Treating Methamphetamine Use Disorder

AAAP/ASAM Guidelines → Implications for our patients

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CEO/Addiction Psychiatrist, 406 Recovery
Consultant, MPCA & CMS

A Primary Care Approach to Treating Substance Use Disorders
March 19, 2025

406Recovery.Care

Disclosures:

Nature of Relationship	*Name of Organization*
CEO/Co Founder	*406 Recovery (Nonprofit)*
Consultant	*Community Medical Services*
Consultant	*MPCA (Nonprofit)*

Objectives

1. Acknowledge: history & epidemiology of methamphetamine use
2. Discuss the short & long-term effects of methamphetamine use
3. Review how methamphetamine works in the brain
4. Evaluate current forms of treatment for MUD

   → The ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder

Patient Case 1

HG is a 37-year-old man who lives between Sidney and Billings, MT who is admitted for endocarditis in the setting of IV meth use. He 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

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:

“Meth is 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”

Medication Assisted Treatment (MAT) is available for most SUDs

- **Stimulant Use Disorder**: Case management, motivational interviewing, Vivitrol (naltrexone IM) + bupropion for meth use (perhaps methylphenidate as well- *even for patients without co-occurring ADHD)*
- **AUD**: naltrexone, gabapentin, disulfiram, acamprosate
- **Opioid Use Disorder (OUD)**: methadone, buprenorphine, naltrexone
- **Kratom**: buprenorphine

*Note for most SUDs: motivational interviewing & 12-step facilitation (i.e. AA, NA) = crux of tx

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Twin Peaks of Treatment Efficacy:

→ ***Relative Efficacy and Role of MAT varies greatly by SUD***

Medication Assisted Treatment

Psychosocial Interventions

Opioid Use Disorder

Medication Assisted Treatment

Psychosocial Interventions

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Methamphetamine Use Disorder

Medication Assisted Treatment

Psychosocial Interventions

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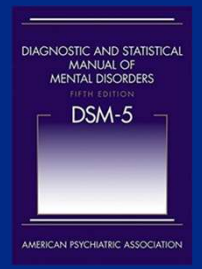
DSM 5 Diagnostic Criteria

Stimulant Use Disorder (e.g. Methamphetamine Use Disorder)



A problematic pattern of amphetamine-type substance, cocaine, or other stimulant use leading to clinically significant impairment or distress, as manifested by ≥2 of the following, occurring within a 12-month period:

1. Stimulants are often taken in larger amounts or over a longer period than was intended
2. There is a persistent desire or unsuccessful efforts to cut down or control stimulant use
3. A great deal of time is spent in activities necessary to obtain, use or recover from the stimulant
4. Craving, or a strong desire or urge to use the stimulant
5. Recurrent stimulant use resulting in a failure to fulfill major role obligations at work, school, or home
6. Continued use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the stimulant
7. Important social, occupational, or recreational activities are given up or reduced because of stimulant use
8. Recurrent stimulant use in situations in which it is physically hazardous
9. Use is continued despite having a persistent/recurrent physical/psychological problem that is caused/exacerbated by the stimulant
10. Tolerance, as defined by either of the following:
    a. A need for markedly ↑ amounts of the stimulant to achieve intoxication or desired effect
    b. A markedly diminished effect with continued use of the same amount of the stimulant
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for the stimulant
    b. The stimulant is taken to relieve or avoid withdrawal symptoms

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

Methamphetamine

A focus on the historical perspective

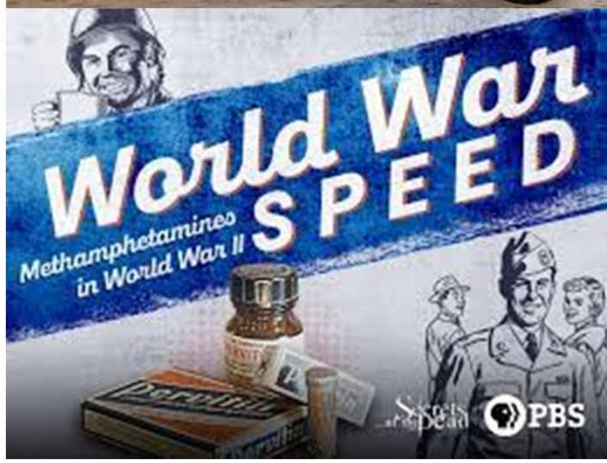
First synthesized from ephedrine in 1893 by Japanese chemist Nagai Nagayoshi

Starting in 1938, Germany began mass marketing methamphetamine under the name “Pervitin”

- Available over the counter

Central role in World War II

- All branches of the combined Wehrmacht armed forces of the Third Reich used it to help with ↑ energy/wakefulness
- Deleterious effects were noticed including agitation, rage & violence



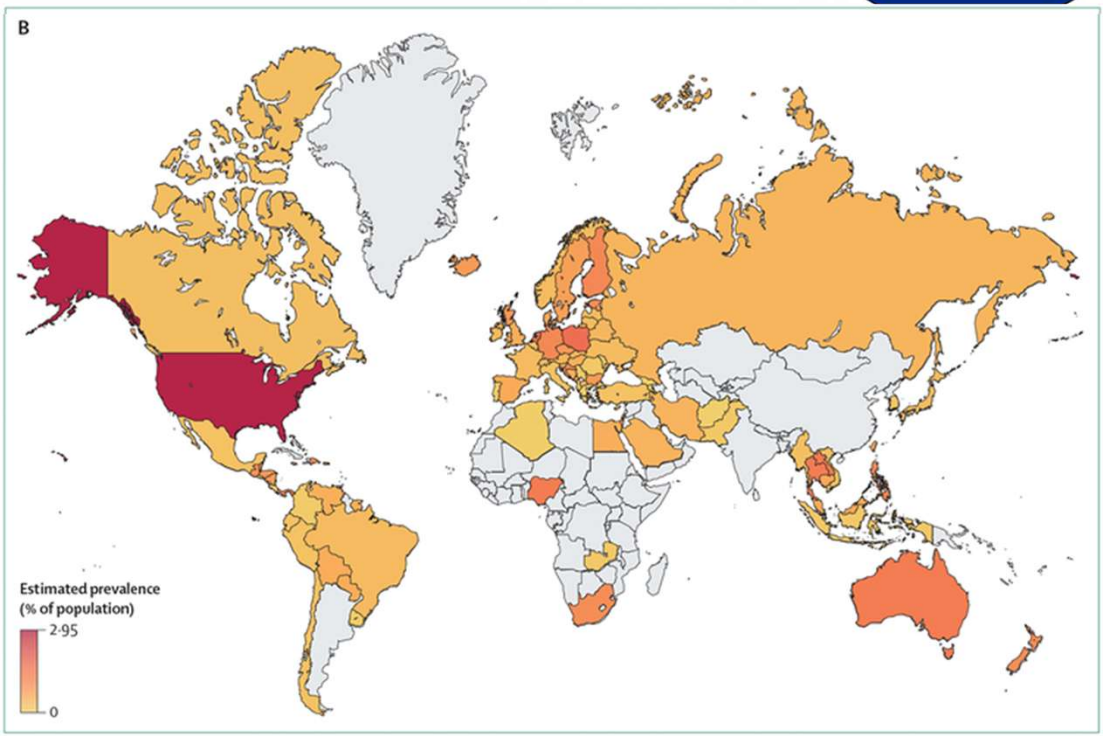
Bull Anesth Hist. 2011 Apr;29(2):21-32.; The Journal of Interdisciplinary History. 2011 Aug;42(2):205-233.

Epidemiology of Use

Cocaine & amphetamines are 2 of the most widely used illicit drugs worldwide

- 2018 UN Office on Drugs & Crime World Drug report estimated (15–64-year-olds):
  - **18.2 million** people used **cocaine**
  - **34.2 million** people used **amphetamines**

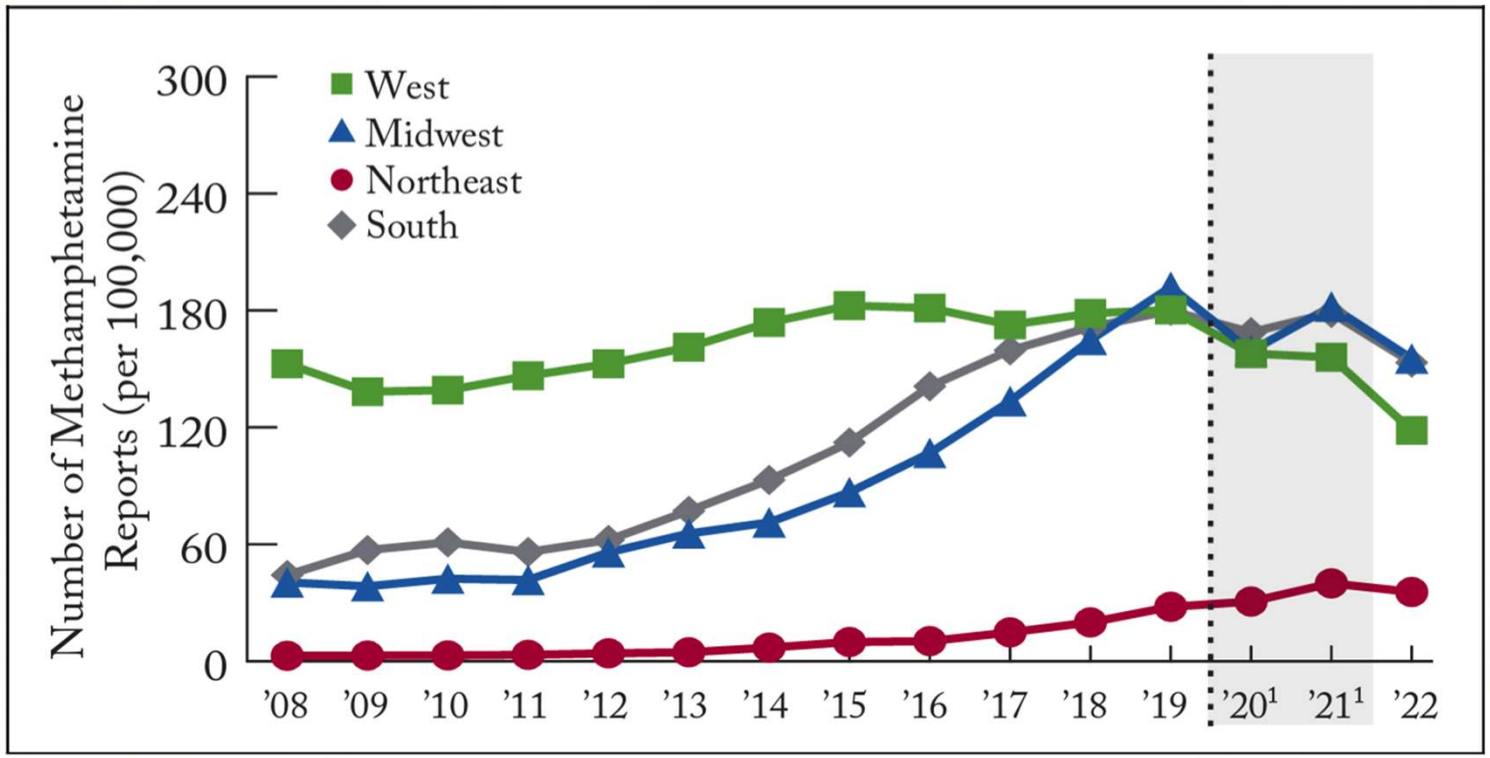
- The highest proportion of amphetamine use was in North America
  - **2.0 million** people (0.7% of U.S. population) used **methamphetamine** in the past year
  - **4.9 million** people (1.8% of U.S. population) misused **Rx stimulants** in the past year



Lancet. 2019 Nov 2; 394(10209): 1652–1667.; Lancet 2013; 382: 1564–74.; UN Office on Drugs and Crime. World drug report 2018 2018. https://www.unodc.org/wdr2018/

Regional Trends in Methamphetamine Use

Per 100,000 people aged 15 or older, Jan 2008-Dec 2022



NFLIS-Drug 2022 Annual Report: https://www.nflis.deadiversion.usdoj.gov/nflisdata/docs/2022NFLIS-DrugAnnualReport.pdf

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

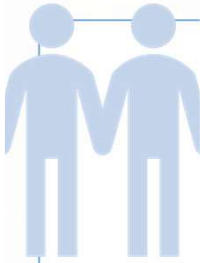
Long-term use

- **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.

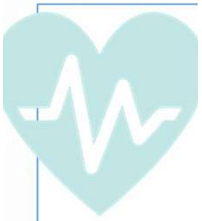
Comorbidities with Stimulant Use

Medical & Psychiatric Complications



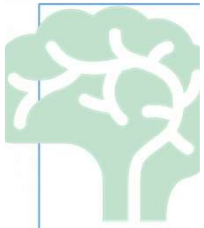
Methamphetamine use is 22.5-fold higher in MSM

- Is an independent risk factor for HIV/STI
- HIV incidence is 40-fold ↑



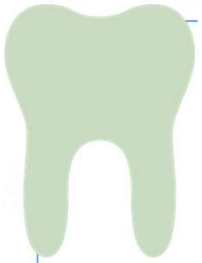
Proportion of total CHF patients having methamphetamine-associated cardiomyopathy is increasing

- Impaired cardiac function is correlated to methamphetamine use



Methamphetamine-induced psychosis occurs in 15-23% of individuals with recreational use

- May be up to 60% in dependent users in treatment settings



Periodontal disease

- Bruxism
- Dental caries
- Xerostomia

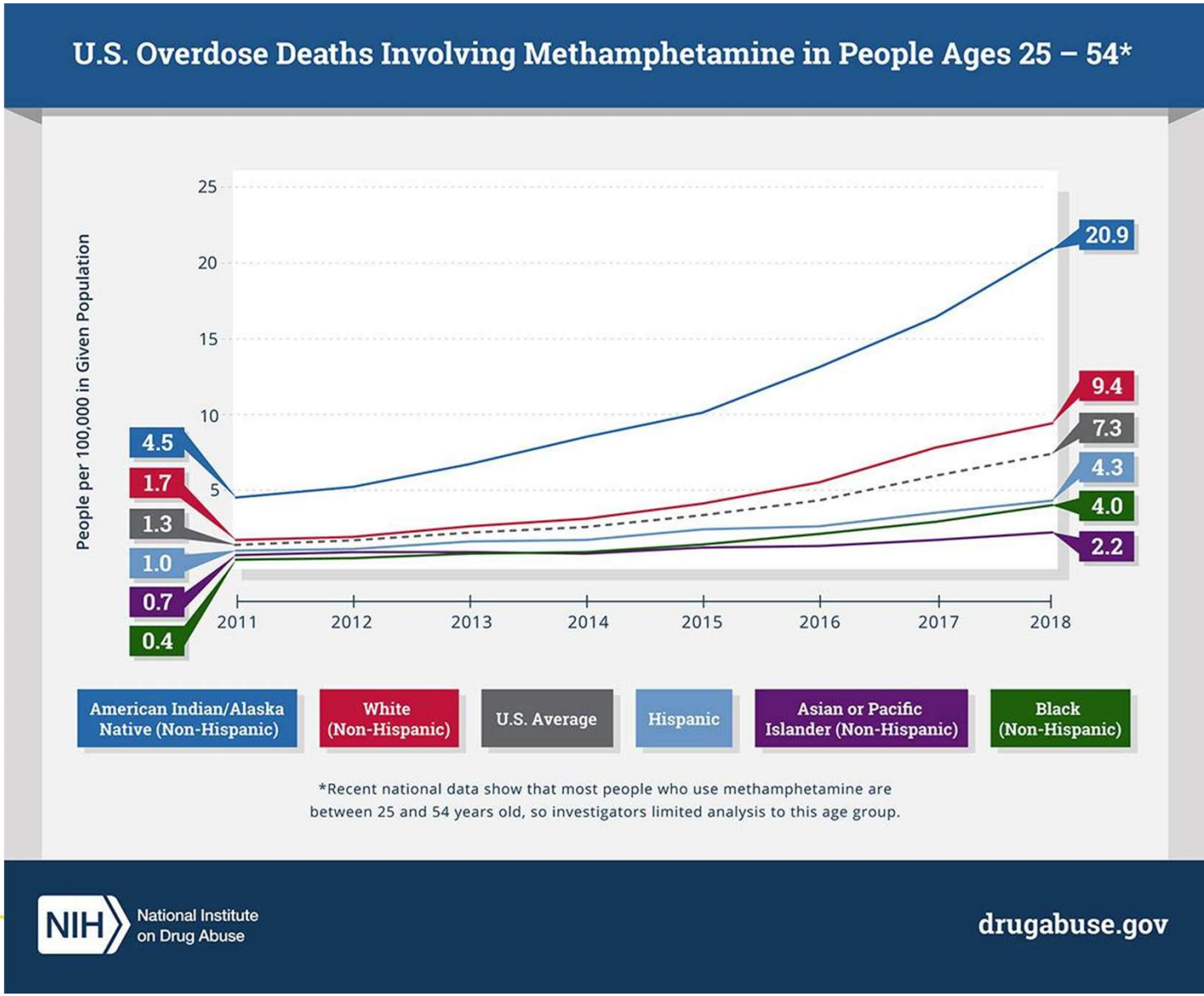
MSM: men who have sex with men; HIV: human immunodeficiency virus; STI: sexually transmitted infection; CHF: congestive heart failure

Arch Gen Psychiatry. 2011;68(11):1168-1175.; Sliman, et al., 2015; Arunogiri, et al., 2000.; New York Heart Association Functional Classification. Arch Intern Med. 1972;129(5):836.

Mortality Rates

Methamphetamine overdose deaths rise sharply nationwide

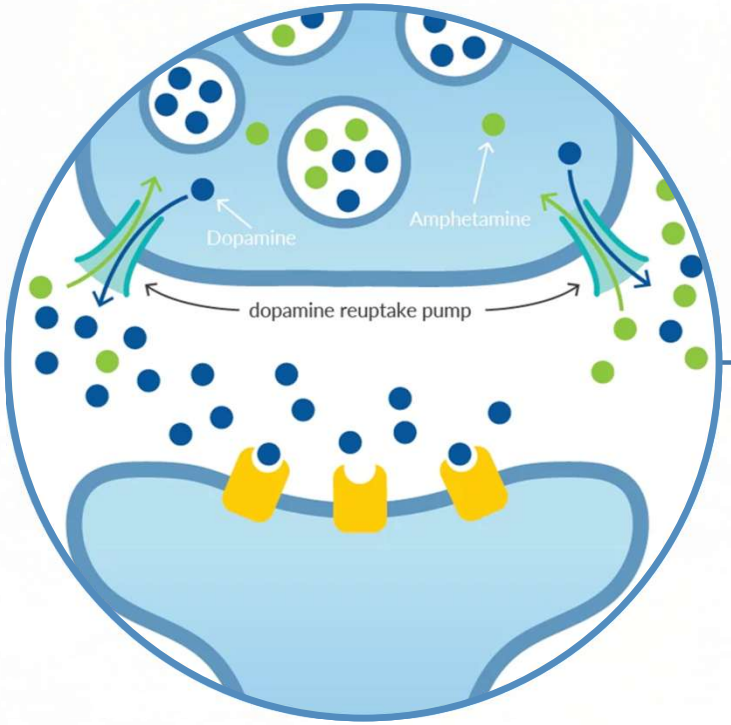
- American Indians & Alaska Natives had the ↑ death rates overall



JAMA Psychiatry.2020.4321 (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

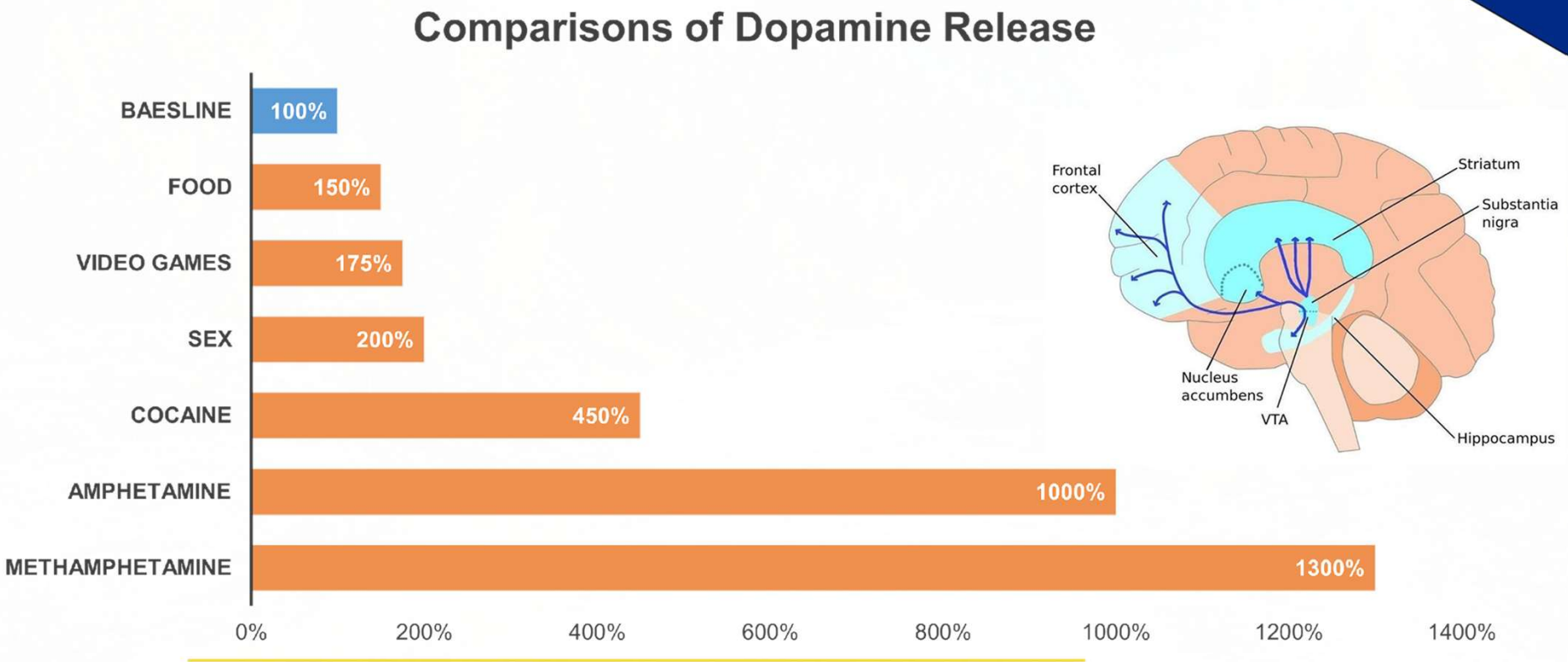
Net Effect: *¡Mucha Dopamina!*

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.

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	Symptomatic treatment (e.g., ↓ depressive symptoms) may prevent relapse	
No specific medication management recommendations	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.

Treatment for Methamphetamine Use Disorder

Evidence-based Psychosocial Interventions

First-line treatment for MUD per ASAM/AAAP

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

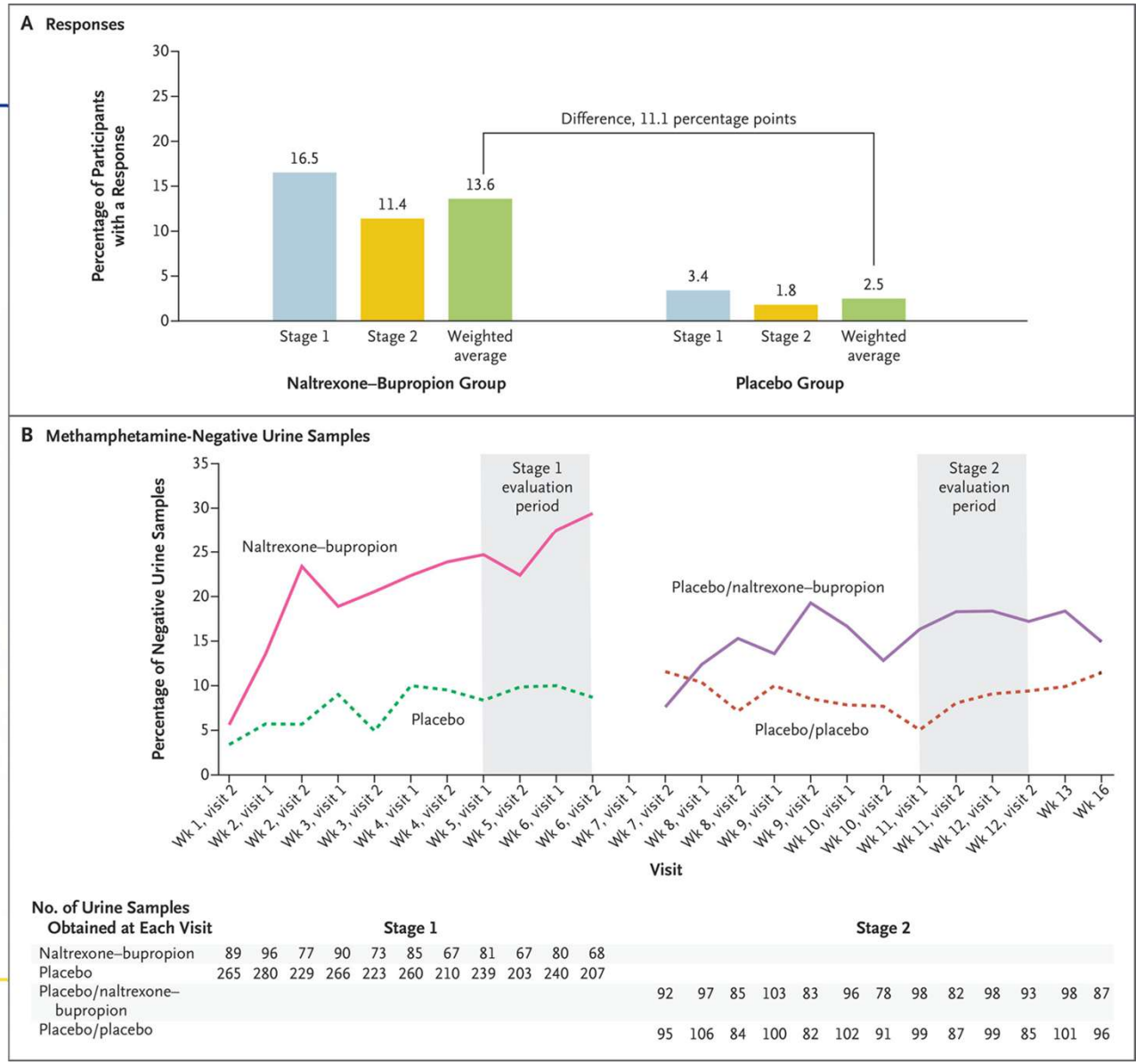
N Engl J Med 2021;384:140-53.

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*



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

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

American Academy *of* Addiction Psychiatry

Translating Science. Transforming Lives.

The ASAM/AAAP

CLINICAL PRACTICE GUIDELINE ON THE

Management of Stimulant Use Disorder

The ASAM/AAAP
CLINICAL PRACTICE GUIDELINE ON THE

Management of Stimulant Use Disorder

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.

1. 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.

1. 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.

1. 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

Methylphenidate (MPH) as Treatment of MUD:

Cited Sources

Study	Study Design	N	Primary Outcome(s)	Demonstrated decrease in Meth Use via 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, NO comment on %
Minařík et al., 2016	Retrospective Cohort	24	Abstinence from meth	+			
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.

Patient Case

HG is a 37-year-old man who lives between Sidney and Billings, MT who is admitted for endocarditis in the setting of IV meth use. He 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

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:

“Meth is 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

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**

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**

Objectives → *Takeaways*

1. Acknowledge: history & epidemiology of methamphetamine use
   Has been very prevalent for some time, since early 1900s
2. Discuss the short & long-term effects of methamphetamine use
   Strong stimulant, altered mood, psychosis and long-term cognitive impact
3. Review how methamphetamine works in the brain
   Massive synaptic surge of dopamine
4. 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)

   Contingency Management

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

   Treat co-occurring disorders

Questions?

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