



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

MEDICATION MANAGEMENT OF STIMULANT USE DISORDER

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DISCLOSURES

- None

OBJECTIVES

1. Describe basics of stimulants and stimulant use
2. Highlight important historical context
3. Discuss reasons that people use stimulants
4. Review evidence for contingency management
5. Review evidence for mirtazapine, bupropion, xr-naltrexone
6. Review evidence for prescribed stimulants
7. Discuss harm reduction for stimulant use

STIMULANTS

- Cocaine and methamphetamine
- Powder or rock form
- Multiple route of administration
- Increase extracellular dopamine and norepinephrine
- Increased stimulation of alpha and beta adrenergic receptors
- Active in central and peripheral nervous system



Images: <https://www.dea.gov/>

STIMULANTS

Euphoric

- Increased energy/alertness
- Sociability
- Elation/euphoria
- Decreased appetite
- Decreased need for sleep

Dysphoric

- Anxiety
- Irritability
- Panic attacks
- Hypervigilance
- Paranoia
- Grandiosity
- Impaired judgement
- Psychosis

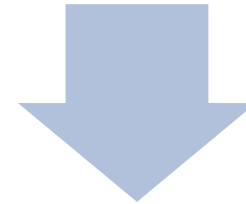
Risks

- Seizure
- Stroke
- Myocardial infarction

STIMULANTS

Withdrawal characterized

- Anhedonia
- Fatigue
- Difficulty concentrating
- Increased sleep duration
- Increased appetite

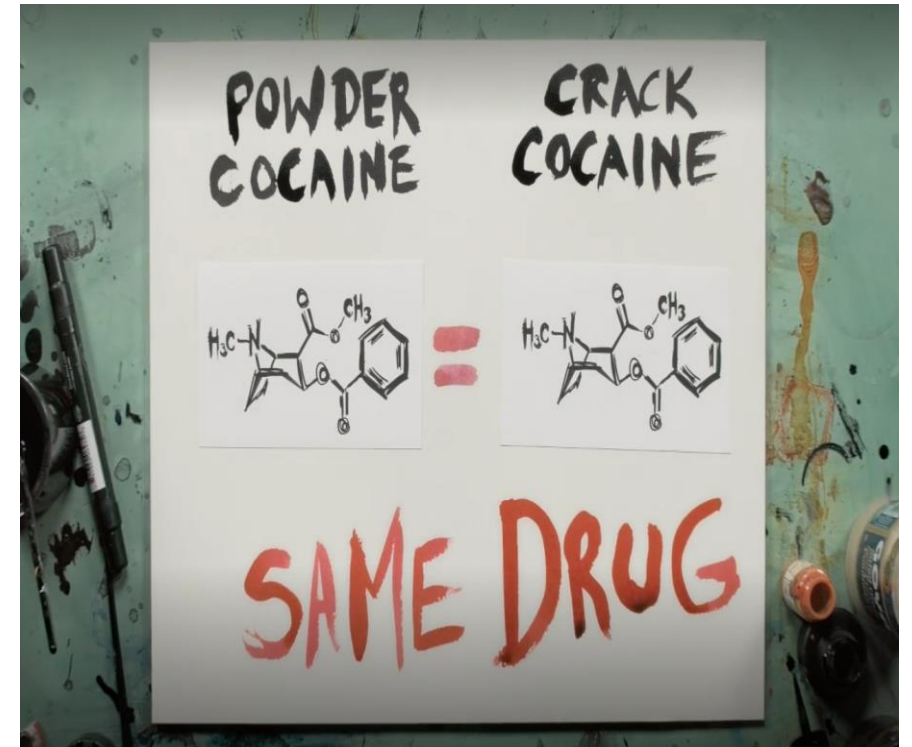


Chronic use

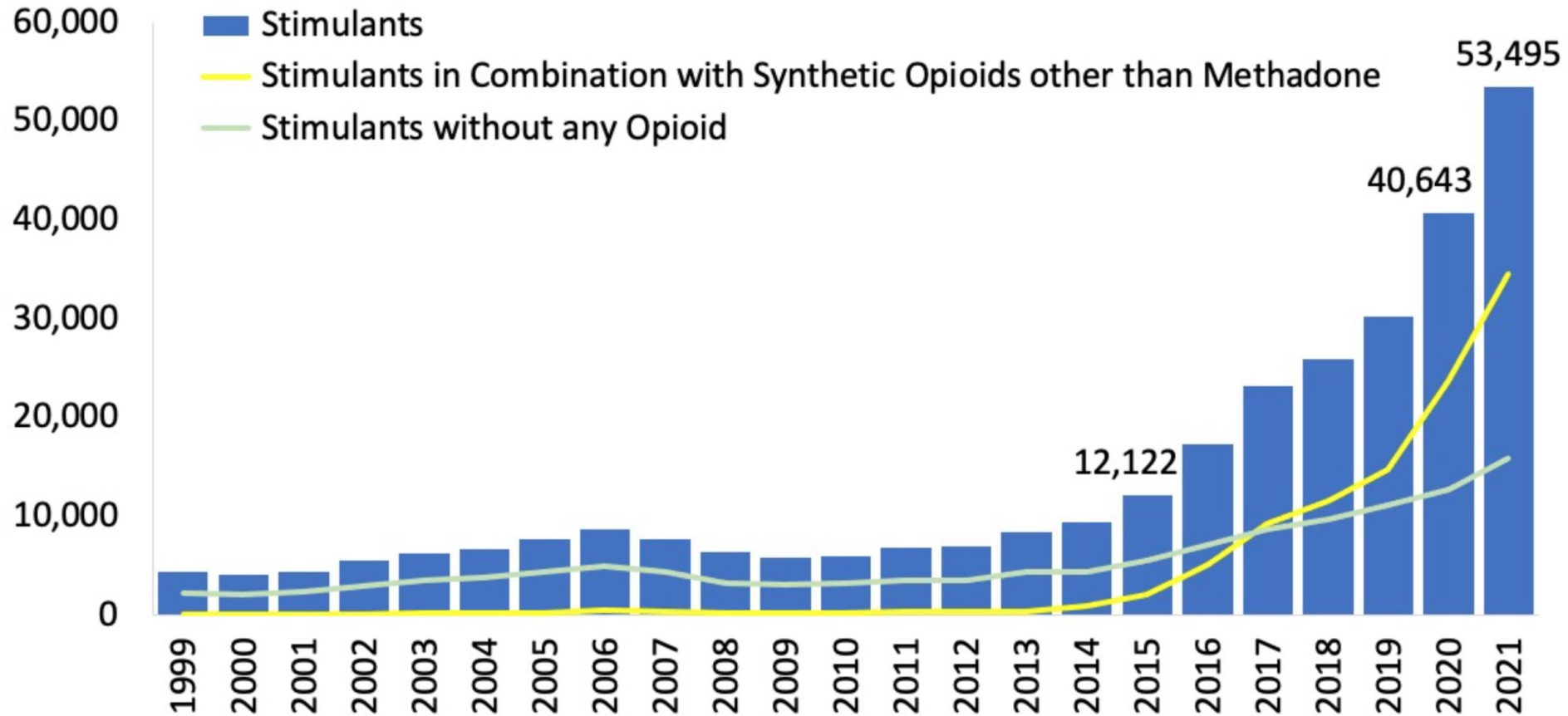
- Cognitive impairment
 - May persist for several months of abstinence
- Persistent psychotic disorder
 - May require antipsychotics

DISCRIMINATORY LEGAL POLICIES

- "Anti-Drug Abuse Act" signed by Regan in 1986 as part of "War on Drugs"
- 100:1 sentencing disparity for crack vs powder cocaine
 - Black Americans more likely to be convicted of crack cocaine offenses
 - White Americans more likely to be convicted of powder cocaine offenses
- "Fair Sentencing Act" decreased disparity to 18:1 under Obama
- "EQUAL" act passed in the house of representatives but failed to pass in the senate

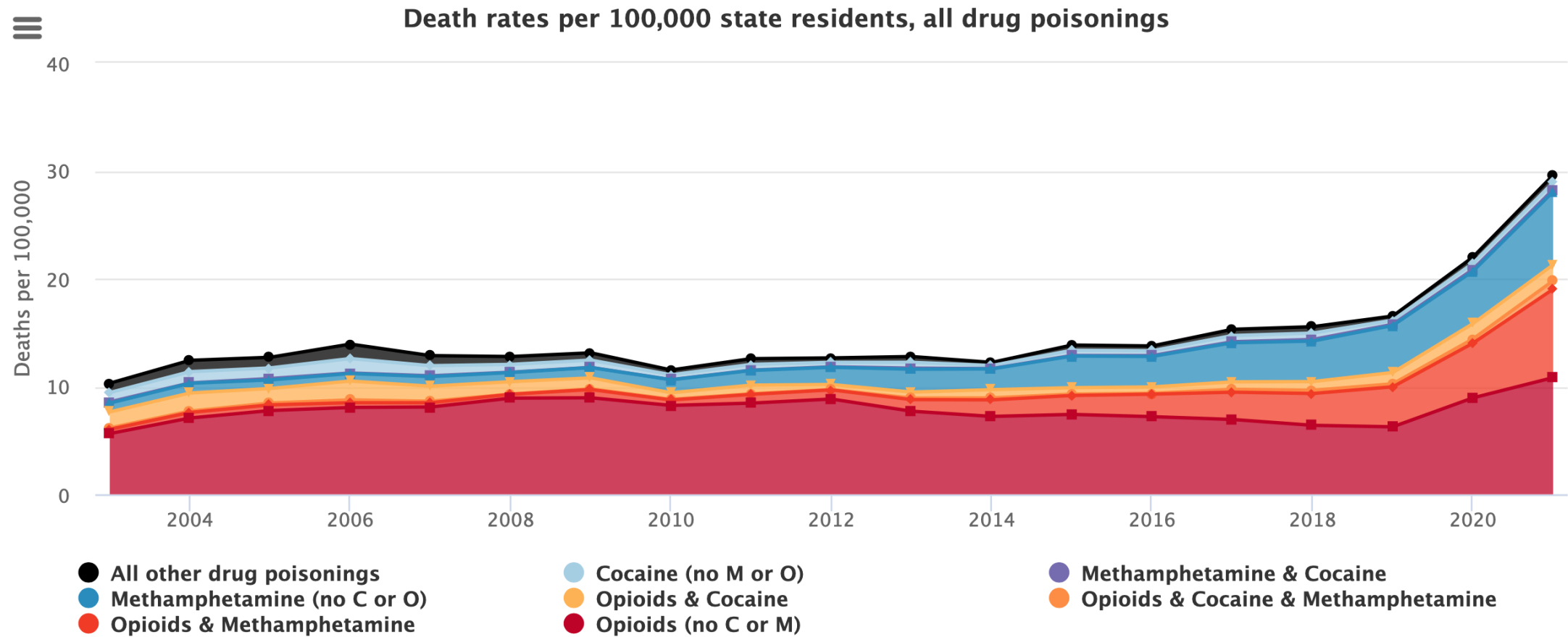


DEATHS INVOLVING STIMULANTS IN US



Graph: <https://nida.nih.gov/research-topics/trends-statistics/overdose-death-rates>

DEATHS INVOLVING STIMULANTS IN WA



Analysis by UW ADAI. For data sources, see text or adai.uw.edu/WAdata

Graph: <https://adai.washington.edu/wadata/deaths.htm>

CASE 1

A is a 32 year old male with stimulant use disorder who presents with chronic lower extremity wounds. He is currently living in a tent and uses methamphetamine to stay awake at night and protect his belongings. He is concerned about his stimulant use and would like to stop using.

REASONS TO USE

Stay awake to stay safe	Balance other substances	Treat mental health	Bond with others
Loose weight	Improve sex	Feel good	Relax
Cope with emotions	Treat pain	Stay awake to work	Manage with stress

SOCIAL DETERMINANTS OF HEALTH

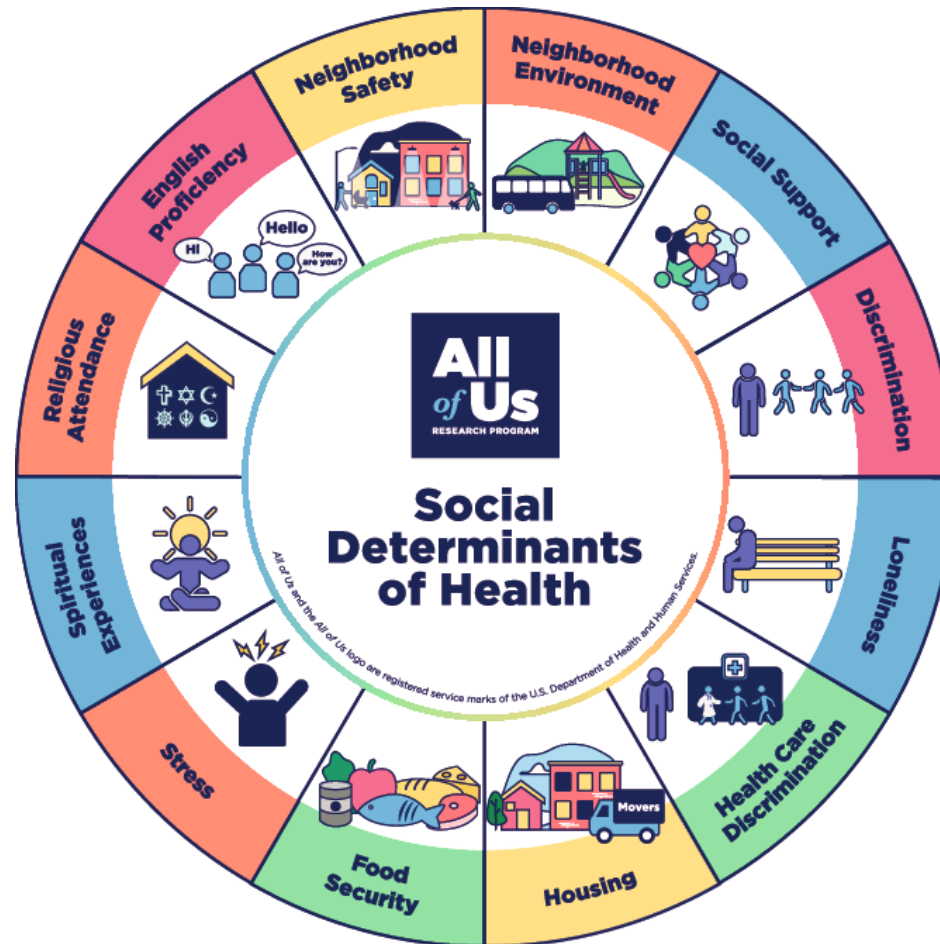


Image: <https://aahd.us/2022/05/all-about-the-social-determinants-of-health/>

CONTINGENCY MANAGEMENT

- Operant conditioning
- Positive reinforcement
- Increase desired behaviors
- Earlier, salient, predictable vs long term benefits
- Difficult to access



Image: <https://ndarc.med.unsw.edu.au/project/incentivise-integrating-contingency-management-methamphetamine-use-routine-clinical-care>

CONTINGENCY MANAGEMENT

Meta-Analysis > [PLoS Med.](#) 2018 Dec 26;15(12):e1002715. doi: 10.1371/journal.pmed.1002715.

eCollection 2018 Dec.

Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis

Franco De Crescenzo ^{1 2 3}, Marco Ciabattini ⁴, Gian Loreto D'Alò ⁴, Riccardo De Giorgi ^{1 2},
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PMID: 30586362 PMCID: [PMC6306153](#) DOI: [10.1371/journal.pmed.1002715](#)

CONTINGENCY MANAGEMENT

- 50 RCTs, 6942 participants
- 12 psychosocial interventions vs treatment as usual (TAU)
- Contingency management (CM) and community reinforcement (CRA) only interventions that increased
 1. Abstinence at 12 weeks (OR 7.60, 95% CI 2.03-28.37, P = 0.002)
 2. Abstinence at end of treatment (OR 2.84, 95% CI 1.24-6.51, P = 0.013)
 3. Abstinence at longest follow up (OR 3.08, 95% CI 1.33-7.17, P = 0.008)
- CM and CRA better efficacy and retention than all other interventions
 1. More effective than CBT (OR 3.08, 95% CI 1.33-7.17, P = 0.008)
 2. More effective than 12 step program (OR 4.07, 95% CI 1.13-14.69, P = 0.031)
 3. Less dropout at 12 weeks (OR 3.92, P < 0.001) and end of treatment (3.63, P < 0.001)

MEDICATIONS

- No FDA approved medications
- No medication that shows consistent benefit
- Literature hard to interpret, small samples, difficult to achieve outcomes (abstinence, negative urines), lots of drop out
- Some medications have good safety profile, enough evidence to consider using

MIRTAZAPINE

Randomized Controlled Trial > [JAMA Psychiatry](#). 2020 Mar 1;77(3):246-255.

doi: [10.1001/jamapsychiatry.2019.3655](https://doi.org/10.1001/jamapsychiatry.2019.3655).

Effects of Mirtazapine for Methamphetamine Use Disorder Among Cisgender Men and Transgender Women Who Have Sex With Men: A Placebo-Controlled Randomized Clinical Trial

[Phillip O Coffin](#)^{1 2}, [Glenn-Milo Santos](#)^{1 3}, [Jaclyn Hern](#)¹, [Eric Vittinghoff](#)⁴, [John E Walker](#)¹, [Tim Matheson](#)¹, [Deirdre Santos](#)¹, [Grant Colfax](#)¹, [Steven L Batki](#)⁵

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PMID: 31825466 PMCID: [PMC6990973](#) DOI: [10.1001/jamapsychiatry.2019.3655](https://doi.org/10.1001/jamapsychiatry.2019.3655)

MIRTAZAPINE

- Double blind RCT
- 120 cisgender men and transgender women who 1) had sex with men and 2) had methamphetamine use disorder
- Mirtazapine 30 mg vs placebo, with background counseling
- Fewer methamphetamine positive urine test results in mirtazapine group vs placebo
 - At week 12 (RR, 0.67 [95% CI, 0.51-0.87])
 - At week 24 (RR, 0.75 [95% CI, 0.56-1.00])
 - At week 36 (RR, 0.73 [95% CI, 0.57-0.96])

BUPROPION

Clinical Trial > [Neuropsychopharmacology](#). 2008 Apr;33(5):1162-70.

doi: 10.1038/sj.npp.1301481. Epub 2007 Jun 20.

Bupropion for the treatment of methamphetamine dependence

Ahmed M Elkashef ¹, Richard A Rawson, Ann L Anderson, Shou-Hua Li, Tyson Holmes, Edwina V Smith, Nora Chiang, Roberta Kahn, Frank Vocci, Walter Ling, Valerie J Pearce, Michael McCann, Jan Campbell, Charles Gorodetzky, William Haning, Barry Carlton, Joseph Mawhinney, Dennis Weis

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PMID: 17581531 DOI: [10.1038/sj.npp.1301481](#)

BUPROPION

- Double blind RCT
- 151 people with methamphetamine use disorder
- Bupropion 150 mg BID vs placebo, and psychotherapy
- Difference in number of non use weeks non statistically significant ($p=0.09$)
 - Subgroup analyses showed significant effect for males and those with lower level of methamphetamine use (less than 18 days per month)

BUPROPION AND XR-NALTREXONE

Randomized Controlled Trial

> [N Engl J Med.](#) 2021 Jan 14;384(2):140-153.

doi: [10.1056/NEJMoa2020214](https://doi.org/10.1056/NEJMoa2020214).

Bupropion and Naltrexone in Methamphetamine Use Disorder

[Madhukar H Trivedi](#)¹, [Robrina Walker](#)¹, [Walter Ling](#)¹, [Adriane Dela Cruz](#)¹, [Gaurav Sharma](#)¹,
[Thomas Carmody](#)¹, [Udi E Ghitza](#)¹, [Aimee Wahle](#)¹, [Mora Kim](#)¹, [Kathy Shores-Wilson](#)¹,
[Steven Sparenborg](#)¹, [Phillip Coffin](#)¹, [Joy Schmitz](#)¹, [Katharina Wiest](#)¹, [Gavin Bart](#)¹,
[Susan C Sonne](#)¹, [Sidarth Wakhlu](#)¹, [A John Rush](#)¹, [Edward V Nunes](#)¹, [Steven Shoptaw](#)¹

Affiliations + expand

PMID: 33497547 PMCID: [PMC8111570](#) DOI: [10.1056/NEJMoa2020214](https://doi.org/10.1056/NEJMoa2020214)

BUPROPION AND XR-NALTREXONE

- Double blind two stage sequential parallel design
 - Stage 1: 0.26:0.74 ratio to receive naltrexone-bupropion or placebo
 - Stage 2: non responders from placebo group randomized 1:1 to receive naltrexone-bupropion or placebo
- 403 participants with methamphetamine use disorder
- XR-naltrexone 380 mg q 3 weeks and bupropion 450 mg daily vs placebo
- More negative urines in treatment group
 - Weighted average response 13.6% with naltrexone-bupropion, 2.5% with placebo (overall treatment effect Of 11.1, $p < 0.001$)

CURRENT TRIALS

- XR-Buprenorphine
 - NIDA CTN-0100 "MURB", Seattle site enrolling now
 - Randomized, double-blind, placebo controlled trial of monthly injectable buprenorphine for methamphetamine use disorder
 - XR-Buprenorphine for people with stimulant use disorder with mild opioid use disorder/opioid misuse
- Psilocybin enhanced psychotherapy
 - Psilocybin-Enhanced Psychotherapy for Methamphetamine Use Disorder, Portland VA

CASE 1

Connect A with resources for housing
Connect A with CM/CRA program
Consider medications if additional
indication

CASE 2

B is a 28 year old woman with ADHD who presents to establish primary care. She reports that she was diagnosed with ADHD as a child and was briefly prescribed stimulants. She recently started using methamphetamine at work and sometimes at home to help her stay focused and complete tasks. She is concerned about the risks of methamphetamine and wonders if prescribed stimulants would be a safer options.

PRESCRIBED STIMULANTS

Randomized Controlled Trial > [JAMA Psychiatry](#). 2023 Jan 1;80(1):31-39.

doi: [10.1001/jamapsychiatry.2022.3788](https://doi.org/10.1001/jamapsychiatry.2022.3788).

Association of Pharmacological Treatments and Hospitalization and Death in Individuals With Amphetamine Use Disorders in a Swedish Nationwide Cohort of 13 965 Patients

[Milja Heikkinen](#)^{1 2}, [Heidi Taipale](#)^{1 2 3}, [Antti Tanskanen](#)^{1 2}, [Ellenor Mittendorfer-Rutz](#)²,
[Markku Lähteenvuo](#)¹, [Jari Tiihonen](#)^{1 4 5}

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PMID: 36383348 PMID: [PMC9669925](#) DOI: [10.1001/jamapsychiatry.2022.3788](https://doi.org/10.1001/jamapsychiatry.2022.3788)

[Free PMC article](#)

PRESCRIBED STIMULANTS

- Nationwide register-based cohort study
- 13965 people with methamphetamine use disorder
- Included medications for SUD, ADHD, mood disorders, antipsychotics
- Stimulants were only medication associated with decreased hospitalization for SUD, any hospitalization or death
 - Lisdexamphetamine decrease in risk of 3 outcomes (aHR 0.82; 95% CI, 0.72-0.94 for SUD hospitalization; aHR, 0.86; 95% CI, 0.78-0.95 for any hospitalization or death; aHR, 0.43; 95% CI, 0.24-0.77 for all-cause mortality)
 - Methylphenidate decrease in all-cause mortality (aHR, 0.56; 95% CI, 0.43-0.74)

CASE 2

Obtain records from B's ADHD diagnosis
Assess impact of ADHD symptoms on current functioning
Consider prescribing stimulants

CASE 3

C is a 48 year old male with stimulant use disorder who presents to discuss hepatitis C treatment. He has now transitioned from injecting to smoking. He is not interested in stopping his methamphetamine use but would like to discuss ways to use more safely.

HARM REDUCTION

Ways to use more safely

Choose safer ways to use

- **Why?** Some ways of using drugs are less risky to your health.
- **How?** Taking drugs by mouth is safer than smoking which is safer than shooting. If you smoke crack, you can use a crack condom for your pipe. You can get clean works at the People's Harm Reduction Alliance or the King County Needle Exchange.

Shoot safer

- **Why?** Avoid overdose, bloodborne illness (HIV and hepatitis C), bacterial infections.
- **How?** Pace yourself until you know the strength of your stash. Shooting into veins in your arms or hands is safer than hitting blind into your groin or into your neck. Rotate sites and shoot downstream if possible. Using new, clean needles and works can help prevent bloodborne illnesses, like HIV and hepatitis C, and other infections.

Avoid mixing drugs

- **Why?** Using stimulants and depressants, like opioids, alcohol or benzos, at the same time can have unexpected effects, put stress on your heart and lead to overdose.
- **How?** Try to stick to one drug at a time, especially when you are unsure of its strength or content.

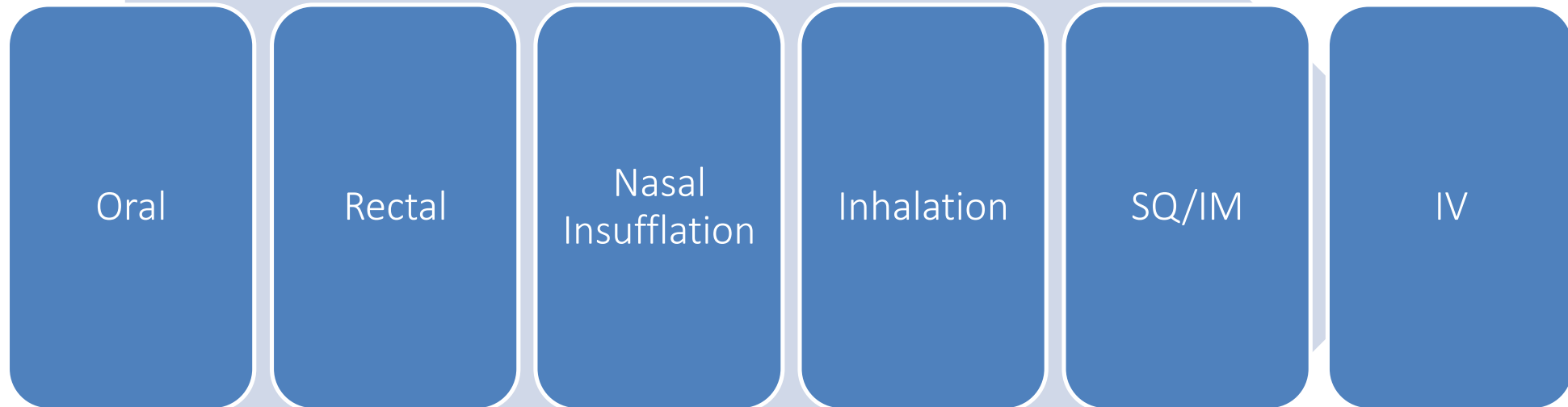
Use with safe people in a safe place

- **Why?** Heavy stimulant use can cause paranoia or aggression that can lead to fights, hassels and arrests. People can take advantage of you when you're high.
- **How?** Avoid using with people you don't know or trust. Use where you feel safe and in control of the surroundings. Do not drive or ride your bike when you are high.

Image: <https://depts.washington.edu/harrtlab/wordpress/wp-content/uploads/2018/11/Safer-Use-Stimulants.pdf>

HARM REDUCTION

Route of administration



HARM REDUCTION

How to prepare your meth pipe:

1 Clean your hands with soap and water or alcohol swabs.



2 Pour crystal meth into pipe.



3 Fit mouthpiece onto pipe.



4 Hold pipe and apply heat to bowl. The flame shouldn't touch the bowl. Keep heat moving around the bowl.




5 Once you begin to see vapour, continue heating pipe and inhale slowly, then exhale immediately (holding in won't get you more high and can burn your lungs).

6 The pipe will be very hot - handle it with care. If the pipe has a crack or chip, throw it out.



Image: <https://www.catie.ca/client-publication/safer-crystal-meth-smoking>

HARM REDUCTION

-  **Green Areas are Safer**
-  **Try to Avoid Yellow Areas**
-  **Red Areas are Dangerous**



HARM REDUCTION

Ways to stay healthier when you use

Prepare for safer sex

- **Why?** Stimulant use can lower your inhibitions and turn up your sex drive.
- **How?** It's a good idea to think ahead and carry condoms, dams, lube and gloves with you. These barriers can prevent unwanted pregnancy and sexually transmitted infections like HIV and hepatitis C.

Test your drugs

- **Why?** You can find out if your drugs are cut with other drugs (like fentanyl) or fillers (like levamisole) that could harm you.
- **How?** Talk to providers about getting a urine drug testing kit and testing liquids before you shoot them. For pills and powders, check out <https://dancesafe.org> for testing kits.

Try to eat

- **Why?** Stimulants can drain your body and dull your appetite. Food and water replenish these important nutrients to help you stay healthy.
- **How?** Try to eat nutritious foods before using, pack healthy snacks and water on the go, and avoid using over a long time. Let your body rest for at least a day after using.

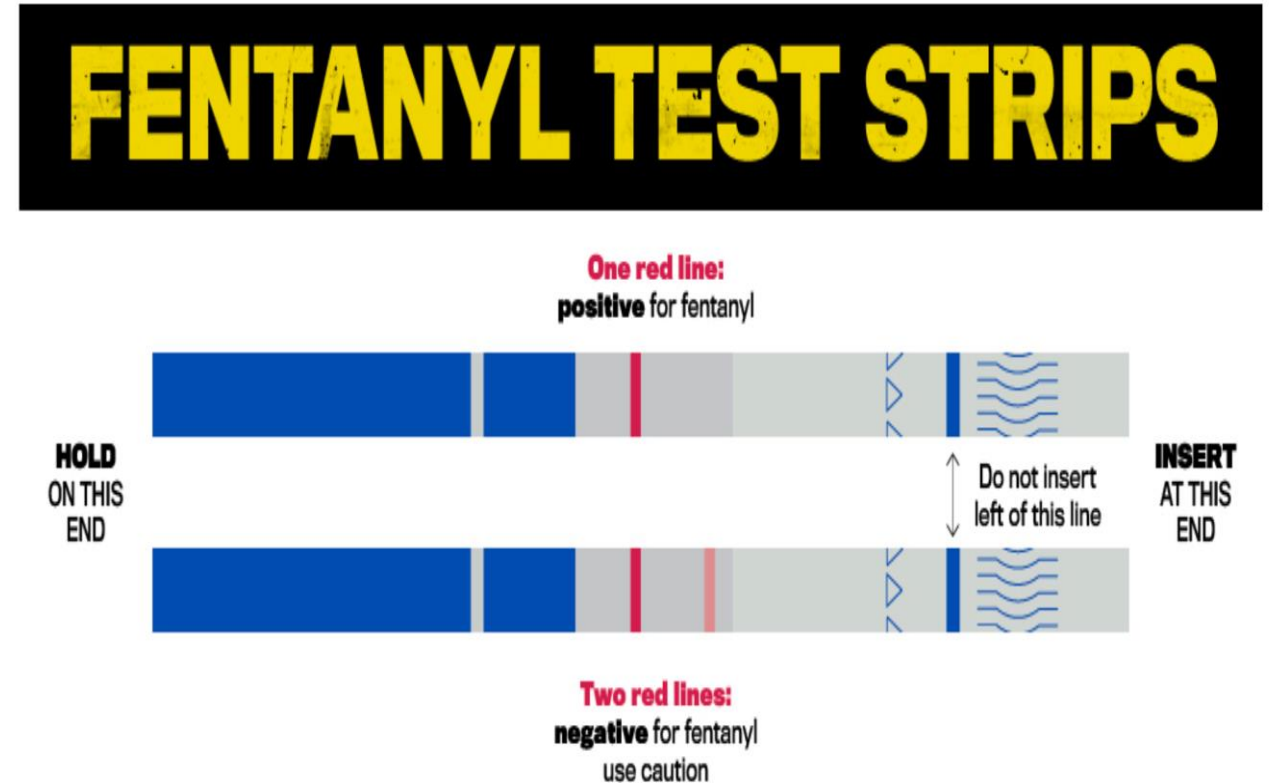
Take care of your mouth

- **Why?** Some stimulants cause mouth dryness, sores, cracks, and teeth clenching.
- **How?** Drink water to keep yourself hydrated, and chew gum to keep your mouth moist and your teeth from grinding. Brushing your teeth can help control increased bacteria due to dry mouth. Use chapstick to prevent lip and mouth cracking.

Image: <https://depts.washington.edu/harrtlab/wordpress/wp-content/uploads/2018/11/Safer-Use-Stimulants.pdf>

HARM REDUCTION

1. Put a small amount (10mg) in clean, dry container.
2. Mix in water (1 tsp for methamphetamine, ½ for other)
3. Place the wavy end in water, wait 15 seconds.
4. Place on flat surface for 2 to 5 minutes.



HARM REDUCTION

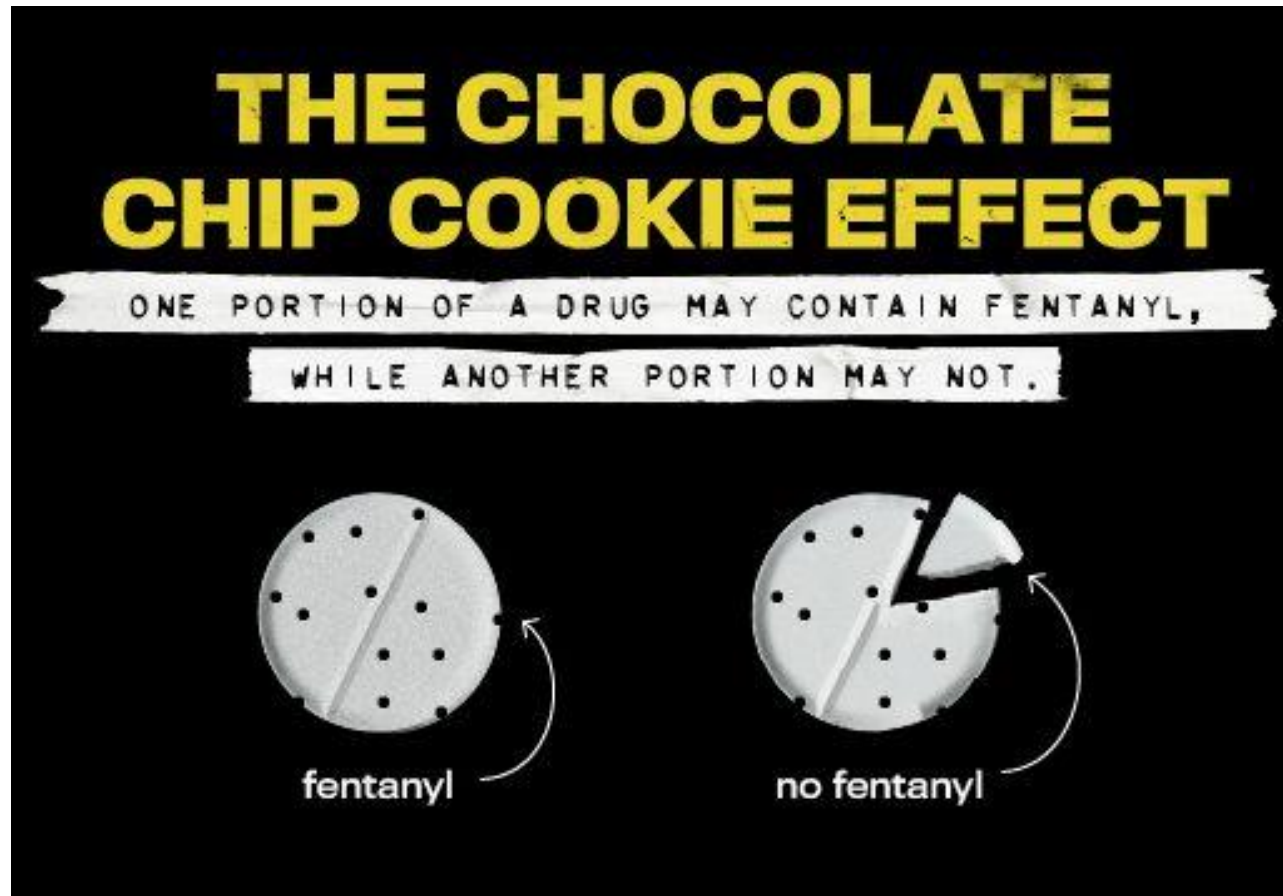


Image: <https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html>

HARM REDUCTION



Image: <https://www.kelley-ross.com/services/naloxone/>

HEPATITIS C TREATMENT

Meta-Analysis > [Lancet Gastroenterol Hepatol.](#) 2018 Nov;3(11):754-767.

doi: [10.1016/S2468-1253\(18\)30304-2](https://doi.org/10.1016/S2468-1253(18)30304-2). Epub 2018 Sep 21.

Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: a systematic review and meta-analysis

[Behzad Hajarizadeh](#)¹, [Evan B Cunningham](#)², [Hannah Reid](#)², [Matthew Law](#)², [Gregory J Dore](#)²,
[Jason Grebely](#)²

Affiliations + expand

PMID: 30245064 DOI: [10.1016/S2468-1253\(18\)30304-2](https://doi.org/10.1016/S2468-1253(18)30304-2)

HEPATITIS C TREATMENT

- 8 studies, 670 participants
- Recent injecting drug use
- 96.9% completed HCV treatment
- 87.4% reached SVR

CASE 3

Affirm HR behaviors C is already doing
Counsel C on other HR behaviors
Treat HCV

PEARLS

- Important to understand why people use stimulants and address underlying social determinants of health
- Contingency management is the gold standard treatment for stimulant use disorder but is difficult to access
- Can consider Mirtazapine and Bupropion off label especially if other indication in addition
- People with stimulant use disorder and ADHD should have ADHD treatment
- Always remember harm reduction
- People with who use stimulants should have HCV treatment

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- Heikkinen M, Taipale H, Tanskanen A, Mittendorfer-Rutz E, Lähteenvuo M, Tiihonen J. Association of Pharmacological Treatments and Hospitalization and Death in Individuals With Amphetamine Use Disorders in a Swedish Nationwide Cohort of 13 965 Patients. *JAMA Psychiatry*. 2023 Jan 1;80(1):31-39. doi: 10.1001/jamapsychiatry.2022.3788. PMID: 36383348; PMCID: PMC9669925.
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