

Opioid Update

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Disclosure

- ▶ I have no commercial financial relationships to disclose
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- ▶ Views expressed in this presentation are mine and do not reflect the position or policy of the US government



Which of the following are true?

RCT evidence has demonstrated that...

- A. For chronic back pain, opioids are more effective than placebo
- B. For acute back pain, naproxen + oxycodone is more effective than naproxen alone
- C. For chronic back pain, opioids reduce pain more than NSAIDs or acetaminophen
- D. A & B, but not C
- E. A, B, and C



Which of the following are true?

In patients receiving prescribed opioid analgesics, higher daily dosage is associated with...

- A. Fatal and non-fatal opioid overdose
- B. Incident depression
- C. Incident opioid use disorder
- D. A and B, but not C
- E. A, B, and C





What's known and what's new in 2016

Opioid benefits

Opioid harms

Management of opioid therapy

Opioid benefits—what's known?

- ▶ Opioids decrease pain intensity more than placebo in short-term
 - ▶ Chronic back pain: Δ ~10 points on 0-100 scale
 - ▶ Hip/knee osteoarthritis: Δ ~7 points on 0-100 scale
- ▶ Insufficient evidence for opioids vs. non-opioids
- ▶ No evidence for effectiveness of long-term opioid therapy

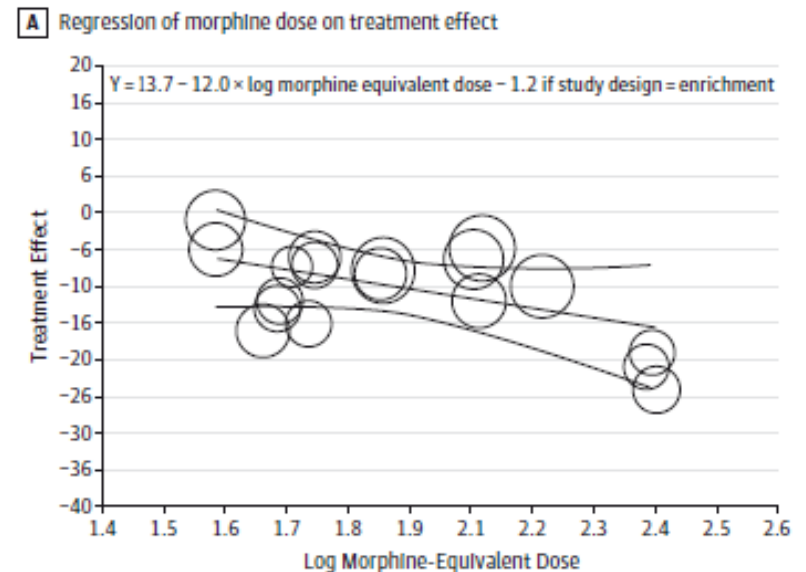
Opioid benefits—what's new?

Original Investigation

Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain A Systematic Review and Meta-analysis

- ▶ Meta-regression of placebo-controlled trials to estimate effect of dose (range 40-240 mg/d) on pain
 - ▶ Association between log dose and pain: statistically significant, but **not clinically significant**
 - ▶ Outcomes of doses above & below 100 mg/d: **no difference**

Figure 3. Effect of Opioid Dose on Treatment Effect



Opioid benefits—what's new?

Original Investigation

Naproxen With Cyclobenzaprine, Oxycodone/Acetaminophen, or Placebo for Treating Acute Low Back Pain A Randomized Clinical Trial

Benjamin W. Friedman, MD, MS; Andrew A. Dym, BS; Michelle Davitt, MD; Lynne Holden, MD; Clemencia Solorzano, PharmD; David Esses, MD; Polly E. Bijur, PhD; E. John Gallagher, MD

- ▶ Participants: Patients presenting to ED with non-traumatic, non-radicular acute low back pain
- ▶ Intervention: Randomized to 10-day course of...
 - ▶ Naproxen plus placebo
 - ▶ Naproxen plus oxycodone/acetaminophen
 - ▶ Naproxen plus cyclobenzaprine
- ▶ Results: **No difference** in pain or physical function at 1 week



What's known and what's new in 2016

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Opioid harms—what's known?

FIGURE 2. Rates* of opioid pain reliever (OPR) overdose death, OPR treatment admissions, and kilograms of OPR sold — United States, 1999–2010

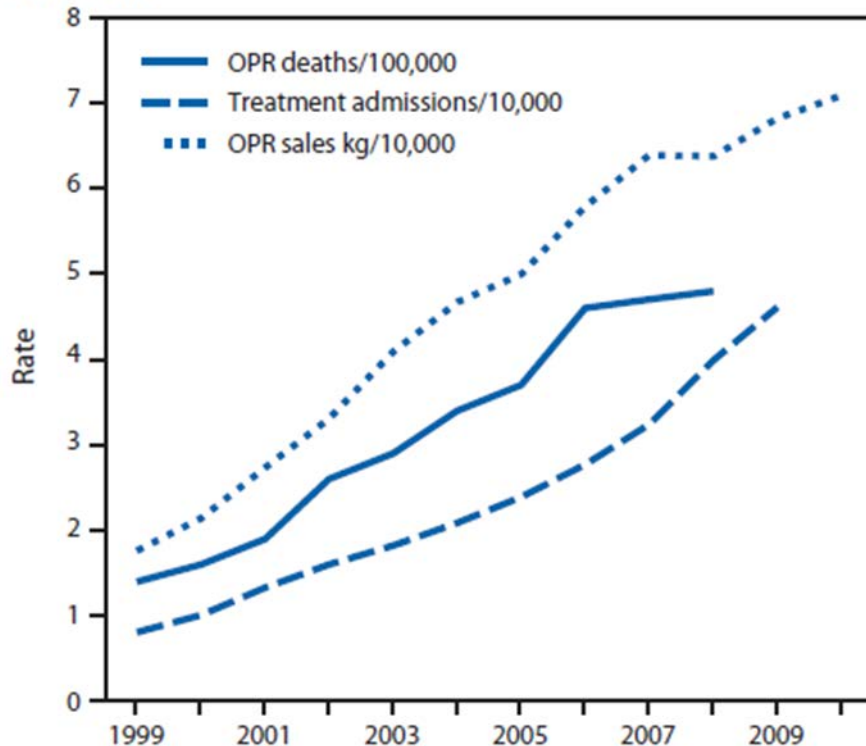


Figure from CDC in Paulozzi et al, MMWR 2011;60:1487–92

- ▶ Among patients prescribed opioids, higher doses predict...
 - ▶ Fatal and non-fatal opioid overdose
 - ▶ Incident and recurrent major depression
 - ▶ Opioid use disorder
 - ▶ Road trauma

Opioid harms—what's new?

ORIGINAL ARTICLE

A Detailed Exploration Into the Association of Prescribed Opioid Dosage and Overdose Deaths Among Patients With Chronic Pain

- ▶ Nested case-control study examining association of dose and death
- ▶ Finding: **No dose cutoff for risk**

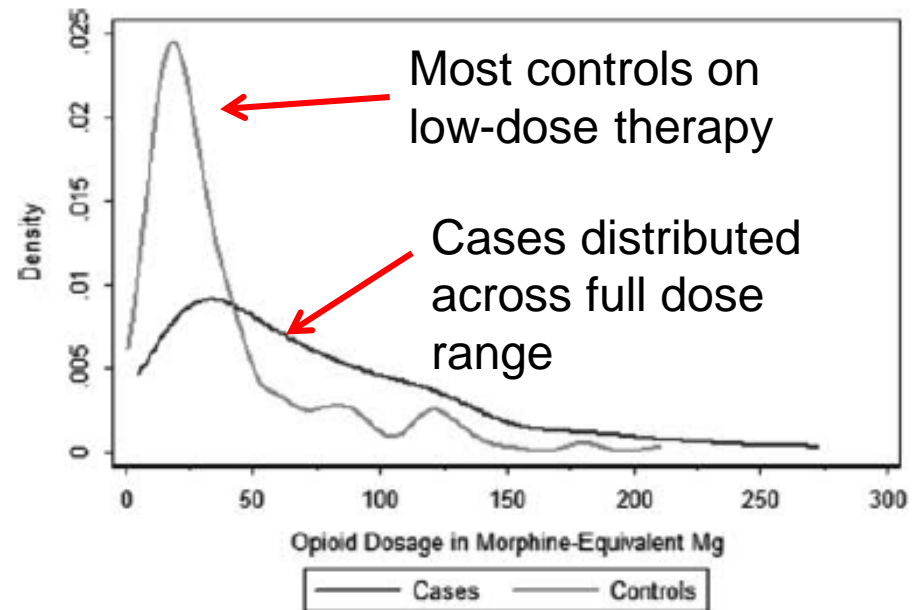


FIGURE 2. Distribution of opioid dosages by group.

Opioid harms—what's new?

ORIGINAL ARTICLE

A Detailed Exploration Into the Association of Prescribed Opioid Dosage and Overdose Deaths Among Patients With Chronic Pain

TABLE 2. Distribution of Opioid Overdose Cases and Controls at Specific Opioid Dosage Levels

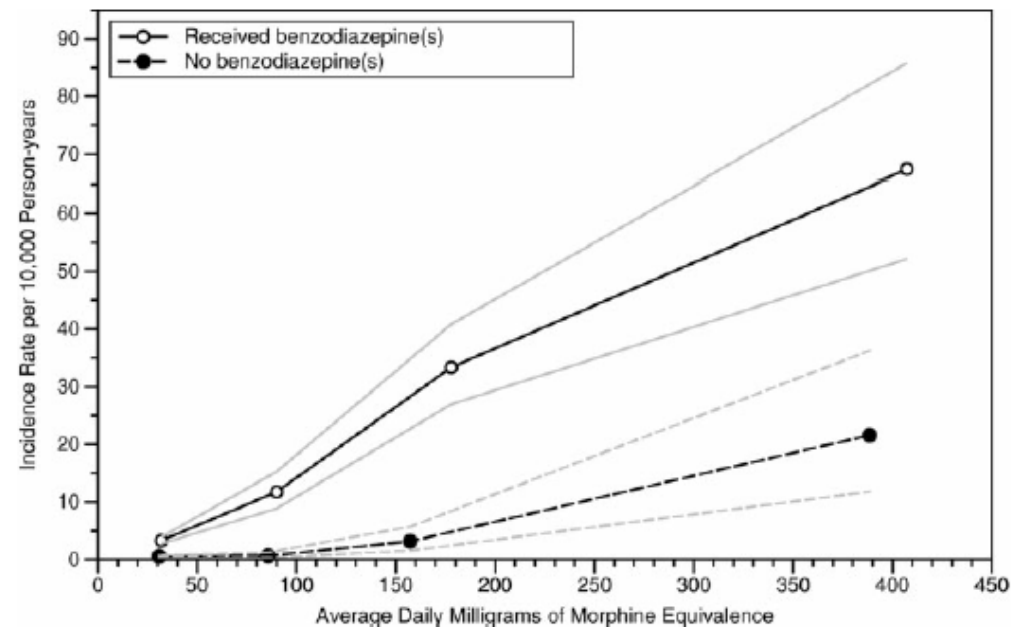
| Dose in MEM | Cases Above (Sensitivity) (%) | Controls at or Below (Specificity) (%) | Likelihood Ratio (+) |
|-------------|-------------------------------|--|----------------------|
| 10 | 97 | 14 | 1.12 |
| 20 | 87 | 41 | 1.47 |
| 30 | 71 | 63 | 1.94 |
| 40 | 66 | 71 | 2.27 |
| 50 | 59 | 76 | 2.50 |
| 60 | 48 | 81 | 2.50 |
| 70 | 45 | 82 | 2.50 |
| 80 | 41 | 84 | 2.60 |
| 90 | 33 | 88 | 2.67 |
| 100 | 31 | 89 | 2.83 |
| 110 | 28 | 90 | 2.82 |
| 120 | 21 | 93 | 3.06 |

Opioid harms—what's new?

Original Research Articles

Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality

- ▶ Cohort study of North Carolina residents
- ▶ Findings: **No dose cutoff for risk**
- ▶ Death rates increased gradually across the full range of opioid dosage
- ▶ **Benzodiazepine increased death rate 10x** (greater Δ at higher doses)



Opioid harms—what's new?

Annals of Internal Medicine

ORIGINAL RESEARCH

Opioid Prescribing After Nonfatal Overdose and Association With Repeated Overdose

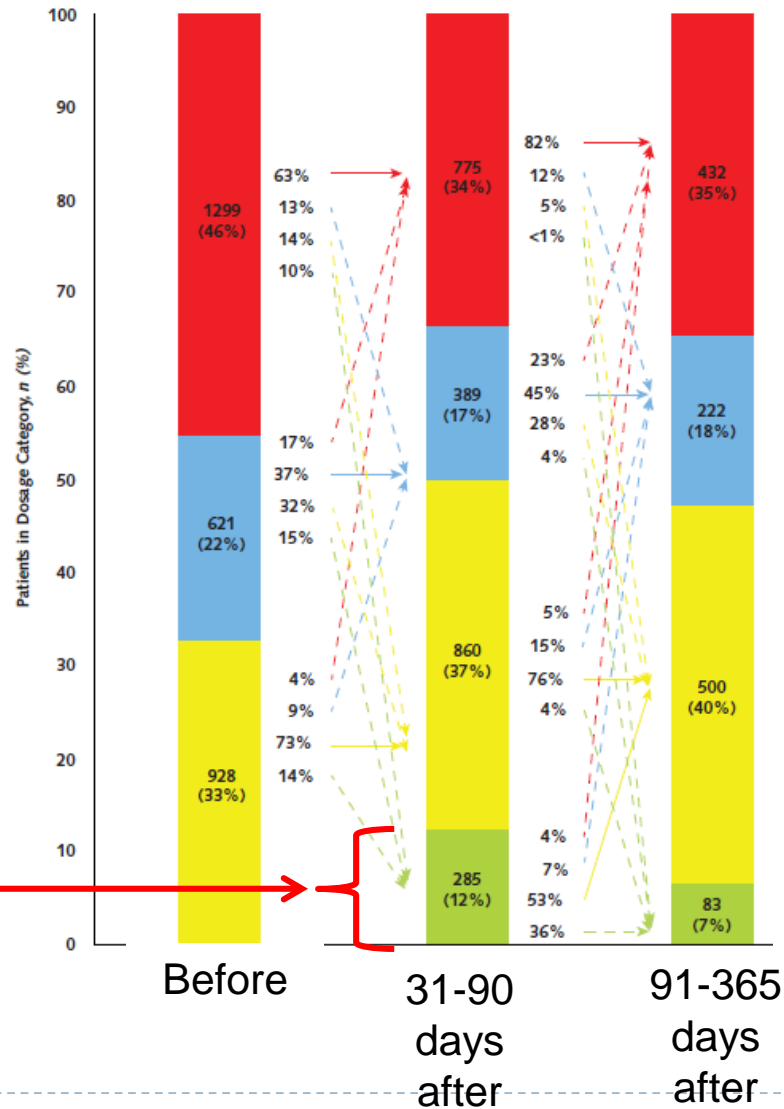
A Cohort Study

- ▶ Cohort of insured patients on long-term opioid therapy who had an initial non-fatal opioid overdose (n=2848)
- ▶ Findings:
 - ▶ **Most continued receiving opioids from same prescriber** (30% switched)
 - ▶ **7% had another overdose** (17% of those on high dose therapy)

Opioid harms—what's new?

Most patients on high-doses before overdose were continued on high-dose therapy

Few patients had opioids discontinued after overdose





What's known and what's new in 2016

Opioid benefits

Opioid harms

Management of opioid therapy

Opioid management—what’s known?

Annals of Internal Medicine

POSITION PAPER

National Institutes of Health Pathways to Prevention Workshop: The Role of Opioids in the Treatment of Chronic Pain

David B. Reuben, MD; Anika A.H. Alvanzo, MD, MS; Takamaru Ashikaga, PhD; G. Anne Bogat, PhD; Christopher M. Callahan, MD; Victoria Ruffing, RN, CCRC; and David C. Steffens, MD, MHS

- ▶ “Particularly striking to the panel was the realization that evidence is insufficient for *every clinical decision that a provider needs to make about the use of opioids* for chronic pain, leaving the provider to rely on his or her own clinical experience.”

Opioid management—what's new?

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

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

- ▶ Target audience: Primary care clinicians
- ▶ Application: Adults with chronic pain outside of palliative or end-of-life care
- ▶ Voluntary guideline based on emerging evidence



CDC Guideline development overview

- ▶ CDC commissioned an updated systematic review and a new contextual review
- ▶ CDC personnel drafted initial recommendations and refined them in Core Expert Group process
- ▶ CDC submitted draft guideline for review by peers, stakeholders, federal partners, and the public
- ▶ Federal advisory committee commissioned an Opioid Guideline Workgroup to review draft recommendations, rationale, evidence reviews, and public/stakeholder feedback
- ▶ Workgroup submitted report to federal advisory committee
- ▶ CDC revised and published final Guideline



Rationale for CDC Guideline

- ▶ No evidence for long-term benefits of opioids
- ▶ Extensive evidence of opioid-related harms
- ▶ Extensive evidence for benefits of a variety of non-opioid approaches to pain



CDC RECOMMENDATIONS

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

- ▶ 1. Non-pharmacological therapy and non-opioid medications are preferred for chronic pain
 - ▶ Consider opioids only if benefits expected to outweigh risks
- ▶ 2. Before starting opioids, establish realistic goals and an “exit strategy”
- ▶ 3. Before starting opioids, discuss realistic potential benefits and known risks

CDC RECOMMENDATIONS

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

4. Prescribe short-acting (IR) meds, not ER/LA meds
5. Use the lowest effective dosage
 - ▶ Use caution at any dosage
 - ▶ Carefully assess benefits/risks of >50 ME mg/day
 - ▶ Avoid >90 ME mg/day
6. For acute pain, use lowest effective dose of IR meds
 - ▶ ≤ 3 days usually sufficient
 - ▶ > 7 days rarely needed
7. Evaluate benefits/harms regularly
 - ▶ Within 1-4 weeks of initiation or dose escalation
 - ▶ At least every 3 months
 - ▶ Taper or discontinue if benefits don't clearly outweigh harms/risks

Evaluating benefits/harms

- ▶ Are treatment goals being met?
 - ▶ Sustained improvement in pain & function?
 - ▶ Common or serious adverse effects?
 - ▶ Early warning signs/elevated risk for serious adverse events?
 - ▶ Evidence of potential opioid use disorder?
- ▶ Do benefits of continuation clearly outweigh harms and risks?
- ▶ Can dosage be reduced or opioids discontinued?



Evaluating benefit

- ▶ Progress toward individual functional goals
- ▶ 30% improvement in PEG scale

Pain on average

What number best describes your pain on average in the past week? (from 0=no pain to 10=pain as bad as you can imagine)

Enjoyment of life

What number best describes how, during the past week, pain has interfered with your enjoyment of life? (from 0=does not interfere to 10=completely interferes)

General activity

What number best describes how, during the past week, pain has interfered with your general activity? (from 0=does not interfere to 10=completely interferes)

CDC RECOMMENDATIONS

ASSESSING RISK AND ADDRESSING HARMS

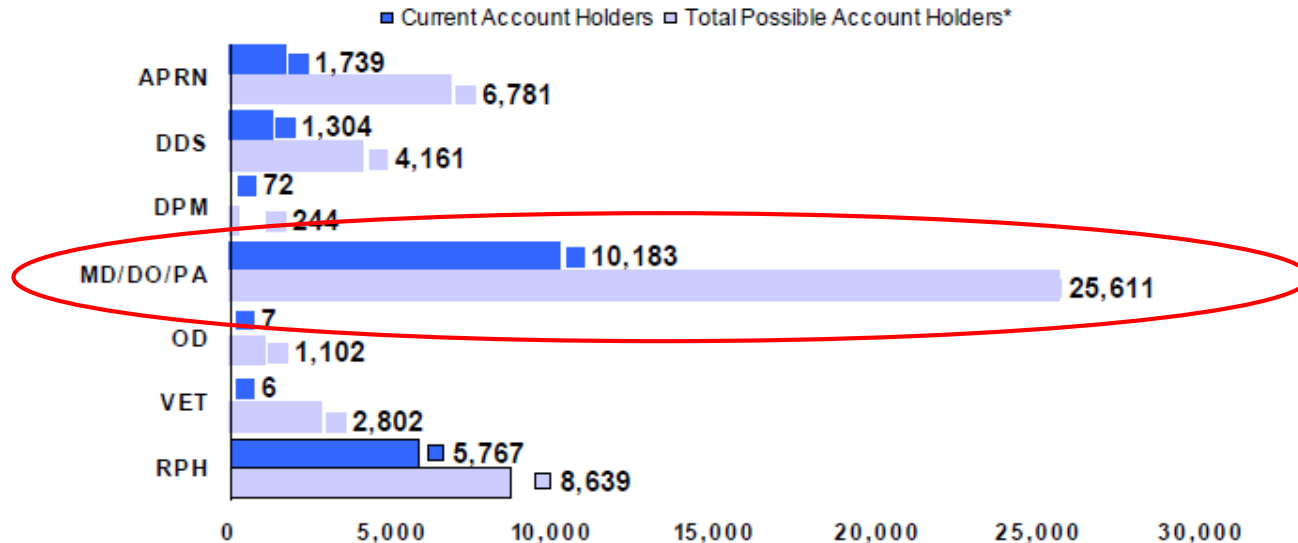
- ▶ 8. Assess risk for opioid-related harms before starting opioids and periodically during therapy
 - ▶ Consider naloxone if risk factors for overdose present
- ▶ 9. Review PDMP every 1-3 months
- ▶ 10. Obtain UDT before prescribing and consider annual UDT
- ▶ 11. Avoid co-prescribing of opioids and benzodiazepines whenever possible
- ▶ 12. Offer or arrange treatment for opioid use disorder

Evaluating risk



System Accounts by Number of Total Possible Within Each Type

Jan 2016—Aug 2016



*Based on total number of MN RPh licensees or MN licensees eligible for DEA registration as of 1/1/2016

CDC guideline—remaining questions

DETERMINING WHEN TO INITIATE OR CONTINUE OPIOIDS FOR CHRONIC PAIN

- ▶ Which patients are good candidates for a trial of conservative opioid therapy?

OPIOID SELECTION, DOSAGE, DURATION, FOLLOW-UP, AND DISCONTINUATION

- ▶ For patients on high-dose/long-term opioids, what are best practices for managing dose reduction?
 - ▶ Are there patients for whom opioids cannot be completely discontinued?

ASSESSING RISK AND ADDRESSING HARMS

- ▶ For patients with comorbid chronic pain and opioid use disorder, what are best practices for managing both conditions?



Summary—Opioids in 2016

- ▶ Evidence is still limited for most clinical questions
 - ▶ Specific opioid prescribing practices are associated with bad outcomes: higher doses, benzodiazepine co-prescription
- ▶ Opioid overdose epidemic is still worsening
- ▶ CDC guidelines define a new standard of care
 - ▶ Opioids are not routine or default therapy for chronic pain
 - ▶ Prescribing should be undertaken only with caution and with the lowest dosage for the shortest time possible
 - ▶ Opioid therapy should be continually reassessed and stopped if not clearly beneficial



Thank you! Questions?

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