Opioids and Chronic Pain

CRIT/FIT 2016

April 2016

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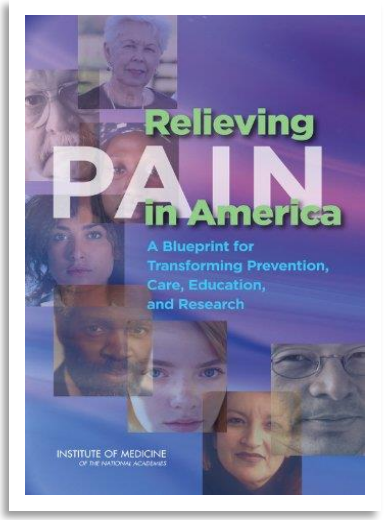
Chronic Pain in Perspective

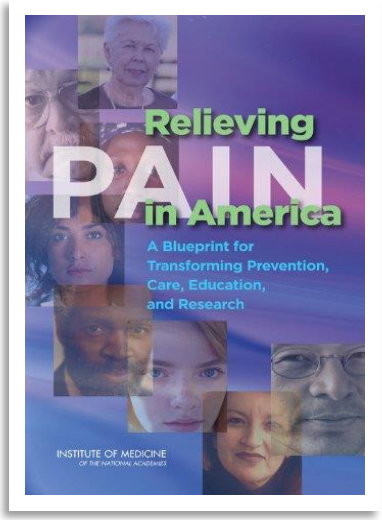


- 100 Million in U.S. with chronic pain
  - 25 million have moderate to severe chronic pain

- **Chronic pain can be a disease in itself**
  - Pathologic, maladaptive disorders of somatosensory pain signaling pathways that persists well after the acute injury
  - Management approaches designed for acute, self-limited pain are inadequate and inappropriate for treating chronic pain

Institute of Medicine. 2011 Relieving Pain in America. Washington DC
Dzau VJ, Pizzo PA. *JAMA* 2014
Walk D, Poliak-Tunis M. *Med Clin N Am*. 2016

Chronic Pain in Perspective

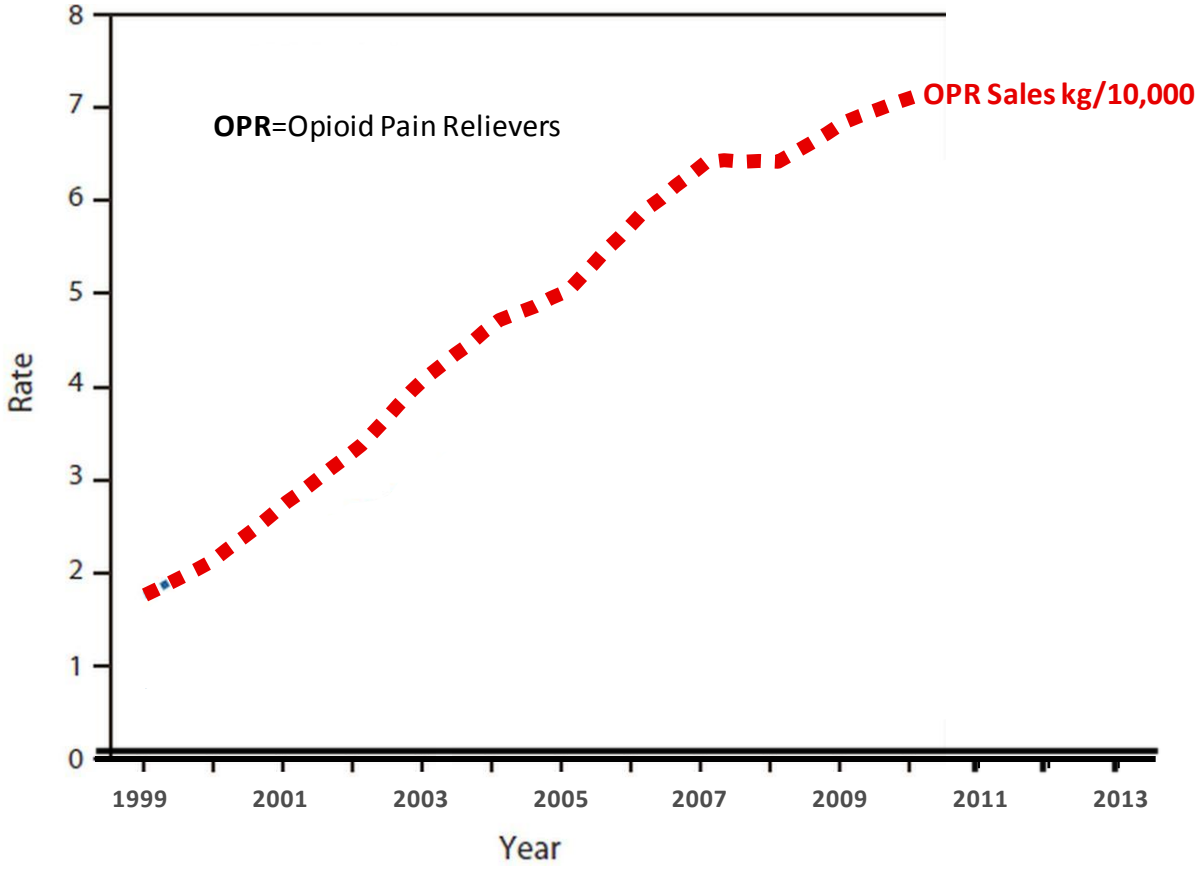


- Significant barriers to adequate pain care
  - Negative attitudes and disparities in pain care
  - Lack of decision support for chronic pain management
  - Financial misalignment favoring use of medications
  - Over-burdened primary care providers

Care must be tailored to each patient's experience

Institute of Medicine. 2011 Relieving Pain in America. Washington DC
Reuben DB et al. *Ann Intern Med*. 2015

Worrisome Trends and Associations



MMWR Nov 4, 2011
Volkow ND et al. *N Engl J Med*. 2014
Tolia VN et al. *N Engl J Med.* 2015

“The pain medication conundrum”

Opinion The New York Times

- Undertreating pain, we are admonished…it violates the basic ethical principles of medicine. On the other hand, we are lambasted for overprescribing pain medications… creating an epidemic of overdose deaths.
- For patients with chronic pain, especially those with syndromes that don’t fit into neat clinical boxes, being judged by doctors to see if they “merit” medication is humiliating and dispiriting. This type of judgment, with its moral overtones and suspicions, is at odds with the doctor-patient relationship we work to develop.

“As Mr. W. and I sat there sizing each other up, I could feel our reserves of trust beginning to ebb. I was debating whether his pain was real or if he was trying to snooker me. He was most likely wondering whether I would believe him…”

Danielle Ofri, MD
Associate Professor at NYU and a physician at Bellevue Hospital
August 2015

“My chronic pain isn’t a crime”

Opinion The Boston Globe

- I will be in chronic pain until I die…I accept it.
- Pain medication is inadequate. But with it I am more consistently functional (homeowner, spouse, parent, teacher, writer, editor).
- Abuse of prescription pain medications is a serious problem; people are dying.
- Ever-tighter regulations…are of dubious value in reducing [abuse] – while causing grave harm to those of us in chronic pain, to the overwhelming majority who take medications for appropriate reasons.

> “Increasingly I am a suspect, treated less as a patient and more as a criminal.”

Donald N.S. Unger, MFA, PhD
Visiting Lecturer English Department, College of the Holy Cross
February 2015

Opioids in Perspective

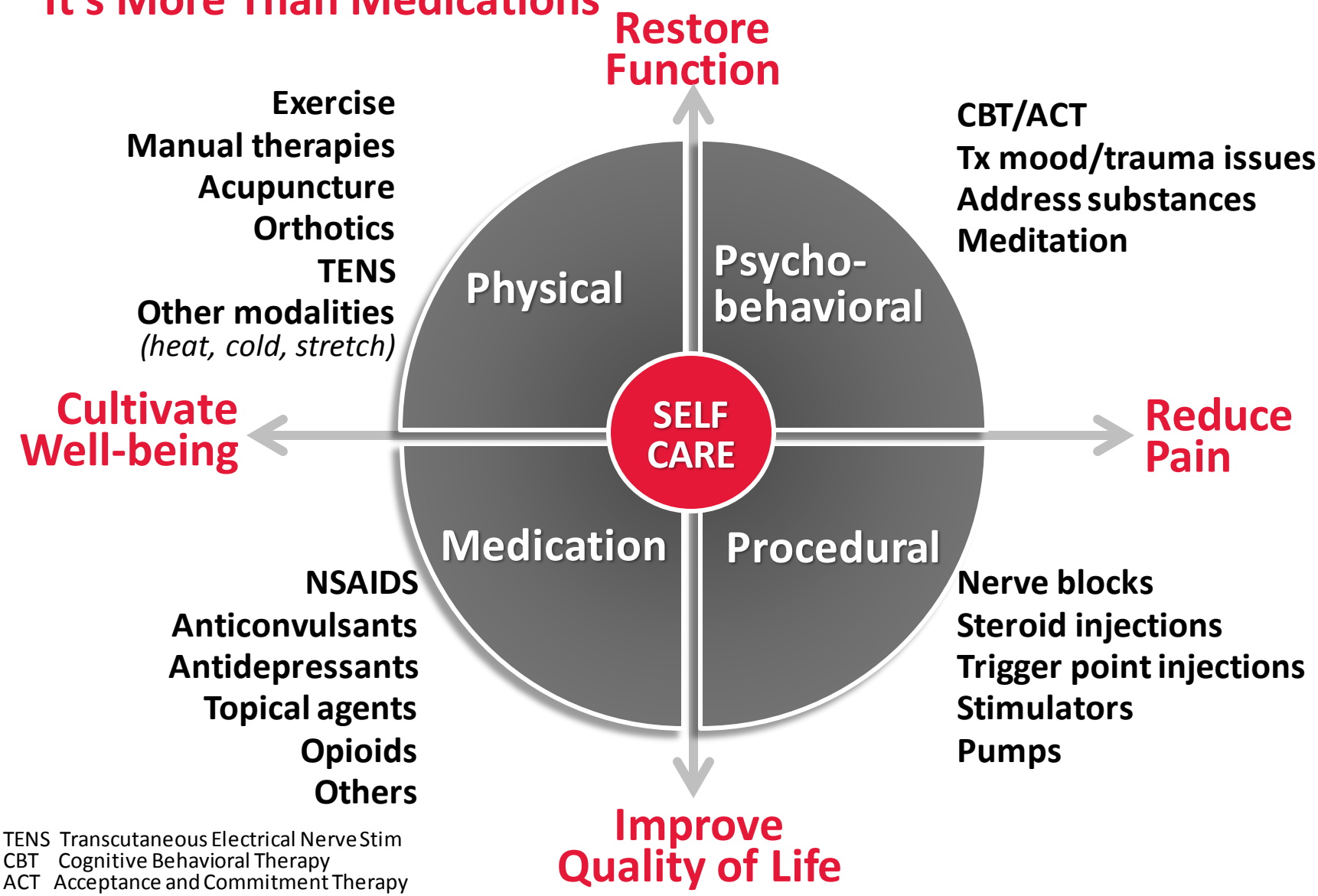
- The efficacy and safety of chronic opioid therapy for chronic pain has been **inadequately studied***
- Opioid prescribing needs to be more selective and conservative
- Opioids for chronic pain…
  - help ***some*** patients
  - harm ***some*** patients
  - are only one tool for managing severe chronic pain
  - are indicated only when alternative safer treatment options are inadequate

*

Chou R et al. *Ann Intern Med* 2015
Dowell D et al. *JAMA* 2016
Manchikanti L et al. *Pain Physician* 2011
Reuben DB et al. *Ann Intern Med* 2015
Volkow ND, McLellan T. *N Engl J Med* 2016

Multidimensional Care

It's More Than Medications



TENS Transcutaneous Electrical Nerve Stim
CBT Cognitive Behavioral Therapy
ACT Acceptance and Commitment Therapy

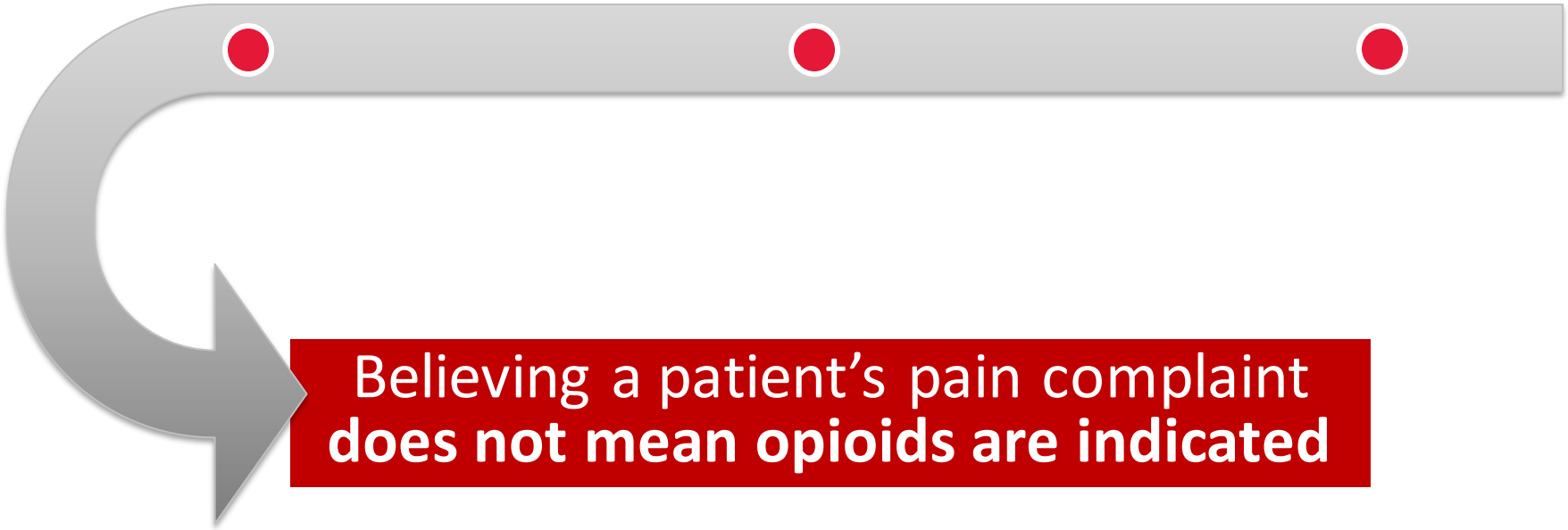
Building Trust

- After you take a thorough pain history…

Show empathy for patient experience

Discuss factors which worsen pain and limit treatment (i.e. substance use, mental health)

Validate that you believe pain is real



Believing a patient's pain complaint **does not mean opioids are indicated**

Opioid Efficacy for Chronic Pain

- Most literature: surveys and uncontrolled case series
- RCTs are short duration (<8 months) with small samples (<300 patients)
- Mostly pharmaceutical company sponsored
- Outcomes
  - Better analgesia with opioids vs. placebo
  - Pain relief modest
  - Mixed reports on function
  - Addiction not assessed

Ballantyne JC, Mao J. *N Engl J Med*. 2003
Chou R et al. *Ann Intern Med*. 2015
Eisenberg E, McNicol ED, Carr DB. *JAMA.* 2005
Furlan AD, et al. *CMAJ.* 2006
Kelso E, et al. *Pain.* 2004
Martell BA, et al. *Ann Intern Med.* 2007
Michna E, et al. *Pain Med* 2014
Noble M, et al. *Cochrane Systematic Reviews*. 2010.

Opioid Efficacy for Chronic Pain

- Proportion of patients with at least 50% pain relief
- N = 442
- Follow-up 7.5 months (mean) to 13 months (1^2 77.3%)

Study Name	Event Rate	Lower Limit	Upper Limit	Total	Proportion
Zenz 1992	0.510	0.413	0.606	51 / 100	
Allan 2005	0.392	0.341	0.445	134 / 342	
	0.443	0.333	0.559		

44.3% of participants had at least 50% pain relief

Noble M et al. *Cochrane Systematic Reviews* 2010.

Variable Response to Opioids

Mu-opioid Receptor

- >100 polymorphisms in the human MOR gene
- Mu-opioid receptor subtypes

Opioid Pharmacokinetics

- Opioid metabolism differs by individual opioid and by individual patient

Not all patients respond to the same opioid in the same way

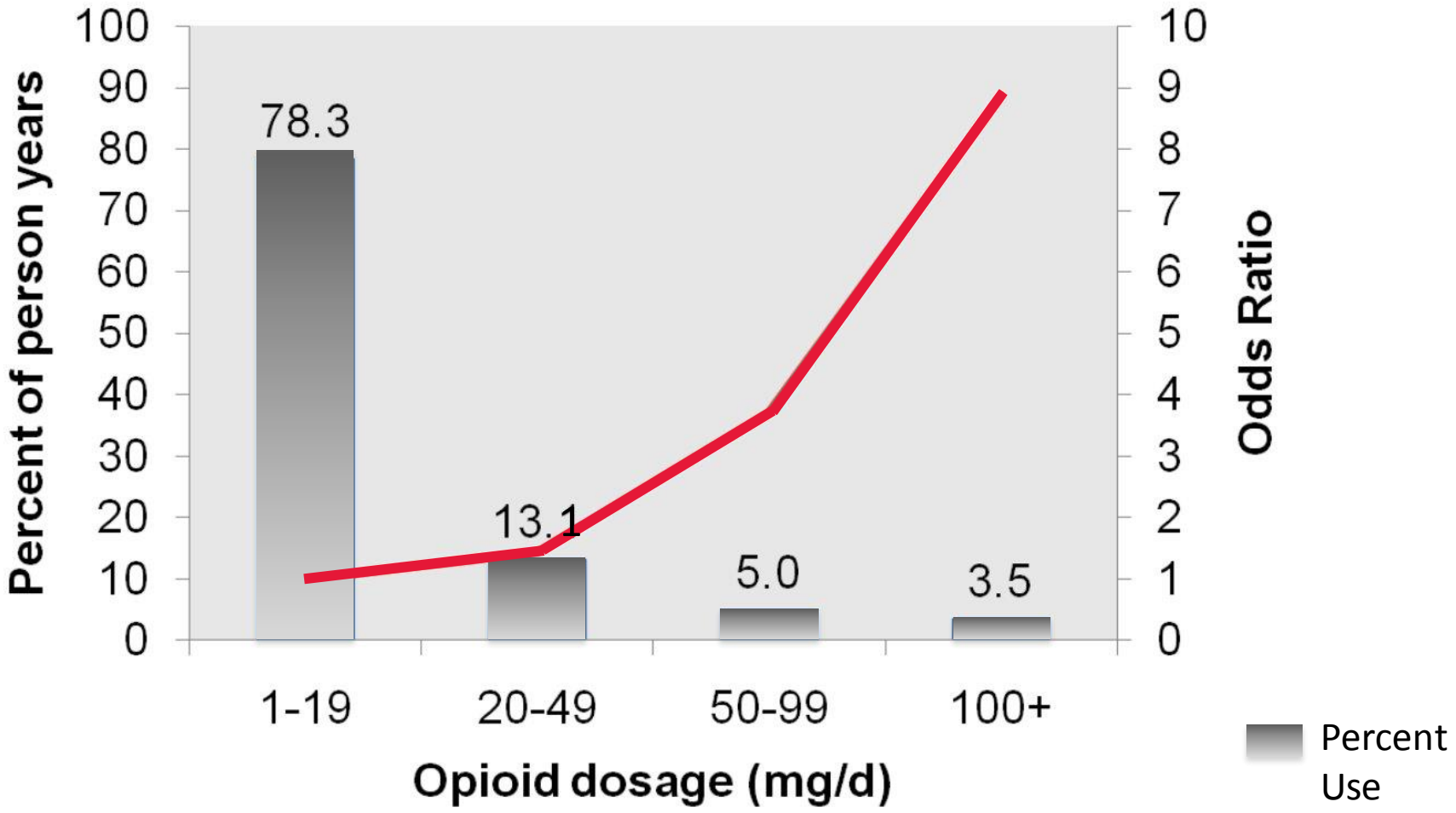
Smith HS. *Pain Physician*. 2008

Opioid Safety and Risks

- **Allergies** are rare
- **Side effects** are common
  - Nausea, sedation, constipation, urinary retention, sweating
  - Respiratory depression – sleep apnea
- **Organ toxicities** are rare
  - Suppression of hypothalamic-pituitary-gonadal axis
- **Worsening pain** *(hyperalgesia in some patients)*
- **Addiction**
- **Overdose**
  - when combined w/ other sedatives
  - at high doses

Dunn KM et al. Ann Intern Med 2010
Li X et al. Brain Res Mol Brain Res 2001
Doverty M et al. Pain 2001
Angst MS, Clark JD. Anesthesiology 2006

Dose and Overdose Risk



Group Health Consort Study, 1997-2005; Dunn KM, et al. Ann Intern Med. 2010

Rates of Problematic Opioid Use in Chronic Pain

Systematic review from 38 studies
(26% primary care settings, 53% pain clinics)

Misuse rates: **21% - 29%** ([95%CI]: 13%-38%)

> **Misuse:** *Opioid use contrary to the directed or prescribed pattern of use, regardless of the presence or absence of harm or adverse effects.*

Addiction rates: **8% - 12%** ([95% CI]: 3%-17%)

> **Addiction:** *Pattern of continued use with experience of, or demonstrated potential for, harm (eg, "impaired control over drug use, compulsive use, continued use despite harm, and craving").*

Vowles KE et al. *Pain.* 2015

Q1

Opioid Misuse Risk

Known Risk Factors

Good Predictors for Prescription Opioid Misuse

- Young age (less than 45 years)
- Personal history of substance use disorder
  - Illicit, prescription, alcohol, nicotine
- Family history of substance use disorder
- Legal history
  - DUI, incarceration
- Mental health problems
- History of sexual abuse

Akbik H, et al. *J Pain Symptom Manage*. 2006
Ives J, et al. *BMC Health Serv Res*. 2006
Liebschutz JM, et al. *J Pain*. 2010
Michna E, et al. *J Pain Symptom Manage*. 2004
Reid MC, et al. *J Gen Intern Med*. 2002

Does my patient have an OUD?

- ✓ ***Tolerance**
- ✓ ***Withdrawal**
- ✓ **Use in larger amounts or duration than intended**
- ✓ **Persistent desire to cut down**
- ✓ Giving up interests to use opioids
- ✓ **Great deal of time spent obtaining, using,** or recovering from **opioids**
- ✓ Craving or strong desire to use opioids
- ✓ Recurrent use resulting in failure to fulfill major role obligations
- ✓ **Recurrent use in hazardous situations**
- ✓ Continued use despite social or interpersonal problems caused or exacerbated by opioids
- ✓ **Continued use despite physical or psychological problems**

*This criterion is not considered to be met for those individuals taking opioids solely under appropriate medical supervision

Mild OUD: 2-3 Criteria
Moderate OUD: 4-5 Criteria
Severe OUD: ≥6 Criteria

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.)

Is the my patient addicted?

Clinical syndrome presenting as…

- ☐ Loss of **C**ontrol
- ☐ **C**ompulsive use
- ☐ **C**ontinued use despite harm

} **Aberrant Medication Taking Behaviors** (pattern and severity)

- **Addiction** is a **behavioral maladaptation**
- **Physical Dependence** is a **biologic adaptation**

Savage SR, et al. *J Pain Symptom Manage.* 2003

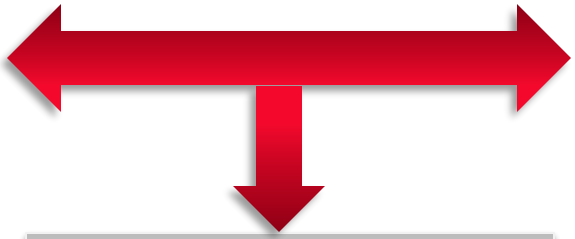
Aberrant Medication Taking Behaviors

The Spectrum of Severity

O	Requests for increase opioid dose
O	Requests for specific opioid by name, “brand name only”

Aberrant Medication-Taking Behaviors

Differential Diagnosis (DDx)



Pain Relief Seeking

- Disease progression
- Poorly opioid responsive pain
- Withdrawal mediated pain
- Opioid analgesic tolerance
- Opioid-induced hyperalgesia

Pain Relief and Drug Seeking

For example, patient with chronic pain, with co-morbid addiction, taking some for pain and diverting some for income

Drug Seeking

- Opioid use disorder/Addiction
- Other psychiatric diagnosis
- Criminal intent (diversion)

Alford DP. *JAMA.* 2013

When Are Opioids Indicated?

- Pain is moderate to severe
- Pain has significant impact on function and quality of life
- Non-opioid pharmacotherapy has been tried and failed
- **Patient agreeable to…**
  - **take opioids exactly as prescribed**
    - e.g., no unsanctioned dose escalation
  - **have opioid use closely <u>monitored</u>**
    - e.g. pill counts, urine drug testing

Always **start low** and **go slow**

"Universal Precautions"

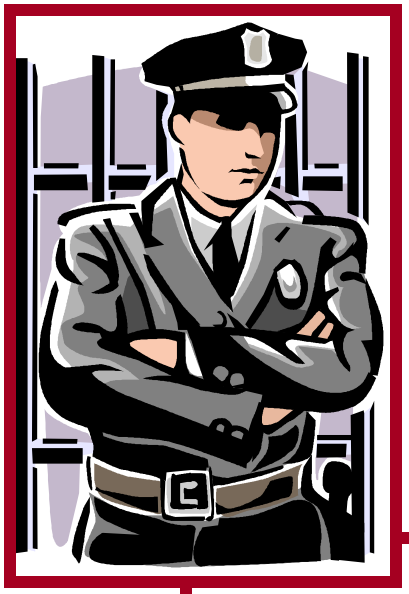
(not evidence-based but has become "standard" of care)

- Agreements "contracts", informed consent
- Monitor for benefit and harm with frequent face-to-face visits
- Monitor for adherence, addiction and diversion
  - Urine drug testing
  - Pill counts
  - Prescription monitoring program data

FSMB Guidelines 2004 www.fsmb.org
Gourlay DL, Heit HA. Pain Medicine 2005
Chou R et al. J Pain 2009

What is the physician's role?

not



Nicolaidis C. Pain Medicine 2011

Implementing Universal Precautions in Pain Medicine

Use a Health-Oriented, Risk Benefit Framework

NOT…

- Is the patient good or bad?
- Does the patient deserve opioids?
- Should this patient be punished or rewarded?
- Should I trust the patient?

RATHER…

Do the benefits of opioid treatment outweigh the untoward effects and risks for this patient (or society)?

Judge the opioid treatment NOT the patient

Nicolaidis C. *Pain Med.* 2011

Assessing Benefit: PEG scale

1. What number best describes your pain on average in the past week:

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

Krebs EE, et al. J Gen Intern Med. 2009

Assessing Risk: Opioid Risk Tool

	Female	Male
Family history of substance abuse		
Alcohol	❑1	❑3
Illegal drugs	❑2	❑3
Prescription drugs	❑4	❑4
Personal history of substance abuse		
Alcohol	❑3	❑3
Illegal drugs	❑4	❑4
Prescription drugs	❑5	❑5
Age between 16-45 years	❑1	❑1
History of preadolescent sexual abuse	❑3	❑0
Psychological disease		
ADHD, OCD, bipolar, schizophrenia	❑2	❑2
Depression	❑1	❑1

Scoring
0-3 low risk
4-7 moderate risk
>8 high risk

Webster LR, Webster RM. Pain Medicine, 2006

Discussing Monitoring with Patients

- Discuss risks of opioid medications
- Responsibility to look for early signs of harm
- Discuss agreements, pill counts, drug tests, etc. as ways that you are helping to protect patient from getting harmed by medications

Use consistent approach (Universal Precautions)
BUT
apply it individually to match risk

Urine Drug Testing

Objective information that can provide:

- **Evidence of therapeutic adherence**
- **Evidence of use or non-use of illicit drugs**

- Discuss urine drug testing openly with patient
  - If I send your urine right now, what will I find in it…
- Document time of last medication use
- One medical data point to integrate with others
  - Cannot discriminate elective use, addictive use and diversion
- Dedicated deceivers can beat the system

Heit HA and Gourlay DL. J *Pain Symptom Manage.* 2004
Christo PJ et al. *Pain Physician.* 2011

Urine Drug Testing

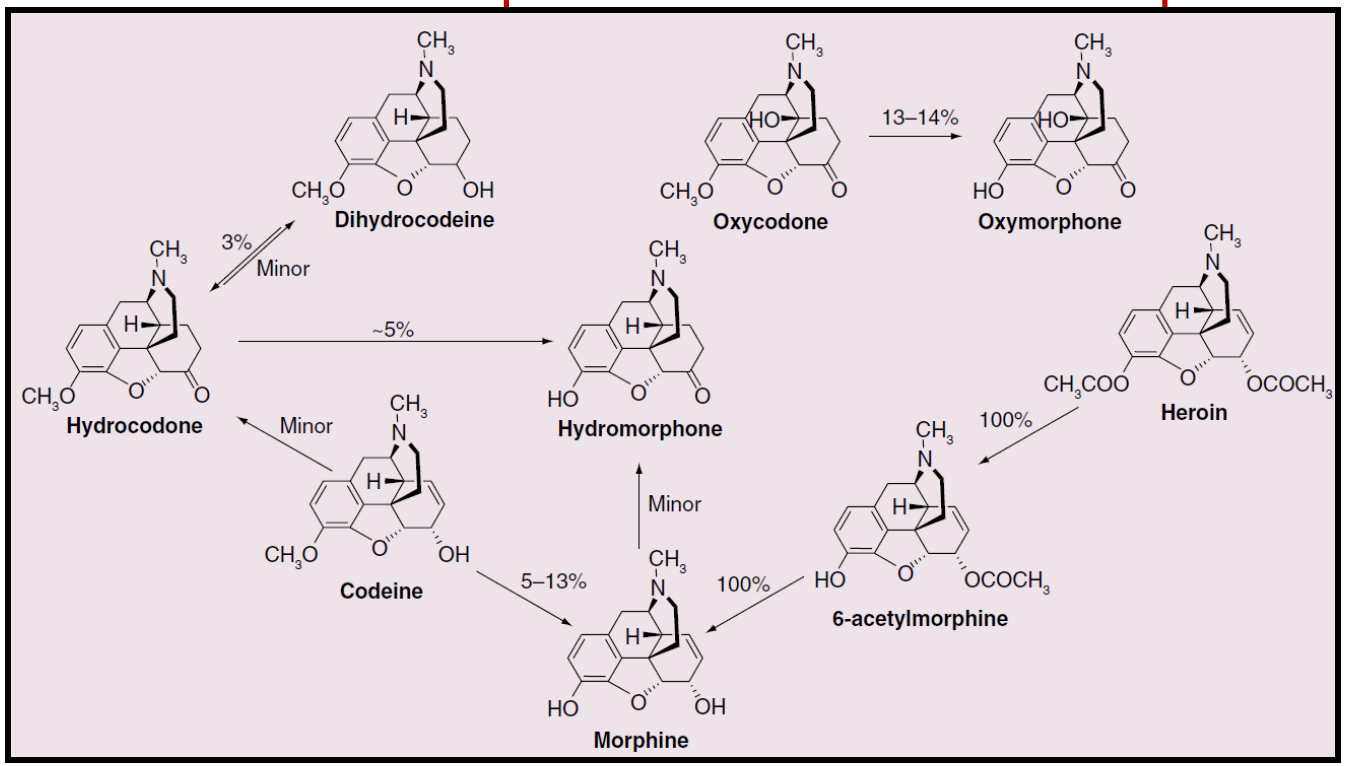
- Urine drug **screens** are usually immunoassays
  - Quick and relatively inexpensive
  - Need to know what is included in testing panel
  - Risk of false negatives due to cut offs
  - Risk of false positives due to cross reactions
  - Unexpected findings can be verified with Gas Chromatography/Mass Spectroscopy (GC/MS)

Identify a toxicologist/clinical pathologist for questions regarding unexpected results

Reisfield GM, et al. *Bioanalysis.* 2009

Urine Drug Testing

- GC/MS **confirmation**
  - Identifies specific molecules - sensitive and specific but more expensive
  - Measurement of urine drug levels is not a valid method of determining the amount of opioid ingested
  - Understand opioid metabolism to interpret GC/MS results



Peppin JF, et al. *Pain Med.* 2012

Heit HA, Gourlay DL. J *Pain Symptom Manage.* 2004

Heit HA, et al. Urine Drug Testing in Clinical Practice; Pharmacom Group Inc., May 2010.

Reisfield GM, et al. *Bioanalysis.* 2009

Pill Counts

Objective information that can:

- Confirm medication adherence
- Minimize diversion

Strategy	
	28 day supply (rather than 30 days) prevents running out on weekends
	Prescribe so that patient should have residual medication at appointments
	Ask patient to bring in medications at each visit
	For identified risks or concerns, can request random call-backs for immediate counts

Prescription Drug Monitoring Programs (PDMP)

- Statewide electronic database on dispensed controlled substance prescriptions
- Prescription data available to prescribers and pharmacists (usually for the past year, and including information on date dispensed, patient, prescriber, pharmacy, medicine, and dose)
- A substantially underutilized resource
  - Many states now mandate use before writing for controlled substances
- Several studies suggest association between PDMP use and positive outcomes related to improving prescribing and reducing prescription drug abuse

www.pdmpexcellence.org/sites/all/pdfs/Brandeis_PDMP_Report.pdf
Haffajee RL, et al. *JAMA.* 2015

Continuation of Opioids

- Before writing the next prescription…you should be convinced that…
  - …there is benefit (pain, function, QOL)
  - …benefits outweigh observed harms/risks

Discontinuing Opioids

- Do not have to prove addiction or diversion - only assess and reassess the risk-benefit ratio
- If patient is unable to take opioids safely or is nonadherent with monitoring then discontinuing opioids is appropriate even in setting of benefits
- Need to determine how urgent the discontinuation should be based on the severity of the risks and harms
- Document rationale for discontinuing opioids

You are abandoning the opioid therapy NOT the patient

Using Risk Benefit Framework

Benefits

Pain
Function
Quality of Life

Risks/Harm

Misuse
Addiction, Overdose
Adverse Effects

Useful to Avoid Pitfalls...

- "But I really, really need opioids."
- "I thought we had a good relationship/I thought you cared about me."
- "If you don't give them to me, I will drink/use drugs/hurt myself."
- "Can you just give me enough to find a new doc?"

RESPONSE:

"I cannot a prescribe a medication that is not helping you (or is hurting you)."

Summary

- Opioids can be effective and safe but are imperfect
- Use risk/harm - benefit framework
- Use consistent approach, but set level of monitoring to match risk
- Judge the treatment and not the patient
- If there is benefit in the absence of harm, continue opioids
- If there is no benefit or if there is harm, discontinue opioids