Opioids in Primary Care: The Good, the Bad, and the Ugly

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Nebraska-South Dakota ACP Combined Meeting

October 2019

Learning Objectives*

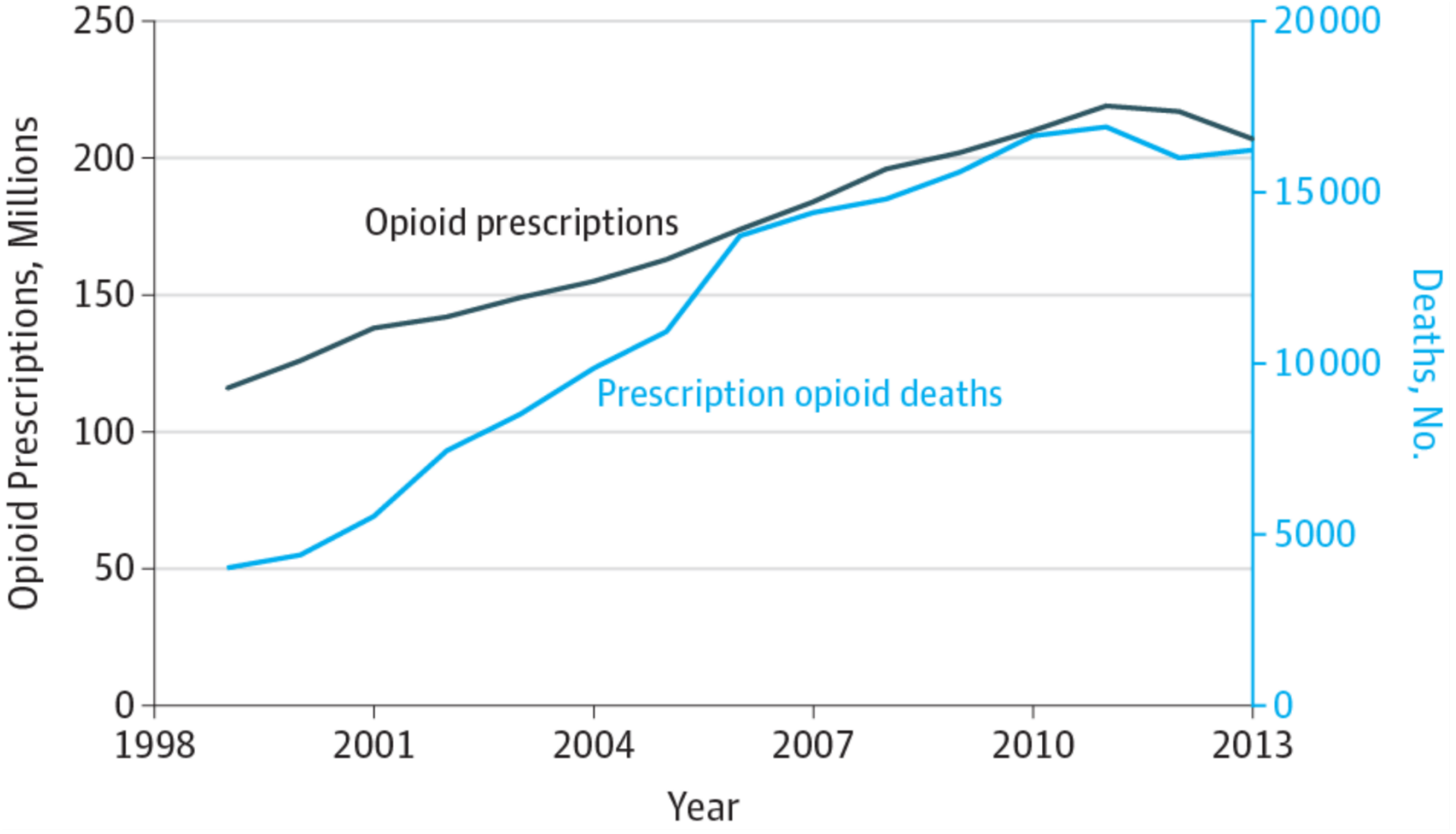
- Become aware of the recent epidemic of opioid overuse and its consequences.
- Describe the factors that have led to over prescribing of opioids for chronic non-cancer pain.
- Be able to describe the differences between nociceptive and neuropathic pain.
- Describe alternative approaches to chronic pain management other than opioids.
- Be aware of the CDC Opioid Prescribing Guidelines for Chronic pain and how to apply them in practice.

The Opioid Epidemic – Statistics

- 259 million opioid prescriptions written in 2012.
- ~ 20% of patients with non-cancer pain are prescribed opioids.
- Between 3% and 4% of adults are prescribed long term opioids.
- ~ 2 million people are dependent on or abuse opioids.
- ~ half of opioid overdose deaths involve a prescription opioid.
- Since 1999 > 180,000 have died from Rx opioid overdoses.
- Prescription opioid death rate has quadrupled since 1999.
- 4 out of 5 heroin users started on prescription opioids.
- Heroin deaths have tripled between 2010 and 2015.

- Source: https://www.cdc.gov/drugoverdose/prescribing/guideline.html

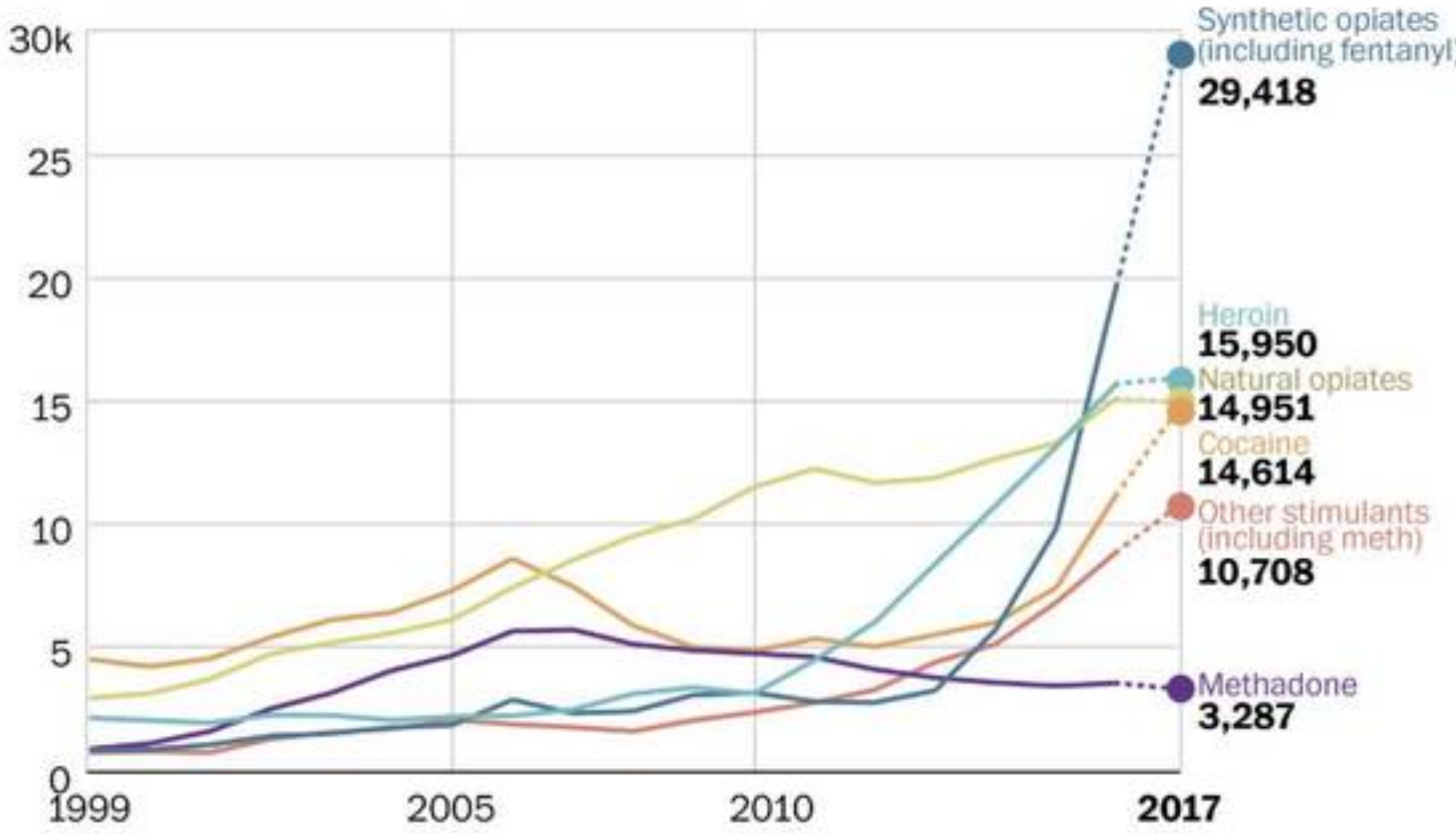
Trends in Opioid Prescribing



JAMA Neurol. 2016;73(5):513-514. doi:10.1001/jamaneurol.2016.0535

Synthetic opiate deaths continue to surge

Annual overdose deaths involving selected drugs



Note: 2017 figures are provisional. Many overdose deaths involve multiple drugs.

Source: Centers for Disease Control and Prevention WAPO.ST/WONKBLOG

Overdose estimates for selected drug types in 2017.

Factors promoting increased opioid prescribing

- Pain as the 5th vital sign
  - Introduced in 1996 by the American Pain Society.
  - Rapid uptake by health care organizations using 1-10 rating scale.
  - Rating scales oversimplify the problem of chronic pain.
- Patient satisfaction as a component of reimbursement
  - Until recently, Medicare reimbursement was partly based on patient satisfaction surveys including questions about pain control.
- Aggressive opioid promotion by the pharmaceutic industry as safe and effective
  - There is little high quality evidence to suggest that long term opioid use is an effective means of chronic pain control.
  - There is ample high quality evidence showing the risks of long term opioid use. E.g. 68.5 excess deaths per 10,000 person years opioid prescribing (for non-cancer pain).

Ray et al. JAMA 2016;315:2415-2423.

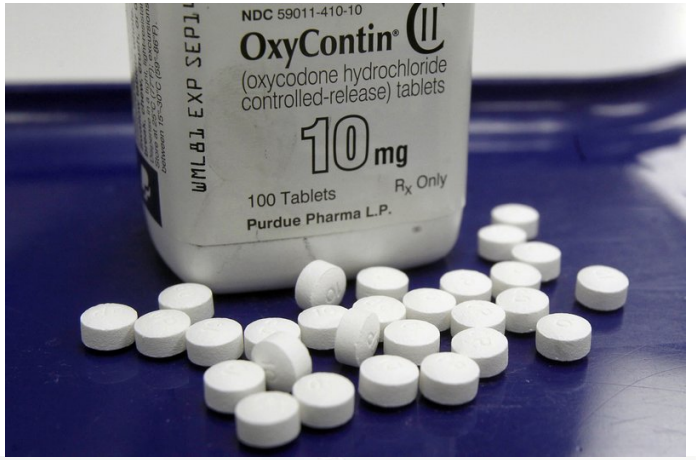
Marketing of Oxycontin

- From 1996 to 2002, Purdue Pharmaceuticals funded > 20,000 pain related educational programs.
- From 1996 to 2001, Purdue conducted > 40 national pain management and speaker training conferences at resorts (all expenses paid) where >5,000 physicians, nurses and pharmacists attended.
- Purdue more than doubled its internal sales force, provided starter coupons for free trails of oxycontin and distributed extensive promotional items.
- Oxycontin heavily promoted for non-cancer pain. Sales reps claimed that risk of addiction was less than 1%.

- Van Zee. AmJPubHealth 2009;99:221-227. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2622774/pdf/221.pdf

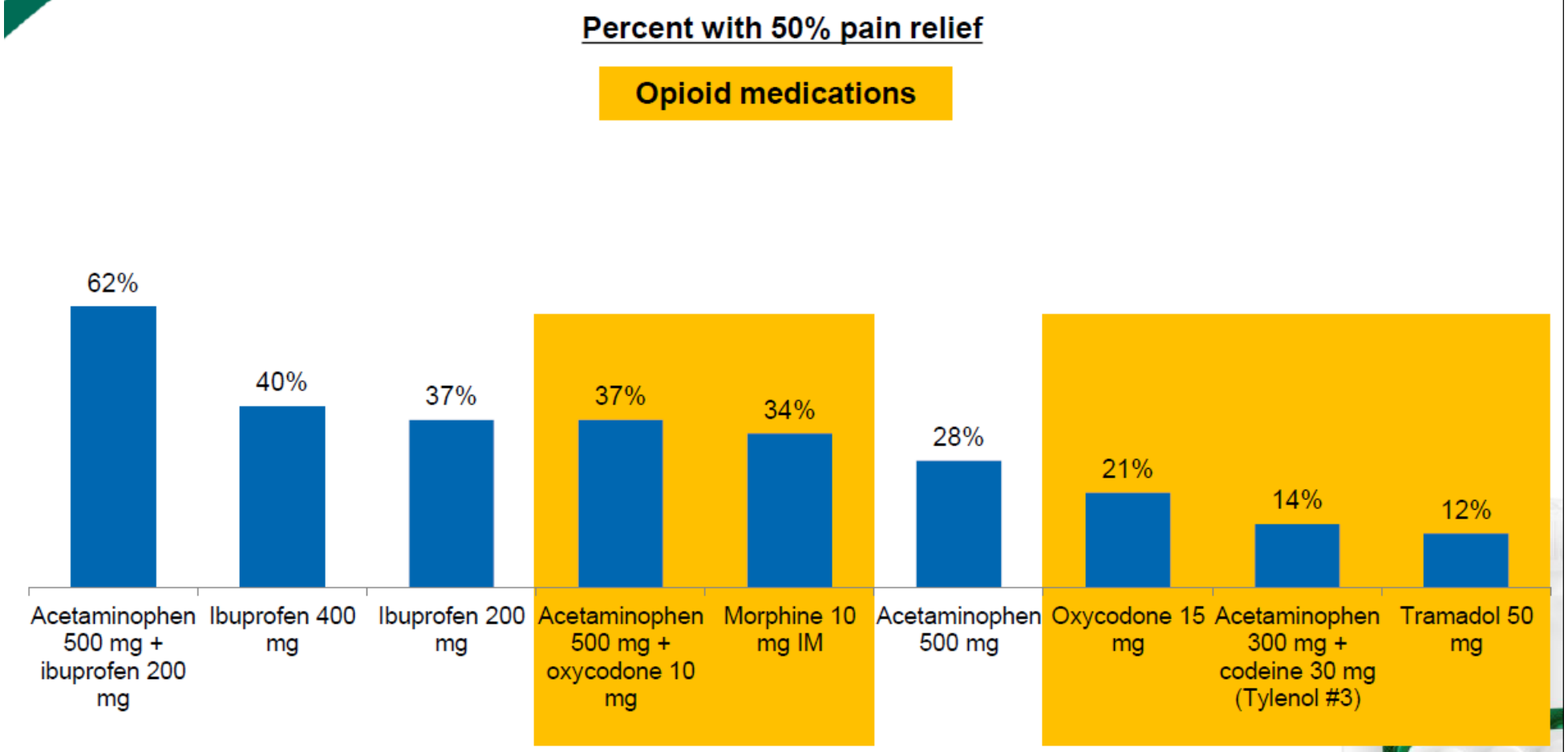
Marketing of Oxycontin (continued)

- In 2001,*The Medical Letter on Drugs and Therapeutics* found oxycodone offered no advantage over appropriate doses of other potent opioids.
- By 2004, Oxycontin was the leading drug of abuse in the US.
- In 2007, Purdue Frederick Co. Inc. and 3 executives plead guilty to criminal misbranding by claiming it was less addictive and less subject to abuse and paid $634 million in fines.
- 2019 Purdue declares bankruptcy in the setting of massive nationwide legal action.



Misperception of opioid analgesic potency

Opioids are not the most effective at providing pain relief.



http://www.nsc.org/NewsDocuments/2016/Doctor-Survey-press-briefing-32416.pdf

Source: Cochran research cited in the NSC white paper, Evidence for the efficacy of pain medications

Under-appreciation of opioid side effects

- Respiratory depression
- Sedation

} Overdose risk

- Constipation & Nausea
- Opioid-induced hyperalgesia
- Addictive potential (Rx opioids similar to heroin)
  - ~25% of chronic pain patients in primary care are opioid dependent
- Immunologic effects
- Hormonal effects

The Challenge of Assessing Pain

- Pain is common
  - 25 million American report daily chronic pain
  - http://americanpainsociety.org/about-us/press-room/nih-study-shows-prevalence-of-chronic-or-severe-pain-in-u-s-adults
- Pain is subjective
- Sometimes pain is feigned
- Pain is modulated by psychosocial factors (especially depression)
- Tissue injury pain (nociceptive) vs. neuropathic pain
- Over-reliance on overly simplistic measures (e.g: 0-10 pain scale)
- Multidimensional assessment tool are somewhat time consuming
  - McGill Pain Questionnaire (5-15 minutes)
  - Brief Pain Inventory (5-15 minutes)
- Establishing realistic goals: improving function vs. elimination of pain
  - “Zero pain is not the goal”

Types of Pain

- Nociceptive pain: Ongoing inflammation or tissue injury
  - E.g.: Rheumatoid arthritis, Toothache, Fracture pain, Post operative pain

- Neuropathic pain: Dysfunction of the nervous system
  - Peripheral neuropathic pain
    - E.g.: Diabetic neuropathy, Trigeminal neuralgia, Post-herpetic neuralgia
  - Sympathetically mediated pain
    - Complex regional pain syndrome
  - Central pain syndromes
    - E.g.: Fibromyalgia, Phantom limb pain

- Note: Opioids are relatively contraindicated in neuropathic pain syndromes

General approach to chronic pain

- Assess both physical and psychosocial dimensions of pain.
- Set realistic goals that emphasize function rather than pain relief.
- Recognize that there is unlikely to be a “quick fix” for chronic pain.
- Use a multi-modal approach that combines behavioral, manipulative, and pharmacologic modalities as appropriate.
- Continue to care for the patient, providing encouragement, empathy, and support.

Non-Opioid approaches to treat chronic pain:

- Non-pharmacologic:
  - Cognitive behavioral therapy
  - Biofeedback
  - Relaxation therapy.
  - Exercise
  - Acupuncture
  - Physical therapy
  - Manipulation
  - Neuromodulation
- Pharmacologic:
  - Acetaminophen
  - NSAIDs
  - Tricyclic antidepressants
    - Nortriptyline
  - SNRIs
    - Venlafaxine
    - Duloxetine
  - Antiepileptics
    - Gabapentin
    - Pregabaline
  - Topical agents
    - Lidocaine patch
    - Capsaicin cream
  - Nerve Blocks/ablations

JAMA | Original Investigation

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain
The SPACE Randomized Clinical Trial

Erin E. Krebs, MD, MPH; Amy Gravely, MA; Sean Nugent, BA; Agnes C. Jensen, MPH; Beth DeRonne, PharmD; Elizabeth S. Goldsmith, MD, MS; Kurt Kroenke, MD; Matthew J. Bair; Siamak Noorbaloochi, PhD

- 240 patients randomized to opioid vs non-opioid pain strategy in steps and followed for 12 months:
  - Step 1: Short acting opioids ± acetaminophen vs. acetaminophen ± NSAIDs
  - Step 2: Extended release opioids vs. tricyclics, gabapentin, topicals
  - Step 3: Fentanyl patch vs. pregabalin, duloxetine, tramadol
- Limit of 100 MME in the opioid group
- Patients were not blinded but outcome assessments were blinded
- No significant difference in pain related function
- Pain intensity significantly better in the non-opioid group
- Increased medication adverse effects in opioid group

JAMA 2018; 319:872-882.

2016 CDC Opioid Guidelines for Chronic Pain

- Chronic pain defined as > 3 months duration
- Guidelines do NOT apply to:
  - Patients in active cancer treatment
  - Patients in palliative care
  - Patients in end-of-life care
- Guidelines were developed based on:
  - Evidence-based literature review
  - Advice from Core Expert Group
  - External comments made to draft guideline

- https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

CDC Guidelines: 1-3 (of 12)

- Non-pharmacologic and non-opioid pharmacologic therapy are preferred for chronic pain.
  - If opioids are used, they should be combined with the above approaches.
- Before starting opioid therapy, clinicians should establish treatment goals including realistic goals for pain and function.
  - An exit strategy should be pre-specified (should benefits not outweigh risks).
  - Continued therapy should be based on meaningful improvement in pain and function.
- Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits.

PEG Score – Average 3 Scores

1: What number from 0-10 best describes your pain in the past week?

2: What number from 0-10 describes how, during the past week pain has interfered with your enjoyment of life?

3: What number from 0-10 describes how, during the past week, pain has interfered with your general activity?

30% improvement from baseline is clinically meaningful

http://mytopcare.org/wp-content/uploads/2013/06/PEG-Pain-Screening-Tool1.pdf

CDC Guidelines 4-6 (of 12)

- When starting therapy, prescribe immediate release opioids instead of extended-release/long-acting (ER/LA) opioids

- When opioids are started, prescribe the lowest effective dosage.
  - Exceed 50 morphine milligram equivalents (MME)/day with caution.
  - Avoid exceeding 90 MME/day.

- When opioids are used for acute pain, prescribe no more than needed for the expected duration of severe pain.
  - Usually 3 days or less
  - Rarely more than 7 days

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

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.

CDC Guidelines 7-9 (of 12)

- Evaluate the benefits and harms within 1-4 weeks of starting therapy or dose escalation and every 3 months thereafter.
  - If benefits do not outweigh harms, taper or discontinue opioids.

- Before starting and periodically during opioid therapy, evaluate risk factors for opioid-related harms: h/o overdose; h/o substance use disorder; dosages > 50 MME/day; concurrent benzodiazepine use.
  - Consider offering naloxone in such cases.

- Use the state Prescription Drug Monitoring Program (PDMP)
  - Before starting and at least every three months thereafter.

CDC Guidelines 10-12 (of 12)

- Use urine drug testing before starting opioids and at least annually during therapy:
  - To assess for prescribed medications
  - To assess for other controlled substances or illicit drugs

- Avoid prescribing opioids and benzodiazepines concurrently.

- Offer or arrange evidence-based treatment for patients with opioid use disorder.
  - Typically medication-assisted treatment (buprenorphine or methadone) plus behavioral therapy.

Nebraska Pain Management Guidance

- Available here: http://dhhs.ne.gov/publichealth/PDMP/Documents/Nebraska%20Pain%20Management%20Guidance%20Document%20v3.2.pdf
- Practical advice on pain management and safer use of opioids.
  - Includes special populations such as children, adolescents, pregnancy, elderly.
  - Tips on having the “difficult conversation” about chronic pain management.
- Contains multiple assessment tools for assessing the risk of opioid dependence as well as for evaluating chronic pain.
- Is concordant with the CDC guidelines.

There’s an App for That…

Download the free Opioid Guideline App today!
https://www.cdc.gov/drugoverdose/prescribing/app.html.

Available on the App Store

ANDROID APP ON Google play

This App, including the calculator, is not intended to replace clinical judgment. Always consider the individual clinical circumstances of each patient.

Example of application in Primary Care

- Nebraska Medicine Midtown Clinic
- Primary Teaching Site for UNMC Internal Medicine Teaching Program
- Patient-Centered Medical Home Certified
  - Integrated behavioral health, social work, and pharmacist support

Chronic pain management approach

- **Patient-centered pain assessment and initial therapy**
  - Physician evaluation of pain and functional limitations
  - Non-opioid approaches preferred and tried first
  - Assessment of risks of opioid therapy and discussion with patients
  - Coordination of pain management plan with other team members

- **Approach to chronic opioid use guided by CDC recommendations**
  - Opioid agreement with explicit dosing limitations
  - Multi-disciplinary pain class required
  - Random urine drug screening
  - Periodic assessment with emphasis on function
  - Limits on dose escalation

Provider and Staff Roles

- Physician
  - Develop and monitor comprehensive pain management plan
- Behavioral health
  - Identify and treat patient psychosocial difficulties
  - Teach skills for coping with pain
- Pharmacy
  - Medication education
  - Design and monitor opioid tapers
  - Comprehensive medication review of pain regimen
- Nurse coordinators
  - Review procedures with patient upon initiation of opioid agreement
  - Goal setting
  - Monitor refill requests for appropriateness
- Social work
  - Access to medication/non-medication resources for pain management

Pain Management Class Goals

- Learn how thoughts, feelings, and behaviors impact pain
- Use pain logs to identify alleviating factors
- Learn coping skills that enhance pain management
- Learn relaxation techniques to help with pain management

- Identify pain medication adverse effects
- Manage expectations of medication effectiveness (focus on functionality)
- Increase awareness of laws concerning controlled substances.
- Understand tolerance, dependence, addiction, overdose.
- Awareness that the ultimate goal of opioid pain medications is to stop them through a controlled taper

Preliminary Outcomes

1. Decreased number of ED visits
2. Decreased positive depression screenings (PHQ-2)
3. Less frustration surrounding opioid refills reported by providers
4. Increased pain medication knowledge and awareness of risk for dependence/ addiction

Summary

- Prescription opioids are overused and abused with consequent morbidity and mortality.
- Chronic pain is common and there are many misperceptions about the optimal way to manage it.
- In general opioids are not the best option for chronic pain.
- Adherence to guidelines for more judicious and safer opioid prescribing may help reduce the epidemic of opioid abuse.
- The optimal approach to chronic pain employs a health care team.

Postscript: What do all these people have in common?

They all died of opioid overdoses

http://www.usatoday.com/story/life/people/2016/06/02/celebrities-who-have-died-addiction/85314450/