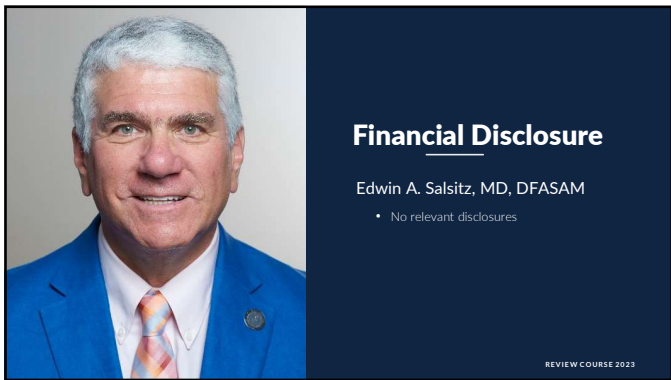
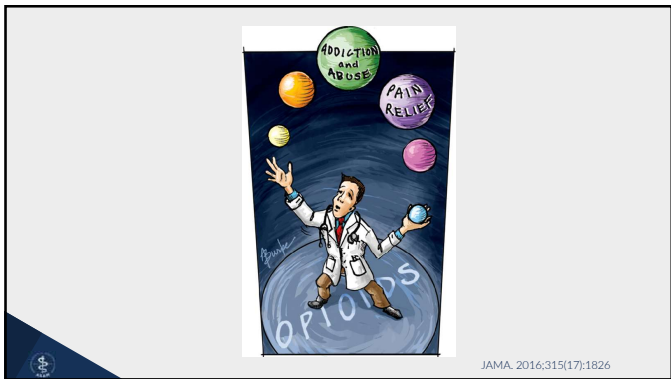


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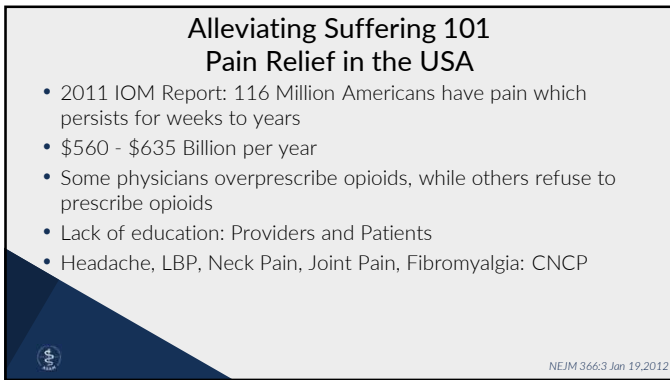
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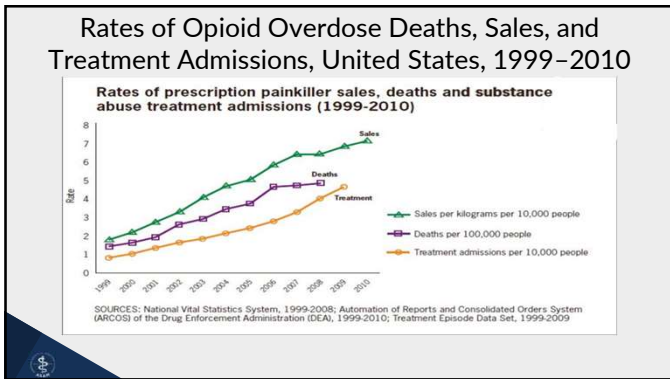
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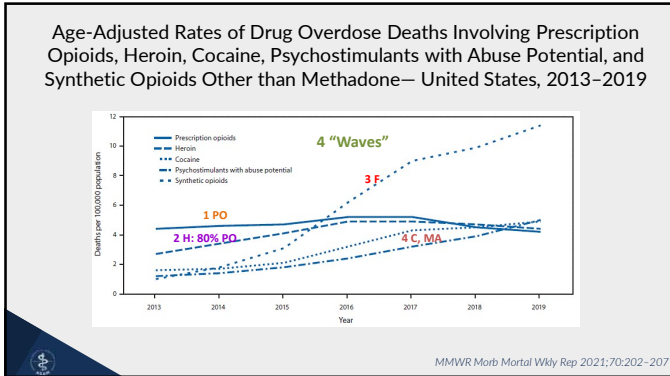
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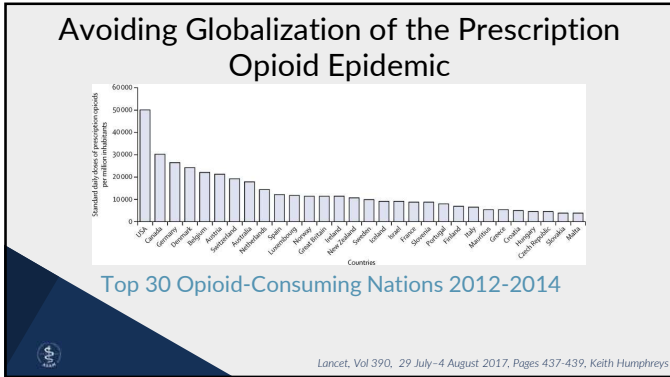
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How Did We Get Here?

REVIEW COURSE 2023

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“Perfect Storm”

ADDITION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 10,000 hospitalized medical patients who were discharged continuously. Although there were 11,382 patients who received at least one narcotic prescription, there were only four cases of narcotic addiction. The addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs prescribed were morphine in two patients, Percodan in one, and hydrocodone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

Jan Puritz
Richard J. Fox, MD
Boston, California Drug
Regulator Program
Waltham, MA 02154 Boston University Medical Center

1. J. H. Mattson, G. S. Shapiro, S. Lewis, G. S. Sakel, Y. Stone D. (1980) *Continuance drug dependence (CDD)*. *PNP*, 21:18-24.
2. Miller, R. K. (1981) *Continuance drug dependence in hospitalized medical patients*. *J Clin Pharmacol*, 21:18-24.

Number and Type of Citations of the 1980 Letter, According to Year.

- 1980→ 2017: 608 citations : ~75% used as evidence that addiction is rare with COT and made no mention that these were hospitalized patients with few doses of opioids.
- 11 other letters from 1980 were cited on average, 11 times.

N Engl J Med 1980; 302: 123.
N Engl J Med 376:22 June 2017

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“Perfect Storm”

- 1995: Introduction of Oxycontin
- 1995: Pain is Fifth Vital Sign
- Publications indicating low risk of addiction
- Thought Leaders with Financial/Pharma Conflicts
- Patient Satisfaction Surveys: "...staff did everything they could to help you with your pain"
- Physicians successfully sued for not treating pain
- No Evidence for long term Effectiveness COT → CNCP
- Physical Dependence vs Addiction

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Doctor liable for not giving enough pain medicine

June 14, 2001 | posted: 12:28 AM EDT (0428 GMT)

HAYWARD, California (CNN)—In a civil case that could have broad ramifications for how patients in pain are treated, a California jury Wednesday found a doctor liable for recklessness and abuse for not prescribing enough pain medication to a patient, who later died of cancer.

The jury in Alameda County Superior Court called on the doctor to pay the patient's family \$1.5 million dollars for pain and suffering of the patient. Under California law, however, the cap for such awards is \$250,000, and the judge will likely reduce the jury's award.

A Doctor Who Prescribed 500,000 Doses of Opioids Is Sent to Prison for 40 Years

Dr. Joel Smithers was convicted of more than 800 counts of illegally prescribing opioids, and jurors found that the drugs he prescribed caused the death of a woman.

By Adel Hassan

Oct 3, 2019

A Virginia doctor who prescribed more than 500,000 doses of opioids in two years was sentenced to 40 years in prison on Wednesday for leading what prosecutors called an interstate drug distribution ring.

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CONCLUSIONS: The 16% of Americans who have mental health disorders receive over half of all opioids prescribed in the United States. Improving pain management among this population is critical to reduce national dependency on opioids.

Adverse Selection

J Am Board Fam Med 2017;30:407 - 417

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New Safety Measures Announced for Opioid Analgesics, Prescription Opioid Cough Products, and Benzodiazepines FDA: August 2016

Table 1. The Danger of Combining Opioids And Benzodiazepines

FDA Warning: Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants

Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

- Reserve concomitant prescribing of (opioid) and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate
- Limit dosages and durations to the minimum required
- Follow patients for signs and symptoms of respiratory depression and sedation

Source: US Food and Drug Administration website. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm1518697>.

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FDA Drug Safety Communication: FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks

This provides updated information to the FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medications with benzodiazepines, requires its strongest warning (<https://www.fda.gov/drugs/drug-safety-communications/ucm1518697>) issued on August 31, 2016.

Safety Announcement

19-20-2017 Based on our additional review, the U.S. Food and Drug Administration (FDA) is advising that the opioid addiction medications buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks. Careful medication management by health care professionals can reduce these risks. We are requiring this information to be added to the buprenorphine and methadone drug labels along with detailed recommendations for minimizing the use of medication-assisted treatment (MAT) drugs and benzodiazepines together.

Buprenorphine and methadone help people reduce or stop their abuse of opioids, including prescription pain medications and heroin. Methadone and buprenorphine have been shown to be effective in reducing the negative health effects and deaths associated with opioid addiction and dependency.¹ These medications are often used in combination with counseling and behavioral therapies, including contingency management (CM), to assist with treatment (CM) of opioid addiction, and patients can be treated with them individually. Buprenorphine and methadone work by acting on the same parts of the brain as the opioid that the patient is addicted to. The patient taking the medication as directed generally does not feel high, and withdrawal does not occur. Buprenorphine and methadone also help reduce cravings² (see Table 1. List of Buprenorphine and Methadone MAT Drugs).

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Intended/Unintended Consequences in Reaction to the Prescription Opioid Epidemic

- Prescription Drug Monitoring Programs: PDMP
- Limits on the quantity and dosage prescribed
- UDTs become standard of care
- Education of prescribers: FDA REMS course on Safe and Effective Opioid Mgt.
- CDC Guidelines
- Tamper Resistant/Abuse Deterrent Formulations
- Patients Physically Dependent on Opioids Left in the Lurch
- **HEROIN: Cheaper, Readily Accessible**
- **FENTANYL/Fentanyl Analogues**

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Physicians' Progress to Reverse the Nation's Opioid Epidemic AMA Opioid Task Force 2018 Progress Report

Year	Total opioid prescriptions (in millions)
2013	251.8
2014	244.5
2015	227.8
2016	215.1
2017	196.0

Source: IQVIA, KQWA

As PDMPs improve, America's physicians and health care professionals are using state PDMPs more than ever.

The AMA Opioid Task Force encourages all physicians to enhance their education.

In 2017, more than **549,700 PHYSICIANS** have completed the AMA Opioid Task Force educational program.

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Journal of Pain Research

Dovepress

EDITORIAL

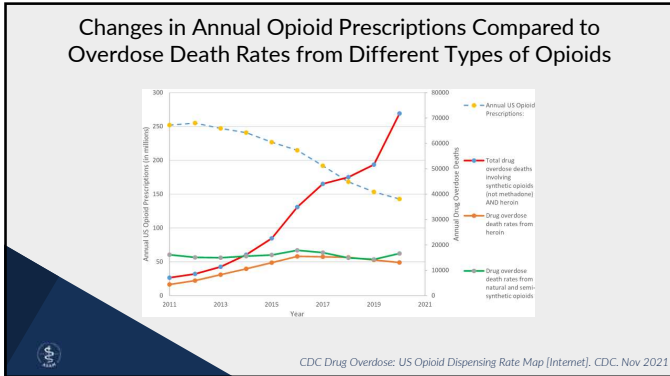
Misinterpretation of the "Overdose Crisis" Continues to Fuel Misunderstanding of the Role of Prescription Opioids

Jeffrey J Bettinger¹, William Amaraquay², Jeffrey Fudin³⁻⁶, Michael E Schatman⁷⁻⁹

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Correspondence: Michael E Schatman, Department of Anesthesiology, Perioperative Care, and Pain Medicine, NYU Grossman School of Medicine, 550 1st Ave., New York, NY, 10016, USA. Tel: +425-647-4880, Email: Michael.Schatman@NYU.Langone.org

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CDC Guidelines: 2016 vs 2022

- Similar Recommendations on Opioids as the last option for chronic pain and in many cases of acute pain. Always start with IR opioids for the shortest duration and lowest effective dose.
- Change in Tone: These are guidelines. Use Clinical Individualized Patient-Centered Judgments as to duration, dose, risk/benefit of COT, and need for tapering
- These Guidelines are not to be used by health systems, pharmacies, insurance companies, medical boards, or governments to determine standard of care

CDC Guidelines at a Glance

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Start With Non-Pharmacologic Therapy

- Physical Therapy, Exercise
- Cold, Heat
- CBT, MI
- Meditation, Mindfulness
- Acupuncture
- Biofeedback
- Massage
- Aquatic Therapy
- Spinal Cord Stimulation (SCS)

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Next Option: Non-Opioid Pharmacotherapy

- Acetaminophen (Efficacy), NSAIDS (Adverse Effects, Cardiac, Elderly)
- Anti-Depressants: TCAs, SSRIs, SNRIs
 - Neuropathic Pain, Nociceptive Pain (e.g., Fibromyalgia), Pain + Depression
- Anti-Convulsants: Gabapentanoids, Topiramate, Carbamazepine
 - Neuropathic Pain, Nociceptive Pain, Migraine Prophylaxis
- Topicals: Lidocaine Patch, NSAIDS, Capsaicin
- "Muscle Relaxants:" Baclofen, Cyclobenzadrine, Methocarbamol, Tizanidine
 - Avoid Benzodiazepines, Carisoprodol (Schedule IV)
- Ketamine: Acute Pain (e.g., ED)
- Interventional Procedures: Epidurals, Nerve Blocks, Neuro-Modulation

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Gabapentanoids: Conclusions

- Significant Misuse Among Patients with SUDs, Primarily OUD Receiving Methadone or Buprenorphine Maintenance.
- Significant Adverse Effects With Therapeutic Doses, and Increased Adverse Effects With Supra-Therapeutic Doses
- Must Adjust for Renal Function
- Full Recovery From Adverse Effects Is The Rule
- **Death Is Uncommon, But Increased In Combination With Opioids**
- Gabapentin Bioavailability ↓ With Increasing Dose
- Weak Evidence For Off Label Pain Treatment
- Should Gabapentin Be Listed On PDMPs (e.g., Ohio, NJ)
- Pregabalin Schedule 5 listed
- Add Gabapentanoids To UDT Screens

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Opioid Pharmacotherapy

- Acute Pain: e.g., Post-Operative, Burn, Severe Trauma
- Limit Duration: NYS-7days
- **Sickle Cell Disease 2022 Guidelines**
- Cancer Pain
- Palliative Care, Hospice
- End of Life Care
- **Chronic Opioid Therapy (COT) for**
 - Chronic Non-Cancer Pain (CNCP)
 - Effectiveness, Safety, Adverse Effects,
 - IR vs. ER

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Opioid Tapering/Deprescribing Strategies

- Patient Requests/Agrees vs Patient Resists
- Alternative Treatment if Pain Still Present
- Clonidine/Lofexidine Tablets and Patches
- alpha 2 centrally acting adrenergic agonists → ↓LC → ↓NE
- Switch to Methadone
- Switch to Buprenorphine
- Symptomatic Meds: NSAIDs, Loperamide, Benzos(short course), non-benzo sleep meds
- Patients report favorable outcomes after tapering
- Opioid Induced Hyperalgesia

*JAMA Internal Medicine May 2018 Volume 178, Number 5
The Journal of Pain, Vol 18, No 11 (November), 2017*

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FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering

FDA Drug Safety Communication

Safety Announcement

[4-9-2023] The U.S. Food and Drug Administration (FDA) has received reports of serious harm in patients who are physically dependent on opioid pain medicines and have their medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.

The U.S. Food and Drug Administration (FDA) has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.

JAMA | Original investigation

Association of Dose Tapering With Overdose or Mental Health Crisis Among Patients Prescribed Long-term Opioids

Alcibi Agripa, MD, MPH, MHS, Gabe King, PhD, David J. Tancredi, PhD, Elizabeth Magnus, MD, PhD, Anthony Levitt, MD, Joshua J. Fenton, MD, MPH

CONCLUSIONS: Among patients prescribed stable, long-term, higher-dose opioid therapy, tapering events were significantly associated with increased risk of overdose and mental health crisis

JAMA, 2021;326(5):411-419

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HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics Oct. 2019

- The CDC Guideline for Prescribing Opioids for Chronic Pain **does not recommend opioid discontinuation when benefits of opioids outweigh risks.**
- Avoid misinterpreting cautionary dosage thresholds. Guideline recommends avoiding or carefully justifying increasing dosages **above 90 MME/day, it does not recommend abruptly reducing opioids from higher dosages.**
- **Avoid dismissing patients from care.**
- **Reinforced in the 2022 Guidelines**

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The Health Effects of Cannabis and Cannabinoids

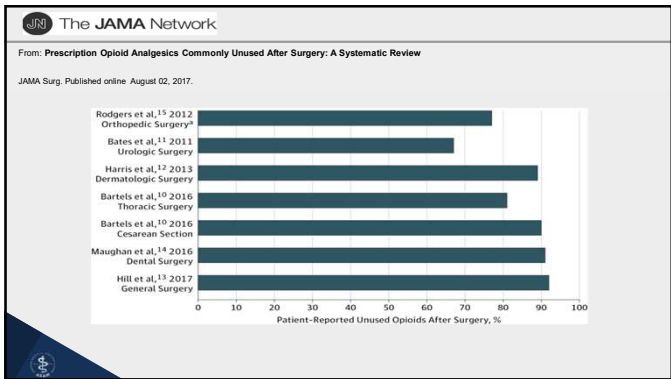
- In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics.
- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.
- In adults with multiple sclerosis (MS) related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.
- For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.

Opioid Use Disorder: Conflicting reports. No RCTs
Controversies About Listing as Eligible Disorder for Medicinal Cannabis by Some States

Conflicting Data on Opioid Overdose Increase/Decrease—likely related to fentanyl not prescription opioids as primary responsible opioid since 2013.

National Academy of Science, Engineering and Medicine. 2017. Journal of Health Economics 88 (2023) 102728

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Opioid Rx Disposal

- DEA Take Back Programs
- Some Pharmacies, Some Police Stations
- Mix with cat litter/coffee grounds, then seal in plastic bag and throw out in trash
- Flush down toilet: environmental issues
 - Fentanyl Patch: Flush only
- DO NOT throw out in trash in Rx bottle

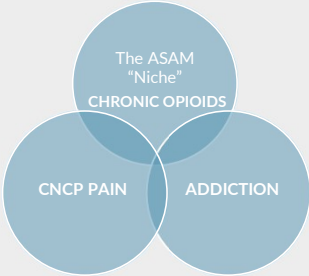
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Co-Prescribe Naloxone



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Complex Intersection



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Pain and Addiction: Definitions

- "Pain is viewed as a biopsychosocial phenomenon that includes **sensory, emotional, cognitive, developmental, behavioral, spiritual and cultural components.**" (IASP website)
- Addiction is a treatable, chronic medical disease involving **complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.** People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

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Pain and Addiction

Ann Quintan-Colwell, PhD, PCSS-O Webinar, 2011.

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Pain and Addiction Limited (e.g., UDT) Objective Measurements

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Biomarkers on the Horizon

First-in-human prediction of chronic pain state using intracranial neural biomarkers

Journal: Nature Neuroscience
DOI: 10.1038/s41593-023-00500-0
Published online 5/22/23

Nature Neuroscience
Published online 5/22/23

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Opioid Sites of Action in the Brain

41

“Exaggerated Response” What Did It Feel Like The First Few Times?

- “All my problems disappeared.”
- “Felt like I was under a warm blanket.”
- “Thought this is how normal people feel.”
- “Forgot about all the abuse.”
- “Felt like the world was at peace.”
- “Totally relaxed.” “Not shy.”
- “Looking at a beautiful sunset.”
- “I was energized!”
- *Liking opioids: this is a vulnerability.*

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Treating Pain in the Addicted Patient

- "Pain patients with a coexisting SUD are among the most challenging patients in medicine."
- Universal Precautions
- "Real Pain" may make opioids less rewarding/euphorogenic
- Addicted Patients Have Pain: Trauma, Lower Thresholds, Medical
- Screening Tests: ORT, SOAPP, others
- **Untreated Pain is a trigger for relapse**
- **Address both pain and addiction**
- **Significant other to secure and dispense opioid meds**
- Psychiatric Co-morbidity
- Active Addiction recovery program
- UDS, pill counts, agreements, etc.
- **Multidisciplinary Pain Program**

Bailey, et al. Pain Medicine 2010; 11: 1803-1818

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Buprenorphine Formulations: FDA Approved for Pain not OUD

- Buprenex® Parenteral (IV, IM)
- Butrans® Transdermal (7 Day)
- Belbuca® Buccal Film (75–900mcg q12h)

- Approved for pain but **NOT** OUDs
- **Can NOT be used OFF LABEL** for OUDs: Violates DATA 2000

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JAMA Network **Open.** JAMA Network Open. 2021;4(9)

Original Investigation | Substance Use and Addiction

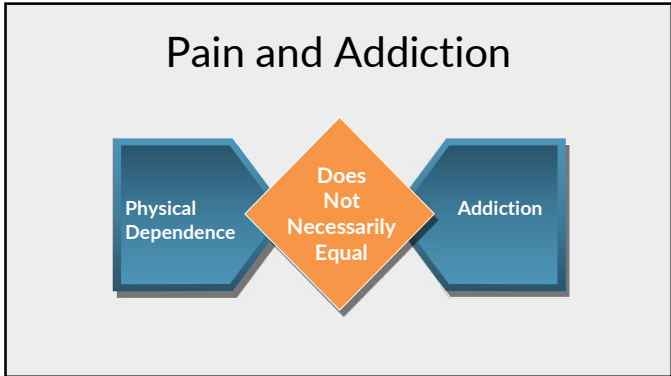
Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain
A Systematic Review

Victoria D. Powell, MD; Jack M. Rosenberg, MD; Avani Yagnik, BS; Claire Garpestad, MD; Praga Lagganthy, MD, MSc; Carol Shannon, MPH; Mark J. Shevlin, MD, MA, F

CONCLUSIONS AND RELEVANCE: In this systematic review, buprenorphine was associated with reduced chronic pain intensity without precipitating opioid withdrawal in individuals with chronic pain who were receiving LTOT. Future studies are necessary to ascertain the ideal starting dose, formulation, and administration frequency of buprenorphine as well as the best approach to buprenorphine rotation.

MEANING: These findings suggest that buprenorphine rotation may be a viable option for mitigating the harms of long-term opioid therapy in individuals with chronic pain who were receiving unsafe opioid analgesic regimens; further studies are needed to examine the best way to accomplish buprenorphine rotation.

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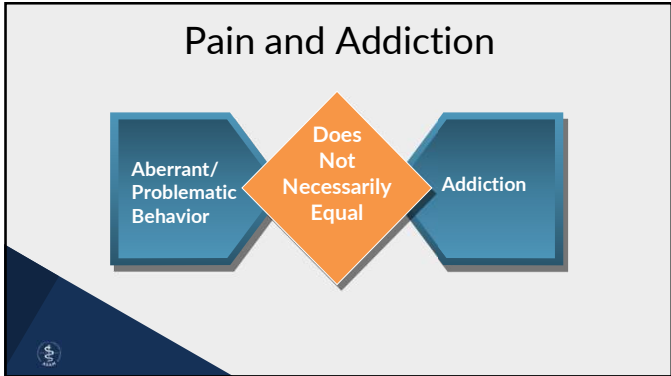
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**Definitions:
Complex Physical Dependence**

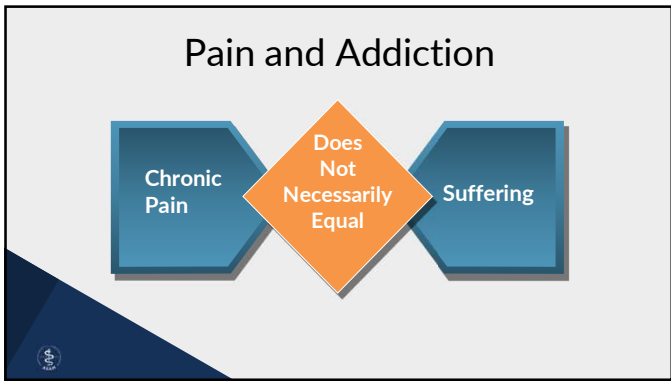
"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, **complex persistent prescription opioid dependence** is a serious consequence of long-term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy."

Opioid Dependence vs Addiction: A Distinction Without a Difference?
Ballantyne J, Sullivan M, Kolodny A. Arch Intern Med. 2012

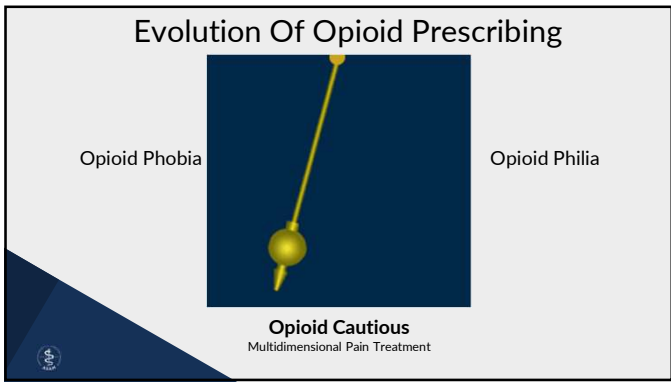
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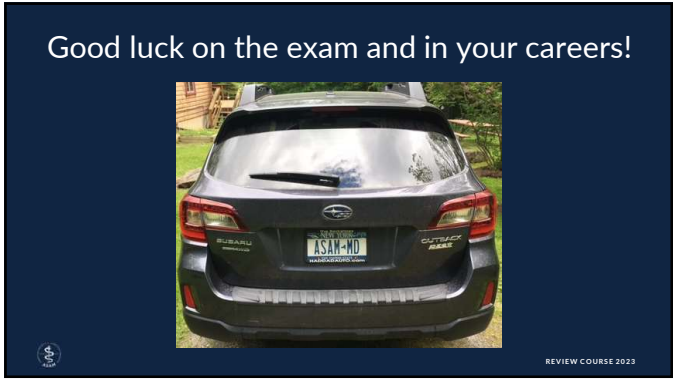


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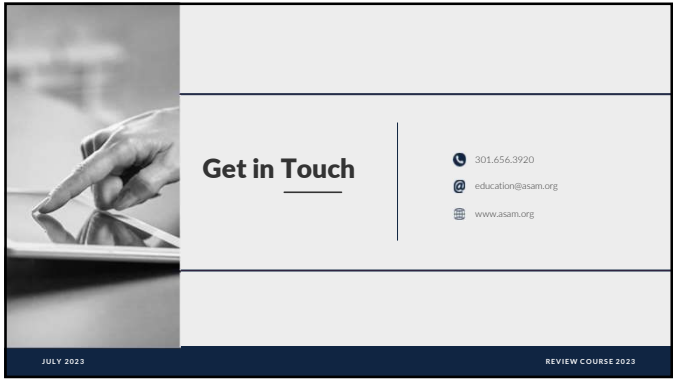
Pain Quotes

- "To have great pain is to have certainty. To hear that another person has pain is to have doubt." "Seeing Pain," Nicola Twilley (2018)
- "Physical Pain does not simply resist language, but actively destroys it." -"The Body in Pain" by Elaine Scarry (1985)
- "Morphine is God's own medicine" Sir William Osler
- We can't live without opioids; we have to learn to live with them.

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