Diagnosis and Management of Prescription Opioid Use Disorders in Primary Care

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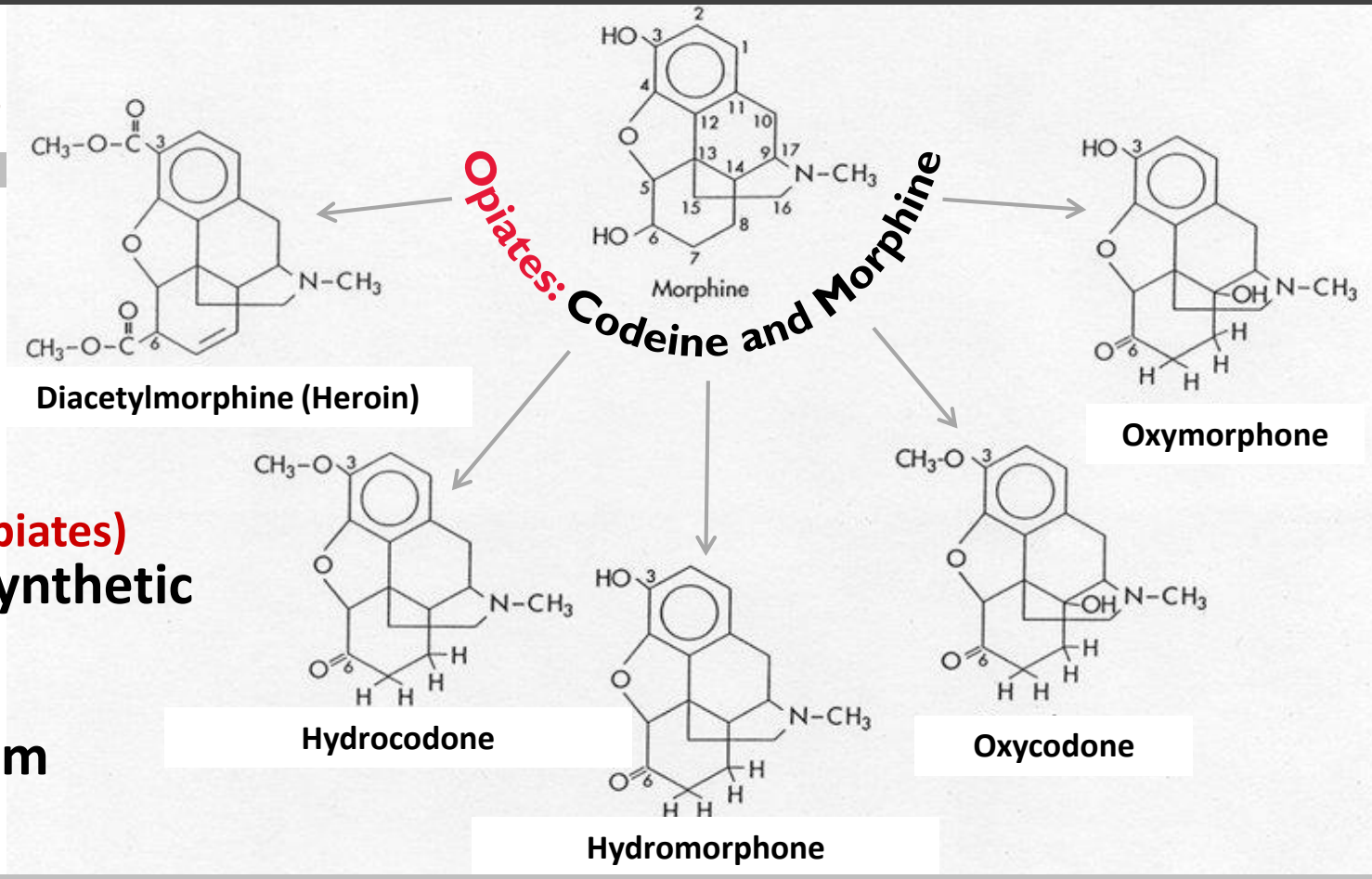
No financial disclosures

Objectives

- Describe the epidemiology and impact of prescription opioid use disorders
- Identify risk factors and signs and symptoms of prescription opioid use disorders.
- Explain the risk-benefit framework when considering opioid therapy
- Understand how to screen and diagnose opioid use disorders in primary care realizing this is difficult to do.
- Describe options for opioid detox and opioid use disorder treatment.

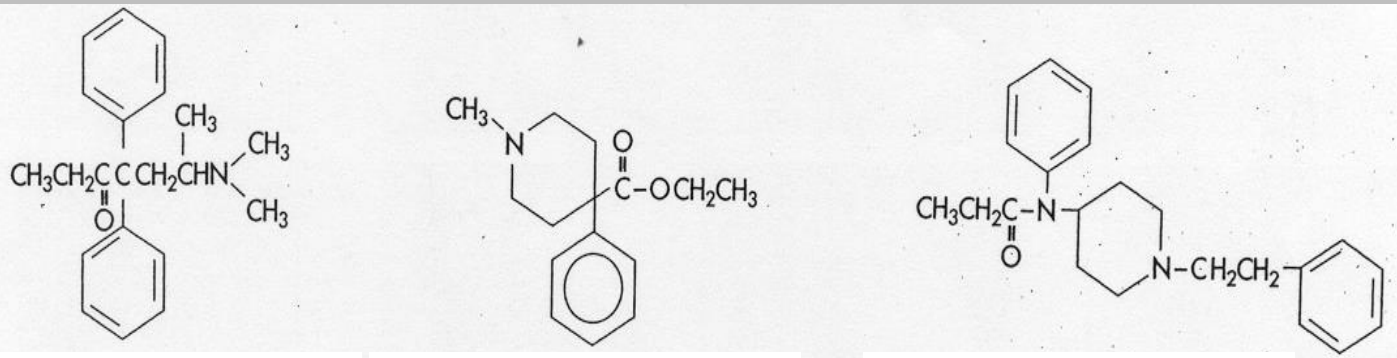
Opioids



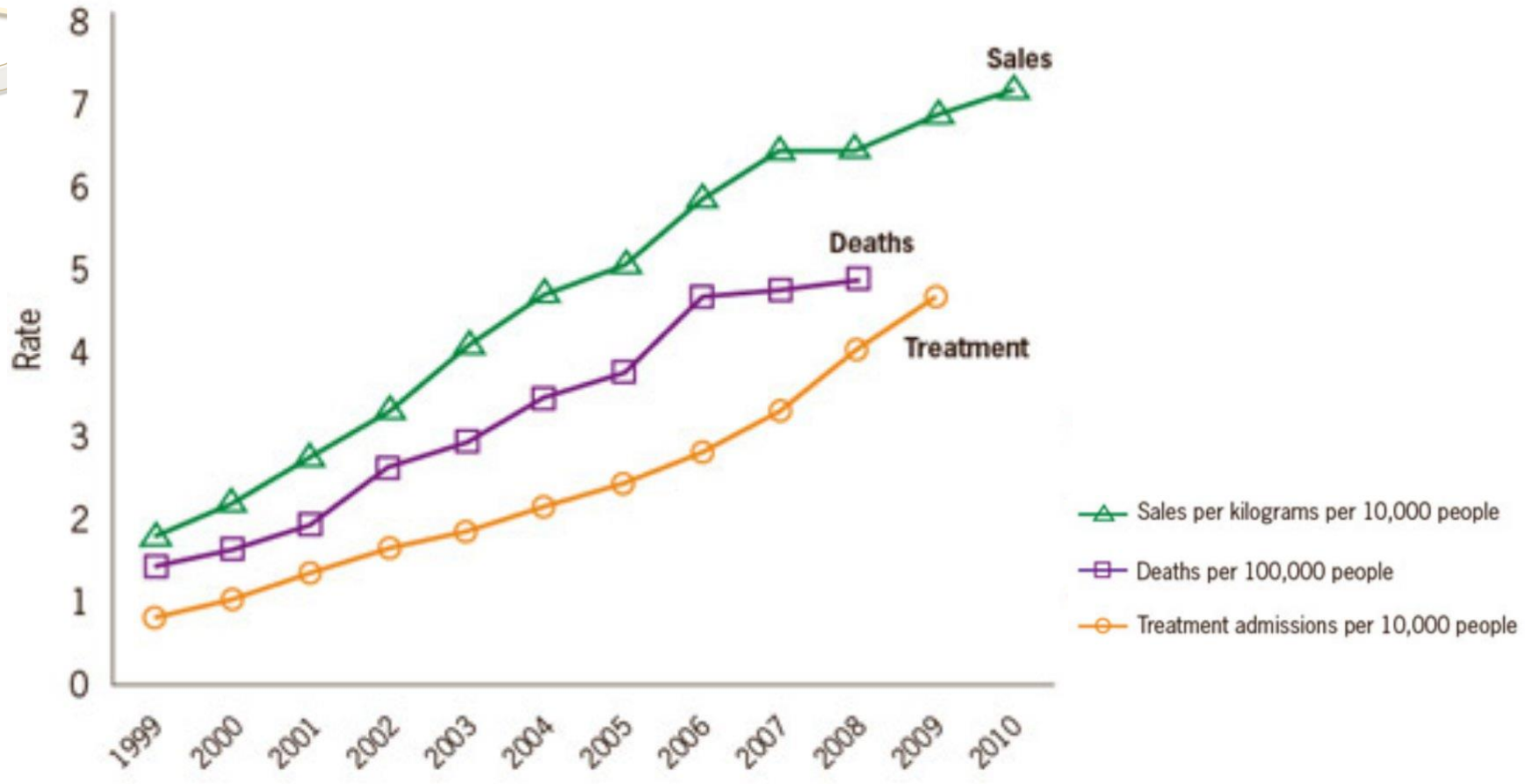
Natural (Opiates) and Semisynthetic

Derived From Opium

Synthetic



Opioid Sales, Deaths and Substance Abuse Treatment Admissions



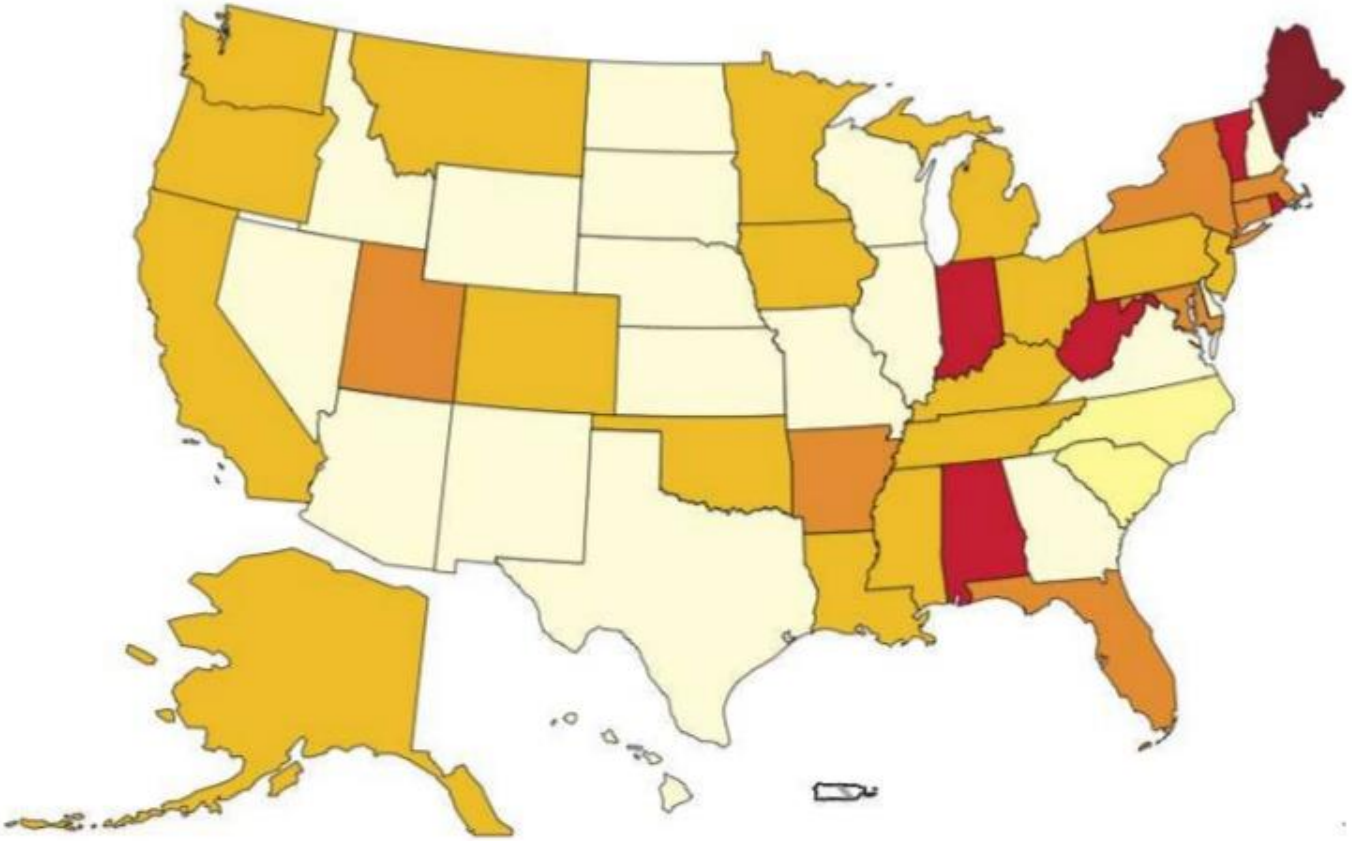
National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System (ARCOS) of the Drug Enforcement Administration (DEA), 1999-2010; Treatment Episode Data Set, 1999-2009.

Substance Use Disorders and Health Care

- Prescription Opioid Abuse Common[1]
  - 4.6% of U.S. Population
    - 6.4% of Oregonians (highest state prevalence)
- High prevalence of SUD in primary care
  - Up to 25% with substance use disorder[2]
  - 4-30% of chronic pain patients
  - 36-50% in HIV-infected patients[3-5]

[1] NSDUH Report 2013
[2] Fleming 1996
[3]Turner BJ, JGIM 2001
[4]Korthuis JSAT 2008
[5]Bing Arch Gen Psych 2001

Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



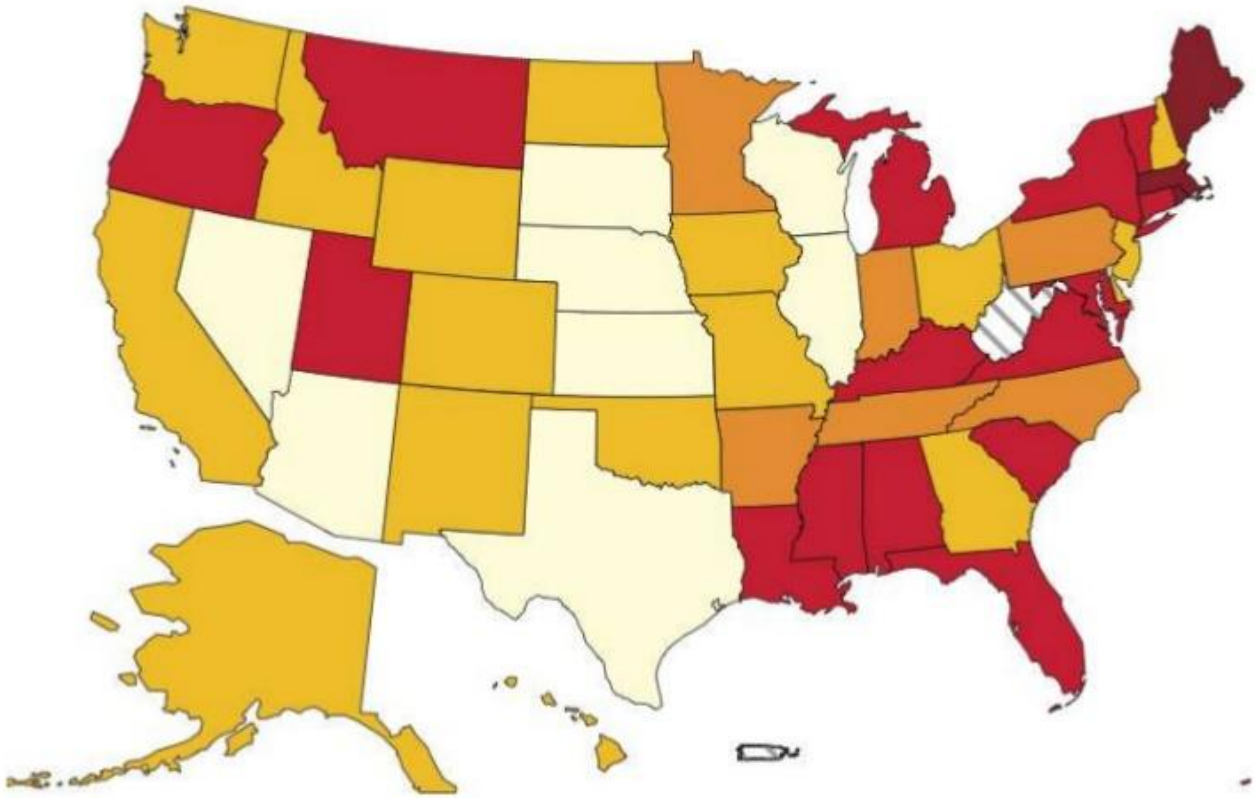
1999

(range 1 - 50)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



2001

(range 1 – 71)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

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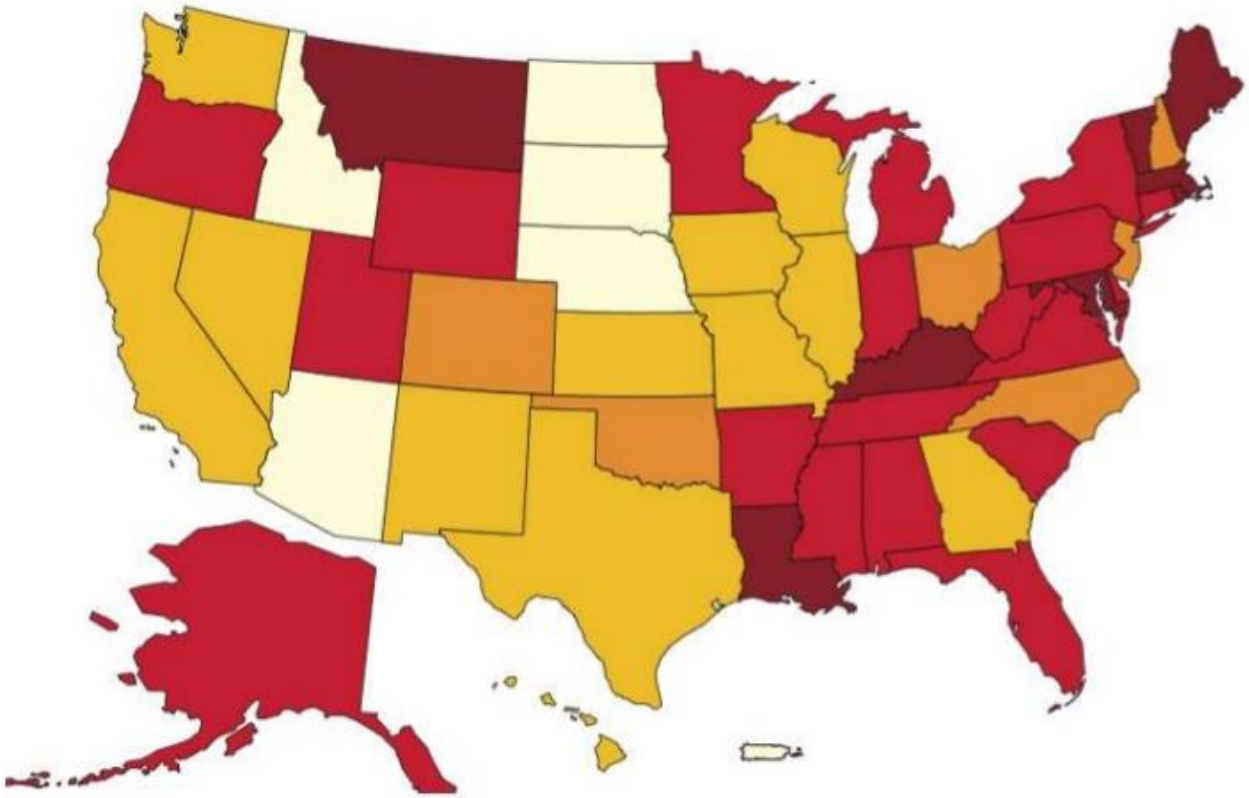


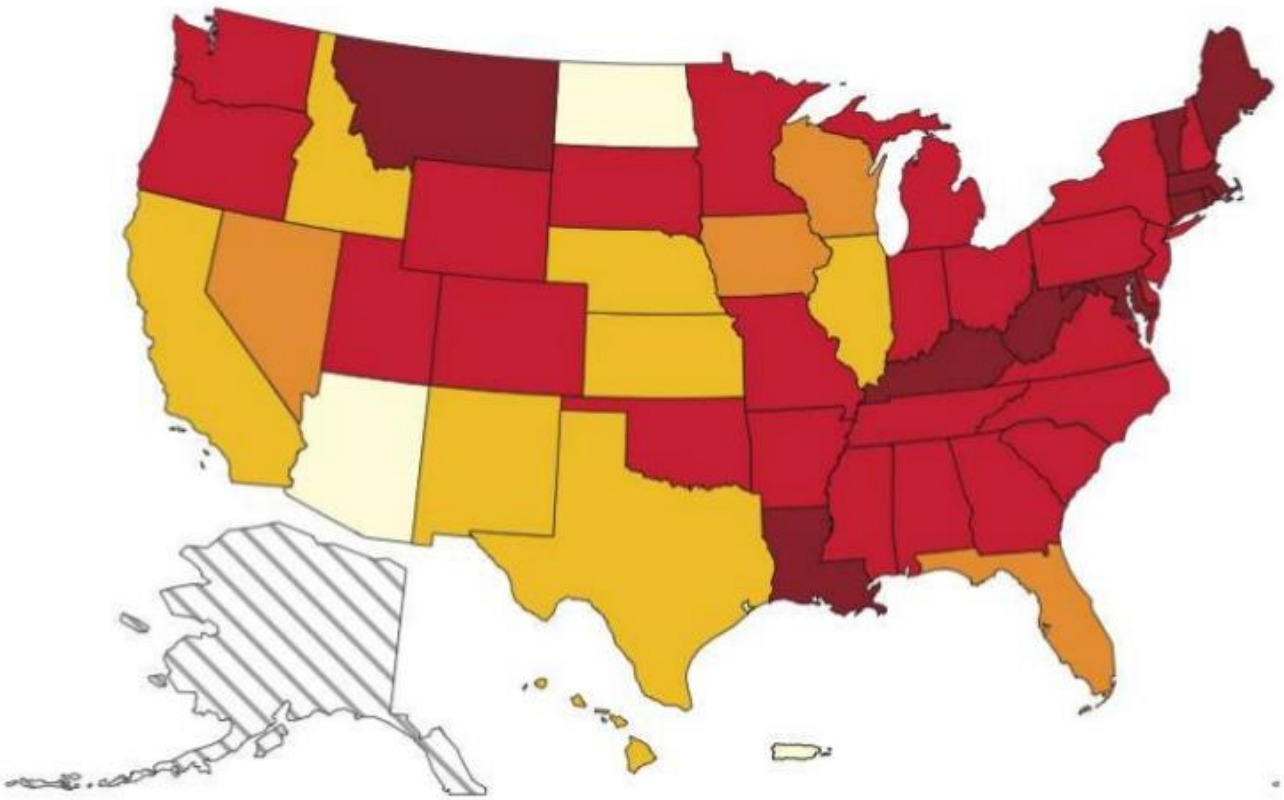
2003

(range 2 – 139)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

Primary non-heroin opiates/synthetics admission rates, by State
(per 100,000 population aged 12 and over)

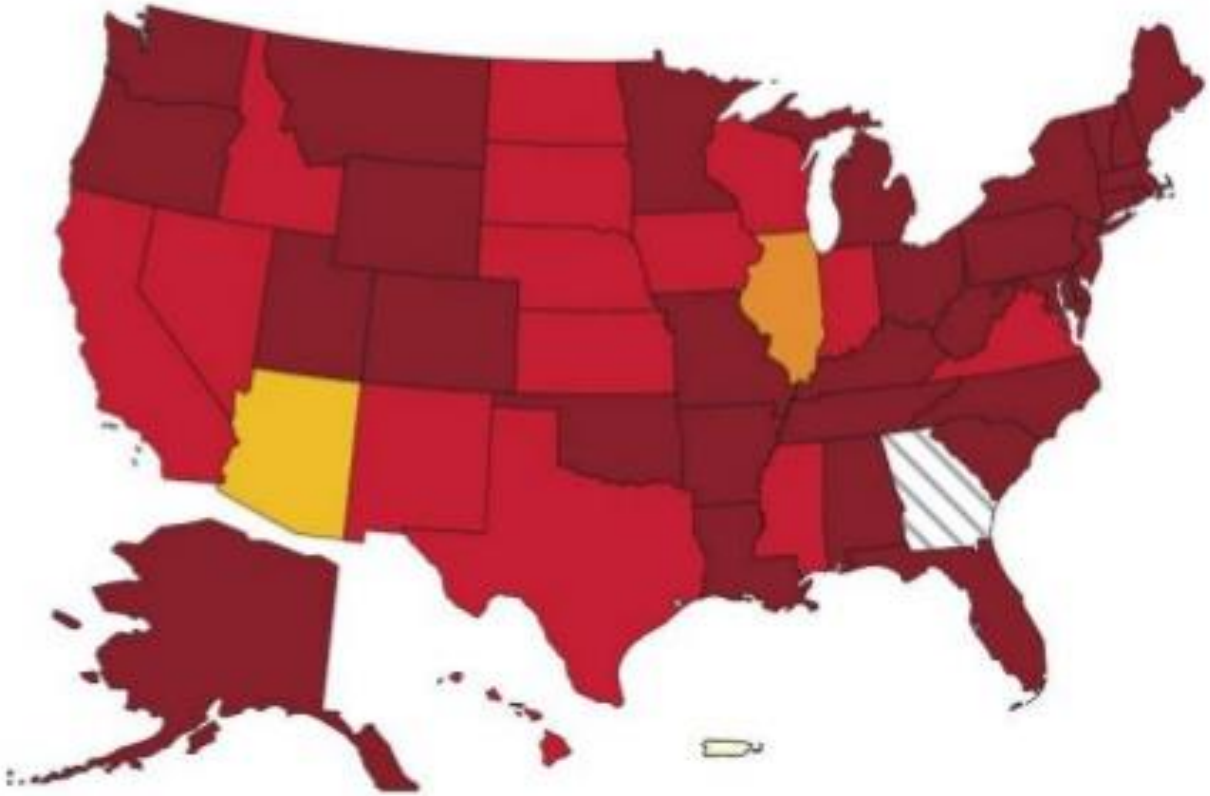


2005
(range 0 – 214)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

Primary non-heroin opiates/synthetics admission rates, by State (per 100,000 population aged 12 and over)



2009

(range 1 – 379)

< 8	15 - 18	45 or more
8 - 14	19 - 44	Incomplete data

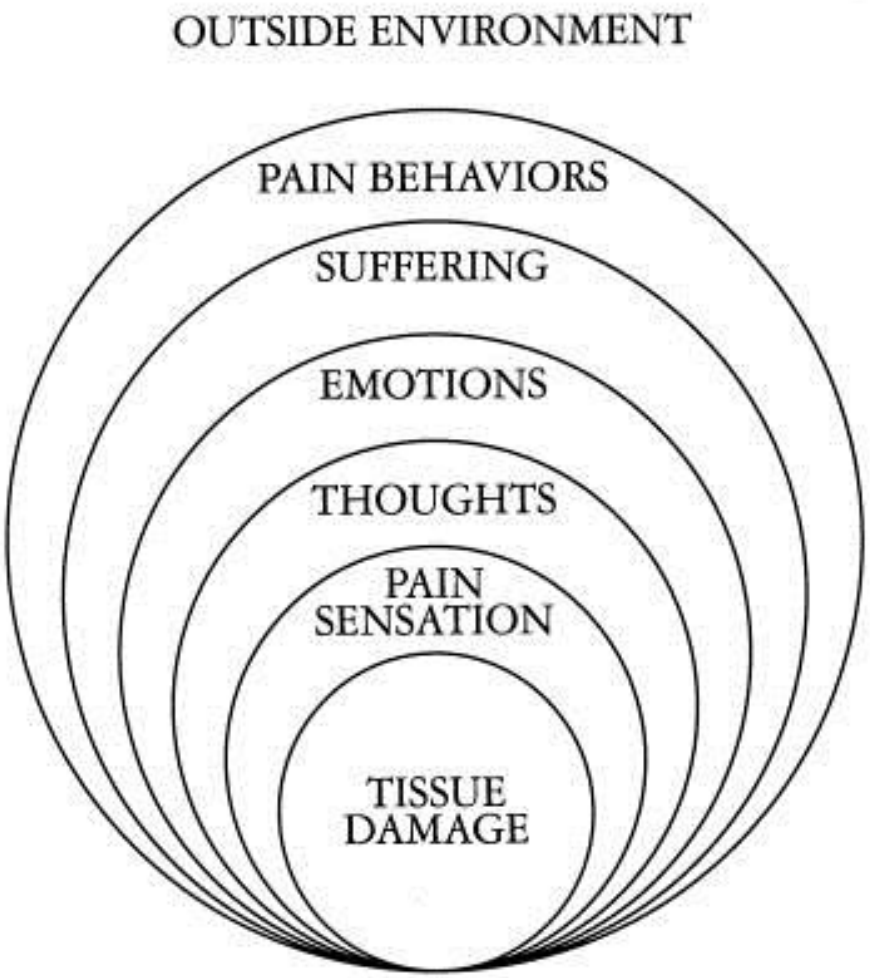
SOURCE: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, Treatment Episode Data Set (TEDS). Data received through 11.03.10.

What we know about chronic opioids for chronic pain

- 26 RCTs showing short-term efficacy for CNCP, max 30% relief with mixed functional benefit, poor work outcomes
- A multitude of other harms including worsening of MH, hyperalgesia, etc…
- Opioid use is concentrated in CNCP population (5% use 70% of opioids)*
- Dose related mortality >100 MED

*Edlund MJ, et al. J Pain Symptom Manage. 2010 Aug;40(2):279-89.

Pain is a multifaceted experience



- Pain is unavoidable, misery is optional
- Intensifiers of pain: fear, anger, guilt, loneliness, helplessness
- Catastrophic thinking
- Limited coping skills
- Passive Approach to Life and Pain

- **Adverse selection** – recipients of chronic opioids are also most likely to abuse opioids*

*Edlund MJ, et al. J Pain Symptom Manage. 2010 Aug;40(2):279-89.

Mr. Smith

- 35 yo obese male who is new to your practice
- Chronic, nonspecific moderately-severe right upper quadrant pain

- Family history of alcoholism
- Denies personal history of substance use

- Multiple ED visits for pain and morphine refills
- Troubled by impact of pain on his work

Mr. Smith's Physical Exam

- Review of prior records suggest extensive work up with no reversible cause for patient's pain
- Normal neurologic, musculoskeletal, and joint exam
- Severe tenderness to palpation in the RUQ
- Elevated PHQ-9 score
- Multiple opioid prescriptions in the past 6 months from various ED providers
- He has been out of his ER morphine for 2 weeks and would like a prescription today

OPIOID RISK TOOL

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	[X]	1	3
	Illegal Drugs	[ ]	2	3
	Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse	Alcohol	[ ]	3	3
	Illegal Drugs	[ ]	4	4
	Prescription Drugs	[X]	5	5
3. Age (Mark box if 16 – 45)		[X]	1	1
4. History of Preadolescent Sexual Abuse		[ ]	3	0
5. Psychological Disease	Attention Deficit Disorder, Obsessive Compulsive Disorder, Bipolar, Schizophrenia	[ ]	2	2
	Depression	[X]	1	1
	TOTAL		———	——— **10**

Total Score Risk Category
Low Risk 0 – 3
Moderate Risk 4 – 7
High Risk ≥8

Webster, Pain Med, 2005

Lab/Imaging Evaluation

- POC UDS = + opioids
- CBC normal
- CMP normal
- Vitamin D mildly low
- Vitamin B12 normal
- CT abdomen with contrast negative

What would you do?

Recommendation for Mr. Smith

- Express concern about his prior use of ER morphine
- Explain that the risks of opioid therapy outweigh the benefits at this point
  - Do not offer a taper due to concern for possible OUD
- Continue work up to render a specific diagnosis
- Offer alternative, safer treatment options
- Schedule follow up with you in 2 weeks

When to say 'no' to a request for long-term opioid therapy

- Patients with current, untreated substance use disorders or mental health disorders should NOT be placed on long-term opioid therapy.
- Definite No
  - Stimulant, benzodiazepine, alcohol, other opioid use disorders
- Proceed with caution
  - Cannabis, tobacco
  - Strong family or personal history of substance use disorder

Saying ‘no’ to a request for opioids

- Alternate evaluation, therapies and continued care should be offered when refusing to write an opioid prescription.
- Continue regular patient visits to re-evaluate goals of care and treatment

Use a 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 Jun;12(6):890-7.

Mr. Smith's outcome

- Extensive work up negative
- Osteopathic evaluation consistent with myofascial pain
- Admitted he was making "homemade opioid tea" from organic poppy seeds and using on a daily basis
- Re-offered addiction treatment
- Pain remained a problem for him

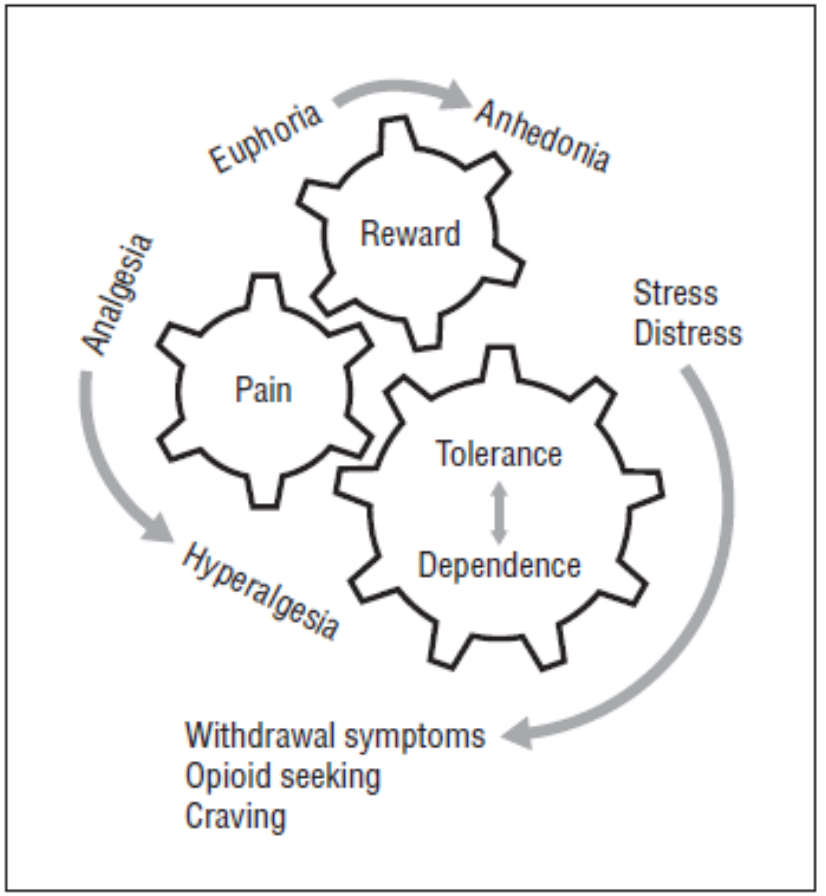
Why do some people become addicted while others do not?

- No single factor can predict addiction
  - **INDIVIDUAL BIOLOGY**– genetics in combination with environmental influences accounts for 40-60% of addiction vulnerability
    - Men may have slightly higher prevalence for opioid use disorders
    - African Americans may have higher prevalence of opioid use disorders
  - **ENVIRONMENTAL** – low socioeconomic status, poor parental support, drug availability, stress, exposure to physical or sexual abuse.
  - **AGE/STAGE OF DEVELOPMENT-** The earlier drug abuse begins, the more likely it will progress to more serious abuse, includes tobacco initiation.

Opioid Dependence vs Addiction

A Distinction Without a Difference?

"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment…Whether or not it is called addiction, complex persistent opioid dependence is a serious consequence of long-term pain therapy."



Ballantyne, Sullivan, Kolodny,. Archives of IM, 2012

Prescribed Opioid Use Disorder Risk

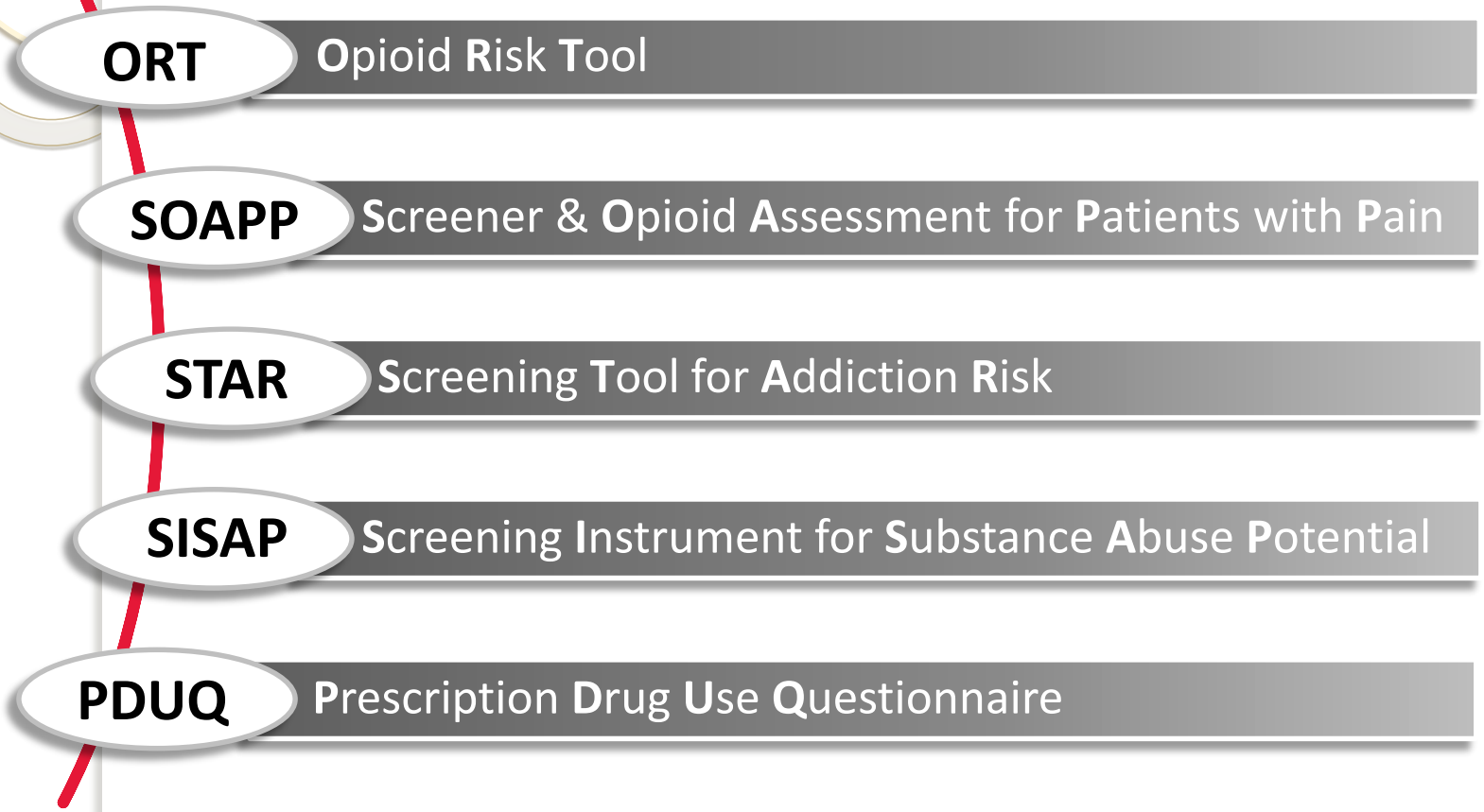
Known Risk Factors

Good Predictors for Prescription Opioid Use Disorder

- Young age (less than 45 years)
- Personal history of substance abuse
- Family history of substance abuse
- Legal history
- Back pain, headache
- Mental health problems
- History of sexual abuse
- High dose of opioids

Akbik H, et al. J Pain Symptom Manage. 2006 Sep;32(3):287-93.
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.
Edlund MJ, et al. J Pain Symptom Manage. 2010 Aug;40(2):279-89.

Validated Questionnaires for Opioid Use Disorder Risk



No "Gold Standard", Not diagnostic
All lack rigorous testing in primary care populations

Moore TM, et al. Pain Med. 2009 Nov;10(8):1426-33.

Objective Measures to detect Opioid Use Disorders

- *Random* Urine Drug Testing
  - Evidence of therapeutic adherence
  - Evidence of use or non-use of illicit drugs
- Prescription Drug Monitoring data
- Pill counts
- Review of past medical records

Heit HA and Gourlay DL. J Pain Symptom Manage Mar;27(3):260-7.
Christo PJ et al. Pain Physician. 2011 Mar-Apr;14(2):123-43.

Physical signs and symptoms of an opioid use disorder

- Track marks
- Irritation of the nose lining or perforated nasal septum
- Diaphoresis
- Frequent illness
- Mood swings, depression, anger, irritability
- Marital problems
- Missing school or work
- Poor performance at school or work
- Financial problems, eg: large recent debt
- Social isolation, loss of friendships

Concerning Behaviors for Opioid Use Disorders

Spectrum: Yellow to Red Flags

- Requests for increase opioid dose
- Requests for specific opioid by name, "brand name only"
- Non-adherence w/other recommended therapies (e.g., PT)
- Running out early (i.e., unsanctioned dose escalation)
- Resistance to change therapy despite AE (e.g. over-sedation)
- Deterioration in function at home and work
- Non-adherence w/monitoring (e.g. pill counts, UDT)
- Multiple "lost" or "stolen" opioid prescriptions
- Illegal activities – forging scripts, selling opioid prescription

Modified from Portenoy RK. J Pain Symptom Manage. 1996 Apr;11(4):203-17.

Primary Care
Single Screening Question

"How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?"

Positive = ≥ 1

Nonmedical Reasons = because of the experience or feeling it caused.

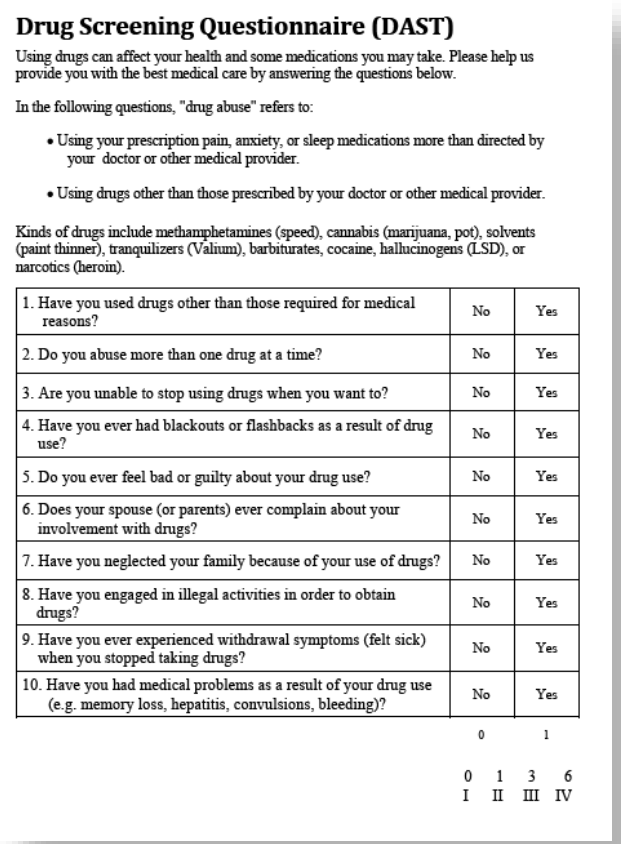
Sensitivity97%
Specificity 79%
Positive likelihood ratios 4.6
Negative likelihood ratios 0.04

Smith PC, *Arch Intern Med.* 2010;170(13):1155–1160.
Saitz, et al. JOURNAL OF STUDIES ON ALCOHOL AND DRUGS / JANUARY 2014

DAST

(Drug Abuse Screening Test)

- **Addresses drugs only**
- **Validated for screening adults**
- **Not diagnostic**
- **Sens: 82-96% Spec: 81-91%**



Drug Screening Questionnaire (DAST)

Using drugs can affect your health and some medications you may take. Please help us provide you with the best medical care by answering the questions below.

In the following questions, "drug abuse" refers to:

- Using your prescription pain, anxiety, or sleep medications more than directed by your doctor or other medical provider.
- Using drugs other than those prescribed by your doctor or other medical provider.

Kinds of drugs include methamphetamines (speed), cannabis (marijuana, pot), solvents (paint thinner), tranquilizers (Valium), barbiturates, cocaine, hallucinogens (LSD), or narcotics (heroin).

1. Have you used drugs other than those required for medical reasons?	No	Yes
2. Do you abuse more than one drug at a time?	No	Yes
3. Are you unable to stop using drugs when you want to?	No	Yes
4. Have you ever had blackouts or flashbacks as a result of drug use?	No	Yes
5. Do you ever feel bad or guilty about your drug use?	No	Yes
6. Does your spouse (or parents) ever complain about your involvement with drugs?	No	Yes
7. Have you neglected your family because of your use of drugs?	No	Yes
8. Have you engaged in illegal activities in order to obtain drugs?	No	Yes
9. Have you ever experienced withdrawal symptoms (felt sick) when you stopped taking drugs?	No	Yes
10. Have you had medical problems as a result of your drug use (e.g. memory loss, hepatitis, convulsions, bleeding)?	No	Yes
	0	1

0 1 3 6
I II III IV

Skinner, 1982. Agency for Healthcare Research and Quality, 2004

THE AMERICAN JOURNAL OF PSYCHIATRY

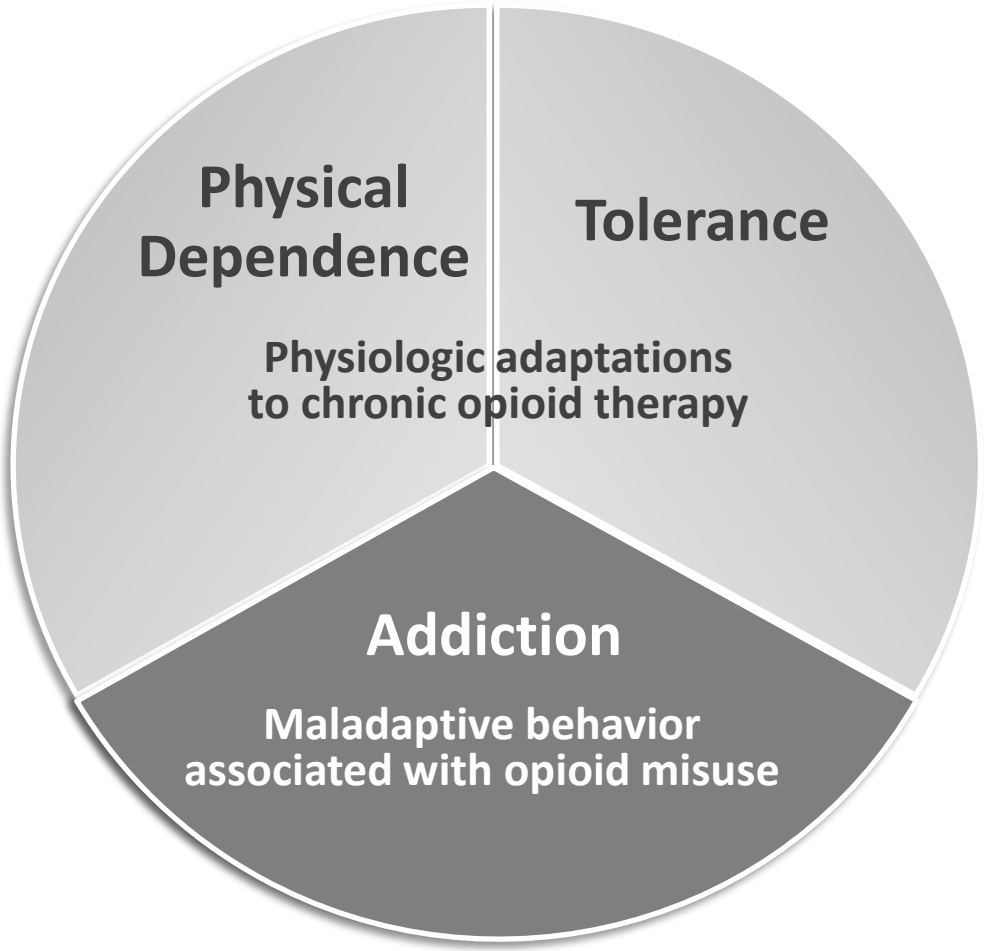
psychiatryonline

From: DSM-5 Criteria for Substance Use Disorders: Recommendations and Rationale
Am J Psychiatry. 2013;170(8):834-851.

	DSM-IV Abuse[a]		DSM-IV Dependence[b]		DSM-5 Substance Use Disorders[c]	
Hazardous use	X	≥1 criterion	–		X	≥2 criteria
Social/interpersonal problems related to use	X		–		X	
Neglected major roles to use	X		–		X	
Legal problems	X		–		–	
Withdrawal[d]	–		X	≥3 criteria	X	
Tolerance	–		X		X	
Used larger amounts/longer	–		X		X	
Repeated attempts to quit/control use	–		X		X	
Much time spent using	–		X		X	
Physical/psychological problems related to use	–		X		X	
Activities given up to use	–		X		X	
Craving	–		–		X	

2-3 = mild SUD, 4-5 = moderate SUD, >6 severe SUD

Physiologic Dependence Vs. Addiction



Savage SR, et al. J Pain Symptom Manage. 2003 Jul;26(1):655-67.

Opioid use disorder in clinical practice

- The 4 C's
  - Loss of Control
  - Compulsive use
  - Continued use despite harms
  - Craving

Savage SR, et al. J Pain Symptom Manage. 2003;26:655-667.

Wendy: pain consultation

- 43 yo female with long history of migraine headaches, high health care utilization, depression, anxiety, sexual abuse as a child, and domestic violence as an adult.
- Sought outpatient treatment for opioid use disorder 6 months ago but never stopped using vicodin
- Currently maintained on daily vicodin and nortriptyline
- Continues to have daily, debilitating migraines

Wendy

- Admits that she craves opioids
- Spends most of her day in bed
- States that she is unable to stop or cut back on opioids
- Increased depression, mental instability when she stops opioids
- Frequently obtains opioids from friends
- Her husband is concerned about her use
- PDMP shows 3 dental prescribers, 3 physician prescribers, and >4 pharmacies

Does she have a problem?

- What sounds like a "straight forward" case persisted for >1 year because no one evaluated subjective or objective measures
- PDMP data was "eye opening" for the patient

Treatment of Prescription Opioid Use Disorders

- Detoxification
- Medication Assisted Treatment
- Outpatient treatment
  - Multidisciplinary Pain Rehabilitation Programs
- Residential treatment

Opioid Detox Options

- No taper is indicated for an active opioid use disorder
- "Cold Turkey"
- Use of adjuvant withdrawal medications
- Outpatient Buprenorphine taper with or without transition to maintenance therapy
- Inpatient detox

Adjuvant Opioid Withdrawal Medications

For sweating, anxiety, agitation

Clonidine 0.1mg by mouth three times daily PRN anxiety
Hold for sedation or dizziness

For anxiety

Hydroxyzine 25-50 mg by mouth every 4-6 hours PRN anxiety

For nausea or vomiting

Phenergan 12.5-25 mg by mouth every 4-6 hours PRN nausea OR Zofran 4mg every 12 hours PRN

For abdominal cramping/diarrhea

Hyocosamine 0.125mg by mouth every 4-6 hours PRN

For increased pain with taper and from opioid withdrawal Ibuprofen 400-600 mg by mouth three times daily PRN

OR Tylenol 500mg by mouth every 4-6 hours PRN pain

Opioid Withdrawal Assessment

Grade	Symptoms / Signs
0	Anxiety, Drug Craving
1	Yawning, Sweating, Runny nose, Tearing eyes, Restlessness Insomnia
2	Dilated pupils, Gooseflesh, Muscle twitching & shaking, Muscle & Joint aches, Loss of appetite
3	Nausea, extreme restlessness, elevated blood pressure, Heart rate > 100, Fever
4	Vomiting / dehydration, Diarrhea, Abdominal cramps, Curled-up body position

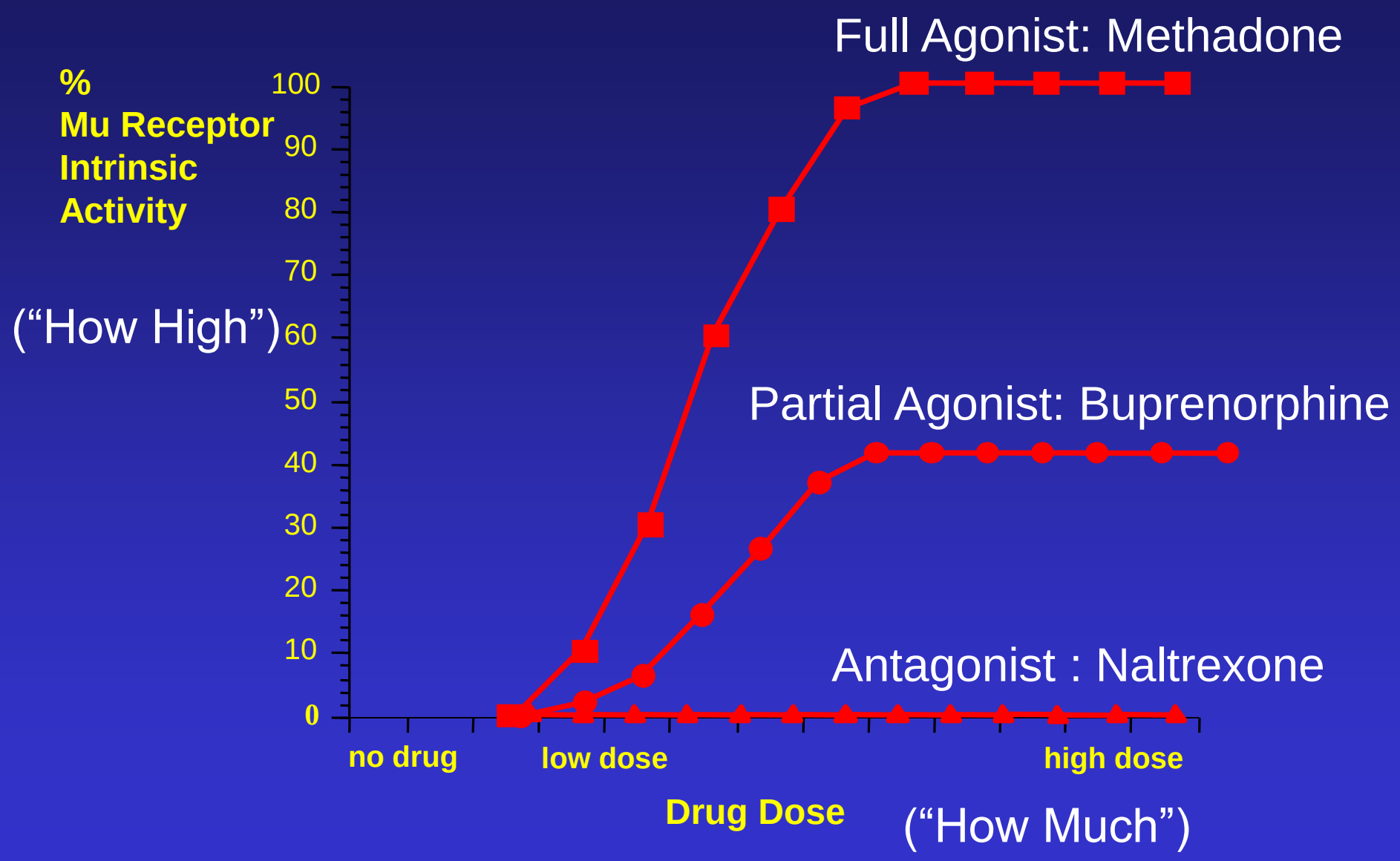
Clinical Opiate Withdrawal Scale (COWS): *pulse, sweating, restlessness & anxiety, pupil size, aches, runny nose & tearing, GI sx, tremor, yawning, gooseflesh (score 5-12 mild, 13-24 mod, 25-36 mod sev, 36-48 severe)*

Maintenance Medication Assisted Treatment Options

- Buprenorphine/naloxone
- Methadone
- Naltrexone (oral)
- Extended-release Naltrexone

All MAT should be coupled with outpatient or residential treatment

Opioid Activity Levels



Buprenorphine (subutex™) /naloxone (Suboxone™) sublingual

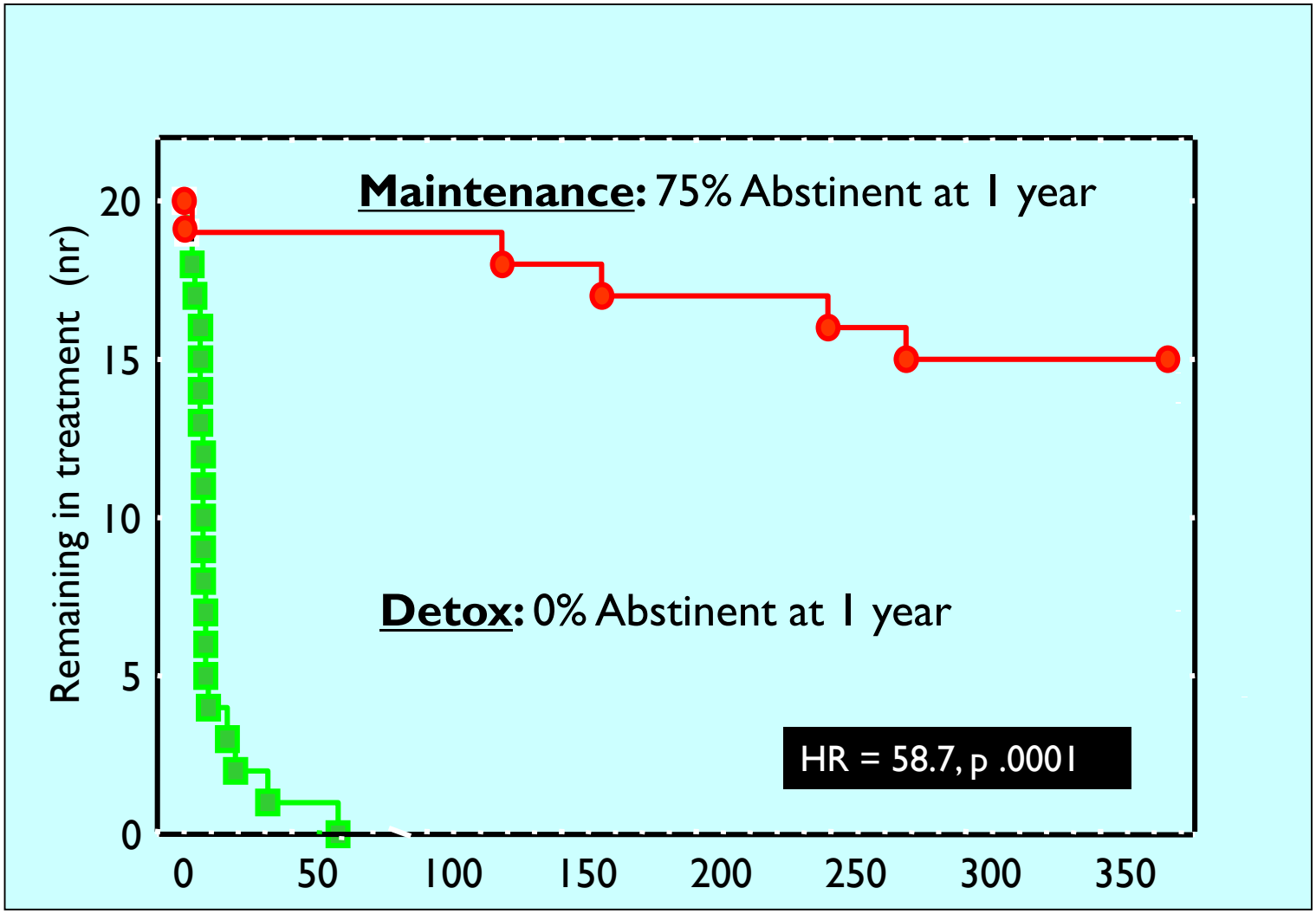
Buprenorphine (subutex™) /naloxone (Suboxone™)

- Partial opioid agonist (plateau effect)
- Less euphoric effect than other opioids
- Paired with antagonist to prevent abuse through injection
- Office based prescribing (DEA waiver, training)
- Is effective for pain management in some patients
- **Less optimal candidate for buprenorphine treatment:**
  - significant psychiatric co-morbidity
  - polysubstance use,
  - frequent relapses in prior treatment attempts
  - discharges from more structured treatment settings
  - pregnancy

Buprenorphine Affinity and Dissociation

- High affinity for mu opioid receptor
  - Competes with other opioids and blocks their effects
- Slow dissociation from mu opioid receptor
  - Prolonged therapeutic effect for opioid dependence treatment
- Low potential for overdose

Treatment Retention: Buprenorphine Detox vs. Maintenance



Kakko, Lancet 2003

Methadone Maintenance Therapy

- Full agonist with long elimination half-life
- Reduces euphoria of subsequent opioid use
- Only licensed methadone clinics are permitted to *dispense* methadone
- Typical effective dose range 60-90mg/day
- SE: QTc prolongation, sedation, drug interactions
- Effective to
  - Increase retention in treatment
  - Reduce use of opioids
  - Reduce human immunodeficiency virus (HIV)

Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database of Systematic Reviews 2009, Issue 3.

Methadone for pain management

- Analgesia for 4-6 hours with daily dosing
- Combine with adjuvant therapies
- Treat underlying cause (if any known) for pain

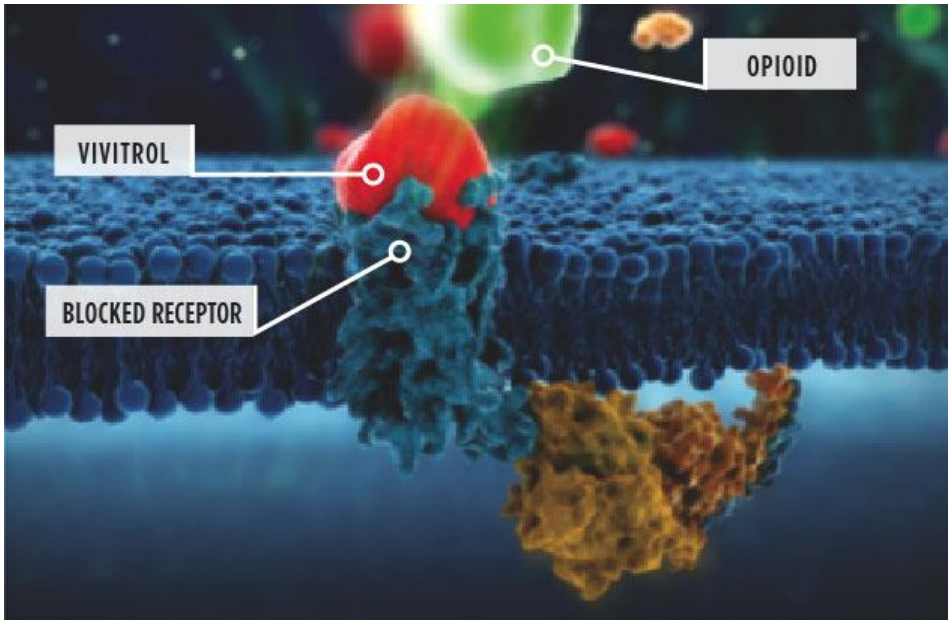
Methadone Vs. Suboxone

- Low dose Buprenorphine (2-6mg) was less effective than methadone in retaining people in treatment.

- Buprenorphine (>7 mg/day) was not different from methadone (≥40 mg/day) in retaining people in treatment or in suppression of illicit opioid use.

Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database of Systematic Reviews 2014, Issue 2.

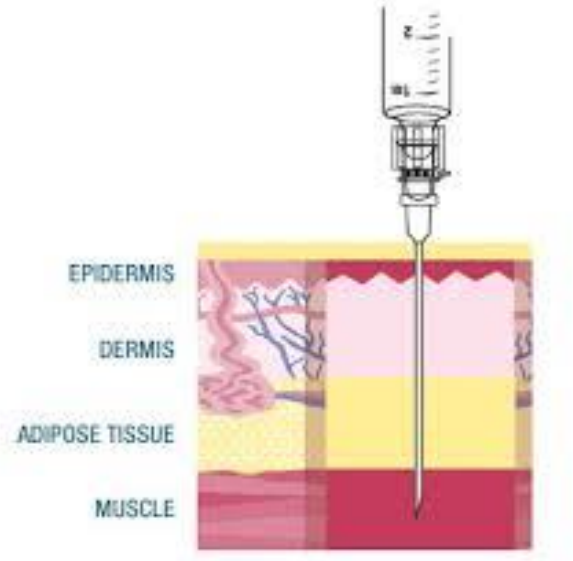
Naltrexone



Two formulations approved in US
Oral Naltrexone (1984)
Extended Release Naltrexone, Vivitrol® (2010)

Opioid receptor antagonist, not controlled
Blocks euphoric effects of opioids
Also treats alcohol dependence
Underutilized in primary care practices

Extended release naltrexone (Vivitrol®)



XR-Naltrexone for Opioid Use Disorder

- Intramuscular injection lasts 28d
- Challenge: Must be opioid-free (5-7 days) to avoid precipitated withdrawal
- Efficacious compared to placebo:
  - Comer: 60 U.S. heroin users at 8 weeks[1]
  - Krupitsky: 250 Russian heroin users at 24 wks[2]
- Potential for direct effects on HIV viral suppression & immune function
  - CD4 κ blockade increases HIV entry[3] and viral killing[4]
  - NTX is toll-like receptor (TLR-4) antagonist; may facilitate CD4 recovery[5]

[1] Comer Arch Gen Psych 2006, [2]Krupitsky Lancet 2011, [3] Wang J Leuk Bio 2006, [4] Gekker Drug Alc Dep 2001, [5] Quin J Cell Biochem 2011

Medication Efficacy For Opioid Dependence

	Treatment Program Retention	Opioid Misuse	Criminal Activity
Methadone	↑ (n=3)[a]	↓ (n=6)[a]	No Effect (n=3)[a]
Buprenorphine	↑ (n=4)[b]	↓ (n=2)[b]	No data
PO NTX	No effect (n=2)[c]	↓ (n=4)[c]	↓ (n=2)[c]
XR NTX	↑ (n=2)[d]	↓ (n=2)[d]	No data

[a]Mattick RP, et al. Cochrane Database Syst Rev 2011;
[b]Mattick RP, et al. Cochrane Database Syst Rev 2018;
[c]Minozzi S, et al. Cochrane Database Syst Rev 2011;
[d]Krupitsky E et al. Lancet. 2011, Comer SD et al. Arch Gen Psychiatry 2006.

Multidisciplinary Pain Rehab Programs

- Treat pain and opioid use disorder
- Maximize active modalities of treatment
- Enhance self-care

- Cleveland Clinic showed low resumption of opioids at 12 months*
  - 22% resumed use
  - Depression predictive of restarting opioids

Huffman, et al. Pain Medicine, 2013.

Pain management after opioid cessation

- Pain may remain high for a several months
- Maximize adjuvant therapies
- Maximize self-care
- Maximize mental health care
- Analgesic expectations from methadone and suboxone

Wendy's outcome

- Detoxed with outpatient suboxone
- Transitioned to suboxone maintenance
- Active engagement with outpatient OUD treatment
- Migraines dramatically improved
- Hospital/ED utilization decreased
- Mental health improved
- Family life improved
- Quality of life improved

Questions? weimerm@ohsu.edu

FREE Substance Use Disorder Resources:

www.coperems.org

www.scopeofpain.com

www.pcsso.org

www.pcssmat.org

March 6, 2015 –Substance Use Disorder Training for PCPs

Buprenorphine	Methadone
Partial agonist	Full agonist
Office-based prescribing	Only through methadone clinics
Can be diverted	Cannot be diverted (easily)
Potential for precipitated withdrawal	Cardiac toxicities
Low overdose risk	High overdose risk
Able to block other opioids	Can block other opioids at higher doses
Minimal drug-drug interactions, except benzodiazepines	Known drug-drug interactions
Can complicate pain treatment	