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Validating Controlled Substances

Manny Alfonso
Baptist Health South Florida, manny.alfonso@baptisthealth.net

Validating Controlled Substances

Manny Alfonso, Pharm.D.
PGY-1 Pharmacy Resident
Baptist Hospital of Miami
Part II

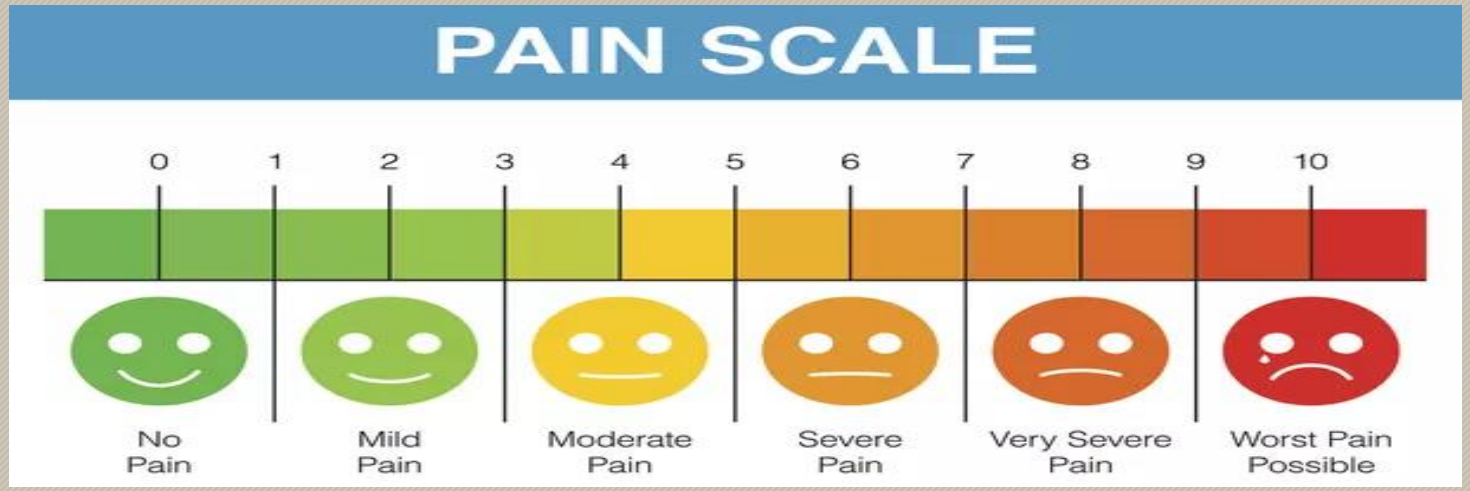
Objectives

- Assess the role of opioids in treatment of acute versus chronic pain
- Identify methods for validating controlled substance prescriptions and review strategies for distinguishing invalid prescriptions
- Outline patient counseling pearls for controlled substances regarding administration, adverse effects, drug interactions, and appropriate storage and disposal
- Discuss the role of naloxone in suspected opioid overdose and review treatment resources for patients with opioid dependence, addiction, misuse, or abuse

Role of Opioids in Pain

What is Pain?

- “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”



Raja SN et al. Revised Intern Asso for the Study of Pain. *Pain*. 2020.

Characteristics of Pain

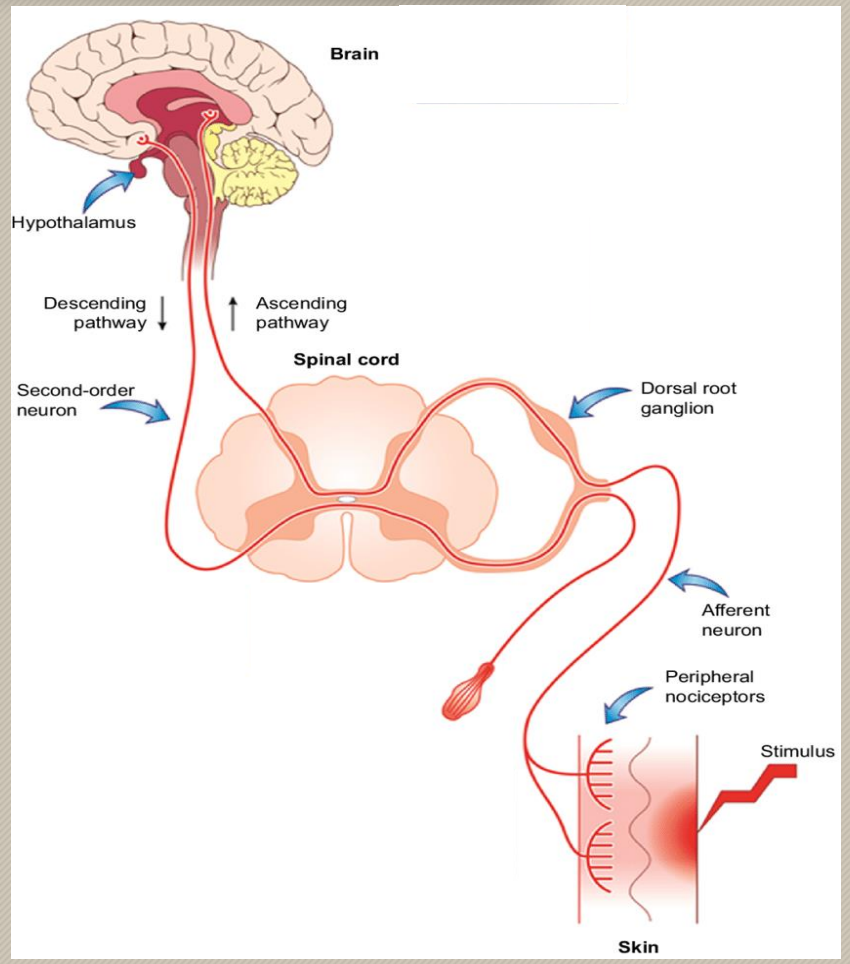
Nociceptive	**Neuropathic**
Sharp	Tingling/numbness
Aching	Burning
Throbbing	Shock-like
Usually localized	Radiating

Kelly D, et al. *Can J Clin Anaeasth*. 2001.

Pathophysiology

Four steps of pain signaling & processing:

1. Transduction
   - Stimulus → nociceptors → action potentials and nerve signaling
2. Transmission
   - Nociceptive sensory nerve fibers → neurons synapse in the dorsal horn of the spinal cord → brainstem, thalamus, and hypothalamus
3. Modulation
   - Neurons descending from brain stem to spinal cord → release chemical messengers modulating transmission of stimuli
4. Perception
   - Recognition of uncomfortable awareness → complex interactions between thalamus, limbic system, and reticular system



Kelly D, et al. *Can J Clin Anaeasth*. 2001.

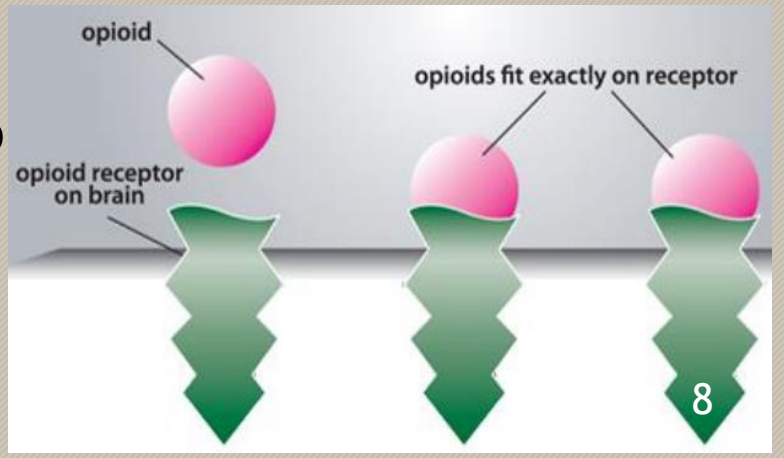
Acute Versus Non-acute/Chronic Pain

	Acute Pain	Non-Acute / Chronic
Definition	• Normal, predicted, physiological, and *time-limited response* to an adverse chemical, thermal, or mechanical stimulus associated with surgery, trauma, or acute illness	• Malignancy, terminal condition, palliative care or serious traumatic injury with an Injury Severity Score (ISS) ≥9 • Chronic nonmalignant pain persisting beyond usual course of disease OR pain persisting >90 days after surgery
Treatment goal	• Cure	• Functionality
Organic cause	• Common	• May not be present
Dependence & tolerance	• Unusual	• Common
Psychological component	• Usually not present	• Major problem
Insomnia & depression	• Unusual	• Common
Symptoms	• Anxiety, tachycardia, tachypnea, hypertensive, diaphoresis, dilated pupils	• Depressed mood, fatigue, lack of motivation, loss of appetite, loss of libido

Argoff C. Mech of Pain transmission.*Curr Med Res Opin*. 2011.

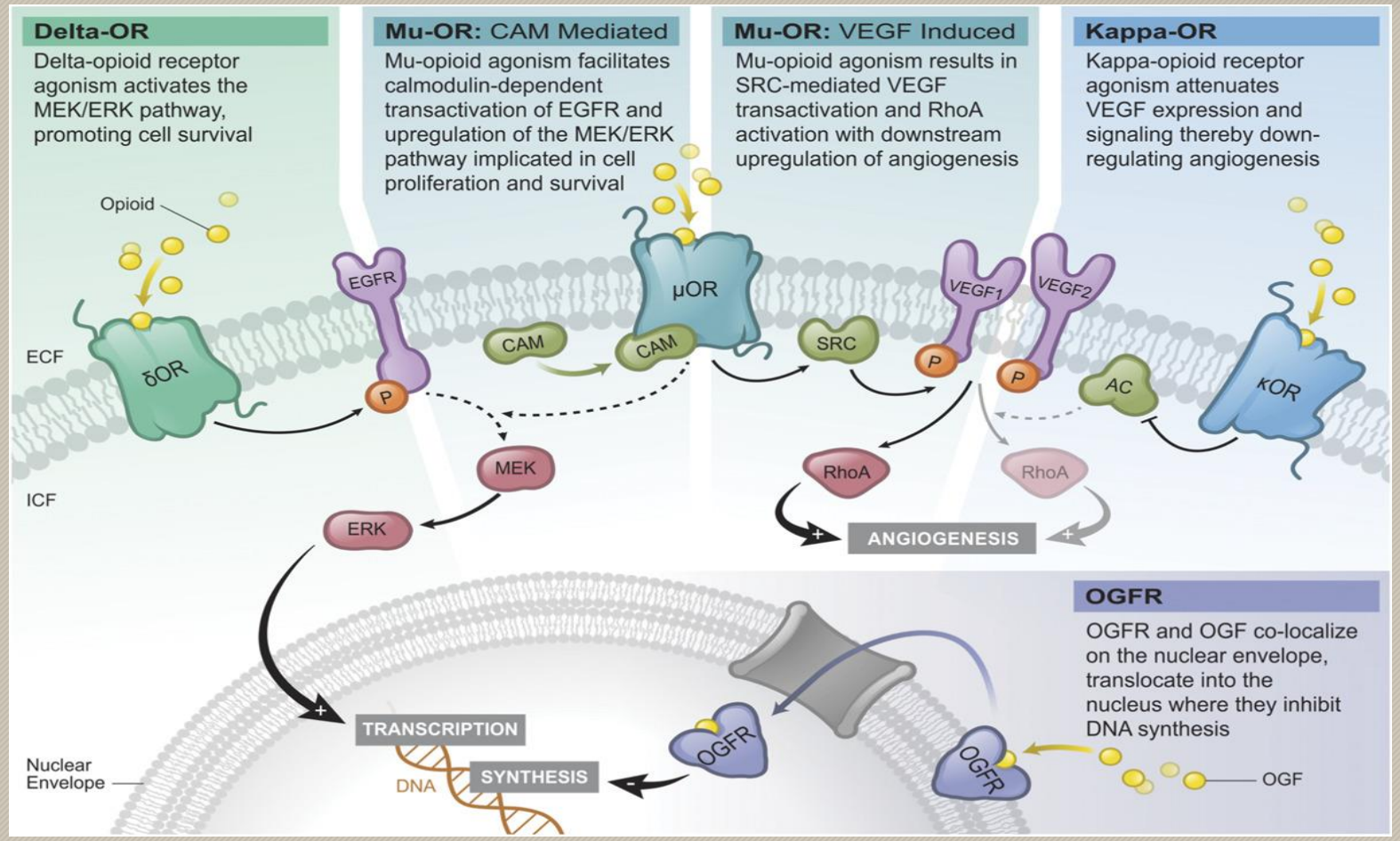
Opioids

- Mechanism
  - Agonist of opioid receptors → inhibition of ascending pain pathway
  - Interacts with 3 primary opioid receptors → μ (Mu), κ (Kappa), & δ (Delta)
- Administration
  - Oral, IV, IM, transdermal patch
- Adverse reactions
  - Nausea & vomiting, constipation, somnolence, dizziness, pruritus, flushing, reduced respiratory rate, decreased libido
- Warnings
  - Initiation of CYP3A4 inhibitors or discontinuing inducers
  - Risk evaluation and mitigation strategy (REMS)



Schiller EY et al. *Opioid Overdose*. 2019.

Opioids Receptors



★Mu:
- Analgesia, euphoria, respiratory depression

★Kappa:
- Hyperalgesia, euphoria, dysphoria, sedation, hypertension

Delta:
- Dopamine release, appetite, suppression

Schiller EY et al. *Opioid Overdose*. 2019.

Common Opioid Agents

Opioid	Brand	Formulation	Concentration	On-Set	Duration
Codeine	Tylenol #3, #4 (+acetaminophen)	Oral tablets	30 mg, 40 mg	15 - 30 minutes	4 - 6 hours
	Phenergan w/Codeine (+promethazine)	Oral solution	10 mg/5 mL		
Fentanyl	Sublimaze	IV	50 mcg/mL	5 minutes	30 - 60 minutes
	Duragesic	Transdermal patch	12 mcg/hour, 25 mcg/hour, 37.5 mcg/hour, 50 mcg/hour, 75 mcg/hour, 100 mcg/hour		
Hydrocodone	IR: Lorcet, Lortab, Norco, Vicodin (+acetaminophen)	Oral tablets	2.5 mg, 5 mg, 7.5 mg, 10 mg	70 - 90 minutes	3 - 4.5 hours
	ER: Hysingla ER, Zohydro	Oral capsules	10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg	14 - 16 hours	12 - 24 hours
Hydromorphone	Dilaudid	Oral tablet	2 mg, 4 mg, 8 mg	15 - 30 minutes	3 - 4 hours
Meperidine	Demerol	Oral tablet	50 mg, 100 mg	3 - 6 minutes	2 - 4 hours
Morphine	MS Contin, Kadian	Oral tablet	15 mg, 30 mg, 60 mg, 100 mg, 200 mg	20 - 40 minutes	3 - 6 hours
Oxycodone	IR: Roxicodone, Percocet (+acetaminophen)	Oral tablet	Roxicodone: 5 mg, 15 mg, 30 mg Percocet: 2.5 mg, 5 mg, 7.5 mg, 10 mg	10 - 30 minutes	3 - 6 hours
	CR: Oxycontin	Oral tablet	10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg	60 minutes	12 hours

Validating Prescriptions for Controlled Substances

Methods for Validating

- Assess therapeutic legitimacy
- Visual authenticity
- Drug Utilization Reviews (DUR)
- Consulting the Prescription Drug Monitoring Program (PDMP)

Assess for Therapeutic legitimacy

Acute

- Limits C-II opioids to 3 days
  - ➢ May be increased to 7 days if determined to be medically necessary
  - ➢ Prescriber ***must*** have "ACUTE PAIN EXCEPTION" on prescription
  - ➢ Limits scheduled II controlled substance opioids to a 14 day supply for post-surgical procedure
    - ❖ Exemption: Does not apply opioids for treatment of addiction

House Bill No. 21: Chapter 2018-13.

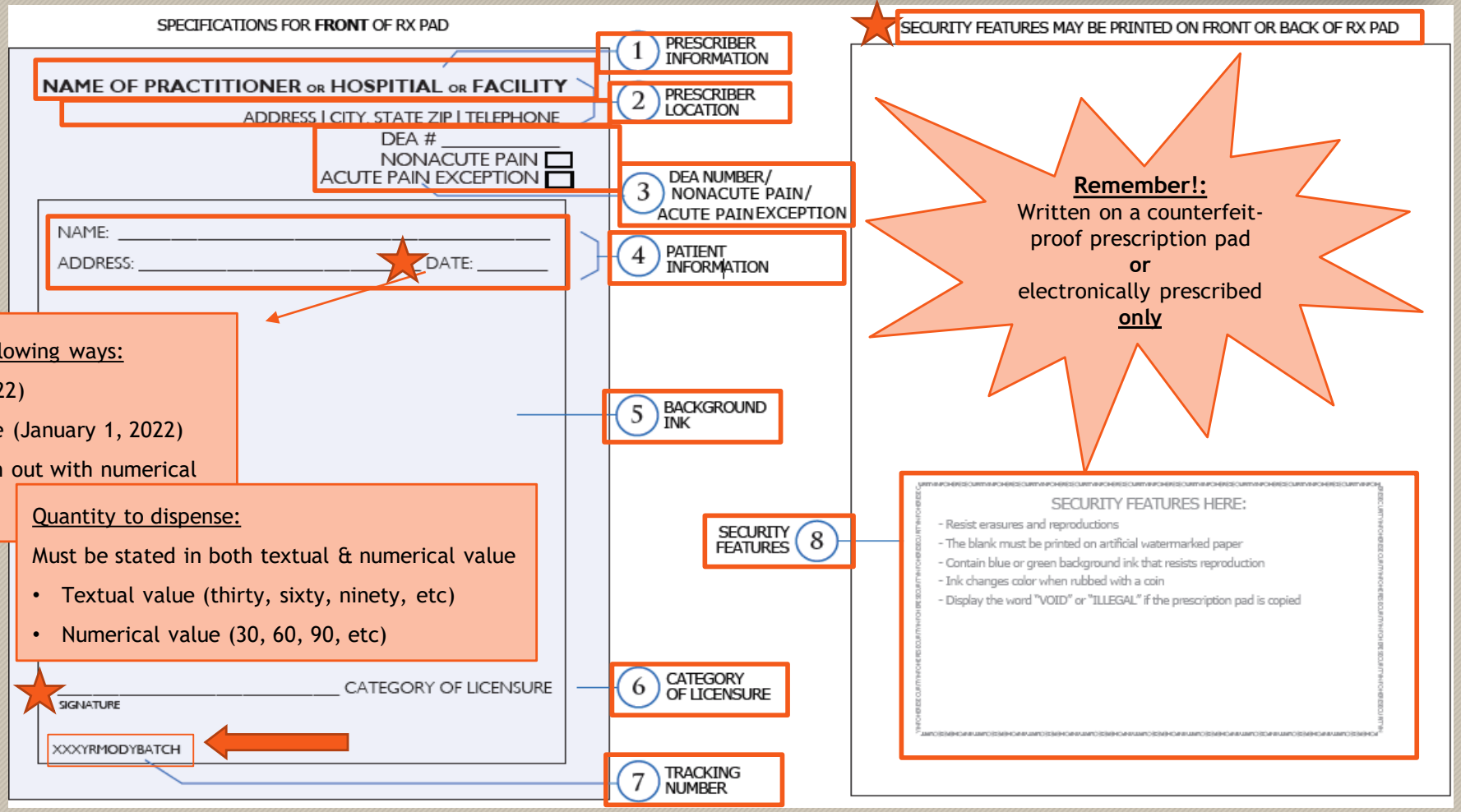
Assess for Therapeutic Legitimacy

Non-Acute/Chronic Pain

- Prescriber ***must*** indicate "NONACUTE PAIN" on the prescription for a C-II
- Patients treated for a traumatic injury with an ISS of ≥9 must be concurrently prescribed an emergency opioid antagonist
  - If this is not received, pharmacist should follow standard policy and procedures and contact prescriber
  - Any changes should be promptly reduced to writing and properly annotated

House Bill No. 21: Chapter 2018-13.

Visual Authenticity



Date reduced in **one** of the following ways:

1. Numerical format (1/1/2022)
2. Month written out in whole (January 1, 2022)
3. Abbreviated month written out with numerical format (Jan. 1, 2022)

Quantity to dispense:

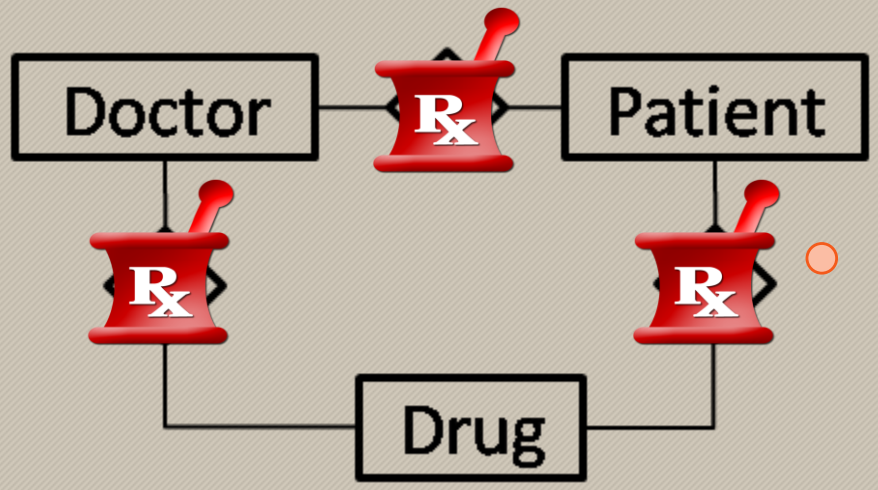
Must be stated in both textual & numerical value

- Textual value (thirty, sixty, ninety, etc)
- Numerical value (30, 60, 90, etc)

Florida Statue 456.42.

Drug Utilization Review

- An authorized, structured, ongoing review of healthcare provider prescribing, pharmacist dispensing, and patient use medication
  - Drug review against predetermined criteria



Pharmacist play a key role:

- ✓ Prevent inappropriate therapies
- ✓ Prevent adverse drug reactions
- ✓ Improve overall effectiveness

Navarro. Drug Utilization Review Strategies. 2008.

Drug Utilization Review

Classified into three categories:

Prospective:
Evaluation before dispensing

- Contraindications
- Precautions
- Therapy interchange & substitutions

Concurrent:
Monitoring during treatment

- Interactions
- High or low doses
- Duplicate therapy

Retrospective:
Reviewing after dispensing

- Over & under utilization
- Abuse & misuse
- Duration of treatment

Navarro. Drug Utilization Review Strategies. 2008.

Drug Utilization Review: Drug Interactions

Drug Class	Interaction with Opioids
Sedative hypnotics (e.g., benzodiazepines, barbiturates)	• ↑ Respiratory depression
Antipsychotic agents & relaxants (e.g., clozapine, cyclobenzaprine)	• ↑ Sedation • ↑ Cardiovascular effects • Variable effects on respiratory depression
Antidepressant agents (e.g., duloxetine, sertraline)	• ↑ Enhance the toxicity of antidepressants

Overholser et al. Opioid pharmacokinetic drug-drug interactions. *Am J Manag Care*. 2011.

Drug Utilization Review: Dosing

Dose†	Centers for Disease Control & Prevention Interpretation
20-50 MME/d*	• Low risk for overdose

50-90 MME/d*	• ↑ Risk for overdose by at least 2-fold
	  • Monitor and assess pain and function
	  • Reducing dose and discontinuation if risks outweigh benefits

>90 MME/d*	• Significant risk for opioid overdose • Conduct and document risk versus benefit reviews

†Morphine milligram equivalents per day (MME/d)
*Thresholds based on overdose risk when opioids are prescribed for pain

CDC. *Annual Surveillance Report of Drug-Related Risks and Outcomes* 2018.

Morphine Milligram Equivalents Calculations

Opioid	Conversion Factor
Codeine	0.15
Fentanyl transdermal	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1 – 20 mg/day	4
21 – 40 mg/day	8
41 – 60 mg/day	10
≥ 61 – 80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

Single opioid prescription:

Vicodin 5/300 mg PO Q4H

1. Calculate total daily dose required
   - 5 mg x 6 = 30 mg/d
2. Look for conversion factor
   - Hydrocodone = 1
3. Multiply daily dose by conversion factor
   - 30 mg/day x 1 = 30 MME/d

Multiple opioid prescriptions:

Percocet 5/325 mg PO QID

plus

Roxicodone 15 mg BID PRN breakthrough pain

1. Calculate total daily dose required for each opioid
   - Percocet 5/325 mg QID = 20 mg/day
   - Roxicodone 15 mg BID = 30 mg/day
2. Look for conversion factor for each opioid
   - Oxycodone = 1.5
3. Multiply total daily opioid dose by conversion factor
   - Percocet → 20 mg/day x 1.5 = 30 MME
   - Roxicodone → 30 mg/day x 1.5 = 45 MME
4. Add total MME
   - 30 MME + 45 MME = 75 MME/d

Fudin J, et al. Safety concerns with the CDC opioid calc. *J Pain Res*. 2017.

Switching Agents

	Equianalgesic Doses (mg)	
Drug	**Parenteral**	**Oral**
Morphine	10	30
Buprenorphine	0.3	0.1 (SL)
Codeine	100	200
Fentanyl	0.1*	NA
Hydrocodone	NA	30
Hydromorphone	1.5	7.5
Meperidine	100	300
Oxycodone	10	20
Oxymorphone	1	10
Tramadol	100	120

*mcg/hour

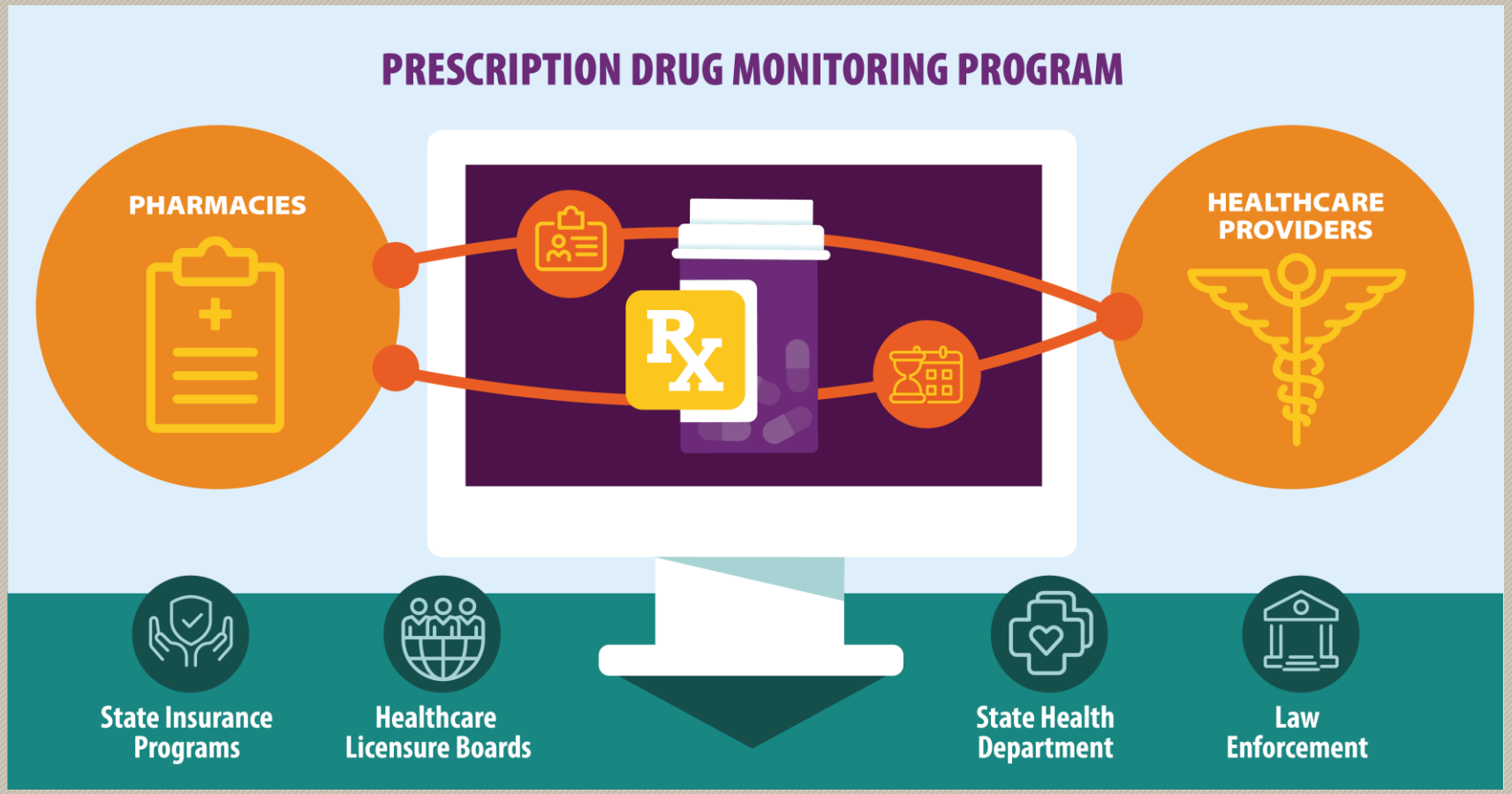
Fudin J, et al. Safety concerns with the CDC opioid calc. *J Pain Res*. 2017.

Drug Utilization Review: Duplications

- The prescribing and dispensing of two or more drugs from the same therapeutic class such that the combined daily dose puts the beneficiary at risk of an adverse medical result or incurs additional program costs without additional therapeutic benefit

Overholser et al. Opioid pharmacokinetic drug-drug interactions. *Am J Manag Care*. 2011.

Prescription Drug Monitoring Program



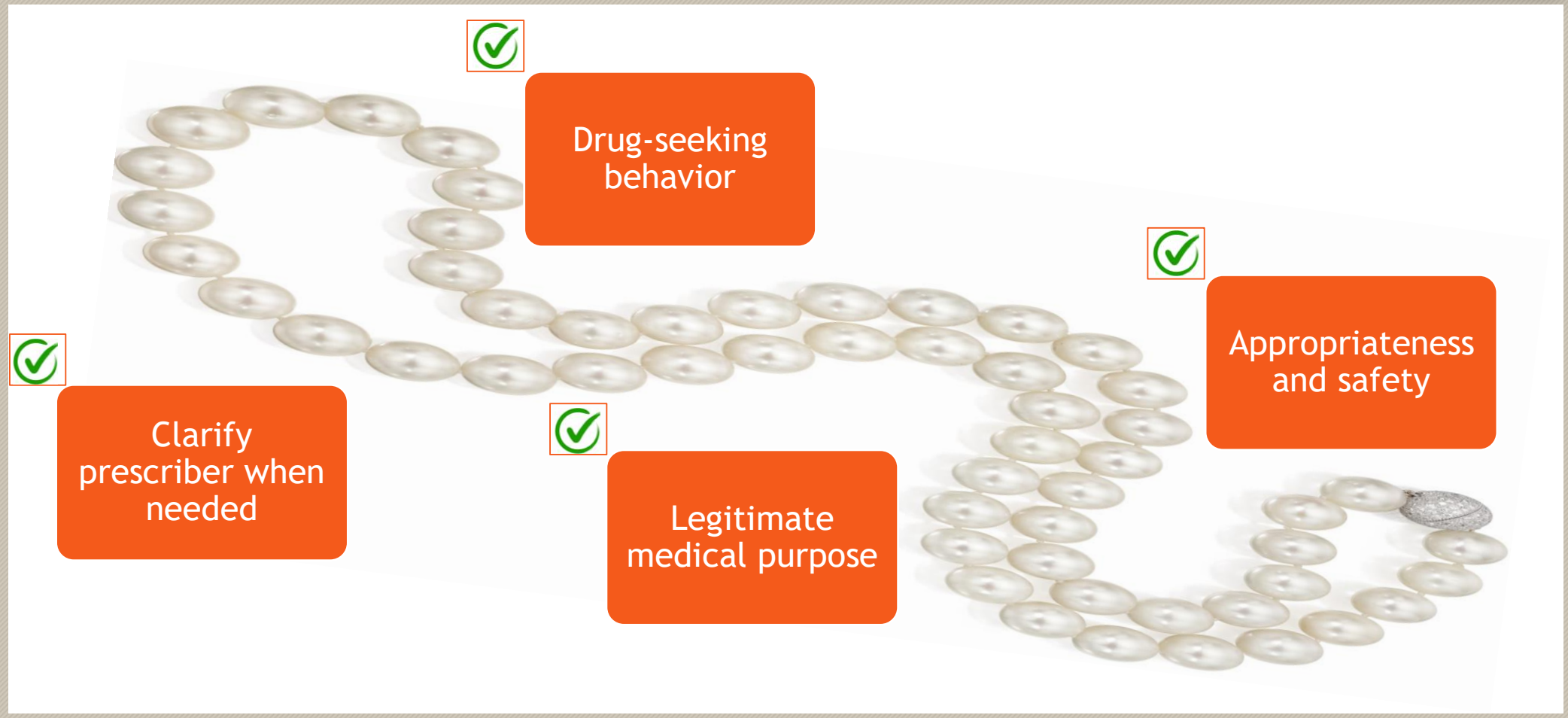
Ozturk et al. Presc Drug Monit Prog & Opioid Presc for DisCond. *Appl Health Econ Health Policy*. 2021.

Prescription Validity

- **Valid:**
  - ✓ Based on a practitioner-patient relationship
  - ✓ Legitimate medical purpose
- **Invalid:**
  - ✗ Not a legitimate medical purpose
  - ✗ Ethical concerns
  - ✗ Outside scope of practice for provider

Florida Statue 64B16-27.831.

Pharmacist Pearls



Patient Counseling for Opioid Medications

Key Points to Consider During Counseling

- Administration 
- Adverse Effects 
- Interactions 
- Storage & disposal 

Administration

- Taken as prescribed
- Following directions on prescription label
- Do not alter original formulation
- Alcohol
- With or without regards to meal
- Do not drive or operate machinery

Schiller EY et al. *Opioid Overdose*. 2019.

Adverse Effects

- Constipation
- Itching
- Drowsiness
- Dry mouth
- Nausea
- Respiratory depression

Schiller EY et al. *Opioid Overdose*. 2019.

Interactions

Food-drug

Drug-drug

Drug-disease

Inform healthcare providers

Vitamins, minerals, & herbals

Alcohol intake

Schiller EY et al. *Opioid Overdose*. 2019.

Storage & Disposal

Storage	Disposal
1. Count & keeping track of quantity	1. Drug disposal kiosks
2. Store in a safe & private area	2. Mail-back programs registered through DEA
3. Away from children & pets	3. Solidifying & deactivating agents
4. Separated from pill boxes	4. DEA National Rx Take Back program
5. Never share with anyone	

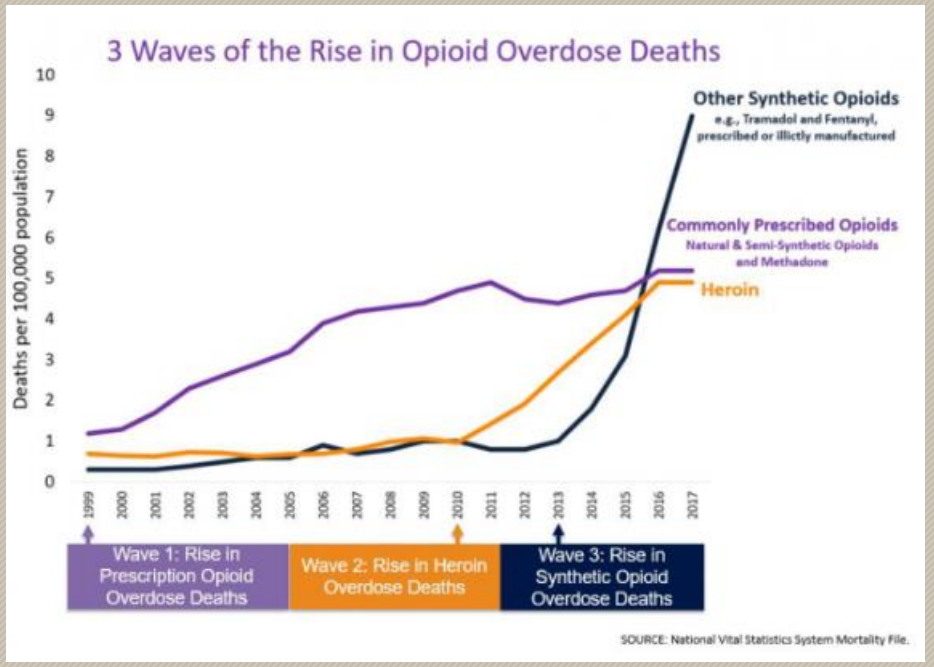
Schiller EY et al. *Opioid Overdose*. 2019.

Opioid Use & Misuse

Overdose

- 130 Americans die each day from an opioid overdose

- 400,000 opioid related deaths (1999-2017)
  - 1990: ↑ Prescribing opioids
  - 2010: ↑ Heroin overdose deaths
  - 2013: ↑ Synthetic opioid overdose deaths



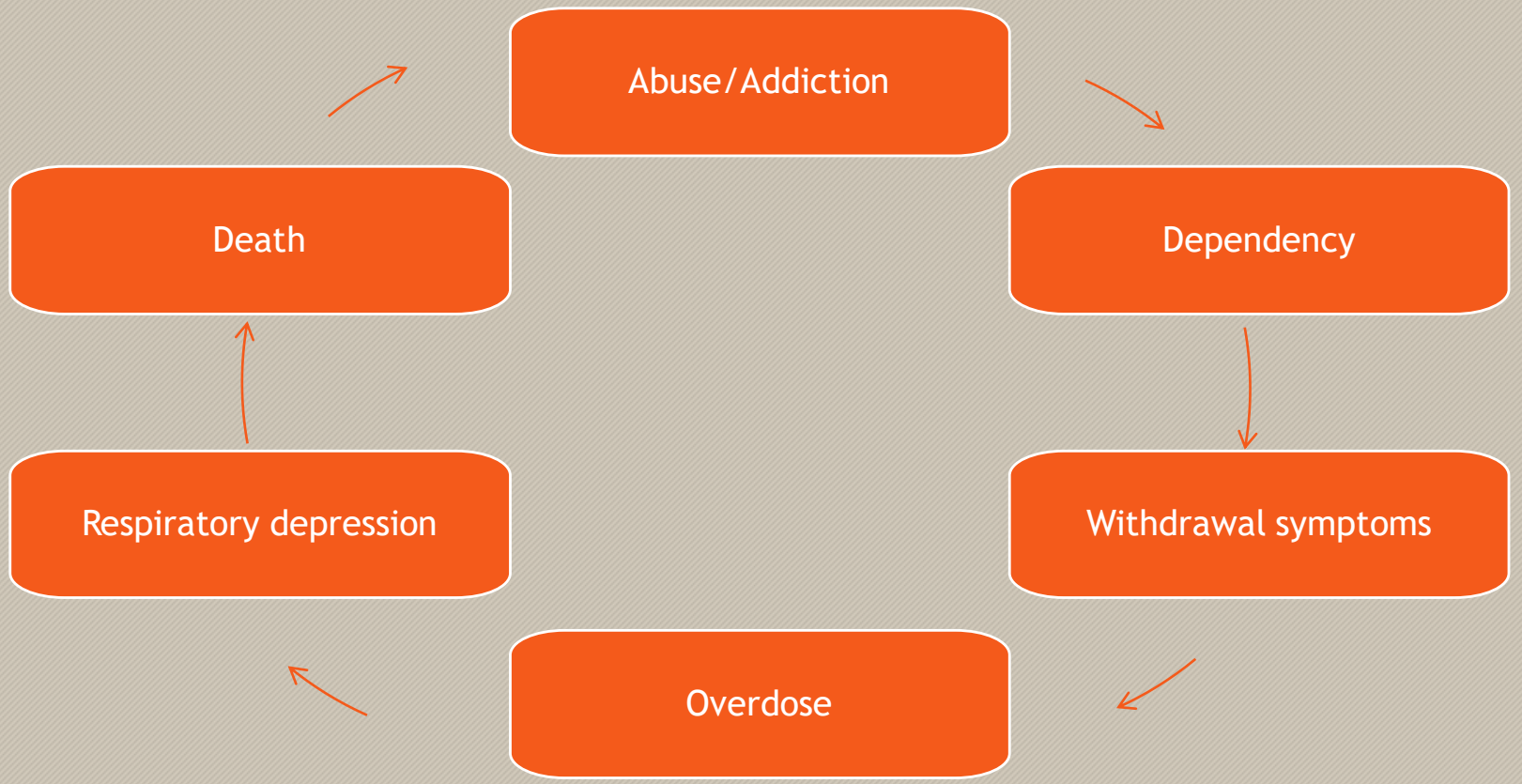
Opioid Overdose. *Centers for Disease Control and Prevention.* 2019.

Identifying Risk Factors for Overdose

- Dependency for chronic pain
- Increasing doses for pain management
- Doses > 50 MME/d
- Concomitant severe medical or psychiatric conditions
- Alcohol or other sedatives combination
- Male gender
- Younger age
- Household members taking opioids
- IV drug use history

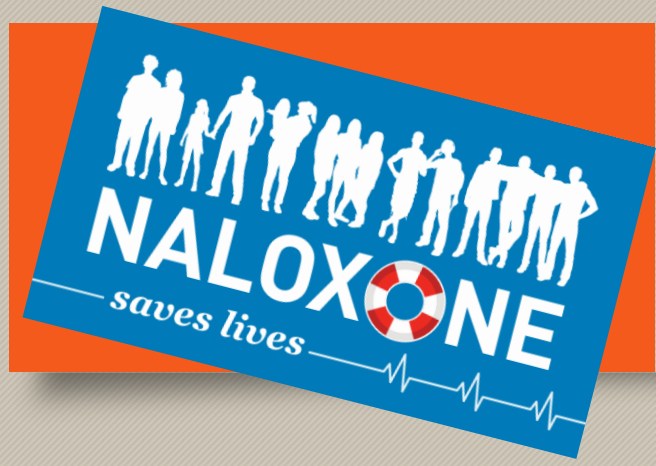
Schiller EY et al. *Opioid Overdose*. 2019.

Serious Risks



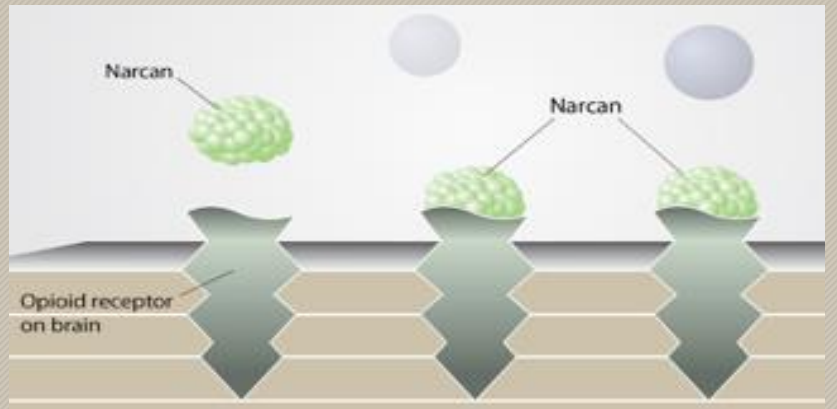
Schiller EY et al. *Opioid Overdose*. 2019.

Naloxone



Naloxone

- Mechanism
  - Opioid antagonist
- Administration
  - Intravenous (IV), intramuscular(IM), subcutaneous(SUBQ), & intranasal
- Onset of action
  - IV: 2 minutes
  - IM, SUBQ: 2 to 5 minutes
  - Intranasal: 8 to 13 minutes
- Duration of action
  - 30 to 120 minutes depending on route
  - IV has a shorter duration of action than IM
    - Note: repeated doses are usually needed
- Dosing
  - IV, IM, SUBQ: Initial: 0.4 to 2 mg; may need to repeat doses every 2 to 3 minutes
- Adverse reactions:
  - Flushing, labile blood pressure, tachycardia, diaphoresis



Narcan Nasal Spray [prescribing information]. *Emergent Devices.* 2020.
Naloxone HCL Inj [prescribing information]. *AuroMedics Pharma.* 2019.

Who is Prescribed Naloxone?

- Title XXXII, Ch. 456.44 of Florida Pharmacy Law:
  - For the treatment of pain related to a traumatic injury
    - ISS of ≥9, a prescriber who prescribes a schedule II controlled substance **must concurrently prescribe an emergency opioid antagonist**, as defined in s. 381.887

- Patients who are considered to be "high risk" for opioid overdose:

History of substance abuse	Opioid doses > 50 MME/d	Benzodiazepine use	Sleep apnea
Pregnancy	Renal/hepatic disease	> 65 years old	Mental health comorbidities

Dreiling J. The Validation of Controlled Drug Prescriptions in Florida. 2020.

Who is Prescribed Naloxone?

2019 Florida statutes, Title XXIX, chapter 381.887:

> "An authorized health care practitioner may prescribe and dispense an emergency opioid antagonist to a patient or caregiver for use in accordance with this section, and **pharmacists may dispense an emergency opioid antagonist pursuant to such a prescription or pursuant to a non-patient-specific standing order for an auto-injection delivery system or intranasal application delivery system**, which must be appropriately labeled with instructions for use"

Dreiling J. The Validation of Controlled Drug Prescriptions in Florida. 2020.

Recognizing an Overdose

High	Overdosing
• Constricted pupils • Muscles are flaccid • Incoherence • Slurred speech • Disoriented • Respond to outside stimulus	• Pinpoint pupils • Loss of consciousness • Awake but unable to speak • Skin/nail/lip color changes • Unresponsive

Schiller EY et al. *Opioid Overdose*. 2019.

Responding to an Overdose

- Call 911
- Administer naloxone
- Perform CPR
- Stay until help arrives

Dosage Forms

Narcan® Nasal Spray	Naloxone for injection
• 4 mg/0.1 mL • Price: $75.00 • No prescription required 	• 0.4 mg/1 mL • Price: $5.27 – $23.72 • First responders no prescription needed 

Narcan Nasal Spray [prescribing information]. *Emergent Devices.* 2020.
Naloxone HCL Inj [prescribing information]. *AuroMedics Pharma.* 2019.

Treatment Resources for Substance Abuse

Required By Florida Law

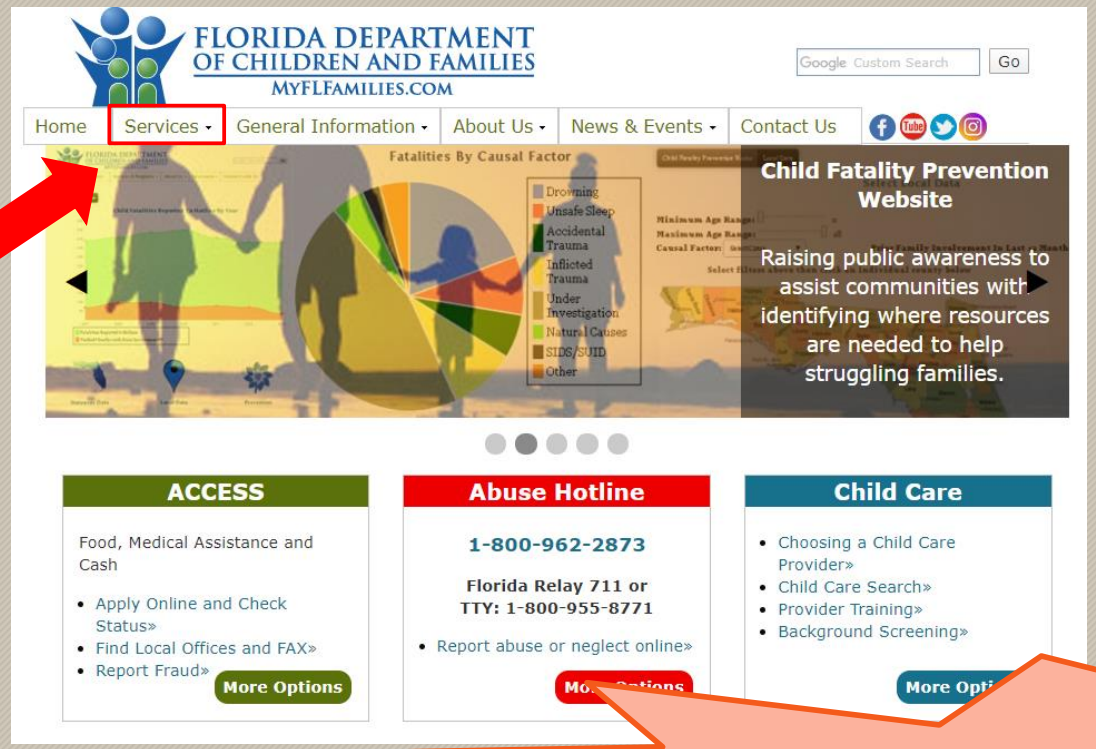
Controlled Substance House Bill 451

- The Florida Department of Health requires all health care providers to include non-opioid alternatives
  - Exception: Provision of emergency services of care or before providing anesthesia

- Health care practitioners must:
  - Inform the patient of available non-opioid alternatives
  - Discuss the advantages and disadvantages of non-opioid alternatives
  - Provide the patient with educational pamphlet
  - Document the non-opioid alternatives considered in the patient's record

House Bill No. 451: Chapter 2019-123.

Treatment Resources

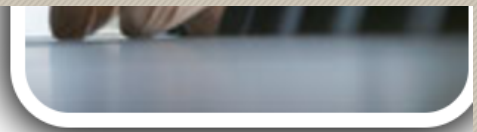


www.myflfamilies.com/service-programs/samh

Substance Abuse and Mental Health (SAMH). Florida Departm ildren and Families.

Treatment Resources

Find Local Services By County



If you or someone you know is in need of substance abuse and/or mental health services, our local managing entities can help you locate available programs. Please choose your county from the drop-down list below for the managing entity contact in your area.

County: Dade ▼ View local provider

Substance Abuse & Mental Health

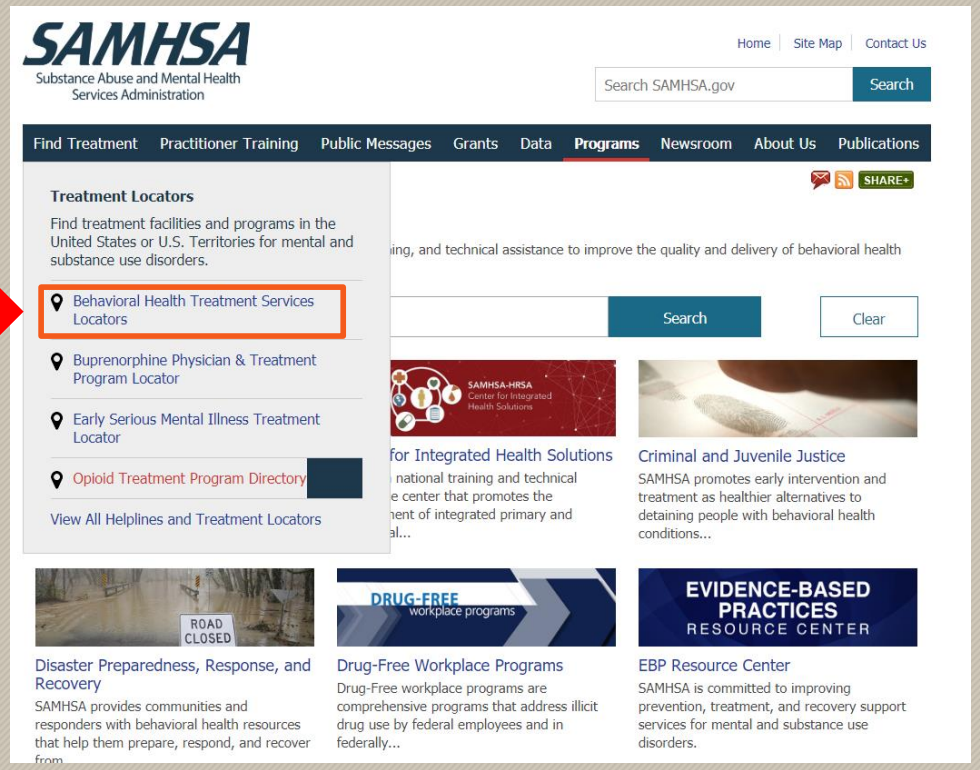
Your Local Provider of Services

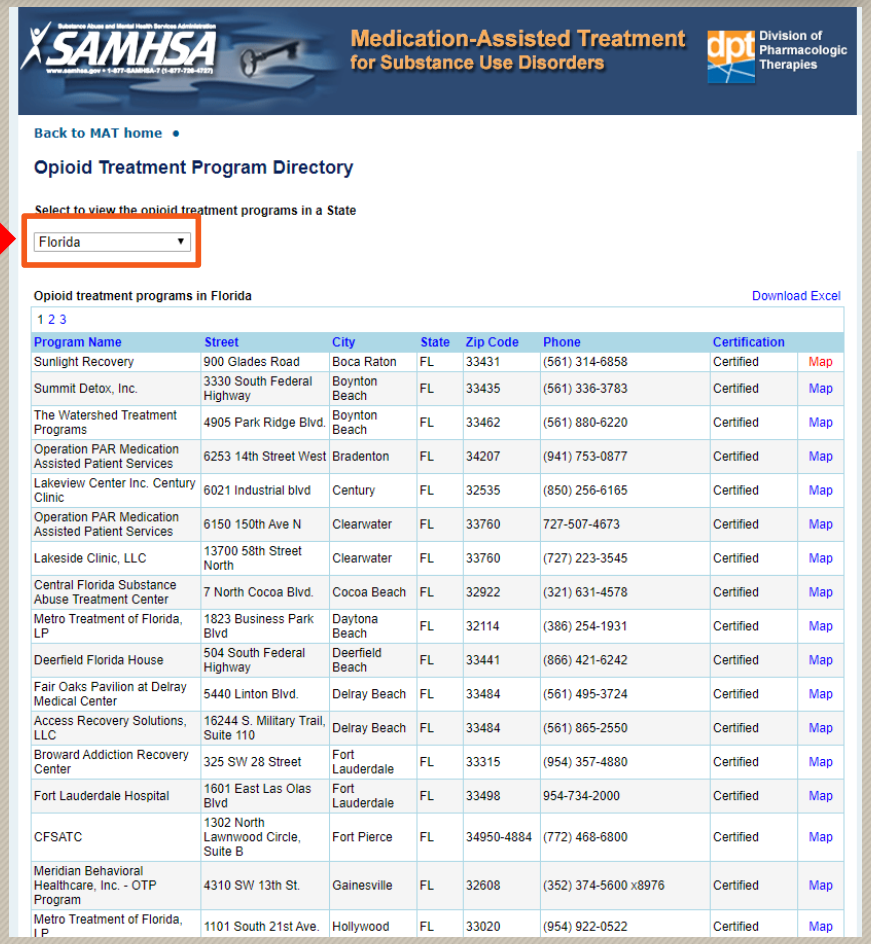
South Florida Behavioral Health Network

Telephone: 888-248-3111

Substance Abuse and Mental Health (SAMH). Florida Department of Children and Families.

Treatment Resources





Program Name	Street	City	State	Zip Code	Phone	Certification	
Sunlight Recovery	900 Glades Road	Boca Raton	FL	33431	(561) 314-6858	Certified	Map
Summit Detox, Inc.	3330 South Federal Highway	Boynton Beach	FL	33435	(561) 336-3783	Certified	Map
The Watershed Treatment Programs	4905 Park Ridge Blvd.	Boynton Beach	FL	33462	(561) 880-6220	Certified	Map
Operation PAR Medication Assisted Patient Services	6253 14th Street West	Bradenton	FL	34207	(941) 753-0877	Certified	Map
Lakeview Center Inc. Century Clinic	6021 Industrial blvd	Century	FL	32535	(850) 256-6165	Certified	Map
Operation PAR Medication Assisted Patient Services	6150 150th Ave N	Clearwater	FL	33760	727-507-4673	Certified	Map
Lakeside Clinic, LLC	13700 58th Street North	Clearwater	FL	33760	(727) 223-3545	Certified	Map
Central Florida Substance Abuse Treatment Center	7 North Cocoa Blvd.	Cocoa Beach	FL	32922	(321) 631-4578	Certified	Map
Metro Treatment of Florida, LP	1823 Business Park Blvd	Daytona Beach	FL	32114	(386) 254-1931	Certified	Map
Deerfield Florida House	504 South Federal Highway	Deerfield Beach	FL	33441	(866) 421-6242	Certified	Map
Fair Oaks Pavilion at Delray Medical Center	5440 Linton Blvd.	Delray Beach	FL	33484	(561) 495-3724	Certified	Map
Access Recovery Solutions, LLC	16244 S. Military Trail, Suite 110	Delray Beach	FL	33484	(561) 865-2550	Certified	Map
Broward Addiction Recovery Center	325 SW 28 Street	Fort Lauderdale	FL	33315	(954) 357-4880	Certified	Map
Fort Lauderdale Hospital	1601 East Las Olas Blvd	Fort Lauderdale	FL	33498	954-734-2000	Certified	Map
CFSATC	1302 North Lawnwood Circle, Suite B	Fort Pierce	FL	34950-4884	(772) 468-6800	Certified	Map
Meridian Behavioral Healthcare, Inc. - OTP Program	4310 SW 13th St.	Gainesville	FL	32608	(352) 374-5600 x8976	Certified	Map
Metro Treatment of Florida, LP	1101 South 21st Ave.	Hollywood	FL	33020	(954) 922-0522	Certified	Map

Substance Abuse and Mental Health (SAMH). Florida Department of Children and Families.

Take Home Points

- Pain is measured depending on perception
- Pain indication is required to comply with state laws and regulations
  - Day-supply with correlation to indication of pain type
    - “ACUTE PAIN EXCEPTION”: 7 day limit
    - “NONACUTE PAIN”: > 7 day
- Pharmacist should take all necessary steps when validating an Rx

Take Home Points

- Provide optimal patient education on the administration, adverse effects, drug interactions, and the appropriate storage and disposal during initial counseling with a new patient or new opioid agent
- Consult PDMP for each new prescription dispensed
- Naloxone should be dispensed to any patient (caregiver) who could possibly be at a potential high risk for misuse or abuse
- Pharmacist should take initiatives to provide available treatment resources for patients with suspected dependence

Let's Test Ourselves

1. T/F: Pain can be objectively measured.
   A. False

2. T/F: When a schedule II controlled substance for opioid is prescribed for pain with an "ACUTE PAIN EXCEPTION," the pharmacist may dispense a up to a 10 day supply.
   A. False

3. T/F: A schedule II opioid must be either written on a counterfeit-proof prescription pad made by a vendor approved by Department of Health or electronically prescribed.
   A. True

Thank You!

References

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