The Science of Substance Use Disorders Integration Summit

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Presentation Length: 1.25 hours



THE SCIENCE OF SUBSTANCE USE DISORDERS

Learning Objectives:

At the end of this presentation participants will be able to:

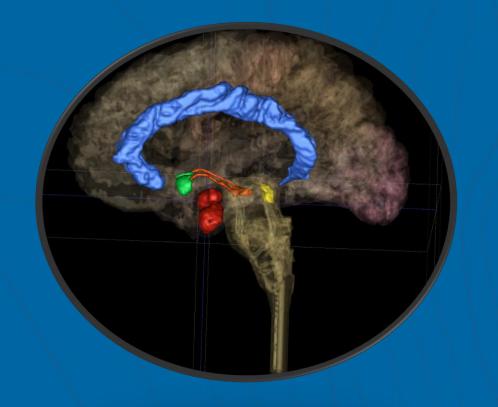
Name at least 1 change that occurs in the brain related to exposure to substances of abuse

State if substance use disorders have the same, greater than or lower rates of response to treatment than other chronic conditions

Summarize how long brain changes last after someone stops using substances Identify one difference between the 2 commonly used medications for alcohol use disorder

List the key difference between the 3 the commonly used medications for opioid use disorder

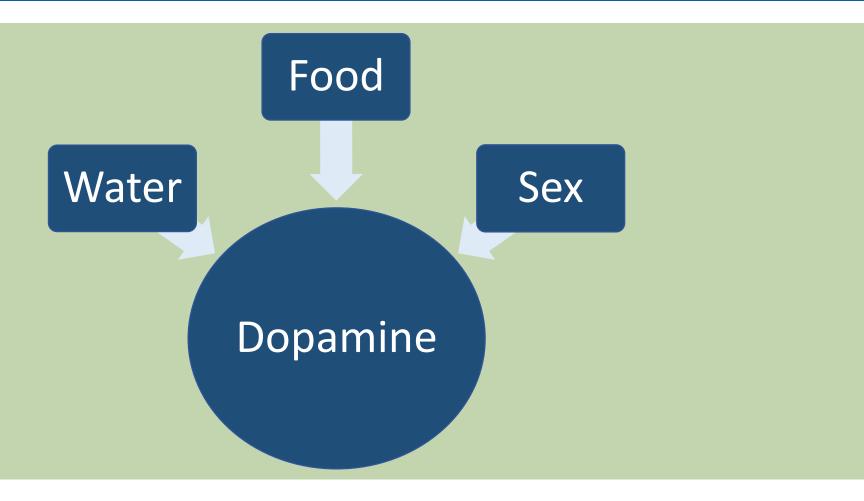




SUBSTANCE USE DISORDERS CHRONIC BRAIN DISEASE



NATURAL REWARDS RELEASE DOPAMINE



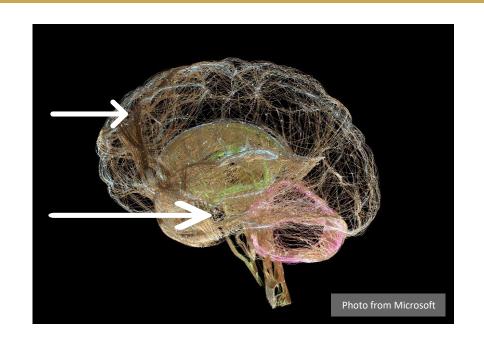


HOW SUBSTANCES OF ABUSE AFFECT THE BRAIN

- All substances of abuse result in the activation of the reward pathway
- The same pathway activated by naturally rewarding substances and events

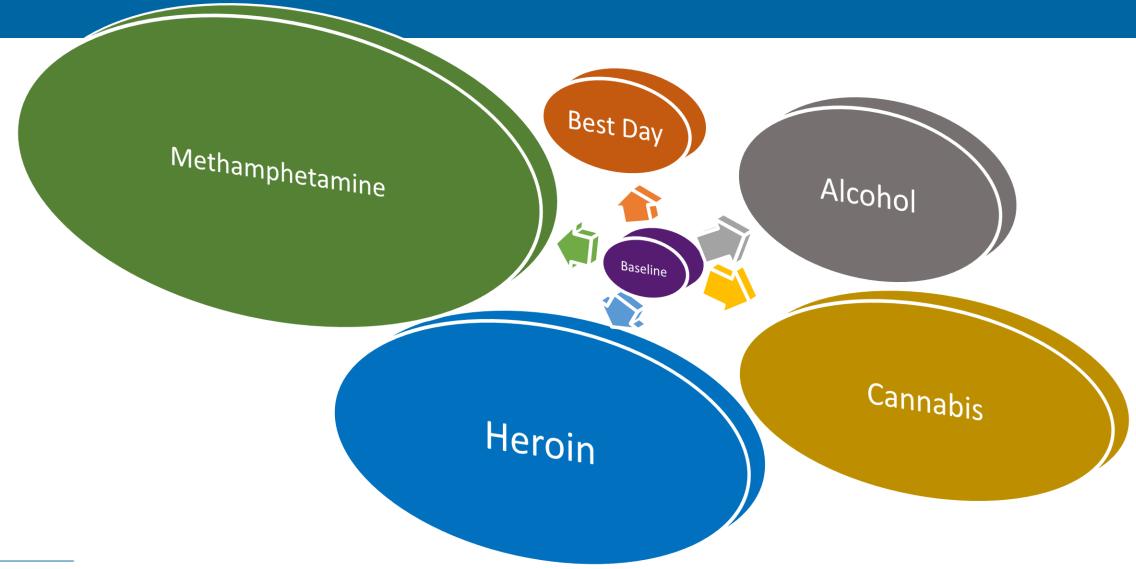
Thinking part of brain

Primitive parts of brain



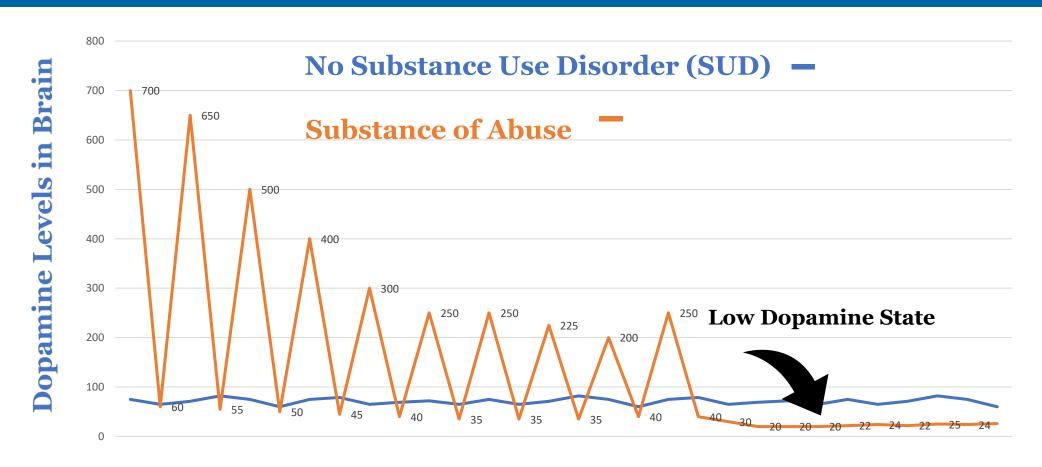


DOPAMINE RESPONSE





BRAIN CHANGES WITH EPISODES OF SUBSTANCE USE



Time



INTENSITY OF CRAVINGS

A direct, or indirect, force pulling someone towards a substance or behavior





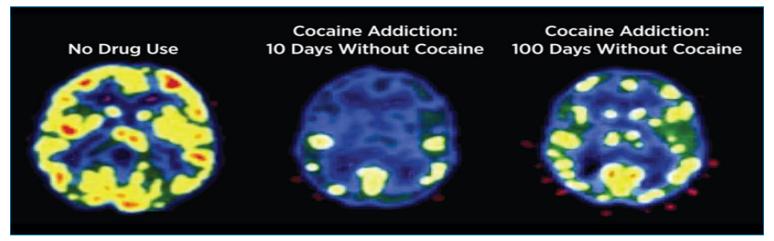




IT TAKES TIME FOR YOUR BRAIN TO RECOVER

- The brain function takes at least 1 year to return to "normal" after you stop substances of abuse
- If you stop treatment before a year, you may lose the medication benefits

How the Brain Changes and Recovers from Drug Use



Source: https://nida.nih.gov/publications/teaching-addiction-science/bringing-power-science-to-bear-drug-abuse-addiction



CHRONIC MEDICAL DISORDERS

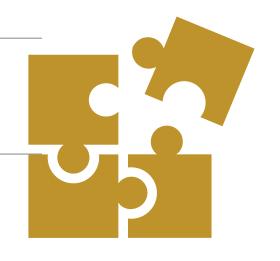


UNDERSTANDING SUBSTANCE USE DISORDERS TO INFORM TREATMENT

Chronic Diseases: Substance Use Disorder (SUD) and Diabetes II

Cause: Genes, Environment and Behavior

Prevention: Change Environmental and Behavior



Treatment: Long Term Medicine and Lifestyle Changes

What is Different?



Features of Chronic Disease

Features	SUD	Hypertension	Diabetes II
Gradual onset	Yes	Yes	Yes
All racial, ethnic, IQ & income	Yes	Yes	Yes
Use of substance not allowed	Yes	Yes	Yes
Use despite negative effects	Yes	Yes	Yes
Can present as life threatening	Yes	Yes	Yes
Taking medication as prescribed	50%	50%	50%
Lifestyle changes needed & help	Yes	Yes	Yes
Return of symptoms after a period without symptoms	Yes	Yes	Yes

Source: McLellan 2000



UNDERSTANDING ADDICTION TO INFORM TREATMENT

Diabetes and Addiction: You make a mistake...what could you lose?

	Diabetes	Addiction
Treatment	No	YES
Custody of Children	No	YES
Freedom (Probation, Incarceration)	No	YES
Housing	No	YES
Family	No	YES
Work Identity	No	YES





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CHRONIC DISEASES OVER TIME

- Remission (no symptoms)
 - Can medication be stopped? Or will symptoms return?
- Better but not in remission
 - Continue treatment
 - Adjust treatment with goal of remission
- Not responding or getting worse
 - Treatment is changed
 - Medications
 - Counseling
 - Self-help program

SCREENING

- >> Screening is the act of identifying if someone is at risk for an illness
- >> Routine screening for chronic diseases is a regular part of a primary care
 - Depression → PHQ9
 - Anxiety → GAD7
 - Gestational diabetes → Glucose challenge test
 - Breast Cancer→ Mammogram
- >> It is important to use a tool that is scientifically validated





UNIVERSAL SCREENING

- Holistic approach supporting:
 - Safe use or abstinence
 - Harm reduction
 - Prevention of dependence
 - Reduces overuse of healthcare resources



Photo Source: Microsoft Stock Icons

- Screen for tobacco, alcohol, illicit and prescriptions drugs at the same time
- Why SUD Screenings Should be Universal:
 - Deciding to screen some patients but not others may introduce the risk of racial, ethnic, socioeconomic, gender, age, and other biases resulting in missed opportunities to identify and intervene
 - It also normalizes SUD one of several chronic diseases that we screen for



SELECTING A VALIDATED SCREENING TOOL

Tool	Substance Type		Patient Age		How tool is administered	
	Alcohol	Drugs	Adults	Adolescents	Self- administered	Clinician - administered
Screening to Brief Intervention (S2BI)	X	X		X	X	X
Brief Screener for Alcohol, Tobacco, and other Drugs (BSTAD)	X	X		X	X	X
Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS)	X	X	X		X	X



Source: https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools

SCREENING RATES

>> Primary Care

- >> 72% were screened for alcohol and 71% for drug use
- >> Self administered screening was associated with greater detection of moderate to high-risk alcohol use compared to staff administered screening
- >> Screening at any appointment type increases rate of screening
- >> Use of counseling script after a positive screen was < 13% in primary care study above



SCREENING RATES

>> Outpatient BH clinics- screening rates varied from 48-100%

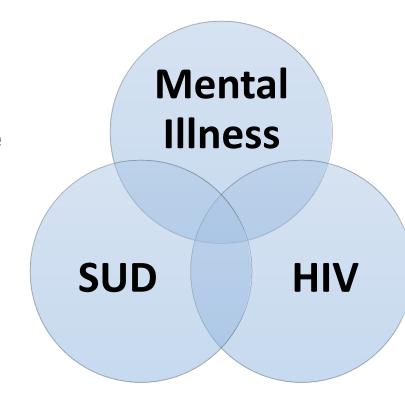
- >> Inpatient
 - >> Detection rates varied by race, ie screening was not done universally
 - >> HIV inpatient care program <50% conducted recommended screening & brief intervention for alcohol



Source: Woodward 2023 Serowik 2021

SUD, HIV AND MENTAL ILLNESS

- >> 54% report moderate to high-risk cannabis use
- >> 40% report moderate to high-risk drinking
- >> 12% report moderate to high-risk cocaine
- >> 11% reported moderate to high risk of amphetamine use
- >> Only 35% of people in 10 <u>outpatient</u> HIV clinics reported talking to primary care provider (PCP) about alcohol use
- >> < 50% of providers in hospital-based HIV care programs conducted recommended screening and brief interventions for reducing alcohol







SBIRT











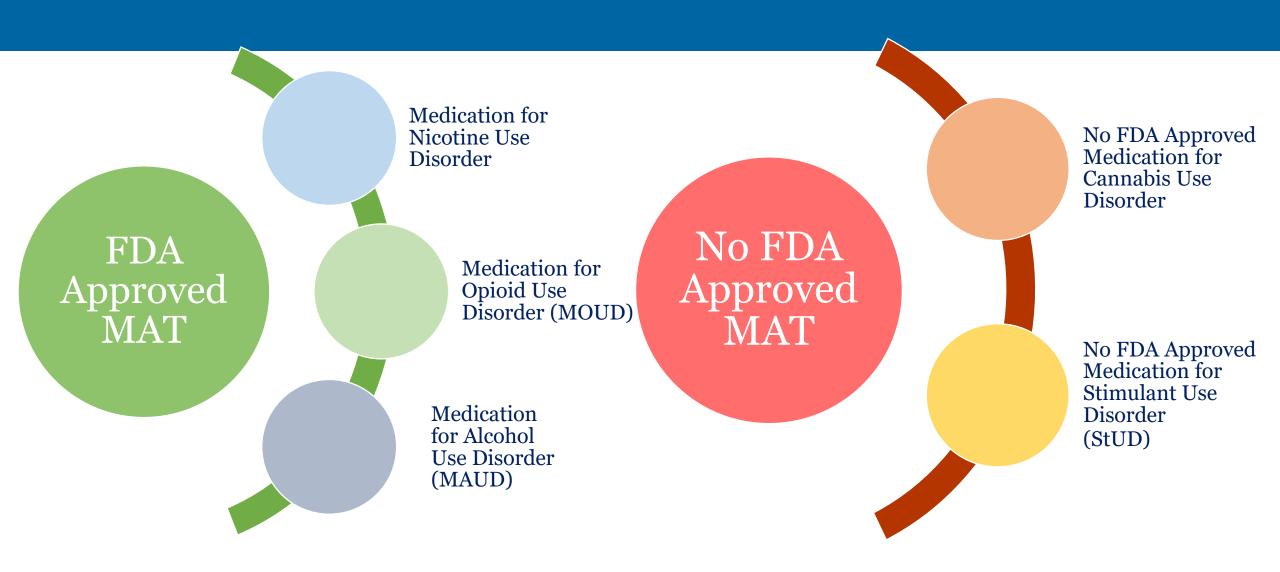
https://www.samhsa.gov/sbirt/resources



MEDICATIONS FOR ADDICTION TREATMENT



FDA APPROVED MEDICATIONS FOR ADDICTION TREATMENT (MAT)

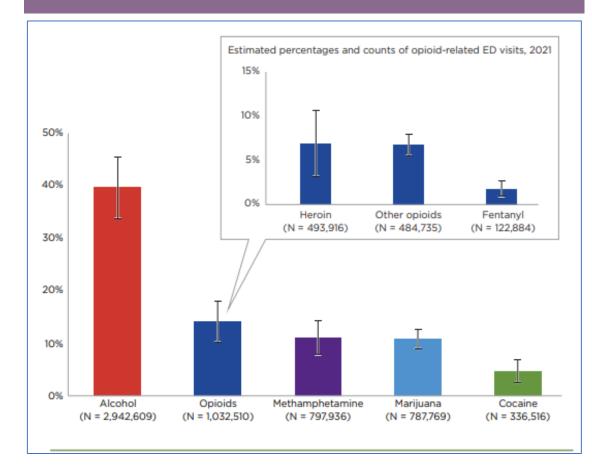




ALCOHOL

- Alcohol is the most used substance of abuse
- Alcohol-related deaths continue to increase
 - 25% increase from 2019 to 2020
- Alcohol-related emergency room visits are higher than for any other substance

Figure 4.1 Estimated percentages and counts of drug-related ED visits by the top five drugs (January 2021-December 2021)





Source: https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR090120.htm#:~:text=%22misuse.%22),Among%20people%20aged%2012%20or%20older%20in%202019%2C%2060.1%20percent

ALCOHOL USE DISORDER

Acamprosate (Campral®)	Naltrexone (Revia® or Vivitrol®)
Decrease drinking & stay in treatment longer	Decrease drinking & stay in treatment longer
Three times per day dosing	Oral daily & long acting injectable every 4 weeks
Drug Interactions: none	Drug Interactions: opioids
Contraindications: severe renal impairment or allergy to medication	Contraindications: on opioids, in withdrawal, or allergy to medication

Source: SAMHSA and NIAAA, Medication for the Treatment of Alcohol Use Disorder: A Brief Guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2015.;chick 2003; Mann 2004; Garbutt 1999; SAMHSA 2015.



MEDICATIONS FOR OPIOID USE DISORDER (MOUD)

BENEFITS OF MEDICATION FOR OPIOID USE DISORDER (MOUD)

Treats withdrawal symptoms

Stabilizes dopamine

Helps people feel normal

Increased attendance in treatment

Decreased cravings

Decreased opioid use

Decreased intravenous drug use and complications

Decreased overdose

Decreases death

Improves functioning Decreased criminal behavior

The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Tsui JI et al., 2014

Metzger DS et al., 1993 Mattick, RP, et al. 2009

Mattick, RP, et al. 2014

Lobmaier, P et al. 2008

Lutgen-Nieves, L. et. al. 2021

Santo, T 2021



FDA APPROVED MOUD & OPIOID OVERDOSE

Agonist Treatment (turns on receptor):

- Methadone approved for cough in 1940s, for OUD 1972
- Buprenorphine-approved in 1981 for pain; oral approved for OUD 2002; patch, implants, and injection later



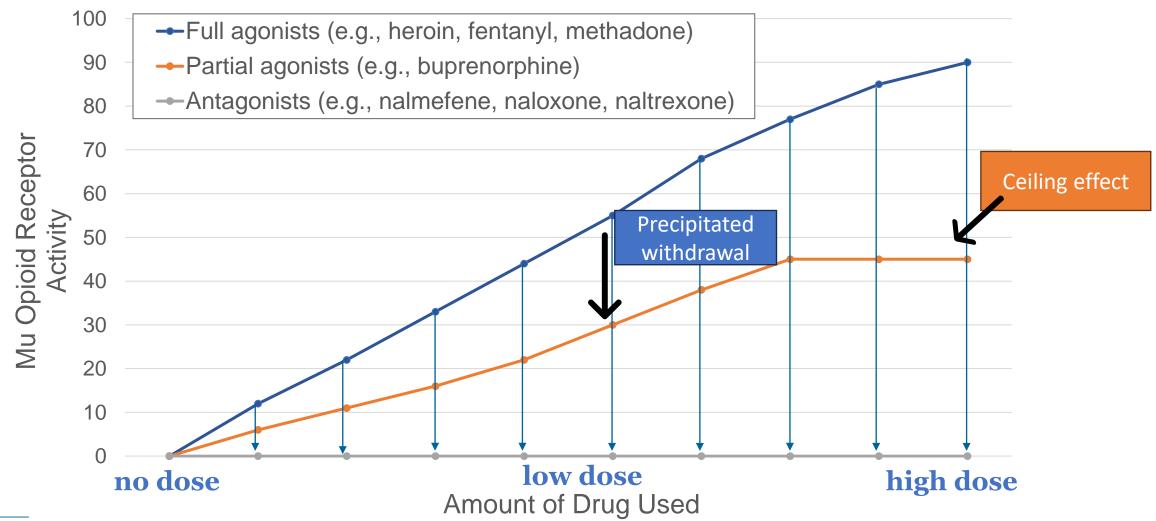
Antagonist Treatment (blocks receptor from being turned on):

- Naltrexone-oral approved 1984; injectable 2006 AUD, OUD 2010
- Naloxone-approved 1961, autoinjector 2014, nasal spray 2015
- Nalmefene- injectable approved 1995; nasal spray 2023





FULL, PARTIAL, OR NO EFFECT



METHADONE



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HIGHLY EFFECTIVE:

- 33% fewer opioid positive tests compared to those receiving no medication*
- 4.4x more likely to stay in treatment*
- Reduced crime**
- Reduced infectious disease***
- Reduced death*****

Sources: * Mattick, 2009, ** Lutgen-Nieves, 2021, *** Tsui, 2014, Metzger, 1993, **** Santo, 2021; Wakeman, 2020



METHADONE: WHAT IS IT AND FOR WHOM?

- Turns on the opioid receptor
- No "ceiling effect"
- Do not need to be in withdrawal to start
- Takes time to reach an effective dose
- Lots of medication interactions

Who should take methadone?

Patients with a more severe OUD

Patients who would benefit from the services available including daily observed dosing required in Narcotic Treatment Programs

Patients who did not reach goals with other medications for opioid use disorder



BUPRENORPHINE

Highly Effective

- 1.82 times more likely to stay in treatment if on 16 mg per day or higher
- Decreased opioid use
- Decreased death

Safer than other opioids because of ceiling effect; higher doses do NOT cause

- Increased "high"
- Decreased breathing



NIDA Medications to Treat OUD Research Report Updated December 2021

Mattick 2014 Cochrane Review
Santo 2021, Wakeman 2020

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BUPRENORPHINE: WHAT AND FOR WHOM?

- Turns on opioid receptor part way
- Has ceiling effect
- Binds more strongly to receptor than full agonists
 - Start buprenorphine when in moderate withdrawal
- Dosing
 - Typical dose is 16-32 mg/day
 - Some patients will need higher doses
- Fewer medication interactions than methadone

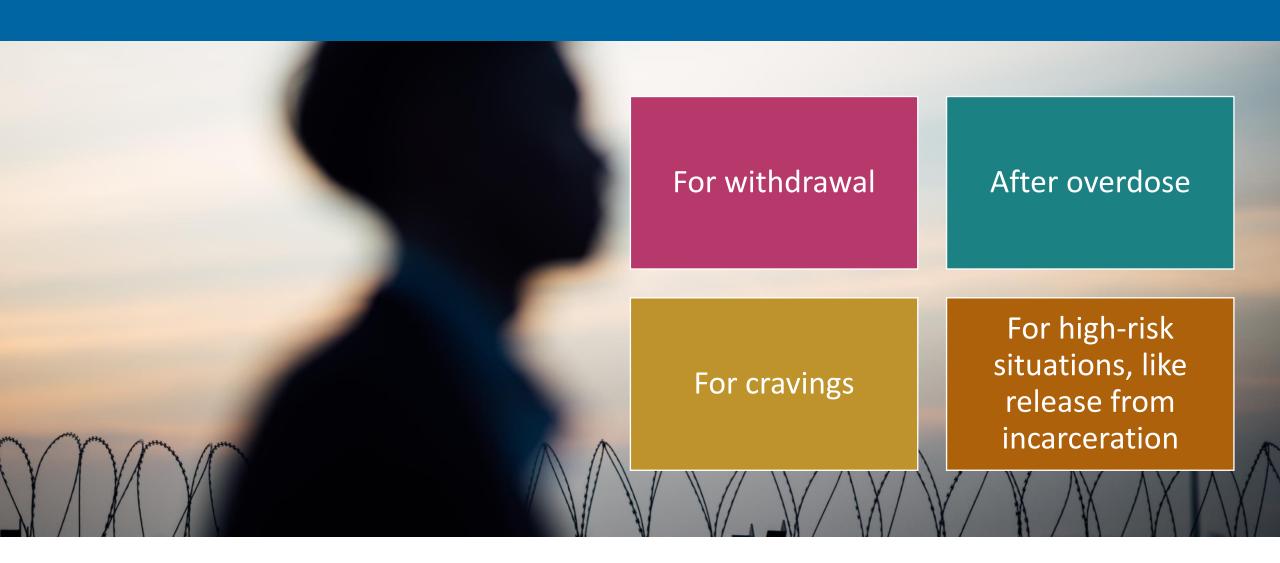
Who should take buprenorphine?

Opioid use disorder or opioid withdrawal

Patient wants agonist treatment



MEDICATION INITIATION FOR OPIOID USE DISORDER





NALTREXONE





NALTREXONE: WHAT AND FOR WHOM?

- Long-acting injection approved for OUD
- Blocks opioid receptor
- Does NOT treat withdrawal or underlying low dopamine level
- Patient must be opioid-free seven days before starting, making it more difficult to start than buprenorphine or methadone
- No evidence of decreased death

Who should take naltrexone?

Patients still getting rewards from normal activities

Patients who did not reach treatment goals with other medications

Can be useful as "back-up" after stopping buprenorphine or methadone, or in high-risk situations



HOW LONG SHOULD SOMEONE BE ON MEDICATION?

Long-term or indefinite treatment with medications for OUD is often needed to maintain outcomes

Discontinuing
buprenorphine or
methadone is usually only
successful in about 15% of
cases

Discontinuing medication without return to opioid use usually occurs, if at all, when people have been treated with MOUD for at least 3 years

Sources: National Academies of Sciences, Engineering, and Medicine. (2019). Nosyk, B. et al. (2012). SAMHSA & the Office of the Surgeon General (2018).



BARRIERS

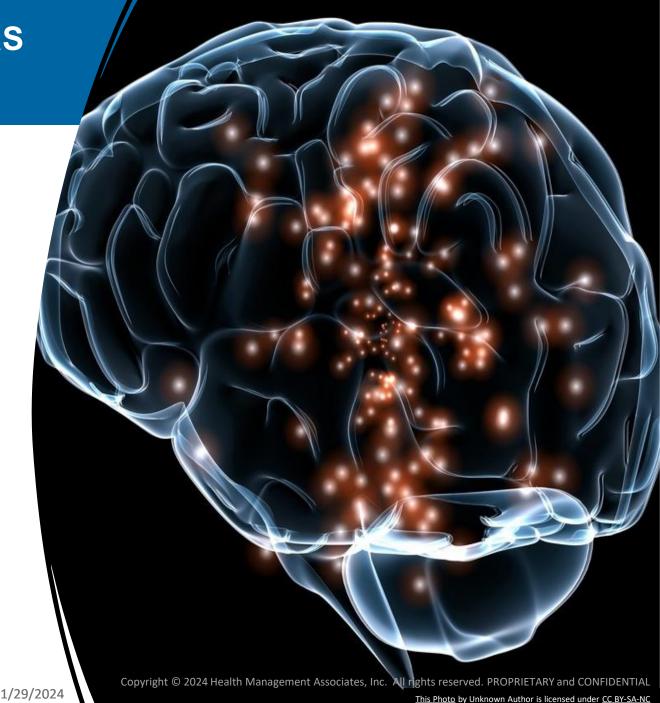


OUR THOUGHTS CAN BE BARRIERS TO TREATMENT

Most common barriers we hear are:

- We are just replacing one addiction for another
- We are just replacing one drug with another
- You can't give meds without counseling
- They need to hit rock bottom before they'll get better





"WE ARE JUST REPLACING ONE ADDICTION WITH ANOTHER"

Substance Use Disorder Diagnostic Criteria

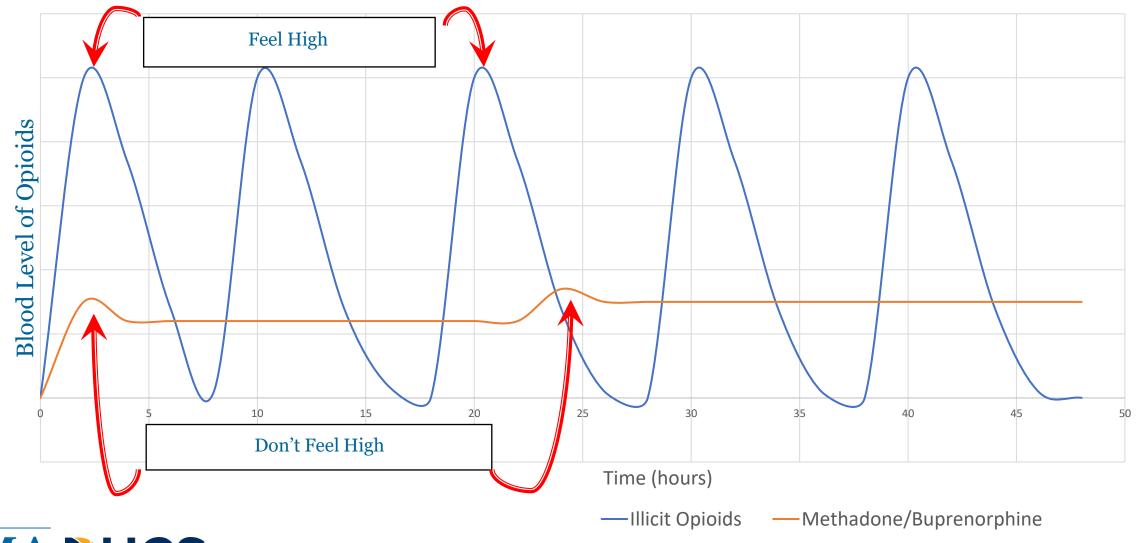
- Using more or longer than you said you would
- 2. You would like to cut down your use
- 3. You spend a lot of time getting, using or recover from drug
- 4. Drug use makes it difficult for you to work, do good in school, or take care of the house
- 5. You continue to use even though you have problems with your family & friends due to using
- 6. You give up activities to use
- 7. You use in dangerous places or times
- 8. You use even though you are having physical or mental problems related to drug use
- You crave the drug
- 10. It takes more drug to have the same effect
- 11. You feel sick if you don't use





PHYSIOLOGICALLY: WE ARE NOT REPLACING ONE DRUG WITH ANOTHER







WHAT IS STIGMA?

- Westfall, Miller and Bazemore '...bad thoughts about mental health or substance use that cause people to have bad behavior"
 - If a person with a problem says, "I should be able to stop on my own," then they might not ask for help.
 - When a doctors says, "it's a waste of my time to help them, they
 will just keep using," then the doctor doesn't offer them
 medication.
- Stigma is born out of thoughts and beliefs...



"UNLESS THERE IS COUNSELING, YOU CAN'T HAVE MOUD"

Improve patient survival (MOUD only)

Source: Sordo 2017, Wakeman 2020, Walley 2020, Santo 2022

Increase retention in treatment (MOUD only)

Source: Mattick 2009 & 2014, Lobmaier 2008

Decrease illicit opiate use and other criminal activity among people with OUD (MOUD only)

Source: Mattick 2009 & 2014; Krupitsky 2011, Lutgen-Nieves, L. 2021

Improve birth outcomes among women who have SUD and are pregnant (MOUD only)

Source: SAMHSA. TIP 63, 2018, ASAM Practice Guidelines for OUD 2020, Mascola 2017

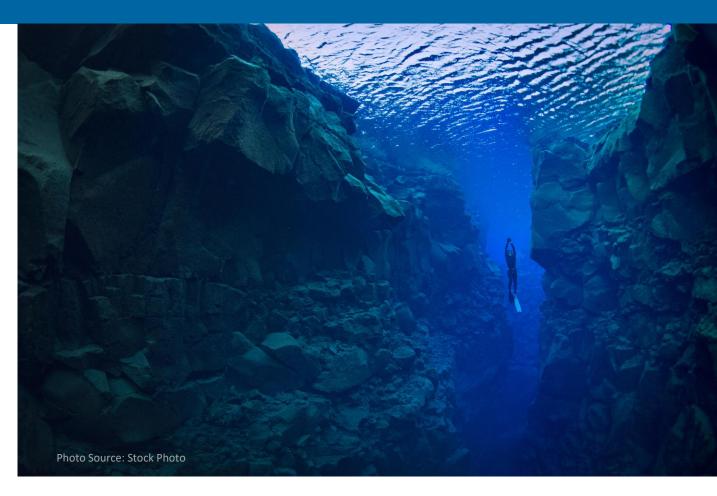
Increase patients' ability to gain and maintain employment (MOUD + behavioral health treatment)

Source: Leary 2016, Guillery 2021, Sun 2015



THEY NEED TO HIT ROCK BOTTOM

- Rock bottom in the era of fentanyl is deceased
- People who are coerced to go into treatment for criminal justice reasons or to maintain a job have similar outcomes to those who choose treatment



Sources: Pilarinos, A., Barker, B., Nosova, E., Milloy, M-J., Hayashi, K., Wood, E., Kerr, T., & DeBeck, K. (2021). Coercion into addiction treatment and subsequent substance use patterns among people who use illicit drugs in Vancouver, Canada. Addiction, 115(1), 97-106. DOI: 10.1111/add.14769

Farabee, D et al. 1998 · The effectiveness of coerced treatment for drug-abusing offenders. Federal Probation, 62(1), 3–10.



DECREASING STIGMA

Listen to people who have gotten better (increase empathy)

Talk about people getting better (SUD is treatable)

Provide information when thoughts are not true

Talk about the whole person not just the problem (person first language)

Talk about how hard it is to get help



STIGMA, THOUGHTS, AND MISINFORMATION

"They need to make better choices. The patient is in this situation because of their own choices."

"Having Narcan encourages people to party."

"I got sober without meds; people should do it without medication."

"It's a waste of time to help them. They haven't hit rock bottom."

"They just keep using." "Having clean needles encourages people to party."

"Treating people with addiction takes up time that could be used for other people."



Sources: Strugar-Fritsch, (2019) McLellan, (2000)

TIME FOR QUESTIONS AND ANSWERS







Abadía-Barrero CE, Castro A. Experiences of stigma and access to HAART in children and adolescents living with HIV/AIDS in Brazil. Soc Sci Med. 2006 Mar; 62(5):1219-28. doi: 10.1016/j.socscimed.2005.07.006. Epub 2005 Aug 15. PMID: 16099573.

ACLU (2022) How the Failure to Provide Treatment for Substance use in Prisons and Jails Fuels the Overdose Epidemic Over-Jailed and Un-Treated.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA.

Andriote. HIV and Clinical Depression APA Fact Sheet 2012, Arlington, VA.

Baser O, Chalk M, Fiellin DA, Gastfriend DR. (2011) Cost and utilization outcomes of opioid-dependence treatments. Am J Manag Care. 17 Suppl 8:S235-48. PMID: 21761950.

Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. Ann Intern Med. 2013 Nov 5;159(9):592-600. doi: 10.7326/0003-4819-1599-201311050-00005. PMID: 24189594; PMCID: PMC5242316. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5242316/

Buprenorphine/naloxone film. Reference ID: 4219642 - Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022410s033,020732s019,020733s023lbl.pdf

Bureau of Justice Assistance. (2022). Managing Substance Withdrawal in Jails: A Legal Brief.

CA Bridge. https://cabridge.org/wp-content/uploads/CA-BRIDGE-PROTOCOL-Bup-after-overdose-reversal-September-2020.pdf

Caritis, Steve N. et al. (2017) An evidence-based recommendation to increase the dosing frequency of buprenorphine during pregnancy. American Journal of Obstetrics & Gynecology, Volume 217, Issue 4, 459.e1 - 459.e6.

Chick, J., Lehert, P., & Landron, F. (2003). Does Acamprosate Improve Reduction of Drinking As Well As Aiding Abstinence? Journal of Psychopharmacology, 17(4), 397–402. doi:10.1177/0269881103174017

Code of Federal Regulation (CFR) surrounding narcotic treatment programs are contained in CFR 41 and 42 and defines for whom and under what circumstances methadone can be used for OUD.

Cunningham, JA, (1999) Untreated remissions from drug use: the predominant pathway. Addict Behav. 24(2):267-70.

Dawson-Rose C, Draughon JE, Zepf R, Cuca YP, Huang E, Freeborn K, Lum PJ. Prevalence of Substance Use in an HIV Primary Care Safety Net Clinic: A Call for Screening. J Assoc Nurses AIDS Care. 2017 Mar-Apr;28(2):238-249. doi: 10.1016/j.jana.2015.12.001. Epub 2015 Dec 11. PMID: 26763795; PMCID: PMC4903083.

D'Onofrio G. et al. (2017) Emergency Department-Initiated Buprenorphine for Opioid Dependence with Continuation in Primary Care: Outcomes During and After Intervention. J GEN INTERN MED 32, 660–666. https://doi.org/10.1007/s11606-017-3993-2.

DOJ Civil Rights Division (2022) The Americans with Disabilities Act and the Opioid Crisis: Combating Discrimination Against People in Treatment or Recovery.

Enforcement Reports. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/209862lbl.pdf

Extended-release injectable buprenorphine. Reference ID: 4188740 - Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda docs/label/2017/209819s000lbl.pdf.

FDA. https://wwwfda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-urges-caution-about-withholding-opioid-addiction-medications#:":text=Safety%20Announcement,central%20nervous%20system%20(CNS).

Garbutt, J. C., West, S. L., Carey, T. S., Lohr, K. N., & Crews, F. T. (1999). Pharmacological Treatment of Alcohol Dependence. JAMA, 281(14), 1318. doi:10.1001/jama.281.14.1318.



Green TC, Clarke J, Brinkley-Rubinstein L, Marshall BDL, Alexander-Scott N, Boss R, Rich JD. Postincarceration Fatal Overdoses After Implementing Medications for Addiction Treatment in a Statewide Correctional System. JAMA Psychiatry. 2018 Apr 1;75(4):405-407. doi: 10.1001/jamapsychiatry.2017.4614. PMID: 29450443; PMCID: PMC5875331.

Guillery SPE, (2021). Quality of Life in Opioid Replacement Therapy: A Naturalistic Cross-Sectional Comparison of Methadone/Levomethadone, Buprenorphine, and Diamorphine Patients. Eur Addict Res. 2021;27(5):371-380. doi: 10.1159/000514192. Epub PMID: 33784698.

Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2019; 393:778.

Harris, AH. et. al. (2005) A Randomised Trial of the Cost Effectiveness of Buprenorphine as an Alternative to Methadone Maintenance Treatment for Heroin Dependence in Primary Care Setting. Pharmacoeconomics. 23 (1): 77-91.

Health Management Associates Institute on Addiction. (2022). Patient Guide to Starting Buprenorphine at Home. Downloaded from: https://addictionfreeca.org/r/sugpob8ybohf

Healthresearchfunding.org(2019) https://healthresearchfunding.org/24-opiate-addiction-recovery-statistics/ 24 Shocking Opiate Addiction Recovery Statistics.

https://bja.ojp.gov/doc/managing-substance-withdrawal-in-jails.pdf

Kakko et al. (2003) 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomized, placebo-controlled trial. Lancet 361(9358):662-8.

Kinlock TW, Gordon MS, Schwartz RP, O'Grady K, Fitzgerald TT, Wilson M. A randomized clinical trial of methadone maintenance for prisoners: results at 1-month post-release. Drug Alcohol Depend. 2007 Dec 1;91(2-3):220-7. doi: 10.1016/j.drugalcdep.2007.05.022. Epub 2007 Jul 12. PMID: 17628351; PMCID: PMC2423344.Krupitsky, et. al. (2011) Injectable extended-release naltrexone for opioid dependence: a double-blind placebo controlled, multicenter randomized trial. Lancet 377: 1506-13.

Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial. Lancet. 2011 Apr 30;377(9776):1506-13. doi: 10.1016/S0140-6736(11)60358-9. PMID: 21529928.

Larochelle, et al. (2018) Medication for opioid use disorder after nonfatal opioid overdose and association with mortality. A cohort study. Annals of Internal Medicine. 169:3;137-45.

Leary, ML (2017) ONDCP webinar: Medication Assisted treatment (MAT) in Prison and Re-entry programs.

Lee, JD et. al. (2018) Comparative effectiveness of extended-release naltrexone vs buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicenter, open label, randomised controlled trial. Lancet 391(10118). 309-318.

Legal Action Center. https://www.lac.org/assets/files/Cases-involving-denial-of-access-to-MOUD.pdf

Lintzeris N. et al. (2013) A Randomised Controlled Trial of Sublingual Buprenorphine-Naloxone Film Versus Tablets in the Management of Opioid Dependence. Drug Alcohol Dependence, 131 (1-2), 119-26.

Lobmaier, P et al. (2008) Sustained-Release Naltrexone For Opioid Dependence. Cochrane Systematic Review.

Lofwall MR, Walsh SL, Nunes EV, Bailey GL, Sigmon SC, Kampman KM, Frost M, Tiberg F, Linden M, Sheldon B, Oosman S, Peterson S, Chen M, Kim S. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial. JAMA Intern Med. 2018 Jun 1;178(6):764-773.

Lutgen-Nieves, L. et. al. (2021) From the General Public to America's Jails: MAT Saves Lives. NCCHC Foundation. Chicago, IL.



Magura, S, et al. Buprenorphine and methadone maintenance in jail and post release: a randomized clinical trial Drug Alcohol Depend 2009; 99 (1-3): 222-30.

Mann, K., Lehert, P., & Morgan, M. Y. (2004). The Efficacy of Acamprosate in the Maintenance of Abstinence in Alcohol-Dependent Individuals: Results of a Meta-Analysis. Alcoholism: Clinical & Experimental Research, 28(1), 51–63. doi:10.1097/01.alc.0000108656.81563.05

Mascola, M. (2017) Opioid Use and Opioid Use Disorder in Pregnancy, Am College of Obstetrics and Gynecology Committee Opinion 711 in conjunction with American Society of Addiction Medicine

Mattick RP, Hall W. Are detoxification programmes effective? Lancet. 1996 Jan 13;347(8994):97-100. doi: 10.1016/s0140-6736(96)90215-9. PMID: 8538351.

Mattick, RP, et al. (2009) Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Systematic Review.

Mattick, RP, et al. (2014) Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Systematic Review.

McLellan AT, Lewis DC, O'Brien CP, Kleber HD. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. JAMA. 2000 Oct 4;284(13):1689-95. doi: 10.1001/jama.284.13.1689. PMID: 11015800

McGinty E, Pescosolido B, Kennedy-Hendricks A, Barry CL. Communication Strategies to Counter Stigma and Improve Mental Illness and Substance Use Disorder Policy. Psychiatr Serv. 2018 Feb 1;69(2):136-146. doi: 10.1176/appi.ps.201700076. Epub 2017 Oct 2. PMID: 28967320; PMCID: PMC5794622.

McNeely J, Adam A, Rotrosen J, Wakeman SE, Wilens TE, Kannry J, Rosenthal RN, Wahle A, Pitts S, Farkas S, Rosa C, Peccoralo L, Waite E, Vega A, Kent J, Craven CK, Kaminski TA, Firmin E, Isenberg B, Harris M, Kushniruk A, Hamilton L. Comparison of Methods for Alcohol and Drug Screening in **Primary Care Clinics**. JAMA Netw Open. 2021 May 3;4(5):e2110721. doi: 10.1001/jamanetworkopen.2021.10721. PMID: 34014326; PMCID: PMC8138691.

Methadone. Reference ID: 3725185 - Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/006134s038lbl.pd.

Metzger DS et al., (1993)"Human Immunodeficiency Virus Seroconversion Among Intravenous Drug Users In- and Out-of-Treatment: An 18-Month Prospective Follow-Up," Journal of Acquired Immune Deficiency Syndromes 6, no. 9: 1049–56. http://www.ncbi.nlm.nih.gov/pubmed/8340896

Miller S et. al. (2019) Principles of Addiction Medicine 6th edition Philadelphia, PA.

Minozzi S, (2011). Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev.2011(4):CD001333. Published 2011 Apr 13. doi:10.1002/14651858.CD001333.pub4

Naltrexone for extended-release injectable suspension. VIVITROL (naltrexone for extended-release injectable suspension) Label. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021897s015lbl.pdf

Naltrexone. REVIA 50 mg Opioid Antagonist Description - Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/018932s017lbl.pdf

National Academies of Sciences, Engineering, and Medicine. (2019). Medications for opioid use disorder save lives. The National Academies Press.

NIDA (2020) Principles of Effective Treatment. Baltimore, MD.

NIDA (2021) Medications to Treat Opioid Use Disorder. Baltimore, MD.

NIDA (2021) Words Matter: Preferred language for talking about addiction. Baltimore, MD.



- NIDA. 2018, February 11. Bringing the Power of Science to Bear on Drug Abuse and Addiction. Retrieved from https://archives.nida.nih.gov/publications/teaching-addiction-science/bringing-power-science-to-bear-drug-abuse-addiction on 2024, January 26
- Nosyk B, Sun H, Evans E, Marsh DC, Anglin MD, Hser YI, Anis AH. Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study. Addiction. 2012 Sep;107(9):1621-9. doi: 10.1111/j.1360-0443.2012.03870.x. Epub 2012 May 8. PMID: 22385013; PMCID: PMC3376663.
- Nunes, EV et. al. (2021) Sublingual Buprenorphine-naloxone compared with injection naltrexone for OUD: A Potential Utility of Patient Characteristics in Guiding Choice of Treatment. Am J Psychiatry178 (7). 600-671.
- Rich JD, McKenzie M, Larney S, Wong JB, Tran L, Clarke J, Noska A, Reddy M, Zaller N. Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomised, open-label trial. Lancet. 2015 Jul 25;386(9991):350-9. doi: 10.1016/S0140-6736(14)62338-2. Epub 2015 May 28. PMID: 26028120; PMCID: PMC4522212.
- SAMHSA, C. for B. H. S. and Q. (n.d.). Key substance use and mental health indicators in the United States: results from the 2019 National Survey on Drug Use and health. Key Substance Use and Mental Health Indicators in the United States: Results from the 2019 National Survey on Drug Use and Health.

 https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRDFWHTML/2019NSDUHFFR090120.htm#:~:text=%22misuse.%22)
 "Among%20people%20aged%2012%20or%20older%20in%202019%2C%2060.1%20percent
- Santo T Jr, et.al. (2022) Association of Opioid Agonist Treatment With All-Cause Mortality and Specific Causes of Death Among People With Opioid Dependence: A Systematic Review and Meta-analysis. JAMA Psychiatry. 2021 Sep 1;78(9):979-993. doi: 10.1001/jamapsychiatry.2021.0976. Erratum in: JAMA Psychiatry. 2021 Sep 1;78(9):1044. Erratum in: JAMA Psychiatry. 79(5):516. PMID: 34076676; PMCID: PMC8173472.
- Schwartz RP, et.al. (2013) Opioid agonist treatments and heroin overdose deaths in Baltimore, Maryland, 1995-2009. Am J Public Health. 2013 May;103(5):917-22. doi: 10.2105/AJPH.2012.301049. Epub. PMID: 23488511; PMCID: PMC3670653.
- Serowik KL, Yonkers KA, Gilstad-Hayden K, Forray A, Zimbrean P, Martino S. Substance Use Disorder Detection Rates Among Providers of General Medical Inpatients. J Gen Intern Med. 2021 Mar;36(3):668-675. doi: 10.1007/s11606-020-06319-7. Epub 2020 Oct 27. PMID: 33111239; PMCID: PMC7947066.
- Snyder H, Chau B, Kalmin MM, et al. High-Dose Buprenorphine Initiation in the Emergency Department Among Patients Using Fentanyl and Other Opioids. JAMA Netw Open. 2023;6(3):e231572. doi:10.1001/jamanetworkopen.2023.1572
- Sordo, L. et. al. (2017) Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ; 357: j1550
- Srisurapanont M, Jarusuraisin N. (2005) Naltrexone for the treatment of alcoholism: a meta-analysis of randomized controlled trials. Int J Neuropsychopharmacol. 8(2):267-80. doi: 10.1017/S1461145704004997. PMID: 15850502
- Strayer, R. J., et al. (2020). "Management of Opioid Use Disorder in the Emergency Department: A White Paper Prepared for the American Academy of Emergency Medicine." J Emerg Med 58(3): 522-546.
- Strauss SM, Rindskopf DM. Screening patients in busy hospital-based HIV care centers for hazardous and harmful drinking patterns: the identification of an optimal screening tool. J Int Assoc Physicians AIDS Care (Chic). 2009 Nov-Dec;8(6):347-53. doi: 10.1177/1545109709350509. Epub 2009 Oct 22. PMID: 19850861
- Strugar-Fritsch, D. (2019). MAT for Opioid Use Disorder: Overcoming Objections. California Health Care Foundation. Oakland, CA. https://www.chcf.org/wp-content/uploads/2019/06/MATOpioidOvercomingObjections.pdf
- Substance Abuse and Mental Health Services Administration and National Institute on Alcohol Abuse and Alcoholism, Medication for the Treatment of Alcohol Use Disorder: A Brief Guide. HHS Publication No. (SMA) 15-4907.

 Rockville, MD: Substance Abuse and Mental Health Services Administration, 2015.



- Substance Abuse and Mental Health Services Administration. (2022). Preliminary Findings from Drug-Related Emergency Department Visits, 2021; Drug Abuse Warning Network (HHS Publication No. PEP22-07-03-001).

 Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/
- Substance Abuse and Mental Health Services Administration. Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63 Publication No. PEP21-02-01-002. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021. https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP21-02-01-002.
- Substance Abuse and Mental Health Services Agency and the Office of the Surgeon General (2018) Facing Addiction in American: The Surgeon General's spotlight on opioids. Washington, D.C. US Dept of Health and Human Services.
- Substance Abuse Mental Health Services Agency. 2020. Substance Use Disorder Treatment for People with Co-occurring Disorders Treatment Improvement Protocol Tip 42. SAMHS. Rockville, MD.
- Tanum, L et. al. (2017) Effectiveness of Injectable Extended-Release Naltrexone vs Daily Buprenorphine-Naloxone for Opioid Dependence. A Randomized clinical noninferiority trial. JAMA Psychiatry 74 (12): 1197-1205.
- The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. Mar/Apr 2020;14(2S Suppl 1):1-91. doi: 10.1097/ADM.
- Tsui JI. et al., (2014) "Association of Opioid Agonist Therapy With Lower Incidence of Hepatitis C Virus Infection in Young Adult Injection Drug Users," JAMA Internal Medicine 174, no. 12: 1974–81, http://archinte.jamanetwork.com/article.aspx?articleid=1918926
- US Department of Health and Human Services SAMHSA SUD Treatment for people with co-occurring disorders TIP 42. (2020) SAMHSA Publication No. PEP20-02-01-004. Rockville, MS. SAMHSA.
- U.S. Department of Health and Human Services. (2024, January 2). Screening and assessment tools chart. National Institutes of Health. https://nida.nih.gov/nidamed-medical-health-professionals/screening-tools-resources/chart-screening-tools
- US Department of Justice Civil Rights Division (2022) The Americans with Disabilities Act and the Opioid Crisis: Combating Discrimination Against People in Treatment or Recovery. Washington D.C.
- Wakeman, SE. et. al. (2020) Comparative Effectiveness of Different Treatment Pathways for Opioid Use Disorder. JAMA Open Network. 3 (2).
- Walley, A. et al. (2020). Association between mortality rates and medication and residential treatment after inpatient medically managed opioid withdrawal: a cohort analysis, Addiction.
- Westfall, J. M., Miller, B. F., & Bazemore, A. W. (2016). No room for prevention: The unintended consequence of Mental Health Stigma Reduction Efforts: Health Affairs Forefront. Health Affairs. Retrieved from https://www.healthaffairs.org/do/10.1377/forefront.20160630.055649/full/
- White AM, Castle IP, Powell PA, Hingson RW, Koob GF. Alcohol-Related Deaths During the COVID-19 Pandemic. JAMA. 2022 May 3;327(17):1704-1706. doi: 10.1001/jama.2022.4308. PMID: 35302593; PMCID: PMC8933830. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8933830/
- Woodward D, Wilens TE, Glantz M, Rao V, Burke C, Yule AM. A systematic review of substance use screening in outpatient behavioral health settings. Addict Sci Clin Pract. 2023 Mar 26;18(1):18. doi: 10.1186/s13722-023-00376-z. PMID: 36967381; PMCID: PMC10041696.

