Best Practices in Prescribing Opioids for Chronic Non-cancer Pain

Opioid Rx has changed over time

- Pre-1995: parsimonious with Rx opioids in US
- 1995-2009: Oxycontin, 5th VS, pt advocacy groups

Causes of Accidental Death in US

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<table>
<thead>
<tr>
<th>Year</th>
<th>Drug-poisoning</th>
<th>Poisoning</th>
<th>Motor vehicle traffic</th>
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<tbody>
<tr>
<td>1980</td>
<td>20</td>
<td>10</td>
<td>20</td>
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<tr>
<td>1990</td>
<td>25</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>2000</td>
<td>30</td>
<td>20</td>
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<td>2010</td>
<td>35</td>
<td>25</td>
<td>25</td>
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Disclosures

- No financial disclosures to report
Opioid Rx has changed over time

- Pre 1995: parsimonious with opioids in US
- 1995-2009: Oxycontin, 5th VS, pt advocacy groups
- 2010-now: dose limits, payor/pharm restrictions

Outline

- Benefits of chronic opioid therapy (a little)
- Risks of chronic opioid therapy (a little)
- Strategies to mitigate risks of chronic opioid therapy

Our case: 54 yo F chronic low back pain

54 yo F presents for primary care after her previous PCP left the clinic where you work.
PMH: HTN, lumbago (Xray shows DJD
Meds:
HCTZ 25 mg qday
Hydrocodone 10/325 mg tid PRN #90 per month
Patient’s insurance plan has introduced incentive payments for having patients on opioids for CNCP re-sign “pain contracts” annually.

54 yo F LBP: “Pain Contracts”?

- Patient’s insurance plan has introduced incentive payments for having patients on opioids for CNCP re-sign “pain contracts” annually.

What effect do “pain contracts” have on patients’ risky behavior while on chronic opioid therapy?

a) None documented.
b) Increased diversion, since the document gives patients the idea to give their friends meds
c) Decreased overuse because patients who are addicted only need the fear of adverse consequences to prevent overuse.
d) Modest decrease in aggregate risky behavior observed in some clinic populations.
54 yo F chronic LBP: “Pain Contracts”?

Patient provider agreements have modest effect on rates of opioid misuse from clinic perspective*

- 7-23% reduction in 4 observational studies with comp
- 30-43% misuse AFTER agreements

*Starrels, 2010

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**The Risk-Benefit Approach**

- Set expectations for benefits
- Outline the risks
- Describe a process for management

**Building a Patient Provider Agreement**

See the UCSF Pain Management Committee’s model Patient-Provider agreement at [http://pain.ucsf.edu/docs/UCSF_Patient_Provider_Agreement_on_Opioids.pdf](http://pain.ucsf.edu/docs/UCSF_Patient_Provider_Agreement_on_Opioids.pdf)
46 yo M LBP: benefits of high doses

46 yo M on disability for chronic low back pain managed with opioids for >10 years. Currently on sustained release oxycodone 80 mg bid and oxycodone 30 mg tid “PRN” advises MA that his pain is 9/10. He took his medication this morning as prescribed.

46 yo M LBP: benefits of high doses

Which is true of opioids for CNCP at or above the equivalent of 200 mg morphine daily (MED)?

a) Case series suggest that MED > 200 mg reduce pain by 50% in ~50% of patients
b) Data supporting the benefits of MED > 200 mg in CNCP are lacking
c) Patients at very high doses have reported worse pain control
d) Both B and C

The benefits of opioids for CNCP

Cochrane: n>4800 show reduction in pain*
50-66% report reducing pain scores by at least half**

Caveats
Max dose 180 mg MED
Few studies longer than 6 months.

The “PEG” tracks benefits of opioids

On a scale of 0-10, over the last week:

What has your average pain been? (0-10)

How much has your pain interfered with your enjoyment of life? (0-10)

How much has your pain interfered with your general activity? (0-10)

Krebs, 2009

*Noble 2010
**Chou 2009; Reuben 2015
Complications of chronic opioids

- Constipation
- Sedation\(^1,2\)
- Opioid overdose\(^2\)
- Death from overdose\(^1,2\)
- Aberrant use, addiction\(^2\)
- ED visits\(^2\)
- Depression\(^2\)
- Psychosocial problems\(^2\)

Complications of chronic opioids

- Falls and fractures\(^1,2\)
- LESS likely to return to work
- Immune dysfunction\(^2\)
- Decreased GNRH, low libido\(^2\)
- Hyperalgesia\(^2\)
- Difficult interactions with the care providers\(^2\)
- Mixing with other sedating drugs associated with increased risk
- Higher doses associated with increased risk

Building a Patient-Provider Agreement

- Purpose: The purpose of this agreement is to protect your access to controlled substances and to protect our ability to prescribe for you.
  1. Your provider has determined that you may be a candidate for opioid therapy because of their potential benefits to decrease pain and/or improve function.
  1. There are several risks which may limit or exit the continued use of opioids. These risks are elevated when combined with alcohol or other drugs.

What is high dose of an opioid?

Which of the following regimens describes the highest dose?

- a) Fentanyl 50 mcg/h td + oxycodone 10 mg tid
- b) MS-Contin 30 mg tid + MS-IR 15 mg tid
- c) Oxycodone 30 mg tid
- d) Extended-release hydrocodone 50 mg bid + hydrocodone/APAP 10/325 mg tid
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What is a high dose of an opioid?

- MSO4 50 mg is about the same as:
  - Codeine 60 mg q4h
  - Oxycodone/APAP 10/325 tid
  - Hydrocodone/APAP 10/500 5 times a day
  - Methadone 5 mg tid
  - Hydromorphone 4 mg tid
  - Oxymorphone ER 7.5 mg bid
  - Fentanyl 12 mcg/hr patch

Who is at risk?

Which of the following patients is most likely to display “aberrant behavior,” divert or misuse prescription opioid medications?

a) 42 yo white M with chronic LBP
b) 35 yo black F with SLE
c) 64 yo Latino F with h/o AUD in remission knee OA
d) More information would help predict
e) Impossible to predict

### Daily Opioid dose (MSO4 eq) | Hazard Ratio for OD (95% CI)
---|---
None | 0.31 (0.12-0.8)
1 to <20 mg | 1
20 to <50 mg | 1.44 (0.57-3.62)
50 to <100 mg | 3.73 (1.47-9.3)
100+ | 8.87 (3.99-19.72)
Any dose | 5.16 (2.14-12.48)

Dunn et al. 2010 Annals
Risk prediction models

Many models attempt to predict aberrant behaviors
a) ORT, SOAPP

“no model adequately predicts ...” (Chou et al, 2009)

Evidence suggests many adverse consequences in “low risk” patients

46 yo F chronic pain: urine drug testing

46 yo F presents for med refill. She is on MS-Contin 30 tid and oxycodone 30 mg bid PRN for fibromyalgia. Her insurance plan has introduced incentive payments for urine drug testing patients on opioids for CNCP

What is the direction and magnitude of the effect of urine drug testing on opioid misuse by patients being treated for CNCP?

a) 15 % increase in misuse
b) 50% decrease in misuse
c) 15% decrease in misuse
d) There is no evidence that urine drug testing affects the rate of opioid misuse in these patients

Urine Drug Testing in COT

Recommended by 9 of 10 guidelines (Nuckols et al., 2014)

Disparities in which patients are tested demonstrated in Philadelphia and SF (Becker, 2010; Bauer, pers comm)
Urine Drug Testing in COT

- Test everyone, with frequency standardized according to risk.
  - 200 mg+ or recent aberrancy: monthly
  - 50-199 mg: quarterly
  - 20-49 mg: annually

But which urine drug tests should I order?

"Adherence" labs
- Opiate tests: please order GC/MS
- Oxycodone
- Methadone

"Abuse" labs
- Amphetamine
- Benzodiazepine
- Cocaine
- ?other

Don’t order a simple “U tox”

Opiate “screen” may be completely negative in patients taking these drugs:

- Codeine
- Morphine
- Hydrocodone
- Hydromorphone
- Oxycodone
- Methadone
- Fentanyl
Don’t order a simple “U tox”

Opiate “screen” should be completely **negative** in patients taking only these medications:

- Codeine
- Heroin
- Hydrocodone
- Hydromorphone
- Opiates
- Methadone
- Morphine
- Fentanyl

Don’t order a simple “U tox”

Opiate “screen” may be **positive** in patients taking these drugs:

- Codeine
- Heroin
- Hydrocodone
- Hydromorphone
- Oxycodone
- Methadone
- Morphine
- Fentanyl

“+opiate” can mean a lot of things

![Diagram of opioids](http://labmed.ucsf.edu/labmanual/mftlng-mtzn/test/test-index.html)
"+amphetamine" can mean a lot of things

"+benzodiazepine" can mean a lot of things

"+cocaine means only one thing"

- Cocaine screen tests for cocaine metabolite (benzoylecgonine), which is unique to cocaine metabolism

Urine Drug Testing in COT, bottom line

#1: Test everyone, with frequency standardized according to risk.
- 200 mg+ or recent aberrancy: monthly
- 50-199 mg: quarterly
- 20-49 mg: annually

#2: Order the right tests, and get to know your lab medicine colleagues
46 yo F: urine drug testing

- Results of patient's urine toxicology test come back:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>negative</td>
</tr>
<tr>
<td>Morphine</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>negative</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>negative</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>negative</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>negative</td>
</tr>
<tr>
<td>Cocaine</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>POSITIVE</td>
</tr>
</tbody>
</table>

46 yo F fibromyalgia and cocaine use

- Patient denies cocaine use at follow-up visit
- PCP advises that ongoing use of cocaine will result in discontinuation of therapy over time.

46 yo F fibromyalgia, cocaine use: taper?

- Patient denies cocaine use at follow-up visit
- PCP advises that ongoing use of cocaine will result in discontinuation of therapy over time.

- Which statement about tapering opioids most accurately reflects the evidence?
  a) Patients using stimulants must be tapered rapidly due to risk of overdose
  b) Opiate withdrawal is non-fatal, rapid taper is safe
  c) Patients who are prescribed opioids for treatment of opiate use disorder are much more likely to relapse when their dose is tapered
  d) None of the above

Tapering Opioids for CNCP: Scylla and Charybdis

<table>
<thead>
<tr>
<th>Tapering is Risky</th>
<th>Maintenance is risky</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tapering MMTP and buprenorphine = relapse (Fiellin 2014)</td>
<td>Active SUD = higher risk of OD, death</td>
</tr>
<tr>
<td>States with dose limitations = increased heroin, treatment for addiction</td>
<td>Higher dose = higher rates of complication</td>
</tr>
</tbody>
</table>
Tapering opioids
- Taper high risk patients very slowly.
- Offer options and let patient choose
  - Drop short-acting daily dose by a pill
  - Convert to mostly short-acting
  - “rotate” to other opioid

Tapering opioids: an example

<table>
<thead>
<tr>
<th>Week</th>
<th>(baseline)</th>
<th>690 mg tid</th>
<th>30 mg qid</th>
<th>200 mg bid</th>
<th>15 mg qid</th>
<th>% decr</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>670 mg bid</td>
<td>18 x 35 mg</td>
<td>28</td>
<td>252</td>
<td>2.0%</td>
<td></td>
<td>0.0%</td>
</tr>
<tr>
<td>4</td>
<td>655 mg bid</td>
<td>17 x 35 mg</td>
<td>28</td>
<td>238</td>
<td>2.3%</td>
<td></td>
<td>0.0%</td>
</tr>
<tr>
<td>6</td>
<td>642 mg bid</td>
<td>16 x 35 mg</td>
<td>28</td>
<td>224</td>
<td>2.3%</td>
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<td>0.0%</td>
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<tr>
<td>8</td>
<td>625 mg bid</td>
<td>15 x 35 mg</td>
<td>28</td>
<td>210</td>
<td>2.4%</td>
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Reducing risk for all patients

Which of the following interventions has been demonstrated to reduce rates of overdose in patients prescribed opioids for CNCP?

a) Implementing pill count visits
b) Random urine toxicology testing
c) Tapering them to lower doses
d) Prescription of naloxone

Reducing risk for all patients

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d) Prescription of naloxone
Reducing risk for all patients

- Reduction in OD among heroin users since late 90’s
- Project Lazarus in NC showed decrease in opioid OD from 47 to 29 per 100,000*

*Albert et al., Pain Med 2011

Checklist for “new” patient

- Diagnosis appropriate for opioids
- Screen for psych dz, incl substance use
- ORT (or other)
- Document specific functional goal
- Make patient aware of risks of opioids
- U tox
- CURES report
- ROI/consent to discuss with previous/current providers
- Consent to discuss with one family member/friend
- Discuss safe storage
- Patient-Provider Agreement/Informed consent
- Rx naloxone and provide teaching to patient/caregiver

http://prescribetoprevent.org/prescribers/palliative/


http://harmreduction.org/shop
## Moving toward improved opioid stewardship

**DURING CHRONIC OPIOID THERAPY:**
- 28 day supply
- No early refills
- Monitor benefits and harms
- Monitor adherence
- Consider ceiling dose

**STOP ANYTIME RISKS > BENEFITS!**

## Summary

- Opioids have limited benefit in CNCP
  - Some patients do well
- Chronic opioids have risks that increase with dose
- Informed consent >> “pain contracts”
- Toxicology testing is tricky but useful
- Tapering is tricky, even when necessary
- Naloxone saves lives with little to no risk