Vermont Center on Behavior & Health

Center on Rural Addiction
UNIVERSITY OF VERMONT

What are the evidence-based treatment options for methamphetamine use disorder?

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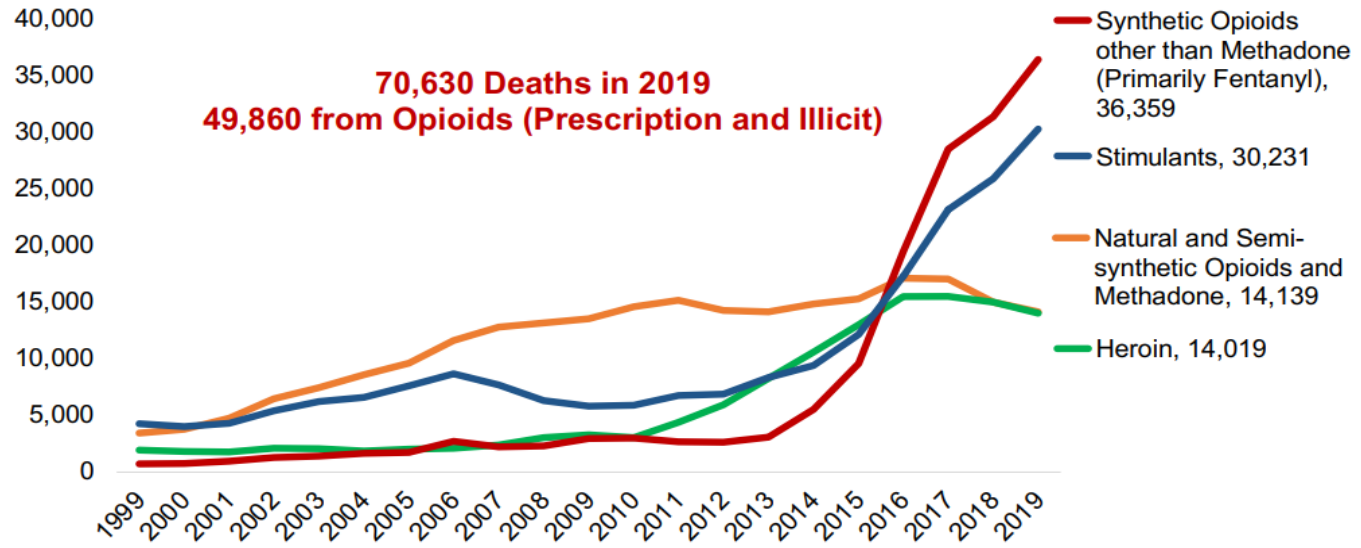
Evolution of Drivers of Overdose Deaths, All Ages

Analgesics → Heroin → Fentanyl → Stimulants



Source: The Multiple Cause of Death data are produced by the Division of Vital Statistics, National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), United States Department of Health and Human Services (US DHHS).

Clinical Challenges for Individuals with Methamphetamine Use Disorder

Overdose death

Limited understanding of stimulant addiction

Ambivalence about need to stop use

Impulsivity/Poor judgement

Cognitive impairment and poor memory

Paranoia

Clinical Challenges with Individuals with Methamphetamine Use Disorder

Anhedonia

Hypersexuality/Hyposexuality

Psychosis

Elevated levels of violence

Powerful Pavlovian trigger-craving response

Poor retention in outpatient treatment

Individuals with methamphetamine use disorder are difficult to engage and retain in treatment

Interest in Reducing Methamphetamine and Opioid Use among Syringe Services Program Participants in Washington State McMahan et al, 2020 Drug and Alcohol Dependence

- In a sample of 583 participants at a Washington State syringe exchange program (443 opioids; 140 methamphetamine), survey data were collected on their attitudes about stopping drug use.
- 82% of the individuals who reported opioids as their main drug expressed an interest in reducing/stopping opioid use
- 46% of individuals who reported methamphetamine as their main drug expressed an interest in reducing/stopping their meth use.

Dropout rates of in-person psychosocial substance abuse treatment: a systematic review and meta-analysis (Lappan et al., Addiction, 2020)

- Meta-analysis of in-person psychosocial SUD treatment.
- Drop out rates in first 90 days of treatment
- 151 studies, with 26,243 participants.
- Results yielded overall average dropout rates, and predictors of dropout.

Substance Targeted and Dropout

Treatment Target	Dropout Rate
Heroin	25.1
Tobacco	25.5%
Alcohol	26.1%
Cocaine	48.7%
Methamphetamine	53.5%

Special Treatment Consideration Should Be Made for the Following Groups

- **People who inject stimulants.**
- **People who use stimulants daily or in very high doses**.
- Women (high rates of physical/sexual abuse).
- Homeless, chronically mentally ill, and/or individuals with high levels of psychiatric symptoms at admission.
- Men who have sex with men (MSM).
- Individuals in medication treatment for OUD.

Harm Reduction Strategies for Individuals who use Stimulants

- Information about medical and psychiatric effects of meth
- Overdose education (fentanyl)
- Syringe exchanges
- Naloxone (for opioid overdose)
- Quiet rooms and wash up/shower rooms
- Condoms/safe sex education
- Topical antibiotic creams and ointments for injection sites
- Water (dehydration)
- Toothpaste/toothbrush

Vermont Interviews

- 45 minute, 1:1 interviews with 25 volunteers who were on methadone (12) or buprenorphine (13) and who gave more than one Ua positive for cocaine (23) or methamphetamine (2), in the past 30 days. (participants received $25 for the interview)
- Participants were asked to respond to:
  - Do you consider your stimulant use a significant problem in your life?
    - 23/25 answered “no”
  - Would additional counseling be helpful to reducing/stopping stimulants?
    - 25/25 answered “no”
    - 5 patients on buprenorphine added that if they were forced to get more counseling they would stop treatment and purchase buprenorphine on the street.
  - If you decided you did want to reduce/stop stimulant use, what would help?
    - 2 patients had been in a Contingency Management project at university and said it was helpful
    - 1 patient said he had been in drug court and the “accountability” had helped
    - 5 patients said assistance with jobs, transportation and developing new recreational activities

Treatment for individuals for methamphetamine use disorder

Evidence-based Practices

- To guide the development of a treatment system that can effectively address the serious public health crisis of methamphetamine it is critical that clinical strategies with the best scientific evidence be used. These strategies are defined as evidence-based practices (EBPs).
- **EBPs are those interventions that are grounded in systematic empirical evidence derived from research guided by the standards of science. (Jennings, 2011)**

Current Status of Treatment Approaches for Methamphetamine Use Disorder

- **Contingency management unanimously (7 systematic reviews and meta-analyses) found to have best evidence of effectiveness**.
- Other approaches with less but clear evidence of support: Cognitive Behavioral Therapy (CBT) and Community Reinforcement Approach (CRA).
- Approach with evidence for treatment of a broad variety of SUD: Motivational Interviewing (MI).
- Approach with recent studies showing benefit to methamphetamine users: Physical Exercise (PE) (e.g., Rawson et al., 2015).

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RESEARCH ARTICLE

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], Cinzia Del Giovane[5], Carolina Cassar[6], Luigi Janiri[3], Nicolas Clark[7], Michael Joshua Ostacher[8,9], Andrea Cipriani[1,2]*

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Meta-Analysis Findings

Network meta-analysis was used to analyze 50 clinical studies (6,943 participants) on 12 different psychosocial interventions for cocaine and/or amphetamine addiction.

The combination of contingency management and community reinforcement approach was the most efficacious and most acceptable treatment, both in the short and long term.

Non-pharmacological interventions for methamphetamine use disorder: a systematic review AshaRani, PV, et al. Drug and Alcohol Dependence, 2020

- 44 Studies reviewed.
- Conclusions: While Contingency Management (CM) interventions showed the strongest evidence favoring the outcomes assessed, tailored CBT alone or with CM was also effective in the target population.

Bentzley BS, Han SS, Neuner S, Humphreys K, Kampman KM, Halpern CH. Comparison of Treatments for Cocaine Use Disorder Among Adults: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2021;4(5):e218049. doi:10.1001/jamanetworkopen.2021.8049

Results and Conclusions Bentzly et al, 2021

Results A total of 157 studies comprising 402 treatment groups and 15 842 participants were included.

Only contingency management programs were significantly associated with an increased likelihood of having a negative test result for the presence of cocaine (OR, 2.13; 95%)

Conclusions In this meta-analysis, **contingency management programs were associated with reductions in cocaine use among adults.**

Contingency Management for the Treatment of Methamphetamine Use Disorder: A Systematic Review Brown and DeFulio, 2020

- A review of 27 studies.
- All included a contingency management intervention for individuals with methamphetamine use disorder.
- Outcomes:
  - Drug abstinence
  - Retention in treatment
  - Attendance/treatment engagement
  - Sexual risk behavior
  - Mood/affect
  - Treatment response predictors

Results of CM Treatments

- Reduced methamphetamine use in 26 of 27 studies.
- Longer retention in treatment.
- More therapy sessions attended; higher use of other services and medical services.
- Reductions in risky sexual behavior.
- Increases in positive affect and decreases in negative affect.

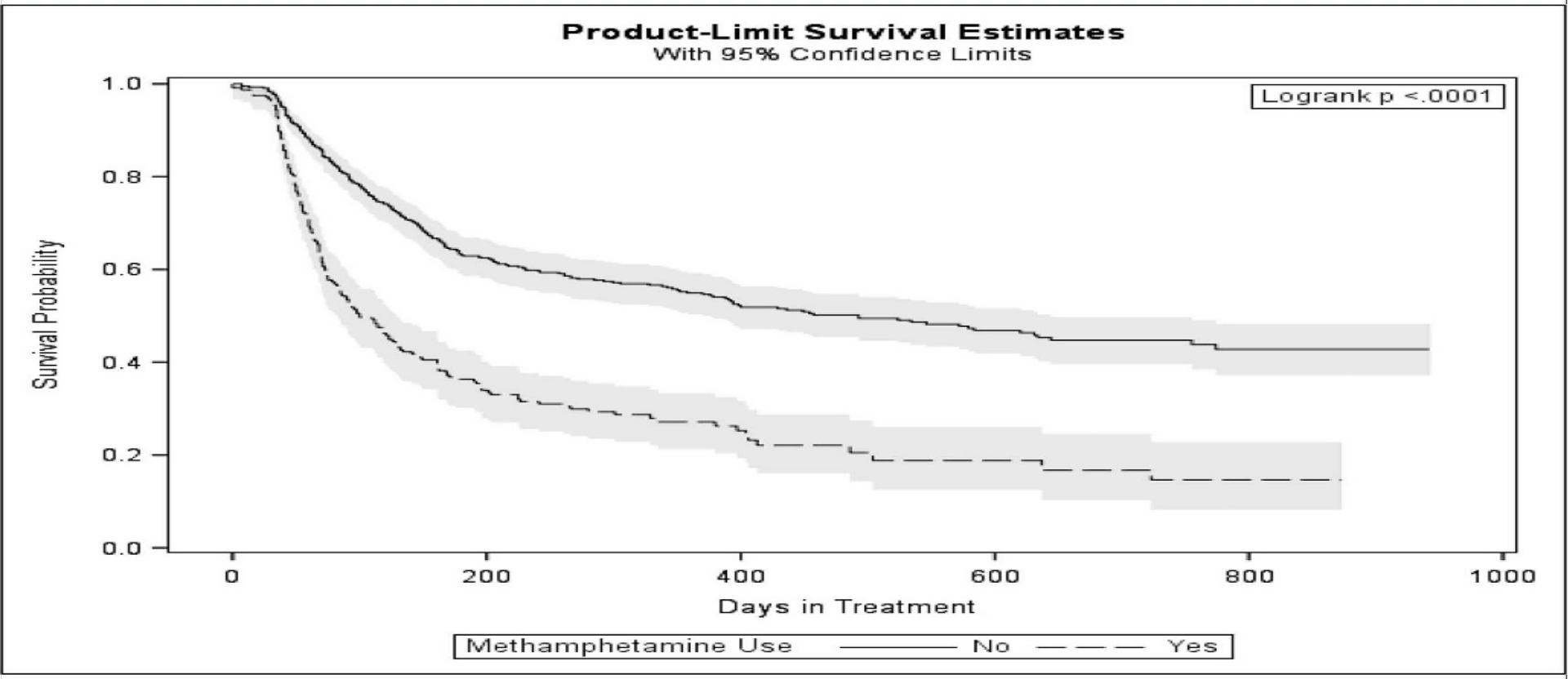
Judith I. Tsui, et al (2020) Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine. Journal of Substance Abuse Treatment 109:80–85

Association Between Methamphetamine Use and Retention Among Patients With Opioid Use Disorders Treated With Buprenorphine

- The study utilized data on adult patients receiving buprenorphine from Washington State Medication Assisted Treatment-Prescription Drug and Opioid Addiction program clinics between November 1, 2015, and April 31, 2018 (N=799). Past 30-day substance use data were collected at baseline, 6-months, and date of program discharge.

- 30% (n=237) of individuals reported meth use at admission. Baseline methamphetamine use was associated with more than twice the relative hazards for discharge in adjusted models (aHR=2.39; 95% CI: 1.94–2.93).

Association Between Methamphetamine Use and Retention Among Patients With Opioid Use Disorders Treated With Buprenorphine



Bolivar, H.A., Klemperer, E.M., Coleman, S.R., Skelly, J., Higgins, S.T. Contingency Management for Patients Receiving Medication for Opioid Use Disorder: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. Published online August 4, 2021. doi:10.1001/jamapsychiatry.2021.1969

Bolivar, H.A., et al. JAMA 2021

These results provide **evidence supporting the use of contingency management in addressing key clinical problems among patients receiving MOUD**, including the ongoing epidemic of comorbid psychomotor stimulant misuse.

Ronsley C, Nolan S, Knight R, Hayashi K, Klimas J, Walley A, et al. (2020) Treatment of stimulant use disorder: A systematic review of reviews. PLoS ONE 15(6): e0234809. https://doi.org/10.1371/journal.pone.0234809

Interventions reviewed

- 29 reviews resulted.
- 11 interventions were examined:
  - Contingency management
  - Cognitive behavioral treatment
  - Acupuncture
  - Antidepressants (e.g., fluoxetine, bupropion)
  - Dopamine agonists (e.g., levodopa)
  - Antipsychotics (e.g., aripiprazole)
  - Anticonvulsants (e.g., topiramate)

Conclusions

- **The strongest body of evidence was for contingency management**.
- Of pharmacologic treatments, psychostimulants appear to be the most promising, but data are insufficient to support clinical use and further research is necessary..
- All other interventions found predominantly negative results.

Responding to global stimulant use: Challenges and opportunities Lancet (Farrell et al, 2019)

Psychosocial interventions other than contingency management have weak and non-specific effects on stimulant problems and there are no effective pharmacotherapies. Substantial research investment is needed to develop more effective, innovative, and impactful prevention and treatment.

Contingency Management (also known as Motivational Incentives)

Contingency Management (CM)

A technique employing the systematic delivery of positive reinforcement for desired behaviors. In the treatment of methamphetamine dependence, vouchers or prizes can be "earned" for submission of methamphetamine-free urine samples or for attendance at treatment sessions.

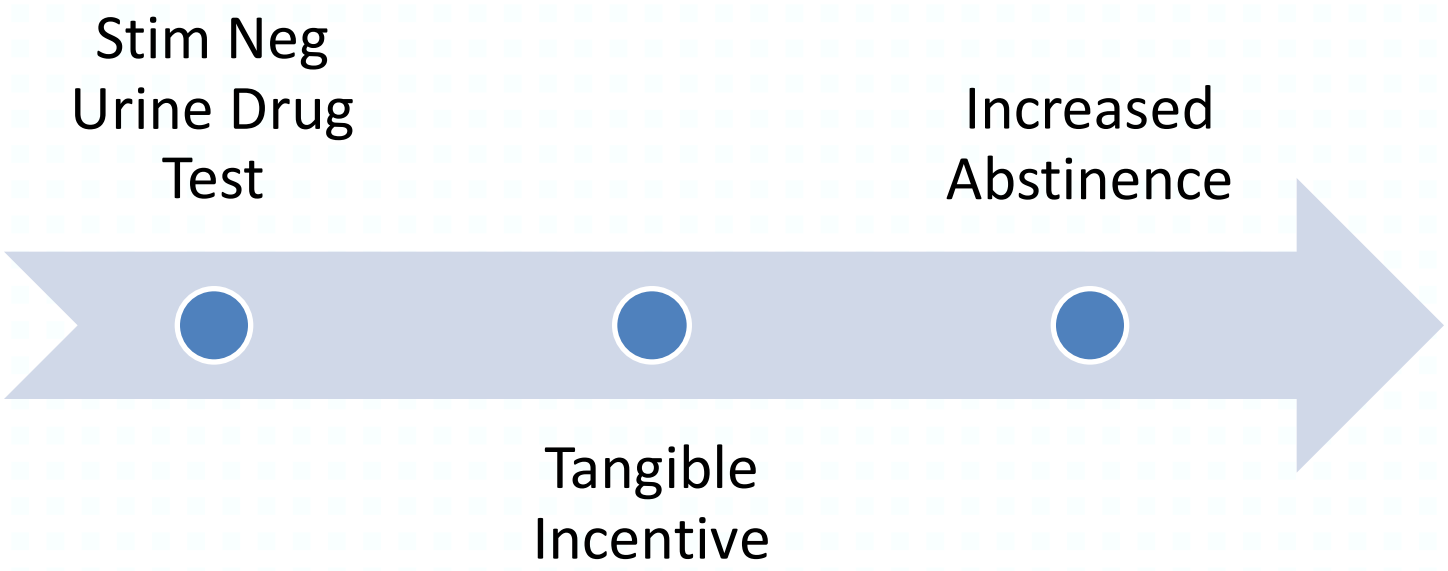
In most CM protocols, the value of the incentive is increased (escalation) as patients perform the target behavior in consecutive UAs or visits. If a positive UA or missed session occurs, the value of the incentive returns to the original value (reset).

Operant Conditioning

Behavior → Consequence → Behavior Change

	Reinforcement (Increase / maintain behavior)	**Punishment** (Decrease behavior)
Positive (add stimulus)	Add pleasant stimulus to **Increase / maintain** behavior	Add aversive stimulus to **Decrease** behavior
Negative (remove stimulus)	Remove aversive stimulus to **Increase / maintain** behavior	Remove pleasant stimulus to **Decrease** behavior

Basics of CM For Stimulants



Key Elements of CM

Target Behavior:

- Objective
- Measurable
- Achievable
- Feasible
- Consistent

CM Incentives:

- Contingent
- Immediate
- Tangible
- Desirable
- Escalating

CM for Stimulants: Target Behavior

Drug Abstinence: Stimulant Negative Urine Drug Test (UDT)

- **Objective:** Self-report is not sufficient
- **Achievable:** 2-4 day detection period
- **Feasible:** point-of-care tests are cheap and provide immediate results
- **Consistent:** 2 times a week

CM for Stimulants: Incentives

- **Contingent:** only provide incentive when UDT negative.
- **Immediate:** deliver incentive immediately after UDT result
- **Tangible:** prizes or gift cards
- **Desirable:** things people want/need and amount that will be motivating
  - Minimum $10/ neg UDT, total of $500 for 12 weeks

CM Incentives: Escalation, Reset, Recovery

- **Escalation Bonus:** incentives get bigger with continuous abstinence
- **Reset:** positive or missed UDT results in
  - No incentive and a reset or cancelation of the escalation bonus
- **Recovery:** the escalation bonus can be recovered after 1 week of abstinence

Challenges to using CM

- Staff resistance to the idea of incentives
  - Overcome with knowledge of the robust benefits from CM
- Challenges of tracking escalation bonus, reset, and recovery
- Where does the funding for incentives come from?

Community Reinforcement Approach

Community Reinforcement Approach

Community Reinforcement Approach (CRA) is a combination of behavioral strategies that address the role of environmental contingencies in encouraging or discouraging drug use, and attempts to rearrange these contingencies so that a non-drug using lifestyle is more rewarding than a using one.

Cognitive Behavioral Therapy (CBT)

Cognitive Behavioral Therapy

- CBT is a form of “talk therapy” based on principles of social learning theory.
  - Used to teach, encourage and support individuals in reducing or stopping their harmful drug use
  - Provides skills aimed at sustaining abstinence
  - Addresses negative thought patterns and helps to develop coping strategies to prevent relapse

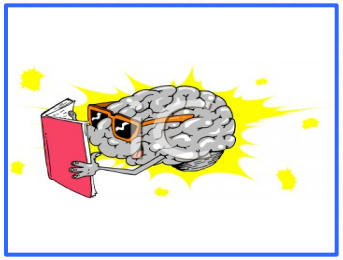
Exercise as a Treatment Intervention for Methamphetamine Dependence

Impact of Exercise on Individuals in Treatment for Methamphetamine Use Disorder Rawson, et al multiple studies

Exercise Group:
1h, 3 days/wk

N=69

Health Education Group:
1h, 3 days/wk



N=66

Exercise Summary

- For individuals in the first 100 days of meth recovery, exercise:
  - Improves physical conditioning
  - Reduces weight gain
  - Improves cardiovascular functioning (increases heart rate variability)
  - Reduces symptoms of anxiety and depression
  - Reduces craving for methamphetamine
  - Enhances recovery of dopamine system
  - Reduces relapse to methamphetamine post discharge (except in very heavy users)

Medications

Medications for Cocaine Use Disorder

Medications with positive studies and under consideration.

- topiramate*
- modafinil*
- bupropion*
- amphetamine salts
- disulfiram (mixed, worse retention)
- propranolol (WD)
- buprenorphine+naltrexone

Medications for Methamphetamine Use Disorder

Medications with positive studies and under consideration

Bupropion/naltrexone
mirtazapine

bupropion
naltrexone
methylphenidate
d-amphetamine
topiramate

Chan B, Freeman M, Ayers C, Korthuis PT, Paynter R, Kondo K, Kansagara D. A systematic review and meta-analysis of medications for stimulant use disorders in patients with co-occurring opioid use disorders. Drug Alcohol Depend. 2020 Nov 1;216:108193. doi: 10.1016/j.drugalcdep.2020.108193. Epub 2020 Aug 1. PMID: 32861136.

Discussion

- An examination of multiple classes of medications used for the treatment of cocaine and methamphetamine use disorders in people with OUD found no strong evidence that any medication was effective in increasing abstinence, reducing use, or improving retention.
- There is almost no evidence regarding treatment of methamphetamine use disorder in people with OUD.
- Antidepressants and disulfiram may worsen treatment outcomes when used for treatment of cocaine use disorders in patients with OUD.

Current implementation efforts with CM

- US Veterans Administration System uses CM, together with CBT and other services as the primary treatment for StimUD
- California initiating a $58 M CM program for 2022-2024.
- Montana and West Virginia pilot projects

- Thank you for your attention
- Questions?

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