

**Utilizing Opioids Safely in Pain  
Management  
2021 Pain Conference  
Ascension Alabama 10/28/2021**

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# Conflict of Interest Disclosure

- **Conflict of Interest**

**Author: Linda Vanni-None**

**1. I have no relevant financial relationships with any ACCME-defined commercial interest to disclose.**

**2. I will not discuss off label use and/or investigational use in my presentation.**

**3. All Ascension planners, reviewers, and course directors have no relevant financial relationships with ACCME-defined commercial interests.**

# Objectives

1. Review the latest practices for assessing acute and chronic pain
2. Summarize current guidelines on the appropriate use of opioids for pain management
3. Describe the pharmacologic agents used in pain management

# What happened?

- 1996 APS president's speech about the need to have pain assessed with the same zeal as vital signs. Ortho third highest prescribers of opioids, dentists
  - Let's talk about hoarding
- Management pain = prescribe opioids
  - Too much drug around
- Things got out of hand
- 76 Million opioid scripts written in 1991
- 219 Million opioid scripts written in 2011, since 2012 opioid scripts have declined
- The jump from legal to illicit use
- 120---number of deaths per day from opioid overdose (CDC, 2017), USA Today 1/29/2018-175 opioid deaths per day



# Other Contributing Factors

- **Illegal activity from prescribers**
- **Diversion in the hospital setting**
- **Heroin is cheap**
- **Effect of the opioid crisis on chronic and cancer pain patients**
- **Money, money, money**
- **You are drug seeking, until proven otherwise**
- **Abuse deterrent medications not covered**

# Tolerance, Physical Dependence & Addiction

## Tolerance

- Effects diminish over time. Tolerance is not an inevitable consequence of chronic opioid therapy

## Physical dependence

- A predictable physiological response that occurs with continuous use
- Manifest by symptoms of withdrawal if use is abruptly discontinued or an antagonist is given
- Taper the dose to prevent withdrawal

## Addiction

- A primary, chronic, neurobiologic disease: impaired control over drug use, compulsive use, craving and continued use despite harm
- Addiction is a complex condition, a brain disease that is manifested by compulsive substance use despite harmful consequence

American Psychiatric Association, 2017

## Pseudo Addiction

“Addiction-like” behavior may signal inadequate pain control or intensification, progression of pain

# Addiction

- Chronic, relapsing, treatable, disease
- Characteristics
  - **Impaired control over drug use**
  - **Compulsive use**
  - **Continued use despite harm**
  - **Craving**
- Research shows strong association between stress and drug craving, and pain may contribute to increased stress

(NIDA)

# **In 2021, significant issues over chronic opioid use remain**

- **Stigma**
- **Using opioids for cancer pain, these medications are not benign, ER**
- **Who will be the writer?**
- **Expense**
- **Addiction**
- **Diversion**



# Safety Issues

- Are we dealing with illegal or legal substances?  
Multi-substances?
- Opioid naïve?
- Are we getting accurate information from the patient, i.e. amount, type of issues?
- Discrimination on our part?
- Ethical treatment?

# The modern ethics dilemma: Opioids for pain management in drug abuser

Mak Wen Yao , 07 Nov 2017

- Travis Rieder, is a research scholar at the Berman Institute of Bioethics at Johns Hopkins University. He wrote "if opioids prevent significant suffering from pain, then the solution to the prescription opioid problem cannot simply be to stop using them. To do so would be to trade one crisis (an opioid crisis) for another (a pain crisis)."
- In the face of debilitating pain, the guiding principle for doctors and other allied health professionals is "to do good" – beneficence that takes patients best interest as the treatment priority.
- In the end, we should acknowledge that the opioid crisis has presented a sophisticated moral dilemma that could not be resolved easily.



# Fentanyl

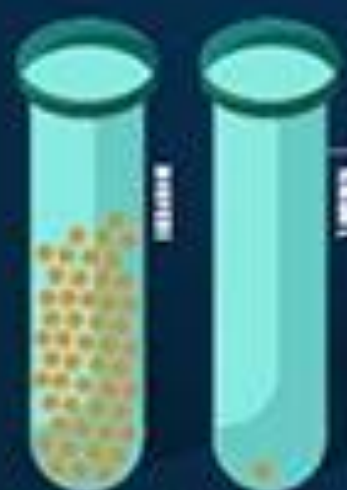
## •Fentanyl and Other Synthetic Opioids:

- primarily sourced from China and Mexico
- the most lethal category of opioids used in the United States
- Traffickers— wittingly or unwittingly— are increasingly selling fentanyl to users without mixing it with any other controlled substances and are also increasingly selling fentanyl in the form of counterfeit prescription pills
- Fentanyl suppliers will continue to experiment with new fentanyl-related substances and adjust supplies in attempts to circumvent new regulations imposed by the United States, China, and Mexico.

# FENTANYL: Overdoses On The Rise

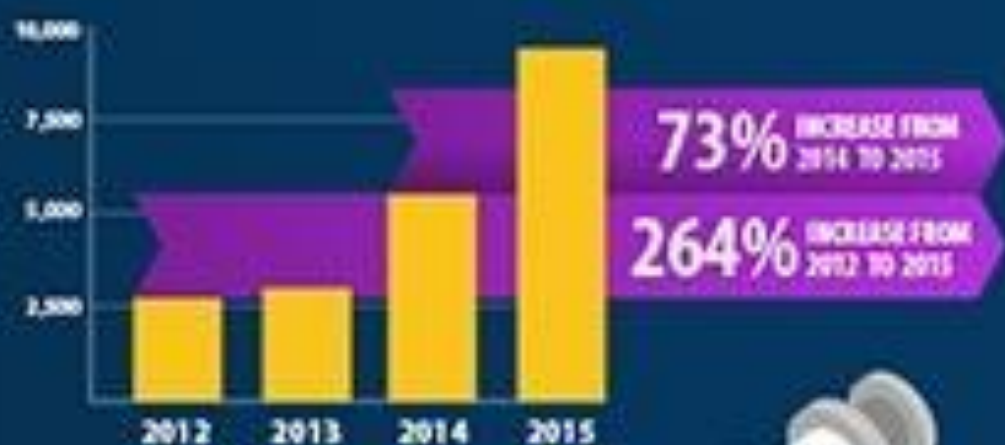


Fentanyl is a synthetic opioid approved for treating severe pain, such as advanced cancer pain. Illicitly manufactured fentanyl is the main driver of recent increases in synthetic opioid deaths.

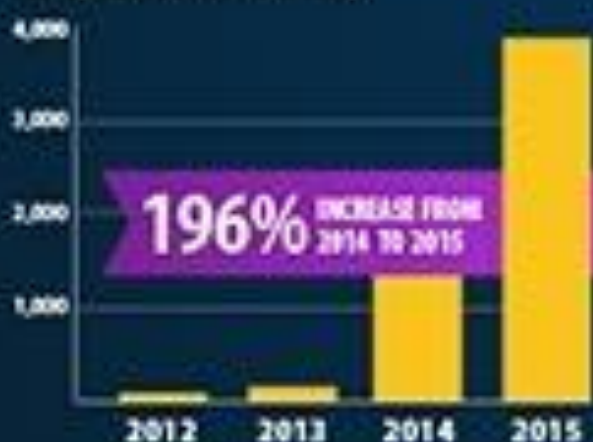


**50-100x  
MORE POTENT  
THAN MORPHINE**

## SYNTHETIC OPIOID DEATHS ACROSS THE U.S.



Ohio Drug Submissions Testing Positive for Illicitly Manufactured Fentanyl



## ILLICITLY MANUFACTURED FENTANYL

Although prescription rates have fallen, overdoses associated with fentanyl have risen dramatically, contributing to a sharp spike in synthetic opioid deaths.



# Fentanyl: where did it all go wrong?

## Fentanyl 27 FEBRUARY 2018 ANALYSIS

- Developed in early 1960's
- When created, most powerful opioid in world
- 100 x stronger than morphine
- FDA approval 1968
- Available for use on own in 1972
- From 1979 onward illicit forms developed in illegal labs
- 1980's transdermal patch developed
- 1998 Actiq approved, cancer pain only
- 2005-2006 off label use rampant
- 2013 street use of Fentanyl climbs
- 2015 Onsolis
- 2016 3<sup>rd</sup> wave of US Opioid Crisis
- Fentanyl deaths up 540% since 2016, China Issues

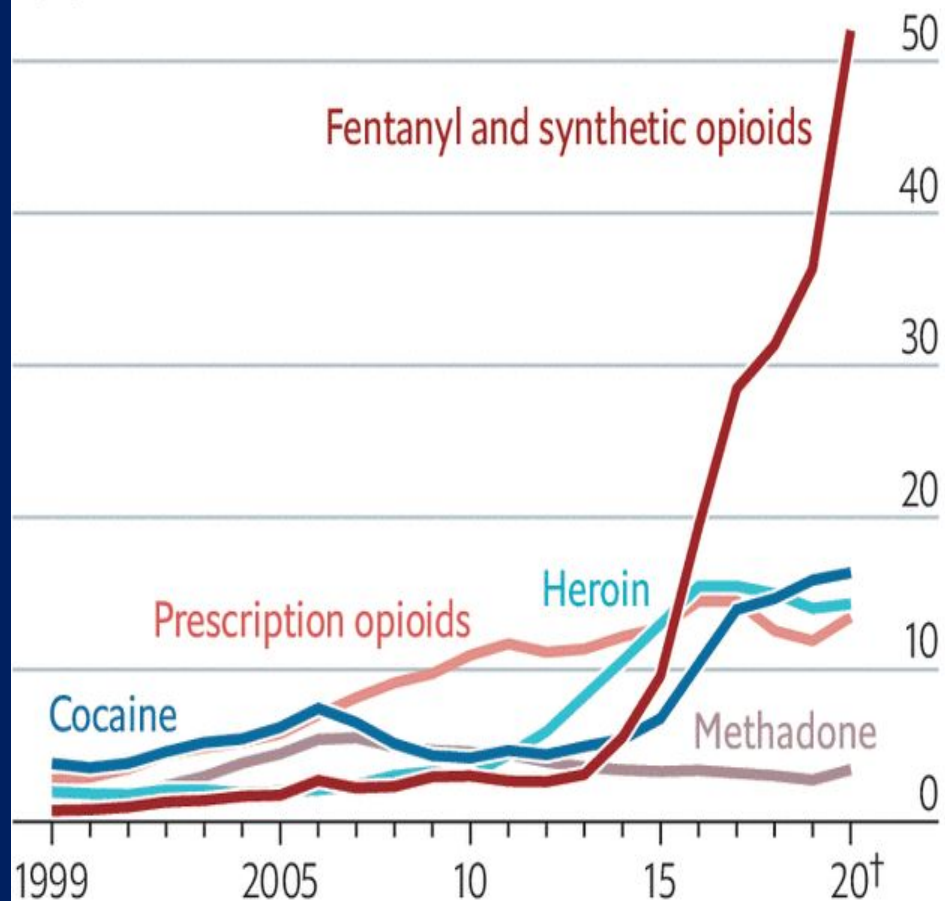




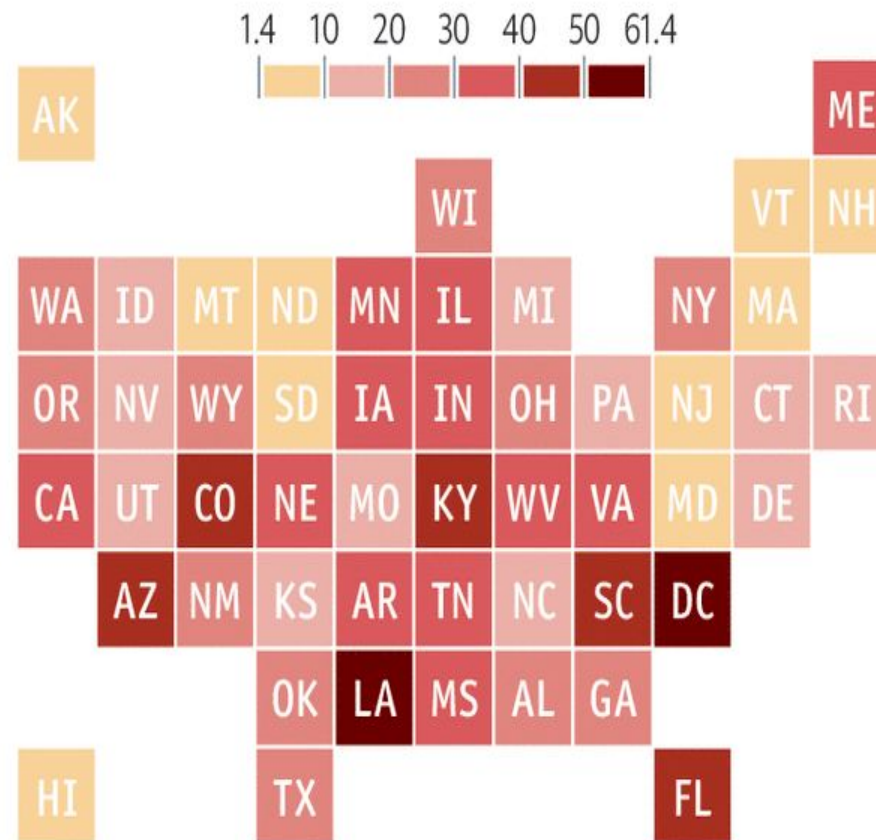
# The other epidemic

United States, drug overdose deaths\*

By year, '000



By state, 2020†, % change on a year earlier



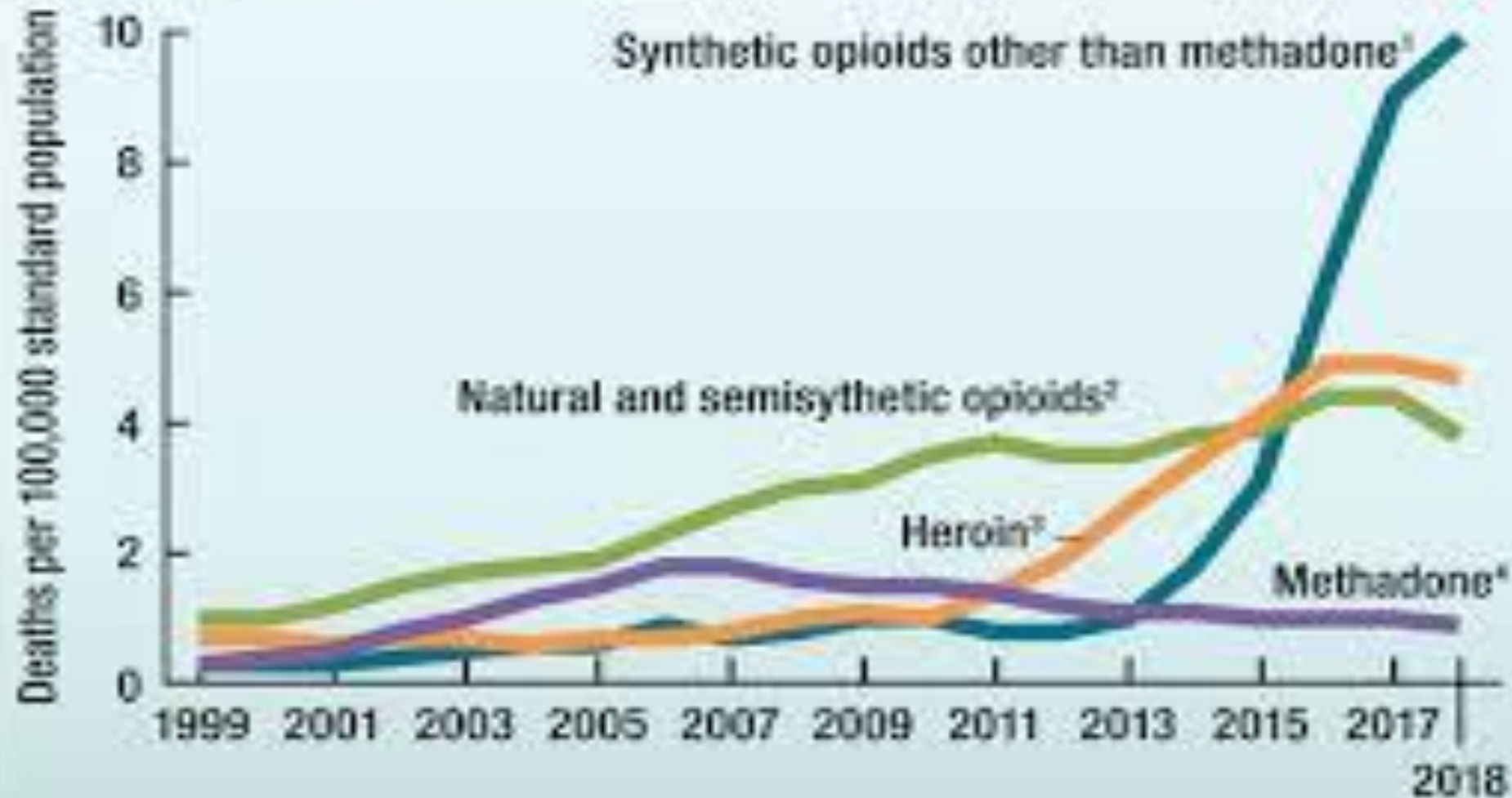
Source: Centres for Disease Control and Prevention

\*Deaths involving multiple opioids counted in each category  
 †12-month ending August 2020, predicted

# NCHS Data Brief ■ No. 356

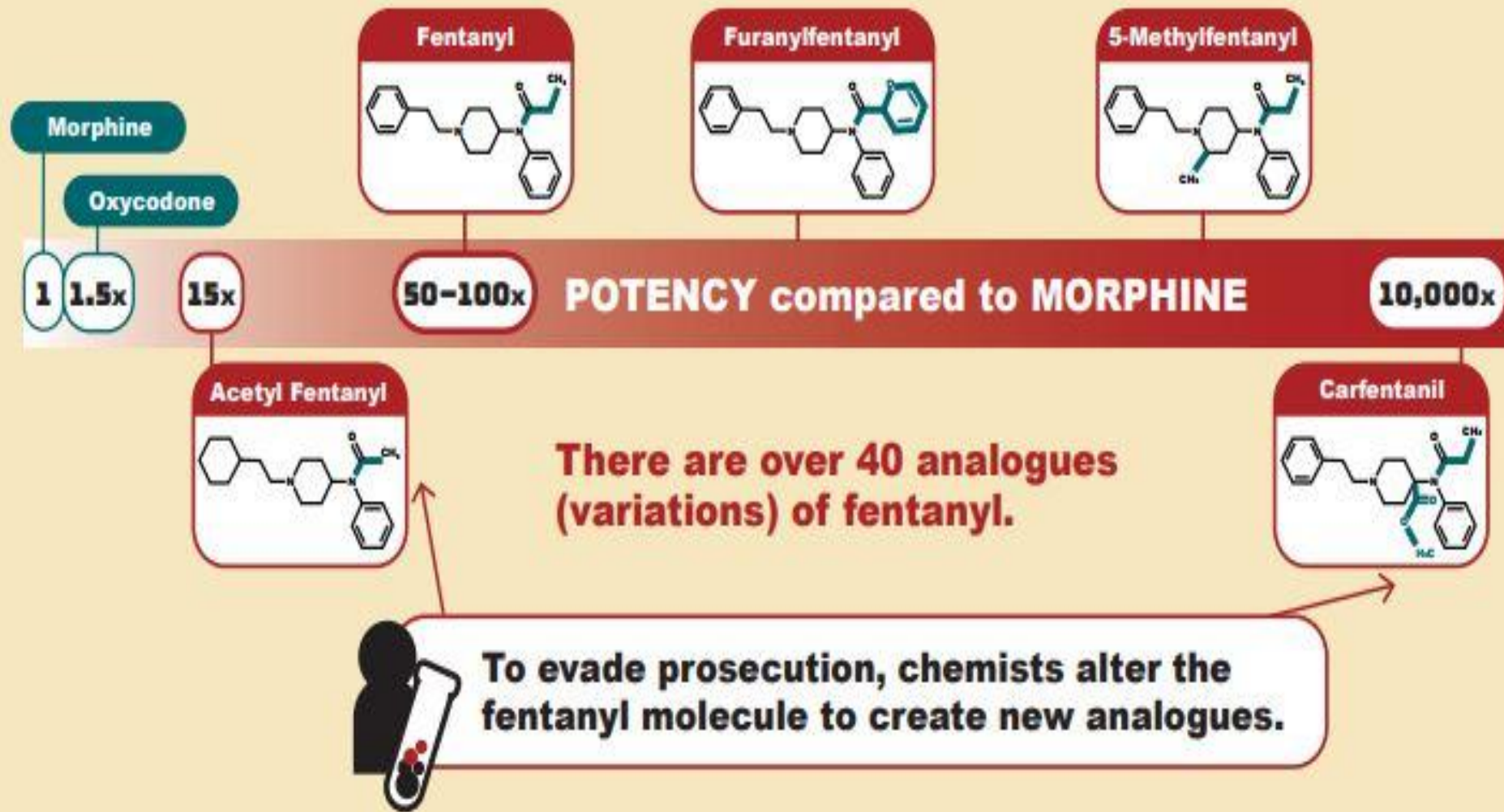
## January 2020

Age-adjusted drug overdose death rates involving opioids, by type of opioid: United States, 1999–2018



# What are fentanyl and fentanyl analogues?

Fentanyl is a synthetic opioid that is 50–100 times more potent than morphine. Doctors prescribe fentanyl in medical settings, but drug traffickers manufacture black market fentanyl and sell it illegally.





# Fentanyl is not just deadly to users.



**Several law enforcement and first responders have overdosed during investigations.**

**In 2016, the DEA urged officers to limit drug testing to lab settings because of the possibility of exposure.**

**Accidental inhalation or ingestion of just a few grains is enough to cause an overdose.**



# Diversion

- Drug **diversion** is a medical and legal concept involving the transfer of any legally prescribed **controlled substance** from the individual for whom it was prescribed to another person for any illicit use. ... The term comes from the "**diverting**" of the **drugs** from their original licit medical purpose.
- [Drug diversion - Wikipedia](#)
- [https://en.wikipedia.org › wiki › Drug diversion](https://en.wikipedia.org/wiki/Drug_diversion)
- In **2018**, doctors were involved in 42.46% of **diversion** incidents, making them the most common diverters, compared to 26.32% in 2017. Nurses were involved in 28.49% of incidents, positioning them as second most likely, as compared to 41% in 2017. Sep 10, 2018
-

# Addictive Disease in Healthcare Providers

- 4,011,911 professional nurses (RNs and LPNs) actively working in the United States  
(Henry J. Kaiser Family Foundation)
- 10% to 15% may be impaired or recovering from substance or alcohol addiction  
American Nurses Association (ANA)
- Ask yourself, is my colleague exhibiting unsafe or borderline unsafe behaviors or practices, or unethical behaviors that violate trust or care standards? Is he or she violating the nurse practice act?

Signs of impairment in the healthcare setting include:

- \* discrepancies on the medication reconciliation report or missing medication brought in by the patient on admission
- \* alterations in verbal or telephone orders
- \* unexplained "wastes" in the opioid count or discrepancies where withdrawals don't match documentation
- \* illegible, incomplete, or missed documentation
- \* immediately going to the bathroom after accessing the medication administration system
- \* patients seem to need more frequent medication, complain of ineffective pain relief, or even dispute receiving an opioid
- \* requests to change to a shift with less supervision
- \* inappropriate behavior or behavior that doesn't fit the situation
- \* nervousness, irritability, or excessive mood swings
- \* frequent absenteeism or tardiness
- \* use of mouthwash, mints, or gum to disguise breath odor

**SEPTEMBER 10, 2018**  
**18.7M pills lost due to**  
**healthcare employee misuse & theft**

- 18.7 million pills and \$164 million were lost due to drug diversion during the first half of 2018.
- This compares to Protenus' previous [report](#), which found 20.9 million pills and \$301.1 million were lost because of diversion incidents throughout all of 2017.
- [Protenus' report](#) is based on 179 incidents of medication tampering, theft or fraud reported in the news between January 1 and June 30, 2018.
- The Baltimore-based organization defined drug diversion as “the transfer of drugs by healthcare workers from a legal use to an illicit one.”
- 166% more legally prescribed opioids were stolen in 2018 than the year prior. 34% of incidents of diverted opioids happened in hospitals, followed by private practices, long-term care facilities and pharmacies. 67% by doctors and nurses.



# Drug Diversion is a Multi-Victim Crime

## Employee Risks:

- Health - morbidity and death
- Progression to illicit substances
- Risky behaviors
- Incarceration
- Loss of employment
- Revocation of license



## Patient Risks:

- Lack of pain control
- Infection risk
- Care by an impaired employee

## Health System Risks:

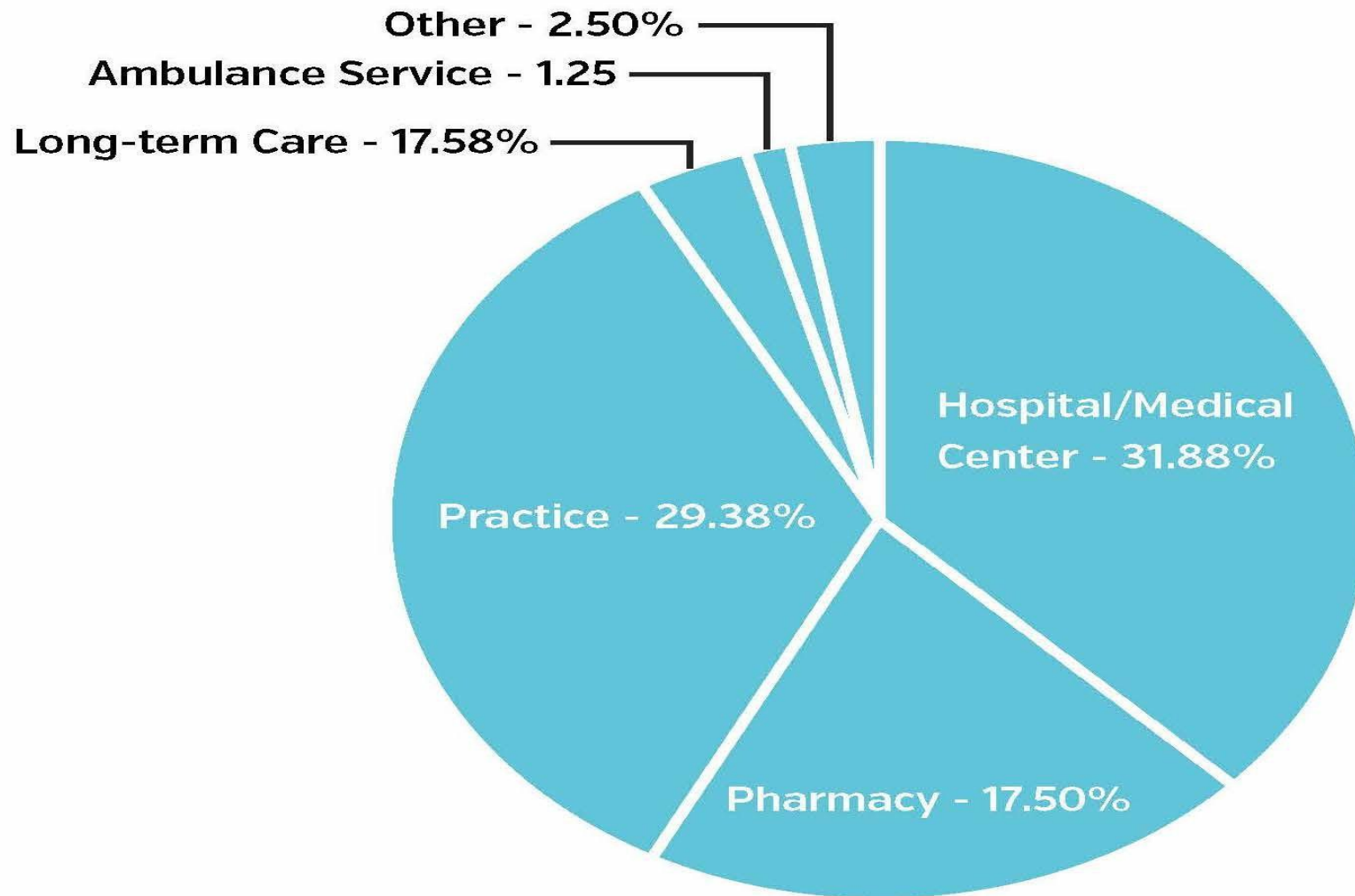
- Patient harm -- *CDC estimates ~30,000 people exposed to Hep C in last decade by infected hospital workers using narcotics intended for patients.*
- Civil and regulatory liability
- Reputation and brand at risk

\*



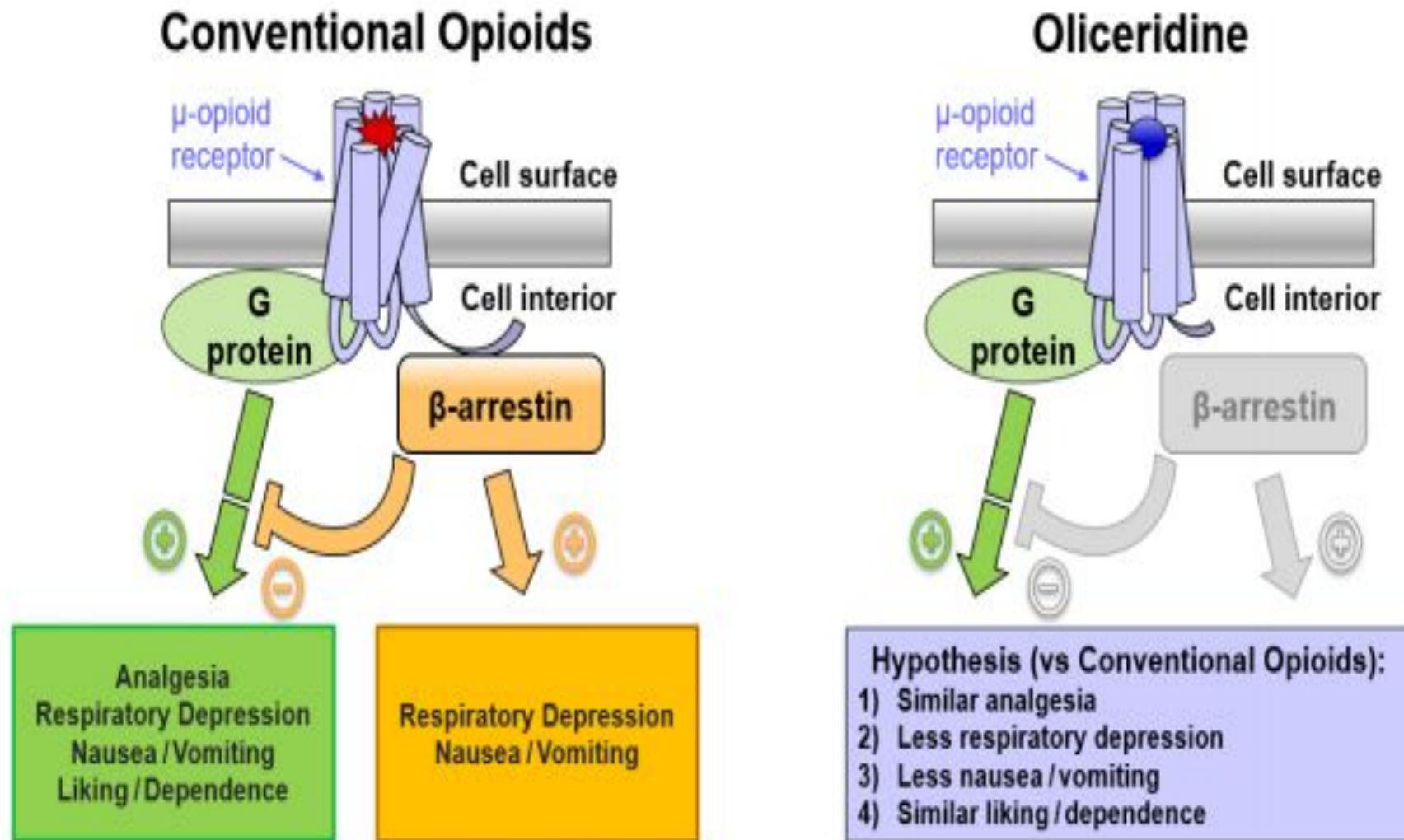
## 2019 DRUG DIVERSION DIGEST

47.2 million doses lost due to healthcare employee misuse and theft in 2018  
Protenus, Inc.



# Oliceridine

Figure 18:  $\mu$ -Opioid Receptor Binding of Conventional Opioids and Oliceridine



# Guidelines

- “Start low and go slow”
  - Use longer dosing intervals
  - Use smaller doses
- Pharmacologic therapy is most effective when combined with nonpharmacologic therapy
- Acetaminophen
  - First line therapy
  - Consider ATC dosing
  - 3-4 grams/24hrs from all sources
- Nonsteroidal anti-inflammatory drugs
  - Should be used with caution
  - Short term
- Opioid analgesics
  - Effective for relieving severe pain
  - Monitor for adverse effects



# Required Opioid Education

PA 246 of 2017 requires prescribers to provide Opioid Education using the state's or similar Start Talking Form when prescribing an Opioid drug. It does not have to be used when prescribing any other controlled substance that does not contain an Opioid.

AutoSave Off MDHHS - Saved to this PC Table Tools Linda Vanni

File Home Insert Draw Design Layout References Mailings Review View Help Design Layout Tell me what you want to do Share Comments

**OPIOID START TALKING**  
**(MUST BE INCLUDED IN THE PATIENT'S MEDICAL RECORD)**  
Michigan Department of Health and Human Services

Patient Name [REDACTED]		Date of Birth [REDACTED]
Name of Controlled Substance containing an Opioid [REDACTED]		
Dosage [REDACTED]	Quantity Prescribed (For a minor, if signature is not the parent or guardian, the prescriber must limit the opioid to a single, 72 hour supply) [REDACTED]	
Number of refills [REDACTED]		

**A controlled substance is a drug or other substance that the United States Drug Enforcement Administration has identified as having a potential for abuse. My provider shared the following:**

- The risks of substance use disorder and overdose associated with the controlled substance containing an opioid.
- Individuals with mental illness and substance use disorders may have an increased risk of addiction to a controlled substance. (Required only for minors.)
- Mixing opioids with benzodiazepines, alcohol, muscle relaxers, or any other drug that may depress the central nervous system can cause serious health risks, including death or disability. (Required only for minors.)
- For a female who is pregnant or is of reproductive age, the heightened risk of short and long-term effects of opioids, including but not limited to neonatal abstinence syndrome.
- Any other information necessary for patients to use the drug safely and effectively as found in the patient counseling information section of the labeling for the controlled substance.
- Safe disposal of opioids has shown to reduce injury and death in family members. Proper disposal of expired, unused or unwanted controlled substances may be done through community take-back programs, local pharmacies, or local law enforcement agencies. Information on where to return your prescription drugs can be found at

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# State Legislation

- Bill 274 Prohibits more than 7-day supply of opioids within a 7 day period for an acute condition
- Bill 270 Must have a bona fide prescriber-patient relationship to prescribe (delayed implementation)
- Bill 47 Requires methadone clinics & physician offices that dispense buprenorphine on premises report to MAPS

# Prescribing Recommendations

## UPDATED 2019

Procedure	Oxycodone* 5mg tablets	Procedure	Oxycodone* 5mg tablets
Laparoscopic Cholecystectomy	10	Hysterectomy – Vaginal, Lap/Robotic, or Abdominal	15
Open Cholecystectomy	15	Cesarean Section	15
Appendectomy – Lap or Open	10	Breast Biopsy or Lumpectomy	5
Hernia Repair – Major or Minor	10	Lumpectomy + Sentinel Lymph Node Biopsy	5
Colectomy – Lap or Open	15	Sentinel Lymph Node Biopsy Only	5
Ileostomy/Colostomy Creation, Re-siting, or Closure	15	Wide Local Excision ± Sentinel Lymph Node Biopsy	20
Open Small Bowel Resection or Enterolysis	20	Simple Mastectomy ± Sentinel Lymph Node Biopsy	20
Thyroidectomy	5	Modified Radical Mastectomy or Axillary Lymph Node Dissection	30
Sleeve Gastrectomy	10	Carotid Endarterectomy	10
Prostatectomy	10	Total Hip Arthroplasty	30
Laparoscopic Anti-reflux (Nissen)	10	Total Knee Arthroplasty	50
Laparoscopic Donor Nephrectomy	10	Dental	0
Cardiac Surgery via Median Sternotomy	15		

\*The recommendations remain the same if prescribing hydrocodone 5mg

# Symptoms of Opioid Withdrawal

- The usual signs
- June's example: patient moved from ICU to the floor
- Overdose victims, after being given Narcan at home by first responders refusing to go to hospital because of Covid----additional doses of Narcan left in the home

# Weaning/Tapering

Opioid naïve post-operative patients

- 1-2 weeks duration of opioids
- 20-25% reduction of discharge dose every 1-2 days

Chou et al, 2016

Problem with new acute pain prescribing guidelines

CDC guidelines, for chronic pain (stable cancer)

- 90 MME max dose, “Say what!!??!!”
- 5-10% per week, sometimes per month

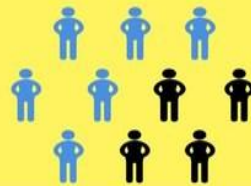


# Reversal Agents

## Emergency Care and the Nation's Opioid Crisis



Nearly **9 in 10** emergency physicians reported the number of patients seeking opioids has increased or remained the same during the past year.



Nearly **6 in 10** reported the detox or rehab facilities were rare or not accessible.

Of all patients who were treated with Naloxone:



.....**10%** of patients treated with Naloxone **died within one year.**

.....Of those, **HALF died within one month.**

"Virtually every emergency physician has seen firsthand the tragedy of opioid addiction," said Paul Kivela, MD, FACEP, president of ACEP. "The consequences of this epidemic are playing out in the nation's emergency departments."



This survey was conducted online between Sept. 21 and Oct. 2, 2017, with 1,261 emergency physicians. There was a response rate of 5.3 percent and a margin of error of 2.7.

American College of  
Emergency Physicians®  
ADVANCING EMERGENCY CARE

## Naloxone (pure opioid antagonist)

Extremely short half life, 1.07-1.53h, normally longer than opioid being reversed. In the inpatient hospital setting (excludes ER), intravenous route, an ampule of naloxone(0.4mg/ml is diluted with 9 mls of saline for a final concentration of 0.04mg/ml). Initial dose of 2-3 mls administered and then titrated for effect to reverse opioid sedation. Caution: Because of short life of naloxone, opioid half life is longer and additional doses of naloxone maybe required. Patient must be continually monitored.



## US approves high-dose opioid reversal nasal Spray from Hikma

Kloxxado 8 mgs. of nasal naloxone

## Flumazenil (benzodiazepine receptor antagonist)

Reversal agent for benzodiazepines, binds to benzodiazepine receptors, enhances GABA effects. IV route, 1 mg. q 2-3 minutes < 60 yo, max, 2.5 mg/dose. >60 yo max dose 1.5 mg/dose. epocrates, athenahealth service (2018)



# **MS tweaks opioid proposal after backlash**

**The agency had received pushback on a proposal that would have meant a prescription for high doses of opioids (90 milligrams of morphine per day or more) automatically wouldn't be filled and the patient would need special permission from their private insurance company in order to receive the medication.**

# Prescription Drug Monitoring Program



Pharmacies

Health Care Providers

State Insurance Programs

Healthcare Licensure Boards

State Health Department

Law Enforcement



**Table I. Schedules of Controlled Substances within the CSA.<sup>3,4</sup>**

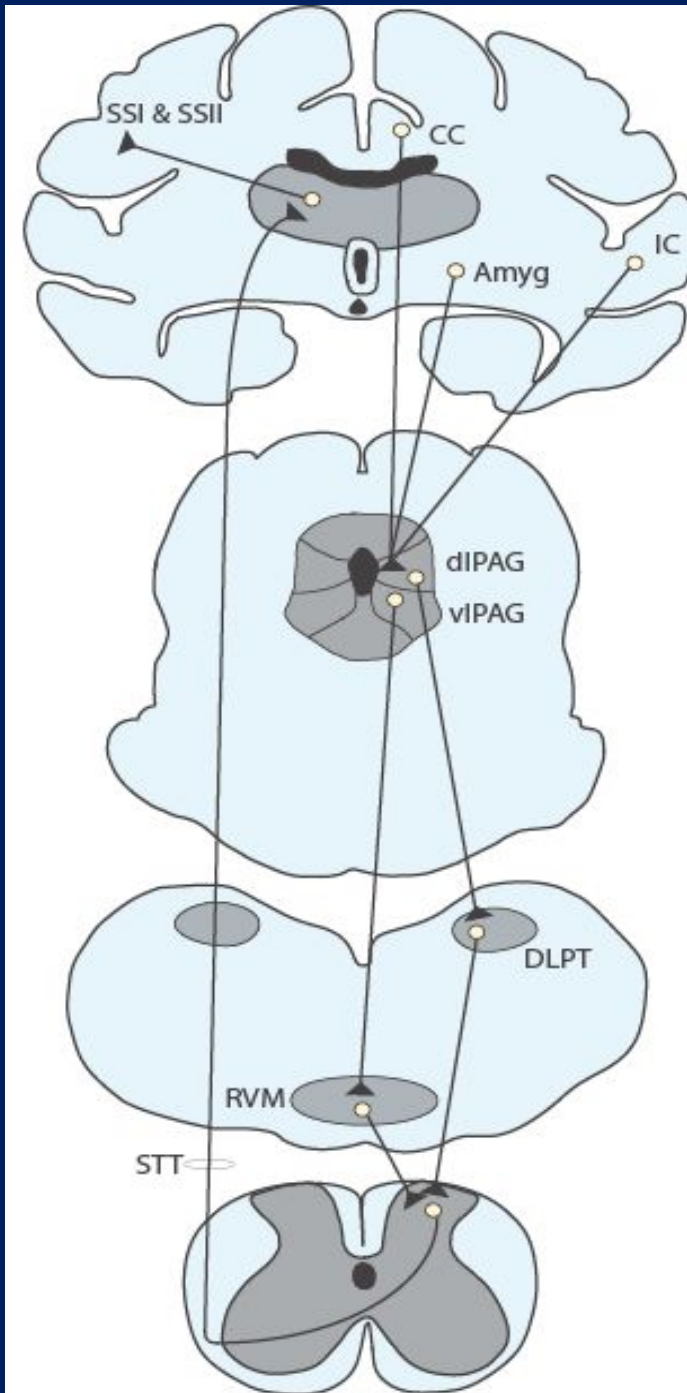
<b>Schedule</b>	<b>Definitions</b>	<b>Examples</b>
Schedule I	No accepted medical use with a lack of accepted safety and high abuse potential; medications within this schedule may not be prescribed, dispensed, or administered for medical use	Heroin, peyote, ecstasy, lysergic acid diethylamide (LSD)
Schedule II	High abuse potential with severe psychological or physical dependence; however, these medications have an accepted medical use and may be prescribed, dispensed, or administered	Morphine, codeine, hydromorphone, methadone, oxycodone, fentanyl, methylphenidate, amphetamine, pentobarbital, combination products with < 15 mg of hydrocodone per dosage unit (eg, Vicodin)
Schedule III	Abuse potential less than Schedules I or II but more than Schedule IV medications; abuse may lead to moderate or low physical dependence or high psychological dependence	Products with < 90 mg of codeine per dosage unit (eg, Tylenol with codeine), dronabinol, anabolic steroids, ketamine
Schedule IV	Abuse potential less than Schedule III but more than Schedule V medications	Propoxyphene, various benzodiazepines, sibutramine
Schedule V	Medications with the least potential for abuse among the controlled substances	Robitussin AC, Phenergan with codeine, pregabalin

# Origin of Opioids

- **Naturally occurring opiates:**
  - Morphine, codeine
- **Semi-Synthetics:**
  - Hydrocodone, oxycodone, hydromorphone
- **Synthetics:**
  - Fentanyl, methadone, meperidine
  - \*\*\*Pseudoallergies: flushing, itching, hives (increase in release of histamine, not antibodies)
  - True Allergy: severe hypotension, swelling of tongue, face, lips, rash, difficulty breathing

(DeDea, L., JA APA, Jan. 2012)

# Opioids: Central



- Increased expression after tissue injury
  - Spinal Cord
  - Brainstem
- Opioids are more effective after inflammation
- Increased central inhibition after inflammation
- Tested in animals

(Sluka, K. 2013. Pain Mechanisms, University of Iowa, Neuroscience)

# Schedule II (C-II)

- High potential for abuse & dependence
- Not currently e prescribed
- Written on tamper proof paper
- Outpatient Rx must be in writing
- Emergency orders may be phoned in; written provided within 72 hours
- No refills allowed

codeine (single)

Fentanyl

meperidine

methylphenidate

oxycodone

tapentadol

dextroamphetamine

hydromorphone

methadone

morphine

pentobarbital

hydrocodone ER & combo

# Opioid Therapy

- Morphine is considered the “Gold Standard”
- 1:300 rule morphine conversion
  - 1 mg of intrathecal morphine = 10 mg of epidural morphine = 100 mg of intravenous morphine = 300 mg of oral morphine  
(This is due to first pass effect)
- When utilizing equianalgesia chart make sure to take into account incomplete cross tolerance due to genetic variances
- There are several applications that can assist in conversion from one opioid to another

# OPIOIDS

## DOSING ISSUES

- Opioids undergo first pass metabolism in the liver, so oral doses are higher than injectable. Potencies vary from one agent to another, also, which must be considered when converting a patient to a different opioid. (Refer to equianalgesic table)
- fentanyl patch 25mcg/hr is roughly equivalent to 50mg/24hrs of oral morphine.

# Dosing Long-Acting Opioids

- Treat patient with immediate-release opioids (morphine, oxycodone) for 48 hours to learn the average daily dose requirement
- Approximately  $\frac{2}{3}$  of estimated daily dose should be prescribed as sustained-release opioid preparation
- Provide supplementary doses of immediate-release opioid for breakthrough pain

# Episodic Pain

- *Breakthrough* is a transitory flare of pain superimposed on an otherwise controlled stable pain syndrome.
- *Incident* pain is predictable 'episodic pain' caused by a physical or psychosocial-spiritual stimulus
- *'End of dose' failure* - long acting opioid does not last expected duration



# Breakthrough Pain

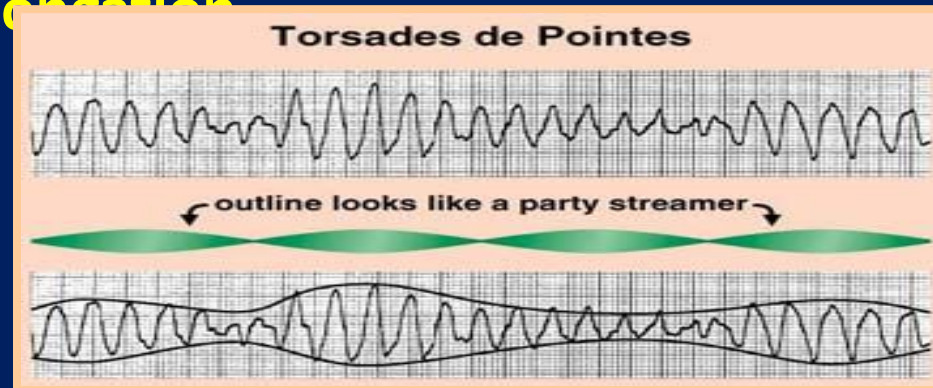
- Doses should be equivalent to about 10%-20% of the 24-hour total dose
- Doses may be given every 2 hours as needed
- Doses of short acting opioid may be taken at same time as sustained-release opioid
- Do not use sustained-release opioid for breakthrough pain
- [www.medscape.com/viewprogram/8253](http://www.medscape.com/viewprogram/8253)

# Federal Regulation

- Prevention of withdrawal in opioid addiction
  - Special annual registration with DEA
  - Use only in an established addiction treatment program
  - Maintenance patients may continue tx when admitted to acute care facility
- Treatment for pain
  - Any clinician licensed to prescribe Schedule II drugs may prescribe methadone for pain

# Methadone Black Box Warning

- Deaths during initiation and conversion from other opioids
- Respiratory depression – chief hazard
- Use of concomitant sedatives including alcohol
- Self-titration – iatrogenic overdose
- QTc prolongation



# Breast Milk Issues

Pump & Dump

Breast Milk for Sale



# Schedule IV (C-IV)

- Less abuse potential than C-III with minimal liability for dependence
- Outpatient Rx can be refilled 6 times within 6 months from date of issue
- Telephone orders acceptable

alprazolam	butorphanol	chloral hydrate
codeine (elixir)	diazepam	diphenoxin/atropine
lorazepam	pentazocine	sibutramine
zaleplon	zolpidem	tramadol (8/18/14)

# Schedule V (C-V)

- Minimal potential for abuse
- Number of refills determined by prescriber
- Some products (cough suppressants, antidiarrheals) may be available without a prescription
  - buprenorphine      diphenoxylate/atropine
  - pregabalin (Lyrica)

As of 1/14/19, per State of Michigan, gabapentin  
Schedule V



# CDC Recommendations Regarding Morphine Milligram Equivalents (MMEs)

## CALCULATING TOTAL DAILY DOSE OF OPIOIDS FOR SAFER DOSAGE

**Higher Dosage, Higher Risk.**

Higher dosages of opioids are associated with higher risk of overdose and death—even relatively low dosages (20-50 morphine milligram equivalents (MME) per day) increase risk. Higher dosages haven't been shown to reduce pain over the long term. One randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy (with average final dosage 52 MME) and maintenance of current dosage (average final dosage 40 MME).

Dosages at or above 50 MME/day increase risks for overdose by at least **2x** the risk at <20 MME/day.

**WHY IS IT IMPORTANT TO CALCULATE THE TOTAL DAILY DOSAGE OF OPIOIDS?**

Patients prescribed higher opioid dosages are at higher risk of overdose death.

In a national sample of Veterans Health Administration (VHA) patients with chronic pain receiving opioids from 2004–2009, patients who died of opioid overdose were prescribed an average of 98 MME/day, while other patients were prescribed an average of 48 MME/day.

Calculating the total daily dose of opioids helps identify patients who may benefit from closer monitoring, reduction or tapering of opioids, prescribing of naloxone, or other measures to reduce risk of overdose.

### HOW MUCH IS 50 OR 90 MME/DAY FOR COMMONLY PRESCRIBED OPIOIDS?

<b>50 MME/day:</b>	<b>90 MME/day:</b>
<ul style="list-style-type: none"> <li>50 mg of hydrocodone (10 tablets of hydrocodone/acetaminophen 5/300)</li> <li>33 mg of oxycodone (~2 tablets of oxycodone sustained-release 15 mg)</li> <li>12 mg of methadone (&lt;3 tablets of methadone 5 mg)</li> </ul>	<ul style="list-style-type: none"> <li>90 mg of hydrocodone (9 tablets of hydrocodone/acetaminophen 10/325)</li> <li>60 mg of oxycodone (~2 tablets of oxycodone sustained-release 30 mg)</li> <li>~20 mg of methadone (4 tablets of methadone 5 mg)</li> </ul>

U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

LEARN MORE | [www.cdc.gov/drugoverdose/prescribing/guideline.html](http://www.cdc.gov/drugoverdose/prescribing/guideline.html)

## HOW SHOULD THE TOTAL DAILY DOSE OF OPIOIDS BE CALCULATED?

- 1 DETERMINE** the total daily amount of each opioid the patient takes.
- 2 CONVERT** each to MMEs—multiply the dose for each opioid by the conversion factor. (see table)
- 3 ADD** them together.

**Calculating morphine milligram equivalents (MME)**

OPIOID (doses in mg/day except where noted)	CONVERSION FACTOR
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

*These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.*

**CAUTION:**

- Do not use the calculated dose in MMEs to determine dosage for converting one opioid to another—the new opioid should be lower to avoid unintentional overdose caused by incomplete cross-tolerance and individual differences in opioid pharmacokinetics. Consult the medication label.

**USE EXTRA CAUTION:**

- Methadone:** the conversion factor increases at higher doses
- Fentanyl:** dosed in mcg/hr instead of mg/day, and absorption is affected by heat and other factors

### HOW SHOULD PROVIDERS USE THE TOTAL DAILY OPIOID DOSE IN CLINICAL PRACTICE?

- Use caution when prescribing opioids at any dosage and prescribe the lowest effective dose.
- Use extra precautions when increasing to ≥50 MME per day\* such as:
  - Monitor and assess pain and function more frequently.
  - Discuss reducing dose or tapering and discontinuing opioids if benefits do not outweigh harms.
  - Consider offering naloxone.
- Avoid or carefully justify increasing dosage to ≥90 MME/day.\*

\* These dosage thresholds are based on overdose risk when opioids are prescribed for pain and should not guide dosing of medication-assisted treatment for opioid use disorder.

LEARN MORE | [www.cdc.gov/drugoverdose/prescribing/guideline.html](http://www.cdc.gov/drugoverdose/prescribing/guideline.html)

# Equianalgesic Dosing

## \*Incomplete Cross Tolerance

Drug	Oral(mg)	IV (mg)	Duration (h)
morphine	30	10	3 - 4
hydromorphone	7.5	1.5	3 - 4
oxymorphone	10	1	> 4
methadone	2-5	2-5	6 - 8?
codeine	200	130	3 - 4
oxycodone	20-30	-	3 - 4
hydrocodone	30	-	3 - 4
meperidine	300	100	2 - 3

# Genetic Polymorphism

UGT 1A1; involved in the glucuronidation of morphine, buprenorphine, and nalorphine.

UGT 1A3/1A4; glucuronidation of TCA.

UGT 2B7; glucuronidation of benzodiazepines.

Genetic polymorphism: population distribution for inheriting liver enzyme activity controlled by a single gene locus.

CYP 2C19 approx. 18% Japanese and African Americans, 3-5% of whites, poor metabolizers with higher plasma conc. of drug substrates.

Ex. Diazepam, imipramine, and phenytoin.

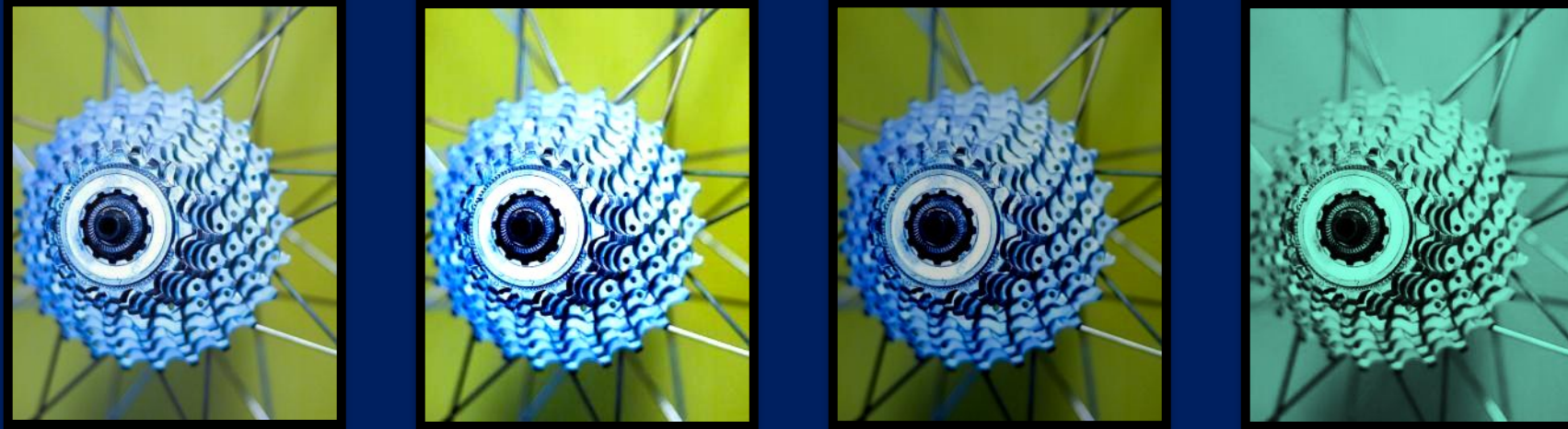
CYP2D6 7-10% whites, 1-4% African Americans inherit autosomal recessive allele on chromosome 22 results in poor metabolism with higher plasma conc., prolonged half lives. Ex. Codeine-cannot convert codeine to morphine, paroxetine, venlafaxine, fluoxetine, desipramine, imipramine, nortriptyline and oxycodone.

(Core, 2002), (Cleary & Hogan, 2007)

## \*\*\*FDA Drug Safety Communications

8/2012 Reviewing the safety of codeine administered post-tonsillectomy/adenoidectomy. 2/20/13 Black box warning issued. Deaths occurred in children ultra-rapid metabolizers with sleep apnea.

# Current Practice is Trial and Error



**50% of Beta Blockers work the first time <sup>2</sup>**

**60% of Depressed patients do not respond fully to the first prescribed Medication <sup>3</sup>**

**Methadone represents less than 5% of all opioid prescriptions, but is responsible for a third of the deaths. <sup>4</sup>**

**There is a 20 fold difference in the dosages of warfarin required to achieve therapeutic effect while the plasma concentrations vary 30-50 fold among individuals receiving the same dose. <sup>5</sup>**

<sup>2</sup> <http://publications.nigms.nih.gov/findings/mario/rightfit.asp>, <sup>3</sup> Science Daily; Dec 15, 2011.

<sup>4</sup> AAPM 25<sup>th</sup> Annual Meeting – Methadone. <sup>5</sup> Personalized Medicine (2005) 2(4), 325-337

# Patient Education

- Set pre-operative realistic expectations regarding pain by using scripting:
  - “Your pain control is very important to us. However, we also need to keep you safe.”
  - “It is normal to have pain after surgery.”
  - “It is our responsibility to keep your pain under control to allow you to do the things you need to do to get better and go home.”
  - “It is your responsibility to keep us informed about your pain, any side effects you experience, and if you are able to do the things you need to do to get better.”
- Communicate with patients about a realistic pain management goal for elective procedures
- Pain control is important, set goals, inform patients about risk benefit ratio and side effects when dosing medications
- Be a patient advocate, the safety of the patient is the first priority
- Education of patients is an important part of pain control



## Know the Facts About Opioid Pain Medication

We care about your comfort and believe that patients with pain deserve safe and effective pain management. Your provider has determined that an opioid pain medication is best for you. Opioid pain medications are available only by prescription and are used to treat moderate to severe pain. You should know that it is not always possible to completely relieve pain. It's important to have a realistic goal for pain relief depending on your condition.

### Opioid Generic Names:

Hydrocodone + Acetaminophen; Codeine + Acetaminophen; Oxycodone + Acetaminophen; Oxycodone; Fentanyl; Morphine; Hydromorphone; Methadone; Buprenorphine; Tramadol

While opioids can be effective in treating pain, there are also risks and side effects to opioid use. It is important for you to know how to safely take these medications. You should also be aware of other options for pain relief.

### Other Things to Try for Pain Relief:

- Meditation / Prayer
- Relaxation - relaxation breath exercise
- Music
- Heat and cold compresses
- Aromatherapy
- Guided imagery
- Distractions—watching TV or reading
- Movement & exercise

### What are the Risks and Side Effects of Opioid Use?

The use of prescription opioids can have side effects, even when taken as directed:

- Breathing problems. Call your doctor right away if you have slow, shallow, or trouble breathing.
- Sleep apnea (pauses in breathing while sleeping). May increase while on opioids.
- Constipation - You should take something to make your bowels move every day.
- Nausea, vomiting, and dry mouth
- Sleepiness, dizziness, lightheaded (may affect walking and working)
- Confusion
- Depression
- Low levels of testosterone that can result in lower sex drive, energy, and strength
- Itching and sweating

## Be Informed on Opioid Use

### While Taking Opioids:

- Do not break or crush your opioid medication unless advised to do so by your prescriber.
- **DO NOT** drive or operate heavy machinery until you know how opioids affect you.
- Do not take more than the maximum daily recommended dose of acetaminophen (<4000 mg).
- **Avoid alcohol.**
- If your doctor has recommended sleep apnea machine, please continue while on opioids.
- Tell your doctor if you are pregnant or breastfeeding - Opioids may harm your baby.
- Opioid toxicity is worse when taken with the medications below, unless specifically advised by your doctor.
  - Anxiety medications (benzodiazepines - such as Xanax or Valium)
  - Muscle relaxants (such as Soma or Flexeril)
  - Sleeping pills (such as Ambien or Lunesta)
  - Other prescription opioids (such as a pain patch)

### Safely Store Your Opioids and Dispose of Any Unused Pills!

- Store medications in a secure place and out of reach of others (this may include visitors, children, friends, and family).
- Safely dispose of unused medications: Find your community drug take-back program or your pharmacy mail-back program, dispose in a sealed bag with wet cat litter or used coffee grounds, or flush them down the toilet, following guidance from the Food and Drug Administration ([www.fda.gov/Drugs/ResourcesForYou](http://www.fda.gov/Drugs/ResourcesForYou)).

### Help Prevent Misuse and Abuse

- Only take your medication as prescribed. If your pain is not controlled with the prescribed dose or the medication is not lasting long enough, call your doctor.
- Never sell or share medications. — Never use another person's opioids. This is dangerous and a crime.
- Presently there is an opioid epidemic and there are new laws to control opioid prescribing and to prevent misuse and abuse.

### Know the Facts about Opioid Addiction

Tolerance, physical dependence, and increased sensitivity to pain are conditions that occur with prolonged opioid use.

Prescription opioids carry serious risks of addiction and overdose, especially with long term use. Misuse or abuse of this drug can lead to overdose and death. An opioid overdose, often marked by slowed breathing, can cause sudden death. Call 911.

➤ Naloxone is the antidote for opioid overdose. Contact your doctor or pharmacist to obtain.

### You are at higher risk of developing a dependence or an addiction to opioids if you:

- Have a history of depression or anxiety - Mental health conditions
- Have a history of using or abusing alcohol, tobacco or drugs (including prescription or street drugs).
- Have a history of long term (chronic) pain
- Take opioids for longer than a week
- Take more pills, more often than your doctor prescribes.

Thank you for keeping informed on Opioid Pain Medication Safety  
The Pain Management Resource Team





# Take Home Principles of Pain Management

- Accept patient's report of pain
- Individualize pain regime. Discuss goals and plans with patient and family.
- Combine pharmacologic and non-pharmacologic therapies.
- If opioids used, aggressively manage side effects (i.e. constipation).
- Persistent pain may require the use of both scheduled and as needed dosing of medications.
- Methadone should only be used by clinicians familiar with its use and risks.
- Before prescribing controlled substances, review the patient's PDMP report
- It is essential for healthcare providers to ethically treat patients with addictive disease related to assessing, treating and managing their pain.