Opioid Prescribing Guidelines: Controversy, Opiophobia, and the Role of the Pharmacist

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Disclosure Statement
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- Astra Zeneca (Speakers Bureau, Advisory Board)
- Clarity (Consultant)
- DepoMed (Advisory Board, Speakers Bureau)
- Endo (Consultant, Speakers Bureau)
- Kaléo (Speakers Bureau, Advisory Board)
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- Millennium Health, LLC (Speakers Bureau, Advisory)
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- Remitigate, LLC (Owner)
- Scilex Pharmaceuticals (Consultant)
Disclosure Statement
Dr. Ernest Dole

- Millennium Health, LLC (Speakers Bureau, Advisory)
Objectives

- Debate the pros and cons for implementation of the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain.
- Discuss the pharmacist’s role, or lack thereof, in the development of the CDC Guideline for Prescribing Opioids for Chronic Pain.
- Summarize controversies related to the development of the CDC Guideline for Prescribing Opioids for Chronic Pain.
- Formulate your own professional opinion related to the CDC Guideline for Prescribing Opioids for Chronic Pain.
Pretest Question #1
Chose the best answer listed below. The CDC Guidelines are:

A. The definitive guide to safe prescribing of opioid medications
B. A political ploy by providers that hate opioid medications
C. Guidelines only
D. A line in the sand
Pretest Question #2
The use of extended release opioids combined with immediate release opioids is advocated by the guidelines

A  TRUE
B  FALSE
Pretest Question #3
The guidelines state that no patient should be prescribed opioid medications above 90 MED

A  YES
B  NO
Setting the Stage (Pro)

A BALANCING ACT
A PUBLIC HEALTH ISSUE
SHARP INCREASE IN OPIOID PRESCRIPTIONS PARALLELS SHARP INCREASE IN DEATHS

National Vital Statistics System, DEA’s Automation of Reports and Consolidated Orders System
Setting The Stage (Pro)

National Overdose Deaths
Number of Deaths from Prescription Opioid Pain Relievers

Source: National Center for Health Statistics, CDC Wonder
Setting the Stage (Pro)

- **Provider Realities**
  - The incidence of alcoholism and addiction in the general population is 5%-10%
  - One addict effects 7-10 people
  - The prevalence of current or past substance use disorders in patients receiving chronic opioids for CNCP may be ~40% or higher
  - Clash of providers & patient’s values

- **Patient Expectations**
  - Of being pain free
  - Of “magic bullet” medications
  - Of unlimited supply of medications
    - Opioids
  - Of not having to do any work
    - Physical therapy
    - Behavioral health
  - Of no consequences for their decisions
    - “Being honest”

- **Pain as the 5th Vital Sign**
Setting the Stage (Con)

- How is chronic non-cancer pain different than cancer pain?
- When do we stop calling it “cancer pain” and start calling it “cancer survivor” and CNCP?
- National Guideline Clearinghouse
  - “Level A rating requires at least two consistent Class I studies”.¹
  - A 12 recommendations are based on case series (level 3 evidence) or expert opinion (level 4 evidence) yet assigned a grade A recommendation.²

1. http://www.cancer.org/docroot/CRI/content/CRI_2_6x_Cancer_Prevalence_How_Many_People_Have_Cancer.asp
Setting the Stage (Con)

But perhaps the most duplicitous in my mind...

- The CDC panel lacked a single clinical pharmacist, much less one with post-graduate training and expertise in pain therapeutics.
- To me, writing drug guidelines without a single pharmacist is like writing diagnostic guidelines without a single medical doctor.
CDC Guidelines

Recommendation #1

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
- Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.
- If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

(Recommendation category A: Evidence type: 3)
Pro CDC Guidelines

- Use nonpharmacologic therapy such as exercise or cognitive behavioral therapy (CBT) to reduce pain and improve function.
- Use nonopioid pharmacologic therapy (nonsteroidal anti-inflammatory drugs, acetaminophen, anticonvulsants, certain antidepressants) when benefits outweigh risks, combined with nonpharmacologic therapy.
- When opioids used, combine with nonpharmacologic therapy and nonopioid pharmacologic therapy to provide greater benefits.
- No therapeutic guideline for any condition that has CNCP endorses opioids as 1st line treatment.
Con CDC Guidelines

- Simply put...
  - No drug should EVER be prescribed for ANY disorder unless benefits outweigh risks.
Recommendation #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 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.

(Recommendation category A: Evidence type: 4)
Goals should be realistic and NOT be to take away ALL pain

Previous opioid prescribing guidelines have been developed by several states and agencies but were inconsistent

Most recent national guidelines are several years old and don’t incorporate the most recent evidence

Before initiating opioid therapy for chronic pain

• Determine how effectiveness will be evaluated.
• Establish treatment goals with patients.
  o Pain relief
  o Function

Assess progress using 3-item PEG Assessment Scale*

• Pain average (0-10)
• Interference with Enjoyment of life (0-10)
• Interference with General activity (0-10)

*30% = clinically meaningful improvement
Con CDC Guideline

- “Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.”
  - Disagree; what about disorders where goal is...
    - comfort care?
    - delayed dysfunction?
  - Examples:
    - Spinal Cord injury
    - Parkinsons Disease
    - ALS, or amyotrophic lateral sclerosis
CDC Guidelines

- Recommendation #3
  - Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

(Recommendation category A: Evidence type: 3)
Pro CDC Guidelines

- Be explicit and realistic about expected benefits.
- Never state medications will take ALL of pain away.
- Emphasize goal of improvement in pain and **function**.
- Discuss
  - serious and common adverse effects
  - increased risks of overdose
    - at higher dosages
    - when opioids are taken with other drugs or alcohol
  - periodic reassessment, PDMP and urine checks; and
  - risks to family members and individuals in the community.
Con CDC Guidelines

- I mostly agree, but...
  - Are the majority of pain-treating clinicians that prescribe opioids pain experts in opioid pharmacotherapeutics, pharmacogenetics, clinical chemistry, etc.?
    - Are clinicians held to this standard with other therapies such as NSAID prescribing, depression, diabetes?
      - Note, yearly deaths from NSAID-induced GI bleeds is similar to RX opioids
    - And why we’re at it, what about deaths from lack of gun control?
      - “...30,000 plus deaths per year that are seen from accidental or purposeful massacres”¹
  - Political?
CDC Guidelines

Recommendation #4

• When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

(Recommendation category A: Evidence type: 4)
Pro CDC Guidelines

- Choose predictable pharmacokinetics and pharmacodynamics to minimize overdose risk
- In general, avoid the use of immediate-release opioids combined with ER/LA opioids.
Con CDC Guidelines

- There is no basis for this and it is perhaps less practical.
  - Discussion...
CDC Guidelines

- Recommendation #5
  - When opioids are started, clinicians should prescribe the lowest effective dosage.
  - Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when 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.

(Recommendation category A: Evidence type: 3)
Doses > 90-100 MED have been associated with ~ 8 times greater chance of accidental overdose

Con CDC Guidelines

- You’re killing me....
- “…≥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.”
- Discussion of publications/studies 1-4*
  - Overall daily dose is important, but it’s very individual
  - The cut-offs chosen are based on “pseudoscience”
  - There is no universally accepted MME
CDC Guidelines

- Recommendation #6
  - Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.
  - 3 days or less will often be sufficient; more than 7 days will rarely be needed.

(Recommendation category A: Evidence type: 4)
Pro CDC Guidelines

- Prescribe the lowest effective dose.
- Do not prescribe ER/LA opioids for acute pain treatment.
- The lower the dose, the lower the risk for OD.
Con CDC Guidelines
CDC Guidelines

- Recommendation #7
  - 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.

(Recommendation category A: Evidence type: 4)
Pro CDC Guidelines

- At follow up, determine whether
  - opioids continue to meet treatment goals
  - there are common or serious adverse events or early warning signs of opioid abuse
  - benefits of opioids continue to outweigh risks
  - opioid dosage can be reduced or opioids can be discontinued
Con CDC Guidelines

- Agreed, mostly, but...
  - if one opioid doesn’t work or isn’t well-tolerated, or both, there may be another good opioid option
## Opioid Therapeutics 101

### Chemical classes of opioids Fudin 2015

<table>
<thead>
<tr>
<th>PHENANTHRENES</th>
<th>BENZOMORPHANS</th>
<th>PHENYLPIPERIDINES</th>
<th>DIPHENYLHEPTANES</th>
<th>PHENYLPROPYL AMINES</th>
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<tbody>
<tr>
<td><strong>MORPHINE</strong></td>
<td><strong>PENTAZOCINE</strong></td>
<td><strong>MEPERIDINE</strong></td>
<td><strong>METHADONE</strong></td>
<td><strong>TRAMADOL</strong></td>
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<td>Buprenorphine*</td>
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<td>Alfentanil</td>
<td>Methadone</td>
<td>Tapentadol</td>
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<td>Butorphanol*</td>
<td>Loperamide</td>
<td>Fentanyl</td>
<td>Propoxyphene</td>
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<td>Pentazocine</td>
<td>Meperidine</td>
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<td>Heroin (diacetyl-morphine)</td>
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<td>Remifentanil</td>
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<td>Hydrocodone*</td>
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<td>Sufentanil</td>
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<td>Oxycodone*</td>
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<td>Oxymorphone*</td>
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**CROSS-SENSITIVITY RISK**

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<tr>
<th>PROBABLE</th>
<th>POSSIBLE</th>
<th>LOW RISK</th>
<th>LOW RISK</th>
<th>LOW RISK</th>
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*Agents lacking the 6-OH group of morphine, possibly decreases cross-sensitivity within the phenanthrene group.

CDC Guidelines

- Recommendation #8
  - Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms.
  - Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (>50 MME/day), or concurrent benzodiazepine use, are present.

(Recommendation category A: Evidence type: 4)
Pro CDC Guidelines

- Assess for co-morbid risk factors
  - Avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing when possible.
  - Use additional caution with renal or hepatic insufficiency, aged >65 years.
  - Ensure treatment for depression, hypothyroidism, hypogonadism is optimized.
  - Consider offering naloxone in Universal Precautions model
Con CDC Guidelines
CDC Guidelines

- Recommendation #9
  - Clinicians should review the patient’s history of controlled substance prescriptions using state PDMP data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him/her at high risk for overdose.
  - Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

(Recommendation category A: Evidence type: 4)
Pro CDC Guidelines

- If prescriptions from multiple sources, high dosages, or dangerous combinations
  - Discuss safety concerns with patient (and any other prescribers they may have), including increased risk for overdose.
  - For patients receiving high total opioid dosages, consider tapering to a safer dosage, consider offering naloxone.
  - If you suspect your patient might be sharing or selling opioids and not taking them, consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal.
  - Consider opioid use disorder and discuss concerns with your patient.
  - Do not dismiss patients from care—use the opportunity to provide potentially lifesaving information and interventions.
Con CDC Guidelines
CDC Guidelines

Recommendation #10

- When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

(Recommendation category B: Evidence type: 4)
Pro CDC Guidelines

- Use UDT to assess for prescribed opioids and other drugs that increase risk
  - Be familiar with screening (immunoassay) & confirmatory (GC-LC/MS) urine drug testing panels and how to interpret results.
  - Ask patient when they last took medication that is to be tested
  - Before ordering urine drug testing
    - explain to patients that testing is intended to improve their safety
    - explain expected results; and
    - ask patients whether there might be unexpected results.
  - Discuss unexpected results with local lab and patients.
  - Verify unexpected, unexplained results using specific test.
  - Do not dismiss patients from care based on a urine drug test result.
Con CDC Guidelines

- Makes sense, but...
  - Limited evidence
  - Potential harmful outcomes (interpretation?)
  - Guidelines are under development
    - Expected in print just prior to ASHP Midyear
      - Here’s the update...
CDC Guidelines

- Recommendation #11
  - Clinicians should avoid prescribing opioid pain medication and benzodiazepines (carisoprodol) concurrently whenever possible.

(Recommendation category A: Evidence type: 3)
Concurrent use of opioids and benzodiazepines increases the risk of accidental OD significantly

Con CDC Guidelines

- Agreed, but alcohol doesn’t receive enough attention
  - ~60% of patients taking opioids were prescribed potentially dangerous medication combinations (eg, opioid plus a benzodiazepine)\(^1\)
  - ~20% to 30% of opioid-related deaths involve alcohol\(^1\)
    - Alcohol may cause some extended-release formulations to rapidly release opioid
    - Benzos, opioids, alcohol, July 2016 Report\(^2\)
  - Of 3883 Opioid-related deaths, 860 (22.1%) involved alcohol
  - Of 1512 Benzo-related deaths, 324 (21.4%) involved alcohol

ED = emergency department; OIRD = opioid-induced respiratory depression.


Recommendations #12

- Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (OUD).

(Recommendation category A: Evidence type: 2)
If opioid use disorder (OUD) is suspected

• Discuss with your patient and provide an opportunity to disclose concerns.

• Assess for OUD using DSM-5 criteria. If present, offer or arrange MAT.
  - Buprenorphine through an office-based buprenorphine treatment provider or an opioid treatment program specialist
  - Methadone maintenance therapy from an opioid treatment program specialist
  - Oral or long-acting injectable formulations of naltrexone (for highly motivated non-pregnant adults)
What We Really Believe
Posttest Question #1
Chose the best answer listed below. The CDC Guidelines are

A. The definitive guide to safe prescribing of opioid medications
B. A political ploy by providers that hate opioid medications
C. Guidelines only *
D. A line in the sand
Posttest Question #2
The use of extended release opioids combined with immediate release opioids is advocated by the guidelines

A  TRUE
B  FALSE  *
Posttest Question #3

The guidelines state that no patient should be prescribed opioid medications above 90 MED

A. YES *
B. NO
Key Takeaways

- **Key Takeaway #1**
  - The CDC Guidelines are GUIDELINES ONLY

- **Key Takeaway #2**
  - While the guidelines are the most current synopsis of current data, the data available for analysis is not strong

- **Key Takeaway #3**
  - The guidelines should not be used by professional boards or insurance companies to influence practice