

# **The Changing World of Pain Management 4/18/24**

**Linda Vanni, MSN, PMGT-BC, ACNS-BC, NP, AP-PMN  
Pain Management, Nurse Practitioner  
Professional Pain Education & Consulting, LLC**

# Objectives

Upon completion of this session, participants will be able to:

- 1) Describe how the opioid epidemic has changed pain management practice.
- 2) Discuss the evolution of pain management in the cancer patient.
- 3) Identify multimodal aspects of current pain management therapy.

# Hot Topics

- Mandatory Education on Pain
- The Opioid Epidemic
- COVID
- From strictly Self Report to Functional Status
- The Switch to Multi-Modal, Opioid Sparing
- Marijuana
- Integrative Therapies

# Continuing Education

- Twenty continuing professional development credits (CPD) every 2-year period. Audiologists and speech-language pathologists must obtain 1 CPD in pain and management in order to renew.

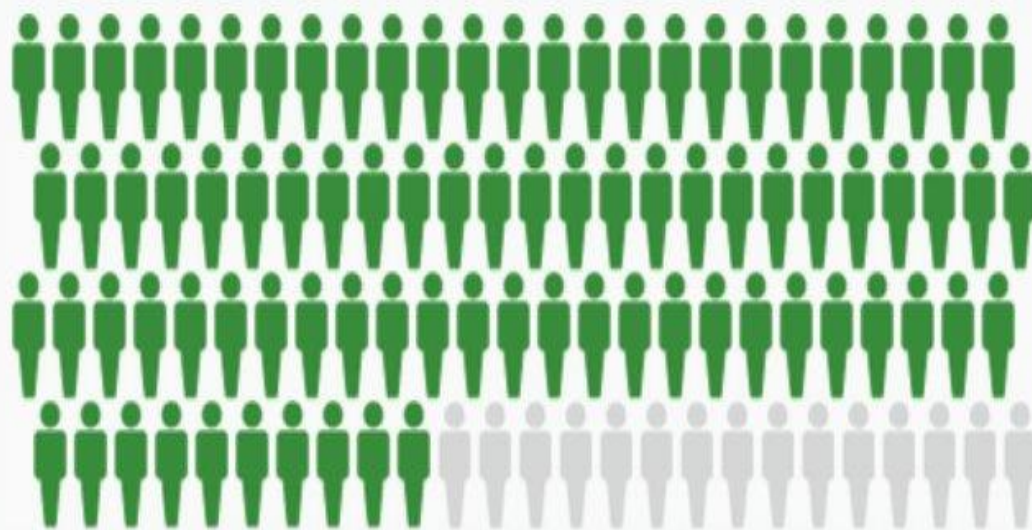
**76.9 billion is spent on the diagnosis and management of low back pain & an additional \$10-\$20 billion is attributed to economic losses in productivity each year.**

**Institute of Health Metrics & Evaluation, 2020**



# Cancer Among Adolescents and Young Adults (AYAs) (Ages 15-39)

## 5-Year Relative Survival Rate



Based on data from SEER 18 2011-2017. Gray figures represent AYAs who have died from cancer within 5 years of diagnosis. Green figures represent those who have survived 5 years or more.

[seer.cancer.gov/statfacts/](https://seer.cancer.gov/statfacts/)



**77 million baby boomers in the U.S. Baby boomers are defined as people born between 1946 and 1964 in the post-World War II era.**

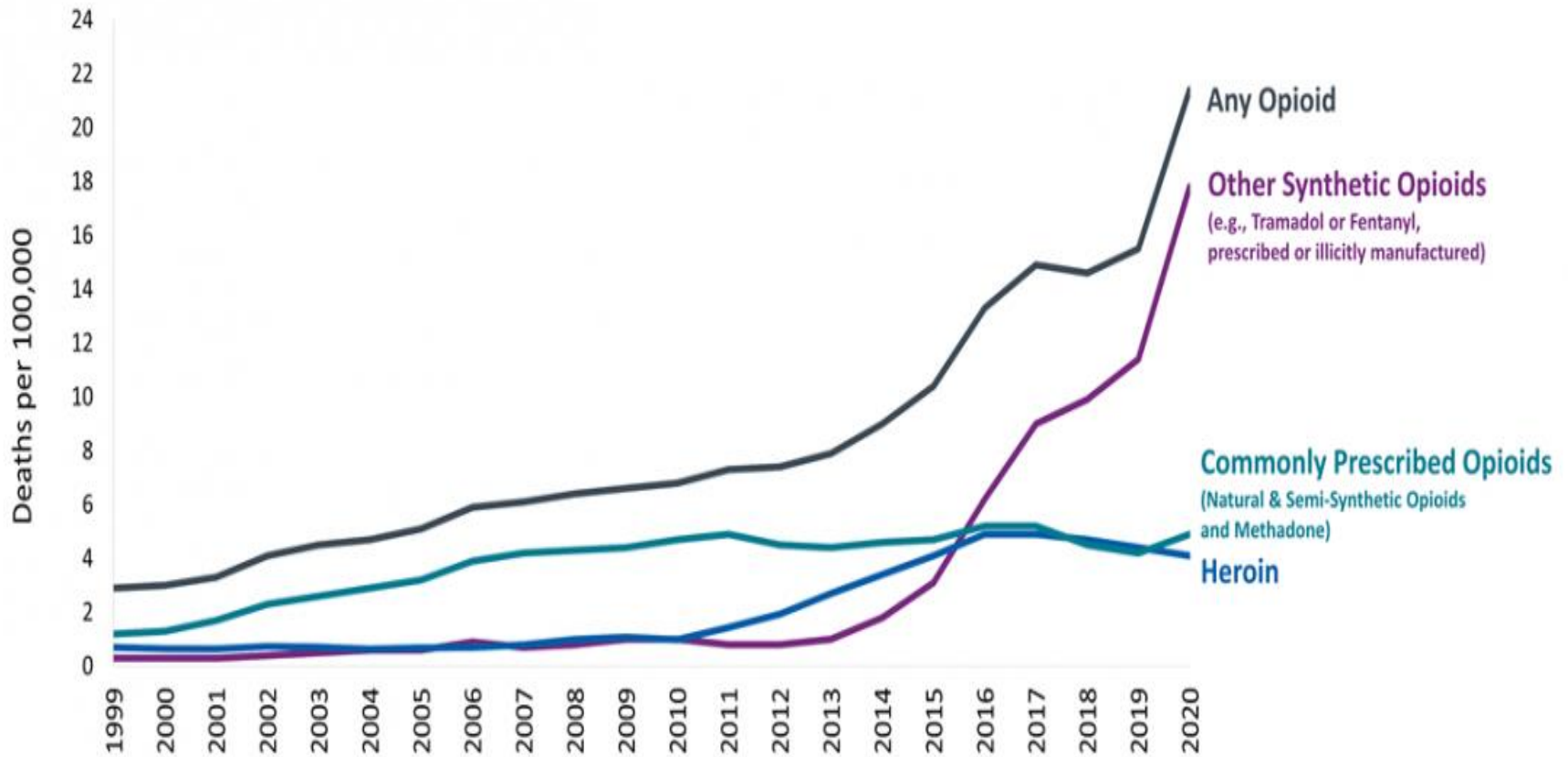
# CAUTION: Over-simplification of Complexities

The screenshot shows the top of a website with the title "PAIN MEDICINE NEWS" in large blue letters. Below the title is a navigation bar with links for SECTIONS, EDUCATION, MULTIMEDIA, MEETINGS, CLASSIFIEDS, and SUBSCRIPTION. There are two featured articles: "For TKA Patients, Use of Psychotropics Increases Consumption of Opioids" and "Can TAP Blocks Be an Alternative for Post-Cesarean Analgesia?". The main article is a commentary by Stephen E. Nadeau, MD, dated July 13, 2022, titled "Origins of Opioid Crisis More Complex Than Stated". The author's bio identifies him as a Professor in the Department of Neurology at the University of Florida. A second author, Richard A. Lawhern, PhD, is also listed as a Patient Advocate in Fort Mill, S.C.

- 2 separate populations
  - Consumers of illicit opioids
  - Patients prescribed opioids for CP
- 2016 CDC guideline
  - Reduced opioid prescribing
  - Opioid OD deaths doubled since then
- Rise in “Pill Mill” Rx since 2000-2012
  - Decreased after 2013
  - Pill Mill customers w/ OUD changed to more Illicits
- Chronic pain pts w/ very low OD rates
- Multiple factors raise OUD risk-not just exposure



# Three Waves of Opioid Overdose Deaths



↑  
Wave 1: Rise in Prescription Opioid Overdose Deaths

↑  
Wave 2: Rise in Heroin Overdose Deaths Started in 2010

↑  
Wave 3: Rise in Synthetic Opioid Overdose Deaths Started in 2013

SOURCE: National Vital Statistics System Mortality File.

# 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

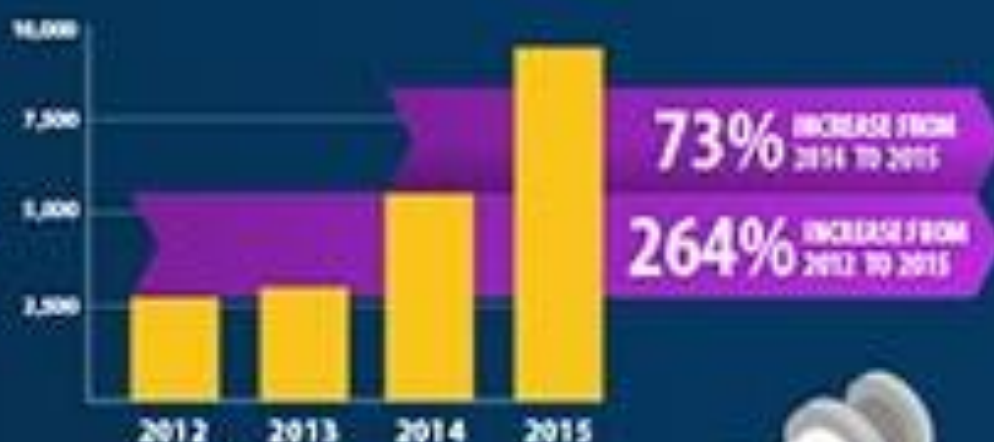


Fentanyl is a synthetic opioid approved for treating severe pain, such as advanced cancer pain. Illicitly manufactured fentanyl is the main driver of recent increases in synthetic opioid deaths.

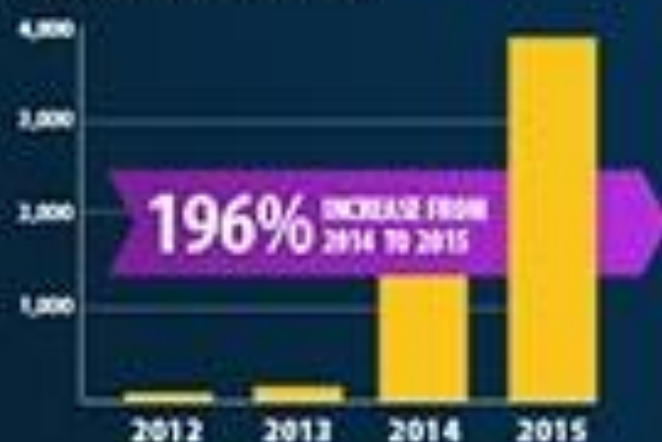


**50-100x  
MORE POTENT  
THAN MORPHINE**

## SYNTHETIC OPIOID DEATHS ACROSS THE U.S.

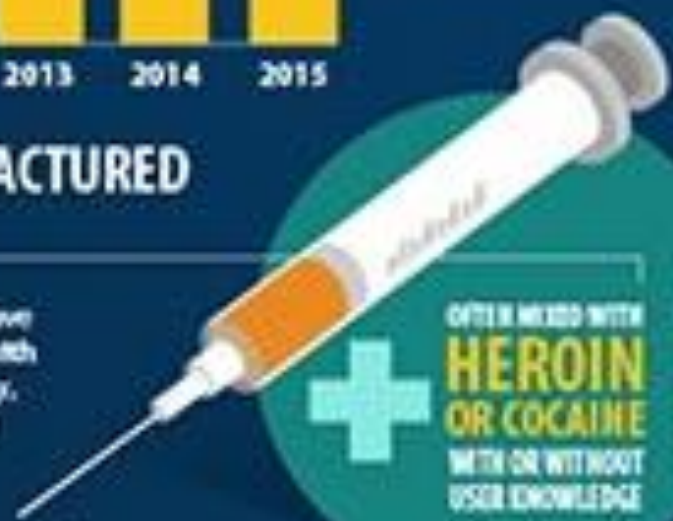


Ohio Drug Submissions Testing Positive for Illicitly Manufactured Fentanyl



## ILLICITLY MANUFACTURED FENTANYL

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



OFTEN MIXED WITH  
**HEROIN  
OR COCAINE**  
WITH OR WITHOUT  
USER KNOWLEDGE

# Xylazine

- Central nervous system depressant
- FDA approved for veterinary use only
- Causes dangerously low heart rate, respiratory rate and blood pressure
- Known on the street as “tranq”
- Often added to illicit opioids to lengthen euphoria
- Repeated use can lead to skin ulcers, abscesses and related complications
- Mediated by drug’s direct vasoconstricting effect on local blood vessels



# COVID-19 and the opioid crisis:

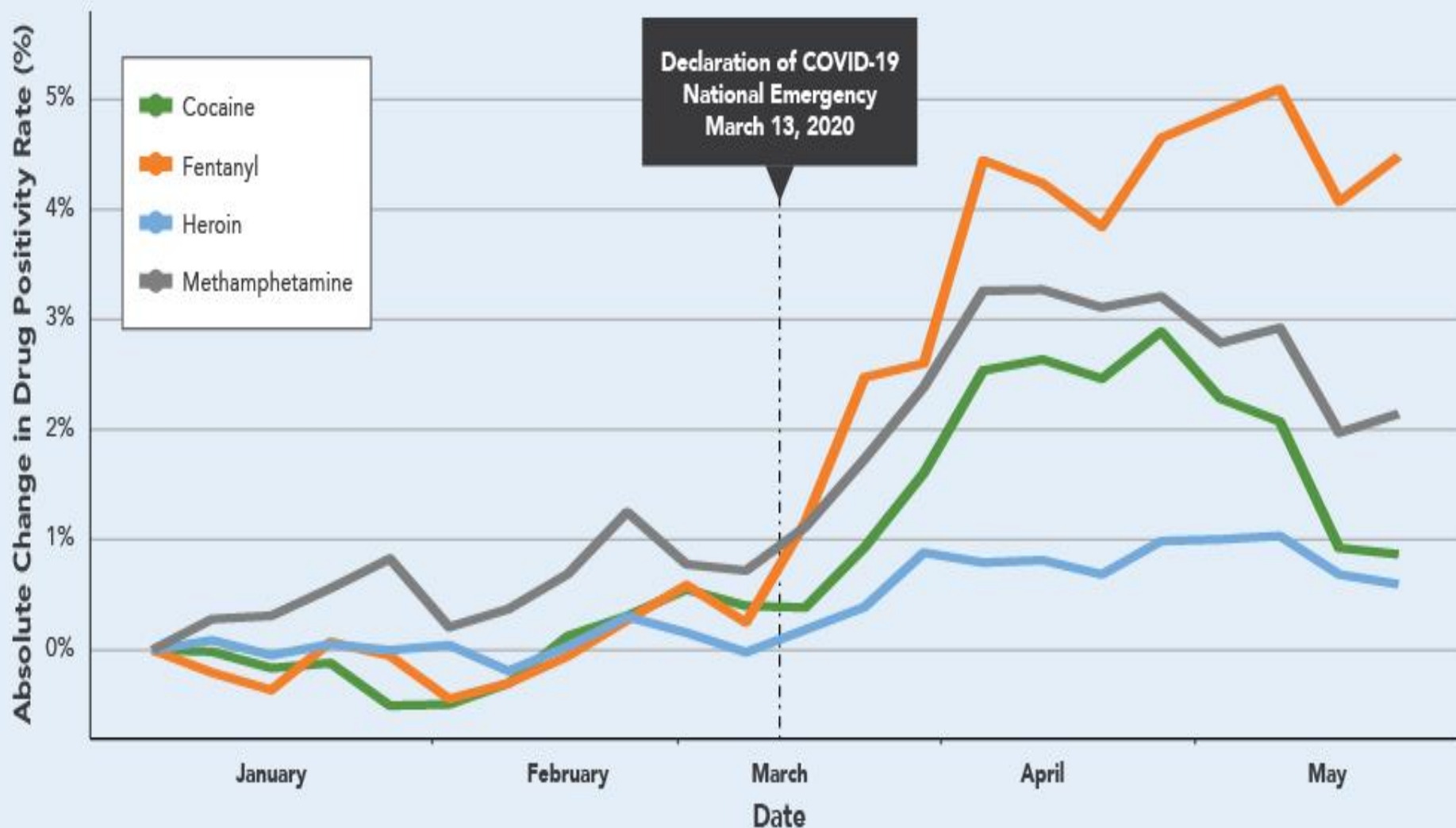
## When a pandemic and an epidemic collide

STACY WEINER, SENIOR STAFF WRITER

JULY 27, 2020

- Researchers say it's too soon to have definitive data on the pandemic's effects, but early numbers are concerning. So far, alcohol sales have risen by more than 25%. A recent analysis of 500,000 urine drug tests by Millennium Health, a national laboratory service, also showed worrisome trends: an increase of 32% for nonprescribed fentanyl, 20% for methamphetamine, and 10% for cocaine from mid-March through May. And suspected drug overdoses climbed 18% in the same period, according to a national tracking system run out of the University of Baltimore.

# Total Study Population Change in Unadjusted Positivity Rate for Cocaine, Fentanyl, Heroin and Methamphetamine



# **Long Hauler's Covid Symptoms**

**COVID-19 Public Health Emergency**

**Expires 5/11/2023**

**In-person visits will be required for  
controlled substance prescribing**

# US Agency Softens Opioid Prescribing Guidelines for Doctors

Mike Stobbe, Associated Press Published:  
November 3, 2022

- *The CDC no longer suggests trying to limit opioid treatment for acute pain to three days.*
- —The agency is dropping the specific recommendation that doctors avoid increasing dosage to a level equivalent to 90 milligrams of morphine per day.
- —For patients receiving higher doses of opioids, the CDC is urging doctors to not abruptly halt treatment unless there are indications of a life-threatening danger. The agency offers suggestions on tapering patients off the drugs.



# Research, Standards and Guidelines for Safe Clinical Practice

- AMA Opioid Task Force Helping Guide (August 2018 update)
- American Pain Society guidelines (2016)
- ANA Position Statement on Ethical Pain Management (2018)
- Numerous guidelines for special populations and conditions,
- ASPMN (2018)
- Revised Joint Commission pain standards (2018)
- CMS Guidelines, finalized (2018)

# 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

# Definition of Pain

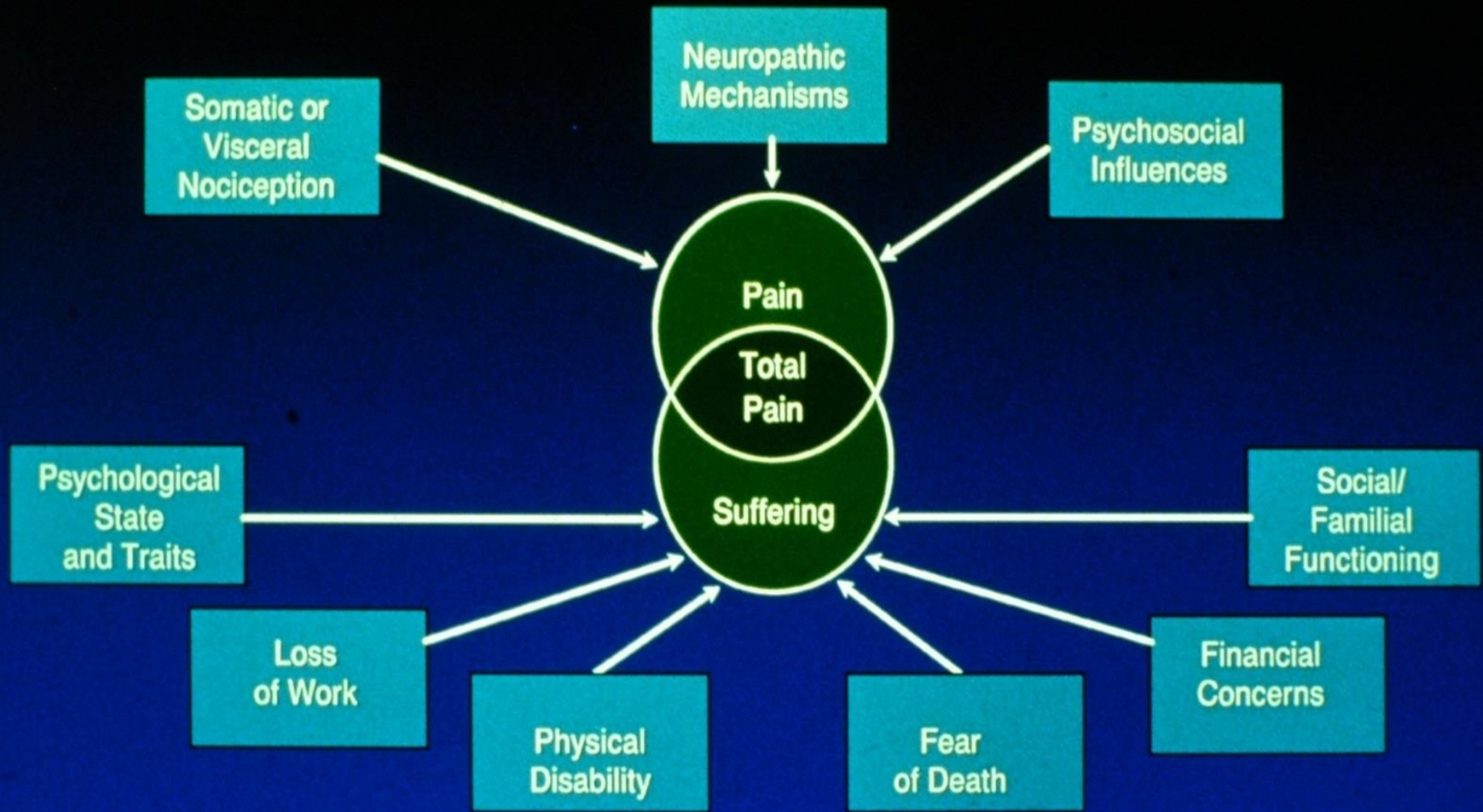
“Pain is whatever the experiencing person says it is, existing whenever he or she says it does.”

- Margo McCaffery, R.N., M.S., FAAN

# Assessment

- **The Problem with Pain-**
  - **No pain-o-meter**
  - **Cultural differences**
  - **Diversity in non-verbal reactions to pain, e.g. stoic, red cell disorder patients**
  - **If a patient has a specific surgery, should all those patients receive the same pain medication (ortho power plans)**
  - **We are influenced by our past experiences with patients**
  - **Our biases, i.e. patient has SUD**
  - **Purely subjective, typically measured with self-report scale 0-10**

# Multifactorial Nature of Pain



(Adapted from Portenoy, 1988)

# Assessment

- Allergies
- Opioid naïve versus opioid tolerant
- Previously effective pain medication
- Under lying medical conditions
- Sleep apnea/CPAP?/obese/neck circumference?
- Multiple surgeries
- History of issues
- Current medications (excellent clue)
- Red flag medications

# Assessment

- The gold standard of pain management assessment is the patient self report on a pain scale from 0 to 10
- The goal of pain management is an awake, alert, functional patient
- Determine if patient is opioid naïve or opioid tolerant

Opioid Naïve: Patients who do not meet the definition of opioid tolerant.

Opioid Tolerant: Patients who are taking at least 60 mg of oral morphine/day, 25 mcg transdermal fentanyl/hour, 30 mg oral oxyCODONE/day, 8 mg oral HYDROmorphone/day, 25 mg oral oxymorphone/day or an equianalgesic dose of another opioid for one week or longer.

- Set realistic expectations from the beginning, sit down with the patient, evaluate if the patient is currently having pain
- Nursing will document a pain score and perception of comfort in the patients electronic record for every patient
- Excellent pain management utilizes adjuvant therapies

# Chronic versus Acute Pain

- Pain in the inpatient setting can be categorized as one of the following: Acute, Chronic, or Acute on Chronic
- Treatment for the type of pain includes multiple modalities that cross over
- Chronic pain in the hospital setting is not something we can immediately affect, but something we must recognize
- We need to look at the patient's functional goals when creating a pain management plan
- Each patient's pain is unique, begin with a thorough assessment
- Patient descriptors will aid in the form of intervention based on pain type



# All about Function

## Pain rating scales

0 1 2 3 4 5 6 7 8 9 10

Numerical Rating Scale (NRS)

No pain Mild pain Moderate pain Severe pain

Visual Rating Scale (VRS)

No pain Visual Analogue Scale (VAS) Worst possible pain



0 1 2 3 4 5  
No hurt Hurts a little bit Hurts a little bit even more Hurts Hurts a whole lot Hurts worst more

Wong's Faces Scale

Note: VAS is usually a research tool

- Patient examinations in physical therapy include, but are not limited to, testing of muscle **function, strength, joint flexibility**, range of motion, **balance and coordination**, posture, respiration, skin integrity, **motor function**, quality of life, and **activities** of daily living.



- Occupational therapy practitioners enable people of all ages to live life to its fullest by helping them promote health, and prevent—or live better with—injury, illness, or disability.



- To all the healthcare professionals practicing in the Rehab specialty including nurses, case managers, physical therapists, occupational therapists, and social workers. You have my deepest respect and admiration!

# Use of Prescription Drug Monitoring Programs (PDMP)

- All 50 states up and running
- Reporting of all controlled substances, many in real time
- Practice patterns for usage varies by state
- Maybe integrated into EMR
- Many PDMPs auto calculate daily MME
- Ability to see multiple states

As of January 1, 2023, Michigan requires all prescriptions be transmitted electronically.

Prescribers are also required to complete prescription history checks through the **Michigan** Automated Prescription System (MAPS) before dispensing or prescribing opioids, benzodiazepines, barbiturates, or carisoprodol.

# gabapentin abuse

- Ohio Substance Abuse Monitoring Network issued alert, February 2017
- Fifth most prescribed drug in nation (GoodRx)
- Can enhance euphoria caused by opioids and stave off drug withdrawals
- Bypasses the blocking effects of medications used for addiction treatment, enabling patients to get “high” while in recovery (STAT, 2017)
- 1/5 of those abusing opioids misuse gabapentin (Addiction, 2016)
- 300 mg pill sells for as little as 0.75 cents on the street

# Sample Drug Report

Alice Testpatient, 118F

Powered by NarxCare

Narx Report Resources

Date: 08/28/2018

Testpatient, Alice

Linked Records

Name	DOB	ID	Gender	Address
Alice Testpatient	01/01/1900	1	Female	555 FAKE DR WICHITA KS 67203
Alice Testpatient	01/01/1900	2	Female	

Report Criteria

First Name	Last Name	DOB
Alice	Testpatient	01/01/1900

Risk Indicators

NARX SCORES

Narcotic Sedative Stimulant  
**271 110 000**

Explanation and Guidance

OVERDOSE RISK SCORE

**110**  
 (Range 000-999)

Explanation and Guidance

ADDITIONAL RISK INDICATORS (0)

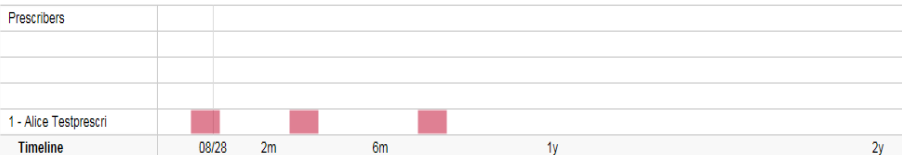
Explanation and Guidance

This NarxCare report is based on search criteria supplied and the data entered by the dispensing pharmacy. For more information about any prescription, please contact the dispensing pharmacy or the prescriber. NarxCare scores and reports are intended to aid, not replace, medical decision making. None of the information presented should be used as sole justification for providing or refusing to provide medications. The information on this report is not warranted as accurate or complete.

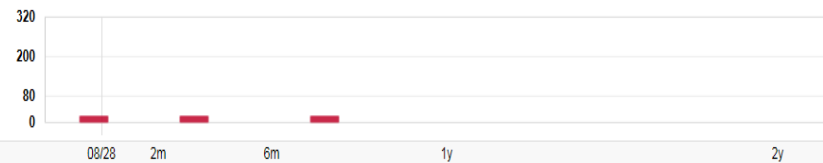
Graphs

RX GRAPH

Narcot  Sed  Stim  Othe



Morphine MgEq (MME)



\*Per CDC guidance, the MME conversion factors prescribed or provided as part of the medication-assisted treatment for opioid use disorder should not be used to benchmark against dosage thresholds meant for opioids prescribed for pain. Buprenorphine products have no agreed upon morphine equivalency, and as partial opioid agonists, are not expected to be associated with overdose risk in the same dose-dependent manner as doses for full agonist opioids. MME = morphine milligram equivalents. LME = Lorazepam milligram equivalents. mg = dose in milligrams.

Summary

Summary	Narcotics* (excluding buprenorphine):	Sedatives*	Buprenorphine*
Total Prescriptions: 3	Current Qty: 88	Current Qty: 0	Current Qty: 0
Total Prescribers: 1	Current MME/day: 18.00	Current LME/day: 0.00	Current mg/day: 0.00
Total Pharmacies: 1	30 Day Avg MME/day: 4.80	30 Day Avg LME/day: 0.00	30 Day Avg mg/day: 0.00

Rx Data

PRESCRIPTIONS

Total Prescriptions: 3  
 Total Private Pay: 3

Fill Date	ID	Written	Drug	Qty	Days	Prescriber	Rx #	Pharmacy	Refill	Daily Dose	Pymt Type	PMP
08/21/2018	2	08/21/2018	ACETAMINOPHEN-COD #3 TABLET	120	30	Al Tes	A00001	Ali (ZZ12)	0	18.00 MME	Private Pay	MI
05/07/2018	1	05/07/2018	ACETAMINOPHEN-COD #3 TABLET	120	30	Al Tes	A00001	Ali (ZZ12)	0	18.00 MME	Private Pay	MI
12/20/2017	1	12/20/2017	ACETAMINOPHEN-COD #3 TABLET	120	30	Al Tes	A00001	Ali (ZZ12)	0	18.00 MME	Private Pay	KS

\*Per CDC guidance, the MME conversion factors prescribed or provided as part of the medication-assisted treatment for opioid use disorder should not be used to benchmark against dosage thresholds meant for opioids prescribed for pain. Buprenorphine products have no agreed upon morphine equivalency, and as partial opioid agonists, are not expected to be associated with overdose risk in the same dose-dependent manner as doses for full agonist opioids. MME = morphine milligram equivalents. LME = Lorazepam milligram equivalents. mg = dose in milligrams.

PROVIDERS

Total Providers: 1

Name	Address	City	State	Zipcode	DEA
Alice Testprescriber	1111 FAKE ST	WICHITA	KS	67203	BR11111111

PHARMACIES

Total Pharmacies: 1

Name	Address	City	State	Zipcode	DEA
Alice's PHARMACY	1111 FAKE ST SEC A	WICHITA	KS	67202	ZZ1234567

# Neural Pathways of Pain

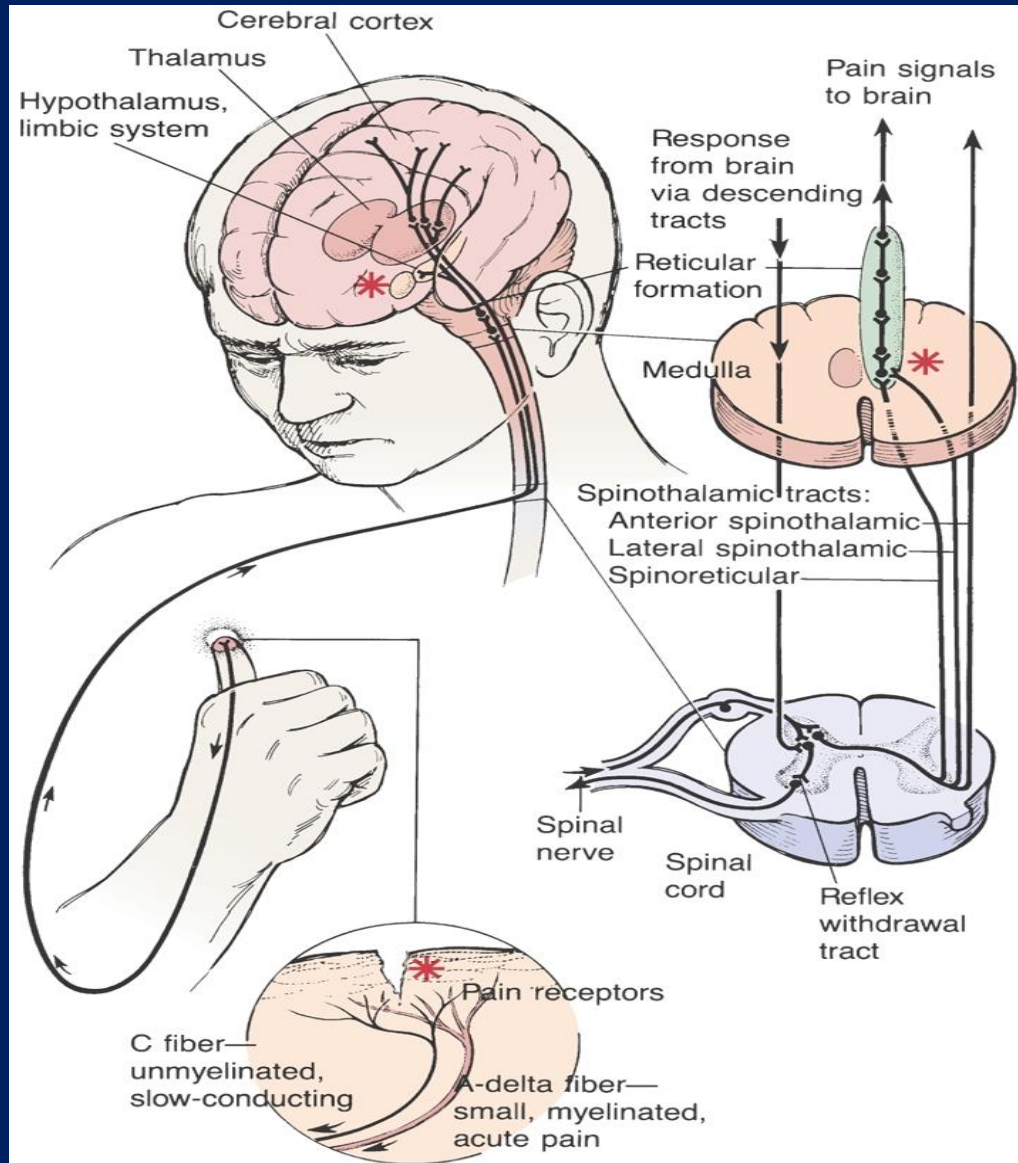


FIGURE 26.1 Neural pathways of pain. (Bullock, B.L. [2000]. *Focus on pathophysiology*. Philadelphia: Lippincott Williams & Wilkins.)

# Facilitating Transduction

- **Biochemical mediators: “Chemical Soup”**

**Prostaglandins**

**Bradykinins**

**Serotonin**

**Histamines**

**Cytokines**

**Leukotrienes**

**Substance P**

**Norepinephrine**

**Treating a specific type  
of pain  
with the wrong type  
of  
medication or therapy!**



# Different Types of Pain

- **Somatic** – localized pain in skin, muscle, bone described as aching, stabbing, throbbing
  - Therapies for somatic pain include NSAIDs (prostaglandin inhibitors), acetaminophen (works centrally), muscle relaxants, ice, and heat
- **Visceral** – non-localized pain in organs or viscera described as gnawing, cramping, aching or sharp
  - Therapies for visceral pain include opioids (occupies opioid receptors), and interventional therapies
- **Neuropathic** – pain caused by nerve damage described as sharp, numbness, burning or shooting
  - Therapies for neuropathic pain include antidepressants (inhibits norepinephrine and serotonin re-uptake), anticonvulsants (blocks voltage-dependent calcium channels), local anesthetics, and interventional therapies **caution: anticonvulsants can cause dizziness, potential for falls. Start low and go slow!**
  - Opioids are not the medication of choice for neuropathic pain
- **These types of pain can occur individually or in combination**

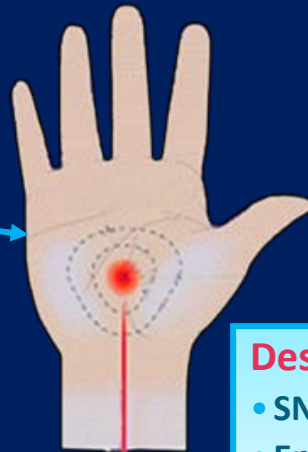
# Multimodal Pain Management Plan



# Multimodal Therapy: Clinical Advantages

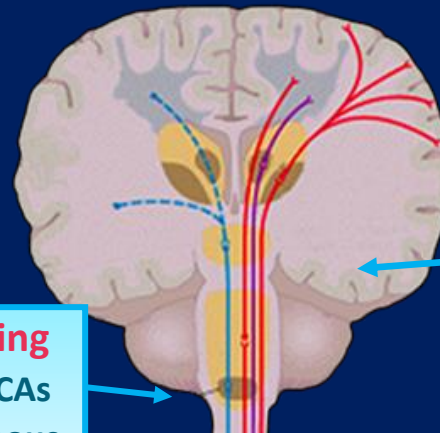
## Peripheral

- Local anesthetics
- Opioids
- Anti-inflammatory agents
- Capsaicin



## Descending

- SNRIs, TCAs
- Endogenous systems

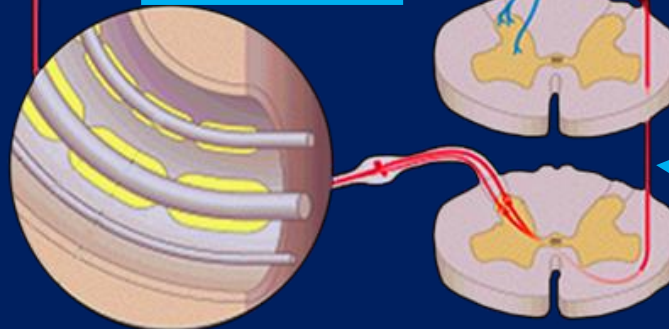


## Central

- Anticonvulsants
- Opioids
- $\alpha_2$ -agonist (clonidine)
- Acetaminophen

## Ascending

- Local anesthetics
- Anticonvulsants
- Opioids
- NMDA antagonists (ketamine)
- $\alpha_2$ -agonist (clonidine)



• Multimodal therapy provides a way to achieve balanced, safer pain therapy<sup>1</sup>

- Improved quality of analgesia<sup>2,3</sup>
- Fewer side effects<sup>2,3</sup>
- Better functional status<sup>4</sup>

1. Gottschalk A, Smith DS. *Am Fam Physician*. 2001;63:1979-1984, 1985-1986.

2. Tippana EM, et al. *Anesth Analg*. 2007;104:1545-1556.

34. Basse L, et al. *Brit J Surg*. 2002;89:446-453.

# Adjuvant Analgesic Medications

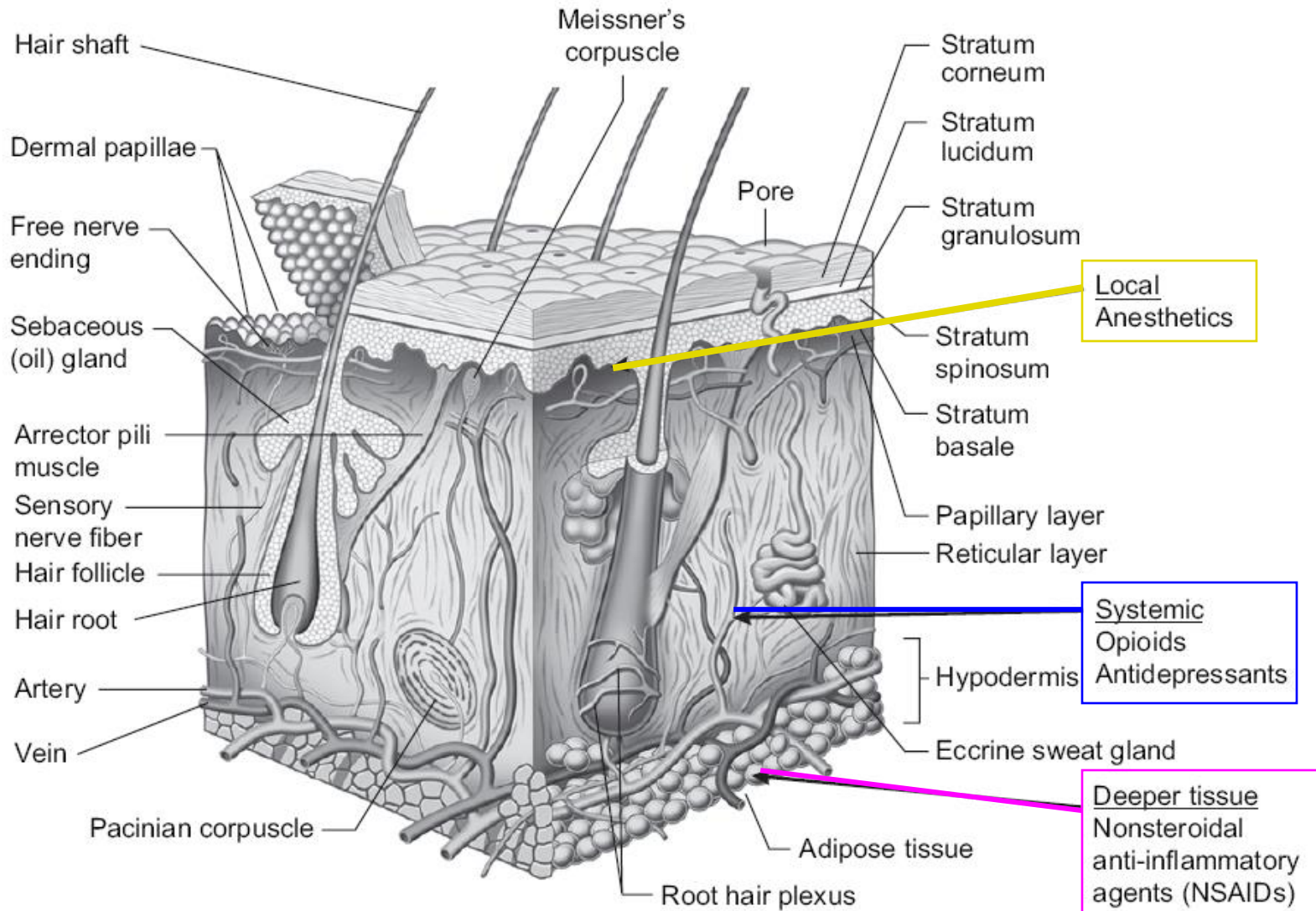
Drug Class	Medication Examples	Use	Clinical Pearls
<b>Antidepressants</b>	Amitriptyline Nortriptyline	Neuropathic Pain	SE: dry mouth, drowsiness, constipation, orthostatic hypotension, urinary retention, confusion. Obtain baseline EKG with history of cardiac disease
<b>SSRI/SNRI Antidepressants</b>	Duloxetine (Cymbalta)	Diabetic peripheral Neuropathy	Should not use with MAOI's (ex. Zyvox). Consider lower starting dose for patients for whom tolerability is a concern.
<b>Antiepileptics</b>	Gabapentin (Neurontin) Pregabalin (Lyrica)	Neuropathic Pain	Adjust Dose for renal Dysfunction. Pregabalin is similar to gabapentin, sometimes more rapid response than gabapentin.
<b>Topical Preparations</b>	Lidoderm patch (topical Lidocaine) Diclofenac Patch	Lidoderm- Neuropathic Pain Diclofenac- Bone Muscle pain	Patch may be cut to fit painful areas. Place only on skin that is clean, dry and intact.
<b>Muscle Relaxants</b>	Baclofen (Lioresal) Methocarbamol (Robaxin)	Muscle Spasm	Gradually increase in 2-4mg increments over 4 weeks.
<b>NSAID</b>	Ibuprofen Naproxen Ketorolac celecoxib	Mild to moderate pain.	Use extreme caution in elderly, cardiac disease, renal dysfunction, and GI bleeding.

# OTC NSAIDs – Awareness of Patient Self-Medication

- NSAIDs ceiling effect must be monitored to avoid toxicity
- Combining NSAIDs increases potential adverse effects, which include:
  - Hepatic dysfunction
  - Bleeding
  - Gastric ulceration
  - Renal failure
- Patient education required for this important class of OTC drugs

# Skin Anatomy

Reference: J. Pain Symptom Manage, 33:342-55, 2007



# Local Anesthetics

Blocks conduction of nerve impulses by decreasing or preventing an increase in the permeability of excitable membranes to  $\text{Na}^+$ .

(Catterall & Mackie, 1996)

# Acetaminophen



- Analgesic, antipyretic
- Well tolerated
- Used for both acute and chronic pain (Pros)
- Used to treat osteoarthritis
- Maximum dose 4000 mg/day, except w/ ETOH
- Inhibits prostaglandin synthetase in the CNS, weak peripheral anti-inflammatory activity, centrally acting. Reinforces the descending inhibitory serotonergic pain pathways (proposed)
- Risk of hepatotoxicity with higher doses, multiple combo products (Cons)
- Renal failure dosing based on creatinine clearance
- Moderately dialyzable
- Antidote – acetylcysteine (Mucomyst, Acetadote)





## SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Acetaminophen is the first-line treatment for most mild to moderate acute pain.	A	8, 18
Ibuprofen and naproxen (Naprosyn) are good, first-line NSAIDs for mild to moderate acute pain based on effectiveness, adverse effect profile, cost, and over-the-counter availability.	A	12, 13
Cyclooxygenase-2 selective NSAIDs are second-line medications for mild to moderate pain based on their similar effectiveness to nonselective NSAIDs and greater costs.	A	13
Celecoxib (Celebrex) alone and an NSAID plus a proton pump inhibitor have the same probability of causing gastrointestinal complications in those at high risk.	B	26, 27
Full opioid agonists may be used if opioids combined with acetaminophen or NSAIDs are insufficient to control moderate to severe pain.	A	14, 15, 31
Tramadol (Ultram) is less effective than hydrocodone/acetaminophen and is a second-line medication for the treatment of moderate to severe pain.	B	16, 39

*NSAID = nonsteroidal anti-inflammatory drug.*

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.*

# Muscle Relaxants for LBP

- Widely used to treat musculoskeletal pain
- Account for 16% of prescriptions written for low back pain in the US despite very limited or inconsistent data about efficacy
- “Muscle relaxants have some limited use for acute LBP, but the effect is small and the risks of abuse are real. No studies support long term use”
- “Skeletal muscle relaxants are an option for short-term relief of acute low back pain, but all are associated with CNS adverse effects (primarily sedation)”

# Anticonvulsants

- 1) Inhibit sustained high-frequency neuronal firing by blocking  $\text{Na}^+$  channels after an action potential, reducing excitability in sensitized C-nociceptors.
- 2) Blockade of  $\text{Na}^+$  channels and increase in synthesis and activity of GABA, in inhibitory neurotransmitter, in the brain.
- 3) Modulates  $\text{Ca}^+$  channel current and increases synthesis of GABA.

(Vallerand, Sanoski & Deglin 2012)

# Tricyclic Antidepressants TCA

- Amitriptyline (Elavil), 10 – 25 mg po hs, usual effective dose 50-150 mg po hs., metabolized CYP<sub>450</sub>: 1A<sub>2</sub>, 2D<sub>6</sub> (primary), 3A<sub>4</sub> substrate, active metabolites incl. nortriptyline. Inexpensive, moderately effective (Pros). High side effect profile (Con). Used for chronic neuropathic pain.
- Nortriptyline (Pamelor, Aventyl HCL), 10 – 25 mg po hs, usual effective dose 50 – 150 mg po hs, metabolized CYP<sub>450</sub>: 2D<sub>6</sub> substrate, active metabolite.
- Desipramine (Norpramin), 10 – 25 mg po hs, usual effective dose 50 – 150 mg po hs, metabolized CYP<sub>450</sub>: 2C<sub>19</sub>, 2D<sub>6</sub> (primary) substrate; active metabolite.  
(McDonald & Portenoy, 2006)

# Breast Milk Issues

Pump & Dump

Breast Milk for Sale



# 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

Meta-Analysis

> [Lancet](#). 2022 Jun 18;399(10343):2280-2293.

doi: [10.1016/S0140-6736\(22\)00582-7](https://doi.org/10.1016/S0140-6736(22)00582-7).

# Opioid versus opioid-free analgesia after surgical discharge: a systematic review and meta-analysis of randomised trials

Julio F Fiore Jr <sup>1</sup>, Charbel El-Kefraoui <sup>2</sup>, Marc-Aurele Chay <sup>3</sup>, Philip Nguyen-Powanda <sup>2</sup>, Uyen Do <sup>2</sup>, Ghadeer Olleik <sup>2</sup>, Fateme Rajabiyazdi <sup>4</sup>, Araz Kouyoumdjian <sup>5</sup>, Alexa Derksen <sup>6</sup>, Tara Landry <sup>7</sup>, Alexandre Amar-Zifkin <sup>8</sup>, Amy Bergeron <sup>8</sup>, Agnihotram V Ramanakumar <sup>9</sup>, Marc Martel <sup>10</sup>, Lawrence Lee <sup>11</sup>, Gabriele Baldini <sup>12</sup>, Liane S Feldman <sup>11</sup>

Affiliations [+](#) expand

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# New 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**
- **Bill No. 166 Beginning June 1, 2018, before prescribing or dispensing to a patient a controlled substance in a quantity that exceeds a 3 – day supply, a licensed prescriber shall obtain and review a report concerning that patient from the electronic system.**



# 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.

# Short Acting Opioids

- morphine – (MSIR, Roxanol)
- hydromorphone – (Dilaudid)
- oxycodone – (OxyIR, Roxicodone, Oxyfast)

# Rapid Release Opioid

- fentanyl – (Actiq, Fentora, Onsolis, Lazanda)

# Suboxone and Butrans

- Buprenorphine/naloxone-Suboxone, Butrans is Buprenorphine
- Antagonist, agonist
- Stop at 3-4 days pre-op??
- Continue through post-op period??



# 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

# Beer's Criteria

- Created in 1991 to improve safety of medication therapy in older adults
- Potentially inappropriate medication
  - All classes of medications
  - Evidence-based, graded tool
  - Assists health care providers in improving medication safety in the geriatric patient
  - Covers side effects and potential adverse effects
    - TCAs: strong anticholinergics
    - NSAIDs: high rate of GIB in pts receiving for 3-6 months



# 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.

## 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

### 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

# 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

# Equianalgesic Dosing

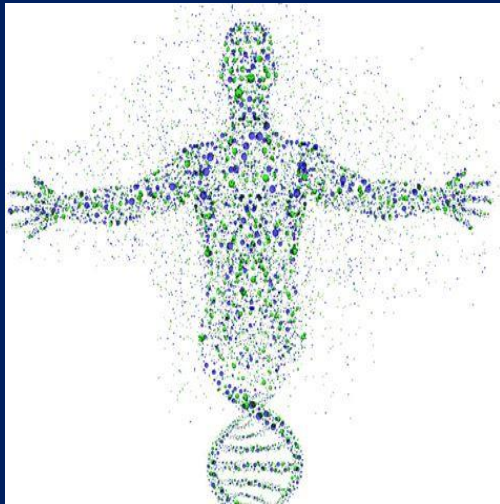
## \*Incomplete Cross Tolerance

<b>Drug</b>	<b>Oral(mg)</b>	<b>IV (mg)</b>	<b>Duration (h)</b>
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



# Exciting New Possibilities

Genomic testing can help identify people with genetic variations so that doctors can make more informed prescribing decisions, reducing the risk of adverse events and increasing the likelihood of treatment success.



## Collaboration

The combined efforts of physicians, universities, the National Institute of Health (NIH) and the FDA are encouraging insurance acceptance and reimbursement by leading with Medicare.

Despite an upfront cost, the realized savings is well worth the investment.

# 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.**

# Reversal Agents

- **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.

- **Flumazenil (benzodiazepine antagonist)**

Reversal agent for benzodiazepines, binds to benzodiazepine receptors, enhances GABA effects.

Intravenous route, 0.2-0.5 mg q min 1 mg., max 5 mg total.



May 31, 2023



# FDA Approves Nalmefene, a Longer-Lasting Opioid Reversal Nasal Spray

Emily Harris

*JAMA*. 2023;329(23):2012. doi:10.1001/jama.2023.9608



# Why Think about Interventional Pain Therapies??

- Longer cancer life expectancy
  - 5-year relative survival rate  to **68%**, 2012-2018
  -  chronic cancer pain (Fallon, et al., 2018)
- Who is responsible for treatment?
- Long term prescribing “Opioid-phobia”

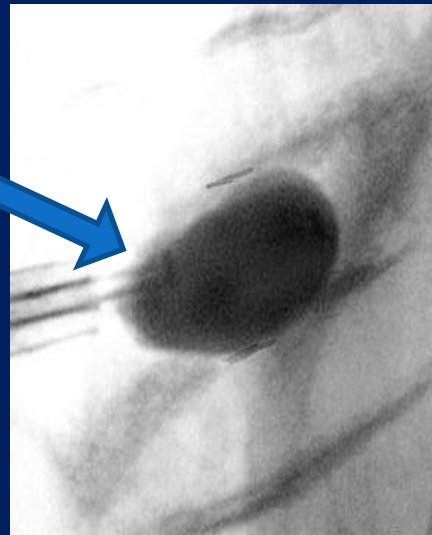
# Interventional Pain Management

Interventional procedures are therapeutic options for managing cancer pain that is uncontrollable by conventional pharmacotherapy and/or patient is experiencing uncontrollable side effects.

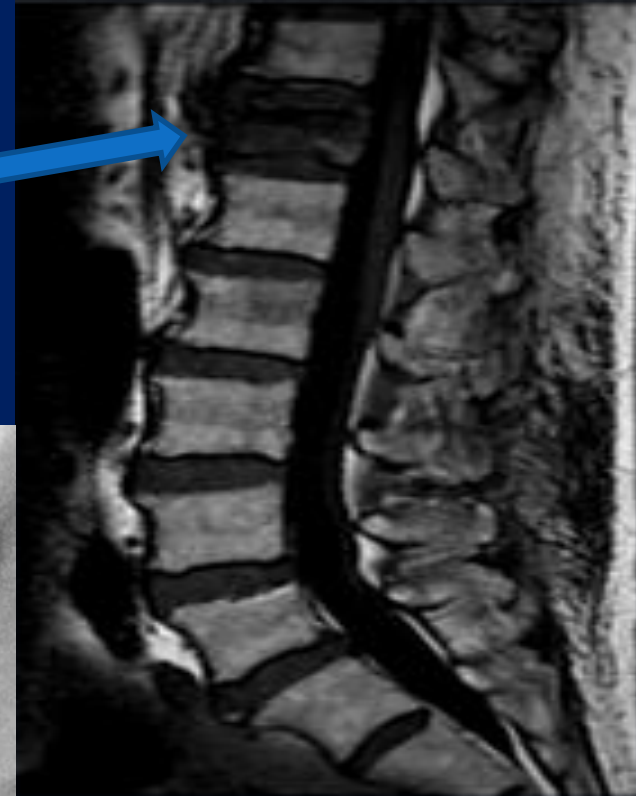
- **Nerve blocks**
- **Neuromodulation**
  - **Intraspinal**
    - **Intrathecal**
    - **Epidural**
- **Vertebral compression fracture stabilization**
- **Neurosurgical intervention**
- **Opioid sparing**

# Percutaneous Vertebroplasty/Kyphoplasty

- Aimed at restoring height and stability in fractured vertebral body
- Treating pain related to vertebral collapse
- Balloon Kyphoplasty creates a void



“Photo by: Linda Vanni



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# Designing a new class of drugs to treat chronic pain

## UC Davis researchers receive \$1.5 million grant

UC Davis School of Medicine September 3, 2019

NaV1.7, NaV1.8 and NaV1.9 have been identified as voltage-gated sodium ion channels critical in pain signaling and transmission

Peptides, such as the tarantula-based toxin ProTx-II, are known to block specific sodium channels

Identifying the most effective peptide design that can block the relevant sodium channels without affecting the activity of other channels.

Improve the design of naturally-occurring ProTx-II peptide by optimizing for potency and selectivity

Trim ProTx-II down to its essential binding parts



# Medical and Recreational Marijuana Use

- Marijuana in all forms is a DEA, Scheduled C-I drug, is federally illegal and for that reason is prohibited in the hospital setting. This applies even if the patient has a state of Michigan Medical Marijuana card.



## LEGALIZATION DAY

AS OF DEC. 6, MICHIGAN IS THE FIRST STATE IN THE MIDWEST TO LEGALIZE ADULT-USE RECREATIONAL MARIJUANA

✓ ADULTS 21 AND UP ARE PERMITTED TO POSSESS AND CONSUME MARIJUANA

✓ UP TO 2.5 OUNCES CAN BE POSSESSED AND TRANSPORTED AT ANY TIME

✓ UP TO 10 OUNCES CAN BE KEPT AT HOME; AMOUNTS HIGHER THAN 2.5 OUNCES MUST BE LOCKED AWAY

✓ UP TO 12 MARIJUANA PLANTS CAN BE GROWN IN THE HOME; MORE WITH A PROPER LICENSE

✗ DRIVING UNDER THE INFLUENCE OF MARIJUANA IS PROHIBITED

✗ CONSUMPTION OF MARIJUANA IN PUBLIC IS PROHIBITED

✗ MUNICIPALITIES MAY BAN RETAIL SALES OF MARIJUANA, BUT CANNOT BAN CONSUMPTION BY ADULTS 21 AND UP

NOTE: MARIJUANA RETAIL SALES ARE NOT EXPECTED TO BEGIN UNTIL 2020



# **“Unexpected Consequences” resulting from legalization of Recreational Marijuana**

- Cyclic vomiting**
- Constant showering**
- Impaired driving**
- New hire urine drug screen failure**

# Subcutaneous Methylnaltrexone

New Drug Application filed 5/30/07,  
approved in 2008

- For treatment of opioid-induced constipation in patients receiving palliative care
- Peripherally acting mu-opioid receptor antagonist
- Without interfering with pain relief
- Single use, pre-filled syringes introduced 2010
- Phase III, oral formulation development for chronic, non-cancer pain patients
- Patents and applications expirations ranging from 2017-2031



# Shingrix

50 yo & older: 0.5 ml IM X 1  
and second vaccine at month 2-6  
for 2 total doses



# Non-Pharm Comfort Guide



- ▶ Relaxation Breathing
- ▶ Visualization
- ▶ Heat/Cold compresses
- ▶ Nature Station
- ▶ Aromatherapy
- ▶ Massage at the bedside
- ▶ Pet Therapy
- ▶ Spiritual Care
- ▶ Quiet Time
- ▶ Movement/repositioning

- ▶ 78% of patients were unaware any non-pharm options available
- ▶ 83% patients said caregivers did not offer them other options besides pain Rx.

# Tricks of the Trade

- Establish a relationship with the patient!
- Do not assume patient is drug seeking
- Listen intently; you would be surprised what the patient may tell you
- Relay the need for accurate information regarding what the patient is actually taking for pain at home
- Discuss with patient how important it is to you that they communicate to you if their pain is being ineffectively managed
- Establish goals, i.e. all about function

# Caring Behaviors in Pain Management

- Establishing a caring relationship in pain management:

Opportunity to meet family members

One of the most vulnerable times

Desperately seeking help and hope!

The feeling of being totally alone

You have the ability to change someone's life EVERYDAY!

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