

MAT TRAINING

PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Opioids for Pain

Understanding and Mitigating Risks

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Roger Chou Disclosures

- Dr. Chou has received funding from the Centers for Disease Control Prevention and the Agency for Healthcare Research and Quality to conduct systematic reviews on opioid- and pain-related topics, but otherwise has no financial relationships related to the content of this presentation to disclose.

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.

Target Audience

- The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.

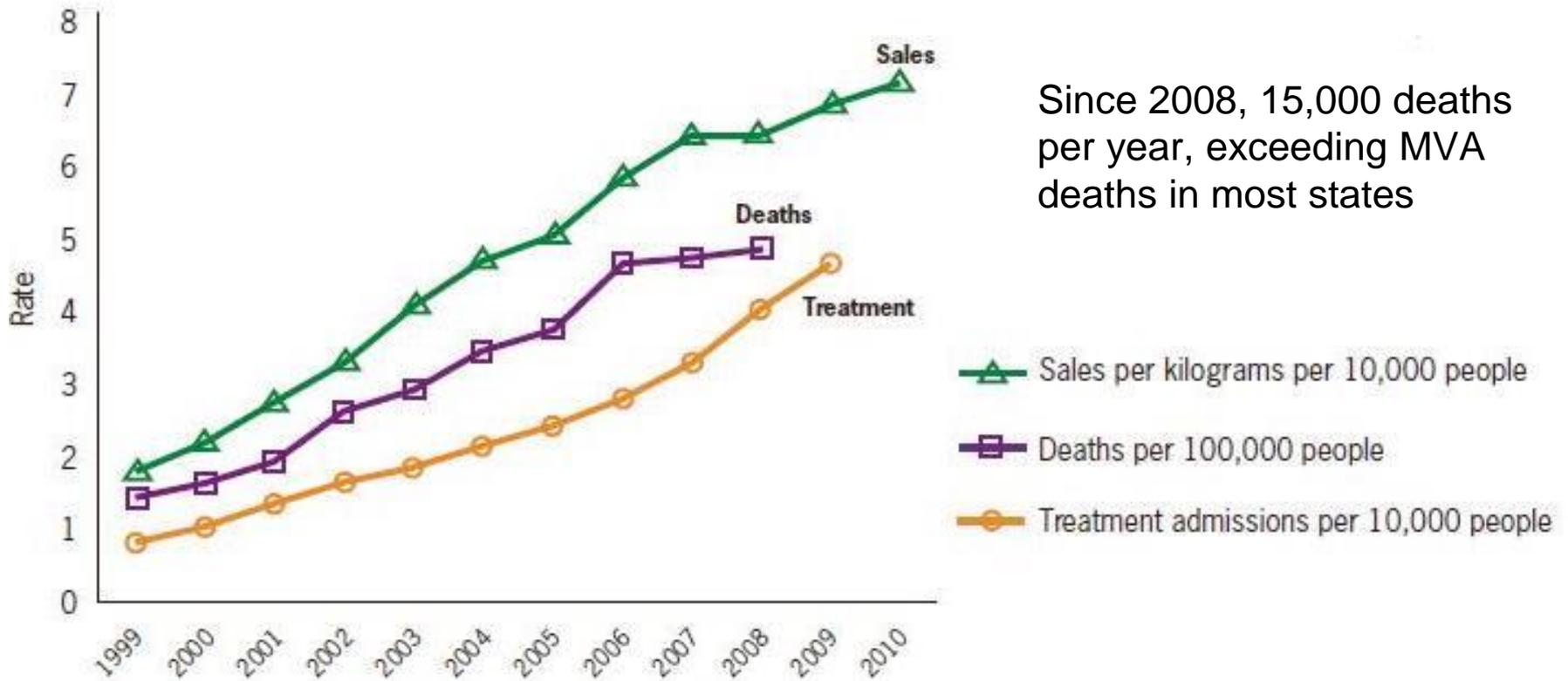
Educational Objectives

- At the conclusion of this activity participants should be able to:
 - Describe risk factors for opioid misuse, opioid use disorder (OUD), and overdose in patients with chronic pain
 - Explain methods for screening and assessment for problematic opioid use
 - Explain methods for monitoring and evaluating patients prescribed opioids for chronic pain to mitigate risks
 - Describe non-opioid treatment approaches for chronic pain

Background

- Chronic non-cancer pain highly prevalent, with substantial burdens
 - Chronic pain: > 3 months
 - Reported by up to 1/3 of adults
- Opioids commonly prescribed for chronic pain
 - 5% of U.S adults on long-term opioids
 - U.S ~ 5% of world's population, use 80% of world's opioids (99% of hydrocodone)
 - Trends indicate prescribing at higher doses, more schedule II
- Opioids: Potential harms to patients as well as to society

Prescription Analgesic Sales, Deaths and Substance Use Disorder Treatment Admissions (1999-2010)



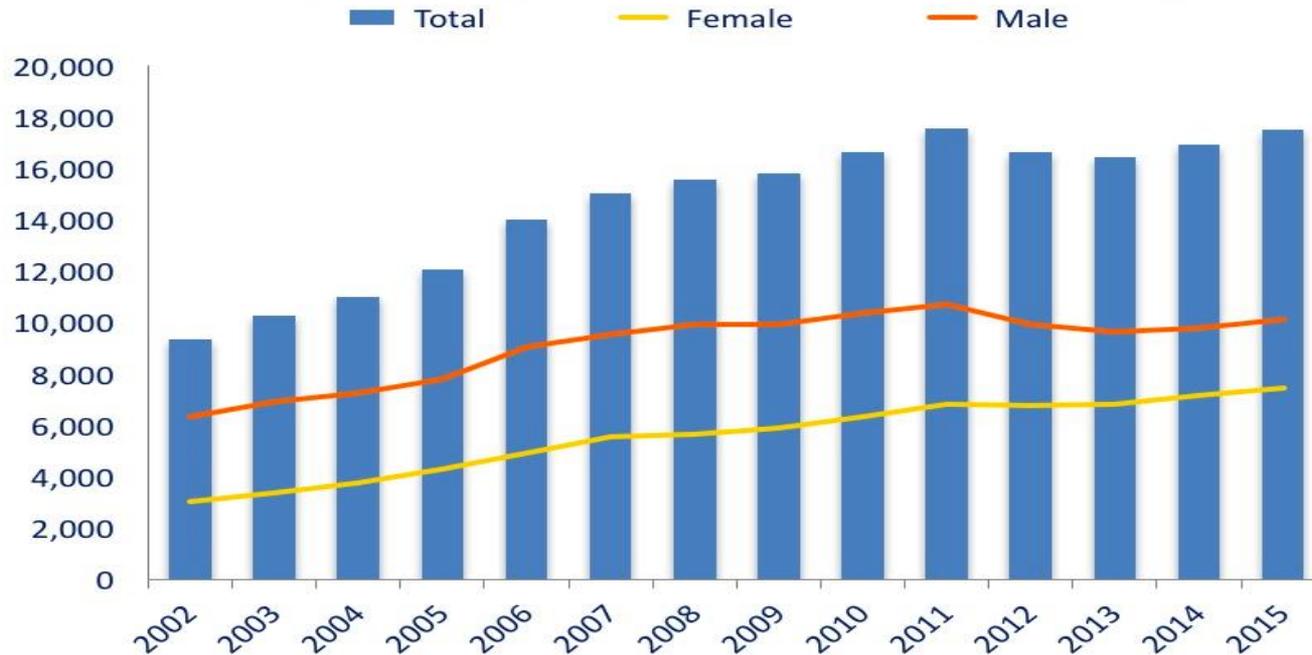
SOURCES: National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009

Risk of Prescription Opioid Overdose



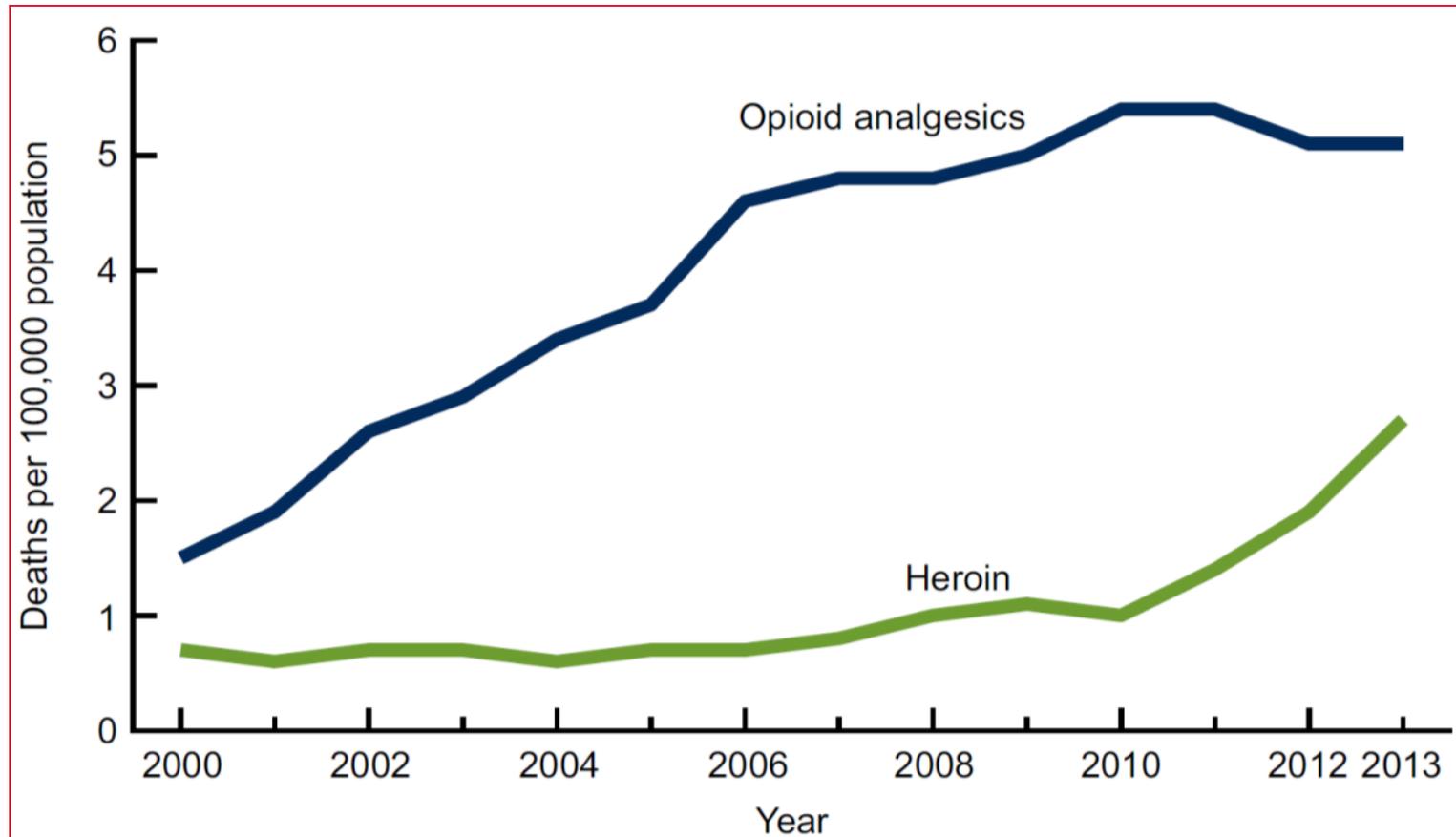
National Overdose Deaths

Number of Deaths from Prescription Opioid Pain Relievers
(excluding non-methadone synthetics)

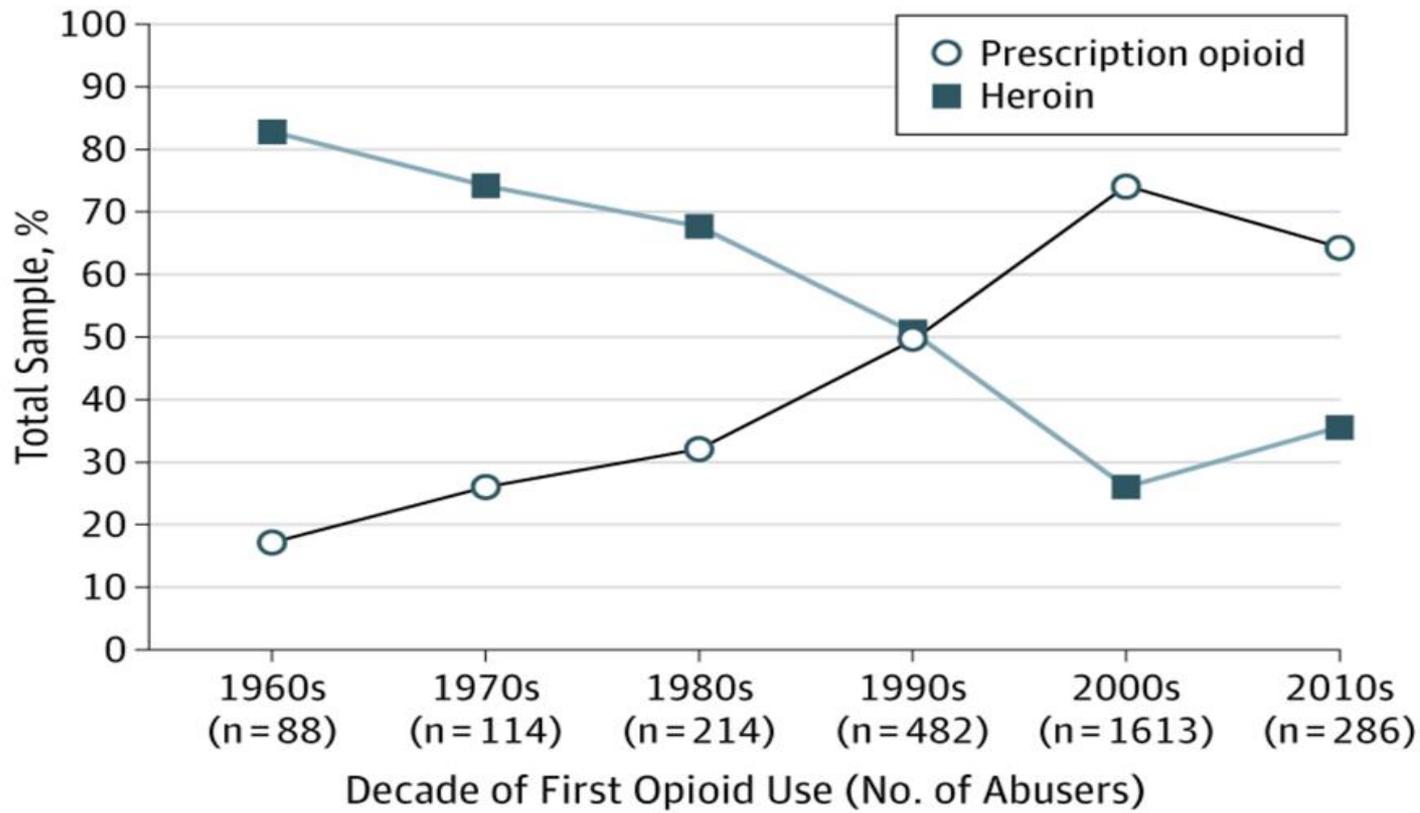


Source: National Center for Health Statistics, CDC Wonder

Opioid Overdose Trends (2000-2013)



First Opioid of Misuse in Those Using Heroin



Opioid Pharmacology

- Opioid mu-receptors mediate analgesic effects and adverse events (AE's)
 - Structure: natural, synthetic, semisynthetic
 - Half-life: 2-4 hours for most, up to 15-60 hours
- Ongoing exposure: tolerance and physical dependence
 - Physical dependence
 - Withdrawal when stopped
 - Tolerance: Higher dose needed to achieve same effects (analgesic and AE's)
 - Individual variability in development of tolerance
 - No theoretical dose ceiling
 - Physical dependence ≠ addiction
 - Addiction is a brain disease characterized by compulsive use

Opioid Misuse in Primary Care



- Likely under-recognized/under-diagnosed
- Published rates of prescription opioid misuse among patients prescribed opioids range from 4% to 26%
 - One study (n=801) based on 2 hour standardized interviews^a
 - 26% purposeful oversedation
 - 39% increased dose without prescription
 - 8% obtained extra opioids from other doctors
 - 18% used for purposes other than pain
 - 20% drinking alcohol to relieve pain
 - 12% hoarded pain medications
- Definitions inconsistent across studies and behaviors evaluated vary in seriousness
- Poorly standardized methods to detect these outcomes
- Data from efficacy trials underestimate risks

Factors Associated With Opioid Overdose in Patients Prescribed Opioids

- Aberrant behaviors
 - Extra doses, unauthorized dose escalation, lost prescriptions, after-hours refill requests, obtaining opioids from multiple prescribers, using unprescribed opioids or other medications/substances, use to treat non-pain symptoms
- Recent initiation of opioids
- Receipt of methadone as an analgesic
- Concomitant use of benzodiazepines
- Substance use disorder
- Psychological comorbidities
- Higher opioid doses

Universal Precautions in Pain Medicine

- Why utilize universal precautions?
 - Predicting opioid misuse is imprecise
 - Protects all patients
 - Protects the public and community health
 - Consistent application of precautions
 - Consistent with clinical practice guidelines
 - Takes pressure off provider
 - Reduces stigmatization of individual patients and bias in management
 - Standardizes systems of care
 - Universal precautions provide a standardized approach while allowing for individualized assessment and management decisions

Common Universal Precautions

- Comprehensive pain assessment including opioid risk assessment
- Formulation of pain diagnosis/es
- Initial opioid prescription should be considered a test or trial; continue or discontinue based on ongoing reassessment of risks and benefits
 - Decision to continue or discontinue opioid therapy should be made regularly (e.g., every 2-3 months)
- Regular face-to-face visits
- Clear documentation

Mitigating Risks Associated with Opioids

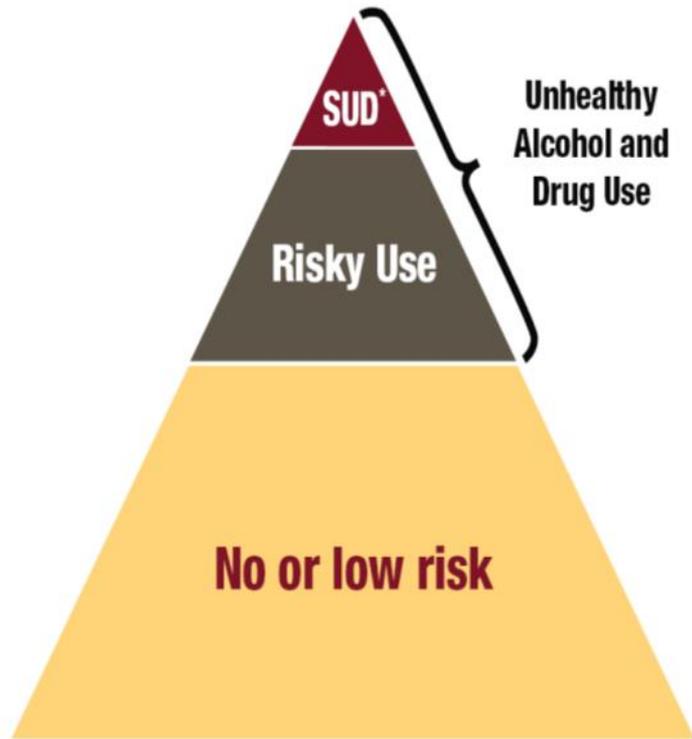
- Careful patient assessment and selection
- Medication agreements
- Avoid higher doses
- Monitoring, including urine drug testing
- Review prescription drug monitoring data
- Avoid sedative-hypnotics (particularly benzodiazepines)
- Addiction, pain, or psychiatric consultation
- More frequent refills with smaller quantities
- Abuse-deterrent formulations
- Naloxone co-prescription
- Evidence on effects of risk mitigation strategies on clinical outcomes (overdose, OUD) is lacking



Patient Selection and Risk Stratification

- Risk assessment in all patients prior to initiating opioids
- Aberrant drug-related behaviors in up to 50% of patients prescribed opioids for chronic pain
 - Strongest predictor personal or family history of alcohol or drug abuse
 - Psychological comorbidities also a factor
- Only consider opioids in patients in whom benefits likely outweigh risks
 - Opioids are not always appropriate
- Tools for risk stratification available

Screening for Unhealthy Substance Use



*Substance Use Disorders

Alcohol

“Do you sometimes drink beer, wine or other alcoholic beverages?”

“**How many times** in the past year have you had 5 (4 for women) or more drinks in a day?”

(positive: > never)

Drugs

“**How many times** in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?”

(positive: > never)

Opioid Misuse Risk Screening Tools

- ORT: Opioid Risk Tool
- SOAPP: Screening & Opioid Assessment for Patients with Pain
- COMM: Chronic Opioid Misuse Measure
- STAR: Screening Tool for Addiction Risk
- SISAP: Screening Instrument for Substance Abuse Potential
- PDUQ: Prescription Drug Use Questionnaire
- No “gold standard”
- Lack rigorous testing

Opioid Risk Tool (ORT)

Mark each box that applies	Female	Male
1. Family history of substance abuse		
Alcohol	<input type="checkbox"/> 1	<input type="checkbox"/> 3
Illegal drugs	<input type="checkbox"/> 2	<input type="checkbox"/> 3
Prescription drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4
2. Personal history of substance abuse		
Alcohol	<input type="checkbox"/> 3	<input type="checkbox"/> 3
Illegal drugs	<input type="checkbox"/> 4	<input type="checkbox"/> 4
Prescription drugs	<input type="checkbox"/> 5	<input type="checkbox"/> 5
3. Age (mark if between 16-45 yrs)	<input type="checkbox"/> 1	<input type="checkbox"/> 1
4. History of preadolescent sexual abuse	<input type="checkbox"/> 3	<input type="checkbox"/> 0
5. Psychological disease		
ADD, OCD, bipolar, schizophrenia	<input type="checkbox"/> 2	<input type="checkbox"/> 2
Depression	<input type="checkbox"/> 1	<input type="checkbox"/> 1
Scoring totals	_____	_____

Administration

- On initial visit
- Prior to opioid therapy
- Predicts misuse behaviors if prescribed opioids

Scoring

- 0-3: low risk (6%)
- 4-7: moderate risk (28%)
- > 8: high risk (>90%)

Screening for Depression

PHQ2

Over the *last 2 weeks*, how often have you been bothered by any of the following problems?

1. Little interest or pleasure in doing things
2. Feeling down, depressed, or hopeless

- **Positive if ≥ 3 points**
 - Test Sensitivity: 83%
 - Test Specificity: 92%



If positive, administer PHQ9

Assess for other Mental Illness (anxiety, PTSD, personality disorders, suicidality)

Medication Agreements

- Informed consent (goals and risks)
- Plan of care
 - Goals of therapy
 - Follow-up and monitoring plan
 - How opioids will be prescribed and refilled
- Signed by both patient and prescriber
- Serves as a patient counseling document and delineates expectations
- Documents plan of care for other clinicians
- Evidence on effects on clinical outcomes lacking

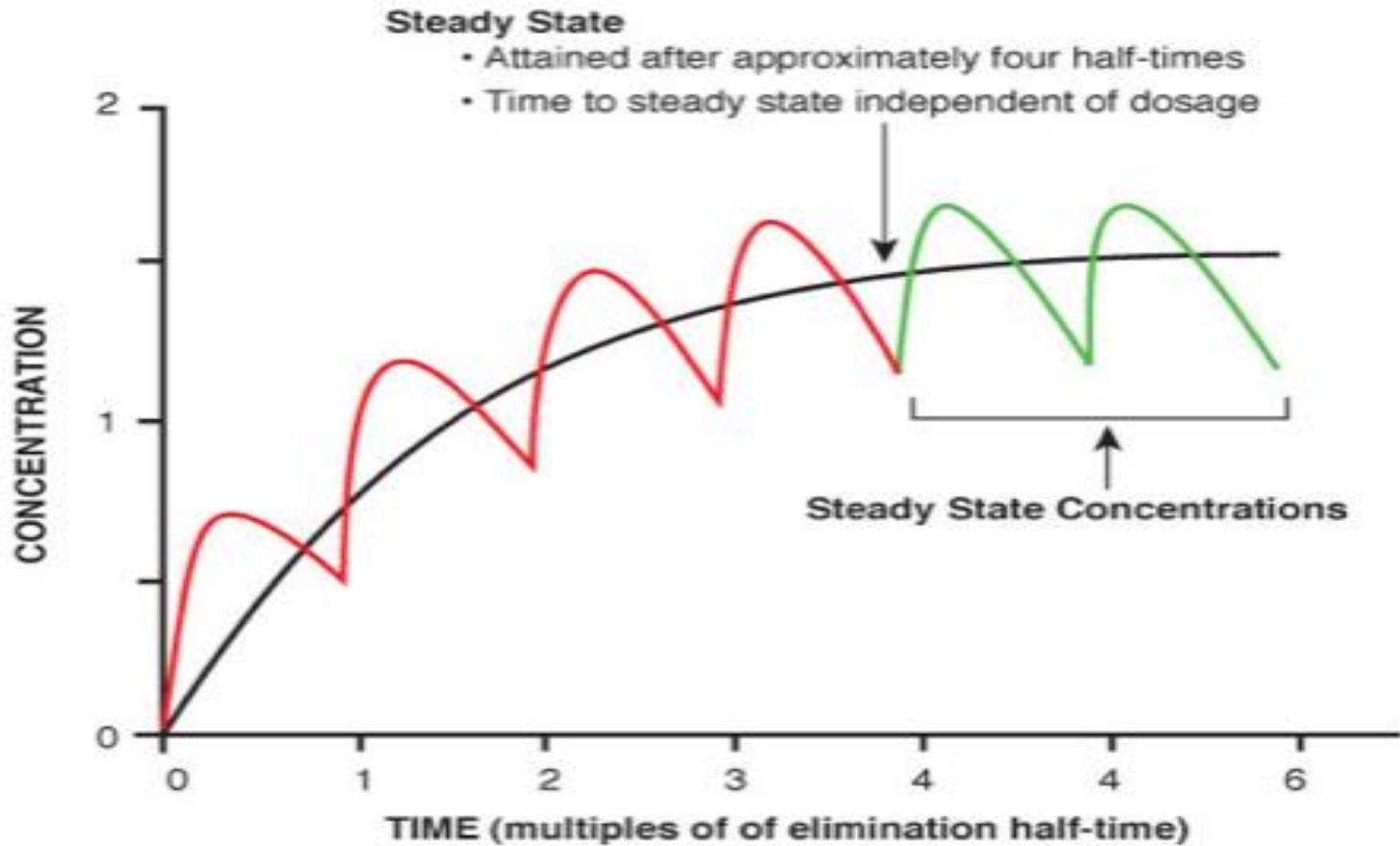
Initiation and Titration of Opioids

- View initial course of opioids as a short-term (e.g., 4 weeks), therapeutic trial
 - The decision to proceed (or continue) with LOT should be a conscious one
 - If opioids are used, should be part of a multimodal strategy
- Start at low doses and titrate cautiously
- Do not initiate therapy with long-acting opioid
 - Insufficient evidence to recommend that all patients be transitioned to round-the-clock, long-acting opioids
- Methadone and fentanyl not recommended as first line options
 - Less predictable and more complicated dosing and pharmacokinetics
 - Buprenorphine is a partial agonist with theoretically lower respiratory risk and might be useful in higher-risk patients; evidence showing decreased overdose risk is lacking and some formulations not approved for chronic pain (only approved for OUD)

Methadone

- Synthetic opioid used for treatment of addiction and pain
- Increased methadone deaths nationwide
 - 1999: 800 deaths → 2008: 4900 deaths
 - 1.7% of opioid rx's in 2009 (9.0% based on morphine equivalent dose [MED]) in 2010^a
 - Involved in 31% of opioid-related deaths, and 40% of single-drug deaths^a
- Half-life 15 to 60 hours, up to 120 hours
 - 60 hour half-life=12 days to steady-state
- Associated with QTc interval prolongation and torsades
 - ECG monitoring at baseline and at higher doses^b

Time to Reach Steady State



Prolonged QTc and Torsades de Pointes

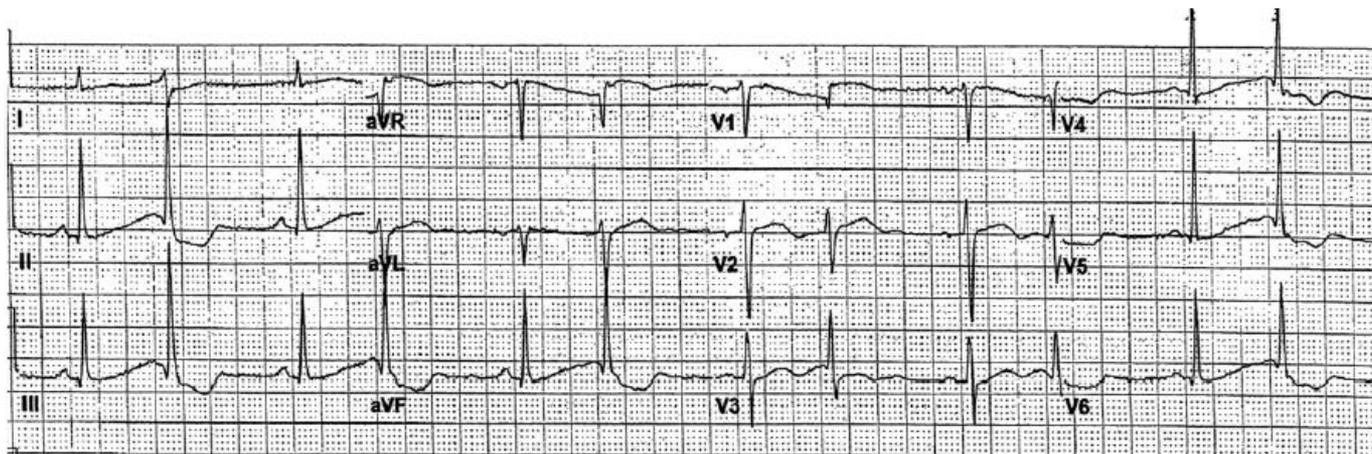


Figure 1 – Admitting ECG shows normal sinus rhythm with atrial bigeminy, nonspecific T-wave abnormality, and QTc prolongation (626 msec).

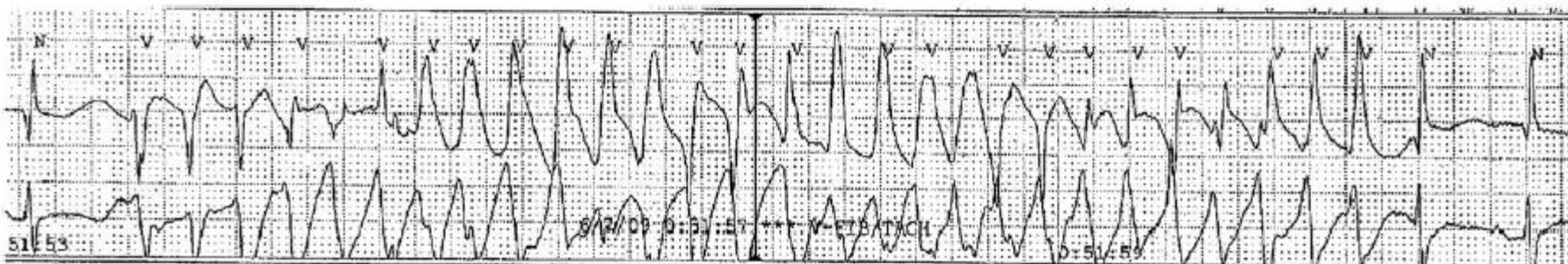


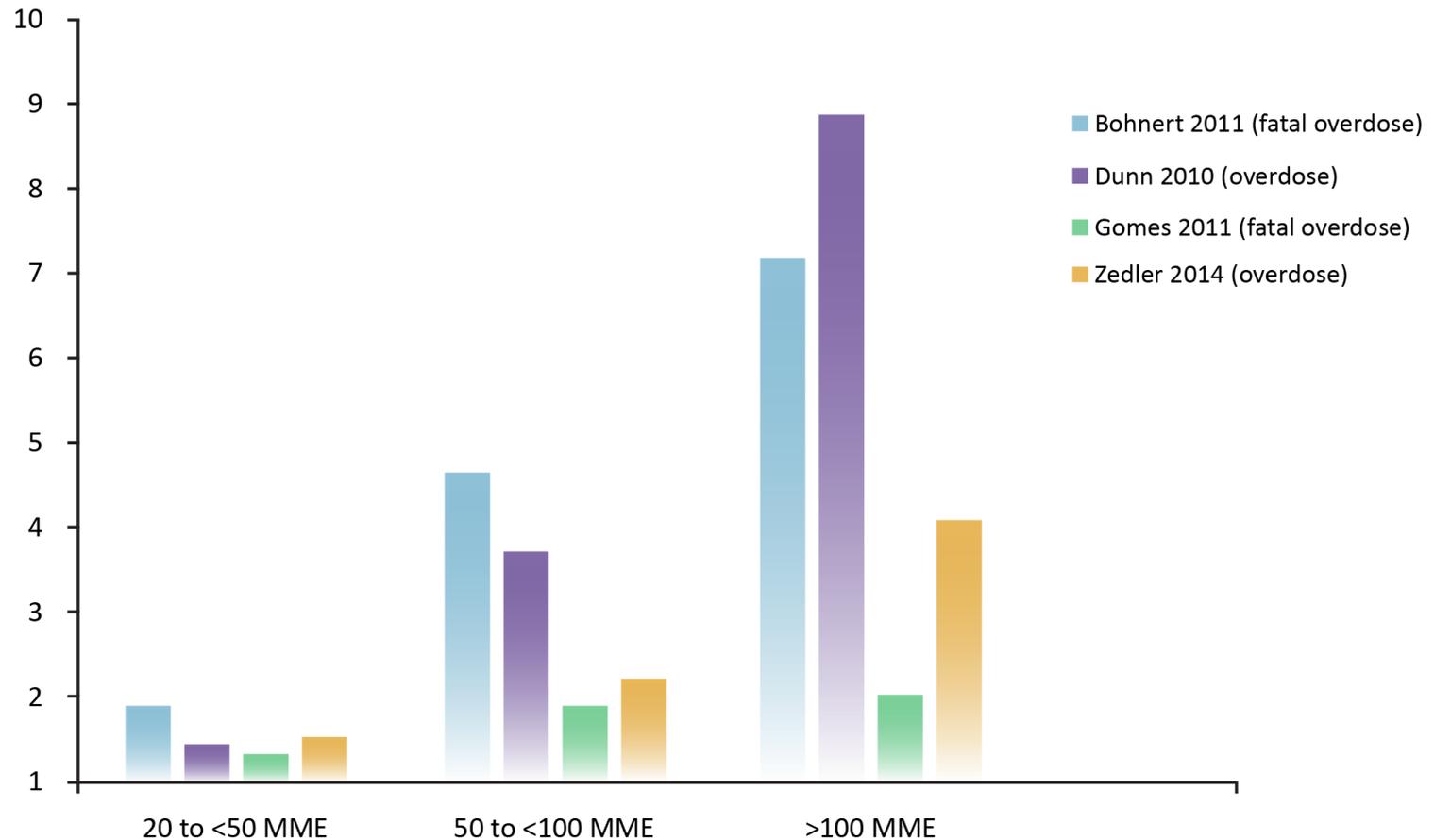
Figure 2 – Rhythm strip shows TdP.

Overdose: Dose-Response Relationship

- Observational studies consistently show an association between opioid dose and risk of overdose or death in patients with chronic pain
- Risk starts to increase at relatively low doses and continues to increase
- Studies matched or adjusted for potential confounders available in administrative databases

Prescribed Opioid Dose (MME) and Risk of Overdose

Odds Ratio or Hazard Ratio for Overdose Relative to 1 to <20 MME



Dosing

- No theoretical ceiling with opioids
 - Benefits of higher doses unclear, ?opioid non-responders
 - Titration to achieve pain relief inconsistent with evidence on benefits
 - Dose-related risk of overdose
- Dose thresholds
 - 2016 CDC guideline: “Caution” at doses >50 MED/day and “avoid” doses >90 MED/day
 - Average dose in overdoses 98 MED/day
 - ~50% of overdoses in patients on <60 MED/day
 - If higher doses used, need for more frequent or intense monitoring and additional risk mitigation strategies

Monitoring Outcomes

- Evaluate patients in multiple domains
 - Focus away from pain as the main goal of treatment
 - No therapy for chronic pain is effective in completely relieving pain
 - Patients can report improvement in pain with no improvement in function
 - Measure function and set functional goals
 - Achievable, measurable
 - Screen for psychological comorbidities
 - Assess sleep issues
 - Screen for substance abuse

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

Urine Drug Tests

- Provides objective information regarding:
 - Self-report unreliable and behavioral observations detect only some problems
 - Evidence of adherence to opioid plan of care
 - Evidence of use or non-use of illicit substances or unprescribed medications
 - May improve adherence
- Perform at baseline and periodically
 - 1-2 times/year for low-risk patients; 3-4 times/year for higher risk
 - Random, scheduled, and /or when concerns arise
 - Discuss expected findings with patient prior to testing
 - Consult with toxicologist/clinical pathologist before acting if patient disputes findings
 - Screening tests requires confirmation
 - Dedicated deceivers can beat the system



Prescription Drug Monitoring Programs

- Available now in almost all states
- Use of PDMPs can identify cases of doctor shopping
- Use of PDMPs variable and generally suboptimal
- PDMPs vary in who can access, information not available across states
- >20 states mandate use before writing for controlled substances (as of June 2014)
- Evidence showing effects of PDMP monitoring on clinical outcomes (overdose, OUD) lacking

Avoid Opioids and Benzo's

- Concomitant benzodiazepine use associated with markedly increased risk of opioid overdose
 - Other medications with respiratory depressant effects may also be associated with similar risks
- Taper benzodiazepines gradually
- Offer evidence-based psychotherapies for anxiety
 - Cognitive behavioral therapy
 - Anti-depressants approved for anxiety
 - Other non-benzodiazepine medications approved for anxiety
- Coordinate care with mental health professionals

Naloxone

- Opioid antagonist that can rapidly reverse opioid overdose; most overdose episodes are witnessed
 - Highly effective in addiction settings
 - Some evidence of effectiveness in chronic pain settings
- CDC recommends for all patients on ≥ 50 MED/day, or other risk factors for overdose
 - Consider for all patients prescribed opioids
- All states have passed Good Samaritan laws providing civil or criminal immunity for administration of naloxone
 - Resources/education: <http://prescribetoprevent.org/>
- Available in FDA-approved IM and IN formulations, also used off-label



Abuse-Deterrent Formulations

- Abuse-deterrent formulations recently approved by FDA or undergoing FDA approval process
 - Designed to be tamper-resistant or co-formulated with medications that reverse opioid effects or produce noxious side effects when tampered with
 - Effectiveness for reducing misuse/substance abuse and improving clinical outcomes unproven
 - Likely to be primarily effective in patients who crush or inject opioids
 - Some patients may seek other prescription or illicit opioids^a

Evaluation of Aberrant Drug-Related Behaviors

- Always evaluate aberrant drug-related behaviors
 - Behaviors vary in seriousness
 - Need to judge seriousness, the cause or causes, likelihood of recurrence, and clinical context
 - Predictors of high likelihood of future aberrant behaviors include 3 or more episodes of aberrant behaviors and sense of “losing control”
 - Serious behaviors include diversion, injecting oral drugs
 - Responses range from patient education and enhanced monitoring to referral to addiction specialist and discontinuation of therapy

Discontinuation of Opioid Therapy

- Taper or wean patients off of long-term opioid therapy [LOT] when they:
 - Engage in serious or repeated aberrant drug-related behaviors or drug abuse/diversion
 - Experience no progress towards meeting therapeutic goals
 - Experience intolerable adverse effects
- Continue to manage pain off opioids
- Have an exit strategy when initiating a trial of LOT
 - Indications for stopping LOT
 - Plans for tapering or discontinuing
 - Reduction in daily dose of 10% per week reasonable starting point
 - Some patients may require slower tapers
 - Know resources for managing addiction and mental health issues



Patients Already on High Doses

- For established patients on ≥ 90 MME/day who meet criteria for taper, initiate taper!
- For patients who do not meet criteria for taper
 - Discuss recent evidence regarding dose-dependent overdose risk
 - Re-evaluate continued use of high opioid dosages
 - Offer opportunity to taper
- Collaborate with the patient on a tapering plan

Opioid Use Disorder

- DSM-5: “A problematic pattern of opioid use leading to clinically significant impairment or distress”
- 2014: 1.9 million Americans with OUD due to prescription drugs, ~600,000 due to heroin
- OUD: Decreased quality of life, negative impacts on morbidity and mortality
- Treatment:
 - FDA-approved medications: agonist (methadone), partial agonist (buprenorphine), antagonist (naltrexone)
 - Block euphoric, sedating effect, decrease craving, mitigate withdrawal
 - Decrease illicit use and misuse of medication, improves social functioning
 - Decrease criminal activity, risks associated with injection drug use

DSM-5 Criteria for 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

Suspected Opioid Use Disorder

- Discuss with your patient and provide an opportunity to disclose concerns.
- Assess for OUD using DSM-5 criteria. If present, offer or arrange medication assisted treatment [MAT].
 - Buprenorphine through an office-based buprenorphine treatment provider or an opioid treatment program specialist
 - Methadone maintenance therapy from an opioid treatment program specialist
 - Oral or long-acting injectable formulations of naltrexone (for highly motivated non-pregnant adults)
- Consider obtaining a waiver to prescribe buprenorphine for OUD (see <http://www.samhsa.gov/medication-assisted-treatment/buprenorphine-waiver-management>) and PCSS waiver offerings

Opioids for Acute Pain

- Opioids generally considered effective for acute pain
 - But, recent data indicates that opioids may be no more effective than an NSAID alone for acute pain
 - In LBP adding oxycodone/acetaminophen to an NSAID did not improve pain or function at 1 week^a
- Use of opioids for “minor” pain associated with increased risk of long-term use
 - Versus no opioid use, opioid within 7 days of minor surgery associated with 44% increased risk of use at 1 year^b
- Prescribing excessive quantities of opioids for acute pain resulting in leftover opioids
 - Source of diversion and unprescribed use
- More judicious use of opioids for acute pain
 - If used, limit opioids to a 3-7 day supply for most acute pain



^aFriedman BW. JAMA 2015;314:1572

^bAlam A. Arch Intern Med 2012;172:425

Opioids for Chronic Pain

- Opioids moderately more effective than placebo for short-term pain relief
 - Effects average 20-30% improvement in pain, 1-2 points vs. placebo
- Data on long-term effectiveness limited
 - Until recently, no placebo-controlled trials >6 months, most trials <8 weeks
 - Uncontrolled studies indicate many discontinuations due to adverse effects (23%) or insufficient pain relief (10%), some patients who continued on opioids experienced long-term pain relief
- Effects on function generally smaller than effects on pain, some trials showed no or minimal benefits
- Optimal results—trials excluded patients at high risk for abuse/misuse, psychological or serious medical comorbidities
- Limited evidence on commonly treated conditions
 - Fibromyalgia, headache, others

SPACE Trial

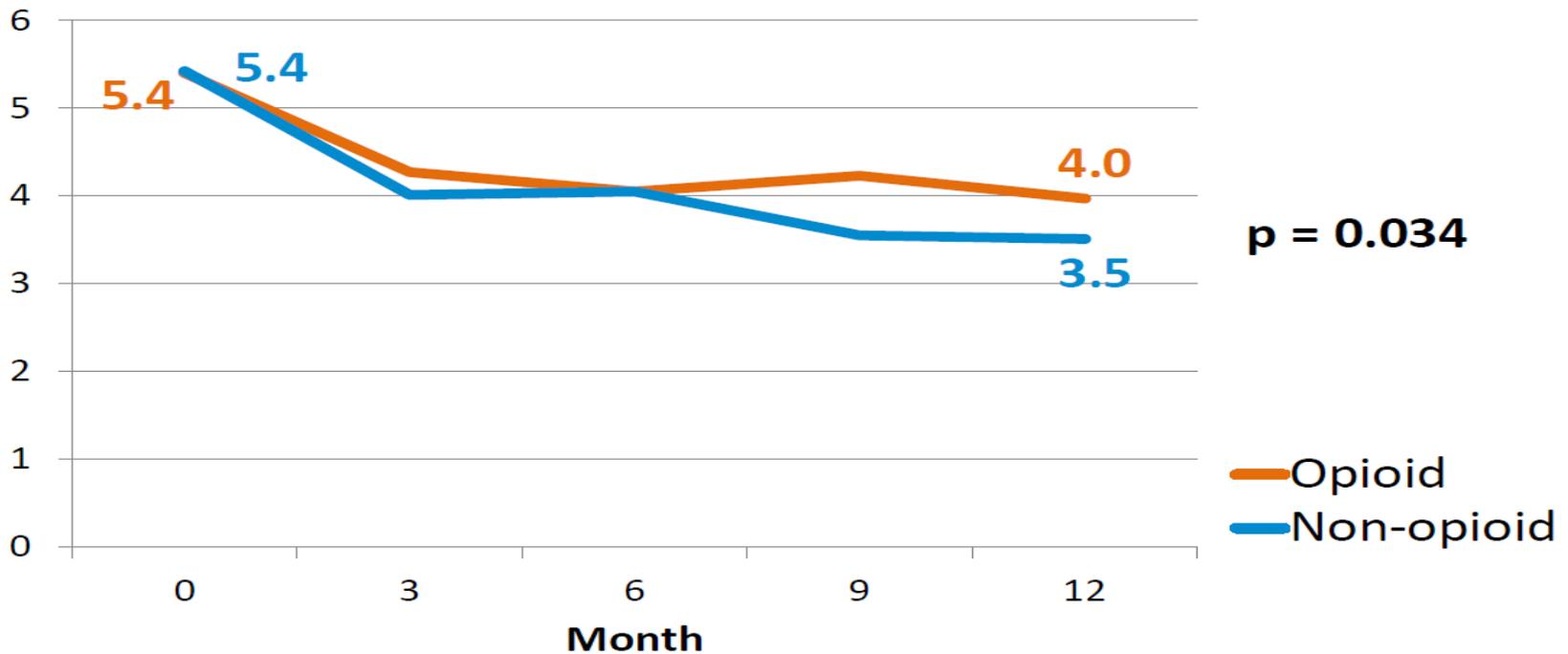
- **RCT of opioid therapy vs. non-opioid therapy for chronic low back pain and osteoarthritis pain (2017)**
 - One year VA trial in primary care, n=240
 - Open-label for patients and clinicians, assessment masked
 - All patients received individualized medication management using collaborative telecare pain management model
 - Opioid daily dose limited to 100 mg morphine equivalents/day
 - At 12 mos: 12% 105-120 mg/day, 23% 75-105 mg/day, 43% 25-75 mg/day, 21% 0-25 mg/day
 - At 12 mos, no difference in function; pain worse in opioid group
 - Clinically significant improvement: Brief Pain Inventory (BPI) interference 59% vs. 61%; BPI severity 41% vs. 54% (p=0.007)
 - Opioids associated with more adverse symptoms; no deaths or OUD

SPACE Trial



Pain intensity

Mean BPI Severity (n=238)

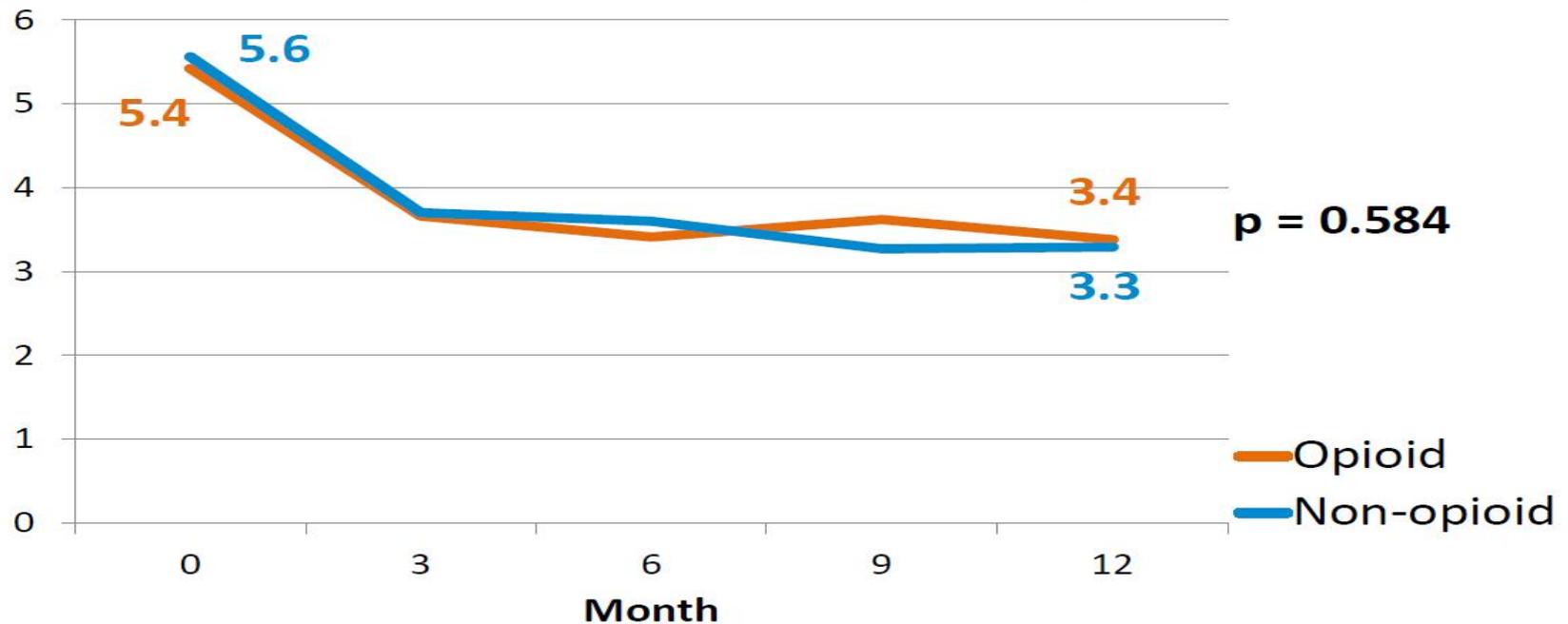


SPACE Trial



Pain interference with function

Mean BPI Interference (n=238)



2016 CDC Guidelines

- **Recommendation #1 (chronic pain)**
 - Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
 - Consider opioid therapy only if expected benefits are anticipated to outweigh risks to the patient.
 - If opioids are used, combine with appropriate nonpharmacologic therapy and nonopioid pharmacologic therapy.
- **Recommendation #6 (acute pain)**
 - When opioids are used for acute pain, prescribe the lowest effective dose of immediate-release opioids and prescribe no greater quantity than needed for expected duration and severity of pain (usually 3 to 7 days)

Approach to Treatment of Pain

- Acute pain
 - Avoid prescribed bed rest, early return to activity as able, heat/cold, OTC analgesics
 - Identify and address psychosocial risk factors early to help prevent transition to chronic pain
- Chronic pain
 - Focus on functional goals and improvement, not just pain
 - Self-care (coping skills, relaxation/meditation, activity/exercise)
 - Identify and address psychosocial contributors to pain
 - Depression, anxiety, PTSD
 - Sleep issues



Non-Opioid Therapies for Pain

- A number of non-opioid therapies are similarly or more effective than opioids, and safer
 - Opioids ≠ effective/good pain management
- Prioritize active over passive modalities
 - Biopsychosocial understanding of chronic pain
 - Active therapies: Psychological treatments, exercise, interdisciplinary rehabilitation, mind-body interventions
 - Actively engage patients with focus on improving function
 - Passive therapies: Medications, physical modalities, complementary and alternative treatments, interventional treatments
 - Main focus is symptom relief
 - Use as an adjunct or bridge to active therapies
- Costs, availability, patient adherence

Cognitive Behavioral Therapy

- **Psychological therapy that integrates:**
 - Cognitive therapy
 - Restructures maladaptive thinking patterns
 - Behavioral therapy
 - Replace undesirable with healthier behaviors
- **Effective for improving pain, disability, mood, maladaptive behaviors**
 - Some effects appear sustained
 - More effective in persons with psychosocial risk factors

Meditation/Relaxation

- Helpful technique for self-management and coping
 - Incorporates some CBT principles
- Distraction, reduce anxiety, reduce sympathetic arousal, reduce muscle tension, altered central processing
- Evidence on effectiveness increasing
 - Mindfulness-based Stress Reduction similarly effective to CBT
- Varied techniques
 - Meditation
 - Progressive muscle relaxation
 - Hypnosis
 - Guided imagery
 - Yoga, Tai Chi—movement-based therapies that incorporate meditation or relaxation principles
 - Related: Biofeedback

Exercise

- Effects on pain and function (and general health!)
 - Impact on fear avoidance behaviors (hurt does not equal harm)
- Many different types for exercise
 - Aerobic, strengthening, stretching, mixed
 - McKenzie, motor control and stabilization, active trunk exercise, others
 - Supervised vs. home, group vs. individual
 - Related: Alexander technique, Pilates, yoga, Tai Chi, others
- Ideally done within a CBT-informed framework
- No technique clearly superior
 - Supervised, individualized exercise programs more effective initially?
 - Handouts and videos for home exercise
 - Start slow, incremental increases; goal is sustained engagement



Interdisciplinary Rehabilitation

- Combines at a minimum psychological treatments and exercise
 - Provided by professionals from at least two different specialties
 - Focus on improvement in function
- Components and intensity of interdisciplinary rehabilitation vary
- More effective than non-interdisciplinary rehab, some evidence of sustained effects
- Lack of availability and reimbursement important barriers
 - May be most effective in persons who fail standard therapies, severe functional deficits, severe psychosocial risk factors

Passive Therapies

- Physical modalities: Evidence limited and difficult to show consistent or sustained benefits
 - Heat similarly effective to NSAIDs for acute LBP
 - Other modalities not generally recommended
- Manipulation, acupuncture, massage: Some evidence of benefit for certain pain conditions
 - Some effects likely non-specific and related to “hand-on” nature
 - If used, as adjunct to active therapies
 - Be aware of costs and discontinue if ineffective in initial trial
 - Expectations of benefit can predict effectiveness
 - Enhanced access to complementary and alternative therapies through the Affordable Care Act

Medications

- Acetaminophen and NSAIDs first-line therapies for many conditions; benefits modest
- Tramadol and tapentadol: Dual mode of action (opioid receptor and centrally acting); tramadol schedule IV and tapentadol schedule II
- Gabapentin and pregabalin: First line for neuropathic pain (pregabalin schedule V); off-label for non-neuropathic pain
- Antidepressants: SNRI's first line for neuropathic pain; TCA's with anticholinergic and cardiac AE's
 - Duloxetine approved for fibromyalgia and chronic back pain
- Skeletal muscle relaxants: Sedating, short-term use for acute pain
 - Cyclobenzaprine (similar to TCA) and tizanidine (similar to clonidine) best-studied
- Benzodiazepines: Avoid!
- Topical lidocaine for neuropathic pain, topical NSAIDs for localized OA

Conclusions

- Very limited data on long-term benefits of opioid therapy, with some evidence showing no benefits versus non-opioid therapy
- Accumulating evidence on serious harms of long-term opioid therapy that appear to be dose-dependent
- Benefits appear limited and harms are significant, suggesting a close balance of benefits to harm
- A more cautious approach to use of opioids for pain is indicated
- Universal precautions, including risk assessment, patient selection, monitoring, and risk mitigation strategies
- Non-opioid therapies preferred
- Assess for and treat opioid use disorder; training for prescribing buprenorphine in office-based settings available

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