Substance Use Disorders: brains, behavior, and diagnosis

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Disclosures

Nothing to disclose

Objectives

1. Review the diagnostic criteria for substance use disorders

2. Understand how and why substance use disorders develop

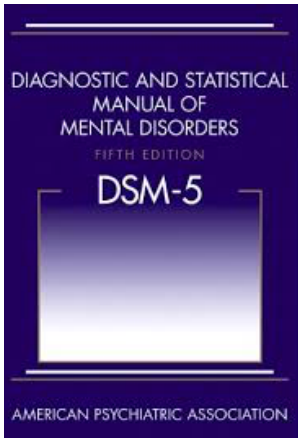
3. Discuss the gray zone between opioid use disorder and pain

Objective 1

Review the Diagnostic Criteria for Substance Use Disorders

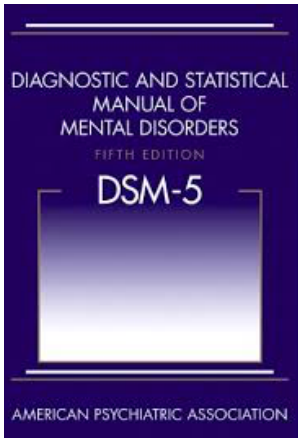
Not Just Use

Disordered Use



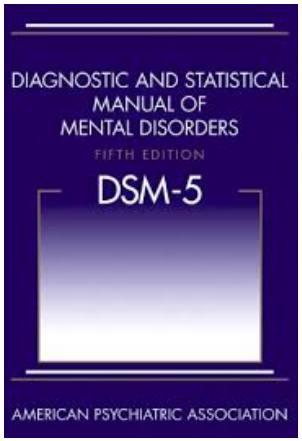
DSM V

Diagnostic and Statistical Manual of Mental Disorders



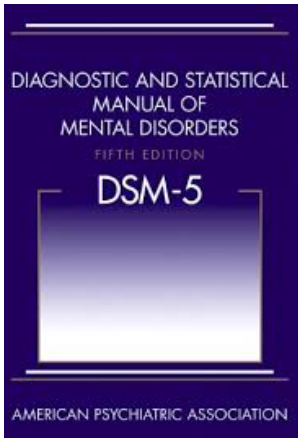
DSM V: Substance Use Disorder

11 criteria



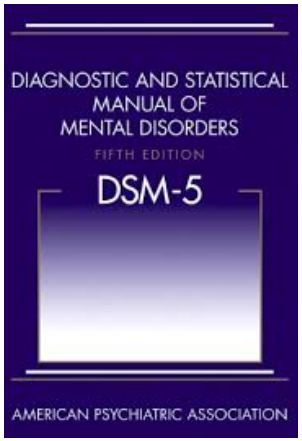
DSM V: Substance Use Disorder

Craving / Compulsion



DSM V: Substance Use Disorder

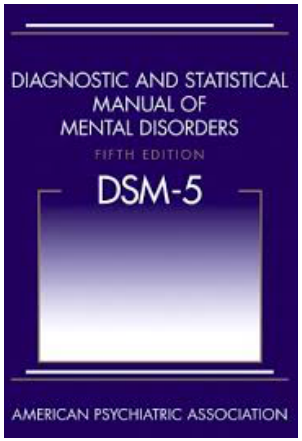
- ☑ Taking in larger amounts or for longer than intended
- ☑ Unsuccessful efforts to cut down
- ☑ Spending a lot of time obtaining the substance
- ☑ Craving or a strong desire to use the substance



DSM V: Substance Use Disorder

Consequences

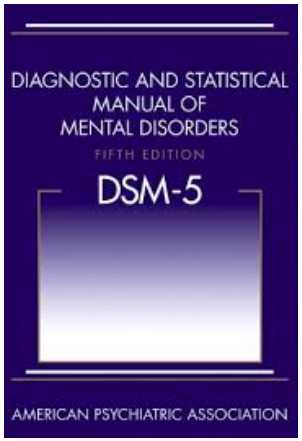
Loss of Control



DSM V: Substance Use Disorder

- ☑ Continued use despite recurring social or interpersonal problems due to use
- ☑ Important activities given up or reduced
- ☑ Recurrent use in physically hazardous situations
- ☑ Persistent / Recurrent physical or psychological difficulties from use
- ☑ Recurrent use resulting in a failure to fulfill major role obligations

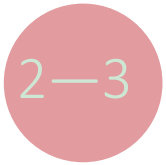

PIE
SADLY, MOTHMAN ALLOWS ANOTHER CRIMINAL TO ESCAPE



DSM V: Substance Use Disorder

- ☑ Tolerance*
- ☑ Withdrawal*

Substance Use Disorder



mild disorder

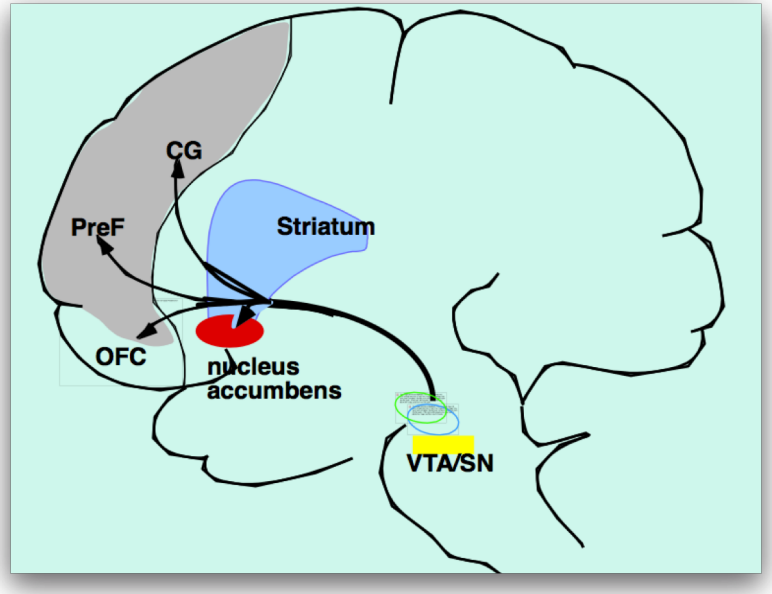
moderate disorder

severe disorder

Craving
Compulsion
Consequences
Loss of Control

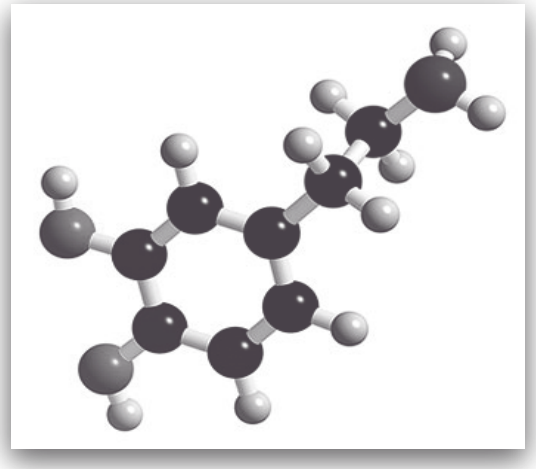
Objective 2

Understand how and why substance use disorders develop

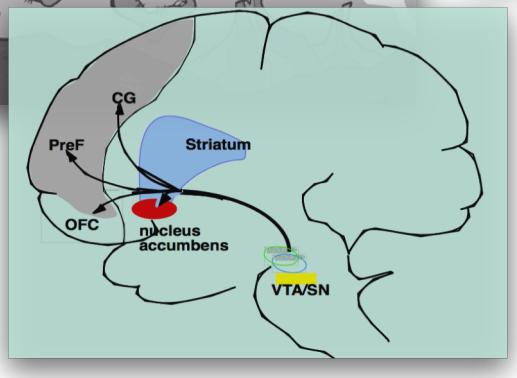

CG
PreF
Striatum
OFC
nucleus
accumbens
VTA/SN

1950s : electrodes

1970s: Dopamine

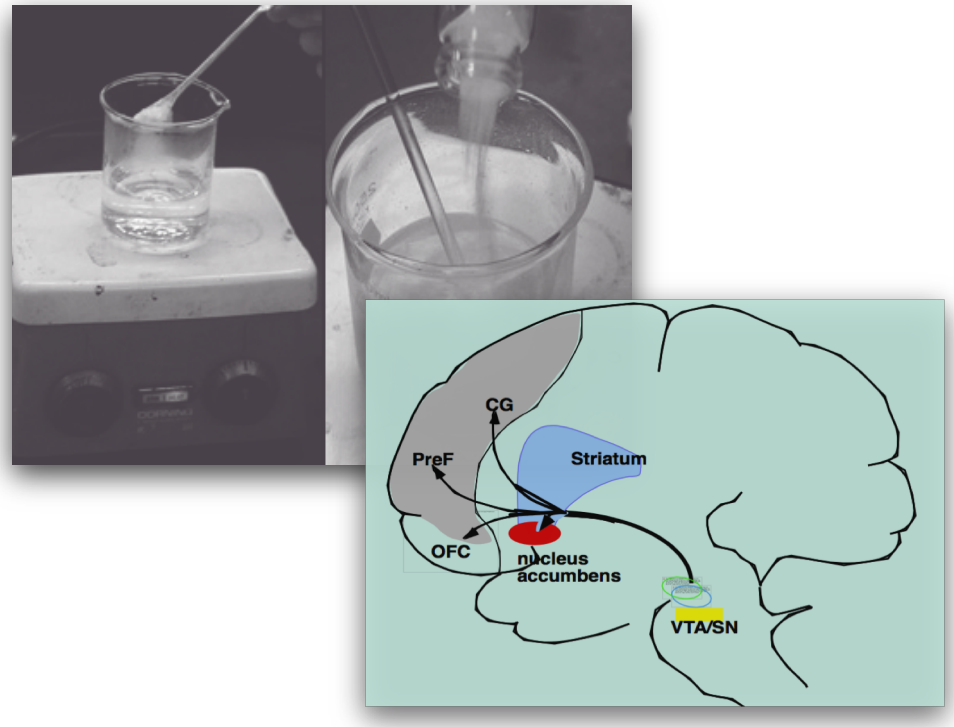


Desire and Drives



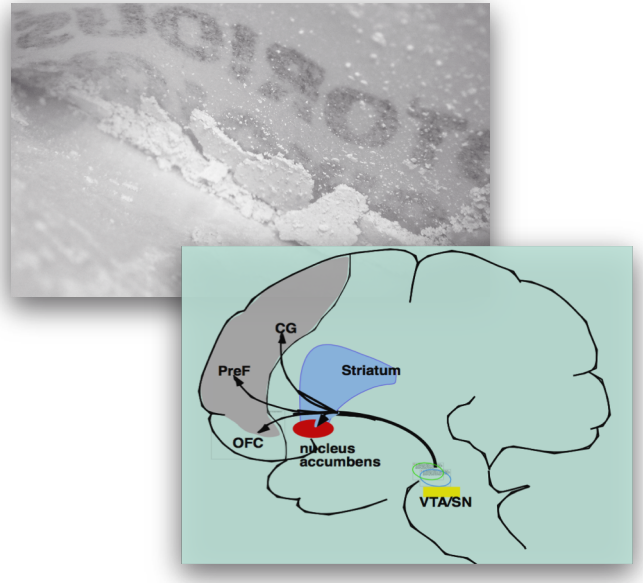
- Mediates responses to food, sex, social interactions
- Connects with memory and emotional centers

Craving



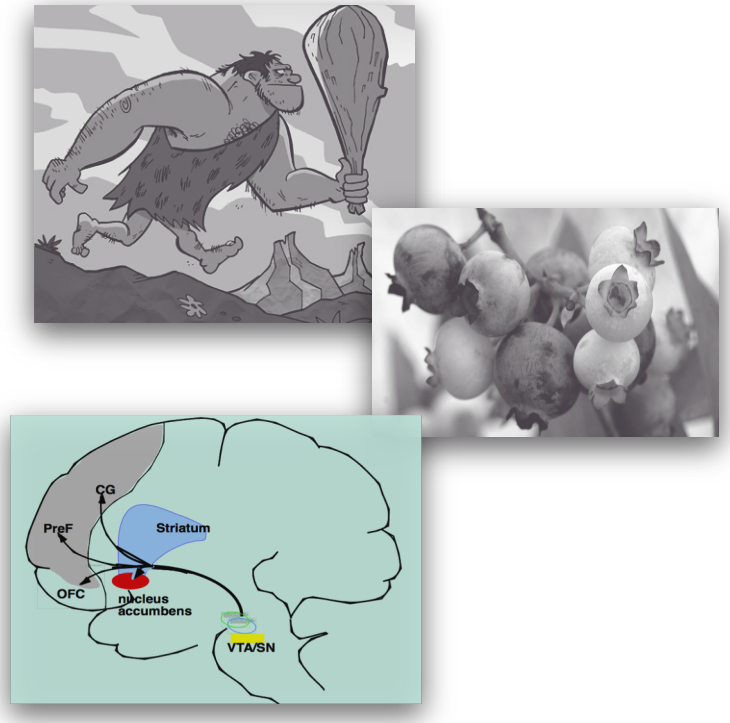
- All addictive drugs activate this pathway
- Drug experience is deeply linked to memory and emotion
- People, places, things associated with drug use can trigger cravings

Liking



- Opioids: Activate DA receptors
- Also activate opioid receptors in NA and produce feeling of satiety, soothing, comfort.

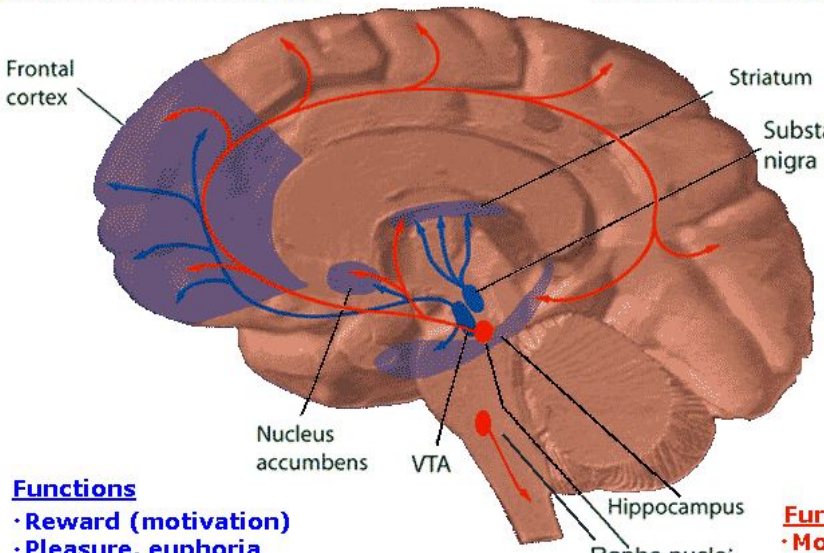
Dysregulation



- Dysregulation: impaired ability of the front of the brain, to regulate what is going on in the older regions of the brain.
- Prefrontal cortex helps determine the risks and benefits of behaviors and make rational choices.
- Repeated activation of the VTA to NAC track slowly strengthens those connections. Habits get hard wired, fast and automatic

Dopamine Pathways

Serotonin Pathways



Functions

- Reward (motivation)
- Pleasure, euphoria
- Motor function (fine tuning)
- Compulsion
- Perseveration

Functions

- Mood
- Memory processing
- Sleep
- Cognition

D1: These receptors are responsive to big pleasure surges and cause to act. The larger the dopamine input, the more likely the action.

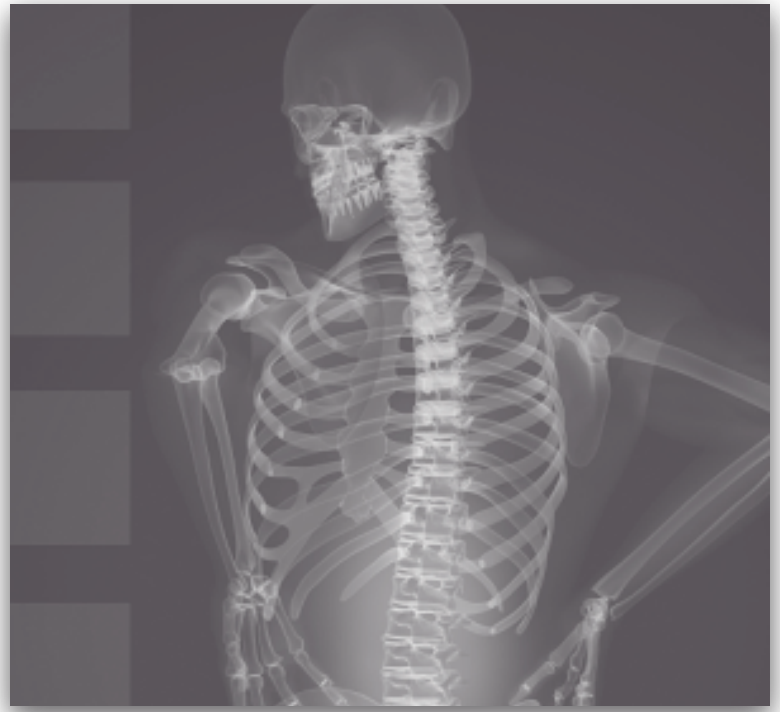
D2: These receptors slow down decision making, allow the frontal cortex to step in. They are responsive to dopamine – but not too much.

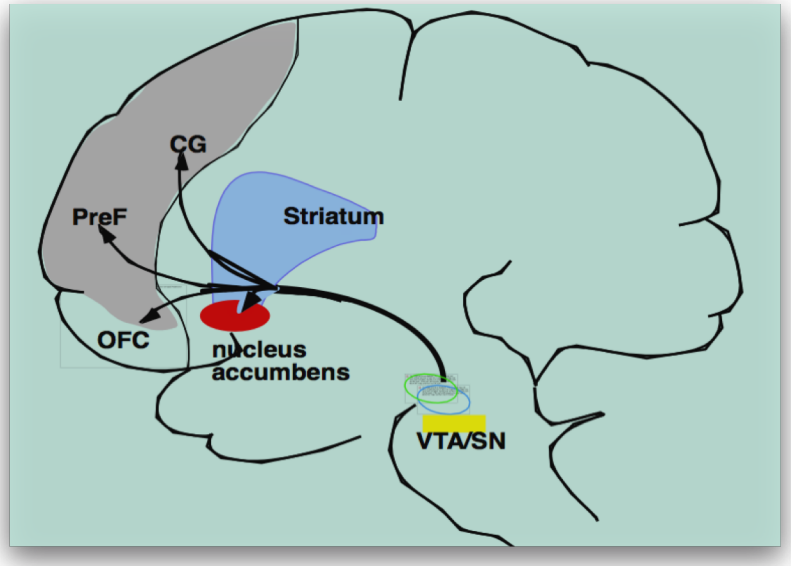
Volkow et al Bioessays 2010
Taylor et al Pain 2016
Dorsook et al Neuroscience and Biobehavioral Reviews 2016


Just
say no

Objective 3

Discuss gray zone between opioid use disorder and pain




CG
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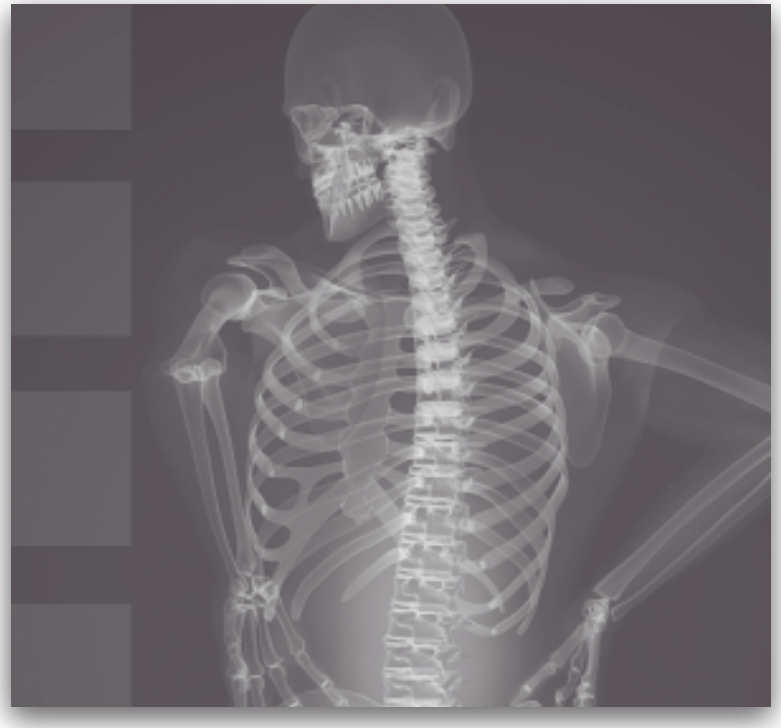


SHARE

Drug Deaths in America Are Rising Faster Than Ever

By JOSH KATZ JUNE 5, 2017

New data compiled from hundreds of health agencies reveals the extent of the drug overdose epidemic last year.

AKRON, Ohio — Drug overdose deaths in 2016 most likely exceeded 59,000, the largest annual jump ever recorded in the United States, according to preliminary data compiled by The New York Times.

The death count is the latest consequence of an escalating public health crisis: opioid addiction, now made more deadly by an influx of illicitly manufactured fentanyl and similar drugs. Drug overdoses are now the leading cause of death among Americans under 50.

Although the data is preliminary, the Times's best estimate is that deaths rose 19 percent over the 52,404 recorded in 2015. And all evidence suggests the problem has continued to worsen in 2017.

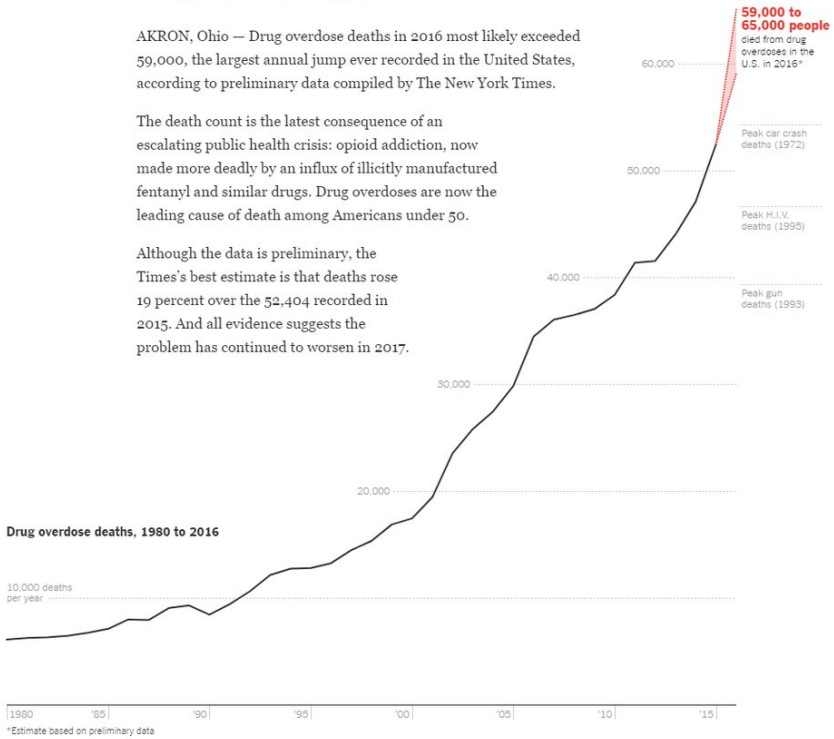


Table 1. 12 Recommendations From the Centers for Disease Control and Prevention For Prescribing Opioids for Chronic Pain

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.

3. Before starting—and periodically during—opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to 50 morphine milligram equivalents (MME) or more per day, and should avoid increasing dosage to 90 MME or more per day or carefully justify a decision to titrate dosage to 90 MME or more per day.

6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than 7 days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/d), or concurrent benzodiazepine use are present.

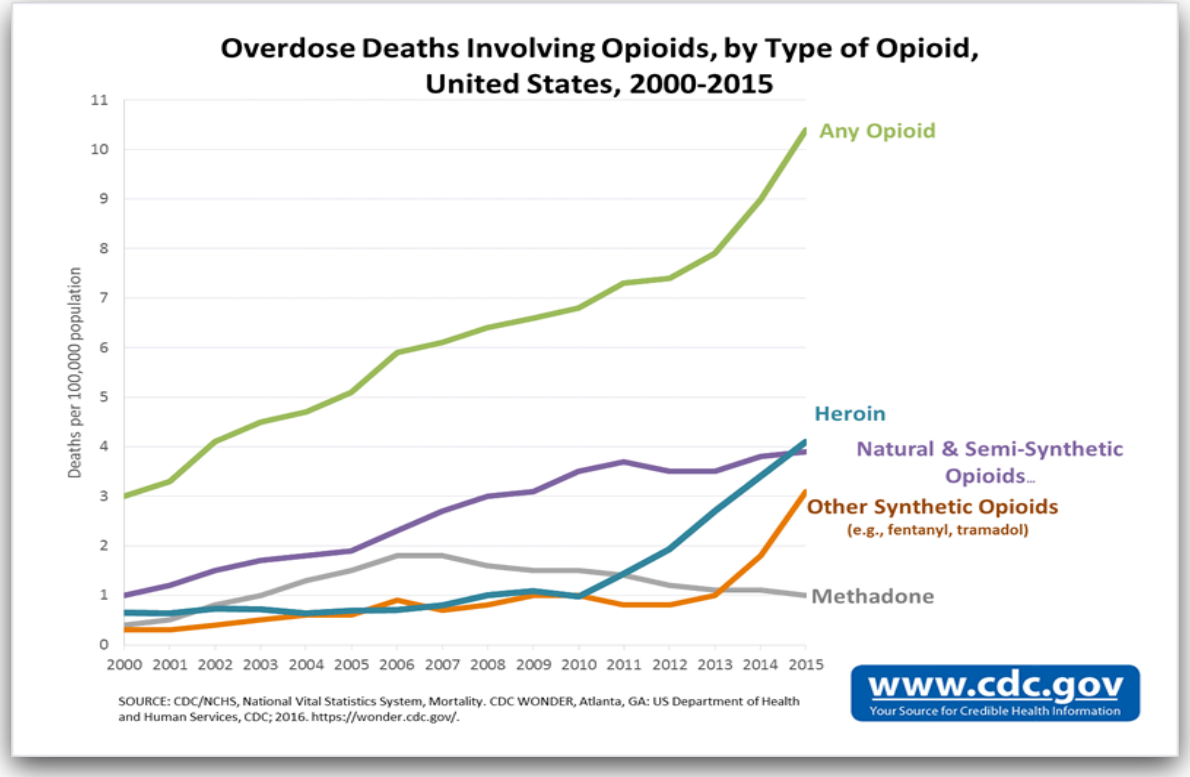
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.

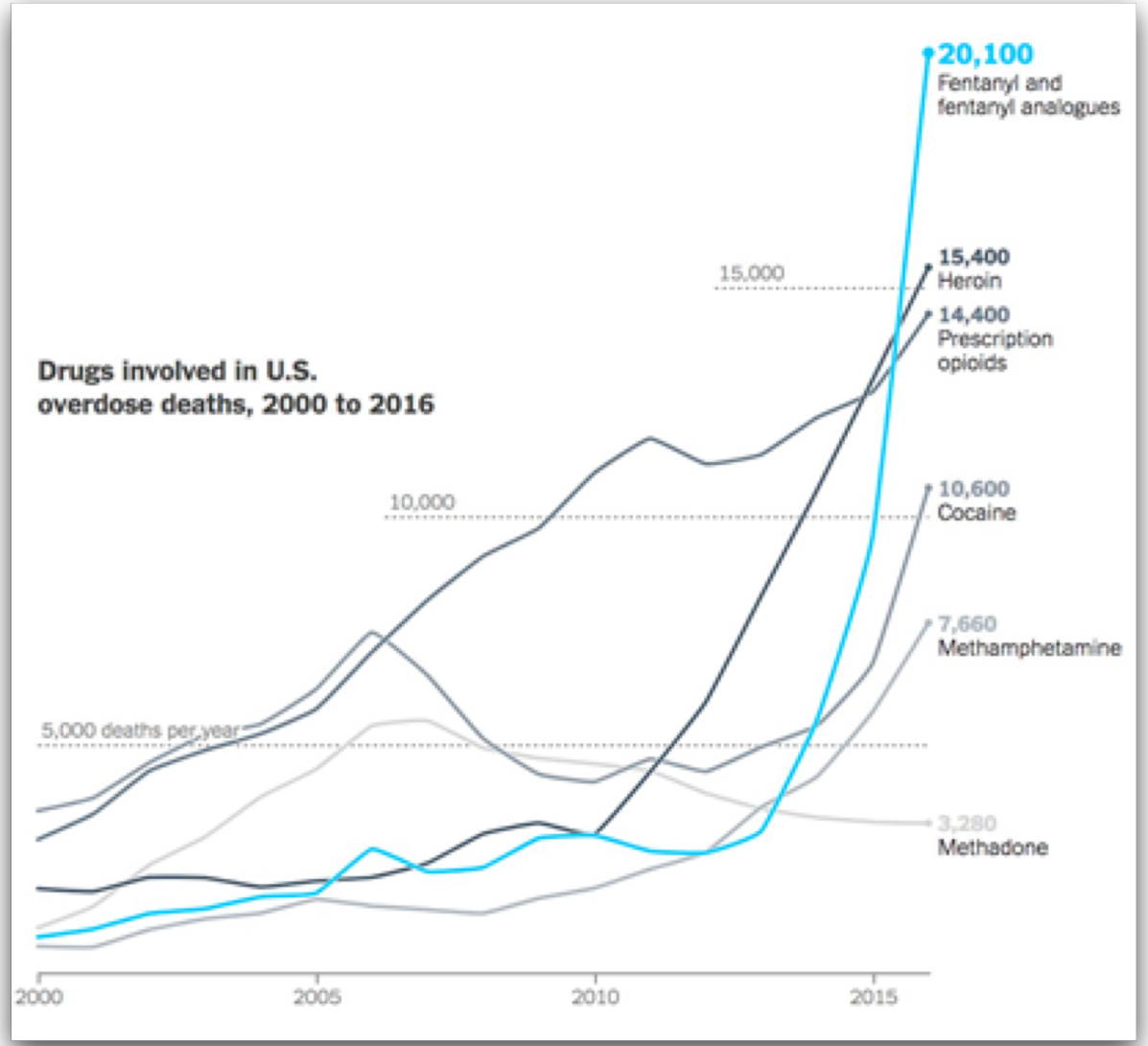
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

Source: 1. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *JAMA*. March 15, 2016. [Epub ahead of print].


Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2015
Deaths per 100,000 population
0
1
2
3
4
5
6
7
8
9
10
11
2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015
Any Opioid
Heroin
Natural & Semi-Synthetic Opioids..
Other Synthetic Opioids
(e.g., fentanyl, tramadol)
Methadone
SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://wonder.cdc.gov/.
www.cdc.gov
Your Source for Credible Health Information


Drugs involved in U.S. overdose deaths, 2000 to 2016
20,100
Fentanyl and fentanyl analogues
15,400
Heroin
14,400
Prescription opioids
10,600
Cocaine
7,660
Methamphetamine
3,280
Methadone
15,000
10,000
5,000 deaths per year
2000
2005
2010
2015

Thank You

Questions?

Administration on Aging and Substance Abuse and Mental Health Services Administration. (2012). *Older Americans behavioral health–Issue brief 5: Prescription medication misuse and abuse among older adults.* Retrieved from https://www.acl.gov/sites/default/files/programs/2016-11/Issue%20Brief%205%20 Prescription%20Med%20Misuse%20Abuse.pdf

Agency for Healthcare Research and Quality. (2014). *Patient characteristics of opioid-related inpatient stays and emergency department visits nationally and by state.* Retrieved from https:// www.hcup-us.ahrq.gov/reports/statbriefs/sb224- Patient-Characteristics-Opioid-Hospital-Stays-ED- Visits-by-State.pdf

Alexander, BK 'Addiction: The View from the Rat Park," www.brucekalexander.com/articles-speeches/rat-park/148-addition-the-view-from-rat-park.

Centers for Disease Control and Prevention, National Center for Injury and Prevention Control, Division of Unintentional Injury Prevention. "Opioid Overdose"

Childress AR et al. Prelude to Passion: Limbic Activation by "Unseen" Drug and Sexual Cues January 30, 2008 PLoS ONE 3(1): e1506.

CMS (Centers for Medicare & Medicaid Services). January 5, 2017. *Opioid Misuse Strategy*.

Coffin PO et al. Nonrandomized Intervention Study of Naloxone Coprescription for Primary Care Patients Receiving Long-Term Opioid Therapy for Pain. Ann Intern Med 2016 Aug 16; 165(4): 245-52.

Comer, SD, et al. Injectable, Sustained-release Naltrexone for the Treatment of Opioid Dependence. Arch Gen Psychiatry 2006.

Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR Recomm Rep 2016;65(No. RR-1):1–49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1

Frenk et al., 2015). Larney, S., Bohnert, A.S., Ganoczy, D., Ilgen, M.A., Hickman, M., Blow, F.C. and Degenhardt, L., 2015. Mortality among older adults with opioid use disorders in the Veteran's Health Administration, 2000–2011. *Drug and Alcohol Dependence*, *147*, pp.32-37.

Koob GF, Volkow ND. Neurocircuitry of Addiction. *Neuropsychopharmacology*. 2010;35(1):217-238.

Krupitisky, e. et al. Injectable Extended-release Naltrexone for Opioid Dependence: A Double-blind, Placebo-controlled, Multicenter Randomized Trial. Lancet 2011

Lee JD et al. Extended-Release Naltrexone to Prevent Opioid Relapse in Criminal Justice Offenders NEJM 2016; 374:1232-1242

Lee Jd, et al. Comparative Effectivenes sof Extended-Release Naltrexone versus Buprenorphine-naloxone for Opioid Relaspse Prevention. The Lancet 2017

Lewis, M. The Biology of Desire: Why Addiction is Not A Disease Public Affairs: New York 2015.

Robins, LN et al. How Permanent Was Vietnam Drug Addiction? Am J Public Health. 1974 December; 64(12 Suppl): 38–43.

Mattson, M., Lipari, R. N., Hays, C., et al. (2017). A day in the life of older adults: Substance use facts. *The CBHSQ Report.* Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/sites/default/files/report_2792/ShortReport-2792.html

Sordo L. eta l. Mortality Risk during and after Opioid Substitution Treatment: Systematic Review and Meta-analysis of Cohort Studies. BMJ 2017

Szalavitz, M. Unbroken Brain: A Revolutionary New Way of Understanding Addiction St. Martin's Press (April 5, 2016)

Tanum, L et al. The Effectiveness of injectable extended-release naltrexone vs daily buprenorphine-naloxone for opioid dependence: a randomized clinical non-inferiority trial. JAMA Psychiatry 2017

Trafton, Jodi New Concepts in the Neurobiology of Pain and Addiction. Lecture at CSAM Addiction Medicine State of the Art Conference October 23, 2015 San Francisco

Substance Abuse and Mental Health Services Administration. (2017). Opioid misuse increases among older adults. *The CBHSQ Report.* Retrieved from https://www.samhsa.gov/data/sites/default/ files/report_3186/Spotlight-3186.html

Substance Abuse and Mental Health Services Administration. (2017). Resources List. Opioid Use in the Older Population. Retrieved from https://www.samhsa.gov/capt/sites/default/files/resources/resources-opiod-use-older-adult-pop.pdf

U.S. Office of the Inspector General. (2017). *Opioids in Medicare Part D: Concerns about extreme use and questionable prescribing.* Retrieved from https://oig.hhs.gov/oei/reports/oei-02-17-00250.asp

Walley, AY et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis *BMJ* 2013; 346 doi: https://doi.org/10.1136/bmj.f174

Weiss A.J., Bailey M.K., O'Malley L., Barrett M.L., Elixhauser A., Steiner C.A., *Patient Characteristics of Opioid-Related Inpatient Stays and Emergency Department Visits Nationally and by State, 2014. HCUP Statistical Brief #224.* June 2017. Agency for Healthcare Research and Quality.