Dosing and Titrating Opioids

Clinician Outreach and Communication Activity (COCA) Call

August 17, 2016

Office of Public Health Preparedness and Response
Division of Emergency Operations

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Planners have reviewed content to ensure there is no bias.

This presentation will not include any discussion of the unlabeled use of a product or products under investigational use.

Objectives

At the conclusion of this session, the participant will be able to:

- Describe the evidence for the association between opioid dosage and opioid therapy benefits and harms.
- Compare and contrast immediate release and extended-release/long-acting opioid formulations.
- Identify methods for calculating morphine milligram equivalent dosage.
- List the steps for titrating opioids to specific dosage thresholds.
- Identify best practices for opioid tapering and discontinuation.

Guideline for Prescribing Opioids for Chronic Pain Call Series

Listen to recordings from previous calls

Call No.	Date	Topic
1	June 22	Guideline for Prescribing Opioids for Chronic Pain
2	July 27	Non-Opioid Treatments
3	August 3	Assessing Benefits and Harms of Opioid Therapy
4	August 17	Dosing and Titration of Opioids

TODAY'S PRESENTER

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Centers for Disease Control and Prevention

TODAY'S PRESENTER

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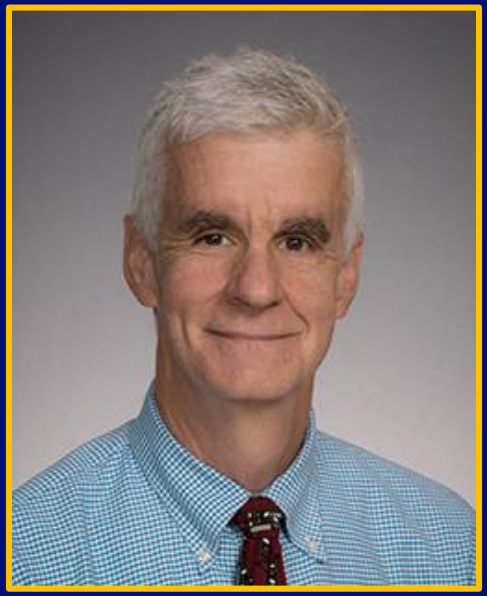
TODAY'S PRESENTER



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CDC Guideline for Prescribing Opioids for Chronic Pain:

Dosing and Titration of Opioids

Deborah Dowell, MD, MPH

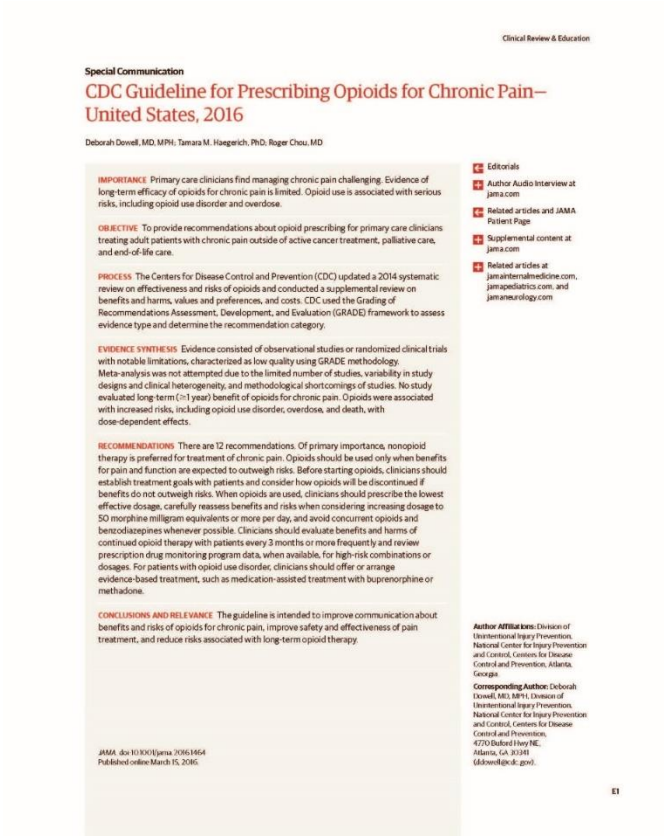
August 17, 2016

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 1
March 18, 2016

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

Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention



Clinical Review & Education

Special Communication

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

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

IMPORTANCE Primary care clinicians find managing chronic pain challenging. Evidence of long-term efficacy of opioids for chronic pain is limited. Opioid use is associated with serious risks, including opioid use disorder and overdose.

OBJECTIVE To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

PROCESS The Centers for Disease Control and Prevention (CDC) updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs. CDC used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to assess evidence type and determine the recommendation category.

EVIDENCE SYNTHESIS Evidence consisted of observational studies or randomized clinical trials with notable limitations, characterized as low quality using GRADE methodology. Meta-analysis was not attempted due to the limited number of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of studies. No study evaluated long-term (≥1 year) benefit of opioids for chronic pain. Opioids were associated with increased risks, including opioid use disorder, overdose, and death, with dose-dependent effects.

RECOMMENDATIONS There are 12 recommendations. Of primary importance, nonopioid therapy is preferred for treatment of chronic pain. Opioids should be used only when benefits for pain and function are expected to outweigh risks. Before starting opioids, clinicians should establish treatment goals with patients and consider how opioids will be discontinued if benefits do not outweigh risks. When opioids are used, clinicians should prescribe the lowest effective dosage, carefully reassess benefits and risks when considering increasing dosage to 50 morphine milligram equivalents or more per day, and avoid concurrent opioids and benzodiazepines whenever possible. Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently and review prescription drug monitoring program data, when available, for high-risk combinations or dosages. For patients with opioid use disorder, clinicians should offer or arrange evidence-based treatment, such as medication-assisted treatment with buprenorphine or methadone.

CONCLUSIONS AND RELEVANCE The guideline is intended to improve communication about benefits and risks of opioids for chronic pain, improve safety and effectiveness of pain treatment, and reduce risks associated with long-term opioid therapy.

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Author Audio Interview at jama.com
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Deborah Dowell, Tamara Haegerich, and Roger Chou

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

Published online March 15, 2016

JAMA®
The Journal of the American Medical Association

Evidence does not support safety of ER/LA opioids relative to immediate-release opioids

- Did not find evidence that ER/LA opioids are more effective or safer than immediate-release opioids
- Higher overdose risk initiating treatment with ER/LA opioids than with immediate-release opioids
- Disproportionate numbers of overdose deaths associated with methadone

Use immediate-release opioids when starting

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)

Additional cautions for

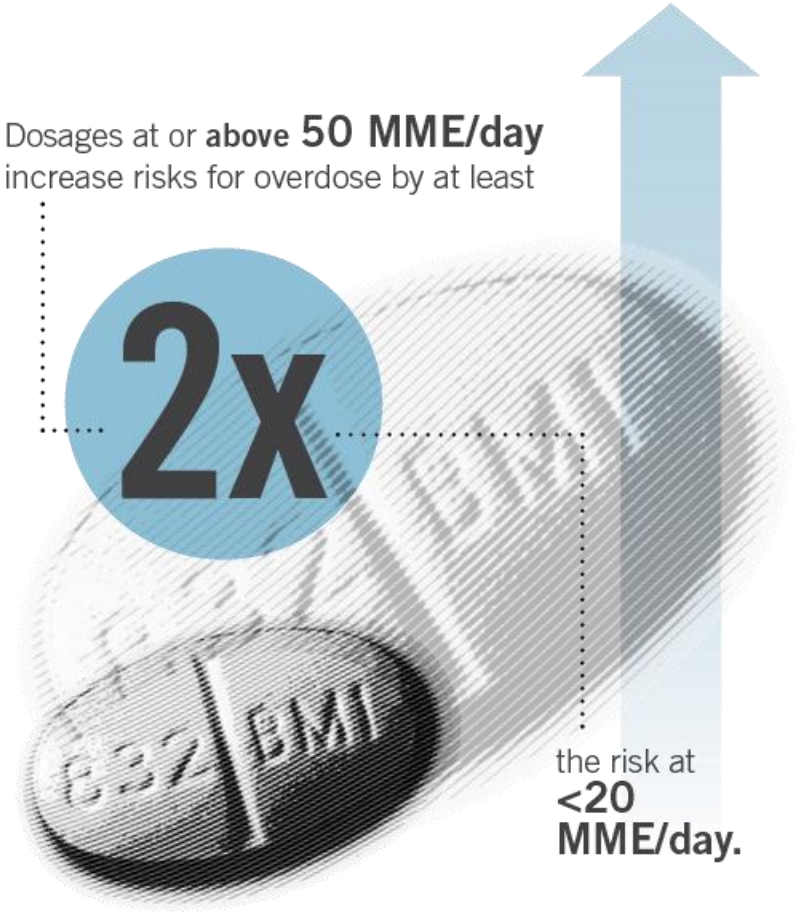
- *Methadone*
- *Transdermal fentanyl*
- *Immediate-release opioids combined with ER/LA opioids*

Higher dosages add risk without clear benefit

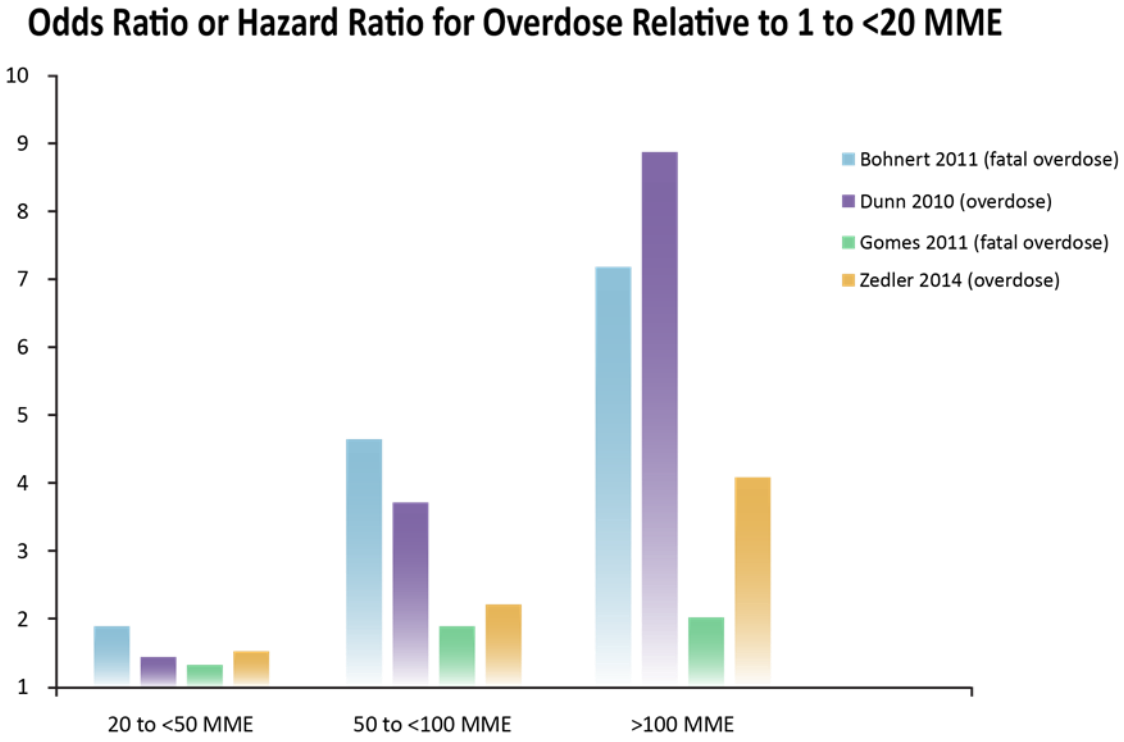
- Benefits of high-dose opioids for chronic pain not established
- RCT*: no difference in pain, function between
  - Liberal dose escalation (average 52 MME)
  - Maintenance of current dosage (average 40 MME)

- Opioid use associated with dose-dependent increased risk of serious harms, including fatal and nonfatal overdose

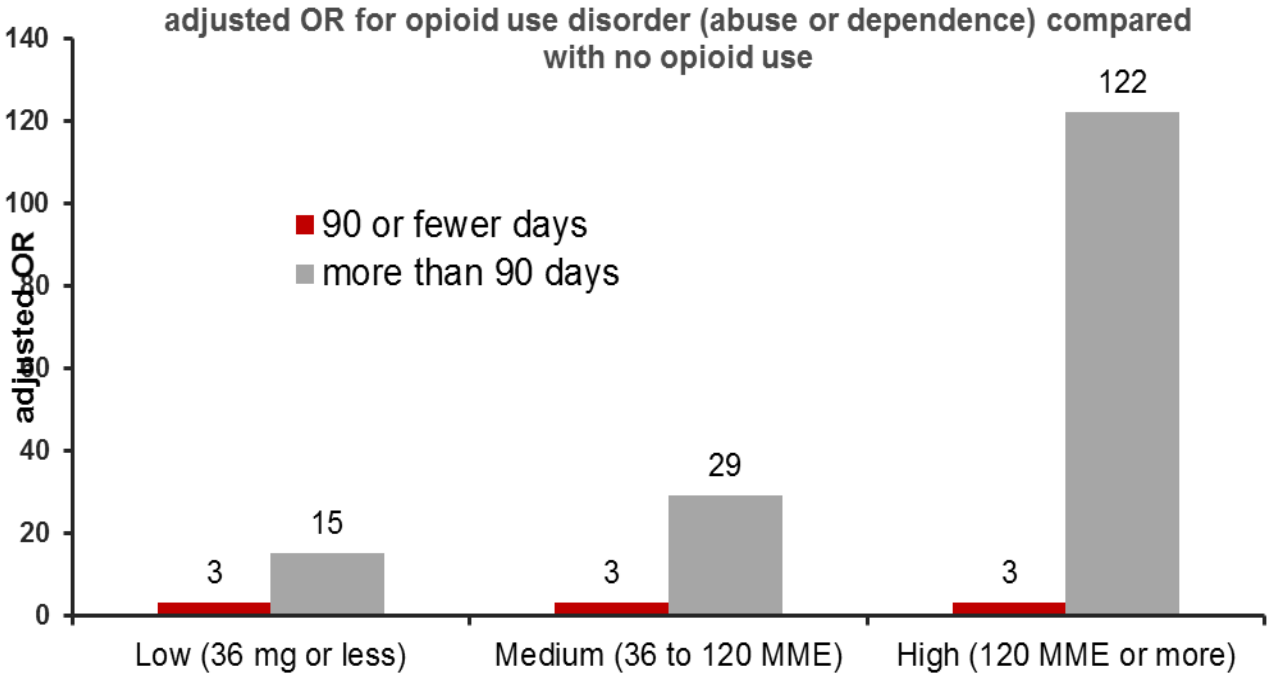
*Naliboff BD, Wu SM, Schieffer B, et al. A randomized trial of 2 prescription strategies for opioid treatment of chronic nonmalignant pain. *J Pain*. 2011;12(2):288-296.


Dosages at or **above** 50 MME/day
increase risks for overdose by at least
2x
the risk at
<20
MME/day.
BMI

Overdose risk increases with opioid dosage



Higher opioid dosages associated with opioid use disorder



Edlund, MJ et al.The role of opioid prescription in incident opioid abuse & dependence among individuals with chronic noncancer pain. *Clin J Pain* 2014; 30: 557-564.

Use caution at any dose and avoid increasing to high dosages

- 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.

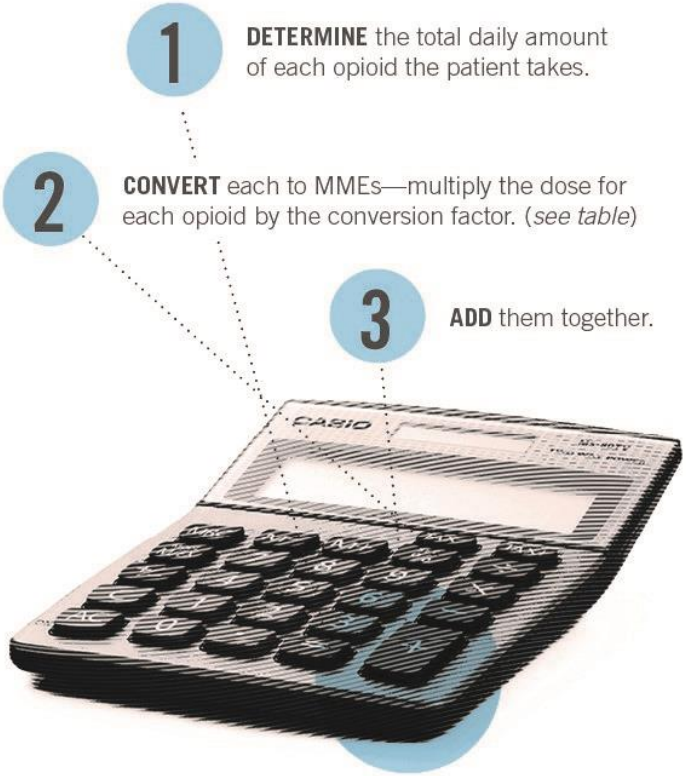
(Recommendation category A: Evidence type: 3)

What about patients already taking high dosages?

- Offer the opportunity to reevaluate continuation of high-dosage opioids in light of recent evidence

- For patients who agree to taper opioids to lower dosages, collaborate on a tapering plan

Calculate MME



CAUTION:
Do not use to convert one opioid to another

Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted)	**CONVERSION FACTOR**
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1-20 mg/day	4
21-40 mg/day	8
41-60 mg/day	10
≥ 61-80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3

Offer a taper if opioids cause harm or are not helping

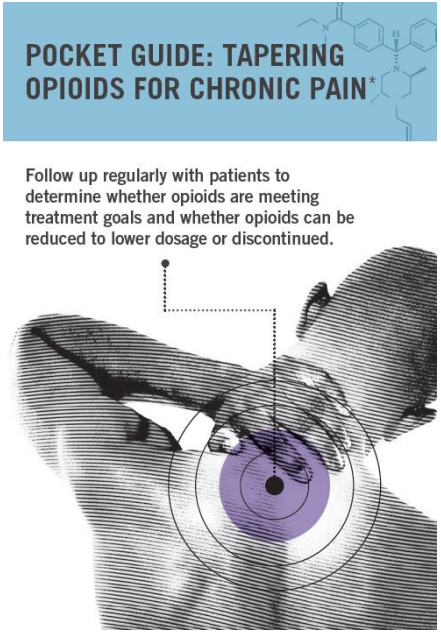
- Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation.
- Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently.
- If benefits do not outweigh harms 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)

Taper slowly enough to minimize withdrawal

- 10% per week is a reasonable starting point
- Some patients do better with slower tapers - 10%/month
- Consider more rapid taper when needed for safety
- Access appropriate expertise during pregnancy
- Optimize pain management and support
  - Anticipate hyperalgesia immediately after tapering
  - Over the long term, most patients report improved function without worse pain

New Resource



Available under the Clinical Tools section of our Guideline resources:
http://www.cdc.gov/drugoverdose/prescribing/resources.html

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CDC Guideline for Prescribing Opioids
for Chronic Pain

DOSING AND TITRATION OF OPIOIDS

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CASE: MS. BROWN

- Ms. Brown is 67 years old and has spinal stenosis
- She has had steadily worsening symptoms of leg pain, lower back pain, leg numbness and tingling, and difficulty walking
- She now finds it difficult to start moving and ambulating in the mornings
- She is motivated to get as well as she can without medication, and has been doing aqua aerobics and graded exercise under the supervision of therapists
- She has tried amitriptyline, gabapentin, and tramadol, but none of these helped
- Her clinician suggested a trial of low dose strong opioid
- She agreed

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WHICH OPIOID?

- Choose something simple with simple pharmacokinetics and pharmacodynamics
- This makes the treatment much safer and easier to manage by patients
- Do not use any of the long acting opioids when starting opioid therapy in an opioid naïve patient
- Long acting opioids include ER/LA opioids, methadone and transdermal fentanyl (fentanyl patches)

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When starting opioids for chronic pain, prescribe IR not ER/LA opioids

4

- Choose predictable pharmacology to minimize overdose risk
- In general, avoid IR combined with ER/LA opioids
- Methadone should not be the first choice for an ER/LA opioid
  - Only providers familiar with methadone's unique risk and who are prepared to educate and closely monitor their patients should consider prescribing it for pain.
- Only consider prescribing transdermal fentanyl if familiar with the dosing and absorption properties and prepared to educate patients about its use.

From the supporting text for Recommendation #4 from the *CDC Guideline for Prescribing Opioids for Chronic Pain*. Recommendation category: A; Evidence type: 4

WHY NOT START WITH LONG ACTING OPIOIDS?

- Dosage forms for ER/LA and transdermal fentanyl are too high for opioid naïve patients, especially elderly patients
- Most patients prefer taking opioids as needed and not round the clock
- Most patients find it easier to control their usage if they are taking opioid as needed and not round the clock
- Overall doses tend to be much lower if IR opioids are taken intermittently and no opioid is taken round the clock

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IS THERE A ROLE FOR LONG-ACTING OPIOIDS?

- Yes, but not at the start of treatment
- Yes, when treating end-of-life pain and some long-term pain conditions
- Yes, when the patient has difficulty controlling usage (e.g. has a substance use disorder)
- Never in conjunction with IR opioids except during palliative or end-of-life pain care

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WHY NOT METHADONE?

- Methadone has very complicated pharmacokinetics
- There are possible cardiac effects including QT prolongation
- There are many drug interactions
- Clearance is idiosyncratic, unpredictable and usually delayed
- Methadone is hard to get off
- Methadone should be reserved for specialists, cancer pain or addiction treatment

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WHY NOT TRANSDERMAL FENTANYL?

- Even the lowest dose is too high for start of therapy
- Absorption can be unreliable
- Heat (e.g. hot showers or baths) can release medication suddenly leading to overdose
- Cannot provide intermittent or as needed doses

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THE CHOICE FOR MS. BROWN

2.5 mg oxycodone (1/2 tablet) every 4 hours as needed

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When opioids are started, prescribe the lowest effective dose

5

- Use caution when prescribing opioids at any dosage
- Carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day
- 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)

AT FOLLOW-UP: MS. BROWN

- She returned to the clinic the following week and reported no improvement but tolerating opioid well and taking it 4 times daily
- Her dose was increased to try and get an effect
- After 2 further dose increases, she stabilized at 5 mg 4 hrly as needed, up to times daily

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Re-evaluate benefits and harms of opioids, and continue therapy only as a deliberate decision

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)

3 MONTH FOLLOW-UP: MS. BROWN

- At her 3 month follow up she came with her daughter who said her mother was drowsy all the time, and getting out and about even less that before

- The decision was made to taper her off the opioid

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HOW TO DO A STRAIGHTFORWARD TAPER

- Do not try to taper too quickly, even for someone who hasn't been on opioids for very long

- A reasonable regime would be:

10% reduction per week until off

- Warn about possible withdrawal symptoms and be prepared to treat withdrawal if it occurs

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CASE: MR. CASEY

- Mr. Casey is a 55 year-old self-employed truck driver who has had back pain for 7 years, starting with a back sprain injury
- He initially had a disc protrusion but that has resolved and he now has an MRI consistent with age and a normal exam
- He has been treated with opioids since the initial sprain injury
- His current regime is 30 mg oxycontin 3 times daily with 30 mg oxycodone 6 times daily as needed (MME 405)

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CASE OF MR. CASEY CONTINUED:

- He has tried other medical and non medical treatments but says none of them work
- He works night to try and make up for time lost during painful episodes
- He doesn't remember what it's like to sleep well
- His wife of 18 years recently asked him to leave because he is dragging down the family
- He is convinced that opioids are the only thing that enable to work

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WHAT ARE YOU GOING TO DO?

- His opioid dose is higher than currently recommended
- His function is poor and his life is in tatters
- He is almost certainly dependent on opioids
- It will be hard to persuade him to taper and hard to achieve a taper
- He will need a lot of ancillary help if he is going to improve

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Re-evaluate benefits and harms of opioids, and continue therapy only as a deliberate decision

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)

BASIC PRINCIPLES OF TAPERING IN A LONG-TERM OPIOID TREATED OR OPIOID DEPENDENT PATIENT

1. Spend time convincing the patient that tapering is the right thing to do (This may take more than one visit)

2. Taper slowly **e.g. 10% reduction per month**

3. Be prepared to stop and give it a rest for a while if it gets difficult

4. As long as the trend is downwards, the amount of time it takes doesn't matter

5. Never go up

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BASIC PRINCIPLES CONTINUED:

6. If surgery or trauma intervene, always go back to the pre-event dose ASAP

7. If it is necessary or desirable to do a rapid taper, buprenorphine is a useful tool

8. Buprenorphine is a useful tool anyway

   GET BUPRENORPHINE TRAINING

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TAPERING OPIOIDS

- **Work with patients to taper opioids down or off when**
  - no sustained clinically meaningful improvement in pain and function
  - opioid dosages >50 MME/day without evidence of benefit
  - concurrent benzodiazepines that can't be tapered off
  - patients request dosage reduction or discontinuation
  - patients experience overdose, other serious adverse events, warning signs.
- **Taper slowly enough to minimize opioid withdrawal**
  - A decrease of 10% per week is a reasonable starting point
- **Access appropriate expertise for tapering during pregnancy**
- **Optimize nonopioid pain management and psychosocial support**

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START LOW AND GO SLOW

- **Start with lowest effective dosage and increase by the smallest practical amount.**
- **If total opioid dosage ≥50 MME/day**
  - reassess pain, function, and treatment
  - increase frequency of follow-up; and
  - consider offering naloxone.
- **Avoid increasing opioid dosages to >90 MME/day.**
- **If escalating dosage requirements**
  - discuss other pain therapies with the patient
  - consider working with the patient to taper opioids down or off
  - consider consulting a pain specialist.

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IF PATIENT IS ALREADY RECEIVING A HIGH DOSAGE

- Offer established patients already taking ≥90 MME/day the opportunity to re-evaluate their continued use of high opioid dosages in light of recent evidence regarding the association of opioid dosage and overdose risk.
- For patients who agree to taper opioids to lower dosages, collaborate with the patient on a tapering plan.

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  - “Click” the Q&A tab at the top left of the webinar tool bar
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  - “Click” ask

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  - Press Star (*) 1 to enter the queue
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  - State your organization and then ask your question

Thank you for joining!

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When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

http://emergency.cdc.gov/coca/calls/2016/callinfo_081716.asp

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