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Understanding and Assessing Opioid Use Disorder in Patients with Chronic Pain

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[2]These individuals were involved in the 2021 review, update, and approved rerelease of this activity.

Educational Objectives

At the conclusion of this activity participants should be able to:

- Describe a neurobiological framework/explanatory model for patients with chronic pain and opioid use disorder
- Recognize that differentiating opioid use disorder from pain is a complex task
- Identify key features of opioid use disorder
- Describe how to perform an opioid use disorder evaluation in primary care

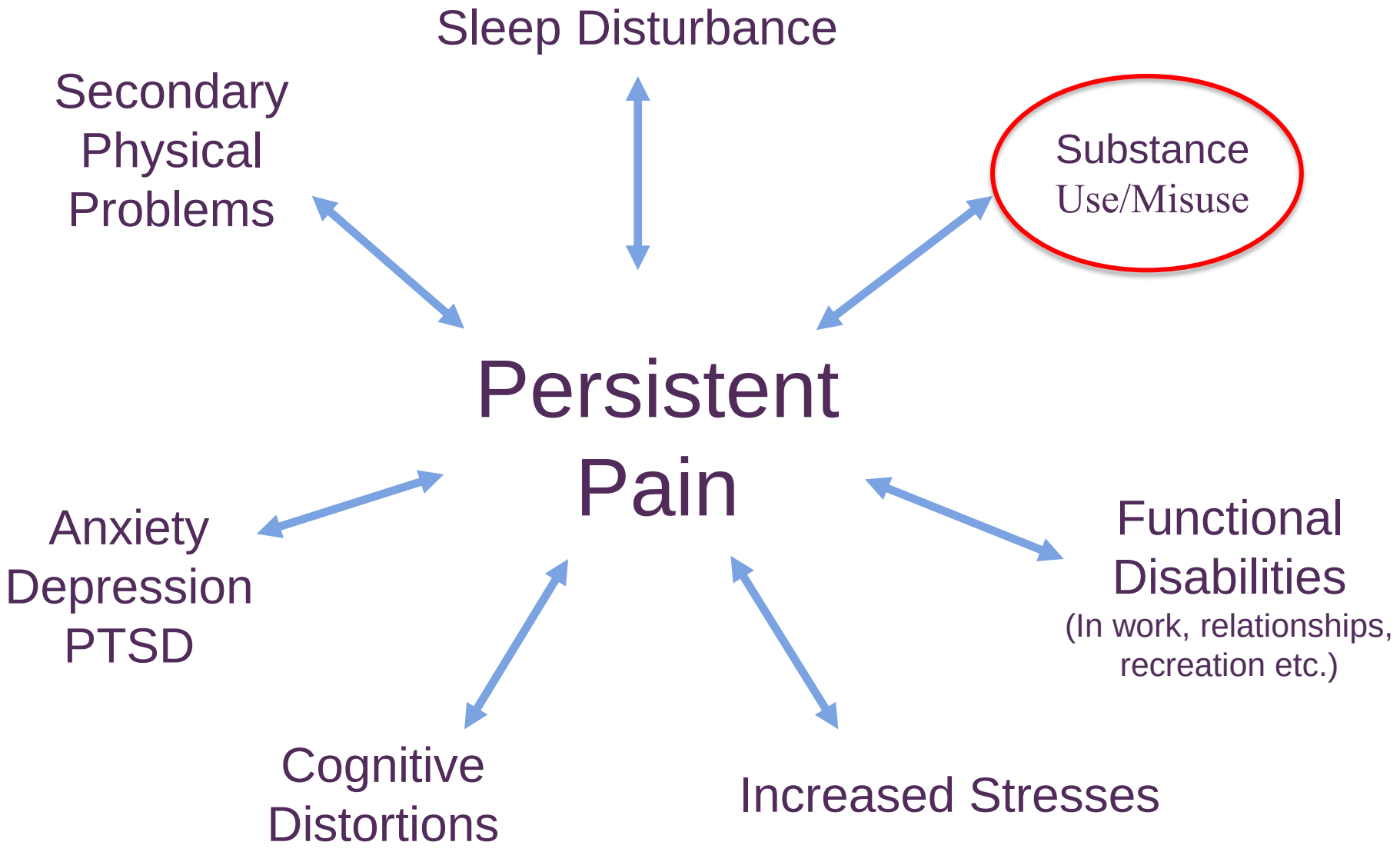
Case

- 35 yo female with chronic daily migraine and diffuse myofascial pain who has been prescribed opioids for 5 years after the birth of her daughter. The patient has severe depression and anxiety, chronic nausea, history of adverse childhood experience (neglect as a child), and obesity. She is a stay at home mother to her 2 children, but frequently has to put the children in daycare because she can not care for them when she has severe migraines. She is also prescribed chronic high dose benzodiazepines by a psychiatrist.

- The patient has a history of losing her opioid prescription, obtaining opioids from another provider, being allergic to most other pain medication options, missing appointments, and frequently asking for opioid dose increases.

Case: Thought Questions

- Does this patient have pain?
- Does this patient have an opioid use disorder?
- What factors place this patient at risk for an opioid use disorder?
- What can you do to help this patient?



Whatever its cause, when pain persists, it often causes secondary problems that can in turn facilitate distress and pain.

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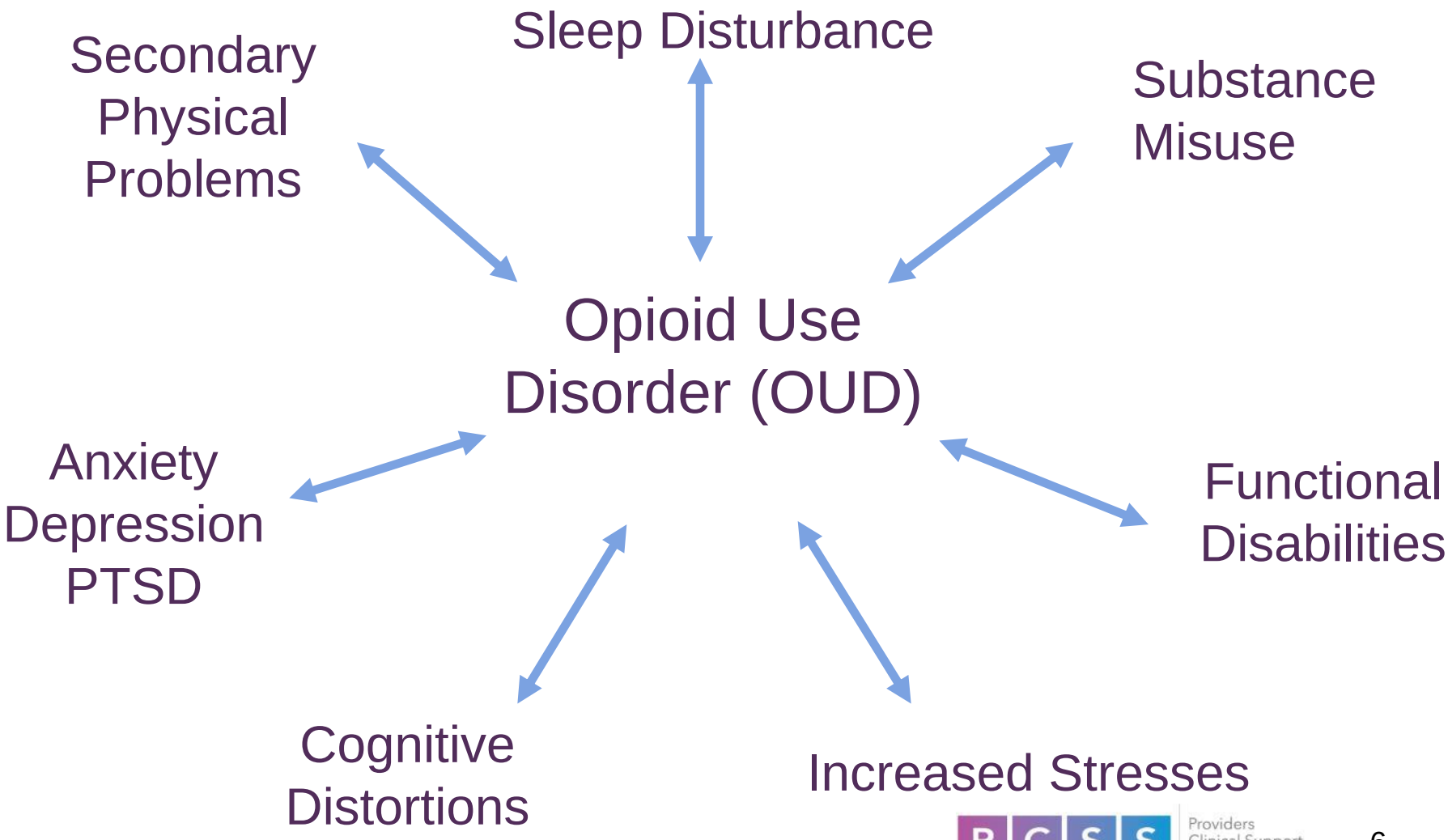
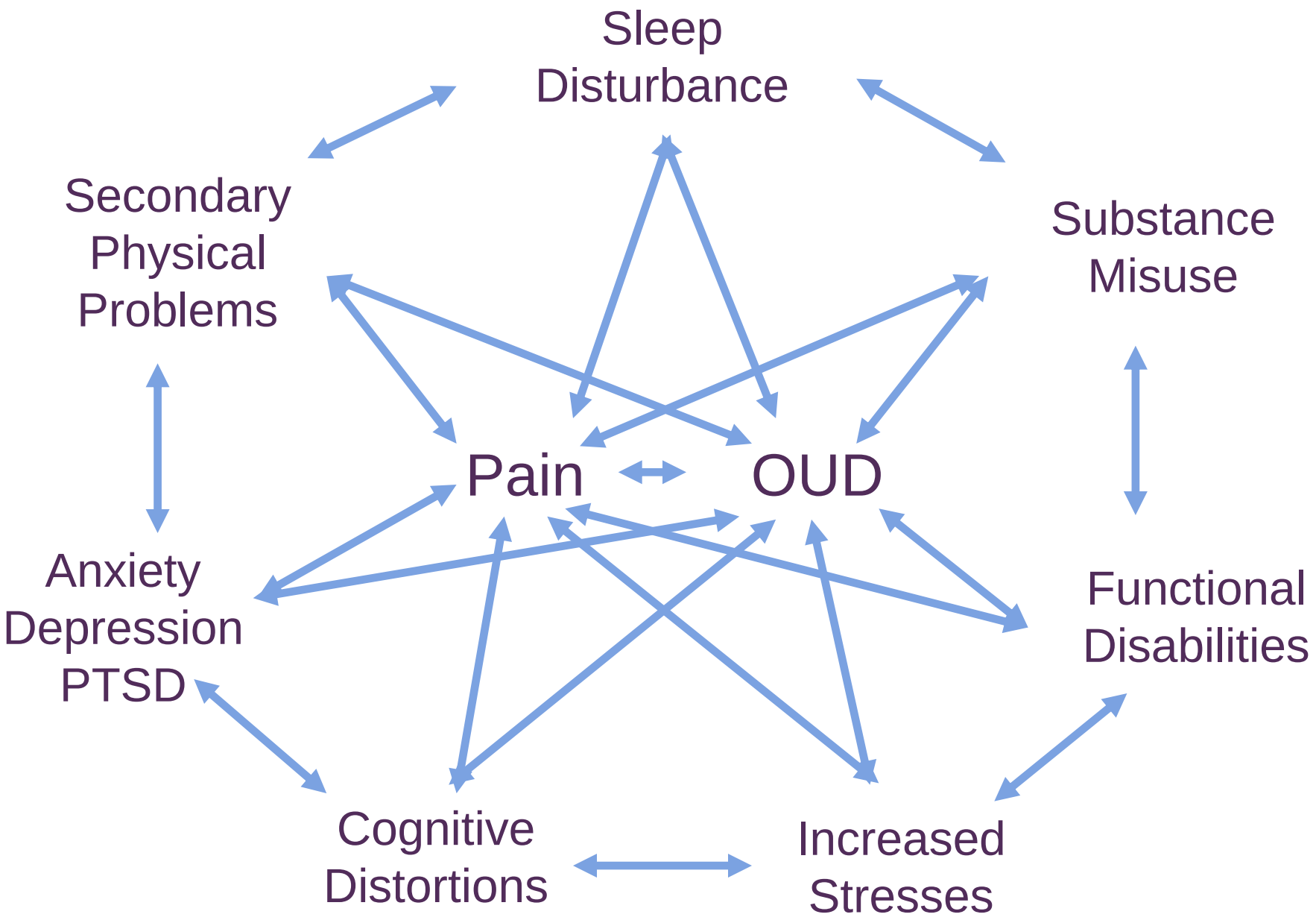
As a chronic condition, OUD shares similar challenges as persistent pain





When OUD and pain co-occur they may reinforce one another. Need to address both to successfully treat pain.

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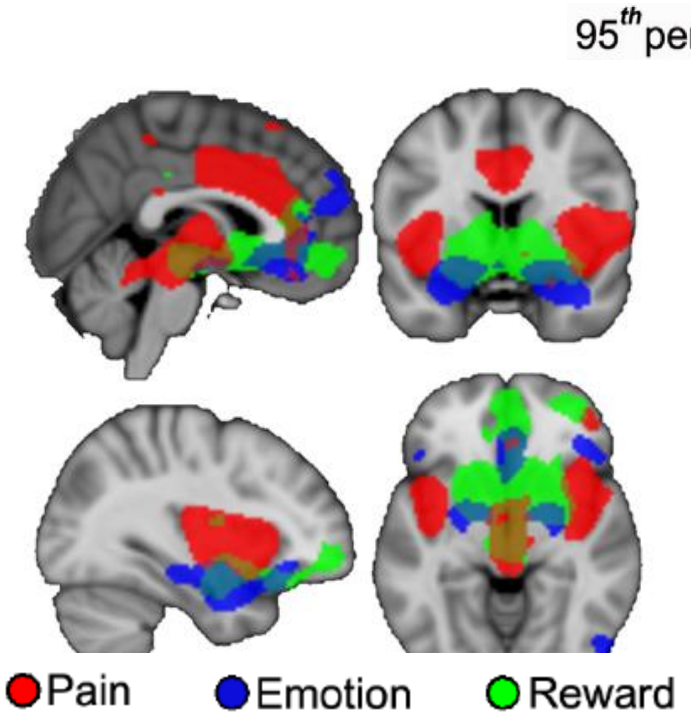
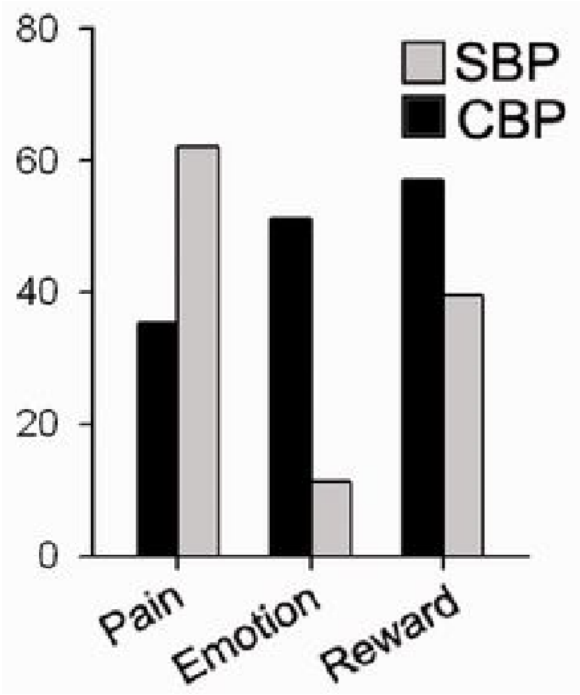
What is the underlying neurobiological mechanism that explains the complex interaction between pain and opioid use disorder?

Understanding Reward and Emotion in Chronic Pain

Reward learning processes may contribute to persistence and amplification of pain

SBP = subacute back pain
CBP = chronic back pain





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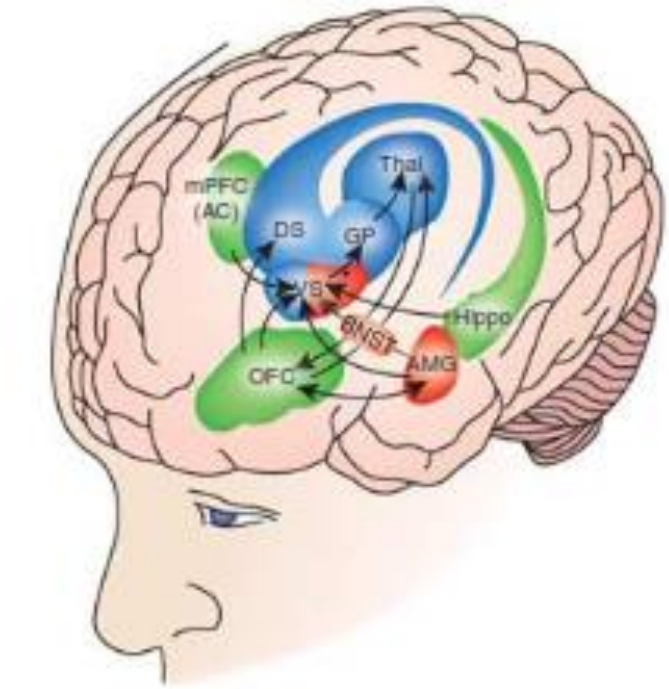
Hashmi JA et al, 2013

Neurocircuitry of Substance Use Disorders

- Three stages of addiction that promote drug-seeking
  - #1: Binge/intoxication (basal ganglia)
    - Effects motivation for a substance via dopamine and opioid peptides
    - Plays a key role in pain-relief seeking also

Koob, Volkow, Neuropsychopharmacology, 2010.

Neurocircuitry of Substance Use Disorders



- Three stages of addiction that promote drug-seeking
  - #2: Withdrawal/Negative Affect Stage (nucleus accumbens and amygdala)
    - Loss of reward
    - Dysphoria
    - Pain
    - anxiety

Koob, Volkow, Neuropsychopharmacology, 2010.

Reward Transmitters Implicated in the Motivational Effects of Repeated Drug Use

Positive Hedonic Effects	Negative Hedonic Effects of Withdrawal
↑ Dopamine	↓ Dopamine – "dysphoria"
↑ Opioid Peptides	↓ Opioid Peptides – pain
↑ Serotonin	↓ Serotonin – "dysphoria"
↑ GABA	↓ GABA – anxiety, panic attacks

Koob, Volkow, Neuropsychopharmacology, 2010.

Anti-Reward Transmitters Implicated in the Motivation Effects of Repeated Drug Use

Positive Hedonic Effects
⇧ Dynorphin – "dysphoria"
⇧ Corticotropin-Releasing Factor (CRF) – stress
⇧ Norepinephrine – stress
These are ACTIVATED in amygdala and ventral striatum during withdrawal

Koob, 2012
Koob, Volkow, Neuropsychopharmacology, 2010.

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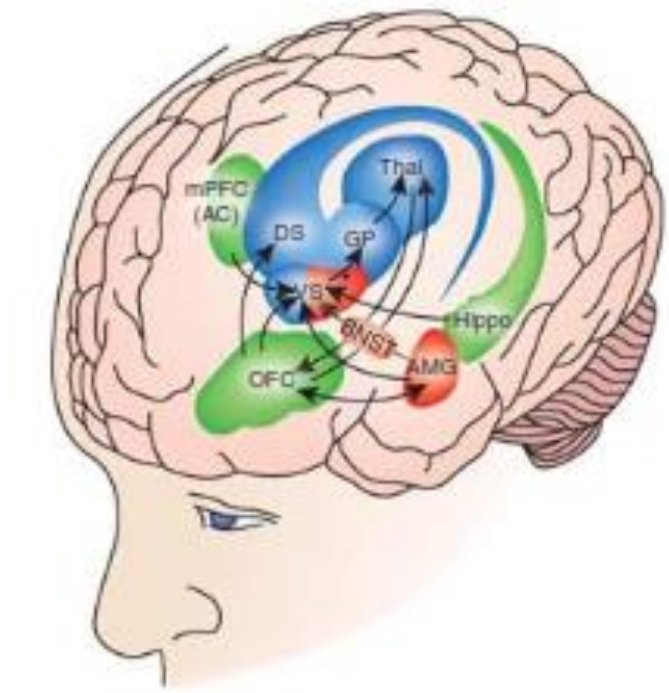
Neurocircuitry of Substance Use Disorders



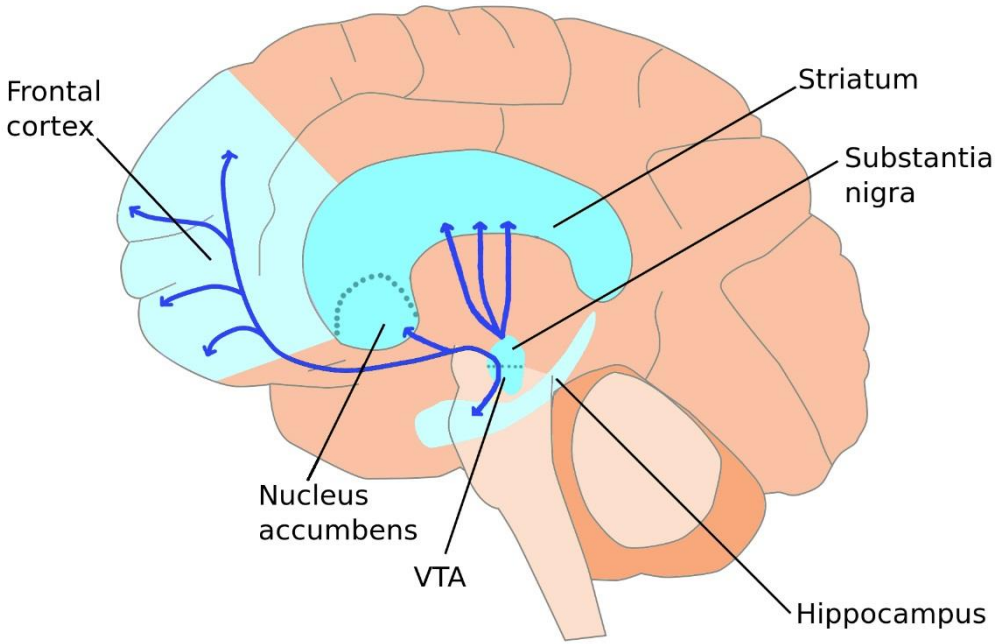
- Three stages of addiction that promote drug-seeking
  - #3: Preoccupation/craving (basolateral amygdala, hippocampus)
    - Loss of executive functioning and decision making
    - Impulsivity
    - Compulsivity
    - Sleep disturbances

Koob, Volkow, Neuropsychopharmacology, 2010.

The Reward System in Pain

A Quick Decision-Making Process:

1. Dopamine neurons* from **Ventral Tegmental Area (VTA)** estimate value of reward/relief-seeking opportunity
2. **Nucleus Accumbens (NAc)** listens, makes decision to proceed
3. **Frontal cortex** also receives information from VTA, can inhibit NAc, but is slow and may be impaired



https://www.oist.jp/news-center/photos/dopamine-pathways

* The larger the dopamine input, the more likely you are to do that behavior

Trafton, 2015

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So What's the Problem?

- The reward system is crucial for survival; if out of balance, it takes over: impulsivity, search for immediate gratification, unable to tolerate distress
- Addictive drugs and search for pain relief can dump tons of dopamine into these circuits
- Addictive drugs increase activity in these neurons, or prolong actions of neurotransmitters they release
- New research show pain relief activates these neurons to drive habitual relief seeking

Trafton, 2015

Example: The Couch

Pain will shape reward learning circuits:

- VTA detects the couch as opportunity for relief, NAc says “go for it!”
- Back pain gets better, and your brain listens: “I got reward!”
- Your brain will refer that relief back to the laying down, reinforce its as new context
- However, the next time you lie down, you may not get as much reward
- If you try something else, you might get more dopamine the next time

People with pain are attracted to quick relief (lying down, guarding, help-seeking, self-medication), but not necessarily recovery

Trafton, 2015

What Happens Over Time?

Chronic dopamine firing reshapes these circuits, making them very fast and hard to control.

Accelerator:
D1 receptor

D1 Receptors: Dopamine in the receptors tells Nucleus Accumbens to say "Yes!"

Brakes:
D2 receptor

D2 Receptors: Activation of these receptors slows decision-making; allows frontal cortex time to step in

Trafton, 2015

Too Much Accelerator is a Bad Thing

- When DA neurons are chronically over-active, they activate D1 receptors:
  - D1 pathway becomes more efficient, speeding up decisions to seek relief
  - Activate anti-reward circuits (dynorphin, CRF, NE)
  - Increase stress response and worsen mood – both amplify pain signals
  - Pain severity increases and relief-seeking behaviors become compulsive

Trafton, 2015

What Happened to the Brakes?

What happened to D2/Inhibitory Pathway?

- Big spikes in dopamine desensitize and internalize D2 receptors
- D2 receptor can't work again until it is recycled (takes an hour) or a new receptor is synthesized

You may ultimately wind up with a system that has no brakes

Trafton, 2015

Summary – An Addiction-Like State

- Coupled with complex social, psychological, and biological stresses, certain people can be “primed” for development of severe chronic, complex pain and opioid use disorder
- Both substance use disorder (SUD) and pain-relief seeking behaviors **activate, and over-stress, the reward system**
- In both SUD and pain, **when the reward system is over-activated, anti-reward neurotransmitters in the limbic system are enhanced**, causing stress, negative affect, impulsivity, inducing compulsive behaviors to alleviate feeling lousy
- In both SUD and chronic pain, **the executive function of the pre-frontal cortex is impaired**, unable to exert control over ventral striatum and limbic system, preventing activities that promote recovery

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Implications for Chronic Pain

- All about dysregulated dopamine
- In rats: increased place preference for opioids, more social anxiety, greater consumption of sugar water

- People with dysregulated dopamine systems are more likely to develop chronic pain:
  - Acute injury chronic pain
  - Drugs that increase dopamine chronic pain
  - Smokers and people given high dose opioids after injury chronic pain even after injury heals

Trafton, 2015

Other Implications for Chronic Pain

- The addicted brain may amplify pain to justify a substance it craves
- Alternating withdrawal and intoxication can physiologically drive pain (sympathetic and psychomotor activation)
- Intoxication may mask pain and permit recurrent injury or overuse
- Intoxication impairs adherence to treatment plan

Trafton, 2015

Which patients with chronic pain are at most risk to develop opioid use disorder?

Risk Factors for Opioid Use Disorder Development

- Published rates of opioid use disorder in people with chronic pain are 4-26%
- Suggests that known risk factors for opioid use disorder in the general population would be good predictors for problematic prescription opioid use
  - Lifetime history of substance use disorder[2]

    -Past alcohol, tobacco[4], cocaine, or cannabis use[1]
  - Family history of substance use disorder, a history of legal problems[3]
  - Heavy tobacco use[4]
  - History of severe depression, anxiety, or PTSD[4]

1. Ives T et al. BMC Health Services Research 2006
2. Reid MC et al JGIM 2002
3. Michna E el al. J Pain and Symptom Management 2004
4. Akbik H et al. J Pain and Symptom Management 2006

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Principle Risk Factors for Opioid Use Disorder

- Younger age, 13-45 years of age
- Previous substance use disorder
- Back pain, headache
- High dose chronic opioid dose

  > 90 mg morphine equivalents/day

Edlund MJ, Martin BC, Devries A, Fan MY, Braden JB, Sullivan MD. *Trends in use of opioids for chronic noncancer pain among individuals with mental health and substance use disorders: the TROUP study*. Clin J Pain. 2010 Jan;26(1):1-8.

Which Individuals are Most Likely to be Prescribed Opioids

- Those with greater number of pain diagnoses
- Those with mental health and substance use disorders
- Adverse selection – recipients of chronic opioid therapy are also most likely to develop opioid use disorder

Concentration of Opioid Use Among Patients with Chronic Pain

- Yearly total opioid use is highly concentrated
- 5% of CNCP patients use 70% of total opioids (in Morphine Equivalent Dosing)
- No other types of prescription medications show this degree of concentration among recipients

Edlund MJ, Martin BC, Fan MY, Braden JB, Devries A, Sullivan MD. *An analysis of heavy utilizers of opioids for chronic noncancer pain in the TROUP study*. J Pain Symptom Manage. 2010 Aug;40(2):279-89.

Why does Adverse Selection Occur?

- Providers want to help patients in pain and have few tools other than prescription pad
- Patients with mental health and substance use disorders and multiple pain problems are more distressed (pain and psychological symptoms) and more persistent in demanding opioid initiation and dose increases
- Providers write opioid prescriptions as a “ticket out of the exam room”

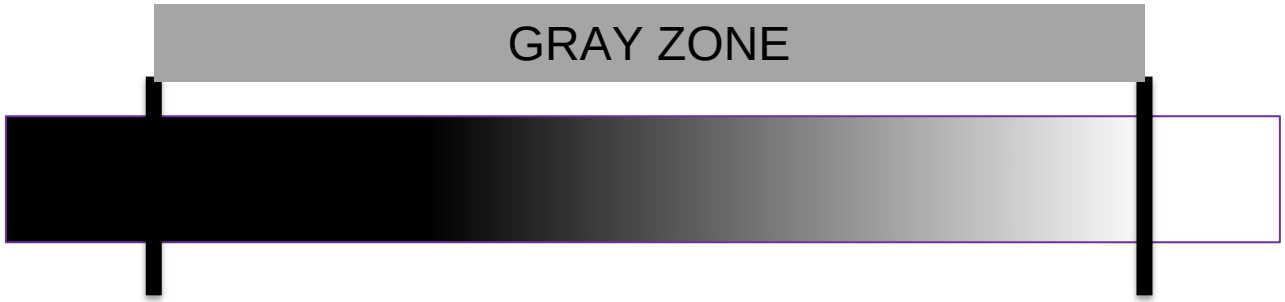
Edlund MJ, Martin BC, Devries A, Fan MY, Braden JB, Sullivan MD. *Trends in use of opioids for chronic noncancer pain among individuals with mental health and substance use disorders: the TROUP study*. Clin J Pain. 2010 Jan;26(1):1-8.

How we think of addiction

How we think of dependence on pain medication

Are they biologically any different?

Photograph: The guardian.

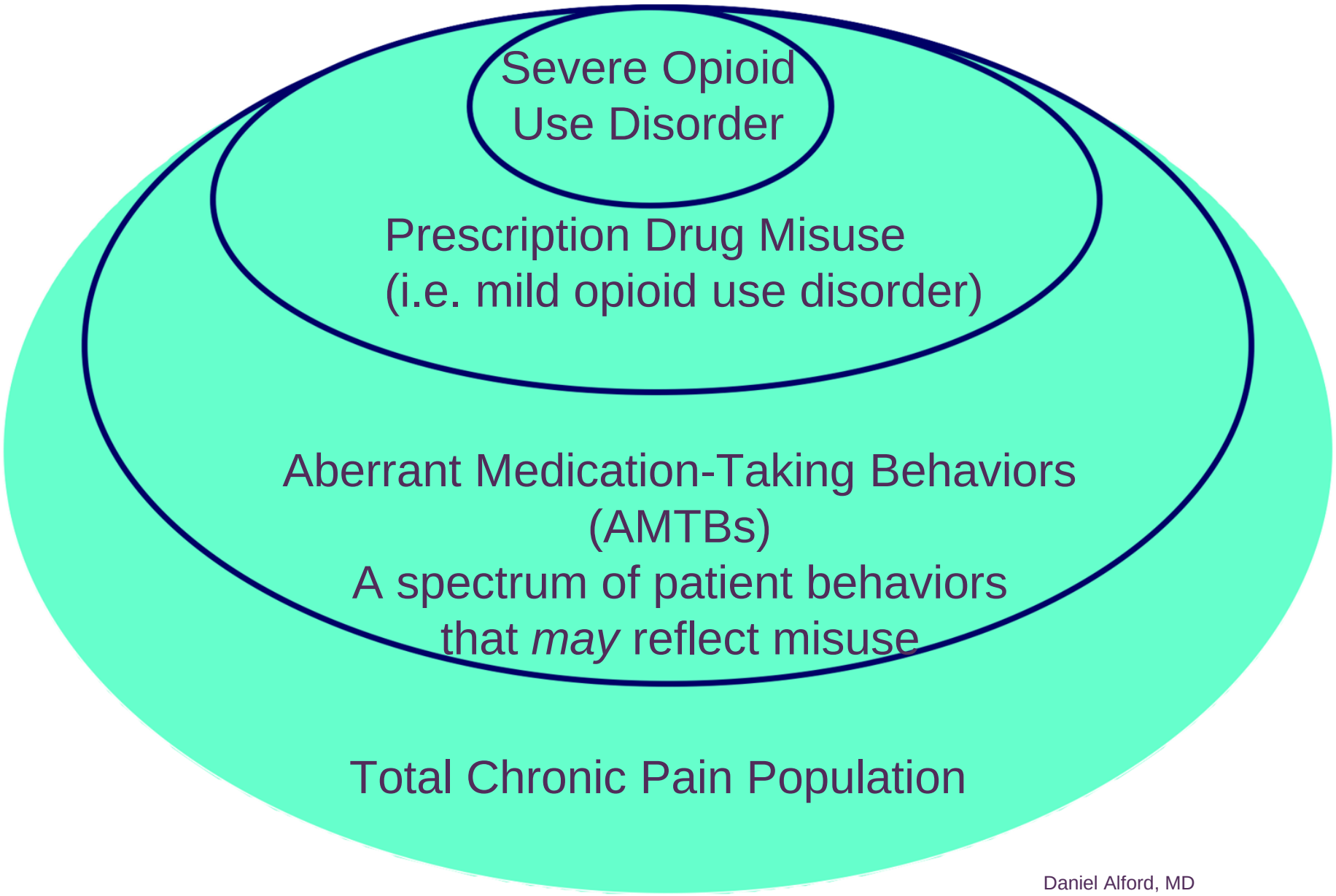


HAS AN ADDICTION

Meets DSM criteria for opioid use disorder

DOES NOT HAVE AN ADDICTION

- No lost prescriptions
- No ER visits
- No early prescriptions
- No requests for dose escalation
- No UDT aberrancies
- No doctor shopping (PMP)



Daniel Alford, MD

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Adapted from Steve Passik. APS Resident Course, 2007

Spectrum of Opioid Use Disorder

- Self medication (chemical coping)
  - Mood
  - Sleep
  - Traumatic memories
- Prevent withdrawal
- Reward (to get high)
- Opioid Use disorder
- Diversion for profit

- **Medication or substance misuse by persons with pain may occur for diverse reasons. Helps to identify and address the driver of misuse. Misuse may be self-limited or may be a sign of opioid use disorder in vulnerable people.**

Continuum of Problematic Opioid Use

Mild indiscretion → Repeated misuse → Opioid use disorder → Severe Opioid Use Disorder (i.e. addiction)

Photo from
http://mediad.publicbroadcasting.net/p/wnpr/files/styles/related/public/201603/PillBottle.jpg

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Behaviors Observed with Use of Opioids

Dependence/addiction develops through pain treatment

- Using opioids to treat pain
- Predominant symptom of withdrawal - pain

Dependence/addiction develops through non-prescribed drug use

- *Need to procure opioid*
- Often use paraphernalia
- Predominant symptom of withdrawal - anhedonia

DSM Criteria

- Social Disruption
- Loss of control over use
- Continued use despite knowledge of harm
- (Craving)

(may not be manifest until off)

Do not accept that anything is wrong other than pain

Accept that they have an opioid use disorder

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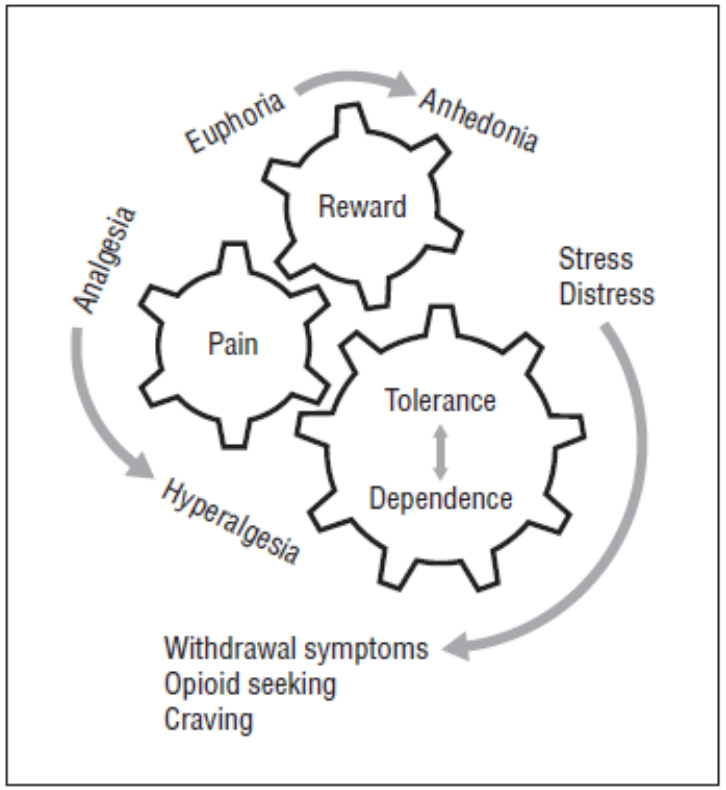
Opioid Dependence vs. Opioid Use Disorder

"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment…Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long-term pain therapy."



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Ballantyne, Sullivan, Kolodny,. Archives of IM, 2012

THE AMERICAN JOURNAL OF PSYCHIATRY

psychiatryonline

From: DSM-5 Criteria for Substance Use Disorders (SUD): Recommendations and Rationale

Am J Psychiatry. 2013;170(8):834-851. doi:10.1176/appi.ajp.2013.12060782

	DSM-IV Abuse[a]		DSM-IV Dependence[b]		DSM-5 Substance Use Disorders[c]	
Hazardous use	X	≥1 criterion	–		X	≥2 criteria
Social/interpersonal problems related to use	X		–		X	
Neglected major roles to use	X		–		X	
Legal problems	X		–		–	
Withdrawal[d]	–		X	≥3 criteria	X	
Tolerance	–		X		X	
Used larger amounts/longer	–		X		X	
Repeated attempts to quit/control use	–		X		X	
Much time spent using	–		X		X	
Physical/psychological problems related to use	–		X		X	
Activities given up to use	–		X		X	
Craving	–		–		X	

DSM-5 Criteria: 2-3 = mild SUD, 4-5 = moderate SUD, >6 severe SUD

Opioid Use Disorder in Clinical Practice

- The 4 C's
  - Loss of Control
  - Compulsive use
  - Continued use despite harms
  - Craving

Savage SR, et al. J Pain Symptom Manage. 2003;26:655-667.

Features of prescription OUD

- Inconsistent health care use patterns (e.g., missed appointments, lack of engagement with non-medication treatments)
- Signs/symptoms of drug use (e.g., intoxication, overdose, track marks)
- Emotional problems/psychiatric issues
- Illicit drug use
- Problematic medication behavior (escalating doses, early refills)
- Family concerns about use
- Functional stagnation, loss of roles
- Extreme difficulty with even a slow opioid taper

Implications

- Concern comes from the “pattern” or the “severity”
- Differential diagnosis

Butler et al. Pain. 2007

Concerning Behaviors for Opioid Use Disorder

Spectrum: Yellow to Red Flags

- ☐ Requests for increase opioid dose
- ☐ Requests for specific opioid by name, "brand name only"
- ☐ Non-adherence w/other recommended therapies (e.g., PT)
- ☐ Running out early (i.e., unsanctioned dose escalation)
- ☐ Resistance to change therapy despite AE (e.g. over-sedation)
- ☐ Deterioration in function at home and work
- ☐ Non-adherence with monitoring (e.g. pill counts, UDT)
- ☐ Multiple "lost" or "stolen" opioid prescriptions
- ☐ Illegal activities – forging scripts, selling opioid prescription

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Modified from Portenoy RK. J Pain Symptom Manage. 1996 Apr;11(4):203-17.

Does the patient with chronic pain who is prescribed opioids have an opioid use disorder?

1. Unable to fulfill role obligations – **MAYBE**
2. Social or interpersonal problems due to use – **MAYBE**
3. Hazardous use – **MAYBE**
4. Tolerance – **DOES NOT APPLY***
5. Withdrawal/physical dependence – **DOES NOT APPLY***
6. Taken in larger amounts or over longer period – **MAYBE**
7. Unsuccessful efforts to cut down or control – **MAYBE**
8. Great deal of time spent to obtain substance – **MAYBE**
9. Important activities given up or reduced – **MAYBE**
10. Continued use despite harm – **MAYBE**
11. Craving – **MAYBE**

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*If opioids are prescribed, this criterion does not apply.

Initial Evaluation of Opioid Use Disorder for the PCP

- Normalize the process as part of Universal Precautions
- Appreciate the fear and stigma associated with opioid use disorder in patients with chronic pain

Initial Evaluation of OUD for PCPs

- Confirm and describe the chronic pain condition
  - Is a diagnosis possible?
  - Would further evaluation prove beneficial?
- Confirm functional improvement with pain medication
  - In the absence of functional improvements, the patient may be experiencing therapeutic failure of opioids
  - No functional benefit = lack of opioid benefit, so why would opioids be continued?
- Confirm and describe that appropriate treatment has been offered or failed
  - Are there treatments that could be optimized?
  - Have non-medication options been tried and/or failed?

Initial Evaluation of OUD for PCPs

- Describe patient's side effects from the medication
- Describe patient's relationship with healthcare providers and any concerning behavior
  - Describe prescription history: lost medications? Stolen medications? Frequent ED visits? Concerning reports from loved ones?
- Describe patient's substance use disorder history or current substance use history
- Describe concomitant psychosocial factors
  - Depression, sexual use history, marital, financial or job stress
  - PHQ-9, GAD, Pain Catastrophizing Scale, Chronic Pain Self-Efficacy

Sullivan MJ, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychol Assess. 1995; 7(4):524–32.
Anderson KO, Dowds BN, Pelletz RE, Edwards WT, Peeters-Asdourian C. Development and initial validation of a scale to measure self-efficacy beliefs in patients with chronic pain. Pain. 1995;63(1):77–84.

Diagnostics

- Random Urine Drug Testing
  - Including evaluation of alcohol use (ethyl glucuronide)
  - See Risk Assessment, Mitigation, and Management Lecture
- Random Pill Counts
- Prescription Drug Monitoring Data
- Review of medical records
- Discuss case with other prescribers and/or family members

Questionnaires

- Current Opioid Misuse Measure (COMM™)
  - Helps to identify patients at high risk for current aberrant medication-taking behavior
  - A high score raises concern for opioid use disorder, but is NOT diagnostic

- Screening Tool for Addiction Risk (STAR)
  - Self-report
  - Corresponds to DSM-IV criteria

Butler SF, Pain. 2007; 130:144-156.
Robert Friedman, et al. Pain Medicine Jun 2003, 4 (2) 182-185

Diagnosis

- There is not ***one*** test or questionnaire that can confirm prescription opioid use disorder.
- The initial PCP evaluation will provide the basis for a risk/benefit determination
- This initial evaluation will place a focus not only on concerning behavior, but also on pain and pain care
  - You can have pain and OUD
  - Treating pain with opioids in the setting of OUD is risky
  - Treating OUD without treating pain is also not likely to be effective
- Based on initial evaluation, consider referral for diagnosis of an OUD if you do not feel comfortable making it
- Ultimately, diagnosis made by DSM V criteria

What Next?

- Make a risk-benefit ratio judgement of the treatment, not the patient.
- If the risks outweigh the benefit, refer the patient and stop or taper opioids
- Continue to treat pain with non-opioid treatments
- Encourage the patient to seek medication assisted treatment for OUD

OUD Medication Treatments
See also PCSS

- Naltrexone (oral or Intramuscular)
  - Opioid antagonist
  - Possible pain relief at very low doses
  - May not work well for patients who have pain

- Methadone
  - Full opioid agonist
  - Analgesia for 4-6 hours
  - Only legally dispensed through a federally qualified opioid treatment program for treatment of OUD

- Buprenorphine
  - Partial opioid agonist
  - Analgesia for 4-6 hours, can be dosed BID or TID for improved pain management
  - Can be utilized to help patients taper off of opioids
  - Office based prescribing with DEA waiver or “X license” after completing online training*
    - Online Waiver Training

*As of 4/27/21 the Practice Guidelines for the Administration of Buprenorphine for Treating Opioid Use Disorder exempt eligible prescribers from federal certification requirements related to training, counseling, and other ancillary services that are part of the process for obtaining a waiver to treat up to 30 patients with buprenorphine.

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Back to the Case

- Patient undergoes a full opioid use disorder assessment and is determined to have a moderate opioid use disorder based on failure to fulfill roles, continued use despite harms, time spent procuring medication, and craving. She is reluctant and scared to consider alternative treatments or seek opioid use disorder treatment, but is appreciative of the honest assessment of her condition. She would like to think about the idea.
- Two weeks later she makes an appointment to see you and seeks treatment for her OUD.
- Three months after stabilizing and starting buprenorphine/naloxone along with cognitive behavioral therapy, she says “Thank you so much for helping me. I am myself again. I am finally enjoying my life with my kids and am thinking about starting a small business.”

Case: Thought Questions

- Does this patient have pain? YES
- Does this patient have an opioid use disorder? YES
- What factors place this patient at risk for an opioid use disorder?
  - Personality traits
  - Young age of opioid initiation
  - Concomitant use of benzodiazepines, possible synergism or cross addiction/dependency
  - Mental illness placing at greater vulnerability for chemical coping
  - Adverse childhood experiences
  - History of medication non-adherence (lost prescriptions, possible compulsive use or medication)
  - Possible frequent bouts of opioid withdrawal from overuse of opioids causing negative affective motivation and craving

Case: Thought Questions

- What can you do to help this patient?
  - Identify underlying biopsychosocial factors that are contributing to her pain
  - Identify neural processes that may be contributing to her behavior
  - Guide her toward activities and treatment modalities that increase D2 receptors (low level dopamine input)
    - Limit use of addictive drugs or medications, tobacco, fast-acting analgesics, etc.
    - Social reinforcement, problem-solving, effective emotional coping, small goal achievement, quality of life activities
  - Offer her safe and effective treatment for her pain and opioid use disorder

Conclusions

- Chronic pain and substance use disorders share many common features that can motivate a person's behaviors
- Diagnosing opioid use disorder during pain management is difficult and requires a thorough evaluation
- Typical substance abuse risk factors probably apply to prescription opioid use disorder
  - High risk groups include young individuals, cigarette smokers with comorbidity psychiatric conditions and high dose opioid analgesic treatment
- Manage opioid use disorder by referring to substance use treatment and considering medication for opioid use disorder, including buprenorphine, methadone, and naltrexone

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PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.
- PCSS Mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medications for opioid use disorder (MOUD)**.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
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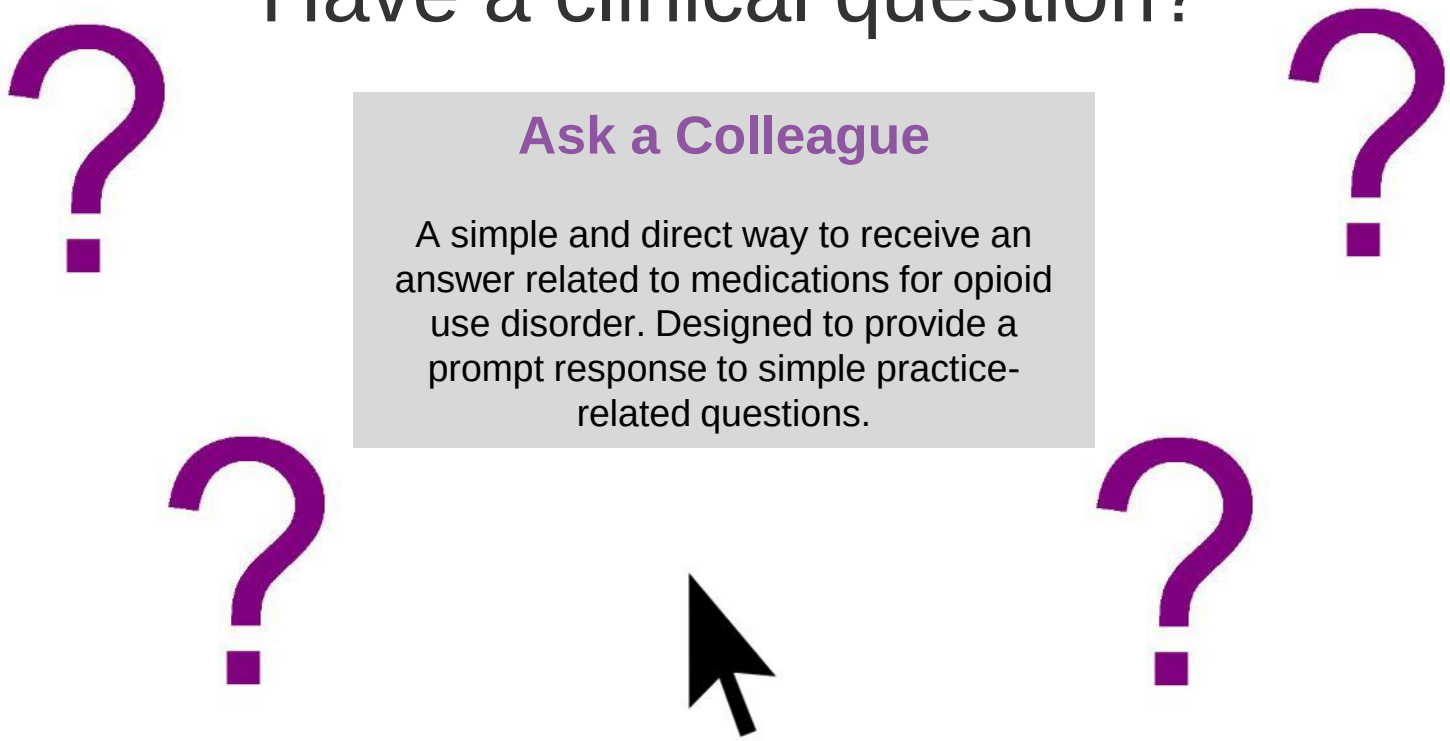

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PCSS is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with:

Addiction Technology Transfer Center	American Society of Addiction Medicine
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American Academy of Pain Medicine	Association for Multidisciplinary Education and Research in Substance use and Addiction
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