

Industry-Funded Provider Education as a Barrier to the Prevention of Opioid Use Disorder

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No pertinent conflicts of interest

“Chronic Pain” exclude cancer-related and end-of-life pain this presentation.

Abbreviations: **LTOT**: Long-Term Opioid Therapy, **MME**: Morphine Milligram Equivalents,

OUD: Opioid Use Disorder, **QOL**: Quality of Life. **RCT**: Randomized Controlled Trial

This presentation refers to U.S. data.

Our approaches to the opioid overdose epidemic are not working.

The increase in opioid prescribing, and the resulting overdose epidemic, primarily involved prescribing for chronic pain. Ballantyne JC 2017 Anesth Analg

There is no substantial evidence that long-term opioids are effective for chronic pain.

The dominant continuing medical education on pain treatment, through the FDA's opioid REMS program, is industry-funded, and promotes the message that LTOT is often "indicated" for chronic pain.

These CME courses emphasize whether and when to initiate opioids for chronic pain, rather how treating chronic pain generally.

The great majority of overdose deaths occur in individuals with OUD.

Most OUD occurs due to exposure to prescription opioids.

The fact that large numbers of Americans are developing new-onset OUD each year is an important factor maintaining the overdose epidemic.

CURRENT EVIDENCE ON OPIOID EFFECTIVENESS:

“Opioids are associated with small improvements versus placebo in pain and function at short-term follow-up (1 to 6 months). In 71 trials, mean difference in pain intensity was -0.79 points on a 0 to 10 scale.

“No differences between opioids versus nonopioid medications at 1 – 6 months in in pain, function, mental health status...”

(AHRQ 2020, updated in 2022)

. . . “effects on pain were attenuated at longer (3 to 6 month) versus shorter (1 to 3 month) follow-up.”

(AHRQ 2020, CDC 2022)

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 and severe harms of long-term opioid therapy.

(VA/DoD 2017)

(OVER TIME, analgesic effectiveness wanes, and adverse events tend to increase).

AHRQ (Agency for Healthcare Research and Quality) 2020: Opioid Treatments for Chronic Pain (Comparative Effectiveness Review) with updates through June 2022: <https://effectivehealthcare.ahrq.gov/products/nonopioid-chronic-pain/research>

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

VA/DoD Clinical Practice Guideline For Opioid Therapy For Chronic Pain. 2017

Some patients appear to be doing well on LTOT, with improvements in both pain and QOL, based on long-term observational studies.

(Ballantyne JC 2008)

Systematic Review: **'Long-term Opioid Management for Chronic Noncancer Pain.'**

25 observational studies after opioid treatment > 6 months for moderate-severe chronic pain, evaluated at 6 - 7.5 months.

There was an overall reduction in pain scores.

('Standardized Mean Difference' for pain reduced by 1.55 (considered to be a large effect size), $P < 0.001$. No clear change in QOL or functional status in this review.

(Noble 2010)

Bear in mind, these are low quality studies without control groups, so it is unclear to what extent outcomes were due to opioid therapy vs. other factors. Also, these studies tend to have high drop-out rates up to about 50%. We now have many RCTs that provide more definitive information on outcomes of opioid therapy.

Ballantyne JC, Shin NS. Efficacy of opioids for chronic pain: a review of the evidence. Clin J Pain. 2008;24:469–478

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

RANDOMIZED CLINICAL TRIALS:

'Opioids for Chronic Noncancer Pain: A Systematic Review and Meta-analysis.' 2018

In 9 RCTs, No difference vs. nonsteroidals.

Follow-up was at least 4 weeks, < 3 months in about half of studies, and 3 – 6 months in about half.

80 RCTs, vs. placebo, opioids reduced pain very slightly.

The average difference was **-0.68 (on a 10 point scale), $P < .001$** (Busse 2018)

The extremely small average effect size is not clinically significant.

The authors, Busse et al., note that a minimum change of 1 point on a 10 point scale (a 10% change) has been described as the threshold for a clinically meaningful change in pain scores, citing Dworkin et al.

(Dworkin 2008)

Other authors have suggested that a minimum change of 2 points (20% change) is the appropriate threshold for clinical significance in pain trials.

(Farrar 2000), (Salaffi 2004), (Haag 2003)

Busse JW, et al. JAMA. 2018 Dec 18;320(23):2448-2460.

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.

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.

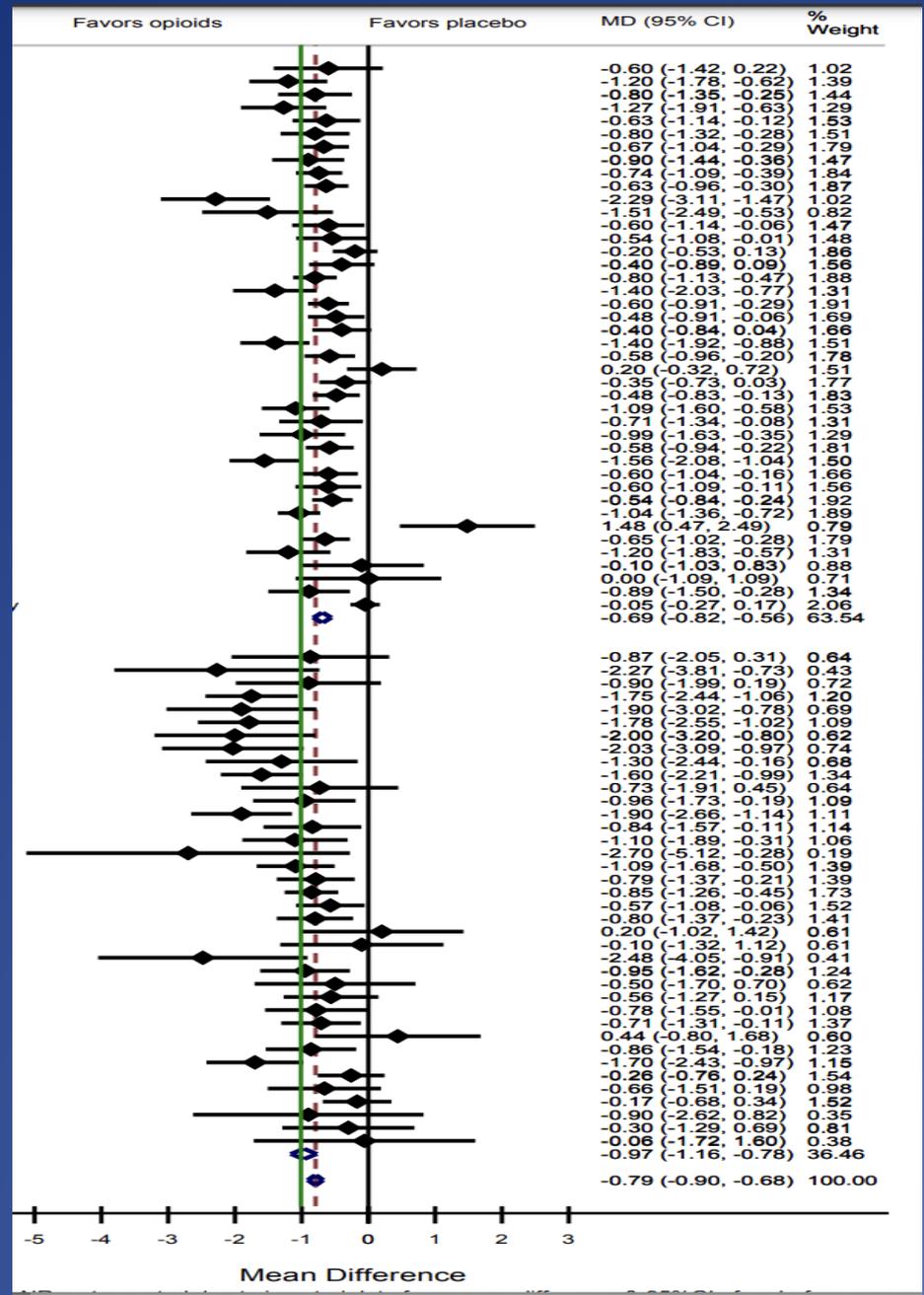
Hagg O, et al. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *European Spine Journal* 2003 Feb;12(1):12-20.

eFigure 2: Pain relief and length of follow-up: <3 months (bottom half) and ≥3 months (top half) from 80 RCTs of opioids vs. placebo.

Black line: 0 difference
 Green line: -1.0 (10 point scale)
 Red dotted line: -0.68 out of 10

This is consistent with the AHRQ's report cited earlier that (1) average effect sizes with LTOT are extremely small, and (2) analgesic effects wane with time.

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



OPIOIDS IN ACUTE PAIN

Opioids are often highly effective for acute pain and should not be withheld in appropriate circumstances. However, they have been shown to be no more effective than NSAIDs in many circumstances in which they are commonly used; Short-term use is associated with increased risk of long-term use over months and years. For most acute pain it is recommended that opioids be limited to a 3-7 day supply.

(PCSS 2023)

Opioid analgesics are widely used for low back pain.

THE ONLY RCT OF OPIOIDS FOR SLOWLY RECOVERING LOW BACK PAIN:

N= 347, Up to 12 weeks duration of non-specific low back and/or neck pain of at least moderate severity, randomized to up to 20 mg oxycodone /day vs. placebo for up to 6 weeks. 310 subjects analyzed.

At 6 weeks there was a trend of **higher pain scores in the opioid group** vs. placebo. + 0.53 points (10 point scale). Not quite statistically significant: 0.53 (95% CI -0.00 to 1.07) p=0.051. More adverse events in the opioid group.

Author's interpretation: "Opioids should not be recommended for acute non-specific low back pain or neck pain..."

(Jones 2023)

PCSS Module 11: Opioids for Pain: Understanding and Mitigating Risks, Roger Chou MD. January 12, 2023;

<https://pcssnow.org/courses/11-opioids-for-pain-understanding-and-mitigating-risks/>

Jones CMP et al. Opioid analgesia for acute low back pain and neck pain (the OPAL trial): a randomised placebo-controlled trial.

402(10398): 304-312, JULY 22, 2023

THE ONLY LONG-TERM RANDOMIZED TRIAL OF OPIOIDS FOR CHRONIC PAIN ('SPACE' TRIAL):

Moderate to severe chronic musculoskeletal pain despite analgesics with interference with enjoyment of life, and general activity. n=240 randomized to an opioid or non-opioid pharmacologic therapy.

At 12 months:

FUNCTION:	No difference.
PAIN:	Slightly worse in the opioid group (P= .03).
ADVERSE SYMPTOMS:	Significantly more common in the opioid group (P= .03)

(Krebs EE et al JAMA. 2018).

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)

Krebs EE, et. al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain. The SPACE Randomized Clinical Trial JAMA. 2018;319(9):872-882.

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)

REMS courses on opioid prescribing

(Risk Evaluation and Mitigation Strategy)

REMS is an FDA program based on a “Blueprint” developed by the FDA with input from stakeholders, notably including opioid manufacturers. The manufacturers hire and select CME providers (medical communication companies) who develop the content of these courses.

The Blueprint is written in general terms, so there is wide latitude for the medical communication companies to develop content that is consistent with both the Blueprint and the manufacturers’ interests. These CME companies are incentivized to create content that is consistent with the manufacturers’ interests in order to maintain this line of business.



The stated purposes of the course are to ...

“ ... help you **safely and effectively manage patients with acute and/or chronic pain**, when appropriate, **with opioid analgesics.**”

... you'll learn how to:

1. Optimize safety when prescribing opioids for acute pain
2. **Determine when opioid analgesics are indicated for chronic pain. (emphasis added)**
3. Assess pain and prescription opioid misuse risk

Etc.

The term “indicated” conveys a level of certainty and consensus that does not exist. This term is used only in opioid REMs courses in this context, not in courses independent of opioid manufacturers.

The courses do include valuable information on managing patients on long-term opioid therapy. This is an important skill needed by more physicians who may inherit so-called ‘legacy patients’ already dependent on long-term opioids. However, the courses emphasize whether, when and how to initiate long-term opioids for chronic pain in those who are opioid-naïve, and give the impression that this should be considered in many patients, despite good evidence that average benefits are not clinically significant, and that well-known severe harms are likely to outweigh benefits.

Opioid Efficacy for Chronic Pain

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 pain-related function over 12 months

Study limitations:⁴

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

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

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

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



(from the REMS course: 'SCOPE of Pain; Safer/Competent Opioid Prescribing Education,' Boston University)

Slide 40: Note the title of the slide.

The middle panel summarizes the trial by Krebs et. al. but does not mention it's primary outcome: that pain was not improved in the opioid group (in fact it was worse), and only mentioned the lack of improvement of function. The narrator focused primarily on the study's possible limitations.

The narrator repeats the information from the last panel, concluding the discussion on opioid efficacy for chronic pain. This clearly conveys that opioids are effective for chronic pain, without mentioning that these were observational studies, that the RCT data show that average pain reduction is clinically insignificant, or that this is contrary to the AHRQ, CDC, & VA/DoD conclusions.

Incidentally, Noble et al. specifically noted that firm conclusions about the particular outcome claimed - are not justified:

"Because this number is substantially heterogenous and because only two studies report this outcome, 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."

(Only later in the course is it noted that "The efficacy of long-term opioid therapy for chronic pain has been inadequately studied.")

When Are Opioids Indicated?

Pain is severe

Pain has significant impact on function and quality of life

Pain type potentially opioid-responsive

(e.g., musculoskeletal or neuropathic but NOT fibromyalgia, migraines)

Inadequate benefit from non-opioid modalities

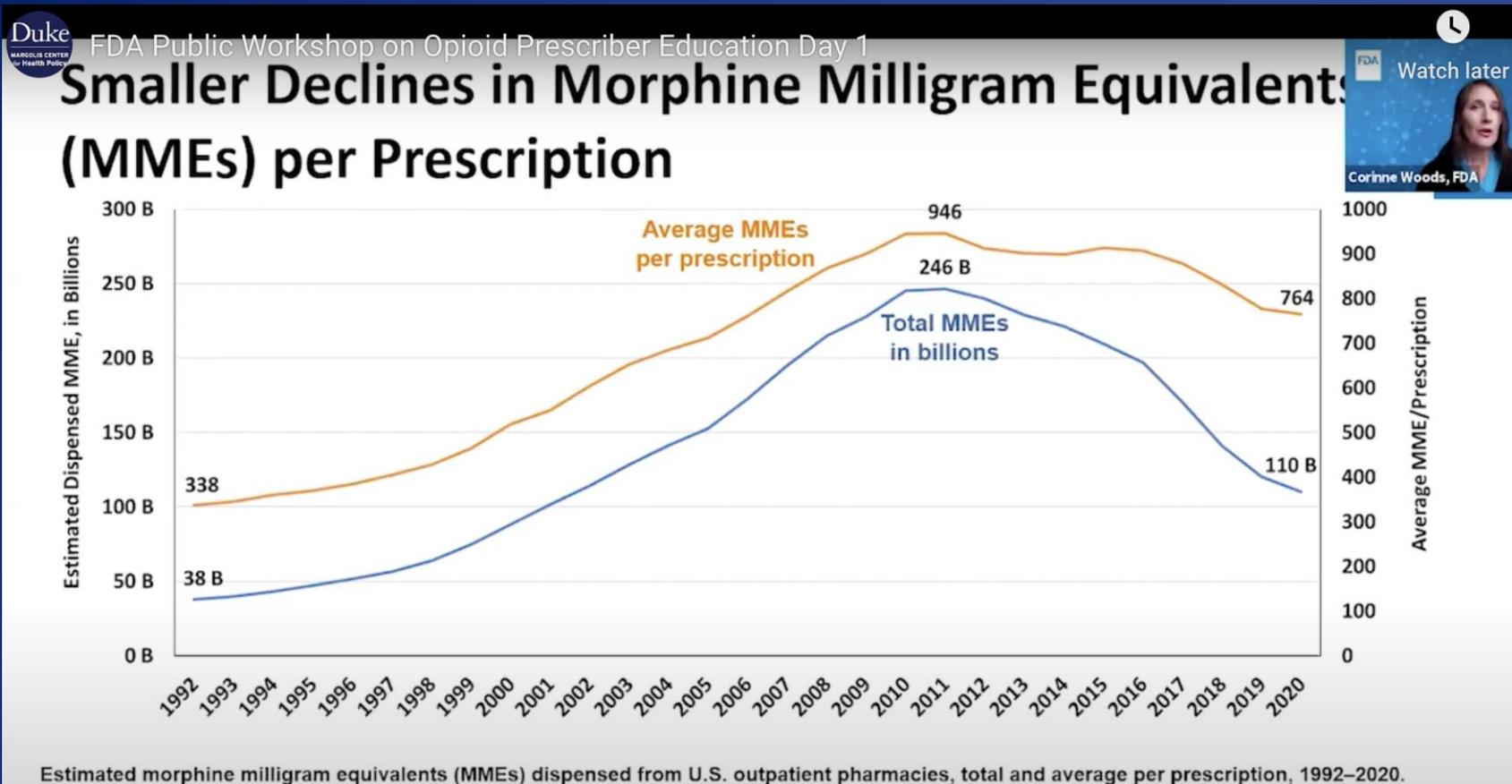
If already on opioids, is there documented benefit?



Slide 54, in the context of **chronic pain**.

These features describe most people with chronic pain. One could conclude that opioids should be used much more often for chronic pain than it already is. Also, the term “indicated” is not appropriate.

CURRENT PRESCRIBED OPIOID VOLUME IS TWICE THE PRE- OPIOID EPIDEMIC BASELINE (From an FDA presentation)



Total U.S. MME was 110 billion in 2020 vs. 38 billion in 1992.

(Per capita MME: 333 MME in 2020 vs. 148 in 1992)

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.

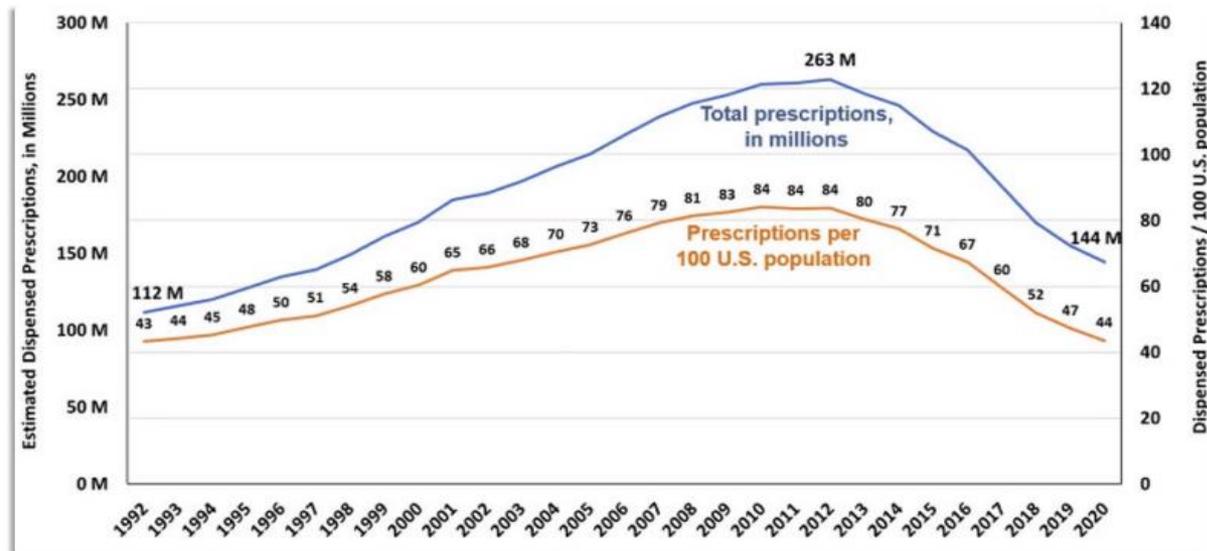
As presented at a 2021 FDA workshop at at 1:15:00.

<https://healthpolicy.duke.edu/events/fda-public-workshop-opioid-prescriber-education>

OPIOID REMS COURSES PRESENT PRESCRIBING INFORMATION SELECTIVELY:

SCOPE of Pain, slide 12:

Trends in Opioid Prescribing for Pain



Racial Differences

Compared to White patients, Black and Hispanic patients are less likely to receive opioid analgesics for pain and when they do it's at a lower dose²

1. www.fda.gov
2. Morden NE, et al. NEJM 2021



All REMS courses reviewed for this presentation selectively present data that **the numbers of opioid prescriptions** have returned to the pre-opioid epidemic baseline, omitting data on opioid volume (MME). This conveys the strong impression that over-prescribing is no longer a problem.

SAMPLE QUESTION & ANSWER

from “Opioid Prescribing: Safe Practice, Changing Lives,” a CORE REMS course:

A 59 year-old with long-standing hypertension and Stage 3 chronic kidney disease continues treatment with disease-modifying anti-rheumatoid drugs for rheumatoid arthritis. Recently she has exhibited increasing pain and further functional decline likely due to progression of RA and osteoarthritis of the hips, knees and feet. She wants to remain as functional as possible. Which of the following is the best next step for addressing this patient's pain?)

- A. Acetaminophen 650 mg. Two tabs a 4 hours prn
- B. Duloxetine 20 mg. Daily
- C. Oxycodone IR 5 mg. Q 4 hours prn. *** “CORRECT ANSWER” according to this course.**
- D. Morphine sulfate ER 15 mg. Q 8 hours
- E. Ibuprofen 600 mg. Q 4 hrs prn

CRITICAL FEATURES OF THE U.S. OPIOID EPIDEMIC NOT COVERED IN OPIOID REMS COURSES:

The great majority of fatal opioid overdoses occur in people with OUD.

(Kolodny 2015), (Washington Post 2023)

The great majority of new cases of OUD result from the use of prescription opioids.

(Compton 2016), (Jones 2013), (Muhuri 2013), (Brands 2004).

U.S. per-capita opioid consumption is greater than that of any other country in the world (As of 2019).

(CRS 2021)

It is estimated that approximately two million Americans develop new-onset long-term opioid dependence each year after routine surgical procedures.

(Brummett 2017)

The total MME (and per-capita MME) is still ~ 2-fold higher in 2020 than in 1992 pre- opioid epidemic.

Total MME was 110 billion in 2020 vs. 38 billion in 1992. (Per capita MME: 333 MME in 2020 vs. 148 in 1992)
(Although opioid prescriptions have declined to pre-epidemic levels).

(IQVIA Institute, 2021), (FDA Workshop 2021)

Kolodny, A. The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction Annu. Rev. Public Health 2015. 36:559–74;
'Overdoses soared even as prescription pain pills plunged' Washington Post. Sept 12, 2023

Compton WM et. al. Relationship between nonmedical prescription-opioid use and heroin use . NEJM. 374 (2) (2016), pp. 154-163.

Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002-2004
and 2008-2010. Drug Alcohol Depend. 2013;132(1-2):95-100.

Muhuri PK, et al. Substance Abuse and Mental Health Services Administration. Associations of nonmedical pain reliever use and initiation of heroin use in
the United States. CBHSQ Data Review. Published August 2013.

Brands, B., (2004). Prescription opioid abuse in patients presenting for methadone maintenance treatment. Drug and Alcohol Dependence, 73(2), 199.

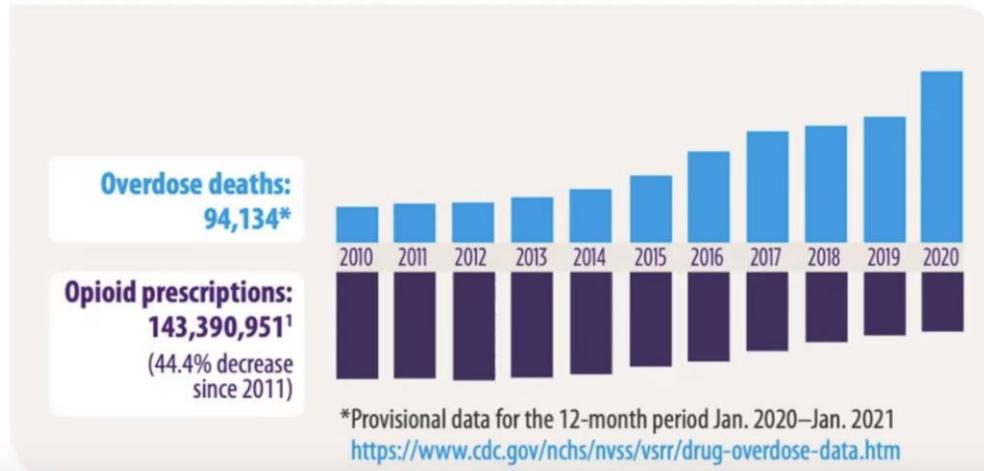
CRS: Congressional Research Service. Consumption of prescription opioids for pain: a comparison of opioid use in the United States and other countries
Washington, DC (2021). <https://crsreports.congress.gov/product/pdf/R/R46805> (pg. 1)

Brummett CM, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg. 2017; 152(6):e170504

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

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

REDUCTIONS IN OPIOID PRESCRIBING HAVE NOT LED TO REDUCTIONS IN OVERDOSE DEATHS



SOURCE: <https://www.ama-assn.org/delivering-care/overdose-epidemic/physicians-progress-toward-ending-nation-s-drug-overdose-epidemic>

All opioid REMS courses reviewed for this presentation display the juxtaposition of the decline in total opioid prescriptions with the increase in overdose deaths, and conveys that that this apparent discrepancy is important (without further explaining it). The gives the impression that prescription opioids are no longer related to overdose deaths, which is not true. (Fentanyl is now the proximate cause of death in most opioid overdoses, but most occurred in individuals who developed OUD from prescription opioids).

REMS Course 2023:

Accompanying narrative (emphasis added).

"**Historical** over-prescribing, & a massive and sustained exposure to opioids ... has fueled the opioid overdose epidemic in the U.S. "As of 2020, **there are still pockets** of the US where prescribed opioids are influencing the number of deaths. **While the prescribing level has gone down**, the number of overdose deaths has continued to rise at an alarming rate."

From the REMS course 'Pain Management and Opioids: Balancing Risks and Benefits' Presented by CO*RE, 2023

<https://elearning.asam.org/products/pain-management-and-opioids-balancing-risks-and-benefits-2023> in Course Introduction, at 4:48 in the video.

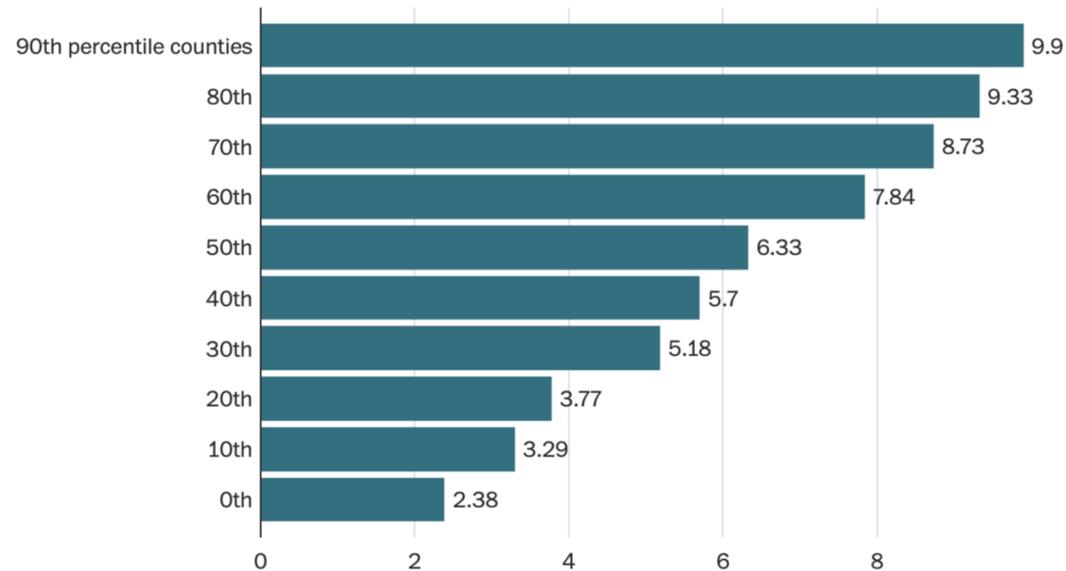
Counties with the highest average doses of legal pain pills per person from 2006 to 2013 suffered the highest death rates in the nation over the subsequent six years.

‘Overdoses soared even as prescription pain pills plunged’ Washington Post. Sept 12, 2023

<https://www.washingtonpost.com/investigations/2023/09/12/us-overdose-deaths-opioid-crisis/>

The Washington Post
Democracy Dies in Darkness

■ 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

Counties with the highest average doses of legal pain pills per person from 2006 to 2013 suffered the highest death rates in the nation over the subsequent six years.

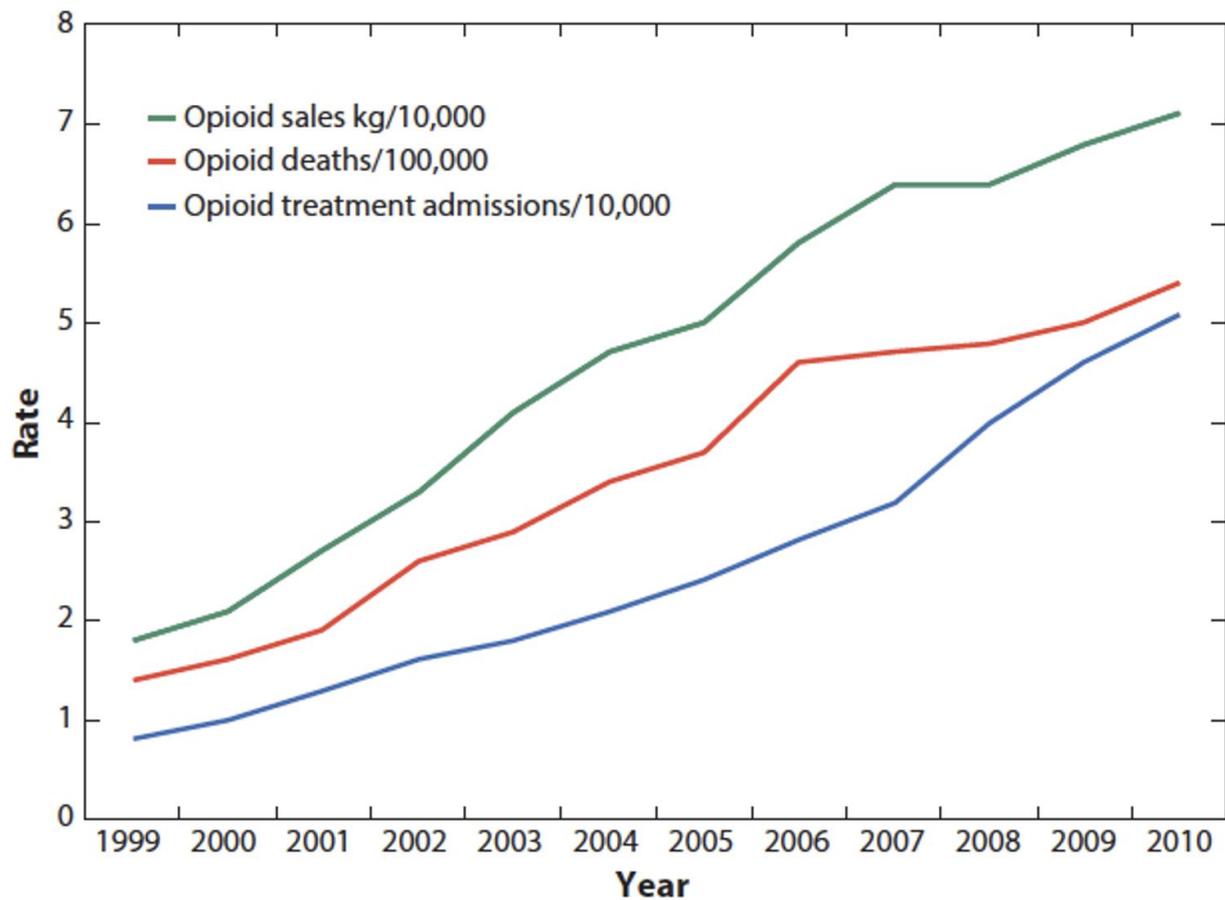


Figure 1

Rates of OPR sales, OPR-related unintentional overdose deaths, and OPR addiction treatment admissions, 1999–2010. Abbreviation: OPR, opioid pain reliever. Source: 10.

Role of the Accreditation Council for Continuing Medical Education (ACCME)

Although the Opioid REMS courses are accredited by the ACCME as being free of commercial bias, these courses appear to include promotional messages coinciding with opioid manufacturers' interests.

(Fugh-Berman, 2021), (Fugh-Berman, 2016)

These publications provide possible reasons for this:

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.

> 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 in 2018 using thematic analysis.

Themes or repeated statements included:

Opioids are an appropriate treatment for chronic pain.

There is no population for whom opioids are absolutely contraindicated or inappropriate.

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

Addiction & overdose are due to street drugs, not prescription opioids.

Etc.

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

REMS education has not been shown to reduce either opioid prescribing, or opioid harms.

(Goodwin 2021)

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.

free: <https://www.painphysicianjournal.com/current/pdf?article=NzI4Mg%3D%3D&journal=137>

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) used Risk Evaluation and Mitigation Strategies (REMS) as tools to mitigate misuse and abuse of opioids. REMS have the potential to help address the opioid crisis, but previous Office of Inspector General work from 2013 raised concerns about FDA's oversight and the overall effectiveness of REMS programs. This review determines the extent to which FDA has held drug manufacturers accountable for mitigating the risk of opioid misuse and abuse through REMS. It complements OIG's past work tracking opioid use among Medicare and Medicaid beneficiaries and provides insight

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

Key Takeaways

Although opioid prescribing has decreased, data quality issues have made it challenging for FDA to determine whether the two REMS for opioids have been effective. Furthermore, REMS may not be well-suited to quickly address the opioid crisis.

the REMS. However, the drug manufacturer is responsible for developing and implementing the program. Following approval of the REMS, the manufacturers submit assessments detailing how the REMS is performing and whether it is meeting its goals to FDA.

The Food and Drug Administration (FDA) can require drug manufacturers to develop and implement a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of a drug outweigh its risks. A REMS is a drug safety program that is intended to mitigate a specific serious risk associated with the use of a drug. FDA can require a REMS if it determines that placing a drug's risks on the FDA-approved drug label is insufficient to protect patients. FDA specifies the requirements and approves

In 2020, the HHS Office of Inspector General (OIG) found that, due to the poor quality of data submitted by opioid manufacturers on REMS' effectiveness through 2017, and due to a lack of baseline data, the FDA was unable to determine whether the opioid REMS improved adverse outcomes of inappropriate prescribing. The FDA then moved away from attempting to measure these outcomes. The OIG found that some manufacturers engage in deceptive marketing practices that undermine the REMS' educational message regarding risk. **The OIG also concluded that REMS is not well-suited to quickly address the opioid crisis.**

CRITICAL DECISION POINTS IN OPIOID PRESCRIBING

NOT COVERED IN OPIOID REMS COURSES:

Decisions regarding:

- Differences in the threshold for prescribing for ACUTE VS. CHRONIC PAIN
- Differences in the threshold for INITIATING OPIOIDS IN OPIOID-NAÏVE INDIVIDUALS vs. **Continuing opioids if already on LTOT.**
- In chronic pain: the Limitations Of “Therapeutic Trials” when initiating long-term opioids.

Acute vs. Chronic pain:

Opioids often highly effective for acute pain; they should not be withheld in appropriate circumstances. Very different than the situation with chronic pain.

Most adverse effects develop over time.

Experts and organizations are increasingly recommending that initiating opioids for chronic pain should be uncommon.

Initiating LTOT if **opioid-naïve** vs. continuing LTOT if **already dependent on LTOT:**

Lack of substantial evidence for chronic pain.

(Some experts & organizations recommend against initiating LTOT, or doing so rarely, for chronic pain).

But abruptly or rapidly tapering LTOT is dangerous, done only in unusual circumstances.

. . . CRITICAL DECISION POINTS IN OPIOID PRESCRIBING

NOT COVERED, OR NOT ADEQUATELY COVERED, IN OPIOID REMS COURSES:

In chronic pain: *the Limitations Of ‘Therapeutic Trials’* when initiating opioids.

(Initiating a ‘therapeutic trial’ makes initiating opioids easier, but tapering off later is often challenging).

Opioids tend to provide good analgesia initially, +/- reduction in “psychic pain.”

Only later do problems tend to arise, e.g. hyperalgesia, waning effectiveness, depression, OUD.

Physical dependence occurs quickly, making even slow tapers challenging.

Tapering can be complex and unpredictable; Tapers often exacerbate pain.

OPIOID TAPERING:

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

Tapering involves risk of overdose and other serious harms, especially with aberrant behaviors, possibly even in stable patients.

(LaRochelle 2022)

Also, in a systematic review, tapering was associated with improvements in pain, function, & QOL in all of the fair-quality studies.

Most tapering attempts did not result in complete discontinuation.

(Frank 2017)

LaRochelle MR Comparative Effectiveness of Opioid Tapering or Abrupt Discontinuation vs No Dosage Change for Opioid Overdose or Suicide for Patients Receiving Stable Long-term Opioid Therapy. JAMA Netw Open. 2022;5(8):e2226523.

Frank JW, et al. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: A systematic review. Ann Intern. Med 2017.

A SUBSET OF PATIENTS ON LTOT ARE NOT ABLE TO TAPER OFF OF OPIOIDS

'COMPLEX PERSISTENT OPIOID DEPENDENCE'

May present as '**aberrancy**' / '**misuse**' / '**concerning behavior**.'

Resembles OUD; Definition not standardized.

May have **poor pain control & function**, aberrant behaviors, psychiatric symptoms, **tapering intolerance**, with greater than usual dysphoria, hyperalgesia during tapering.

(Manhapa 2020)

“Physical dependence on opioid pain treatment is not necessarily easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, ...it is a serious consequence of long-term pain treatment.”

(Ballantyne 2012)

Manhapa A, et al. Complex Persistent Opioid Dependence with Long-term Opioids: a Gray Area That Needs Definition, Better Understanding, Treatment Guidance, and Policy Changes. J Gen Intern Med. Dec 2020; 35(Suppl 3):964-971.

Ballantyne JC et al. Opioid Dependence vs Addiction: A Distinction Without a Difference? Arch Intern Med . 2012 Sep 24;172(17):1342-3.

ONE IN TEN PATIENTS TREATED FOR CHRONIC PAIN HAVE OUD.

ONE IN FIVE HAVE ABERRANT BEHAVIORS/OPIOID MISUSE.

This may provide a clue into rates of adverse events related to long-term opioid therapy.

In clinical practice, “adverse selection” describes the phenomenon of those at highest risk for complications being most likely to receive opioid therapy by a factor of 2 – 8.

(Quinn 2017)

In contrast, randomized trials, and other trials of safety and efficacy, typically exclude subjects with mental health disorders, opioid misuse and substance use disorder.

OID : <8% (Volkow 2018)

OID: **8 - 12 %** (Vowles 2015)

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

OID in PCP settings: 3 - 26% (CDC 2016)

opioid misuse / aberrant behaviors: **15 - 26%** (Volkow 2018)

Opioid Misuse: **21 - 29%** (Vowles 2015)

Quinn PD et al. Incident and long-term opioid therapy among patients with psychiatric conditions and medications: a national study of commercial health care claims. *Pain*. 2017;158(1):140-8.

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

WHAT TO DO ABOUT ABERRANT BEHAVIORS IN LTOT?

Of about a dozen studies reviewed on how to respond to aberrant behaviors in the treatment of pain with opioids, the study below is the only one identified that describes a potentially effective approach:

RANDOMIZED TRIAL TO PREVENT MISUSE WITH LTOT:

A structured cognitive behavioral training was administered monthly for 6 months to those at risk for, or with a history of, opioid misuse. At 6 months the experimental group had significantly lower scores on the Drug Misuse Index vs. the control group: 26.3% vs. 73.7%. . (Jamison 2012)

CLINICAL PEARL FOR RESPONDING TO ABERRANT BEHAVIORS (from Joseph A. Adams MD):

Careful, repeated screening for features of OUD, while normalizing craving and loss of control.

YOU CAN SAY TO THE PATIENT: “It is not uncommon for people to find that they sometimes use the medicine for stress, or that they are often thinking about their next dose. Or they might sometimes have trouble controlling the number of pills they take. If you have experienced anything like this: not to worry, I believe I can help.” With OUD, refer or treat for OUD.

If criteria for OUD are not met, treating patients with methadone or buprenorphine (or possibly slow release oral morphine) for pain may help control misuse and achieve stability. NOTE: Initiating methadone is dangerous and may cause overdose due to its very prolonged and unpredictable half-life.

It is illegal in the U.S. to prescribe methadone for OUD outside of an Opioid Treatment Program, or to prescribe any prescription medicine for OUD that isn't FDA-approved for OUD, including some brands of buprenorphine.

Jamison RN ...Substance misuse treatment for high-risk chronic pain patients on opioid therapy: A randomized trial. Pain 2010; 150:390-400.

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

TYPE OF SURGERY:	NEW DEVELOPMENT OF PERSISTENT OPIOID USE:	REFERENCE:
Various:	5%	Clarke 2014, Alam 2012, Waljee 2017
<u>Both minor & major:</u>	6%	Brummett CM 2017
Orthopedics:	8%	Goesling J 2016
Curative CA	10%	Lee JS 201
Hand:	13%	Johnson SP 2016
Back:	13%	Deyo RA 2018

Brummett et al estimate that >two million people per year who are opioid naïve may initiate long-term opioid use following elective surgery.

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. Iatrogenic 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/

SUCCESSFUL REDUCTIONS OF OPIOID PRESCRIPTIONS IN HOSPITALS:

After a 5 month educational intervention for hospital physicians, the median post-op opioid prescription went from 250 to 75 mg. (MME) after laporoscopic cholecystecomy, (p <.001) without change in pain or refill requests. (U of Mich, Ann Arbor)

(Howard 2018)

Changing the electronic health record's default number of opioid pills significantly reduces opioid prescribing in post-operative, and ED settings.

(Chiu 2018), (Delgado 2018)

Howard R, et al. Reduction in opioid prescribing through evidence-based prescribing guidelines. *JAMA Surg.* 2018;153:285–287.

Chiu AS, et al. Association of lowering default pill counts in electronic medical record systems with postoperative opioid prescribing. *JAMA Surg*, 153 (2018), pp. 1012-1019

Delgado, MK *et al.* Association between electronic medical record implementation of default opioid prescription quantities and prescribing behavior in two emergency departments. *J Gen Intern Med*, 33 (2018), pp. 409-411

Adult Prescribing Recommendations

Procedure	Oxycodone 5mg tablets*
Breast Cancer Surgery	
Breast Biopsy or Lumpectomy	0-5
Lumpectomy + Sentinel Lymph Node Biopsy	0-5
Sentinel Lymph Node Biopsy Only	0-5
Simple Mastectomy + Sentinel Lymph Node Biopsy	0-20
Modified Radical Mastectomy + Sentinel Lymph Node Biopsy	0-30
Cardiothoracic Surgery	
Cardiac Surgery via Median Sternotomy	0-25
Dentistry	
Dental Extraction	0
Obstetrics and Gynecology	
Hysterectomy - Vaginal or Laparoscopic/Robotic or Abdominal	0-10
Cesarean Section	0-20
Orthopaedic Surgery	
Total Hip Arthroplasty	0-30
Total Knee Arthroplasty	0-40
Urology	
Prostatectomy	0-10
Vascular Surgery	
Carotid Endarterectomy	0-5

Procedure	Oxycodone 5mg tablets*
General Surgery	
Anti-reflux (Nissen) - Laparoscopic	0-5
Enterolysis - Laparoscopic	0-5
Excision of Rectal Tumor - Transanal	0-5
Thyroidectomy	0-5
Appendectomy	0-10
Cholecystectomy - Laparoscopic or Open	0-10
Colectomy - Laparoscopic or Open	0-10
Donor Nephrectomy - Laparoscopic	0-10
Enterostomy Closure - Laparoscopic	0-10
Gastrorrhaphy	0-10
Hernia Repair - Minor or Major	0-10
Ileostomy/Colostomy Creation, Re-sitting, or Closure	0-10
Pancreatectomy	0-10
Sleeve Gastrectomy	0-10
Small Bowel Resection or Enterolysis - Open	0-10
Melanoma Surgery	
Sentinel Lymph Node Biopsy Only	0-5
Wide Local Excision + Sentinel Lymph Node Biopsy	0-20

[The Michigan Opioid Prescribing Engagement Network \(michigan-open.org\)](https://michigan-open.org) developed this evidence-based guide of average numbers of oxycodone tablets usually needed after various surgeries, used in education of hospital physicians.



Reducing Postoperative Opioid Prescribing

Opioid Prescribing Toolkit

The toolkit below includes sample performance reports, action plans, worksheets, recommended readings and more.

Quality Initiative Summary

View the initiative summary to learn why SCW started this initiative, what we are trying to change in practice, and how we will implement the changes.

Events & Resources

Check here for upcoming events related to the postoperative opioid prescribing initiative, resources that we think would be beneficial for our members, and more.

OPIOID OVERPRESCRIBING CAUSES HARMS:

"The USA and Canada have experienced **an epidemic of opioid prescribing, which has been a driver** of the current public health emergency of **OD**.

"The consequences of this over-prescribing have been severe. Prescription sales of opioids for pain management have increased alongside increases in opioid-related deaths.

"An important risk factor for OUD and for overdose deaths is the availability and volume of prescriptions of opioid pain medication . . . it is not surprising that countries that have much higher prescribing rates for opioids have greater rates of non-medical use and opioid overdose deaths."

Strang J, Volkow ND, et. al. Opioid use disorder (Review). Nat Rev Dis Primers. 2020 Jan 9;6(1):3.

OVERPRESCRIBING IS STILL CAUSING HARMS

GOVERNMENT AGENCIES' CURRENT ONLINE STATEMENTS:

NIH

National Institutes of Health HEAL Initiative

"encourage safer opioid prescribing"

HHS

Dept of Health & Human Services (under Primary Prevention of Overdose):

"Reduce clinically inappropriate prescribing of medications with misuse potential."

CMS

Center for Medicare and Medicaid Services:

"Over Prescriber Support Strategy (OPSS)"

CDC

Centers for Disease Control and Prevention:

"When the Prescription Becomes the Problem" . . .

"To reverse this epidemic, we need to improve the way we treat pain."

NIH: <https://heal.nih.gov/research/cross-cutting-research/translating-data-action-prevent-overdose>
HHS: www.hhs.gov/overdose-prevention/
CMS: https://qioprogram.org/sites/default/files/2022-01/OPSS_Fact_Sheet_508_08-16-2021.pdf
CDC: <https://www.cdc.gov/opioids/basics/prescribed.html>

REDUCING OVERPRESCRIBING CAN ALSO CAUSE HARM:

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

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.

“Legacy patients”: approximately 8 million Americans on chronic opioids for pain and not able to come off easily. Older doctors are retiring. Many PCP providers do not want to accept the care of these patients, who may risk abrupt discontinuation, OUD and death from overdose or suicide.

Features of both pain and possible addiction together are common, and many patients have a difficult time finding either addiction medicine or pain medicine physicians willing to treat them.

We want to reduce irresponsible prescribing, NOT irresponsibly reduce prescribing.

We also want to reduce initiating long-term opioids in opioid-naïve patients for chronic pain.

...The Field is Changing:

Possibly the best course on pharmacological treatment of chronic pain:

Online Course: 'Pain & Addiction: Essentials'

Available online from ASAM: The American Society of Addiction Medicine.

ASAM.org - 'education' - 'e-learning center'. Module 4 (of 6): Pharmacological Treatment Approaches (1 hr.) presented by **Donald Teater, MD, MPH**

Lead facilitator, expert panel for the CDC Guidelines for Prescribing Opioids for Chronic Pain.

Lead Medical Advisor at the National Safety Council, effort to reduce opioid abuse & overdose (2013-16)

This course notes that:

- Average effect sizes of analgesia from opioid therapy are not clinically significant.)
- Opioids for chronic pain should not be prescribed unless there has first been every effort to explore non-opioid and non-pharmacologic options. . .
It should be a rare patient where we initiate opioids for chronic pain.
- Suggests that if a physician was considering starting a long-term opioid for chronic pain, buprenorphine would be preferred due to safety (Identical to a recommendation from the 2022 VA/DoD Clinical Practice Guideline on Opioid Therapy for Chronic Pain).

. . . From the Course: 'Pain & Addiction: Essentials' from the Am Society of Addiction Medicine

For chronic pain, behavioral approaches become more important than medication approaches, e.g. CBT, ACT (Acceptance & Commitment Therapy), motivational interviewing.

Thoughts and emotions become the major drivers of *chronic* pain.

In chronic low back pain, fibromyalgia, and chronic headaches, long-term outcomes are often worsened by the use of long-term opioids.

SIMILARITIES BETWEEN CHRONIC PAIN AND OPIOID USE DISORDER:

Very commonly co-occur with one another

Both typically associated with co-occurring mental health sx which are strongly predisposing.

Treatment generally requires addressing psychosocial factors.

For either condition It may be difficult or impossible to taper off of long-term opioids.

PAIN REPROCESSING THERAPY (PRT)

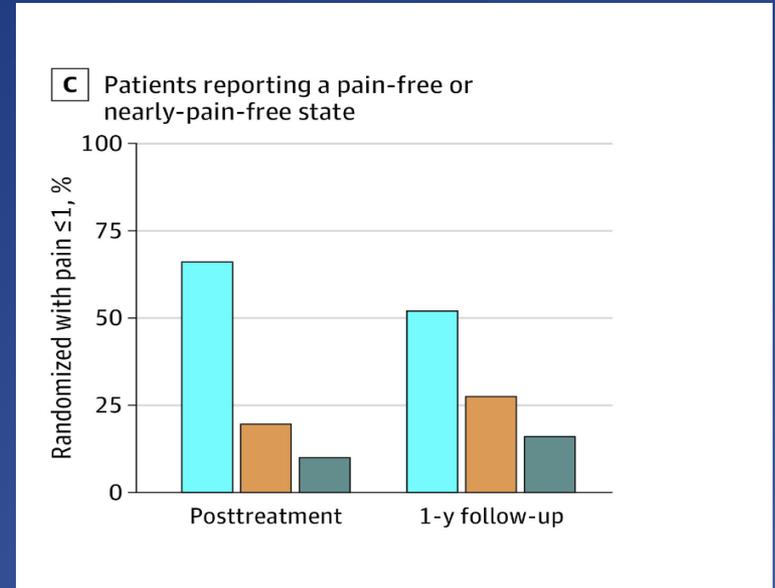
85% of cases of chronic back pain (CBP) are "primary CBP," for which a peripheral etiology cannot be identified, and maintenance factors include fear, avoidance, and beliefs that pain indicates injury.

PRT aims to help patients reconceptualize their pain as due to nondangerous brain activity rather than peripheral tissue injury, using cognitive, somatic, and exposure-based techniques.

n=151, chronic back pain randomized to PRT X 4 wks vs. usual care vs. saline injection. Greater pain reduction in the PRT group ($P < 0.001$) with benefits largely maintained after 12 months.

www.painreprocessingtherapy.com

(Ashar 2022)



PAIN NEUROSCIENCE EDUCATION (PNE) (closely related to PRT)

An educational method to reduce patients' fear and anxiety about their pain condition, used with motivational interviewing to increase activity.

Seven RCTs comprising 479 participants, with significant reductions in pain with a large effect size (Hedges' $g = -0.730$), $p = 0.019$.

(Lin 2023)

Ashar YK, Gordon A, Schubiner H, et al. Effect of Pain Reprocessing Therapy vs Placebo and Usual Care for Patients With Chronic Back Pain. A Randomized Clinical Trial JAMA Psychiatry. 2022;79(1):13-23.

Lin LH et al. Pain neuroscience education for reducing pain and kinesiophobia in patients with chronic neck pain: A systematic review and meta-analysis of randomized controlled trials. Eur J Pain. 2023 Sep 11.

PSYCHOLOGICAL INTERVENTIONS:

In meta-analyses, psychological interventions for chronic pain, such as CBT, ACT, behavioral therapy or social support, have shown small to moderate reductions in pain intensity

and modest improvements in catastrophizing beliefs, physical functioning, and some effects on improving mental health.

(Blasco-Belled 2023)

CBT: Cognitive Behavioral Therapy

ACT: Acceptance & Commitment Therapy

Blasco-Belled A, et al Positive psychology interventions can improve mental health for chronic pain patients: a systematic review and meta-analysis. Psychol Health. 2023 Aug 29:1-17. Online ahead of print.

2-page handout / poster
for patients:

'What Should I Know About Opioids and Living With Chronic Pain?'

Excerpt:

"If I Take Opioids for Chronic Pain, Should I Decrease or Stop?"

There are many indicators that you should consider gradually decreasing or stopping your opioid medication . . .

Make a plan with your doctor to gradually decrease your use.

Consider stopping opioids if you continue to have poor pain control and difficulty functioning in your life while taking opioids; **studies show that if opioids are decreased slowly, pain and function can actually improve...**"

(Leyde 2020)

Leyde S, Azari S. JAMA internal medicine 2020. PMID: 32453391.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2765691>

Reducing the risks of opioid use for chronic pain

Even when taken as directed, opioids can cause negative effects such as tolerance, dependence, increased sensitivity to pain, depression, fatigue, constipation, low sex hormone levels, itching, sweating, and overdose.

Ways to reduce your risk while taking opioids

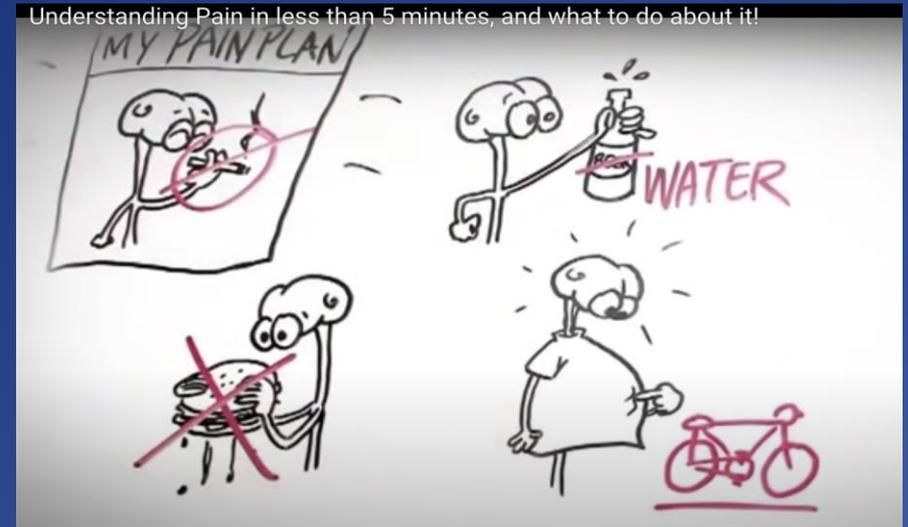
-  Avoid drinking alcohol and using recreational drugs.
-  Avoid taking other sedatives such as muscle relaxants and sleep medications.

-  Take your medication as prescribed.
-  Visit your doctor routinely to assess pain control, physical function, quality of life, and safety.
-  Talk with your doctor about naloxone, which reverses opioid overdose and can be kept at home in case it is needed.
-  Inform your doctor if you begin to feel any negative effects or if you begin to crave more medication than is prescribed.
-  Store your medication in a safe place so other people cannot get to it.
-  Consider working with your doctor to gradually decrease the dose of your opioid medication.



Excellent 5 minute video for patients on the role of modifiable nervous system sensitivity in chronic pain:

https://www.youtube.com/watch?v=C_3phB93rvI





SELECTED PROVIDER RESOURCES:

Podcast Episode: Unlearning Your Pain w/ Dr Howard Schubiner.

https://www.youtube.com/watch?v=rYz_ApWYeg0

(Pain Reprocessing Therapy; “Unlearn Your Pain”)

Lucid Lane

An organization that can provide virtual tapering services for opioids if needed, and behavioral health services, billing most commercial insurance carriers.

<https://lucidlane.com/>

PharmedOut

A project at Georgetown University Medical Center that advances evidence-based prescribing and educates health care professionals and students about pharmaceutical and medical device marketing practices. Provides education and information about CME courses free of industry sponsorship.

<https://sites.google.com/georgetown.edu/pharmedout/home>

Physicians for Responsible Opioid Prescribing (PROP)

A non-profit organization comprised of healthcare professionals whose mission is to reduce opioid-related morbidity and mortality by promoting cautious and responsible prescribing practices

www.supportprop.org

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.



thebmj

covid-19 Research ▾ Education ▾ News & Views ▾ Campaigns ▾ Jobs ▾

Feature » Essay

Industry-funded medical education is always promotion—an essay by Adriane Fugh-Berman

BMJ 2021 ; 373 doi: <https://doi.org/10.1136/bmj.n1273> (Published 04 June 2021)

Cite this as: BMJ 2021;373:n1273

Fugh-Berman, A. Industry-funded medical always promotion—an essay by Adriane Fugh-BMJ 2021;373:n1273.

Fugh-Berman A and Batt S "This May Sting a Bit": Cutting CME's Ties to Pharma. VIEWPOINT. JUN 2006

AMA Journal of Ethics®

Illuminating the Art of Medicine

VIEWPOINT
JUN 2006

"This May Sting a Bit": Cutting CME's Ties to Pharma

Adriane Fugh-Berman, MD and Sharon Batt, MA

Citation PDF Altmetric

‘Responding to the opioid crisis in North America and beyond: recommendations of the Stanford–Lancet Commission.’ The Lancet. 2022;399(10324):555-604.

authors: Prof Keith Humphreys PhD, Chelsea L Shover PhD, Christina M Andrews PhD, Amy S B Bohnert PhD, Prof Margaret L Brandeau PhD, Prof Jonathan P Caulkins PhD, Jonathan H Chen MD, Mariano-Florentino Cuéllar JD, Prof Yasmin L Hurd PhD, Prof David N Juurlink MD, Prof Howard K Koh MD, Prof Erin E Krebs MD, Prof Anna Lembke MD, Prof Sean C Mackey MD, Prof Lisa Larrimore Ouellette PhD, Brian Suffoletto MD, Prof Christine Timko PhD. [https://www.thelancet.com/article/S0140-6736\(21\)02252-2/fulltext](https://www.thelancet.com/article/S0140-6736(21)02252-2/fulltext)

first **“Key Message”**

“Profit motives ... will continue to generate harmful over-provision of addictive pharmaceuticals unless regulatory systems are fundamentally reformed. . .”

“The Commission recommends ... insulating medical education from industry influence ...”

(among other recommendations)

SOME NON-REMS PROVIDER TRAINING RESOURCES

comments by Joseph Adams , MD

Course: 'Pain & Addiction: Essentials' - Am Society of Addiction Medicine

(American Society of Addiction Medicine) ASAM.org - 'education' - 'e-learning center'. (Donald Teater MD).

EXCELLENT, BEST; preented earlier. (behind a paywall)

SOME NON-REMS PROVIDER TRAINING RESOURCES

comments by Joseph Adams, MD

Course: 'CDC's 2022 Clinical Practice Guideline for Prescribing Opioids for Pain'

<https://www.cdc.gov/opioids/healthcare-professionals/training/overview.html>

Determining Whether or Not to Initiate Opioids for Pain.

...Maximize the use of nonpharmacologic and nonopioid pharmacologic therapies ...

Consider initiating opioid therapy if expected benefits for pain and function > risks. **Vague, not specific enough.**

TAPERING:

Consider tapering to a reduced opioid dosage or tapering and discontinuing when:

Opioids have not meaningfully improved pain or function,

Benefit-risk balance is unclear

Higher dosages without evidence of benefit from the higher dosage.... **All excellent**

Scenario: Jamie C: chronic pain Severe LBP, DDD, 1 yr of multiple non-opioid therapies, hard to get to P.T.

Correct Answer: Dr. says: "I think we should try an opioid.... We've talked about this."

No nuance, no pros & cons, no shared decision-making. Is there a "right" answer?

Scenario: Brenda R: spinal stenosis, s/p surgery, prevents being active, no risk factors, Can't sleep, hardly can get out of bed.

Which prescription? Low dose for 3 days (wants to rest before starting P.T.) **Good.**

... SOME NON-REMS PROVIDER TRAINING RESOURCES

comments by Joseph Adams, MD

Multiple courses on pain at <https://pcssnow.org/> search for 'pain' (PCSS: Providers Clinical Support System)

Course: 2. Basics of Pain Treatment

<https://pcssnow.org/courses/2-basic-tenets-pain-treatment/>

Presenter(s): Michael Saenger, MD, *Seddon Savage, MD, *R. Corey Waller, MD, MS, Roger Chou, MD,

Kevin A. Sevarino, MD, PhD, Melissa Weimer, DO, MCR, FASAM

Published: June 1, 2021

Identify and address psychosocial contributors to pain

Emphasize active (psycho-behavioral, exercise, interdisciplinary rehab)

over passive modalities (medications, complementary/alternative treatments)

CBT: 4 slides, Meditation/Relaxation: 1 slide, Promoting Self care - 1 slide, Exercise - 2 slides

Interdisciplinary Rehab: 2 slides, Physical modalities: 2 slides. Complementary and Integrative: 2 slides

Above: all excellent.

For chronic pain, analgesics effectiveness for short-term pain is small to moderate, and limited for function; evidence very limited on long-term effects (emphasized). Very good

Muscle relaxants are all sedating, some better studied than others. Helpful.

CHRONIC PAIN: "Use opioids "only if benefits are expected to outweigh risks". Too vague.

Migraine, Fibromyalgia: Opioids not preferred or not mentions. Good.

Neuropathic: Op: 2nd line. 3rd line: Lamotrigine Carbamazepine, Topical Capsaicin I disagree.

Chronic DJD: Op: 2nd line. I disagree.

Chronic LBP: 1st Line: NSAIDs, 2nd Line: SNRI, Tramadol; Consider short-term trial of opioids in Carefully Selected Pts.

I disagree; a "trial" in chronic pain is likely long-term. Other experts: opioids in chronic LBP more likely to harm than help.

Scenario: Chronic LBP. An opioid is not among the options. Good.

Overall: Too aggressive with opioids for chronic pain, but very helpful discussion of non-pharmacologic therapies.

... SOME NON-REMS PROVIDER TRAINING RESOURCES comments by Joseph Adams , MD

Course: 3: Opioid Therapy For Pain: An Evidence Review.

<https://pcssnow.org/courses/3-opioid-therapy-pain-evidence-review/>

Presenter: Roger Chou MD Published: June 1, 2021.

Summary of the state of the evidence based on AHRQ 2020 review.

Excellent

Slides showing trends only go through 2010.

dated

Slide 9: Graph: After 1990, prescription opioids became the first drug of abuse in those using heroin. Important

EVIDENCE ON OPIOID THERAPY FOR CHRONIC NON-CANCER PAIN:

SHORT TERM vs. PLACEBO

Pain intensity (71 trials): Mean difference -0.79 points (on a 0-10 scale)

Pain response (44 trials): RR 1.35

Function (44 trials): Decrease: Standardized mean difference -0.22

SHORT TERM VS. NONOPIOIS: No difference in intensity, response or function

LIMITATIONS: High loss to follow-up; No trials of LTOT vs. CBT, exercise, or interdisciplinary rehab. Good

SPACE trial (12 mo. RCT): 3 slides

HARMS: OUD, misuse falls/fractures, poorer function, hypogonadism. (mostly by cross-sectional studies)

A small proportion of patients account for the majority of opioids prescribed.

(In one study, 5% of opioid users accounted for 48% to 70% of total use).

"Adverse selection" in clinical practice, persons at highest risk are most likely to receive high dose opioids"

Mitigating Risks Associated with Opioids: Fails to include that LTOT should rarely be initiated for chronic pain

Scenario: Inherited a patient on very high dose opioids with multiple risk factors, though no aberrant behavior.

Correct Answer: Slowly taper (over 2 years) with goal to get to a much lower dose. Good

OVERALL RECOMMENDATION FOR CHRONIC PAIN:

"In appropriately selected patients, who do not respond to non-opioids, view an initial course of opioids as a short-term therapeutic trial; Initiating LTOT for chronic pain should be rare.

Viewing this initiation as a therapeutic trial is very likely to result in LTOT

... SOME NON-REMS PROVIDER TRAINING RESOURCES

comments by Joseph Adams , MD

Course: Essentials of Good Pain Care: A Team-Based Approach Safely Manage Acute and Chronic Pain

AMA Ed Hub> AMA STEPS Forward> By Topic. <https://edhub.ama-assn.org/steps-forward/module/2702759>
STEPS to Promote Safe and Effective Pain Treatment in Your Practice include . . .

...

Prescribe Opioids Safely and Have a Discontinuation Plan.

Does not seem appropriate as a key step

There is an absence of high-quality data on opioid effectiveness for chronic pain.⁸ Although more studies are needed, there is evidence that suggests that discontinuing long-term opioid therapy may actually improve pain, function, and quality of life for some patients. Multiple meta-analyses have demonstrated that long-term opioid therapy provides little benefit to patients. (with references).

Very good.

The lowest effective opioid dose of immediate-release opioids for the shortest therapeutic duration should be prescribed; often, 3 days is sufficient.

Very good

What can I do for a patient at high risk of OUD with chronic pain?

Physicians can consider an alternative therapy to opioids for patients at high risk. Explain to patients who are high-risk that their safety is always the number one concern. Offer alternatives to opioid therapy as described in STEP 4. For high-risk patients in whose case the patient and the physician jointly decide the benefit of opioids outweighs the risk, the care team should employ extra monitoring and risk mitigation strategies, including more frequent toxicology testing, naloxone prescription, consideration of pill counts, shorter duration of prescriptions, and more frequent follow-up visits. Care must be taken to avoid stigmatizing the patients who may benefit from long-term opioid therapy; for example, this “extra care” should be communicated with patients from the beginning so they do not feel like they are being singled out because of their chronic pain condition.

Poor. Suggests that there is no category of patient who is a poor opioid candidate as long as they are monitored.

Physicians can watch for unexpected changes in the patient's risk profile and consider discontinuing opioid therapy when a patient's risk-to-benefit ratio increases.

Downplays the complexities of tapering.

Overall: Very poor

BUPRENORPHINE FOR CHRONIC PAIN:

"I myself believe that buprenorphine is the opioid of choice, if we're going to use any opioid for the treatment of chronic pain."

Donald Teater, MD, MPH, ASAM course; 'Pain & Addiction: Essentials,' Lead facilitator, expert panel for the CDC Guidelines

Consideration of changing full opioids to buprenorphine is a strategy endorsed by the Health and Human Service Guidelines (HHS) for Discontinuation of Long-Term Opioid Analgesics.

https://www.hhs.gov/opioids/sites/default/files/2019-10/Dosage_Reduction_Discontinuation.pdf

(But no evidence of effectiveness of either buprenorphine or full opioids for chronic pain).

BUPRENORPHINE VS. FULL OPIOIDS FOR CHRONIC PAIN:

Safe (overdose is rare)

No hyperalgesia

Very unlikely to cause addiction (vs. physical dependence)

There appears to be no tolerance to analgesia (less need for dose escalation)

Fewer opioid side effects (drowsiness, hypogonadism, QT interval, cognitive effects, constipation, etc.)

More effective in neuropathic pain.

May have beneficial effects for depression or anxiety.

Withdrawal symptoms may be milder.

Anecdotal evidence of usefulness in aberrancy/ Chronic Persistent Opioid Dependence

(any diversion is more likely to be 'therapeutic diversion')

Davis, M. P. (2012). Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain. *The Journal of Supportive Oncology*, 10(6), 209–219. free: <https://doi.org/10.1016/j.suponc.2012.05.002>

The Ins and Outs of Prescribing Buprenorphine; Updated January 13, 2022 Katie Fitzgerald Jones & Jessica Merlin
<https://www.capc.org/blog/part-2-the-ins-and-outs-of-prescribing-buprenorphine/>

DOES REDUCING PRESCRIPTION OPIOIDS DRIVE PEOPLE TO HEROIN / FENTANYL?

Throughout the opioid epidemic, people have transitioned from prescription to illicit opioids, especially after developing OUD. This likely occurs in individual circumstances.

In 2013 - 2014 when fentanyl use was beginning to rise, opioid prescribing was near its peak.

“Evidence does not support the hypothesis that initiatives intended to reduce opioid prescribing increase illicit opioid-related overdose at a population level.” (Dowel 2017), (Dowel 2016)

“The rise in heroin overdose preceded any substantial controls on opioid prescribing, at a time when “80% of Americans who *initiated heroin use started with prescription opioids.*”

“... most of those who die from heroin and fentanyl overdoses are previous or current users of prescription opioids.” (Humphreys 2022)

“The increase in the rates of heroin use preceded changes in prescription-opioid policies, and there is no consistent evidence of an association between the implementation of policies related to prescription opioids and increases in the rates of heroin use or deaths.” (Compton 2016)

Dowell D, Haegerich TM. Changing the Conversation About Opioid Tapering. Ann Intern Med. 2017 Aug 1;167(3):208-209

Dowell D, et. al. Mandatory provider review and pain clinic laws reduce the amounts of opioids prescribed and overdose death rates. Health Aff (Millwood). 2016;35: 1876–1883.

Humphreys K, et al. ‘Responding to the opioid crisis in North America and beyond: recommendations of the Stanford–Lancet Commission.’ The Lancet. 2022;399(10324):555-604.

Compton WM ... Relationship between nonmedical prescription-opioid use and heroin use. N Engl J Med 2016;374:154-163

No reliable way to predict serious harms from opioids

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

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

<https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm>

“No instrument has been shown to be associated with high accuracy for predicting opioid overdose, addiction, abuse, or misuse.”

Opioid Treatments for Chronic Pain SYSTEMATIC REVIEW April 16, 2020 AHRQ (Agency for Healthcare Research and Quality)

<https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research>

However, risk assessment can reduce risks somewhat, and is recommended.

THANK YOU

Joseph A. Adams, MD, FASAM

Please contact me for questions, comments,
or just to let me know you're interested or to keep in touch.

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RESOURCES for the presentation:

'Industry-Funded Provider Education as a Barrier to the Prevention of Opioid Use Disorder'

9/25/2023

Joseph A. Adams, MD, FACP joadamsmd@gmail.com

AHRQ: Agency for Healthcare Research and Quality 2020 report: Opioid Treatments for Chronic Pain, including updates through March 2022.

<https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research>

CDC Clinical Practice Guideline for Prescribing Opioids for Pain. 2022

<https://www.cdc.gov/mmwr/volumes/71/rr/rr7103a1.htm>

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE USE OF OPIOIDS IN THE MANAGEMENT OF CHRONIC PAIN <https://www.healthquality.va.gov/guidelines/pain/cot/>

Review of observational studies:

Noble, M, et. al. Long-term opioid management for chronic noncancer pain. Cochrane Database Syst Rev. 2010 Jan 20;2010(1):CD006605. free: <https://pubmed.ncbi.nlm.nih.gov/20091598/>

Review of RCTs:

Busse JW, et al. Opioids for Chronic Noncancer Pain: A Systematic Review and Meta-analysis JAMA. 2018 Dec 18;320(23):2448-2460. Free: free: <https://pubmed.ncbi.nlm.nih.gov/30561481/>

(The only RCT of opioids in slowly recovering low back pain):

Jones CMP et al. Opioid analgesia for acute low back pain and neck pain (the OPAL trial): a randomised placebo-controlled trial. 402(10398): 304-312, JULY 22, 2023

Abstract: <https://pubmed.ncbi.nlm.nih.gov/37392748/>

(THE ONLY LONG-TERM RCT OF OPIOIDS FOR CHRONIC PAIN):

Krebs EE, et. Al. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain. The SPACE Randomized Clinical Trial free: <https://jamanetwork.com/journals/jama/fullarticle/2673971>

(The volume of prescribed opioids in MME is currently double what it was before the opioid epidemic: 110 billion MME in 2020 vs. 38 billion in 1992):

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>

(The great majority of fatal opioid overdoses occur in people with OUD):

(Kolodny 2015), (Washington Post 2023)

Kolodny, A. The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction *Annu. Rev. Public Health* 2015. 36:559–74;

Abstract: <https://pubmed.ncbi.nlm.nih.gov/25581144/>

Article: ‘Overdoses soared even as prescription pain pills plunged’ *Washington Post*. Sept 12, 2023

(The great majority of new cases of OUD result from the use of prescription opioids):

(Compton 2016), (Jones 2013), (Muhuri 2013), (Brands 2004).

Compton WM et. al. Relationship between nonmedical prescription-opioid use and heroin use. *NEJM*. 374 (2) (2016), pp. 154-163.

free: <https://www.nejm.org/doi/full/10.1056/nejmra1508490>

Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002-2004 and 2008-2010. *Drug Alcohol Depend.* 2013;132(1-2):95-100. Abstract: <https://pubmed.ncbi.nlm.nih.gov/23410617/>

Muhuri PK, et al. Substance Abuse and Mental Health Services Administration. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. *CBHSQ Data Review*. Published August 2013.

free: <https://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm>

Brands, B., (2004). Prescription opioid abuse in patients presenting for methadone maintenance treatment. *Drug and Alcohol Dependence*, 73(2), 199.

free: <https://www.sciencedirect.com/science/article/pii/S0376871603002904>

(U.S. per-capita opioid consumption is greater than that of any other country in the world):

CRS: 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)

(Systematic evaluation of commercial bias in opioid REMS programs;

The program has not reduced opioid prescribing, nor harms):

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
free:

<https://www.painphysicianjournal.com/current/pdf?article=NzI4Mg%3D%3D&journal=137>

(Role of the Accreditation Council for Continuing Medical Education):

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).

free: <https://www.researchgate.net/publication/352133867> Industry-funded medical education is always promotion-an essay by Adriane Fugh-Berman

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.

free:

<https://www.researchgate.net/publication/287211552> CME stands for commercial medical education And ACCME still won't address the issue

(Opioid tapering was associated with improvements in pain, function, & QOL):

Frank JW, et al. Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: A systematic review. Ann Intern. Med 2017.

free: <https://www.acpjournals.org/doi/10.7326/M17-0598>

("Complex persistent opioid dependence" - patients who may not be able to taper off of opioids after developing physical dependence):

Manhapra A, et al. Complex Persistent Opioid Dependence with Long-term Opioids: a Gray Area That Needs Definition, Better Understanding, Treatment Guidance, and Policy Changes. J Gen Intern Med. Dec 2020; 35(Suppl 3):964-971.

free: <https://pubmed.ncbi.nlm.nih.gov/33159241/>

Ballantyne JC et al. Opioid Dependence vs Addiction: A Distinction Without a Difference? Arch Intern Med. 2012 Sep 24;172(17):1342-3.

<https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/1309576>

(New onset of long-term opioid dependence is one of the most common complications of routine surgery;

Two million people per year who are opioid naïve may initiate long-term opioid use following elective surgery):

Brummett CM, et al. New persistent opioid use after minor and major surgical procedures in US adults. JAMA Surg. 2017;152(6):e170504

free: www.ncbi.nlm.nih.gov/pubmed/28403427

(etc.)

Michigan Open ((Opioid Prescribing Engagement Network) <https://michigan-open.org/>

(An important risk factor for OUD and for overdose deaths is the availability and volume of prescriptions of opioid pain medication):

Strang J, Volkow ND, et al. Opioid use disorder (Review). Nat Rev Dis Primers. 2020 Jan 9;6(1):3

Abstract: <https://pubmed.ncbi.nlm.nih.gov/31919349>

(Possibly the best online training course on pharmacological treatments of chronic pain):
Online Course: 'Pain & Addiction: Essentials'
Available online from ASAM: The American Society of Addiction Medicine.
ASAM.org - 'education' - 'e-learning center'. Module 4 (of 6): Pharmacological Treatment
Approaches presented by Donald Teater, MD, MPH

PAIN REPROCESSING THERAPY (PRT)

Ashar YK, Gordon A, Schubiner H, et al. Effect of Pain Reprocessing Therapy vs Placebo and Usual Care for Patients With Chronic Back Pain. A Randomized Clinical Trial JAMA Psychiatry. 2022;79(1):13-23.

Free: <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2784694>
www.painreprocessingtherapy.com

Podcast Episode: Unlearning Your Pain w/ Dr Howard Schubiner.
https://www.youtube.com/watch?v=rYz_ApWYeg0

PAIN NEUROSCIENCE EDUCATION (PNE)

Lin LH et al. Pain neuroscience education for reducing pain and kinesiophobia in patients with chronic neck pain: A systematic review and meta-analysis of randomized controlled trials. Eur J Pain. 2023 Sep 11

Abstract: <https://pubmed.ncbi.nlm.nih.gov/37694895/>

(Excellent 2-page handout for patients):

Leyde S, Azari S. 'What Should I Know About Opioids and Living With Chronic Pain?' JAMA internal medicine 2020. PMID: 32453391.

free: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2765691>

Excellent 5 minute video for patients on the role of modifiable nervous system sensitivity in chronic pain: free: https://www.youtube.com/watch?v=C_3phB93rvI

Lucid Lane

An organization that can provide virtual tapering services for opioids if needed, and behavioral health services, billing most commercial insurance carriers. <https://lucidlane.com/>

PharmedOut

A project at Georgetown University Medical Center that advances evidence-based prescribing and educates health care professionals and students about pharmaceutical and medical device marketing practices. Provides education and information about CME courses free of industry sponsorship. <https://sites.google.com/georgetown.edu/pharmedout/home>

Physicians for Responsible Opioid Prescribing (PROP)

A non-profit organization comprised of healthcare professionals whose mission is to reduce opioid-related morbidity and mortality by promoting cautious and responsible prescribing practices
www.supportprop.org

'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.

Free: <https://www.motherjones.com/politics/2018/04/doctors-are-required-to-receive-opioid-training-big-pharma-funds-it-what-could-go-wrong/>

Fugh-Berman, A. Industry-funded medical education is always promotion—an essay by Adriane Fugh-Berman BMJ 2021;373:n1273.

Abstract: <https://www.bmj.com/content/373/bmj.n1273>

Fugh-Berman A and Batt S "This May Sting a Bit":
Cutting CME's Ties to Pharma. VIEWPOINT. JUN 2006

free:

<https://journalofethics.ama-assn.org/article/may-sting-bit-cutting-cmes-ties-pharma/2006-06>

("Profit motives ... will continue to generate harmful over-provision of addictive pharmaceuticals unless regulatory systems are fundamentally reformed. . .")

Responding to the opioid crisis in North America and beyond: recommendations of the Stanford-Lancet Commission.' The Lancet. 2022;399(10324):555-604.

free: [https://www.thelancet.com/article/S0140-6736\(21\)02252-2/fulltext](https://www.thelancet.com/article/S0140-6736(21)02252-2/fulltext)

(Buprenorphine as a frontline agent for chronic pain):

Davis, M. P. (2012). Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain. The Journal of Supportive Oncology, 10(6), 209-219.

free: <http://accurateclinic.com/wp-content/uploads/2016/03/Twelve-Reasons-for-Considering-Buprenorphine-as-a-Frontline-Analgesic-in-the-Management-of-Pain-2012.pdf>