Pre-existing psychiatric disorders are associated with increased risk of opioid misuse
  - Mood disorders: depressive disorder, bipolar I disorder,
  - Anxiety disorders: panic and generalized anxiety disorders
  - Opioid misuse more likely to lead to full OUD when these disorders are present.
- Opioid misuse also associated with later development of mental illness.

Depression: Prevalence

Most prevalent mood disorder among patients with OUD.

44% to 54% lifetime depression



Depression: Impact on MAT

- Patients with vs patients without comorbid depression:
  - Less likely to respond well to treatment
  - More likely to relapse to opioid use
  - Respond well to psychiatric intervention
  - Sometimes depression can be a manifestation of a substance use disorder and can remit rapidly after patients cease misuse
- Screening instruments:
  - Patient Health Questionnaire
  - Hospital Anxiety and Depression Scales
  - Geriatric Depression Scale
  - Edinburg Postnatal Depression

Anxiety Disorders: Prevalence

- Lifetime prevalence
  - OUD (abuse and dependence): 36%
    - Opioid dependence: 61%
  - Generalized anxiety disorder
    - Opioid dependence: 22%
  - Phobia
    - Opioid dependence: 33%

Anxiety Disorders: Impact on MAT

- Poorer quality of life
- Greater likelihood of treatment dropout
- Abuse of other substances (e.g., benzodiazepines)
- Routine treatment with pharmacotherapy is appropriate
  - Caution needed regarding use of benzodiazepines given risk of respiratory depression and lethality

Posttraumatic Stress Disorder: Prevalence

- Common among people with substance use disorders. Most common among OUD relative to other substance use disorders.
- 40.6% of people with drug dependence reported symptoms of PTSD and were diagnosed with PTSD.

Posttraumatic Stress Disorder: Impact on MAT

- ↑PTSD = ↑ severity of drug problems
- PTSD symptoms can overlap with those of opioid withdrawal
  - E.g., hypervigilance, exacerbated startle response, insomnia
- Opioid use may be a kind of self-medication for PTSD
- Good outcomes for OUD, but poor outcomes for co-occurring PTSD

Treatment for PTSD should be integrated with treatment for OUD.

Suicidality: Prevalence

- Almost half of opioid users have a past suicide attempt.
- Suicide among opioid users is approximately a third higher than in the general population.
- Up to 7% of those with opioid users die from suicide each year.
  - 20% of suicides are associated with opioids (heroin and prescription pain killers)
- In a matter of 15 years (1999 to 2014), suicide with opioid poisoning increased from 2% to 4%.

Suicidality: Impact of Treatment and MAT

- Impact of treatment: Treatment decreases risk of suicidal ideation and attempts.
- Assessment
  - Assess relative risk of committing suicide when suicidality is reported or suspected.
  - Assess whether patient wants to kill himself/herself, has access to lethal means of suicide, and “has a plan”.
  - Consider screens like the Columbia-Suicide Severity Rating Scale.

Personality Disorders: Prevalence

- Lifetime prevalence: 50%
  - More than 4x the prevalence than the general population
  - Borderline personality disorder ~50%
  - Antisocial personality disorder ~40%

Personality Disorders: Impact on MAT

- Increased difficulty of treating OUD
  - Inflexibility and maladaptive thoughts/behaviors can strain doctor-patient relationship (e.g., impulsivity, emotional reactivity)
- May not respond as well
- Are less likely to complete treatment
- Are more prone to relapse to opioid misuse after successful treatment
- Consider the following:
  - Additional time learning a patient's individual challenges
  - Additional care in communications and efforts to build trust
  - Referring patients to a higher level of care if above precautions are not possible or are ineffective

ADHD

- More careful instructions when instructing patients on correct buprenorphine usage and dosing, considering the patient's attention span
- Additional treatment structure
- Additional follow-up phone calls during induction and stabilization
- Additional psychosocial support (e.g., 12-step program)

Polysubstance Use

- Cocaine use is most common among patients with addiction to heroin
  - 75% concurrent use
- Alcohol can be abused by licit and illicit drug users.
- Benzodiazepines are lethal with opioids
  - Goal should be to decrease or discontinue use of benzodiazepines
  - BHPs can help patients address anxiety in other ways
- Marijuana is commonly used because it helps manage withdrawal symptoms.

Differentiating Between Opioid-Induced vs. Opioid Independent Psychiatric Disorders

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Order of Onset	Psychiatric disorder not a cause of opioid misuse if it developed after the patient began using opioids.
Family History	Family history of mental illness increases likelihood that mental illness is independent of opioid misuse.
Symptoms During Abstinence	Psychiatric disorders that persist during periods of abstinence (from both opioids and all other substances of abuse) are much more likely to be independent of opioid misuse.

Treatment of Induced Psychiatric Disorders

- Resolve once opioid use stops (especially depression)
- Stability as first therapeutic step
  - Psychiatric intervention necessary only in severely affected patients (i.e., suicidal patients)
- Reverse treatment sequence may be necessary, i.e., stabilization of psychiatric illness before buprenorphine treatment

Module 4 Summary

- Motivational interviewing is effective. It can facilitate connecting with patient and can help enhance motivation to seek treatment.
- Use of screening instruments is valuable.
- Buprenorphine treatment is indicated for moderate to severe OUD.
- Dual diagnosis of OUD with other forms of mental illness is common and can affect treatment.
- BH providers can help address mental health concerns underlying OUD.

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