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Florida Validation of Controlled Substances Continuing Education – FL APPROVED

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We live in an "Opioid Crisis" where someone dies approximately every 7 minutes from drug overdose. So just how do we end this "Opioid Crisis", or at least, how do we as healthcare professionals contribute to the progress of moving society in the right direction? In this monograph, we will review overall pain management etiology; risk reduction strategies (psychological and opioid risk screenings, urine drug monitoring, etc.), numerous non-pharmacological and pharmacological treatment options (with particular attention on opioid medications), opioid overdose reversal treatments; along with not only how to identify drug seeking and diversion behaviors, but possible actions to take when the behaviors are suspected. The Florida PDMP known as E-FORCSE will of course also be discussed for its expected impact on adherence and diversion. We will also review Federal and Florida specific controlled substance laws and trends such as controlled substance classifications, prescribing authorities, the 2018 Florida Statue Update, the naloxone standing order, and DEA Red Flags. Unlike opioids, this monograph is intended to open one's eyes, elevate blood pressure and/or heart rate, and increase cognition!

Learning Objectives

Pharmacist

1 Recognize how to ensure access to controlled substances for all patients with a valid prescription, while also assessing prescriptions for

4 Recognize proper storage and disposal protocols for controlled substances.

5 Recall protocols for addressing and resolving problems

7 Identify the most clinically important patient counseling considerations for patients utilizing opioid medications.

appropriate therapeutic value and detecting prescriptions not based on legitimate medical purpose.

2 Recall the legal expectations and intentions of utilizing the Florida Prescription Drug Monitoring Program's Database (E-FORCSE).

3 Recall the laws and rules related to the prescribing and dispensing of controlled substances in Florida.

recognized during the drug utilization review including drug/drug interactions, side effects, high dose and low dose guidelines, and other therapeutic concerns.

6 Recognize the relevance of the Florida standing order for naloxone for the emergency treatment of opioid overdose.

8 Recall available treatment resources for opioid physical dependence, addiction, misuse, or abuse.

9 Recall pain management non-pharmacological and pharmacological (both opioid and non-opioid) treatment options and respective dosage and patient counseling considerations.

Accreditation

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Target Audience

Pharmacists

Universal Activity Number

Pharmacist
0798-0000-20-216-H08-P

Credit Hours

2.0 Hour

Activity Type

Knowledge-Based

CE Broker Tracking Number

20- 709367

Activity Release Date

November 1, 2020

Activity Offline Date

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ACPE Expiration Date

November 2, 2023

Educational Support Provided By

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Florida Validation of Controlled Substances Continuing Education

https://www.flrules.org/gateway/sysMessage.asp?ENO=E004

All Florida licensed pharmacists must complete a Board-approved 2-hour continuing education course on the Validation and Counseling of Prescriptions for Controlled Substances and Opioids during every pharmacist license renewal period. The course may count towards the mandatory 30 hours of continuing education required for licensure renewal and must include the following:

- *a) Ensuring access to controlled substances for all patients with a valid prescription;*
- *b) Use of the Prescription Drug Monitoring Program's Database;*
- *c) Assessment of prescriptions for appropriate therapeutic value;*
- *d) Detection of prescriptions not based on a legitimate medical purpose;*
- *e) The laws and rules related to the prescribing and dispensing of controlled substances.*
- *f) Proper patient storage and disposal of controlled substances;*
- *g) Protocols for addressing and resolving problems recognized during the drug utilization review to include but not limited to the following:*
    - *a. Drug/drug interactions;*
    - *b. Side effects;*
    - *c. High dose/low dose guidelines; and*
- *h) Education on the provision of section 381.887, F.S., Emergency treatment for suspected opioid overdoses and on the State Surgeon General's Statewide Standing Order for Naloxone (eff. May 19, 2017) for as long as the Order is valid and effective.*
- *i) Pharmacist initiated counseling of patients with opioid prescriptions;*

Available treatment resources for opioid physical dependence, addiction, misuse, or abuse.

The laws and Rules Related to the Prescribing and Dispensing of Controlled Substances

- Controlled Substance Act of 1970 [United States Code Title 21 (Food & Drugs), Chapter 13 (Drug Abuse Prevention & Control)]: https://www.deadiversion.usdoj.gov/21cfr/21usc/
- Florida Statue [Title 46 (Crimes) Chapter 893 (Drug Abuse Prevention & Control)]: http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0800-0899/0893/0893.html
- Florida House Bill 21 of 2018 (1st Major Update Since 2011): https://www.flmedical.org/Florida/Florida_Public/Docs/FMA-Opioid-HB21.pdf

*These 3 references utilized to provide bottom-line pharmacy practice effort details herein unless otherwise noted.

Prescribing & Dispensing Prescription Medications

Overall, a prescription for a controlled substance must always be dated and manually signed on the date when issued. The prescription must include the patient's full name & address, the practitioner's full name, address, and DEA registration number, along with the drug name, strength, dosage form, quantity prescribed, directions for use, and the number of refills (if any).

Florida Statute requires a health care practitioner licensed to prescribe medicinal drugs, including controlled substances, who *maintains a system of electronic health records*, or who prescribes medicinal drugs as an owner, an employee, or a contractor of a licensed health care facility or practice that maintains such a system and who is prescribing in his or her capacity as such an owner, an employee, or a contractor, may *only electronically transmit prescriptions* for such drugs.

A health care practitioner who maintains a system of electronic health records and is unable to electronically transmit prescriptions for medicinal drugs may request a one year waiver from the electronic prescribing requirement under certain circumstances at: https://floridasnursing.gov/forms/Electronic-Prescribing-Waiver.pdf.

Conversely, if a healthcare practitioner does not utilize an electronic health record, a hardcopy (paper) prescription for a controlled substance must be written in ink or indelible pencil or typewritten and must be manually signed by the practitioner on the actual date of issuance. A practitioner's delegate (e.g. nurse practitioner, secretary, etc.) may be designated by the practitioner to prepare prescriptions ahead of time with everything except the practitioner's actual signature (and not the reverse of a practitioner signing an empty prescription pad for a delegate to then complete at a later date). The signing practitioner is responsible for ensuring that the prescription conforms to all requirements of the federal and state law and regulations.

When a pharmacist receives an electronic, hardcopy (paper), or even verbal prescription with anything raising suspicion that it was also electronically submitted to another pharmacy, the pharmacist must communicate with the other pharmacy to ensure that there was not an actual dispensing, and voiding the prescription if so.

C-II Prescriptions cannot be refilled. However, a prescriber may issue multiple prescriptions for the same C-II medication, as long as all signed and dated on the same date of issue, with the respective future-use prescriptions having a statement of "do not fill until date" included within the prescription (as long as still within the prescriber's scope of practice and there is no risk of diversion, misuse, or abuse for the patient).

If a prescriber is not able to efficiently electronically send a C-II prescription to a pharmacy, a prescriber may transmit a C-II prescription to the pharmacy via facsimile (i.e. fax) to expedite the filing for the prescription. The original hardcopy paper C-II prescription must be presented to the pharmacist for review *prior* to the actual dispensing of the controlled substance.

In an emergency, a practitioner may call in a C-II prescription to the pharmacy, allowing the pharmacist to dispense the prescription provided that the quantity is limited to an amount adequate to treat the patient only during the emergency period. The prescriber must provide a signed written prescription to the pharmacist within 7 calendar days. The pharmacist must notify the DEA if the prescription is not received in that timeframe. Of note, during the COVID-19 state of emergency, the time frame was extended from 7 calendar days to 14 calendar days (DEA COVID Prescribing).

Every law typically has noted exceptions, as the legislation involving C-II faxed prescriptions does as well. A faxed C-II prescription may serve as the original prescription in any of the following scenarios where the C-II medication is for:

- Compounding for direct patient administration by parenteral, intravenous, intramuscular, subcutaneous, or intraspinal infusion
- A resident of a long-term care (LTC) facility
- A patient enrolled in hospice certified and/or paid for by Medicare or licensed by the state, and the practitioner will indicate on the prescription that it is for a patient in hospice

C-III, C-IV, and C-V prescriptions may be transmitted to a pharmacy via hardcopy (paper), verbally, or by fax, and may include authorized refills. C-III and C-IV prescriptions may only be refilled up to 5 times within 6 months of the date the prescription was signed by the prescriber. A pharmacist may not dispense more than a 30-day supply of a C-III medication upon an oral prescription in Florida.

Ensuring Access to Controlled Substances For All Patients with a Valid Prescription

A valid prescription involves both a practitioner-patient relationship and a legitimate medical purpose. Both a prescriber and a pharmacist have an individual corresponding responsibility to ensure the validity of a prescription, not one or the other, both. A prescriber issuing an invalid prescription and a dispenser filling an invalid prescription will both be subject to the penalties for violating the federal controlled substance act, which is recognized as a felony.

Florida statue defines the process of validating a prescription as the process implemented by a pharmacist to determine that the prescription was issued for a legitimate medical purpose. Concern sometimes arises for multiple reasons which we'll discuss shortly, but not every suspicion results in a prescription absolutely not being filled. However, when suspicion does arise, a pharmacist shall attempt to resolve any validity concerns to ensure the validity of a

prescription utilizing one's professional judgement, based on respective knowledge, training, and experience. In addition to reviewing the validity of a prescription for a legitimate medical purpose, a pharmacist must also confirm that a prescription is in the usual course of professional practice of the prescriber. Once having confirmed the both the validity of a prescription and the usual course of professional practice of the prescriber, a pharmacist should not fear disciplinary action from the Florida Board of Pharmacy or any other regulatory or enforcement agency.

In order to validate a controlled substance prescription, a pharmacist must first validate prescriber's DEA registration number. All DEA registration numbers are a combination of two letters followed by seven numbers according to the following rules:

TWO LETTERS

1. First letter: Type of prescriber
    - A/B/F/G: Doctors of Medicine, Osteopathy, Dentistry, or Veterinary Medicine
    - M: Midlevel practitioners (i.e. nurse practitioner, physician Assistant, & midwives)
    - X: Medication Assisted Treatment Provider Waiver (DATA 2000)
2. Second letter: First letter of the practitioner's last name

SEVEN NUMBERS

1. Add the odd numbers (1st, 3rd, & 5th)
2. Add the even numbers (2nd, 4th, & 6th)
3. Double the even number sum, and add to the odd number sum
4. The last digit of the overall sum is the last DEA Number Digit

DEA Number Example Case

AP1234561

- Dr. **P**ayne, Pain Management Specialist MD **(A)**
- Odd Numbers: 1 + 3 + 5 = 9
- Even Number: 2 + 4 + 6 = 12
- Combination: 9 + 12 = 2**1**

When validating a prescription, a pharmacist must always keep the following points in mind:

- No one shall interfere with a pharmacist exercising independent professional judgment
- A pharmacist shall ensure that communication with a patient is not overheard by others
- If at any time a pharmacist determines with professional judgment that concerns on the validity of a prescription cannot be resolved, the pharmacist shall refuse to fill (dispense)

Before a pharmacist refuses to fill a prescription based solely upon a concern with the validity of the prescription, a pharmacist must attempt to resolve any concerns with the validity of the prescription by performing the following:

1. Initiate communication with a patient (or representative) to acquire information relevant to the prescription's validity
2. Initiate communication with the prescriber (or agent) to acquire information relevant to the prescription's validity
3. In lieu of either 1 or 2, but not both, the pharmacist may elect to access the Prescription Drug Monitoring Program Database (PDMP) to acquire information relevant to the prescription's validity (In other words, a pharmacist must communicate with a patient and prescriber, or only a patient and review the PDMP, or only a prescriber and review the PDMP)

If a patient refuses to cooperate with a pharmacist attempting to acquire information relevant to the prescription's validity, the minimum standards for refusing to fill a prescription will not be required.

Detection of Prescriptions Not Based on a Legitimate Medical Purpose

Controlled Substance Classifications

Knowing the respective controlled substance classes of opioid medications can be helpful for healthcare professionals to understand so as to ascertain what professionals can prescribe medications from various controlled substance classes based on state laws. The C-IV, or C4, class contains tramadol and pentazocine/naloxone products. The C-III, or C3, class contains acetaminophen/codeine and dihydrocodeine products along with buprenorphine products specifically utilized in pain management (As per DATA2000, not for substance-use disorder, or addiction). The C-II, or C2, class contains tapentadol, morphine, hydrocodone, hydromorphone, oxycodone, oxymorphone, levorphanol, methadone, and fentanyl. The C-I class includes diacetylmorphine (i.e. Heroin).

Healthcare professionals encounter situations that balance preventing drug diversion and ensuring appropriate patient care daily. The US Drug Enforcement Agency (DEA) developed the below "red flags" for prescribers and dispensers as a resource of what to be on the lookout for as healthcare professionals in those precarious situations. Reporting Prescription Drug Abuse to the DEA can be accomplished via telephone by calling: 1-877-RX-ABUSE. (DEA Red Flags).

Prescriber

- Cash only patients and/or no acceptance of worker's compensation or private insurance
- Prescribing of the same combination of highly-abused drugs
- Prescribing the same, typically high, quantities of pain drugs to most or every patient
- High number of prescriptions issued per day
- Out-of-area patient population

Dispenser

- Dispensing a high percentage controlled to non-controlled drugs
- Dispensing high volumes of controlled substances generally
- Dispensing the same drugs & quantities prescribed by the same prescriber
- Dispensing to out-of-area or out-of-state patients
- Dispensing to multiple patients with the same last name or address
- Sequential prescription #s for highly diverted drugs from the same prescriber
- Dispensing for patients of controlled substances from multiple practitioners
- Dispensing for patients seeking early prescription fills

In addition to the prescriber and dispenser DEA "Red Flags", there are patient behaviors that rise prescription validity concerns as well such as:

- Patient shows physical symptoms of controlled substance abuse, such as needle tracks, or scars on the neck, arms, feet, or ankle
- Patient's statements and conduct suggest abuse of controlled substances, such as appearing sedated, confused, intoxicated, or exhibiting withdrawal symptoms
- Patient obtains same or similar controlled substance prescriptions from multiple prescribers without respective prescribers being aware of the other prescriptions
- Patient obtains same or similar controlled substance prescriptions from multiple pharmacies without respective pharmacies being aware of the other prescriptions
- Patient presents several prescriptions written for controlled and non-controlled substances, but only wants the controlled substance medication(s) dispensed (e.g. prescription opioid and antibiotic prescriptions presented to pharmacy, but patient requests to only fill/dispense the opioid)
- Patient has a history of concerning statements and actions when filling controlled substance prescriptions

Conversely, there are stereotypical situations that provide a certain level of professional judgement comfort to a pharmacist when presented with a controlled substance prescription, particularly for an opioid medication. However, a pharmacist should not proceed with a false premonition based on any stereotypical situation. These are examples of such situations:

- Patient has consistently received non-controlled substance prescriptions for the past 6 months
- Patient is not paying out of pocket (i.e. not paying with cash, rather utilizing insurance coverage)
- Patient has a consistent recent (or overall) history of "on-time' prescriptions fills and refills, with no "fill/refill too soon" concerns
- Prescription directions are consistent with FDA-approved labeling (e.g. indication, dosage interval, etc.)

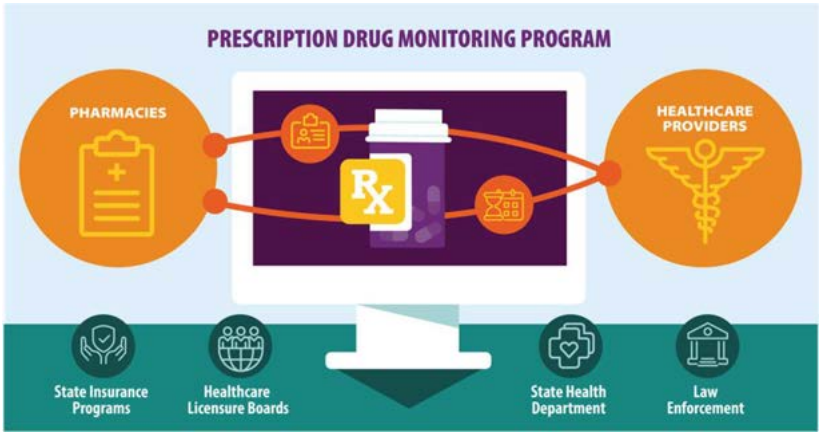
A dispensing pharmacist must constantly be aware of the possibility of encountering forged or altered prescriptions (i.e. fraudulent prescriptions), with a handful of examples including:

- Prescriber Paper prescription pads stolen from prescribers' offices (Eliminated by e-prescribing)
- Scratched-out or added-on writing on a hardcopy (paper) prescription
- Non-uniform ink color on a hardcopy (paper) prescription
- Printed paper prescription pads mirroring those of an actual prescriber with incorrect contact information
- Verbal prescriptions left on a pharmacy's voicemail system for prescribers
- A Prescription looking or sounding "too good to be true" (e.g. legible hand writing or verbally stating prescription information in a perfect order on a prescription pad)
- Hardcopy (paper) prescription appears to be a photocopy
- Directions are written on a hardcopy (paper) prescription with not abbreviations

Best practices of pharmacists to prevent prescription fraud include:

- Know the prescriber and respective signature
- Have local prescribers' DEA registration numbers easily accessible in the pharmacy
- Verify a government ID of every patient, every time
- Review the state PDMP (E-FORCSE) when filling every prescription

Use of the Prescription Drug Monitoring Program's Database



Prescription drug monitoring programs (PDMPs) are useful tools in monitoring medication adherence and avoiding drug abuse and diversion. PDMPS are not the panacea answer to preventing drug abuse and diversion, but are one major tool amongst others that needs to be universally and consistently utilized to reach its full potential. Yet with participation by prescribers and dispensers typically being voluntary, usage has historically been well below half of healthcare professionals across the country (Brandeis University, October 2014). Practical reasons exist for the barrier(s) to universal implementation such as electronic integration into prescribing and dispensing software programs. Thankfully, there are grassroots efforts across the country directly addressing the concern of integration. Additionally, there exists a program that aesthetically and clinically conveys the respective mundane and repetitive information universally within state PDMPs to show a color-coated score that simplifies the data analysis for a prescriber and/or dispenser (NarxCheck, n.d.). The day will hopefully come when both prescribing and dispensing computer software and electronic healthcare records automatically review a nationally integrated PDMP, but in the meantime, healthcare professionals have a moral responsibility to do no harm, which can be aided with the consistent review of a respective state's PDMP.

The Florida Prescription Drug Monitoring Program, known as E-FORCSE® (Electronic-Florida Online Reporting of Controlled Substance Evaluation Program), was created by the 2009 Florida Legislature in an initiative to encourage safer prescribing of controlled substances and to reduce drug abuse and diversion within the state of Florida. (Florida Health E-FORCSE Home Page)

Prescribers and dispensers are required to review E-FORCSE before prescribing and dispensing respectively for every new prescription (even if a renewal from a previous medication). Dispensers of controlled substances are required to report to E-FORCSE ***each*** time a controlled substance in schedules II, III, IV, and V are dispensed to a patient, as soon thereafter as possible but no later than close of business the day after the prescription is dispensed, unless one or more of the following statutory exemptions applies:

- Nonopioid Schedule V
- Administering the controlled substance directly to a patient
- Hospital, emergency room, nursing home, ambulatory surgical center, hospice, or intermediate care facility for the developmentally disabled
- Administering or dispensing to a patient in the Department of Corrections
- Administering or dispensing to a person under the age of 16
- When dispensing a one time, 72-hour emergency resupply of a controlled substance
- System is not operational or requestor has technological or electrical failure
- When a state-declared or nationally declared disaster suspends reporting

The initial offense penalty for not reviewing E-FORCSE is being subject to a non-disciplinary citation for the initial offense. The subsequent offense penalty for not reviewing E-FORCSE is disciplinary action against the health care practitioner's license. Even a "zero dispensing" activity needs to be reported to E-FORCSE by the close of the next business day. The penalty for not reporting controlled substance dispensing to E-FORCSE is a first-degree misdemeanor.

Controlled substance dispensing information that must be reported to E-FORCSE includes:

- Prescriber
    - Name, DEA Registration Number, NPI Number, & Date of Prescription
- Pharmacy
    - Full Name, Address, DEA Registration #, & Florida Pharmacy Permit Number
- Patient
    - Full name, address, telephone number, & Date of Birth
    - Name of Individual picking up prescription & Type/Issuer of Identification
- Prescription
    - Date filled, Payment Method, & Whether an Initial Prescription or Refill
- Medication
    - Name, Strength, Quantity, & NDC Number

Exemptions for overall reporting to E-FORCSE are attained at: https://forms.office.com/Pages/ResponsePage.aspx?id=gI_NKEQ8J0uBoM0rA6MbjTnNU-2qGcdHpmNOMX7FE7hUNloxQ01PWEkwWUFESEZBNFRWU1FXV1lPNyQlQCN0PWcu

The Florida Drug-Related Outcomes Surveillance and Tracking System (FROST), which provides updated dynamic data reporting is available at: https://public.tableau.com/views/FloridaDrug-RelatedOutcomesSurveillanceandTrackingSystem/Home?:embed=y&:%20display_count=no&:showVizHome=no.

The Florida Prescription Drug Monitoring Program (PDMP) known as E-FORCSE (Electronic-Florida Online Reporting of Controlled Substance Evaluation Program is available at:
https://florida.pmpaware.net/login

2018-2019 Florida Prescription Drug Monitoring Program Annual Report (FL PDMP Report)

1. Increase in Enrollment and Utilization
    - Since the 2018 House Bill 21 took effect mandating prescribers and dispensers to review E-FORCSE, there has been a 43% and 100% increase in dispenser and prescriber registrations, respectively. As of June 2019, dispensers and prescribers made over 50 million all-time PDMP queries.

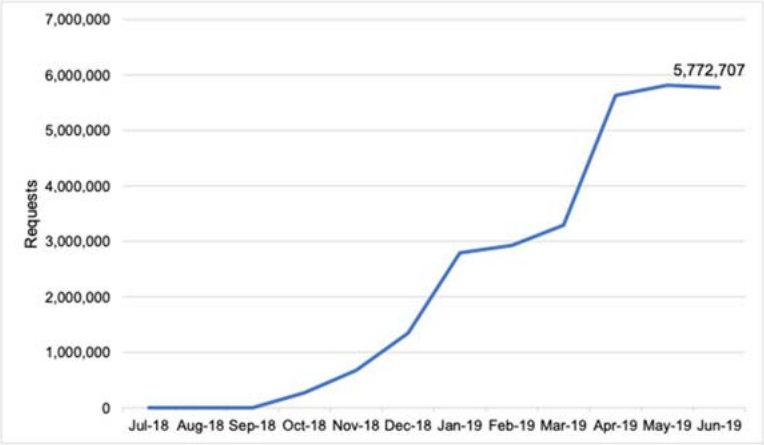


Figure 5. Queries requested through Electronic Health Recordkeeping System Integrations, July 2018 – June 2019.

2. Reduction of Opioid Prescriptions Dispensed
    - From 2018 to 2019, there was a 14% decrease in the number of C-II through C-IV opioid prescriptions dispensed to patients, and a 53% decrease in the average daily morphine milligram equivalents (MMEs) per prescription.

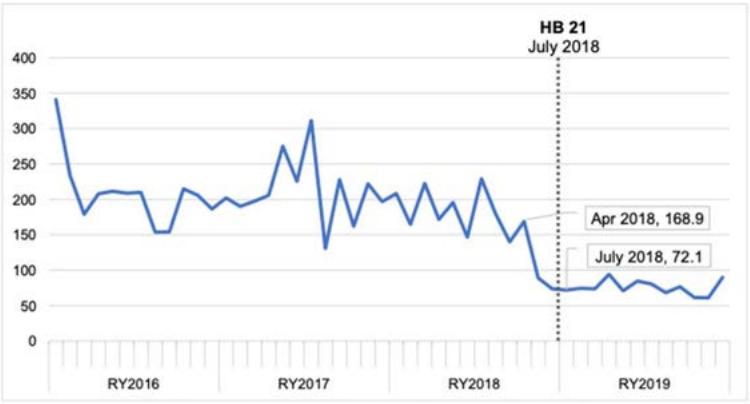
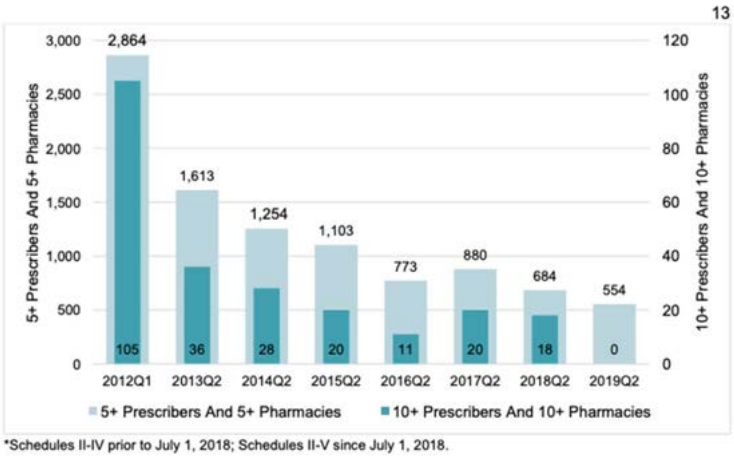


Figure 4. Average daily Morphine Milligram Equivalent (MME) per schedule II opioid prescription.

3. Reduction in Multiple Provider Episodes (MPE)
    - Since implementing the monitoring, analysis, and proactive notification of MPEs in 2009, Florida has seen an 80% reduction in the number of individuals having MPEs.



*Schedules II-IV prior to July 1, 2018; Schedules II-V since July 1, 2018.

Figure 1. Number of individuals obtaining controlled substance prescriptions* from 5/10 or more prescribers and 5/10 or more dispensers within a 90-day period, January 2012 – June 2019.

4. Increase in Electronic Health Recordkeeping Integration
    - 455 entities' electronic health recordkeeping (EHR) systems across the states
5. Increase in Data Sharing
    - As of the end of 2019, there were 16 states sharing PDMP data the Florida.

Once a Fraudulent Prescription, Drug Seeking, or Drug Diversion is Suspected

Working with healthcare professionals and other professionals concerning patients suspected of drug seeking behavior and diversion is often not something that many are comfortable pursuing. As with any other clinical or administrative decision, if one leaves out personal or judgmental biases, and proceeds with a calm, collected, knowledgeable, and well researched approach, the entire endeavor will lead itself to a path of success.

If uncertainty exists regarding the nature of the unintended result of a risk reduction action such as a PDMP review, a urine drug screen/test, or a random/scheduled pill count, the healthcare professional(s) may consider arranging for an in-person meeting with the identified patient to have an open conversation to clarify the patient's actions and concerns. Prior to initiating that important conversation, a healthcare professional should research all aspects of the respective patient related scenario including opening communications with any other respective healthcare professionals involved directly or indirectly with the respective patient case. If abuse or diversion is confirmed, treatment can continue with alternative therapies (i.e. non-controlled substances), the patient should be referred to a substance-use disorder (addiction) specialist/program or an entity that can facilitate that connection, and law enforcement should be contacted if concern for the safety of others exists.

Available Treatment Resources for Opioid Physical Dependence, Addiction, Misuse, or Abuse

- SAMHSA'S National Helpline: 1-800-662-HELP (4357)
- SAMHSA Opioid Information: www.samhsa.gov/atod/opioids
- Narcotics Anonymous: 818-773-9999
- Nar-Anon (Family & Friends): 1-800-477-6291
- Drug Enforcement Administration (DEA): www.dea.gov
- DEA's Operation Prevention: www.operationprevention.com
- DEA's Diversion Control Program: www.DEAdiversion.usdoj.gov
- Food & Drug Administration (FDA): www.FDA.gov
- National Association of Boards of Pharmacy (NABP): www.nabp.net
- National Association of State Controlled Substances Authorities (NASCSA): www.nascsa.org
- Office of National Drug Control Policy (ONDCP): www.whitehousedrugpolicy.gov
- HHS (Health & Human Services) Opioid Information: www.hhs.gov/opioids
- Federation of State Medical Boards: www.FSMB.org
- Florida Board of Pharmacy: www.floridaspharmacy.gov

Respect or all those directly or indirectly involved in the specific patient case should be upheld always, while also ensuring both a procession within mandated laws and an appropriate level of patient care. As goes the umbrella healthcare professionals' oath to "do no harm."

General Epidemiology of Pain

Across the globe, more than 1.5 billion people suffer from chronic pain. In the United States, chronic pain affects approximately 100 million people, which is more than those affected by diabetes, heart disease, and cancer combined, with 26, 16, and 12 million people respectively affected. Approximately 75 million Americans, one in every four, have suffered from pain that lasts longer than 24 hours and millions more suffer from acute pain. Chronic pain is the most common cause of long-term disability (Painmed.org, 2017).

Approximately 2 million Americans live with prescription opioid dependence or abuse opioids (SAMSHA, 2013). Studies have shown a strong and consistent linear relationship between the number of opioids sold and distributed (i.e. prescribed and dispensed) with morbidity and mortality associated with these chemicals (Paulozzi LJ B. D., 2006). Of those who began their opioid abuse in 2000s, 75% stated that their first regular opioid was a prescription opioid (TJ Cicero, 2014), although there were no specifics provided as to the actual respective acquisition of those prescription opioids being legitimate or illicit. In 2017, there were 70,237 drug overdose deaths in the United States. Therefore, approximately 192 Americans die every day due to drug overdose, equating to one American dying approximately every 7 minutes. More specifically, each and every day in the United States, approximately 120 people die from an opioid overdose, one death every 12 minutes (Hedegaard H, 2018). Additionally, in our country a baby is born dependent on opioids approximately every 25 minutes (Tolia, 2015). These staggering statistics demonstrate how bad this situation is, and why it has been generally regarded as a national epidemic or crisis (Paulozzi LJ J. C., 2011) (Jones CM, 2013).

Pain Anatomy, Physiology, & Terminology

Nociception is the sensory nervous system's response to harmful stimuli. The general cascade of nociception begins with transduction where sensory is translated into electricity, as when a radio transduces radio waves into sound waves. The next part of nociception is conduction where the pain sensory moves from the peripheral nervous system into the central nervous system, as when heat from a hot cooking pan is conducted from the pan to a metal spoon touching the

inside of the pan. Next is transmission where electricity is converted into neurotransmitters such as glutamate, norepinephrine, or dopamine, as when television signals are transmitted over open air to a receiver television. Next is perception where the neurotransmitters elicit a sensory experience within the thalamus of the brain, as is with one's perception being different on any given topic such as a glass being half full or half empty. Finally, and sometimes included within the perception phase, is modulation where the brain adjusts pain sensory via the descending pathways (away from the brain) within the nervous system (all previous phases were in the ascending pathway, or to the brain), like one playing a trump card in pinochle or a joker card in poker.

Pain is typically understood to involve both the nervous system and the musculoskeletal system, yet it transcends to all the systems of the body such as the endocrine, cutaneous, cardiovascular, and immunological systems. Within the endocrine system, pain related neurohormones are released from various points in the body such as the hypothalamus, pituitary gland, thyroid (thyroxine), adrenal glands (cortisol, DHEA, etc.), and the ovaries (estrogen/progesterone) or testes (testosterone). Each of these neurohormones plays a vital role in communicating with other systems of the body to facilitate responses to the experience of pain. Upon injury to the skin, the cutaneous system has activated skin receptors releasing vasodilators which affect the cardiovascular system (veins/arteries) and stimulate the immunological response of releasing cytokines and other mediators to ultimately stimulate nociceptors within the nervous system. The overall encompassing idea is that pain involves all the systems of the body.

Analgesia is derived from the Greek language meaning "without pain" or lack of pain. Anesthesia means lack of sensation. Chronic pain is defined as experiencing the sensation of pain for a period longer than the expected time to heal, but is commonly referred to as pain lasting greater than 3 months, although we will review how the Florida Statue conversely defines acute pain in a moment. Allodynia is a painful response to a normally unpainful stimulus. Hyperalgesia is an extremely painful response to a normally minimal painful stimulus. Tolerance develops when a higher dose is needed for the same response. Dependence develops when the body exhibits withdrawal symptoms upon discontinuation of the substance. Substance-use disorder or addiction is a medical condition where the brain exhibits changes relating to a craving for a substance.

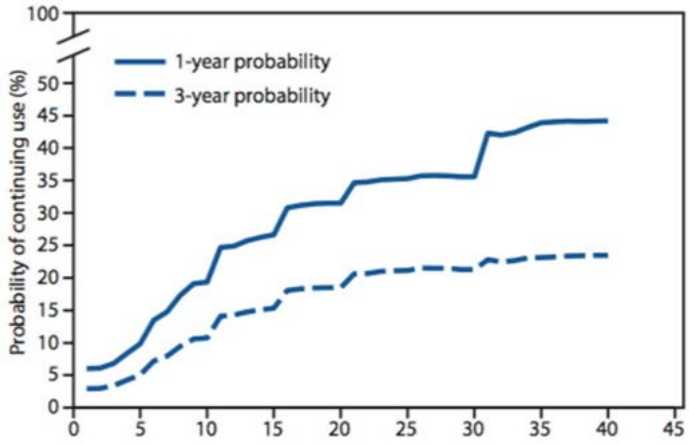
Acute Pain

Florida statue defines acute pain is defined as "the normal, predicted, physiological, and time-limited response to an adverse chemical, thermal, or mechanical stimulus associated with surgery, trauma, or acute illness". This does not include pain related to cancer, a terminal condition, palliative care, nor a traumatic injury with an Injury Severity Score of 9 or greater. Florida now allows a maximum 3-day supply for a CII opioid prescription for acute pain, which can become a 7-day supply if all the following criteria are met:

- More than a 3-day supply is needed based on the professional judgment of the prescriber
- The prescriber indicates "Acute Pain Exception" on the prescription
- The prescriber documents in the medical records the acute medical condition and lack of alternative treatment options that justify a 7-day supply instead of a 3-day supply

There is limited data supporting the utilization of long-term opioid medication utilization for pain, which does not mean that it should be absolutely avoided, yet does imply that it should not be universally deployed. The day supply of initial opioid prescribing patterns for opioid-naïve patients has shown an association with an increasing higher likelihood of long-term opioid medication utilization (Shah MMWR, 2017). Of note, that refers to chronic opioid use, not opioid use disorder (addiction). Now that does not automatically result in a monumental risk concern, yet it does propel healthcare professionals to realize that one can, or perhaps should, consider supplying no more than a couple day supply of any opioid medication as an initial prescription for all patients, regardless of risk, but perhaps especially for those screening for a higher risk based on the aforementioned opioid risk screening tools.

One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply* of the first opioid prescription — United States, 2006–2015 (Shah MMWR, 2017)



Chronic Pain

When prescribing a CII opioid prescription for non-acute pain (e.g. chronic nonmalignant pain, etc.), the prescriber must indicate "Non-Acute Pain" on the prescription.

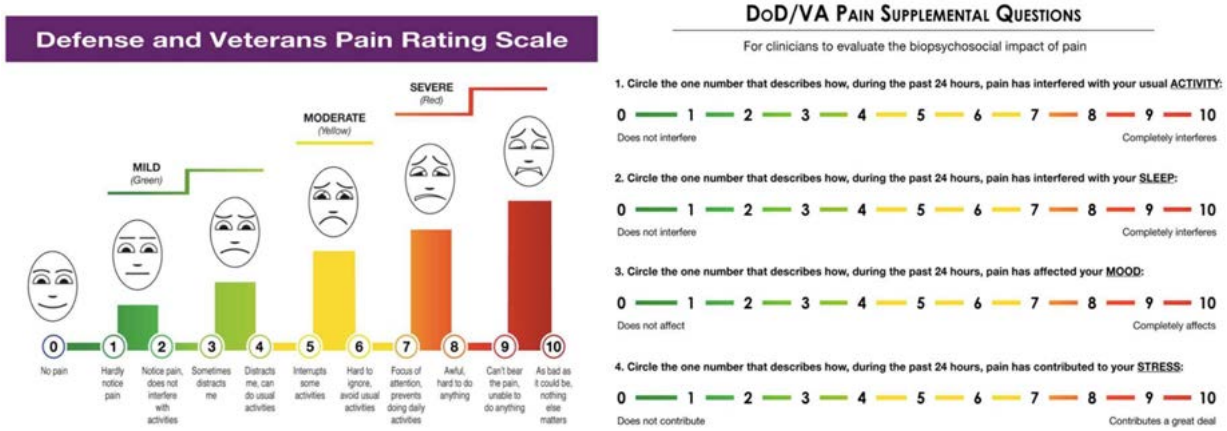
Traumatic Injury Pain

When a practitioner prescribes a CII substance for the treatment of pain related to a traumatic injury with a severity score of 9 or greater, the practitioner must concurrently prescribe an emergency opioid antagonist (e.g. naloxone). However, there is no law stating that the opioid antagonist prescription must absolutely be filled at a pharmacy.

Pain Diagnosis

Subjective assessments include subjective pain scales (i.e. classic 1 to 10 rating) and/or functional pain assessments on topics such as activities of daily living (ADLs) or the "PQRST" assessment. Examples of activities of daily living include walking up sets of stairs within a home, completing tasks necessary for employment, or even merely walking outside to get the mail. The "PQRST" assessment includes questions revolving around what precipitates or palliates one's pain (P), the quality (Q), the region and radiation (R), the severity (S), and the temporal factors (T) of one's pain.

The single best pain scale that I actually utilize for my patients in pain is the DVPRS (after you say it dozens of times, it just rolls right off the tongue, but certainly not initially). The DVPRS basically combines all your favorite approaches to common pain scales including color, emotional faces, and of course numbers. However, and here's the part that can really improve one's patient care, on the backside of the pain scale printout are four powerful questions assessing a patient's activity, sleep, mood, and stress. I've often said, I may never be able to help change a patient's pain number, however, affecting at least one of these items sounds much more like a SMART goal in being Specific, Measurable, Attainable, Realistic, and Timely (DVPRS Pain Scale).



Objective assessments include physical exam findings, such as range of motion, dermatomes, or myotomes. Other objective findings include both laboratory results such as inflammation markers or vitamin levels, or radiological findings such as MRIs, X-Rays, or CT Scans.

Types of Pain

There is debate as to how to universally classify all types of pain involving nociceptive, neuropathic, inflammation, and mixed pain types. However, generally speaking, most agree that there are definitely at least two core types of pain: nociceptive and neuropathic.

Nociceptive pain arises from noxious stimuli affecting thermal, mechanical, or chemical receptors (nociceptors) in normal tissues (Merck Manual, 2017). Nociceptive pain can be further classified into somatic or visceral. Somatic nociceptive pain involves the outer organs, and generally produces a localized aching or throbbing pain. Visceral nociceptive pain involves internal organs with examples including a localize tumor or Irritable Bowel Syndrome.

Neuropathic pain stems from an abnormal processing of sensory input by the Central Nervous System (CNS) and/or Peripheral Nervous System (PNS) (Merck Manual, 2017). Central neuropathic pain can occur because of injury to the CNS or PNS, such as is seen with phantom leg pain, or be the result of a dysregulation of the autonomic nervous system, such as is seen in complex regional pain syndrome (CRPS). Peripheral neuropathic pain manifests itself from damage to a specific nerve with an example being trigeminal neuralgia, or can be distributed among a regional grouping of nerves with examples being diabetic neuropathy or post-herpetic neuralgia. Before going further into comprehensive pain management with or without opioid pain medications, let's first review the laws and regulations that Florida pharmacists must always comply with while treating patients in pain.

Assessment of Prescriptions for Appropriate Therapeutic Value

There are multiple specific efforts that a pharmacist can conduct and/or discuss with a prescriber in order to ensure a legitimate medical use and appropriate therapeutic value including the utilization of Patient & Provider(s) Agreements.

An umbrella strategy for reducing patient risk with the use of pain management medications is to have a thorough review of the mutually agreed upon pain management treatment plan between a patient and a provider within a patient and provider agreement, sometimes known as a contract or consent form. A patient and provider agreement are an invaluable tool to ensure progress towards specific, measurable, attainable, realistic, and timely goals. A patient and provider agreement can also serve as a roadmap for how to progress, or even cease, an agreed upon treatment plan.

Best practices amongst pain management specialists suggest a patient and provider agreement to include appropriate goals (i.e. improvement in function, reduction in pain, and end of therapy), periodic reassessment of a patient's psychological state, risk, pain, function, and the treatment profile; drug interaction review; adverse effects of medications; proper medication storage and disposal of medications; prescription drug monitoring program (PDMP) results, urine drug screening and/or testing; naloxone education and supply as necessary; medication pill counts; medication risks to others if shared; having a treatment co-manager if needed, and a contingency plan for any violations of the agreement.

Psychological Evaluation

Another best practice within pain management is to perform an initial and annual psychological evaluation for patients taking medications with addictive properties. Life circumstances evolve for everyone; thus, risk can also change over time, warranting ongoing monitoring of risk factors.

Currently the PHQ-2 depression screening instrument is not only one of the go-to screening tools for depression, but is also something that can be completed conversationally in a mere two questions. The purpose of the PHQ-2 is not to diagnose, but to be utilized as a brief initial screen for depression, where positive screening results should be further evaluated with the PHQ-9 to determine whether they meet criteria for a depressive disorder. The two main questions within the PHQ-2 screening tool revolved around how often the following occurred in the last two weeks: 1. Little interest or little pleasure in doing things, and 2. Feeling down, depressed, or hopeless. All healthcare professionals can easily familiarize themselves with the PHQ-2 brief depression screening to utilize as a tool for determining when to refer for an actual diagnosis.

Opioid Risk Screenings

It is vitally important to bear in mind that all patients being considered for the utilization of opioid medications should be screened for risk of substance misuse regardless of his or her respective previous exposure to opioid medications. There is debate amongst healthcare professionals as to whether more in-depth research on the evidence of the opioid risk screenings may be needed, especially for use in populations beyond patients experiencing chronic pain. However, it is currently generally accepted as best practice to employ a risk screening for any patient currently taking or being considered for opioid medication (Chou R, 2009). One of the natural questions to arise regarding the results of an opioid risk screening, is whether higher risk results disqualify a patient from being a candidate for receiving opioid medications. Results of an opioid risk screening neither demand nor inhibit the use of opioid medications for a given patient, yet results more so emphasize the degree to which more patient education is needed on risk reduction strategies, while also suggesting when the utilization of opioid medications may be of higher risk.

One can classify the currently available opioid risk screenings into those to be utilized for opioid-naïve patients or those to be utilized for opioid-experienced patients. The screenings useful for patients being considered for opioid treatment include one of the most widely utilized screenings known as the Opioid Risk Tool (ORT), the relatively newer Opioid Risk Tool for Opioid-Use Disorder (ORT-OUD) (Cheatle M., 2019), the Drug Abuse Screening Test (DAST), the Diagnosis, Intractability, Risk, & Efficacy Score (DIRE), and the Screener and Opioid Assessment for Patients with Pain (SOAPP). The SOAPP can be utilized for opioid-experienced patients as well. With that in mind, the opioid screenings useful for patient already receiving opioid treatment include the Current Opioid Misuse Measure (COMM), the Pain Medication Questionnaire (PMQ), and the Prescription Drug Use Questionnaire. (CDC, 2016)

Drug-Drug, Pharmacokinetic, Pharmacodynamic, & Pharmacogenic Interactions

Pain management medications interact with other medications just as often and easily as any other medications interact. Thus, a review of a patient's entire medication profile to assess for drug interactions is pivotal to ensure the proper selection and dosage of a patient's pain medication(s). Hepatic cytochrome P450 (CYP-450) enzymes of particular concern with multiple pain medications, such as opioid medications, include 2D6 and 3A4. Obviously, these are synonymous with numerous other non-pain management or even adjuvant pain management medications, and thus need to be specifically considered.

Pharmacogenics (PGx) is the study of the role of genetics in the human body's response to medications. Numerous physiological systems of the human body, such as metabolic enzymes or drug receptors, can exhibit genetic variability resulting in altered drug-responses. For instance, if a patient's genetic composition facilitates a change in how a patient metabolizes a pain medication, then the selection and dosage of the pain medication may need altered. Two of the most common CYP450 enzymes that have shown pharmacogenomic involvement with pain management medications include 2C9 and 2D6. CYP-2C9 substrates include pain medications such as ibuprofen and celecoxib, and CYP-2D6 substrates include codeine, dextromethorphan, tramadol, duloxetine, venlafaxine, and tricyclic antidepressants. Pharmacogenetic testing can be performed to help forecast a patient's response to a given medication before initializing the treatment plan. For example, a CYP2D6 poor metabolizer may not receive adequate analgesia from tramadol, whereas, an ultra-rapid metabolizer may experience unnecessary side effects because of having more of the active metabolites present.

Urine Drug Screens/Tests

Urine drug screenings and tests are important tools in facilitating not only truthful conversations between healthcare professionals and patients, but also in medication adherence monitoring and the detection of illicit substance use. In general, one must also remember that an illicit substance is either a substance that is illegal by law and/or a substance that is use either for an unintended purpose or by an unintended person. All healthcare professionals need the most up-to-date and comprehensive medication information, including both legal medications and illicit substances, to provide a high level of patient's care.

Urine drug screenings are typically known as the "cup" method, and more specifically as the lower cost, yet qualitative examination. Urine drug screenings often include a strip on the cup labeled "OPI" which will show results for the most common structural class of opioids known as phenanthrenes which include morphine, diacetylmorphine (Heroin), codeine, hydrocodone, and oxycodone. However solely screening for the phenanthrene structural class of opioid medications does not screen for other opioids such as methadone or fentanyl.

Urine drug testings are typically known as the more sophisticated chemical testings (i.e. Gas Chromatography Mass Spec), and more specifically as the higher cost, yet quantitative

examination. In general, a urine drug screening can neither legally confirm nor deny the absolute presence of a substance, but can indicate the need for more specific testing via urine drug testing, which specifically identify all present substances, with correlating amounts of the substances, within the urine sample. Urine drug screens (not tests) have been conversationally compared to over-the-counter urine pregnancy tests in that there is not only a possibility for false negatives or false positives, but also that the over-the-counter urine pregnancy test may tell if one is pregnant, but certainly not to the specificity of the sex of the fetus.

Regardless of the lack of absoluteness in results, urine drug screenings are very frequently utilized within community, family practice, and primary care settings. Before administering a urine drug screen, a healthcare professional should be fully educated on cross-contaminants, testing time periods, and anticipated results based on the original substance and its respective metabolites. Asking a patient for a complete medication profile including prescription, over-the-counter, supplements, illicit substances, and even short-term medications can ensure that the results of a urine drug screening can be relied on, with a special concern for avoiding cross contaminants. The following chart highlights the active metabolites of the specified opioid medications that would be expected to at least a minor degree within a urine drug testing (note: not screening).

Opioid Ingested	Urine Drug Test Expected Results (Based on Active Metabolites, not including inactive metabolites)
morphine	morphine & hydromorphone*
hydromorphone	hydromorphone
hydrocodone	Hydrocodone, dihydrocodeine*, & hydromorphone
codeine	codeine, hydrocodone*, dihydrocodeine*, morphine, & hydromorphone
oxycodone	oxycodone & oxymorphone
oxymorphone	oxymorphone
fentanyl	fentanyl
tramadol	tramadol
methadone	methadone
heroin	heroin, morphine, & hydromorphone

*Very low levels (Smith, Opioid Metabolism, 2009)

Protocols For Addressing And Resolving Problems Recognized During The Drug Utilization Review

Florida statue defines a Drug Utilization Review (DUR) as an authorized, structured, ongoing review of prescribing, dispensing, and use of medication. DUR encompasses a drug review against predetermined criteria that results in changes to drug therapy when these criteria are

not met. A prospective DUR evaluates a patient's planned medication(s) before a medication is dispensed. Pharmacists should routinely perform prospective DURs in their daily practice by reviewing medication dosages and interactions.

A pharmacist shall review the patient record and each new and refill prescription presented for dispensing in order to promote therapeutic appropriateness by identifying the following 7 drug utilization review efforts:

- Over-utilization or under-utilization
- Therapeutic duplication
- Drug-disease contraindications
- Drug-drug interactions
- Incorrect drug dosage or duration of drug treatment
- Drug-allergy interactions
- Clinical abuse/misuse

Upon recognizing any of the above, the pharmacist shall take appropriate steps to avoid or resolve the potential problems which shall, if necessary, include consultation with the prescriber (Florida Code).

Pain Management Treatment Options

Non-pharmacological Treatment Options

Non-pharmacological treatment options can be separated into two distinct groups of Active vs Passive treatments, which may help to facilitate conversations around acceptance and agreement upon a selected non-pharmacological treatment options between a healthcare professional and a patient. “Active” treatments require some form of action during the treatment on behalf of the patient, whereas “Passive” treatments do not necessarily actually require a patient do perform any action.

Active	Passive
Cardio and/or Resistance Exercise	
Aquatic Exercise	
Walking Aids	Nutrition
Yoga	Heat or Cold
Tai Chi	TENS or EMS Devices
Qigong	Hyperbaric Oxygen
Meditation	Spinal Manipulation (Chiropractor)
Hypnosis	Massage
Relaxation	Ultrasound
Cognitive Behavioral Therapy (CBT)	Paraffin Wax
Acceptance & Commitment Therapy (ACT)	Infrared Light
Biofeedback	Spinal Traction
Graded Motor Imagery	Acupuncture
Occupational Therapy	
Physical Therapy	

Acetaminophen

Acetaminophen is an abbreviated name for n-acetyl-p-aminophenol. Additionally, the abbreviation "APAP" is extracted from n-*A*cetyl-*P*-*A*mino*P*henol, and the brand proprietary name Tylenol® is extracted from n-ace*TYL*-p-aminoph*ENOL*. Acetaminophen inhibits prostaglandin synthesis in the Central Nervous System (CNS), thus giving its antipyretic properties. The toxic metabolite via CYP1A2/2E1/3A4 metabolism is referred to as NAPQI, which is what derives the medication's maximum recommended doses of 3 grams for over-the-counter use and patients >/= 65 years of age, 4 grams under prescriber supervision, and 2 grams for patients with liver or kidney impairment (Clinical Pharmacology. Internet Database.)

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit lymphocytes, neutrophils, and prostaglandin synthesis in both the central nervous system (CNS) and the peripheral nervous system (PNS). NSAIDs can be useful in the treatment of inflammatory conditions such as rheumatoid arthritis, fever. NSAIDs can also be helpful in the management of gout due to the increased urinary excretion of urates. NSAIDs must be used with caution in asthma, due to the increased production of leukotrienes, and in impaired renal function, due to the decrease in glomerular filtration rate (GFR). The relative selectivity of each NSAID medication for either COX-1 or COX-2 inhibition is of importance for patients with either a higher risk of gastrointestinal issues or cardiovascular issues. In general, patients with a higher gastrointestinal risk should receive NSAIDs that are more COX-2 selective with the possible addition of a proton pump inhibitor, whereas patients with a higher cardiovascular risk should receive NSAIDs that are more

COX-1 selective. Overall examples of NSAIDs (in relative order of COX-2 selectivity to COX-1 selectivity) include etodolac, meloxicam, celecoxib, diclofenac, sulindac, piroxicam, ibuprofen, naproxen, indomethacin, ketoprofen, ketorolac, and aspirin.

L-Methylfolate

Folate is the natural version of synthetic folic acid, which is metabolized to dihydrofolate (DHF), and then tetrahydrofolate (THF), which is then metabolized by the methylenetetrahydrofolate reductase (MTHFR) enzyme to L-Methylfolate, which is bioactive to assist in the formation of monoamines such as serotonin, norepinephrine and dopamine. Those monoamines help facilitate the body's sensory status regarding conditions such as depression or pain sensation. Thus, a deficiency in L-Methylfolate will result in an alteration of status in those medical conditions. L-Methylfolate supplementation may increase monoamine synthesis and augment a patient's depression therapy or pain management as demonstrated in several studies (Trippe B, 2016). L-Methylfolate is available as multiple prescription products with doses of 3mg, 7.5mg, and 15mg, and ranging vastly in respective price ranges as compared to the unregulated non-FDA approved supplement versions available in various doses.

Topical Formulations

Topical medication formulations are very useful not only for the reducing one's pain and improving function, but primarily in accomplishing those goals while avoiding systemic exposure and additional side effects. Examples of commonly utilized topical pain medications include topical NSAIDs, tricyclic antidepressant (doxepin), lidocaine +/- prilocaine, capsaicin, counterirritants (i.e. menthol, camphor, etc.), salicylates, or arnica.

Tri-Cyclic Antidepressants (TCAs)

Antidepressants exhibit their respective mechanisms of action on neurotransmitters within the nervous system, such as dopamine, serotonin, norepinephrine, and so on. Antidepressants that are observed to be effective in pain management have a mechanism of action involving norepinephrine (NE). Therefore, antidepressant medications not directly effective in pain management include selective serotonin reuptake inhibitors (SSRIs), and to some degree trazodone (mainly affecting serotonin) and nefazodone (norepinephrine effects lost with chronic use). However, one must always also keep in mind that pain is very psychological, and if a medication positively influences one's mood, then it may also indirectly affect one's perception of pain.

Tricyclic antidepressants (TCAs) mainly affect norepinephrine, and thus are observed to be effective in pain management. Secondary amines have less side effects and shorter half-lives relative to tertiary amines such as amitriptyline. Secondary amines include both desipramine, the metabolite of imipramine, and nortriptyline, the metabolite of amitriptyline. Anticholinergic and antihistaminic related side effects of TCAs include orthostatic hypotension, drowsiness, & withdrawal upon abrupt discontinuation (Clinical Pharmacology. Internet Database.).

Serotonin & Norepinephrine Re-Uptake Inhibitors (SNRIs)

Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) include duloxetine, venlafaxine, desvenlafaxine, milnacipran, & levomilnacipran. SNRIs exhibit their pain management mechanism of action on norepinephrine (NE). The relative scale of potency/action on NE amongst adjuvant TCA and SNRI pain medications ranks nortriptyline as the highest potency to act upon NE, followed by milnacipran, amitriptyline, duloxetine, venlafaxine, and desvenlafaxine (Vaishnavi SN, 2004). Common side effects of SNRIs include nausea, dry mouth, fatigue, and somnolence (Clinical Pharmacology. Internet Database.).

Atypical Antidepressants

Two atypical antidepressants that have been observed to be effective in pain management include bupropion and mirtazapine. Bupropion exhibits its mechanism of action as a norepinephrine & dopamine reuptake inhibitor, while mirtazapine exhibits its mechanism of action as a noradrenergic (alpha-blocking) & specific serotonergic antidepressant.

Anti-Epileptic Drugs (AEDs)

Epilepsy prevention medications exhibit their seizure management effects on the body's nervous system by affecting the electrical current passed along neurons and their pain management effects on the body's nervous system by increasing the Gamma-Amino-Butyric Acid (GABA) facilitated inhibition of pain sensation. First generation AEDs include carbamazepine, phenytoin, & valproic acid. Second generation AEDs include lamotrigine, levetiracetam, topiramate, oxcarbazepine, & zonisamide. Unique side effects of particular AEDs compared to other pain management medications include rashes and an increased bone fracture risk (Clinical Pharmacology. Internet Database.).

Gabapentinoids

Gabapentinoids act upon Gamma-Amino-Butyric Acid (GABA) channels, like benzodiazepines, ethanol, and sedative hypnotics. The action is on calcium channels, not the actual GABA receptors, to ultimately increase GABA's inhibition of pain sensation. Common gabapentinoids include gabapentin, pregabalin, and a structural analog of GABA named baclofen (typically referred to as a "muscle relaxant"). Gabapentin's maximum daily dosage is 3,600mg per day, while it can also be noted that its bioavailability decreases with higher than average doses, so much so that many experts agree that clinical effects peak at 1,200mg per day. Gabapentin is highly lipophilic (crossing the Blood-Brain-Barrier) and is excreted unchanged in the urine. Common side effects of gabapentin include sedation/fatigue, dizziness, ataxia, & neuropathic edema (which ironically is not affectively treated with water pills). Gabapentin is a classic example of the mantra for "start low, go slow" dosing. Conversely, pregabalin has a relatively quicker dose titration period and a higher potency (i.e. 6x) than gabapentin (Clinical Pharmacology. Internet Database.).

“Muscle Relaxants”

Muscle relaxant medications are intended to be used for the relief of muscle spasticity and spasms with acute pain, yet are not recommended for chronic everyday use. These medications are classified as either exhibiting action on muscle spasticity (stiffness) or musculoskeletal conditions (spasms).

Medications referred to as muscle relaxants observed to be effective for stiffness include tizanidine, baclofen, and dantrolene. Tizanidine is a structural analog of clonidine and is thus an alpha-2 agonist, best dosed at bedtime to avoid daytime drowsiness. Baclofen is a structural analog of Gamma-Amino-Butyric Acid (GABA). Dantrolene is the one true muscle relaxant exhibiting its actions on peripheral muscles.

Medications referred to as muscle relaxants observed to be effective for spasms include carisoprodol, cyclobenzaprine, orphenadrine, methocarbamol, metaxalone, and chlorzoxazone. Carisoprodol is metabolized to meprobamate, a barbiturate, and is actually banned in Europe. Cyclobenzaprine is structurally related to amitriptyline and began its history of utilization as a TCA. Orphenadrine is a structural analog of diphenhydramine. Methocarbamol is a carbamate derivative of guaifenesin, a structural analog of mephenisin (concerns for respiratory depression), and has a unique possible side effect of dark brown, black, or green colored urine. Metaxalone has a relatively lower risk of sedation, and its bioavailability increases when taken with high fat meals. Chlorzoxazone has a unique possible side effect of turning urine orange, red, or purple (Clinical Pharmacology. Internet Database.).

Opioids

Opioid receptors naturally occurring in the human body include Mu, Kappa, Sigma, Delta receptors. The vast majority of current opioid pain medications exhibit analgesic effects as action on Mu opioid receptors.

Traditional Opioids

Codeine (acetaminophen/codeine) has a higher chance of patients experiencing two of the more common opioid side effects of nausea/vomiting and constipation. Morphine is a Mu agonist and the control standard of opioid pain medications for relative dosage. Hydrocodone and its metabolite hydromorphone are both in the C2 class of medications, even though there is a four-fold difference in potency. Similarly, both oxycodone and its metabolite oxymorphone are in the C2 class of medications, even though there is a two-fold difference in potency. Oral pentazocine (with naloxone) is a weak Mu antagonist and a weak Kappa agonist. Dihydrocodeine is available as combination products with caffeine added along with either acetaminophen or aspirin. Fentanyl is a fully synthetic and highly potent opioid with

numerous dosage forms. Meperidine is also a fully synthetic opioid. Buprenorphine is a partial Mu agonist and Kappa antagonist with a unique "ceiling effect" where relatively lower doses provide pain relief without progressing to a euphoric feeling nor comparative higher chance of respiratory depression. Buprenorphine also exhibits a very high relative affinity for Mu receptors. Buprenorphine is available alone for both pain management (mcg doses) and opioid-use disorder (mg doses) or in combination with naloxone solely for opioid-use disorder (Clinical Pharmacology. Internet Database.).

Mixed Action Opioids

Tramadol is a weak Mu agonist and serotonin norepinephrine reuptake inhibitor (SNRI) with a maximum immediate release daily dose of 400mg and maximum extended release daily dose of 300mg. Tramadol requires hepatic and renal impairment dosing adjustments, and a monitoring for serotonergic interactions and symptoms. Tapentadol is a weak Mu Agonist & norepinephrine reuptake inhibitor with a relatively faster onset and less serotonergic activity and concerns compared to tramadol. Levorphanol is a fully synthetic opioid with multiple mechanisms of action including being a Mu, Delta, & Kappa Agonist; NMDA Antagonist; serotonin and norepinephrine reuptake inhibitor (SNRI); Anticholinergic medication. Methadone is a Mu agonist; NMDA Antagonist; serotonin and norepinephrine reuptake inhibitor (SNRI). Methadone has two enantiomers with the D-methadone enantiomer exhibiting the primary analgesic effects. The pharmacokinetics of methadone include a half-life of *8 to 150 hours* while being metabolized by CYP-450 enzymes (3A4, 2B6, 2C9 2C19, & 2D6) and PgP (Clinical Pharmacology. Internet Database.). These variable pharmacokinetic factors warrant a relatively very low initial dose (i.e. 15mg/day) with no dose titrations in the initial week of therapy, followed by a gradual increase of approximately 10mg/day each week (Webster, 2012).

Pharmacist Initiated Counseling Of Patients With Opioid Prescriptions

Pharmacists are required by law to offer patient counseling (i.e. answer questions, provide information on how to best take a medication, expected side effects, and so on) when dispensing prescription medication(s) (OBRA 1990). A chief responsibility of all healthcare professionals is educating patients, and often, that education is on basic concerns that can greatly help a patient in everyday life such as side effects, drug interactions, proper dosage, and storage and disposal.

Morphine Milligram Equivalents (MMEs)

One of the most important concepts for the selection, dosage, and patient education of opioid pain medications is the morphine milligram equivalent (MME). The MME can be explained in a different paradigm involving citrus fruits such as oranges, grapefruits, lemons, and limes which all contain various amounts citrus or potency of citric acid. The relative comparison of how much "citrus" is in each citrus fruit could become known as the "citrus content equivalent", much like the degree of opioid potency in any opioid medications relative to morphine as a baseline standard. In essence, the realized role of the MME is to express an opioid's potency.

To most easily utilize the MME conversation factors seen below, as adopted from the 2016 CDC Opioid Guidelines with 2017 updates, one can multiply the MME factor by the opioid dosage for a given patient to calculate the overall MMEs the patient is receiving. Typically, that total MME amount is divided by a given time frame to result in a Morphine Equivalent Daily Dose (MEDD), otherwise known as a daily MME. The CDC Chronic Pain Opioid Guidelines of 2016 state that a daily MME level >/= 50 should only be used with caution and a daily MME level >/= 90 should be avoided unless a clinician can carefully justify the titration. According to a study published in the Annals of Internal Medicine in 2010, the approximate adjusted hazard ratio (or relative likelihood of overdose) for a patient receiving >/= 100 morphine milligram equivalent (MME) of any opioid medication per day is eleven, thus showing the importance of healthcare professionals being familiar with the concept of MMEs. A table of MME conversion factors is provided below for reference, yet if a healthcare professional learns that morphine and hydrocodone each have an MME conversion factor of 1, while oxycodone has an MME conversion factor of 1.5, one can relatively easily calculate a respective patient's MME/Day, or MEDD, level.

Type of Opioid	MME Factor
Transdermal Buprenorphine	12.6 (then divide by days)
Buprenorphine Tablet/Film	30 (for mg doses)
Codeine	0.15
Dihydrocodeine	0.25
Transdermal Fentanyl	7.2 (then divide by days)
Hydrocodone	1
Hydromorphone	4
Levorphanol	11
Meperidine	0.1
Methadone	4, 8, 10, & 12 (Progressive)
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Pentazocine	0.37
Tapentadol	0.4
Tramadol	0.1

Adapted from: (CMS, 2015), (CDC, 2016)

Morphine Milligram Equivalent (MME) Patient Case

Let's practice the MME math with figuring out the MME of an acetaminophen/codeine 300mg/30mg tablet (commonly referred to as "Tylenol #3"). One must simply multiple the codeine 30mg by the codeine 0.15 MME Factor. This results in an MME of 4.5, which, although relatively low, is almost indistinguishable to that of a tablet of hydrocodone/apap 5/325mg (MME Factor 1). I only mention because, although the street value of the "Tylenol #3" is observed to be remarkably lower than that of hydrocodone or oxycodone, its clinical expectations are almost mirrored. Considering that the goal of healthcare professionals need to be to recognize not only addressing a patient's pain, but also considering the prescription drug supply chain implications, regardless of legality, one could say that the utilization of acetaminophen/codeine tablets instead of hydrocodone/acetaminophen tablets may reduce the risk of drug diversion and/or medication misuse when concentrating on the drug supply chain beyond the direct patient and practioner relationship.

Opioid Metabolism

It is important to understand how an opioid, or any medication, is metabolized in the human body considering pharmacogenetic differences and possible drug-drug interactions (Smith, Opioid Metabolism, 2009). The CYP-2D6 enzyme is involved in the metabolism of codeine, hydrocodone, oxycodone, methadone and tramadol. The CYP-3A4 enzyme is involved in the metabolism of oxycodone, methadone, tramadol, and fentanyl (Clinical Pharmacology. Internet Database.).

Opioid Side Effects

The package inserts of all opioid medications contain each of the following as possible side effects to opioid medications: constipation, neuralgia, itching, Sedation, Respiratory Depression, Bradycardia, Hypotension, QT Prolongation, Nausea & Vomiting, Central Sleep Apnea, Edema, Urine Retention, Miosis (Pupil Constriction), Myoclonus (muscle jerking), and Hypogonadism (decreased estrogen or testosterone).

One of the most common side effects of opioids is itching due to stimulation of the release of histamine. Second generation antihistamines such as loratadine, cetirizine, or fexofenadine can prevent/treat the itching side effect with minimal respective side effects. Another common side effect of opioids is sedation, which can be addressed by educating patients on the likelihood of feeling tired and/or confused to best accommodate their daily life. A basic yet incredibly important counseling point is to have patients avoid operating machinery or driving, especially while adjusting to opioid medication dosage for an appropriate period.

Another very common side effect of opioid medications is constipation [Opioid Induced Constipation, (OIC)]. For OIC, healthcare professionals should encourage patients to utilize a diet with adequate fiber & fluid intake, and utilizing a stepwise approach including docusate +/- Senna, followed by Polyethylene Glycol-3350, followed by either a chloride channel activator (i.e. lubiprostone) if the constipation was present prior to opioid therapy, or a peripheral opioid antagonist (i.e. alvimopan, methylnaltrexone, naldemedine, naloxegol, with only naldemedine being an oral formulation being able to be taken without regard to food) if the constipation resulted from opioid therapy. It is invaluable to also consider that any given patient has most likely already attempted over-the-counter self-care options once finally resorting to talking with a healthcare professional, given the sensitive nature of GI issues in conversations. Thus, it is inherently important to discuss previous treatments, as with any clinical scenario.

Opioid Tapering

The goal of opioid tapering is to safely decrease the need for the prescription opioid pain medication, while still addressing the respective patient's pain management concerns. Approaches to tapering range from a slow 10% reduction per week to a more aggressive 25-50% reduction every few days depending on the original MME dosage and duration of the opioid therapy. In general, a slower taper will produce fewer unpleasant symptoms of withdrawal. Opioid withdrawal symptoms are uncomfortable, but are not dangerous nor life-threatening under standard clinical care, thus opioids can be stopped abruptly when the risks outweigh the benefits. (Association, 2014)

Opioid Conversion

If the same opioid medication is being converted from immediate-release (IR) to extended-release (ER) formulation, one can directly convert the IR MME daily dose to an ER MME daily dose. (Clinical Pharmacology. Internet Database.)

Opioid Rotation

If an opioid mediation is being rotated to a different opioid medication, more caution than a simple conversion of formulations is warranted. First, calculate the MME based equianalgesic dose of the new opioid. Then determine the automatic dose reduction percentage based on the following strategies.

If switching to methadone, then utilize a 75-90% equianalgesic dosage reduction. If switching to a new route of administration for the same drug, utilize a 25% equianalgesic dosage reduction. If the patient is receiving a higher risk MME dose, is not Caucasian, elderly, or medically frail, utilize a 50% equianalgesic dosage reduction. Additionally, assess patient pain severity to decide upon an additional increase or decrease of 15-30% to enhance pain management effectiveness or avoid causing withdrawal symptoms.

Continually assess the patient for effectiveness and safety of the new dosage. Healthcare professionals may want to provide a "rescue dose" supply at 5-15% of the total daily MME for as needed use by the patient during the opioid rotation (Fine P, 2009).

Proper Patient Storage And Disposal Of Controlled Substances

A chief responsibility of all healthcare professionals is educating patients, and often, that education is on basic concerns that can greatly help a patient in everyday life. Educating patients on proper medication storage and disposal can involve straightforward information, yet sometimes is even debated amongst healthcare professionals. The most important aspects of proper medication storage can be summarized as consistently putting mediations away, with a safety cap locked on, after every use in a cool, dry, and secure storage location out of the reach and sight of children and pets, and within a locked device if controlled substances are involved. (Education, 2016). Patients also need to know that if someone accidentally takes an unintended medication or dosage, the Poison Center (1-800-222-1-222) should be contacted immediately or even the "911" emergency service if person is unconscious or having a seizure. Many medicine cabinets are installed in bathrooms, which some healthcare professionals may inadvertently recommend consistent storage within, even though the humidity of the bathroom shower and/or bath is not a suitable location to store medications unless the room is well ventilated.

The FDA recommends three different methods of medication disposal including disposal through a DEA sponsored Take-Back Program, a DEA-Authorized collector, or via a specific process within household trash. The FDA recommended process for disposal of medications within household trash is summarized as removing medications from original container and mixing with an undesirable substance (i.e. coffee grounds, dirt, etc.) in a sealable container or bag. Additionally, for a few dozen controlled substance medications (a listing of mainly opioids), the FDA recommends removal from the home by flushing them down the toilet or sink (FDA Drug Disposal, 2016).

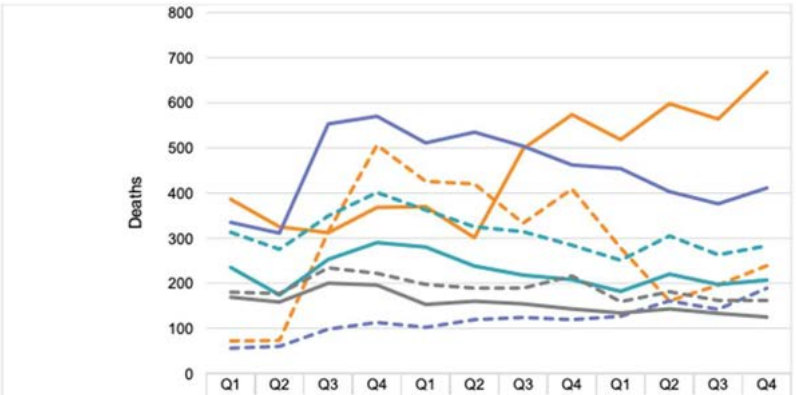
Education On The Emergency Treatment For Suspected Opioid Overdoses and On The State Surgeon General's Statewide Standing Order For Naloxone

Naloxone is a reversal agent for opioid overdose as it reverses opioid induced respiratory depression. Naloxone is available in multiple formulations including a 0.4mg/ml IM injection, 0.4mg/ml auto-injection, 2mg/2ml intranasal solution, and the 4mg nasal spray. Candidates for the education and supply of naloxone include:(Instructions for Healthcare Professionals: Prescribing Naloxone, 2016)

- Current or past opioid-use disorder or opioid overdose
- Current higher risk dose opioid use (>/=50mg MME per day) or opioid rotation
- Receiving any opioid prescription for pain plus:
    - Respiratory Condition (i.e. Smoking, COPD, emphysema, asthma, sleep apnea, etc.)
    - Renal dysfunction, hepatic disease, cardiac illness, HIV/AIDS
    - Concurrent alcohol use
    - Concurrent sedative or antidepressant prescription
    - Who may have difficulty accessing EMS (i.e. distance, rural, etc.)?
- Voluntarily request naloxone by oneself or a caregiver

Florida's standing order for naloxone authorizes pharmacists who maintain a current active license practicing in a pharmacy located in Florida that maintains a current active pharmacy permit to dispense one of the following naloxone formulations to emergency responders for administration to persons exhibiting signs of opioid overdose. Emergency responders include law enforcement, firefighters, paramedics and emergency medical technicians. The pharmacy must maintain a copy of the Standing Order for Naloxone if dispensing naloxone pursuant to the order. Incorporated in this Standing Order for Naloxone is the expectation that the SAMHSA Opioid Prevention Toolkit Five Essential Steps for First Responders be followed. Approved Options for intranasal or Auto -Injector Administration include the auto-injector, the naloxone 2mg/2mL, and the Narcan nasal spray (Florida Naloxone Standing Order).

Florida Drug Overdose Trends



	Q1 2016	Q2 2016	Q3 2016	Q4 2016	Q1 2017	Q2 2017	Q3 2017	Q4 2017	Q1 2018	Q2 2018	Q3 2018	Q4 2018
Fentanyl	386	325	312	368	370	301	498	574	518	598	564	668
Fentanyl Analogs	72	73	314	506	426	420	333	409	278	161	196	239
Cocaine	335	311	553	570	511	535	504	462	454	403	376	411
Methamphetamine	56	60	98	113	102	119	124	119	127	161	142	189
Heroin	235	174	253	290	280	238	218	208	182	220	197	207
Morphine	313	275	349	401	362	325	314	284	251	305	263	283
Oxycodone	169	158	200	196	153	160	154	143	134	143	133	125
Alprazolam	180	177	234	222	197	189	189	216	159	181	162	162

Figure 9. Quarterly drug overdose deaths by contributing drug in Florida, 2016 – 2018.

(FL Drug Overdose Trends)

As one can see from the Florida Drug Overdose Trends chart, over the past few years there are a few substances of abuse trends that are worth noting, especially in relationship, although rather indirectly to prescription-controlled substances. In Florida, the one substance of abuse that easily stands out in having an upward trend of overdoses is fentanyl (and its analogs to a lesser fluctuating degree) along with methamphetamine having a gradual increase. This trend is observed to be relatively consistent across the United States as well as what I would refer to as the "4th Wave of the Opioid Crisis", the major methamphetamine and fentanyl/analog problem plaguing our country and globe right here and now.

The natural question is "How did we get here?". There's enough "blame" to go around for everyone including particular (but not all) poppy growers, manufacturers, distributors and wholesalers, prescribers, dispensers, insurance companies, government, street dealers, cartels, and even patients. That blame, or perhaps better stated as responsibility, is real at all levels, yet many times over sensationalized. For instance, when it comes to the overwhelming vast majority of healthcare professionals (minus the few that end up in criminal situations), there is a universal misleading sensationalization of healthcare professional's involvement in the opioid crisis. We, as healthcare professionals, are clearly within the general supply chain of opioid medications (and all controlled substances), however, one particular study is constantly misinterpreted by media with headlines to the tune of "75% of Heroin utilizers began their use with prescription opioids" (TJ Cicero, 2014). Who hasn't seen two dozen of those headlines? However, details matter. Yes,

prescription opioids, but that does not necessarily mean that the eventual Heroin utilizing individuals began their respective use with prescription opioids attained directly from prescribers and dispensers. In fact, another study shows that 2/3rds actually attained said prescription opioids from family, friends, or street dealers for free or cash (2017 DEA Assessment). On top of that, another study shows that those utilizing substances of abuse were not aiming for the euphoric effects, rather relief from various pain and psychological issues, which is what we as healthcare professionals typically specialize in (2018 DEA Assessment). That being said, we as pharmacists have a corresponding responsibility to confirm the validity of controlled substance prescriptions (and all prescriptions), as previously reviewed herein, to ensure a legitimate medical utilization and the appropriate scope of practice for the prescriber. In the grander picture, we pharmacists, as healthcare professionals, still do have a (legal) responsibility to counsel patients on medication concerns minimally by OBRA ’90, but more so in our professional oath to provide optimal patient care. The pain management treatment plan diversity and multiple risk reduction strategies discussed herein are a great place to start. Year-after-year, we as pharmacists, are shown to have public trust via Gallop polls, and now is the time to go a step further and show just how much we care. Afterall, no one cares how much you know until one knows how much you care.

References

1. Association, C. M. (2014). *Pain Management Guidelines.*
2. Brandeis University, C. o. (October 2014). *Mandating PDMP Participation by Medical Providers: Current Status and Experience in Selected States.* Retrieved from http://www.pdmpexcellence.org/sites/all/pdfs/COE_briefing_mandates_2nd_rev.pdf
3. CDC. (2016). *CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016.* Morbidity and Mortality Weekly Report.
4. Cheatle M., e. a. (2019). Development of the Revised Opioid Risk Tool to Predict Opioid Use Disorder in Patients with Chronic Non-Malignant Pain. *Journal of Pain*.
5. Chou R, e. a. (2009). Opioids for Chronic Non-Cancer Pain: Prediction and Identification of Aberrant Drug-Related Behaviors: A Review of the Evidence for an American Pain Society and American Academy of Pain Medicine Clinical Practice Guideline. *Journal of Pain*, 131-146.
6. *Clinical Pharmacology*. (July 2020). Retrieved from www.clinicalpharmacology.com
7. CMS. (2015, March). *Opioid EQ Conversion Factors*. Retrieved from www.cms.gov/Medicare/Prescription-Drug-
8. Controlled Substance Act of 1970 [United States Code Title 21 (Food & Drugs), Chapter 13 (Drug Abuse Prevention & Control)]: https://www.deadiversion.usdoj.gov/21cfr/21usc/
9. DEA 2017 National Drug Threat Assessment (NDTA). Retrieved from: https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf.
10. DEA 2018 National Drug Threat Assessment (NDTA). Retrieved from: https://www.dea.gov/documents/2018/10/02/2018-national-drug-threat-assessment-ndta.
11. DEA Prescribing Guidelines during COVID. Retrieved from: https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-023)(DEA075)Decision_Tree_(Final)_33120_2007.pdf
12. DEA Red Flags. National Associations of Boards of Pharmacy (NABP) Pharmacist's Resources. Retrieved from: https://nabp.pharmacy/initiatives/pharmacist-resources/.
13. DVPRS Pain Scale. Department of Defense & Veterans Pain Rating Scale. Retrieved from https://www.va.gov/PAINMANAGEMENT/docs/DVPRS_2slides_and_references.pdf
14. *FDA Drug Disposal*. (2016, March). Retrieved 2017, from https://www.fda.gov/forconsumers/consumerupdates/ucm101653.htm
15. Fine P, P. R. (2009). Establishing "Best Practices" for Opioid Rotation: Conclusions of an Expert Panel. *Journal of Pain and Symptom Management*, 418-425.
16. Florida Code 64B16-27.810. Retrieved from: https://www.flrules.org/gateway/ruleno.asp?id=64B16-27.810
17. Florida Drug Overdose Trends. Retrieved from: (http://www.floridahealth.gov/statistics-and-data/e-forcse/laws-rules/2019-pdmp-annual-report.pdf.

18. Florida Health E-FORSCE Homepage. Retrieved from: http://www.floridahealth.gov/statistics-and-data/e-forcse/index.html.
19. Florida House Bill 21 of 2018 (1st Major Update Since 2011): https://www.flmedical.org/Florida_Public/Docs/FMA-Opioid-HB21.pdf
20. Florida Naloxone Standing Order. Retrieved from: http://www.floridahealth.gov/licensing-and-regulation/ems-system/_documents/standing-order-naloxone.pdf).
21. Florida PDMP Annual Report of 2019. Retrieved from: http://www.floridahealth.gov/statistics-and-data/e-forcse/laws-rules/2019-pdmp-annual-report.pdf
22. Florida Statue [Title 46 (Crimes) Chapter 893 (Drug Abuse Prevention & Control)]: http://www.leg.state.fl.us/statutes/index.cfm?App_mode=Display_Statute&URL=0800-0899/0893/0893.html
23. Hedegaard H, M. A. (2018). *Drug overdose deaths in the United States, 1999–2017.* National Center for Health Statistics (NCHS).
24. *Instructions for Healthcare Professionals: Prescribing Naloxone.* (2016, January 12). Retrieved from Prescribe to Prevent: http://www.prescribetoprevent.org/wp-content/uploads/2012/11/one-pager_12.pdf
25. Jones CM, M. K. (2013). Pharmaceutical Overdose Deaths, United States, 2010. *JAMA, 309*, 657-659.
26. *Merck Manual*. (2017, March). Retrieved from www.merckmanual.com
27. *NarxCheck*. (n.d.). (Appriss Health) Retrieved from https://apprisshealth.com/solutions/narxcare/
28. Ominus Budget Reconciliation Act of 1990 (OBRA '90). Retrieved from: https://www.ssa.gov/history/pdf/Downey%20PDFs/Omnibus%20Budget%20Reconciliation%20Act%20of%201990%20Vol%204.pdf.
29. *Painmed.org*. (2017, February). Retrieved from www.painmed.org
30. Paulozzi LJ, B. D. (2006). Increasing Deaths from Opioid Analgesics in the United States. *Pharmacoepidemiol Drug Safety, 15*, 618-627.
31. Paulozzi LJ, J. C. (2011). *Overdoses of Prescription Opioid Pain Relievers — United States, 1999–2008.* Morbidity and Mortality Weekly Report (MMWR). CDC.
32. SAMSHA. (2013). *National Survey on Drug Use and Health (NSDUH).* Retrieved from http://w ww.samhsa.gov/data/sites/default/files/NSDUH-SR200-RecoveryMonth-2014/NSDUH-SR200-RecoveryMonth-2014.htm
33. Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use- United States, 2006-2015. MMWR Morb Mortal Wkly Rep 2017; 66: 265-269.
34. Smith, H. (2009). Opioid Metabolism. *Mayo Clin Proc*, 613-624.
35. TJ Cicero, e. a. (2014). The Changing Face of Heroin Use in the United States. *JAMA Psychiatry*, 821-826.

36. Tolia, V. (2015). Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs. *The New England Journal of Medicine*, 2118-2126.
37. Trippe B, e. a. (2016). Nutritional Management of Patients with Diabetic Peripheral Neuropathy with L-methylfolate-methylcobalamin-pyridoxal-5-phosphate: Results of a Real-World Patient
38. Experience Trial. *Current Medical Research & Opinion*, 219-227.
39. Webster, L. (2012). What are best safety practices for use of methadone in the treatment of pain? *Practical Pain Management*.

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LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1a. PHARMACISTS ONLY: Does this lesson meet the learning objectives? (Circle choice).

Recognize how to ensure access to controlled substances for all patients with a valid prescription, while also assessing prescriptions for appropriate therapeutic value and detecting prescriptions not based on legitimate medical purpose.	YES	NO
Recall the legal expectations and intentions of utilizing the Florida Prescription Drug Monitoring Program's Database (E-FORCSE).	YES	NO
Recall the laws and rules related to the prescribing and dispensing of controlled substances in Florida.	YES	NO
Recognize proper storage and disposal protocols for controlled substances.	YES	NO

Recall protocols for addressing and resolving problems recognized during the drug utilization review including drug/drug interactions, side effects, high dose and low dose guidelines, and other therapeutic concerns.	YES	NO
Recognize the relevance of the Florida standing order for naloxone for the emergency treatment of opioid overdose.	YES	NO
Identify the most clinically important patient counseling considerations for patients utilizing opioid medications.	YES	NO
Recall available treatment resources for opioid physical dependence, addiction, misuse, or abuse.	YES	NO
Recall pain management non-pharmacological and pharmacological (both opioid and non-opioid) treatment options and respective dosage and patient counseling considerations.	YES	NO

2. Was the program independent & non-commercial? YES NO

3. Relevance of topic Low Relevance Very Relevant
   1 2 3 4 5 6 7

4. What did you like MOST about this lesson? _____
_____

5. What did you like LEAST about this lesson? _____
_____

6. How would you improve this lesson? _____
_____

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1. A practitioner licensed to prescribe medicinal drugs, including controlled substances, in Florida who maintains a system of electronic health records, and does not have any confirmed waiver may provide prescriptions:
    a. Electronically
    b. Verbally
    c. Hardcopy (Paper)
    d. All of the above

2. Which of the following could be a possible DEA registration number for a prescriber whose last name begins with the letter "P"?
    a. PB1234561
    b. PA1234561
    c. AP1234561
    d. AP6543211

3. Before a pharmacist refuses to fill a prescription based solely upon a concern with the validity of the prescription, a pharmacist must attempt to resolve any concerns with the validity of the prescription by performing the following:
    a. Communicate with the patient and prescriber
    b. Communicate with patient and review respective E-FORCSE report
    c. Communicate with prescriber and review respective E-FORCSE report
    d. Any of the above

4. Which of the following opioid medications is recognized by the DEA as a C-II medication?
    a. Buprenorphine
    b. Diacetylmorphine
    c. Tapentadol
    d. Tramadol

5. Which of the following opioid medications is recognized by the DEA as a C-III medication?
    a. Buprenorphine
    b. Hydromorphone
    c. Methadone
    d. Tramadol

6. DEA "Red Flags" for dispensers include:
    a. Dispensing a high ratio of non-controlled to controlled medications
    b. Dispensing the same medications and quantities prescribed by the same prescriber for multiple patients
    c. Consistently dispensing controlled substances for patients from one single practitioner
    d. Not consistently dispensing for patients seeking early prescription fills

7. In Florida, at what point are dispensers required to review E-FORCSE before dispensing a patient's medication:
    a. New prescriptions
    b. New and refill prescriptions
    c. Every 3 months
    d. Every 6 months

8. As of 2017, an American citizen statistically dies from a drug overdose every:
    a. 5 minutes
    b. 7 minutes
    c. 10 minutes
    d. 17 minutes

9. Florida allows a prescriber to utilize professional judgement, documentation, and indicating "Acute Pain Exception" on a C-II acute pain prescription to prescribe a maximum day supply of:
    a. 3 Days
    b. 7 days
    c. 10 days
    d. 14 days

10. Which of the following initial opioid prescription day supplies has at least a 25% observed increase in the likelihood of a patient continuing on to chronic opioid utilization?
    a. 3 Days
    b. 5 Days
    c. 1 Week
    d. 2 Weeks

11. Which of the following pain scales combines, emotional faces, and numbers, while also including questions on a patient's activity, sleep, mood, and stress?
    a. DVPRS
    b. ELMNOP
    c. PQRST
    d. QRSTUV

12. Which of the following is a psychological screener that can be administered in a conversational manner in mere seconds with two questions?
    a. PHQ-2
    b. PHQ-9
    c. ORT-2
    d. ORT-9

13. Which of the following opioid risk screenings has proven utility for utilization with opioid-experienced patients who are being screened personally by a healthcare professional?
    a. Current Opioid Misuse Measure (COMM)
    b. Opioid Risk Tool (ORT)
    c. Pain Medication Questionnaire (PMQ)
    d. Prescription Drug Use Questionnaire (PDUQ)

14. Which of the following opioid medications could possibly produce a positive urine drug screening for hydromorphone?
    a. Codeine
    b. Hydrocodone
    c. Morphine
    d. All of the above

15. What is the FDA approved maximum daily dosage stated on over-the-counter (OTC) self-care acetaminophen products?
    a. 3,000mg
    b. 3,500mg
    c. 4,000mg
    d. 4,500mg

16. Which of the following opioids has the highest observed chance of producing the side effects of nausea/vomiting and constipation?
    a. Codeine
    b. Hydrocodone
    c. Morphine
    d. Oxycodone

17. How many MMEs per day would a patient utilize if applying a transdermal fentanyl 12.5mcg/hr patch every 72 hours?
    a. 25
    b. 30
    c. 50
    d. 60

18. How many MMEs per day would a patient utilize if taking oxycodone ER 20mg 1 tablet by mouth twice daily?
    a. 40
    b. 50
    c. 60
    d. 80

19. As stated in the OBRA '90 federal law, pharmacists are required by law to offer patient counseling when dispensing prescription medication(s). Which of the following is/are examples of this patient counseling required by law?
    a. Verbally ask patient to sign a paper or electronic signature log
    b. Verbally explain when and how to best take the medication
    c. Placing a side effect sticker on the prescription vial as non-verbal communication
    d. All of the above

20. According to a 2017 DEA National Drug Threat Assessment, the majority of misused prescription opioid pills leading to 75% of heroin utilizers' first exposure to prescription opioids (as per a 2014 JAMA Psychiatry article) were attained from:
    a. Doctors
    b. Nurse
    c. Pharmacists
    d. Outside the Healthcare System