Methamphetamine Use Disorders

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Faculty Disclosure

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- (Co)Edited Straight Talk About Psychiatric Medications for Kids (Guilford); ADHD Across the Lifespan (Cambridge), MGH Comprehensive Clinical Psychiatry (Elsevier), MGH Psychopharmacology and Neurotherapeutics (Elsevier)

Some of the medications discussed may not be FDA approved in the manner in which they are discussed including diagnosis(es), combinations, age groups, dosing, or in context to other disorders (e.g., substance use disorders)

LATEST NEWS

Overshadowed by opioids, meth is back and hospitalizations surge

Publish date: November 27, 2018

By Anna Gorman, Kaiser Health News

Clinical Psychiatry News

The number of people hospitalized because of amphetamine use is skyrocketing in the United States, but the resurgence of the drug largely has been overshadowed by the nation's intense focus on opioids.

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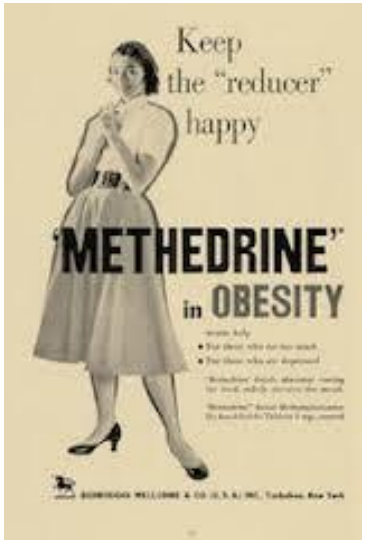
Amphetamine-related hospitalizations jumped by about 245% during 2008-2015, according to a recent study in the Journal of the American Medical Association. That dwarfs the rise in hospitalizations from other drugs, such as opioids, which were up by about 46%. The most significant increases were in Western states.

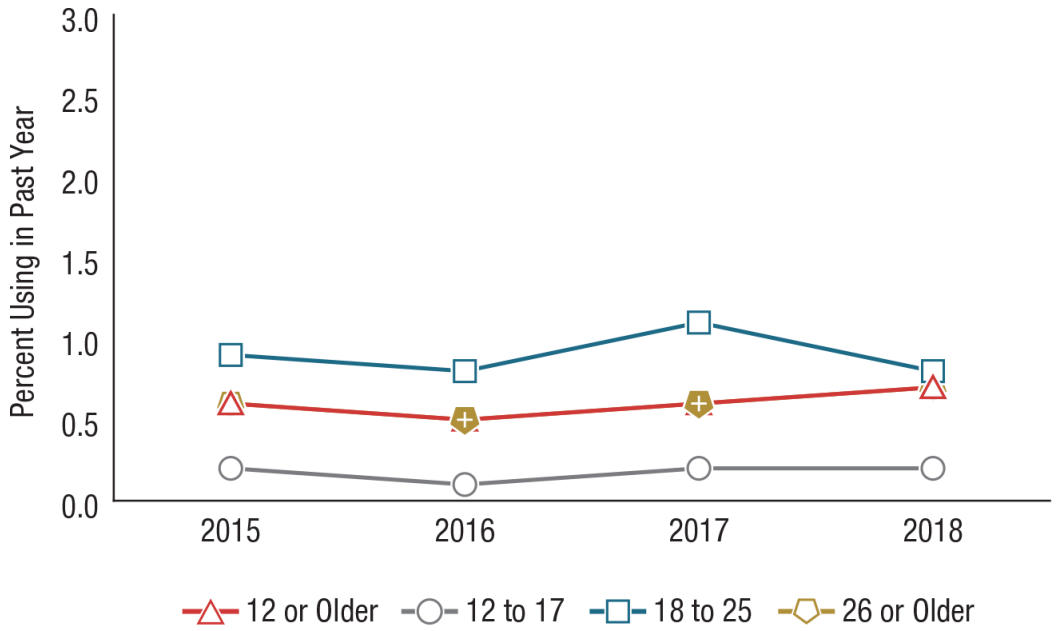
Methamphetamine: Epidemiology

- 4.7% lifetime use
- 0.4% past year; 0.2% past month
- Amphetamine type stimulants are second most frequently used illicit class in world
- Use in US for obesity, mood, & ADHD—use peaked in 1967



Courtney and Roy, Drug Alc Dep 2014: 143: 11-21

Past Year Methamphetamine Use among People Aged 12 or Older: 2015-2018



Age	2015	2016	2017	2018
12 or Older	0.6	0.5+	0.6	0.7
12 to 17	0.2	0.1	0.2	0.2
18 to 25	0.9	0.8	1.1	0.8
26 or Older	0.6	0.5+	0.6+	0.7

+ Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.

Results from the 2018 National Survey on Drug Use and Health: SAMHSA 2019

Methamphetamine Related Hospitalizations are Increasing

Figure 1. Amphetamine-Related Hospitalizations in the United States, 2003 to 2015

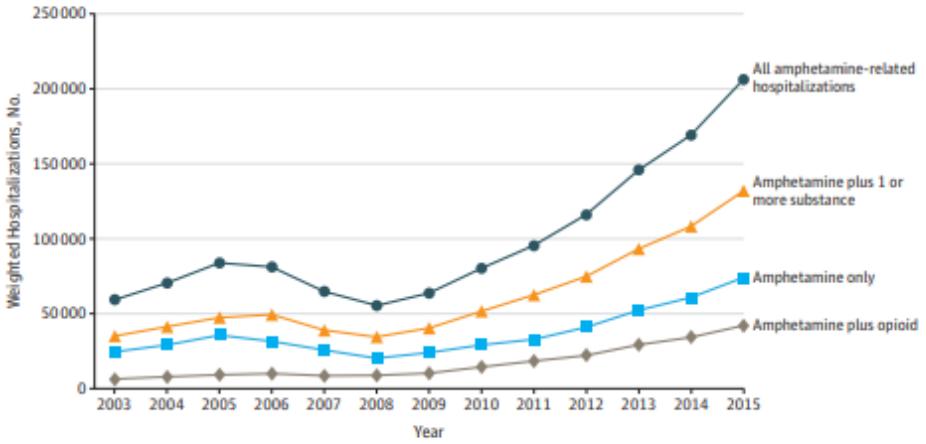
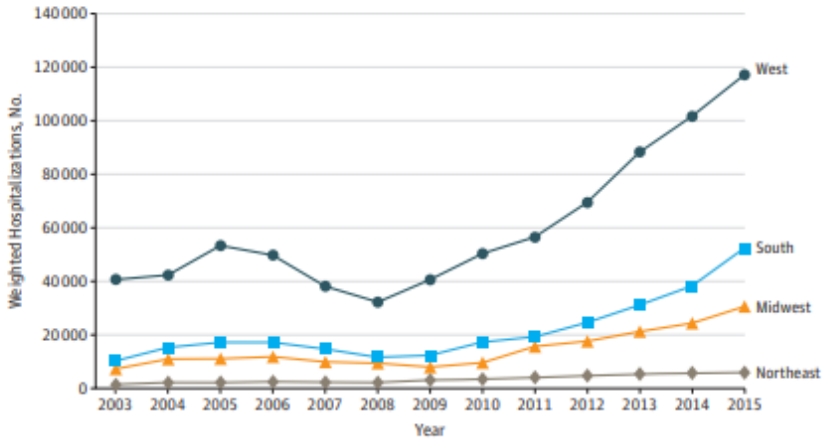


Figure 2. Amphetamine-Related Hospitalizations by US Census Region, 2003 to 2015



JAMA Network Open. 2018;1(6):e183758. doi:10.1001/jamanetworkopen.2018.3758

(Winkelman et al., JAMA, 2018)

Methamphetamine basics

- Mixture of pseudoephedrine and ephedrine
- New manufacturer decreased with reduced pseudoephedrine availability
- Cost down from 270$/gm in 2007 to 80$/gm currently
- Purity from 40% to 80%
- Available as powder (tablet) or crystalline form (“ice” “Crystal Meth”)
- Urine Detection: <4 days (7d if heavy use)
- High: immediate if smoked/injected; slower onset (<20 min) but long duration (8-12h) if po/intranasal/pr

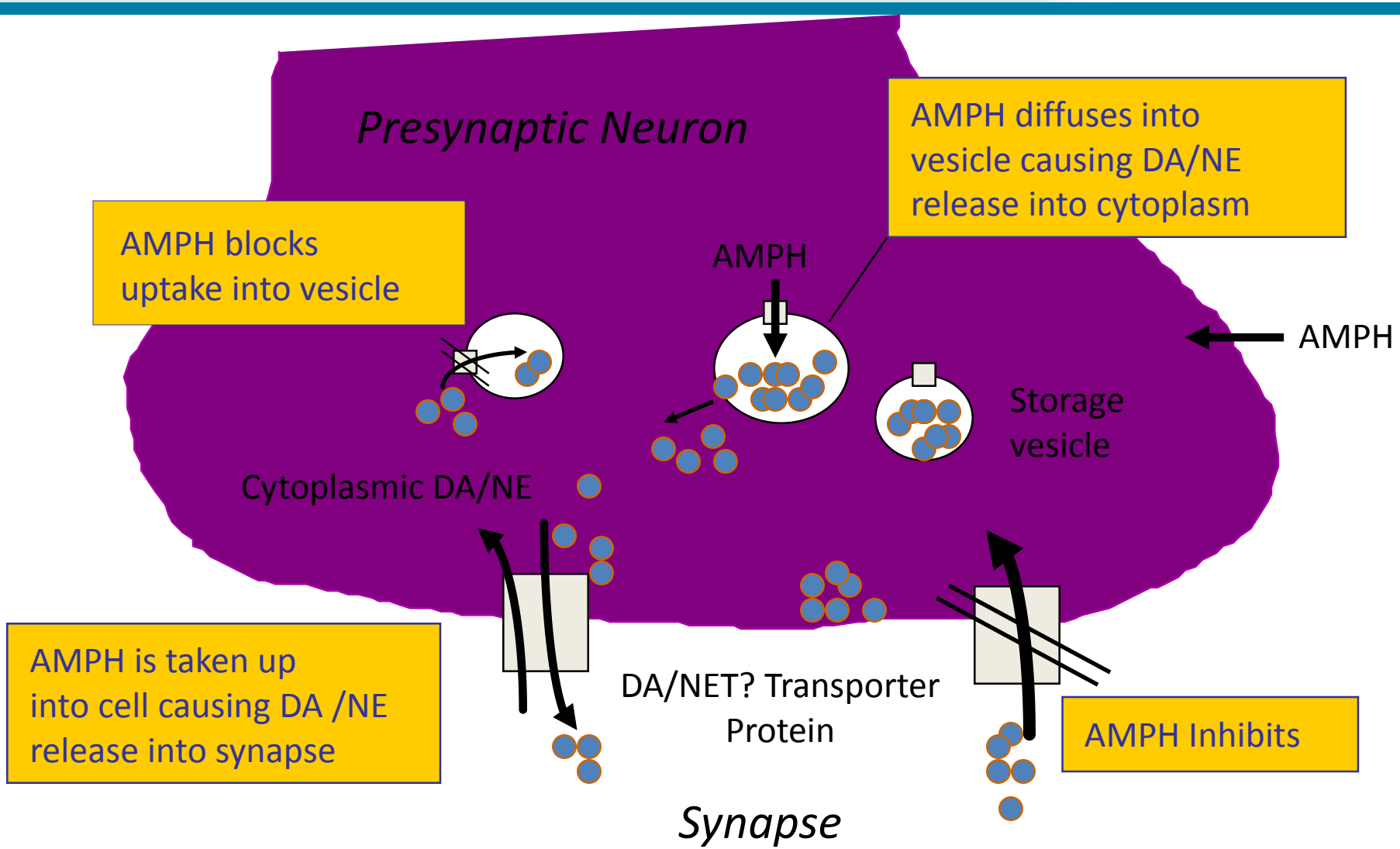
Methamphetamine neurobiology

Related to dopamine, norepinephrine and serotonin systems

- Presynaptic neuronal release with depletion
- Downstream involvement in opioid system

The Mechanisms of Action of (Meth)Amphetamine

(Wilens T. J Clin Psych 2006; Paulus and Stewart, JAMA Psychiatry 2020: 77:959-966).



Methamphetamine: Presentation

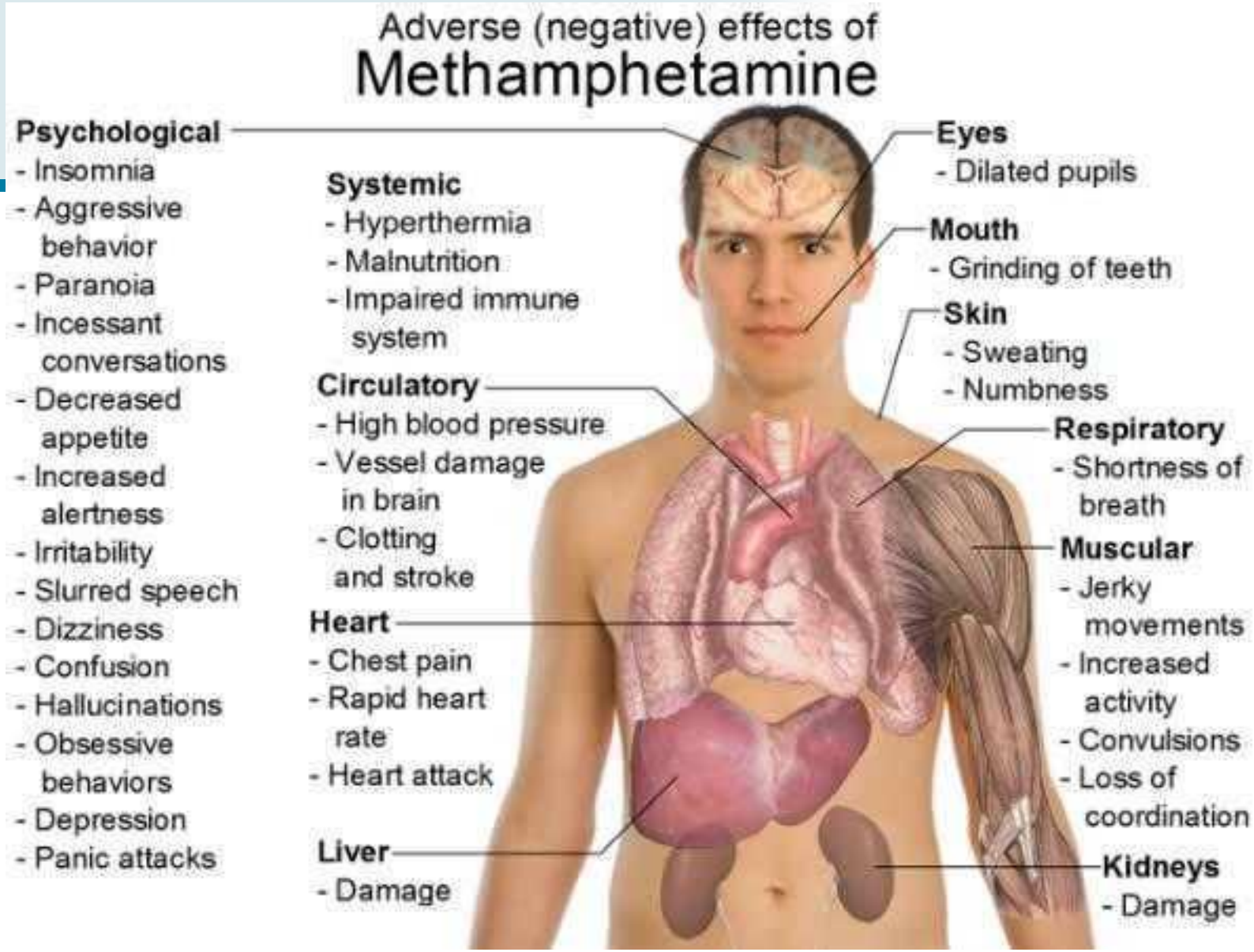
- Drawn face
- Weight loss
- Skin erosions
- Mucosal infarcts
- Skin erosions, scars
- MSE: Anhedonia/depression, anxiety, executive functioning deficits (prominent)
- Severe urges and cravings

Image: http://mentalhealthtreatment.net/blog/treating-the-physical-scars-of-crystal-meth-addiction-and-heroin-addiction-in-recovery/

Methamphetamine: Clinical Effects

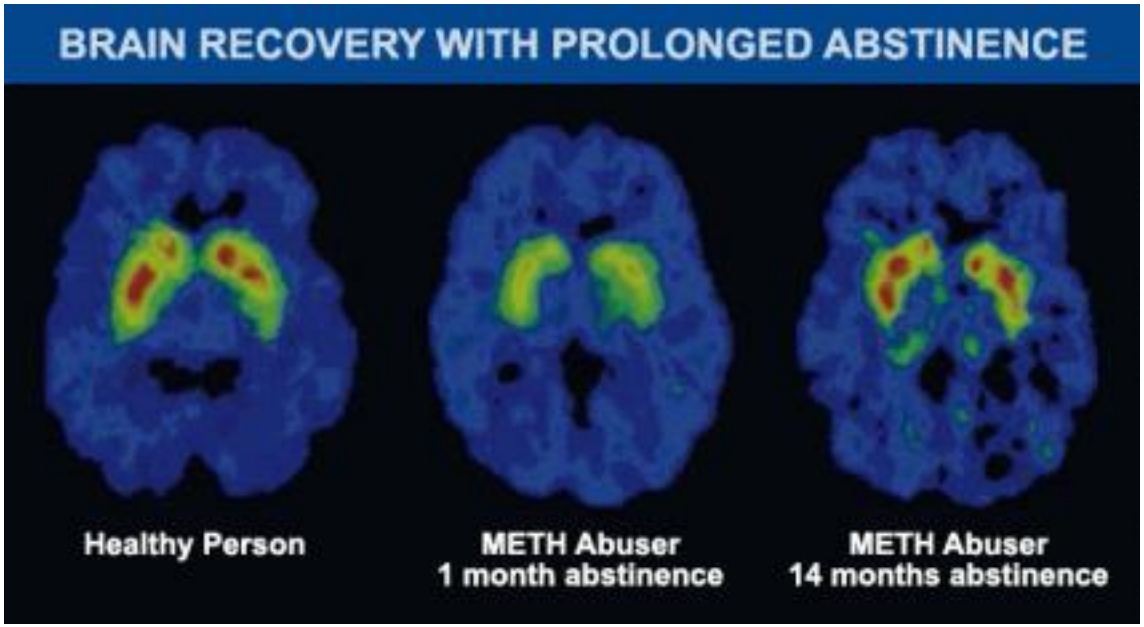
- Potent CNS Stimulation
  - Disinhibition, euphoria, elevation, enhanced sense of self, energy
  - Tachycardia, increased heart rate
- Adverse
  - Acute: anxiety, talkativeness, paranoia, psychosis, stereotypies/picking, dyskinesias, cardiovascular/stroke, hyperthermia, circulatory failure
  - Chronic: depression, neurotoxicity & neurocognitive dysfunction (executive dysfunction), cardiovascular
- Withdrawal (immediate to two+weeks)
  - Depression most common (anhedonia)

Courtney and Ray, Drug Alc Dep: 2014:143: 11-20



http://journeymalibu.com/drug-rehabs/methamphetamine-addiction-rehab/

Methamphetamine: Recovery Takes Time



Methamphetamine Treatment

- Some similarities to cocaine use disorder
- Amongst the most difficult SUD to treat
  - Engagement and Retention
- Inpatient management issues
- Most data suggest psychosocial interventions most effective
- Twelve Step/ Rational Recovery
- Cognitive Behavioral Therapy +/- MI
  - Caveat: Executive functioning deficits
- Contingency Management
- Time abstinent

Lee and Rawson, Drug Alc Rev 2008: 27: 309-17
Cadet and Gold, Curr Psychiatry, 2017: 11: 15-20

Review

Non-pharmacological interventions for methamphetamine use disorder: a systematic review

PV AshaRani*, Aditi Hombali, Esmond Seow, Wei Jie Ong, Jit Hui Tan, Mythily Subramaniam

A B S T R A C T

Background: Meth… …lers in-
creasing exponen… …needs.
This systematic r… …cal ap-
proaches for the …
Methods: Five ele… …ng and
Allied Health Lite… …les that
were published b… …endent
reviewers. A syste… …ducted
to appraise the e…
Results: A total o… …vioural
therapy (CBT), c… …petitive
transcranial mag… …moting
abstinence, reduc… …ved the
strongest evidenc… …in the
target population…
Conclusions: Beha… …tamine
use disorder. Fut… …sample
sizes and high dr…

Highlights

- Non pharmacological interventions are effective in treating METH use disorder.
- Contingency management and cognitive behavioural therapy yield better outcomes.
- Heterogeneity noted across the studies in terms of methodology and interpretation.
- The methodology should be standardised to allow comparison across the studies.

PV AshaRani, et al. *Drug and Alcohol Dependence.* 2020;212(7):108060

Review of Studies: Efficacy of Meds Used to Treat Amphetamine Use Disorder

Drug Class	# of Studies	Abstinence	Use	Harm	Retention
Antidepressants: Overall	9	No diff.	**Mixed findings**	No diff.	No diff.
Sertraline		No diff.	N/A	No diff.	N/A
Mirtazapine		N/A	**Yes**+	No diff.	No diff.
Buproprion		No diff.	No diff.	No diff.	No diff.
Anticonvulsants: Overall	2	No diff.	No diff.	No diff.	No diff.
Topiramate*		No diff.	**Yes**	No diff.	No diff.
Baclofen		No diff.	No diff.	No diff.	No diff.
Gabapentin		No diff.	No diff.	No diff.	No diff.
Stimulants: Overall	11	No diff.	**Mixed findings**	No diff.	N/A
Methylphenidate*		No diff.	**Yes**	No diff.	No diff.
Dexamphetamine		No diff.	No diff.	No diff.	No diff.
Atomoxetine		N/A	No diff.	No diff.	No diff.
Antipsychotics: Aripiprazole	2	No diff.	No diff.	No diff.	No diff.
Opioid Antagonists: Naltrexone	4	No diff.	**Mixed findings**	No diff.	No diff.
Other: Varenicline	5	N/A	No diff.	No diff.	No diff.

* Demonstrated evidence of effectiveness
+Authors deemed study methodologically flawed; evidence is insufficient

Chan, B., Freeman, M., Kondo, K., Ayers, C., Montgomery, J., Paynter, R., & Kansagara, D. (2019). Pharmacotherapy for methamphetamine/amphetamine use disorder – A systematic review and meta-analysis. Addiction, (ePub ahead of print). doi: 10.1111/add.14755

Methamphetamine: Treatment (2)

- **No FDA approved agents for meth use disorder**
- **Ascorbic acid/Vitamin C for acute intoxication mgmt**
- **Bupropion effective in less severe cases**
- **Modafinil + CBT effective in HIV+ cases**
- **Naltrexone for general amphetamine misuse**
  - **Implantable or high dose may be preferred**
- **Topiramate reduced meth in MSM-short but not longer term**
  - **May be better for relapse prevention (e.g. abstinent at start)**

Karilla et al.Br J Clin Pharm; 2010:69:578-592 Lee and Rawson, Drug Alc Rev 2008: 27: 309-17; Colfax et al. Arch Gen Psych 2011: 68: 1168-75; Cadet and Gold, Curr Psychiatry, 2017: 11: 15-20; Mousavi et al, Arch Iran Med 2015: 18: 28-33: Shottenfeld et al. Drug Alc Dep 2018: 186 130-7; Wang et al Front Psychiatry, 2019: 10: 656.

Methamphetamine: Treatment (2)

- **Mirtazapine (30 mg)-**
  - **RCT: tested in MSM (improved meth and risk behaviors)**
- **Atomoxetine in bup+amph disorders: best in adherent sample**
- **Craving reduction**
  - **Multiple attempts have not been successful**
  - **Some efficacy with substitution therapy (e.g. d-amphetamine), cholinesterase inhibitors, NAC, bupropion, nicotine, naltrexone**
- **Treating psychosis (2^{nd} > 1^{st} generation antipsychotics): careful with EPS**

Karilla et al.Br J Clin Pharm; 2010:69:578-592 Lee and Rawson, Drug Alc Rev 2008: 27: 309-17; Colfax et al. Arch Gen Psych 2011: 68: 1168-75; Cadet and Gold, Curr Psychiatry, 2017: 11: 15-20; Mousavi et al, Arch Iran Med 2015: 18: 28-33: Shottenfeld et al. Drug Alc Dep 2018: 186 130-7; Wang et al Front Psychiatry, 2019: 10: 656.

Methamphetamine Inpatient Detoxification/Management Protocol

- Goal: Ensure patient is medically/psychiatrically safe, assist with acute w/d management including urges/cravings, setting up for longer-term abstinence (avoidance of drug for brain health).
- Please complete comprehensive medical evaluation with additional emphasis on vital signs, heart rate/rhythm disturbances, pulmonary status, oral/dental care, skin excoriations, or topical infections.
- Vitamin C 1000 mg po BID for 48 hours
- Encourage po intake of fluids, snacks, and meals. Hold meal for later administration if patient unable to attend a meal.
- Reduce stimulation -have patient housed in quiet room with minimal light and sound. Manage behavioral agitation with reducing stimuli, speaking quietly, and interacting in a non-confrontational manner. Continue to monitor patient when in reduced stimulation setting.
- Allow patient to sleep PRN with continued vital sign and other safety checks. Patient may be excused from group and other community-type groupings if sleeping, Do not discharge patient for missing groups or individual counseling if the patient is sleeping. Encourage patient to exercise while awake.
- For agitation, use low dose diphenhydramine (Bendryl) 25 mg po QID-hold for disinhibition. For panic or anxiety, use chlordiazepoxide (Librium) 25 mg po TID-hold for disinhibition. For moderate-to-severe agitation or paranoia or psychosis-use quetiapine (Seroquel) 25-50 mg po TID-hold for worsening of symptoms. Call MD if patient has auditory or visual hallucinations.
- After day 2, use methylphenidate 5-10 mg po BID (8-10AM, 2-4 PM) for severe urges, cravings, or depressive symptoms. Hold for worsened agitation, paranoia, anxiety, motor spasms/tics, or cardiovascular symptoms (e.g. palpitations). Hold PM dose if causing insomnia. For insomnia, in addition to PRN medications, consider mirtazepine 15-30 mg qHS.
- If aftercare established, consider trials of bupropion SR/XL (Wellbutrin; less severe cases, prominent mood symptoms), topirimate (more severe cases, urges/cravings), naltrexone (alone or in combination with bupropion), mirtazepine (sleep, mood, anxiety symptoms), methylphenidate or modafinil (urges/cravings, anhedonia), and/or quetiapine (paranoia, psychosis, sleep). Avoid the use of aripiprazole (Abilify)

(Wilens et al unpublished 2021)

Summary: Cocaine & Methamphetamine

- **Both classes of substances with pronounced "stimulant – like" effects**
- **Nonfatal but intense withdrawal and cravings**
- **Treatment engagement and retention challenging**
- **Use of psychosocial treatments necessary**
- **Limited replicated trials demonstrating medication efficacy**
- **Somewhat longer time for brain recovery relative to other misused substances**