

Assisting Patients with Opioid Addiction Treatment

Steven Wright, MD



ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Every effort has been made to ensure the accuracy of the data presented here. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.

Indivior Inc. has provided unrestricted funding to support the program.

DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

The following individual in a position to control content for this session have disclosed the following relevant financial relationships:

- Steven Wright, MD, disclosed a relationship with Millennium Health (pharmacogenetics), Indivior (Suboxone, Recovery Oriented Care), Astra Zeneca-Daiichi Sankyo (Movantik), Pernix Therapeutics (Zohydro ER), Depomed (Nucynta, Nucynta ER), Endo Pharmaceuticals (Belbuca), Purdue Pharma (Butrans Oxycontin, Hysingla ER), Collegium Pharmaceuticals (Xtampza), Cordant Health Solutions (Drug testing) - Speakers' Bureau; Millennium Health (pharmacogenetics) – Manuscript Preparation Assistance.

All other individuals in a position to control content for this activity have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Steven Wright, MD

Consultant, Medical Pain Management and Addiction.

Dr. Wright is a graduate of Case Western Reserve University School of Medicine, Cleveland, Ohio. He was in family medicine practice for 32 years, and is now active in addiction medicine and medical pain management. He focuses on these areas through consulting, public speaking, advocacy, policy development, education, medical legal work, and medical provider assessment and supervision. Dr. Wright's clinical interests include the neurophysiology and treatment of pain and addiction. In particular, he focuses on etiology, pharmacogenetics, opioids, psychiatric medications, and cannabis, with an emphasis on adverse consequences, best practices, and systems of care. Dr. Wright actively participates in the Colorado Pain Society as vice president and physician liaison; the Colorado Society of Addiction Medicine treasurer, and delegate; the Prescription Drug Abuse Committee of the Colorado Medical Society; and the Colorado Consortium for Prescription Drug Abuse. He is involved in a variety of related projects and speaks across the country on opioids, opioid-induced constipation, cannabis, pharmacogenetics, and risk managing controlled medication use.

Learning Objectives

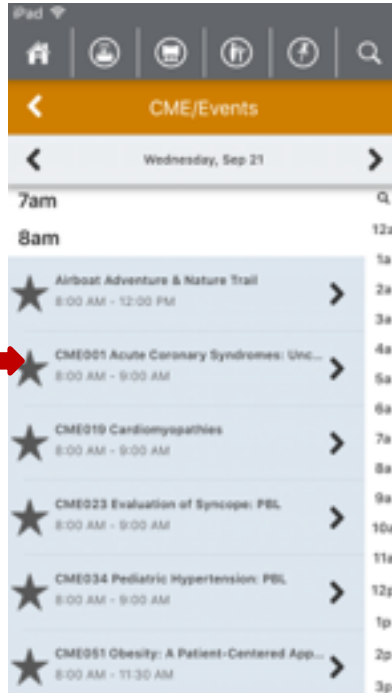
1. Outline the problems associated with opioids, including addiction.
2. Outline non-pharmacologic and pharmacologic approaches to opioid addiction, including the FDA approved medications: methadone, buprenorphine, and naltrexone.
3. Consider the benefits and challenges of becoming an FDA waived physician for medication assisted treatment of opioid addiction .
4. Develop a patient-centered approach to the patient with opioid addiction.

Audience Engagement System

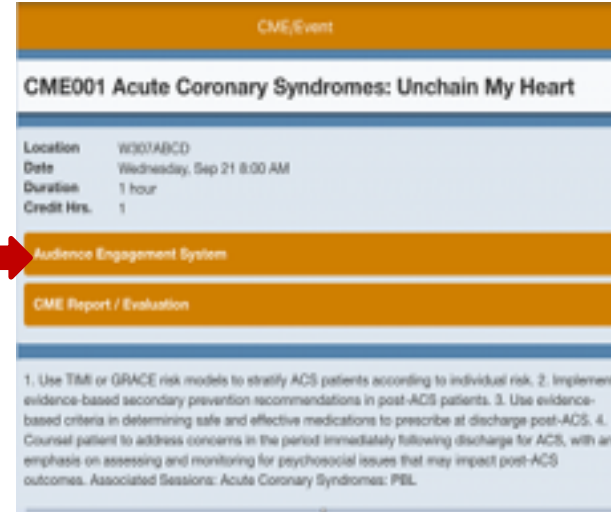
Step 1



Step 2




Step 3





A more terrible lord over Mankind
than even Death itself

- Albert Schweitzer

A photograph of several red poppies with long green stems, set against a clear, bright blue sky. The flowers are in various stages of bloom, with some fully open and others partially visible. The lighting is bright, highlighting the vibrant red of the petals.

God's Own Medicine - Osler

Opioid Efficacy

- Acute / Postop pain analgesia:
 - Well established ¹⁻¹¹
 - Knowledge application suboptimal ^{12,13}
 - Can lead to chronic pain ^{12,14}
- Chronic pain analgesia for long-term use:
 - Literature mixed ¹⁵⁻²¹
 - Evidence insufficient overall ^{11,12,22-24}
 - Problems with study design:
 - Non-naturalistic studies
 - 1y placebo-controlled severe pain trials unethical

Opioid Efficacy References

- 1 Jones. Acute injury Rx NSAID v other. *Coch Database Syst Rev.* 2015;7:CD007789
- 2 Chou. Postop pain Rx guide APS, ASRPM, ASA. *J Pain.* 2016;17(2):131-7
- 3 Dworkin. Pharmacologic Rx neuropathic pain. *Pain.* 2007;132(3):237-51
- 4 Humble. Amputation, thoracotomy, mastectomy pain Rx. *Eur J Pain.* 2015;19(4):451-65
- 5 Blondell. Pharmacologic Rx acute pain. *Am Fam Phys.* 2013;87(11):766-72
- 6 Chou. Acute, chronic LBP meds guide. *Ann Int Med.* 2007;147(7):505-14
- 7 Dijkstra. Prehospital trauma Rx. *Eur J Pain.* 2014;18(1):3-19
- 8 Manterola. Acute abdomen pain Rx. *Coch Database Syst Rev.* 2011 Jan 19;(1):CD005660
- 9 Davis. Cancer pain opioid guide. *Onc (Williston Park).* 2007;21(10):1229-38
- 10 Khan. Opioid v adjuvant analgesics. *Am J Hosp Palliat Care.* 2011;28(5):378-83
- 11 Manchikanti. ASIPP guide for opioids. *Pain Physi.* 2012;15(3 Suppl):S1-65
- 12 Sinatra. Inadequate acute pain Rx causes, consequences. *Pain Med.* 2010;11(12):1859-71
- 13 Albrecht. Trauma acute pain undertreatment. *Br J Anes* 2013;110(1):96-106
- 14 Kehlet. Persistent postop pain: risk factors, prevention. *Lancet.* 2006;367(9522):1618-25
- 15 Manchikanti. LT opioid: chronic nonCA pain. *Pain Phys.* 2011;14:91-12
- 16 Deshpande. Opioids, chronic LBP. *Coch Database Syst Rev.* 2007 Jul 18;(3):CD004959
- 17 Colson. Review: opioid efficacy in cancer. *Pain Phy.* 2011;14:E85-E102
- 18 Papaleontiou. Elderly nonCA pain, opioids. *J Am Ger Soc.* 2010; 58:1353-69
- 19 da Costa. Opioids for OA knee, hip. *Coch Database Syst Rev.* 2014 Sep 17;9:CD003115
- 20 Dillie. QOL associated with qd opioids. *J Am Board Fam Med.* 2008;21(2):108-17
- 21 Trescot. Opioids in chronic nonCA pain. *Pain Phys.* 2008;11(2 Suppl):S5-S62
- 22 CDC opioid prescribing guide for chronic pain 2016 Accessed 4/12/16
- 23 Chou. LT opioids in chronic pain effectiveness, risks. *AIM.* 2015;162(4):276-86
- 24 Chaparro. Opioids in chronic LBP. *Coch Database Syst Rev.* 2013 Aug 27;(8):CD004959

BAYER Pharmaceutical Products

HEROIN-HYDROCHLORIDE

is pre-eminently adapted for the manufacture of cough elixirs, cough balsams, cough drops, cough lozenges, and cough medicines of any kind. Price in 1 oz. packages, \$4.85 per ounce; less in larger quantities. The efficient dose being very small (1-48 to 1-24 gr.), it is

The Cheapest Specific for the Relief of Coughs

(In bronchitis, phthisis, whooping cough, etc., etc.)


WRITE FOR LITERATURE TO

FARBENFABRIKEN OF ELBERFELD COMPANY

SOLE AGENTS

40 **Stone Street**, NEW YORK

Opioids Have Consequences

- 
- Diversion
 - Misuse
 - Non-medical use
 - Addiction
 - Overdose
 - Death

- Psychomotor (small effects) ¹⁻³
- Hypogonadism in men ^{4,5}
- Drowsiness 3-88% ^{2,6-9}
- Falls / Fractures ^{10,11}
- Depression ¹² except buprenorphine ¹²
- Opioid Bowel Dysfunction ^{5,13,14}
 - 3-85% nausea, vomiting ⁸
 - 5-97% constipation ^{5,8,14,15}

¹ Larsen. LT opioid psychomotor effects. *Anaesthesist*. 1999;48(9):613-24

² Dassanayake. Benzodiazepine, antidepressant, opioid & driving. *Drug Saf*. 2011;34(2):125-56

³ Soyka. Opioids and traffic safety - focus on buprenorphine. *Pharmacopsych*. 2014;47(1):7-17

⁴ Bawor. Testosterone suppression in opioid users. *Drug Alc Dep*. 2015;149:1-9

⁵ Birthi. Hypogonadism associated with LT opioids. *J Opioid Manag*. 2015;11(3):255-78

⁶ Zlott. Mechanisms pharmacologic agents contribute to fatigue. *PMR*. 2010;2(6):451-5

⁷ Wiffen. Opioid impact: consciousness, appetite thirst. *Coch Database Syst Rev*. 2014;5:CD011056

⁸ Kalso. Opioids in chronic non-cancer pain: systematic review. *Pain*. 2004;112(3):372-80

⁹ Oosten. Opioid AEs in cancer-related pain. *J Pain*. 2015;16(10):935-46

¹⁰ Bushel. Medication fall injury risk among older people. *Eur J Pub Health*. 2014;25(3):527-32

¹¹ Solomon. Comparative analgesic safety in elderly arthritics. *Arch Int Med*. 2010;170(22):1968-76

¹² Schemer. Prescription opioid duration increases depression risk. *Ann Fam Med*. 2016;14:54-62

¹³ Bodkin. Buprenorphine for refractory depression. *J Clin Psychopharmacol*. 1995;15(1):49-57

¹⁴ Panchal. Opioid-induced bowel dysfunction. *Int J Clin Pract*. 2007;61(7):1181-7

¹⁵ Szigethy. Narcotic bowel syndrome. *OIC. Curr Gastroenterol Rep*. 2014;16(10):410

¹⁶ Rosti. Opioid-related bowel dysfunction. *Eur Rev Med Pharmacol Sci*. 2010;14(12):1045-50

**Good judgment
comes from experience,
and a lot of that
comes from bad judgment.**

- Will Rogers

Dual Problems

A photograph of a mountain goat and a black dog standing on a rocky cliff edge. The goat is in the foreground, facing left, and the dog is behind it, also facing left. The background shows a vast, hazy mountain range under a cloudy sky.

100,000,000 with pain ¹
> 18,000 opioid-related deaths ²

¹ Institute of Medicine. Relieving Pain in America. 2011. Accessed 3/23/16

² CDC: Deaths Involving Opioid Analgesics, Heroin. Accessed 7/12/16

Definition of Trouble

- Diversion Transfer from a lawful to unlawful channel ^{1,2}
- Misuse Use in a way other than intended ³
- Non-medical use Use for reason(s) other than intended ^{3,4}
- Addiction Compulsive use + negative outcomes ⁵

- Overdose Related to
 Overdose death Respiratory depression ⁶
 Torsades de Pointes (methadone) ⁷

¹ Inciardi. Prescription opioid abuse and diversion. *Pain Med.* 2009;10(3):537-48

² Larancel. Definitions related to opioids. *Drug Alc Rev.* 2011b;30:236-45

³ WHO. *Lexicon of alcohol, drug terms* Accessed 4/2/16

⁴ Del Fabbro. Assessment, management of chemical coping. *J Clin Oncol.* 2014;32(16):1734-8

⁵ ASAM. *Definition of Addiction.* 2011 Accessed 4/2/16

⁶ Pattison. Opioids and control of respiration. *Br J Anes.* 2008;100(6):747-58

⁷ Paulozzi. Risk for methadone OD. 1999-2010. *MMWR Weekly.* 2012;61(26):493-7

Epidemiology of Trouble

- US 5% of world population
80% of world's opioids 99% of world's hydrocodone ¹
- Diversion 0.7% patients prescribed opioids are doctor shoppers ²
Strong association with OD deaths ³
- Misuse 20% of those prescribed ^{4,5} ↓ from 2003-2013 ⁶
33% ↑ misuse if opioid started before 12th grade ⁷
- Addiction Prescription opioids: ↑ to 2 million Heroin: ↑ to 0.5 million ^{6,8}
Present in up to 95% opioid OD deaths ^{9,10}

¹ Manchikanti. Opioid therapeutic use, abuse, nonmedical use. *Pain Phys.* 2010;13(5):401-35

² McDonald. Estimating prevalence opioid diversion. *PLoS One.* 2013;8(7):e69241

³ Hall. Patterns of abuse among unintentional OD fatalities. *JAMA.* 2008;300(22):2613-20

⁴ Sullivan. Opioid possible, probable misuse in commercial, Medicaid. *Pain.* 2010;150(2):332-9

⁵ Reutsch. Empirical view of opioid dependence. *J Manag Care Pharm.* 2010;16(1 Suppl B):S9-13

⁶ Han. NMU Rx opioid use, OUD among 18-64yo US 2003-2013. *JAMA.* 2015;314(14):1468-78

⁷ Miech. Rx opioids in adolescence, future misuse. *Pediatrics.* 2015;136(5)

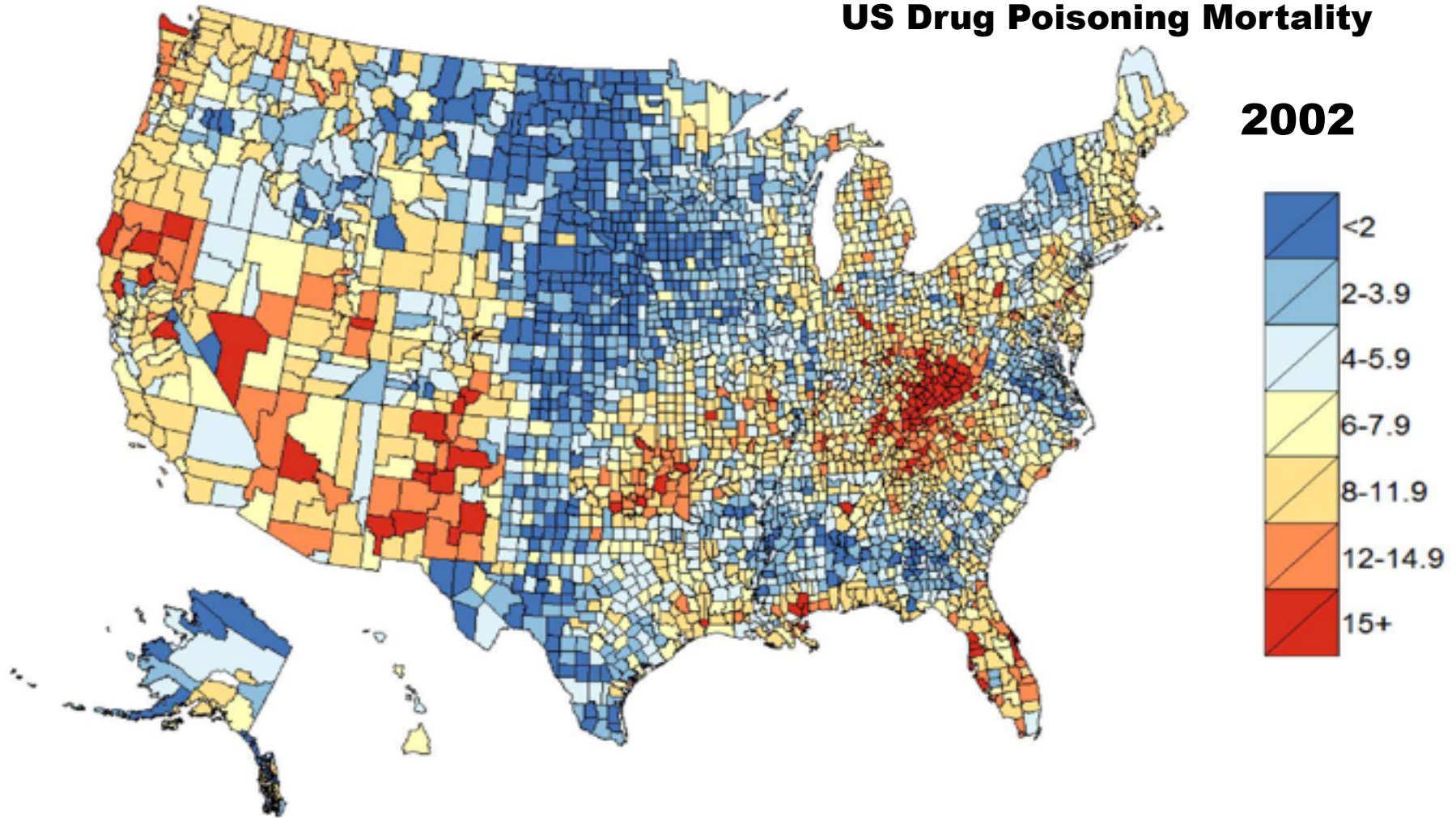
⁸ SAMHSA. 2013 National Survey on Drug Use and Health Accessed 4/3/26

⁹ Paulozzi. OD death methadone v other opioids in West Virginia. *Addiction.* 2009;104(9):1541-8

¹⁰ Hall. Abuse patterns in unintentional pharmaceutical OD fatalities. *JAMA.* 2008;300(22):2613-20

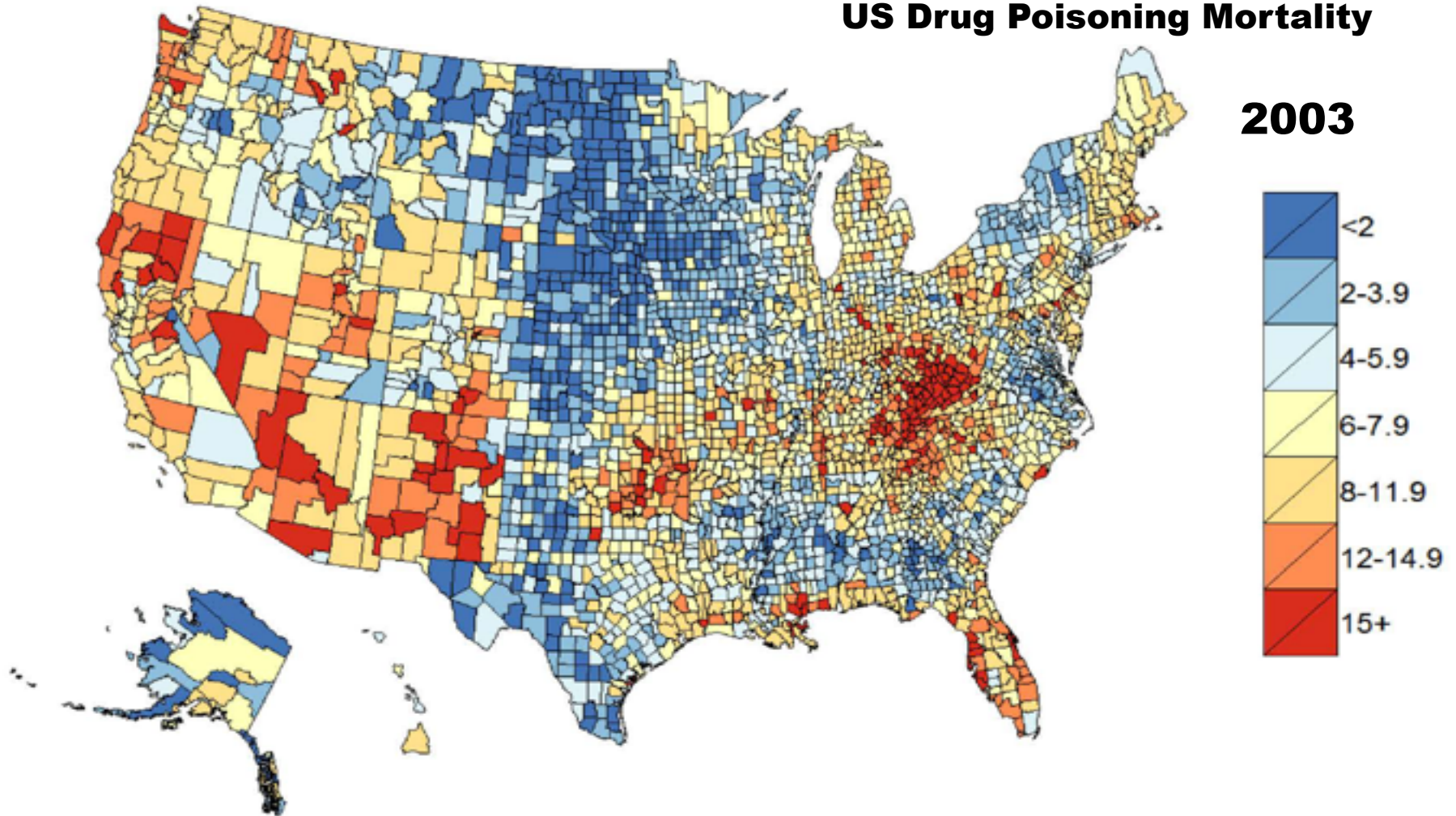
US Drug Poisoning Mortality

2002



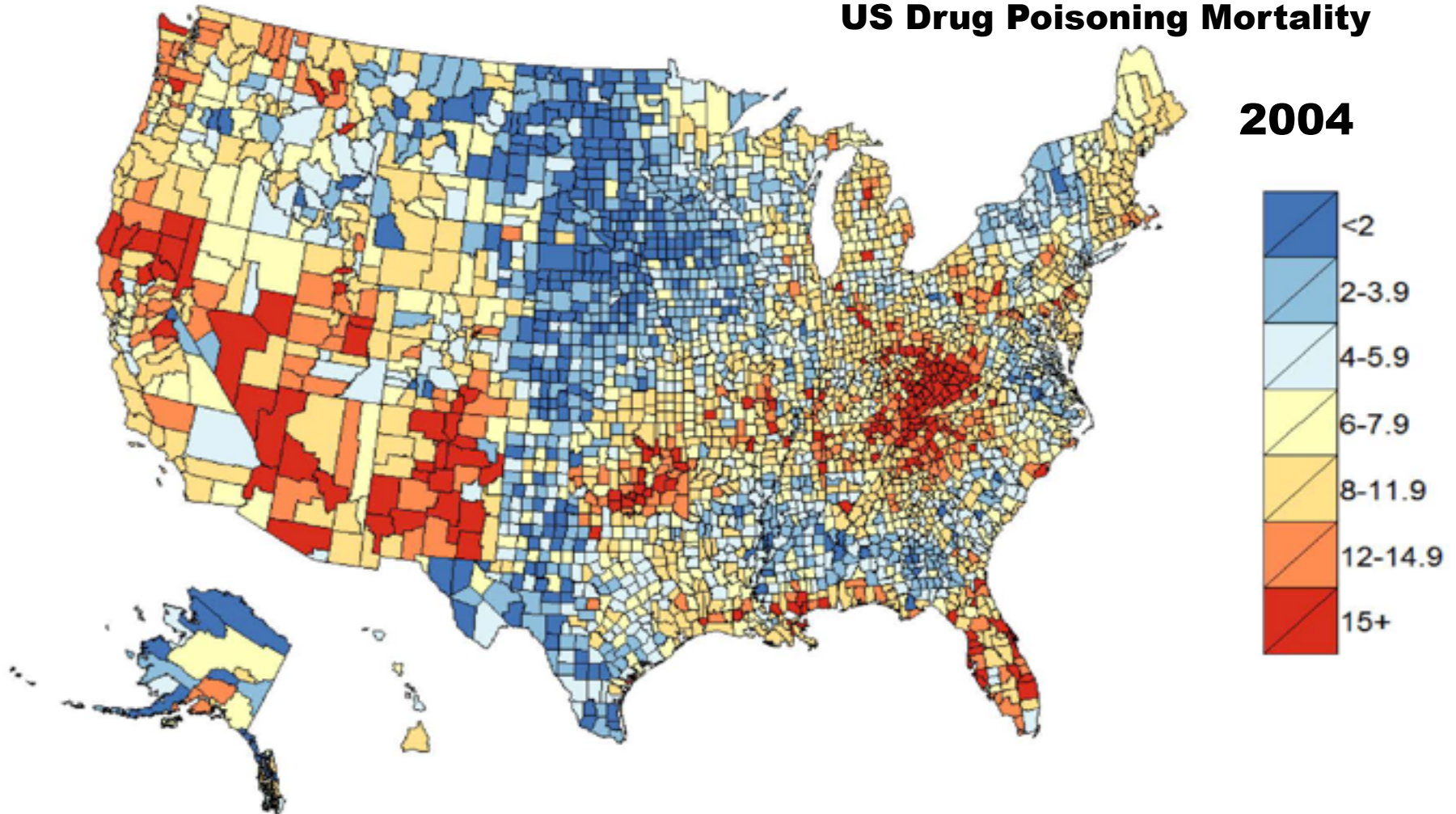
US Drug Poisoning Mortality

2003



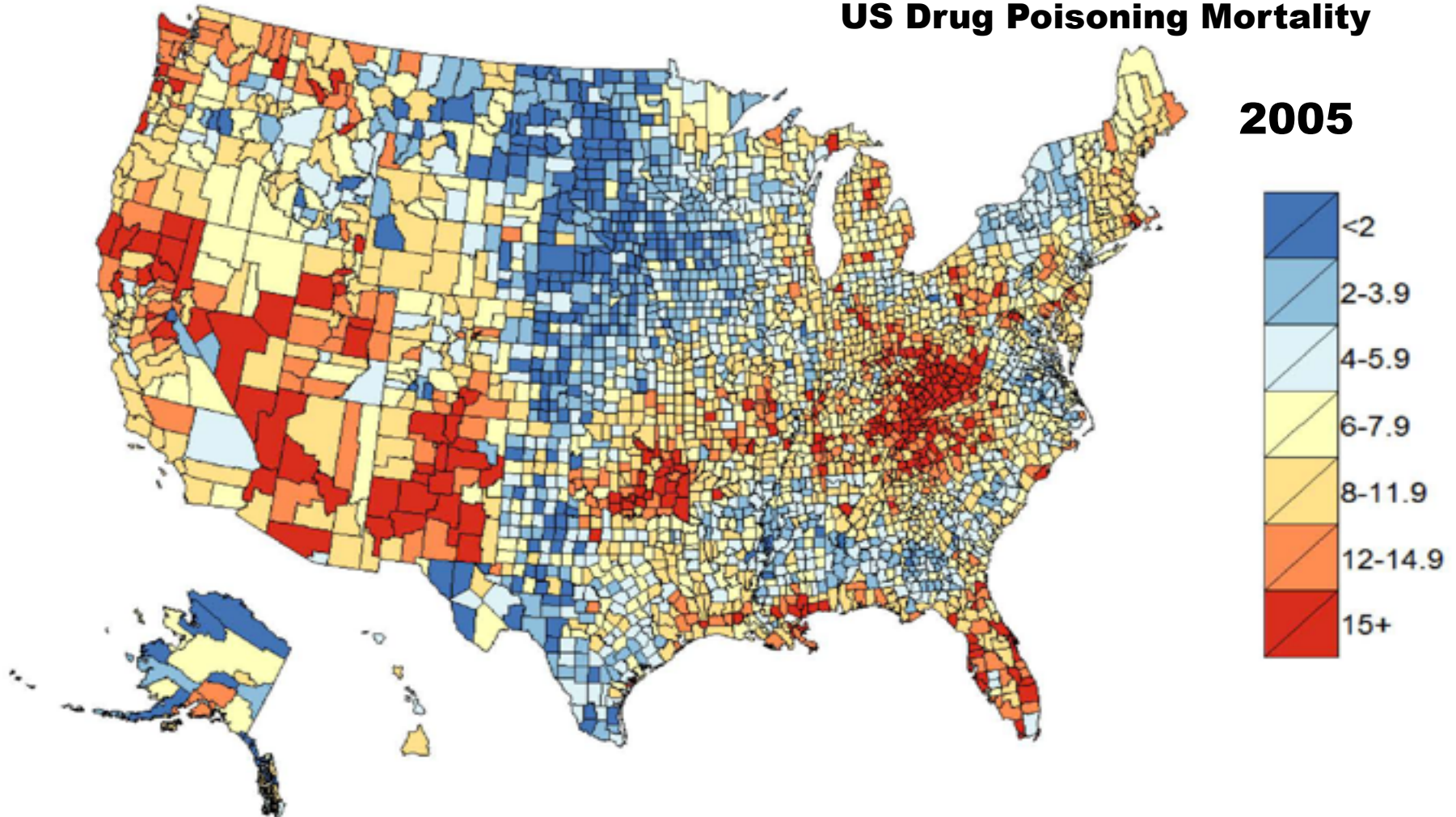
US Drug Poisoning Mortality

2004



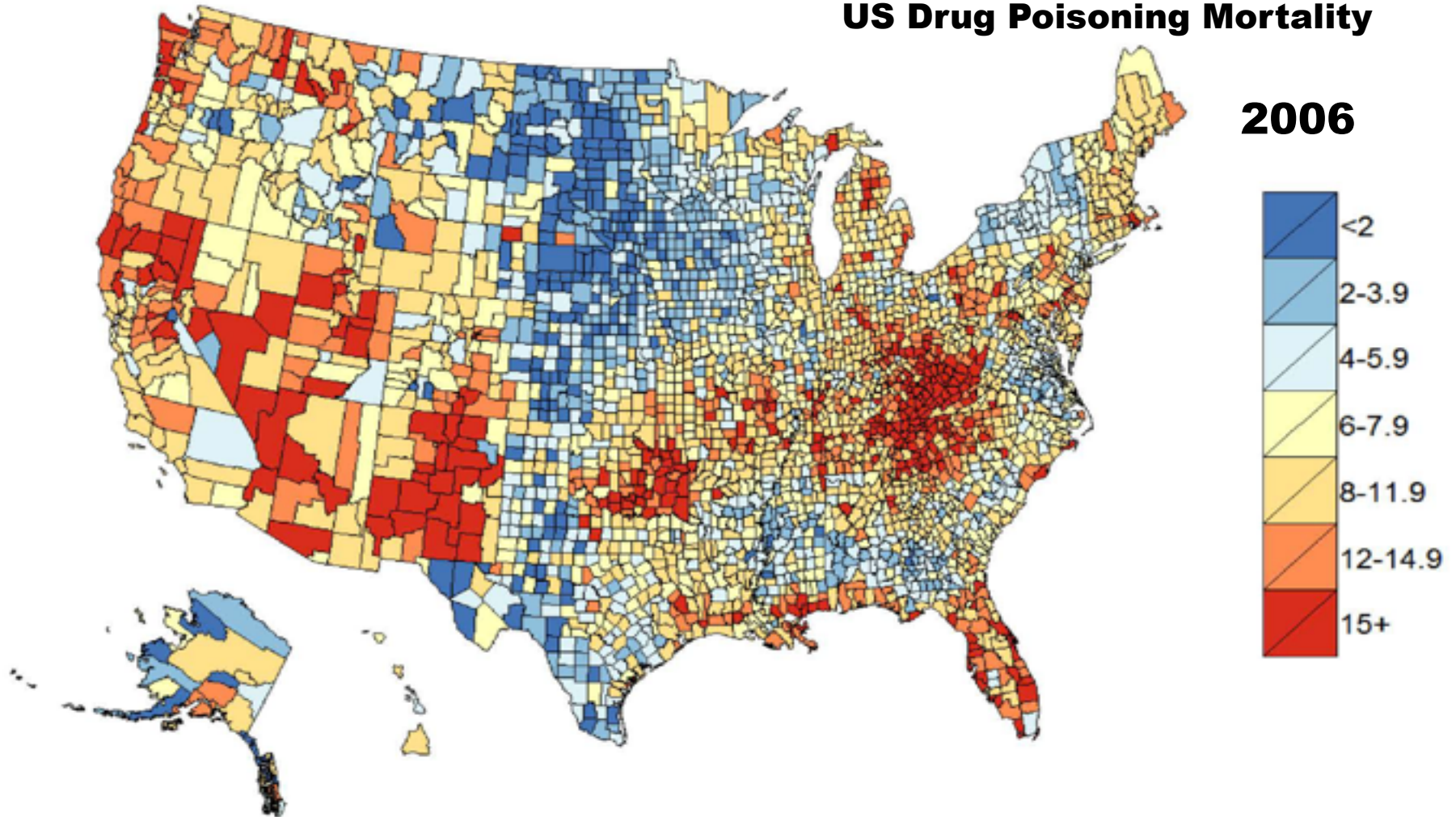
US Drug Poisoning Mortality

2005



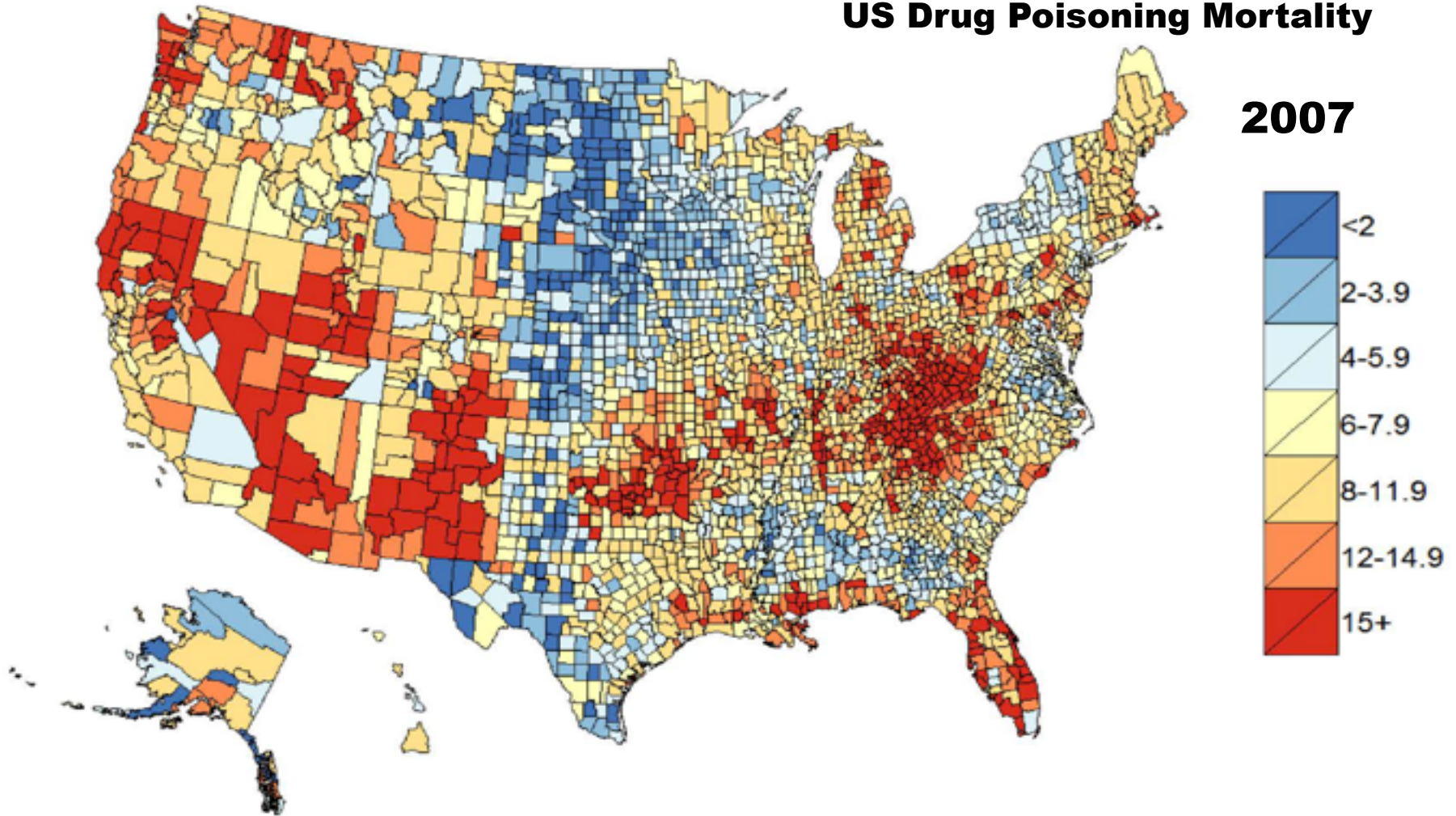
US Drug Poisoning Mortality

2006



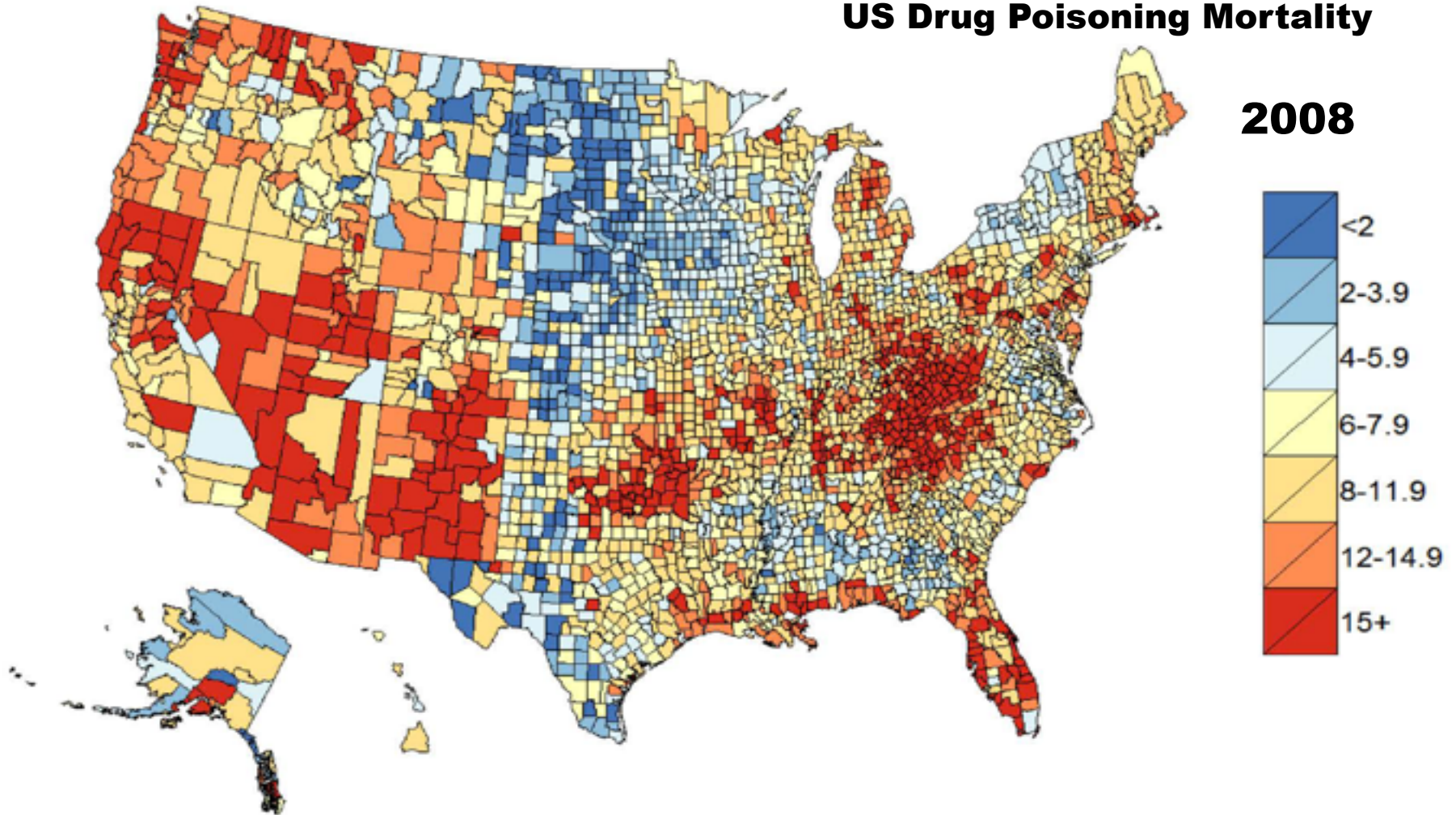
US Drug Poisoning Mortality

2007



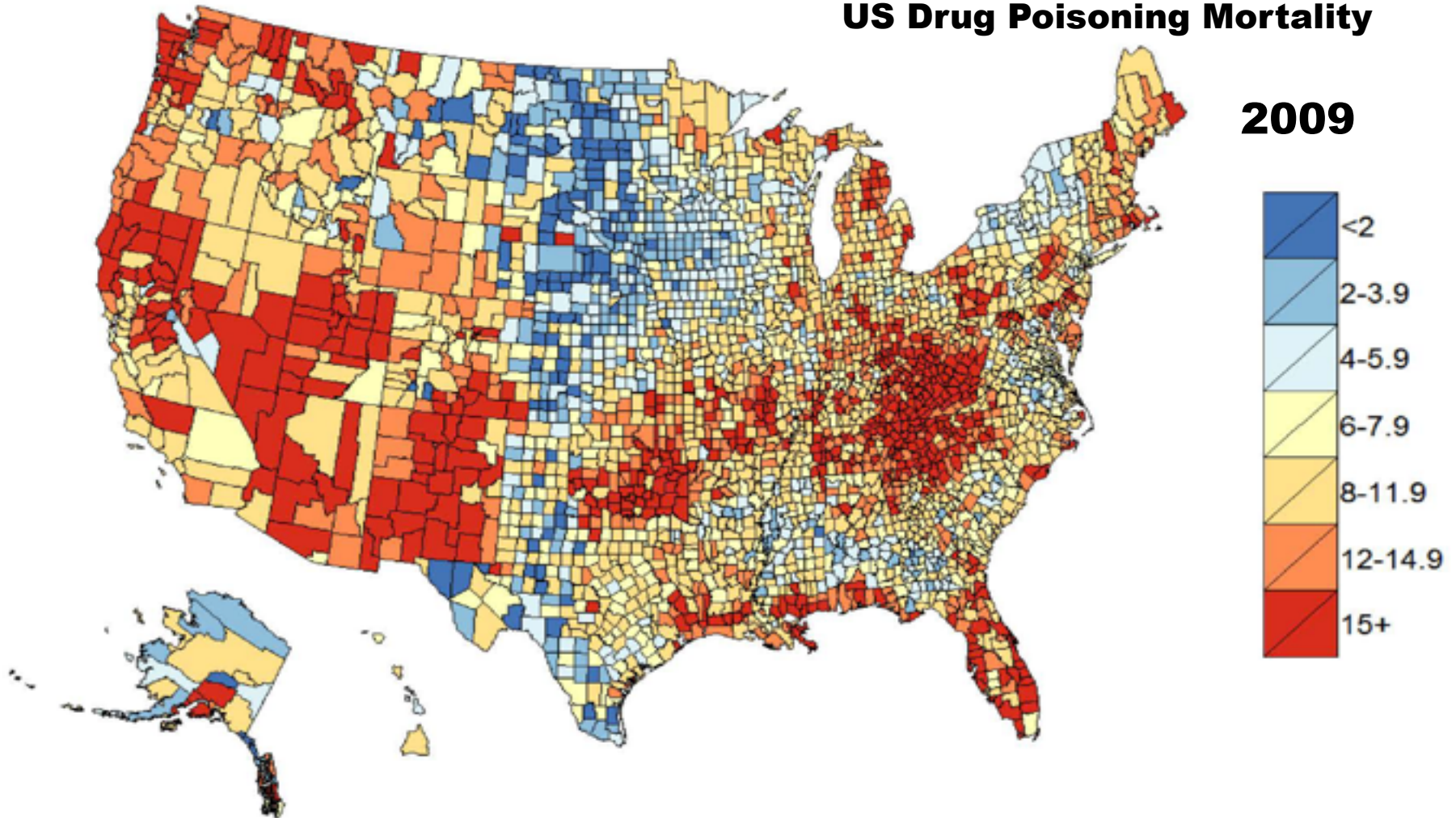
US Drug Poisoning Mortality

2008



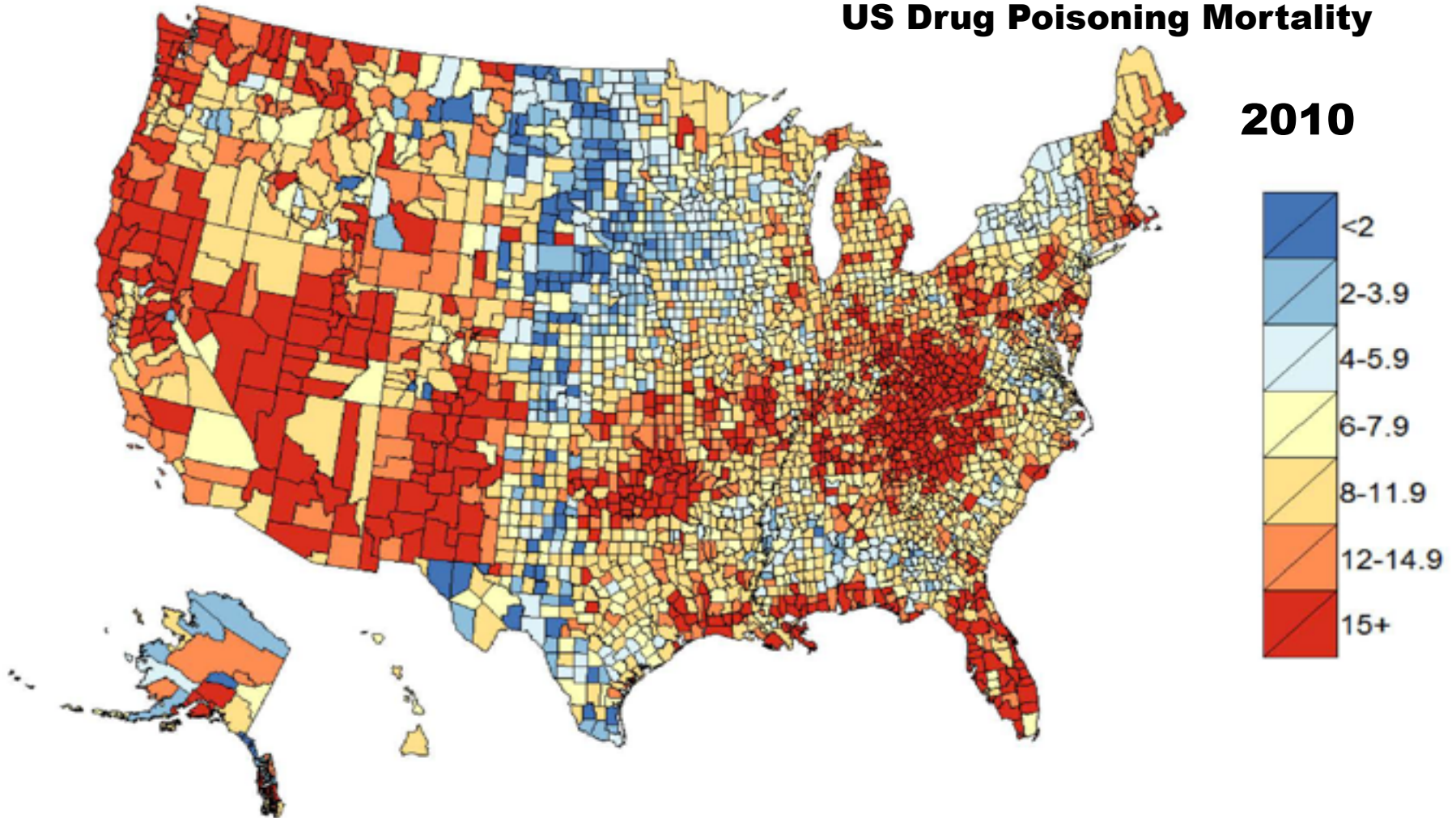
US Drug Poisoning Mortality

2009



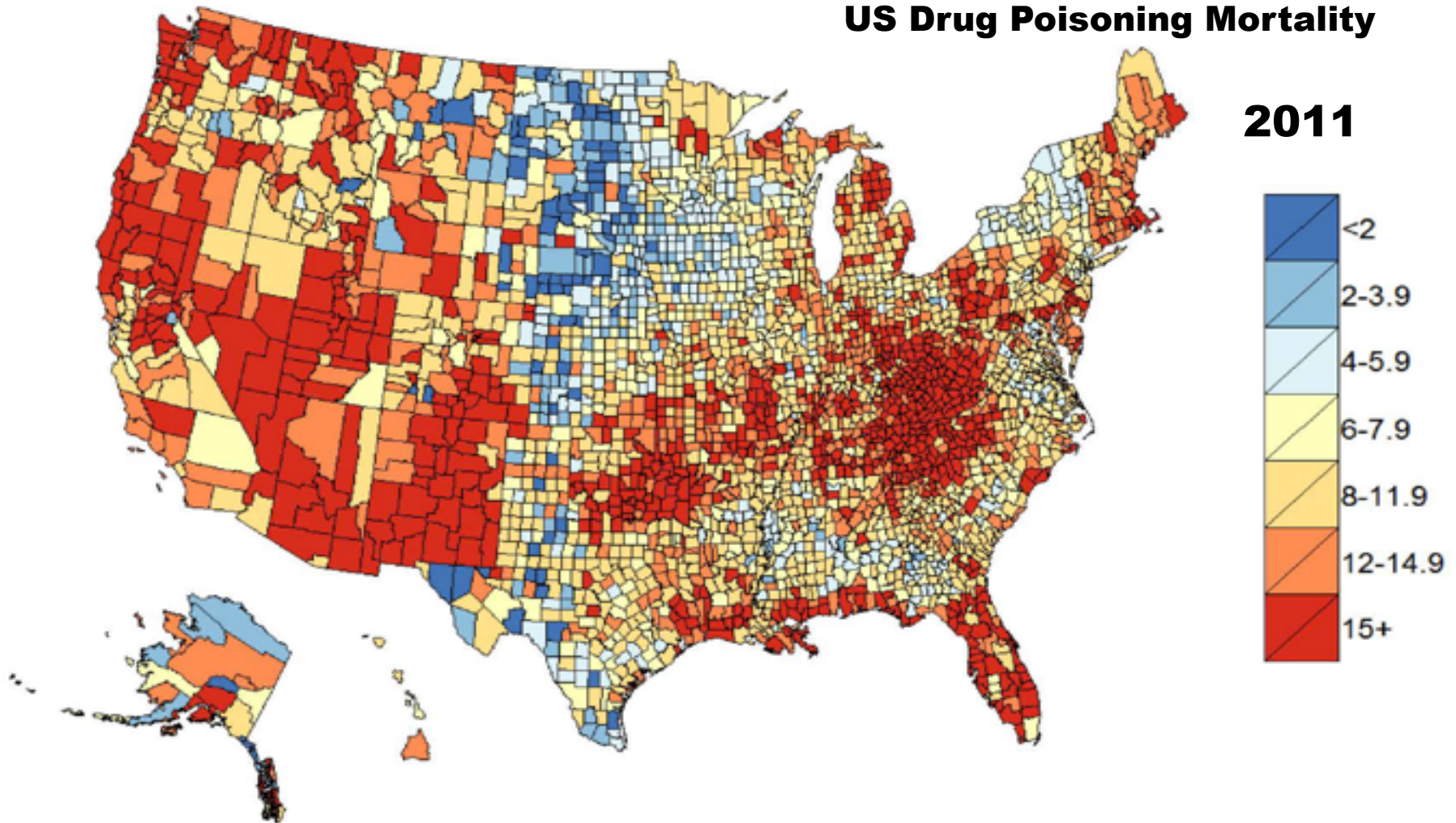
US Drug Poisoning Mortality

2010



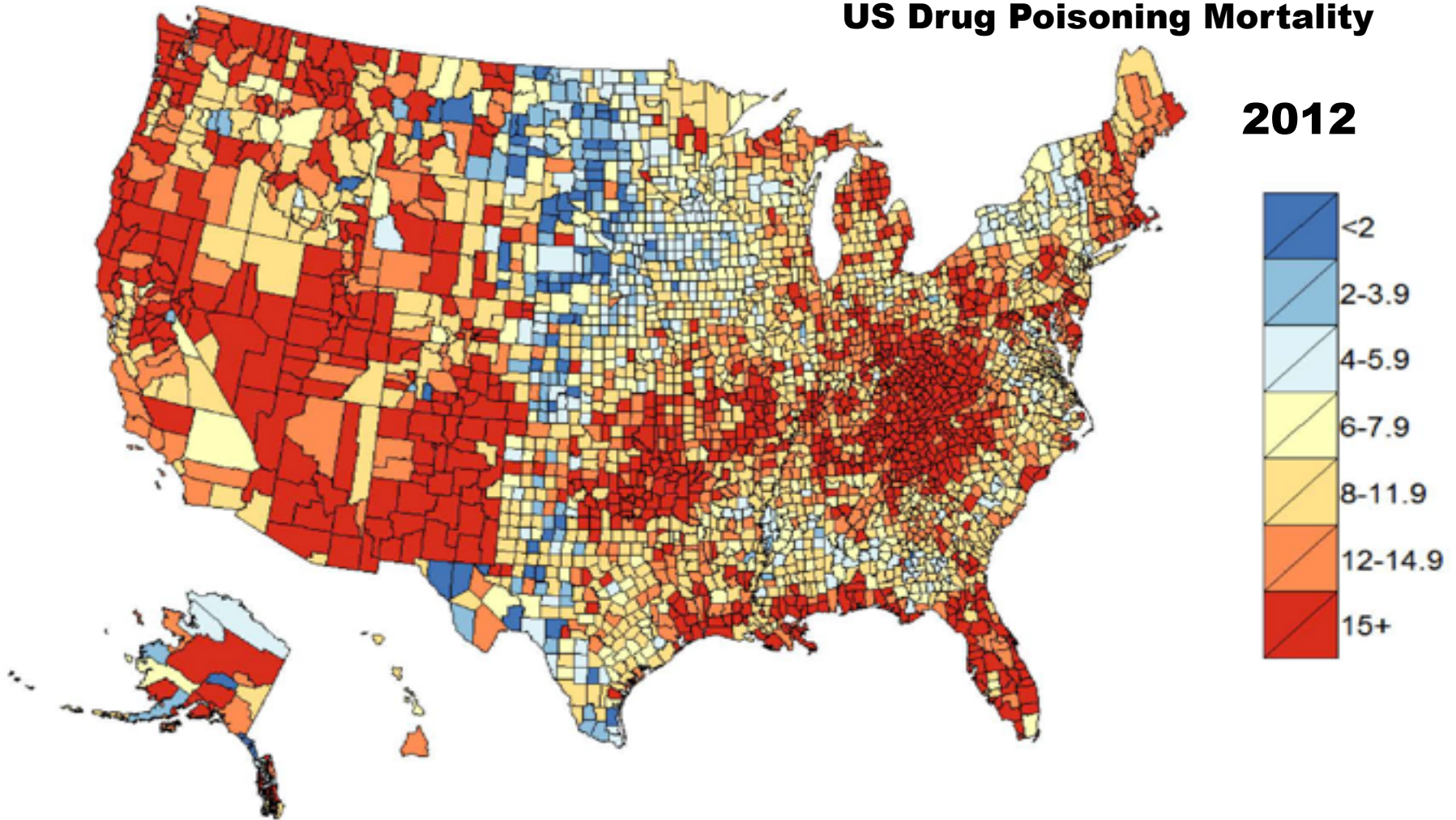
US Drug Poisoning Mortality

2011



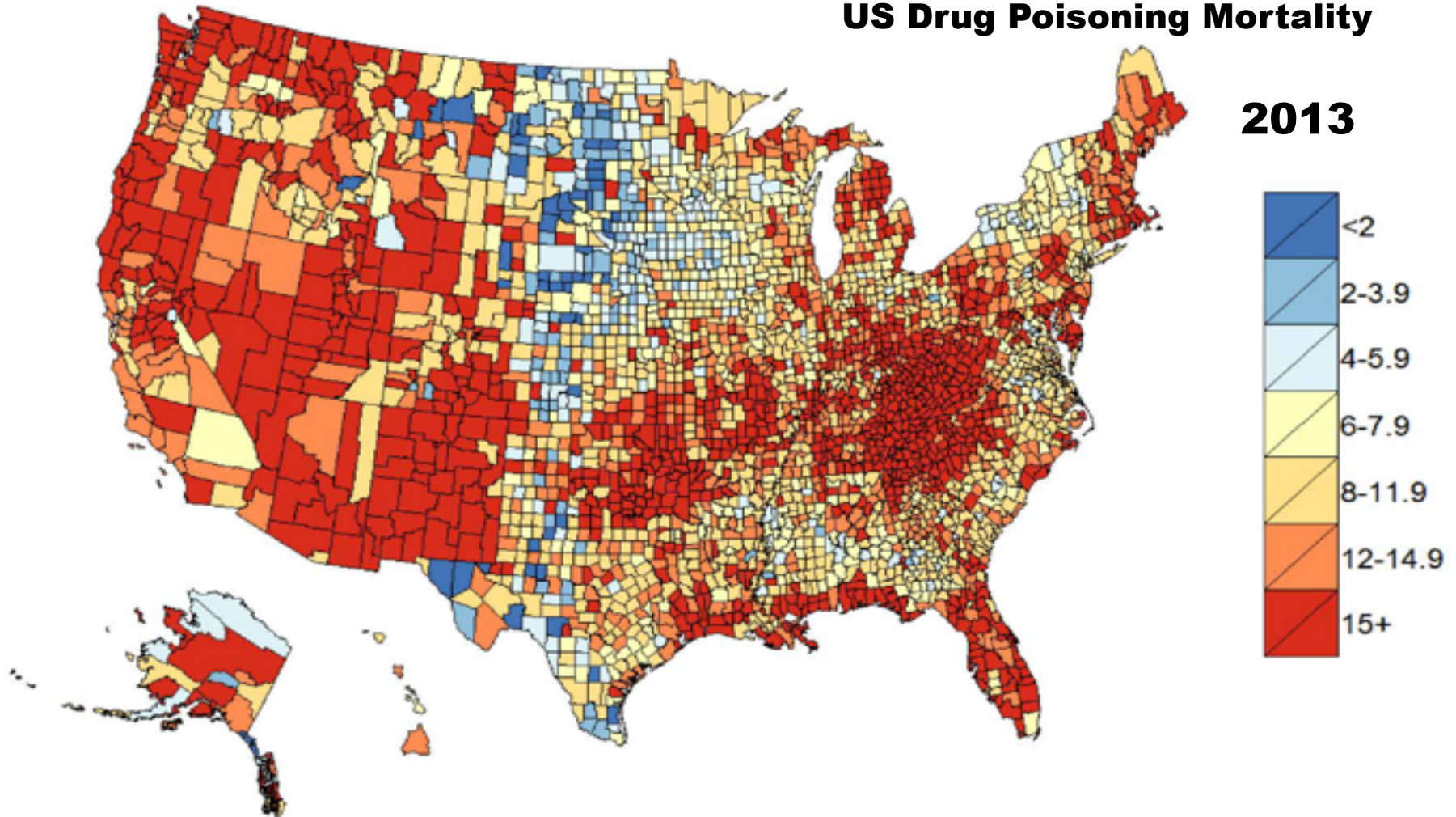
US Drug Poisoning Mortality

2012

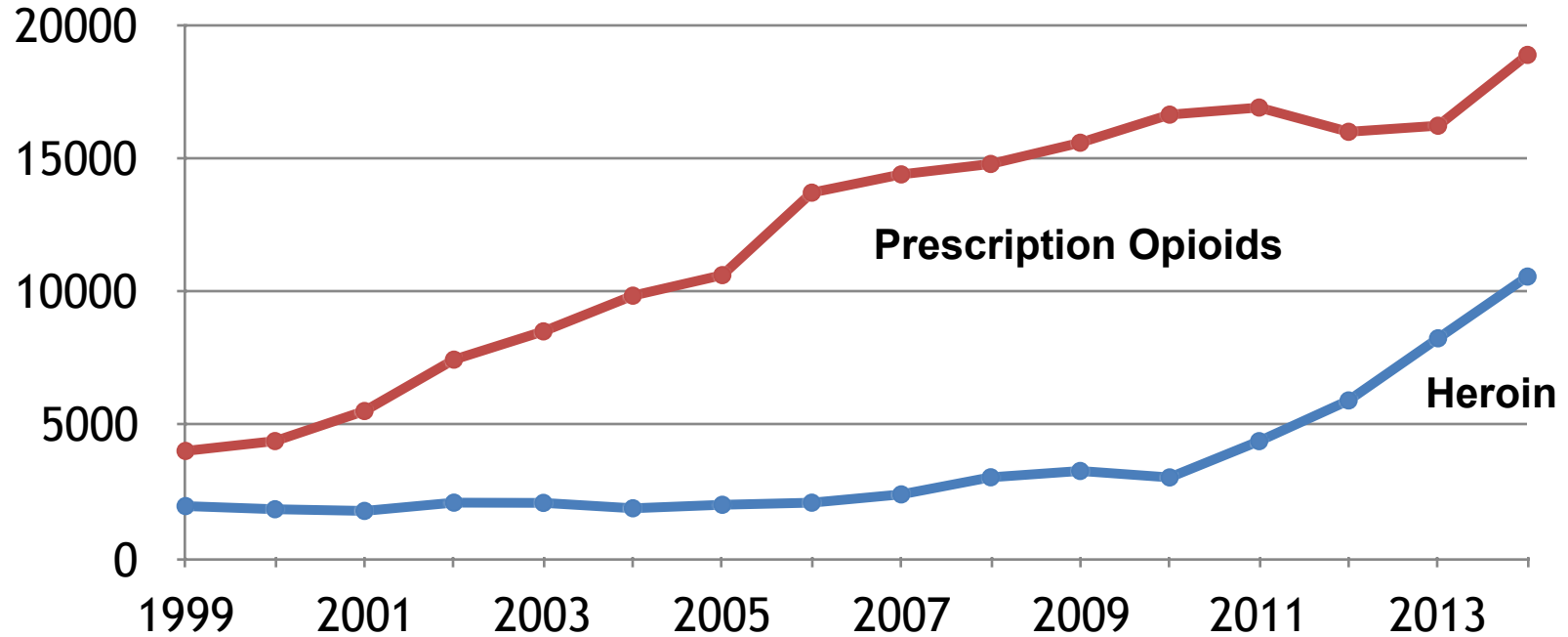


US Drug Poisoning Mortality

2013



Opioid Overdose Deaths Total US Deaths



Heroin

- Route of administration: Smoked Injected
- Vietnam
 - 45% soldiers used opium or heroin in Vietnam ¹
 - 5% heavy users addicted on return to US ^{1,2}
- Severity of addiction
 - > that for prescribed opioids ³
 - Injectors > non-injectors ³
- Recent increases in use, addiction, OD death probably independent of efforts to address prescription opioid problems ⁴⁻⁸

¹ Robins. VN vets' rapid recovery from heroin addiction. *Addiction*. 1993;88:1041-54

² Robins. How permanent was VN drug addiction? *Am J Pub Hlth*. 1974;64(Suppl 12):38-43

³ Potter Buprenorphine, methadone for opioid, heroin. *J Stud Alc Drug*. 2013;74(4):605-13

⁴ Compton. Relationship between NMU Rx opioids and heroin. *NEJM*. 2016;374:154-63

⁵ Dart. Opioid abuse, mortality US trends. *NEJM*. 2015;372(3):241-8

⁶ Cicero. ADF & Rx epidemic. *JAMA Psych*. 2015;72:424-9

⁷ Johnson. OD death decline after Florida policy changes. *MMWR*. 2014;63(26):569-74

⁸ Rudd. Heroin OD death ↑- 28 states.. *MMWR*. 2014;63(39):849-54

Opioid Overdose: Background Etiology

- Co-occurring
 - Medications
 - Respiratory disease
 - Sleep apnea
 - Prolonged QT (methadone)
- Suicide ¹
- Pseudoaddiction
- Memory problem
- Opioid Addiction ^{2,3}

¹ Madadi. Suicide by means of opioid OD in chronic pain patients. Curr Pain Headache Rep. 2014;18(11):460

² Paulozzi. OD death methadone v other opioids in West Virginia. Addiction. 2009;104(9):1541-8

³ Hall Abuse patterns, unintentional OD fatalities. JAMA. 2008;300(22):2613-20

Opioid Prescribing Risk Management

Stepwise Process to Help Ensure Safe Use

- 1) Risk Assessment
 - a) Risk evaluation
 - b) Risk stratification
- 2) Risk Mitigation
- 3) Risk Monitoring
- 4) Aberrancy Management

Follow-Up Pain Management Visit

- Subjective 5 A's ^{1,2}
 - **A**ctivities (function)
 - **A**nalgesia
 - **A**ffect
 - **A**dverse events
 - **A**bserrancies

¹ After Passik. Tool: assess, document outcomes in chronic pain, opioids. Clin Ther. 2004;26(4):552-61

² Kirsch. 4 A's for ongoing monitoring chronic pain. Medscape Neurol. 2005 Accessed 4/14/16

Top 10 Reasons for My Medication Issue

6) Oxycodone in my Urine? That CAN'T Be!

But I Did have Sex with my Husband who takes it!

7) I lost my pills when THREE Trees Fell on my house

8) The Deer ate them off the Picnic table

9) I was Eating my Percocet over the Sink when they Fell in!

10) Sorry I'm Late I got Arrested ...I'm in a Rush!
I need my refill ...

1) You won't Believe This!

I took off Fast The Pen Popped off the Dash

Hit the Prescription lying on the Car Seat

That's why there was a 1 in Front of the 20 Vicodin
Once I got to the Pharmacy !!

2) They Fell on the Floor All these Ants Carried them Off
I just watched in Amazement !

3) I Don't know HOW they ended in the Microwave

4) My Parakeet Carried the Bottle out the Window

5) I buy Syringes because my Trainer told me
to Inject B12 4 Times a Day

Aberrancy Management

- Aberrancy = Deviation from controlled substance agreement
- Present in 5-80% of pain patients on opioids ¹⁻³
- Response options:
 - Coach adherence ⁴
 - Refer, diagnose, treat opioid addiction ⁵
 - Discontinue opioid - non-judgmental ⁶
 - Discharge from practice - therapeutically

¹ Martell. Ppoids for chronic back pain. AIM. 2007;146(2):116-27

² Fishbain. % chronic nonCA pain patients on opioids develop addiction, aberrancy. Pain Med. 2008;9(4):444-59

³ Fleming. Reported aberrancies of substance misuse in 1^o care. Pain Med. 2008;9(8):1098-106

⁴ Jamison. Substance misuse Rx for high-risk chronic pain patients on opioids. Pain. 2010;150:390-400

⁵ Compton. Should opioid abusers be discharged from opioid analgesic therapy? Pain Med. 2008;9(4):383-90

⁶ Peppin. Managing pain while mitigating risk Accessed 4/25/16

Addiction

- *Not* Basic drive in all persons
- *Not* Simply physical dependence ¹
- *Not* To be confused with pseudo-addiction ²⁻⁴
- *Is* Chronic disease of brain reward ^{5,6} characterized by

Compulsion

Loss of control

Continuation despite negative consequences ^{7,8}

Based on craving: “*Needing*” not “*Liking*” drug ^{9,10}

¹ Savage. Definitions: use of opioids. J Pain Symp Manage. 2003;26(1):655-67

² Weissman. Opioid pseudoaddiction - an iatrogenic syndrome. Pain. 1989;36(3):363-6

³ Passik. Pseudoaddiction revisited. Pain Manag. 2011;1(3):239-48

⁴ Elander. Sickle cell pain, pseudoaddiction. J Pain Symp Manage. 2004;27(2):156-69

⁵ American Society of Addiction Medicine. Definition of addiction. 2011 Accessed 3/29/16

⁶ Hasin. DSM-5 criteria for SUDs. Am J Psych. 2013;170(8):834-51

⁷ Smith. Cocaine abuse Dx, Rx. J Sub Abuse Treat. 1984;1(1):5-9

⁸ Savage. Addiction assessment in pain treatment. Clin J Pain 2002;18:S28-38

⁹ Miller. Craving alcohol and drugs. J Addict Dis. 2001;20(3):87-104

¹⁰ Richard. Brain circuits: reward, motivation. Neurosci Biobehav Rev. 2013;37(9 Pt A):1919-31

Opioid Addiction

Shares Features with Other Chronic Diseases ¹

- Involuntary ¹
- Distinct neurophysiology ^{2,3}
- Genetically based 60-80% Environmentally influenced ^{1,4}
- Identifiable: Screening → Diagnosis ⁵
- Treatable *Not* curable ¹
- Predictable course treated, untreated ¹
- 2^o problems like intimate partner violence,⁶ hepatitis, HIV ⁷
- 10-15% patients on chronic opioids - studies vary widely ⁸⁻¹⁵

¹ McLellan. Drug dependence, a chronic medical illness. JAMA. 2000;284(13):1689-95

² Koob. Neurocircuitry of addiction. Neuropsychopharmacology. 2010;35(1):217-38

³ Sabatinelli. Pleasure activates NA, MPC. J Neurophysiol. 2007;98(3):1374-9

⁴ Blum. Genetic Addiction Risk Score. Mol Neurobiol. 2014;50(3):765-96

⁵ Bowman. Reducing health consequences of opioid addiction. Am J Med. 2013;126(7):565-71

⁶ Dube. Exposure to abuse among adults witnessing IPV (as children). Violence Vict. 2002;17(1):3-17

⁷ MacArthur. Opioid substitution & HIV with IVDU. BMJ. 2012;345:e5945

⁸ Fishbain. Addiction % in chronic nonmalignant pain patients on opioids. Pain Med. 2008;9(4):444-59

⁹ Boscarino. OUD prevalence in chronic pain. J Addict Dis. 2011;30(3):185-94.

¹⁰ Edlund. Risk of opioid abuse, dependence with chronic opioids. Drug Alc Dep. 2010;112:90-8

¹¹ Noble. LT opioids for chronic noncancer pain. Coch Database Syst Rev. 2010;20:CD006605

¹² Manchikanti. Controlled substance abuse, illicit drug use in chronic pain. Pain Phys. 2006;9(3):215-25

¹³ Cowan. Survey of chronic noncancer pain patients prescribed opioids. Pain Med. 2003;4(4):340-51

¹⁴ Vowels. Rates of opioid misuse, abuse, addiction in chronic pain. Pain. 2015;156(4):569-76

¹⁵ Højsted. Addiction to opioids in chronic pain. Eur J Pain. 2007;11(5):490-518

Addiction Terminology

- Equivalent to Opioid Use Disorder (OUD) ¹
- DSM-5 combined substance “abuse” and “dependence” ²
 - “Abuse” Pejorative ^{3,4}
Better “Non-Medical Use”
 - “Dependence” Ambiguous ⁵
Physical dependence: Tolerance Withdrawal
- “Addiction” Stigmatizing ?
Can replace with Opioid Use Disorder ¹
Person first language: “Person with addiction...”

¹ American Psych Assoc. (2013). Diagnostic & statistical manual: DSM-5. Washington DC: APA Accessed 3/28/16

² American Psych Publishing. DSM-5 Substance-Related and Addictive Disorders Accessed 3/28/16

³ Saitz. Recommending against terminology that can stigmatize. J Addict Med. 2016;10(1):1

⁴ WHO. Lexicon of alcohol, drug terms Accessed 4/2/16

⁵ Savage. Definitions: use of opioids. J Pain Symptom Manage. 2003;26(1):655-67

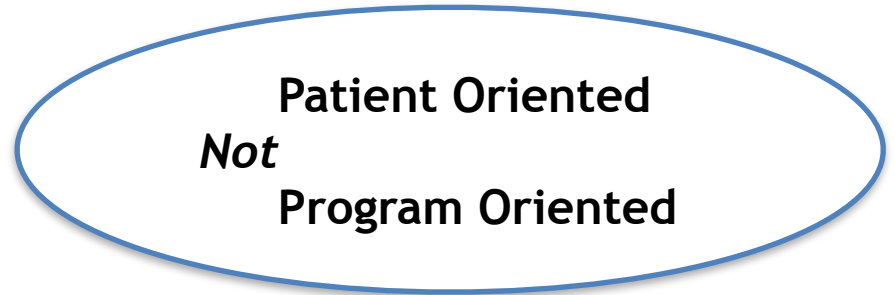
Polling Question

Which opioid addiction treatment approach is *not* supported by evidence ?

- A. Addiction therapy
- B. Narcotics Anonymous
- C. Medication management
- D. Brief interventions

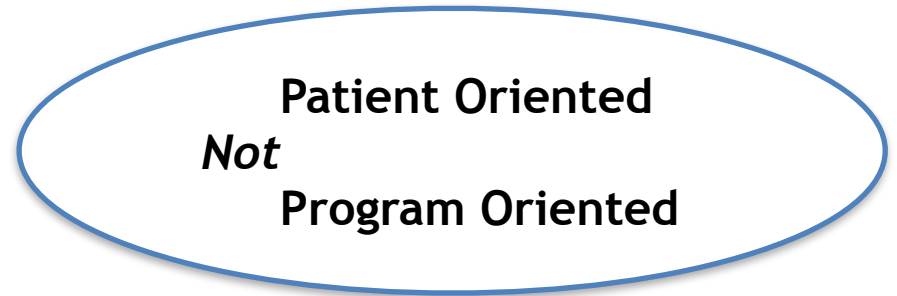
Opioid Use Disorder Treatment

- Mutual Help Programs
- Addiction Therapy
- Medication Management



Opioid Use Disorder Treatment

- Mutual Help Programs
- Addiction Therapy *
- Medication Management *



* Addiction treatment services: Provided professionally ¹

Mutual Help Programs

- Not *self* - help — *Mutual* help
- 12-step or other formats
- Peer Recovery Coaching ¹

- Narcotics Anonymous
- Pills Anonymous or Prescriptions Anonymous
- Alcoholics Anonymous

- Effective ²⁻¹³ Dose: weekly ^{9,11}
- Accessible
- Inexpensive

**Professional Role:
12-step
Facilitation**

¹ SAMHSA - BRSS TACS: Addiction recovery peer service roles. 2010. Accessed 7/19/16

² Gossop. NA, AA meeting attendance and outcomes. *Addiction*. 2008;103(1):119-25

³ Humphreys. Encouraging posttreatment self-help. *Alc Clin Exp Res*. 2007;31(1):64-8

⁴ Kelly. Youth Rx outcomes, 12-step attendance. *Drug Alc Dep*. 2013;129(1-2):151-7

⁵ Kelly. 12-step strengthens adolescent addiction Rx. *Drug Alc Dep*. 2010;110(1-2):117-25

⁶ Vederhus. High effectiveness of self-help. *BMC Psych*. 2006;6:35

⁷ Kaskutas. AA effectiveness: faith meets science. *J Addict Dis*. 2009;28(2):145-57

⁸ Krentzman. How AA, NA) work. *Alcohol Treat Q*. 2010;29(1):75-84

⁹ Hoffman. Effective Rx for alcohol, drug disorders. *Psych Clin North Am*. 1993;16(1):127-40

¹⁰ Witbrodt. 12-step attendance, abstinence over 9y J Sub Abuse Treat. 2012;43(1):30-43

¹¹ Humphreys. Self-help for alcohol and drugs. *J Sub Abuse Treat*. 2004;26(3):151-8

¹² Cloud. Dose, underutilization of 12-step. *Recent Dev Alc*. 2008;18:283-301

¹³ Monterosso. Behavioral economics of will in addiction recovery. *Drug Alc Dep*. 2007;90 Suppl 1:S100-11

Addiction Therapy

- Motivational Enhancement Therapy (MET)
- Cognitive Behavioral Therapy (CBT)
- Supportive- Expressive Therapy
- Contingency Management
- Trigger Management
- Network Therapy
- Peer Coaching
- Social Support
- Drug Court

Effective

- Opioid addiction: 2 RCTs - beneficial results ^{1,2}
- “Substance” or “Drug” abuse: Beneficial ³⁻¹⁰
 - Effect size varies by meta-analysis:
 - Very strong ⁴
 - Meaningful ⁵
 - Small ^{6,7}
 - Benefit tends to ↓ over time ⁵
 - Moderators of benefit uncertain ⁷
- Guideline support with reservation ¹¹⁻¹²

¹ McAuliffe. Recovery training + self help for opioid addicts. J Psychoact Drugs. 1990;22:197-209

² Bickel. Adding behavioral Rx to opioid detox. J Consult Clin Psych 1997;65:803-10

³ Azrin. Behavior therapy: drug abuse controlled Rx outcome study. Behav Res Ther. 1994;32(8):857-66

⁴ Windsor. CBT meta-analysis: race, substance use. Cultur Divers Ethnic Minor Psych. 2015;21(2):300-13

⁵ Waldron. CBT: adolescent substance abuse. Addiction. 2004;99 Suppl 2:93-105

⁶ Magill. CBT with adult alcohol, illicit drug users: meta-analysis. J Stud Alc Drugs. 2009;70(4):516-27

⁷ Blodgett. SUD continuing care effectiveness: meta-analysis. J Sub Abuse Treat. 2014;46(2):87-97

⁸ Schumacher. Cost, effectiveness: substance abuse Rx for homeless. J MH Policy Econ. 2002;5(1):33-42

⁹ Woody. Psychotherapy for opiate addicts. Arch Gen Psych. 1983;40(6):639-45

¹⁰ Kaminer. Adolescent substance abuse evidence-based practice. Curr Psych Rep. 2002;4(5):397-401

¹¹ NICE: Drug misuse psychosocial intervention guidelines. 2008. Accessed 7/16/16

¹² VA / DoD: SUD management guideline. 2015. Limited recommendation. Accessed 7/16/16

Medication Management

- Withdrawal meds: Preparation for treatment
- Adjunctive symptom meds: Post-acute withdrawal
- Anti-Craving meds: Primary medication management

Medication Management Opioid Withdrawal

- Opioid withdrawal symptoms ^{1,2}
 - Yawning, shakes, sweats, rhinorrhea
 - Pain: Generalized, abdominal, back
 - GI: Nausea, vomiting, diarrhea
 - Restlessness, anxiety, insomnia
 - ↑ pupils, HR, BP
- Adults: Can *feel* life threatening, not fatal
- Neonates: Can *be* life-threatening, death rare ^{3,4}

Withdrawal Treatment = Preparation for Treatment

- Opioid withdrawal with opioids
Agent initiated → Tapered off
 - Methadone ⁵⁻⁹
 - Buprenorphine ⁷⁻¹³
 - Tramadol ^{6,9,13}

¹ Fudin. Opioid withdrawal medication options. *Prac Pain Manage.* 2015;15(9)

² SAMHSA: Buprenorphine for opioid addiction guide. 2004. Accessed 7/16/16

³ Lam. OUD adverse perinatal outcomes. *Aust NZ J Ob Gyn.* 1992;32(3):216-21

⁴ Finnegan. Effects of maternal opiate abuse on the newborn. *Fed Proc.* 1985;44(7):2314-7

⁵ Amato. Methadone at tapered doses for opioid WD. *Coch Database Syst Rev.* 2013 Feb 28;(2)

⁶ Zarghami. Tramadol v methadone for opiate WD RCT. *J Addict Dis.* 2012;31(2):112-7

⁷ Seifert. Buprenorphine v methadone opioid detox. *Pharmacopsych.* 2002;35(5):159-64

⁸ NICE: Opioid detox guideline. 2008. Accessed 7/17/16

⁹ Diaper. Detox Rx strategies. *Br J Clin Pharm.* 2014;77(2):302-14

¹⁰ Assadi. Opioid detox with buprenorphine high dose RCT. *J Sub Abuse Treat.* 2004;27(1):75-82

¹¹ Gowing. Buprenorphine for opioid WD. *Coch Database Syst Rev.* 2006;(2)

¹² Ziedonis. Buprenorphine-naloxone, clonidine opioid WD. *NIDA. Drug Alc Dep.* 2009;99(1-3):28-36

¹³ Chawla. Buprenorphine v tramadol in heroin detox. *J Opioid Manag.* 2013;9(1):35-41

Medication Management

Opioid Withdrawal

- Supported abrupt withdrawal: Tapering will not work in addiction
- Monitor severity with Clinical Opioid Withdrawal Scale (COWS) ^{1,2}
- Withdrawal meds given prn symptoms expected over 5d ³⁻⁵
 - Up to 3w for Buprenorphine Methadone
 - Avoid benzodiazepines

Pain	Naproxen	220 mg	PO	#20
Back spasm	Cyclobenzaprine	10 mg	PO	#20
Abdominal cramps	Hyoscyamine	0.125 mg	SL	#20
Shakes / sweats	Clonidine ⁵⁻⁸	0.1 mg	PO	#20

¹ MedCalc: COWS calculator. Accessed 7/17/16

² Wesson. The Clinical Opiate Withdrawal Scale. J Psychoact Drugs. 2003;35(2):253-9

³ Fudin. Opioid withdrawal medication options. Prac Pain Manage. 2015;15(9)

⁴ Diaper. Detox Rx strategies. Br J Clin Pharm. 2014;77(2):302-14

⁵ Donaher. Managing opioid addiction with buprenorphine. AFP. 2006;73(9):1573-8

⁶ Gowing. α 2-adrenergic agonists for opioid WD. Coch Database Syst Rev. 2016 May 3;(5)

⁷ Albertson. α 2 adrenoceptor agonists in WD Rx. J Med Tox. 2014;10(4):369-81

⁸ Ziedonis. Buprenorphine-naloxone, clonidine for opioid WD. NIDA. Drug Alc Dep. 2009;99(1-3):28-36

FDA Approved Medications For Opioid Addiction Treatment

- Methadone Full mu-opioid agonist
- Buprenorphine Partial mu-opioid agonist
- Naltrexone Mu-opioid antagonist

Polling Question

Which of the following is true about methadone ?

- A. Any appropriately DEA registered physician can prescribe for opioid addiction
- B. Associated cardiac failure can be fatal
- C. Should be dosed < 60 mg po qd for opioid addiction
- D. Constipation is the most common side effect

Methadone

- [Schedule II](#)
- Full mu-opioid agonist ¹
- Long duration of clinical action for opioid addiction
- Approved for opioid addiction ²
Supervised oral administration ²
- Requires SAMHSA certification as Opioid Treatment Program (OTP) ^{2,3}
Cannot prescribe for opioid addiction unless from within OTP
- [Locate Methadone Opioid Treatment Program](#)

¹ SAMHSA: Buprenorphine for opioid addiction guide. 2004. Accessed 7/16/16

² SAMHSA: OTP federal guidelines. 2015. Accessed 7/17/16

³ SAMHSA: Application for OTP certification. Accessed 7/22/16

Methadone for Opioid Addiction

- Effective ¹⁻⁹ Guideline supported ¹⁰⁻¹⁶
- Initiation: Progressively ↑'d supervised qd po dosing ¹³⁻¹⁷
- Maintenance: Oral 60-100 mg po qd or higher ¹⁶⁻²⁰
- Duration of use: Indefinite Individualized ²¹
- Discontinuation: By taper over months ^{21,22}
Abrupt withdrawal: 3-4 week withdrawal symptoms

¹ Dole. Med Rx for heroin addiction. JAMA. 1965;193(8):646-50

² Mattick Buprenorphine v placebo, methadone in OUD. Cochr Database Syst Rev. 2014 Feb 6;2

³ Fullerton. Med-assisted Rx with methadone review. Psych Serv. 2014;65(2):146-57

⁴ Nosyk. QOL improvement in opioid agonist Rx. Drug Alc Dep. 2015;157:121-8

⁵ Mattick. Methadone v no opioid replacement for OUD. Cochr Database Syst Rev. 2009 Jul 8;(3)

⁶ Minozzi. Maintenance agonist for OUD in pregnancy. Cochr Database Syst Rev. 2013 Dec 23;(12)

⁷ Sees. Methadone maintenance v 180d psychosoc enriched detox for OUD. JAMA. 2000;283:1303-10

⁸ Potter. Buprenorphine-naloxone, methadone for Rx opioid, heroin. J Stud Alc Drug. 2013;74(4):605-13

⁹ Barnett. Methadone maintenance cost-effectiveness. Mt Sinai J Med. 2000; 67(5-6):365-74

¹⁰ VA / DoD: SUD management guideline. 2015. Accessed 7/16/16

¹¹ Soc OB Gyn Canada: Substance use in pregnancy. 2011. Accessed 7/18/16

¹² WHO: SUD management in pregnancy. 2014. Accessed 7/18/16

¹³ APS: Methadone safety guide. 2014. Accessed 7/17/16

¹⁴ SAMHSA: OTP federal guidelines. 2015. Accessed 7/17/16

¹⁵ APS: Methadone safety guide. 2014. Accessed 7/17/16

¹⁶ SAMHSA. Med-assisted Rx for opioid addiction in OTPs: TIP 43. 2005. Accessed 7/22/16

¹⁷ Baxter. Safe methadone induction, stabilization. J Addict Med. 2013;7(6):377-86

¹⁸ Eap. Methadone pharmacokinetic interindividual variability. Clin Pharmacol. 2002; 41(14):1153-93

¹⁹ Fareed. Methadone maintenance OUD dosing guide. J Addict Dis. 2010;29(1):1-14

²⁰ Farré. Retention, opioid use in methadone maintenance. Drug Alc Dep. 2002;65(3):283-90

²¹ Winstock. Coming off methadone, buprenorphine. Int J Drug Pol. 2011;22(1):77-81

²² Senay. Rate of methadone WD. Arch Gen Psych. 1977;34:361-7

Methadone Adverse Reactions

- GI: Nausea, vomiting, abdominal pain, constipation ¹
- Overdose death high ↑ with CNS depressants ²⁻⁸
- Respiratory depression ⁹⁻¹¹
 - ↑ with CNS depressants
 - Resuscitate with naloxone by bolus
- QT ↑ → torsades de pointes ↑ with benzodiazepines ¹²⁻¹⁴

¹ Pergolizzi. Opioid-induced constipation. Pain Med News. August 27, 2015

² Paulozzi. Risk for methadone OD 1999-2010. MMWR. 2012;61(26):493-7

³ Rudd. Drug & opioid OD deaths: US 2000-2014. MMWR. 2016;64(50):1378-82

⁴ Paulozzi. OD death methadone v other opioids in West Virginia. Addiction. 2009;104(9):1541-8

⁵ Hall. Abuse patterns in unintentional pharmaceutical OD fatalities. JAMA. 2008;300(22):2613-20

⁶ Baxter. Safe methadone induction, stabilization. J Addict Med. 2013;7(6):377-86

⁷ Srivastava. Methadone induction doses, safety. J Addict Dis. 2006;25(3):5-13

⁸ Hendrikson. Methadone, Rx drug OD. NCSL Legisbrief. 2014;22(45):1-2

⁹ Lee. NMU benzos + buprenorphine, methadone toxicity. Drug Alc Dep. 2014;138:118-23

¹⁰ Nielsen. Buprenorphine + benzos, toxicity. Addiction. 2007;102(4):616-22

¹¹ Wang. Central sleep apnea on stable methadone. Chest. 2005;128(3):1348-56

¹² Chou. Methadone OD, cardiac arrhythmia review. J Pain. 2014;15(4):338-65

¹³ Peles. Prospective study: QTc in methadone maintenance. J Addict Med. 2013;7:428-34

¹⁴ Bunten. Gene variants, methadone-related death. Addiction Biol. 2011;16:142-4

Methadone Adverse Reactions

- CNS: HA, dizziness, confusion, dyscognition, psychomotor ¹⁻⁴
- Drug-drug interactions ^{5,6} > *50 interactions* In part related to
 - Concurrent sedating meds
 - 90% protein binding
 - P450 metabolism: 8 enzymatic sites
- Non-medical use Addiction Diversion ⁷⁻⁹
- Neonatal abstinence syndrome ¹⁰⁻¹²
- Accidental childhood ingestion ¹³

**Partial
List**

¹ Soyka. Opioids, traffic safety - focus on buprenorphine. *Pharmacopsych*. 2014;47(1):7-17
² Loeber. Neuropsych, buprenorphine, methadone. *Am J Drug Alc Abuse*. 2008;34(5):584-93
³ Soyka. Cognition: methadone, buprenorphine. *J Clin Psychopharm*. 2008;28(6):699-703
⁴ Strand. Driving on methadone, buprenorphine. *Traffic Inj Prev*. 2013;14(1):26-38
⁵ Kapur. Methadone drug-drug interactions. *Crit Rev Clin Lab Sci*. 2011;48(4):171-95
⁶ McCance-Katz. Drug interactions: methadone, buprenorphine. *Am J Addict*. 2010;19(1):4-16

⁷ Coplan. TD buprenorphine v other LA opioid abuse. *Pain Week Abstracts*. 2014;33
⁸ Surrat. Street prices of Rx opioids. *Pain Week Abstracts*. 2012;113:172
⁹ Maxwell. Buprenorphine, methadone use & abuse indicators. *Am J Addict*. 2010;19(1):73-88
¹⁰ Minozzi. Agonist Rx in pregnancy. *Cochr Database Syst Rev*. 2013 Dec 23;(12)
¹¹ Lund . Buprenorphine, methadone in pregnancy. *Sub Abuse*. 2013;7:61-74
¹² Bagley. Neonatal abstinence management. *Addict Sci Clin Pract*. 2014;9(1):19
¹³ Martin. Childhood ingestion of methadone, buprenorphine. *Curr Drug Saf*. 2011;6(1):12-6

Polling Question

Which of the following is true about buprenorphine ?

- A. Any appropriately DEA registered physician can prescribe for opioid addiction
- B. Maintenance use should be limited to 2 years
- C. Can cause withdrawal in patients on other opioids
- D. Associated QT prolongation can be fatal

Buprenorphine

- Schedule III ¹
- Partial mu-opioid agonist: High affinity, slow dissociation, low intrinsic activity ^{2,3}
- Long duration of clinical action for addiction ^{2,4-7}
- Approved for opioid addiction
 - Single agent **Sublingual "mono" tablet** or **Implant**
 - Combination 4:1 with naloxone **Sublingual, buccal tablet or film** ^{2,7}
- Requires FDA waiver to prescribe ⁸
- Locate physicians **Waived to Prescribe** or **Waived + Provides Implant**

¹ DEA. Rescheduling buprenorphine to schedule III. Fed Regist. 2002;67(194):62354-70

² Ling. Buprenorphine for opioid addiction. Pain Manag. 2012;2(4):345-50

³ Walsh. Buprenorphine partial agonist, blockade effects. J Pharm Exp Ther. 1995; 274(1):361-72

⁴ Boas. Fentanyl, buprenorphine clinical actions, binding. Br J Anaesth. 1985;57(2):192-6

⁵ Greenwald. Buprenorphine duration of action. Biol Psych. 2007; 61(1):101-10

⁶ Kuhlman. IV, SL, buccal buprenorphine pharmacokinetics. J Anal Tox. 1996;20(6):369-78

⁷ Orman. Buprenorphine-naloxone for opioid dependence. Drugs. 2009;69(5):577-607

⁸ SAMHSA: Buprenorphine Waiver Management Accessed 7/15/16

Buprenorphine

- Effective ¹⁻⁹ Guideline supported ¹⁰⁻¹⁴
- Initiation: Induction of the patient in withdrawal ^{12,15-17}
- Maintenance: Transmucosal 2-24 mg qd ^{12,15,16,18} Implant ¹⁹⁻²¹
- Duration of use: Individualized Indefinite ^{15,22,23}
- Discontinuation: By taper over months ²³⁻²⁶
Abrupt withdrawal: 3-4 week withdrawal symptoms

¹ Jasinski. Buprenorphine: potential for treating narcotic addiction. Arch Gen Psych. 1978;35(4):501-16

² Mattick. Buprenorphine v placebo, methadone in OUD. Cochr Database Syst Rev. 2014 Feb 6;(2)

³ Minozzi. Maintenance agonist Rx for OUD in pregnancy. Cochr Database Syst Rev. 2013 Dec 23;(12)

⁴ Nielsen. Opioid agonist Rx for Rx for OUD. Cochr Database Syst Rev. 2016;(5)

⁵ Colson. Office-based OUD Rx. Pain Phys. 2012;15(3 Suppl):ES231-6

⁶ Thomas. Medication-assisted Rx with buprenorphine. Psych Serv. 2014;65(2):158-70

⁷ Clay. Persistence, healthcare use with buprenorphine-naloxone. J Med Econ. 2014;17(9):626-36

⁸ Orman. Buprenorphine-naloxone in OUD review. Drugs. 2009;69(5):577-607

⁹ Potter. Buprenorphine-naloxone, methadone for Rx opioid, heroin OUD. J Stud Alc Drug. 2013;74(4):605-13

¹⁰ VA / DoD: SUD management guideline. 2015. Accessed 7/16/16

¹¹ WHO: SUD management in pregnancy. 2014. Accessed 7/18/16

¹² SAMHSA: Buprenorphine for opioid addiction guide. 2004. Accessed 7/16/16

¹³ Farmer. Buprenorphine for OUD guide. Sub Abus. 2015;36(2):209-16

¹⁴ Center Addiction & MH: Buprenorphine-naloxone for OD guide. 2011. Accessed 7/16/16

¹⁵ Donaher. Managing OUD with buprenorphine. AFP. 2006;73(9):1573-8

¹⁶ Ling. Buprenorphine for OUD. Pain Manag. 2012;2(4):345-50

¹⁷ Nielsen. Buprenorphine induction: heroin v Rx opioid users. J Sub Abuse Treat. 2012;43(3):285-90

¹⁸ Khemiri. Buprenorphine-naloxone dose, duration, resource use. Postgrad Med. 2014;126(5):113-20

¹⁹ Ling. Buprenorphine implant for OUD. Pain Manag. 2012;2(4):345-50

²⁰ Rosenthal. Buprenorphine implants in OUD Rxd SL buprenorphine. JAMA. 2016;316(3) [Epub before print]

²¹ Ling. Buprenorphine implants for OUD RCT. JAMA. 2010;304(14) [Epub online]

²² Weiss. Buprenorphine-naloxone, counseling. Drug Alc Dep. 2014;140:118-22

²³ Bentzley. Buprenorphine maintenance discontinuation. J Sub Abuse Treat. 2015;52:48-57

²⁴ Sigmon. Buprenorphine taper duration. JAMA Psych. 2013;70(12):1347-54

²⁵ Dunn. Buprenorphine detox duration outcomes review. Drug Alc Dep. 2011;119(1-2):1-9

²⁶ Mannelli. ER naltrexone in OUD after buprenorphine induction. Drug Alc Dep. 2014;138:83-8

Buprenorphine: Transmucosal

- Buprenorphine
 - 30-60% bioavailable SL, buccal ¹
 - Reduces opioid withdrawal and craving ²
 - Blocks effects of other opioids used while on buprenorphine ^{3,4}
 - Precipitates withdrawal if on other opioids when started ⁵
 - Produces physical dependence ⁶
- Naloxone in combination product
 - 7% bioavailable SL, buccal ⁷
Does not alter buprenorphine effect when used SL, buccal ^{2,4,7-9}
 - 100% bioavailable if injected ⁷
To deter abuse *Not* FDA labeled as abuse deterrent ^{2,4,7-9}

¹ Kuhlman. IV, SL, buccal buprenorphine pharmacokinetics. J Anal Tox. 1996;20(6):369-78

² Ling. Buprenorphine for opioid addiction. Pain Manag. 2012;2(4):345-50

³ Walsh. Buprenorphine partial agonist, blockade effects. J Pharm Exp Ther. 1995; 274(1):361-72

⁴ Strain. Hydromorphone blockade by buprenorphine-naloxone, buprenorphine. Psychopharm. 2002;159:161-6

⁵ Rosado. Buprenorphine / naloxone precipitates methadone WD. Drug Alc Dep. 2007;90(2-3):261-9

⁶ Eissenberg. Buprenorphine physical dependence potential. J Pharm Exp Ther. 1996;276(2):449-59

⁷ Orman. Buprenorphine / naloxone for opioid dependence. Drugs. 2009;69(5):577-607

⁸ Mammen. Buprenorphine-naloxone efficacy, abuse. Expert Opin Pharmther. 2009;10(15):2537-44

⁹ Harris. Buprenorphine v naloxone combined pharmacokinetics, effects. Clin Pharmkinet. 2004;43:329-40

Buprenorphine Adverse Events

- GI: Nausea, vomiting, abdominal pain, constipation ¹
- Overdose death *rare* ↑ with CNS depressants ²⁻⁴
- Respiratory ↓ despite ceiling effect ⁵⁻¹¹
↑ with CNS depressants
Resuscitate by naloxone *continuous infusion* ⁵
- QT ↑ *Not* clinically significant ^{1,12}

¹ Ling. Buprenorphine for opioid addiction. Pain Manag. 2012;2(4):345-50

² Tracqui. Buprenorphine-related deaths in France. J Anal Tox. 1998;22:430-4

³ Selden. Tox findings in buprenorphine related deaths. Forensic Sci Int. 2012;220:284-90

⁴ Hakkinen. Benzos, alcohol & fatal buprenorphine OD. Eur J Clin Pharm. 2012;68:301-9

⁵ Dahan. Respiratory depression ceiling with buprenorphine. Br J Anes. 2006; 96(5):627-32

⁶ Walsh. Buprenorphine ceiling effects at high doses. Clin PharmTher. 1994;55:569-80

⁷ Ciraulo. Multiple SL buprenorphine tabs in dose-escalation trials. J Clin Pharm. 2006;46(2):179-92

⁸ Boyd. Serious buprenorphine ODs in Helsinki. Acta Anes Scand. 2003;47(8):1031-3

⁹ Farney. Sleep disordered breathing on buprenorphine/naloxone. Eur Respir J. 2013;42(2):394-403

¹⁰ DeVido. Sleep-disordered breathing on buprenorphine-naloxone. J Op Manag. 2015;11(4):363-6

¹¹ Lee. Nonmedical benzos use + buprenorphine, methadone. Drug Alc Dep. 2014;138:118-23

¹² Poole. QTc with buprenorphine-naloxone. J Addict Med. 2016;10(1):26-33

Buprenorphine Adverse Events

- CNS: Headache, dizziness, confusion, dyscognition, psychomotor¹⁻⁶
- Drug-drug interactions^{1,7} In part related to
 - Concurrent sedating meds
 - 90% protein binding
 - P450 metabolism: 3A4
- Non-medical use Addiction Diversion⁸⁻¹³
- Neonatal abstinence syndrome¹⁴⁻¹⁶
- Accidental childhood ingestion¹⁷⁻¹⁹

**Partial
List**

¹ Ling. Buprenorphine for opioid addiction. Pain Manag. 2012;2(4):345-50

² Loeber. Neuropsych function buprenorphine, methadone. Am J Drug Alc Abuse. 2008;34(5):584-93

³ Soyka. Cognition: methadone, buprenorphine. J Clin Psychopharm. 2008;28(6):699-703

⁴ Strand. Driving on methadone, buprenorphine. Traffic Inj Prev. 2013;14(1):26-38

⁵ Soyka. Opioids, traffic safety - focus on buprenorphine. Pharmacopsych. 2014;47(1):7-17

⁶ Strand. Driving on methadone, buprenorphine. Traffic Inj Prev. 2013;14(1):26-38

⁷ McCance-Katz. Drug interactions: methadone, buprenorphine. Am J Addict. 2010;19(1):4-16

⁸ Lofwall. Buprenorphine diversion, misuse review. J Addict Med. 2014;(5):315-26

⁹ Middleton. Intranasal buprenorphine, buprenorphine-naloxone. Addiction. 2011;106:1460-73

¹⁰ Larance. Diversion, injection of buprenorphine-naloxone film. Drug Alc Depend. 2014;136:21-7

¹¹ Larance. Buprenorphine diversion, injection: Australia. Drug Alc Dep. 2011;118:265-73

¹² Johanson. National surveys: buprenorphine diversion, abuse. Drug Alc Dep. 2012;120:190-5

¹³ Maxwell. Buprenorphine, methadone use & abuse indicators. Am J Addict. 2010;19(1):73-88

¹⁴ Minozzi. Agonist Rx in pregnancy. Cochr Database Syst Rev. 2013 Dec 23;(12)

¹⁵ Lund . Buprenorphine, methadone in pregnancy. Sub Abuse. 2013;7:61-74

¹⁶ Bagley. Neonatal abstinence management. Addict Sci Clin Pract. 2014;9(1):19

¹⁷ Martin. Childhood ingestion of methadone, buprenorphine. Curr Drug Saf. 2011;6(1):12-6

¹⁸ Lavonas. Buprenorphine exposures of children. J Pediatr. 2013;163:1377-83. e1371-3

¹⁹ Hares. Toxicity of buprenorphine ODS in children. Pediatrics. 2008;121(4):e782-6

Polling Question

Which of the following is true about naltrexone ?

- A. As an opioid antagonist, it has no GI side effects
- B. Indicated for both opioid and alcohol addiction
- C. Effective both orally or by depot IM for opioid addiction
- D. It blocks opioids and can result in opioid craving

Naltrexone

- Not scheduled
- Competitive mu-opioid antagonist ^{1,2}
- Long duration of clinical action for addiction ^{1,3-5}
- Approved for addiction
 - Oral Naltrexone Alcohol addiction
 - Depot IM Naltrexone Alcohol addiction ⁶⁻¹⁰ *and* Opioid addiction
- Locate Physicians who can Provide

¹ Ling. Buprenorphine for opioid addiction. Pain Manag. 2012;2(4):345-50

² Walsh. Buprenorphine partial agonist, blockade effects. J Pharm Exp Ther. 1995; 274(1):361-72

³ Boas. Fentanyl, buprenorphine clinical actions, binding. Br J Anaesth. 1985;57(2):192-6

⁴ Greenwald M, Johanson CE, Bueller J, et al. Buprenorphine duration of action. Biol Psych. 2007; 61(1):101-10

⁵ Kuhlman. IV, SL, buccal buprenorphine pharmacokinetics. J Anal Tox. 1996;20(6):369-78

⁶ Ciraulo. ER naltrexone early Rx response in alcoholism. J Clin Psych. 2008;69(2):190-5

⁷ Lapham. ER naltrexone effects, holiday drinking in alcoholism. J Sub Abuse Treat. 2009;36(1):1-6

⁸ Lee. ER naltrexone for alcoholism in 1^o care. J Sub Abuse Treat. 2010;39(1):14-21

⁹ Pettinati. ER naltrexone in higher severity alcoholism. Alc Clin Exp Res. 2011;35(10):1804-11

¹⁰ O'Malley. ER naltrexone in alcoholism after abstinence. J Clin Psychopharm. 2007;27(5):507-12

Naltrexone for Opioid Addiction

- Oral form mixed results ^{1,2} Meta-analysis: Ineffective ³
- IM depot form effective ⁴⁻⁹ Guideline supported ¹⁰

- Initiation: *Only after* opioid withdrawal complete
- Maintenance: Monthly IM depot injection
- Dose: Deep IM gluteal injection 380 mg
- Duration of use: Individualized Indefinite
- Discontinuation: Abruptly OK

¹ Mannelli. Naltrexone in post-detox opioid dependence. J Clin Psychopharm 2007;27(5):468-74

² Azatian. Clonidine & naltrexone in opioid addiction. J Addict Dis. 1994;13(1):35-52

³ Minozzi. Oral naltrexone for opioid dependence. Coch Database Syst Rev. 2011 Apr 13;(4)

⁴ Comer. Injectable, SR naltrexone for opioid dependence RCT. Arch Gen Psych. 2006; 63(2):210-8

⁵ Krupitsky. Injectable ER naltrexone for opioid dependence RCT. Lancet. 2011; 377(9776):1506-13

⁶ Krupitsky. Injectable ER naltrexone for opioid dependence LT. Addiction. 2013;108(9):1628-37

⁷ Syed. ER IM naltrexone in opioid dependence review. CNS Drugs. 2013;27(10):851-61

⁸ Gastfriend. IM ER naltrexone; evidence. Ann N Y Acad Sci. 2011;1216:144-66

⁹ Mannelli. ER naltrexone in opioid dependence after buprenorphine induction. Drug Alc Dep. 2014;138:83-8

¹⁰ VA / DoD: SUD management guideline. 2015. Accessed 7/16/16

Naltrexone Adverse Events

- Not associated with euphoria, non-medical use, addiction, OD death, respiratory depression, accidental childhood exposures
- Precipitates withdrawal if on opioids
- GI: Nausea, vomiting, abdominal pain, constipation, hepatic impairment
- Fatigue, somnolence, sedation, dizziness
- Depression, anxiety, suicidality
- Injection site reactions
- Headache, myalgias

**Partial
List**

¹ Comer. Injectable, SR naltrexone for opioid dependence RCT. Arch Gen Psych. 2006; 63(2):210-8
² Krupitsky. Injectable ER naltrexone for opioid dependence RCT. Lancet. 2011; 377(9776):1506-13
³ Krupitsky. Injectable ER naltrexone for opioid dependence LT. Addiction. 2013;108(9):1628-37

⁴ Syed. ER IM naltrexone in opioid dependence review. CNS Drugs. 2013;27(10):851-61
⁵ Gastfriend. IM ER naltrexone: evidence. Ann N Y Acad Sci. 2011;1216:144-66

Medication Management: Comparisons

- Opioid use disorder efficacy
Methadone = Buprenorphine overall Methadone retention better ¹⁻⁶
- Respiratory depression / OD
Methadone > Buprenorphine ⁷ Depot Naltrexone none
- Neonatal Abstinence Syndrome
Methadone > Buprenorphine ^{3,4,8} Depot Naltrexone none
- Cognitive, psychomotor dysfunction
Methadone > Buprenorphine ⁹⁻¹¹ Depot naltrexone none
- Non-medical use:
Depot Naltrexone none

¹ Connock. Methadone, buprenorphine for OUD. Health TechAssess. 2007;11(9):1-171, iii-iv

² Nielsen. Opioid agonist Rx for Rx OUD. Coch Database Syst Rev. 2016;(5)

³ Minozzi. Maintenance agonist for OUD in pregnancy. Coch Database Syst Rev. 2013 Dec 23;(12)

⁴ Lund. Buprenorphine-naloxone, buprenorphine, methadone in pregnancy. Sub Abuse. 2013;7:61-74

⁵ Mattick Buprenorphine v placebo, methadone in OUD. Coch Database Syst Rev. 2014 Feb 6;2

⁶ Potter. Buprenorphine-naloxone, methadone maintenance for OUD. J Stud Alc Drugs. 2013;74(4):605-13

⁷ Lee. Nonmedical benzos use + buprenorphine, methadone. Drug Alc Dep. 2014;138:118-23

⁸ Jones. NAS after methadone or buprenorphine. NEJM. 2010;363(24):2320-31

⁹ Soyka. Opioids, traffic safety - focus on buprenorphine. Pharmacopsych. 2014;47(1):7-17

¹⁰ Soyka. Buprenorphine v methadone maintained patients: psychomotor RCT. J Clin Psychphar. 2005;25(5):490-3

¹¹ Mintzer. Methadone, buprenorphine psychomotor, cognitive effects. Heroin Addict Relat Clin Probl.. 2007;9(1):5-24

Medication Management Initial Selection

Consider access, coverage, cost, preference, prior success

- Combined opioid and alcohol addiction: Naltrexone
- Combined opioid and cocaine addiction: Buprenorphine ¹⁻⁴
Buprenorphine not FDA approved for cocaine addiction
- Prolonged QTc: Buprenorphine Naltrexone
- Anticipated cardiovascular instability in withdrawal: Methadone
- Significant xerostomia: Methadone Naltrexone

¹ Buprenorphine does not have FDA approval for cocaine addiction

² Ling. Buprenorphine-naloxone + naltrexone for cocaine dependence. *Addiction*. 2016;111(8):1416-27

³ Foltin. Cocaine self-administration, cocaine. *Behav Pharm*. 1994;5(1):79-89

⁴ Montoya. Buprenorphine for concurrent opiate, cocaine dependence. *Clin Pharm Ther*. 2004;75(1):34-48

Opioid Addiction Medication Prescribing Requirements

- Methadone [Patient Education](#)
DEA registration for Schedule II
Federally qualified Opioid Treatment Program
- Naltrexone by depot injection [Patient Education](#)
Refrigerator
Capacity to inject
- Buprenorphine [Patient Education](#)
DEA registration for Schedule III
FDA waiver for medication assisted treatment
Certification to perform implants, if providing

Buprenorphine: FDA Waiver

- To prescribe approved Schedule III, IV, V opioids in opioid addiction ¹⁻³
- Requirements ⁴
 - License under state law
 - DEA registration to prescribe controlled substances
 - Physicians: 8 hour approved training ⁵⁻⁷ *or* addiction board certification ⁸⁻¹⁰
 - PAs, NPs: 24 hour approved training
 - Capacity to refer for counseling
 - Record keeping
- Limitations
 - 30 patients 1st year ¹
 - 100 patients after 1 year ^{1,11}
 - New: 275 patients ^{1,12}

¹ Dept HHS. 42 CFR Part 8: Med Assisted Treatment for OUD. Fed Regist. 2016;81(131)
² SAMHSA Waiver Notification Form SMA-167 Accessed 7/22/16
³ SAMHSA: Buprenorphine Waiver Management Accessed 7/15/16
⁴ SAMHSA: Buprenorphine Qualification Requirements Accessed 7/15/16
⁵ SAMHSA: Buprenorphine Training Links Accessed 7/15/16
⁶ PCSS-MAT: Buprenorphine waiver training
⁷ ASAM: Buprenorphine Course October 5, 2016, Washington DC Hilton Accessed 7/22/16
⁸ American Board of Addiction Medicine Accessed 7/22/16
⁹ American Board of Psychiatry & Neurology Accessed 7/22/16
¹⁰ American Osteopathic Academy of Addiction Medicine Accessed 7/22/16
¹¹ SAMHSA Online Notification Form to Increase Patient Limit
¹² SAMHSA. Med Assisted Rx for OUD. Final rule. Fed Regist. 2016;81(131):44711-39

Opioid Addiction Treatment Combinations

Evidence-based data does not necessarily address individualized needs

- Adding Mutual Help to Addiction Therapy: No data
- Adding Mutual Help to Medication Management: No data
- Adding Addiction Therapy to Medication Detox: Beneficial ^{1,2}
- Adding Addiction Therapy to Medication Management:
Studies mixed ³⁻¹⁵ Reviews mixed ^{16,17} Meta-analysis - no benefit ¹⁸
- Adding psychiatric treatment for psychiatric problems: Beneficial ^{19,20}

¹ Amato. Psychosoc + med v med for opioid detox. Coch Database Syst Rev. 2011;(9)

² Bickel. Adding behavioral Rx to buprenorphine in detox. J Consult Clin Psych. 1997;65(5):803-10

³ Montoya. Psychotherapy attendance, buprenorphine Rx. J Subs Abuse Treat. 2005;28(3):247-54

⁴ Stein. Buprenorphine retention in 1^o care. J Gen Int Med. 2005;20(11):1038-41

⁵ Weiss. Buprenorphine-naloxone, counseling. Drug Alc Dep. 2014;140:118-22

⁶ Weiss. Counseling in buprenorphine-naloxone Rx. Arch Gen Psych. 2011;68(12):1238-46

⁷ Woody. Psychotherapy for opiate addicts. Arch Gen Psych. 1983;40(6):639-45

⁸ McLellan. Psychosocial in substance abuse Rx. JAMA. 1993;269(15):1953-9

⁹ Rothenberg. Behavioral naltrexone Rx in opiate dependence. J Sub Abuse Treat. 2002; 23(4):351-60

¹⁰ Carroll. Behavioral Rx, naltrexone in opioid dependence. Arch Gen Psych. 2001;58(8):755-61

¹¹ Subramaniam. Abstinence predict: buprenorphine-Rx. J Am Acad Child Adol Psych. 2011;50(11):1120-8

¹² Nunes. Behavioral Rx, po naltrexone for opioid dependence. Am J Drug Alc Abuse. 2006;32(4):503-17

¹³ Fiellin. CBT in 1^o care-based buprenorphine RCT. Am J Med. 2013;126(1):74.e11-7

¹⁴ Ling. Behavioral Rx in buprenorphine maintenance RCT. Addiction. 2013;108(10):1788-98

¹⁵ Galanter. Network therapy & buprenorphine maintenance. J Sub Abuse Treat. 2004;26(4):313-8

¹⁶ Copenhaver. Counseling, buprenorphine, opioid dependence. Am J Drug Alc Abuse. 2007;33(5):643-54

¹⁷ Orman. Buprenorphine-naloxone use in opioid dependence review. Drugs. 2009;69(5):577-607

¹⁸ Amato. Psychosocial + agonist v agonist in opioid dependence. Coch Database Syst Rev. 2011;(10)

¹⁹ Beaulieu. Managing comorbid mood, SUD. Ann Clin Psych. 2012;24(1):38-55

²⁰ Baigent. Managing patients with dual Dx. Curr Opin Psych 2012;25(3):201-5

Follow-Up Visit: Outcomes

- Subjective 5 A's¹
 - **A**ctivities (function)
 - **A**bstinence
 - **A**ffect
 - **A**dverse events
 - **A**berrancies

¹ After Passik. Tool to assess, document pain outcomes in chronic pain patients receiving opioids. Clin Ther. 2004;26(4):552-61

Follow-Up Visit for Outcomes

- Mutual Help Involvement

Ask about Service work

- Addiction Therapy Involvement

Ask about Trigger management plan

- Medication Management Response

Ask about Efficacy / Side effects

Follow-Up Visit for Outcomes

- Subjective 5 A's¹
 - **A**ctivities (function)
 - **A**bstinence
 - **A**ffect
 - **A**dverse events
 - **A**bserrancies

¹After Passik. Tool to assess, document pain outcomes in chronic pain patients receiving opioids. Clin Ther. 2004;26(4):552-61

Risk Monitoring

- Behavioral aberrancies: Reported Observed ¹⁻⁵
- Online prescription database: PDMP ⁶⁻⁹
- Body fluid drug testing: Urine Oral fluid ⁶⁻¹²
Methadone maintenance → Methadone, EDDP
Buprenorphine prescribed → buprenorphine, norbuprenorphine
No other opioids, illicit, alcohol should be seen
- Pill / Film counts if indicated ^{6,8,12,13}

¹ Martell. Opioids for chronic back pain. AIM. 2007;146(2):116-27

² Fleming. Reported aberrancies of substance misuse in 1^o care. Pain Med. 2008;9(8):1098-106

³ Fleming. SUDs in patients on opioids in 1^o care. J Pain. 2007;8(7):573-82

⁴ Addiction Behaviors Checklist Accessed 4/25/16

⁵ Wu. Addiction Behaviors Checklist validation. J Pain Symp Manag. 2006;32(4):342-52

⁶ Alturi. Opioid abuse prevention in chronic pain. Pain Phys. 2012;15:ES177-89

⁷ Hamill-Ruth. Objective data for med misuse risk. Pain Med. 2013;14(12):1900-7

⁸ Hall. Abuse patterns, unintentional OD fatalities. JAMA. 2008;300(22):2613-20

⁹ Chang. PDMP, pill mill laws, high-risk opioid prescribers. Drug Alc Dep. 2016;165:1-8

¹⁰ Manchikanti. Adherence monitoring, substance abuse in chronic pain. Pain Phys. 2006;9:57-60

¹¹ Gourlay. Urine Drug Testing in Clinical Practice Monograph. 2015 Accessed 4/25/16

¹² Bujold. Improving narcotic use in chronic nonmalignant pain. J Opioid Manag. 2012;8(6):363-7

¹³ Viscomi. Pill counts & pill rental. Clin J Pain. 2013;29(7):623-4

Practice Recommendations

Screen *all* patients for *all* potentially addicting substances (SORT A)

Secondarily screen opioid users for problematic use (SORT A)

If opioid use is problematic, evaluate for opioid addiction (SORT A)

Use Motivational Interviewing to facilitate change ¹⁻⁸ (SORT C)

Use culturally ⁹⁻¹¹ and trauma informed ¹²⁻¹⁸ approaches (SORT A)

Establish treatment goals with the patient (SORT C)

¹ Lundahl. Motivational interviewing effectiveness. J Clin Psych. 2009;65(11):1232-45

² Burke Motivational interviewing meta-analysis. J Consult Clin Psych. 2003;71(5):843-61

³ Dunn. Brief interventions, motivational interviewing. Addiction. 2001;96(12):1725-42

⁴ Jensen. Motivational interviewing, adolescent substance use. J Consult Clin Psych. 2011;79(4):433-40

⁵ Strobbe. SBIRT substance use in 1^o care. Prim Care. 2014;41(2):185-213

⁶ Harris. SBI for alcohol, other abuse. Adol Med State Art Rev. 2014;25(1):126-56

⁷ Saitz. SBI drug use in 1^o care. J Addict Med. 2014;4(3):123-30

⁸ Carney. Early interventions for substance-using adolescents. Sub Abuse Treat Prev Pol. 2012;7:25

⁹ Guerrero. Implementing cultural competence in addiction Rx. Eval Program Plann. 2013;40:74-81

¹⁰ Guerrero. Medicaid payment acceptance, cultural competence in SUD Rx. Drug Alc Dep. 2013;132(3):555-61

¹¹ Rowan. Cultural interventions, SUD Rx in Indigenous populations. Sub Abuse Treat Prev Pol. 2014;9:34

¹² Dube. Exposure to abuse among adults witnessing IPV as children: implications. Violence Vict. 2002;17(1):3-17

¹³ De Venter. Adverse childhood experience & MH in adults. review. Tijdschr Psychiatr. 2013;55(4):259-68

¹⁴ Schäfer. Sexual violence & special needs in patients OUD. Addict Behav. 2014;39(12):1691-4

¹⁵ Xu. Adult victims of sexual violence & alcohol, related conditions. Psych. 2013;76(3):223-40

¹⁶ Brown. Trauma-informed practice in addiction Rx collaborative model. J Psychoact Drug. 2013;45(5):386-93

¹⁷ Covington. Women & addiction: trauma-informed approach. J Psychoact Drug. 2008;Suppl 5:377-85

¹⁸ Covington. Trauma-informed, gender-responsive drug Rx for women. J Psychoact Drug. 2008;Suppl 5:387-98

Practice Recommendations: Opioid Addiction

Recommend patient involvement in mutual help programs (SORT A)

Recommend professional addiction therapy (SORT A)

Treat with methadone, naltrexone, or buprenorphine (SORT A)

Provide overdose rescue education and naloxone¹⁻⁹ (SORT A)

Collaborate, co-locate, and integrate with addiction therapy team¹⁰⁻¹² (SORT A)

Monitor for and respond to continued opioid use (SORT A)

¹ Clark. Community opioid OD prevention, naloxone distribution. J Addict Med. 2014;8(3):153-63

² Green. Evaluation of OD training and naloxone distribution programs. Addiction. 2008;103(6):979-89

³ Walley. Opioid OD prevention with naloxone for those on methadone. J Sub Abuse Treat. 2013;44(2):241-7

⁴ Coffin. Cost-effectiveness of distributing naloxone to heroin users. AIM. 2013;158(1):1-9

⁵ Strang. OD training, take-home naloxone for opiate users. Addiction. 2008;103(10):1648-57

⁶ Dwyer. Opioid ed, nasal naloxone rescue kits in ED. West J Emerg Med. 2015;16(3):381-4

⁶ Dwyer. Opioid ed, nasal naloxone rescue kits in ED. West J Emerg Med. 2015;16(3):381-4

⁷ SAMHSA: Opioid Overdose Toolkit Accessed 7/22/16

⁸ NASADAD: State legislation to ↑ access to Rx for opioid OD. 2015. Accessed 7/22/16

⁹ Barry. Integrating buprenorphine Rx into office-based practice. J Gen Int Med. 2009;24(2):218-25

¹⁰ DeFlavio. Buprenorphine therapy barriers of family physicians. Rural Remote Health. 2015;15:3019

¹¹ Pating. New systems of care for SUDs. Psych Clin North Am. 2012;35(2):327-56

Relapse

- Common: 40-60%
Frequency similar to other chronic disease ¹
- “Congratulations - you made it back”
- “It’s not failure, if we do something about it”
- “Now, what do we need to do that we weren’t doing before”
- Risk factors ²
 - Stress ²
 - Craving ²
 - Psychiatric disease ³
 - Being around substance users ²

¹ McLellan. Drug dependence, a chronic medical illness. JAMA. 2000;284(13):1689-95

² Hoffman. Effective Rx for alcohol and drug disorders. Psychiatr Clin North Am. 1993;16(1):127-40

³ Baigent. Managing patients with dual Dx in psych practice. Curr Opin Psych. 2012;25(3):201-5

Recovery

“Drug users have special problems
not solved by just getting them off drugs”¹


- Harm Reduction:
Continued compulsive use *but* negative consequences limited
Med management *not* substituting one addiction for another²
Med management *also* reduces harm: mortality, HIV, hepatitis²
- Abstinence: Off drug(s)
- Sobriety: Resolving negative consequences of drug use
- Recovery: Engaging a full life with meaning and purpose

¹ Robins. VN vets' rapid recovery from heroin addiction. *Addiction*. 1993;88:1041-54

² Park. Med management for addiction. *R I Med J*. 2013;97(10):20-4

Recovery Oriented Care

- Addiction *is not* inherent in the substance or person alone
- Addiction *is* inherent in a person's *relationship* to the substance
- Recovery:
Developing ing relationship with living that has meaning and purpose in the absence of compulsion with harm
- Recovery Oriented Care
Treatment and services directed towards recovery and not just abstinence



I told you
I was sick.

Sue Rangell
1964 - 2013

Questions ??

sleighwright@gmail.com



Billing & Coding

When services performed in conjunction with:

Office Visit 992xx *

Preventive medicine counseling and/or risk factor reduction interventions 99401-99404 (billable in 15 minute increments)

*Time-based selection documentation criteria:

- Face-to-face time
 - greater than 50% spent counseling/coordinating care
-

Interested in More CME on this topic?

aafp.org/fmx-pain