Summary for CDC or Seedy Sea? What Do the Guidelines Mean?

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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Summary

This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.

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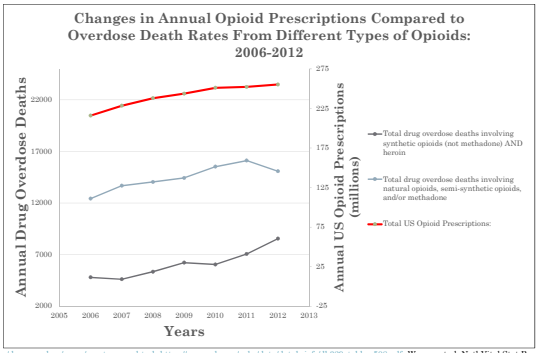
Changes in Annual Opioid Prescriptions Compared to Overdose Death Rates From Different Types of Opioids: 2006-2012



https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html; https://www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf; Warner et al. Natl Vital Stat Rep. 2016;65(10):1-15.

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Other Factors Setting the Stage

- Shift in Patient Expectations:
  - Being "pain free"
  - "Magic bullet" of medications
  - Relatively unlimited supply of opioid medications
- Marketing from Opioid Companies
  - What above the government, third party payers, FDA, etc?
- Pain as the 5th Vital Sign

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Debate #1

Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.

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Morphine Milligram Equivalent Thresholds Wegrzyn- CDC

- Lowest effective dose at initiation and maintenance phase
- High doses of opioids interferes with ability to taper/stop opioids
  - Safety measure
- Majority of benefits seen with low dose opioids
  - Adverse effects drastically increase with higher doses
- Increased mortality risk >40 MME
  - Ballantyne JC, et al

Ballantyne JC, Murinova N. Kreuhin DL. Opioid Guidelines are a necessary response to the opioid crisis. Clin Pharmacol Ther. 2018 Jun;103(6):946-949
Bohnert AS, Valenstein M, Bair MJ, etal. Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths. *JAMA*. 2011;305(13):1315-1321. doi:10.1001/jama.2011.370

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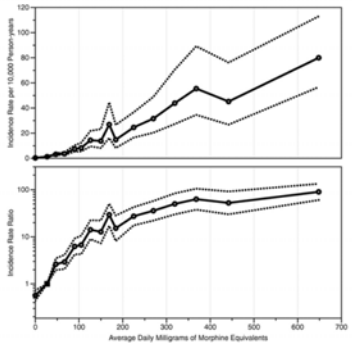

Dasgupta N, Funk MJ, Proescholdbell S, et al. Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality. Pain Med. 2016 Jan; 17(1):85-98

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- Doses > 90-100 MME have been associated with ~ 8 times greater chance of accidental overdose

Ballantyne JC, Murinova N, Kreshin DL. Opioid Guidelines are a necessary response to the opioid crisis. Clin Pharmacol Ther. 2018 Jun;103(6):946-949
Bohnert AS, Valenstein M, Bair MJ, etal. Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths. *JAMA*. 2011;305(13):1315-1321. doi:10.1001/jama.2011.370

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Cleary- Pain Specialist

- The MEDD myth: the impact of pseudoscience on pain research and prescribing-guideline development
- How do you calculate morphine equivalence?
- Patient specific factors:
  - Genetics
  - Drug interactions
  - Variations in organ function
  - Height, weight, gender, etc.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4809143/

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Calculation of MME: Rennick A.

- 319 included (MDs, PharmDs, and NPs)
- Asked to provide MME for hydrocodone 80mg, fentanyl 75mg/hour (1800mcg/day), methadone 40mg, oxycodone 120mg, and hydromorphone 48mg
- Reference for calculation also collected
- MME for fentanyl, hydrocodone, hydromorphone, methadone, and oxycodone were: 176 (±117) mg, 88 (±42) mg, 192 (±55) mg, 193 (±201) mg, and 173 (±39) mg

Rennick A, Atkinson T, Cimino NM et al. Variability in Opioid Equivalence Calculations. Pain Med. 2015 Sep 9. doi: 10.1111/pme.12920. [Epub ahead of print]

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Calculation of MME: Rennick A.

- A total of 124 (46%) respondents identified using personal knowledge as a resource
- Online calculator at 83 (31%), a textbook table at 45 (17%), and a conversion table from a journal at 15 (6%)

Rennick A, Atkinson T, Cimino NM et al. Variability in Opioid Equivalence Calculations. Pain Med. 2015 Sep 9. doi: 10.1111/pme.12920. [Epub ahead of print]

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Cleary- Pain Specialist

- The recommendation is based on one randomized unblinded study in 135 patients (94% males; 74% have musculoskeletal pain) who received 40 MME/day compared to 52 MME/day
  - Recommendation was generalized to "chronic non cancer pain" and recommended "to avoid increasing dosage to ≥90 MME/ day" which was NOT evaluated by the referenced study
- Arbitrary cutoffs not based on science

Dowell D. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. Regulations.gov. Available at: http://www.regulations.gov/#!documentdetail;d=cdc-2015-0112-0002. Accessed April 2016. = http://www.regulations.gov/#!documentDetail;D=CDC-2015-0112-0002

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Debate #2

Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

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Wegrzyn- CDC

- Establish realistic goals
  - NOT to eliminate ALL pain
- Assessment of functionality creates measurable benchmarks for treatment - Ensure benefits outweigh risks
- Prior to initiating therapy
  - Establish treatment goals
    - Pain relief
    - Function
- 3-item PEG Scale for Assessment
  - Average Pain Scale (0-10)
  - Interference with Enjoyment of life (0-10)
  - Interference with General activity (0-10)

*30% - benchmark for clinically meaningfully improvement

Krebs EE, Lorenz KA, Bair MJ, et al. Development and Initial Validation of the PEG, a Three-item Scale Assessing Pain Intensity and Interference. J Gen Intern Med. 2009 Jun; 24(6): 733–738.

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Cleary- Pain Specialist

- Several conditions are associated with severe and enduring chronic pain->functional improvement may NOT be feasible
- Improvement in quality of life?!
- Often times this statement causes providers to taper or discontinue therapy all together
- NOT ALL OPIOIDS ARE CREATED EQUAL
  - Not seeing benefit from one does not mean all can be ruled out

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Cleary- Pain Specialist

- "Benefits do not outweigh risks"-> arbitrary statement leaves a LOT for interpretation
- Definition not standard across ALL patients and ALL chronic pain conditions
- Risk of overdose can be determined prior to prescribing using the RIOSORD tool

Zedler B, Saunders W, Joyce A, et al. Validation of a screening risk index for overdose or serious prescription opioid-induced respiratory depression prescription opioid use and deaths from overdose or opioid-induced respiratory depression. Presented at the 2015 AAPM Annual Meeting. March 2015.

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Debate #3

Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

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Wegrzyn- CDC

- "The willingness and ability to stop opioids is key to safe prescribing"
  - Ballantyne JC, et al.
- Continuous monitoring
  - Target to treatment goals
  - Early warning signs for misuse/abuse
  - Risks vs. benefits

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Cleary- Pain Specialist

- HOW DO YOU TAPER!?
- Lack of training and education for medical professionals on what we have already discussed…and how to undo what has already been done
  - Mezei L et al. concluded that education for North American medical students is limited, variable, and often fragmentary" > 80% of attending physicians rate their education on chronic pain during medical school as "inadequate"
  - Yanni et al. identified lack of confidence in treating chronic pain among physicians, where 59% of the participants rated the education on pain management as "fair" or "poor"
- Increase in heroin use and overdose deaths while prescribing is decreasing-> harder to obtain? 4/5 heroin users start with RX

1.Mezei et al. Pain Education in North American Medical Schools. The Journal of Pain, 12:12 (December), 2011: 1199-1208
2.Yanni LM, et al. Preparation, confidence, and attitudes about chronic noncancer pain in graduate medical education. J Grad Med Educ 2010 (2):260–268

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% CHANGE IN OPIOID PERSCRIBING PER COUNTY, U.S. 2010–2015

2016 data available at:
https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6712a1-H.pdf

Opioid prescribing measures	Decrease (%)	Stable (%)	Increase (%)
MEDD per capita	49.6	27.8	22.6
Overall prescribing rate	46.5	33.8	19.6
High-dose prescribing rate	86.5	6.7	6.9
Average daily MME per prescription	72.1	25.7	2.2

Guy GP, et al. MMWR Morb Mortal Wkly Rep. 2017;66:697–704

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Debate #4

USE IMMEDIATE-RELEASE OPIOIDS WHEN STARTING When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/ long-acting (ER/LA) opioids.

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Cleary- Pain Specialist

- No medical evidence supporting this claim
- What meets the needs of the patient
- IR vs. ER PK?
- Opioids with multiple mechanisms of action may be more beneficial
- Deaths associated with ER opioids skewed:
  - Patients are sicker
  - Abuse of ER opioids more likely to result in death due to dose dumping

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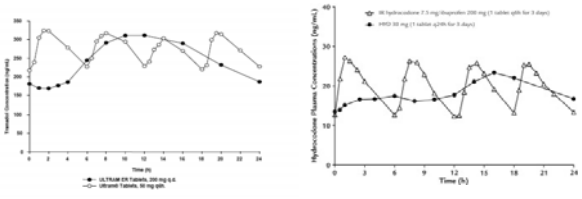
IR vs. ER



https://www.rxlist.com/ultram-er-drug.htm#clinpharm
https://www.sciencedirect.com/science/article/pii/S0149291815013036#f0015

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ER/LA increases deaths - Wegrzyn-CDC

- Lower the dose, lower risk for overdose
- Allows for predictable pharmacokinetics and pharmacodynamics
  - Minimize overdose risks
- Physician error – knowledge deficits
  - Methadone
- Avoid combination of immediate-release opioids in combination with ER/LA opioids

Webster LR, Cochella S, Dasgupta N, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. Pain Med. 2011;12(Suppl 2):S26–S35

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What can we AGREE upon?

- Use strategies to mitigate risk
  - Urine drug screens
  - PMP data
  - Controlled substance agreement
- Avoid co-prescribing of opioids and benzodiazepines
- Co-prescribing of naloxone
- Short durations for acute pain
- Offer treatment for opioid use disorder (OUD)
  - Medication assisted treatment (MAT)
- Use nonpharmacologic and nonopioid therapies FIRST!

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How do we really feel?

Dr. Cleary Dr. Wegrzyn

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So where are we now?

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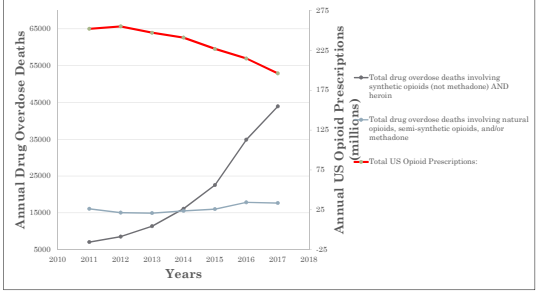
Changes in Annual Opioid Prescriptions Compared to Overdose Death Rates from Different Types of Opioids: 2011-2017



https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html; https://www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf; Warner et al. Natl Vital Stat Rep. 2016;65(10):1-15.

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Potential Consequences from the Guidelines

- Misapplication to populations outside the scope of the guideline
  - Cancer patients, acute/post-op pain, acute sickle cell crises, etc
- Polices that encourage hard limits and abrupt tapering
  - Medical groups, insurances, and state governments
- Potentially increased rates of suicide?

Kroenke K et al. Pain Med. 2019;20(4):724-735

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The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JUNE 13, 2019

No Shortcuts to Safer Opioid Prescribing

Deborah Dowell, M.D., M.P.H., Tamara Haegerich, Ph.D., and Roger Chou, M.D.

Since the Centers for Disease Control and Prevention (CDC) released its Guideline for Prescribing Opioids for Chronic Pain in 2016,[1] the medical and health policy communities have largely embraced ommended dosage and duration thresholds and policies that encourage hard limits and abrupt tapering of drug dosages, resulting in sudden opioid discontinuation or dismissal of patients

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Key Takeaways

- The CDC guidelines are JUST GUIDELINES
- There needs to be flexibility when using any type of guidelines, but especially when we are dealing with high risk medications like opioids
- The "opioid crisis" continues, and is perhaps worsening, despite the major implementation of the guidelines
- It is important to commend the authors for clarifying themselves
  - Although kind of ironic, don't' we think?

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Questions/Comments?

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