Complex chronic pain, opioid prescribing and opioid use disorder: Pitfalls, pearls and new directions

William C. Becker, MD
Assistant Professor, General Internal Medicine
VA Connecticut Healthcare System
Yale University School of Medicine

June 23, 2017

The PRIME Center
Pain Research, Informatics, Medical comorbidities, and Education
Enhancing Pain Care for Veterans

I have no conflicts of interest related to the content of this presentation.

Learning objectives

- Appreciate chronic pain and opioid use disorder as distinct entities that commonly co-occur
- Understand complexities of and tips for making an opioid use disorder diagnosis in patients on long-term opioid therapy for chronic pain
- Learn about potential roles for buprenorphine in managing complex chronic pain

Poll Question

In a given month, I write approximately this number of prescriptions for long-term opioid therapy:

A) 0, I'm not a prescriber
B) 0, I'm a prescriber but I don't prescribe
C) a handful (1-5)
D) 6-20
E) > 20

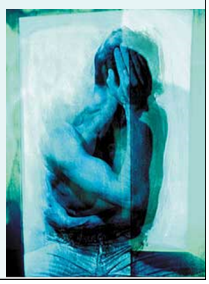
Poll Question

Complex chronic pain and related opioid issues are:

A) The most challenging thing I treat clinically
B) Among the most challenging things I treat
C) Sometimes challenging, sometimes not
D) Not particularly challenging
E) Downright easy
F) N/A; I'm not a clinician

Chronic pain: ubiquitous and costly

- Point prevalence: 25% in U.S. adults; 10% with disabling chronic pain that limits work and family activity
- Second most common reason for outpatient visits
- Annual national economic cost estimated up to $635 billion



Chronic pain: neuronal plasticity and central sensitization

Neuronal plasticity

Peripheral nerve injury → recruitment of macrophages and glial cells → dysregulated nerve regeneration of c-fibers

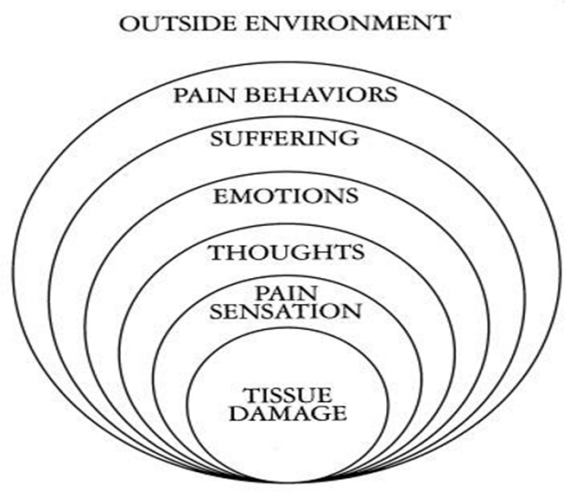
⇩

Central sensitization

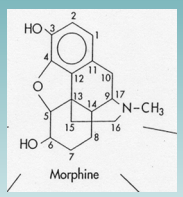
Excess of c-fibers in dorsal horn → lowered pain thresholds

Woolf CJ. Pain 2011

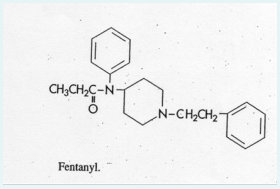
Complexity of chronic pain



Deardorff, WW. APA 2008.



Opioid analgesics



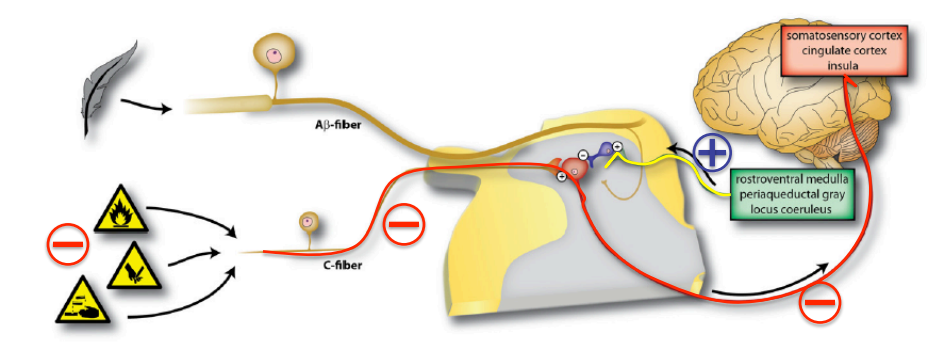
Morphine equivalent dose

- Method of standardizing potency across various opioid compounds
- Based on equianalgesic tables from dose ranging studies
- Example:
  20 mg oxycodone TID
  =
  90 mg morphine
  equivalent daily dose

Equianalgesic dose (MG)	Opioid (oral)
30	Morphine
7.5	Hydromorphone
20	Oxycodone
30	Hydrocodone

http://www.agencymeddirectors.wa.gov/Calculator/DoseCalculator.htm

Activation of mu receptors



Sequelae of long-term opioids

Tolerance → higher doses required to achieve same analgesic effect over time

+

Withdrawal → characteristic symptoms upon abrupt cessation or lowering of opioid dose

---

"PHYSIOLOGIC DEPENDENCE"

Opioid-induced hyperalgesia → paradoxical worsening of pain with higher doses

Opioid use disorder (DSM-5)

Physiologic sequelae

- Tolerance
- Withdrawal
- Opioid craving

Loss of control

- Greater amounts of use or longer period of use than intended
- Persistent desire but unsuccessful efforts to cut down
- Inordinate amount of time obtaining, using, or recovering

Adverse consequences

Summary of 5 criteria:

- Important social, occupational or recreational activities given up or reduced due to opioid use or recurrent opioid use despite physical or psychological problems caused or worsened by use

DSM-5 criteria vs. pain literature guided criteria

DSM-5	Pain literature
• Failure to fulfill major roles	• Multiple prescribers
• Use in physically hazardous situations	• Frequent ED visits
• Persistent interpersonal problems	• Multiple drug "allergies
• Unsuccessful efforts to cut down	• Running out of meds early
• Great deal of time obtaining	• Frequent phone calls to clinic
• Giving up activities	• Prescription losses
• Craving	• Anger/temper with clinicians/staff
• Continued use despite knowledge of harm	

Adapted from Ballantyne & Stannard PAIN: CLINICAL UPDATES • DECEMBER 2013

False dichotomy

~~*Is this pain or is this opioid use disorder? (..if it's "real pain" and not addiction, opioids are probably indicated)*~~

- The patient *HAS* pain.
  - The patient may also have opioid use disorder.
- What is the optimal treatment plan for the pain?
  - What is the optimal treatment plan for pain if opioid use disorder is co-occurring?

Other important toxicities

- Constipation
- Itching
- Nausea/vomiting
- Hypogonadism
- Opioid-induced hyperalgesia
- Sedation
- Impaired cognition
- Falls/motor vehicle accidents
- Blunted respiratory drive
- ***Non-fatal and fatal overdose***

Odds of overdose by increasing dose

	Dunn	Gomes	Bohnert
Dose* (mg/day)	**HR (95% CI)**	**OR (95% CI)**	**HR (95% CI)**
1-<20	1.00 (REF)	1.00 (REF)	1.00 (REF)
20-<50	1.2 (0.4-3.6)	1.3 (0.9-1.8)	**1.9 (1.3-2.7)**
50-<100	**3.1 (1.0-9.5)**	**1.9 (1.3-2.9)**	**4.6 (3.2-6.7)**
≥100 or 100-199	**11.2 (4.8-26.0)**	**2.0 (1.3-3.2)**	**7.2 (4.9-10.7)**
≥200		**2.9 (1.8-4.6)**	

*morphine equivalent

Dunn et al. Annals IM 2010; Gomes et al. Archives IM 2011; Bohnert et al. JAMA 2011

Evidence for long-term use

- "Despite the identification of 26 treatment groups with 4768 participants, the evidence regarding the effectiveness of long-term opioid therapy in chronic non-cancer pain is too sparse to draw firm conclusions..."
- Medium effect size in study completers, but they were small proportion of sample
- No long-term studies included functional outcomes

Noble, M. The Cochrane Collaboration. 2010

What are we treating?

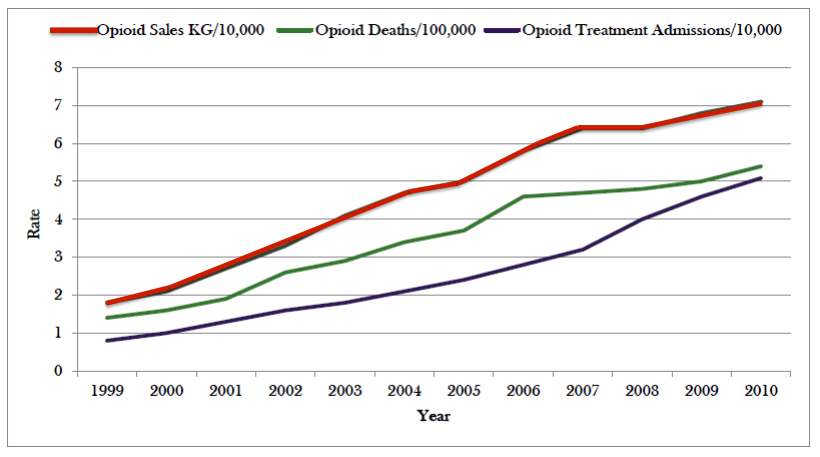
- The people who "respond" to opioid treatment/stay on opioids long term may be actually medicating emotional distress: "Chemical coping"
- Mental health diagnoses increase risk of overdose and other harms.
- Some experts believe opioid treatment interferes with effectiveness of actual evidence-based MH treatment.

Sullivan and Ballantyne. Arch IM, 2012.

Opioids for chronic pain: important limitations

- Central sensitization—driver of much of chronic pain--may not be responsive to long-term opioids.
- Opioids may initially "work" but the body adapts to them, necessitating higher doses.
- Higher doses long-term → increased risk of toxicity/ adverse effects, both acute and chronic.
- Are "responders" mostly benefitting from treatment of emotional distress, for which better/safer treatments exist?

Lockstep trends in prescribing and harm



http://www.nsc.org/RxDrugOverdoseDocuments/evidence-summary-opioid-sales-use-and-increase-in-opioid-overdose.pdf

CDC Guideline for Prescribing Opioids for Chronic Pain


Special Communication

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

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

- Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

- 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.

Assessing Risk and Addressing Harms of Opioid Use

- Clinicians should offer or arrange evidence-based treatment for patients with opioid use disorder when that diagnosis is evident.

Case

Mr. M is 58-year-old man with chronic low back pain who presents to transfer care; pain specialist will no longer see him because he lost private insurance**.**

CC: "*I'm in a rut*."

PMHx: lumbar spondylosis, PTSD

Pertinent data:

–Morphine SA 60 mg TID, oxycodone IR 10 mg q6 hours;

–Opioid therapy started 2004 at 30 mg MEDD→240 mg MEDD

–Lorazepam 0.5 mg TID

–Sedentary but intermittent high intensity activity

ROS: Daily moderate-severe pain interfering with ADLs, nightmares, snoring, erectile dysfunction, feels blah most days

Opioid use disorder (DSM-5)

Physiologic sequelae

- Tolerance
- Withdrawal
- Opioid craving

Loss of control

- Greater amounts of use or longer period of use than intended
- Repeated unsuccessful efforts to cut down
- Inordinate amount of time obtaining, using, or recovering

Adverse consequences

Summary of 5 criteria:

- Important social, occupational or recreational activities given up or reduced due to opioid use or recurrent opioid use despite physical or psychological problems caused or worsened by use

Physiologic dependence

Problem list

Poorly controlled chronic pain with pervasive pain-related functional interference → BENEFIT is absent

Poorly controlled PTSD

Sleep-disordered breathing

Erectile dysfunction

Elevated risk of overdose death (240 mg MEDD) and physiologic dependence

→ HARM/RISK are prohibitive

Options

A) Opioids don't work for chronic pain and I am not comfortable writing those doses; you'll need to ask someone else
B) There is no imminent safety issue; continue at current dose for now but will start taper with 2nd prescription
C) It's clear that harm is already outweighing benefit. I can work with you to get you to a safer dose (or off altogether), but that will need to start with the first prescription I write.
D) Arrange inpatient detoxification

Framing the low benefit conversation

- Empathy
- Concern
- Shared responsibility
- Optimism

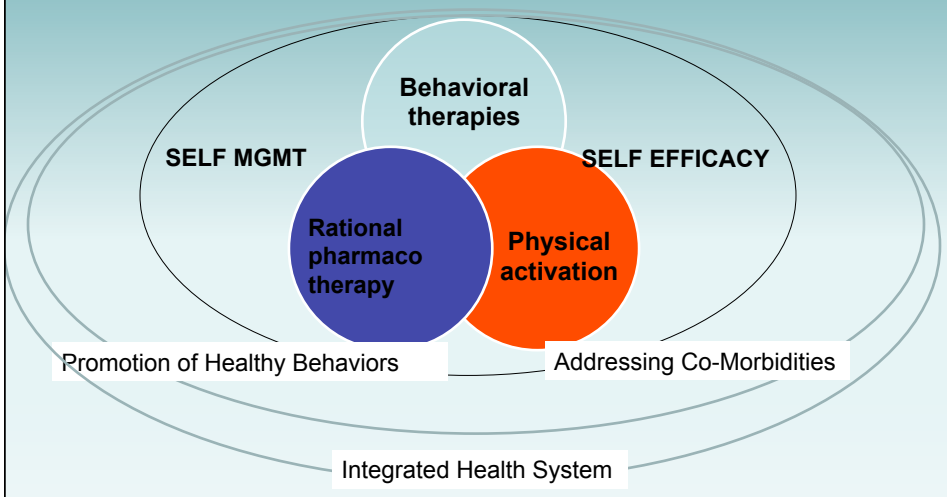
Tapering/discontinuing in low benefit

- Very little evidence to guide
- Patients report increased willingness when offered empathy, support, reassurance
- Anecdotal evidence:
  - Start with long-acting: decrease in 5-10% of overall dose *rarely* noticeable
  - Success in each step down breeds success
  - Offer pt option to "pause" PRN
- See Dr. Joseph Frank's CSAM webinar
  https://player.vimeo.com/video/215259225

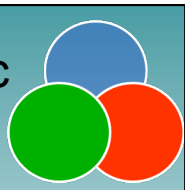
Plan for this patient…

- Optimize pain care
  - Behavioral therapies
  - Physical activation
  - Rational non-opioid pharmacotherapy
- Optimize opioid management
  - Decrease dose
  - Therapeutic monitoring: Treatment agreement, UDTs, PDMP checks

Evidence-based high value chronic pain care



Evidence-based non-pharmacologic treatments for chronic pain



Physical activation

- Structured exercise
- Physical therapy
- Yoga
- Tai Chi
- Aqua-therapy

Behavioral treatments

- Cognitive behavioral therapy
- Mindfulness based stress reduction

Other techniques

- Chiropractic
- Acupuncture
- Trigger point injections
- Intra-articular injection
- TENS
- Nerve blocks

Non-opioid pharmacologic options

- NSAIDs
- Acetaminophen
- Gabapentanoids (gabapentin, pregabalin)
- SNRIs (duloxetine, venlafaxine)
- Topicals (capsaicin, NSAIDs, lidocaine)

Optimizing treatment of co-occurring conditions

- Major depression, anxiety, other MH conditions
- Diabetes, OSA and other chronic conditions
- Substance use disorders

Therapeutic monitoring

Assess and re-assess the 5 As

1. Analgesia: 11- pt Numeric Rating Scale
2. Activities of daily living (function): "**Your goal** was to get back in your walking routine. How is it going?"
3. Adverse effects: detailed questions
4. Addiction/overuse: Is the patient oversedated? Is the patient running out early? Does the urine drug test unprescribed drugs/meds?
5. Adherence to the treatment agreement: Is the patient no-showing appointments? Does the patient have multiple prescribers?

Urine drug testing

- Performs better than physician impression
- Learn how to order and interpret first; *then*, incorporate into clinical practice

Katz, Fanciullo. Clin J Pain, 2002

Goals of urine drug testing

- Improve Patient Care and Safety:
  - Facilitates doctor-patient communication
  - Provides objective information
  - Confirms use of prescribed medication: Adherence testing
  - Confirms lack of use of non-prescribed medications and illicit drugs

Heit,H.A. and Gourlay, D.L. *J Pain Sympt Mgt*. 2004.

How to discuss UDT

- New patient initiating on opioids: (as part of treatment agreement discussion)
  - "This is our routine practice as a patient safety issue."
- Patient says: "But I'm not a drug addict":
  - "Routine testing…not singling anyone out."
- Patient says: "I refuse":
  - "We can't prescribe if we're unable to do the routine safety monitoring discussed in the treatment agreement."

Heit, H.A.; Gourlay, D.L. *J Pain Sympt Mgt.* 2004.

Laboratory testing procedures

First:

Screening:

- Enzyme-Mediated Immunoassay (EIA)

If any unexpected findings, then:

Confirmatory:

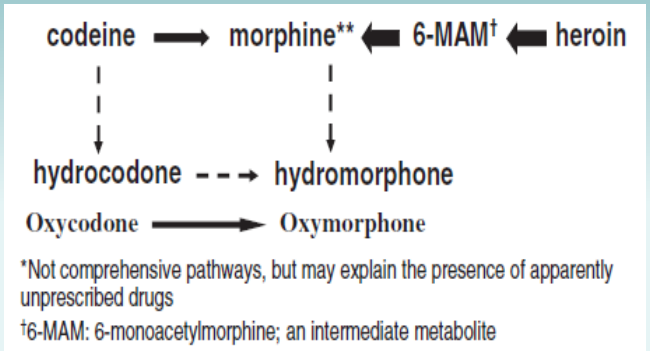
- Gas Chromatography/ Mass Spectrometry

Katz, N. and Fanciullo, G.J. *Clin J Pain*. 2002.

Sample two-stage EMIT then GC/MS (rx is oxycodone CR 20 mg TID)

- EMIT:
  - Amph (-)
  - BZD (-)
  - Barb (-)
  - Cannab (-)
  - Cocaine (-)
  - Methadone (-)
  - Opiate (+)
  - Oxycodone (+)
  - PCP (-)
- Opiate GC/MS:
  - Codeine (-)
  - Morphine (-)
  - Hydrocodone (-)
  - Hydromorphone (-)

Metabolism of Opioids



*Not comprehensive pathways, but may explain the presence of apparently unprescribed drugs

†6-MAM: 6-monoacetylmorphine; an intermediate metabolite

Gourlay, D. L. and Heit, H.A. *Pain Med.* 2009; 10: (S2): S115-S123.

Identifying opioid use disorder

- Your role:
  - Partner with the patient
  - Be transparent/forthright/non-judgmental
- In the treatment agreement:
  - I want to ensure your safety
  - I will be monitoring [*in these ways*]
  - Specifically, I'm looking for [*safe use behavior*]
  - If you demonstrate lack of safety, it is my duty to stop the therapy and transition you to safer therapy
- *If patient evidences recurrent problematic behavior, that suggests loss of control, requiring close evaluation for opioid use disorder*

Patient started the taper…

- Felt that he was totally pre-occupied with pill count
- Was craving next dose despite absence of withdrawal symptoms
- Frustrated that he wanted to cut back but couldn't

OUD pattern has emerged

Physiologic sequelae

- Tolerance
- Withdrawal
- ✓ Opioid craving

Loss of control

- Greater amounts of use or longer period of use than intended
- ✓ Repeated unsuccessful efforts to cut down
- Inordinate amount of time obtaining, using, or recovering

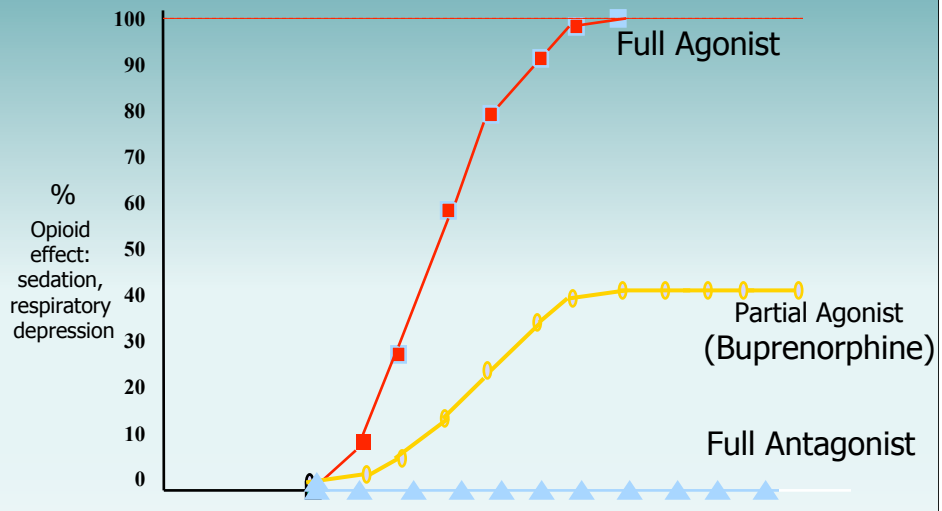
Adverse consequences

Summary of 5 criteria:

- Important social, occupational or recreational activities given up or reduced due to opioid use or recurrent opioid use despite physical or psychological problems caused or worsened by use

Physiologic dependence

Buprenorphine: a partial μ agonist



Increasingly, we are offering bup/nx before OUD develops

- "We now know more about safety problems related to opioids and we are concerned about your health and safety. We recognize that we/("the system") prescribed you these medications so now we want to help you be safer while still managing your pain."
- Constrained choice: slow taper (e.g. 10% every 2-4 weeks) vs. quick taper off and rotation to buprenorphine.
- Possible outcomes if choosing bup/nx:
  - Bup/nx works better for pain/overall well-being → WIN
  - Bup/nx works about the same → WIN
  - Bup/nx nowhere near as effective → try to stay on 2-3 weeks, potentially restart full agonists at <50% prior dose

A word about dose, etc

- Difficult to make conclusive statements…Rough guidelines:
  - Pre rotation dose > 120 mg MEDD → 4 mg TID
  - Pre rotation dose 60-120 mg MEDD → 2 mg TID
  - Pre rotation dose <60 mg MEDD → 2 mg BID
- For induction of patient on > 120 mg MEDD:
  - Halve their dose every day until ~100-120 mg MEDD →
  - Stop; Await withdrawal
  - Start bup/nx
  - We do ~90% "home inductions"
- If prescribing for pain only, X-license not needed *OR* if you have X-license, for pain does not count towards cap

Document

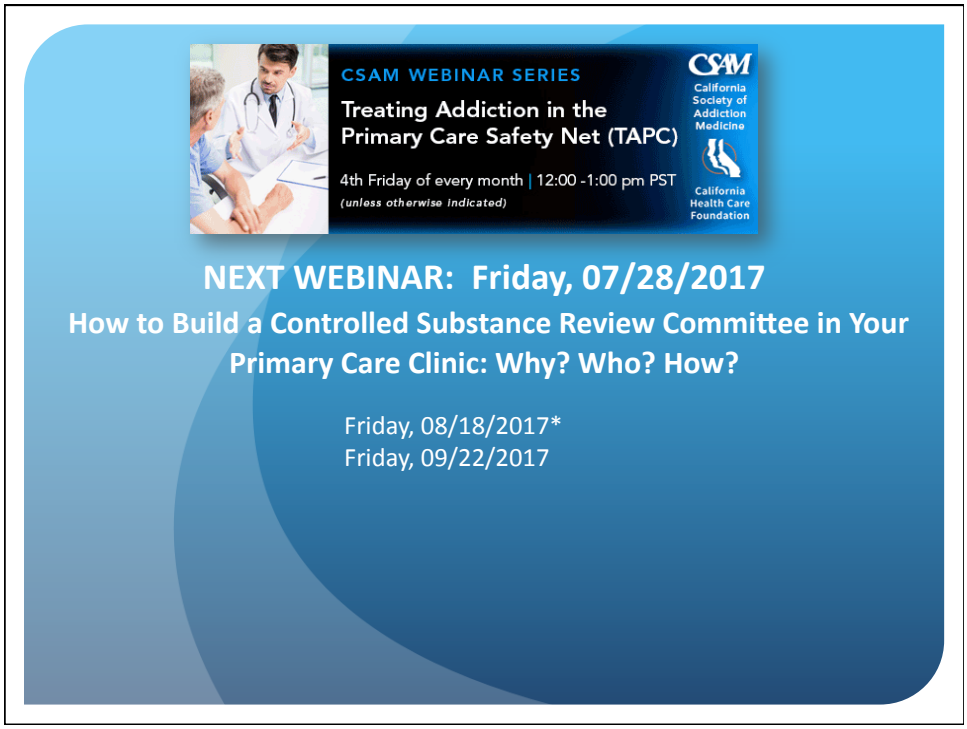
- Indication for treatment
- Discussion of potential harm and benefit
- Treatment plan
- Results of assessment and reassessment with each visit
- Response to problems

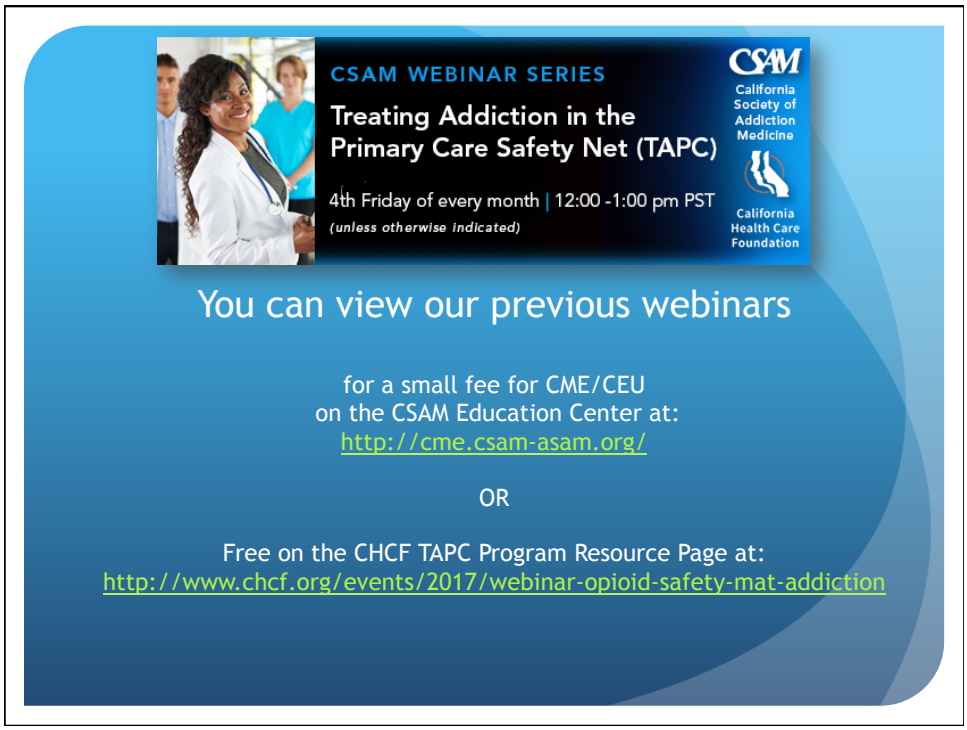
We are at a crossroads…

- There are many patients already on long-term opioid therapy that would likely not have been started in the first place if we knew then what we know now.
- For patients **already on long-term therapy** consider this stance:
  - *Continue if favorable benefit to harm/ratio*
  - Avoid dose escalation
  - Be vigilant for indications to lower the dose/ discontinue, potentially rx bup/nx
  - Avoid stigmatizing – patients are not "at fault" for where things stand today.

Summary

- Chronic pain is common, marked by functional disability and affective distress.
- Evidence supports multi-modal treatment that promotes patient self management as the most effective management strategy.
- Opioids have a limited role in chronic pain.
- When used, opioids should be monitored carefully and discontinued when harm outweighs benefit. Buprenorphine can play a helpful role.


CSAM WEBINAR SERIES
Treating Addiction in the Primary Care Safety Net (TAPC)
4th Friday of every month | 12:00 -1:00 pm PST
(unless otherwise indicated)
CSAM
California Society of Addiction Medicine
California Health Care Foundation
NEXT WEBINAR: Friday, 07/28/2017
How to Build a Controlled Substance Review Committee in Your Primary Care Clinic: Why? Who? How?
Friday, 08/18/2017*
Friday, 09/22/2017


CSAM WEBINAR SERIES
Treating Addiction in the Primary Care Safety Net (TAPC)
4th Friday of every month | 12:00 -1:00 pm PST
(unless otherwise indicated)
CSAM
California Society of Addiction Medicine
California Health Care Foundation
You can view our previous webinars
for a small fee for CME/CEU
on the CSAM Education Center at:
http://cme.csam-asam.org/
OR
Free on the CHCF TAPC Program Resource Page at:
http://www.chcf.org/events/2017/webinar-opioid-safety-mat-addiction

Thank you for participating in today's webinar.

Stay online after the webinar ends
and you will be connected to the post webinar
quiz and evaluation.

You will also receive a link via email.

Save the date!
CSAM Addiction Medicine Review Course
and Board Exam Preparation
August 24 - August 27, 2017
Hilton San Francisco Union Square