



SCOPE of Pain

Safe and Competent Opioid Prescribing Education

| | |
|--------------------|--|
| Trainers | <ul style="list-style-type: none">• Donald Harrell• Meg Rumfield• Claire Saadeh• Karel Schram |
| Venue: | Joint Provider Surveyor Training |
| City: | Grand Rapids |
| State: | Michigan |
| Date: | Tuesday, April 1, 2014 |
| Disclosure: | None of the trainers have anything to disclose |

Part 1 of 3



Overview



- **42 year old female**
- **Hypertension**
- **Type 2 diabetes with painful neuropathy**
- **Chronic low back pain**

Past Medical History

- **Type 2 diabetes mellitus x 8 years**
 - Painful diabetic neuropathy x 2 years
- **Hypertension**
- **Chronic low back pain**
- **Tobacco dependence**
- **Alcohol dependence (in recovery 10 yrs)**
- **Obesity**



Mary Williams
Case Study

Current Medications

- **Metformin** 1000 mg 2x/day
- **Lisinopril** 10 mg 1x/day
- **Hydrochlorothiazide** 12.5 mg 1x/day
- **Aspirin** 81 mg 1x/day

Current Pain Medications

- **Oxycodone/APAP** 5mg/325 mg
1-2 tablets every 4-6 hours
- **Gabapentin** 300 mg 3x/day



***Previous* Pain Medications**



- **NSAIDs** (inadequate pain relief and upset stomach)
- **Acetaminophen** (inadequate pain relief)
- **Tricyclic antidepressants** (inadequate pain relief and dry mouth)
- **Tramadol** (inadequate pain relief)
- **Acetaminophen with codeine** (inadequate pain relief)

Mary Williams

Case Study

Social History



- **Receptionist** - law office 20 hrs/week
- **Married** - husband manages hardware store
- **Children** - ages 6, 12 and 15 years

Substance Use History

- **Alcohol dependence** (in recovery for past 10 years)
- **Tried marijuana** in high school
- **No recent history of illicit drug use**
- **Smokes tobacco** 1 pack per day for the past 25 years

Family History

- **Family history of substance abuse**
 - Mother died from complications of alcoholic cirrhosis

Assessing Chronic Pain and Opioid Misuse Risk



Learning Objectives: Presentation 1

- Discuss prevalence of chronic pain in the US
- Discuss prevalence of the use and misuse of opioid analgesics
- Describe the pharmacology, efficacy and safety of opioid analgesics
- Describe the components of a thorough opioid misuse risk assessment for a potential candidate for chronic opioid therapy

Mary Williams Case Presentation

- Visiting provider for first time
- Previous PCP moved out of state

Takes 4 to 8 oxycodone/APAP tablets per day for chronic pain

- Makes it possible for her to go to work

Best pain relief 8 tablets per day

- Previous PCP limit of 150 tablets per month
- Afraid she would become “addicted”

She hopes to get enough medication to consistently take 8 tablets per day

Mary Williams Case Presentation

***Very careful
not to run out
early***

***Gets anxious
if supply runs
out early in
month***

***Nausea,
vomiting and
diarrhea
upon running
out***

***Has enough
medication to
last one week***

***Brought in her
previous
medical
records***

Mary Williams Case Presentation

- **Severe pain in feet**
Burning, numbness and tingling
- **Trouble sleeping** and “**depressed**”
because of her chronic pain
- Pain **worse at night**
- Due to only taking 3-4 tablets/day
because it is end of month

**States pain
is “20”
on a scale
of 0 - 10**

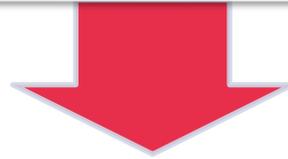
Assessing Pain



Building Trust

Patient Issues

Patients will assume that
you don't believe their pain complaints

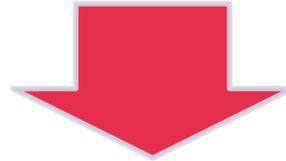


Often demonstrated by
exaggerating pain scores

Building Trust

Patient Issues

Some patients with adequate pain relief
Believe it is not in their best interest to report pain relief



Fear that medication will be reduced

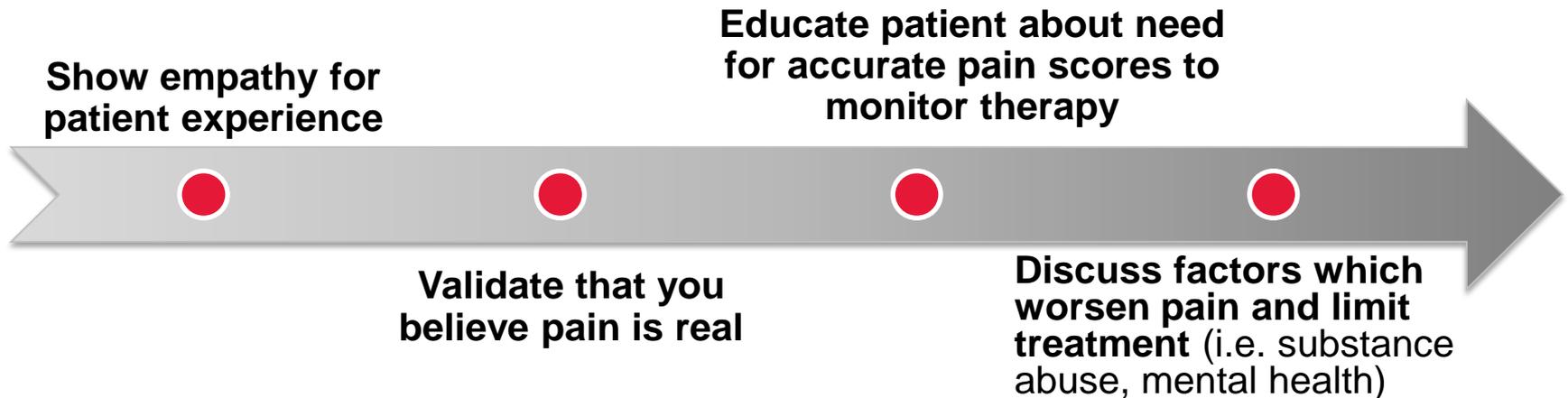


Fear that physician may decrease efforts
to diagnose problem

Building Trust

Provider Strategies

- Assume patient fears you think pain is not real or not very severe
- After you take a thorough pain history...



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

Pain Assessment

- Pain scales
 - Numeric rating
 - Visual analog
 - Faces scale

Mary Williams

Case Study

PEG Scale Assessment

In the past week:



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Case Study

Physical

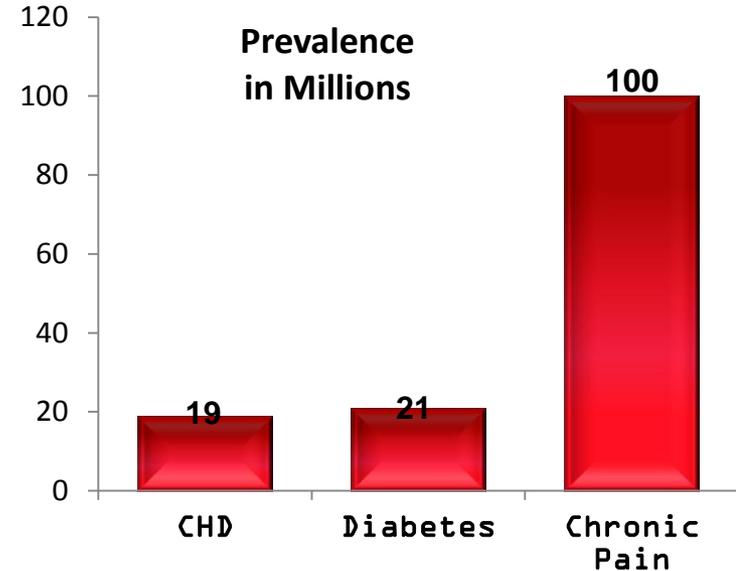


- Normal vital signs
- Weight 220 lbs (BMI 32 = obese)
- No acute distress
- Normal cardiopulmonary exam
- Spine normal alignment, negative straight leg test
- No Achilles tendon reflex bilaterally
- Diabetic foot exam:
 - No lesions/ulcerations
 - Palpable pulses
 - Monofilament testing bilaterally 4/5

Scope of the Problem

100 Million in U.S. with Chronic Pain

- 42% with pain lasting over one year
- 33% report pain as disabling
- 63% have seen primary care physician for help



\$600 Billion Annual Costs

- Healthcare expenses
- Lost income
- Lost productivity

Chronic Pain is Complex

Genetic Predispositions

- Structure and function of the nervous system
- Molecular basis for response to pain and/or analgesia

Environmental Stressor Effects

- Work, home

Social Effects

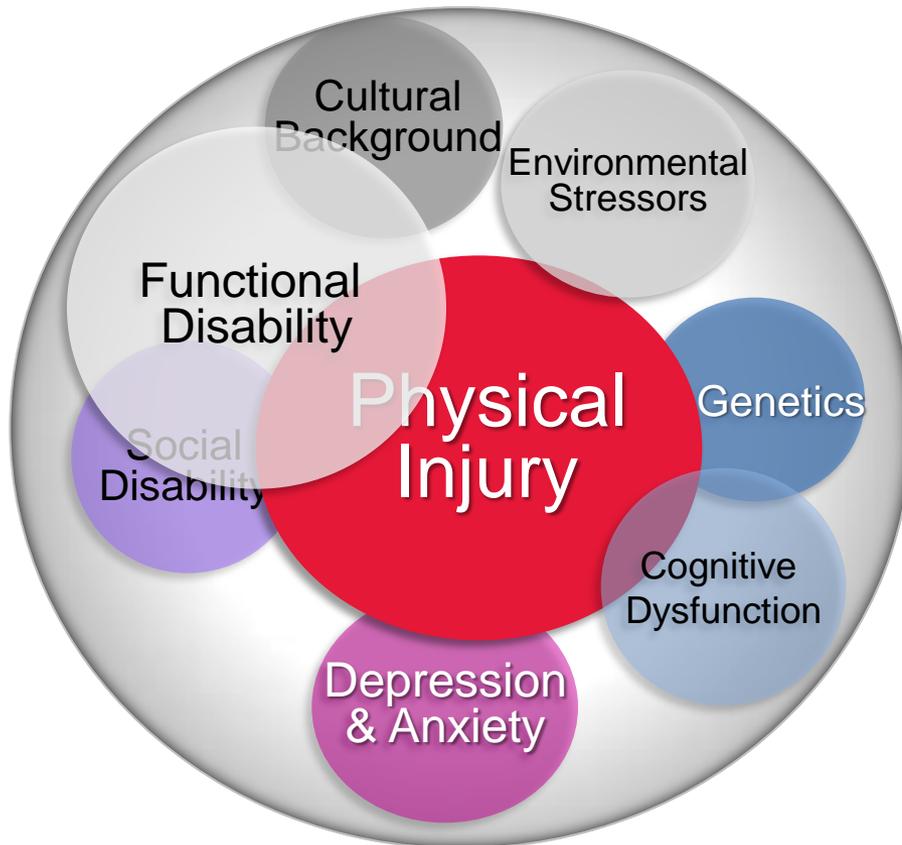
- Socially determined constructs of pain, suffering and disability
- Beliefs about pain treatment

Chronic Pain Affected by Co-Morbidities

| Condition | Incidence Chronic Pain Patients | References |
|----------------------------|------------------------------------|------------------------------|
| Depression | 33 - 54% | Cheatle M, Gallagher R, 2006 |
| | | Dersh J, et al., 2002 |
| Anxiety Disorders | 16.5 - 50% | Knaster P, et al., 2012 |
| | | Cheatle M, Gallagher R, 2006 |
| Personality Disorders | 31 - 81% | Polatin PB, et al. 1992 |
| | | Fischer-Kern M, et al., 2011 |
| PTSD | 49% veterans 2% civilians | Otis, J, et al., 2010 |
| | | Knaster P, et al., 2012 |
| Substance Use Disorders | 15 - 28% | Polatin PB, et al. 1992 |
| | | Cheatle M, Gallagher R, 2006 |

Psychiatric Co-Morbidities

Patient "A" Pain 8/10



Screening for Unhealthy Substance Use

Alcohol

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

Screening for Mental Illness

Patient Health Questionnaire (PHQ 2, PHQ 9)

Other psychiatric history – anxiety, PTSD

Suicidal, homicidal

Mental status and competency

Screening for Depression

PHQ2 Patient Health Questionnaire

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

- **Interpretation**
 - Positive if 3 or more points
- **Administer PHQ9 if positive**
- **Efficacy**
 - Test Sensitivity: 83%
 - Test Specificity: 92%

Scoring:

| | |
|---|-------------------------|
| 0 | Not at all |
| 1 | Several days |
| 2 | More than half the days |
| 3 | Nearly every day |

Mary Williams Case Study

Screenings: Substance Abuse and Depression

- Screened negative for unhealthy substance use and depression



Opioid Pharmacology



When are Opioids Indicated?

Pain is moderate to severe

Pain has significant impact on function

Pain has significant impact on quality of life

Non-opioid pharmacotherapy has failed

If already on opioids, is there documented benefit

Mary Williams

Case Study



YES Pain is moderate to severe

YES Pain has significant impact on function

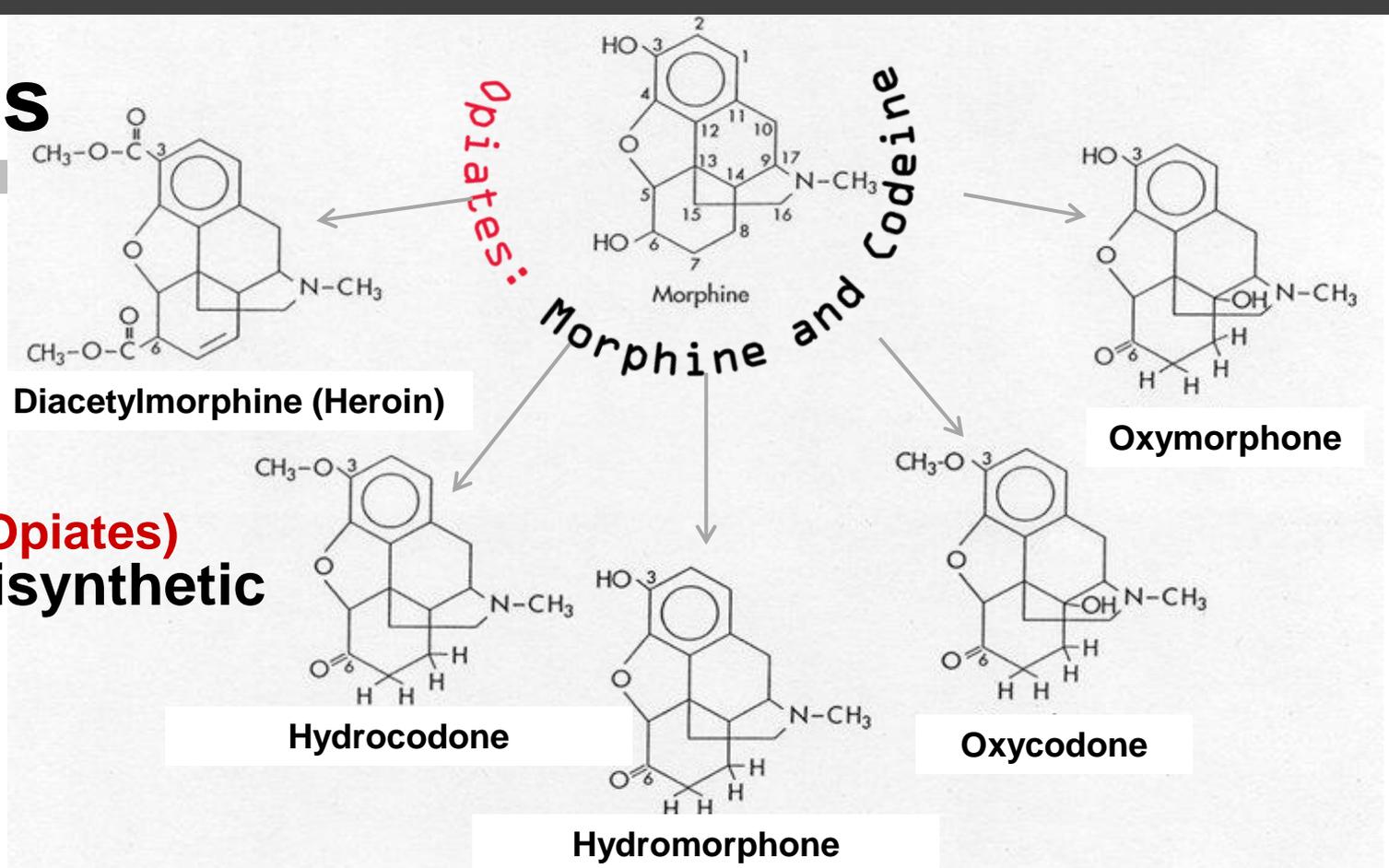
YES Pain has significant impact on quality of life

YES Non-opioid pharmacotherapy has failed

NOT KNOWN

If already on opioids, is there documented benefit

Opioids



**Natural (Opiates)
and Semisynthetic**

Opioid Chemical Classes with Examples

Phenathrenes *prototypical opioids*

- Morphine, Codeine, Hydromorphone, Hydrocodone, Oxymorphone, Buprenorphine

Benzomorphans

- Pentazocine

Phenylpiperidines

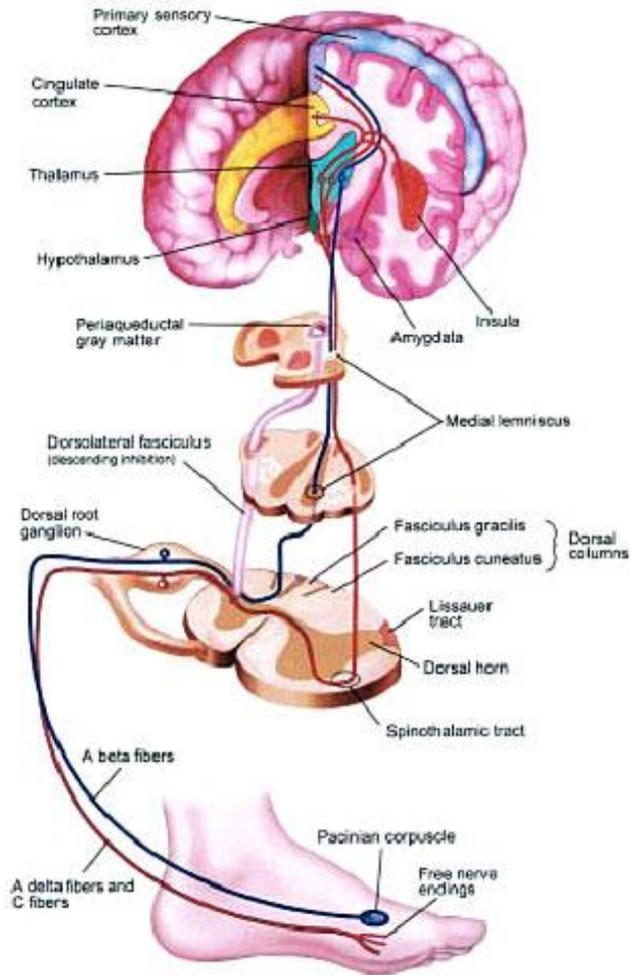
- Fentanyl

Diphenylheptanes

- Methadone

Activation of Mu Receptors

Opioid Pharmacodynamics



- Turn on descending inhibitory systems in the midbrain
- Prevent ascending transmission of pain signal
- Inhibit terminals of C-fibers in the spinal cord
- Inhibit activation of peripheral nociceptors

How Good are Opioids for Chronic Pain?

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

Ballantyne JC, Mao J. N Engl J Med. 2003 Nov 13;349(20):1943-53.

Kelso E, et al. Pain. 2004 Dec;112(3):372-80.

Eisenberg E, McNicol ED, Carr DB. JAMA. 2005 Jun 22;293(24):3043-52.

Furlan AD, et al. CMAJ. 2006 May 23;174(11):1589-94.

Noble M, et al. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD006605.

Variable Response to Opioids



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

Variable Response to Opioids

Mu Receptor

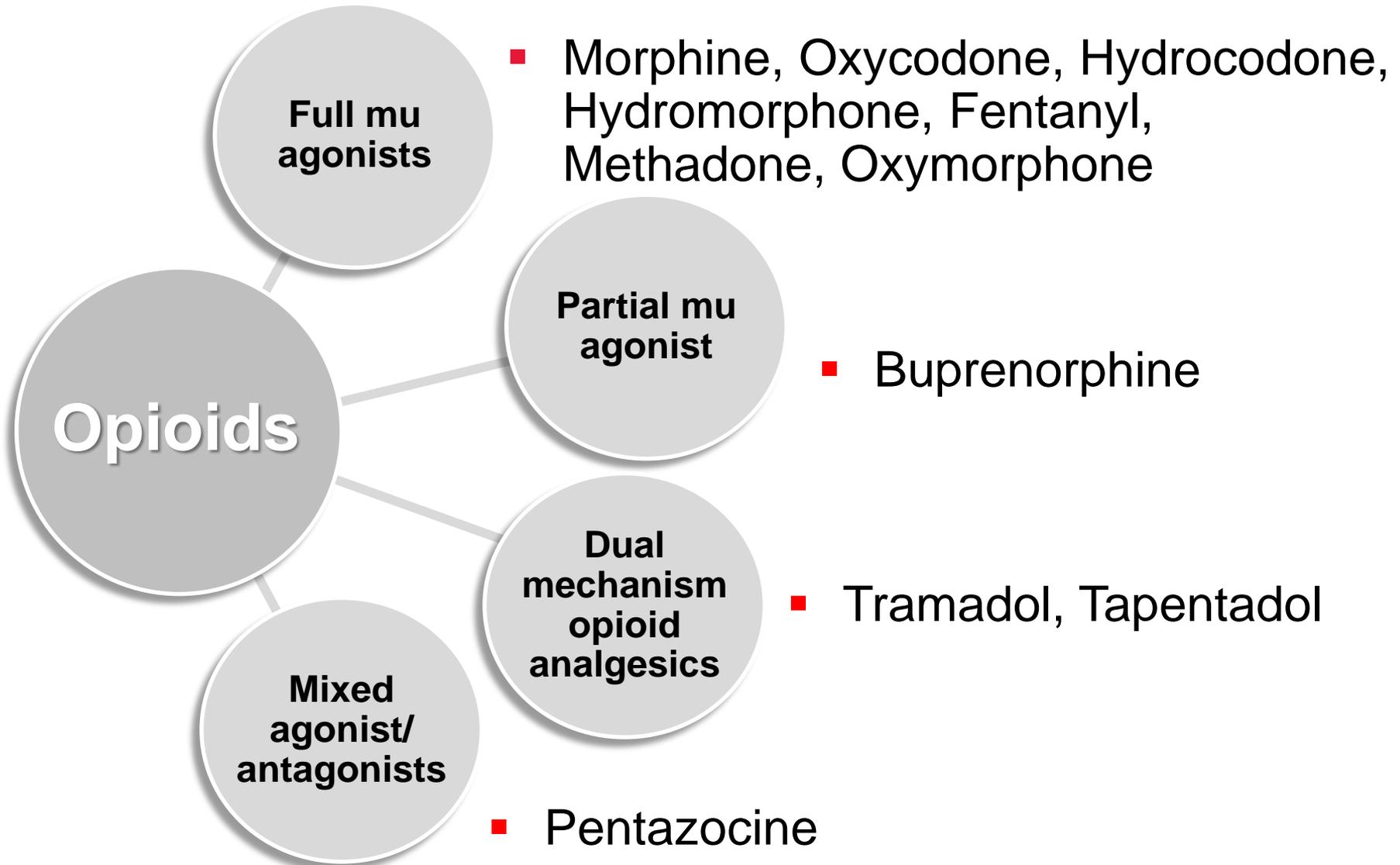
- G protein-coupled receptor family, signal via second messenger (cAMP)
- >100 polymorphisms in the human MOR gene
- Mu receptor subtypes

Variable Response to Opioids

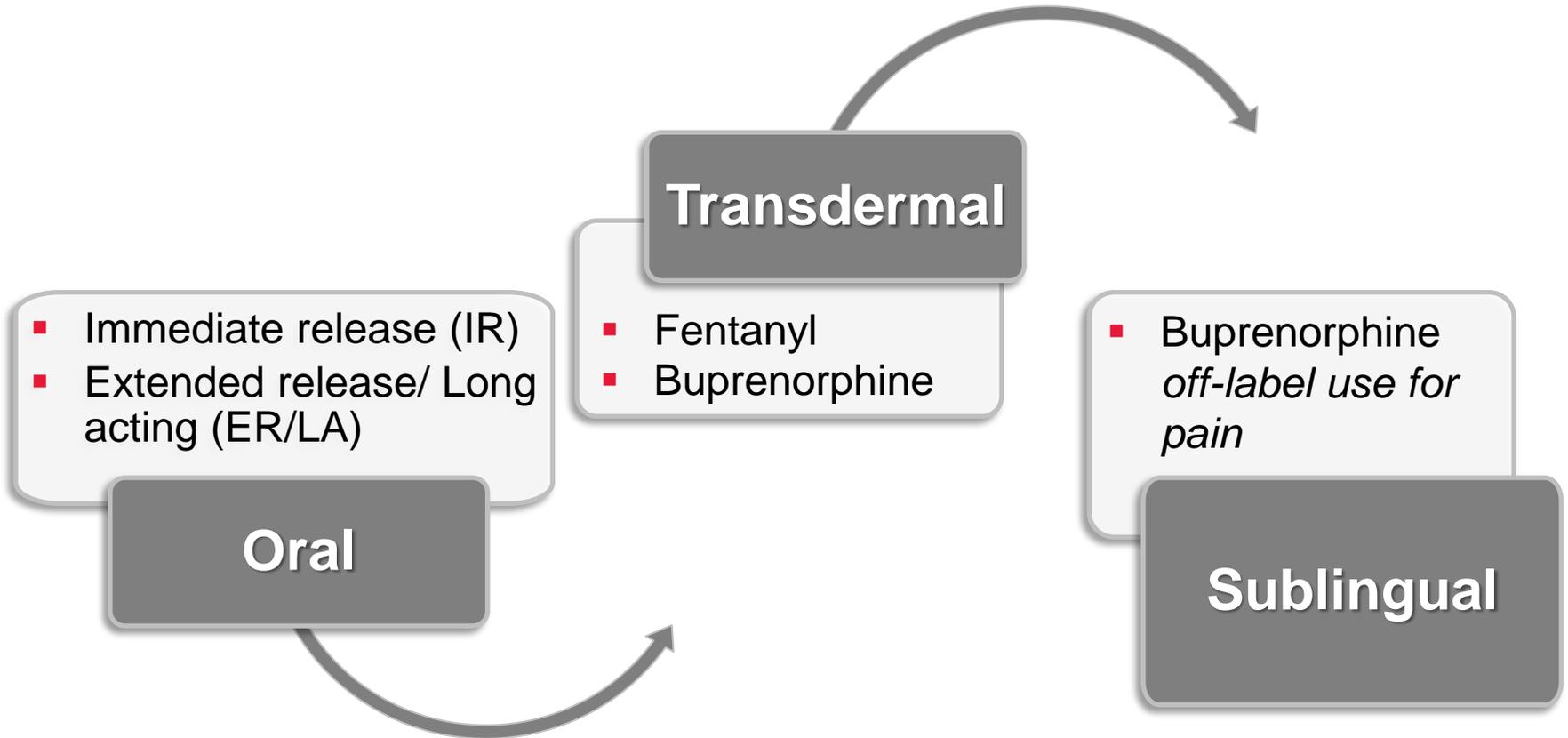
Opioid Pharmacokinetics

- Opioid metabolism differs by individual opioid and by individual patient
- Most opioids are metabolized by the cytochrome P450 (CYP) system
 - Codeine may be ineffective in ~10% of Caucasians due to genetic polymorphisms in CYP2D6
- Trial of several opioids may be needed to find acceptable balance between analgesia and tolerability

Opioid Choices with Examples



Opioid Formulations and Routes



Transdermal Preparations

- Fentanyl and Buprenorphine
- Convenient dosing
 - Fentanyl every 72 hours
 - Buprenorphine every 7 days
- Slow onset and delayed offset
- Requires predicable blood flow and adequate subcutaneous fat
- Absorption is altered with fever, broken skin, edema
- Some with metal foil backing and not compatible with MRI

Opioid Choice

Immediate Release (IR)

- Morphine
- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone
- Tramadol
- Tapentadol

- Codeine

Extended Release / Long-acting (ER/LA)

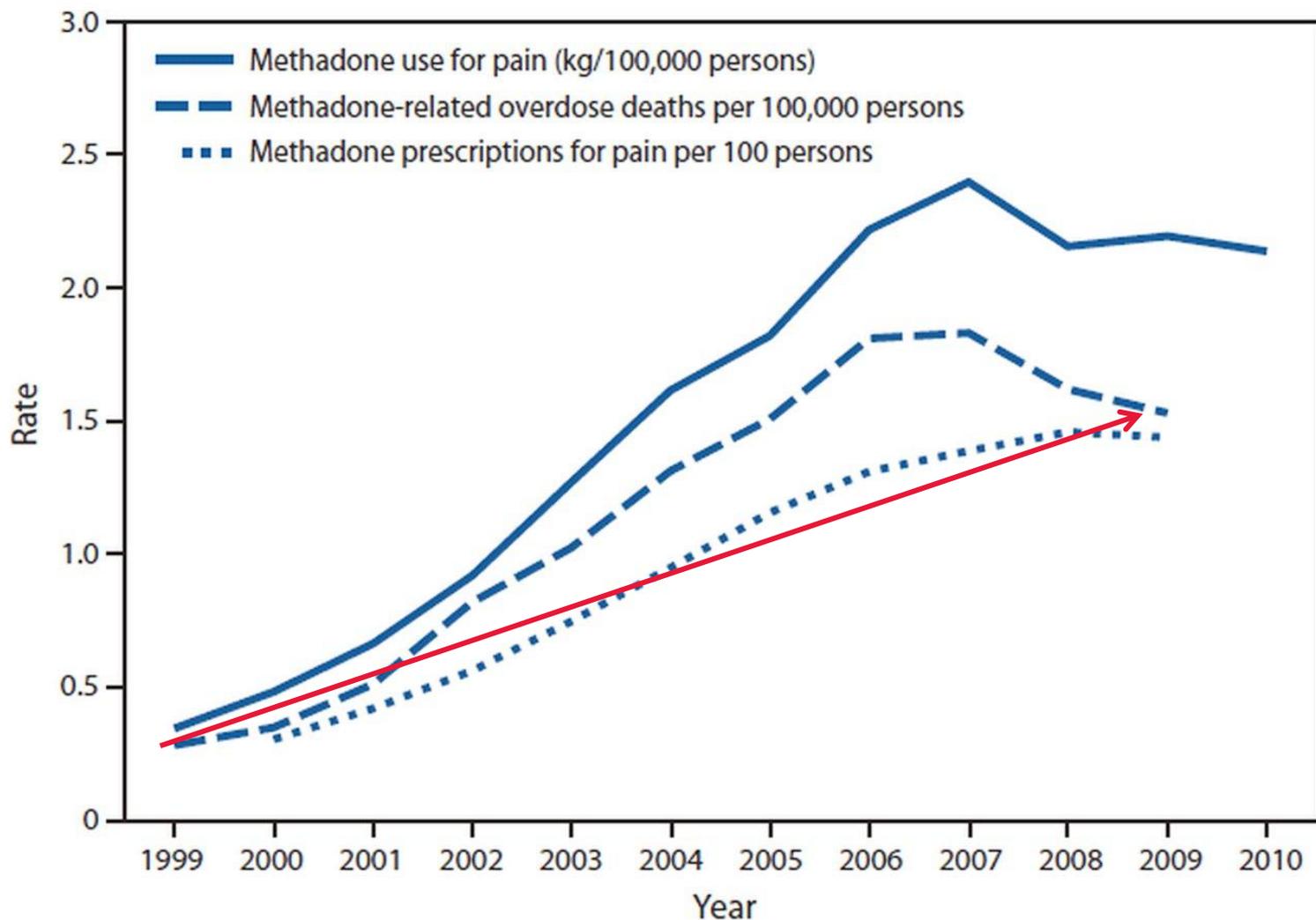
- Morphine
- Hydrocodone
- Hydromorphone
- Oxycodone
- Oxymorphone
- Tramadol
- Tapentadol

- Methadone
- Fentanyl transdermal
- Buprenorphine transdermal

Selected Opioids With Unique Properties



Methadone is Different



Methadone is Different

The problem...

- Long, variable, unpredictable half-life
 - Analgesia 6-8 hours
 - Serum $t_{1/2}$ 20-100 hours
- QTc prolongation, risk of torsade de points

Some possible advantages...

- Mu opioid agonist, NMDA receptor antagonist
 - Potentially less tolerance, better efficacy in neuropathic pain
- No active metabolites
- Inexpensive, small dosage units (5mg tablets)

Dual Mechanism Opioids

Tramadol

- Mu-opioid agonist and NE and serotonin reuptake inhibitor
- Seizure risk
- Physical dependence
- Not scheduled as controlled substance BUT has addiction potential

Tapentadol

- Mu-opioid agonist and NE reuptake inhibitor
- Seizure risk
- Physical dependence
- Schedule II controlled substance with addiction potential

Resources on Specific Opioids

Providers

e.g., dosing, specific product risks, limitations for use in patients with gastrointestinal problems such as inability to swallow, feeding tubes or malabsorption issues

- <http://dailymed.nlm.nih.gov/dailymed>
- www.accessdata.fda.gov/scripts/cder/drugsatfda/
- **Package inserts on ER/LA website**
- **Adverse events to be reported to FDA**
www.fda.gov/Drugs/InformationOnDrugs/ucm135151.htm

Patients

e.g., side effects, drug-drug interactions including CNS depressants, safe disposal

- **Materials:**
www.er-la-opioidrems.com/lwgUI/rems/products.action
- **Medication guide given at the pharmacy**

Opioid Risks

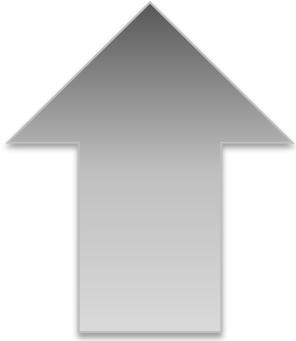


Issues Preventing Opioid Prescribing

| Issues | Prevalence |
|---|------------|
| Potential for patients to become addicted | 89% |
| Potential for patients to sell or divert | 75% |
| Opioid side effects | 53% |
| Regulatory/law enforcement monitoring | 40% |
| Hassle and time required to track/refill | 28% |

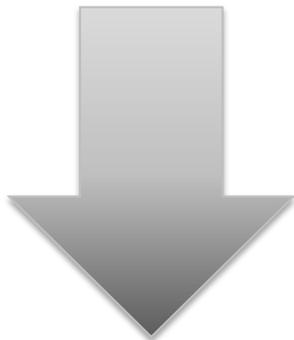
Opioid Tolerance and Physical Dependence

Both tolerance and physical dependence are physiological adaptations to chronic opioid exposure



Tolerance:

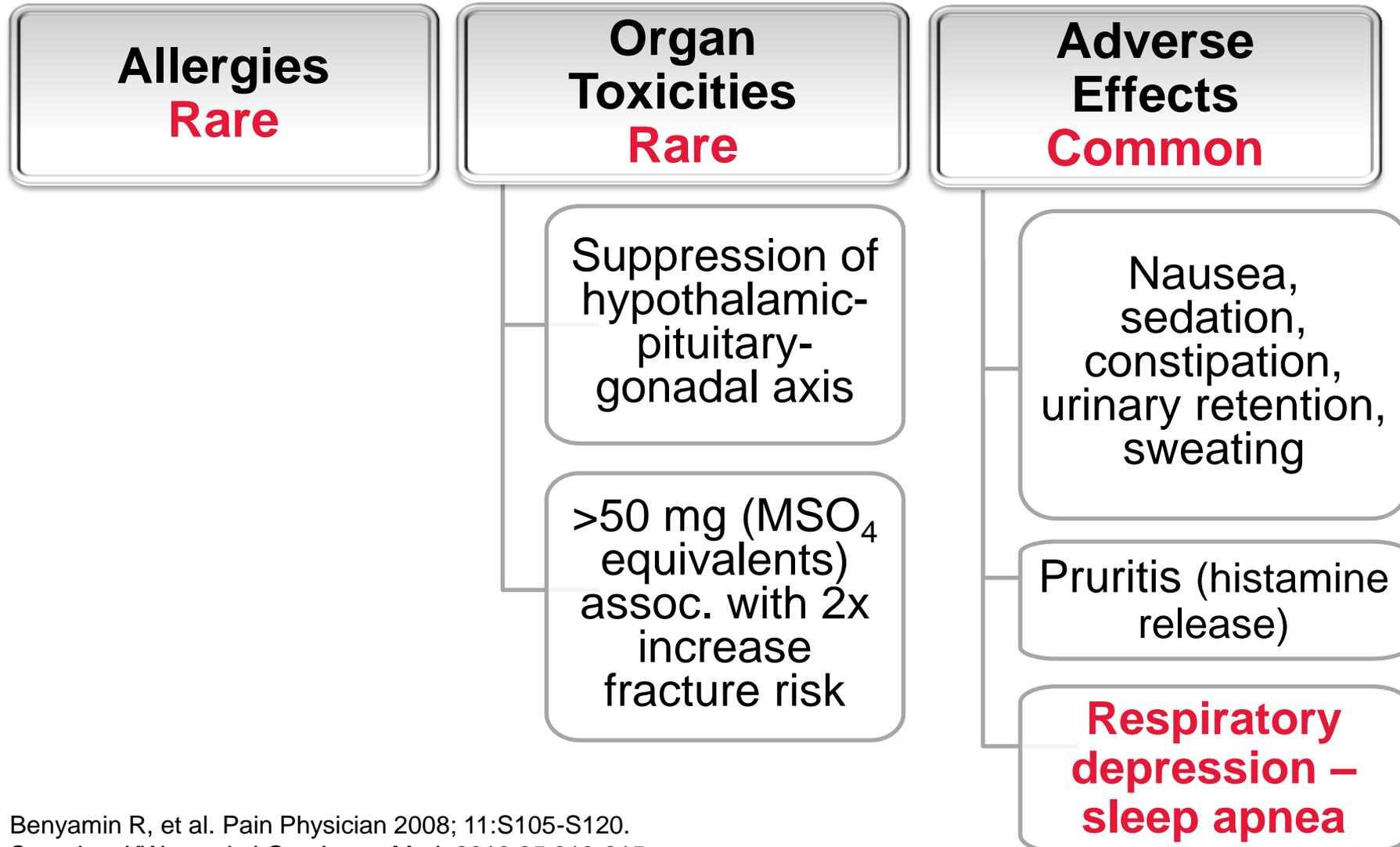
- Increased dosage needed to produce specific effect
 - Develops readily for CNS and respiratory depression
 - Less so for constipation
 - Unclear about analgesia



Physical Dependence:

- Signs and symptoms of withdrawal by abrupt opioid cessation, rapid dose reduction

Opioid Safety and Risks



Respiratory Depression

- Depression of the medullary respiratory center
- Decreased tidal volume and minute ventilation
- Right-shifted CO₂ response
- Hypercapnea, hypoxia and decreased oxygen saturation
- Various agonist-type opioids do appear to differ in potential for ventilatory depression in humans
- Immediately life threatening
- The key to remember is that sedation occurs before respiratory depression therefore it is a warning sign that the patient is overmedicated

Managing Opioid Adverse Effects

Nausea and vomiting

Usually resolves in few days, antiemetics, switch opioids

Sedation

Mostly during initiation or change in dose

Decrease dose

Constipation

Most common and should be anticipated

Senna laxatives, bowel stimulants, switch opioids; avoid bulking agents

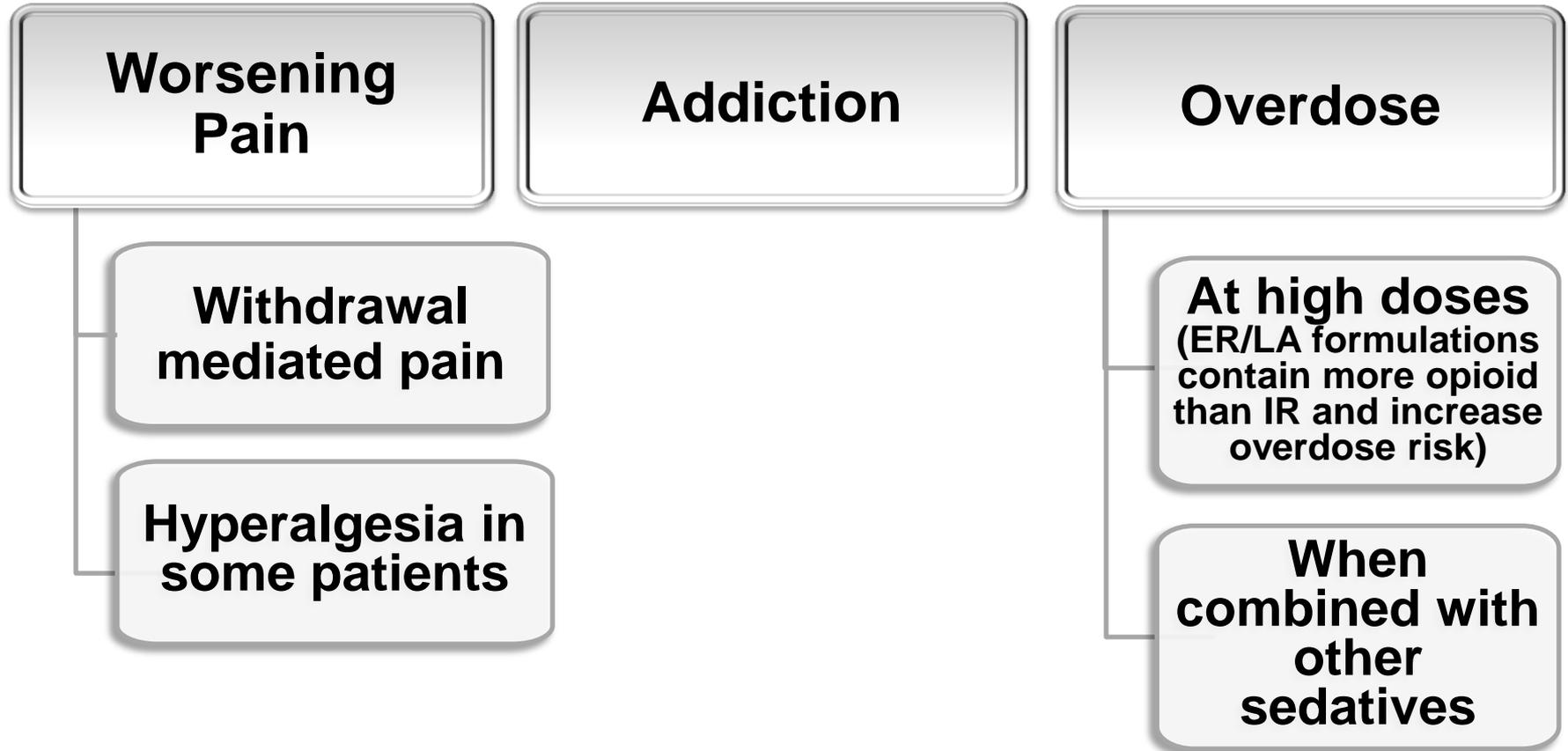
Pruritis

Switch opioids, antihistamines

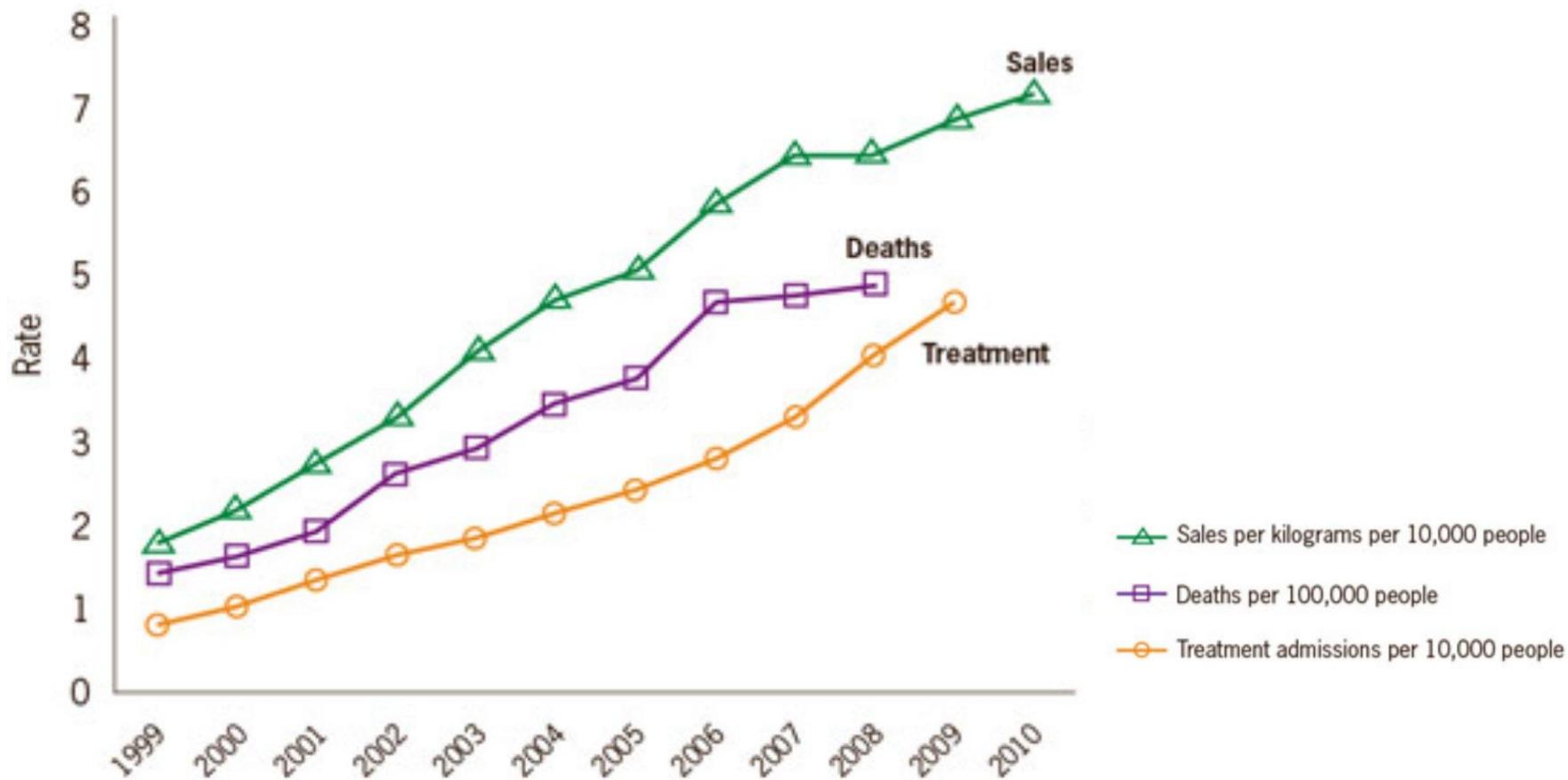
Urinary Retention

Switch opioids

Opioid Safety and Risks

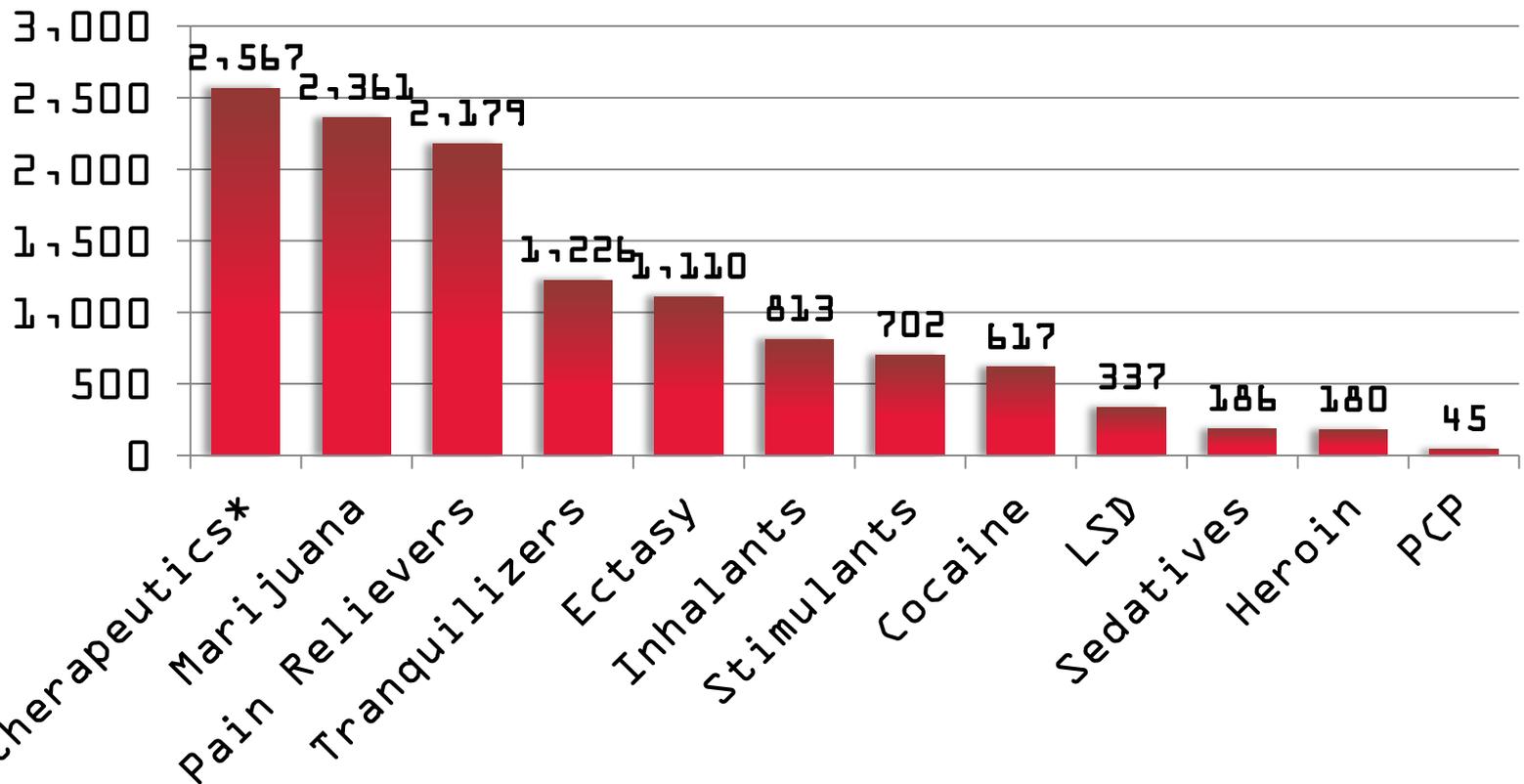


Rates of Prescription Opioid Sales, Deaths and Substance Abuse Treatment Admissions



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.

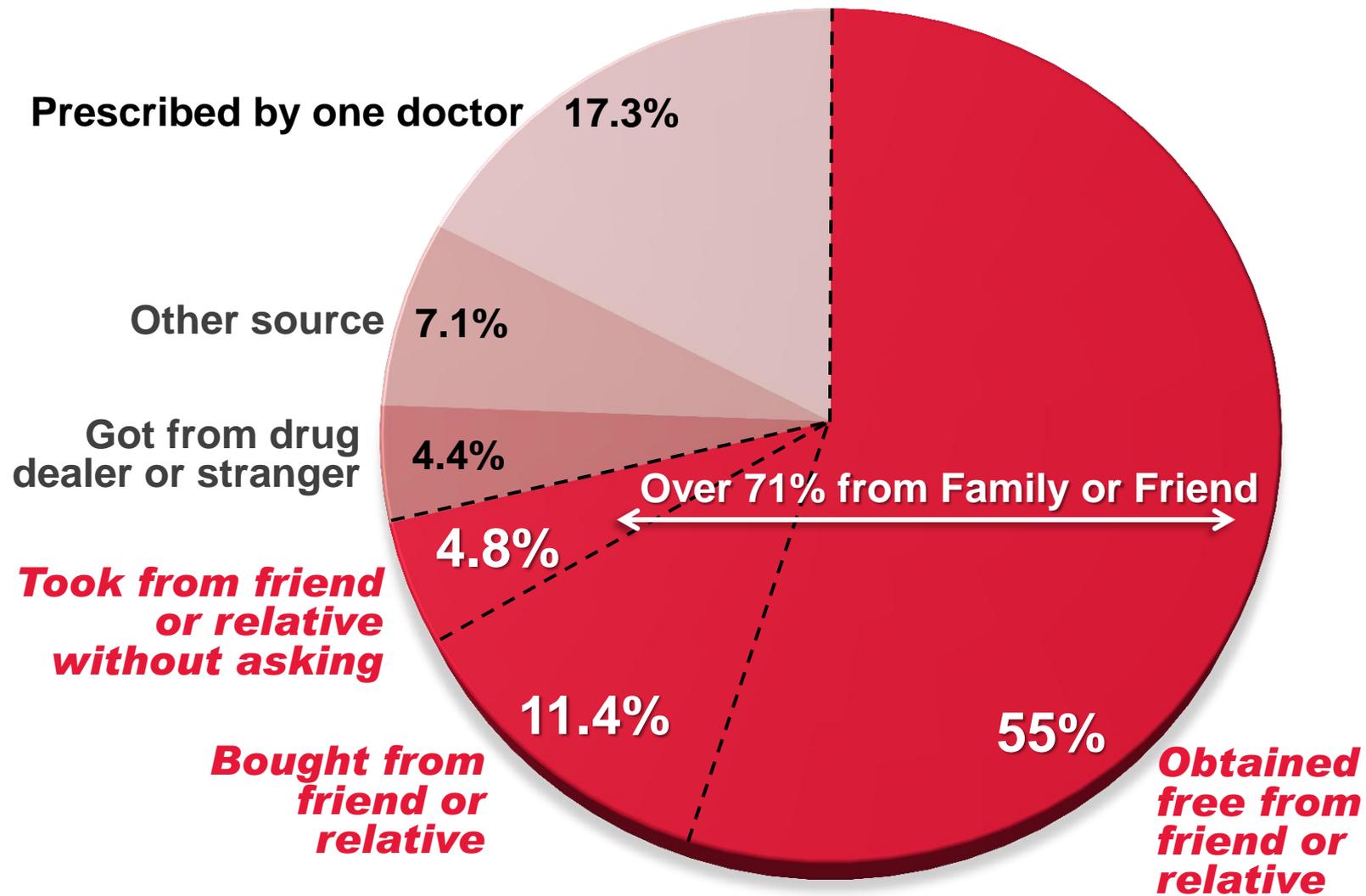
New Users: Specific Illicit Drugs



* Includes pain relievers, tranquilizers, stimulants, and sedatives.
Note: The specific drug refers to a drug that was used for the first time, regardless of whether it was the first drug used or not.

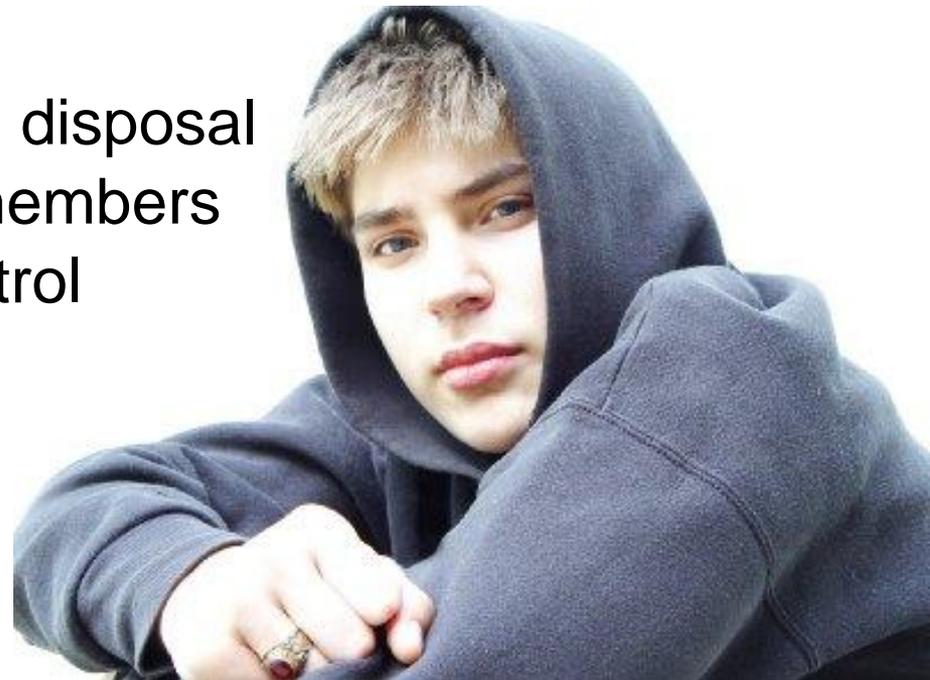
Where Pain Relievers Were Obtained

Over 71% from Family or Friend



Collateral Opioid Risk

- Risks
 - Young children ingestion and overdose
 - Adolescents experimentation leading to overdose and addiction
- Mitigating risk
 - Safe storage and disposal
 - Educate family members
 - Have poison control number handy



Opioid Addiction Risk

- True incidence and prevalence of addiction in chronic pain populations prescribed opioids is unknown due to different criteria used to define addiction in different studies
- The range in prevalence reported is 0-50%

Opioid Misuse Risk

Known Risk Factors

Good Predictors
for
problematic
prescription
opioid use

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

Akbik H, Butler SF, Budman SH, et al. J Pain Symptom Manage 2006;32(3):287-293.

Ives J, et al. BMC Health Serv Res. 2006 Apr 4;6:46.

Liebschutz JM et al. J Pain. 2010 Nov;11(11):1047-55.

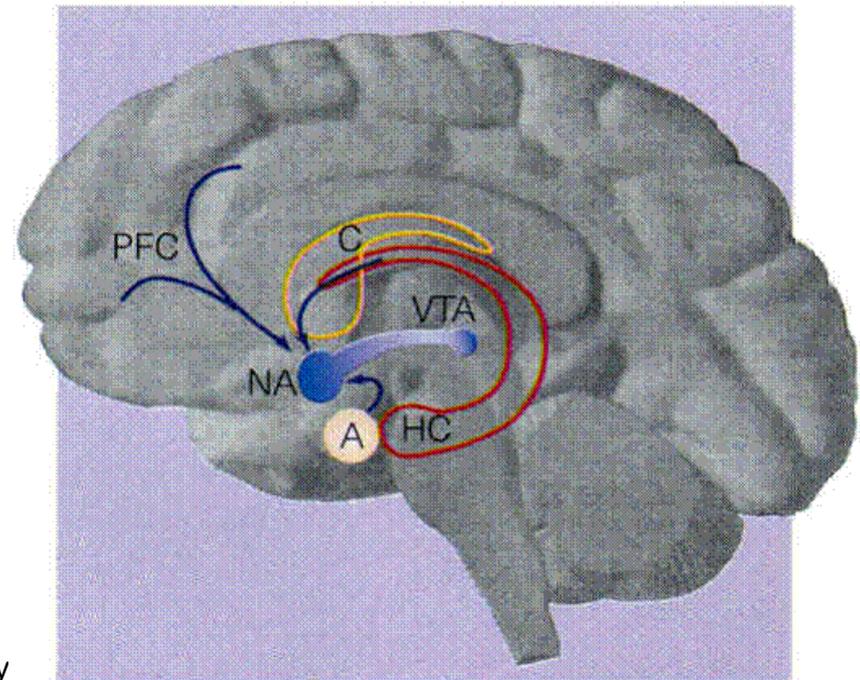
Michna E, et al. J Pain Symptom Manage. 2004 Sep;28(3):250-8.

Reid MC, et al. J Gen Intern Med. 2002 Mar;17(3):173-9.

Why Patients Become Addicted to Opioids

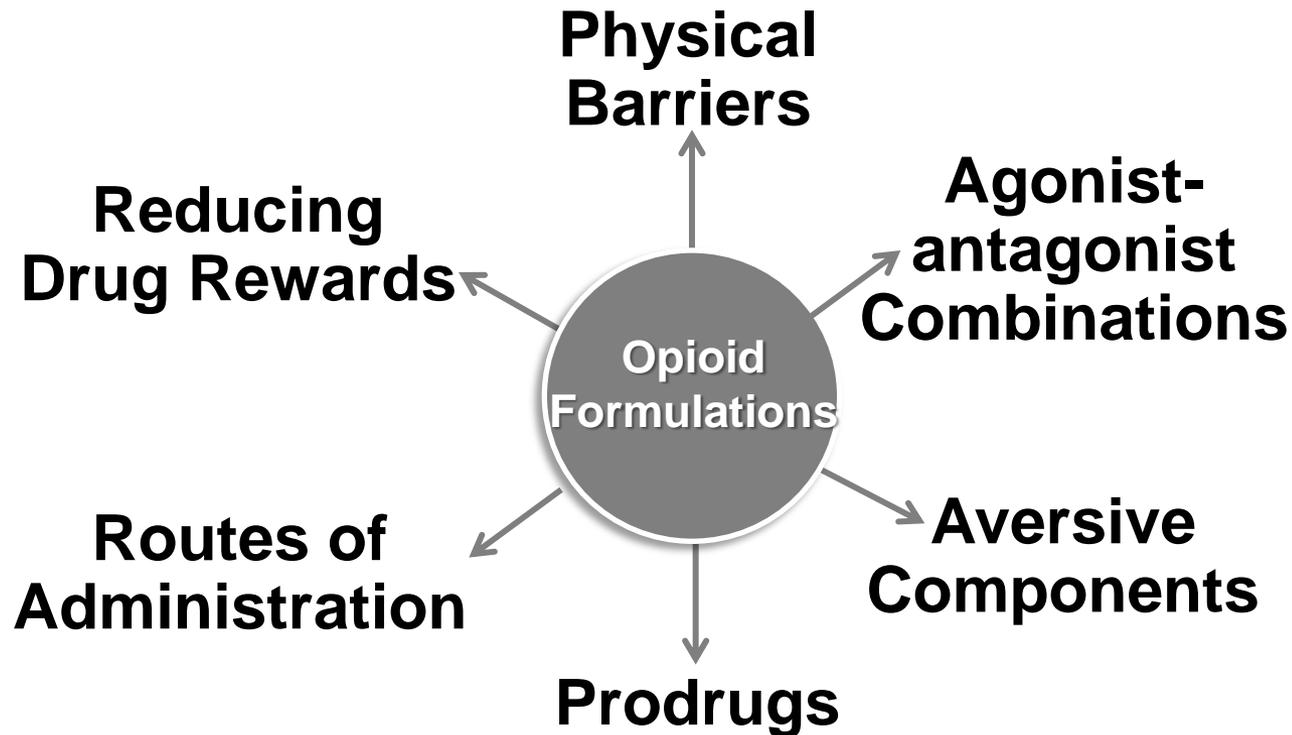
Opioids activate mu receptors in midbrain = “reward pathway” causing euphoria

- Dopaminergic system that is very reinforcing
- Most rewarding are fast onset opioids
- ER/LA should be less rewarding if taken as prescribed but are very rewarding if adulterated (e.g., crushed, chewed)



Abuse Deterrent/Resistant Formulations

In Development



Currently there are NO PROVEN abuse deterrent/resistant opioids or formulations

Drug-Drug Interactions

Profiles vary among the different opioids and opioid formulations

Central nervous system depressants (*alcohol, sedatives, hypnotics, tricyclic antidepressants*)

- Can have potentiating effect on sedation and respiratory depression caused by opioids

Some ER/LA opioid formulations

- May rapidly release opioid (dose dump) when exposed to alcohol
- Some drug levels may increase without dose dumping when exposed to alcohol

Diuretics

- Opioids can reduce efficacy by inducing release of antidiuretic hormone (ADH)

Some Opioids (*methadone, buprenorphine*)

- Can prolong the QTc interval

Concomitant drugs that act as inhibitors or inducers of various cytochrome P450 enzymes

- Can result in higher or lower than expected blood levels of some opioids

Important Resource: DailyMed



<http://dailymed.nlm.nih.gov/dailymed>

**Daily
Med**
Current
Medication
Information

- Updated medication content and labeling
 - Search and download
- Reformatted drug labeling easier to read
- National Library of Medicine (NLM) provides as a public service; does not accept advertisements

Risk in Elderly

- Drug-drug interactions
- Drug-disease interactions
 - CHF, chronic liver and renal disease
 - Dementia
- Decline in therapeutic index
- Age-related predisposition to adverse drug effects
- Start low and go slow



Risk Assessment



Assess for Opioid Misuse Risk

Prior to Prescribing

- Validated questionnaire
- Urine drug testing
- Check state prescription drug monitoring program data (if available)
- Review old medical records
- Talk to previous provider (if possible)

Validated Questionnaires

ORT

Opioid Risk Tool

SOAPP

Screening & Opioid Assessment for Patients with Pain

STAR

Screening Tool for Addiction Risk

SISAP

Screening Instrument for Substance Abuse Potential

PDUQ

Prescription Drug Use Questionnaire

***No “Gold Standard”
Lack of rigorous testing***

Mary Williams

Case Study

Opioid Risk Tool Score



| | Female | Male |
|--|---|----------------------------|
| 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 |
| 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 checked="" type="checkbox"/> 5 ✓ | <input type="checkbox"/> 5 |
| Age between 16-45 years | <input type="checkbox"/> 1 | <input type="checkbox"/> 1 |
| History of preadolescent sexual abuse | <input type="checkbox"/> 3 | <input type="checkbox"/> 0 |
| Psychological disease | | |
| ADHD, OCD, bipolar, schizophrenia | <input type="checkbox"/> 2 | <input type="checkbox"/> 2 |
| Depression | <input type="checkbox"/> 1 | <input type="checkbox"/> 1 |

SCORING
 0-3 Low Risk
4-7 Moderate Risk
 >8 High Risk

Opioid Misuse Risk Stratification

How should it be used?

Level of concern that should be communicated to the patient

- **“Despite being in recovery from alcoholism, you are at higher risk for developing problems with the opioid pain medication.”**

Level of monitoring that should be implemented

- **Frequency of visits, urine drug testing, etc.**
- **High risk patients may need to agree to random call-backs**

Need for pain and/or addiction consultant

- **If available**

Some patients may be too risky for opioids analgesics

- **e.g., patient with recent opioid addiction**

Prescription Drug Monitoring Programs

Clinical tool that supports safe prescribing and dispensing

May help prevent or stop harm from drug diversion, misuse and abuse

Specifics vary from state to state

Can provide:

- Patient's prescription history for Schedule II–V
- Solicited reports online; real time or delay of days to weeks
- Unsolicited reports on patients with “questionable activity”

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Case Study



- Patient agrees to return in one week
- Provider has time to check records and Prescription Drug Monitoring Program (PDMP)
- Patient has left a Urine Drug Test (UDT)

Summary Points: Presentation 1

Opioids:

- can be beneficial for some
- side effects are common but can be managed
- can be harmful for some
- carry significant risk including overdose and addiction
- misuse risk can be assessed using systematic approach which includes validated risk assessment questionnaires

Mary Williams Case Presentation

Review of Ms. Williams' medical records

Progress notes, medication lists are reconciled

Radiology reports

- Lumbar degenerative joint disease
- Mild spinal stenosis

No evidence of misuse of her opioid prescriptions

Lack of adequate documentation about pain and functional benefits in her old record

She is likely benefiting from opioids

States she is able to continue working on current medications

Moderate risk for prescription opioid misuse based on the Opioid Risk Tool score

Questions for Next Visit

Initiating Opioid Therapy Safely

Clinician Concerns:

- Should I change her opioid prescription?
- Should I change the opioid dose?
- What about any other adjuvant medications or therapies?
- What sort of treatment plan should I develop?

