Pain Management and Opioids:

Balancing Risks and Benefits

PRESENTED BY
CO*RE, THE COLLABORATION FOR
REMS EDUCATION

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UPDATED 2019

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STRONG MEDICINE FOR CALIFORNIA

DISCLOSURE:

Dr. Havens and all staff involved in this content declare that neither they nor members of their immediate families have had financial relationships with the manufacturers of goods or services discussed, or corporate supporters of this event.

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ACKNOWLEDGMENTS

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This activity is supported by an independent educational grant from the Opioid Analgesic REMS Program Companies (RPC). Please see **this document** for a list of REMS Program Companies. This activity is intended to be fully compliant with the Opioid Analgesic REMS education requirements issued by the U.S. Food and Drug Administration.

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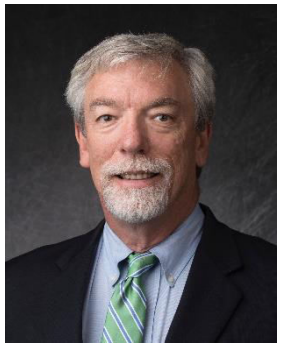

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NO CO*RE FACULTY HAS ANY RELEVANT FINANICAL RELATIONSHIPS

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

Misuse, abuse, diversion, addiction, and overdose of opioids in the United States have created a serious public health epidemic.

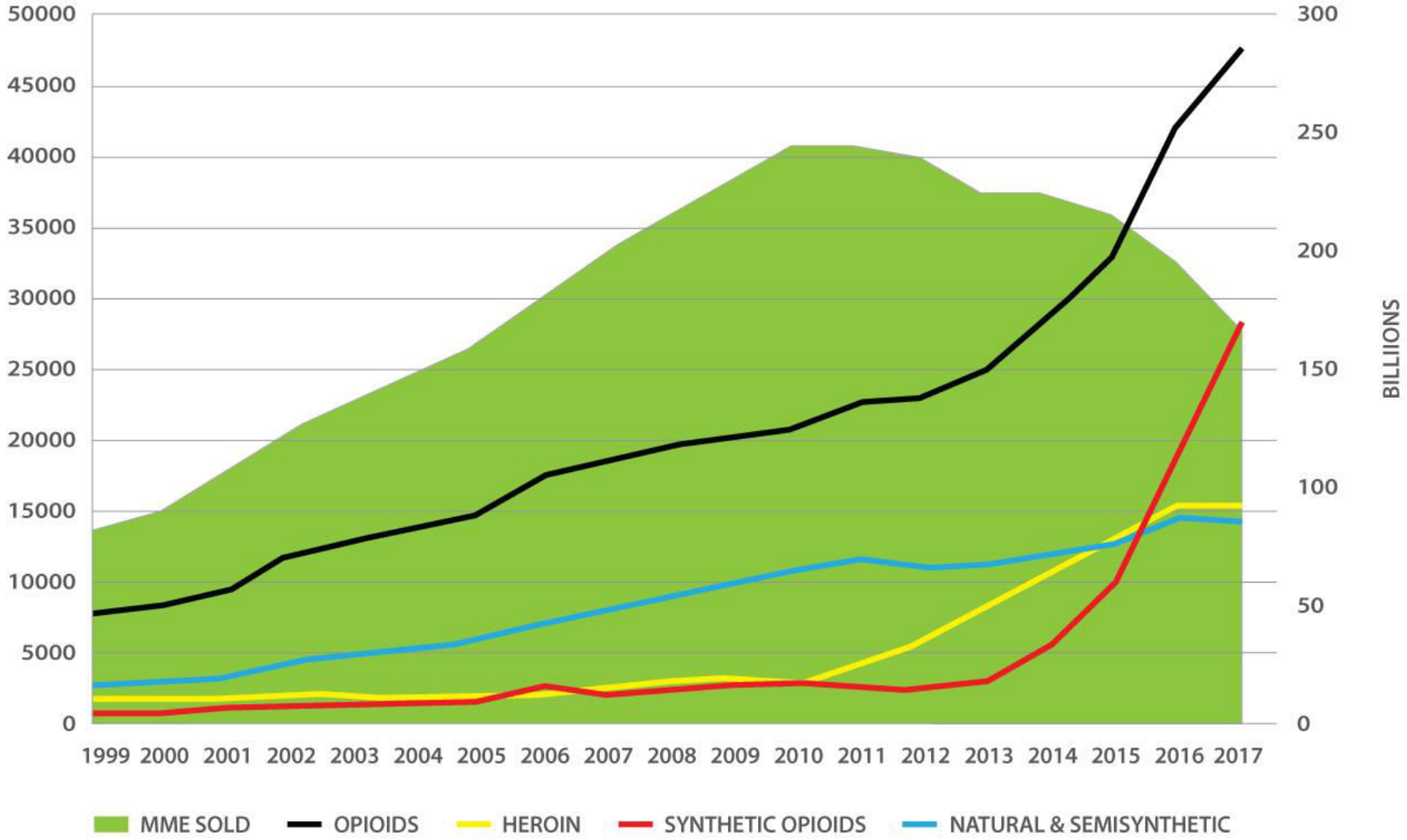
When prescribed well, and used as prescribed, opioids can be valuable tools for effective pain management.

There is potential for unintended consequences of inadequately managed pain from far-reaching prescribing restrictions.

This course is in alignment with the FDA Opioid Analgesics REMS Education Blueprint.

This course does not advocate for or against the use of opioids. We intend to help healthcare 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.

PRESCRIBING PATTERNS AND OPIOID-RELATED DEATHS



SOURCE: CDC, Prescription Opioid Data

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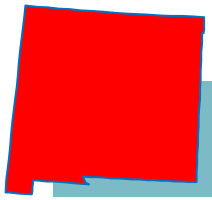
Opioid Prescribing Rates & Overdose Deaths



Prescribing Rates (per 100 people)

	2014	2016	2017
NM	72	65	56

Opioid Overdose Deaths

NM 2017	332	US 2017	47,600

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

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OPIOID ANALGESICS ARE SCHEDULE II SUBSTANCES

SCHEDULE	DESCRIPTION	EXAMPLES
I	High potential for abuse; no currently accepted medical use	Heroin, LSD, cannabis, ecstasy, peyote
II	High potential for abuse, which may lead to severe psychological or physical dependence	Hydromorphone, methadone, meperidine, oxycodone, fentanyl, morphine, opium, codeine, hydrocodone combination products
III	Potential for abuse, which may lead to moderate or low physical dependence or high psychological dependence	Products containing ≤ 90 mg codeine per dose, buprenorphine, benzphetamine, phendimetrazine, ketamine, anabolic steroids
IV	Low potential for abuse	Alprazolam, benzodiazepines, carisoprodol, clonazepam, clorazepate, diazepam, lorazepam, midazolam, temazepam, tramadol
V	Low potential for abuse	Gabapentin, pregabalin, cough preparations containing ≤ 200 mg codeine/100 ml

Complete list of products covered under the Opioid Analgesic REMS available at: https://opioidanalgesicrems.com/RpcUI/products.u

FENTANYL AND FENTANYL ANALOGUES

OD deaths from fentanyl and fentanyl analogues, such as carfentanil, have increased 540% in three years.

Street fentanyl is illegally manufactured; it is generally NOT a diverted pharmaceutical product.

Two causes of fentanyl OD death: opioid-induced **respiratory depression** and **rigid chest wall syndrome**; higher or repeated doses of naloxone are required to reverse a fentanyl overdose.

Fentanyl is also found in heroin, cocaine, and methamphetamine.

Photo source: New Hampshire State Drug Laboratory

RISKS VERSUS BENEFITS

RISKS

- Misuse, diversion, and addiction
- Abuse by patient or household contacts
- Interactions with other meds and substances
- Risk of neonatal abstinence syndrome
- Inadvertent exposure/ingestion by household contacts, especially children
- Life-threatening respiratory depression
- Overdose, especially as ER/LA formulations contain more MME than IR

BENEFITS

- Analgesia
  - Reliable pain control
  - Quick analgesia (particularly with IRs)
- Continuous, predictable (with ER/LAs)
- Improved function
- Improved quality of life

SOURCE: Nicholson, B. Pain Pract. 2009;9(1):71-81. http://onlinelibrary.wiley.com/doi/10.1111/j.1533-2500.2008.00232.x/abstract

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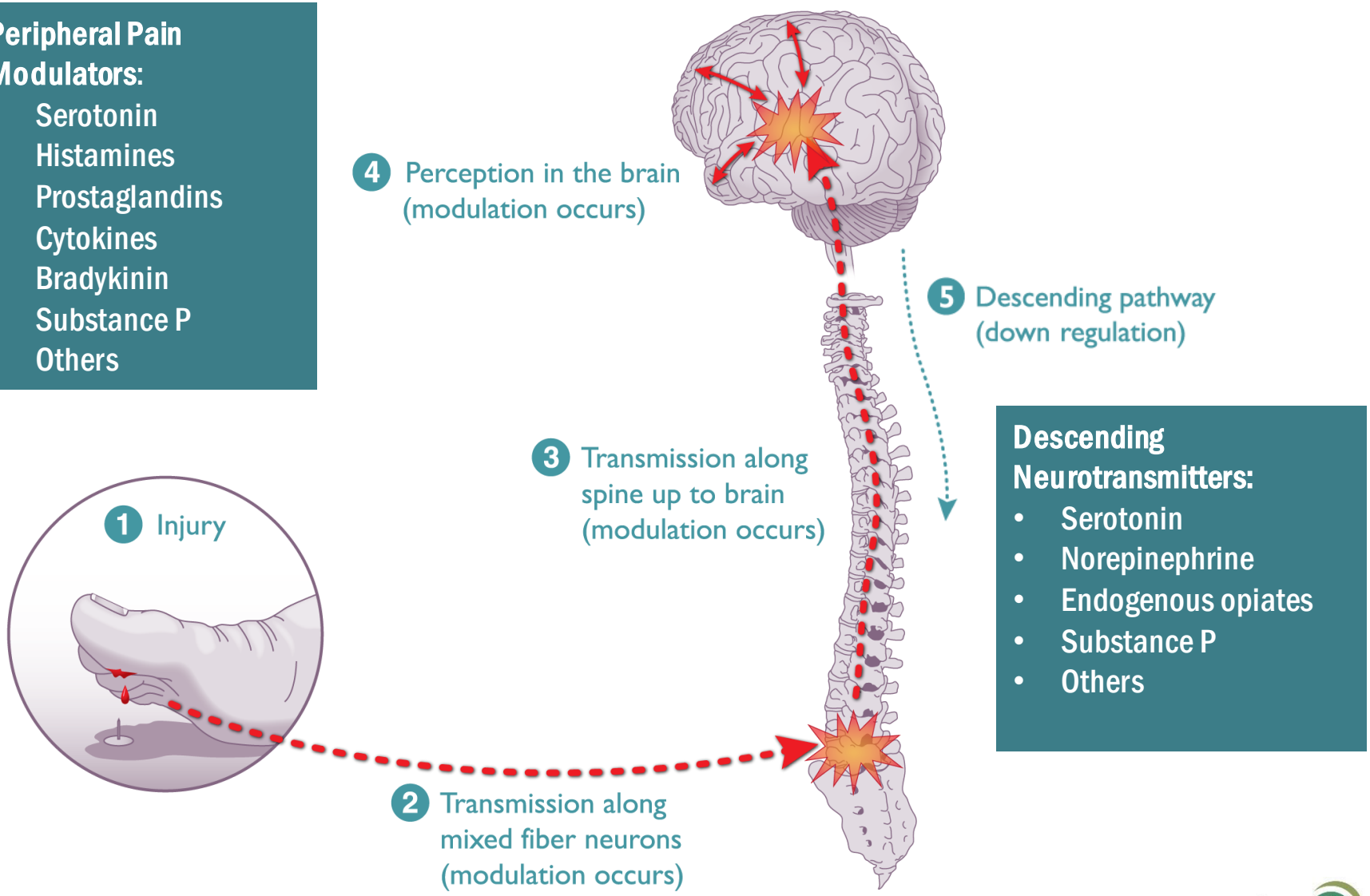
CHAPTER 1
PAIN

THE NEUROMECHANISMS OF PAIN

Peripheral Pain Modulators:

- Serotonin
- Histamines
- Prostaglandins
- Cytokines
- Bradykinin
- Substance P
- Others



Descending Neurotransmitters:

- Serotonin
- Norepinephrine
- Endogenous opiates
- Substance P
- Others

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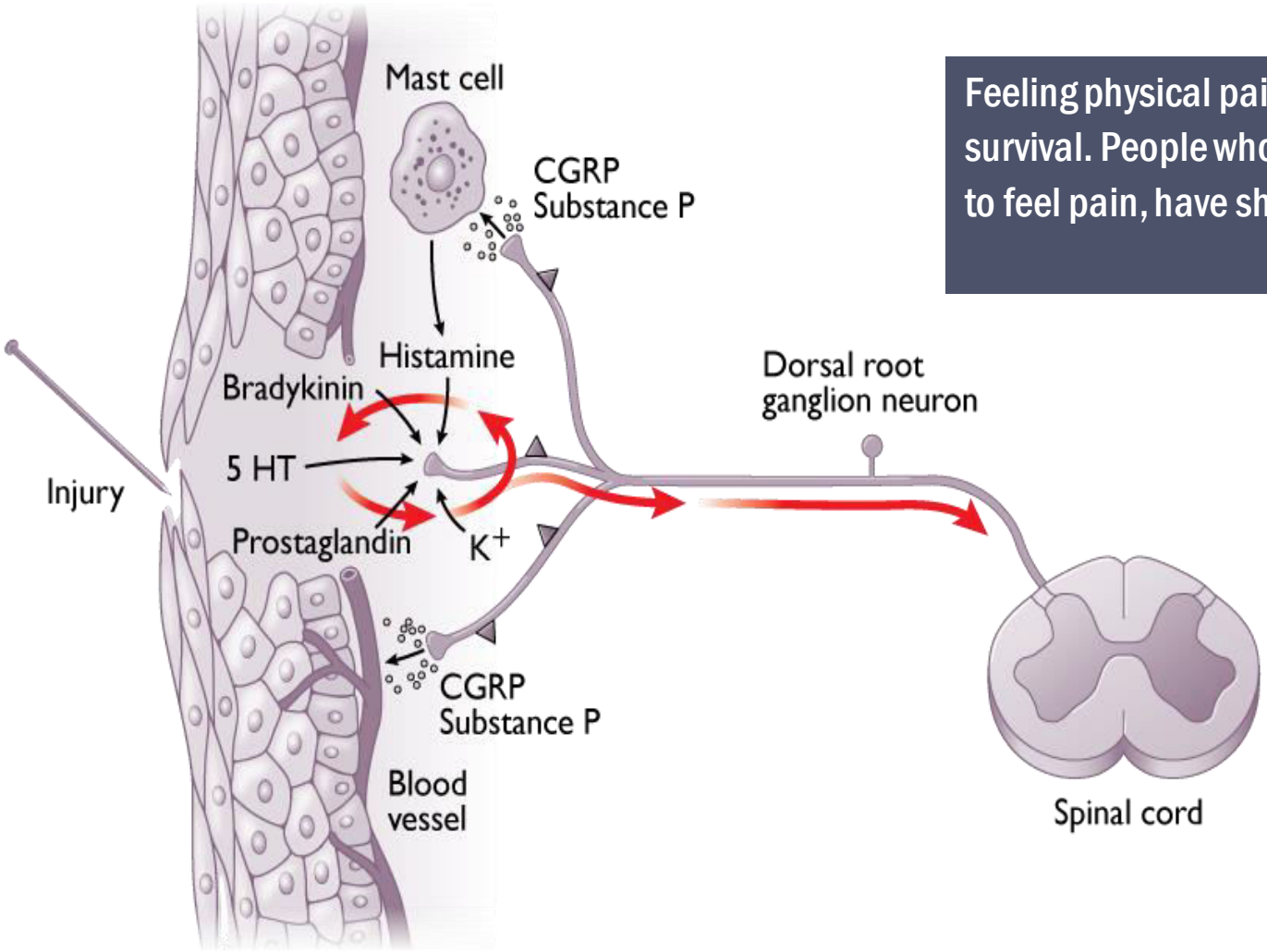
MEDIATORS OF PERIPHERAL NOCICEPTION



Feeling physical pain is vital for survival. People who lose the ability to feel pain, have shorter life spans.

With thanks to Allan Basbaum and David Julius, University of California, San Francisco

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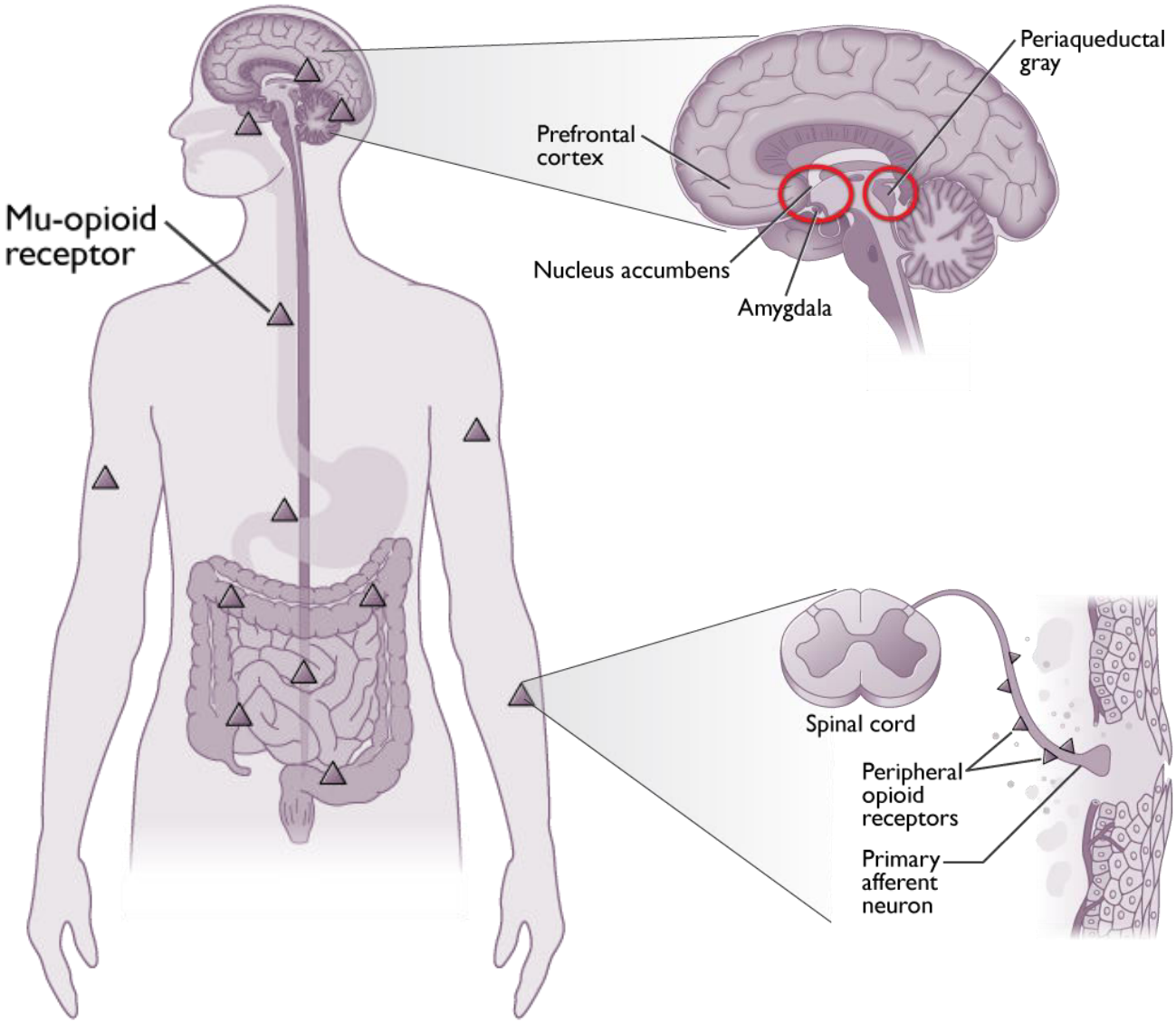
OPIOID RECEPTOR LOCATIONS



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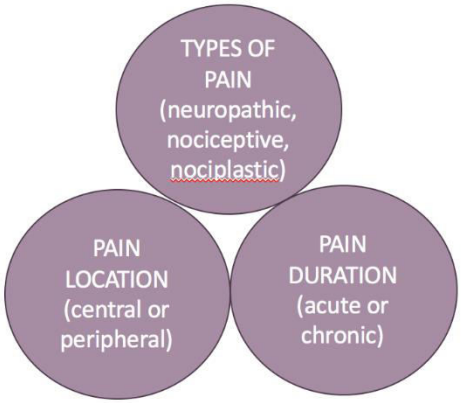
TYPES OF PAIN

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; *typically* chronic	Primary injury and secondary effects
Postoperative pain, sports injuries, arthritis, sickle cell disease, mechanical low back pain	Fibromyalgia, irritable bowel syndrome, CRPS, non-specific low back pain	Post-herpetic neuralgia, trigeminal neuralgia, distal polyneuropathy, neuropathic low back pain	

Possible development of chronic pain after an acute injury.



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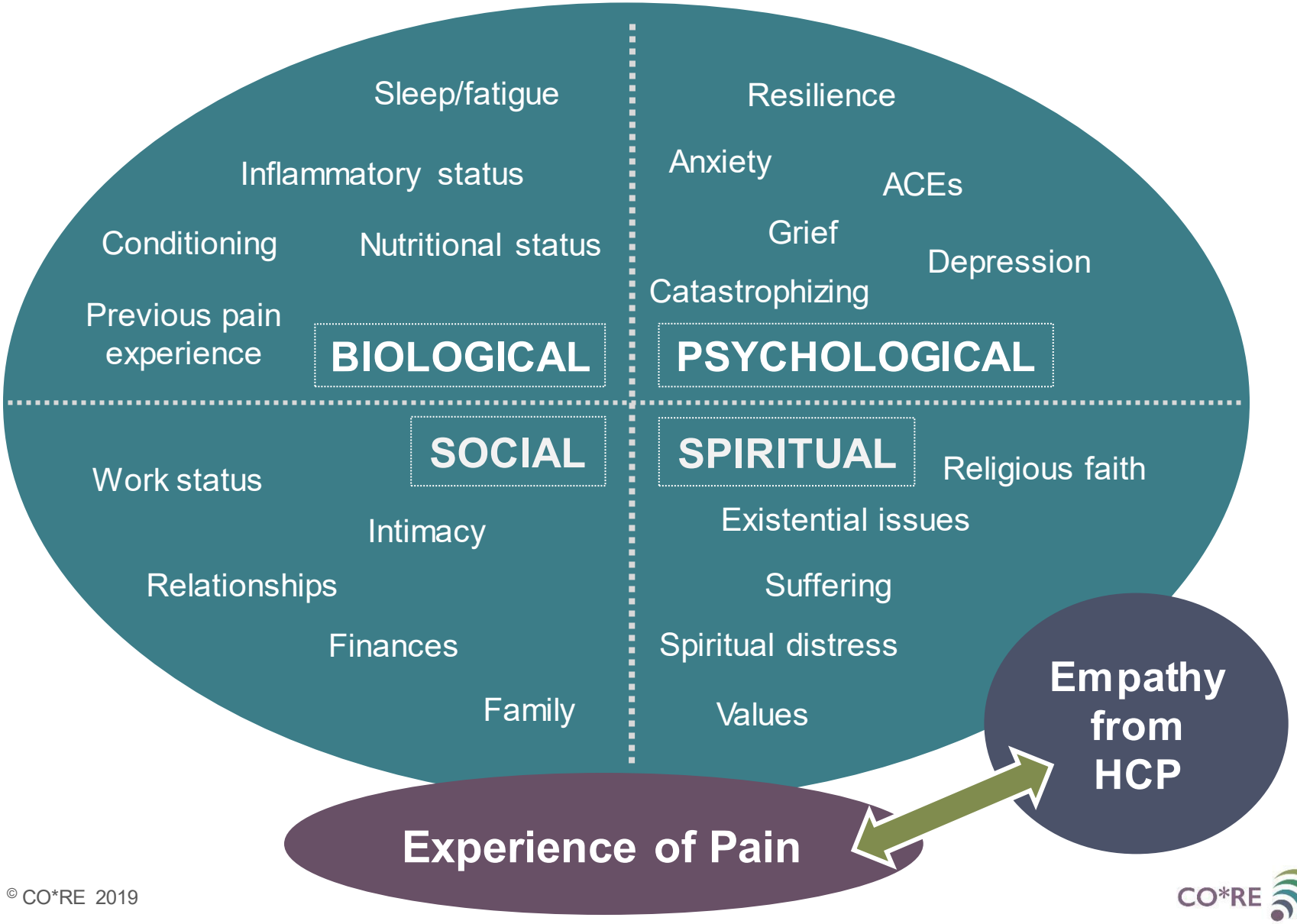
THE BIOPSYCHOSOCIAL SPIRITUAL CONTEXT OF PAIN



PAIN CATASTROPHIZING

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

SOURCE: Pain Catastrophizing Scale © 2009 Dr. Michael JL Sullivan

- "*Tell me about your pain…*"
- Listen for rumination, feelings of hopelessness, or anticipation of negative outcomes.
- These feelings are important to identify because they can prolong and intensify pain; or lead to higher levels of suffering and altered perception of pain.
- If identified, shift to "*tell me about your life.*"

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CHAPTER 2
TERMINOLOGY

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) [from the *DSM-5*®]
Drug-seeking, aberrant/problematic behavior	Using medication not as prescribed
Addict	Person with substance use disorder (SUD)
Clean/dirty urine	Positive/negative urine drug screen

SOURCES: SAMHSA Resource: https://www.samhsa.gov/capt/sites/default/files/resources/sud-stigma-tool.pdf
Scholten W. Public Health. 2017;153:147-153. DOI: 10.1016/j.puhe.2017.08.021

WORDS MATTER: DEFINITIONS

Misuse	Use of a medication in a way other than the way it is prescribed
Abuse	Use of a substance with the intent of getting high
Tolerance	Increased dosage needed to produce a specific effect
Dependence	State in which an organism only functions normally in the presence of a substance
Diversion	Transfer of a legally controlled substance, prescribed to one person, to another person for illicit (forbidden by law) use
Withdrawal	Occurrence of uncomfortable symptoms or physiological changes caused by an abrupt discontinuation or dosage decrease of a pharmacologic agent
MME	Morphine milligram equivalents; a standard opioid dose value based on morphine and its potency; allows for ease of comparison and risk evaluations
Chronic non-cancer pain (CNCP):	Any painful condition that persists for ≥ 3 months, or past the time of normal tissue healing, that is not associated with a cancer diagnosis

SOURCES: SAMHSA Resource: https://www.samhsa.gov/capt/sites/default/files/resources/sud-stigma-tool.pdf
World Health Organization, Ensuring Balance in National Policies on Controlled Substances.
https://www.who.int/medicines/areas/quality_safety/GLs_Ens_Balance_NOCP_Col_EN_sanend.pdf

CHAPTER 3
ASSESSMENT

PAST MEDICAL AND TREATMENT HISTORY

NONPHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

PHARMACOLOGIC STRATEGIES AND EFFECTIVENESS

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**

GENERAL EFFECTIVENESS OF CURRENT PRESCRIPTIONS

OBTAIN A COMPLETE SOCIAL AND PSYCHOLOGICAL HISTORY

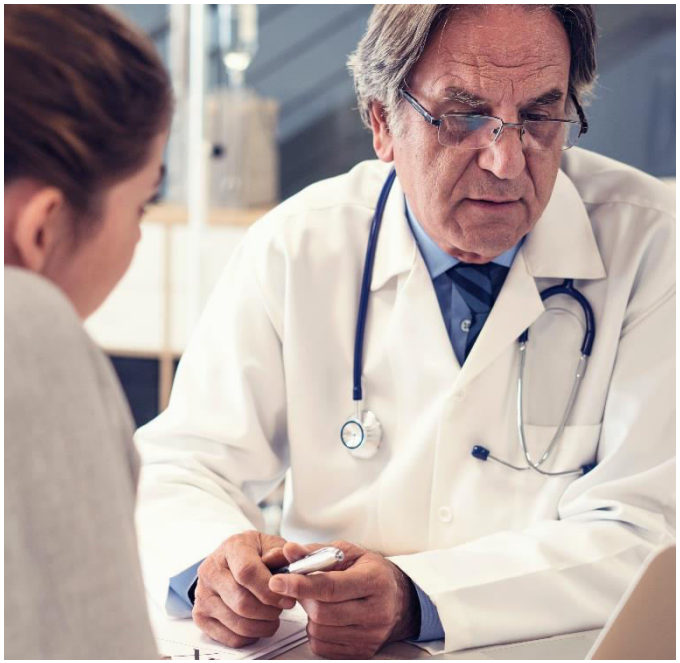
SOCIAL HISTORY

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

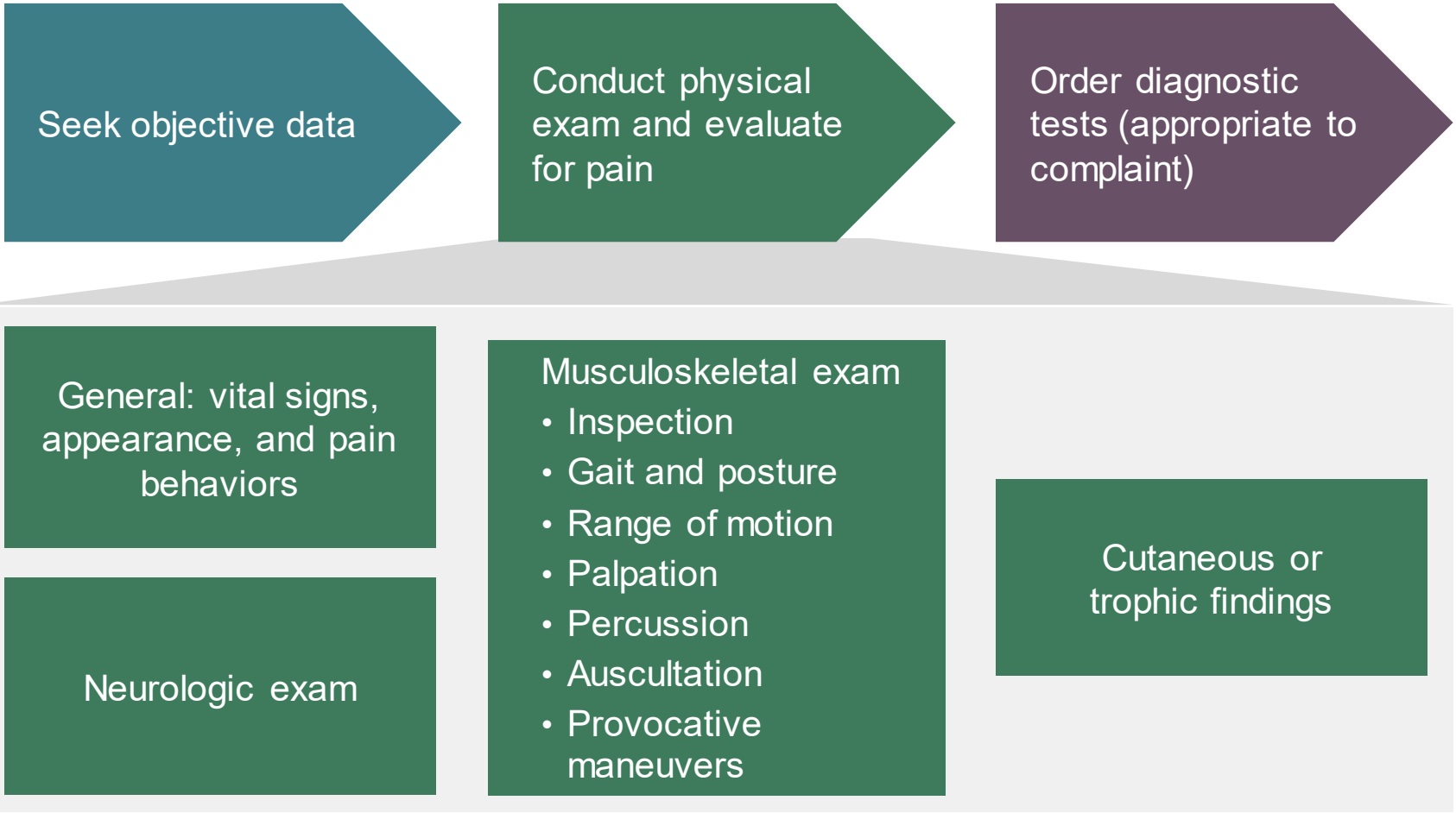
PSYCHOLOGICAL HISTORY

Screen for:

- Mental health diagnoses, depression, anxiety, PTSD, current treatments
- Alcohol, tobacco, and recreational drug use
- History of adverse childhood experiences
- Family history of substance use disorder and psychiatric disorders



PHYSICAL EXAM AND ASSESSMENT



SOURCES: Lalani I, Argoff CE. History and Physical Examination of the Pain Patient. In: Raj's Practical Management of Pain. 4th ed. 2008:177-188; Chou R, et al. J Pain. 2009;10:113-130.

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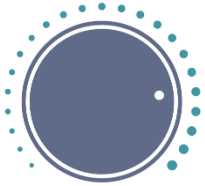
PAIN ASSESSMENT

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

SOURCES: Heapy A, Kerns RD. Psychological and behavioral assessment. In: Raj's Practical Management of Pain. 4th ed. 2008:279-295; Zacharoff KL, et al. Managing Chronic Pain with Opioids in Primary Care. 2nd ed. Newton, MA: Inflexion, Inc.;2010.

PAIN ASSESSMENT TOOL BOX

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

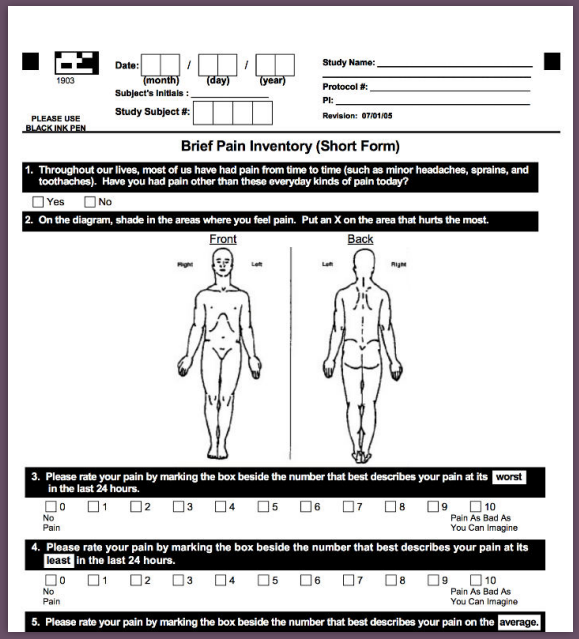
PEG

Childhood Trauma Questionnaire

ACE

Assessment in Advanced Dementia

PAINAD



Brief Pain Inventory (Short Form)

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?
☐ Yes ☐ No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.

Front Back

3. Please rate your pain by marking the box beside the number that best describes your pain at its worst in the last 24 hours.
☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10
No Pain — Pain As Bad As You Can Imagine

4. Please rate your pain by marking the box beside the number that best describes your pain at its least in the last 24 hours.
☐0 ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 ☐8 ☐9 ☐10
No Pain — Pain As Bad As You Can Imagine

5. Please rate your pain by marking the box beside the number that best describes your pain on the average.

Brief Pain Inventory

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

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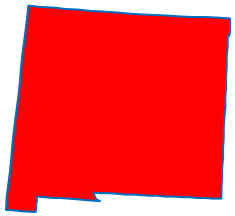
PRESCRIPTION DRUG MONITORING PROGRAMS (PDMPs)

PDMPs are state-run, electronic databases that track controlled substance prescriptions in a state.

PDMP DATABASES	BENEFITS
• Provide a full accounting of the controlled substance prescriptions filled by a patient • Nearly all are available online 24/7 • Required in most states; know your state laws	• Identify potential drug misuse/abuse • Discover existing prescriptions not reported by patient • Opportunity to discuss with patient • Determine if patient is using multiple prescribers/pharmacies • Identify drugs that increase overdose risk when taken together

PDMP: Prescription Drug Monitoring Program



General	• **New Mexico Prescription Monitoring Program** www.nmpmp.org/ • Administered by the **Board of Pharmacy** • **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 **within 1 business day of** dispensing • Unsolicited reports/alerts **are sent to prescribers, dispensers, law enforcement, and licensing boards** • New Mexico **does share** data with other states' PDMPs • 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 Jan. 2019
http://www.pdmpassist.org/content/pdmp-maps-and-tables Aug. 2018

CHAPTER 4

CREATING THE PAIN TREATMENT PLAN

HOW IS PAIN RESOLVED?

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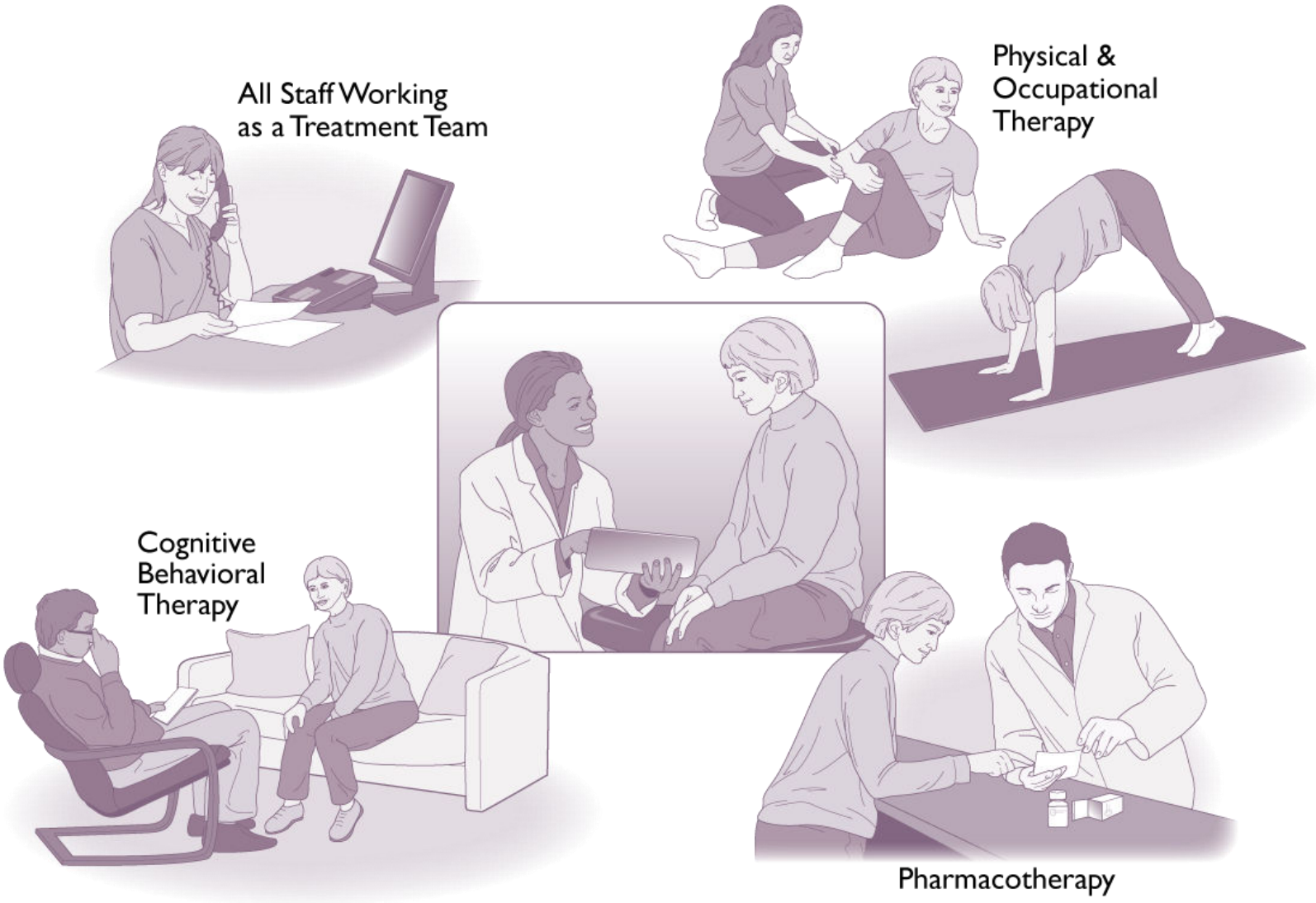
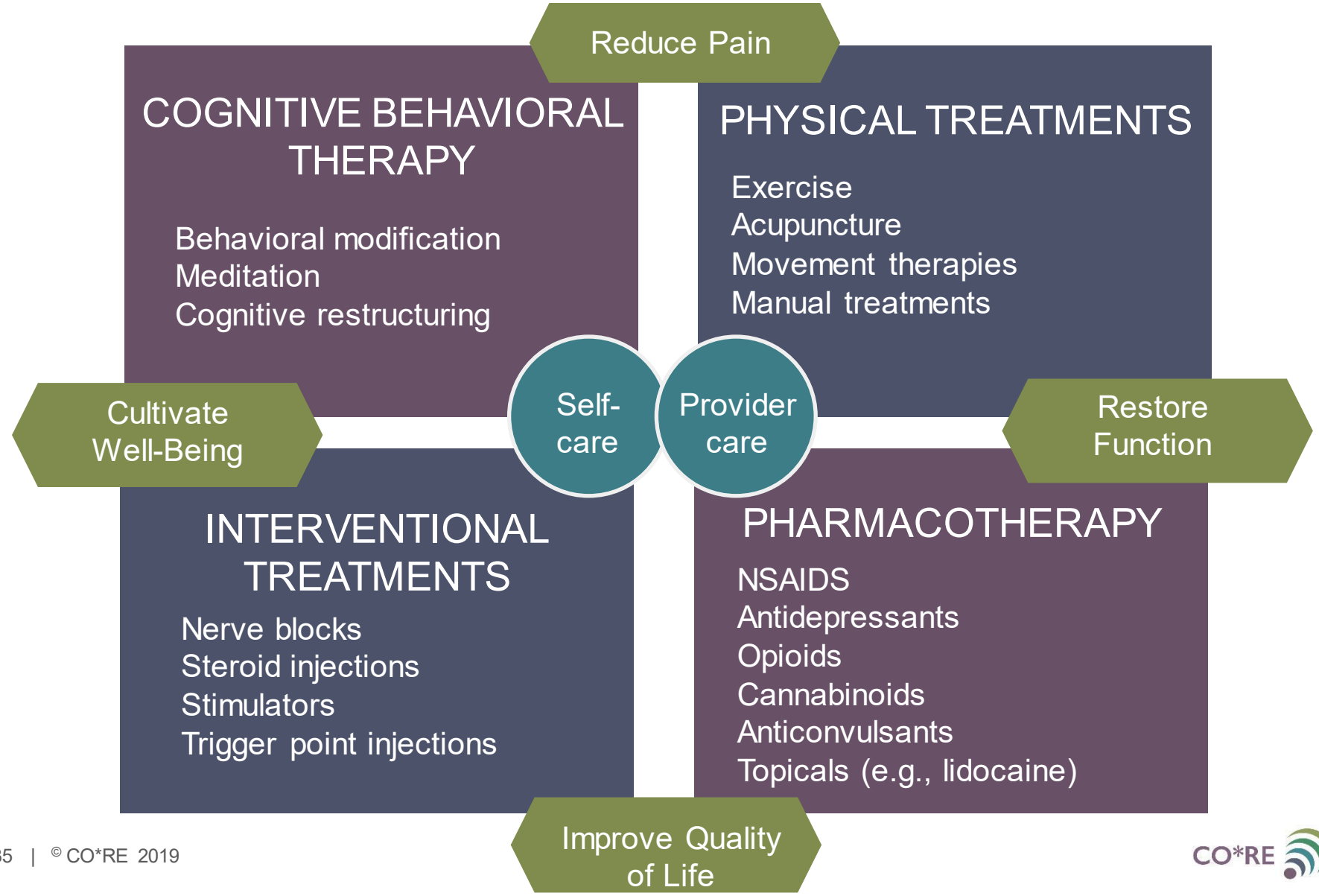
COMPONENTS OF A MULTIMODAL TREATMENT PLAN FOR PAIN



PAIN MANAGEMENT GOALS AND TREATMENT OPTIONS: A MULTIMODAL APPROACH



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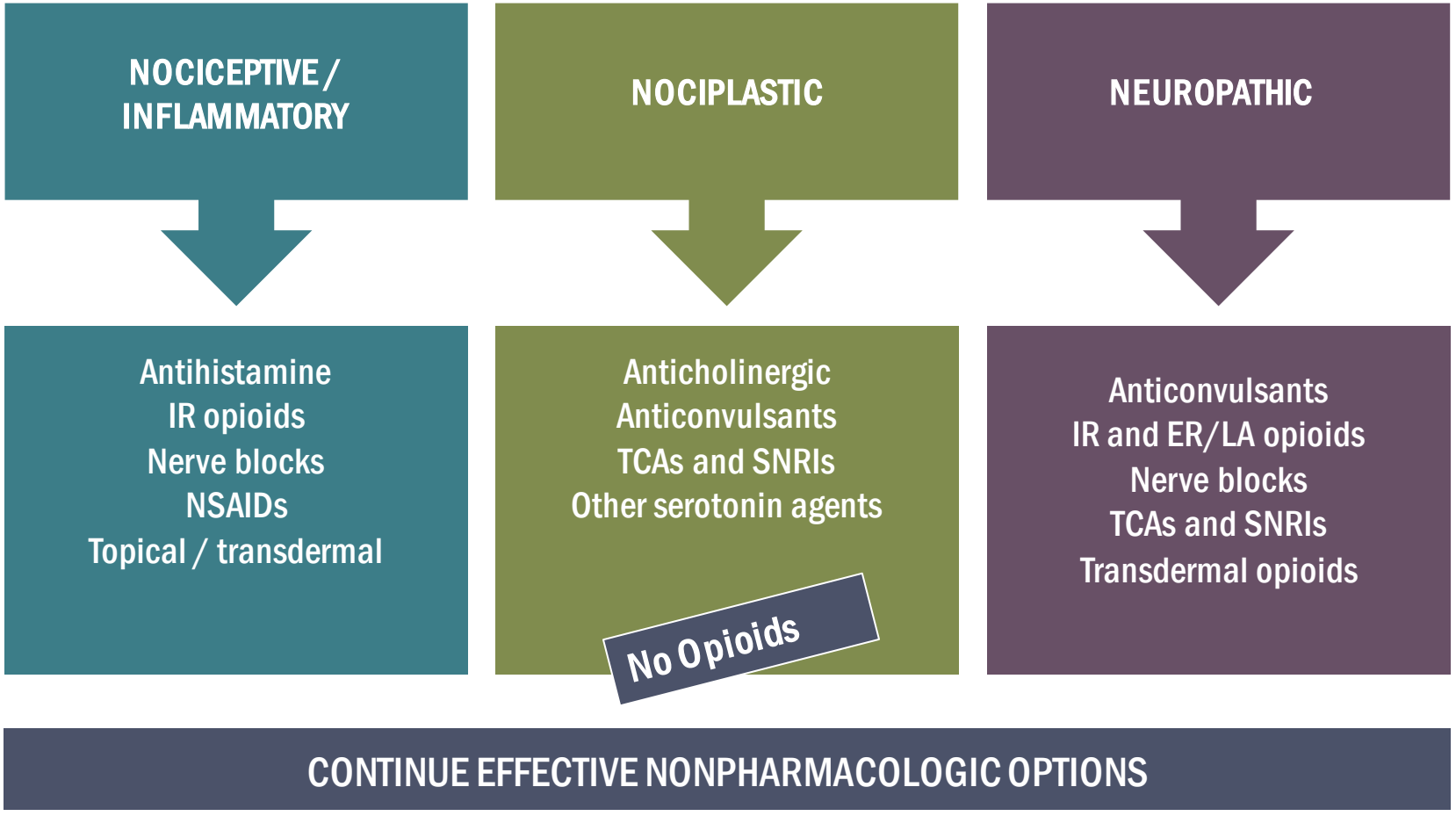
EVIDENCE-BASED NONPHARMACOLOGIC TREATMENTS

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



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WHEN TO CONSIDER A TRIAL OF AN OPIOID

A 52 y/o male construction worker presents complaining of worsening burning and tingling in his feet at night. He states that his diabetes in under control since he has been on insulin. He takes gabapentin at bedtime. He requests something stronger for pain at night.

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Name	Substance Class	Mechanism of Action	Recommended Dosage	Grade of Recommen-dation
Amitriptyline	TCA	Inhibition of NE and 5HT transporter (1);*	10-50 mg/day	Weak for
Cyclobenzaprine	TCA derivative	1; **	10-40 mg/day	Weak for
Duloxetine	SNRI	1	20-120 mg/day	Weak for
Milnacipran	SNRI	1	100-200 mg/day	Weak for
Pregabalin	Anti-convulsant	Modulation of $\alpha 2\delta$ subunit of presynaptic Ca channel (2);	300-450 mg/day	Weak for
Gabapentin	Anti-convulsant	2; increased GABA turnover	1200 mg/day	Weak for
Tramadol	Opioid	μ agonist; 1	150 mg/day	Weak for

*5-HT_{2A}, 5-HT_{2C}, 5-HT_6, 5-HT_7 receptor antagonism
**5-HT_{2A} receptor antagonism

GRADE system for making recommendations

modified from Schmidt-Wilcke & Diers. 2017.

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 neuropathic or nociceptive pain that is moderate to severe

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. 2010.

Case Discussion: Jacob

Jacob, a 30 year old man who suffers with fibromyalgia.

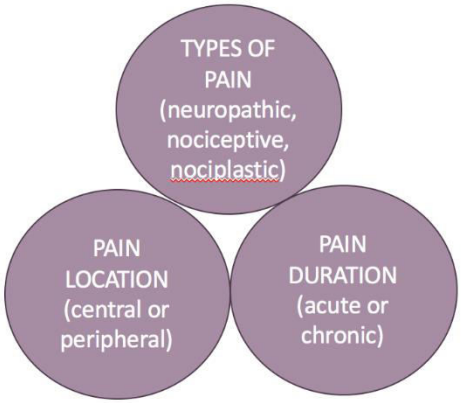
What is the best opioid for him?

What if he suffers with alcohol use disorder?

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; *typically* chronic	Primary injury and secondary effects
Postoperative pain, sports injuries, arthritis, sickle cell disease, mechanical low back pain	Fibromyalgia, irritable bowel syndrome, CRPS, non-specific low back pain	Post-herpetic neuralgia, trigeminal neuralgia, distal polyneuropathy, neuropathic low back pain	

Possible development of chronic pain after an acute injury.



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WHEN TO CONSIDER A TRIAL OF AN OPIOID

60 y/o with chronic disabling osteoarthritis pain. Non-opioid therapies have not provided relief and there is no psychiatric/medical comorbidity or person/family substance abuse history.

How would you assess this patient's appropriateness for a trial of opioid therapy?
What screening tools would you utilize prior to initiation of treatment?
What would be your initial choice of medication and why?

INITIATING OPIOIDS

- Begin with IR
- 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
- Co-prescribe naloxone (if indicated)
- Co-prescribe 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 3 months; if benefits do not outweigh harms, optimize other therapies and work to taper and discontinue

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

New Mexico recommendations

- H and P
- Written treatment plan including goals
- Opioid risk screening
- Informed consent
- Start as trial of short acting

Silent on

- UDT
- Check PDMP
- Naloxone

Prescribing Limits, Status & Education Requirements

Initial prescribing limits for acute pain: None

	Physician	Physician Assistant	Advanced Practice Nurse
Prescriber Status	Licensed	Schedule II-V	Schedule II-V
Education Requirements	5 hrs./3 yrs.	3 hrs./2 yrs.	5 hrs./2 yrs.

http://www.fsmb.org/siteassets/advocacy/key-issues/continuing-medical-education-by-state.pdf April 2019
https://ballotpedia.org/Opioid_prescription_limits_and_policies_by_state Feb 2019
www.netce.com/ce-requirements/

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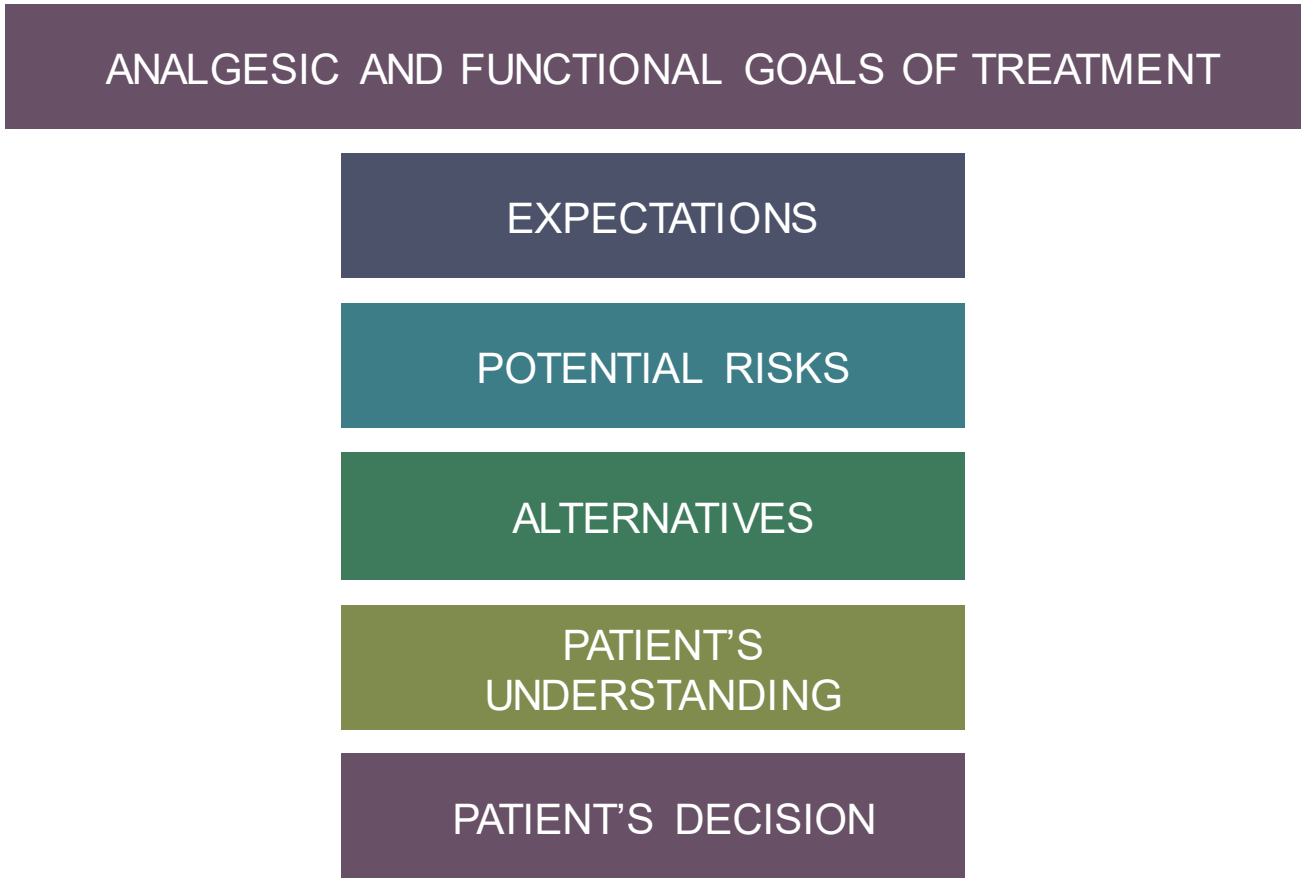
INFORMED CONSENT

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 UDT and pill counts
- Refill procedure
- Identify behaviors indicating need for discontinuation
- Exit strategy
- Signed by both

PPA NONADHERENCE

Behavior outside the boundaries of agreed-on treatment plan

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

Any of these behaviors merits **investigation**: proceed with caution

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

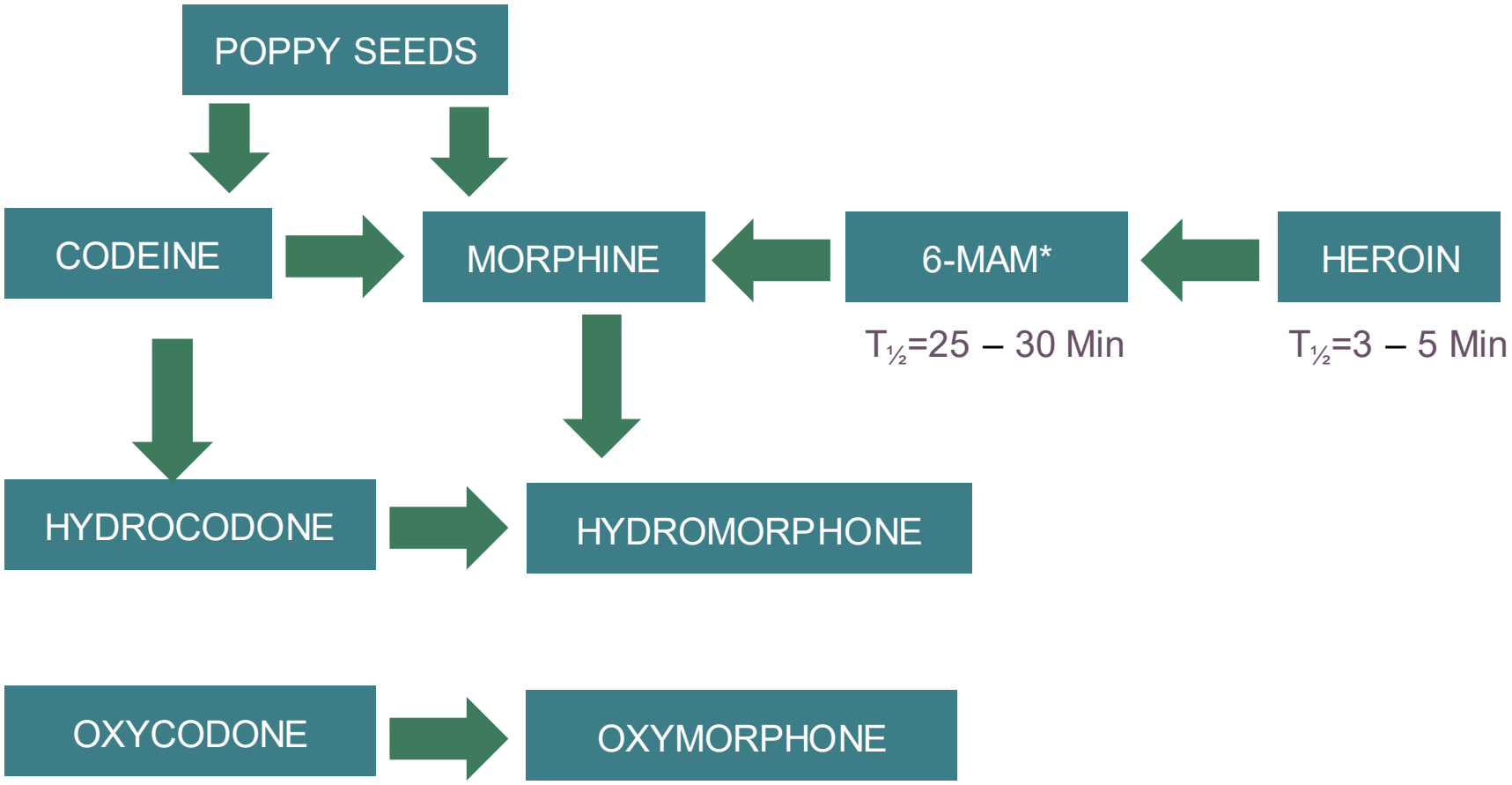
- Recommend UDT before first prescription (baseline) then intermittently, depending on clinical judgment and state regulations
- Document time and date of last dose taken
- Be aware of possible false positives or negatives
- Clarify unexpected results with the lab before confronting patient to rule out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

SCREENING VERSUS CONFIRMATORY UDTS

	SCREENING	CONFIRMATORY
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 or synthetic opioids	High
Specificity (power to detect an individual drug)	Varies (can result in false positives or false false negatives)	High
Turnaround	Rapid	Slow
Other	Intended for a drug-free population, may not may not be useful in pain medicine.	Legally defensible results

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

EXAMPLES OF OPIOID METABOLISM



*6-MAM=6-Monoacetylmorphine

OPIOID MISUSE RISK ASSESSMENT TOOLS

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

TOOLS FOR PATIENTS CONSIDERED FOR OPIOID THERAPY
ORT-OUD Opioid Risk Tool
SOAPP® Screener and Opioid Assessment for Patients with Pain
DIRE Diagnosis, Intractability, Risk, and Efficacy score

TOOLS FOR SUBSTANCE USE DISORDER
CAGE-AID Cut down, Annoyed, Guilty, Eye-Opener tool, Adapted to Include Drugs
RAFFT Relax, Alone, Friends, Family, Trouble
DAST Drug Abuse Screening Test
CTQ Childhood Trauma Questionnaire
ACEs Adverse Childhood Experiences

Also for patients with chronic pain:

- Get a baseline UDT
- Check the PDMP

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A CLOSER LOOK AT THE ORT-OUD

Opioid Risk Tool – OUD (ORT-OUD)

This tool should be administered to patients upon an initial visit prior to beginning or continuing opioid therapy for pain management. A score of 2 or lower indicates low risk for future opioid use disorder; a score of >/= 3 indicates high risk for opioid use disorder.

Mark each box that applies	YES	NO
Family history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Personal history of substance abuse		
Alcohol	1	0
Illegal drugs	1	0
Rx drugs	1	0
Age between 16-45 years	1	0
Psychological disease		
ADD, OCD, bipolar, schizophrenia	1	0
Depression	1	0
Scoring totals		

SOURCE: Cheatle, M., et al. JPain 2019; Jan 26.

Substance use disorder history does not prohibit treatment with opioids, but may require additional monitoring and expert consultation or referral.

Scoring:

- **≤ 2: low risk**
- **≥ 3: high risk**

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OPIOID SIDE EFFECTS AND ADVERSE EVENTS

SIDE EFFECTS	ADVERSE EVENTS
Respiratory depression	Falls or fractures
Opioid-induced constipation (OIC)	Addiction
Myoclonus (twitching or jerking)	Overdose
Sedation, cognitive impairment	Hospitalization
Sweating, miosis, urinary retention	Disability or permanent damage
Allergic reactions	Death
Hypogonadism	
Tolerance, physical dependence,	

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

OPIOID-INDUCED RESPIRATORY DEPRESSION

MORE LIKELY TO OCCUR:

- In elderly, cachectic, or debilitated patients
- If given concomitantly with other drugs that depress respiration
- In patients who are opioid-naïve or have just had a dose increase
- Opioids are **contraindicated** in patients with respiratory depression or conditions that increase risk

HOW TO REDUCE RISK:

- Ensure proper dosing and titration
- **Do not overestimate** dose when converting dosage from another opioid product
  - Can result in fatal overdose with first dose
- Instruct patients to swallow tablets/capsules whole
  - Dose from cut, crushed, dissolved, or chewed tablets/capsules may be fatal, particularly in opioid-naïve individuals

NALOXONE

What it is:

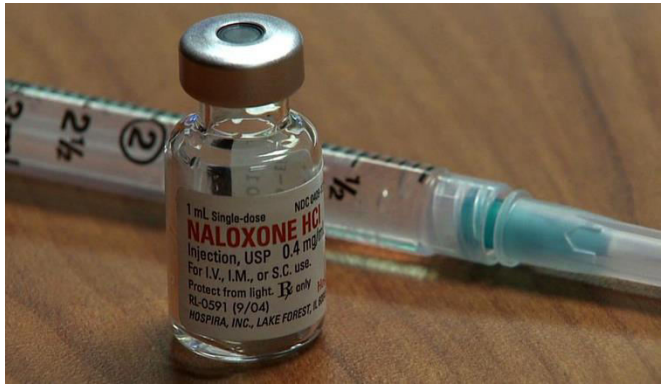
- An opioid antagonist administered intranasally (most common) or parenterally
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia; may precipitate acute opioid withdrawal

What to do:

- Discuss an overdose plan with patients
- Consider offering a naloxone prescription to all patients prescribed opioids; some states *require* co-prescribing
- Involve and train family, friends, partners, and/or caregivers in the proper administration of naloxone
- Check to see if pharmacy dispenses it
- Check expiration dates and replace expired naloxone
- In the event of known or suspected overdose **call 911** and administer naloxone

NALOXONE OPTIONS

- Available as auto-injector, intramuscular injection, or nasal spray
- Cost and insurance coverage vary
- Make use of tutorial videos to demonstrate administration
- Store at room temperature
- Dispose of used containers safely



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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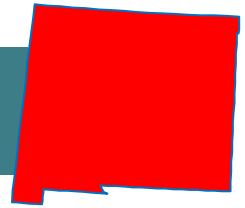
Naloxone Regulation



Effective date	• **March 2016**
Criminal Immunity	• Prescribers: **No** • Dispensers: **Yes** • Lay People: **Yes**
Also Available	• Without Prescription: **Yes** • To 3rd Party: **Yes** • By Standing Order: **Yes**
Carried by First Responders	• **Yes**

https://www.networkforphl.org/_asset/qz5pvn/legal-interventions-to-reduce-overdose.pdf Dec. 2018
www.pdaps.org

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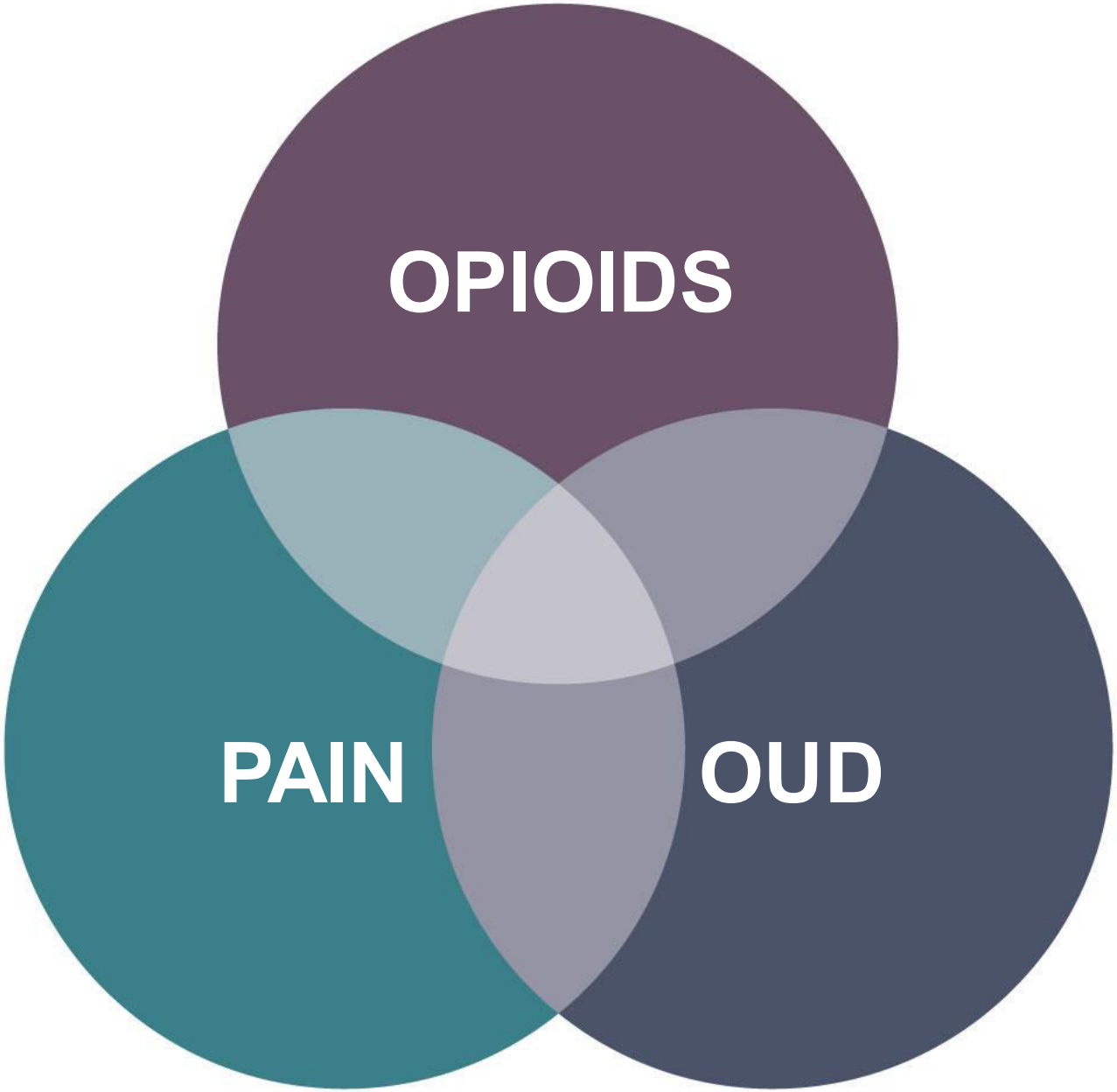
CHAPTER 7

UNDERSTANDING OPIOID USE DISORDER (OUD)



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OPIOIDS

WHAT IS THE RISK FOR MY PATIENT?

- Risk of opioid use disorder in patients on chronic opioid therapy (COT) for chronic non-cancer pain (CNCP) is up to **26%**
- Risk is always highest with past history of substance use disorder (SUD) or psychiatric comorbidity

SOURCE: Boscarino, J. Addictive Dis., 2011;30(3):185-194, http://www.tandfonline.com/doi/abs/10.1080/10550887.2011.581961

WHAT IS ADDICTION?

OFFICIAL ASAM DEFINITION:

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

PRACTICAL DEFINITION:

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

SUBSTANCE USE DISORDER: DSM-5 CRITERIA

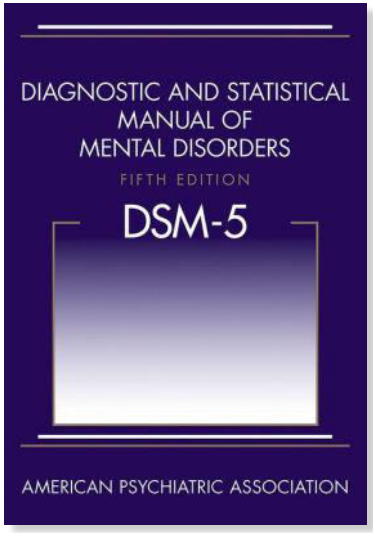
1. Tolerance*
2. Withdrawal*

LOSS OF CONTROL

3. Using larger amounts and/or for longer periods
4. Inability to cut down on or control use
5. Increased time spent obtaining, using, or recovering
6. Craving/compulsion

USE DESPITE NEGATIVE CONSEQUENCES

7. Role failure at work, home, school
8. Social, interpersonal problems
9. Reducing social, work, recreational activity
10. Physical hazards
11. Physical or psychological harm



- 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). 2013

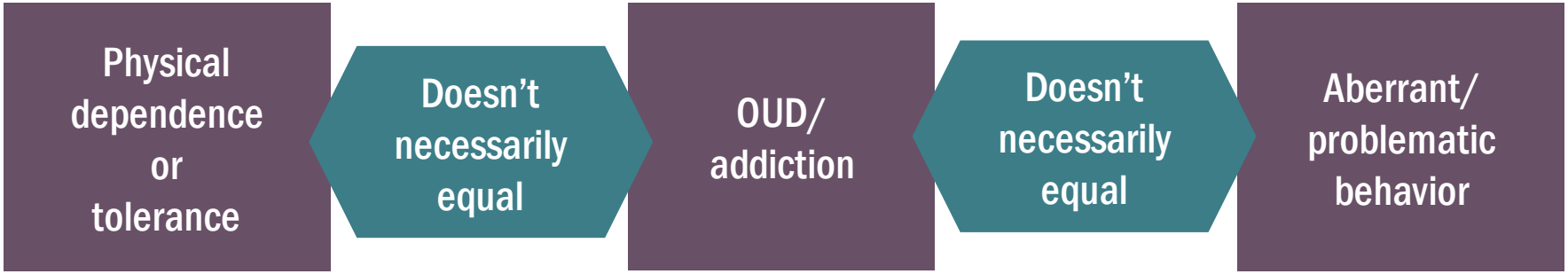
PAIN, OUD, AND OPIOIDS

The DSM-5 criteria for opioid use disorder may be misleading in the context of *prescribed opioids* for the treatment of pain.

The usual illegal, illicit issues do not pertain.

Harm may be masked under these conditions.

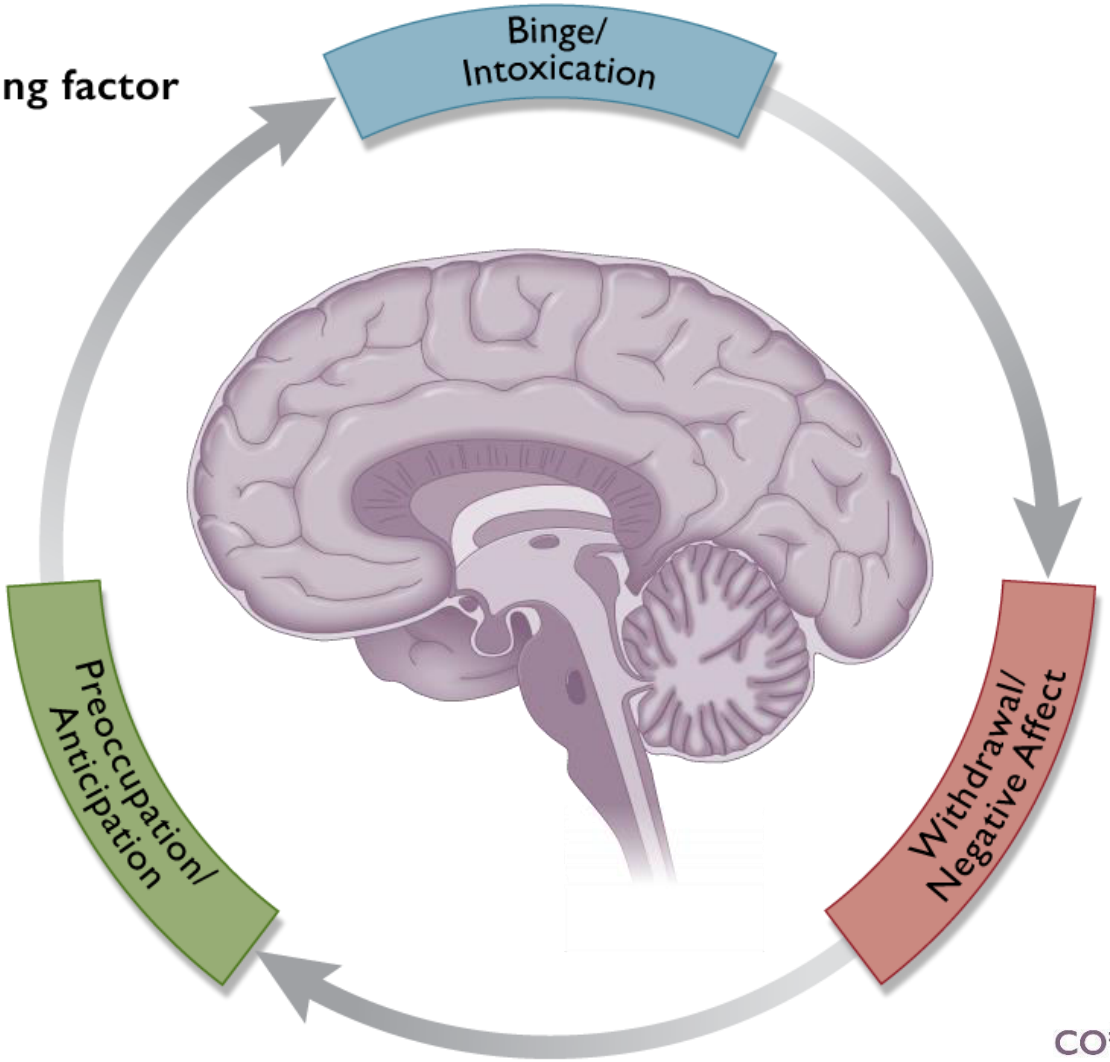
WORDS MATTER



THE CYCLE OF SUBSTANCE USE DISORDER

NEUROTRANSMITTERS

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



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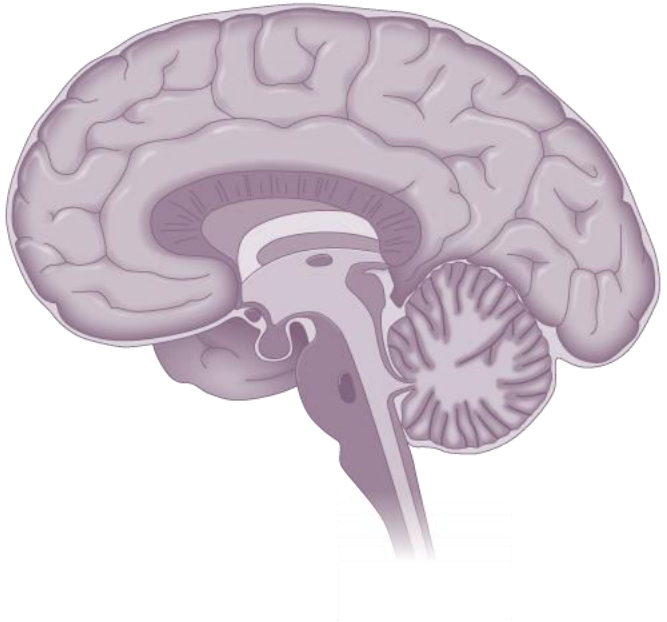
WHO IS VULNERABLE TO OPIOID MISUSE OR OUD?

Those with psychiatric comorbidities

19% of people who have mental health disorders in United States receive 51% of the prescribed opioids.

The probability of long-term opioid use increases most sharply in the first days of therapy, particularly after 5 days or 1 month of opioids has been prescribed.



TREATMENT OF OPIOID USE DISORDER

- Medication options for addiction treatment (MAT)
  - Methadone (Schedule II)
  - Buprenorphine (Schedule III)
  - Naltrexone (not a controlled substance)
- Supplementary psychosocial and recovery support services
  - Housing, childcare, support groups, employment services
- Temporal considerations
  - Frequency of administration (daily versus long-acting formulations)
  - Length of treatment
    - No recommended time period for treatment
    - Patients who discontinue and resume risk overdose and death

TREATING PAIN IN THE PATIENT WITH OUD

- Remember that untreated pain is a trigger for relapse
- Must address *both* pain and opioid use disorder
- Avoid other potentially problematic medications
- Consider a multidisciplinary pain program

- Consider buprenorphine for both pain and OUD
- Consider using opioids that do not metabolize to other prescribed medications
- Enlist patient's family/ significant other to secure and dispense opioids
- Recommend an active recovery program
- Remember to use UDT, PDMP, pill counts, PPA

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

OPIOID ANALGESICS WITH BENZODIAZEPINES, NICOTINE, AND ALCOHOL

- More than 30% of opioid overdoses involve benzodiazepines (BZDs); both are CNS depressants
- Nicotine and alcohol use are risk factors for misuse of prescribed opioids
- Nicotine users are co-prescribed BZDs and muscle relaxants (MRs) with opioids to a greater extent than non-nicotine users



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

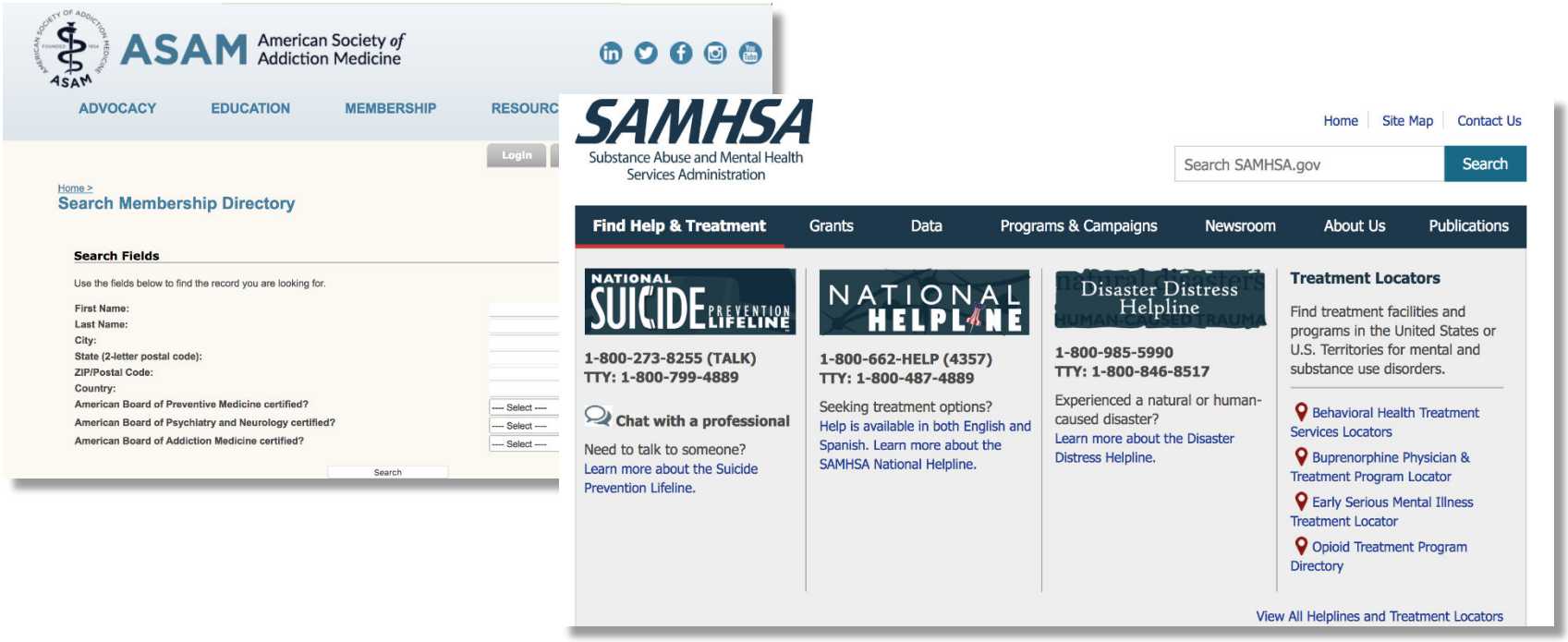
BUPRENORPHINE

- If using for pain, you don't need a waiver
- If using to treat OUD, you need a waiver
- The most commonly prescribed pharmacotherapy for the treatment of OUD
- Partial mu-agonist with "plateau effect" for respiratory depression
- Good efficacy and safety profile
- FDA-approved buprenorphine products for pain:
  - Butrans: 7-day transdermal patch
  - Belbuca: buccal mucosal film; BID dosing

REFERRALS AND TREATMENT CENTERS

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

ASAM resources: https://www.asam.org/resources/resource-links
SAMHSA locator: https://findtreatment.samhsa.gov/locator
AAAP locator: https://www.aaap.org/patients/find-a-specialist/



Cannabis and Pain

PRESENTED BY
CO*RE, THE COLLABORATION FOR
REMS EDUCATION

CO*RE

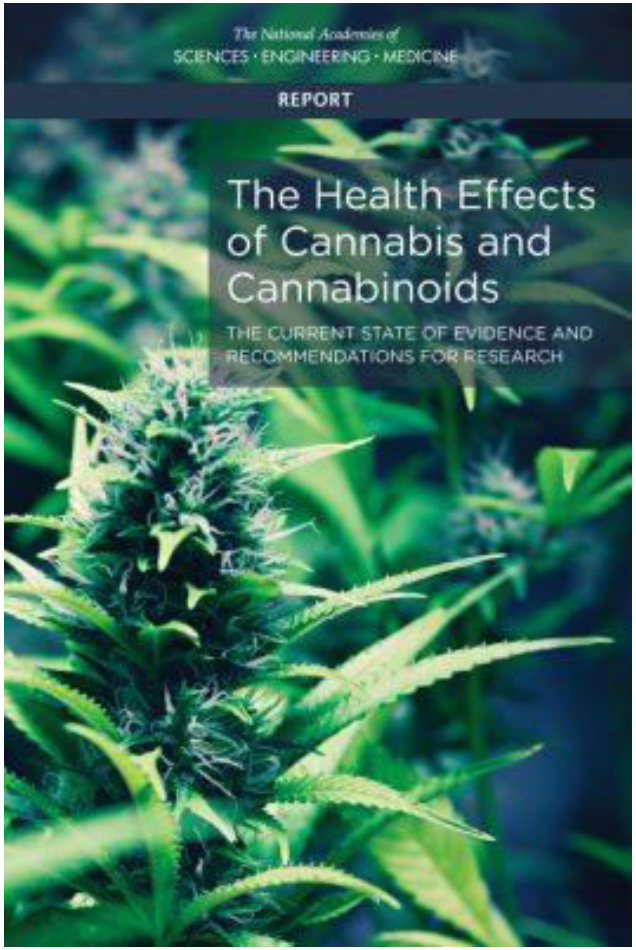
June 2019

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

CANNABIS and CANNABINOIDS



- DEA Schedule 1 ("high abuse potential") yet state laws and regulations vary
- There is evidence that cannabis or selective cannabinoids (cannabidiol) are effective for chronic pain treatment in adults
- More research is needed
- Concern for high risk groups: children, adolescents, pregnant women

SOURCE: The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. A National Academy of Science publication (2017)

EVIDENCE FOR PAIN

Twenty-seven trials:

- Low-level evidence for neuropathic pain
- No evidence for other pain populations

Eleven systemic reviews and 32 primary studies:

- Increased adverse events such as motor vehicle accidents, psychotic symptoms, short-term cognitive impairment

- *Limitations: Not methodologically rigorous, heterogeneous products, few long-term studies, few studies in older populations*

SOURCE: Nugent et al, Ann Intern Med 2017

EVIDENCE FOR PAIN

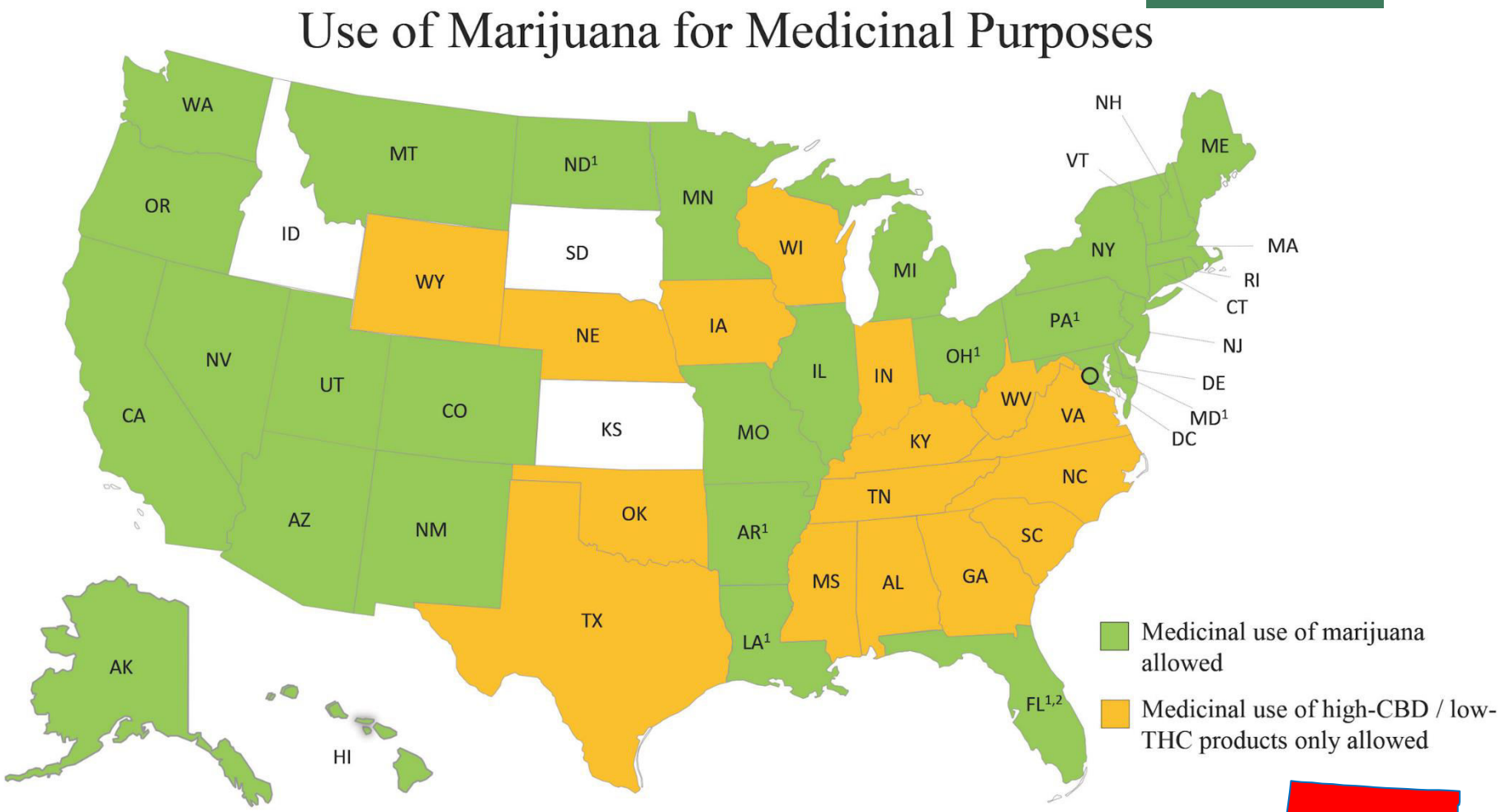
In a 2015 meta-analysis:

- Eight studies showed some pain reduction vs placebo (37% vs 31%, OR 1.41)
- Five studies showed reduction in pain score vs placebo (WMD -0.46)
- Adverse effects: dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, hallucination
- *Limitations: Not methodologically rigorous, heterogeneous products, few long-term studies, few studies in older populations*

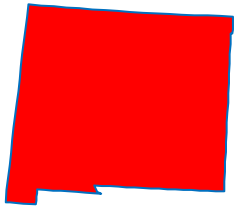
SOURCE: Whiting et al, JAMA 2015

Marijuana Status

Medical



Recreational | **Not legal for recreational use in New Mexico**



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 a schedule I drug, can have legal consequences, depending on your state
  - Avoid high frequency
  - Avoid synthetics
- Use PPA and document conversations about risks
- Seek institutional legal counsel to reduce liability


SPECIAL
POPULATIONS

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

SOURCE: 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.

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, breast feeding 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 high-risk OB/Gyn who will ensure appropriate treatment for the baby

- Perform universal screening to avoid neonatal abstinence syndrome

- For women using opioids on a daily basis, consider methadone or buprenorphine

SOURCES: Chou R, et al. J Pain. 2009;10:113-30; ACOG Committee on Obstetric Practice, August 2017

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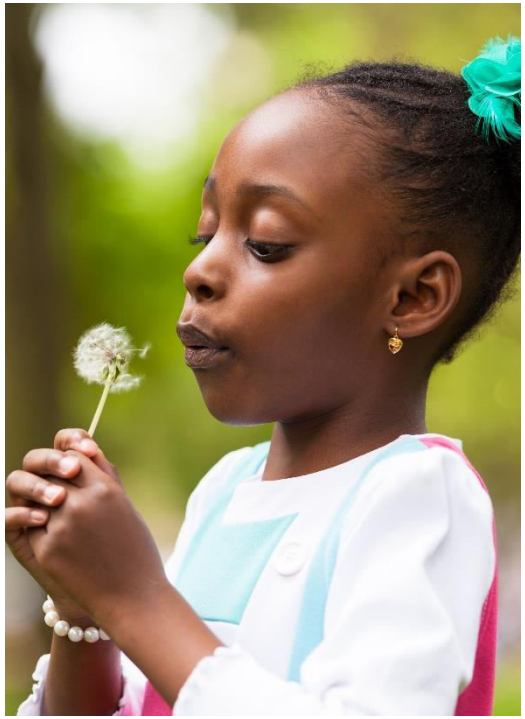
CHILDREN AND ADOLESCENTS

HANDLE WITH CARE: JUDICIOUS & 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
- Oxycodone ER dosing changes for children ≥ 11



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)
- Persons with dementia/ nonverbal patients
- Persons with obesity
- Persons with renal/ hepatic impairment
- Persons with psychiatric disorders
- Persons at end-of-life
- Persons with substance use disorder

CHAPTER 5

MANAGING PATIENTS ON OPIOID ANALGESICS

INITIATING OPIOIDS

- Begin with IR
- 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
- Co-prescribe naloxone (if indicated)
- Co-prescribe 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 3 months; if benefits do not outweigh harms, optimize other therapies and work to taper and discontinue

There are differences in benefit, risk 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 their 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 PDMP (when clinically indicated or legally mandated)
- Use urine drug testing (UDT)
- Reassess risk of 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

PPA NONADHERENCE

Behavior outside the boundaries of agreed-on treatment plan

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

Any of these behaviors merits **investigation**: proceed with caution

OUD/SUD RISK ASSESSMENT TOOLS (ONCE TREATMENT BEGINS)

PMQ
Pain Medication Questionnaire

COMM
Current Opioid Misuse Measure

PDUQ
Prescription Drug Use Questionnaire

SBIRT
Screening, Brief Intervention, and Referral to Treatment

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

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

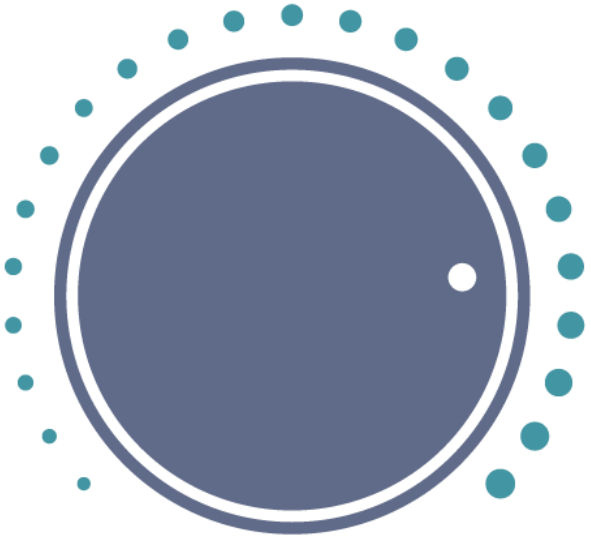
- Especially within 24 – 72 hours of initiating therapy and increasing dosage

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

- 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

OPIOID-INDUCED HYPERALGESIA



- An increased sensitivity to pain
- 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 progression
- Usually occurs at high MME dosages and over long periods of time
- A physiological phenomenon that can happen to anyone

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

IMPORTANT

FOR 1 WEEK OR LONGER

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/RpcUI/products.u

OPIOID TOLERANCE VERSUS PHYSICAL DEPENDENCE

TOLERANCE

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

PHYSICAL DEPENDENCE

- Occurs when an organism 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

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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 (EDT)

Many different versions:

- Published
- Online
- Online interactive
- Smart-phone 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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EXAMPLE OF 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)

MU-OPIOID RECEPTORS AND INCOMPLETE CROSS TOLERANCE

MU-OPIOIDS BIND TO MU RECEPTORS

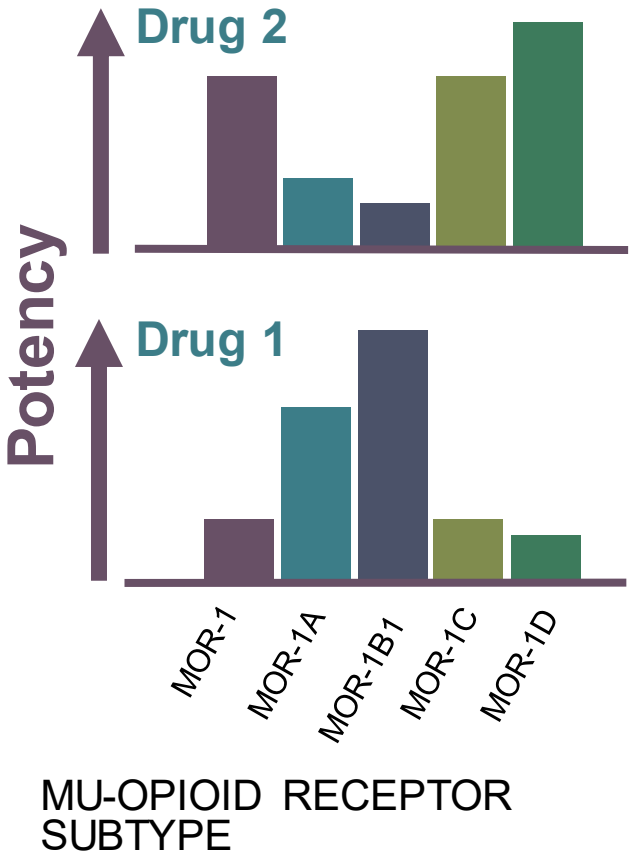
MANY MU RECEPTOR SUBTYPES

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



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GUIDELINES FOR OPIOID ROTATION

Calculate equianal-gesic 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	CLOSER TO 25% REDUCTION IF PATIENT
• Is receiving a relatively high dose of current opioid regimen • Is elderly or medically frail	• Does not have these characteristics • Is changing route of administration

*75% – 90% reduction for methadone

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GUIDELINES FOR OPIOID ROTATION *(continued)*

IF SWITCHING TO METHADONE:

- Standard EDTs 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

GUIDELINES FOR OPIOID ROTATION: SUMMARY

VALUES FROM EDT*	PATIENT OPIOID VALUES	SOLVE FOR X	AUTOMATICALLY REDUCE DOSE
$\frac{\text{Value of current opioid}}{\text{Value of new opioid}}$	$\frac{\text{24-hr dose of current opioid}}{\text{X amount of new opioid}}$	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 aberrant/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

- Response to growing non-medical-use problem
- An ER/LA opioid with properties to meaningfully deter abuse, even if they do not fully prevent abuse
  - 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

REASONS FOR DISCONTINUING OPIOIDS

PAIN LEVEL DECREASE IN STABLE PATIENTS

INTOLERABLE AND UNMANAGEABLE AEs

NO PROGRESS TOWARD THERAPEUTIC GOALS

MISUSE OR ABERRANT 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

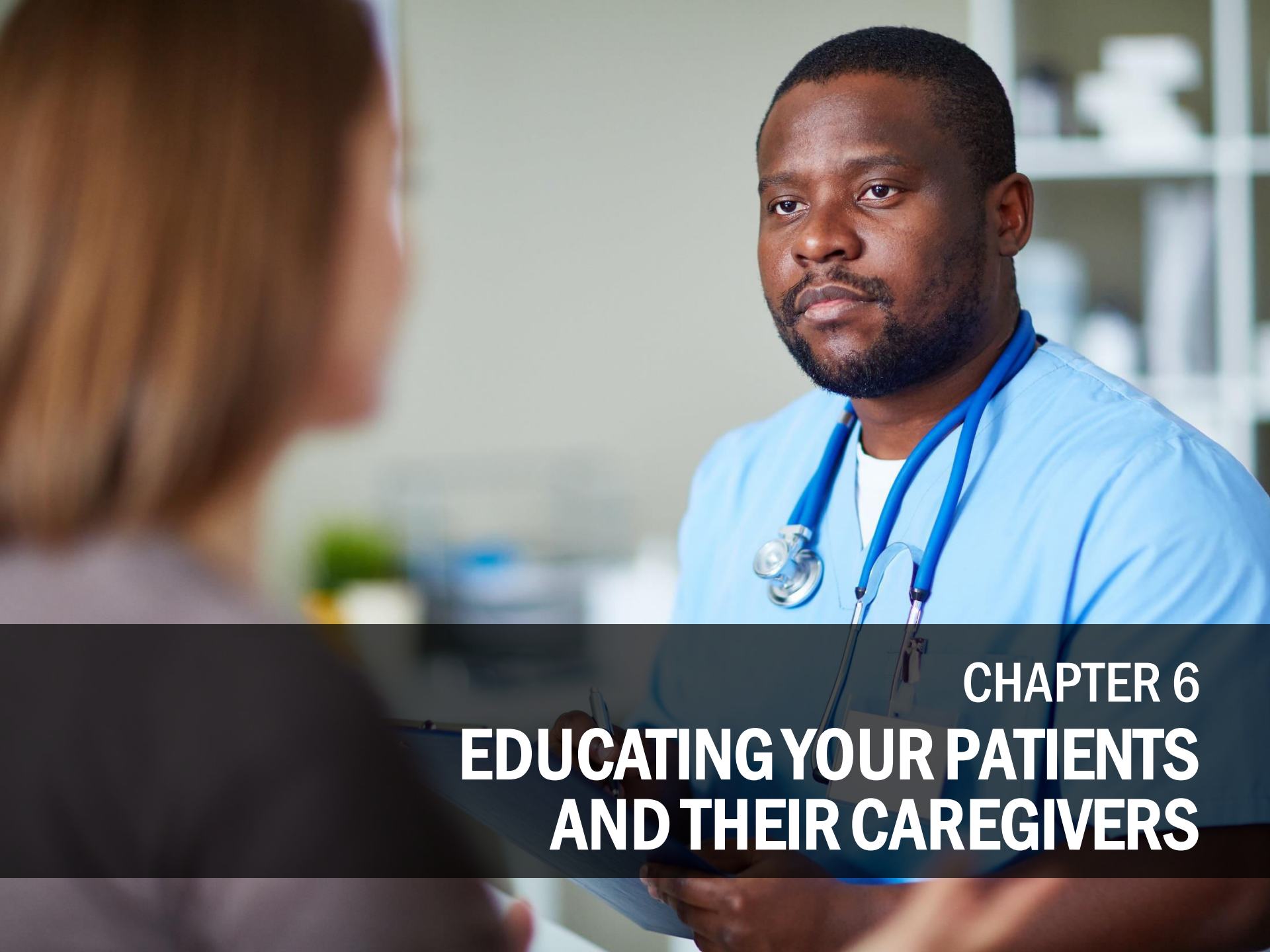
TAPER DOSE WHEN DISCONTINUING

- 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
- If opioid use disorder or a failed taper, refer to an addiction specialist or consider opioid agonist therapy
- Counseling and relaxation strategies needed

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, and treatment plans.



CHAPTER 6

EDUCATING YOUR PATIENTS AND THEIR CAREGIVERS

COUNSEL PATIENTS ABOUT PROPER USE

- Take opioid as prescribed
- Adhere to dose regimen
- Use least amount of medication necessary for shortest time
- Do not abruptly discontinue or reduce dose; taper safely to avoid withdrawal symptoms
- Properly handle missed doses
- Notify HCP if pain is uncontrolled
- Manage side effects
- Inform HCP of ALL meds being taken
- Never share or sell opioids: can lead to others' deaths, against the law
- Use caution when operating heavy machinery and driving

Read the opioid **drug package insert** received from the pharmacy **every time** an opioid is dispensed

USE PATIENT COUNSELING DOCUMENT

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

CLICK TO DOWNLOAD

https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_Analgesic_2018_09_18_Patient_Counseling_Guide.pdf

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PROVIDE ANTICIPATORY GUIDANCE ON OPIOID SIDE EFFECTS AND ADVERSE EVENTS

- Respiratory depression: most serious
- Opioid-induced constipation (OIC): most common
- Sexual dysfunction and other endocrine abnormalities
- Tolerance, physical dependence, hyperalgesia
- Allergic reactions
- Sedation, cognitive impairment
- Falls and fractures
- Sweating, miosis, urinary retention
- Hypogonadism
- Myoclonus (twitching or jerking)
- Addiction in vulnerable patients
- Overdose and death

WARN PATIENTS

Never break, chew, crush, or snort an opioid tablet/capsule, or cut or tear patches or buccal films prior to use

- May lead to rapid release of opioid, causing overdose and death
- If patient is unable to swallow a capsule whole, refer to drug package insert to determine if appropriate to sprinkle contents on applesauce or administer via feeding tube

Use of CNS depressants or alcohol with opioids can cause overdose and death

- Use with alcohol may result in rapid release and absorption of a potentially fatal opioid dose, known as “dose dumping”
- Use with other depressants such as sedative-hypnotics (benzodiazepines), anxiolytics, or illegal drugs can cause life-threatening respiratory depression

OPIOID-INDUCED RESPIRATORY DEPRESSION

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

Greatest risk: during initiation of therapy 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

SIGNS OF OVERDOSE POISONING CALL 911

- Person cannot be aroused or awakened 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

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NALOXONE

What it is:

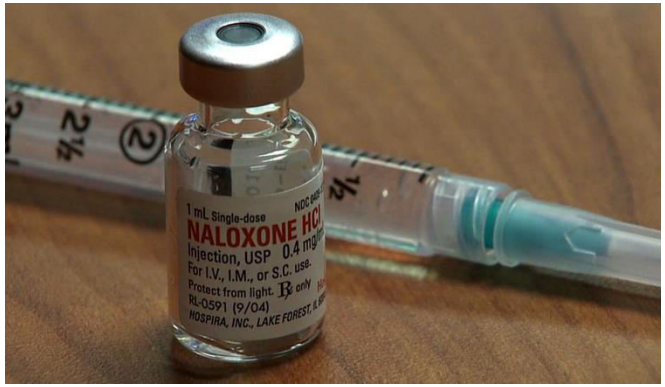
- An opioid antagonist administered intranasally (most common) or parenterally
- Reverses acute opioid-induced respiratory depression but will also reverse analgesia; may precipitate acute opioid withdrawal

What to do:

- Discuss an overdose plan with patients
- Consider offering a naloxone prescription to all patients prescribed opioids; some states *require* co-prescribing
- Involve and train family, friends, partners, and/or caregivers in the proper administration of naloxone
- Check to see if pharmacy dispenses it
- Check expiration dates and replace expired naloxone
- In the event of known or suspected overdose **call 911** and administer naloxone

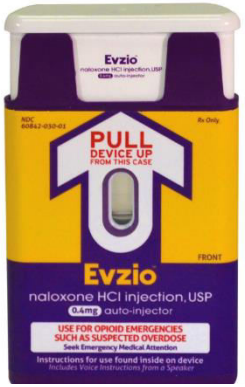
NALOXONE OPTIONS

- Available as auto-injector, intramuscular injection, or nasal spray
- Cost and insurance coverage vary
- Make use of tutorial videos to demonstrate administration
- Store at room temperature
- Dispose of used containers safely



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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SAFE OPIOID STORAGE AND DISPOSAL

STEP 1: MONITOR

- Note how many pills are in each prescription
- Keep track of dosage and refills
- Make sure everyone in the home knows

STEP 2: SECURE

- Keep meds in a safe place (locked cabinet or box)
- Store away from children, family, visitors, and pets
- Encourage parents of your teen's friends to secure their prescription

STEP 3: DISPOSE

- Discard expired or unused meds
- Consult drug package insert for best disposal method

SOURCE: McDonald E, Kennedy-Hendrick A, McGinty E, Shields W, Barry C, Gielen A. Pediatrics. 2017;139(3):e20162161

WHERE AND HOW TO DISPOSE OF UNUSED OPIOIDS

Authorized Collection Sites

- Use the DEA disposal locator website to find sites near you: https://apps.deadiversion.usdoj.gov/pubdispsearch
- Search Google Maps for "drug disposal nearby"

Mail-Back Packages

- Obtain from authorized collectors

Other Options

- Drug take-back days (local pharmacies or local law enforcement)
- Flush
- Trash (mix with noxious element)
- Fold patch in half so sticky sides meet, then flush

SOURCES. Department of Justice, Diversion Control Division, Disposal Act: General Public Fact Sheet (June 2018), https://www.deadiversion.usdoj.gov/drug_disposal/fact_sheets/disposal_public_06222018.pdf; FDA. Where and How to Dispose of Unused Medicines, https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm

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Our session stops here, but your review continues…

For detailed information, prescribers can refer to prescribing information available online via DailyMed at www.dailymed.nlm.nih.gov or https://opioidanalgesicrems.com/RpcUI/products.u

Please visit the CO*RE Tools Repository
http://core-rems.org/opioid-education/tools/

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Your participation in this test allows CO*RE to report de-identified numbers to the FDA.

Strong test participation will demonstrate that clinicians have voluntarily engaged with this important material and are committed to patient safety and improved outcomes.

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