# Opioid Epidemic: Myths versus Facts

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# More specifically…

- Where were we?
- Where we are now?
- How we got here (dispelling the myths)?
- Clarification of alternative facts

# Objectives

1. Interpret current opioid usage and outcomes data
2. Summarize the neurobiology of addiction
3. Evaluate facts and myths associated with opioid usage and mortality
4. Recognize at least 3 medical disorders of “epidemic proportion” other than opioid abuse that may involve addictive personality
5. Summarize pharmacist strategies to address the opioid epidemic and mitigate opioid risk

# Pre / Post Test #1

Nonmedical use of opioid analgesics from early 2000 to the mid-2000's have…

A. increased approximately 50%

B. decreased approximately 50%

C. remained the same

D. have fluctuated up and down

# Pre / Post Test #2

Which of the following is true regarding morphine equivalent daily equivalent (MEDD) doses?

A. There is general consensus of what constitutes an MEDD

B. The Internet posted CDC calculator should be used to provide accurate morphine equivalents for methadone conversions

C. Online opioid conversion calculators by states and federal agencies are generally consistent in terms of MEDD

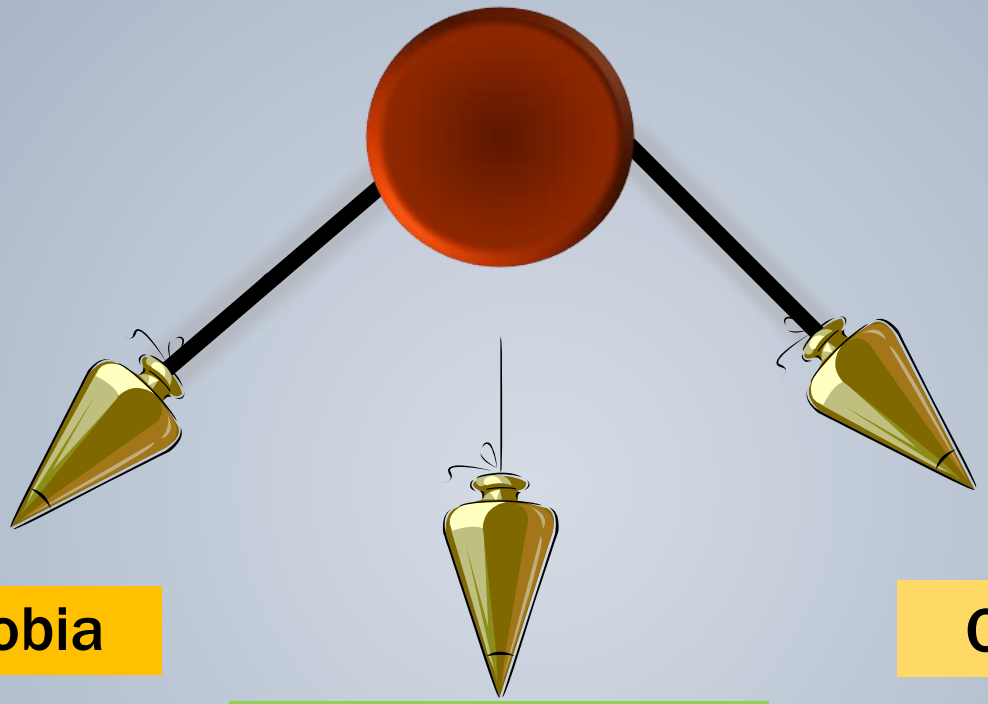
D. There is no general consensus on what constitutes an MEDD

# Pre / Post Test #3

Select the correct sequence of least to highest baseline addiction vulnerability

A. Alcohol, illicit drugs, nicotine
B. Illicit drugs, alcohol, nicotine
C. Nicotine, alcohol, illicit drugs
D. They all have equal vulnerability

# The Opioid Pendulum



**Opiophobia**

**Opiophillia**

**Balance of Addiction Medicine and Pain Management Principles[1]**

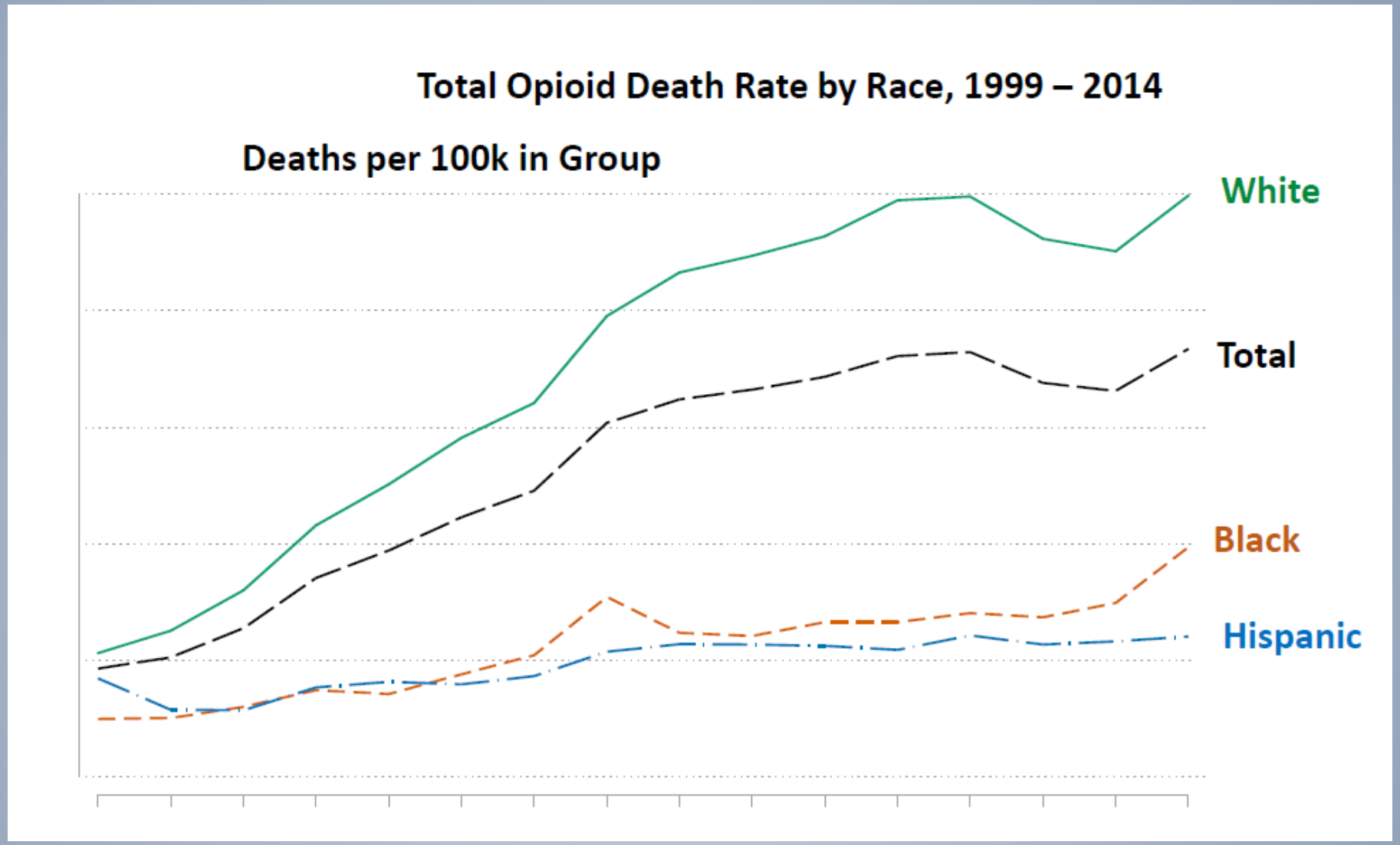
Gourlay, D.L. et al. (2005). Universal precautions in pain medicine: A rational approach to the treatment of chronic pain. *Pain Medicine, 6(2),* 107-112.

# Two Types of Opioid Consumers

1. Opioid abuse disorder
   - Heroin
   - Carfentanil
   - RX opioids
   - Other
2. Legitimate opioid consumers (RX)
   - Long-term opioid therapy v. short-term acute pain
3. A combination of #1 and #2 above

# Myths about Opioid Addiction in the U.S.

- Opioid Abuse is dominated by the African-American community
- Increased opioid RX's are the cause of overdose deaths
- Addiction starts with teens using opioids




Krane E. using National Vital Statistics System of the CDC and Prevention Multiple Cause of Death files for 1999-2014. Available at Pacing Event-ADE Deep Dive Opioid Use. Partnership for Patients and Communities, US Dept. HHS. https://www.healthcarecommunities.org/ResourceCenter/PartnershipforPatientsLibrary.aspx?CategoryId=836036&EntryId=110138

## Drug Overdose Death Data

Opioids—prescription and illicit—are the main driver of drug overdose deaths. Opioids were involved in 42,249 deaths in 2016, and opioid overdose deaths were five times higher in 2016 than 1999.

In 2016, the five states with the highest rates of death due to drug overdose were West Virginia (52.0 per 100,000), Ohio (39.1 per 100,000), New Hampshire (39.0 per 100,000), Pennsylvania (37.9 per 100,000) and (Kentucky (33.5 per 100,000).

Significant increases in drug overdose death rates from 2015 to 2016 were seen in the Northeast, Midwest and South Census Regions. States with statistically significant increases in drug overdose death rates included Connecticut, Delaware, Florida, Illinois, Indiana, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Jersey, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, South Carolina, Tennessee, Texas, Vermont, Virginia, West Virginia, and Wisconsin.[1]

https://www.cdc.gov/drugoverdose/data/index.html

# CDC Newsroom



## U.S. drug overdose deaths continue to rise; increase fueled by synthetic opioids

### Press Release

Embargoed Until: Thursday, March 29, 2018, 1:00 p.m. ET

**Contact:** Media Relations

(404) 639-3286

An in-depth analysis of 2016 U.S. drug overdose data shows that America's overdose epidemic is spreading geographically and increasing across demographic groups. The report, from researchers at the Centers for Disease Control and Prevention (CDC), appears in today's issue of MMWR.

Drug overdoses killed 63,632 Americans in 2016. Nearly two-thirds of these deaths (66%) involved a prescription or illicit opioid. Overdose deaths increased in all categories of drugs examined for men and women, people ages 15 and older, all races and ethnicities, and across all levels of urbanization.

CDC's new analysis confirms that recent increases in drug overdose deaths are driven by continued sharp increases in deaths involving synthetic opioids other than methadone, such as illicitly manufactured fentanyl (IMF).

"No area of the United States is exempt from this epidemic—we all know a friend, family member, or loved one devastated by opioids," said CDC Principal Deputy Director Anne Schuchat, M.D. "All branches of the federal government are working together to reduce the availability of illicit drugs, prevent deaths from overdoses, treat people with substance-use disorders, and prevent people from starting using drugs in the first place."

https://www.cdc.gov/media/releases/2018/p0329-drug-overdose-deaths.html

# Alternative Facts - 1

## Deaths from Opioid Overdoses Now Higher Than Car Accident Fatalities

CDC estimates more than 42,000 people overdosed on opioids in 2016.

https://www.healthline.com/health-news/deaths-from-opioid-overdoses-higher-than-car-accident-fatalities#modal-close

# The Opioid Epidemic: A Crisis Years in the Making

By Maya Salam

Oct. 26, 2017

The current opioid epidemic is the deadliest drug crisis in American history. Overdoses, fueled by opioids, are the leading cause of death for Americans under 50 years old — killing roughly 64,000 people last year, more than guns or car accidents, and doing so at a pace faster than the H.I.V. epidemic did at its peak.

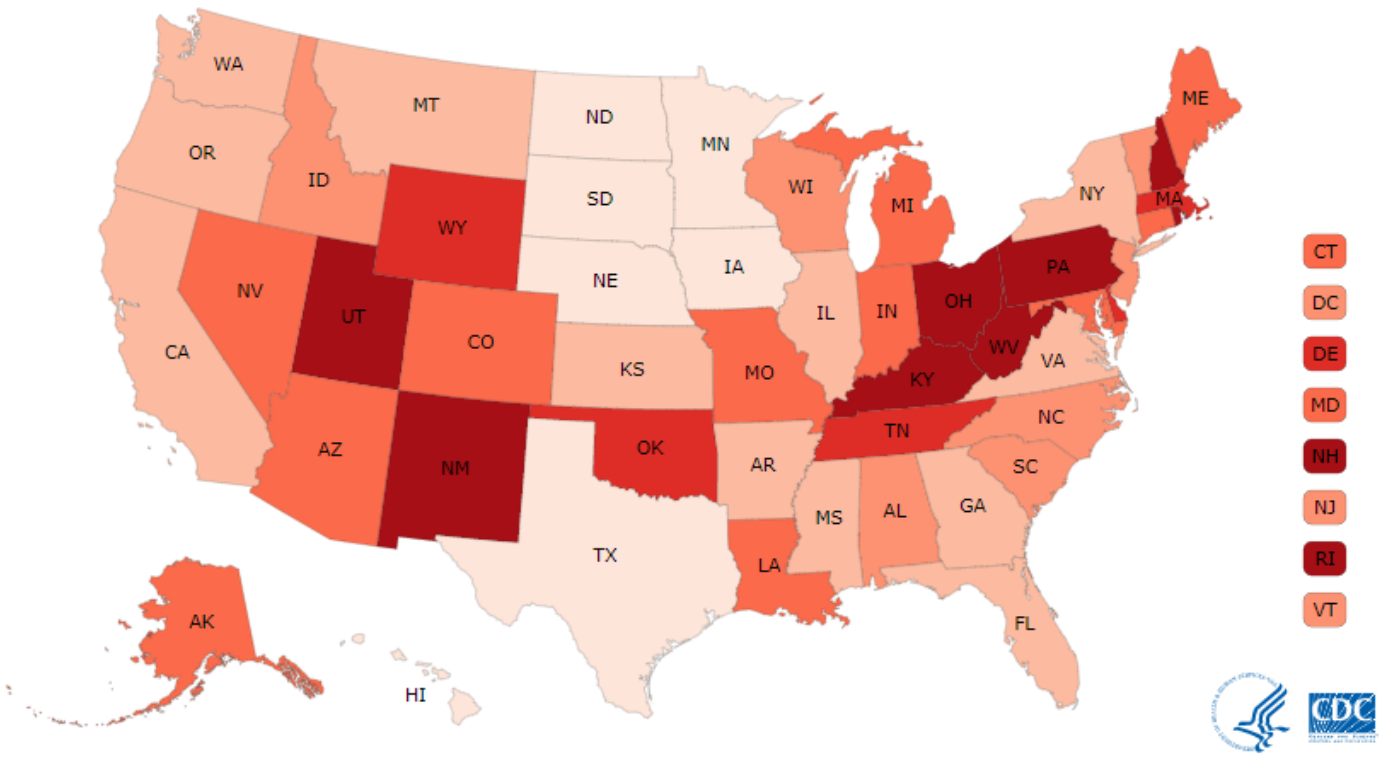
President Trump declared the opioid crisis a "public health emergency" on Thursday, though he did not release additional funding to address it. Had he declared it a "national emergency," as he promised to do in August, it would have led to the quick allocation of federal funds.

# Alternative Facts - 2

https://www.nytimes.com/2017/10/26/us/opioid-crisis-public-health-emergency.html

2015-2016 Increases | 2014-2015 Increases | 2016 | 2015 | **2014** | Rates | Data Sources

## Number and age-adjusted rates of drug overdose deaths by state, US 2014



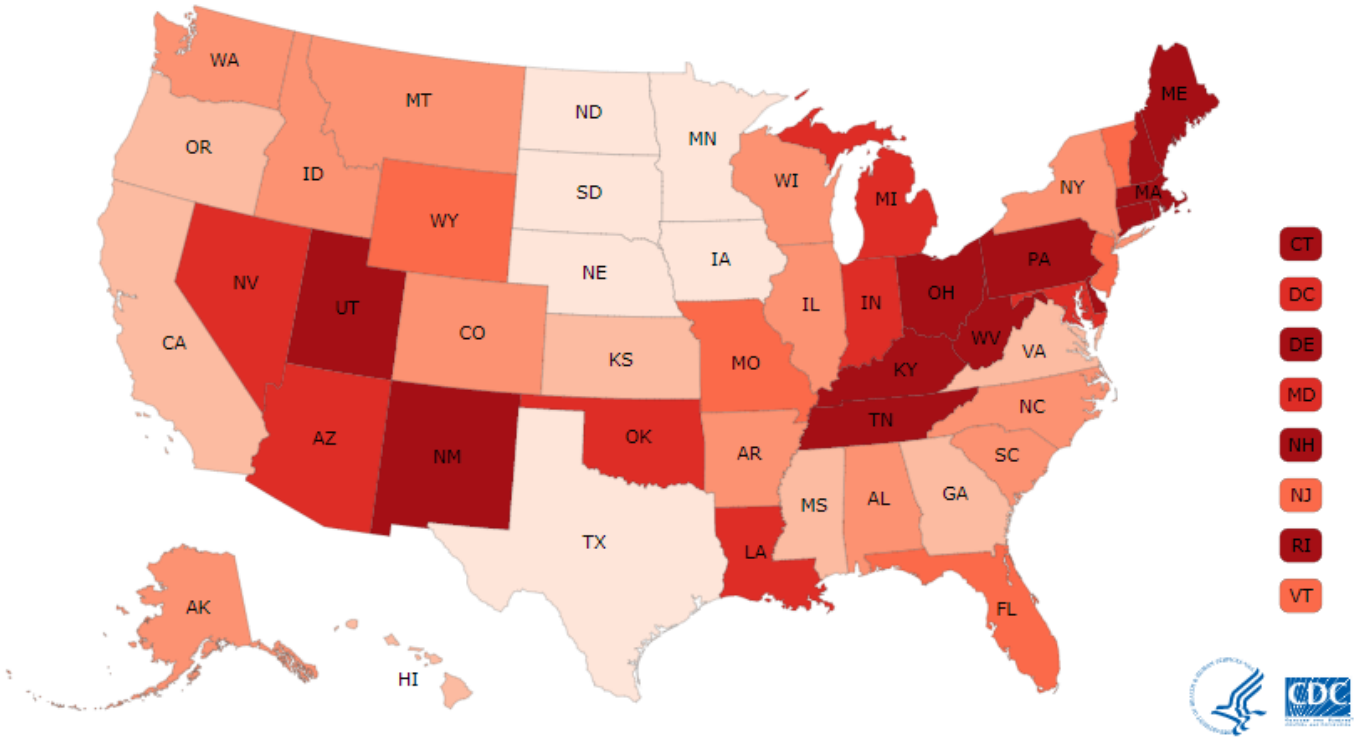

2014 Age-adjusted rate

- 6.3 to 11.0
- 11.1 to 13.5
- 13.6 to 16.0
- 16.1 to 18.5
- 18.6 to 21.0
- 21.0 to 35.5

https://www.cdc.gov/drugoverdose/data/index.html

2015-2016 Increases | 2014-2015 Increases | 2016 | **2015** | 2014 | Rates | Data Sources

## Number and age-adjusted rates of drug overdose deaths by state, US 2015



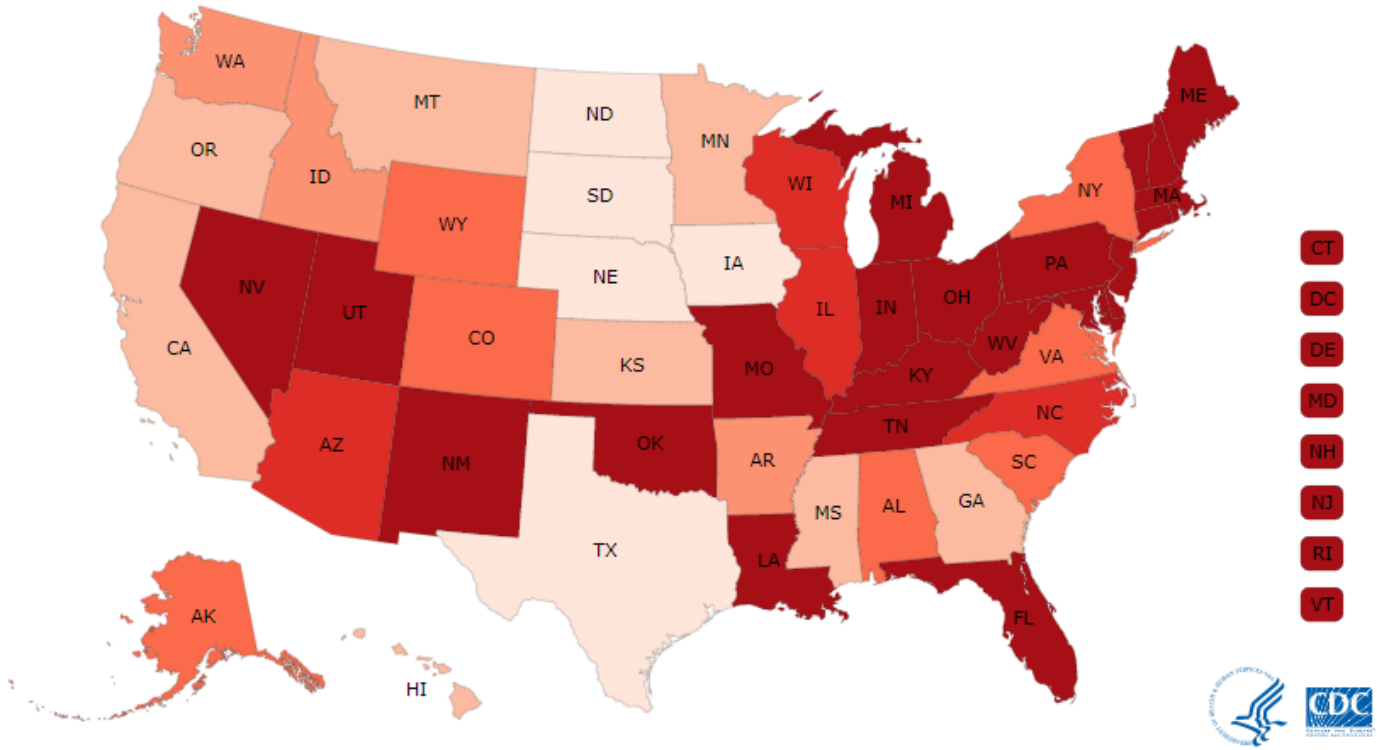

2015 Age-adjusted rate

- 6.9 to 11.0
- 11.1 to 13.5
- 13.6 to 16.0
- 16.1 to 18.5
- 18.6 to 21.0
- 21.0 to 41.5

https://www.cdc.gov/drugoverdose/data/index.html

2015-2016 Increases | 2014-2015 Increases | **2016** | 2015 | 2014 | Rates | Data Sources

## Number and age-adjusted rates of drug overdose deaths by state, US 2016



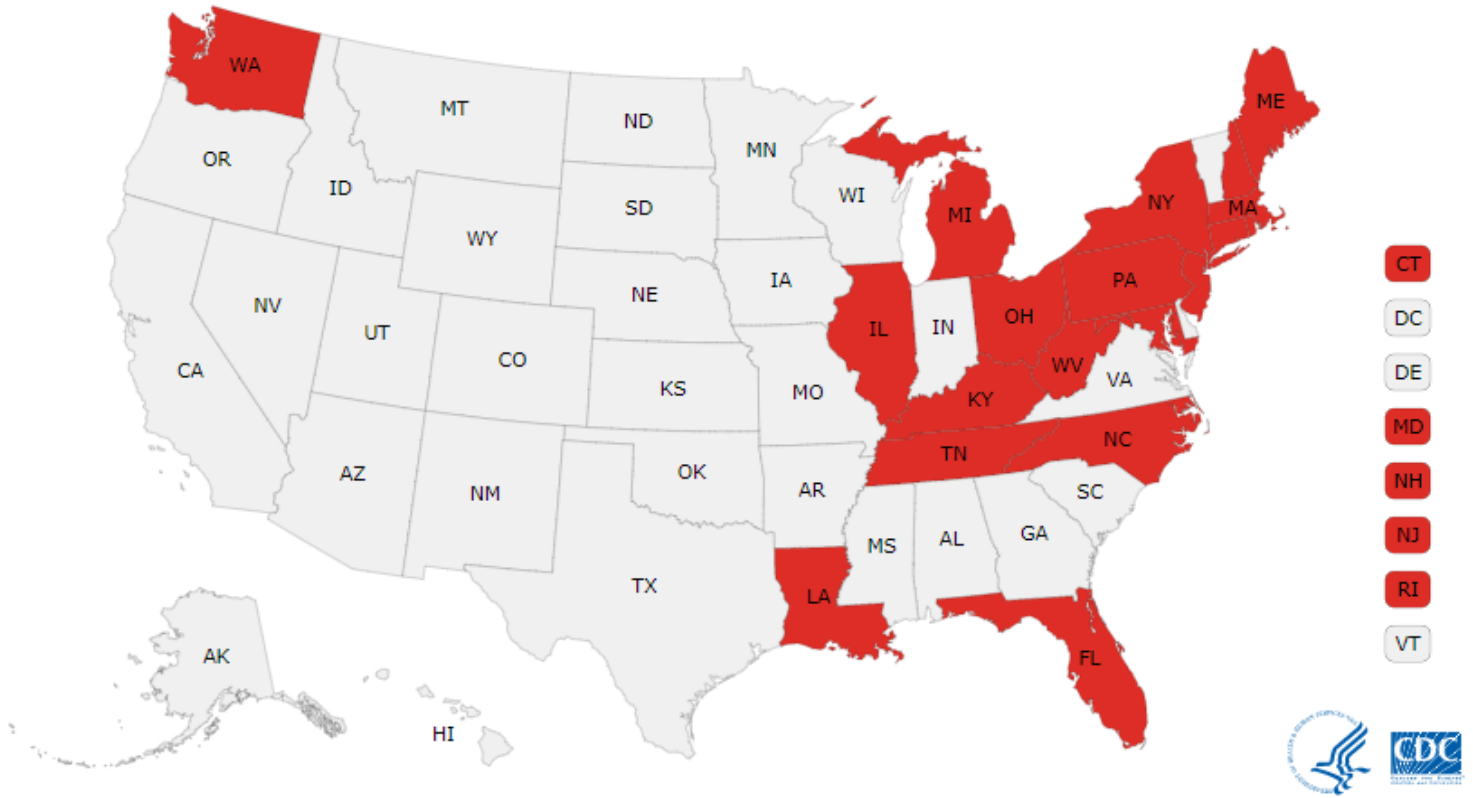

Legend

- 6.9 to 11.0
- 11.1 to 13.5
- 13.6 to 16.0
- 16.1 to 18.5
- 18.6 to 21.0
- 21.1 to 52.0

https://www.cdc.gov/drugoverdose/data/index.html

2015-2016 Increases | **2014-2015 Increases** | 2016 | 2015 | 2014 | Rates | Data Sources

## Statistically significant drug overdose death rate increase from 2014 to 2015, US states




### Statistically significant increase

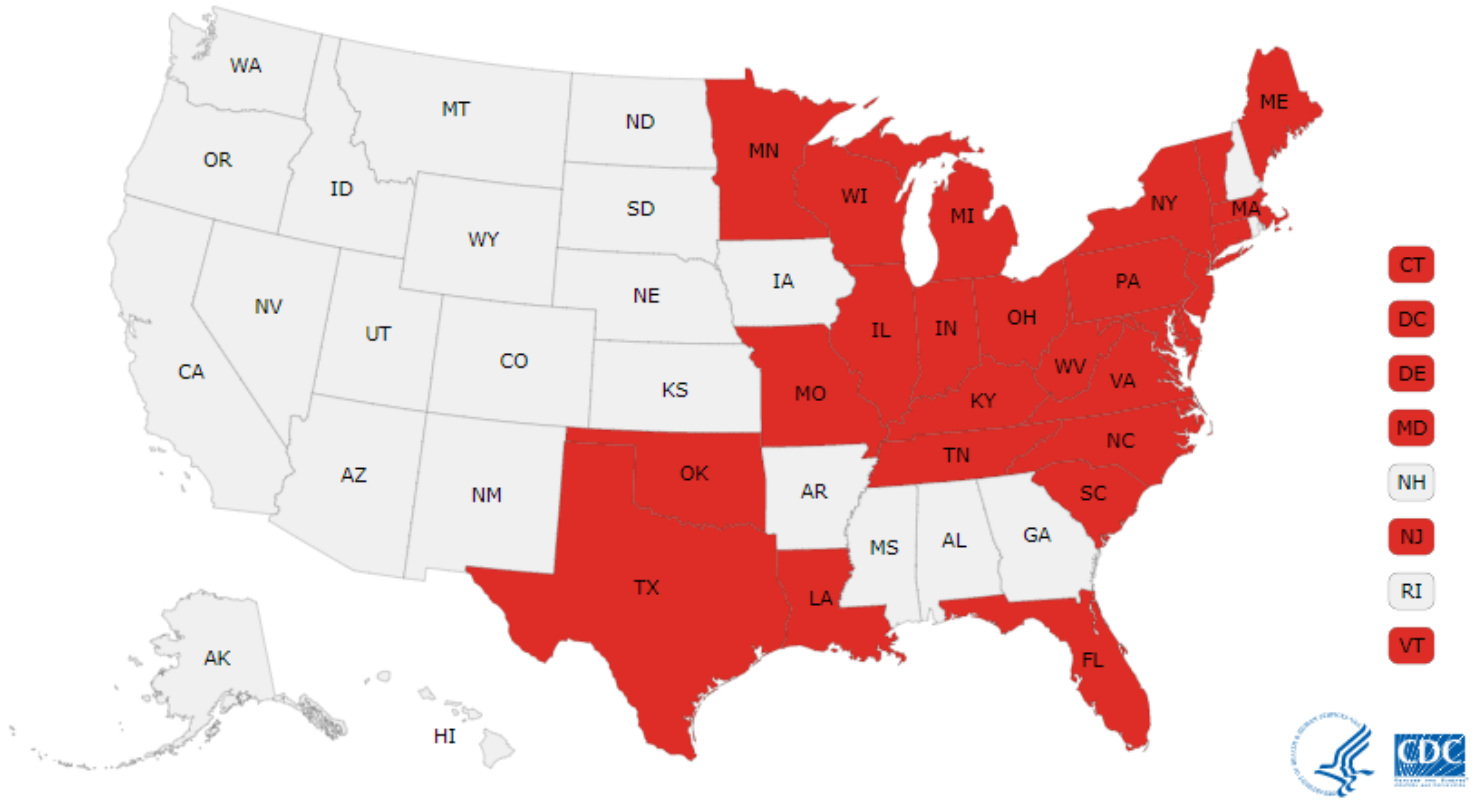
Statistically significant increase from 2014 to 2015

- No
- Yes

https://www.cdc.gov/drugoverdose/data/index.html

2015-2016 Increases | 2014-2015 Increases | 2016 | 2015 | 2014 | Rates | Data Sources

## Statistically significant drug overdose death rate increase from 2015 to 2016, US states




Statistically significant increase

Statistically significant increase from 2015 to 2016

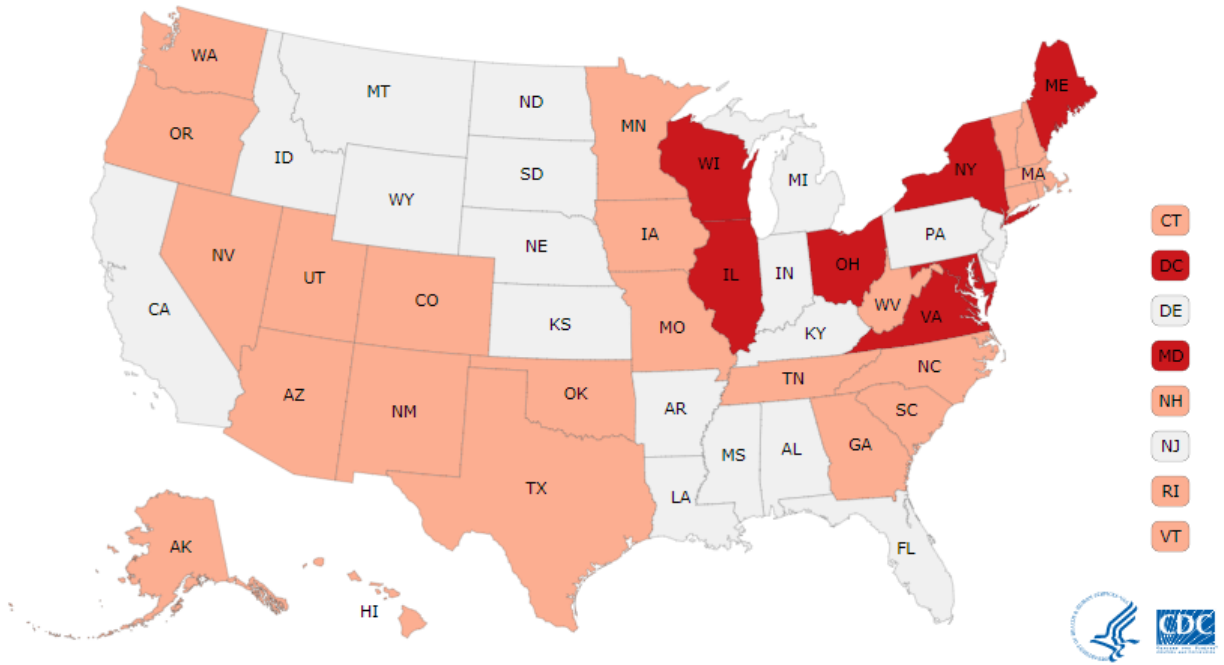
No

Yes

https://www.cdc.gov/drugoverdose/data/index.html

Key Data | Prescription Opioid Map | Prescription Opioid Graph

**Statistically significant changes in drug overdose death rates involving prescription opioids by select states, United States, 2015 to 2016**




- did not meet inclusion criteria
- increase
- decrease
- stable - not significant

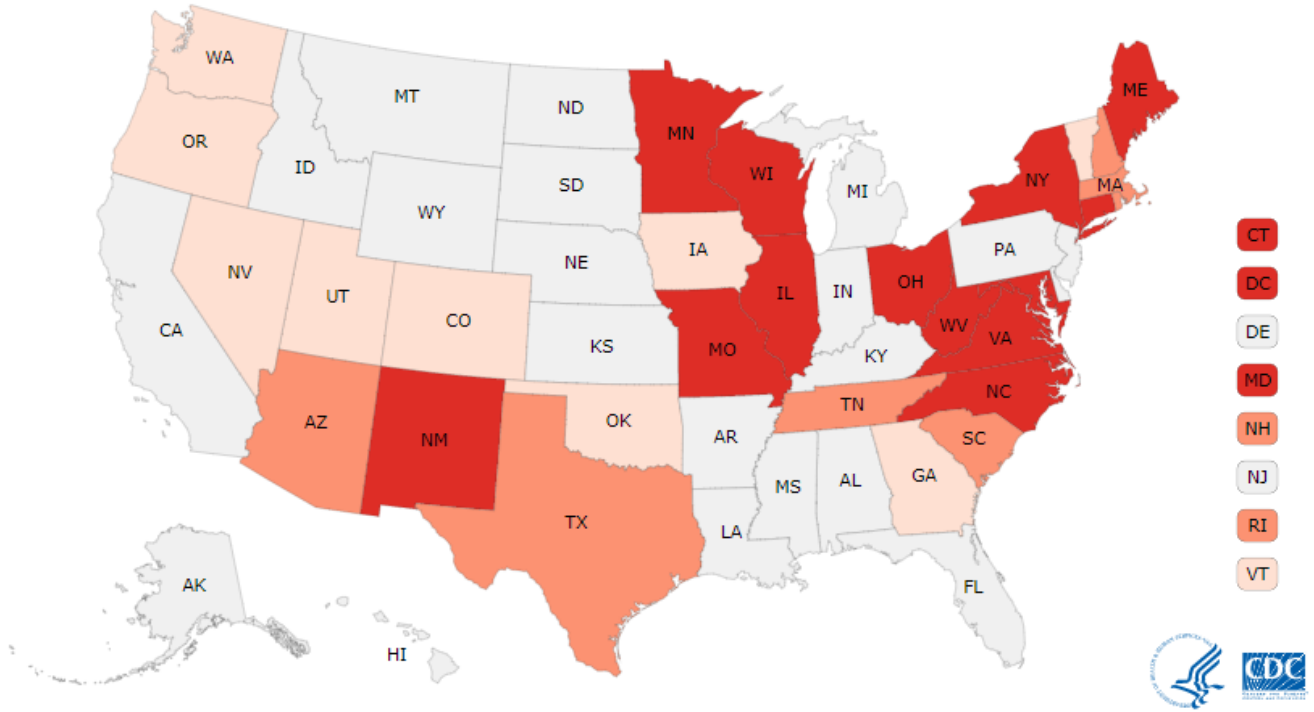
About This Map

Statistically significant change in rate, 2015-2016

Statistically significant changes in drug overdose death* rates involving prescription opioids† by select states,†† United States, 2015 to 2016.

https://www.cdc.gov/drugoverdose/data/overdose.html

## Statistically significant changes in drug overdose death rates involving synthetic opioids by select states, United States, 2015 to 2016




### About This Map

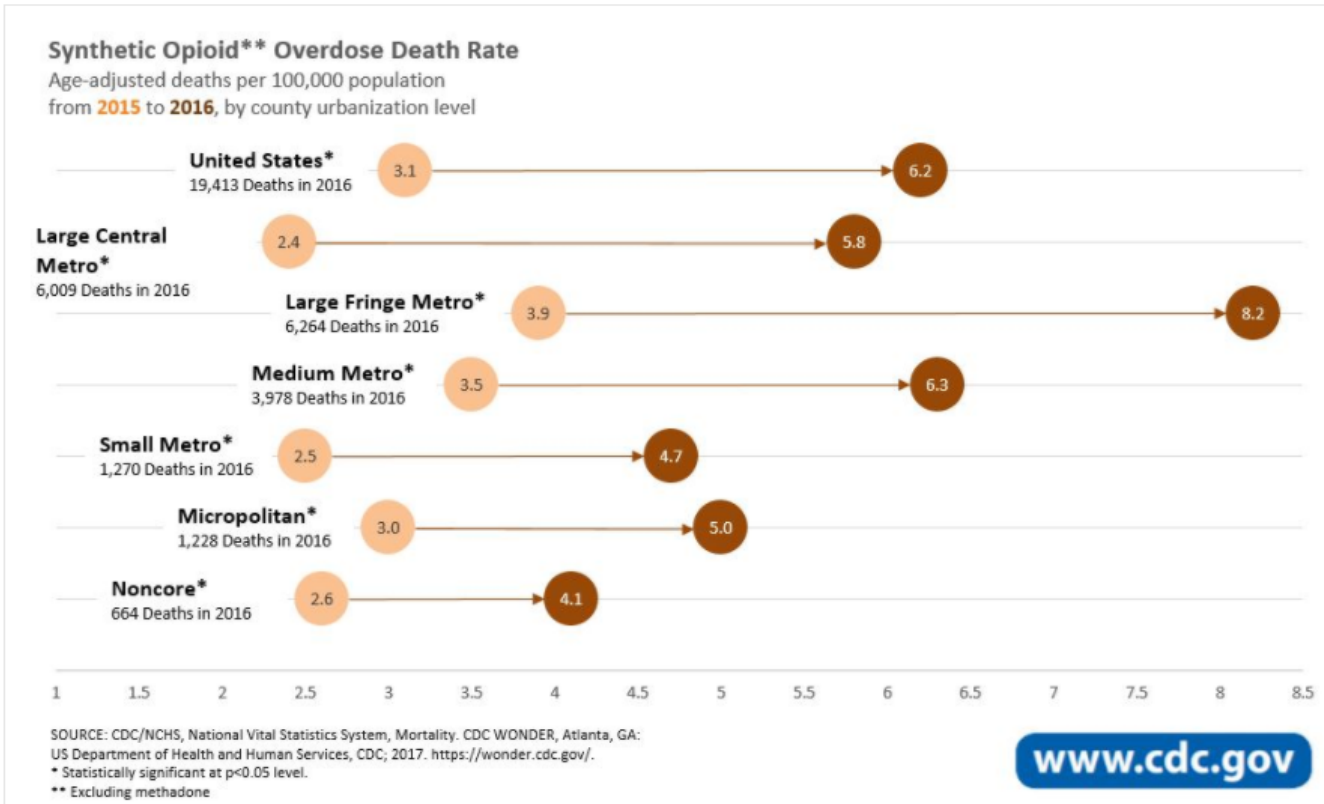
Statistically significant change in rate, 2015-2016

Statistically significant changes in drug overdose death* rates involving synthetic opioids (excluding methadone)† by select states,†† United States, 2015 to 2016.

Note: Rate comparisons between states should not be made due to variations in reporting across states.

https://www.cdc.gov/drugoverdose/data/overdose.html

Key Data | Synthetic Opioids Map | **Synthetic Opioids Graph**

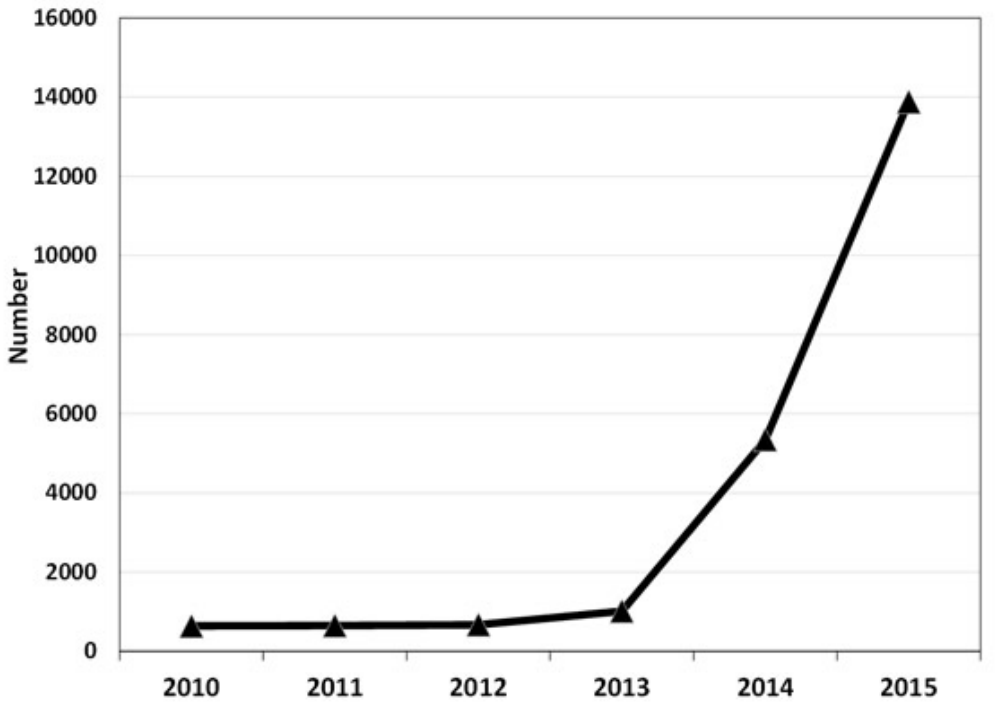



- **Large central metro**—Counties in metropolitan statistical areas of 1 million or more population that:
  - Contain the entire population of the largest principal city
  - Have their entire population contained in the largest principal city
  - Contain at least 250,000 inhabitants of any principal city
- **Large fringe metro**—Counties of 1 million or more population that did not qualify as large central metro counties.
- **Medium metro**—Counties of populations of 250,000 to 999,999.
- **Small metro**—Counties of populations less than 250,000.
- **Micropolitan**—Counties in micropolitan statistical areas that have a population of at least 10,000 but less than 50,000.
- **Noncore**—Nonmetropolitan counties that did not qualify as micropolitan.

https://www.cdc.gov/drugoverdose/data/overdose.html

Key Data | 2010-2015 Graph | 2013 Map | 2014 Map | 2015 Map | 2014-2015 Change Map | 2015 Rate Map

Number of Reported Law Enforcement Encounters Testing Positive for Fentanyl in the US: 2010 - 2015




www.cdc.gov
Your Source for Credible Health Information

*This graph uses data from the DEA National Forensic Laboratory Information System (NFLIS) on the number of law enforcement drug submissions that test positive for fentanyl from 2014 to 2015 as of July 1, 2016.

https://www.cdc.gov/drugoverdose/data/fentanyl-le-reports.html

# Schedule I Imported Fentanyl Derivatives

- Methoxyacetyl fentanyl
- 3-methylfentanyl, 3-methylthiofentanyl, China White
  - Alpha-methylfentanyl, alpha-methylthiofentanyl
  - Beta-hydroxy-3-methylfentanyl, beta-hydroxyfentanyl, beta-hydroxythiofentanyl
- Para-fluoroisobutyryl fentanyl
- Acetyl fentanyl
- Acetyl-alpha-methylfentanyl
- Acryloylfentanyl
- Butyryl fentanyl
- Cyclopentyl fentanyl
- Cyclopropyl fentanyl
- Furanyl fentanyl
- Isobutyryl fentanyl
- Tetrahydrofuranyl fentanyl
- Ortho-fluorofentanyl or 2-fluorofentanyl
- Ocfentanil
- Para-chloroisobutyryl fentanyl
- Para-fluorobutyryl fentanyl
- Para-fluorofentanyl
- Para-methoxybutyryl fentanyl
- Thiofentanyl
- Valeryl fentanyl

https://www.ncbi.nlm.nih.gov/pccompound/?term=fentanyl

# Are deaths due to carfentanil?

- 2015 New Hampshire data:
  - ✓351 total opioid deaths
  - ✓28 died of heroin as a single-drug overdose
  - ✓**Fentanyl was a factor in 253 of the overdose deaths!**

Costantini C, et al. "Death by Fentanyl". Documentary, aired December 3, 2016. (NH State Medical Examiner data)

- 2017 New Hampshire data (January 1-April 13, 2017):
  - ✓0 deaths from heroin alone
  - ✓18 deaths due to fentanyl
  - ✓2 deaths from a heroin-fentanyl combination
  - ✓86 deaths pending toxicology reports

Leclerc C. More people now dying from fentanyl than heroin in New Hampshire. WMUR on Demand. April 13, 2017.

# Percentage of counties with changes in opioid prescribing United States, 2010–2015

| Opioid prescribing measures | Decrease (%) | Stable (%) | Increase (%) |
|---|---|---|---|
| MEDD per capita | 49.6 | 27.8 | 22.6 |
| Overall prescribing rate | 46.5 | 33.8 | 19.6 |
| High-dose prescribing rate | 86.5 | 6.7 | 6.9 |
| Average daily MME per prescription | 72.1 | 25.7 | 2.2 |

Guy GP, et al. MMWR Morb Mortal Wkly Rep. 2017;66:697–704.

RAWSTORY US WORLD SCIENCE TECH MEDIA TRUMP

# Trump's false war on opioids will only punish patients

NEWSWEEK
06 APR 2018 AT 12:46 ET

Flipboard Facebook Twitter LinkedIn More 1.1K

https://www.rawstory.com/2018/04/trumps-false-war-opioids-will-punish-patients/

# Real Data v. Alternative Facts

- The CDC states that roughly 60,000 people die each year from drug overdoses.
  - Many people assume this is opioids ONLY.
  - It includes all drugs combined (prescription, over the counter, licit and illicit)
- Even 63,632 is inflated
  - Includes both prescription opioids, street opioids (heroin and illicit fentanyl analogs)
    - By lumping together the two dissimilar groups
      - CDC claims that more than 40,000 people die each year from opioid overdoses
      - The real number is likely in the 10,000-15,000 range
- CDC data shows that in 2015:
  - Half of the overdose deaths involving prescription opioids also involved a benzodiazepines, alcohol, and methamphetamine
- Real Fact: Deaths from prescription opioids alone is probably about 5,000

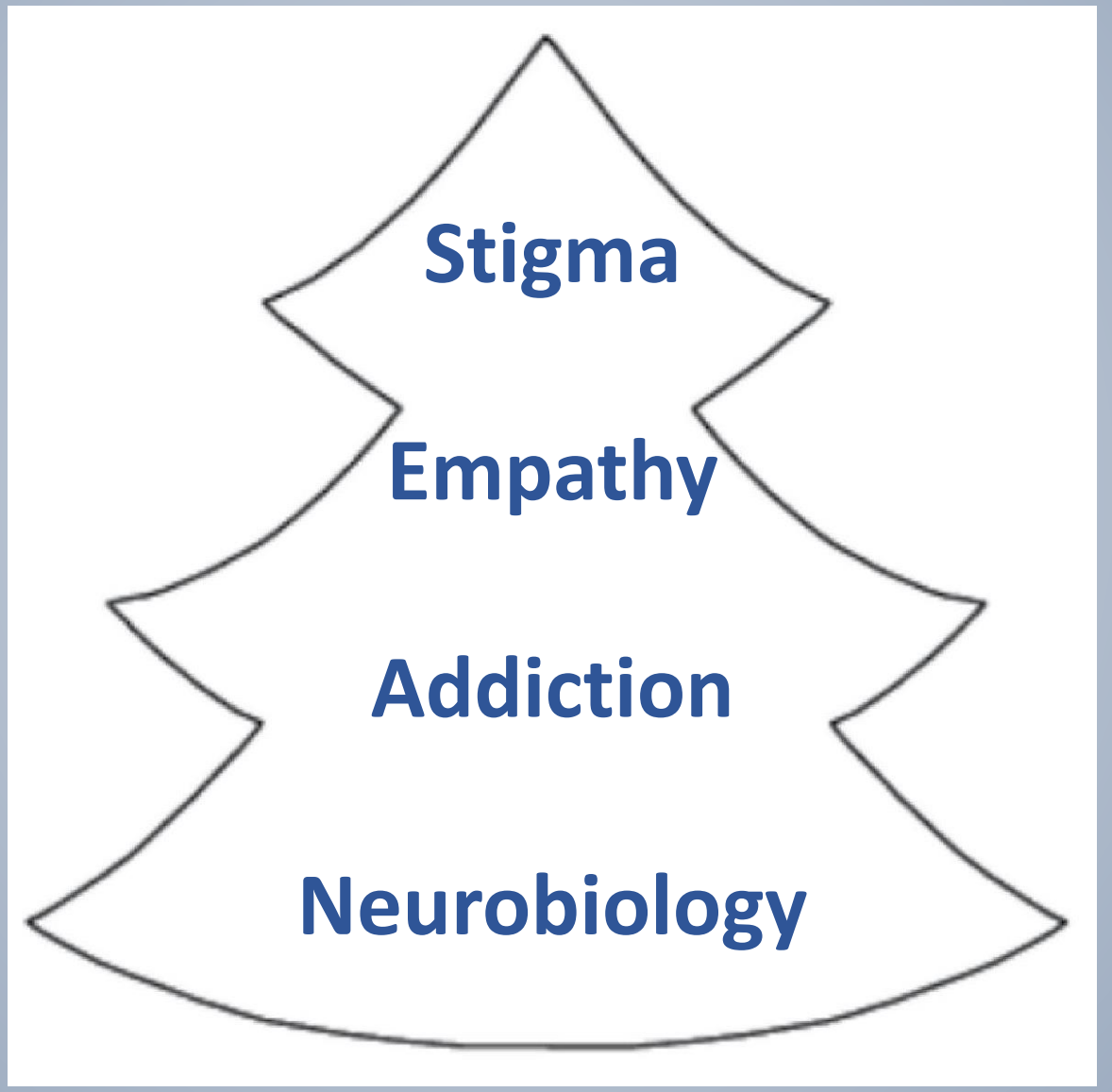

1. https://www.cdc.gov/drugoverdose/data/index.html
2. https://www.rawstory.com/2018/04/trumps-false-war-opioids-will-punish-patients/

# NSAID Mortality
# Putting things in perspective…

| | |
|---|---|
| Number of NSAID Deaths | 16,500 |
| Data Source | Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS)1 |
| Study Type | 1999 observational study |

Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. *J Rheumatol*. 1999;26(Suppl 56):18-24.

# Definitions



# Stigma

1. A mark of disgrace or infamy; a stain or reproach, as on one's reputation. a mental or physical mark that is characteristic of a defect or disease: the stigmata of leprosy. a place or point on the skin that bleeds during certain mental states, as in hysteria.
2. People coping with mental illness have a lot more to deal with than just the disorder itself. Many people report that the stigma of mental illness, and the prejudices they encounter because of it, is nearly as bad as the disorder's symptoms themselves.


1. http://www.dictionary.com/browse/stigma
2. https://www.healthyplace.com/stigma/stand-up-for-mental-health/what-is-stigma/

# Empathy

- Empathy means 'the ability to understand and share the feelings of another' (as in both authors have the skill to make you feel empathy with their heroines)
- Sympathy means 'feelings of pity and sorrow for someone else's misfortune' (as in they had great sympathy for the flood victims)

https://en.oxforddictionaries.com/definition/empathy

# Addiction (ASAM-short)

- A primary, chronic disease involving brain dysfunction which encompassing reward, motivation, memory and related circuitry.
  - Includes biological, psychological, social and spiritual manifestations.
  - Compulsive reward seeking
    - relief by substance use and other behaviors
    - Examples?

https://www.asam.org/quality-practice/definition-of-addiction

# Addiction (continued)

- Inability to abstain
- Impairment in behavioral control and craving
- Diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response.

https://www.asam.org/quality-practice/definition-of-addiction

# Improvement Needed in Healthcare System

- Chronicity
- Conditions requiring motivational/psychiatric component
- Communication amongst professionals
- Continual risk assessment
- Conditions that involve socio-economic status
- Stigmatization


- Goldney RD, et al. Depression, diabetes, and quality of life: A population study. Diabetes Care. 2004; 27(5): 1066-1070.
- Patrick DL, et al. Symptom management in cancer pain: Pain, depression, and fatigue. Journal of the National Cancer Institute, 2003; 95(15): 1110-1117.
- Winkleby MA, et al. Social class disparities in risk factors for disease: Eight-year prevalence patterns by level of education. Preventative Medicine. 1990; 19: 1-12.

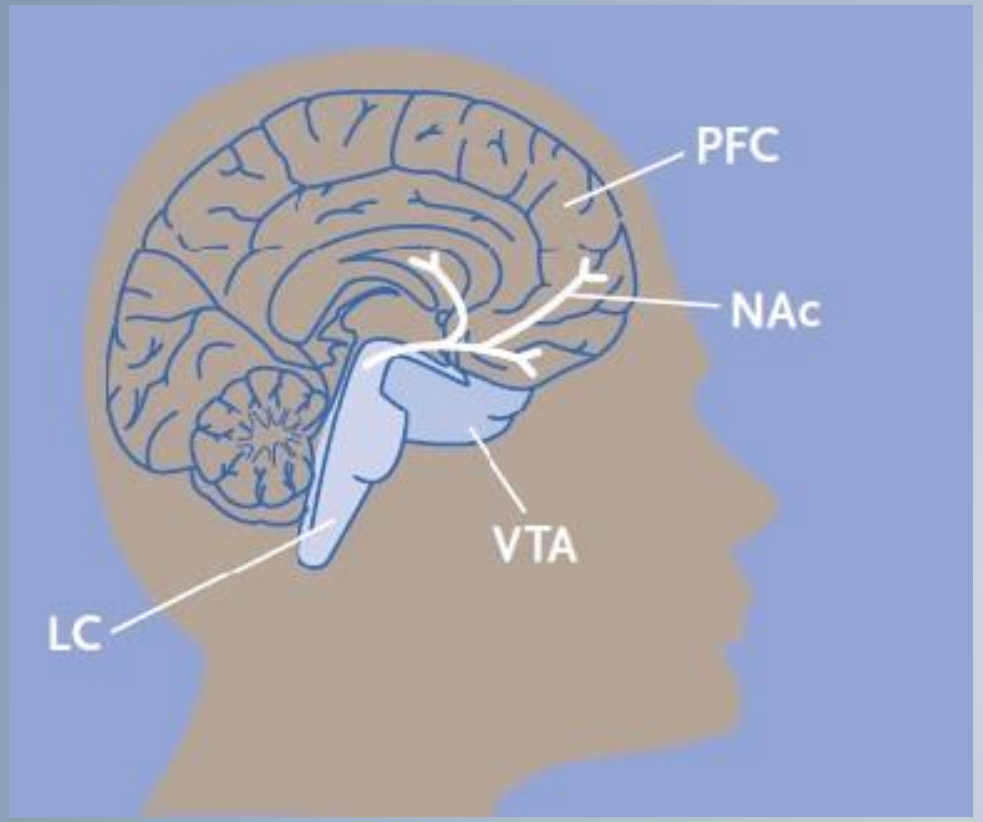
# Base Rates of Addiction/Abuse: Vulnerabilities in the Population

- 8.7% Illicit Drugs
- 12.5% Alcohol
- 26.5% Nicotine


- SAMHSA 2011 National Survey on Drug use and Health
- Hasin DS, et al. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States. Arch Gen Psychiatry. 2007; 64(7): 830-842.

# Neurobiology 101

# Mesolimbic Reward System




VTA: ventral tegmental area
NAc: nucleus accumbens
PFC: prefrontal cortex
LC: locus ceruleus

## Stages of Addiction Cycle

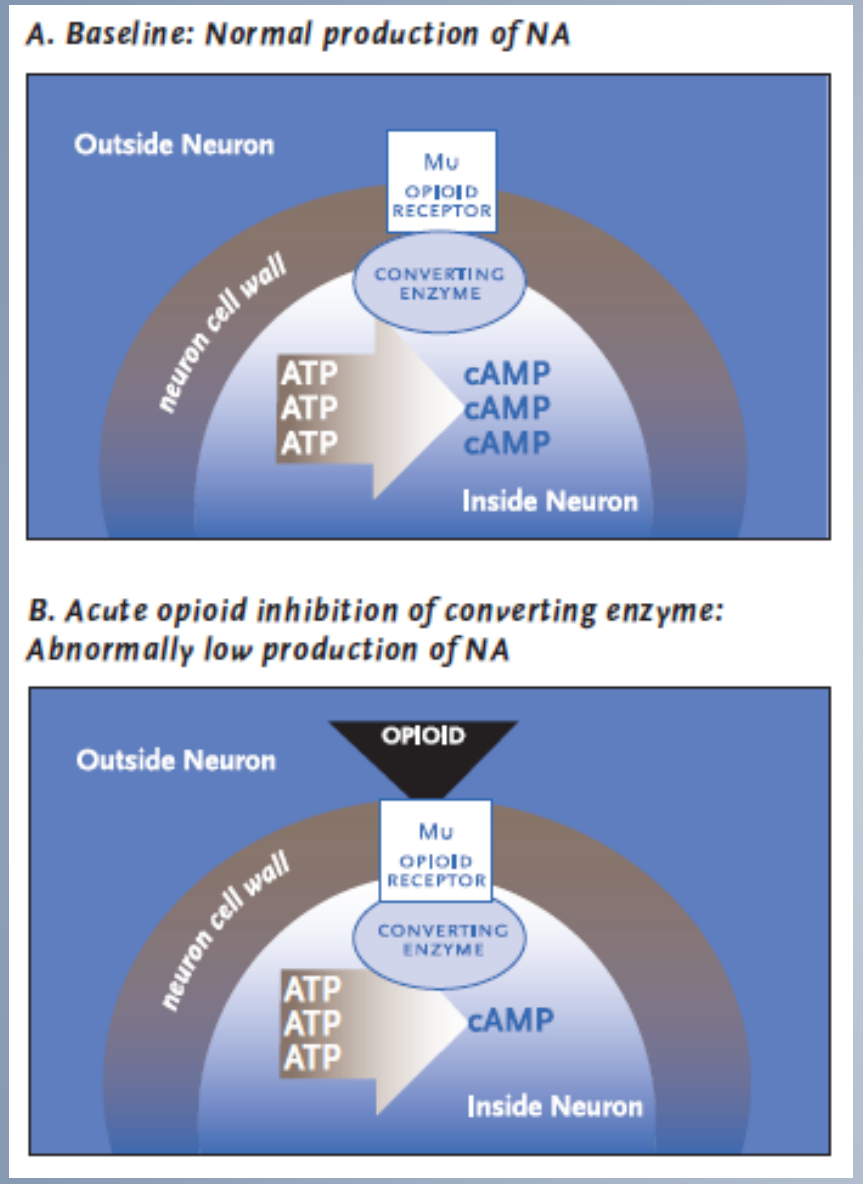
a. Binge and Intoxication
b. Withdrawal and Negative Affect
c. Preoccupation and Anticipation

1. Kosten, T. R., & George, T. P. (2002). The neurobiology of opioid dependence: implications for treatment. *Science & Practice Perspectives*, *1*(1), 13.
2. Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine*, *374*(4), 363-371.

| Stage of Addiction | Neuroadaptive Changes | | |
|---|---|---|---|
| **Binge and Intoxication** | Euphoria | Feeling Happy | Escaping depression, anxiety, or agitation |
| **Withdrawal and negative Affect** | Reduced Energy | Reduced Pleasure | Feeling dysphoric |
| **Preoccupation and anticipation** | Anticipation | Craving | Obsessing /Planning for Drug |

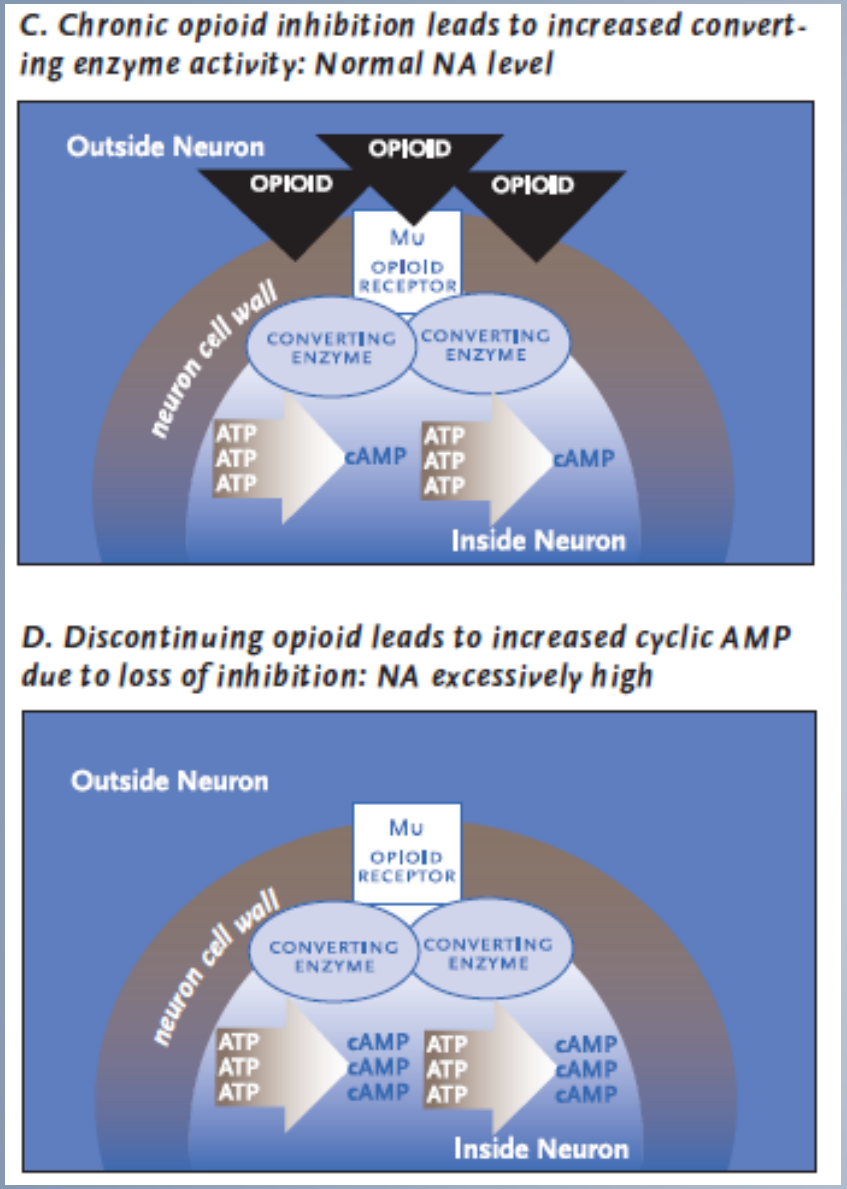
Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine*, *374*(4), 363-371.

# Neurobiological Explanation for Dependence and Withdrawal




# What's the impact of diminished noradrenalin?

Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine*, *374*(4), 363-371.




# Can we explain the physiological symptomatology?

Volkow, N. D., Koob, G. F., & McLellan, A. T. (2016). Neurobiologic advances from the brain disease model of addiction. *New England Journal of Medicine*, *374*(4), 363-371.

Substance Abuse is Complex
Political rhetoric attempts to simplify the issues…

- Genetic
- Psychiatric
- Social
- Environmental
- Economic

# Addiction is not Simply a Disease of Exposure

Exposure is necessary but not sufficient

- ✓Exposure to drug
- ✓Vulnerable person
- ✓Vulnerable time

Savage SR, Kirsh KL, Passik SD. Challenges in using opioids to treat pain in persons with substance use disorders. Addiction science & clinical practice. 2008 Jun;4(2):4.

# Addiction Comes in All Varieties

# Medical Problems Involving Addiction

- Diabetes
- Obesity
- Lung Cancer
- GERD[1]

1. Yoshikawa I, et al. Long-term treatment with proton pump inhibitor is associated with undesired weight gain. World J Gastroenterol. 2009; 15(38): 4794-4798.

# Does formulation selection matter?

**Fentanyl Patch**

**Fentanyl TIRF**

Included with permission from Dr. Steven Passik with revisions

# Could this have ended badly?

## Newsflash, April 2013
## Louisville Player Shatters Leg During Elite 8 Game

Louisville athlete Kevin Ware, 2013

- ✓Exposure to drug
- ✓Vulnerable person
- ✓Vulnerable time

Aleccia J. Gruesome basketball injury for Ware a 'freak accident,' doc says. NBC News. Apr 01, 2013. http://www.wrcbtv.com/story/21842623/gruesome-basketball-injury-for-ware-a-freak-accident-doc-says

# Strategies: Assess Abuse Risk

| Risk Assessment Tools | Question Formats | Indications | Advantages | Disadvantages | Scoring | Validated |
|---|---|---|---|---|---|---|
| SOAPP[1] | 5, 14, 24 | 1° Care, Assess for high abuse risk, suitability for long term opioid tx, preferable to ORT in high-risk populations | Best psychometrics, less susceptible to deception, 5-10 minutes | Dependent on patient reporting, Copyrighted | Numeric, simple to interpret | Yes, 14 quest ion studied in 396 pts |
| SOAPP-R[2] | 24 | Primary Care | 5 minutes, Cross-validated, Less susceptible to overt deception c/t SOAPP | Less sensitive and less specific than SOAPP | Numeric, simple to interpret | Yes, 283 pts |
| ORT[3] | 5 | Categorizes patients as low risk, moderate risk, and high risk | Less than 1 minute, simple scoring, high sensitivity & specificity when stratifying patients | 1 question in the ORT is limited by patient's knowledge of family history of substance abuse | Numeric, simple to interpret | Yes, (male and female), Preliminary Validation in 185 patients at 1 pain clinic, high degree of sensitivity and specificity |
| DIRE[4] | 7, by pt interview | risk of opioid abuse and suitability of candidates for long term opioid therapy | 2 minutes, score correlates well with patient's compliance& efficacy of long term opioid therapy | Prospective validation needed | Numeric, simple to interpret | ?, Retrospective validation only of 61 pts over 38 months |


1. J Pain Symptom Manage 2006;32:287–93
2. J Pain. 2008 April; 9 (4): 360-372
3. Pain Med 2005;6:432–42
4. J Pain 2006;7:671–81

# Strategies: Assess Misuse Risk

| Opioid Misuse Tools | Question Formats | Indications | Advantages | Disadvantages | Scoring | Validated |
|---|---|---|---|---|---|---|
| PADT[5] | N/A | To streamline the assessment of outcomes in patients with chronic pain, 2 sided chart note based on 4-A's* | 5 minutes, Documents progress over time, Complements a comprehensive clinical evaluation | Not intended to be predictive of drug-seeking behavior or predict positive or negative outcomes to opioid therapy | N/A | Further studies needed to confirm the reliability and validity, Studied in 388 patients by 27 clinician |
| COMM[6] | 17 | To assess aberrant medication related behaviors of chronic pain patients | 10 minutes, Useful in assessing & reassessing adherence to opioid RX(s) | Long term reliability is unknown | Numeric | 222 pts, Long term reliability is unknown, Validated in small study, needs to be replicated |
| ABC[7] | 20 questions | Ongoing clinical assessment of chronic pain patients on opioid therapies | Concise and easy to score<br>Studied in the VA setting | Needs validation in non-VA setting. | Score of ≥3 indicates possible inappropriate opioid based on Y/N answers | Studied 136 veterans in a multidisciplinary VA Chronic Pain Clinic |


5. Clin Ther 2004; 26:552–61
6. Pain. 2007 July; 130(1-2):144-156
7. J Pain Symptom Manage 2006;32:342-351

# Conclusions / What should pharmacist not do?

1. Perpetuate false information and rhetoric
2. Deny prescriptions based solely on MEDD
3. Assume that MEDD is accurate
4. Avoid counseling when patient “forfeits” it
5. Prejudge patients receiving chronic opioid therapy
6. Dispense opioids combined with sedative-hypnotics without carefully checking the reasons with patient and prescriber

# Conclusions / What should pharmacists **do**?

1. Check PDMP
2. Participate & promote educational programs for patients, pharmacists, and other clinicians
3. Be a team player with prescribers
4. In an ideal world
   - ✓ Assess risk for OIRD, abuse, and misuse prior to discharge and when dispensing RX in community
5. Treat each patient with “individualized” approach
6. Evaluate for and provide naloxone for in-home use

# Pre / Post Test #1

Nonmedical use of opioid analgesics from early 2000 to the mid-2000's have…

A. **increased approximately 50%**
B. decreased approximately 50%
C. remained the same
D. have fluctuated up and down

# Pre / Post Test #2

Which of the following is true regarding morphine equivalent daily equivalent (MEDD) doses?

A. There is general consensus of what constitutes an MEDD

B. The Internet posted CDC calculator should be used to provide accurate morphine equivalents for methadone conversions

C. Online opioid conversion calculators by states and federal agencies are generally consistent in terms of MEDD

**D. There is no general consensus on what constitutes an MEDD**

# Pre / Post Test #3

Select the correct sequence of least to highest baseline addiction vulnerability

A. Alcohol, illicit drugs, nicotine

**B. Illicit drugs, alcohol, nicotine**

C. Nicotine, alcohol, illicit drugs

D. They all have equal vulnerability