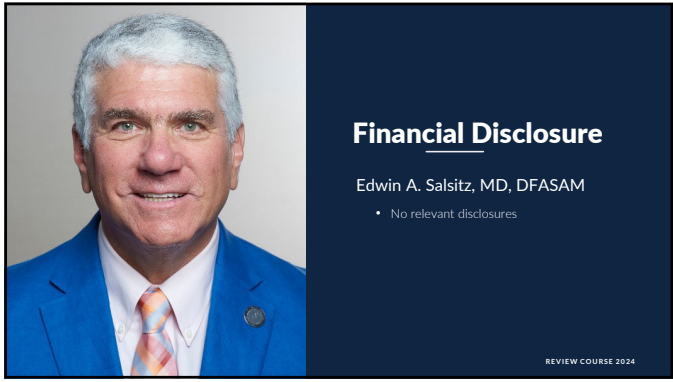
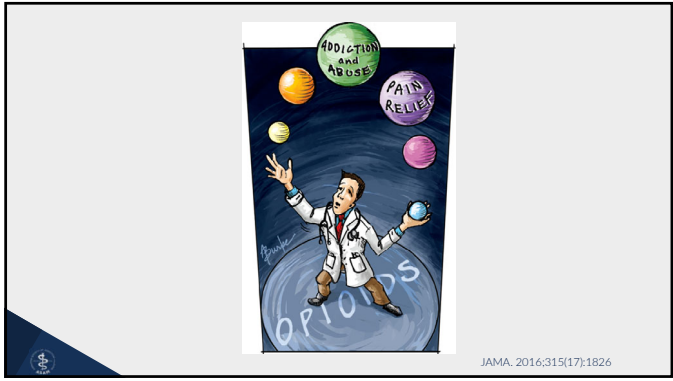




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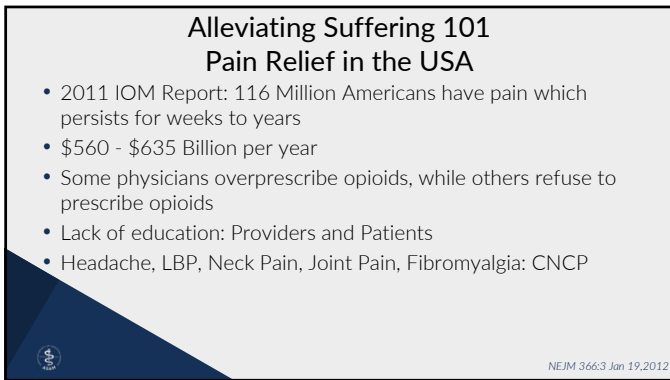
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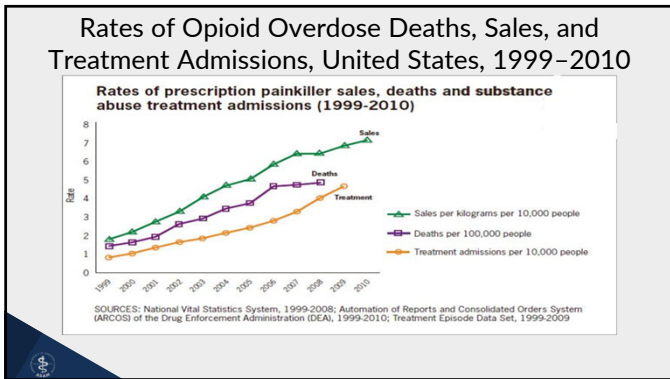
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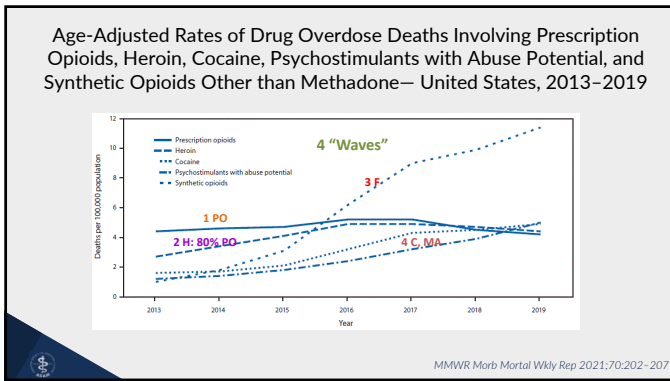
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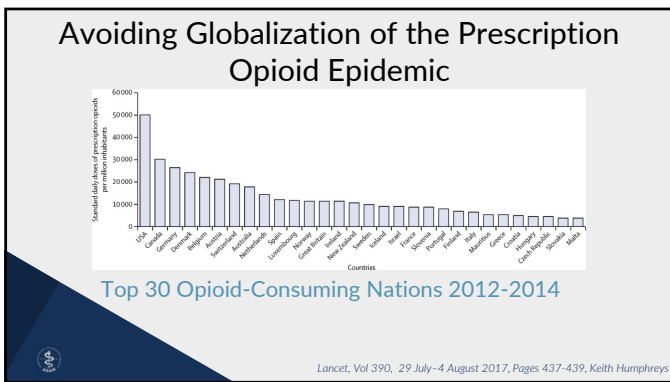
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8

How Did We Get Here?

REVIEW COURSE 2024

9

"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 30,706 hospitalized medical patients who were discharged continuously. Although there were 13,382 patients who received at least one narcotic prescription, there were only four cases of narcotically induced addiction in patients who had no history of addiction. The addiction was considered major in one case and minor. The drugs prescribed were morphine in two patients, Percodan in one, and hydrocodone in one. We conclude that drugs administered to hospitalized patients are safe, and the development of addiction is rare in medical patients with no history of addiction.

Just Puzos
Hazardous Drug
Responsible Program
Boston University Medical Center
Waltham, MA 02154

1. Jish H, Mattison GS, Shapiro S, Lewis GS, Sakata Y, Stone D. Complications drug addiction. JAMA. 1978; 239:1404-1406.
2. Miller RR, Zisk H. Clinical effects of morphine in hospitalized medical patients. J Clin Pharmacol. 1976; 16:356-364.

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*

10

"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

11

ORIGINAL RESEARCH

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

Background: The extent to which adults with mental health disorders in the United States receive appropriate pain management remains unclear.

Objective: We performed a cross-sectional study of a nationally representative sample of the general population of 18-year-old patients from the National Comorbidity Replication to estimate the prevalence of prescription opioid use among adults with mental health disorders.

Design: We analyzed data from the 2009-2012 National Comorbidity Replication, a nationally representative sample of 18-year-old patients from the National Comorbidity Replication.

Setting: The study was conducted in the United States.

Participants: The study included 18-year-old patients from the National Comorbidity Replication.

Measurements and Main Results: We found that 16% of patients with mental health disorders received a prescription opioid in the past 12 months, compared with 10% of patients without mental health disorders.

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

12

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/tcm518697>.

13

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**

14

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

Year	Prescriptions (millions)
2013	251.8
2014	244.5
2015	227.8
2016	215.1
2017	196.0

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

Physicians using prescription drug monitoring programs (PDMPs) are doubling compared to 2014. In 2017, 48% of physicians used a PDMP, up from 24% in 2014. Source: Xperient, IQVIA.

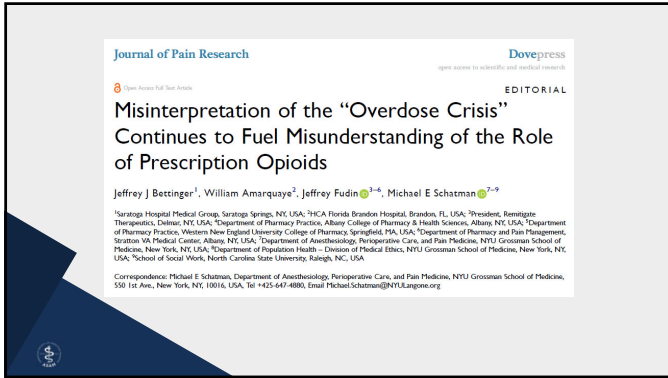
The AMA Opioid Task Force encourages all physicians to enhance their education.

In 2017, more than **549,700 PHYSICIANS** completed the AMA Opioid Task Force educational program. Source: AMA, American Medical Association. www.ama-assn.org

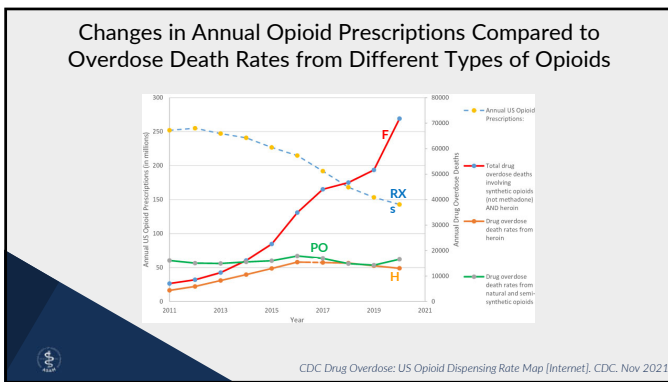
Physicians are helping to improve access to high-quality, evidence-based treatment for opioid use disorder.

Over 100,000 physicians have completed the AMA Opioid Task Force educational program. The AMA encourages all physicians to complete the program. Source: AMA, American Medical Association. www.ama-assn.org

15



16



17

- 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 be used by health systems, pharmacies, insurance companies, medical boards, or governments to determine standard of care.

18

Start With Non-Pharmacologic Therapy

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

19

Non-Pharmacologic Therapy

Figure 2. Age-Standardized Prevalence of Use of Complementary Health Approaches for Pain Management Among Adults Using Each Approach in 2002, 2012, and 2022

JAMA February 20, 2024 Volume 331, Number 7

20

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: Gabapentinoids, 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

21

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

22

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

23

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

24

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, Aphra A. Turner, PhD, Emily B. Devine, PharmD, PhD, MEd, Ryan N. Hansen, PharmD, PhD, Jason D. Salzman, PhD, Ian Brennan, MPH, Tracy Dore, MEd, Christina Brungton, MPH, and Richard A. Deyo, MD, MPH

Background: Increases in prescriptions of opioid medications for chronic pain have been accompanied by increases in opioid overdose, abuse, and other harms and controversy about long-term consequences.

Purpose: To evaluate evidence on the effectiveness and harms of long-term (≥ 12 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 Ovid® catalogs (2008 through August 2018); relevant studies from a prior review; reference lists; and OpenWebPage.

Study Selection: Randomized trials and observational studies that treated 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: The study of opioid therapy versus no opioid therapy evaluated long-term (> 1 year) outcomes related to pain (ORs); quality of life, opioid misuse, or addiction (ORs); and

fair-quality observational studies suggest that opioid therapy for chronic pain is associated with increased risk for overdose, opioid abuse, hospitalizations, emergency department and fracture of cervical spine, although there are risk factors for each of these outcomes; for some harms, higher doses are associated with an 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-analytic could not be done, and publication bias could not be assessed. The placebo-controlled trials and inclusion criteria evidence may be subject to many confounders and outcomes, and observational studies were limited in their ability to address potential biases.

Conclusions: 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;162:376-396. doi:10.7554/ajim.112011 www.annals.org For author disclosures, see end of text. This article first 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

25

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**

Chou R, et al. J Pain. 2009;10:113-30.

26

Can You Land the Opioid Plane?



27

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

28

29

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 Assessment

[4-9-2019] The U.S. Food and Drug Administration (FDA) has received reports of serious harm to patients who are physically dependent on opioid pain medicines and who, having those medicines discontinued or the dose rapidly decreased, have experienced 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 Aguiar, MD, MPH, MHS, Gabe King, PhD, Daniel J. Torzbeck, PhD, Elizabeth Magnus, MD, PhD, Anthony Jorvat, 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

30

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**

31

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

32

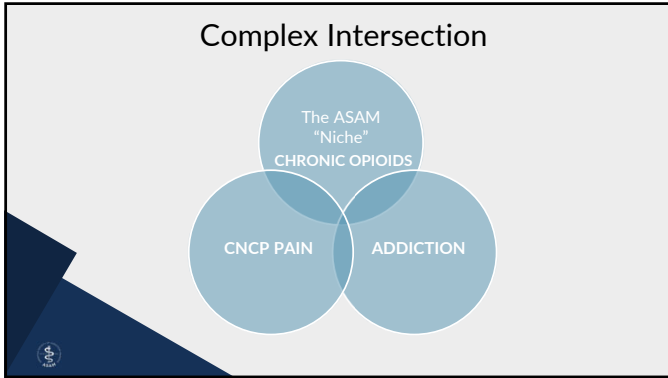
Co-Prescribe Naloxone Formulations



Naloxone 8mg nasal spray
Opioid overdose can happen anywhere. Be ready.

- Narcan® (Naloxone HCl) nasal spray 8 mg
- Evzio®
- Nalmetene

33

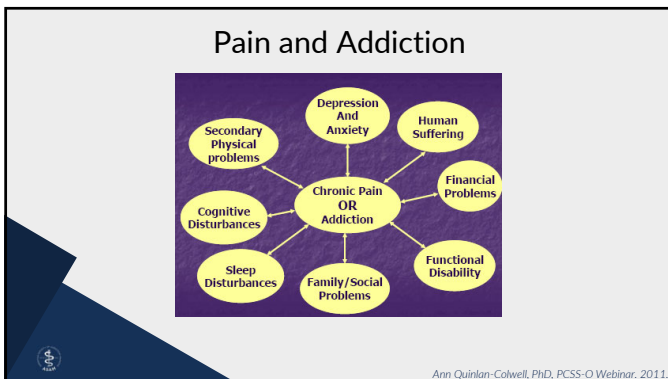


34

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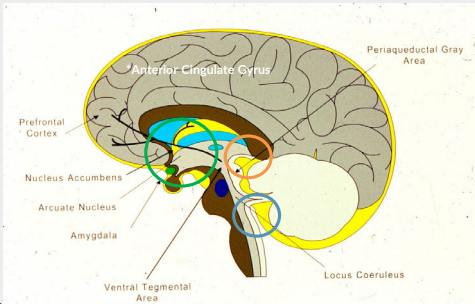
Pain and Addiction
Limited (e.g., UDT) Objective Measurements



The image shows two pieces of medical equipment. On the left is a blue blood pressure cuff with a gauge and tubing. On the right is a handheld urine drug testing device (UDT) with a digital display and a test strip inserted into it.

37

Opioid Sites of Action in the Brain



The diagram shows a sagittal section of the human brain with several regions highlighted in different colors and labeled. The highlighted regions include the Prefrontal Cortex (blue), Nucleus Accumbens (green), Arcuate Nucleus (orange), Amygdala (red), Ventral Tegmental Area (purple), Anterior Cingulate Gyrus (yellow), Periaqueductal Gray Area (light blue), and Locus Coeruleus (dark blue).

38

“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.*

39

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**

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

40

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

41

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

Original Investigation | Substance Use and Addiction

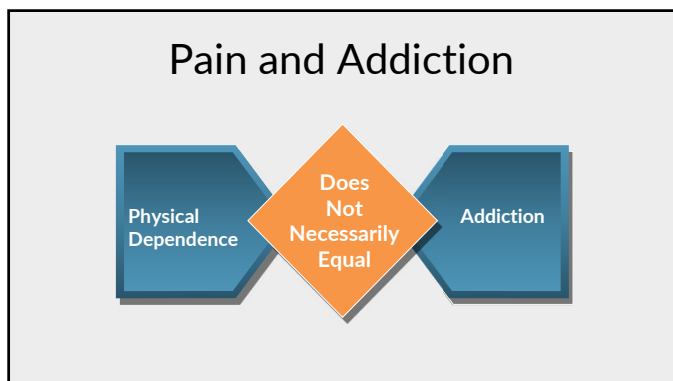
Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain A Systematic Review

Victoria D. Powell, MD; Jack M. Rosenberg, MD; Avani Yiganti, BS; Claire Garpestad, MD; Praga Laggerty, MD, MSc; Carol Shannon, MPH; Mark J. Sheara, 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.

42



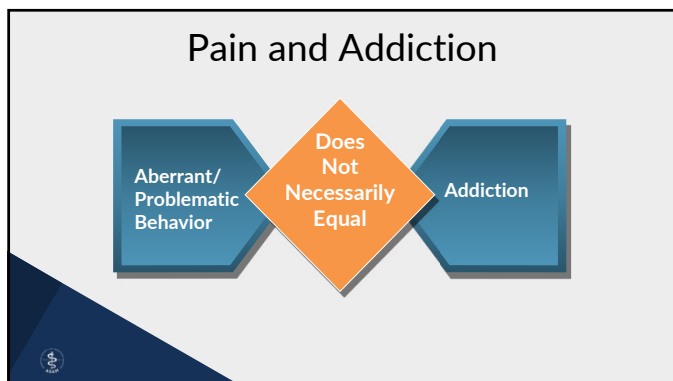
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**Definitions:
Complex Physical Dependence**

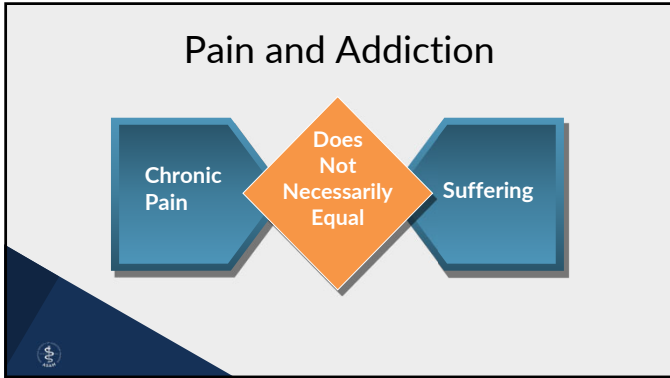
"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether 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

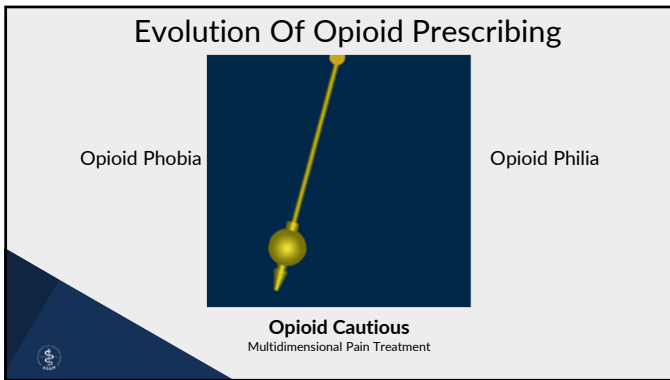
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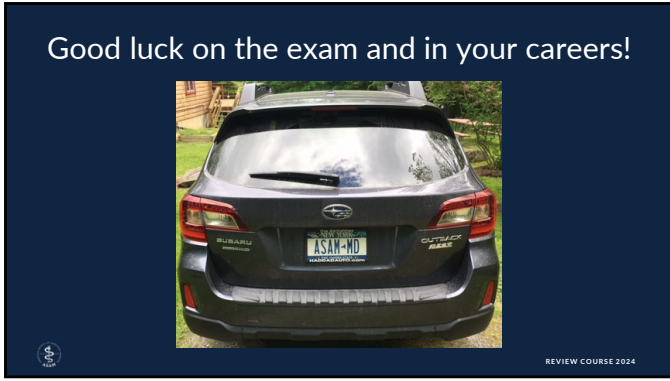
The slide is titled "Pain Quotes". It contains three bullet points:

- "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

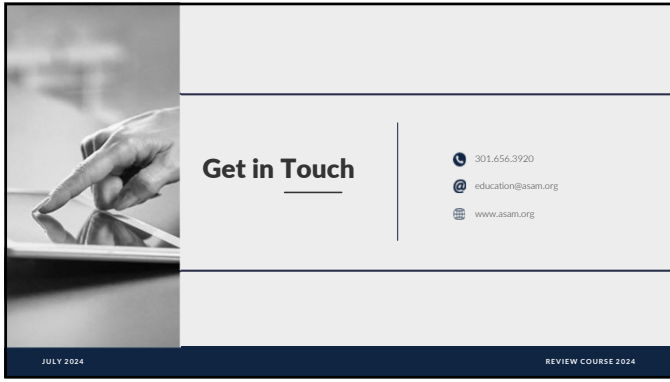
A fourth line of text is present at the bottom: "We can't live without opioids; we have to learn to live with them."

A small logo is visible in the bottom-left corner of the slide.

48



49



50
