

TREATING PAIN IN THE PATIENT WITH SUBSTANCE USE DISORDER

Ebtesam Ahmed, Pharm.D., M.S.

Clinical Professor

Clinical Pharmacist Specialist

St. John's University College of Pharmacy

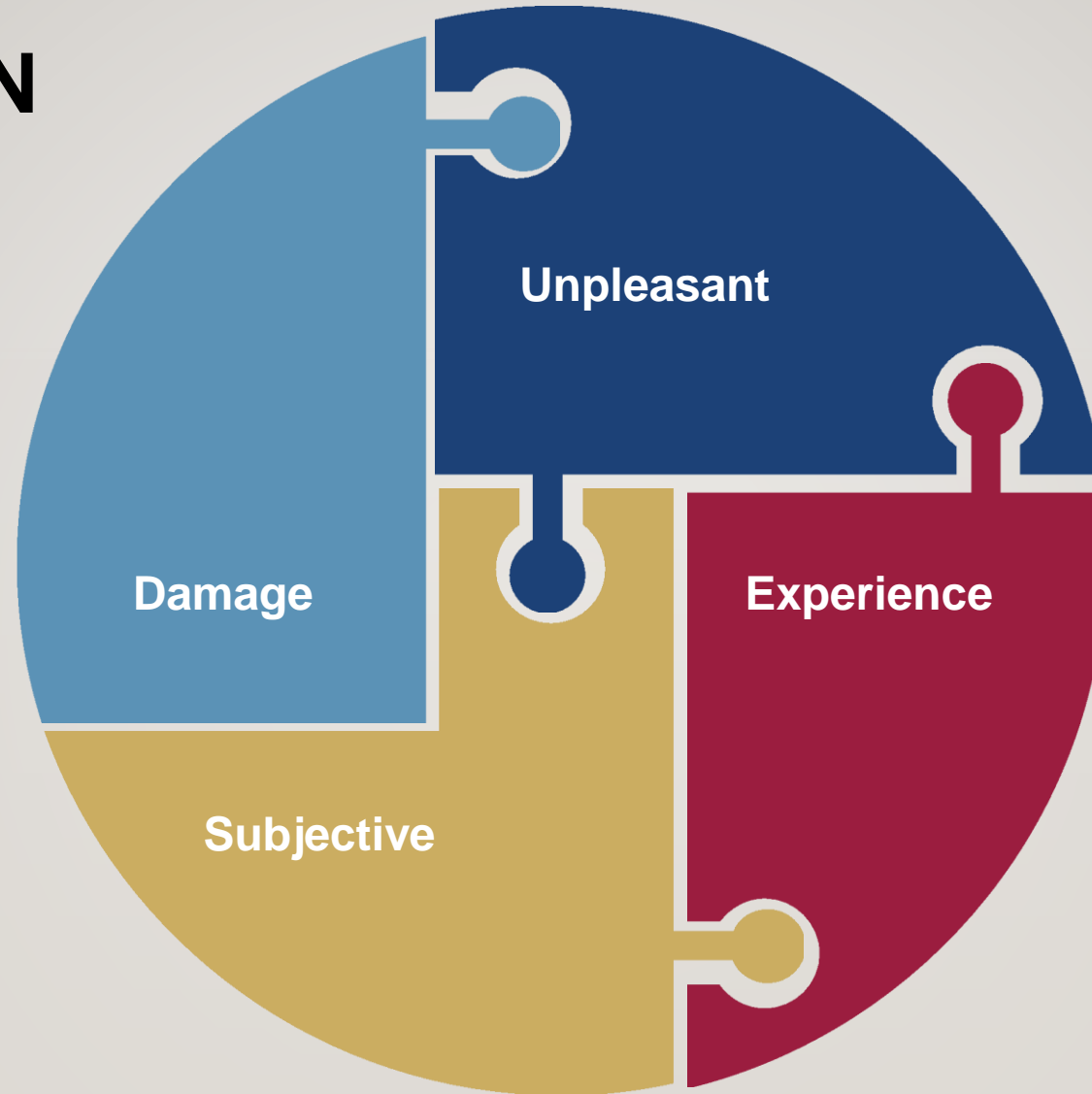
FINANCIAL RELATIONSHIP DISCLOSURES

- Ebtesam Ahmed: no financial relationships or other interests to disclose
- Bennett Doughty: Speaker's Bureau for PsychU-Otsuka, Speaker for AchieveCE
- Nicole Cieri-Hutcherson (planning committee): no financial relationships or other interests to disclose
- Chung-Shien Lee (planning committee): Advisory Board for Takeda
- Calvin Meaney (planning committee): Advisory Board for GSK, Consultant for Wolters Kluwer
- This activity is funded by NYSACCP and NYSCHP, no external funding was received for this program.

LEARNING OBJECTIVES

1. Explain the pharmacology of medication assisted therapy and its interaction with common pain medications
2. Describe barriers to optimal pain management in patients with substance use disorder
3. Summarize pain management treatment strategies in patients with substance use disorder

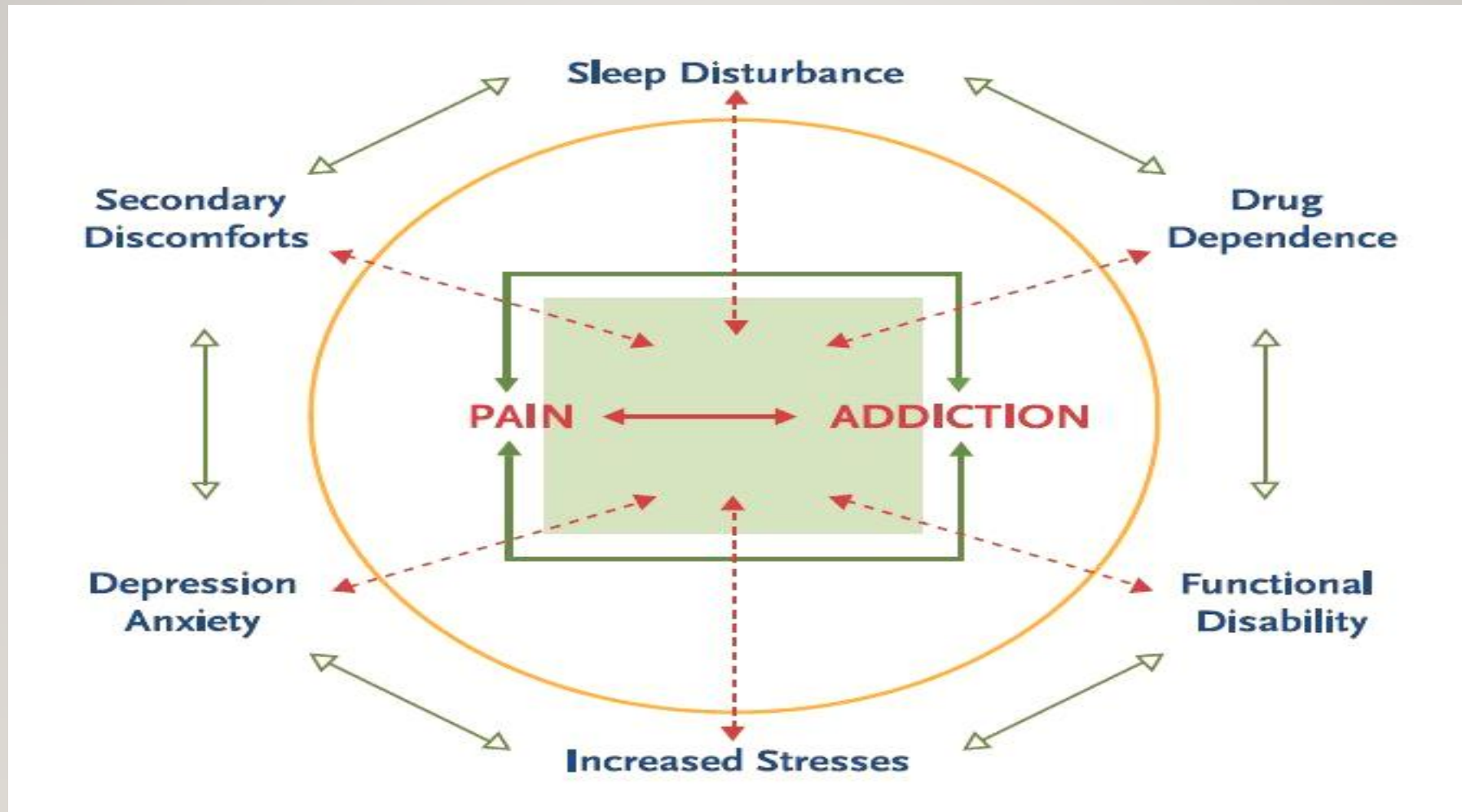
DEFINING PAIN



THE IMPACT OF PAIN:



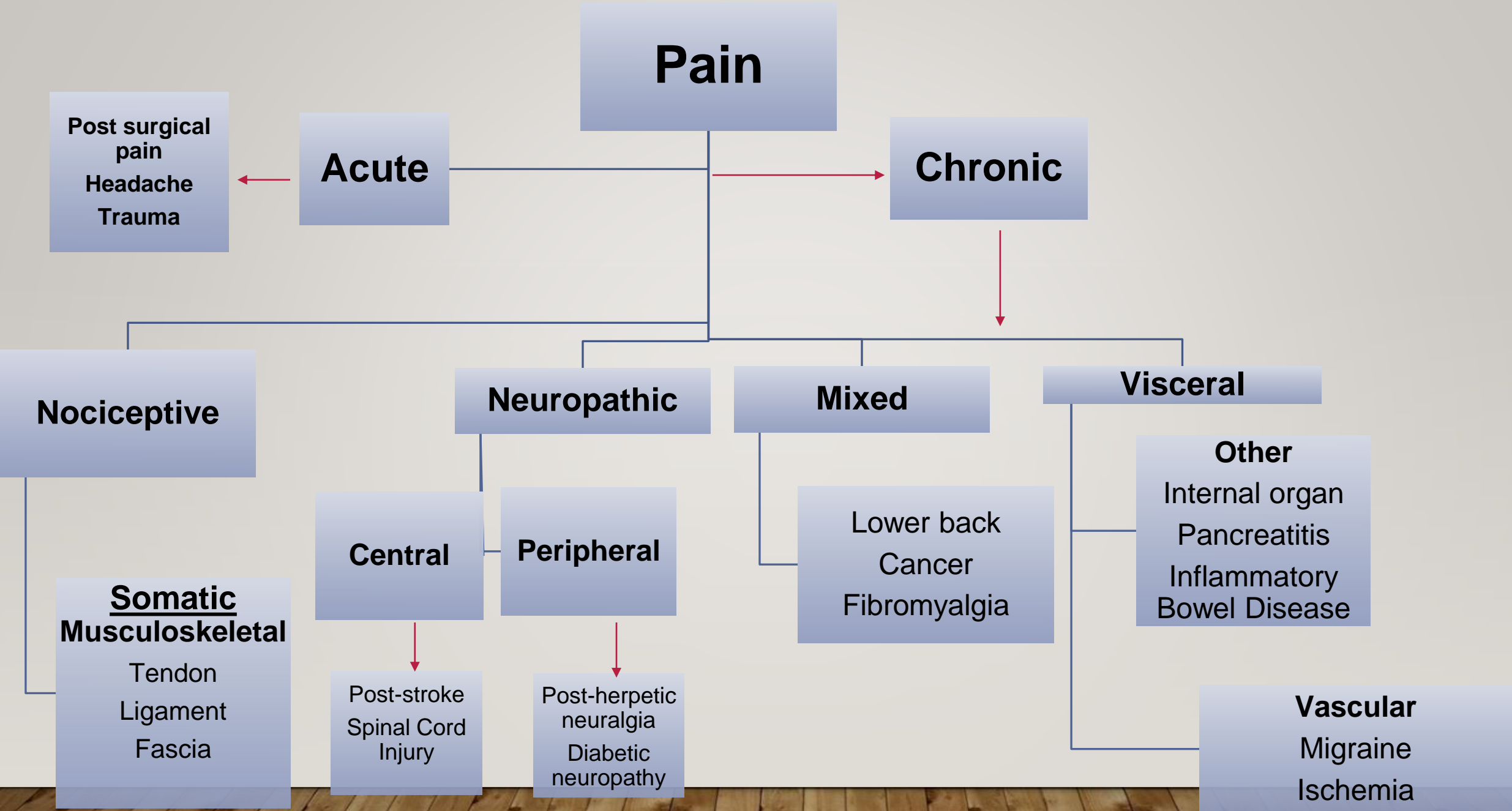
Relationship: Pain & Addiction



UNDER TREATMENT OF PAIN

- **Under treatment of pain** is a significant concern in populations with substance use disorders
- Barriers to inadequate pain management:
 - Institutional practices
 - Inadequate training and skills of clinicians
 - Lack of access to health care, pain management care
 - Reluctance of physicians to prescribe opioid
 - Reluctance of patients to seek medical care:
 - Stigma
 - Fear of relapse





ACUTE PAIN

- Usually associated with an acute physical condition- etiology identifiable
- Generally **self-limited**
- Often primarily nociceptive
- Sympathetic responses, increased blood pressure (BP), pulse (P), diaphoresis
- Failure to treat acute pain properly **may lead to chronic pain**

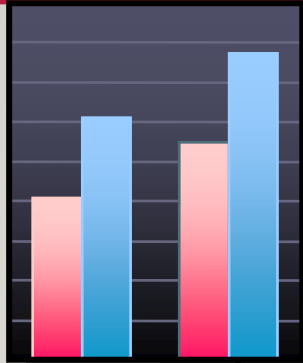
CHRONIC PAIN

- No longer serves **survival** or beneficial purpose
- Lingered past limits normally associated with **tissue healing**
- May persist because of chronic **ongoing tissue pathology**
 - Degenerative Joint Disease
 - Chronic pancreatitis
 - Progressive cancer
- Engenders secondary problems
 - Sleep disturbance; anxiety; depressive symptoms; loss of normal functioning; increased stress associated with losses

Pain Assessment

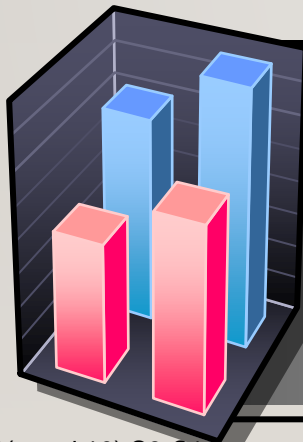


PAIN ASSESSMENT TOOLS



Unidimensional scales¹

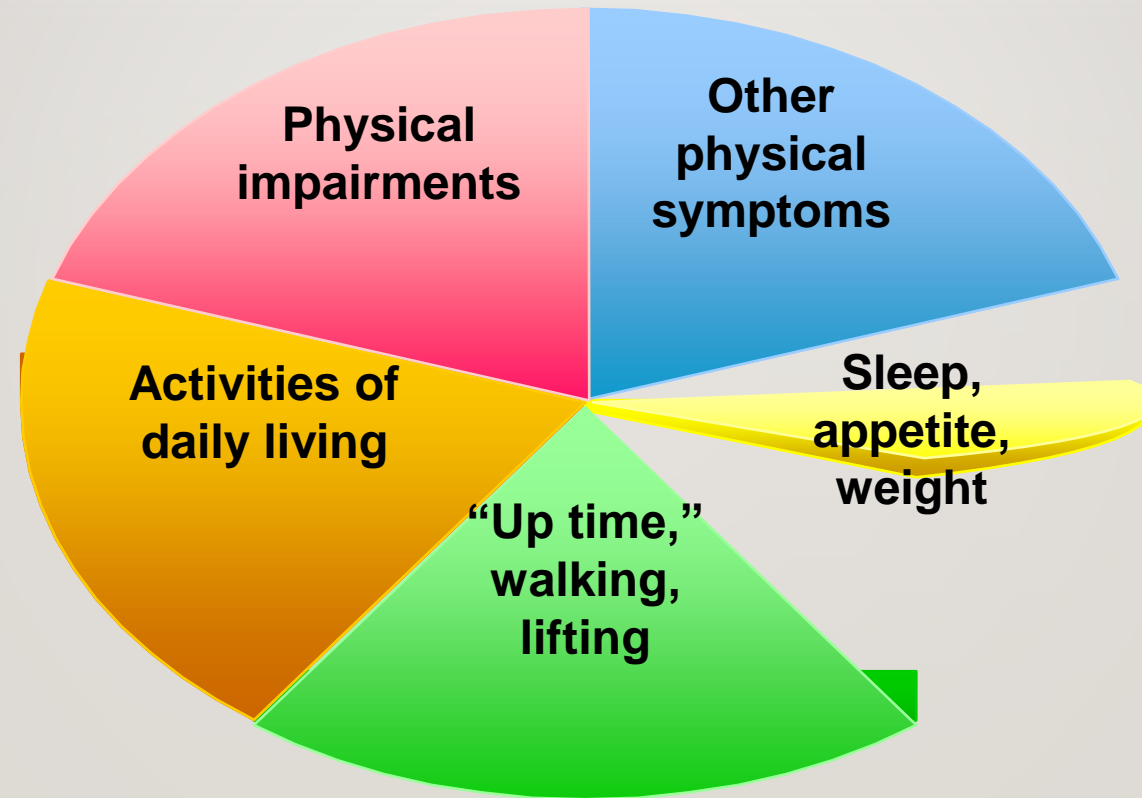
- Numeric Rating Scale
- Verbal Rating Scale
- Visual Analog Scale
- Faces Pain Rating Scale



Multidimensional scales

- Brief Pain Inventory
- McGill Pain Questionnaire

FUNCTIONAL ASSESSMENT



PSYCHOSOCIAL ASSESSMENT

- Psychologic symptoms/ disorders
- Mood
- Coping ability
- Cognition

- Ability to work
- Housekeeping tasks
- Parenting
- Hobbies



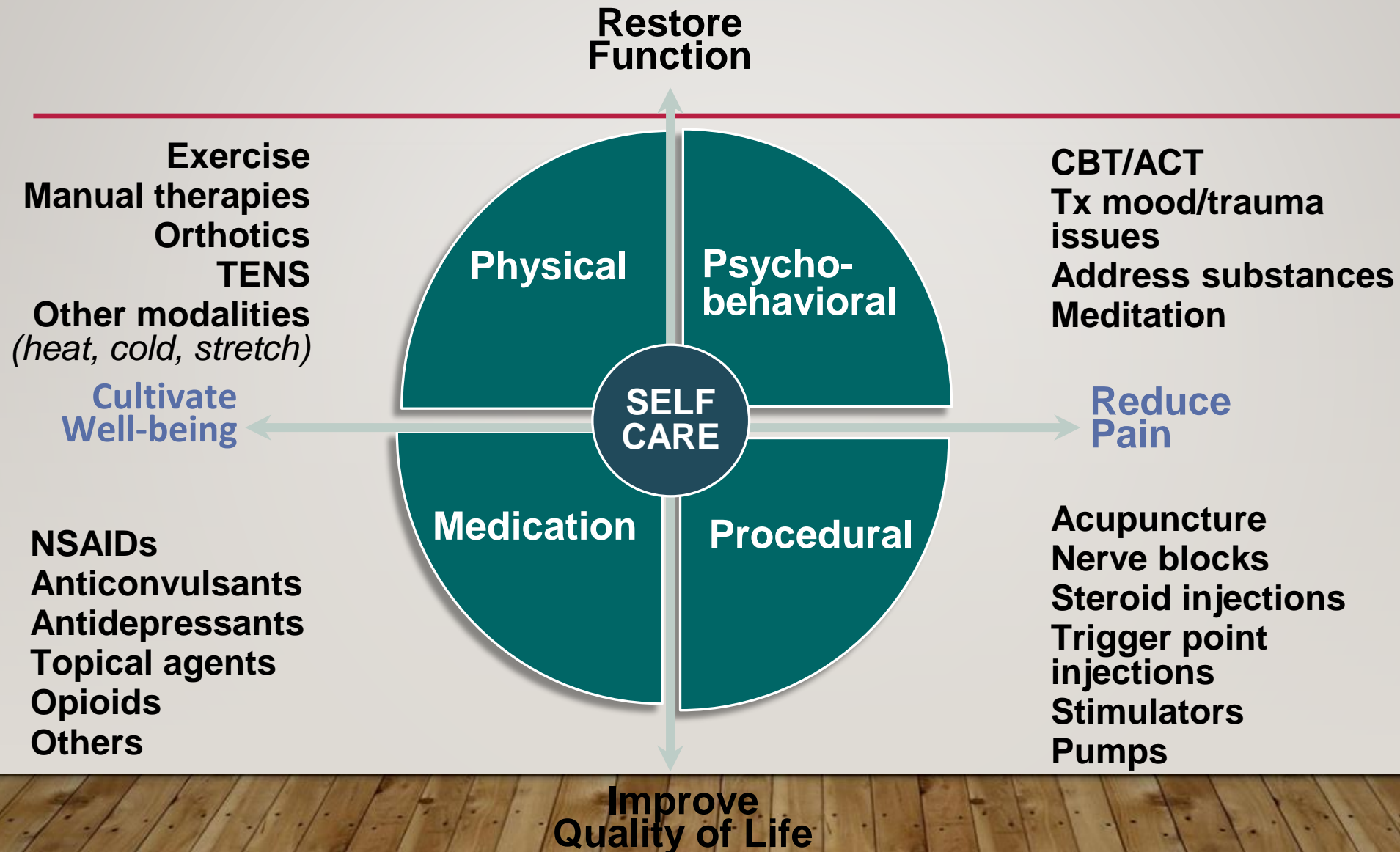
- Family disturbances
- Social support
- Intimacy

- Family history of chronic pain/illness
- Financial impact
- Cultural influences
- Beliefs, values, spiritual orientation

PAIN ASSESSMENT MNEMONIC - PQRSTU

- Provoke or Palliate: What makes the pain better or worse?
- Quality: What does the pain feel like? Is it sharp, dull, stabbing, burning?
- Radiation: Does the pain radiate, and to where?
- Severity: How severe is the pain?
- Time: When did the pain start, and how long has it lasted?
- U (you): What is the impact of pain on you?

MULTIDIMENSIONAL CARE FOR CHRONIC PAIN



PHARMACOLOGIC PAIN THERAPY

- Nonopioid Analgesic Agents (NSAIDs)
- Anticonvulsant Agents
- Muscle Relaxants
- Vitamin D deficiency
- Antidepressant Agents
- Alpha Adrenergic Agents
- Topical Agents
- Opioid Analgesics

NON-PHARMACOLOGIC THERAPY

- Heat
- Physical therapy
- Exercise
- Cognitive-behavioral therapy (CBT)
- Chiropractic care
- Yoga
- Relaxation Therapy
- Meditation
- Interventional pain
- Sleep evaluation
- Recreational Therapy

CATEGORIES OF OPIOID ANALGESICS

Category	Benefits	Drugs
<p>Short-acting: Used to manage intermittent and breakthrough pain</p>	<ul style="list-style-type: none"> ▪ Easier to titrate ▪ More rapidly attained steady-state plasma concentrations 	<ul style="list-style-type: none"> ▪ Morphine sulfate Hydromorphone ▪ Codeine Fentanyl ▪ Hydrocodone Oxymorphone ▪ Oxycodone
<p>Long-acting: For treating chronic pain in patients with consistent pain levels</p>	<ul style="list-style-type: none"> ▪ Makes around-the-clock therapy possible ▪ Dosing convenience and flexibility ▪ Relative steady-state concentrations of opioid concentrations in the blood 	<ul style="list-style-type: none"> ▪ Morphine (sustained-release) Methadone ▪ Oxycodone (sustained-release) Hydrocodone ▪ Transdermal fentanyl Oxymorphone ▪ Hydromorphone (sustained-release) Levorphanol

OPIOID DEPENDENCE, TOLERANCE, PSEUDOADDICTION, AND ADDICTION

Physical dependence: Withdrawal syndrome would occur if the medication is discontinued abruptly, the dose is reduced rapidly, or an antagonist is administered.

Tolerance: A greater amount of medication is needed to maintain the therapeutic effect or loss of effect over time

Addiction: A treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.

CHOOSING AN OPIOID: FACTORS TO CONSIDER

Patient's pain intensity

Coexisting disease (e.g., hepatic,
renal impairment)

Patient response to previous opioid
treatment

Pharmacokinetics

Formulary considerations

ASSESSMENT OF ADDICTION RISK

- Thorough history
- Establish risk factors
 - ORT (Opioid Risk Tool)
 - SOAPP (Screener and Opioid Assessment for Patients in Pain)
 - NIAAA Screen (National Institute on Alcohol Abuse and Alcoholism)
 - COMM (Current Opioid Misuse Measure)
- Psychiatric Comorbidities
- Genetic Factors and Predisposition
- Social/Familial Circumstances

PAIN MANAGEMENT GOALS OF THERAPY FOR PATIENTS WITH OPIOID USE DISORDER (OUD)

Prevent withdrawal

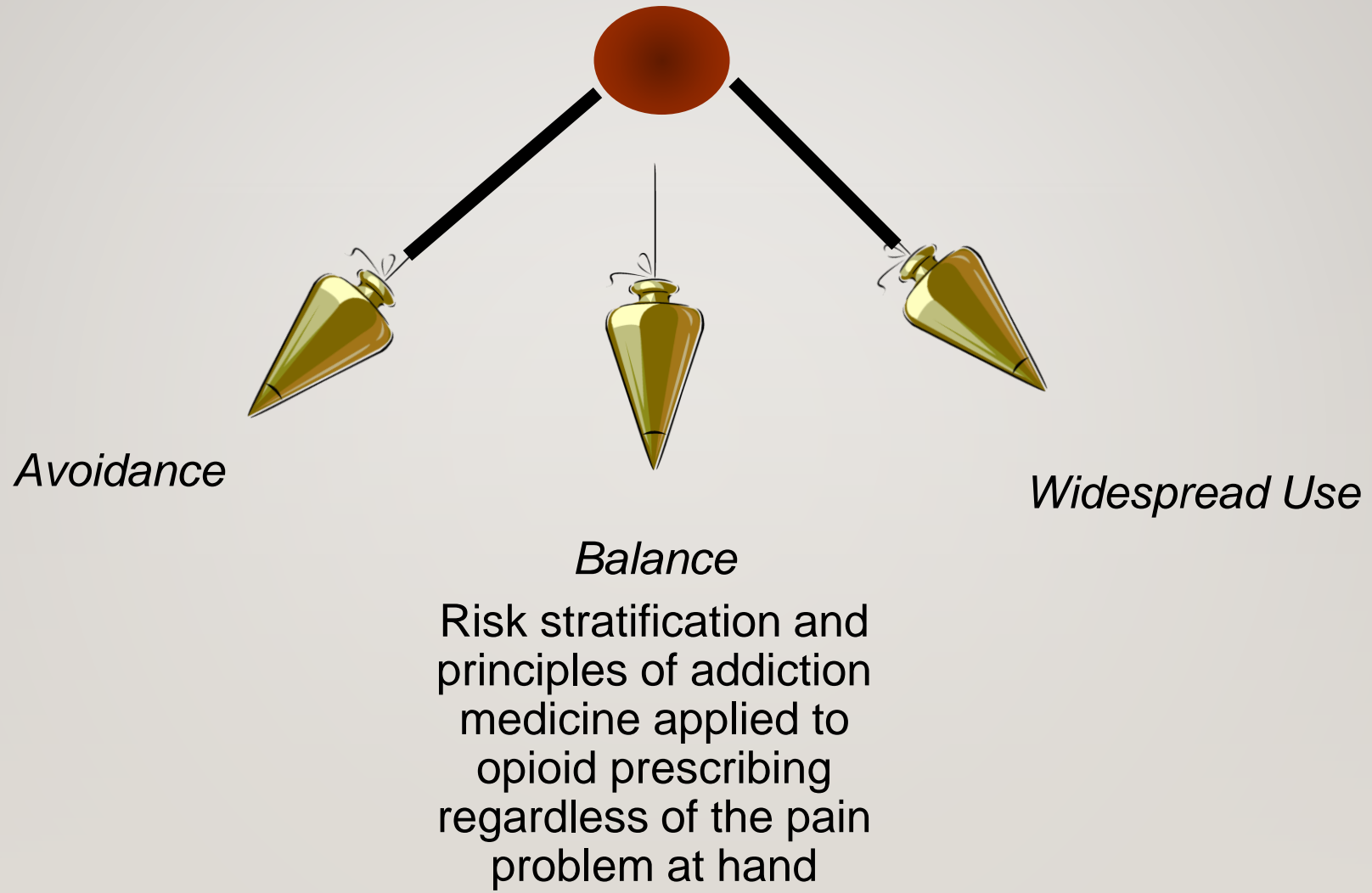
Provide effective analgesia

Prevent relapse to addiction

Effective treatment of opioid addiction (maintenance opioid therapy)

Treatment of psychiatric disorders such as anxiety

THE OPIOID PENDULUM



PAIN BEHAVIORS VS SUSPECT BEHAVIORS

- Disease of addiction
- Addiction:
 - Impaired control over drug use
 - Compulsive use
 - Continued use despite harm
 - Craving
- Disease of pain
- “Drug-seeking” vs “seeking relief of pain”
 - Polypharmacy (comorbidities depression, insomnia, anxiety)
 - Doctor shopping (if under-treated)
 - Aberrant behaviors (doubling up, sharing, borrowing)

Similar behaviors but goals are different



UNIVERSAL PRECAUTIONS IN PAIN MEDICINE

- Reassesses pain score and level of functioning
- Regularly assess the “Five As”:
 - Analgesia
 - Activity
 - Adverse reactions
 - Aberrant behavior
 - Adhering to the treatment agreement
- Review pain diagnosis and co-morbid conditions
- Documentation

URINE DRUG SCREENING: A COMPLEX INTERPRETATION

- Improves patient safety
- Provides objective data
- Can assess both adherence and misuse
- Performed via:
 - Enzyme-mediated Immunoassay (screening)
 - Gas chromatography/mass spectrometry (confirm)

ADJUVANT ANALGESICS

- Multipurpose analgesics
 - Corticosteroids
 - Antidepressants
 - Alpha-2 adrenergic agonists
 - Cannabinoids
 - Topical therapy: Lidocaine, capsaicin, and others
- Drugs used for neuropathic pain
 - Anticonvulsants
 - Antidepressants
- Drugs used for bone pain or bowel obstruction

ROLE OF PATIENT EDUCATION IN PAIN MANAGEMENT

- A critical component of an effective management plan
- Increases patient
 - Understanding of etiology
 - Understanding of the management plan
 - Adherence to the analgesic regimen
- Provides information in writing
- Encourages questions
- Involves family member/caregiver
- Encourages patients to complete a pain management diary

TEAMWORK WITH PHARMACIST

- The pharmacist is a critical member of the treatment team and patient's "Circle of Care"
- Open dialogue between prescriber and dispensing pharmacist to minimize risk while enhancing patient care
- The pharmacist can offer prescribers valuable insight and help modify treatment plans:
 - Ensuring pain is adequately addressed
 - Knowing treatment options and how to utilize them

SUMMARY

- Acute and chronic pain syndromes are prevalent among patients with multiple conditions including chronic malignant and non-malignant pain.
- Knowledge of the multidimensional nature and physiology of pain
- Understanding that pain and addiction have a synergistic relationship
- Best practice recommends a comprehensive approach with interventions using multiple modalities of care

TREATING PAIN IN THE PATIENT WITH SUBSTANCE USE DISORDER

Bennett Doughty, PharmD, BCPS, BCPP

Clinical Assistant Professor

Clinical Psychiatric Pharmacy Specialist

Binghamton University School of Pharmacy

DSM-5 DIAGNOSIS

Impaired Control	Social Problems	Risky Use	Physical Dependence
Using more of a substance or more often than intended Wanting to cut down or stop using but not being able to	Neglecting responsibilities and relationships Giving up activities they used to care about because of substance use Inability to complete tasks at home, school, or work	Use in risky settings Continued use despite known problems	Needing more of the substance to get the same effect (tolerance) Having withdrawal sx when a substance isn't used

ABC'S OF ADDICTION

Addiction is characterized by:

- Inability to consistently **Abstain**;
- Impairment in **Behavioral** control;
- **Craving**; or increased “hunger” for drugs or rewarding experiences;
- **Diminished recognition** of significant problems with one’s behaviors and interpersonal relationships; and
- A dysfunctional **Emotional** response.
- Addiction is a chronic, relapsing disease of the brain with multiple consequences.

RISK FACTORS

- Co-occurring psychiatric disorders
- Demographics – males, younger adults, single individuals, unemployed
- Having deceased parents
- Personality traits (e.g. novelty seeking, impulsivity)
- Exposure to substance – early the age, stronger risk
- Stressful external environment (e.g. home, work)
- Genetic risk (40-60%?)/family history

NUMBERS OF PAST YEAR ILLICIT DRUG USERS AMONG PEOPLE AGED 12 OR OLDER: 2020

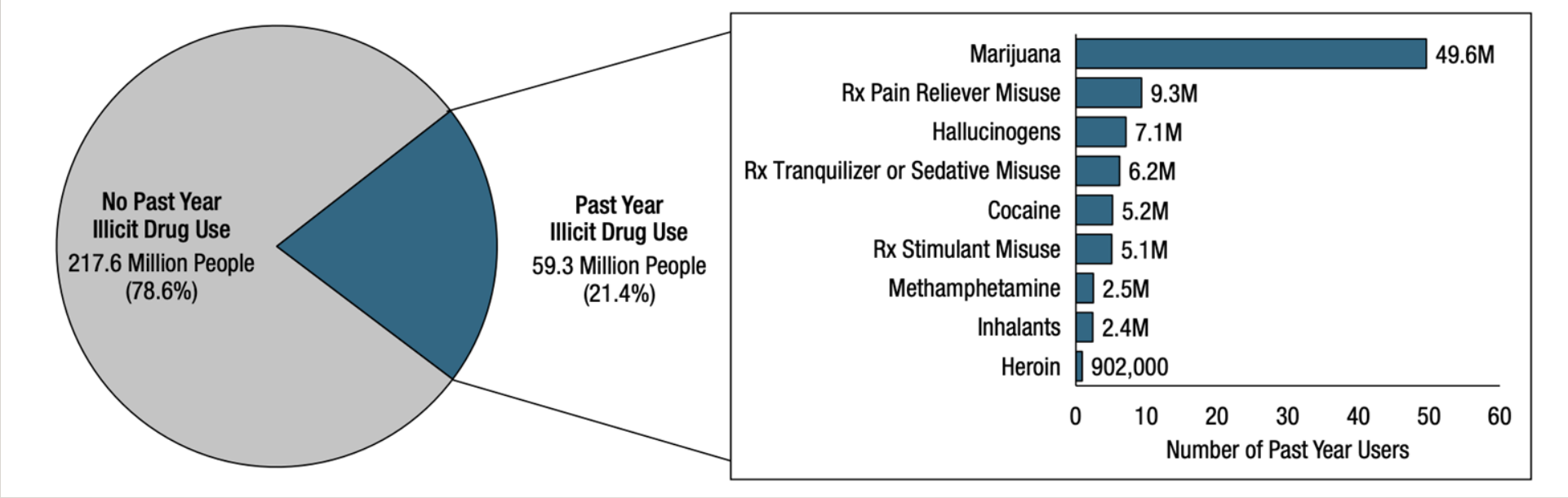
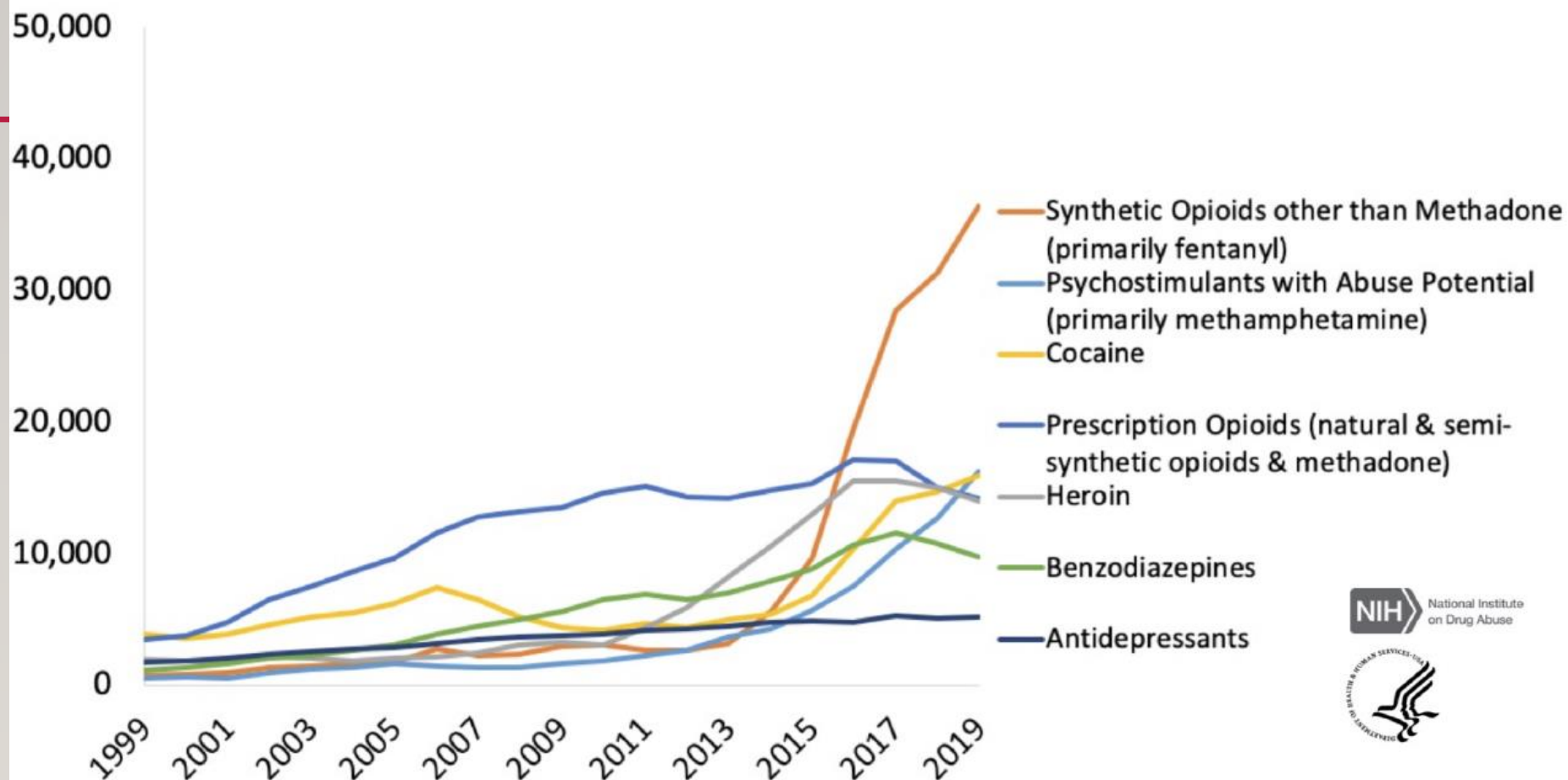
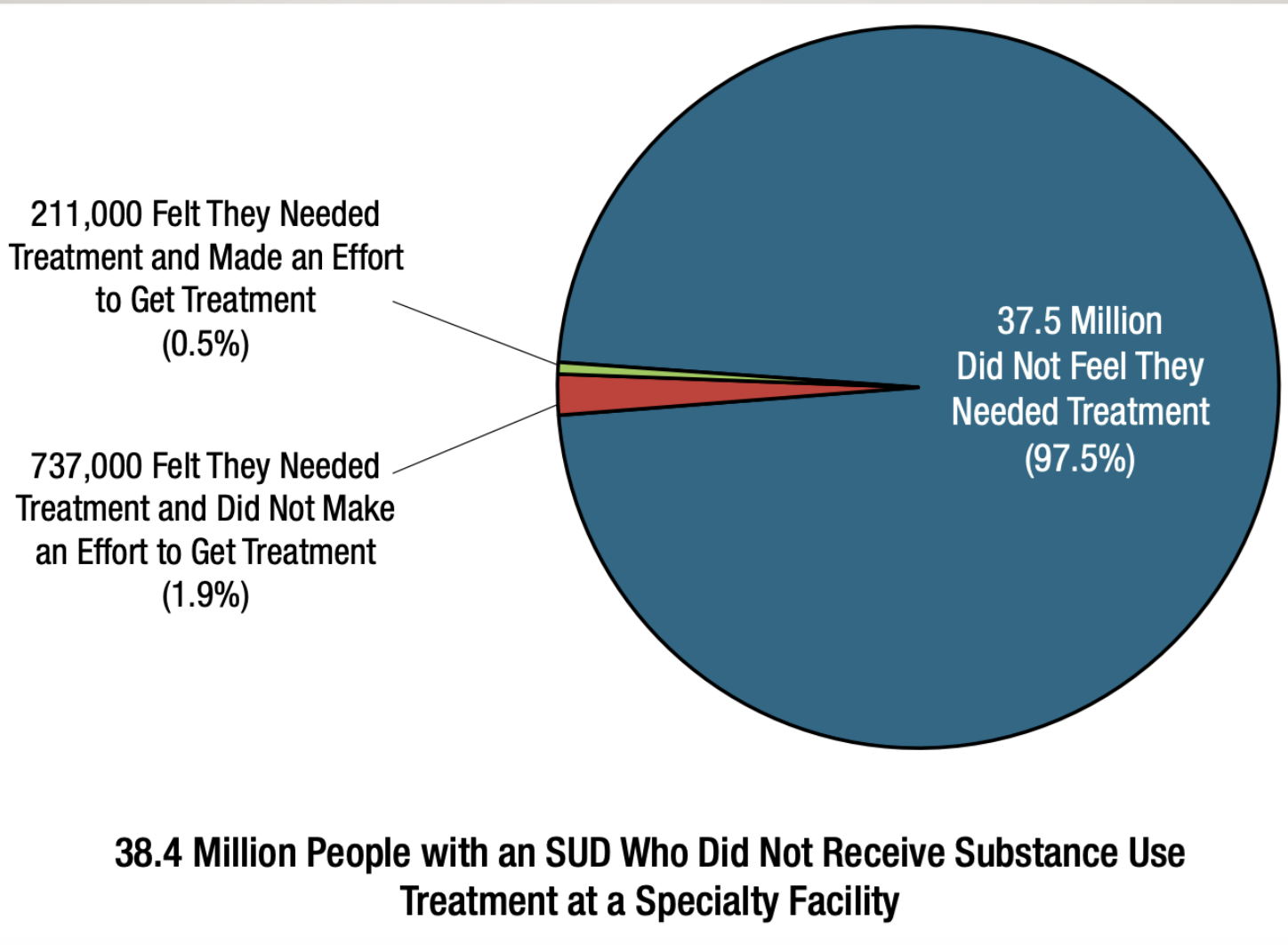


Figure 2. National Drug-Involved Overdose Deaths*, Number Among All Ages, 1999-2019

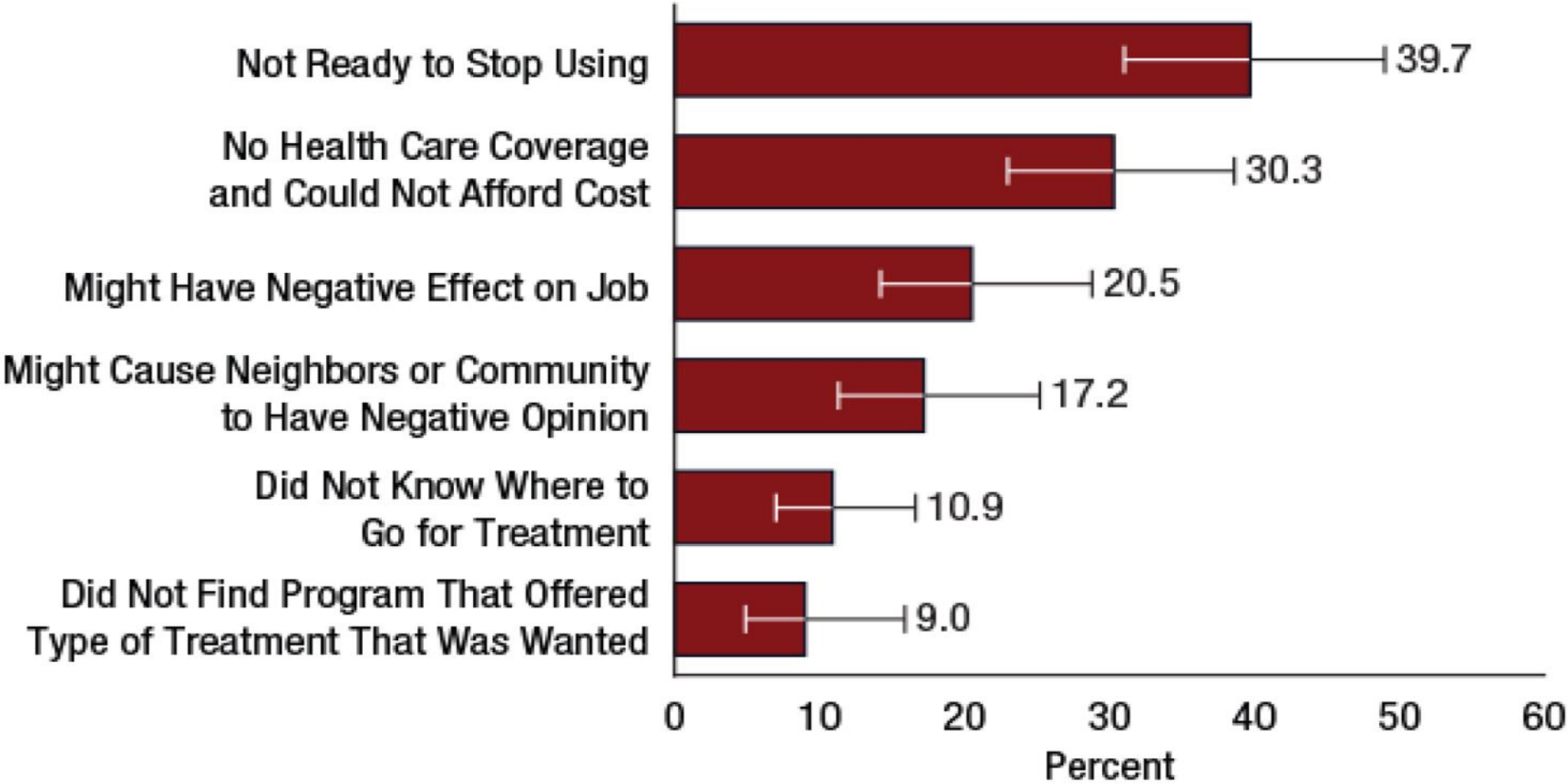


*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2019 on CDC WONDER Online Database, released 12/2020.

Figure 45. Perceived Need for Substance Use Treatment: Among People Aged 12 or Older with a Past Year Substance Use Disorder (SUD) Who Did Not Receive Substance Use Treatment at a Specialty Facility in the Past Year; 2020



REASONS FOR NOT RECEIVING SUBSTANCE USE TREATMENT IN THE PAST YEAR AMONG PEOPLE AGED 12 OR OLDER WHO FELT THEY NEEDED TREATMENT IN THE PAST YEAR: PERCENTAGES, 2017



SYMPTOMS

Opioid Intoxication	Opioid Withdrawal
<ul style="list-style-type: none">- Drowsiness/coma- Slurred speech- Impaired attention/memory- Bradycardia/hypotension- Pinpoint pupils (miosis)- Respiratory depression	<ul style="list-style-type: none">- Dysphoria- N/V- Myalgias- Lacrimation/rhinorrhea- Mydriasis, piloerection, sweating- Diarrhea- Yawning- Fever- Sleeplessness

RATING SCALES

- Clinical Opiate Withdrawal Scale (COWS)
 - 11-item clinician rated assessment tool
 - Used clinically to follow withdrawal symptoms/medication effectiveness
 - Scored from 0 (asymptomatic) – 5 (severely symptomatic)
 - Scoring:
 - 5-12: mild
 - 13-24: moderate
 - 25-36: moderately severe
 - >36: severe withdrawal

SCREENING, BRIEF INTERVENTION, AND REFERRAL TO TREATMENT

SBIRT is a comprehensive approach to the delivery of early intervention and services for persons with substance use disorders, as well as those who are at risk of developing these disorders.

- Screening quickly assesses the severity of substance use and identifies the appropriate level of treatment.
- Brief intervention focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.
- Referral to treatment provides those identified as needing more extensive treatment with access to specialty care.

TREATMENT GUIDELINES

Intervention	APA (2006)	BAP (2012)
1 st Line	Opioid intoxication: naloxone	Opioid Withdrawal: alpha-2-adrenergic agonists, buprenorphine, methadone
	Opioid Withdrawal: buprenorphine, methadone	
	Opioid Dependence: buprenorphine, methadone	
2 nd Line	Opioid Withdrawal: clonidine	Opioid Withdrawal: slow-release oral morphine
	Opioid Dependence: naltrexone IM	Opioid Dependence: naltrexone IM

	Methadone	Naltrexone	Buprenorphine
MOA at Mu Receptors	Agonist	Antagonist	Partial Agonist
Phase of Treatment	Medically supervised withdrawal, maintenance	Prevention of relapse to opioid misuse, following medically supervised withdrawal	Medically supervised withdrawal, maintenance
ROA	Oral	Oral, IM	SL, buccal, subdermal implant, SC ER injection
Regulations and Availability	Schedule II; only available at federally certified OTPs and the acute inpatient hospital setting for OUD treatment	Not a scheduled medication; not included in OTP regulations; requires prescription; office-based treatment or specialty substance use treatment programs, including OTPs	<p>Schedule III; requires waiver to prescribe outside OTPs</p> <p>Implant: Prescribers must be certified in the Probuphine REMS Program, which requires special training for providers</p> <p>Subcutaneous Injection: Healthcare settings and pharmacies must be certified in the Sublocade REMS Program and only dispense the medication directly to a provider for administration</p>

	Methadone	Naltrexone	Buprenorphine
Possible Adverse Effects	<p>Constipation, hyperhidrosis, respiratory depression, sedation, QT prolongation, sexual dysfunction, severe hypotension including orthostatic hypotension and syncope, misuse potential, neonatal abstinence syndrome</p>	<p>Nausea, anxiety, insomnia, precipitated opioid withdrawal, hepatotoxicity, vulnerability to opioid overdose, depression, suicidality, muscle cramps, dizziness or syncope, somnolence or sedation, anorexia, decreased appetite or other appetite disorders</p> <p>Intramuscular: Pain, swelling, induration (including some cases requiring surgical intervention)</p>	<p>Constipation, nausea, precipitated opioid withdrawal, excessive sweating, insomnia, pain, peripheral edema, respiratory depression (particularly combined with benzodiazepines or other CNS depressants), misuse potential, neonatal abstinence syndrome</p> <p>Implant: Nerve damage during insertion/removal, accidental overdose or misuse if extruded, local migration or protrusion</p> <p>Subcutaneous Injection: Injection site itching or pain, death from intravenous injection</p>
<p>SAMHSA. (2021). Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63. Kampman, K., & Jarvis, M. J Addict Med, 9(5):358-367.</p>			

	Methadone	Naltrexone	Buprenorphine
Evidence in OUD	MET has been the gold-standard treatment since FDA approval in 1960s; Cochrane reviews have demonstrated MET's favorable treatment retention rate compared to placebo treatments and reduced rates of opioid positive urine drug screens	NTX is best reserved for highly motivated OUD patients (e.g. mandated treatment by a professional licensing board), as Cochrane reviews confirm the poor clinical utility of NTX due to poor adherence and low treatment retention; XR-NTX was approved in 2010 and has more encouraging data	Since passing of Drug Abuse Treatment Act in 2000, BUP has been used for office based management of OUD resulting in greater access and less stigmatized treatment; Cochrane reviews have noted BUP's inferiority to MET for treatment retention, but BUP performs equally well in reduction of opioid positive urine drug screen rates
Metabolism	Hepatic, primarily via CYP3A4 (consider HIV medications), 2B6, 2C19; half-life 9 to 87 hours	Metabolized via non CYP-mediated dehydrogenase to an active metabolite	Hepatic; primarily by CPY3A4 to active metabolite; half-life 37 hours for sublingual vs 27 hours for buccal
Interactions	Inhibits CYP2D6 moderately; major substrate of CYP3A4 and 2B6	None known enzymatic interactions, but will induce opioid withdrawal if administered in an opioid-using individual	Weak inhibitor for CYP1A2, 2A6, 2C19, and 2D6; major substrate of CYP3A4

SAMHSA. (2021). Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63.

Kampman, K., & Jarvis, M. J Addict Med, 9(5):358-367.

EXHIBIT 3D.1. Buprenorphine Transmucosal Products for OUD Treatment

PRODUCT NAME/ ACTIVE INGREDIENT	ROUTE OF ADMINISTRATION/ FORM	AVAILABLE STRENGTHS	RECOMMENDED ONCE- DAILY MAINTENANCE DOSE
Bunavail²³⁵ <ul style="list-style-type: none"> Buprenorphine hydrochloride Naloxone hydrochloride 	Buccal film	2.1 mg/0.3 mg 4.2 mg/0.7 mg 6.3 mg/1 mg	Target: 8.4 mg/1.4 mg Range: 2.1 mg/0.3 mg to 12.6 mg/2.1 mg
Generic combination product^{236,237} <ul style="list-style-type: none"> Buprenorphine hydrochloride Naloxone hydrochloride 	Sublingual tablet, film	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg	Target: 16 mg/4 mg Range: 4 mg/1 mg to 24 mg/6 mg*
Generic monoproduct^{238,239} <ul style="list-style-type: none"> Buprenorphine hydrochloride 	Sublingual tablet	2 mg 8 mg	Target: 16 mg Range: 4 mg to 24 mg*
Suboxone^{240,241} <ul style="list-style-type: none"> Buprenorphine hydrochloride Naloxone hydrochloride 	Sublingual film	2 mg/0.5 mg 4 mg/1 mg 8 mg/2 mg 12 mg/3 mg	Target: 16 mg/4 mg Range: 4 mg/1 mg to 24 mg/6 mg*
Zubsolv^{242,243} <ul style="list-style-type: none"> Buprenorphine hydrochloride Naloxone hydrochloride 	Sublingual tablet	0.7 mg/0.18 mg 1.4 mg/0.36 mg 2.9 mg/0.71 mg 5.7 mg/1.4 mg 8.6 mg/2.1 mg 11.4 mg/2.9 mg	Target: 11.4 mg/2.9 mg Range: 2.9 mg/0.71 mg to 17.2 mg/4.2 mg

*Dosages above 24 mg buprenorphine or 24 mg/6 mg buprenorphine/naloxone per day have shown no clinical advantage.^{244,245}

Adapted from material in the public domain.²⁴⁶

BUPRENORPHINE IMPLANT (PROBUPHINE)

- Approved in May 2016
- Indicated for patients stabilized on low-moderate doses of transmucosal buprenorphine
 - Studies done in patients on no more than buprenorphine SL 8mg/day
- Consists of four implants inserted subdermally into upper arm for up to 6 months of treatment

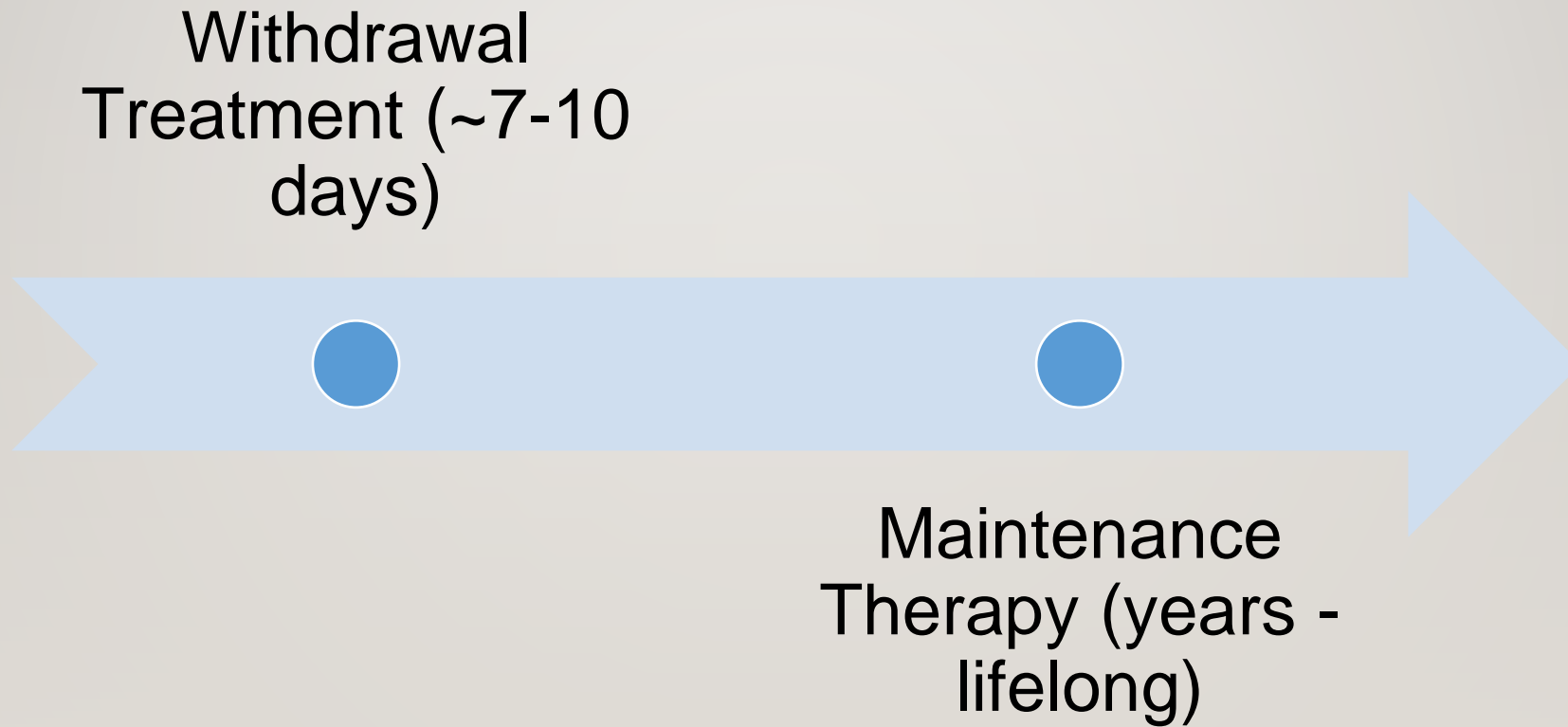


BUPRENORPHINE ER INJECTION (SUBLOCADE)

- Approved in November 2017
- Indicated for the treatment of moderate - severe OUD in patients who have initiated treatment with a transmucosal buprenorphine product, followed by dose adjustment for a minimum of 7 days
- Appropriate for patients initiated on buprenorphine SL 8-24mg/day



TREATMENT ALGORITHM



ADJUNCTIVE TREATMENT

- Clonidine: alpha-2-adrenergic agonist
 - Used for some symptoms of opioid withdrawal: N/V, diarrhea, cramps, sweating
 - Initial dose: 0.1mg three times daily
- Other symptoms:
 - Diarrhea: loperamide
 - Vomiting: antiemetic – prochlorperazine
 - Insomnia: sleep aide – trazodone
 - Anxiety: hydroxyzine
 - Muscle-cramps: Ibuprofen

ONE LAST THOUGHT...

- <https://disposemy meds.org/>
- https://deادiversion.usdoj.gov/drug_disposal/



CASE DISCUSSIONS



CASE 1

A 30-year-old woman with a history of recent intravenous (IV) drug use is admitted to the observation unit for IV antibiotics after the incision and drainage of an antecubital abscess. She has a history of opioid and cocaine dependence. She receives IV morphine followed by IV hydromorphone for acute pain, as she had a significant debridement performed. After the procedure, she is demanding increasingly higher doses of IV opioids, and the observation unit team is becoming uneasy regarding the dose and frequency of opioid medications that she is receiving. The nursing staff raises concerns that she has tampered with her IV tubing and may be using her IV to “inject something.”

CASE 2

A 27-year-old woman on buprenorphine-naloxone (Suboxone®) for treatment of opioid dependence is admitted to the hospital with severe abdominal pain due to a perforated gastric ulcer. She received hydromorphone in the ED, and is urgently taken to the operating room. Postoperatively, she is on a patient-controlled analgesic (PCA) pump containing fentanyl. Her last dose of buprenorphine-naloxone was 20 h prior to the surgery; her daily dose is 16 mg.

CASE 3

A 20-year-old man is brought to the emergency department (ED) by his family for evaluation. His family reports that he failed out of school in his second year at a local community college. He admits to escalating struggles with prescription pain pills (prescription opioids), and then heroin use. He appears to be in opioid withdrawal; he describes anorexia and diarrhea, and is yawning and sweating on exam. He has a COWS score of 15, indicating moderate withdrawal.

His provider orders clonidine, ondansetron, and 2/0.5 mg sublingual buprenorphine/naloxone, with a plan to observe him in the ED. The provider subsequently receives a concerned call from the hospital pharmacist.

CFR 21 - 1306.07 ADMINISTERING OR DISPENSING OF NARCOTIC DRUGS.

A practitioner may administer or dispense directly (but not prescribe) a narcotic drug listed in any schedule to a narcotic dependent person for the purpose of maintenance or detoxification treatment...

Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than three days and may not be renewed or extended.

CASE 4

A 55-year-old African American woman with a history of IVDU was recently diagnosed with multiple myeloma. She was started on chemotherapy for her MM. She presented to the palliative care clinic complaining of severe mid back pain. She has been trying to find a pain specialist who would treat her pain, but every specialist has been very reluctant to treat her cause of her PMH. She states that the pain affects her functioning, sleep, and appetite, so her performance status is 1. The patient was hospitalized twice due to an overdose of morphine; she was self-buying from the streets to manage her pain. She is in the clinic in tears begging the palliative specialist to manage her pain.

QUESTIONS?
