Rise of Methamphetamine: New Risks, Current Treatments

Richard A. Rawson, PhD
Research Professor, Vermont Center for Behavior and Health
Professor Emeritus, UCLA Department of Psychiatry and Biobehavioral Sciences

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Target Audience

- The overarching goal of PCSS is to train healthcare professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well for the prevention and treatment of substance use disorders.
Welcome!

Richard A. Rawson, PhD
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Educational Objectives

• At the conclusion of this activity participants should be able to:
  ▪ Examine trends and impacts of methamphetamine use
  ▪ Identify clinical challenges and strategies for treating individuals who use stimulants
  ▪ Examine the evidence for medications and treatment interventions for stimulant use
No disclosures.

**Person-first language**: I am making a concerted effort to use person-first language to refer to individuals who use drugs/alcohol and/or are in treatment for substance use disorder (e.g. “Individuals who use cocaine or methamphetamine”), rather than more stigmatizing terms (e.g. “addict” or “cocaine/methamphetamine users”). Because old habits are difficult to change, I may inadvertently use the older and more stigmatizing terminology. I apologize in advance.

*The content of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.*
Methamphetamine

• In the 1990s and early 2000s, meth made from the decongestants, pseudoephedrine and ephedrine, poured out of domestic labs like those in the early seasons of “Breaking Bad.”
• Narcotics squads partially became hazmat teams.
Methamphetamine Availability Reduced

• In 2005, Congress passed the Combat Methamphetamine Act, which put pseudoephedrine products behind the counter, limited amounts purchased, and tracked purchasers.
• Although some meth makers tried “smurfing,” meth cases plummeted.
• With no more meth lab explosions on the nightly news, the public forgot about the drug.
• Mexican drug cartels stepped in improving production with higher potency and lower price ($2,000 per pound; down from $8,000).
Methamphetamine Lab Incidents

Figure 76. Number of Methamphetamine Laboratory Incidents, 2000 – 2017.

Source: El Paso Intelligence Center National Seizure System as of June 12, 2018
Methamphetamine Today

• Methamphetamine produced via P2P method is much more potent and potentially lethal.

• 2018: United States border agents seizing 10 to 20 times the amounts they did a decade ago.

• 2014-2020: Fentanyl-contaminated meth and cocaine became more prevalent. In many parts of the US, virtually all meth and cocaine have fentanyl included at the source.

• June 2020: Isotonitazene—commonly referred to as “iso”, a synthetic version of etonitazene is now found in individuals who overdose from cocaine in the Midwest.
Potential Lethal Dose
Heroin, Fentanyl and Carfentanil

Comparing the size of lethal doses of heroin, fentanyl, and carfentanil. The vials here contain an artificial sweetener for illustration. (New Hampshire State Police Forensic Laboratory)
Evolution of Drivers of Overdose Deaths:

- Analgesics
- Heroin
- Fentanyl
- Stimulants

Data from CDC WONDER Database
People who use Opioids who Test Positive for Stimulants at Emergency Departments
(Chawarski, 2020)

• 38% of 396 people who use opioids tested positive for stimulants at emergency departments

• Characteristics of people who use both opioids and stimulants:
  - Younger; white (69%); higher rates of incarceration
  - Higher rates of injection (79% vs 47%)
  - Higher rates of HCV
  - More had overdosed (23% vs 13%)
  - Unstable housing (67% vs 49%)
People who use Opioids who Test Positive for Stimulants at Emergency Departments
(Chawarski, 2020)

Most (38%) were in the Midwest and West

Baltimore: 6%
New York: 7%
Cincinnati: 32%
Seattle: 80%
Cocaine and Psychostimulant Overdose Deaths by Race/Ethnicity, 2017

Source: CDC NVSS, 2019
Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine

Journal of Substance Abuse Treatment
109 (2020) 80–85
Judith I. Tsui, et al.
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 and 6-months, as well as date of program discharge.

- 30% (n=237) 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
Impacts of Methamphetamine Use
Medical Issues Related to Methamphetamine Use
Neurobiology, Clinical Presentation, and Treatment of Methamphetamine Use Disorder
Paulus and Stewart, JAMA Psychiatry, 2020

- Neurotoxicity, cognitive effects
- Cardiovascular and cerebrovascular symptoms
- Need for pharmacologic interventions
Neurotoxicity

- Excessive dopamine results in damaged cell structures
- Cell death
- Activation of dopamine D3 receptors resulting in hyperthermia
- Disruption of the blood-brain barrier
- Overall the altered brain state is consistent with degenerative central nervous system diseases.
Cognition

• Soon after cessation of methamphetamine use:
  ▪ Poor performance on motor and processing tasks
  ▪ Poor performance on verbal fluency and attention

• Even after prolonged abstinence:
  ▪ Poor learning efficiency and comprehension
  ▪ Poor visual-spatial processing
  ▪ Slow processing and psychomotor speed
Cognition

• It is estimated that more than 2/3 of those with methamphetamine use disorder show cognitive impairment.

• Impairment is associated with older age, longer duration of use, and greater frequency of use.

• May limit ability to follow through with treatment, comprehend advice and direction in treatment, and generally achieve good treatment outcomes.
Methamphetamine and Violence

Foulds et al., 2020

- Review of 28 studies.
- Compared to no use, amphetamine use was associated with a 2-fold increase in the odds of hostility or violence.
- Frequent use increases the risk of violent behavior.
- Other risk factors included: psychotic symptoms, alcohol or other drug use, psychosocial problems, and impulsivity.
Cerebrovascular and Cardiovascular Disease

• Leading causes of death with methamphetamine use disorder
• Strokes are increasing most often with young men
• Strokes are primarily hemorrhagic

• Associated with methamphetamine use:
  ▪ Pulmonary hypertension
  ▪ Cardiac arrhythmia
  ▪ Cardiomyopathy
77 articles reviewed reporting stroke in young adult (<45) methamphetamine users.
81 hemorrhagic, 17 ischemic strokes reported.
Hemorrhagic associated with oral or injection route of administration.
Ischemic associated with inhalation.
Following hemorrhagic stroke, 1/3 died.
Following ischemic stroke, 1/5 died.
Stroke and Methamphetamine Use in Young Adults: A Review
Lappin et al., 2017

• Treatment providers should be aware of the heightened risk of stroke in young methamphetamine users.

• Be aware of early signs and symptoms:
  ▪ Numbness
  ▪ Headache
  ▪ Speech and language difficulty
  ▪ Vision problems
  ▪ Dizziness
Smid, Metz and Gordon (2019) Stimulant Use in Pregnancy – an under-recognized epidemic among pregnant women

Stimulant Use in Pregnancy
Smid et al., 2019

• Women are disproportionately vulnerable to stimulant use and abuse.
• Vulnerability is related to hormones and reinforcement of gender constructs.
• Women progress faster from first exposure to addiction.
• Prenatal stimulant use is more common than opioid use.
Stimulant Use in Pregnancy
Smid et al., 2019

• Meta-analysis of 31 studies found cocaine use during pregnancy increased risk of pre-term delivery, low birth weight, small for gestational age, earlier gestational age at delivery, and reduced birth weight (Gouin, 2011).

• Meta-analysis of 8 studies found methamphetamine use during pregnancy was associated with earlier gestational age at delivery, lower birth weight, and smaller head circumference (Kalaitzopoulos, 2018).

• Infants with prenatal exposure to methamphetamine exhibit jitteriness, drowsiness, and respiratory distress suggesting withdrawal.

• Cocaine and methamphetamine are excreted in breastmilk and contraindicate breastfeeding.
Stimulant Use in Pregnancy
Smid et al., 2019

- Long-term follow-up of 204 methamphetamine-exposed maternal-child pairs and 208 unexposed (Derauf et al., 2007).
- At one month, 33% methamphetamine-exposed mothers did not have custody compared to 2% of unexposed.
- At age 3 years, heavy prenatal methamphetamine use (≥3 days per week) was associated with anxiety/depression and attention problems.
- At age 7.5 years, methamphetamine-exposed children had poorer cognitive function.
Collision of the COVID-19 and the Addiction Epidemics
Volkow, 2020

- Chinese Center for Disease Control report fatality rate of 6.3% for people with chronic respiratory diseases compared to 2.3% overall.
- People who smoke, vape, use opioids or have an SUD are vulnerable.
- Opioid use causes hypoxemia.
- Methamphetamine use causes pulmonary damage.
- Social distancing increases risk of overdose with fewer people available to administer naloxone.
- **Isolation, stress, anxiety, and depression can lead to more substance use and more fatal overdoses.**
Clinical Challenges
Clinical Challenges with Stimulant Dependent Individuals

- Overdose death
- Limited understanding of stimulant addiction
- Ambivalence about need to stop use
- Impulsivity/poor judgement
- Cognitive impairment and poor memory
Clinical Challenges with Stimulant Dependent Individuals, cont’d

- Anhedonia
- Hypersexuality
- Violence and psychosis
- Powerful Pavlovian trigger-craving response
- Elevated rates of psychiatric co-morbidity
- Very poor retention in outpatient treatment
Special Treatment Consideration Should Be Made for the Following Groups

- People who use injectable drugs.
- 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).
- People who use stimulants who are under the age of 21.
- Individuals in medication treatment for OUD.
Clinical Interventions
Harm Reduction Strategies for Stimulant Users

- 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
Treatment for Individuals with Stimulant Dependence
Systematic Reviews and Meta-analyses
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 *

1 Department of Psychiatry, University of Oxford, Oxford, United Kingdom, 2 Oxford Health NHS Foundation Trust, Warneford Hospital, Oxford, United Kingdom, 3 Institute of Psychiatry and Clinical Psychology, Catholic University of the Sacred Heart, Rome, Italy, 4 School of Hygiene and Preventive Medicine, University of Rome Tor Vergata, Rome, Italy, 5 Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland, 6 Department of Dynamic and Clinical Psychology, Sapienza University of Rome, Rome, Italy, 7 Mental Health and Substance Abuse, World Health Organization, Geneva, Switzerland, 8 Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California, United States of America, 9 Department of Psychiatry, VA Palo Alto Health Care System, Palo Alto, California, United States of America
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.
Twenty-seven randomized controlled studies (3663 participants) fulfilled inclusion criteria and had data that could be used for at least one of the main comparisons.

The comparisons between different type of behavioral interventions showed results in favor of treatments with some form of contingency management in respect to both reducing dropouts and lowering cocaine use.
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.
• 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.
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 methamphetamine users.
• 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.
Treatment Response Predictors

- HIV negative.
- Fewer years of lifetime drug use.
- Less methamphetamine use at baseline.
- Caucasian.
- Lower monthly income; more years of education.
- Those who spent vouchers vs those who accumulated them did better.
- Those who recently injected did not do as well.
Conclusions

• Contingency management effectively reduces methamphetamine use.

• CM produces broad beneficial effects beyond targeted behaviors.

• Outpatient clinics that treat methamphetamine use disorder should implement CM.
The three major challenges to using CM

- Medicaid regulations that restrict the amount of incentives that can be given to patients to $75 per patient per year
- Where does the funding for incentives come from?
- Staff resistance to the idea of incentives
  - Patients should not have to be “paid” or “bribed”; recovery is the reward
  - Motivation needs to come from within
Current Status of Treatment Approaches for Methamphetamine Use Disorder

- Contingency management unanimously (5 systematic reviews and meta-analyses) found to have the most robust evidence of effectiveness.
- Other approaches with lesser but 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 individuals with methamphetamine use disorder: Physical Exercise (PE). (e.g. Rawson et al, 2015)
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 (D2/D3 receptors)
  ▪ Reduces relapse to methamphetamine post discharge (except in very heavy users)
Medications
Medications for Methamphetamine Use Disorder

Medications with positive studies and under consideration:

- Bupropion
- Mirtazapine *****
- Naltrexone
- Methylphenidate
- D-amphetamine
- Topiramate
TRUST: Treatment of Individuals who Use Stimulants

An Integrated Behavioral Model
TRUST: The Components

TRUST is an integrated, evidence-based, multi-component program for the treatment of individuals with stimulant use disorders. The contents of this program will include strategies including:

1. Motivational incentives (based on contingency management research),
2. Elements of cognitive behavioral therapy,
3. Elements of community reinforcement approach,
4. Motivational interviewing skills,
5. Physical exercise,
6. Self-help (12-Step; Moderation management) program participation encouraged.

In addition, an appendix will include a set of other EBPs to augment the core program at the discretion of each organization.
TRUST: The Priorities

1. Establish a positive, compassionate, respectful, non-judgmental relationship with individuals who use stimulants to promote their engagement and retention in treatment. Individuals in treatment die from overdose and other causes at lower rates than those who are not in treatment.

2. Provide incentives to promote participation (retention) in treatment. Retention is the single most important measure of treatment benefit. All treatment benefits (e.g. reduced drug use and criminal involvement, improved employment and other measures of functioning) are directly associated with treatment retention.

3. Provide respectful evidence-based guidance/information/support to stimulant-using individuals that can help them make changes in their lives that will promote a reduction/discontinuation of methamphetamine/cocaine use.
Summary/Takeaways

• The methamphetamine being used in 2020 is more lethal than in earlier years due to more potent formula and addition of fentanyl.
• New research has provided a better understanding of the medical and psychiatric consequences of methamphetamine use.
• Behavioral treatments, particularly contingency management, have evidence of efficacy.
• There are no medications with FDA approval for the treatment of individuals with methamphetamine use disorder.
Questions?

Richard A. Rawson, PhD
rrawson@mednet.ucla.edu
PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.

- PCSS Mentors are a national network of providers with expertise in addictions, pain, evidence-based treatment including medications for addiction treatment.

  - 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.

  - No cost.

For more information visit: https://pcssNOW.org/mentoring/
PCSS Discussion Forum

Have a clinical question?

Ask a Colleague
A simple and direct way to receive an answer related to medication-assisted treatment. Designed to provide a prompt response to simple practice-related questions.

http://pcss.invisionzone.com/register
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