CDC Opioid Guidelines for Primary Care: Is Evidence-Based Medicine Under Attack?

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Disclosures

Consulting:
- Collegium
- Daiichi Sankyo
- Endo
- MyMatrixx
- Pfizer
- Scilex
- Teva

Research:
- Grunenthal

Consultant: CDC/ Opioid Guideline Workgroup (OGW)
Overview

• Heroin overdose and opioid conundrum
• PROP impact on CDC
• CDC Opioid Guideline “process”
• Review Evidence Based Medicine
• 12 recommendations
• Closure of Seattle Pain Centers
• WA State pain “crisis”
Opioid Conundrum

The problem:
Existing guidelines vary in recommendations, and primary care providers say they receive insufficient training in prescribing opioid pain relievers. It is important that patients receive appropriate pain treatment, and that the benefits and risks of treatment options are carefully considered.

- **259 million**
  In 2012, health care providers wrote 259 million prescriptions for opioid pain relievers – enough for every American adult to have a bottle of pills.

- **300% increase**
  Prescription opioid sales in the United States have increased by 300% since 1999, but there has not been an overall change in the amount of pain Americans report.

- **2 million**
  Almost 2 million Americans, age 12 or older, either abused or were dependent on opioid pain relievers in 2013.

- **16 thousand**
  In 2013, more than 16,000 people died in the United States from overdose related to opioid pain relievers, four times the number in 1999.
Patients, Clinicians, the Public Struggling & Behaving Badly
Who is dying? Are we missing something?

Morbidity and Mortality Weekly Report (MMWR)

CDC, MMWR. Weekly/ August 26, 2016/65(33):837-843.
Abuse, Misuse, Addiction

MEDs
Dose Thresholds

Diversion, Overdose
Evidence
CDC Opioid Guidelines for Primary Care
Do opioids work for chronic pain?

Single-Entity Hydrocodone Extended-Release Capsules in Opioid-Tolerant Subjects with Moderate-to-Severe Chronic Low Back Pain: A Randomized Double-Blind, Placebo-Controlled Study

Noble M, Treadwell JR, Tregear SJ, Coates VH, Wiffen PJ, Akafomo C, Schoelles KM
“Every patient with pain has the right to have both pain assessed and pain relieved. No patient has the right to an opioid drug if that treatment is not appropriate.”

- Kathleen M Foley, MD
- Joseph Fins, MD
- Charles Inturrisi, PhD

1. Strike the term “moderate” from the indication for non-cancer pain
2. Add a maximum daily dose, equivalent to 100 mg of morphine for non-cancer pain
3. Add a maximum duration of 90-days for continuous daily use for non-cancer pain

**FDA Response**

- “Opioid trials based on randomized, controlled clinical trials 12 weeks. For chronic pain, it is difficult to ensure subject participation in controlled trials beyond 12 weeks. FDA is not aware of adequate and well-controlled studies of opioid use longer than 12 weeks.”

- “There is a relationship between increasing opioid dose and risk of certain AEs. Available information does not demonstrate relationship is necessarily a causal one.”

- **Opioid MED and death**: Greater association among > 100 mg MED vs 1-19 MED. Point of at which increase in deaths changes benefit to risk assessment cannot be determined. Dose response relationship should be analyzed treating opioid use as a continuous variable.

- Cited data on long-term opioid use and addiction do not establish a threshold for maximum duration of use.
Long-Acting (LA)/ Extended Release (ER) Opioids

Indication:

“ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.”

- Addiction, Abuse, and Misuse
- Life-threatening Respiratory Depression
- Accidental Exposure
- Neonatal Opioid Withdrawal Syndrome
- Interaction With Alcohol
Dosing and Monitoring

Doses >200 mg oral morphine equivalents/day should prompt re-evaluation and increased monitoring.

APS/AAPM Opioid Guidelines for Chronic Noncancer Pain

Do not exceed 120 mg of oral morphine equivalents/day without either demonstrated improvements in function and pain or first obtaining a consultation with pain management expert.

Washington State Medical Directors Guideline on Opioid Dosing

AAPM, American Academy of Pain Medicine; APS, American Pain Society.
CDC Mission

Intended for primary care clinicians who are treating patients with chronic pain (i.e., pain > 3 months or past the time of normal tissue healing) in outpatient settings.

CDC, March 15, 2016.
Draft CDC Guideline for Prescribing Opioids for Chronic Pain, 2016: Summary of Stakeholder Review Group Comments and CDC Response

- Transparency in process, no empathy for patients, not patient-centered, ignored Federal Advisory Committee Act
- Opposing evidence of dose limitations at 50 and 90 MME/day
- Evidence built on systematic reviews from 2009 and 2014
- Changed study criteria to 1 yr, and then “no evidence” claim

cdc.gov
Comment Period

- Scientific Society’s Response (AAPMR, APS, ABPM)
- Multispecialty Work Group
- Providence Health System/ Swedish Health System
IOM Standards for Practice Guidelines

1. Establish transparency
2. Management and disclosure of conflict of interest
3. Guideline development group composition
4. Evidence based on systematic review of literature
5. Strength of rating for the clinical recommendations
6. Articulation of clinical recommendations in standardized form
7. External review
8. Keeping guidelines updated

CDC Guidelines for Opioids: Process

**Evidence:**
- APS/AAPM Opioid Guidelines 2009
- AHRQ systematic review of 2014

**Process:**
- Core Exert Group (CEG)
- Stakeholder Review Group (SRG)
- Draft Document, Federal Review (80 FR 77351)
  Public comment through Jan 13, 2016
- National Center for Injury Prevention & Control (NCIPC) Board of Scientific Counselors
- Opioid Guideline Workgroup (OGW)

GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN

When to initiate or continue

Selection of opioids, dosage, follow-up, and discontinuation

Risk Management

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

CLINICAL REMINDERS

- Use immediate-release opioids when starting
- Start low and go slow
- When opioids are needed for acute pain, prescribe no more than needed
- Do not prescribe ER/LA opioids for acute pain
- Follow-up and re-evaluate risk of harm, reduce dose or taper and discontinue if needed

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

When opioids are started, clinicians should prescribe the lowest effective dose. Clinicians should use caution when prescribing opioids at any dosage, should carefully measure evidence of individual benefits and risks when considering increasing dosage to 60 morphine milligram equivalents (MME/day), and should avoid increasing dosage to 90 MME/day or carefully justify a decision to initiate dosage at 90 MME/day.

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, an immediate-release opioid should be used for the expected duration of pain, and a sustained-release opioid will often be used.

When starting opioid therapy for chronic pain, clinicians should consider the patient’s history of controlled substance prescriptions, any current prescription drug monitoring program (PDMP) data, and other relevant data. Clinicians should consider the patient’s history of chronic or cancer pain, and should be cautious when initiating opioid therapy for the first time at a high level.

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

When prescribing opioids for chronic pain, clinicians should avoid prescribing opioid pain medications and benzodiazepines concurrently whenever possible.

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ASSESSING RISK AND ADDRESSING HAZARDS OF OPIOID USE

Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should consider the patient’s history of controlled substance prescriptions, any current prescription drug monitoring program (PDMP) data, and other relevant data. Clinicians should consider the patient’s history of chronic or cancer pain, and should be cautious when initiating opioid therapy for the first time at a high level.

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What is Evidence Based Medicine (EBM)?
GRADE Evidence Type or Quality

1. **Randomized clinical trials (RCTs)** or overwhelming evidence from **observational studies**
2. **RCTs** with important limitations or exceptionally strong evidence from **observational studies**
3. **Observational studies** or **RCTs** with notable limitations
4. **Observational studies** with important limitations, **RCTs** with several limitations, clinical experience and observations
## GRADE: Final Evidence Type

<table>
<thead>
<tr>
<th>Evidence Type</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>One can be very confident that true effect lies close to that of the estimate of the effect</td>
</tr>
<tr>
<td>2</td>
<td>True effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</td>
</tr>
<tr>
<td>3</td>
<td>Confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect</td>
</tr>
<tr>
<td>4</td>
<td>One has very little confidence in the effect estimate, and true effect is likely to substantially different from estimate of effect</td>
</tr>
<tr>
<td>Insufficient evidence</td>
<td>No studies are present</td>
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</table>
# 1. When to initiate or continue opioids

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Evidence Category/ Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. If opioids used, should be in combination with non-opioid pharmacologic therapy.</td>
<td>A, 3</td>
</tr>
<tr>
<td>2</td>
<td>Establish treatment goals. Continue only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.</td>
<td>A, 4</td>
</tr>
<tr>
<td>3</td>
<td>Discuss with patients known risks and realistic benefits of opioid therapy and responsibilities of patient and clinician.</td>
<td>A, 3</td>
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2. Selection of opioids, dosage, duration, follow-up, and discontinuation

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Evidence Category, type</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>When starting opioids, prescribe immediate release instead of ER/LA opioids</td>
<td>A, 4</td>
</tr>
<tr>
<td>3</td>
<td>Confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>One has very little confidence in the effect estimate, and true effect is likely to substantially different from estimate of effect</td>
<td>A, 4</td>
</tr>
<tr>
<td>6</td>
<td>Prescribe no greater quantity than needed for expected duration of pain</td>
<td>A, 4</td>
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<tr>
<td></td>
<td>- 3 days or less will often be sufficient</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- &gt; 7 days is rarely needed</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Evaluate benefits and harms within 1-4 wks</td>
<td>A, 4</td>
</tr>
<tr>
<td></td>
<td>Re-evaluate every 3 months or more frequently</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IF benefits do not outweigh harms, taper down or discontinue</td>
<td></td>
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</tbody>
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Long Term Analgesic Effectiveness of COAT

- CDC Opioid Guideline review of evidence excluded any study not longer than 12 months
- Analgesic trials for FDA approval are 3 months duration
- Most analgesic trials now use enriched enrollment study models
- Nonresponders & subjects unable to tolerate are excluded then randomized to placebo or study drug
- FDA requires 1 yr long term safety studies (OL, OLE)

OL: Open Label
OLE: Open Label Extension
Long Term Analgesic Effectiveness of COAT > 6 months

- 268 studies reviewed, 70 included
- 13,686 patients in RCTs, OL, and OLE studies

**Results:**
- Average pain score improvement 2% to 82% improvement
- 86% reported on > 25% reduction in pain
- 75% reported > 30% reduction in pain
- 15% of studies reported on functional change including positive correlation between clinically significant change in pain and physical function scores

OL: Open Label
OLE: Open Label Extension

### 3. Risk management: assessing risk & addressing harms

<table>
<thead>
<tr>
<th>#</th>
<th>Recommendation</th>
<th>Evidence Category, type</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Evaluate risk factors for opioid related harms. Consider offering naloxone with increase in risk for overdose, substance abuse history, higher opioid dosages &gt; 50 MME/day, benzodiazepine use</td>
<td>A, 4</td>
</tr>
<tr>
<td>9</td>
<td>Check PDMP for high dosages and prescriptions from other providers.</td>
<td>A, 4</td>
</tr>
<tr>
<td>10</td>
<td>Use urine drug testing to identify prescribed substances and undisclosed use</td>
<td>B, 4</td>
</tr>
<tr>
<td>11</td>
<td>Avoid concurrent benzodiazepine and opioid prescribing</td>
<td>A, 3</td>
</tr>
<tr>
<td>12</td>
<td>Arrange treatment for opioid use disorder if needed, including office-based treatment in combination with behavioral therapies for patients with opioid use disorder</td>
<td>A, 2</td>
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</tbody>
</table>
CDC Guidelines for Prescribing Opioids for Chronic Pain

• CDC’s recommendations are made on the basis of a systematic review of best available evidence.
• Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient’s clinical situation, functioning, and life context.
• The recommendations in the guideline are voluntary, rather than prescriptive standards.
• Clinicians should consider the circumstances and unique needs of each patient when providing care.

### Six Domains of Appraisal of Guidelines for Research & Evaluation

1. Explicit scope and purposes  
   - +/-
2. Stakeholder involvement  
   - ?
3. Rigor of development  
   - ?
4. Clarity of presentation  
   - Y
5. Applicability  
   - ?
6. Editorial independence  
   - ?

"While we are largely supportive of the guidelines, we remain concerned about the evidence base informing some of the recommendations, conflicts with existing state laws and product labeling, and possible unintended consequences associated with implementation, which includes access and insurance coverage limitations for non-pharmacologic treatments, especially comprehensive care, and the potential effects of strict dosage and duration limits on patient care.”

Patrice A. Harris, MD, the AMA board chair-elect
Checklist for prescribing opioids for chronic pain

For primary care providers treating adults (18+) with chronic pain ≥ 3 months, excluding cancer, palliative, and end-of-life care

**Checklist**

When CONSIDERING long-term opioid therapy
- Set realistic goals for pain and function based on diagnosis (e.g., walk around the block).
- Check that non-opioid therapies tried and optimized.
- Discuss benefits and risks (e.g., addiction, overdose) with patient.
- Evaluate risk of harm or misuse.
  - Discuss risk factors with patient.
  - Check prescription drug monitoring program (PDMP) data.
  - Check urine drug screen.
- Set criteria for stopping or continuing opioids.
- Assess baseline pain and function (e.g., PEG scale).
- Schedule initial reassessment within 1–4 weeks.
- Prescribe short-acting opioids using lowest dosage on product labeling; match duration to scheduled reassessment.

If RENEWING without patient visit
- Check that return visit is scheduled ≤ 3 months from last visit.

When REASSESSING at return visit

Continue opioids only after confirming clinically meaningful improvements in pain and function without significant risks or harm.
- Assess pain and function (e.g., PEG); compare results to baseline.
- Evaluate risk of harm or misuse:
  - Observe patient for signs of over-sedation or overdose risk.
  - If yes: Taper dose.
  - Check PDMP.
  - Check for opioid use disorder if indicated (e.g., difficulty controlling use).
  - If yes: Refer for treatment.
- Check that non-opioid therapies optimized.
- Determine whether to continue, adjust, taper, or stop opioids.
- Calculate opioid dosage morphine milligram equivalent (MME)
  - If ≥ 50MME/day total (≥ 50 mg hydrocodone; ≥ 33 mg oxycodone), increase frequency of follow-up; consider offering naloxone.
  - Avoid ≥ 90 MME/day total (≥ 90 mg hydrocodone; ≥ 60 mg oxycodone), carefully justify; consider specialist referral.
- Schedule reassessment at regular intervals (≤ 3 months).

**Reference**

**Evidence about opioid therapy**
- Benefits of long-term opioid therapy for chronic pain not well supported by evidence.
- Short-term benefits small to moderate for pain; inconsistent for function.
- Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.

**Non-opioid therapies**
Use alone or combined with opioids, as indicated:
- Non-opioid medications (e.g., NSAIDs, TCAs, SNRIs, anti-convulsants).
- Physical treatments (e.g., exercise therapy, weight loss).
- Behavioral treatment (e.g., CBT).
- Procedures (e.g., intra-articular corticosteroid).

**Evaluating risk of harm or misuse**
Known risk factors include:
- Illegal drug use; prescription drug use for nonmedical reasons.
- History of substance use disorder or overdose.
- Mental health conditions (e.g., depression, anxiety).
- Sleep-disturbed breathing.
- Concurrent benzodiazepine use.

Use drug testing: Check to confirm presence of prescribed substances and for undisclosed prescription drug or illicit substance use.

Prescription drug monitoring program (PDMP): Check for opioids or benzo derivatives from other sources.

**Assessing pain & function using PEG scale**
PEG score = average 3 individual question scores (30% improvement from baseline is clinically meaningful)

01: What number from 0–10 best describes your pain in the past week?
0 = “no pain”; 10 = “worst you can imagine”

02: What number from 0–10 describes how, during the past week, pain has interfered with your enjoyment of life?
0 = “not at all”; 10 = “complete interference”

03: What number from 0–10 describes how, during the past week, pain has interfered with your general activity?
0 = “not at all”; 10 = “complete interference”
Implications for Patients

- More cautious and thoughtful approach for using controlled substances
- Greater education for patient and family members of the dangers of misuse, abuse, addiction, and diversion
- Possible undertreatment of pain for patients
- Stigmatization of “chronic pain patients”
- Providers “not treating chronic pain patients” and overwhelming pain medicine resources, access
- Increase mortality and adverse events with use of other pharmacologic agents
Letter to American Doctors

• Take the pledge at www.TurnThe TideRx.org

• Build a national movement
  – CDC Opioid Prescribing Guideline
  – Screen patients for opioid use disorder
  – See addiction at a chronic disease, not a moral failing

http://www.businessinsider.com/letter-surgeon-general-sent-every-doctor-on-opioids-2016-8
Healthcare System Impact

- 11,600 patients seen in last 6 months
- 50% Medicaid, 40% Medicare, 10% private insurance
- > 200 intrathecal pump patients
- Patients directed back to PCPs, CDC
- Local community-wide response
- Access to care limited
- Pain patients stigmatized
Patients flood ERs, hospitals after pain clinics' shutdown

Located in northwest Portland, the clinic was one of several pain clinics that closed after a state panel identified potential abuse of painkillers.

LOOKING FOR AN EYE DOCTOR?

Call 206.860.4550 to schedule an appointment.

Patients look for new treatment after pain center closures

After state suspends doctor, pain patients scramble for help

Headaches abound as former patients at shuttered Seattle Pain Center try to access records

Seattle Pain Center records
Present Impact to Swedish Pain Service

- Received 700 calls from external patients
- Received 80 new completed Epic referrals
- SPC managed 240 intrathecal pumps
- SPS will be taking on 90-100 new long term pump patients
  - UW
  - VM
  - Multicare
  - Others
4 Seattle Pain Center Patient Types

1. “Established” Swedish Primary Care providers.
2. “External” SPC patients. A patient without SPC providers at Swedish or our partner affiliates.
3. External or Established SPC patients who in the past have had intrathecal pump devices placed or managed by Swedish Pain Services or Swedish Neuroscience Institute (SNI).
4. Presenting to any Swedish ED or Urgent Care.
3 Categories for Patient “Risk Level”

a. **Low**: < 90 MED/day
b. **Medium**: >90, < 120 MED and deemed to be compliant with treatment, appropriate with tox screening

c. **High**: > 120 MED/day
d. Psychosocial risk factors
   - depression, anxiety, addiction history, age
   - history of aberrant drug-related behavior
   - medical comorbidities
#1. Has Established Swedish PCP

- Intake person explains policy at PCP office, schedules re-evaluation with PCP
- PCP re-evaluation checklist
  - Patient agreement, medication consent
  - Urine toxicology screen
  - PDMP
  - GAD-7, PHQ-9
  - Assess patient
- Patient referred to SPS in Epic (“Ref Pain”)
- SPS Evaluation & Optimization

LOW Risk  MEDIUM Risk  HIGH Risk
Opinions and Bias Matter
“Evidence Based Medicine”

“Method of integrating individual clinical expertise with the best available evidence from systematic research.”  

“The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.”

2. Evidence-based medicine. A new approach to teaching the practice of medicine. JAMA 1992;268:2420-5.
Summary

• CDC Guidelines will be helpful in educating physicians, improving communication, and decreases misuse, abuse, and overdoses from opioids
• Methodological flaws, scope, cannot be ignored
• Pain providers need to be familiar with the 12 recommendations, but also aware of short-comings and potential pitfalls
• Most recommendations based on poor or very poor evidence. “Contextual evidence” needs to be more deeply scrutinized
• Messaging around heroin overdose crisis, opioid overdose crisis, and appropriate treatment of pain patients remains blurred
• Increasing access to care for legitimate patients has been ignored
• Pain patients have been unknowingly stigmatized
“Evidence does not make decisions. People do.”

RB Haynes, 2002
Thanks

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