PRESCRIPTION OPIOIDS IN CHRONIC PAIN: AN OVERDOSE PREVENTION OPPORTUNITY

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No pertinent conflicts of interest

Abbreviations

CME Continuing Medical Education

CNCP Chronic Non-Cancer Pain

MME Morphine Milligram Equivalents

MOUD Medications for Opioid Use Disorder

OD Overdose

OIH Opioid-Induced Hyperalgesia

OUD: Opioid Use Disorder

PDMP Prescription Drug Monitoring Program

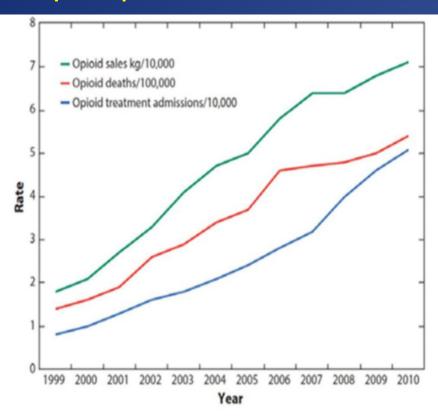
RCT Randomized controlled trial

REMS Risk Evaluation and Mitigation Strategy, an FDA program

Although fentanyl is now the *proximate* cause of most opioid deaths,

Prescription opioids are often the *underlying* cause.

Rates of opioid prescriptions, OUD, and opioid-related deaths have increased in tandem through the first half of the opioid epidemic.



CDC chart 1999–2010, February 28, 2018, Congressional testimony "Combatting the Opioid Crisis," made before the Committee on Energy and Commerce, Subcommittee on Health U.S. House of Representatives (5): "The CDC has shown that a sharp increase in prescriptions for opioids resulted in a corresponding rise in addiction and overdose deaths. This is a CDC graph. The green line represents opioid prescribing, the red line represents opioid deaths, and the blue line represents opioid addiction. The green line went up as opioid prescriptions started to soar, it led to parallel increases in addiction and overdose deaths (6)".

PRESCRIPTION OPIOIDS STILL LEAD TO OUD AND OD <u>IN THE FENTANYL ERA</u> 1 OF 2

"Preventing the development of OUD or opioid overdose deaths ... can be achieved by preventing exposure to opioids..." - American College of Preventive Medicine

Livingston 2022

"More judicious opioid prescribing is necessary so that fewer individuals develop OUD in the first place."

Of individuals with a non-fatal opioid overdose in 2015 – 2016 in BC, Canada, a current opioid prescription was associated with 8-fold higher odds of subsequent overdose. Those with long-term prescriptions had a 3-fold higher rate of overdose than those with short-term prescriptions.

Smolina

Of opioid-related deaths in 2016 in Ontario, a third had an active opioid prescription & > three quarters were dispensed an opioid in the three years before death. 80% of those treated for opioid toxicity in an ED had received a prescription opioid in the previous 3 years.

Gomes

Livingston CJ, et. Al. 'American College of Preventive Medicine: Addressing the Opioid Epidemic Through a Prevention Framework.' Am J Prev Med. 2022 Sep;63(3):454-465.

Rao IJ, Humphreys K, Brandeau ML. Effectiveness of Policies for Addressing the US Opioid Epidemic: A Model-Based Analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. Lancet Reg Health Am. 2021 Nov;3:100031

Smolina K, et. al. Prescription-related risk factors for opioid-related overdoses in the era of fentanyl contamination of illicit drug supply: retrospective case-control study. Subst Abus. 2022;43(1):92-98.

Gomes T, et al. Contributions of prescribed and non-prescribed opioids to opioid related deaths: population based cohort study in Ontario, Canada. BMJ. 2018 Aug 29:362:k3207

PRESCRIPTION OPIOIDS STILL LEAD TO OUD AND OD <u>IN THE FENTANYL ERA</u> 2 OF 2

1 in 8 adolescents are diagnosed with an SUD in the five years following short-term opioid prescriptions after hospitalization for injury between 2011–2013. Each additional outpatient opioid prescription increased the incidence of SUD by 55%. 1 in 10 experience an overdose in the five years following initiation of long-term outpatient opioid prescribing.

Bell

Opioid prescriptions in 2016 predicted opioid-related overdose deaths from both prescription & and illicit opioids. Risk factors included opioid days' supply ≥91 days and average morphine milligram equivalent daily dose. Indications of OUD (prescriptions for MOUD) conferred the highest risk.

Ferris

There is a parallel increase in U.S. opioid treatment admissions and opioid overdose deaths at least through 2019.

Aubry

Bell TM, et al. Outpatient Opioid Prescriptions are Associated With Future Substance Use Disorders and Overdose Following Adolescent Trauma.

Ann Surg. 2022 Dec 1;276(6):e955-e960.

Ferris LM, et. al. Predicting Opioid Overdose Deaths Using Prescription Drug Monitoring Program Data.

Am J Prev Med. 2019 Dec;57(6):e211

Aubry L, Carr BT. Overdose, opioid treatment admissions and prescription opioid pain reliever relationships: United States, 2010- 2019. Front Pain Res (Lausanne). 2022 Aug 4;3:884674.

MORTALITY AFTER EXPOSURE TO PRESCRIPTION OPIOIDS IS OFTEN DELAYED

(making the link between prescription opioids and subsequent fatal illicit opioid OD less obvious).

Of those with an opioid-related death (2013 -2016) after the use of prescribed opioids, most had not had an active prescription for 1-3 years prior to death.

(Gomes)

OUD & fatal OD in 2019 occurred after initiation of prescription opioids a decade earlier.

Reduced U.S. opioid prescribing has already averted ~ 10 000 deaths and are likely to avert five times as many deaths within a decade, relative to 2010 prescribing rates.

(Alexander)

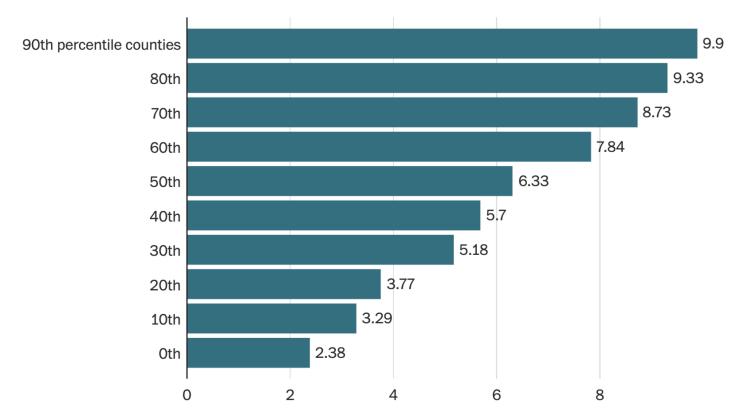
Gomes T, et al. Contributions of prescribed and non-prescribed opioids to opioid related deaths: population based cohort study in Ontario, Canada. BMJ. 2018 Aug 29:362:k3207.

Alexander GC, et. al Effect of reductions in opioid prescribing on opioid use disorder and fatal overdose in the United States: a dynamic Markov model. Addiction. 2022 Apr;117(4):969-976.

More illicit opioid deaths followed years of higher doses of pain pills

The 300 U.S. counties that received the most doses of prescription pain pills per capita from 2006 through 2013 later had the highest death rate from illicit opioids like heroin and fentanyl.

Annualized heroin/fentanyl death rate per 100,000 from 2014 to 2019



Source: Automation of Reports and Consolidated Orders System, CDC Mortality data

STEVEN RICH / THE WASHINGTON POST

PRESCRIPTION OPIOID SALES ARE HIGHLY CORRELATED WITH <u>SUBSEQUENT</u> HEROIN & FENTANYL DEATHS

The Washington Post gained access to the DEA ARCOS database tracking every opioid sold in the U.S. **county-by-county.**

This <u>sales</u> data were correlated with subsequent <u>county-by-county</u> <u>deaths</u> from heroin and fentanyl in CDC data. . .

National Vital Statistics System, CDC Provisional County-Level Drug Overdose Death Counts CDC's Provisional Drug Overdose Death Counts / Vital Statistics System.

... and published in September 2023.

"Users first got hooked by pain pills, ... then turned to cheaper and more readily available street drugs ..."

U.S. OPIOID PRESCRIBING

"The increase in opioid prescribing has occurred mainly because of increased prescribing *for chronic pain*."

Ballantyne

Most opioid prescribing occurs among <u>a small minority of prescribers</u>.

Most top-decile prescribers are general, family medicine, internal medicine, and midlevel practitioners.

Paulozzi

Per-capita consumption of prescription opioids is greater in the U.S. than in any other country. (as of 2019)

Congressional Research Service

Ballantyne JC. Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions. Anesth Analg. 2017 Nov;125(5):1769-1778. Review.

Paulozzi LJ, et. Al. Centers for Disease Control and Prevention (CDC). MMWR Surveill Summ. 2015 Oct 16;64(9):1

Congressional Research Service. Consumption of prescription opioids for pain: a comparison of opioid use in the United States and other countries. Washington, DC (2021). https://crsreports.congress.gov/product/pdf/R/R46805 (pg. 1)

~ ONE IN TEN, TO ONE IN FOUR PATIENTS TREATED FOR CHRONIC PAIN HAVE <u>OUD</u>

~ ONE IN FIVE HAVE OPIOID MISUSE / ABERRANT USE

OPIOID USE DISORDER:

<8% (Volkow 2018)

8 - 12 % (Vowles 2015)

(In Pain clinic settings): 2 - 14% (CDC 2016)

(In PCP settings): **3 - 26**% (CDC 2016)

25% (Boscarino 2020)

OPIOID MISUSE / ABERRANT BEHAVIORS:

5 - 26% (Volkow 2018) **21 - 29%** (Vowles 2015)

Vowles KE, et al. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. Pain. 2015;156(4):569-576.

Dowell D et al. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016 JAMA. 2016 Apr 19; 315(15): 1624–1645. Volkow N, ... McLellan T. Use and Misuse of Opioids in Chronic Pain. Review Annu Rev Med. 2018 Jan 29;69:451

Boscarino JA, et al. Opioid medication use among chronic non-cancer pain patients assessed with a modified drug effects questionnaire and the association with opioid use disorder. J Pain Res. 2020;13:2697–2705.

NEW ONSET OF PERSISTANT OPIOID USE: A COMMON SURGICAL COMPLICATION:

NEW DEVELOPMENT OF

TYPE OF SURGERY: PERSISTENT OPIOID USE: REFERENCE:

Both minor & major: 6% Brummett CM 2017

Various: 5% Clarke 2014, Alam 2012, Waljee 2017

Orthopedics: 8% Goesling J 2016

Curative CA 10% Lee JS 2017

Hand: Johnson SP 2016

Back: 13% Deyo RA 2018

Clarke H, et al. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. BMJ 2014;

Alam A, et al. Long-term analgesic use after low-risk surgery: a retrospective cohort study. Arch Intern Med 2012; 172:425–430.

Waljee, JF et al. latrogenic Opioid Dependence in the United States Are Surgeons the Gatekeepers?

Annals of Surgery: April 2017 - Volume 265 - Issue 4 - p 728-730

Brummett CM, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg. 2017;152(6):e170504 www.ncbi.nlm.nih.gov/pubmed/28403427

Goesling J, et al. Trends and predictors of opioid use after total knee and total hip arthroplasty. Pain.

2016;157(6):1259-1265. Full free: www.ncbi.nlm.nih.gov/pmc/articles/PMC4868627/

Lee JS, et al. New persistent opioid use among patients with cancer after curative-intent surgery.

J Clin Oncol. 2017;35(36):4042

Johnson SP et al. Risk of Prolonged Opioid Use Among Opioid-Naïve Patients Following Common Hand

Surgery Procedures. J Hand Surg Am. 2016 Oct;41(10):947-957. www.ncbi.nlm.nih.gov/pubmed/27692801

Deyo RA et al. Use of prescription opioids before and after an operation for chronic pain (lumbar fusion surgery).

Pain 2018 Jun;159(6):1147 www.ncbi.nlm.nih.gov/pmc/articles/PMC5955818/

EVIDENCE OF EFFECTIVENESS, OR LACK THEREOF: OPIOID TREATMENT FOR CHRONIC PAIN Review of 71 RCTs , AHRQ, 2022

AHRQ: Agency for Healthcare, Research & Quality

(1)

For opioids **compared to non-opioid pharmacotherapy:**

Evidence of lack of effectiveness at 1 – <6 months, and at 12 months. No evidence of effectiveness for chronic pain 6-<12 months

(2)

For opioids **compared to placebo**:

Slight effectiveness for pain with an avg reduction of 0.8 points out of 10 at 1 – <6 months.

* This is below the threshold for a clinically meaningful change in pain scores.

No-evidence of effectiveness at 6-<12 months, or at 12 months.

AHRQ: Systematic Review: Opioid Treatments for Chronic Pain. 2022. Agency for Healthcare Research and Quality. https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research.

Chou, Roger: Presentation: ASAM Pain and Addiction: Common Threads Course XXV - April 2024 Session 2: The State of Evidence-based Pain Care, accessed 7-29-2024

https://elearning.asam.org/products/asam-pain-and-addiction-common-threads-course-xxv-2024#tab- product_tab_contents__18 Feb;12(1):12-20.

A similar review of 80 RCTs of opioids **vs. placebo** for chronic noncancer pain with essentially the same avg results.

(Busse et al)

Mean change in pain score:

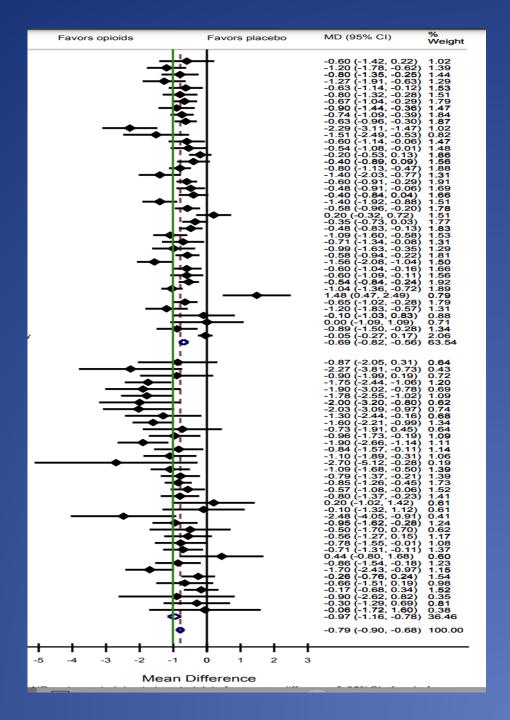
Black line: 0 difference

Green line: -1.0 (10 point scale)

Dotted red line: mean results of -0.68 out of 10 points on average.

(Average effect size is not *clinically* significant).

Busse JW, et al. 'Opioids for Chronic Noncancer Pain: A Systematic Review and Meta-analysis.' JAMA. 2018 Dec 18;320(23):2448-2460.



THRESHOLD FOR CLINICALLY MEANINGFUL IMPROVEMENTS IN PAIN SCORES:

Dworkin et. al. 2008 proposed a **1** point threshold as a meaningful improvement (on a scale from 1-10).

The review by Noble et. al., 2022, noted <u>2 points</u> as a minimum meaningful change in pain scores (10 point scale), citing Farrar 2000, Salafi 2004, and Hagg 2003.

The 2022 CDC Guidelines noted <u>30%</u> as a meaningful improvement for pain and function, citing the review by Ostello 2008.

Approximately two thirds of the 44 studies in the 2022 AHRQ review that defined a meaningful improvement in pain scores used **30%** as the threshold.

(Pain intensity is a limited measure of burden, tolerability, pain interference, & quality of life, which are also affected by confidence in managing pain, psychological factors, etc.).

Sullivan &Ballantyne 2023, Adams 2018

Dworkin RH, et. al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain. 2008;9(2):105-121.

Noble, M. Long-term opioid management for chronic noncancer pain. Review Cochrane Database Syst Rev. 2010 Jan 20;2010(1):CD006605.

Farrar JT. What is clinically meaningful: outcome measures in pain clinical trials. Clinical Journal of Pain 2000;16(2 Supplement):S106-12.

Salaffi F, et al. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. European Journal of Pain 2004 Aug;8(4):283-91.

Hagg O, et al. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *European Spine Journal* 2003 Feb;12(1):12-20.

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

Ostello RWJG, et al. Interpreting change scores for pain and functional status in low back pain: towards international consensus regarding minimal important change. Spine 2008; 33:90–4

AHRQ: Systematic Review: Opioid Treatments for Chronic Pain. 2022. Agency for Healthcare Research and Quality. https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research

Sullivan, Mark and Ballantyne, Jane, The Right to Pain Relief and other Deep Roots of the Opioid Epidemic. Oxford University Press 2023, New York, NY. pg 99 – 100. Adams MH, et al. Prevalence and correlates of low pain interference among patients with high pain intensity who are prescribed long-term opioid therapy.

J Pain. 2018; 19:1074-1081.

PUBLISHED TRIALS MAY OVER-ESTIMATE OPIOID BENEFITS

Trials of long-term opioids for CNCP may not be fully generalizable to patients not enrolled in clinical trials, which generally exclude psychiatric co-morbidities (associated with poor response). But these co-morbidities are over-represented in real-world treatment ("adverse selection").

Sehgal

The few RCTs of efficacy of opioids have rarely extended past 3 months, the length of time after which pain is considered to be chronic.

NASEM
(With time, response to opioid treatment tends to decrease, and opioid-induced hyperalgesia tends to increase,).

Sehgal N., J. Colson, and H.S. Smith. 2013. Chronic pain treatment with opioid analgesics: Benefits versus harms of long-term therapy. Expert Review in Neurotherapeutics 13(11):1201-1220.

NASEM: National Academies of Sciences, Engineering, and Medicine. 2017. Pain Management and the Opioid Epidemic:

Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use. Washington, DC: The National Academies Press. Pg. 53-54.

INSUFFICIENT EVIDENCE OF OPIOID EFFECTIVENESS IN CNCP

There is "**insufficient evidence** to determine long-term benefits of opioid therapy for chronic pain."

(CDC 2022)

"There is a mounting body of research detailing the **lack of benefit** . . . of long-term opioid therapy."

(VA/DoD 2017)

(CNCP: Chronic Non-Cancer Pain)

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 **VA/DoD** Clinical Practice Guideline For Opioid Therapy For Chronic Pain. 2017

VA/DoD Clinical Practice Guidelines Use of Opioids in the Management of Chronic Pain (2022)

"Recommendation #1. We recommend against initiation of long-term opioid therapy for chronic pain.

Strength of recommendation: (Strong evidence)"

(VA/DoD Chronic Pain 2022)

National Institute for Health and Care Excellence:

"Do not initiate opioids to manage chronic primary pain in people aged 16 years and over." (NICE 2021)

"...we have little if any evidence that long-term opioids improve outcomes for chronic pain. It should be a rare patient where we start long-term opioids."

'ASAM Pain & Addiction: Essentials Online,' American Society of Addiction Medicine.

VA/DoD Clinical Practice Guidelines Use of Opioids in the Management of Chronic Pain (2022)

https://www.healthquality.va.gov/guidelines/pain/cot/

NICE: Nat'l. Inst for Health and Care Excellence. Chronic Pain (Primary and Secondary) in Over 16s: Assessment of all Chronic Pain and Management of Chronic Primary Pain. https://www.nice.org.uk/guidance/NG193
Modules presented by Donald Teater, MD, MPH ('Pain & Addiction: Essentials,' ASAM)

'ASAM Pain & Addiction: Essentials Online,' American Society of Addiction Medicine; modules presented by Donald Teater, MD, MPH,

ASAM.org - 'education' - 'e-learning center'

https://elearning.asam.org/products/the-asam-pain-addiction-essentials-online-module-4-treatment-pharmacological-approaches

POTENTIAL HARMS OF REDUCING OPIOID PRESCRIBING:

Overdose or suicide due to injudicious opioid tapering. Chou 2021 Lack of access to pain treatment, especially in minoritized populations.

Patients tapering off of opioids in the years following the 2016 CDC Guidelines for pain were 3 times more likely to die of an overdose.

James 2023

<u>PDMPs</u> and <u>'Pill Mill' laws:</u> are associated with <u>INCREASED</u> use of illicit opioids, and overdose deaths.

(but also with <u>**REDUCED** risky prescribing</u>, and prescription opioid overdose in the longer term)

Cerdá 2023

Chou R, et al, Treatments and Technologies Supporting Appropriate Opioid Tapers. AHRQ Publication No. 21-EHC019. Rockville, MD: Agency for Healthcare Research and Quality; April 2021.

James JR, et al. Mortality after discontinuation of primary care—based chronic opioid therapy for pain: a retrospective cohort study August 2019]. J Gen Intern Med.

Cerdá M, Krawczyk N, et. al. The Future of the United States Overdose Crisis: Challenges and Opportunities.

Milbank Q. 2023 Apr;101(S1):478-506.



Released 9/26/2024; Expires 9/30/2025

One of the OPIOID REMS COURSES (Risk Evaluation Management Strategy).

This is an FDA program funded by manufacturers who also have a role in *hiring faculty and content creators*.

More than half a million U.S. clinicians have taken these courses since 2013.

Opioid Efficacy for Chronic Pain



41

Meta-analyses (3-6 m f/u)

- Opioids vs placebo (high quality studies)
 Opioids with statistically significant, but small, improvements in pain^{1,2} and physical functioning²
- Opioids vs nonopioids (low-mod quality studies)
 Similar benefits²

RCT³ found opioids
not superior to
nonopioids for improving
musculoskeletal painrelated function over 12
months

Limitations to generalizability:4

- Excluded patients already on long-term opioids
- 89% of eligible patients declined to be enrolled

Two longer term followup studies found **44.3%** on chronic opioids for chronic pain had **at least 50% pain relief** ⁵

5. Noble M, et al. Cochrane Syst Rev. 2010

(Slide 41 REMS course: 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' Boston University, expiration: 9/30/2025)

Narrator, discussing last panel: "...pretty much everything you need to know is on this slide . . . There were two longer-term follow-up studies that found 44.3 percent on opioids for chronic pain had at least 50 percent pain relief. So, if that is your outcome measure – 50 percent pain relief – about half achieved it." **This concludes the discussion of "Opioid Efficacy for Chronic Pain."**

^{1.} Meske DS, et al. J Pain Res. 2018

^{2.} Busse JW, et al. JAMA. 2018

^{3.} Krebs EE, et al. JAMA. 2018

^{4.} Webster L. Pain Med. 2019

NOTE THAT ... (1)

These were *observational studies*, at odds with RCT data and conclusions of the CDC and VA/DoD Practice Guidelines.

(2)

The authors of the cited reference, Noble, et al, concluded:
"We do not believe that any firm conclusions regarding the precise proportion of participants who have at least 50% pain relief can be drawn at this time."

and

"...the evidence regarding the effectiveness of long-term opioid therapy in CNCP is too sparse to draw firm conclusions..."

(last panel, prior slide):

Two longer term followup studies found **44.3%** on chronic opioids for chronic pain had **at least 50% pain relief** ⁵

41

5. Noble M, et al. Cochrane Syst Rev. 2010

Pain is severe Pain has significant impact on function and quality of life Pain type potentially opioid-responsive nociceptive or neuropathic pain but less so for nociplastic pain and headache syndromes (e.g., migraines) Inadequate benefit from non-opioid modalities If already on opioids, is there documented benefit (pain, function, quality of life)?

Slide 58: Opioids and Chronic Pain in Perspective

"Opioids for chronic pain are indicated after alternative safer options are inadequate." (emphasis added)

(Slides 57, 58: REMS course: 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' Boston University, expiration: 9/30/2025)

(In the context of chronic pain)

The conditions in which this course claims that opioids are "<u>indicated</u>" are very common (severe pain; inadequate benefit from non-opioid modalities...).

The suggestion that opioids are "<u>indicated</u>" goes beyond the evidence and beyond any major published recommendations.

WHEN TO CONSIDER A THERAPEUTIC TRIAL OF IR OPIOID

Patient has failed to adequately respond to non-opioid and nonpharmacological interventions

Patient has moderate to severe nociceptive or neuropathic pain

Potential benefits are likely to outweigh risks



Chou R, et al. J Pain. 2009;10:113-130.

Dowell D et al. MMWR Recomm Rep 2022 Nov. 4;71(3):1-95. DOI: http://dx.doi.org/10.15585/mmwr.rr7103a1.

VA/DoD Clinical Practice Guideline. (2022). Use of Opioids in the Management of Chronic Pain Work Group. Washington, DC: U.S. Government Printing Office.





'Pain Management & Opioids: A Patient-Centered Approach ' (a CO*RE / Opioid REMS course created Jan 2025)

Similarly, in a REMS course created Jan 2025, the phrase "When to consider..." suggests that a trial of opioids should be considered in the circumstances listed.

This suggestion goes beyond the evidence, beyond any major guideline, and beyond the three references cited:

"Chou R, et al. Pain. 2009; 10:113-130

"Dowel MMWR 2022 Nov. 4;71(3):1-95

"The VA/DoD Clinical Practice Guideline. (2022). Use of Opioids in the Management of Chronic Pain Work Group. Washington, D.C."

(Continued ...)



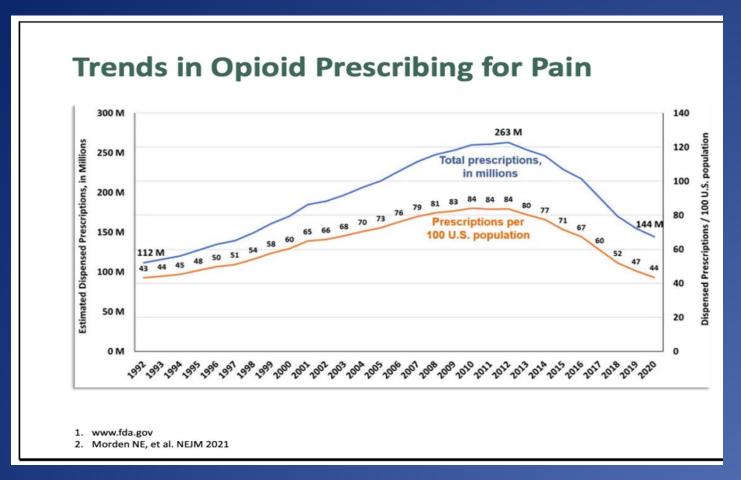


None of the three cited references recommend that initiating a trial of opioids should be considered in the circumstances listed.

The Dowell citation (CDC Clinical Practice Guideline for Prescribing Opioids for Pain 2022) never describes circumstances where a trial of opioids should be considered and states that there is "insufficient evidence to determine long-term benefits of opioid therapy for chronic pain."

The 3rd citation, the 2022 VA/DoD Guideline, states: "Recommendation #1:
"We recommend against the initiation of opioid therapy for the management of chronic non-cancer pain. Strength of Recommendation: Strong."

OPIOID REMS COURSES PRESENT PRESCRIBING RATES SELECTIVELY:



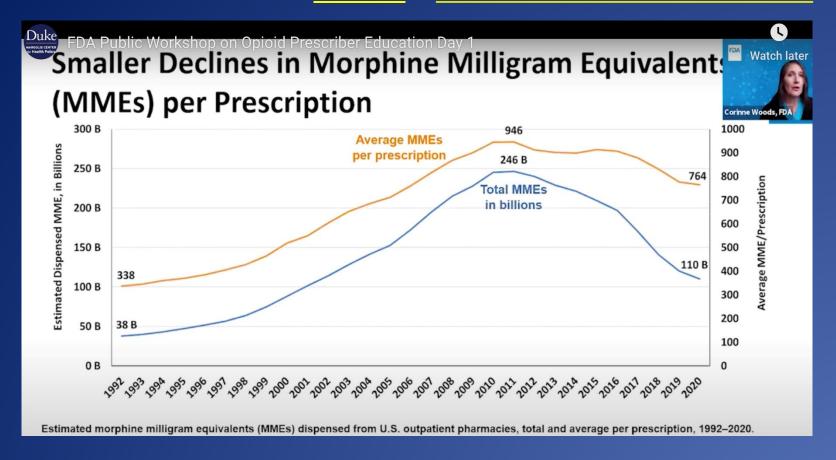
(Slide 12: REMS course: 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' Boston University, expiration: 9/30/2025)

TOTAL NUMBERS OF PRESCRIPTIONS per capita have returned to the level they were at the start of the opioid epidemic.

But the volume of prescribed opioids in terms of morphine milligram equivalents per capita is not presented.

(continued . . .)

MODERN PRESCRIBED OPIOID VOLUME IS TWICE THE PRE-EPIDEMIC BASELINE



Per capita MME: <u>147</u> in 1992; <u>332</u> in 2020

Aitken, M., et. Al. Prescription Opioid Trends in the United States: Measuring and Understanding Progress in the Opioid Crisis, IQVIA Institute for Human Data Science, December 2020.

IQVIA Institute, "National Prescription Audit" extracted March 2021, U.S. Census Bureau.

As presented at a 2021 FDA workshop at at 1:15:00. https://healthpolicy.duke.edu/events/fda-public-workshop-opioid-prescriber-education

Part 2, Slide 37: Lack or Loss of Benefit

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

What are the next steps? . . .

- Add or increase non-opioid and non-pharmacologic treatment
- Add breakthrough medications
- Switch to a different opioid ("rotation")
- Avoid dose escalation to "high" dose opioids

Part 2, Slide 36: Opioid-Induced Hyperalgesia (OIH)

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

..."Uncertain on whether tapering or switching to a different opioid is more effective..."

There is no mention of consideration of rotation to buprenorphine for loss of benefit, OIH, poor functional status, or for reducing risk in this course.

Instead, four slides address risk / lack of benefit by adding opioids for breakthrough pain or rotation to other opioids, strategies which may increase risk.

In another Opioid REMS course (created Jan 2025: 'Pain Management & Opioids: A Patient-Centered Approach') there is likewise no mention of consideration of rotation to buprenorphine for loss of benefit, OIH, poor functioning, or for reducing risk. *

^{*} Although slide 67 on ER/LA opioids simply lists "consider transition to buprenorphine" with a brief comment by the narrator; "it has that safety factor."

Instead, there are five slides on adding opioids for breakthrough pain and opioid rotation (slides 71, 72, 73, 76, and 77).

COMPARED WITH FULL AGONIST OPIOIDS, BUPRENORPHINE FOR CHRONIC PAIN CAN REDUCE RISKS / INCREASE EFFECTIVENESS Slide 1 of 2

"Recommendation: For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk of overdose and misuse."

VA/DoD

A 2020 expert panel from the American Academy of Pain Medicine recommended that "buprenorphine be considered over Schedule II opioids such as fentanyl and oxycodone in managing chronic pain. . ."

Bissaillon

"Management of Opioid Misuse That Does Not Meet Criteria for Opioid Use Disorder ... For patients who choose to but are unable to taper, clinicians can ... offer buprenorphine treatment. . ." CDC 2022

The Dept of Health and Human Services encourages consideration of buprenorphine for pain management for patients "on high opioid dosages unable to taper despite worsening pain and/or functioning with opioids." HHS

Buprenorphine is associated with less respiratory depression, overall mortality and fewer fatal overdoses, and fewer adverse effects than full agonist opioids. In a review of 22 studies, buprenorphine rotation was associated with reduced pain without serious adverse effects.

Powell

VA/DoD Clinical Practice Guidelines Use of Opioids in the Management of Chronic Pain, 2022
Bissaillon A, et al. Is buprenorphine safe for the treatment of chronic pain in adults? Evidence-Based Practice. September 2022
CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022
HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics 2019
Powell VD,... Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review.

JAMA Netw Open. 2021 Sep 1;4(9):e2124152.

COMPARED WITH FULL AGONIST OPIOIDS, BUPRENORPHINE FOR CHRONIC PAIN CAN REDUCE RISKS / INCREASE EFFECTIVENESS Slide 2 of 2

Strategies to transition to buprenorphine are "already being used across the US, including at many top academic institutions, for chronic pain." ... "The existing evidence and expert consensus are sufficient to support a [buprenorphine] microdose cross-taper without an opioid-free period."...

Training programs should be updated to facilitate this approach.

Raheemullah

42 patients with severe musculoskeletal (64%), cancer (21%) or neuropathic (19%) pain were converted from high-dose morphine (120 to >240 mg/day) to transdermal buprenorphine due to insufficient analgesia and intolerable side effects. Patients experiencing good/very good pain relief increased from 5% to 76% (P < 0.001). Freye

35 chronic pain patients treated with high-dose opioid-agonists (mean 550 MME/day) were converted to SL buprenorphine. After 2 months the mean pain score decreased from 7.2 to 3.5 (P < 0.001), Quality of life scores improved from 6.1 to 7.1 (P = 0.005).

Buprenorphine has a ceiling effect for sedation, constipation, and respiratory depression, but not for pain. Manhapra

Compared to full agonist opioids, buprenorphine ...

... has a ceiling effect for respiratory depression but not for pain, a relative lack of psychiatric effects, potent analgesia with antihyperalgesic properties, little or no immunosuppressive effect, less constipation, no serotonin syndrome, no clinically significant QT prolongation at and above generally used doses, and is less likely to suppress the gonadal axis. ... "There is more than enough data to compel providers to consider buprenorphine as a first-line opioid choice for patients with chronic pain who require a long-acting opioid." Rudolf

Raheemullah A, et al. Buprenorphine Microdosing Cross Tapers: A Time for Change. Int J Environ Res Public Health. 2022

Freye E, et al. Opioid rotation from high-dose morphine to transdermal buprenorphine (Transtec) in chronic pain patients. Pain Pract 2007; 7:123-129

Daitch D, et al. Conversion from high-dose full-opioid agonists to sublingual buprenorphine reduces pain scores and improves quality of life for chronic pain patients Pain Med. 2014 Dec;15(12):2087

Manhapra A, et al. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. Subst Abus. 2018;39(2):152-161. Rudolf GD. Buprenorphine in the Treatment of Chronic Pain. Phys Med Rehabil Clin N Am. 2020 May;31(2):195-204. Review.

SPECIAL POPULATIONS: OLDER ADULTS

RISK FOR RESPIRATORY DEPRESSION

Age-related changes in distribution, metabolism, excretion; absorption less affected

ACTIONS

- Monitor
 - Initiation and titration
 - Concomitant medications (polypharmacy)
 - Falls risk, cognitive change, psychosocial status
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated, non-opioid-tolerant patients
- Start low, go slow, but GO

'Pain Management & Opioids: A Patient-Centered Approach (a CO*RE / Opioid REMS course created Jan 2025)

(Also lists: "Routinely institute a bowel regimen" and "Patient and caregiver reliability/risk of diversion")

No mention of rotation to (or initiating with) buprenorphine due to increased risk.

The slide appears to be encouraging the use of opioids in older adults:

"Start low, go slow, but GO" (Capitalized



Part 2, Slide 8: BUPRENORPHINE: A partial opioid agonist

Lists formulations approved for pain or OUD, with dosing information.

Notes the possibility of precipitated withdrawal.

"Taper prior opioid to <30 MME before starting buprenorphine"

Part 2, Slide 13: Opioid Choice Summary

- Duration and onset of action
 - Consider pattern of pain: intermittent vs. constant
- Patient's prior experience (effects & side effects)
 - Mu-opioid receptor polymorphisms and differences in opioid metabolism
- Patient's level of opioid tolerance (assess before starting ER/LA opioid formulations)
- Age, other medications and diseases
- Route of administration
- Cost and insurance issues

Opioid-Induced Hyperalgesia (OIH)

Paradoxical enhanced pain sensitivity in patients on chronic opioids (> 1 month)

Underlying pathophysiology and true incidence is unknown

(Slides from 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education' expiration: 9/30/2025)

OPIOID CHOICE:

The overall <u>safety</u> of various opioids as a criteria to consider, e.g. for risk of hyperalgesia, functional impairment, misuse, addiction, or overdose, is not mentioned in this REMS course.

(continued ...)

DRUG CHARACTERISTICS TO CONSIDER BEFORE PRESCRIBING Mechanism of Route of Dosing Strength administration action interval Key Productinstructions Specific drug Formulation specific safety (indications, uses, interactions concerns contraindications) ER/LA: Use **Specifics** Relative Potential . effects of about product only in opioid potency to sudden conversions. tolerant morphine discontinuation if available (MME) patients Opioid product information available at https://opioidanalgesicrems.com/products.html · Immediate Release (IR): rapid onset of analgesia, relatively short duration of effect Extended Release/Long-Acting (ER/LA): potentially longer onset of action, longer duration of effect; formulation allows for QD or BID dosing; less frequent dosing CO*RE CO*RE 2024

'Pain Management & Opioids: A Patient-Centered Approach ' (a CO*RE / Opioid REMS course created Jan 2025)

OPIOID CHOICE:

In this REMS course, "<u>safety concerns</u>" as an opioid criteria to consider is listed <u>only in</u> this slide, but not mentioned by the narrator, who does mention most of the other characteristics listed. *

^{* (}Except, elsewhere, there is mention of a debate about increased risk of hyperalgesia, addiction with ER/LA opioids).

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

... "Only consider opioids if expected benefits (pain/function) > risks." ...

The statement is ineffective as guidance.

(Prescribers generally do not prescribe medicine if they estimate that benefits do not outweigh risks).

More meaningful guidance would be:

- (1) Initiating long-term opioids for chronic non-cancer pain (CNCP) should be infrequent, and
- (2) If an opioid is initiated for CNCP, buprenorphine is generally preferred. *
- * Both of these guidance messages are included in:
- The VA/DoD Clinical Practice Guidelines: Opioids in the Management of Chronic Pain (2022),
- 'The ASAM Pain & Addiction: Essentials Online' ASAM.org 'education' 'e-learning Center'

Part 2. Slide 27: Implementing Opioid Stewardship

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

Subtitle: "Prescribing Opioids Safely, correctly, and under the right circumstances"...

The word "safely" is misleading and minimizes risks.

Risks typically increase after physical dependence has developed, when it may be difficult / risky to change course.

The risk of harm is not reliably predictable or modifiable:

"No validated, reliable way exists to predict which patients will experience serious harm from opioid therapy and which patients will benefit from opioid therapy."

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

"Estimates of diagnostic accuracy for various risk prediction instruments were highly inconsistent, and there was no evidence on the effectiveness of risk mitigation strategies ... with the exception of one study that found provision of naloxone was associated with decreased emergency department visits."

AHRQ: Systematic Review: Opioid Treatments for Chronic Pain. 2022. Agency for Healthcare Research and Quality.

"There is no safe opioid prescribing"

Slide 17: RISK FACTORS: DEVELOPING CHRONIC POSTSURGICAL PAIN.

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

Lists "Patient-Related Factors,... Intra-Operative Factors, ...

and Postoperative Pain factors:

Uncontrolled high intensity pain, Longer duration of post-op pain."

Does not include duration/dose of post-op prescription opioids as a modifiable factor for subsequent overdose, misuse, and long-term use.

Duration of post-op opioid prescription was the strongest predictor of misuse.

Brat

A retrospective study of patients with disabling low back pain: Compared to the group receiving no early opioids in the first 15 days, groups receiving more early opioids had more disability duration, prolonged opioid use, risk of surgery, and medical costs, which increased in a dose-dependent manner. The highest early opioid group had 3 times the risk of surgery and 6 times the risk of receiving late opioids.

Webster

Post - procedure opioids were associated with subsequent opioid use and abuse.

Schroeder

Discharge opioid prescription ≥ 400 MMEs was a factor associated with long-term use.

Goyal

Brat GA, et al. Postsurgical prescriptions for opioid naive patients and association with overdose and misuse:

Webster BS, et al. Relationship Between Early Opioid Prescribing for Acute Occupational Low Back Pain and Disability Duration, Medical Costs, Subsequent Surgery and Late Opioid Use. Spine (2007)1;32(19):2127.

Schroeder AR, et al. Association of Opioid Prescriptions From Dental Clinicians for US Adolescents and Young Adults With Subsequent Opioid Use and Abuse. JAMA internal medicine. 2019;179(2):145.

Goyal A, et al. Opioid Utilization Following lumbar Arthrodesis: Trends and Factors Associated With Long-Term Use. Spine; 43(17), 1208-1216. retrospective cohort study. BMJ. 2018. BMJ 2018;360:j5790

REDUCTIONS IN OPIOID PRESCRIBING HAVE NOT LED TO REDUCTIONS IN OVERDOSE DEATHS Overdose deaths: 94,134* **Opioid prescriptions:** 143,390,951¹ (44.4% decrease since 2011) *Provisional data for the 12-month period Jan. 2020—Jan. 2021 https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

From the REMS course 'Pain Management and Opioids - Balancing Risks and Benefits' CO*RE (Collaboration for REMS Education) 2023 (expired, inaccessible)

Through 2023/2024 a number of Opioid REMS courses emphasized the apparent discrepancy between increasing OD deaths and <u>declining opioid prescriptions</u>, implying that prescription opioids are no longer related to deaths from illicit opioids.

Verbatim accompanying narrative, emphasis added:

"<u>Historical</u> over-prescribing... has fueled the opioid overdose epidemic ... <u>there are still pockets</u> of the US where prescribed opioids influence the number of deaths."

(See earlier slides with evidence of the opposite conclusion).



'DOCTORS RECEIVE OPIOID TRAINING. BIG PHARMA FUNDS IT.
WHAT COULD GO WRONG? It doesn't look like promotion. It looks like education.'

Julia Lurie Mother Jones magazine April 2018. www.motherjones.com (search for title)

"It is evident that the REMS system is not robust enough to combat the forces pushing for inappropriate use. The FDA should be in charge of developing REMS ..."

It's time to wake up from the REMS cycle; By Judith Garber | July 1, 2019 https://lowninstitute.org/its-time-to-wake-up-from-the-rems-cycle/

> Pain Physician. 2021 Aug;24(5):E529-E538.

Increase your Confidence in Opioid Prescribing: Marketing Messages in Continuing Medical Education Activities on ER/LA Opioids

Benjamin Goodwin ¹, Hwa-Pyung David Lim ², Judy Butler ³, Daniel Paglia ⁴, Matthew T Dempsey ³, Bonnie O Connor ⁵, Adriane Fugh-Berman ⁶

Affiliations + expand PMID: 34323440

Free article

Systematically analyzed all online opioid REMS activities 2016 – 2018 using thematic analysis.

Sample of themes or repeated statements included:

Opioids are safe & effective for chronic pain,

Many activity titles included the word "safe."

Screening and monitoring tools are effective for preventing opioid-related problems.

Case: "Mary Williams," with alcohol use disorder - at "moderate risk;" The right answer is that it is acceptable to initiate opioids for chronic pain in this case.

Quote: "You can never go wrong with opioids if you start low and go slow."

Goodwin B, et. al. Increase your Confidence in Opioid Prescribing: Marketing Messages in Continuing Medical Education Activities on ER/LA Opioids. Pain Physician . 2021 Aug;24(5):E529-E538.

No Evidence of Effectiveness of Opioid REMS

(Part 1)

U.S. Department of Health and Human Services

Office of Inspector General Report in Brief

September 2020, OEI-01-17-00510



Why OIG Did This Review
While the opioid crisis continued
with nearly 47,000 deaths in 2018,
the Food and Drug Administration

FDA's Risk Evaluation and Mitigation Strategies: Uncertain Effectiveness in Addressing the Opioid Crisis

No Evidence of Effectiveness of Opioid REMS

(Part 2)

The FDA has been unable to determine the effectiveness of the Extended Release / Long Acting (ER/LA) opioid REMS (which later became the Opioid REMS) due to limitations in the manufacturers' survey methods. The authors concluded that "the FDA should establish a credible evaluation plan for REMS."

Heyward J, Olson L, Sharfstein JM, Stuart EA, Lurie P, Alexander GC. Evaluation of the Extended-Release/Long-Acting Opioid Prescribing Risk Evaluation and Mitigation Strategy Program by the US Food and Drug Administration: A Review. JAMA Intern Med. 2020 Feb 1:180(2):301

According to a former Sr. FDA Commissioner, "Instead of bold, effective action [to address the use of prescription opioids], the FDA has implemented the Risk Evaluation and Mitigation Strategy programs that ... do not even meet the limited criteria set out by the FDA."

Invited Commentary. December 30, 2019 William K. Hubbard. Getting Serious About Opioid Regulation. JAMA Intern Med. 2020 Feb 1;180(2):309-310.

Opioid REMS courses are accredited by the American Council for Continuing Medical Education (ACCME) as being free of commercial bias.

However

- Messages that are misleading, coinciding with manufacturers' interests, are evident.
- The ACCME claims that CME is not industry-supported.
 However, payments for hotels, caterers, food, Audio/Visual, advertising and exhibition fees <u>are not counted as industry support.</u>
- The ACCME depends on payments from entities providing industry-sponsored education a disincentive to identify commercial bias.
- Opioid Manufacturers hire, and can fire, the CME companies that create content.

Fugh-Berman A. Industry-funded medical education is always promotion—an essay by Adriane Fugh-Berman BMJ: British Medical Journal Vol. 373, (Jun 4, 2021).

Fugh-Berman, A. et al. CME stands for commercial medical education: and ACCME still won't address the issue. 2016 Mar;42(3):172-3.

The following POLICY MEASURES to reduce opioid-related deaths are recommended by the prestigious Stanford-Lancet Commission:

- Reduced opioid prescribing for acute pain,
- Reduced opioid prescribing for chronic pain,
- Reduced opioid prescribing for pain of intermediate duration,
- PDMPs, naloxone availability, and other interventions

 Rao

These policies may *increase* use of illicit opioids in the short-term, but reduce it in the long term.

Cerdá, Rao

An American College of Preventive Medicine 'Key Strategy' to address the opioid epidemic:

Decrease exposure to opioids.

Livingston 2022

"Epidemics do not generally fade without a preventive component. . .

More judicious opioid prescribing is necessary so that fewer individuals develop OUD in the first place."

Rao IJ, et al. Effectiveness of Policies for Addressing the US Opioid Epidemic: A Model-Based Analysis from the Stanford-Lancet Commission on the North American Opioid Crisis. Lancet Reg Health Am. 2021 Nov;3:100031

(Commission members: Keith Humphreys, Ph.D., Christina Andrews, PhD, Amy Bohnert, PhD, Margaret L. Brandeau, PhD, Jonathan Caulkins, PhD, Jonathan Chen, MD, PhD, Mariano-Florentino Cuéllar, JD, PhD, Yasmin Hurd, PhD, David Juurlink, MD, PhD, Howard Koh, MD, MPH, Erin Krebs, MD, Anna Lembke, MD, Sean. Mackey, MD, PhD, Lisa Larrimore Ouellette, PhD, Chelsea Shover, PhD, Brian Suffoletto, MD, Christine Timko, PhD)

Cerdá M, Krawczyk N, et. Al. The Future of the United States Overdose Crisis: Challenges and Opportunities.

Milbank Q. 2023 Apr;101(S1):478-506.

Livingston CJ, et. Al. 'American College of Preventive Medicine: Addressing the Opioid Epidemic Through a Prevention Framework.'

Am J Prev Med. 2022 Sep;63(3):454-465.

Slide 5: ABOUT THE PROGRAM:

('SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025)

"THROUGH THE CASES PRESENTED IN THIS PROGRAM, YOU WILL LEARN HOW TO ...

- Assess for prescription opioid misuse risk . . .
- Monitor patients prescribed opioids for benefits and harms . . .
- Use a risk-benefit framework when initiating, maintaining, modifying, or tapering opioids
- Diagnose and manage patients with opioid use disorder with or without concurrent pain."

All Opioid REMS include an overwhelming emphasis the role of opioids.

With the evident influence of opioid manufacturers over content, these courses may tend to reduce effectiveness of CNCP treatment and sustain opioid over-prescribing and the incidence of OUD and of OD.

Titles of most slides in: 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' expiration: 9/30/2025

PART 1, Slide: 17	Slide 11: Abuse Deterrent/Resistant Formulations [of Opioids]
Slide 14: Understanding Pain and Opioids	Slide 13: Opioid Choice Summary
Slide 5: About the Program (about opioids)	Slide 16: Case study: Change Opioid Regimen
Slide 19: Case Study (on opioids)	Slide 17: Universal Precautions When Prescribing Opioids
Slide 24: Case Study (on <mark>opioids</mark>)	Slide 18: Patient Provider Agreement (includes: safer opioid use
Slide 25: Case Study (on opioids)	Slide 22: Minimum Level of Monitoring Based on Risk: includes Opioid Risk Tool Slide
Slide 26: Case Study (on opioids)	23: Monitoring and Documentation: Office Visits (includes opioids)
Slide 35: Non-Opioid Pharmacotherapies	Slide 24: What is the clinician's role? Judge the opioids treatment, not the patient
Slide 36: Non-Opioids Pharmacotherapies	Slide 25: Discussing Monitoring risks of opioids
Slide 37: Opioids	Slide 26: Safer Opioid Prescribing is a lot of work! [displays title only]
Slide 38: Opioid Analgesics	Slide 27: Implementing Opioid Stewardship
Slide 39: Opioid Tolerance and Physical Dependence	Slide 28: Community Pharmacist) includes naloxone [an opioid antagonist]
Slide 40: Opioid Efficacy and Safety? [Displays title only]	Slide 28: Case study – (on <mark>Opioids</mark>)
Slide 41: Opioid Efficacy for Chronic Pain	Slide 30: Case study – (on <mark>Opioids</mark>)
Slide 42: Opioid Safety and Risks	Slide 31: Case study – (on <mark>Opioids</mark>)
Slide 43: Managing <mark>Opioid</mark> Adverse Effects	Slide 32: Case study – (on <mark>Opioids</mark>)
Slide 44: Opioids and Patient Considerations	Slide 33: Worrisome Medication-Taking Behaviors [re: Opioids]
Slide 45: Opioids: Drug-Drug Interactions	Slide 36: Opioid-Induced Hyperalgesia
Slide 46: Problematic <mark>Opioid</mark> Use in Chronic Pain.	Slide 37: Lack or Loss of Benefit [of Opioids]
Slide 47: Collateral <mark>Opioid</mark> Risk	Slide 38 Consider Breakthrough Medication. (including opioids)
Slide 48: Higher Dose <mark>Opioids</mark>	Slide 39: Consider Switching Opioids
Slide 49: Higher Dose <mark>Opioids</mark>	Slide 40: Opioid Conversion Tables
Slide 51: Risk Factors for Opioid -Related Harm	Slide 41: Case study – (on <mark>Opioids</mark>)
Slide 57: When Are Opioids Indicated?	Slide 42: Case study – (on Opioids)
Slide 58: Opioids and Chronic Pain in Perspective	Slide 43: Case study – (on Opioids)
Slide 59: Patients on Opioid Therapy from Previous Clinician	Slide 44: Case study – (on Opioids)
Slide 60: Assess for Opioid Misuse Prior to Prescribing	Slide 46: Continued Lack of Benefit (all items about opioids)
Slide 61: Case Study (on <mark>Opioids</mark>) Slide 62: Questions for Next Visit [half of items on opioids]	Slide 47: Discussing Continued Lack of Benefit (several items about <mark>opioids</mark>) Slide 48: Discontinuing Opioids
and the control of th	Slide 49: Opioid Discontinuation Risks
Slide 63: Summary Part 1: Opioids	Slide 50: Risk-Benefit Framework (re: opioids)
DADT 3	Slide 51: Case study – (on Opioids)
PART 2:	Slide 52: Case study – (on Opioids)
Slide 2: Part 2: Safer <mark>Opioid</mark> Prescribing [Title only] Slide 3. Case Study (on <mark>opioids</mark>)	Slide 53: Case study – (on Opioids)
Slide 4: Opioid choices (buprenorphine buccal, transdermal: listed among 20 opioids]	Slide 54: Stigma, Chronic Pain, and <mark>Opioids</mark>
Slide 5: Choosing IR/SA vs ER/LA Opioids	Slide 55: Tapering Opioids
Slide 6: IR/SA vs ER/LA Opioid Uncertainties	Slide 56: Tapering Opioids – General Approach
Slide 7: Transdermal Fentanyl	Slide 57: Case study – (on Opioids)
Slide 8: Buprenorphine: a partial opioid agonist	Slide 58: Case study – (on <mark>Opioids</mark>)
Slide 9: Methadone is Complex	Slide 59: Case study – (on Opioids)
Slide 10: Dual Mechanism Opioids	Slide 60: Discussing Possible (Opioid Diversion
	Slide 61: Case study – (on Opioids)
	Slide 69: Summary Part 2 (multiple items about opioids). FINAL SLIDE

Despite REMS courses' emphasis on opioids, opioids are NOT the mainstay of chronic pain management

"All the evidence shows that any medications we choose might reduce patients' sensory pain by no more than about 15%. That's not a dramatic change for these folks. Medications do have a role, but it's not a central role in the treatment of chronic pain."

'ASAM Pain & Addiction Essentials Online'

Same improvement in pain outcomes when opioids are tapered off: In an interdisciplinary pain rehabilitation intervention there were similar improvements across six sites in pain-related functioning (22%) and pain catastrophizing (31%), significant at the p < 0.001 level in all sites,

including two of the sites where all subjects were weaned off of opioids.

Murphy

In RCTs comparing treatment (of at least 1 month) with opioids vs. non-opioids, there is no difference in pain outcomes vs. nortriptyline (3 trials), celecoxib (3 trials), diclofenac, celecoxib (3 trials), diclofenac, detamine, or mailto:mailto:celecoxib, diclofenac, ketamine, or mailto:celecoxib, or mailto:celecoxib, or mailto:celecoxib, or <

AHRQ: Systematic Review: Opioid Treatments for Chronic Pain. 2022. Agency for Healthcare Research and Quality.

Table 9: Study characteristics of trials of opioids versus nonopioids. Pg. 67

'ASAM Pain & Addiction: Essentials Online,' American Society of Addiction Medicine; modules presented by Donald Teater, MD, MPH, ASAM.org - 'education' - 'e-learning center'

Murphy JL, et al. The resurrection of interdisciplinary pain rehabilitation: outcome across a Veterans Affairs collaborative. Pain Med. 2021; 22:430-443.

THANK YOU

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