Pain Management and Opioids:

Balancing Risks and Benefits

PRESENTED BY

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UPDATED SEPTEMBER 2022

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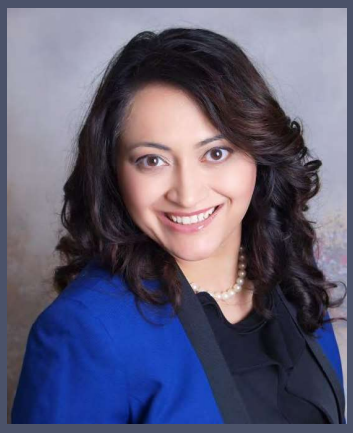

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Dr. Anita Gupta specializes in anesthesiology and pain medicine. Dr. Gupta is notably, recognized for breakthroughs related to the drug crisis as the American Society of Anesthesiologists appointed Gupta to advocate at the U.S. Food and Drug Administration (FDA) to expand the use of naloxone to address overdoses.

CALIFORNIA ACADEMY OF FAMILY PHYSICIANS
STRONG MEDICINE FOR CALIFORNIA

DISCLOSURE:

Anita Gupta has no relevant financial relationship with ineligible companies.

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ACKNOWLEDGMENTS

Presented by the California Academy of Family Physicians, a member of the CO*RE Collaborative, ten interdisciplinary organizations working together to improve pain management and prevent adverse outcomes. For more information about CO*RE, visit http://core-rems.org/.

This activity is supported by an independent educational grant from the Opioid Analgesics REMS Program Companies (RPC). This activity is intended to be fully compliant with the Opioid Analgesic (OA) REMS education requirements issued by the U.S. Food and Drug Administration. For more information about the Opioid Analgesics REMS, visit https://opioidanalgesicrems.com/RpcUI/products.u.

Scan the QR code to go to the FDA OA REMS Blueprint

MATE ACT AND STATE REQUIREMENTS

MATE Act

As of June 27, 2023, DEA registrants are to have completed a total of at least 8 hours of training on treatment and management of patients with opioid or other substance use disorders. This activity meets the criteria outlined by SAMHSA to count toward this training requirement.

State Requirements

This course also meets many states' requirements for pain education.

THE CO*RE COLLABORATIVE

This course does not advocate for or against the use of opioids.

We intend to help clinicians manage pain without putting vulnerable patients at risk for misuse or opioid use disorder. The goal is to keep our patients, our communities, and ourselves SAFE.

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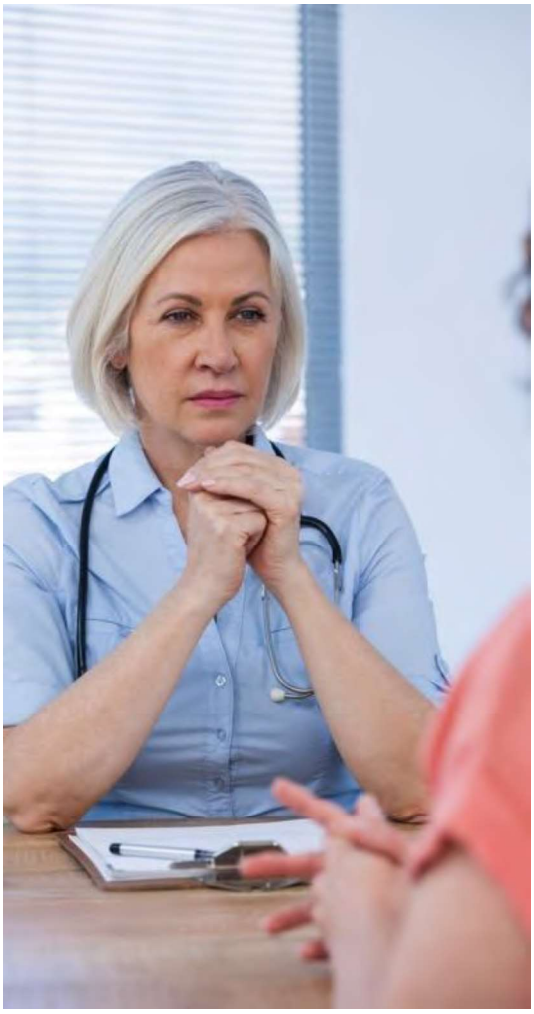
None of the Faculty Advisors, Reviewers, or Planners for this educational activity have relevant financial relationships with ineligible companies to disclose.

This course is based on the FDA's Opioid Analgesic REMS (FDA Blueprint, Sept. 2018) and existing guidelines, including the 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain.

BY THE END OF THIS SESSION YOU WILL BE ABLE TO:

- Describe the pathophysiology of pain as it relates to the concepts of pain management.
- Accurately assess patients in pain.
- Develop a safe and effective pain treatment plan.
- Identify evidence-based non-opioid options for the treatment of pain.
- Identify the risks and benefits of opioid therapy.
- Manage ongoing opioid therapy.
- Recognize behaviors that may be associated with opioid use disorder.



WHY ARE WE HERE?

CO*RE STATEMENT

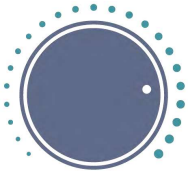
Historical over-prescribing, a massive and sustained exposure to opioids, and a gap in treatment availability have fueled the opioid overdose epidemic in the United States.

When prescribed well, and used as prescribed, opioids can be valuable tools for effective pain management.

Unintended consequences may occur from both under-prescribing (unmanaged pain) and over-prescribing (injudicious use of opioids).

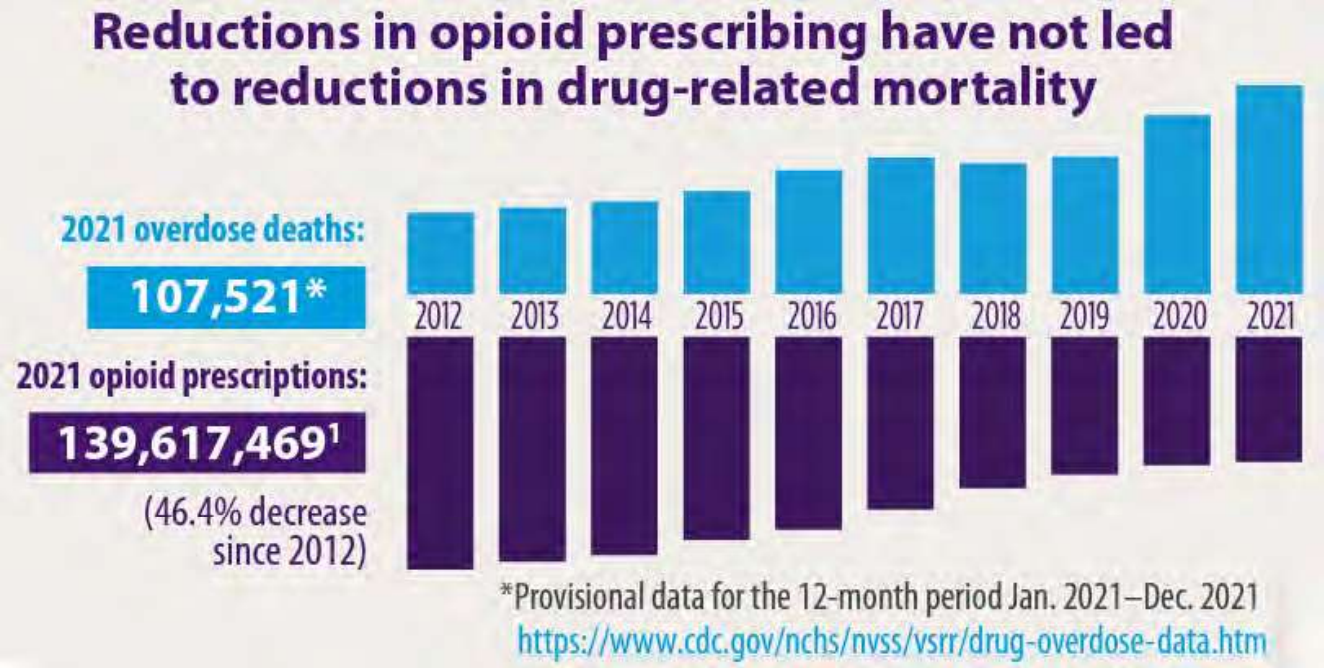
This course does not advocate for or against the use of opioids. We intend to help health-care providers manage pain without putting vulnerable patients at risk for misuse or opioid use disorder. The goal is to keep our patients, our communities, and ourselves SAFE.

TYPES OF OPIOIDS



NATURALLY OCCURRING OPIATES	SEMI-SYNTHETIC OPIOIDS	SYNTHETIC OPIOIDS
Codeine Morphine	Buprenorphine Hydrocodone Hydromorphone Oxycodone Oxymorphone	Alfentanil Fentanyl Methadone Remifentanil Tapentadol Tramadol

AGONISTS	PARTIAL AGONISTS	ANTAGONISTS
Codeine Methadone Morphine Oxycodone	Buprenorphine Nalbuphine	Naloxone Naltrexone



Source: https://www.ama-assn.org/system/files/ama-overdose-epidemic-report.pdf

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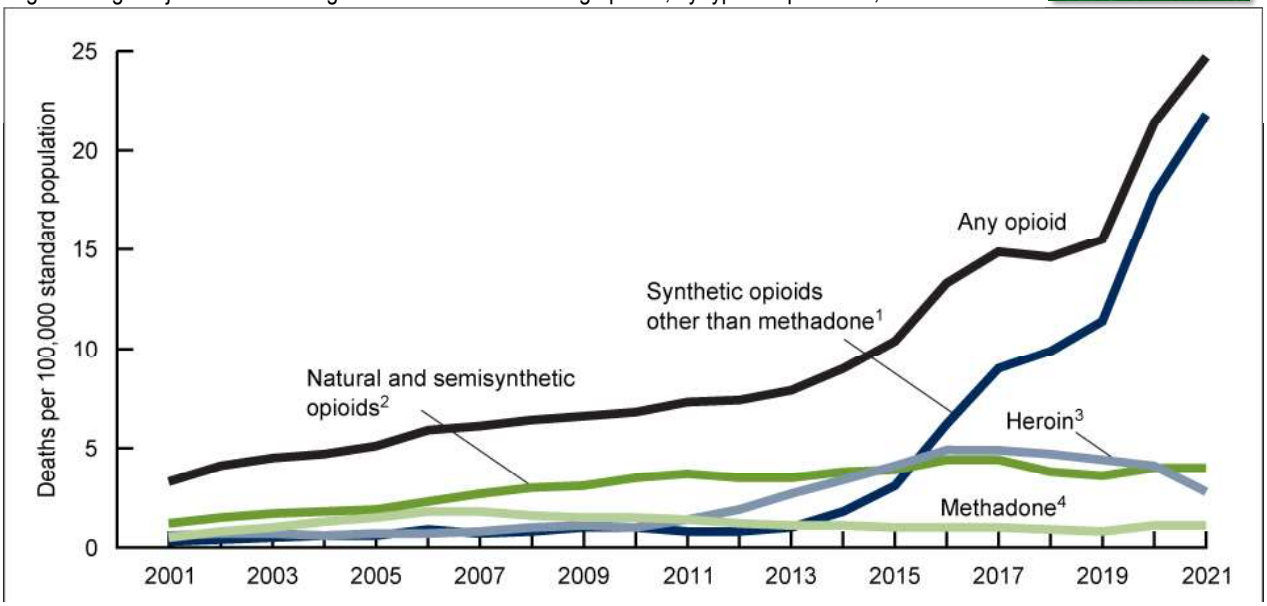
OPIOID OVERDOSE DEATHS BY TYPE OF OPIOID

Figure 4. Age-adjusted rate of drug overdose deaths involving opioids, by type of opioid: US, 2001-2021



Source: https://www.cdc.gov/nchs/images/databriefs/451-500/db457-fig4.png

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CDC Stop Overdoses

https://www.youtube.com/watch?v=zu_WtBrmScs

Opioid Prescribing Rates & Overdose Deaths

Prescribing Rates (per 100 people)

	2018	2019	2020
IL	45	43	40.2

Office of National Drug Control Policy (ONDCP)

Opioid Overdose Death Rate Per 100,000 Population

IL 2022	24.5	US 2022	24.8

https://www.cdc.gov/drugoverdose/rxrate-maps/
https://www.kff.org/state-category/health-status/opioids/

RISKS VERSUS BENEFITS OF PRESCRIBED OPIOIDS

POTENTIAL RISKS

- Life-threatening respiratory depression/overdose
- Development of SUD/OUD
- Diversion
- Inadvertent exposure to family and pets
- Interactions with other meds and substances
- Neonatal abstinence syndrome
- Physiologic dependence and withdrawal

POTENTIAL BENEFITS

- Analgesia
- Option for patients with contraindications for non-opioid analgesics
- Relieves suffering
- May improve function and quality of life

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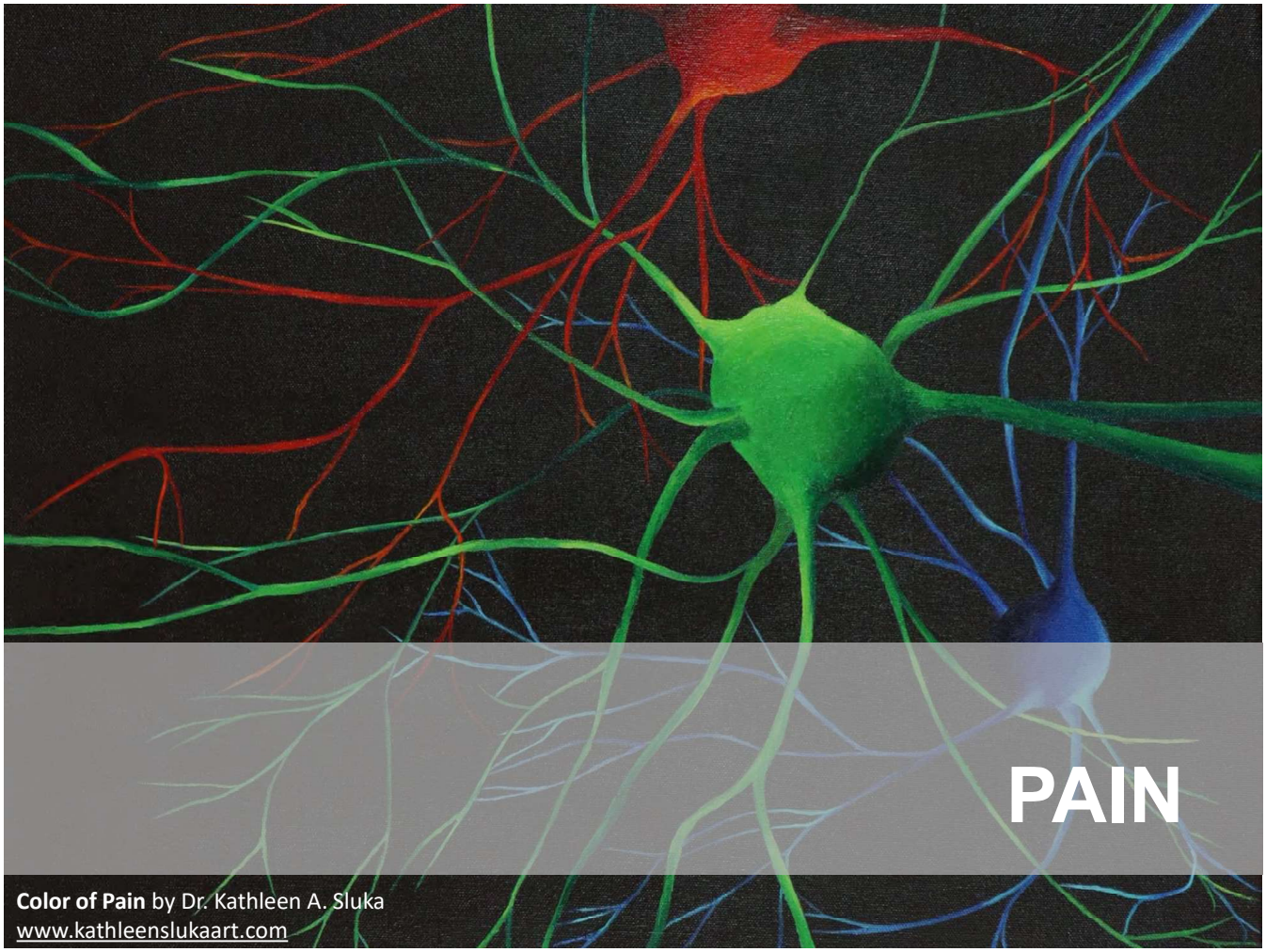
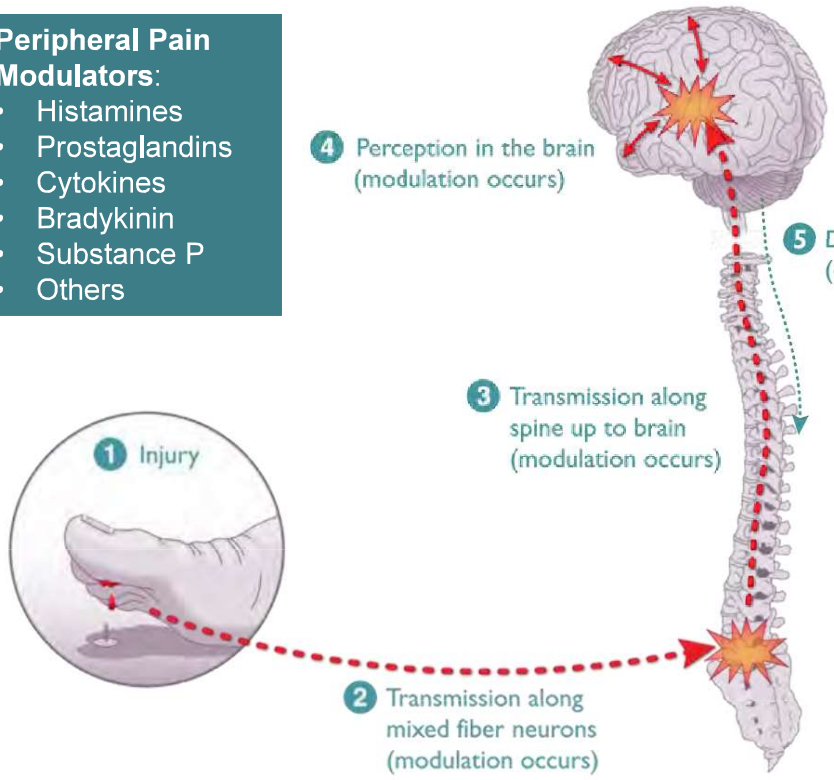


Color of Pain by Dr. Kathleen A. Sluka
www.kathleenslukaart.com

THE NEUROMECHANISMS OF PAIN

Peripheral Pain Modulators:
- Histamines
- Prostaglandins
- Cytokines
- Bradykinin
- Substance P
- Others



Descending Neurotransmitters:
- Serotonin
- Norepinephrine
- Endogenous opiates
- Others

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PAIN

"An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."

—IASP (July 2020)

ACUTE	CHRONIC
• Acute pain duration of < 1 month • Sudden onset, self-limiting • Ideally resolves with healing • Triggered by tissue damage and inflammation • Has protective value • Inflammatory mediation • **Subacute**, pain that continues for 1-3 months, can become chronic	• Lasting 3 months or longer • Generally steady-state or worsening • Persists beyond normal healing period • Serves no value • Peripheral and central sensitization

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TYPES OF PAIN

NOCICEPTIVE / INFLAMMATORY	NOCIPLASTIC	NEUROPATHIC	MIXED TYPES (NOCICEPTIVE / NEUROPATHIC)
Pain in response to an injury or stimuli; *typically* acute	Pain that arises from altered nociceptive function; *typically* chronic	Pain that develops when the nervous system is damaged; chronic	Primary injury and secondary effects
Post-operative pain, sports injuries, arthritis, sickle cell disease, mechanical low back pain	Fibromyalgia, irritable bowel syndrome, nonspecific low back pain	Post-herpetic neuralgia, trigeminal neuralgia, distal polyneuropathy, CRPS, neuropathic low back pain	

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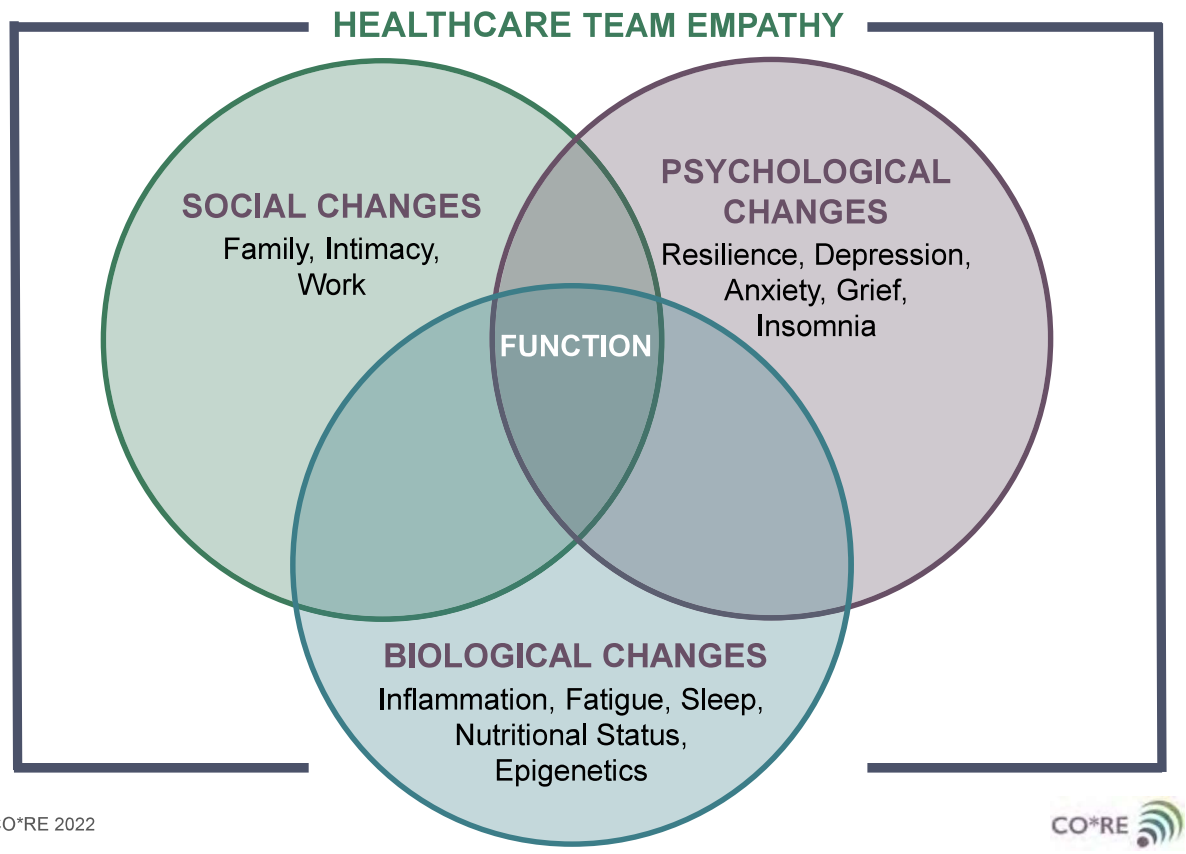
THE EXPERIENCE OF PAIN: A BIOPSYCHOSOCIAL MODEL



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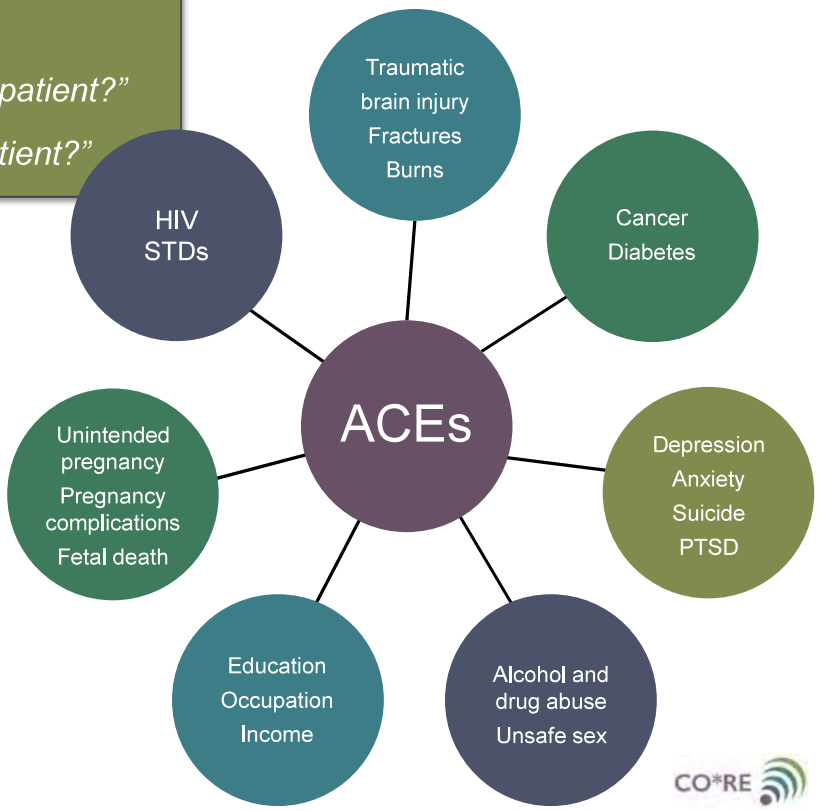
ADVERSE CHILDHOOD EXPERIENCES (ACEs)

A shift in focus…

from *"what's wrong with this patient?"*

to *"what happened to this patient?"*



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WORDS MATTER: LANGUAGE CHOICE CAN REDUCE STIGMA

"*If you want to care for something, you call it a flower; if you want to kill something, you call it a weed.*" —DON COYHIS

COMMONLY USED TERM	PREFERRED TERM
Addiction	Substance use disorder (SUD) or opioid use disorder (OUD) [from the *DSM-5-TR*®]
Drug-seeking, aberrant/problematic behavior	Using medication not as prescribed
Addict/user	Person with a substance use disorder (SUD) or an opioid use disorder (OUD)
Dirty urine/failing a drug test	Testing positive on a urine drug screen
Abuse or habit	Misuse or "use other than prescribed"

SOURCE: https://nida.nih.gov/research-topics/addiction-science/words-matter-preferred-language-talking-about-addiction

PAIN ASSESSMENT

DESCRIPTION OF PAIN

Location

Intensity

Quality

Onset/ duration

Variations/ patterns/rhythms

WHAT RELIEVES THE PAIN?

WHAT CAUSES OR INCREASES THE PAIN?

EFFECTS OF PAIN ON PHYSICAL, EMOTIONAL AND PSYCHOSOCIAL FUNCTION

PATIENT'S CURRENT LEVEL OF PAIN AND FUNCTION

SOURCE: Hogans, B., Barreveld, A. (Eds.). *Pain Care Essentials*, New York, NY: Oxford University Press. 2020.

MEDICAL AND TREATMENT HISTORY

RELEVANT ILLNESSES

PAST AND CURRENT OPIOID USE

- Query your state's Prescription Drug Monitoring Program (**PDMP**) to confirm patient report
- Contact past providers and obtain prior medical records
- For opioids currently prescribed, note the opioid, dose, regimen, and duration
- Determine whether the patient is **opioid-tolerant**

NONPHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

BARRIERS TO PREVIOUS TREATMENT STRATEGIES

PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

PDMP DATABASES	BENEFITS
• Reports on opioid prescriptions filled by patient • Nearly all are available online 24/7 • 54 operational PDMPs in the U.S. • In some states, prescribers are required to access; know your state laws	• Lower rates of prescription opioid-related hospitalization and ED visits • Reduction in "doctor shopping" • Reduction in prescribing high doses and over-prescribing • Identify drugs that increase overdose risk when taken together (such as benzodiazepines, gabapentinoids, opioids, and other sedatives)

Limitations: Often under-used, can be time consuming, may not have access to bordering state data, lack of intuitive format, privacy issues, no national PDMP connection

Multiple prescriptions from different providers is most predictive of opioid misuse.

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PDMP: Prescription Drug Monitoring Program

General	• **Illinois Prescription Monitoring Program** www.ilpmp.org/ • Administered by **Department of Human Services** • **Schedule II-V** are monitored • **Dispensers and prescribers are required** to register and input data • Before prescribing, there **is an obligation** to review under certain circumstances • Prescribers **can authorize** a registered delegate
Reporting	• Must be entered into PDMP **at the end of the next business day** after dispensing • Unsolicited reports/alerts **are sent** to prescribers and dispensers only • Illinois **does share** data with other states' PDMP with authorization • Out-of-state pharmacies **are required** to report to the patient's home state • Patient **will not be notified** if their record has been accessed

https://namsdl.org/doc-library/?fwp_document_type=map January 2019
http://www.pdmpassist.org/content/pdmp-maps-and-tables January 2023

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Prescribing Limits, Status and Education Requirements

Initial prescribing limits for acute pain: None

	Physician	PA	Advanced Practice Nurse
Prescriber Status	Licensed	Schedule II-V	Schedule II-V
Education Requirements	3 hrs./3 yrs.	10 hrs./2 yrs.	10 hrs./2 yrs.

The Medication Access and Training Expansion (MATE) Act requires new or renewing Drug Enforcement Agency (DEA) registrants, as of June 27, 2023, to have completed a total of at least eight hours of training on opioid or other substance use disorders. This course meets the criteria outlined by Substance Abuse and Mental Health Services Administration (SAMHSA) to count toward this training requirement

http://www.fsmb.org/siteassets/advocacy/key-issues/continuing-medical-education-by-state.pdf, January 2023
Opioid prescription limits and policies by state – Ballotpedia, April 4, 2022
www.netce.com/ce-requirements/
https://www.asam.org/education/dea-education-requirements

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OBTAIN A COMPLETE SOCIAL AND PSYCHOLOGICAL HISTORY

SOCIAL HISTORY

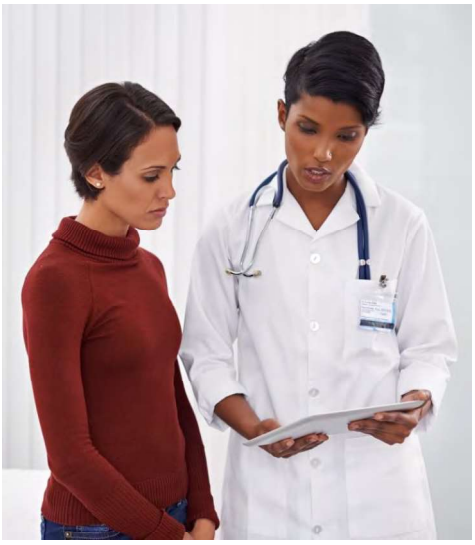
Employment, cultural background, social network, relationship history, legal history, and other behavioral patterns

PSYCHOLOGICAL HISTORY

Screen for:

- Mental health diagnoses, depression, anxiety, PTSD, current treatments
- Alcohol, tobacco, and other drug use
- History of Adverse Childhood Experiences (ACES)
- Family history of substance use disorder and psychiatric disorders

Depression and anxiety can be predictors of chronic pain



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PHYSICAL EXAM AND ASSESSMENT

Seek objective data

Conduct physical exam and evaluate for pain

Order diagnostic or confirmatory tests

General: vital signs, appearance, and pain behaviors

Neurologic exam

Musculoskeletal exam
- Inspection
- Gait and posture
- Range of motion
- Palpation
- Percussion
- Auscultation
- Provocative maneuvers

Cutaneous or trophic findings

SOURCE: Hogans, B., Barreveld, A. (Eds.). Pain Care Essentials, New York, NY: Oxford University Press. 2020.

PAIN ASSESSMENT TOOLBOX

http://core-rems.org/opioid-education/tools/

Pain Assessment Tools

BPI or 5 A's

Functional Assessment

SF-36, PPS, Geriatric Assessment

Pain intensity, Enjoyment of life, General activity

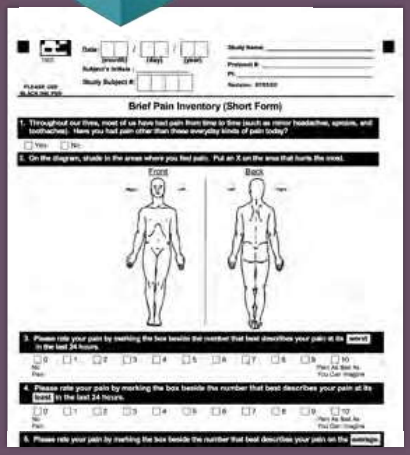
PEG

Adverse Childhood Experience Questionnaire

ACE

Assessment in Patients Unable to Self-Report

Hierarchy of Pain Assessment | **PAINAD**



Brief Pain Inventory (BPI)

Psychological Measurement Tools (PHQ-9, GAD-7, etc.)

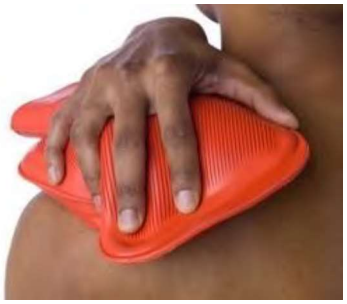
ASSESSMENT IS NOT A ONE-TIME OCCURRENCE

Assessment of a patient's response to pain treatment is a continual process:

- Routinely check the PDMP
- Check in with your patients
- Reassess to identify the underlying source of pain
- Investigate comorbid conditions that may arise
- Ask if patient is willing to engage with other modalities
- Modify plans as needed

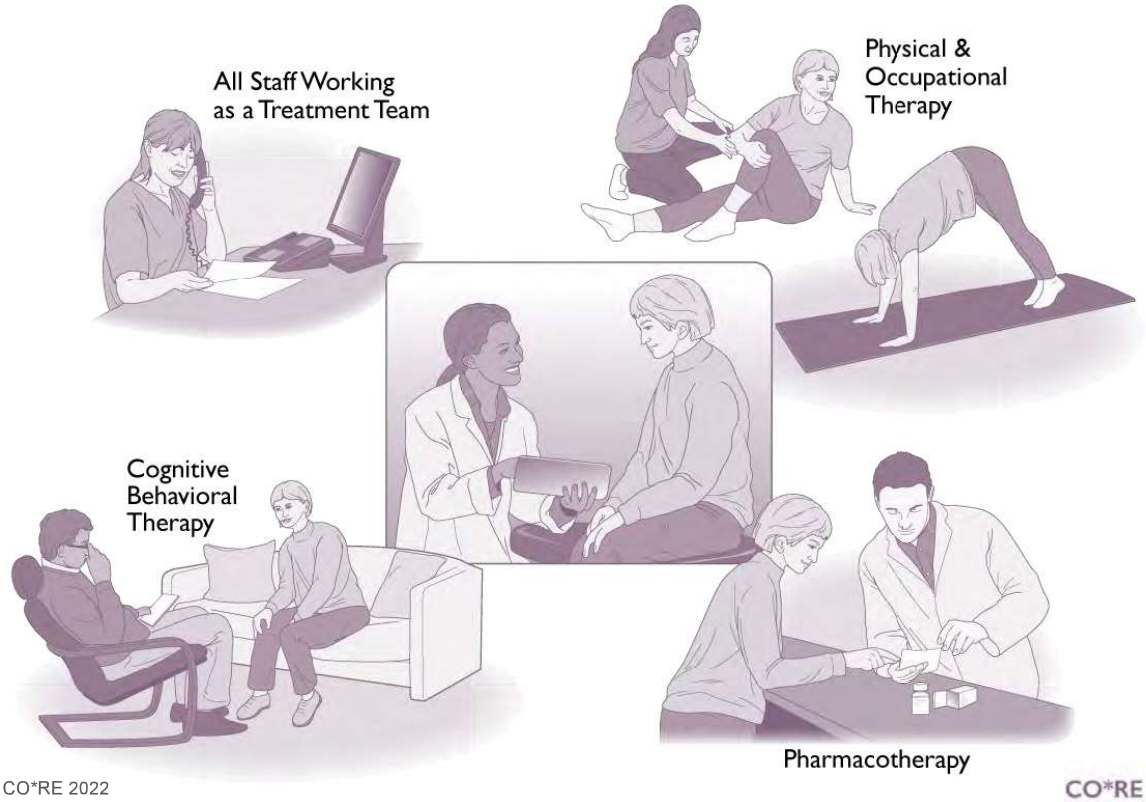
CREATING THE PAIN TREATMENT PLAN



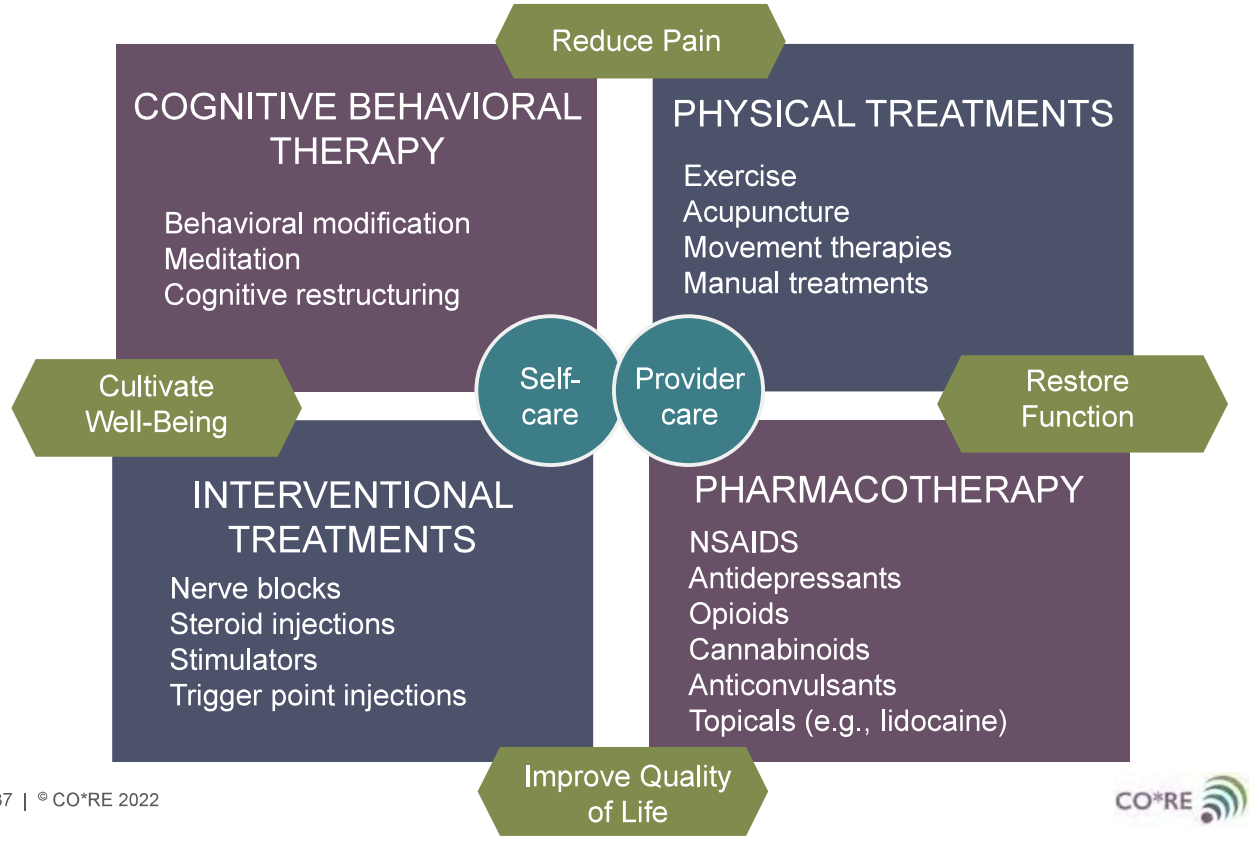



HOW IS PAIN MANAGED?

COMPONENTS OF A MULTIMODAL TREATMENT PLAN FOR PAIN

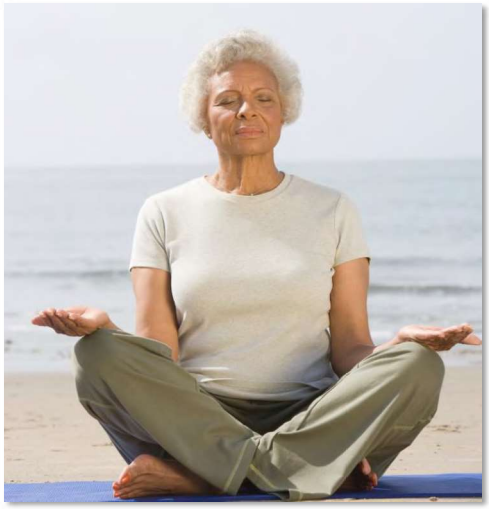


PAIN MANAGEMENT GOALS AND TREATMENT OPTIONS: A MULTIMODAL APPROACH



EVIDENCE-BASED NONPHARMACOLOGIC TREATMENTS

What is appropriate for your patient?



- Tai Chi
- Yoga
- CBT and ACT
- Acupuncture
- PT/OT/aquatic
- Mindfulness meditation
- OMT
- Massage therapy
- Chiropractic
- Neuromodulation or surgical approaches (in some situations)

CBT = cognitive behavioral therapy; ACT = acceptance commitment therapy; OMT = osteopathic manipulative therapy

PHARMACOLOGIC TREATMENTS BY TYPE OF PAIN

CONTINUE EFFECTIVE NONPHARMACOLOGIC OPTIONS

NOCICEPTIVE / INFLAMMATORY	NOCIPLASTIC	NEUROPATHIC
IR opioids Nerve blocks NSAIDs Topicals and patches	Anticholinergic Anticonvulsants TCAs and SNRIs Other serotonin agents **No Opioids**	Anticonvulsants IR and ER/LA opioids Gabapentinoids Nerve blocks TCAs and SNRIs Transdermal opioids

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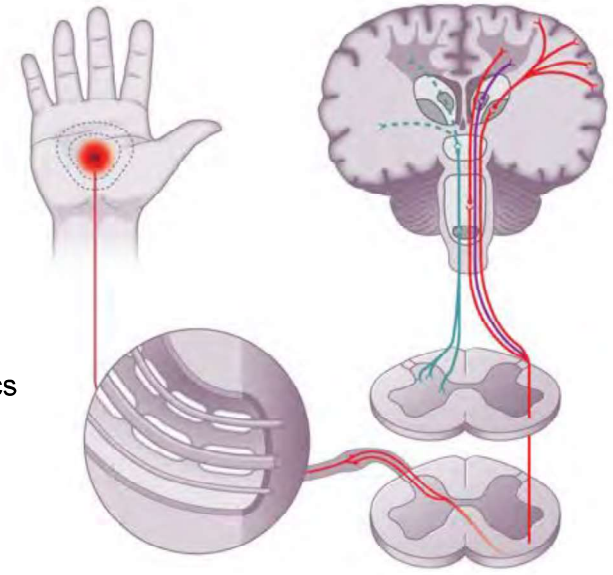
POTENTIAL SITES OF ACTION FOR ANALGESIC AGENTS

Peripherally Mediated Pain:

- Acetaminophen
- NSAIDs
- Opioids
- Topical anesthetics



Centrally Mediated Pain:

- Alpha-2 agonists
- Anticonvulsants
- Ca^{+} channel antagonists
- NMDA RAs
- Opioids
- TCA/SNRI antidepressants

Most commonly, pain conditions are a combination of peripherally and centrally mediated processes

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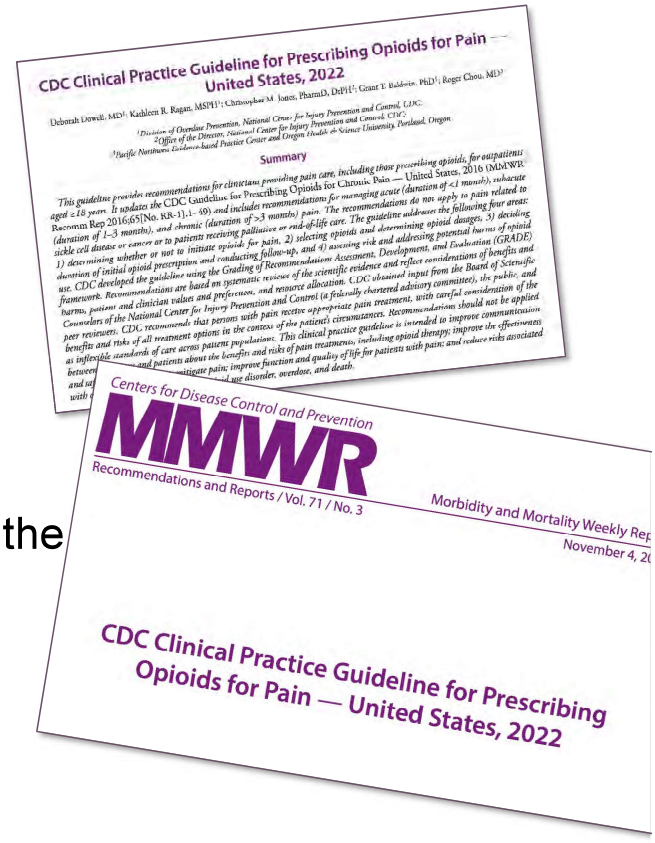
DRUG CHARACTERISTICS TO CONSIDER BEFORE PRESCRIBING

Route of administration	Mechanism of action	Strength	Dosing interval
Key instructions (indications, uses, contraindications)	Specific drug interactions	Formulation	Product-specific safety concerns
Specific information about product conversions, if available	Use in opioid tolerant patients	Relative potency to morphine (MME)	

Opioid product information available at https://opioidanalgesicrems.com/products.html.

2022 CDC GUIDELINE

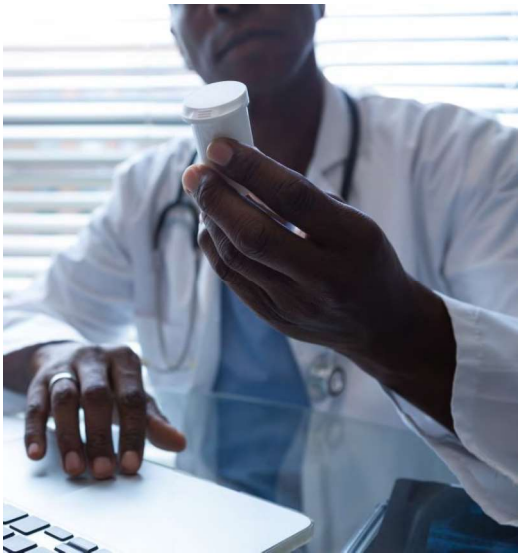
- Clinician recommendations for patients aged ≥18 years
- Summary of current research
- Flexible; encourages patient-centered decision making
- Emphasizes the importance of the individual & clinical judgement
- This is a clinical tool, not a law, regulation or policy



https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm

CONSIDER AN OPIOID ONLY WHEN:

- Potential benefits are likely to outweigh risks
- Patient has failed to adequately respond to non-opioid and nonpharmacological interventions
- Patient has moderate to severe nociceptive or neuropathic pain



Begin as a therapeutic trial

SOURCES: Chou R, et al. J Pain. 2009;10:113-130. Department of Veterans Affairs, Department of Defense. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. 2017.

OLDER ADULTS

RISK FOR RESPIRATORY DEPRESSION

- Age-related changes in distribution, metabolism, excretion; absorption less affected

ACTIONS

- Monitor
  - Initiation and titration
  - Concomitant medications (polypharmacy)
  - Falls risk, cognitive change, psychosocial status
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
- Start low, go slow, but GO
- Routinely initiate a bowel regimen
- Patient and caregiver reliability/risk of diversion

SOURCEs: American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. J Am Geriatr Soc. 2009;57:1331-46; Chou R, et al. J Pain. 2009;10:113-30.

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WOMEN OF CHILDBEARING POTENTIAL

Neonatal opioid withdrawal syndrome is a potential risk of opioid therapy

GIVEN THIS POTENTIAL RISK, CLINICIANS SHOULD:

- Discuss family planning, contraceptives, breastfeeding plans with patients
- Counsel women of childbearing potential about risks and benefits of opioid therapy during pregnancy and after delivery
- Encourage minimal/no opioid use during pregnancy, unless potential benefits outweigh risks to fetus
- Refer to a qualified provider who will ensure appropriate treatment for the baby

- Perform universal screening to avoid neonatal opioid withdrawal syndrome (NOWS)

- **For women using opioids on a daily basis, ACOG recommends buprenorphine or methadone**

ACOG = American College of Obstetricians and Gynecologists
SOURCES: Chou R, et al. J Pain. 2009;10:113-30; ACOG Committee on Obstetric Practice, August 2017

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CHILDREN AND ADOLESCENTS

HANDLE WITH CARE: JUDICIOUS AND LOW-DOSE USE OF IR FOR BRIEF THERAPY

THE SAFETY AND EFFECTIVENESS OF MOST OPIOIDS ARE UNESTABLISHED

- Pediatric analgesic trials pose challenges
- Transdermal fentanyl approved in children ≥ 2 years
- Oxycodone ER dosing changes for children ≥ 11 years

ER/LA OPIOID INDICATIONS ARE PRIMARILY LIFE-LIMITING CONDITIONS

WHEN PRESCRIBING ER/LA OPIOIDS TO CHILDREN:

- Consult pediatric palliative care team or pediatric pain specialist or refer to a specialized multidisciplinary pain clinic

SOURCES: Berde CB, et al. *Pediatrics.* 2012;129:354-364; Gregoire MC, et al. Pain Res Manag 2013;18:47-50; Mc Donnell C. Pain Res Manag. 2011;16:93-98; Slater ME, et al. Pain Med. 2010;11:207-14.

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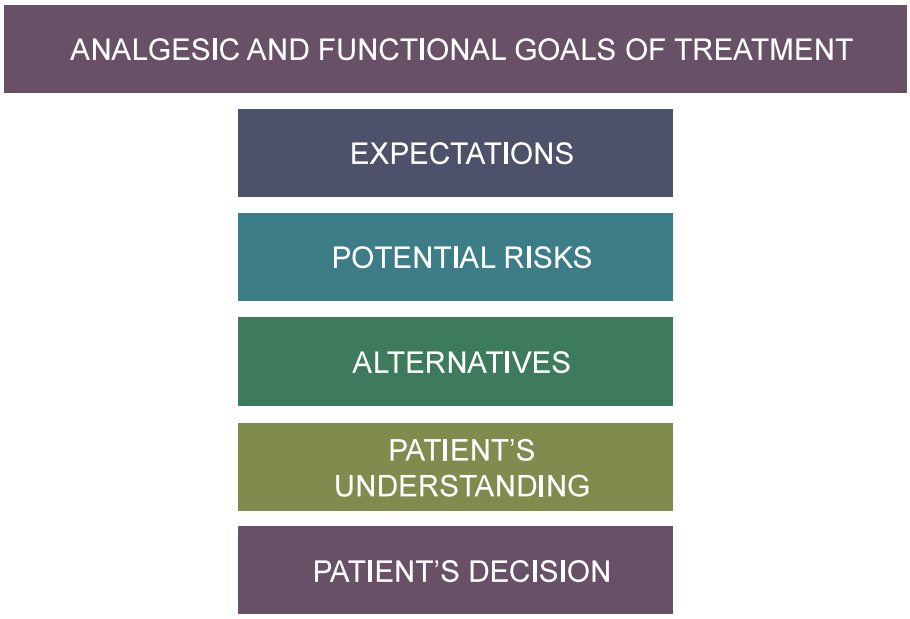
OTHER POPULATIONS NEEDING SPECIAL TREATMENT CONSIDERATIONS

Persons with…

- Sleep disorders or sleep-disordered breathing (sleep apnea)
- Dementia/nonverbal patients
- Obesity
- Renal/hepatic impairment
- Psychiatric disorders
- Life-limiting illness
- Substance use disorder

INFORMED CONSENT

When initiating a pain treatment plan, confirm patient understanding of informed consent to establish:



PATIENT PROVIDER AGREEMENT (PPA)

Reinforce Expectations For Appropriate And Safe Opioid Use

- Clarify treatment plans and goals
- One prescriber
- Consider one pharmacy
- Safeguards
  - Do not store in medicine cabinet
  - Keep locked (medication safe)
  - Do not share or sell
- Instructions for disposal when no longer needed
- Prescriber notification for any event resulting in a pain medication prescription
- Follow-up plan
- Monitoring
  - Random urine drug test (UDT) and pill counts
- Refill procedure
- Identify behaviors indicating need for discontinuation
- Exit strategy
- Signed by both

PATIENT PROVIDER AGREEMENT NONADHERENCE

Behavior outside the boundaries of agreed-on treatment plan

Unsanctioned dose escalations or other noncompliance with therapy on 1 or 2 occasions	Multiple dose escalations or other noncompliance with therapy despite warnings
Unapproved use of the drug to treat another symptom	Prescription forgery
Openly acquiring similar drugs from other medical sources	Obtaining prescription drugs from nonmedical sources

Any of the above behaviors merits **investigation**: proceed with caution

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OPTIMIZING PATIENT CARE THROUGH TELEHEATH

New CO*RE CE/CME Module

- Series of four short videos
- Help HCPs conduct successful telehealth patient visits
- Available online https://learningipma.org

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MANAGING PATIENTS ON OPIOID ANALGESICS

INITIATING OPIOIDS

- Begin a therapeutic trial with an immediate release (IR) opioid
- Prescribe the lowest effective dosage
- Use caution at any dosage, but particularly when:
  - Increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day
  - Carefully justify a decision to titrate dosage to ≥ 90 MME/day
- Always include dosing instructions, including daily maximum
- Be aware of interindividual variability of response
- Have PPA, baseline UDT, and informed consent in place
- Co-prescribe naloxone and bowel regimen
- Re-evaluate risks/benefits within 1–4 weeks (could be as soon as 3–5 days) of initiation or dose escalation
- Re-evaluate risks/benefits every 1–3 months; if benefits do not outweigh harms, optimize other therapies and work to taper and discontinue

There are differences in benefits, risks, and expected outcomes for patients with chronic pain and cancer pain, as well as for hospice and palliative care patients.

ONGOING AND LONG-TERM MANAGEMENT OF PATIENTS ON OPIOID ANALGESICS

PERIODIC REVIEW OF PAIN

- Is the patient making progress toward functional goals?
- Reset goals if required or indicated; develop reasonable expectations
- Monitor for breakthrough pain
- Review adverse events/side effects at each visit
  - Evaluate bowel function
  - Screen for endocrine function as needed
  - Report adverse events to the FDA website
  - Implement opioid rotation, as indicated

Prescribers should report serious AEs and medication errors to the FDA: https://www.fda.gov/media/76299/download or 1-800-FDA-1088

ONGOING AND LONG-TERM MANAGEMENT OF PATIENTS ON OPIOID ANALGESICS

MONITORING FOR SAFETY

- Check Prescription Drug Monitoring Program (PDMP)
- Use urine drug testing (UDT)
- Reassess risk of substance use disorder (SUD) and/or OUD
- Monitor adherence to the treatment plan
  - Medication reconciliation
  - Evaluate for nonadherence

DISCONTINUING AND TAPERING

- When is opioid therapy no longer necessary?

MONITORING PAIN AND SUBSTANCE USE DISORDER

PAIN – 5 A's	SUD – 5 C's
• **A**nalgesia • **A**ctivity/Function • **A**berrant/Problematic behavior, not present • **A**dverse events • **A**ffect	• **C**ontrol, loss of • **C**ompulsive use • **C**raving drug • **C**ontinued use • **C**hronic problem

URINE DRUG TESTING (UDT)

- Urine testing is done **FOR** the patient, not **TO** the patient
- Helps to identify drug misuse/addiction
- Assists in assessing and documenting adherence

CLINICAL CONSIDERATIONS

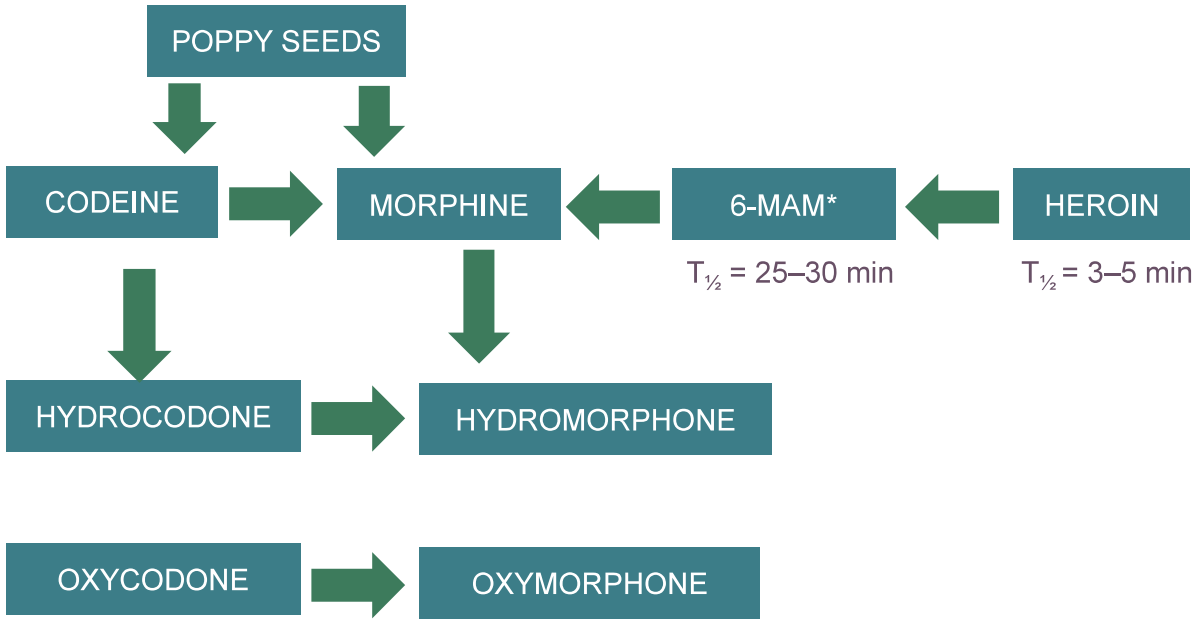
- Recommend UDT before first prescription (baseline), then intermittently, depending on clinical judgment and state regulations
- Document time and date of last dose taken
- Be aware of possible false positives or negatives
- Clarify unexpected results with the lab before confronting patient to rule out poor specimen or error

SCREENING VERSUS CONFIRMATORY UDTs

	SCREENING (Office-based)	CONFIRMATORY (Send to lab)
Analysis technique	Immunoassay	GC-MS or HPLC
Sensitivity (power to detect a class of drugs)	Low or none when testing for semi-synthetic or synthetic opioids	High
Specificity (power to detect an individual drug)	Varies (can result in false positives or false negatives)	High
Turnaround	Rapid	Slow
Cost/Other	Lower cost; intended for a drug-free population; may not be useful in pain medicine	Higher cost; legally defensible results

GC-MS = gas chromatograph-mass spectrometry; HPLC = high-performance liquid chromatography

EXAMPLES OF OPIOID METABOLISM

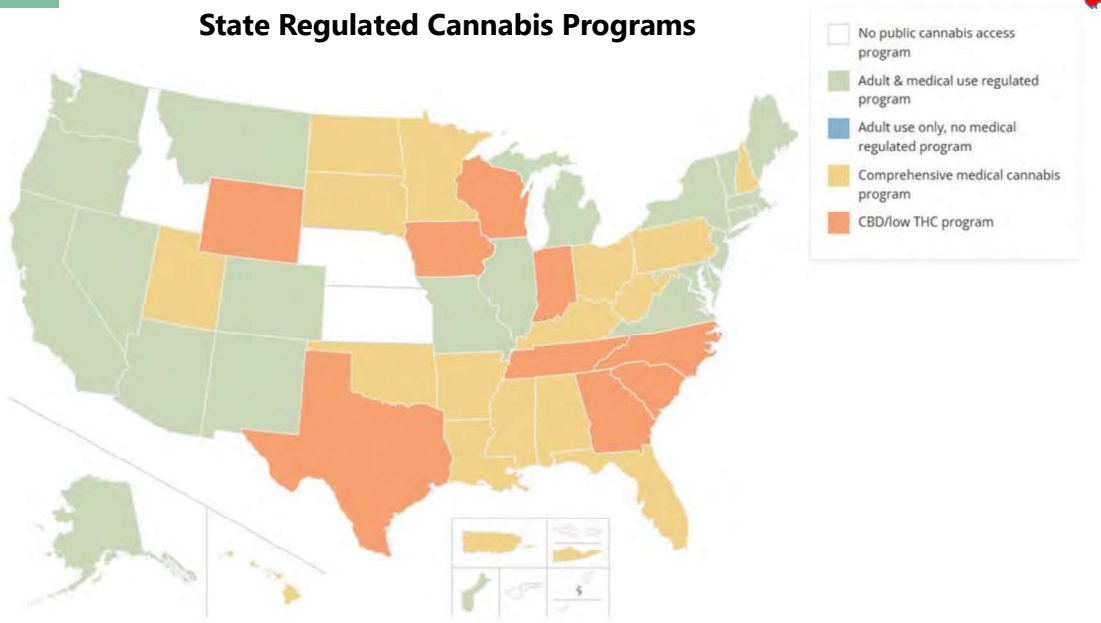


*6-MAM = 6-Monoacetylmorphine

Marijuana Status

Medical

State Regulated Cannabis Programs



Recreational

Legal for recreational use in Illinois

https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx, April 2023

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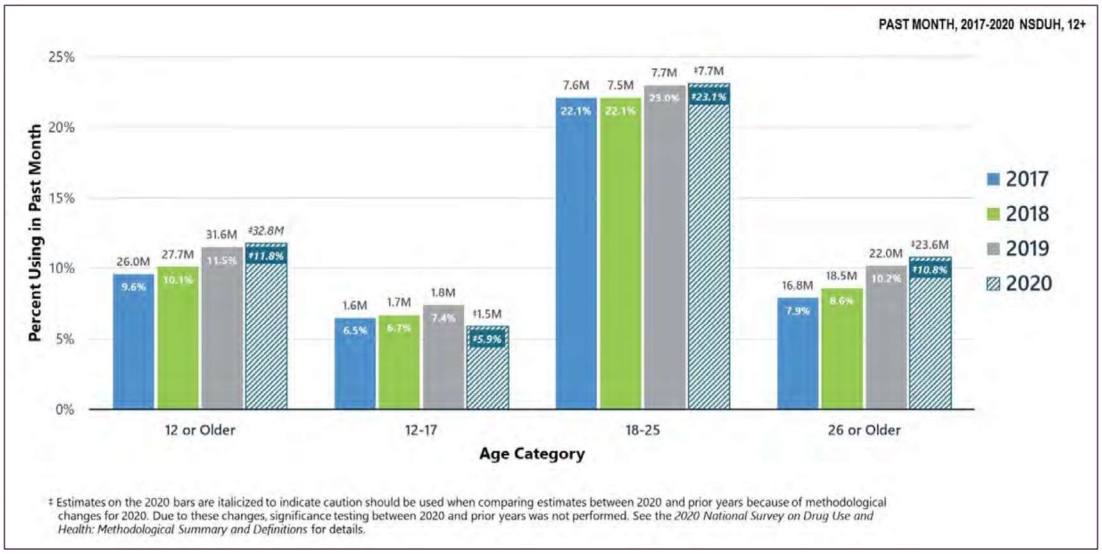
EPIDEMIOLOGY & RECENT TRENDS



- Most commonly-used federally illicit substance in the U.S.
- 44% of people aged 19-30 used in the last year with daily use at 11%, all time highs
- Use is increasing among those 12+ and 26 +

SOURCES: SAMHSA 2020 report from National Survey on Drug Use and Health (NSDUH)
https://monitoringthefuture.org/wp-content/uploads/2023/07/mtfpanel2023.pdf

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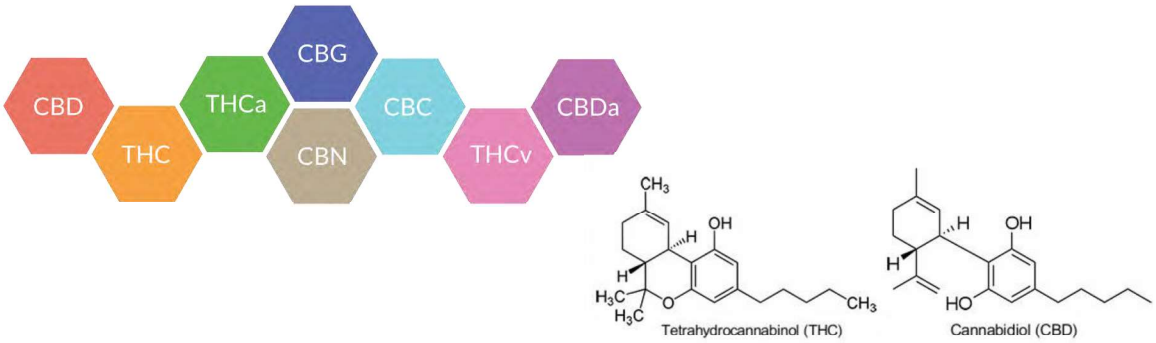
CHEMICAL COMPOSITION

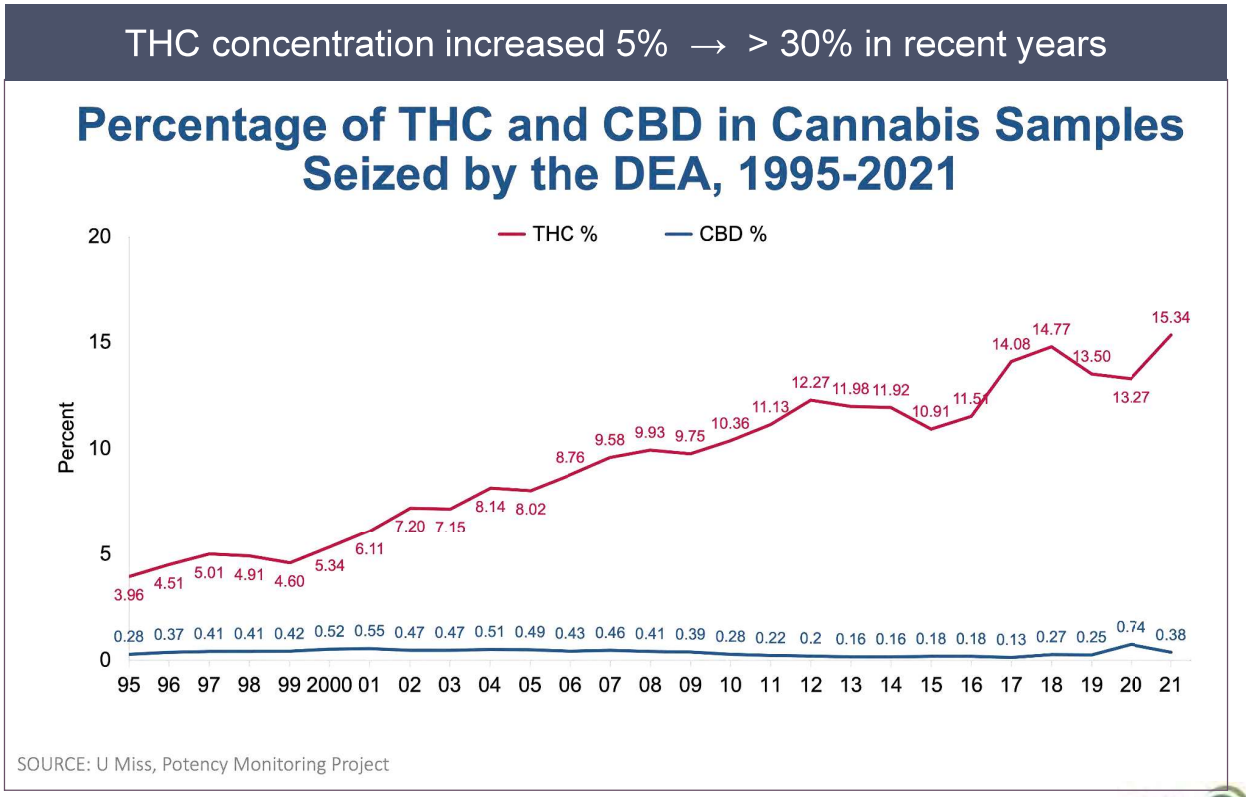
- Over 100 cannabinoids in cannabis plants, most unstudied
- THC associated with more negative effects (high, addiction)
- CBD thought to be potentially more therapeutic
- Preparations often labeled with inaccurate THC & CBD content
- Varying concentration, other cannabinoids may have health effects



SOURCE: Hayakawa, K. et al. Therapeutic Potential of Non-Psychotropic Cannabidiol in Ischemic Stroke. Pharmaceuticals **2010**, 3, 2197-2212

INCREASED THC POTENCY OVER TIME

THC concentration increased 5% → > 30% in recent years



SOURCE: U Miss, Potency Monitoring Project

Preparations

PREPARATIONS	DESCRIPTION	USE
MARIJUANA	Dried plant product consisting of leaves, stems, and flowers	Smoked or vaporized
HASHISH	Concentrated resin cake	Ingested or smoked
TINCTURE	Cannabinoid liquid extracted from plant	Consumed sublingually
HASHISH OIL	Oil obtained from Cannabis plant by solvent extraction	Smoked or vaporized
INFUSION	Plant material mixed with nonvolatile solvents (e.g., butter, cooking oil)	Ingested

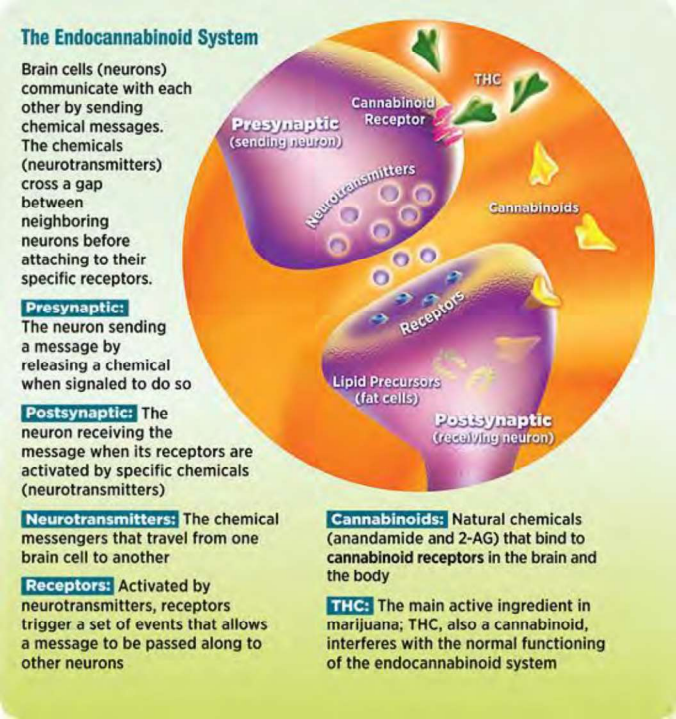
SOURCE: Hill 2015, JAMA

SYNTHETIC CANNABIONOID PRODUCTS

- Typically chemicals sprayed onto dried plant product
- Examples: K2, Spice, Joker, Black Mamba, Kush, KronicSynthetic chemicals sprayed onto dried, shredded plant product
- Mimic THC, bind strongly to same receptors → stronger effects
- Could cause changes in mood/perception, psychosis, tachycardia, vomiting, violent behavior, SI, renal impairment, seizures, death
- Often undetectable in standard urine drug tests
- Warn patients against using these products, severe adverse effects

SOURCE: SAMHSA 2019, NY Dept Pub Health, DEA drugabuse.gov

MECHANISM: HOW DOES CANNABIS WORK?



- Endogenous cannabinoids originate from postsynaptic membrane
- Act on presynaptic cannabinoid receptors
- Modulate release of neurotransmitters (e.g., dopamine)
- Exogenous cannabinoids co-opt this system
- Also affects 5HT, alpha, TRPV, TRPA receptors

SOURCE: NIDA 2011

THEORETICAL MECHANISMS FOR ANALGESIA

- Cells in injured tissue release endocannabinoids
- CB1-r in brain, spinal cord → mitigate sensitization, inflammation
- CB2-r in brain, spinal cord, dorsal root ganglion → reduce inflammatory hyperalgesia
- Long-term studies of exogenous cannabinoids and pain still needed; other mechanisms possible
- Caution with any drug where subjective pain improves, but has addictive properties (e.g., alcohol, opioids, benzodiazepines)

SOURCE: Hill 2017 Cannabis and Cannabinoid Res

PERCEPTIONS OF MEDICAL EFFICACY vs DATA

Perceptions

- 81% of patients believe marijuana has at least one benefit
- 66% of patients believe in pain benefit

Data

- Systematic Review of RTCs: 2021: Outcomes had low or very low-quality evidence, neither supporting nor refuting efficacy
- Meta analysis 2022: Placebo contributes significantly to pain reduction in cannabis clinical trials
- Review 2022: High THC:CBD products (>98% THC) associated with 25% reduction in pain in short-term studies of variable quality

SOURCE: Keyhani et al, Annals of Int Med 2018; Fisher et al Pain 2021; Gedin et al, JAMA 2022, , McDonagh Ananls 2022

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OPIOID-SPARING THEORY vs DATA

Theory: If cannabis products treat pain, patient may use these products and reduce their use of opioids

Data

- States with medical cannabis have modestly lower rates of opioid prescribing and risky opioid prescribing
- **2019 Study:** Association between med cannabis and reduced opioid mortality has **reversed** over time
- **2021 Meta Analysis:** Opioid-sparing effects remain uncertain due to very low evidence
- **2022 Meta Analysis:** Preclinical/observational studies show opioid-sparing effect, but higher-quality RCTs do not
- **2023 Living Systematic Review:** Cannabis impact on use of opioids remains insufficient

SOURCES: Shah et al, JGIM 2019, Noori et al BMJ Open 2021; Nielsen Neuropsychopharm 2022; Chou et al, AHRQ, 2023.

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MEDICAL INDICATIONS

Psychiatric:

- Not well-studied or FDA-approved for any psychiatric condition

Non-Psychiatric FDA Approvals:

- Nausea, vomiting related to chemotherapy
- Anorexia/wasting related to HIV
- Rare childhood forms of epilepsy

The American Psychiatric Association has a Position Statement Against the Use of Cannabis for PTSD and a Position Statement in Opposition to Cannabis as Medicine

SOURCE: APA 2019; US FDA2020 FDA and Cannabis: Research and Drug Approval Process

FDA-APPROVED CANNABINOIDS

Medication	Type	Indication
Dronabinol (Marinol; Syndros)	Synthetic	Anorexia/wasting in AIDS patients
Nabilone (Cesamet)	Synthetic	Nausea, vomiting in chemotherapy patients
Cannabidiol (Epediolex)	Plant-derived	Lennox-Gastaut; Dravet's

SOURCE: fda.gov

CLINICAL CONSIDERATIONS

- Individual risk stratification is crucial
  - Person/family history of mental health, addictions
  - Baseline psychosis risk
  - Risks related to driving, work, education, parenting
  - Medical, cognitive issues worsened by cannabis
- Counsel patients
  - Federally, cannabis is illegal (Schedule 1)
  - States vary
  - Review harm reduction strategies
- Use PPA and document conversations about risks
- Seek institutional legal counsel to reduce liability

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CANNABIS AND HARM REDUCTION

- Abstinence is best way to avoid health risks
- Avoid early-age initiation
- Avoid high frequency use (daily or near daily)
- Choose low-potency THC or balanced THC:CBD ratios
- Abstain from synthetic products
- Avoid combustible products, non-smoking methods preferable

- Avoid deep/risky inhalation
- Abstain from cannabis-impaired driving
- High-risk populations should avoid use (e.g., psychosis, addictions)
- Track use over time, including metered dosing

SOURCE: Adapted from Fischer et al, 2017. American J Public Health Policy

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WHEN TO MOVE FROM IR TO ER/LA OPIOIDS

PRIMARY REASONS

- Maintain stable blood levels (steady state plasma)
- Longer duration of action
- Multiple IR doses needed to achieve effective analgesia
- Poor analgesic efficacy despite dose titration
- Less sleep disruption

OTHER POTENTIAL REASONS

- Patient desire or need to try a new formulation
- Cost or insurance issues
- Adherence issues
- Change in clinical status requiring an opioid with different pharmacokinetics
- Problematic drug-drug interactions

CONSIDERATIONS FOR CHANGE FROM IR TO ER/LA OPIOIDS

DRUG AND DOSE SELECTION IS CRITICAL

Some ER/LA opioids or dosage forms are only recommended for opioid tolerant patients

- ANY strength of transdermal fentanyl or hydromorphone ER
- Certain strengths/ doses of other ER/LA products (check drug prescribing information)

MONITOR PATIENTS CLOSELY FOR RESPIRATORY DEPRESSION

- Especially within 24–72 hours of initiating therapy and increasing dosage

INDIVIDUALIZE DOSAGE BY TITRATION BASED ON EFFICACY, TOLERABILITY, AND PRESENCE OF ADVERSE EVENTS

- Check ER/LA opioid product PI for minimum titration intervals
- Supplement with IR analgesics (opioid and non-opioid) if pain is not controlled during titration

SOURCES: Chou R, et al. J Pain. 2009;10:113-130; FDA. Education Blueprint Healthcare Providers Involved in the Treatment and Monitoring of Patients with Pain 09/2018, https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_analgesic_2018_09_18_FDA_Blueprint.pdf

EMERGENCE OF OPIOID-INDUCED HYPERALGESIA

- An increased sensitivity to pain
- Usually occurs at high MME dosages and over long periods of time
- A physiological phenomenon that can happen to anyone
- Consider this explanation if:
  - Pain increases despite dose increases
  - Pain appears in new locations
  - Patient becomes more sensitive to painful stimuli
  - Patient is not improving in the absence of underlying cause or disease progression

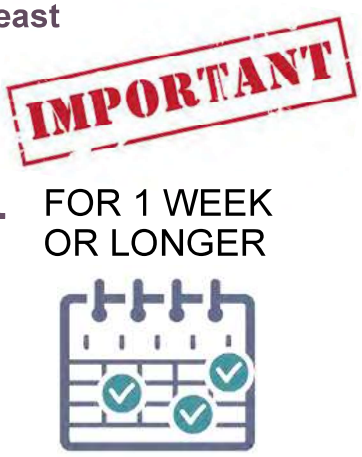
SOURCE: Yi P, Pryzbylkowski P. Opioid induced hyperalgesia. Pain Medicine 2015; 16: S32-S36

OPIOID TOLERANCE

If opioid tolerant, still use caution at higher doses

Patients considered opioid tolerant are taking at least

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/hour
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of another opioid



Also use caution when rotating a patient on an IR opioid to a different ER/LA opioid

Products restricted to opioid tolerant individuals include transdermal fentanyl (Duragesic) and hydromorphone (Exalgo).

SOURCE: The Opioid Analgesics Risk Evaluation & Mitigation Strategy product search, https://opioidanalgesicrems.com/products.html

OPIOID TOLERANCE VERSUS PHYSICAL DEPENDENCE

TOLERANCE

- Occurs when increased dose is needed to maintain the functional status no longer achieved by current dose
- Remember CNS and respiratory depression can develop with dose increase

PHYSICAL DEPENDENCE

- Occurs when an individual only functions normally in the presence of the substance
- Abrupt discontinuation or dosage decrease causes uncomfortable symptoms of withdrawal

Both **tolerance** and **physical dependence** are physiological adaptations to chronic opioid exposure and **DO NOT** equal addiction or opioid use disorder

OPIOID ROTATION

DEFINITION

A change from an existing opioid regimen to another opioid with the goal of improving therapeutic outcomes or to avoid AEs attributed to the existing drug

RATIONALE

Used when differences in pharmacologic or other effects make it likely that a switch will improve outcomes

- Effectiveness and AEs of different mu-opioids vary among patients
- Patient tolerant to first opioid might have improved analgesia from second opioid at a dose lower than calculated from an equianalgesic dosing table (EDT)

SOURCES: Fine PG, et al. J Pain Symptom Manage. 2009;38:418-425; Knotkova H, et al. J Pain Symptom Manage. 2009;38:426-439; Pasternak GW. Neuropharmacol. 2004;47(suppl 1):312-323.

EQUIANALGESIC DOSING TABLES (EDTs)

Many different versions:

- Published
- Online calculators
- Smartphone apps

Vary in terms of:

- Equianalgesic values
- Whether ranges are used
- **Which opioids are included:** May or may not include transdermal opioids, rapid-onset fentanyl, ER/LA opioids, or opioid agonist-antagonists

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START WITH AN EDT FOR ADULTS

	EQUIANALGESIC DOSE		USUAL STARTING DOSE	
DRUG	SC/IV	PO	PARENTERAL	PO
Morphine	10 mg	30 mg	2.5–5 mg SC/IV q3–4hr (1.25–2.5 mg)	5–15 mg q3–4hr (IR or oral solution) (2.5–7.5 mg)
Oxycodone	NA	20 mg	NA	5–10 mg q3–4hr (2.5 mg)
Hydrocodone	NA	30 mg	NA	5 mg q3–4hr (2.5 mg)
Hydromorphone	1.5 mg	7.5 mg	0.2–0.6 mg SC/IV q2–3hr (0.2 mg)	1–2 mg q3–4hr (0.5–1 mg)

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MU-OPIOID RECEPTORS AND INCOMPLETE CROSS TOLERANCE

MU-OPIOIDS BIND TO MU RECEPTORS

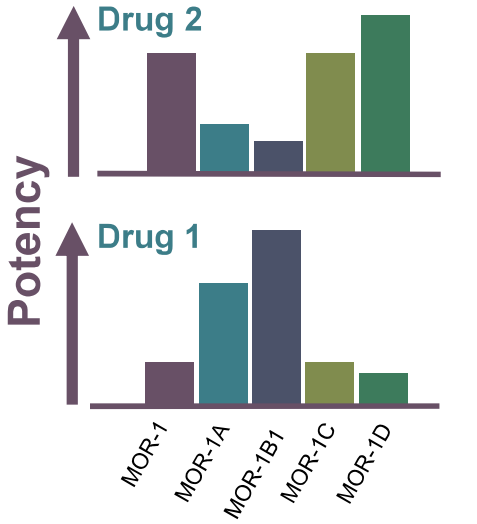
MANY MU RECEPTOR SUBTYPES

Mu-opioids produce **subtly different** pharmacologic responses based on distinct activation profiles of mu receptor subtypes

MAY HELP EXPLAIN:

Interpatient variability in response to mu-opioids

Incomplete cross tolerance among mu-opioids



GUIDELINES FOR OPIOID ROTATION

Calculate equianalgesic dose of new opioid from EDT

REDUCE CALCULATED EQUIANALGESIC DOSE BY 25%–50%*

SELECT % REDUCTION BASED ON CLINICAL JUDGMENT

CLOSER TO 50% REDUCTION

IF PATIENT…

- Is receiving a relatively high dose of current opioid regimen
- Is elderly or medically frail

CLOSER TO 25% REDUCTION

IF PATIENT…

- Does not have these characteristics
- Is changing route of administration

*75%–90% reduction for methadone

GUIDELINES FOR OPIOID ROTATION *(continued)*

IF SWITCHING TO METHADONE:

- Standard equianalgesic dosing tables are less helpful in opioid rotation to methadone
- For opioid tolerant patients, methadone doses should **not** exceed 30–40 mg/day upon rotation
  - Consider inpatient monitoring, including serial EKG monitoring
- For opioid-naïve patients, do **not** give methadone as an initial drug

IF SWITCHING TO TRANSDERMAL:

- **Fentanyl:** calculate dose conversion based on equianalgesic dose ratios included in the drug package insert

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GUIDELINES FOR OPIOID ROTATION: SUMMARY

VALUES FROM EDT*	PATIENT OPIOID VALUES	SOLVE FOR X	AUTOMATICALLY REDUCE DOSE
Value of current opioid / Value of new opioid	24-hr dose of current opioid / X amount of new opioid	Equianalgesic 24-hr dose of new opioid	By 25%–50%†

Frequently assess initial response	Titrate dose of new opioid to optimize outcomes	Calculate supplemental rescue dose used for titration at 5%–15% of total daily dose‡

* If switching to transdermal fentanyl, use equianalgesic dose ratios provided in PI.
†If switching to methadone, reduce dose by 75%–90%.
‡If oral transmucosal fentanyl used as rescue, begin at lowest dose irrespective of baseline opioid.

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BREAKTHROUGH PAIN (BTP)

PATIENTS ON STABLE ATC OPIOIDS MAY EXPERIENCE BTP

- Due to disease progression or a new or unrelated pain
  - Target cause or precipitating factors
- Dose for BTP: Using an **IR, 5%–15%** of total daily opioid dose, administered at an appropriate interval
- **Never use ER/LA for BTP**

CONSIDER ADDING

- PRN IR opioid trial based on analysis of benefit versus risk
  - There is a risk for problematic drug-related behaviors
  - High-risk: Add only in conjunction with frequent monitoring
  - and follow-up
  - Low-risk: Add with routine follow-up and monitoring
- Consider non-opioid drug therapies and nonpharmacologic treatments

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ABUSE-DETERRENT FORMULATION (ADF) OPIOIDS

Drug formulations designed to discourage misuse

- An ER/LA opioid with properties to meaningfully deter misuse (less likely to be crushed, injected, or snorted)
- Consider as one part of an overall strategy
- Mixed evidence on the impact of ADF on misuse
- Overdose is still possible if taken orally in excessive amounts
- These products are expensive with no generic equivalents

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CONSIDERATIONS FOR RE-EVALUATING OPIOID USE

PATIENT MOVES PAST THE POINT OF NEED	INTOLERABLE AND UNMANAGEABLE AEs	NO PROGRESS TOWARD THERAPEUTIC GOALS	RISKS OUTWEIGH BENEFITS

MISUSE BEHAVIORS

- One or two episodes of increasing dose without prescriber knowledge
- Sharing medications
- Unapproved opioid use to treat another symptom (e.g., insomnia)
- Use of illicit drugs or unprescribed opioids
- Repeatedly obtaining opioids from multiple outside sources
- Prescription forgery
- Multiple episodes of prescription loss
- Diversion

Even at prescribed doses, opioids carry the risk of misuse, abuse, opioid use disorder, overdose, and death

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TOOLS TO REASSESS OUD/SUD RISK

SBIRT
Screening, Brief Intervention, and Referral to Treatment

TAPS
Tobacco, Alcohol, Rx, and Other Substances

PDUQ
Prescription Drug Use Questionnaire

PMQ
Pain Medication Questionnaire

COMM
Current Opioid Misuse Measure

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APPROACHES TO SUPPORT THE DISCONTINUATION DECISION

- Discontinue through a taper schedule
- If OUD suspected:
  - Begin treatment: Medications for Opioid Use Disorder (MOUD)
  - Refer to an OUD specialist
- Consider rotation to partial agonist (e.g., buprenorphine)
- No single approach is appropriate for all patients
- May use a range of approaches, from a slow 10% dose reduction per week to a more rapid 25%–50% reduction every few days
- To minimize withdrawal symptoms in patients physically dependent on opioids, consider medications to assist with withdrawal (clonidine, NSAIDs, antiemetics, antidiarrheal agents)

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CONSULTING A PAIN SPECIALIST

- Appropriate when you feel you cannot provide the level of care needed
- First ensure you have a reliable specialist to refer to
- To find a pain specialist in your area:
  - Consult with state boards
  - Consult with colleagues
  - Use online resources
  - Consult payment source
- Prior to referral, contact the specialist and ask what is needed for referral

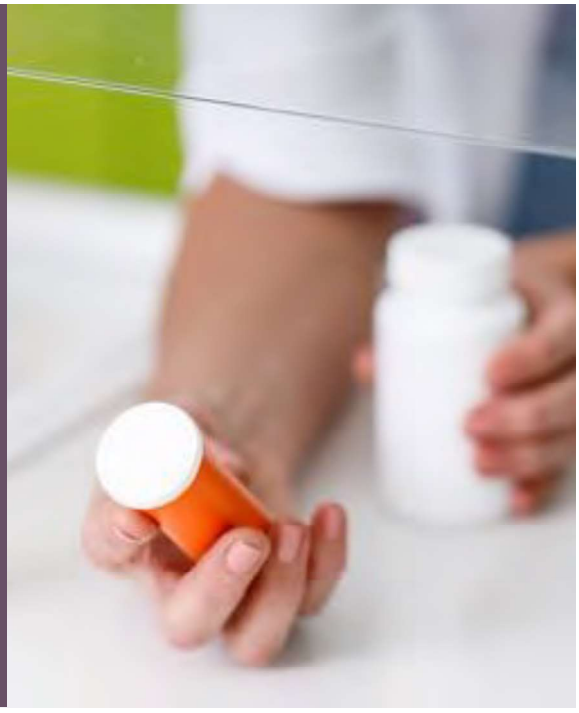
Adequately **DOCUMENT**
all patient interactions,
assessments, test results,
treatment plans,
and expectations.

Case Scenario

https://www.youtube.com/watch?v=2Akj9riF5Sw

COUNSEL PATIENTS ABOUT PROPER USE

- Take opioid as prescribed
- Use least amount of medication necessary for shortest time
- Use caution with long-term opioid use patients; avoid abrupt discontinuation or dose reduction; taper safely to avoid withdrawal symptoms
- Notify HCP if pain is uncontrolled
- Report side effects to HCP
- Inform HCP of ALL meds and supplements being taken
- Never share or sell opioids: can lead to others' deaths, against the law
- Use caution when operating heavy machinery and driving



USE FDA PATIENT COUNSELING DOCUMENT

- What are opioids?
- What are the risks and benefits?
- How to take safely

https://tinyurl.com/5n6z2dta

What You Need to Know About Opioid Pain Medicines

This guide is for you! Keep this guide and the Medication Guide that comes with your medicine so you can better understand what you need to know about your opioid pain medicine. Go over this information with your healthcare provider. Then, ask your healthcare provider about anything that you do not understand.

What are opioids?

Opioids are strong prescription medicines that are used to manage severe pain.

What are the serious risks of using opioids?

- Opioids have serious risks of addiction and overdose.
- **Too much opioid medicine in your body can cause your breathing to stop – which could lead to death.** This risk is greater for people taking other medicines that make you feel sleepy or people with sleep apnea.
- **Addiction** is when you crave drugs (like opioid pain medicines) because they make you feel good in some way. You keep taking the drug even though you know it is not a good idea and bad things are happening to you. Addiction is a brain disease that may require ongoing treatment.

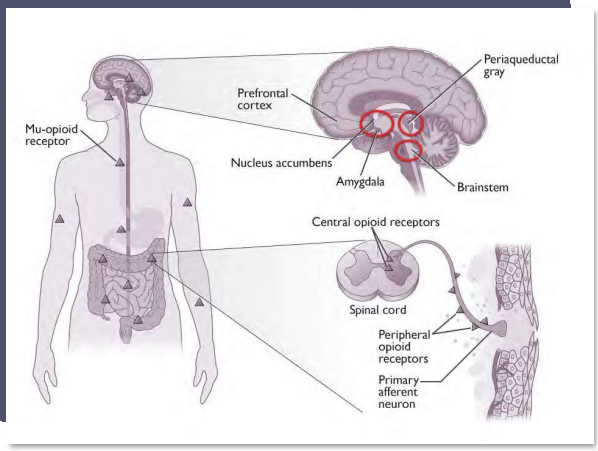
Risk Factors for Opioid Abuse:

- You have:
  - a history of addiction
  - a family history of addiction

- Take your opioid medicine exactly as prescribed.
- Do not cut, break, chew, crush, or dissolve your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider.
- When your healthcare provider gives you the prescription, ask:
  - How long should I take it?
  - What should I do if I need to taper off the opioid medicine (slowly take less medicine)?
- Call your healthcare provider if the opioid medicine is not controlling your pain. Do not increase the dose on your own.
- Do not share or give your opioid medicine to anyone else. Your healthcare provider selected this opioid and the dose just for you. A dose that is okay for you could cause an overdose and death for someone else. Also, it is against the law.
- Store your opioid medicine in a safe place where it cannot be reached by children or stolen by family or visitors to your home. Many teenagers like to experiment with pain medicines. Use a lock- box to keep your opioid

PROVIDE ANTICIPATORY GUIDANCE ON OPIOID SIDE EFFECTS AND ADVERSE EVENTS

- Overdose and death: respiratory depression
- Opioid-induced constipation (OIC): most common
- Nausea, vomiting, GERD
- Sexual dysfunction and other endocrine abnormalities (hypogonadism)
- Tolerance, physical dependence
- Hyperalgesia
- Allergic reactions
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Myoclonus (twitching or jerking)
- Opioid use disorder (OUD)



COUNSEL PATIENTS AND CAREGIVERS

WARNINGS (Safe Administration)	WHAT TO LOOK FOR (Safety Concerns)
• Never break, chew, crush, or snort an opioid tablet/capsule • Never cut or tear patches or buccal films • If patient cannot swallow, determine if appropriate to sprinkle contents on applesauce or administer via feeding tube • Use of CNS depressants or alcohol with opioids can cause overdose	• Cravings • Being unable to fulfill work/family obligations • Nodding off • Taking more than prescribed

OPIOID-INDUCED RESPIRATORY DEPRESSION

If not immediately recognized and treated, may lead to respiratory arrest and death

More likely to occur in opioid-naïve patients during initiation or after dose increase

Instruct patients/family members to:

- Screen for shallow or slowed breathing
- Deliver NALOXONE
- **CALL 911**

Instructions may differ if patient is on hospice or near end of life

Greatest risk: when co-prescribed with a benzodiazepine

SIGNS OF ACCIDENTAL OPIOID POISONING: CALL 911

- Person cannot be aroused or is unable to talk
- Any trouble with breathing, heavy snoring is warning sign
- Gurgling noises coming from mouth or throat
- Body is limp, seems lifeless; face is pale, clammy
- Fingernails or lips turn blue/purple
- Slow, unusual heartbeat or stopped heartbeat

Administer Naloxone

CO*RE

NALOXONE

WHAT IT IS:

- An opioid antagonist administered intranasally (most common) or parenterally
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia; may precipitate acute opioid withdrawal
- No misuse potential

WHAT TO DO:

- Discuss an overdose plan with patients; involve family/caregivers
- Ensure family/caregivers have access to naloxone; some states *require* co-prescribing
- Involve and train family, friends, partners, and/or caregivers in the proper administration of naloxone
- Know your local naloxone resources (e.g., the library, community centers)
- Check expiration dates and replace expired naloxone
- In the event of known or suspected overdose, **call 911** and administer naloxone

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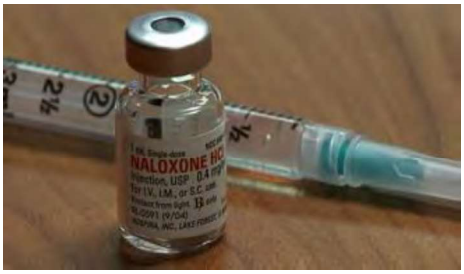
NALOXONE OPTIONS

- Available as auto-injector, intramuscular injection, or nasal spray
- Cost and insurance coverage vary
- Make use of tutorial videos or live demonstration to educate patient/family/caregiver on proper administration
- Store at room temperature



Naloxone vials

Narcan nasal spray

Evzio (auto-injector)

Trade names are used for identification purposes only and do not imply endorsement.

SOURCE: FDA Information About Naloxone, https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm472923.htm

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Naloxone Regulation

Effective date	• **January 2019**
Criminal Immunity	• Prescribers: **Yes** • Dispensers: **Yes** • Lay People: **Yes**
Also Available	• Without Prescription: **Yes** • To 3rd Party: **Yes** • By Standing Order: **Yes**
Carried by First Responders	• **Yes**

On March 29, 2023, FDA announced approval of Narcan (naloxone hydrochloride) Nasal Spray (NNS) for use as a nonprescription opioid overdose reversal agent. OTC NNS commercially available Sept 2023. Other naloxone products will remain prescription drugs.

State Naloxone Access Rules and Resources - SAFE Project, January 2023
http://legislativeanalysis.org/wp-content/uploads/2023/02/Naloxone-Access-Summary-of-State-Laws.pdf
https://www.thefdalawblog.com/2023/03/2023-is-the-year-for-otc-naloxone 3/30/2023

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How to Use Naloxone Spray
https://www.youtube.com/watch?v=odlFtGNjmMQ

WHAT IS ADDICTION?

PRACTICAL DEFINITION:

Addiction is the continued use of drugs or activities, despite knowledge of continued **harm** to one's self or others.

OFFICIAL ASAM DEFINITION:

Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences. Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

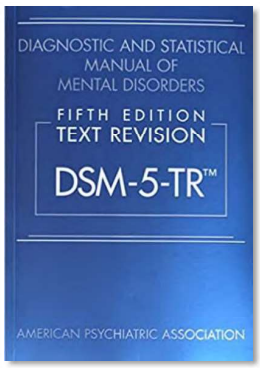
OPIOID USE DISORDER: DSM-5-TR CRITERIA

Be alert to these factors in your patients on long-term opioid therapy

1. Taking larger amounts and/or for longer periods than intended
2. Persistent desire or inability to cut down or control use
3. Increased time spent obtaining, using, or recovering
4. Craving/compulsion to use opioids
5. Role failure at work, home, school
6. Social or interpersonal problems
7. Reducing social, work, recreational activity
8. Physical hazards
9. Physical or psychological harm

❖ Tolerance

❖ Withdrawal

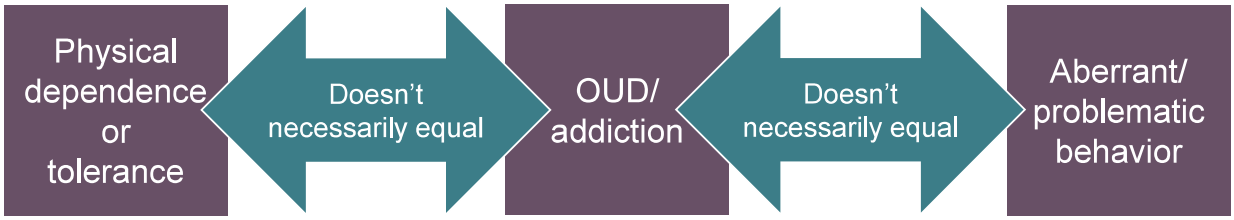


- 2–3 = mild
- 4–5 = moderate
- ≥6 = severe

❖ **Not valid if opioid is taken as prescribed**

SOURCE: APA. Diagnostic and Statistical Manual of Mental Disorders (DSM-5-TR). 2022

WORDS MATTER



HOW TO IDENTIFY RISK FOR MY PATIENTS

10%–26% of patients on chronic opioid therapy (COT) for chronic noncancer pain (CNCP) may develop OUD

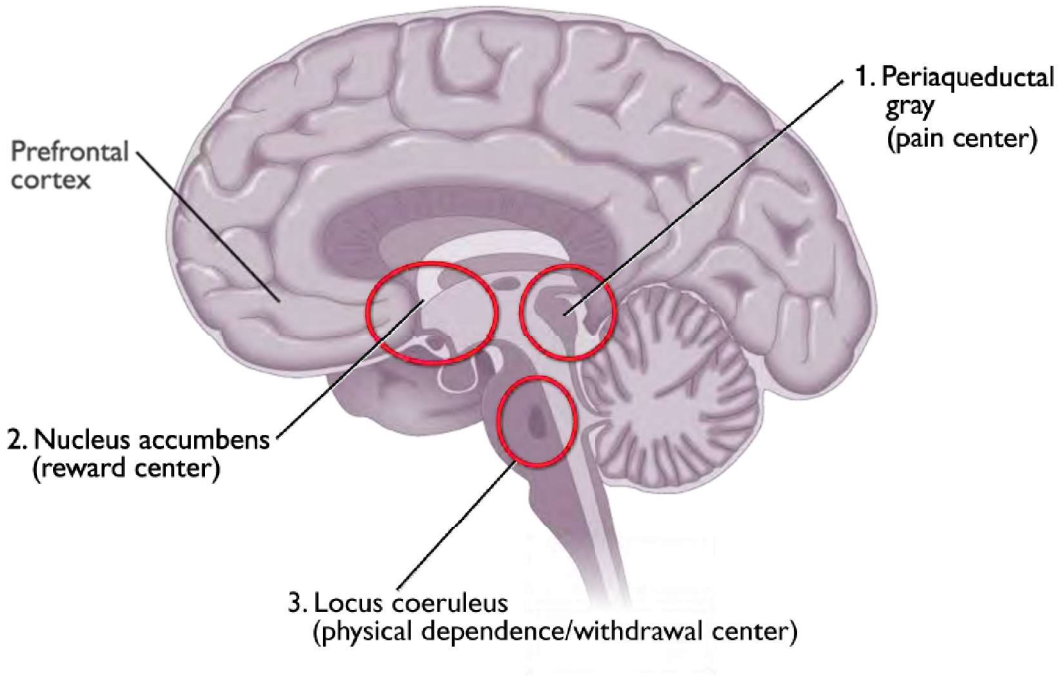
What to look for:

- High dosages
- Prolonged use
- Low hedonic tone
- Mental health disorders
- Past history of substance use disorder

Clinical judgment is key.

SOURCE: Chou R, et al. Ann Intern Med. 2015;162:276-86

OPIOID RECEPTORS IN THE BRAIN: RELATIONSHIP TO ANALGESIA, OUD, AND WITHDRAWAL



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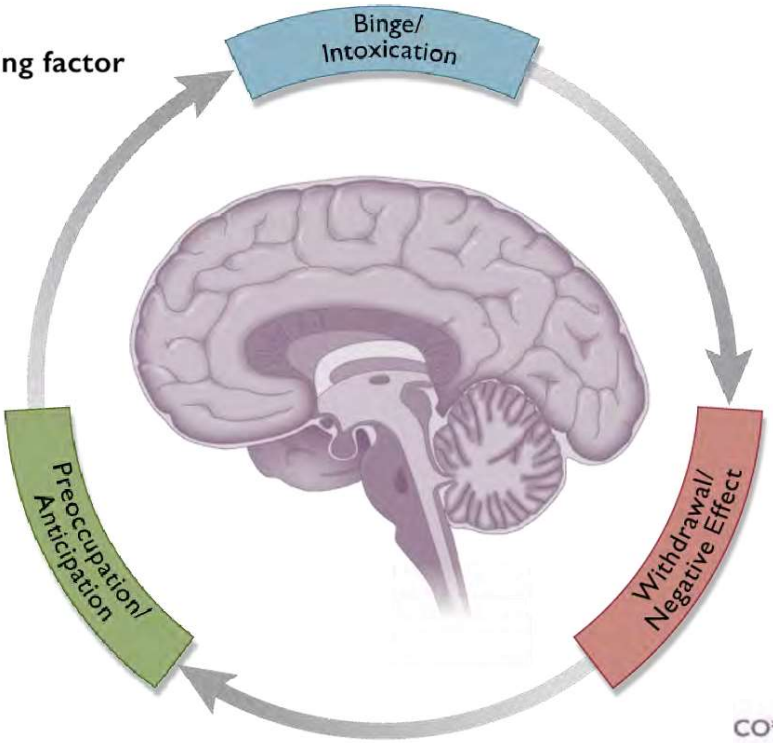
THE CYCLE OF SUBSTANCE USE DISORDER

NEUROTRANSMITTERS

- Dopamine
- Opioid peptides
- Corticotropin-releasing factor
- Dynorphin
- Glutamate



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Medication for Opioid Use Disorder (MOUD)

- Important and evidence-based medication that saves lives
- You can start from your office, as an outpatient
- Patients with OUD have decreased mortality when treated

There are three medication options:

1. Buprenorphine (Schedule III)
2. Methadone (Schedule II)
3. Naltrexone (not a controlled substance)

Are we just replacing one drug with another?
Myth or fact?

CO*RE

BUPRENORPHINE

- The most commonly prescribed pharmacotherapy for the treatment of OUD
- Partial mu-agonist with "plateau effect" for respiratory depression
- Good efficacy and safety profile
- Congress eliminated the X-waiver requirement to prescribe Bup
- All DEA-licensed HCPs can prescribe without patient number caps
- Long-acting and sublingual form indicated to treat opioid withdrawal and craving

FDA-approved bup products for pain:

- Butrans: 7-day transdermal patch
- Belbuca: buccal mucosal film; BID dosing

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AVOID OTHER SUBSTANCES THAT COULD CONTRIBUTE TO AN ACCIDENTAL OVERDOSE

- Benzodiazepines (BZDs), sedatives, muscle relaxants; they are CNS depressants
- More than 30% of opioid overdoses involve benzodiazepines (BZDs)
- Use a comprehensive SUD evaluation to support recovery efforts for all substances

SOURCE: NIDA. Takaki H, et al. Am Journal Addictions. 2019;1-8.

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USE A WHOLE-PERSON APPROACH WHEN TREATING A PATIENT WITH OUD FOR PAIN

- Must address *both* pain and opioid use disorder
- Remember that untreated pain is a trigger for return to use
- Avoid other potentially problematic medications
- Consider a multimodal pain program, including non-pharma options
- Avoid stigmatizing patients who are on long-term opioids for pain

- Consider buprenorphine for both pain and OUD
- Enlist patient's family/caregivers to secure and dispense opioids
- Recommend an active recovery program
- Remember to use PDMP
- Use screening methods (UDT, pill counts, PPA) to identify challenges and initiate discussion

SOURCE: Bailey J, et al. Pain Med 2010;11:1803-1818.

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REFERRALS AND TREATMENT CENTERS

ASAM, SAMHSA, and AAAP are all helpful referral resources.

ASAM resources:
https://asam.ps.membersuite.com/directory/SearchDirectory_Criteria.aspx
SAMHSA locator: https://findtreatment.samhsa.gov/locator
AAAP locator: https://www.aaap.org/patients/find-a-specialist/

IN SUMMARY

- There is a place for opioids, but use caution
- Use multimodal therapies as part of the pain management care plan
- Screen for OUD risk with a validated instrument
- Continually reassess patients using opioids
- Patient and family/caregiver education is essential
- If you suspect OUD, begin treatment

Please complete your post-test 😊

Complete the brief post-test for CE/CME credit
Your participation helps the FDA reach its goals for REMS education

THANK YOU!

WWW.CORE-REMS.ORG