

#### Pain and Addiction: Trends and Treatments

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#### Financial Disclosure

Edwin A. Salsitz, MD, DFASAM

• No relevant disclosures





## The Epidemic of Untreated Pain

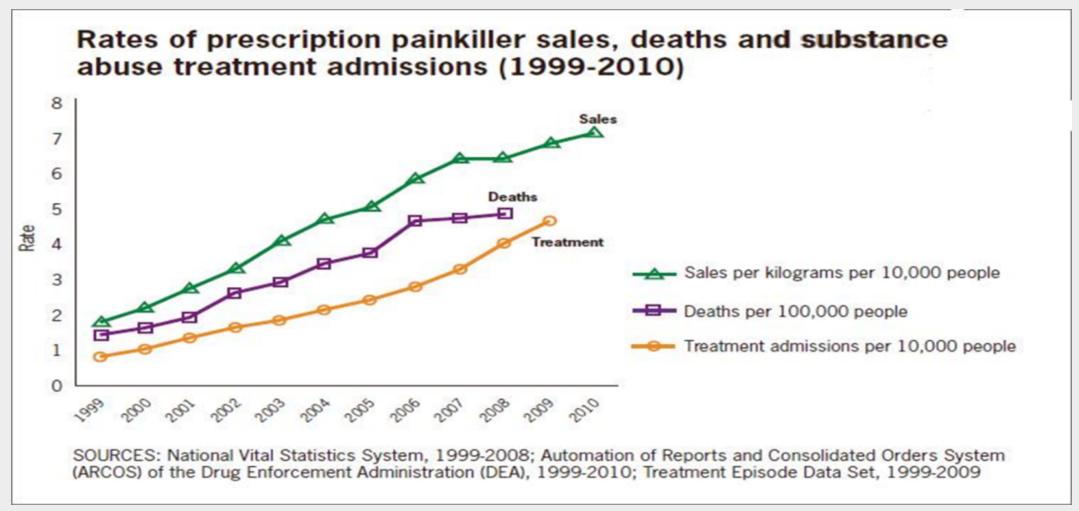


# Alleviating Suffering 101 Pain Relief in the USA

- 2011 IOM Report: 116 Million Americans have pain which persists for weeks to years
- \$560 \$635 Billion per year
- Some physicians overprescribe opioids, while others refuse to prescribe opioids
- Lack of education: Providers and Patients
- Headache, LBP, Neck Pain, Joint Pain, Fibromyalgia: CNCP

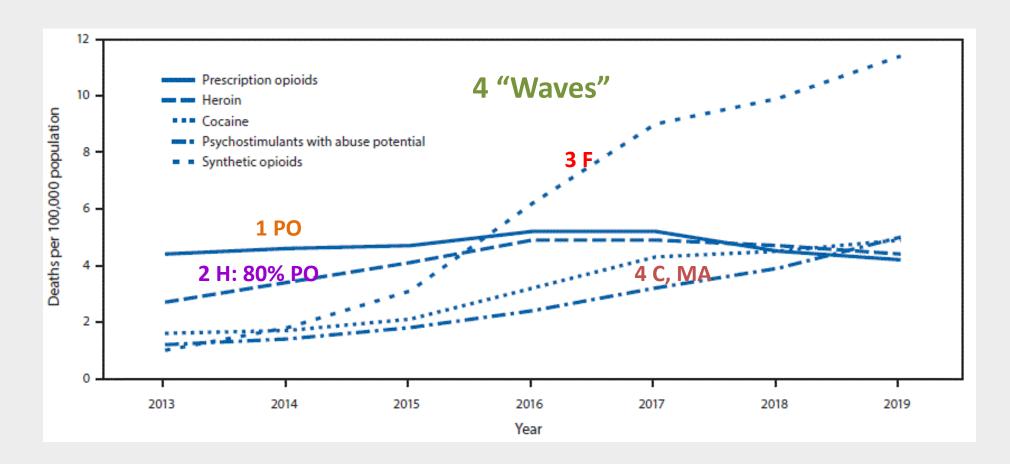


# Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010



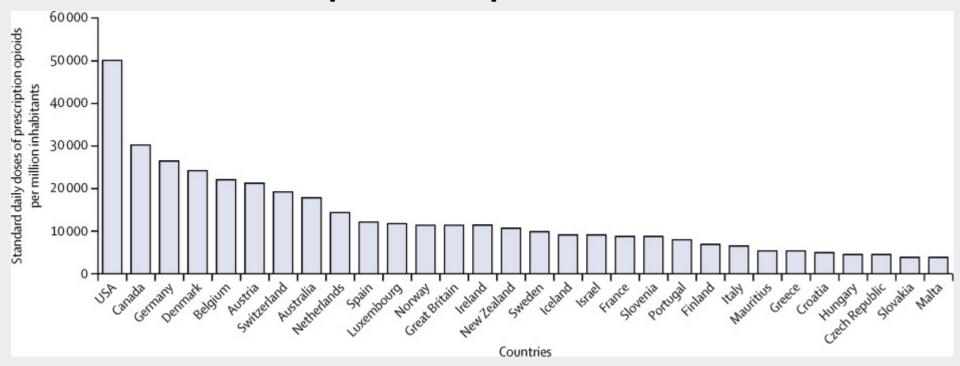


# Age-Adjusted Rates of Drug Overdose Deaths Involving Prescription Opioids, Heroin, Cocaine, Psychostimulants with Abuse Potential, and Synthetic Opioids Other than Methadone— United States, 2013–2019





## Avoiding Globalization of the Prescription Opioid Epidemic



Top 30 Opioid-Consuming Nations 2012-2014



#### How Did We Get Here?



#### "Perfect Storm"

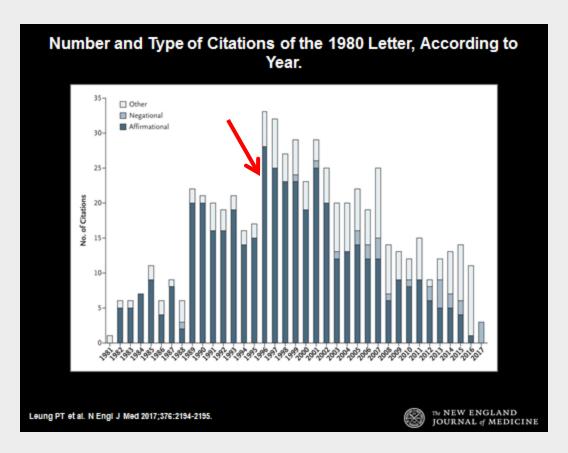
#### ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients¹ who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare inmedical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
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Waltham, MA 02154

- Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind Y, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
- Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.



- 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.



#### "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



#### ORIGINAL RESEARCH

Prescription Opioid Use among Adults with Mental Health Disorders in the United States

Matthew A. Davis, MPH, PhD, Lewei A. Lin, MD, Haiyin Liu, MA, and Brian D. Sites, MD, MS

Background: The extent to which adults with mental health disorders in the United States receive opioids has not been adequately reported.

Methods: We performed a cross-sectional study of a nationally representative sample of the noninstitutionalized U.S. adult population from the Medical Expenditure Panel Survey. We examined the relationship between mental health (mood and anxiety) disorders and prescription opioid use (defined as receiving at least 2 prescriptions in a calendar year).

Results: We estimate that among the 38.6 million Americans with mental health disorders, 18.7% (7.2 million of 38.6 million) use prescription opioids. Adults with mental health conditions receive 51.4% (60 million of 115 million prescriptions) of the total opioid prescriptions distributed in the United States each year. Compared with adults without mental health disorders, adults with mental health disorders were significantly more likely to use opioids (18.7% vs 5.0%; P < .001). In adjusted analyses, having a mental health disorder was associated with prescription opioid use overall (odds ratio, 2.08; 95% confidence interval, 1.83–2.35).

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. (1) on Board Fam Med 2017;30:407–417.)



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



## 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/ucm518697.

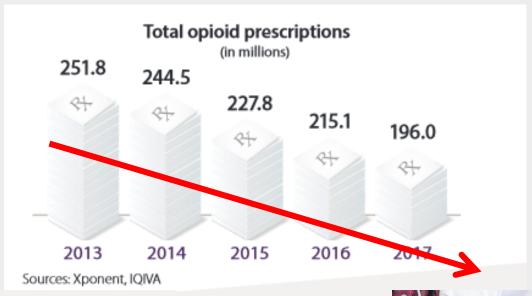


# Intended/Unintended Consequences in Reaction to the Prescription Opioid Epidemic

- 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



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



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

Prescription drug monitoring programs (PDMPs) are databases used to help inform physicians' clinical decisions. To optimize PDMP use, the AMA advocates for PDMPs to be integrated into physicians' clinical workflow to provide data at the point of care.

1,546,099+
471,896
2014
2017

Today, more than 1.5 million physicians and other health care professionals are registered in state-based PDMPs. Between 2016 and 2017, more than 241,000 individuals registered.<sup>2</sup>



Physicians and other health care professionals made more than 300.4 million PDMP queries in 2017—a 121 percent increase from 2016 and a 389 percent increase from 2014.<sup>3</sup> The AMA Opioid Task Force encourages all physicians to enhance their education.



offered by the AMA, state and specialty societies.

Physicians are helping to improve access to high-quality, evidence-based treatment for opioid use disorder.

There are now **more than 50,000** physicians certified to provide in-office buprenorphine for the treatment of opioid use disorder across all 50 states—a **42.2 percent increase** in the past 12 months.

The AMA is encouraged that in the past year, nearly 15,000 physicians have become trained and certified to provide in-office buprenorphine.

To help ensure patients receive care, health insurance companies, Medicaid, and other payers must now remove administrative barriers, such as prior authorization for medication assisted treatment (MAT).



#### Journal of Pain Research

**Dove**press

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EDITORIAL

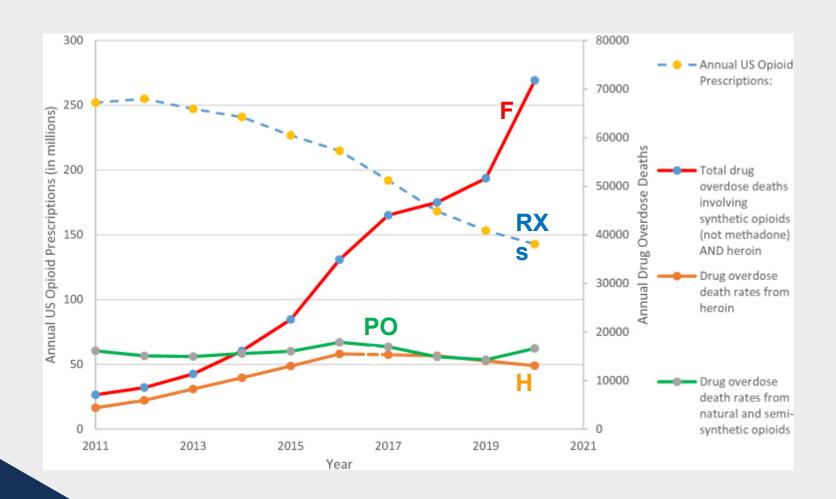
#### Misinterpretation of the "Overdose Crisis" Continues to Fuel Misunderstanding of the Role of Prescription Opioids

Jeffrey J Bettinger<sup>1</sup>, William Amarquaye<sup>2</sup>, Jeffrey Fudin 10<sup>3-6</sup>, Michael E Schatman 10<sup>7-9</sup>

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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@NYULangone.org

#### Changes in Annual Opioid Prescriptions Compared to Overdose Death Rates from Different Types of Opioids





#### 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 to treat CNCP, and need for tapering.
- These Guidelines are not to used by health systems, pharmacies, insurance companies, medical boards, or governments to determine standard of care.

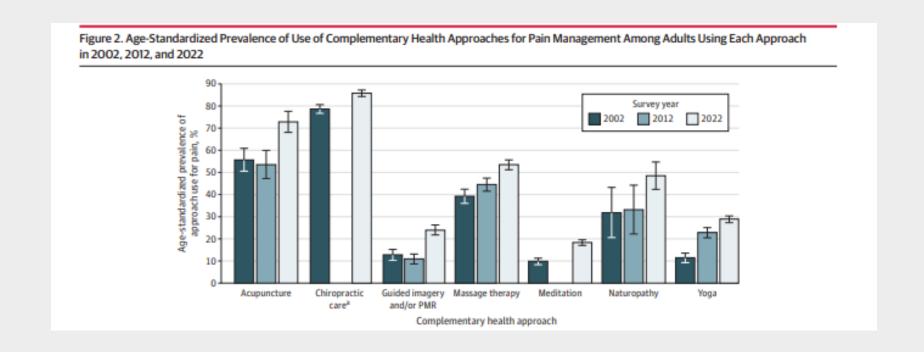


### Start With Non-Pharmacologic Therapy

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



## Non-Pharmacologic Therapy



### Next Option: Non-Opioid Pharmacotherapy

- Acetaminophen (Efficacy), NSAIDS (Adverse Effects, Cardiac, Elderly)
- Anti-Depressants: TCAs, SSRIs, SNRIs
  - Neuropathic Pain, Nociplastic Pain (e.g., Fibromyalgia), Pain + Depression
- Anti-Convulsants: Gabapentanoids, Topiramate, Carbamazepine
  - Neuropathic Pain, Nociplastic 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



#### 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
- 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



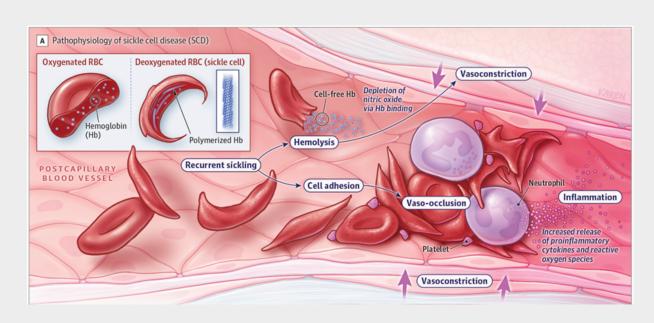
### Opioid Pharmacotherapy

- 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



### Special Mention: Sickle Cell Disease

- Severe Acute and Chronic Pain
- Reduced Life Expectancy
- Prejudice and Stigma
- Racial Disparities in Opioid Rx
- Placed in the Cancer, Palliative Care and End of Life Category in the 2022 Revised CDC Guidelines
- Increasing Evidence for Buprenorphine Efficacy as COT



#### **REVIEW**

#### **Annals of Internal Medicine**

## The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH

**Background:** Increases in prescriptions of opioid medications for chronic pain have been accompanied by increases in opioid overdoses, abuse, and other harms and uncertainty about long-term effectiveness.

**Purpose:** To evaluate evidence on the effectiveness and harms of long-term (>3 months) opioid therapy for chronic pain in adults.

**Data Sources:** MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL (January 2008 through August 2014); relevant studies from a prior review; reference lists; and ClinicalTrials.gov.

**Study Selection:** Randomized trials and observational studies that involved adults with chronic pain who were prescribed long-term opioid therapy and that evaluated opioid therapy versus placebo, no opioid, or nonopioid therapy; different opioid dosing strategies; or risk mitigation strategies.

Data Extraction: Dual extraction and quality assessment.

Data Synthesis: No study of opioid therapy versus no opioid therapy evaluated long-term (>1 year) outcomes related to pain, function, quality of life, opioid abuse, or addiction.

fair-quality observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction, although there are few studies for each of these outcomes; for some harms, higher doses are associated with increased risk. Evidence on the effectiveness and harms of different opioid dosing and risk mitigation strategies is limited.

**Limitations:** Non-English-language articles were excluded, meta-analysis could not be done, and publication bias could not be assessed. No placebo-controlled trials met inclusion criteria, evidence was lacking for many comparisons and outcomes, and observational studies were limited in their ability to address potential confounding.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

Ann Intern Med. 2015;162:276-286. doi:10.7326/M14-2559 www.annals.org
For author affiliations, see end of text.

This article was published online first at www.annals.org on 13 January 2015.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

2015



### **Initiating Opioid Treatment: CNCP**

- Prescribers should regard initial treatment as a therapeutic trial
  - May last from several weeks to several months; start with IR Opioid
  - Decision to proceed w/ long-term treatment should be intentional and based on careful consideration of outcomes during the trial
    - Progress toward meeting therapeutic goals
    - Functional Improvement
    - Presence of opioid-related adverse effects
    - Changes in underlying pain condition
    - Changes in psychiatric or medical comorbidities
    - Identification of problematic drug-related behavior, addiction, or diversion



## Can You Land the Opioid Plane?





## 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  $\rightarrow \psi$ LC $\rightarrow \psi$ 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





#### New Opioid Limits Challenge the Most Pain-Prone



Paula Span
THE NEW OLD AGE JUNE 6, 2016



Irene Cohen, 69, may represent the future of older pain patients: less of a reliance on opioid painkillers and more of an emphasis on exercise and other nonmedicinal therapy.

#### Patients in Pain, and a Doctor Who Must Limit Drugs

By JAN HOFFMAN MARCH 16, 2016













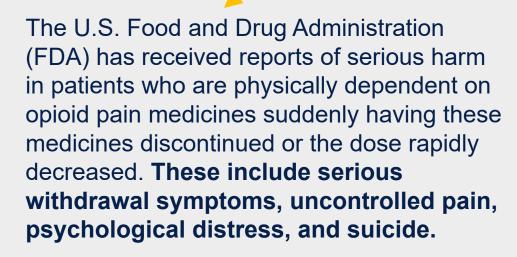


## FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering

FDA Drug Safety Communication

#### Safety Announcement

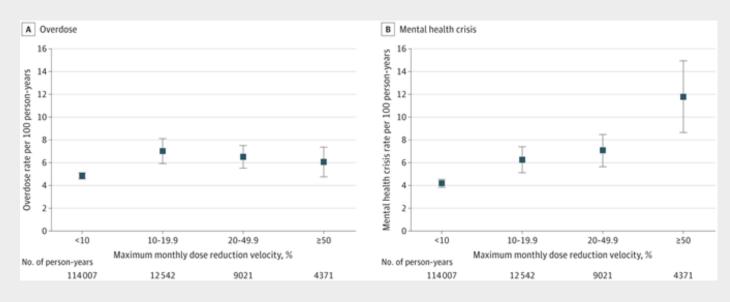
[4-9-2019] The U.S. Food and Drug Administration (FDA) has received reports of serious harm in natients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.



#### JAMA | Original Investigation

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

Alicia Agnoli, MD, MPH, MHS; Guibo Xing, PhD; Daniel J. Tancredi, PhD; Elizabeth Magnan, MD, PhD; Anthony Jerant, 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



#### 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 and Incorporated into the 2022 Guidelines



### 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



#### Co-Prescribe Naloxone Formulations















## **Complex Intersection**

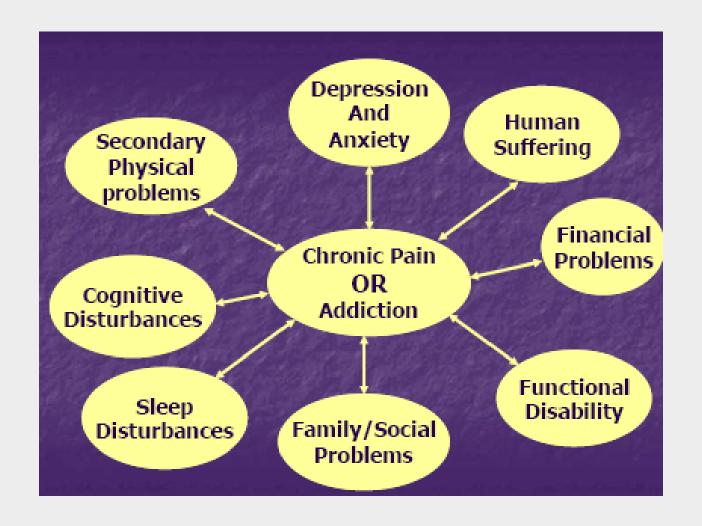


#### Pain and Addiction: Definitions

 "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.

#### Pain and Addiction





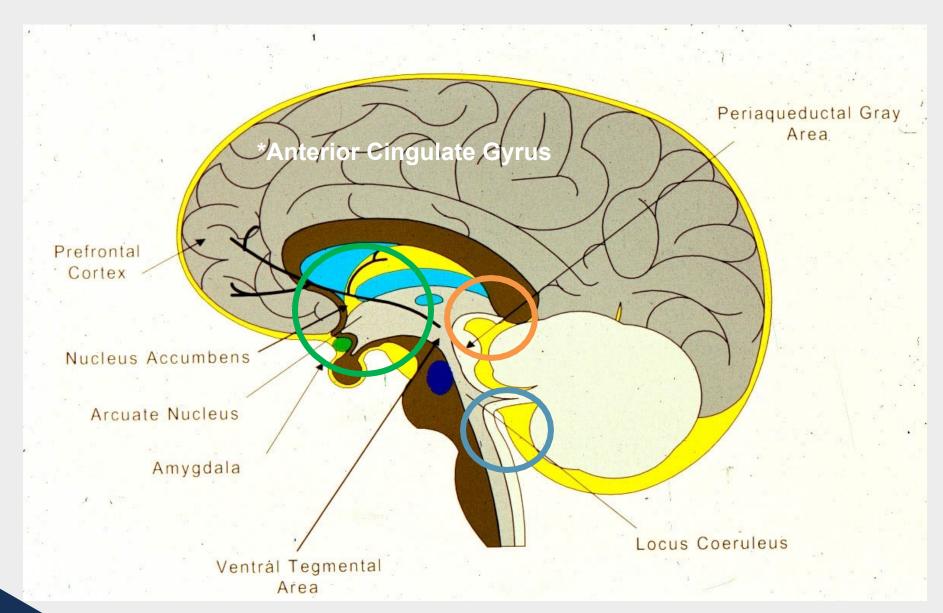
#### Pain and Addiction Limited (e.g., UDT) Objective Measurements







## Opioid Sites of Action in the Brain





# "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.



#### 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: Consider the Bupe Formulations approved for OUD
- Significant other to secure and dispense opioid meds
- Psychiatric Co-morbidity
- Active Addiction recovery program
- UDS, pill counts, agreements, etc.
- Multidisciplinary Pain Program



# Buprenorphine Formulations: FDA Approved for Pain not OUD

- Buprenex® Parenteral (IV, IM)
- Butrans<sup>®</sup> Transdermal (7 Day)
- Belbuca® Buccal Film (75—900mcg q12h)

- Approved for pain but <u>NOT</u> OUDs
- Can NOT be used OFF LABEL for OUDs: Violates DATA 2000





#### 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 Yaganti, BS; Claire Garpestad, MD; Pooja Lagisetty, MD, MSc; Carol Shannon, MPH; Maria J. Silveira, MD, MA, M

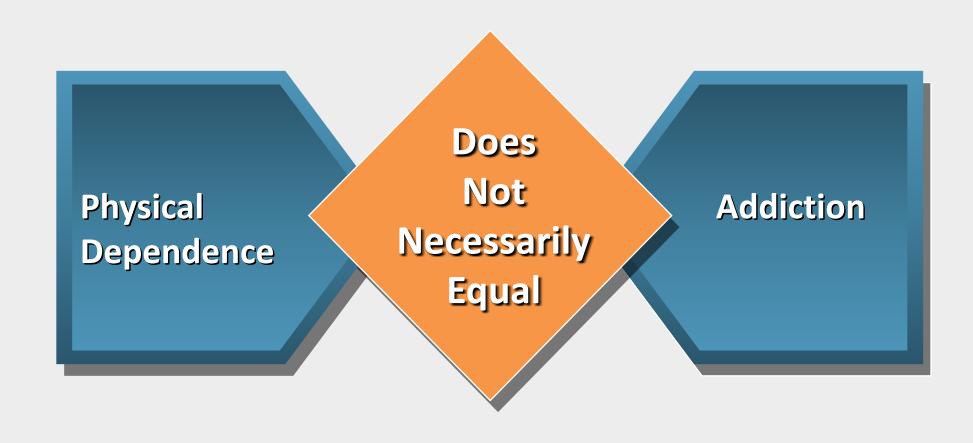
CONCLUSIONS AND RELEVANCE: In this systematic review, buprenorphine was associated with reduced chronic pain intensity without precipitating opioid withdrawal in individuals with chronic pain who were receiving LTOT. Future studies are necessary to ascertain the ideal starting dose, formulation, and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



# Pain and Addiction

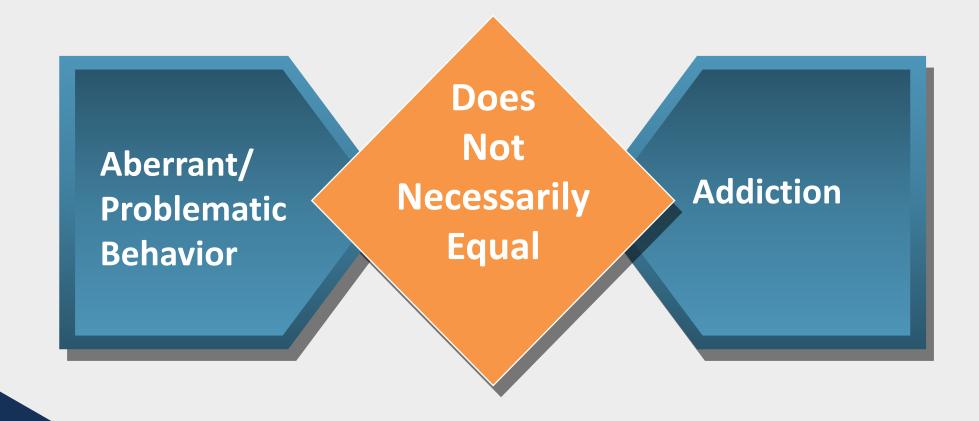


### Definitions: Complex Physical Dependence

"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."

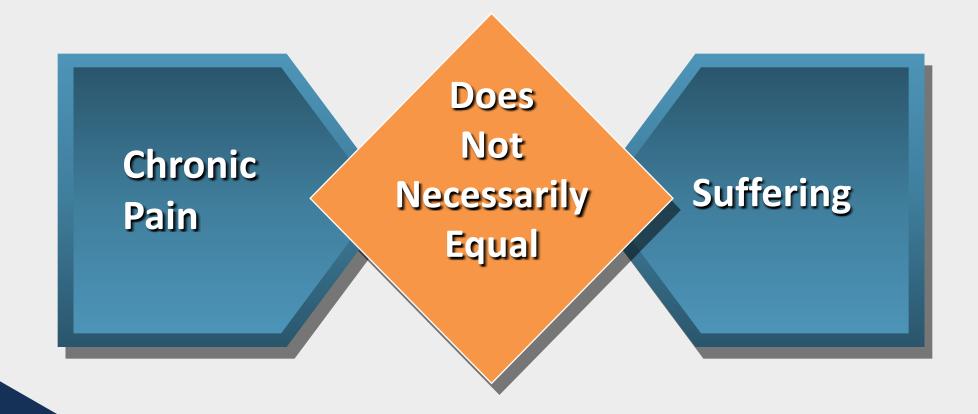


### Pain and Addiction





#### Pain and Addiction





#### **Evolution Of Opioid Prescribing**

Opioid Phobia

Opioid Philia



Multidimensional Pain Treatment



#### 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.



### Good luck on the exam and in your careers!







#### Get in Touch

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JULY 2024 **REVIEW COURSE 2024**