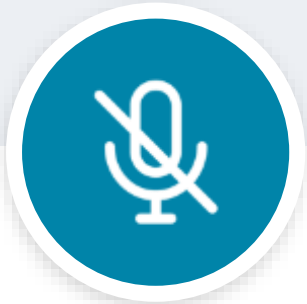
Welcome!



Mute

Minimize Interruptions

Please make sure to mute yourself when you aren't speaking.

Chat

Go Ahead, Speak Up!

Use the Zoom chat to ask questions and participate in activities.

Naming

Add Your Organization

Represent your team and add your organization's name to your name.

Tech Issues

Here to Help

Chat Host privately if are having issues and need tech assistance.

While we wait, please rename yourself.

Addiction Treatment Starts Here
Prescriber Forum Session #3

“Didactic Teaching on Stimulant Use Disorders Prescribing”

November 19, 2021 | 12 – 1pm (PT)

CCI CENTER FOR CARE INNOVATIONS

+

DHCS

Today's Presenter

Joe Sepulveda, MD, FAPA, FASAM

Chief of Psychiatry

Medical Director, Substance Use Disorder Services

Family Health Centers of San Diego

CCI ATSH Prescribers Forum

Stimulant Use Disorder & Evidence-based Treatment 101

Joe Sepulveda, M.D., FAPA, FASAM
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Medical Director, Substance Use Disorder Services
Medication-Assisted Treatment (MAT) Program
Psychiatric Nurse Practitioner Program
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Diplomate of the American Board of Preventive Medicine—Addiction Medicine
Fellow of the American Psychiatric Association
Fellow of the American Society of Addiction Medicine

Agenda

- Overview of Amphetamines
- Methamphetamines vs. Cocaine
- Physical and Psychological effects of Amphetamines
- Toxicology testing for stimulants
- Evidence-based psychosocial interventions
- Medications for Stimulant use (none are FDA approved)
- Key Principles for treating Stimulant Use Disorder – "Take Home Message"
- Stimulants and Fentanyl
- Comprehensive care

Disclosures

Joe Sepulveda, M.D., FAPA, FASAM

No financial conflicts of interest

None of the medications discussed in this presentation are FDA approved for any Stimulant Use Disorder

Amphetamine-Type Stimulants & Cocaine

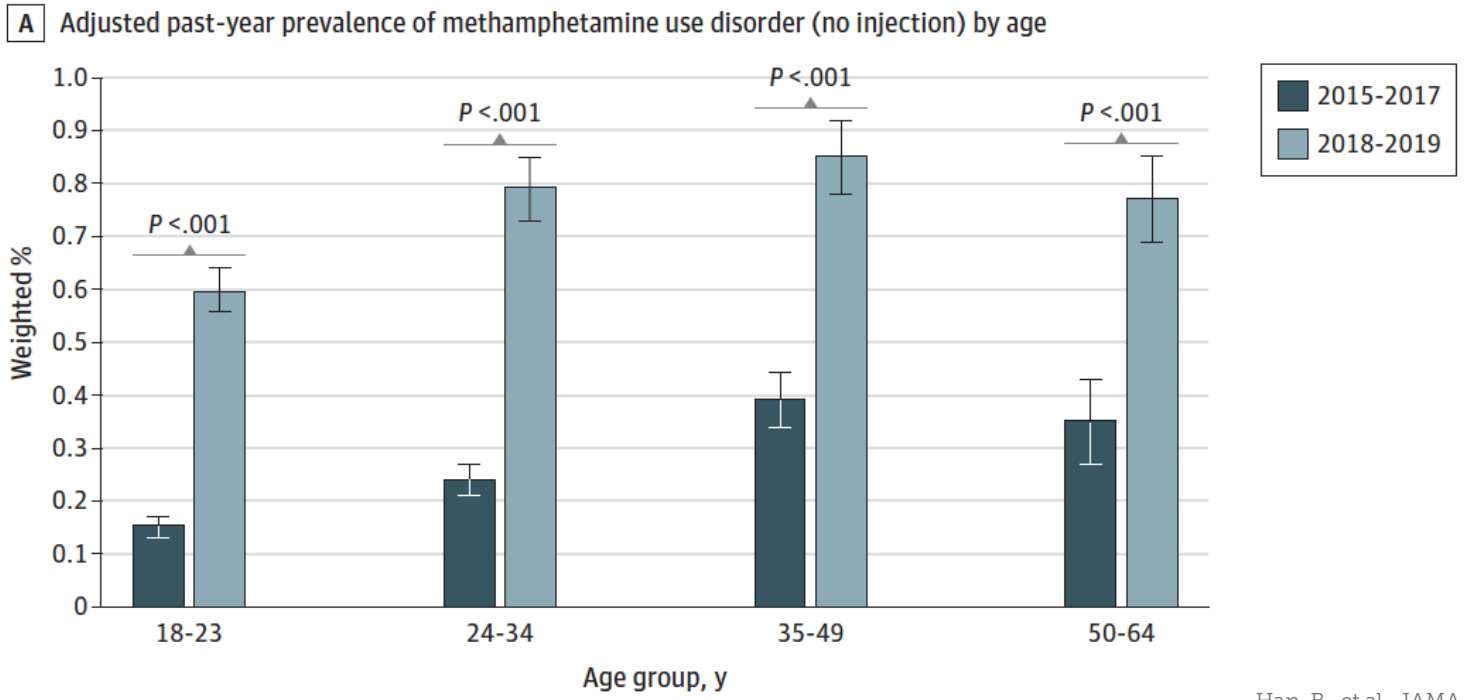
Examples of Stimulants

- Cocaine
- Methamphetamine
- Amphetamine-type stimulants (e.g. MDMA/Ecstasy)
- Prescription stimulants (e.g. mixed amphetamine salts, dextroamphetamine, methylphenidate)
- Other Amphetamine-type stimulants (e.g. bath salts)

Methamphetamine Use Disorder in the U.S.

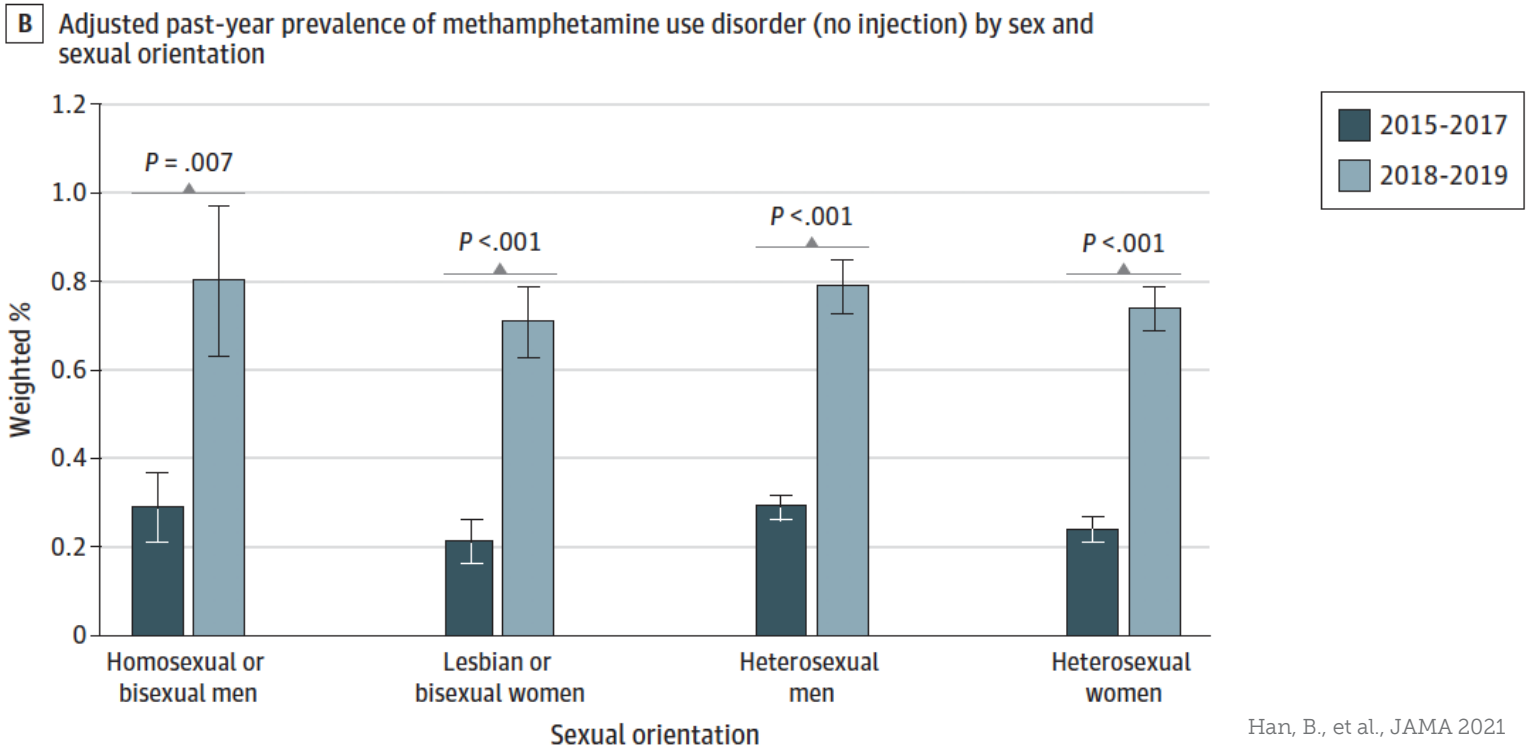
&

Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years



Han, B., et al., JAMA 2021

Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years



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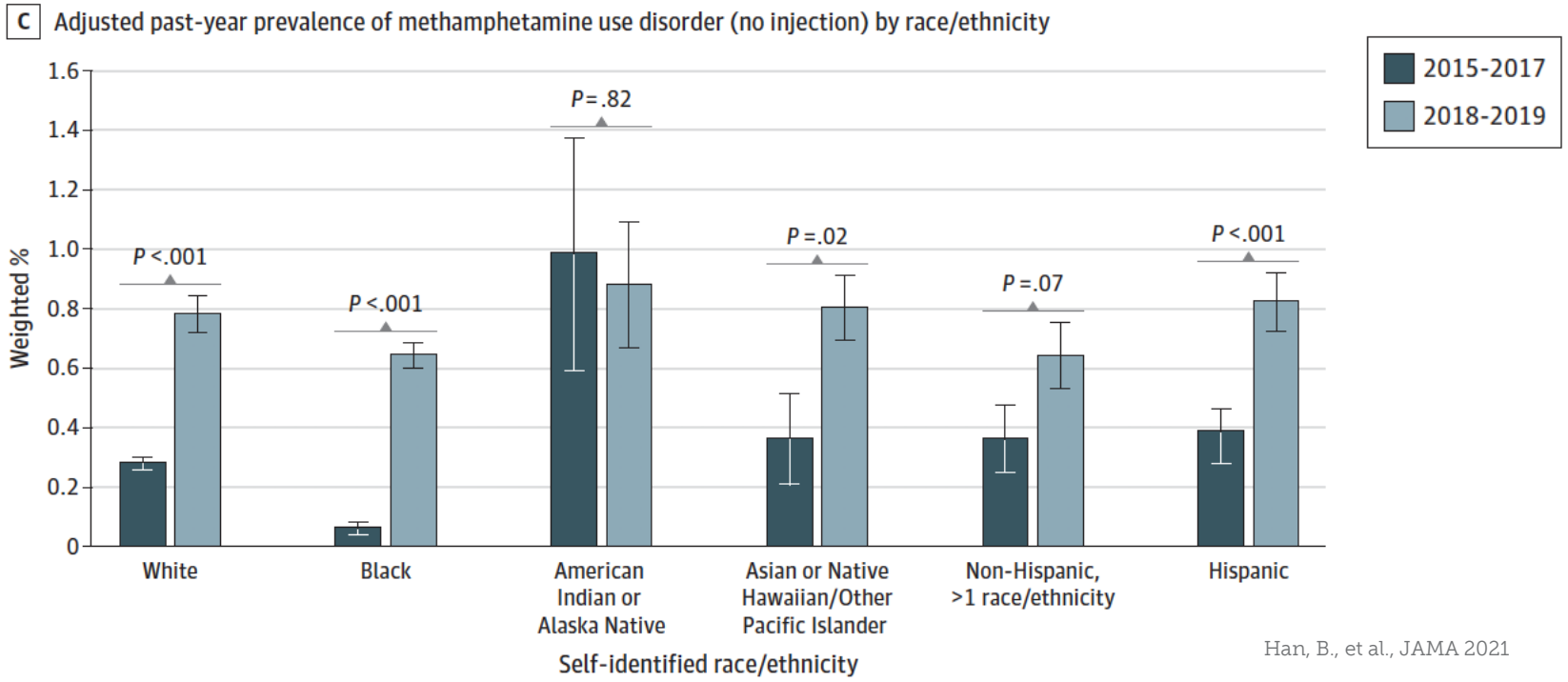
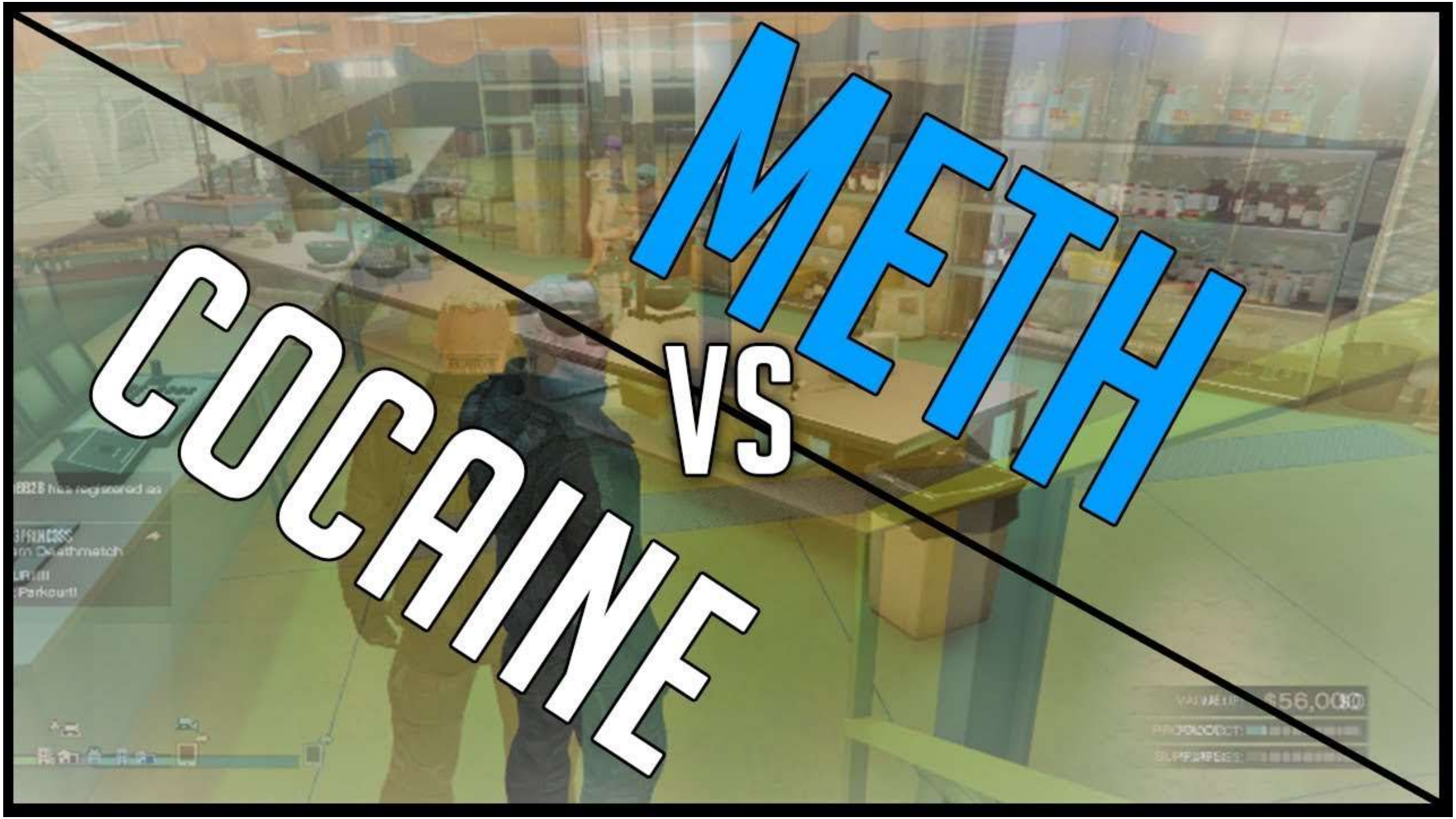
Methamphetamine Use Disorder Among US Adults Aged 18 to 64 years



Han, B., et al., JAMA 2021


METH
VS
COCAINE

Cocaine vs. Methamphetamine

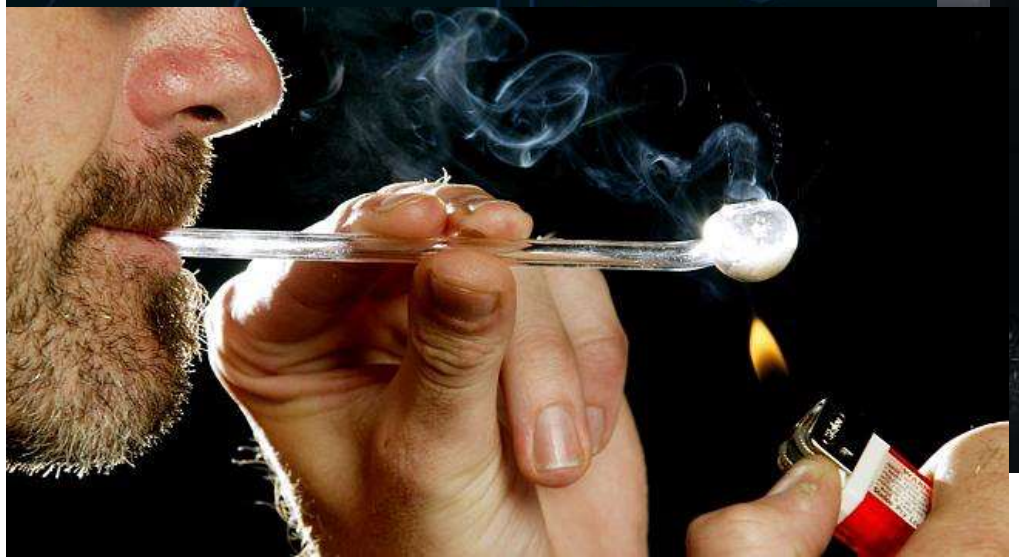
Cocaine

- Plant-derived
- Effects last 1-2 hours
- T½: 1 hour
- Mechanism: mainly DA/NE reuptake
- ***NOT*** directly neurotoxic
- Withdrawal → 1-2 days

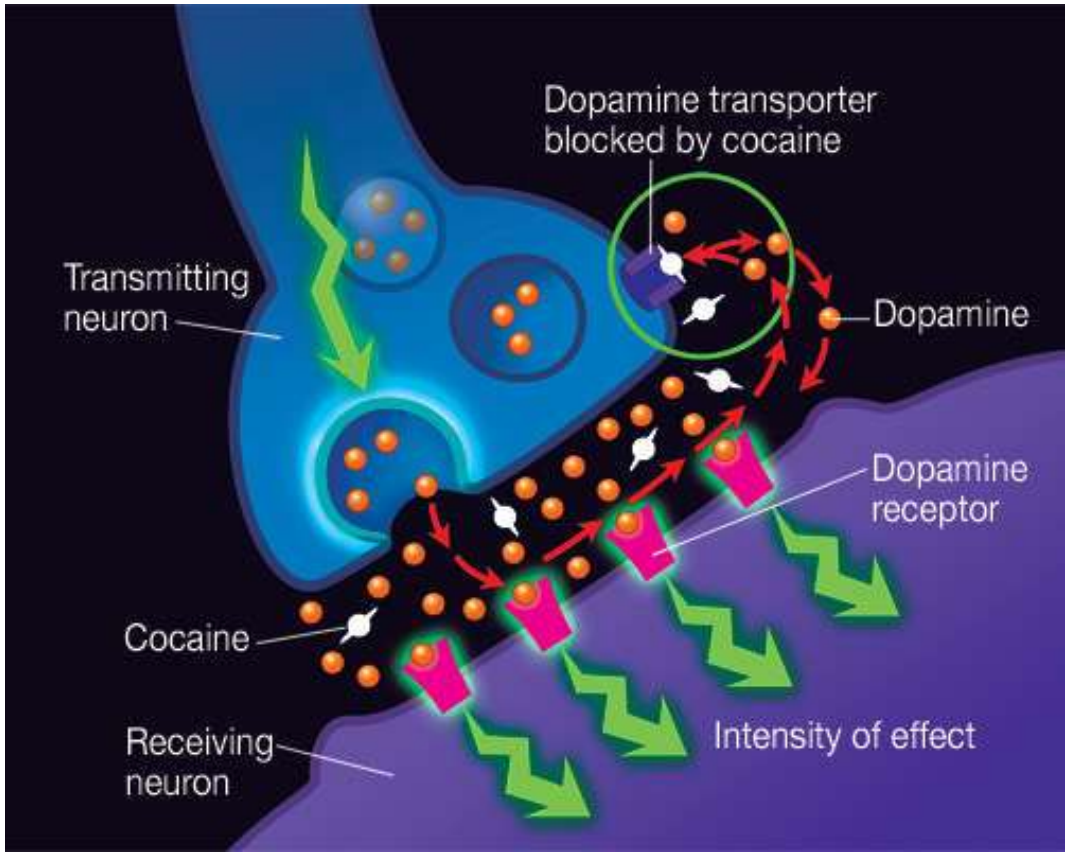
Methamphetamine

- Synthetic
- Effects last 10-20 hours
- T½: 12 hours
- Mechanism: mainly DA/NE release
- Neurotoxicity
- Withdrawal → *SEVERAL* days


$C_{17}H_{21}NO_4$
COCAINE
R1



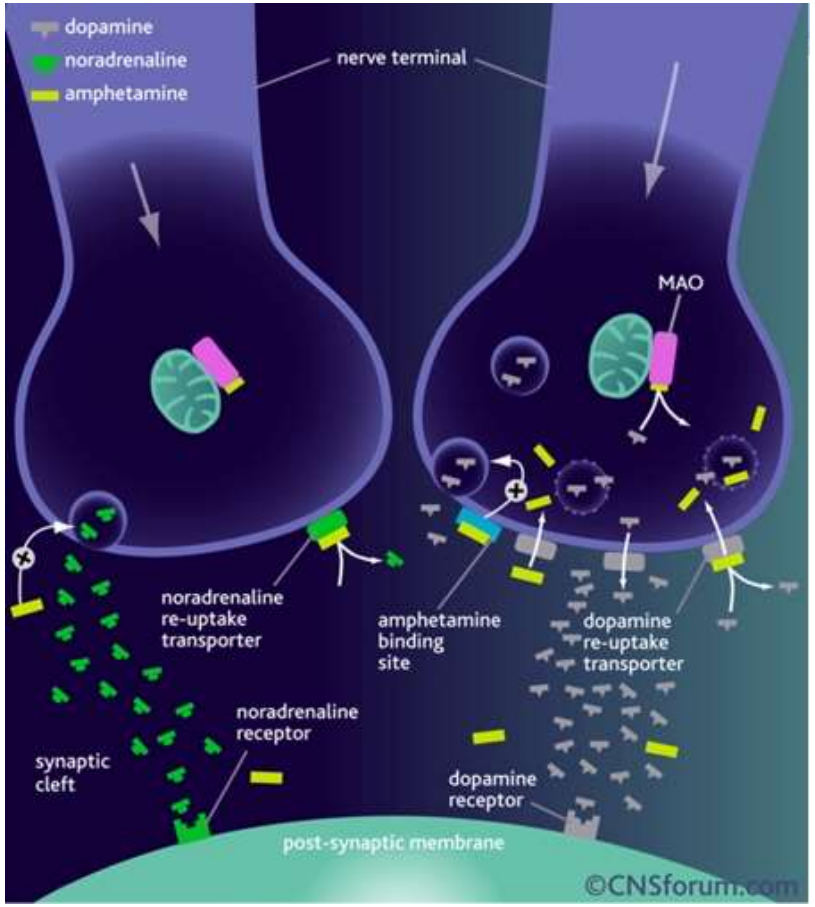
Pharmacology of Cocaine



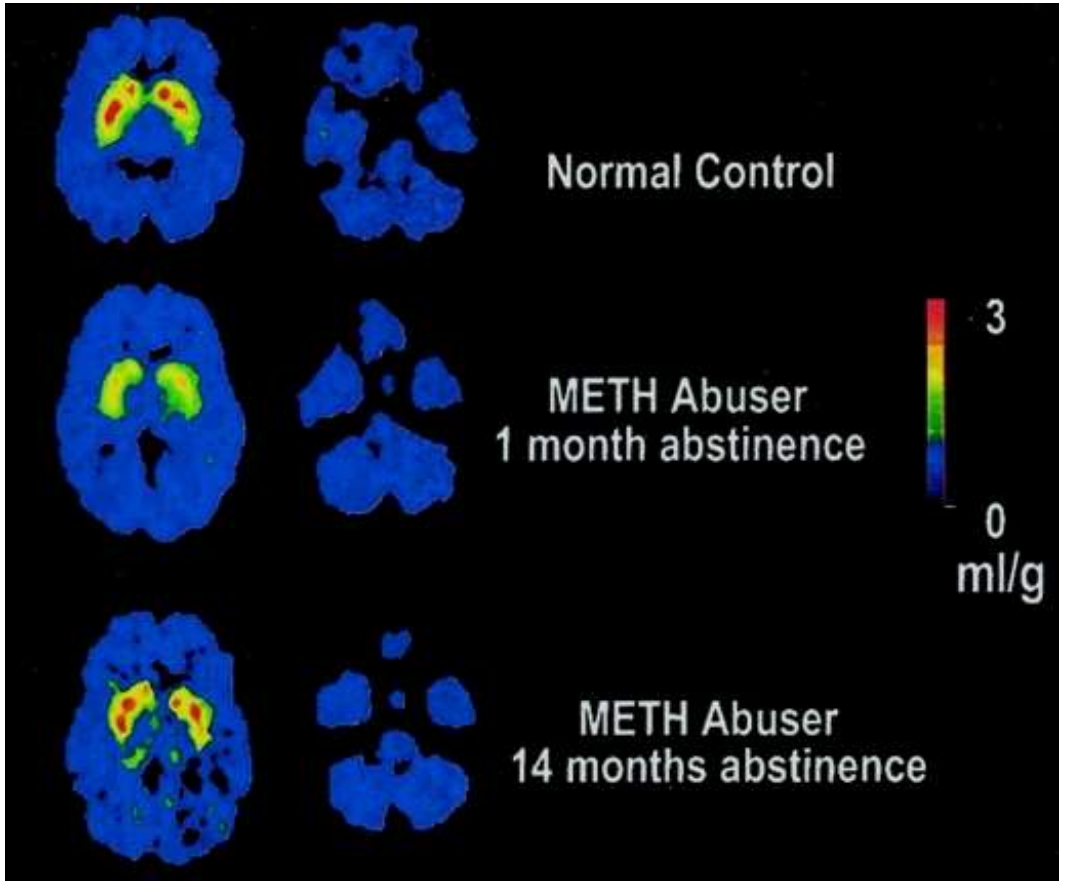
Methamphetamine

Pharmacology of Methamphetamine

- Blocks Reuptake
- Facilitates release of newly formed catecholamine
- Blocks break down of catecholamine in the neuron

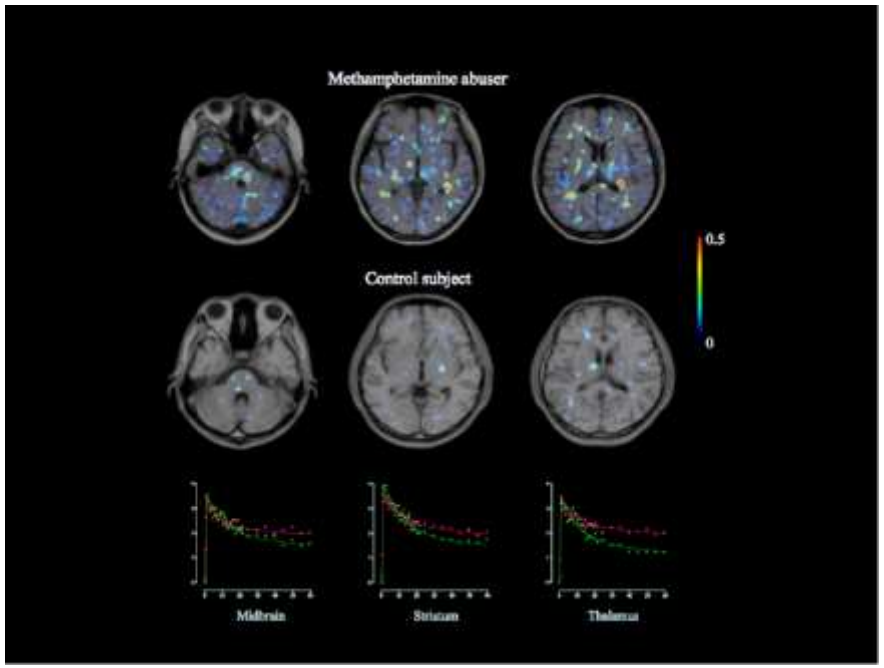


Destruction and Recovery of Dopamine Transporter in Meth Users

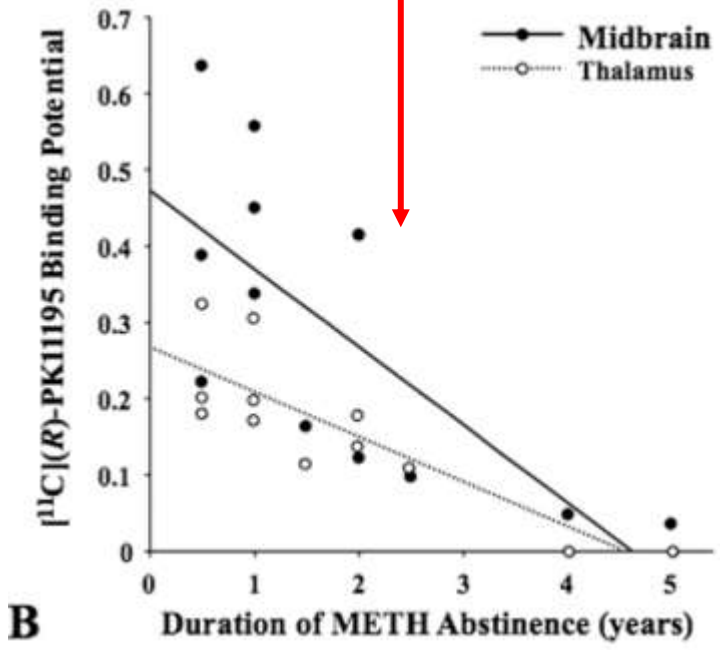


Nora D. Volkow et al., J. Neurosci. 2001

Meth is toxic to the brain triggering glial activation and neuroinflammation



Neuroinflammation persists despite years of abstinence and may trigger relapse



Sekine, Y., et al., J Neurosci. 2008

Acute Physical & Psychological Effect of Stimulants

Physical

Increase

- Energy/productivity
- Heart Rate
- Blood pressure
- Respiration
- Pupil size

Decrease

- Appetite (weight loss)
- Sleep
- Reaction Time

Psychological

Increase

- Energy
- Confidence
- Alertness
- Mood/Euphoria
- Sex Drive
- Talkativeness

Decrease

- Boredom
- Loneliness
- Timidness

NIDA, 2019

Chronic Psychological Effects of Stimulants

- Hallucinations
- Paranoia
- Psychosis
- Depression
- Concentration
- Memory loss
- Irritability
- Anger
- Panic reactions
- Fatigue
- Insomnia
- Confusion

NIDA, 2019

Physical Effects of Chronic Stimulant Use

Organ system damage

Cardiac

- Heart Failure
- Cardiomyopathy
- Myocarditis
- Myocardial infarction
- Arrhythmia → Sudden Death
- Tachycardia
- Reduced heart rate variability
- Microvascular Dz
- Accelerated CAD→ Catacholamine excess

Respiratory

- Pulmonary HTN
- Pleuritic chest pain
- Edema
- Decrease capacity

Neurological

- Movement disorders
  - Parkinson's
  - Tremor
- Neurocognitive Impairment
- Seizures
- Hemorrhage
- Cerebral vasculitis

Dental

- Cavities
- Tooth Erosion
- Periodontal Dz

Hepatic Failure

- Rhabdomyolysis

Renal failure

- Rhabdomyolysis → Renal tubular obstruction

NIDA, 2019; Lappin et al, 2018; Curtin et al, 2015; Callaghan et al, 2011; Turnipsee et al, 2003; Karch, 2002; Rhee et al., 1998; Wallace et al, 1999

Drug Testing: Stimulants

Oral fluid testing

- Shorter detection windows than urine

Serum Testing

- For acute intoxication

Hair testing

- Longer period of detection (e.g. up to 90 days)
- Better for detection of heavy, frequent use

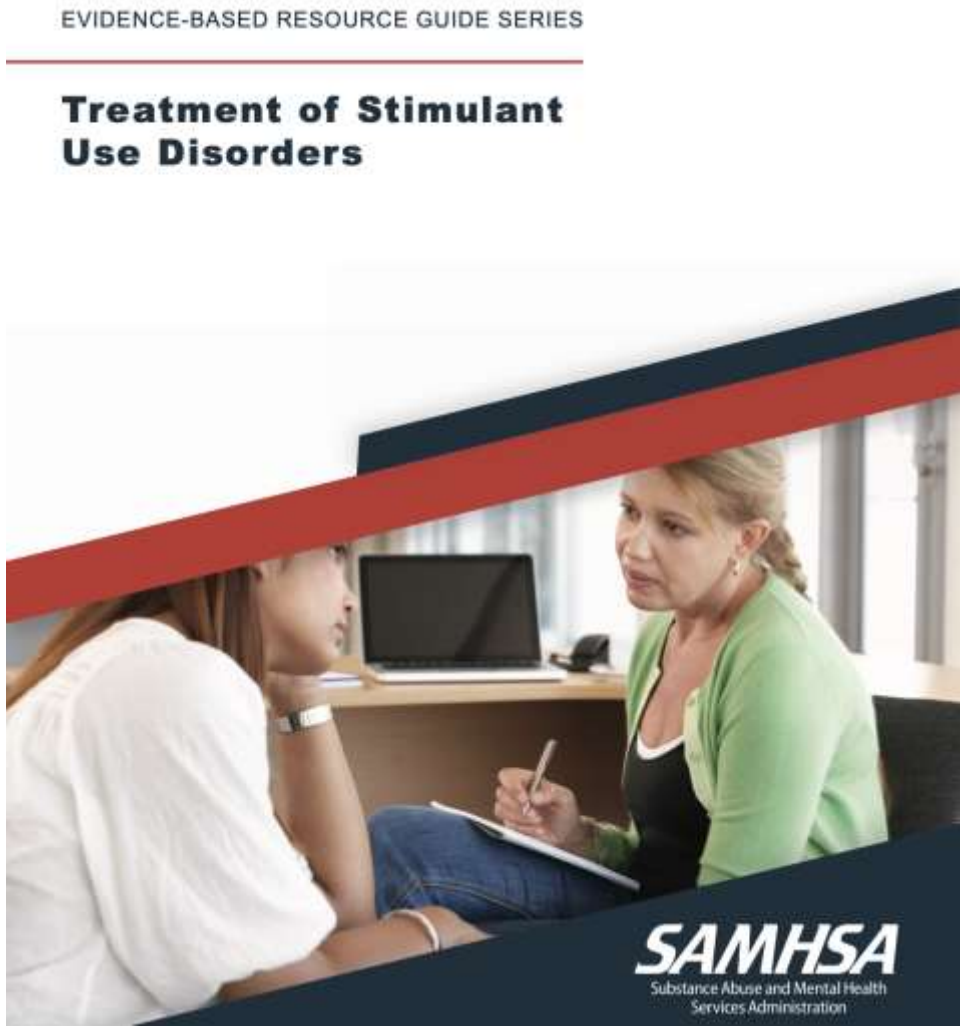
Urine Drug Testing: Stimulants

Amphetamine, Methamphetamine

- Detection window approximately 2-3 days
- False positives: pseudoephedrine, bupropion, labetolol, ranitidine, trazodone, TCA's
- Low sensitivity for detection of MDMA
- 2 methamphetamine isomers: D (CNS) and L (Peripheral)

Cocaine

- Detection window 2-4 days
- Primary metabolite: Benzoyleconine
- False positives **RARE**



https://store.samhsa.gov/product/Treatment-of-Stimulant-Use-Disorder/PEP20-06-01-001

Four psychosocial treatments

Summary of Evidence Review

Practice	Motivational Interviewing	Contingency Management	Community Reinforcement Approach	Cognitive Behavioral Therapy
Review rating	Strong Evidence	Strong Evidence	Strong Evidence	Strong Evidence
Focus of the practice	Resolving clients' ambivalent feelings and insecurities and enhancing the internal motivation needed to change their behavior	Positively reinforcing desired behaviors	Identifying behaviors that reinforce stimulant use and making a substance-free lifestyle more rewarding than one that includes substances	Helping clients improve the quality of their lives not by changing their circumstances, but altering their perceptions of those circumstances
Can be used in outpatient healthcare settings	✓	✓	✓	✓
Can be used in inpatient healthcare settings	✓	✓	✓	✓
Specific training available	✓	--	✓	✓
Web-based version available	--	✓	✓	✓
Can be practiced by peers	✓	--	--	--
Has been used successfully with males and females	✓	✓	✓	✓
Special populations with whom the practice has been successfully implemented	Men who have sex with men	Men who have sex with men; Co-occurring opioid use disorder; Severe mental disorders	Adolescents	--
Intensity and Duration of Treatment	No prescribed intensity and duration	No prescribed intensity and duration; typically 12 weeks	No prescribed intensity and duration; recommended for 24 weeks	No prescribed intensity and duration; typical range of 5 to 10 months

https://store.samhsa.gov/product/Treatment-of-Stimulant-Use-Disorder/PEP20-06-01-001

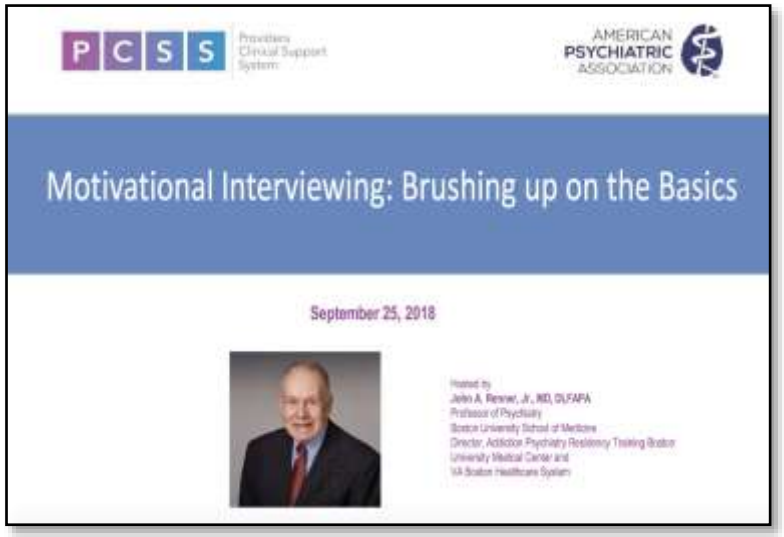
Motivational Interviewing (MI)

- Evoke change talk from individuals overcome ambivalent feelings and insecurities
- In the process, individuals become more likely to make the changes that they verbalize.
- MI does not have a prescribed time period

Motivational Interviewing (MI)

- Five principles
  - Empathy through reflective listening
  - Identify discrepancies between patient's goals/values and current behaviors
  - Avoid arguments and direct confrontations
  - Adjust to a patient's resistance rather than opposing it directly
  - Support self-efficacy and optimism

Motivational Interviewing: Resources



Available at: http://pcssnow.org/event/motivational-interviewing-brushing-up-on-the-basics and http://motivationalinterviewing.org

Contingency Management (CM)

- Basic Assumptions of CM
  - Substance use can be reduced using operant conditioning
  - Useful in promoting treatment retention and adherence
  - Incentives for negative urine tests useful in decreasing drug use

Applications of Contingency Management

- Behavioral targets:
  - Counseling attendance
  - Drug use

- Reinforcing consequences:
  - Money (or vouchers)
  - Privileges (e.g. take-home doses)

Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, ctndisseminationlibrary.org/PPT/485Stitzer.ppt

Contingency Management (CM)

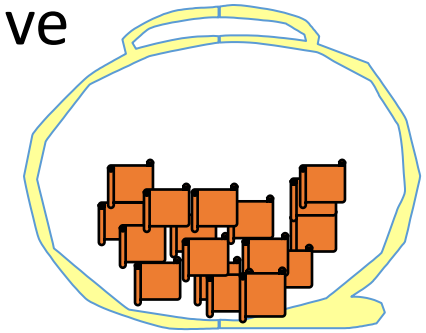
- Key Concepts
  - Behavior to be modified (e.g. stimulant use) must be objectively measured
  - Behavior to be modified (e.g. urine toxicology tests) must be monitored frequently
  - Reinforcement must be immediate
  - Penalties for unsuccessful behavior (e.g. +UDS) include withholding the reinforcer

Nancy Petry's Fishbowl

Fishbowl Method

Incentive = draws from a bowl

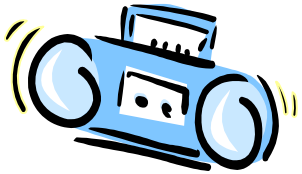
- Draws earned for each negative urine
- Number of draws can escalate
- Bonus draws can be given for consecutive weeks of abstinence



Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, ctndisseminationlibrary.org/PPT/485Stitzer.ppt

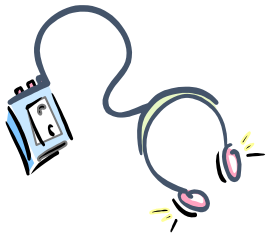
Half the fishbowl slips are winners
Win frequency inversely related to cost

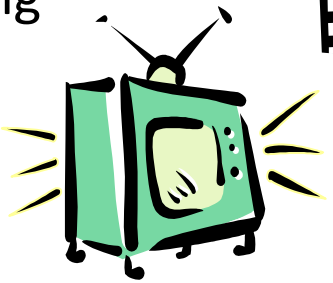
- largest chance of winning a small $1 prize



- moderate chance of winning a large $20 prize

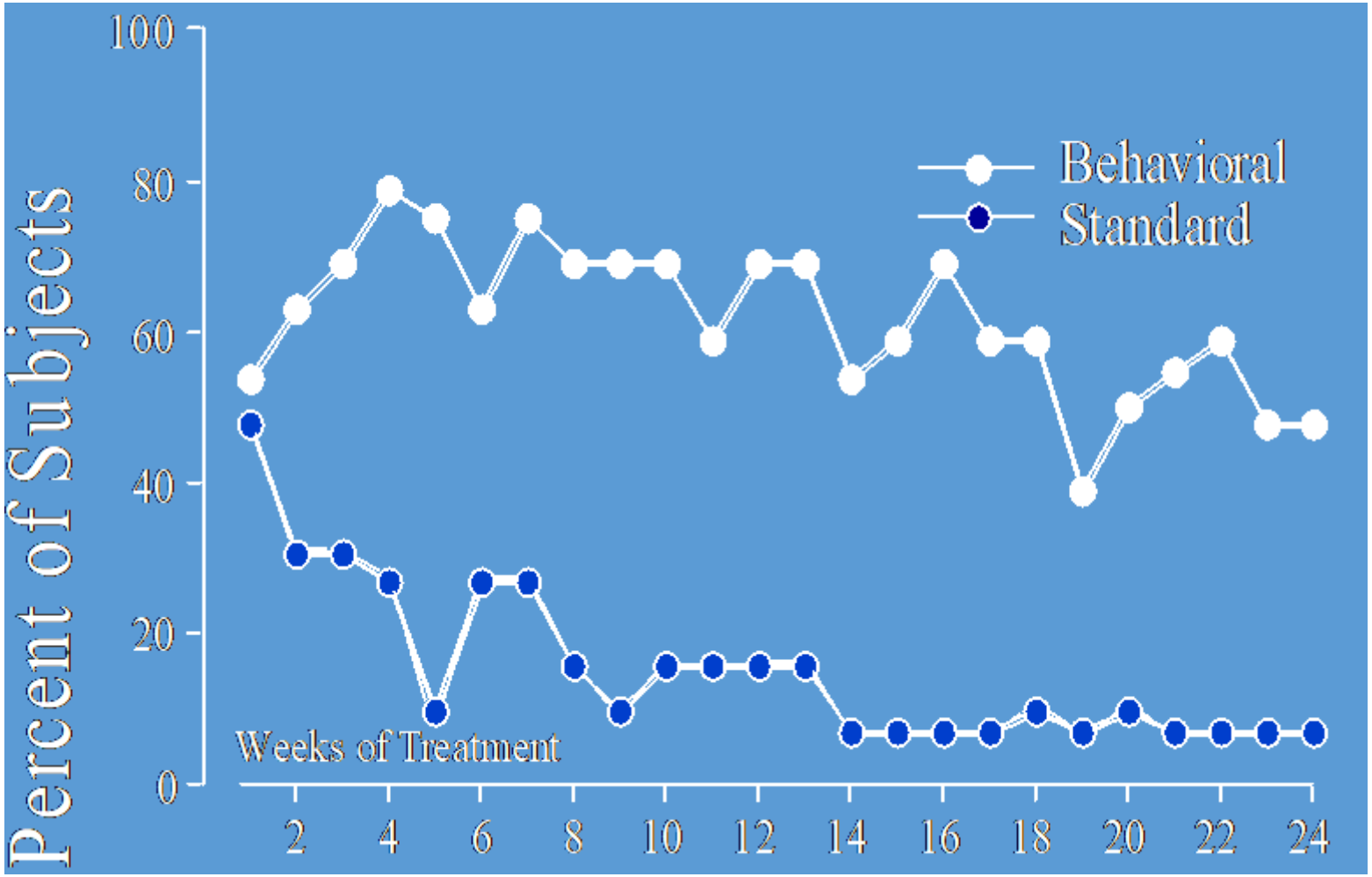
- small chance of winning a jumbo $100 prize





Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, ctndisseminationlibrary.org/PPT/485Stitzer.ppt

Voucher Incentives in Treatment



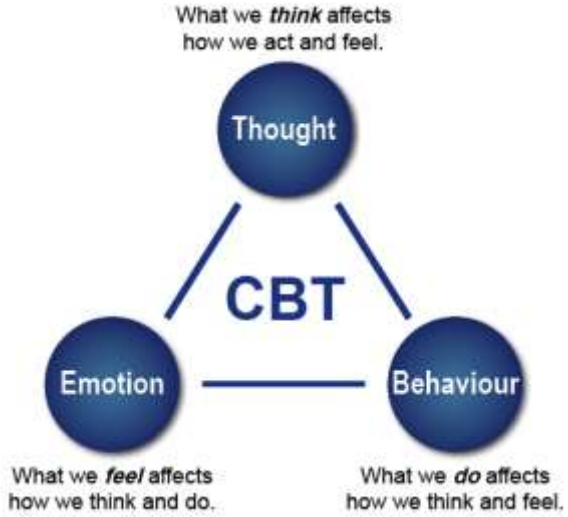
Higgins ST, Budney AJ, Bickel WK, Hughes JR, Foerg F, Badger G. Achieving cocaine abstinence with a behavioral approach. Am J Psychiatry. 1993 May;150(5):763-9. doi: 10.1176/ajp.150.5.763. PMID: 8480823. http://pubmed.ncbi.nlm.nih.gov/8480823

Slide Credit: Maxine Stitzer, Ph.D., Johns Hopkins University SOM, ctndisseminationlibrary.org/PPT/485Stitzer.ppt

Community Reinforcement Approach (CRA)

Cognitive Behavioral Therapy (CBT)

- Patients trained to evaluate faulty patterns of thinking, actions, and negative feelings associated with their drug use
- Tailored to the needs of the individual and their unique experiences with their stimulant use
- Standard therapeutic session last ~50 minutes
- Counseling period last ~5-10 months



Medications for Stimulant Use Disorder (MAT for StUD)

Medications for Methamphetamine Use Disorder (none are FDA approved)

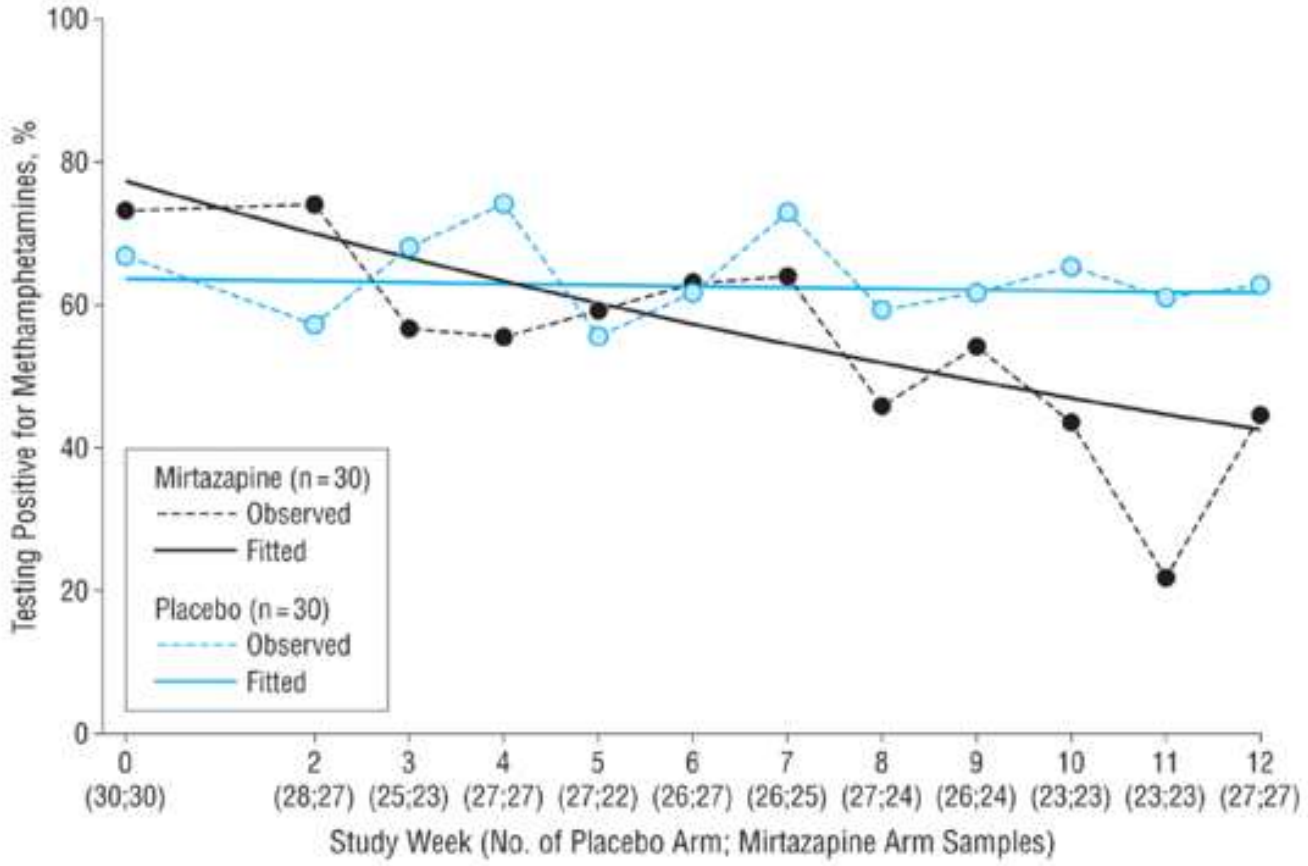
- Naltrexone LAI and high dose bupropion (small effect)
- Mirtazapine (two small studies)
- Bupropion (low-level users who will adhere)
- Topiramate (low-level users)
- Naltrexone (for those who had already stopped using methamphetamine for 2+ weeks)

- Dextroamphetamine (one small study)
- Methylphenidate (moderate to high dose in frequent users/those with ADHD)

http://custom.cvent.com/10D3BAE39269457884C1D96DE1DF8D8D/files/f9dd789e619c417e8d753a1c767a28b8.pdf

http://vimeo.com/390978438/7e844d0b02

Mirtazapine 30mg QD vs. placebo in meth dependent MSM (N=60)



Colfax, GN, et al., Arch Gen Psychiatry. 2011 Nov.; 68(11): 1168-1175

Mirtazapine

- Start mirtazapine at 15 mg qHS and increase to 30mg qHS after 7 days
- Treats Depression, Anxiety and helps with Insomnia
- Common side effects:
  - Weight gain
  - Sedation

Bupropion: dopamine-norepinephrine re-uptake inhibitor for meth?

Randomized trial of bupropion SR 150 mg bid vs placebo for 12 weeks in methamphetamine users with ***less than daily meth use***

Total sample	Bupropion (N=41)	Placebo (N=43)	P value
End of treatment abstinence	29% (12)	14% (6)	0.087

Only 32% (13/41) of bupropion participants were deemed medication adherent via week 6 plasma bupropion level. Adherence was strongly associated with end of treatment meth abstinence.

Bupropion only	Adherent (N=13)	Non-adherent (N=28)	P value
End of treatment abstinence	54% (7)	18% (5)	0.018

Heinzerling KG., Addiction. 2014

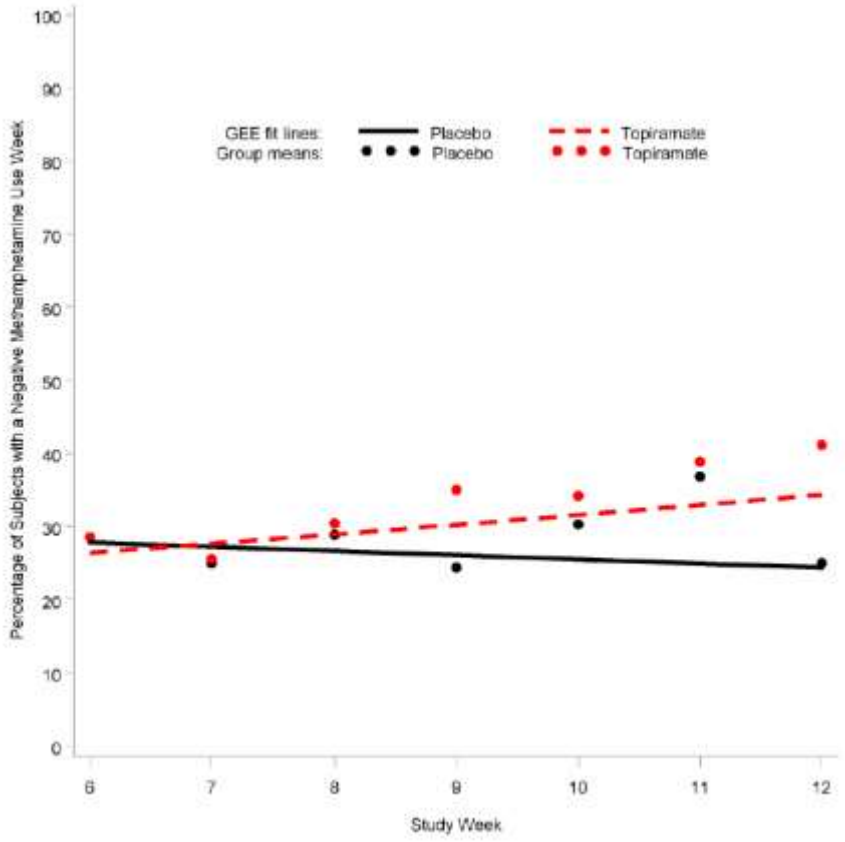
Bupropion

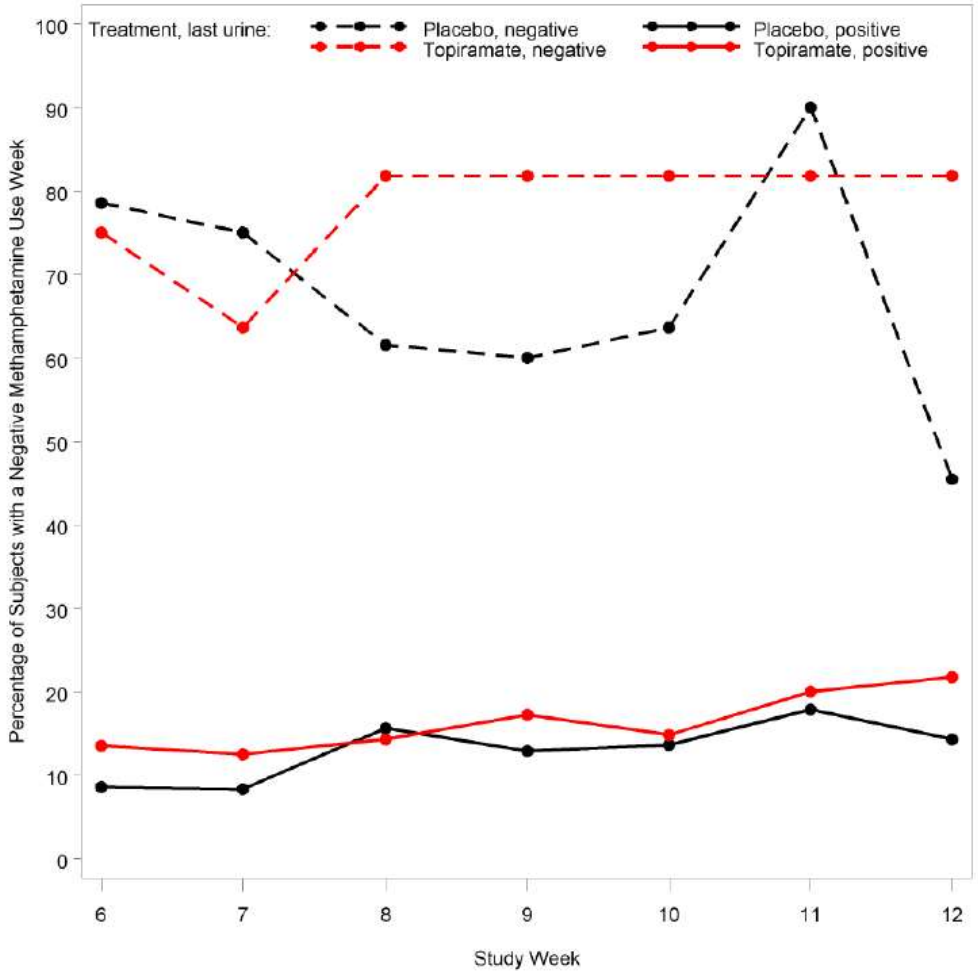
- Start Bupropion XL 150 mg daily for 7 days, then 300 mg daily thereafter

- Avoid in those who:
  - Abuse ETOH/Sedatives or undergoing abrupt ETOH/Sedative discontinuation
  - Bulimia/Anorexia Nervosa
  - Patients with increase risk of Seizures

- Common side effects: Dry mouth, anxiety, insomnia

Topiramate





Elkashef, A., et al., Addiction, 2012

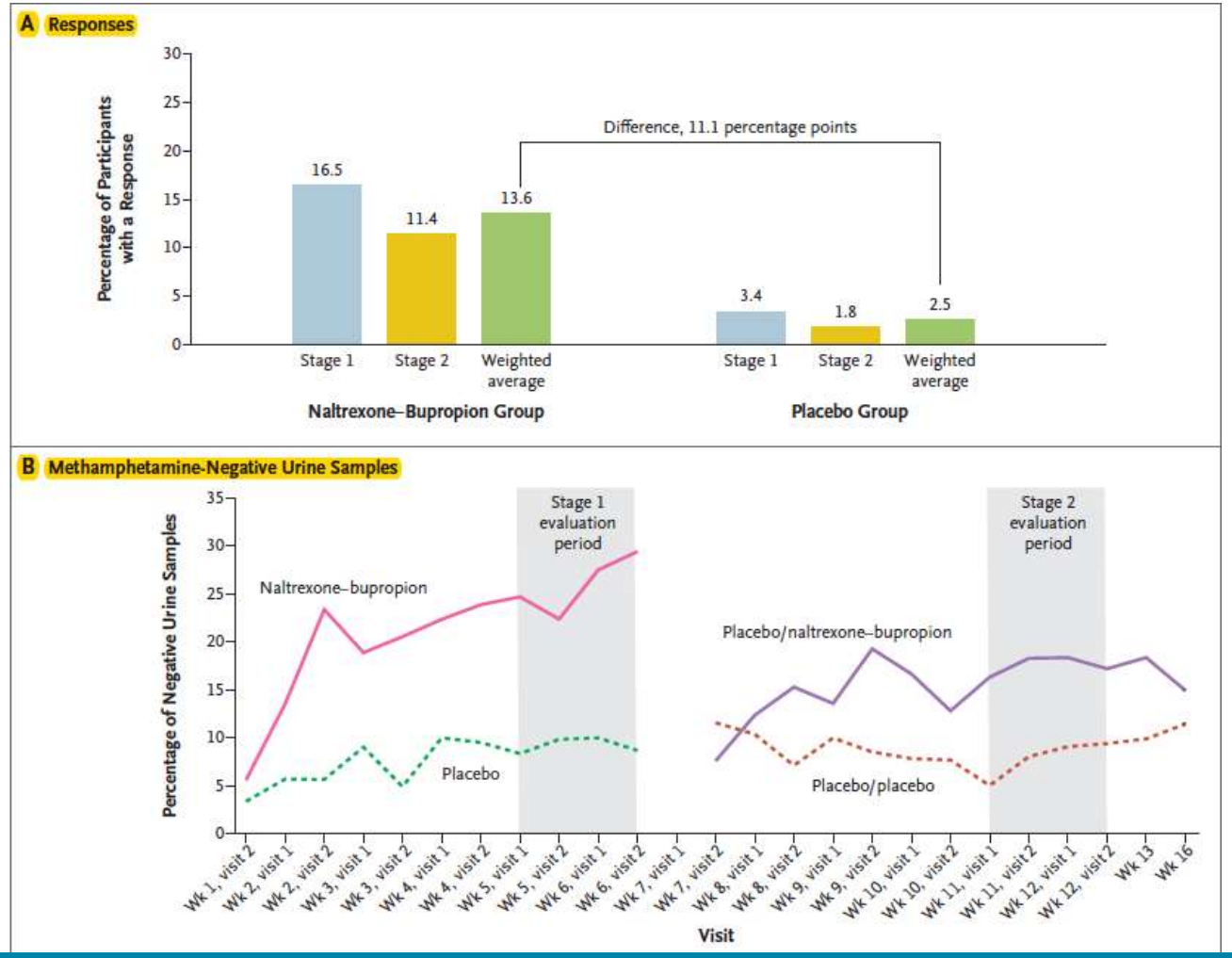
Topiramate

- Start 25mg qHS and titrate up in 25 to 50mg increments as tolerated over a month until the patient is taking either 100mg BID or 200mg qHS, or until the patient's maximum tolerated dose is reached

- Do NOT neglect to provide contraceptive treatments to appropriate patients of childbearing age who are prescribed topiramate.

- Kidney Stones: Use with other carbonic anhydrase inhibitors, other drugs causing metabolic acidosis, or in patients on a ketogenic diet should be avoided

Naltrexone LAI + Bupropion XL



Trivedi, M.H., NEJM, 2021

Naltrexone PO and Naltrexone LAI + Bupropion XL

- Patients must be opioid-free for a minimum of 7-10 days before starting Naltrexone treatment

- Administer Naltrexone extended-release injectable suspension 380mg via intramuscular injection monthly or oral naltrexone 50mg daily

- Naltrexone extended-release injectable suspension in combination with bupropion XL (In the study previously shown):

    - Administer Naltrexone extended-release injectable suspension 380mg via intramuscular injection **every three weeks** in combination with Buproprion XL

    - Titrated Buproprion XL 150mg on day 1, 300mg on day 2, and 450mg daily beginning day 3.

    - Doses can be reduced to alleviate adverse effects although in the trial the prescribing clinicians were encouraged to attempt to raise the dose back up to the 450mg daily dose.

Medications for Cocaine Use Disorder (none are FDA approved)

- Sertraline (abstinent from cocaine and experiencing depression)
- Topiramate (low-level users)
- Modafinil (if the client does not have alcohol use disorder)

- Methamphetamine Sustained Release
- Combination of Mixed Amphetamine Salts-Extended Release and Topiramate
- Mixed Amphetamine Salts-Extended Release (high dose if +ADHD)
- Dextroamphetamine Sustained Release

http://custom.cvent.com/10D3BAE39269457884C1D96DE1DF8D8D/files/f9dd789e619c417e8d753a1c767a28b8.pdf

http://vimeo.com/390978438/7e844d0b02

Stimulant Use Disorder Treatment Key Principles

- Avoid Confrontation
- Therapeutic Alliance
- Meeting the patient where they are at
- Motivational Interviewing
- CM ± CRA
- CBT
- Counseling plus meds
- Frequent Follow-up Visits
- Exercise

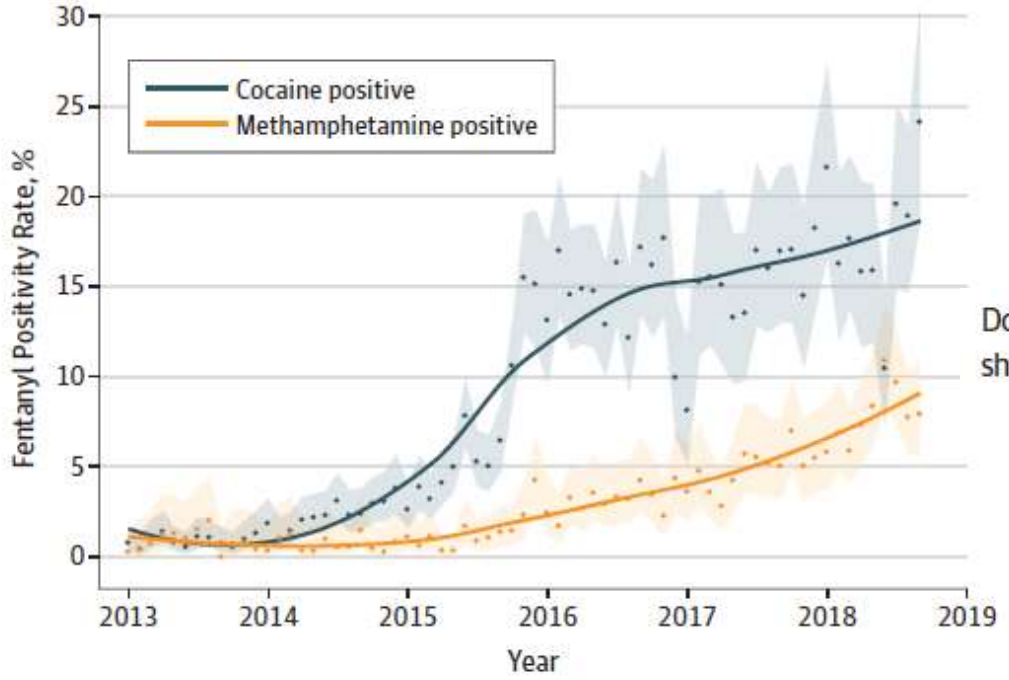
Stimulant Use Disorder Treatment Key Principles

Follow-Up

- Monitor whether patient is achieving their goals
  - If patient not responding to treatment → reassess and adapt or change treatment(s)
  - Develop tracking protocols (e.g., EHR registry) for ensuring population-based follow-up

Methamphetamines and Fentanyl

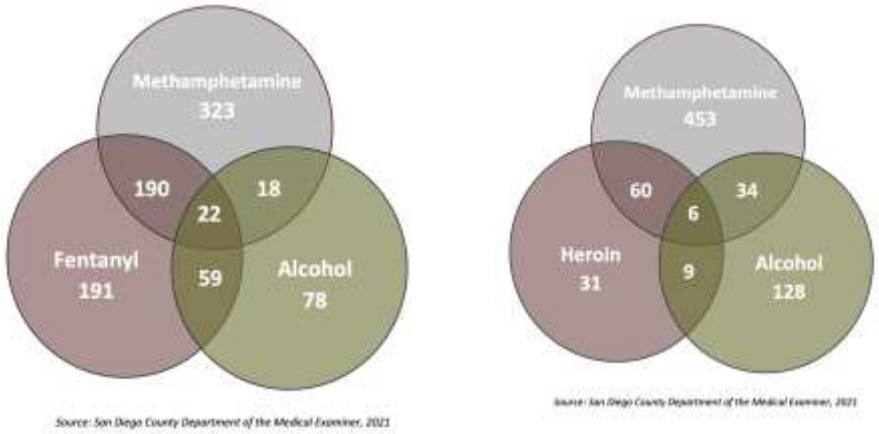
Figure. Nonprescribed Fentanyl Positivity Among Urine Drug Test Results Positive for Cocaine or Methamphetamine

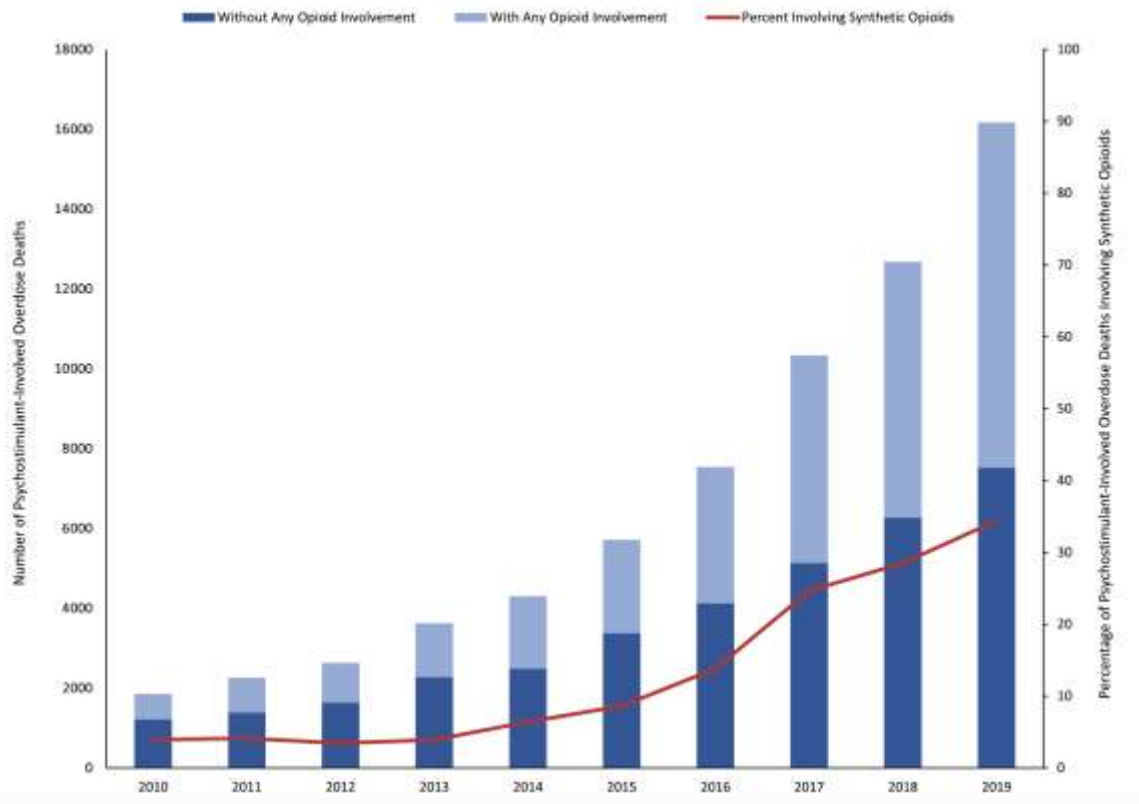


Dots represent monthly fentanyl positivity values; shaded areas, binomial 95% CIs.

LaRue et al, 2019

“Goofball” = Risky Use leading to Deadly results





San Diego County Meth Strike Force 2021 Report Card
Jones, C M., et al., Ann. N.Y. Acad. Sci., 2021

Don’t forget to provide comprehensive care

- StUD patients require comprehensive care!
  - Physical health issues
  - Co-morbid substance use
  - Mental Health
  - Psychosocial issues
- Patient education
  - Narcan!!!

- Laboratory workup recommended
  - CBC
  - CMP
  - Hepatitis A, B & C
  - Pregnancy test
  - STD/HIV screen
  - Urine toxicology, comprehensive

References

1. Substance Abuse and Mental Health Services Administration. (2020). *Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health* (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from http://www.samhsa.gov/data
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Poll

1. On a scale of 1-5, please select the number that best represents your experience with today's session.

5 – Excellent
4 – Very Good
3 - Good
2 - Fair
1 – Poor

2. Please select the number that best represents your response to the statement: Today's session was a valuable use of my time.

5 – Strongly Agree
4 - Agree
3 - Neutral
2 - Disagree
1 – Strongly Disagree

3. I can apply learnings from today's webinar to my MAT work.

5 – Strongly Agree
4 - Agree
3 - Neutral
2 - Disagree
1 – Strongly Disagree

Coming Up – Session #4 (final session)

Friday, December 3, 12-1pm PT

Topic: Office Hours – Prescribing Medications for OUD and StUD

Come with questions, challenges, and case examples you'd like to discuss on the call with Dr. Sepulveda and other attendees.

For registration information, go here:
https://www.careinnovations.org/events/atsh-peer-forums-registration/#prescriber

Any questions? Email meaghan@careinnovations.org


THE END


ANY
QUESTIONS?