Opioids and Chronic Non-Cancer Pain

Panakeia or Siren’s Song

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

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Please note: An erratum has been published for this report. To view the erratum, please click here.

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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 affected individuals who were involved in the development of the guideline.
Case 1

You are seeing one of your primary care patients for routine 3 month follow-up. He is 59 years old. His medical problems include well-compensated systolic heart failure due to ischemic heart disease (EF 45%), type II diabetes mellitus controlled on metformin plus glargine, and stage III chronic kidney disease. He has struggled to exercise in recent years due to severe post-traumatic osteoarthritis of his right knee for which he has tried physical therapy, scheduled acetaminophen, and corticosteroid injection – none of which provided lasting relief. He has also seen an orthopedist who tells him he should “wait a little longer before consider knee replacement.”
In clinic your patient shares, “You know doctor a few weeks ago I was doing some landscaping and had to move this big rock then that night I had terrible back pain. I would have come and seen you but it got better so quickly over the weekend. Anyway, that evening the pain was so bad that I took one of my wife’s pain pills left over from her surgery (hydrocodone 10 mg/acetaminophen 325mg) and it really helped my knee – I was even able to walk around a bit that evening without my usual limp.”
Case 1 continued . . .

He goes on to share, “We’ve been watching my granddaughter after school since her parents are working. She keeps asking me to take her down to the park but I have to tell her, ‘Pop can’t walk that far because of his knee.’ I really wish I could take her down to the park but my knee hurts every day.” Your patient has no history of substance abuse and no significant mental health problems.
In light of his goal, which would be the best option for ongoing management of his knee pain?

1. Controlled release morphine 15mg twice daily
2. Hydrocodone 5mg/acetaminophen 325mg three times daily as needed
3. Methadone 5mg three times daily as needed
4. Diclofenac 75mg twice daily as needed
General Principles in Managing Chronic Pain

1. Recognize CNCP is a chronic disease fundamentally different from acute pain or cancer pain. Take adequate time to develop a treatment plan.

2. Validate symptoms and empathize. Consider reversible physical causes. Adequately document details of CNCP.

3. Address the problem from biopsychosocial perspective recognizing that psychiatric co-morbidity is the rule. Avoid making a distinction between physical and psychological causes of pain.
General Principles in Managing Chronic Pain - Continued

4. Detailed assessment of functional status. Establish a time line for achieving specific, realistic goals.

5. Correct misconceptions if present. Educate about core strategy. Negotiate a treatment plan with regular clinical follow-up.

6. Incorporate non-pharmacological approaches to the treatment plan emphasizing regular physical activity.

7. Re-evaluate polypharmacy. Recommended evidenced-based pharmacotherapy.
Recognize CNCP is a chronic disease fundamentally different from acute pain or cancer pain. Take adequate time to develop/modify a treatment plan.
A 45 year old man comes to clinic complaining of low back pain. Over the last 6 months he has been seen 4 times in acute care settings for “flares of back pain” and each time he has gotten a prescription for hydrocodone/acetaminophen. The last time he got a prescription for 100 tablets of 10mg hydrocodone and he has been taking 4 tablets/day. This past week his wife lost her job which has been their principal source of income as he has struggled to hold down work because of his back problems. He is clearly distressed.
1. Prescribe hydrocodone/apap 10mg/325mg every 6 hours for breakthrough pain.

2. Prescribe gabapentin 300mg every 8 hours.

3. Prescribe extended release morphine 15mg every 12 hours.

4. Schedule short-term follow-up and refer to a counselor if patient amenable.

5. Prescribe fluoxetine 20mg qday.
Association of Number of Prescriptions for Controlled Substance with Risk of Unintentional Drug Overdose

*Pain Medicine* 2012; 13:87-95
The Cancer Pain Model

- Historical under-treatment leading to comprehensive patient education efforts.
- Patients have a “right to pain control”.
- Pain as “5th vital sign”.
- Clinical experience dominated by acute and advancing disease.
- Improvements in treating cancer pain extrapolated to chronic non-cancer pain in the outpatient setting.
What Is Chronic Pain?

• Complex condition with a myriad of causes and perpetuating factors including psychiatric co-morbidity.

• Little correlation between pain complaints, findings on physical exam, and results of diagnostic testing.

• A poorly understood, challenging to treat, chronic disease state.

• It is not acute pain or pain of malignancy!
How Is Chronic Non-Cancer Pain Different From Cancer Pain?

- Treatment horizon is much longer.
- Treatment goals different – need to target functional status rather than comfort only.
- Goal is not “no pain”.
- Chronic pain is stable – no need for rapid adjustments in treatment strategy.
- Limited or no role for breakthrough dosing of medications.
Correct misconceptions if present. Educate about core strategy. Negotiate a treatment plan with regular clinical follow-up.
Embarking on Treatment

• Reinforce that goal of complete resolution of pain unrealistic.
  - “We hope to get the pain out of the driver’s seat and into the back seat.”

• Like other chronic diseases requires multi-faceted approach.
  - lifestyle modification
  - emphasis on coping skills
  - non-pharmacological modalities
  - pharmacological modalities
  - specialty care

• Negotiate with patient elements to include.
  - “We can try that medication as long as you agree to walk most days of the week and keep a log of your activity.”
The challenge of opioids

“The undertreatment of pain in today’s society is not justified . . .”

“From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States.”
Risks of Opioids
Physiological Risks

- Acute
  - GI adverse effects
  - GU adverse effects
  - Falls
  - Respiratory Depression

- Chronic
  - Hormonal
    - Sexual Dysfunction
  - Hyperalgesia
Prevalence of Opioid AE’s in RCT’s

Adverse event (AE) rates with opioid and placebo in chronic non-malignant pain.

Arthritis Research & Therapy 2005; 7:R1046-R1051
Chronic Physiologic Effects

- Opioids inhibit the production of multiple hypothalamic, pituitary, gonadal, and adrenal hormones.
- A growing body of literature, based on animal and human studies, indicates that chronic exposure to opioids alters pain sensitivity.
Opioid-induced androgen deficiency

Substance Abuse and Opioids

• Prevalence of substance use disorders in studies has varied widely – 0% to 50%.
  – 801 adults, daily opioid therapy from primary care practices of 235 FPs and internists in 6 health care systems in Wisconsin. Point prevalence:
    • Any substance use disorder = 9.7%
    • Opioid use disorder = 3.8%

• Risk of de novo addiction is still felt to be relatively low.

*Journal of Pain 2007; 8:573-582*
Opioid Misuse

1 year incidence of opioid misuse in a cohort of patients enrolled within an academic GIM practice. (N=196)

<table>
<thead>
<tr>
<th>Opioid Misuse</th>
<th>Number (%)</th>
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<tbody>
<tr>
<td>Opioid Misuse</td>
<td>62 (31.6% of total)</td>
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<tr>
<td>Stimulants</td>
<td>25 (40.3)</td>
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<tr>
<td>Negative Urines</td>
<td>15 (24.2)</td>
</tr>
<tr>
<td>Multiple Prescribers</td>
<td>10 (16.1)</td>
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<tr>
<td>Inconsistent Urines</td>
<td>9 (14.5)</td>
</tr>
<tr>
<td>Prescription Forgery</td>
<td>2 (3.2)</td>
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<tr>
<td>Diversion</td>
<td>1 (1.6)</td>
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Table 5: Multivariate Analysis: Predictors of Opioid Misuse #

<table>
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<tr>
<th>Model</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age</td>
<td>0.95 (0.90 – 0.99)</td>
<td>0.027</td>
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<tr>
<td>Drug or DUI Conviction</td>
<td>2.58 (1.01 – 6.59)</td>
<td>0.030</td>
</tr>
<tr>
<td>History of Cocaine Abuse</td>
<td>4.30 (1.76 – 10.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>History of Ethanol Abuse</td>
<td>2.60 (1.12 – 6.26)</td>
<td>0.048</td>
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BMC Health Services Research 2006; 6:46
Association of Mean Daily Dosage of Opioid Analgesics With Risk of Unintentional Opioid-Related Overdose Death

ARI = 0.15%
NNH = 666

ARI = 0.25%
NNH = 400

Figure 3. Association of Mean Daily Dosage of Opioid Analgesics With Risk of Unintentional Opioid-Related Overdose Death

Other Dose Related AE’s

- Opioid Use Disorder
- Depression
- Fracture
- MVA
- Suicide

Benefits of Opioids
Evidence for Use of Opioids

- Anecdotal evidence emerged in the 1980’s.
- By 1992 eight surveys described a total of 642 patients. Efficacy was “good” in greater than 75% of patients. Doses of opioids were generally low.
- Now approximately 25 RCTs.
1. Around 1000 highly selected subjects excluding any with history of problems with drug/alcohol abuse.
2. Studies done mostly in specialty clinics further biasing the population and limiting generalizability.
3. Average duration of these studies is just over 6 weeks. None > 1 year.
4. Results typically show decreases in pain on visual analog scales at the cost of significant side effects. Withdraw rates in treatment arms are high.
5. Average reduction in pain is about 30%.
6. Limited improvement in measures of functional status within certain domains but results are inconsistent.
Impact of Opioids in Danish Population

Fig. 2. SF-36 scores in the various investigation groups. PG, pain group; CG, control group. BP, bodily pain; GH, general health; MH, mental health; PF, physical function; RE, role emotional; RP, role physical; SF, social function; VT, vitality.

Is it possible to effectively use opioids for chronic pain in the primary care clinic?

Yes, in some cases.

Probably.
“Chronic opioid therapy can be an effective therapy for carefully selected and monitored patients with chronic non-cancer pain. However, opioids are also associated with potentially serious harms, including opioid-related adverse effects and outcomes related to the abuse potential of opioids.”
Balancing Risks and Benefits
Patient Selection

- Realistic expectations of patient
- No red flags for opioid misuse
- Clear goals of functional improvement
- Adequately treated depression
- Willingness to engage in all facets of treatment plan, e.g. regular exercise
The most overlooked aspect of chronic pain management in primary care setting is need to establish concrete metric of functional improvement.

“What were you hoping to get done today that your pain keeps you from doing?”
Long Range Treatment Goals

• Improve functional role.
• Enhance interpersonal relationships and psychological integrity.
• Increase physical activity.
• Decrease reliance on health care system.
• Improve quality of life.
Depression and Chronic Pain

• Numerous studies have shown, “strong associations between chronic pain and psychiatric comorbidity”.

• Depression affects clinical presentation and treatment response.

• Depression is undertreated.

• Co-existing pain and depression may be a final common presentation reached by a number of pathways – reciprocal relationship.
Exercise and Chronic Pain

- All patients with chronic pain should try to do some regular exercise.
- Consider PT referral to help set up a plan.
- If the patient says, “I can’t exercise because of my pain” say:
  - “Although exercise may hurt at first, there’s a good chance that by starting with a little daily exercise and slowly increasing the amount you do, your body will get stronger and you’ll be better able to cope with your pain.”
Patients for opioid trial

1. Pain complaint is well-defined and regional (e.g. spinal stenosis).
2. No history of substance abuse including alcohol.
3. Depression is adequately treated.
4. Engaged in regular physical activity.
5. Failed all other treatment strategies.
Red Flags - poor candidates for starting or continuing opioids

- History of substance abuse.
- Vague pain history or pain “all over”.
- Polypharmacy with multiple other medications with CNS effects.
- History of frequent requests for early refills or dose increases.
- High doses of opioids (above 180mg morphine or mophine equivalent).
- History of medications lost or stolen more than once.
- Risks of harm (e.g. sleep apnea, CKD)
Prior to Starting Opioids

- Opioid use agreement
- PMP/MPDR
- Urine Drug Screen
Prescription Monitoring Program (PMP)

Prescription Monitoring Program

Legislation in 2007 gave the Department of Health authority to create a Prescription Monitoring Program (PMP). The program's purpose is to improve patient care and stop prescription drug misuse by collecting all the records for Schedule II, III, IV and V drugs. This information is then made available to medical providers and pharmacists as a tool in patient care.

The state law that created the program is RCW 70.225.

The program is a patient safety tool. Practitioners have access to the information before they prescribe or dispense drugs.

This can help prevent overdoses and misuse, and promote referrals for pain management and treatment of addiction.

The program rules took effect August 27, 2011. The program started date collection from all dispensers October 7, 2011.

See the PMP Dispensers information webpage for information on data submission. Providers may register online.
Patient Care Agreements

- Consensus guidelines detail the necessity of informed consent.
- Consent can be accomplished using written agreement describing conditions under which opioids are prescribed.
- “Contracts are widely used in chronic opioid therapy.” Efficacy not established though has become standard of care.

- Most important points to focus on:
  - No early refills.
  - No pain medications from other clinics or providers.
  - No refills by phone.
  - Urine toxicology.
  - Adherence to schedule of dosing.
  - Change in pain intensity requires re-evaluation.
Urine Toxicology Pearls

• Monitoring for illicit drug use
  – Host of drugs can cause false positive amphetamines

• Adherence testing
  – Oxycodone not detected on many routine toxicology screens
  – Hydrocodone metabolized to hydromorphone

• Discrepant result ≠ discharge from clinic
Using Opioids

• Start low dose, short-acting opioids only.

• Let patients know that this is a test and arrange for early follow-up for dose titration.

• Explicitly define a ceiling dose at outset of treatment. Avoid high-dose opioid therapy.

• Anticipate monthly follow-up visits.

• Document functional status and/or quality of life goals.

• NO benzodiazepines

• Consider prescribing naloxone
1 month follow-up

• An assessment period of 1 month may be sufficient to determine responsiveness to opioid therapy.

• Lack of response at 1 month strongly predicts subsequent non-response.

• 30% reduction in PEG?
  - average pain intensity (P)
  - interference with enjoyment of life (E)
  - interference with general activity (G)
3 Month Reassessmeent

- Does COT continue to meet functional treatment goals?
- Has pt experienced AEs?
- Any signs of opioid use disorder?
- Do benefits still outweigh risks?
- Can opioid dosage be reduced/discontinued?
Case 1 revisited . . .

• 59 yo with well-compensated systolic HF due to ischemic heart disease (EF 45%), type II DM, and stage III CKD
• Severe post-traumatic OA of his knee - he has tried PT, acetaminophen, and corticosteroid injection - none of which provided relief
• Orthopedist who tells him he should “wait a little longer before consider knee replacement”
• Hydrocodone helped knee pain
• Wishes he could take granddaughter to the park but knee prevents that . . .
• Has no history of substance abuse and no significant mental health problems
A 42 year old male patient with a personal history of alcohol abuse and chronic neck, shoulder and back pain following a lifting injury at work is transferring his care but arrives late without any medical records. He reports that he takes 10 - 15 tablets of 5mg oxycodone each day. He will be out of oxycodone tomorrow and requests that you refill his medication for one month as he is leaving town to visit his family for “a few weeks”. The plan you offer is:
a. Switch to oxycodone SR 30mg every 12 hours.
b. Refer the patient to a pain clinic.
c. Refill the oxycodone and start venlafaxine.
d. Avoid prescribing opioids at this visit, offer clonidine, and ask patient to facilitate transfer of medical records.
e. Tell the patient he clearly has a problem with drug abuse.
New Patients Already On Opioids

• If uncertain if good candidate - resist pressure to prescribe on 1st visit.

• Contact past providers and obtain outside records - confirm past doses, treatment history.

• Patients often switch providers due to non-adherence with care plans.

• Remember treatment of chronic pain is not an emergency - opioid withdrawal is not life threatening.
- It is OK to Say “No” -

• Many patients with chronic pain are poor candidates for chronic opioids.

• If you say “No” you can offer:
  - exercise program.
  - counseling to work on coping.
  - treating other medical problems such as depression.
  - using NSAID’s, acetaminophen, TCA’s, anti-convulsants.
Discontinuing Opioids

• You are not terminating care. You are only discontinuing opioids.
• Write out a schedule over 14 - 28 days based on how high a dose the patient is on.
• Divide the schedule into 3 parts and decrease the dose as follows:
  - 1st step = 75%
  - 2nd step = 50%
  - 3rd step = 25%
  - 4th step = off
• Patients starting at very high doses lengthen the final stages of the taper. For example, divide a 28 day period into 4 parts, and decrease as follows
  - 1st step = 75%
  - 2nd step = 50%
  - 3rd step = 25%
  - 4th step = 15%
  - 5th step off
### More on Opioid Tapers

- Voluntary participation and slow tapers
- Multidisciplinary and multimodal care emphasizing non-pharmacologic and self-management strategies
- Close follow-up
- Pain severity, function, and quality of life *may* improve after opioid tapering


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#### Summary of Findings

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<tr>
<th>Outcome</th>
<th>Studies, n</th>
<th>Participants, n</th>
<th>Study Design</th>
<th>Study Quality</th>
<th>Results</th>
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<tr>
<td>Effectiveness of strategies to reduce or discontinue LTOT</td>
<td>67</td>
<td>12,546</td>
<td>RCT: 11</td>
<td>Good: 3</td>
<td>Multiple intervention types examined, with heterogeneity of patient populations, study completion, and rates of opioid reduction and discontinuation</td>
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<tr>
<td>Effect of dose reduction or discontinuation on patient outcomes</td>
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<td></td>
<td>CO: 8</td>
<td>Fair: 13</td>
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<tr>
<td>Pain severity</td>
<td>36</td>
<td>7,674</td>
<td>UO: 48</td>
<td>Poor: 51</td>
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<tr>
<td>Function</td>
<td>17</td>
<td>4,809</td>
<td>RCT: 4</td>
<td>Good: 0</td>
<td>8 of 8 fair-quality studies reported improved pain</td>
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<td></td>
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<td></td>
<td>CO: 6</td>
<td>Fair: 8</td>
<td>21 of 28 poor-quality studies reported improved pain, 4 reported no change, and 3 reported worse pain</td>
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<tr>
<td></td>
<td></td>
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<td>UO: 26</td>
<td>Poor: 28</td>
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<tr>
<td>QOL</td>
<td>12</td>
<td>2,880</td>
<td>RCT: 1</td>
<td>Good: 0</td>
<td>3 of 3 fair-quality studies reported improved QOL</td>
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<td></td>
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<td>CO: 0</td>
<td>Fair: 3</td>
<td>4 of 9 poor-quality studies reported improved QOL, 4 reported no change, and 1 reported worse QOL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>UO: 11</td>
<td>Poor: 9</td>
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</table>

Discontinuing opioids without taper

• Clonidine 0.1 mg po bid for 48 hours.
  - Dispense 4 tablets.

• Clonidine transdermal patch TTS-2 (0.2 mg/24 hr) q 7 days.
  - May repeat if symptoms persist at end of 7 days.
  - Dispense 2-4 patches.

• Patient should start with both clonidine tabs and patch on day one as it takes 24-48 hrs for the patch to become effective.
Key Points

• CNMP is best understood as a chronic disease dissimilar to cancer pain.

• CNMP is never an emergency.

• Therapy should focus on improving quality of life by improving function and decreasing pain but complete resolution of the pain is unrealistic.

• The mainstay of non-pharmacological treatment is physical exercise.

• Depression is common. Data supports the use of medication in almost all patients even if overt depression is not obvious.
• Other therapy includes anticonvulsants and topical agents.

• The data supporting opioid use are severely limited by duration of studies. Chronic opioid analgesics may benefit a small subset of patients. Use short-acting opioids at low dose.

• The risk of adverse events is substantial. Data strongly suggests significant safety risks at MED > 100 mg/day.

• Widespread use of opioids in the primary care setting is not indicated. It is okay to say “no” – however don’t abandon patients.
Comments and Questions