Methamphetamine

Use & Its Treatment

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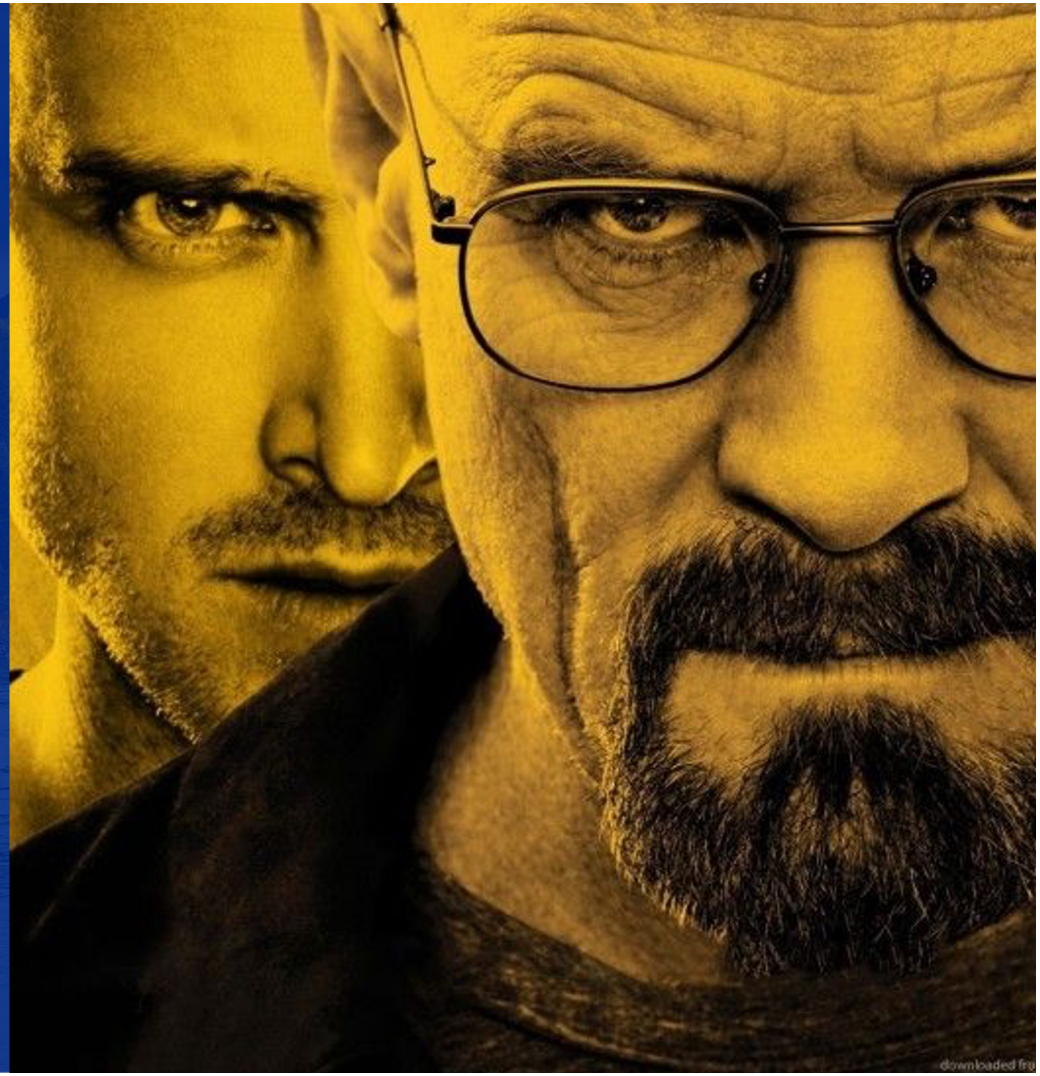
A Primary Care Approach to Treating SUD
May 29, 2024



Patient Case 1

HG is a 37-year-old man who lives between Sidney and Billings, MT who was recently diagnosed with cardiomyopathy (most likely meth-induced). He is currently unemployed and marginally housed, with a past psych hx of longstanding depressive symptoms, no prior hx of psychosis. Has prior h/o of IV heroin use and, more recently has been intermittently smoking fentanyl.

Patient Case 1

Oftentimes feels extreme anxiety and has thoughts, “that scare me… I think a group of people are stalking me… I don’t know who they are… but seeing them all over.”

Uses >1g of methamphetamine daily, remarks: “I thought I had it under control, recently I starting injecting… now I just can’t stop.”

Notes sparse fentanyl use, he is currently on methadone 120 mg PO qday.

Otherwise, he is currently off psychotropics: “only the meth really touches me.”

Notes some potential interest in use reduction/cessation but voices overall ambivalence, remarks:

> *“I mean… it’s awesome… it makes the sex great, but I was here at the hospital not long ago… I recently ended up here because of bad burns on my skin… I’m not sure how I got them… maybe I messed up putting bleach on my athlete’s foot”*

Objectives

1. Discuss the short & long-term effects of methamphetamine use
2. Review how methamphetamine works in the brain
3. Evaluate current forms of treatment for MUD
   → translate into treatment for patients with co-occurring OUD

Signs & Symptoms

Stimulant Intoxication

Behavioral & psychological symptoms

- Feeling "high," euphoria, restlessness, anxiety, agitation, psychosis, hyperactivity, hypervigilance, talkativeness, tension, alertness, grandiosity, anger, impaired judgment

Physical symptoms

- Pupil dilation, headache, bruxism, dyspnea, chest pain, tachycardia, ↑ BP, MI, tremor, hyperreflexia, motor tics, stereotyped movements, seizure activity, cerebral hemorrhage or infarct, N/V, myoglobinuria, acute renal failure, hyperthermia, rhabdomyolysis, death

Bath salts

- Euphoria, ↑ sociability & sex drive, paranoia, agitation, hallucinatory delirium, & psychotic and violent behavior

Stimulant Withdrawal

Withdrawal from stimulants causes symptoms opposite from those seen during intoxication (e.g., fatigue, hypersomnia, ↓ mood, ↑ appetite, & psychomotor retardation)

Feelings of depression may be severe enough to lead to suicidal ideation

Symptoms of craving for stimulants may persist for months, time to symptom resolution varies depending on the individual

Titus-Lay, E. Substance-Related Disorders. CPNP Psychiatric Pharmacotherapy Review. 2022.

Effects of Use

Clinical effects of methamphetamine are almost immediate

Short-term use

- ↑ energy and alertness
- ↓ need for sleep
- Euphoria and/or other mood changes: irritability, anxiety, aggression, and/or panic
- ↑ sexuality
- Excessive talking
- Tightened jaw muscles/ teeth grinding
- Dry mouth
- Loss of appetite
- Disorganized thinking
- Itching
- Sympathetic nervous system: diaphoresis, mydriasis, ↑ HR & other CV changes

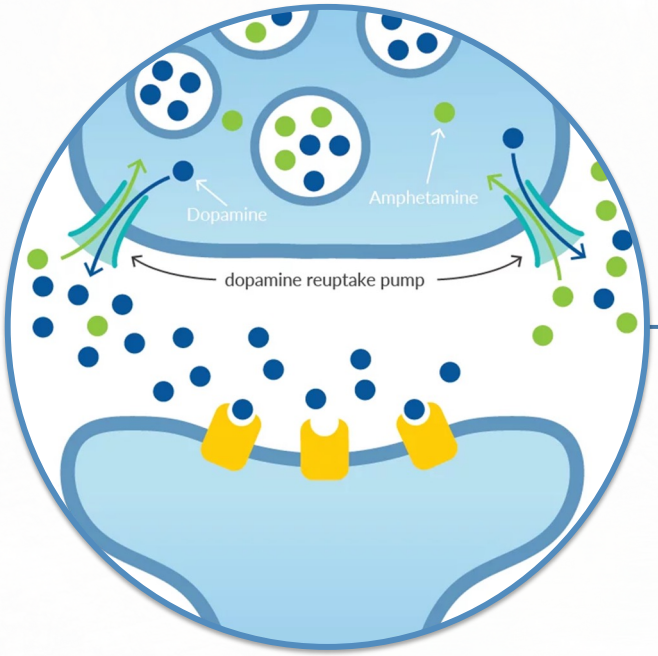
Long-term use

- **Psychosis**
- Sleep disruption/insomnia
- Apparent mania vs. mixed episode
- High risk sexual behavior/STIs
- Tooth decay/damaged dentition
- Meth sores from skin picking
- Cognitive Impairment
- Cardiovascular complications:
  - Malignant hypertension, arrhythmias, aortic dissection, myocardial infarction, stroke, & cardiomyopathy
  - **↑ mortality**

NIDA. "What are the long-term effects of methamphetamine misuse?." National Institute on Drug Abuse, 12 Jan. 2022.;
NIDA. "What are the immediate (short-term) effects of methamphetamine misuse?." National Institute on Drug Abuse, 13 Apr. 2021.

Pathophysiology

Methamphetamine Mechanism of Action (MOA)



Highly potent psychostimulant that ↑ synaptic levels of DA >> NE, & 5HT through ↑ release & blocked reuptake

- ↑ DA production
- ↑ availability of DA & NE
- Reversal of neurotransmitter transport through plasma membrane
- Blocking the activity & expression of transporters (especially for DA)
- Inhibiting enzymatic breakdown of neurotransmitters

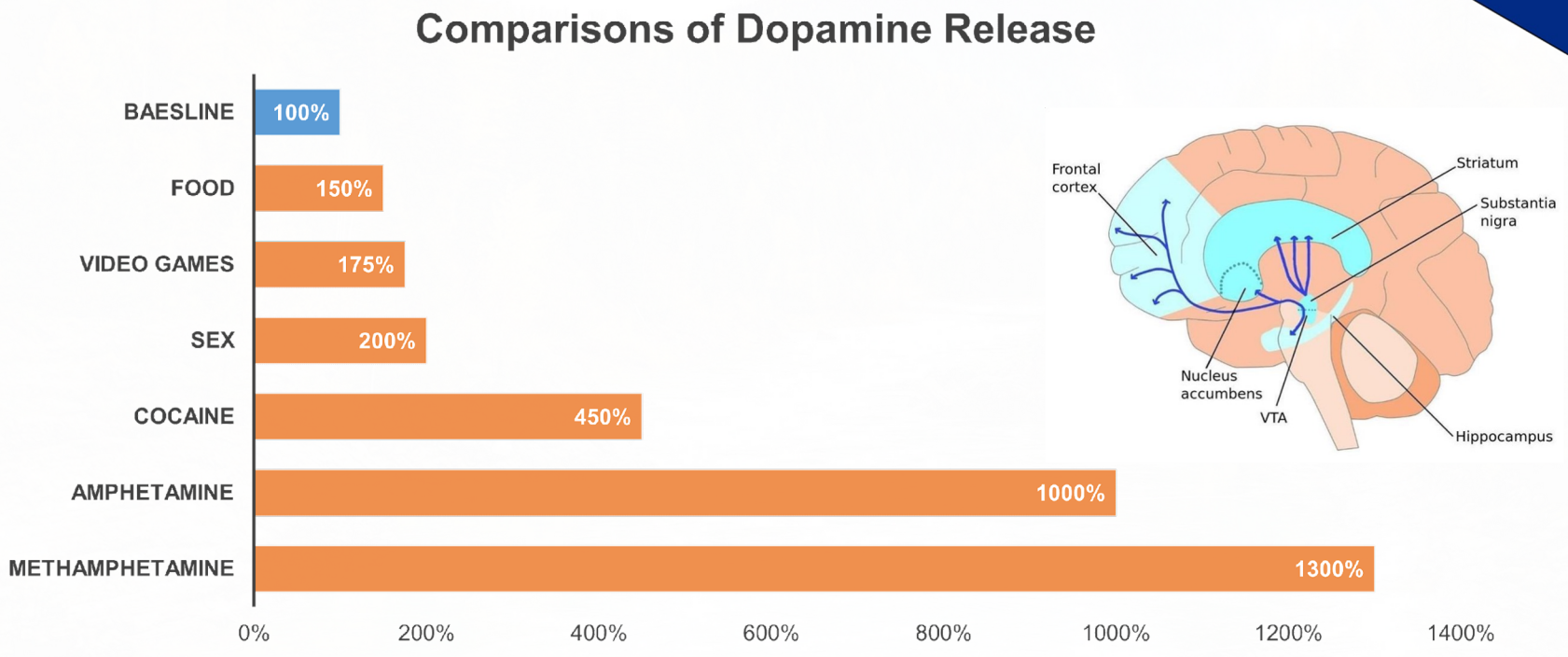
Net Effect: *¡Mucha Dopamina!*

DA: dopamine; NE: norepinephrine; 5HT: serotonin

Titus-Lay, E. Substance-Related Disorders. CPNP Psychiatric Pharmacotherapy Review. 2022.

Pathophysiology of Stimulant UD

Dopamine Release from Natural Rewards vs Stimulants



Di Chiara et al., Neuroscience, 1999.; Fiorino and Phillips, J. Neuroscience, 1997.; Ferguson, 2018.


Psychosocial & Pharmacologic Treatment
Options for StimUD

Treatment Guidance

There are no medications FDA approved for StimUD

Stimulant Intoxication	Symptomatic management – monitor vital signs for ↑ HR, temperature, & BP – may need IV hydration	Provide a quiet & cool environment – helps ↓ agitation & overreaction to external stimuli with close observation
	Benzodiazepines – symptomatic approach for anxiety, agitation, seizures, & HTN	
	Antipsychotics	Most patients with stimulant-induced psychosis recover spontaneously – may use antipsychotics until psychosis clears
Stimulant Withdrawal No specific medication management recommendations	Symptomatic treatment (e.g., ↓ depressive symptoms) may prevent relapse	
	Withdrawal symptoms (e.g., cravings, depression) may persist if untreated	
	Medication management with antidepressants may be necessary for significant depressive symptoms	

Titus-Lay, E. Substance-Related Disorders. CPNP Psychiatric Pharmacotherapy Review. 2022.

Evidence-based Psychosocial Interventions

First-line treatment for MUD

Individual or Group Drug Counseling

- Outpatient & inpatient outpatient therapy (IOT)

Cognitive Behavioral Therapy (CBT)

Motivational Interviewing

Behavioral Approaches

- Contingency Management (NNT = 5)
  - Behavior modification intervention which reinforces desired behaviors through incentives
- Cue Exposure Therapy
  - A behavioristic psychological approach to treating SUDs whereby individuals are exposed to relevant drug cues to extinguish conditioned responses

Community Reinforcement Approach

- Focus on healthier, more adaptive ways to meet social & emotional needs than substance use by providing rewards or withholding negative consequences in response to measurable behavior

Clinical Psychology Review 2017;57:195-207.; Addiction. 2004 Jun;99(6):708-17.; Arch Gen Psychiatry. 1999;5(6):493.; J Consult Clin Psychol. 1998 Oct;66(5):832-7.;
NNT = number needed to treat

The NEW ENGLAND JOURNAL of MEDICINE

Bupropion and Naltrexone in Methamphetamine Use Disorder

Madhukar H. Trivedi, M.D., Robrina Walker, Ph.D., Walter Ling, M.D., Adriane dela Cruz, M.D., Ph.D., Gaurav Sharma, Ph.D., Thomas Carmody, Ph.D., Udi E. Ghitza, Ph.D., Aimee Wahle, M.S., Mora Kim, M.P.H., Kathy Shores-Wilson, Ph.D., Steven Sparenborg, Ph.D., Phillip Coffin, M.D., M.I.A., et al.

Why naltrexone + bupropion for MUD?

- Naltrexone:
  - Reduces reinforcing effects of amphetamine, craving
  - May decrease likelihood of relapse
- Bupropion:
  - Reduces cue craving
  - May decrease methamphetamine use

Study design:

- Multisite, double-blind, two-stage, placebo-controlled trial
- 403 adults with moderate to severe MUD
  - IM Naltrexone 380 mg every 3 weeks
  - Oral extended-release bupropion 450 mg per day
- Included psychosocial component

N Engl J Med 2021;384:140-53.

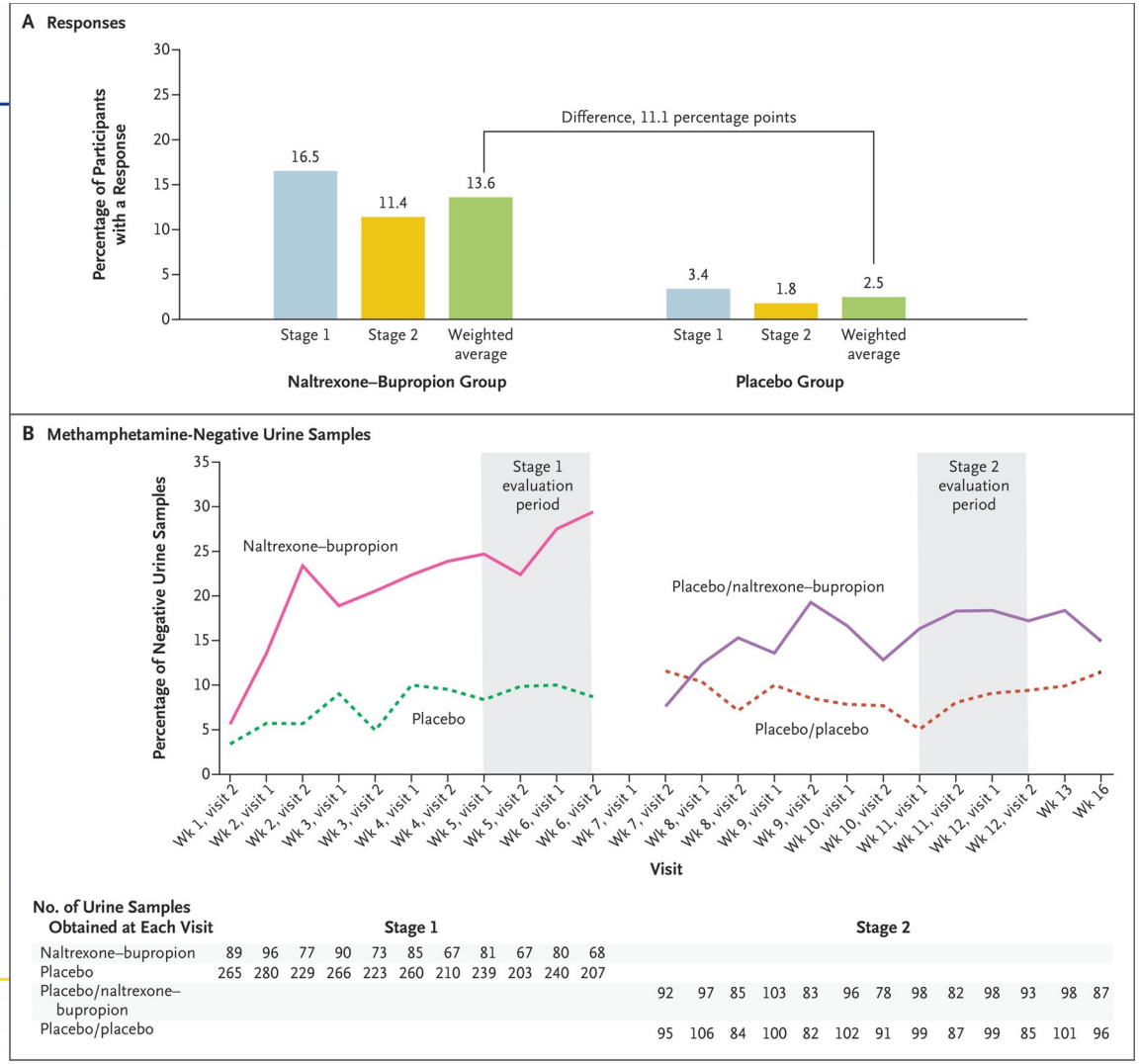
Study Results

Weighted avg. response* across the 2 stages:

- 13.6% for naltrexone–bupropion
- 2.5% with placebo
- Overall treatment effect of 11.1% (p<0.001)
- NNT = 9

**Response = at least 3/4 urine drug screens negative for methamphetamine*

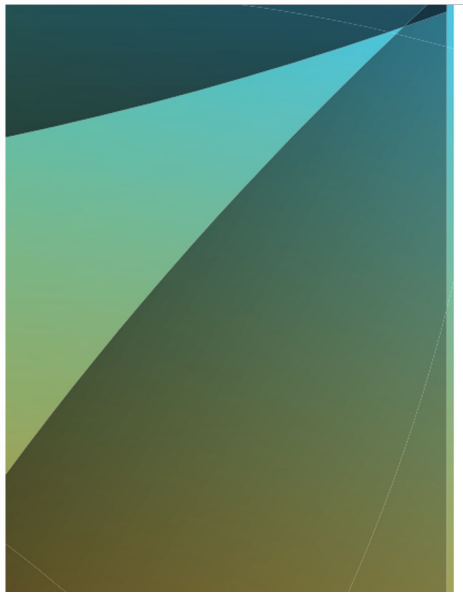
N Engl J Med 2021;384:140-53.; NNT = number needed to treat



No. of Urine Samples Obtained at Each Visit	Stage 1											Stage 2											
Naltrexone–bupropion	89	96	77	90	73	85	67	81	67	80	68												
Placebo	265	280	229	266	223	260	210	239	203	240	207												
Placebo/naltrexone–bupropion												92	97	85	103	83	96	78	98	82	98	93	98	87
Placebo/placebo												95	106	84	100	82	102	91	99	87	99	85	101	96

American Academy *of* Addiction Psychiatry

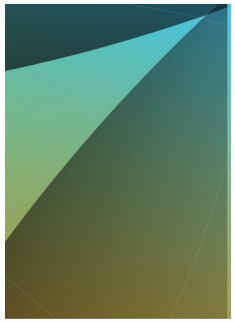
Translating Science. Transforming Lives.



The ASAM/AAAP

CLINICAL PRACTICE GUIDELINE ON THE

Management of Stimulant Use Disorder



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20. For patients with ATS use disorder, clinicians can consider prescribing a long-acting MPH formulation to promote reduced use of ATS (*Low certainty, Conditional Recommendation*).

    a. Clinicians can give long-acting MPH formulations additional consideration for patients with moderate or higher frequency of ATS use at treatment start (ie, 10 or more days per month; *Low certainty, Conditional Recommendation*).

    b. Clinicians can give long-acting MPH formulations additional consideration for patients with co-occurring ADHD, as these medications can also reduce ADHD symptoms (*Low certainty, Conditional Recommendation*).

    c. When prescribing a long-acting MPH formulation, clinicians can consider dosing at or above the maximum dose approved by the FDA for the treatment of ADHD to effectively reduce ATS use (*Low certainty, Weak Recommendation*).

The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder. J Addict Med. 2024 May-Jun 01;18(1S Suppl 1):1-56. doi: 10.1097/ADM.0000000000001299. PMID: 38669101

Methylphenidate as Treatment of MUD: Cited Sources

The ASAM/AAAP
CLINICAL PRACTICE GUIDELINE ON THE
Management of Stimulant Use Disorder

1. Ling W, Chang L, Hillhouse M, et al. Sustained-release methylphenidate in a randomized trial of treatment of methamphetamine use disorder: Methylphenidate for methamphetamine use. Addiction. 2014;109(9):1489-1500. doi:10.1111/add.12608 371.

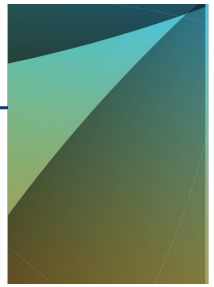
2. Miles SW, Sheridan J, Russell B, et al. Extended-release methylphenidate for treatment of amphetamine/methamphetamine dependence: a randomized, double-blind, placebo-controlled trial: Methylphenidate in amphetamine dependence. Addiction. 2013;108(7):1279-1286. doi:10.1111/add.12109 372.

3. Minařík J, Gabrhelík R, Malcolm R, Pavlovská A, Miller P. Methylphenidate substitution for methamphetamine addiction and implications for future randomized clinical trials: a unique case series. J Subst Use. 2016;21(4):435-438. doi:10.3109/14659891.2015.1045047 373.

4. Rezaei F, Emami M, Zahed S, Morabbi MJ, Farahzadi M, Akhondzadeh S. Sustained release methylphenidate in methamphetamine dependence treatment: a double-blind and placebo-controlled trial. DARU J Pharm Sci. 2015;23(1):2. doi:10.1186/s40199- 015-0092-y

The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder. J Addict Med. 2024 May-Jun 01;18(1S Suppl 1):1-56. doi: 10.1097/ADM.0000000000001299. PMID: 38669101

Methylphenidate (MPH) as Treatment of MUD: Citations



The ASAM/AAAP
CLINICAL PRACTICE GUIDELINE ON THE
Management of Stimulant Use Disorder

Study	Study Design	N	Primary Outcome(s)	Demonstrated ↓Meth in UDS?	Other Finding	Commented on ADHD sx?	Comments
Ling et al., 2014	RCT	110	(i.) MA use self-reported for the last 30 days of trial and (ii.) UDS	+	No difference in retention with MPH	+	Higher ADHD sx burden in MPH group
Miles et al., 2013	RCT	79	(i.)self-reported days of MA use and (ii.) UDS	-	Higher retention with MPH	-	Screened for ADHD but % not noted
Minařík et al., 2016	Retrospective Cohort	24	Abstinence from meth	+	High co-occurrence of ADHD in treatment responders. Regular, low-dose meth users responded best.	+	ADHD dx via clinical interview or historic dx in childhood
Rezaei et al., 2015	RCT	56	(i.) Methamphetamine craving and (ii.) UDS	+	Decreased meth cravings with MPH	+	Excluded childhood ADHD dx

The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder. J Addict Med. 2024 May-Jun 01;18(1S Suppl 1):1-56. doi: 10.1097/ADM.0000000000001299. PMID: 38669101

ADDICTION SSA SOCIETY FOR THE STUDY OF ADDICTION

Review

Pharmacotherapy for methamphetamine/amphetamine use disorder—a systematic review and meta-analysis

Brian Chan, Michele Freeman, Karli Kondo, Chelsea Ayers, Jessica Montgomery, Robin Paynter,

Why methylphenidate for MUD?

- Design: Systematic review and meta-analysis of pharmacotherapy options for treating methamphetamine / amphetamine use disorder.

- Key Results:

  → Methylphenidate: low-strength evidence suggests that methylphenidate may reduce MA use:

  - One study showed a slight increase in MA/A-negative urine drug screens (UDS) from 2.8% to 6.5% (p=0.008).
  - Another study showed an improvement from 16% to 23% in MA/A-negative urine drug screens, with a significance level of p=0.04. Note: high rate of co-occurring ADHD**

*Tiihonen J., Kuoppasalmi K., Fohr J. et al. A comparison of aripiprazole, methylphenidate, and placebo for amphetamine dependence. Am J Psychiatry 2007; 164: 160–2.

**Konstenius M., Jayaram-Lindstrom N., Guterstam J., Beck O., Philips B., Franck J. Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. Addiction 2014; 109: 440–9.

Chan, Brian, et al. "Pharmacotherapy for methamphetamine/amphetamine use disorder—a systematic review and meta-analysis." Addiction 114.12 (2019): 2122-2136.

Return to Patient Case 1

Patient Case 1

HG is a 37-year-old man who lives between Sidney and Billings, MT who was recently diagnosed with cardiomyopathy (most likely meth-induced). He is currently unemployed and marginally housed, with a past psych hx of longstanding depressive symptoms, no prior hx of psychosis. Has prior h/o of IV heroin use and, more recently has been intermittently smoking fentanyl.

Patient Case 1

Oftentimes feels extreme anxiety and has thoughts, “that scare me… I think a group of people are stalking me… I don’t know who they are… but seeing them all over.”

Uses >1g of methamphetamine daily, remarks: “I thought I had it under control, recently I starting injecting… now I just can’t stop.”

Notes sparse fentanyl use, he is currently on methadone 120 mg PO qday.

Otherwise, he is currently off psychotropics: “only the meth really touches me.”

Notes some potential interest in use reduction/cessation but voices overall ambivalence, remarks:

> *“I mean… it’s awesome… it makes the sex great, but I was here at the hospital not long ago… I recently ended up here because of bad burns on my skin… I’m not sure how I got them… maybe I messed up putting bleach on my athlete’s foot”*

How do you proceed?

Select all that apply:

1. Insist on abstinence from meth prior to prescribing any medication
2. Tolerate meth use so long as he is only using < 1 g daily
3. Prescribe bupropion and IM naltrexone as medication-assisted treatment (MAT) for meth use disorder
4. Start methylphenidate as MAT for meth use d/o
5. Engage in motivational interviewing targeting meth use reduction/cessation
6. Proceed to treat psychosis and depression with evidence-based pharmacological treatment
7. Provide contingency management

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5. **Engage in motivational interviewing targeting meth use reduction/cessation**
6. **Proceed to treat psychosis and depression with evidence-based pharmacological treatment**
7. **Provide contingency management**

How do you proceed?

Discharge Med Regimen

1. Abilify 20 mg PO qHS (following Olanzapine 10 mg PO qHS during first few days of hospitalization)
2. Sertraline 50 mg PO qday with plan to likely increase to 100 mg PO qday in the near future

F/U:

Referred to EMCMHC to establish care via their TRUST program's SUD counseling initiative that features **contingency management**

Case 2

BN is a 38-year-old divorced woman with a history of criterion A trauma, trauma-related symptoms as well as current alcohol (began at age 15), cannabis, IV methamphetamine use, fentanyl and other opioid use. She recently lost her job and is currently homeless secondary to the financial impact of her use. She has 3 children in grade school.

- She recently started inpatient treatment and left AMA after 3 days and has continued to use many substances.
- She presents to care noting that she wants treatment to become stable and succeed in her new job at a fast food restaurant.

Case 2 Continued

On assessment she notes:

- ❑ a history of suicide attempt 8 years ago by hanging
- ❑ significant concern as to whether she has Bipolar D/O as she is constantly anxious, moods are up and down and she is very “stressed out” and has difficulty sleeping
- ❑ Reports dx of ADHD and prior treatment with methylphenidate in high school.
- ❑ She is motivated to start her new job and wants to start classes at the community college and “turn her life around for her kids.”
- ❑ Last use: 8 hours ago: Oxycodone 30mg + IV methamphetamine (uncertain how much)

How would you proceed?

Select all that apply:

1. Insist on abstinence from substances prior to prescribing any medication.

2. Prescribe Narcan

3. Prescribe buprenorphine as MOUD

4. Engage in motivational interviewing targeting substance use reduction/cessation

5. Educate regarding benefits of mutual-help group involvement

6. Proceed to treat depression, anxiety, ADHD and trauma-related symptoms with pharmacotherapy

7. Engage in Contingency Management

How would you proceed?

Select all that apply:

1. Insist on abstinence from substances prior to prescribing any medication.

2. Prescribe Narcan

3. Prescribe buprenorphine as MOUD

4. Engage in motivational interviewing targeting substance use reduction/cessation

5. Educate regarding benefits of mutual-help group involvement

6. Proceed to treat depression, anxiety, ADHD and trauma-related symptoms with pharmacotherapy (including methylphenidate or Vyvanse for tx of ADHD)

7. Engage in Contingency Management

Urine Tox. Results after MOUD start

Day 1: 04/2021 -Initiation of Treatment
Oxycodone: 223
Methamphetamine: 377
THC: 15

Week 1:
Norbuprenorphine/Buprenorphine: 1000/490
Amphetamine: 438
Methamphetamine: 521
THC: 19

Week 2:
Norbuprenorphine/Buprenorphine: 113/198
THC: 110
Amphetamine: 438
Methamphetamine: 521

Urine Tox. Results after MOUD start *continued*

Week 3:
Hydrocodone: + 146
Norbuprenorphine/buprenorphine: 587/337
Amphetamine: 108
Methamphetamine: 231
THC: 177

Week 4:
Norbuprenorphine/buprenorphine: 617/421
Amphetamine: 0
Methamphetamine: 0
THC: 144

Objectives

1. Discuss the short & long-term effects of methamphetamine use
2. Review how methamphetamine works in the brain
3. Evaluate current forms of treatment for MUD
   → translate into treatment for patients with co-occurring OUD

Objectives → *Takeaways*

1. Discuss the short & long-term effects of methamphetamine use
   Strong stimulant, altered mood, psychosis and long-term cognitive impact
2. Review how methamphetamine works in the brain
   Massive synaptic surge of dopamine
3. Evaluate current forms of treatment for MUD

   Psychosocial (CM) has greatest impact, possible place for naltrexone IM + bupropion and methylphenidate (especially if patient has co-occurring ADHD and is otherwise appropriate)

   → translate into treatment for patients with co-occurring OUD

   Contingency Management *(naltrexone is frequently NOT a viable option due to opioid agonist therapy)*

   MOUD→ *improved stability associated with decreased meth use*

   Treat co-occurring disorders

Questions?

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