

Treatment Options? What Treatment Options? -- Making Sense of the Methamphetamine Mess

PARTNERSHIP



HEALTHPLAN
of CALIFORNIA
A Public Agency

Jeffrey DeVido, MD, MTS

3/12/2020; 12pm

Behavioral Health Clinical Director,
PHP

Chief, Addiction Services, Marin
County BHRS



Agenda

12:00 to 12:05 PM

Welcome/Housekeeping Rules

Liezel Lago, Continuing Education Program Coordinator

12:05 to 12:10 p.m.

Introduction

Jeffrey DeVido, MD, MTS

Behavioral Health Clinical Director, Partnership Health Plan of California

12:10 to 12:55 p.m.

Treatment Options? What Treatment Options? Making Sense of Methamphetamine

12:55 to 1:00 p.m.

Question & Answer Discussion

1:00 p.m.

Adjourn



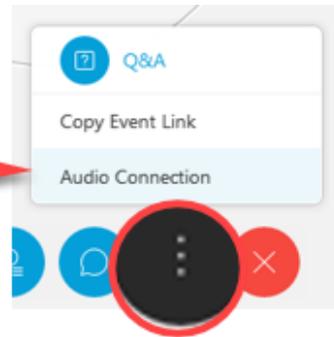
No Conflict of Interest

- Presenter has signed the Conflict of Interest form and has declared there is no conflict of interest and nothing to disclose for this presentation.
- *CME – Approved for 1.00 AAFP elective credits.*
- ***CME credit is for physicians, physician assistants and other healthcare professionals whose continuing educational requirements can be met with AAFP CME.*
- *CE - Provider approved by the California Board of Registered Nursing, Provider #CEP16728 for 1 hours.*

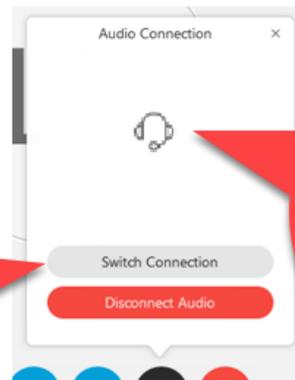
Housekeeping

To avoid echoes and feedback, we request that you use the telephone instead of your computer audio for listening and talking during the webinar.

Click
Audio Connection



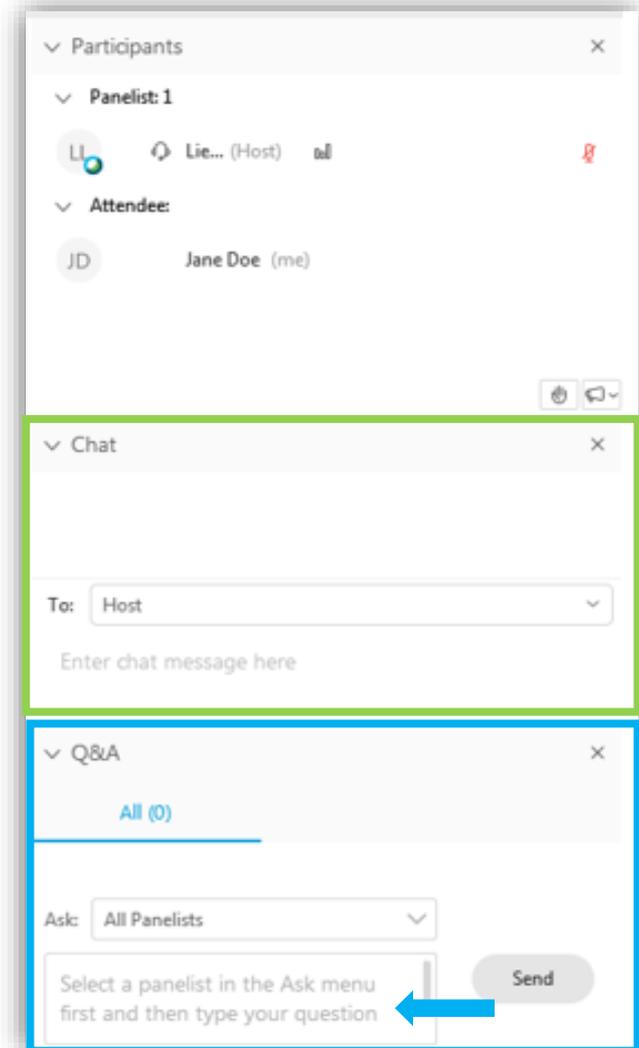
Click
*****Switch Connection**
to change from
computer to phone.



This icon indicates the computer audio is selected for audio. We will not be able to hear you if the computer audio does not have a microphone. Please use the chat box or Q&A box to communicate with the host and panelist(s).

Housekeeping

- All participants have been muted to eliminate any possible noise interference/distraction.
- Participants are encouraged to type questions in the “Q&A” box and comments in the “Chat” box.





Jeffrey DeVido, MD, MTS

About Us



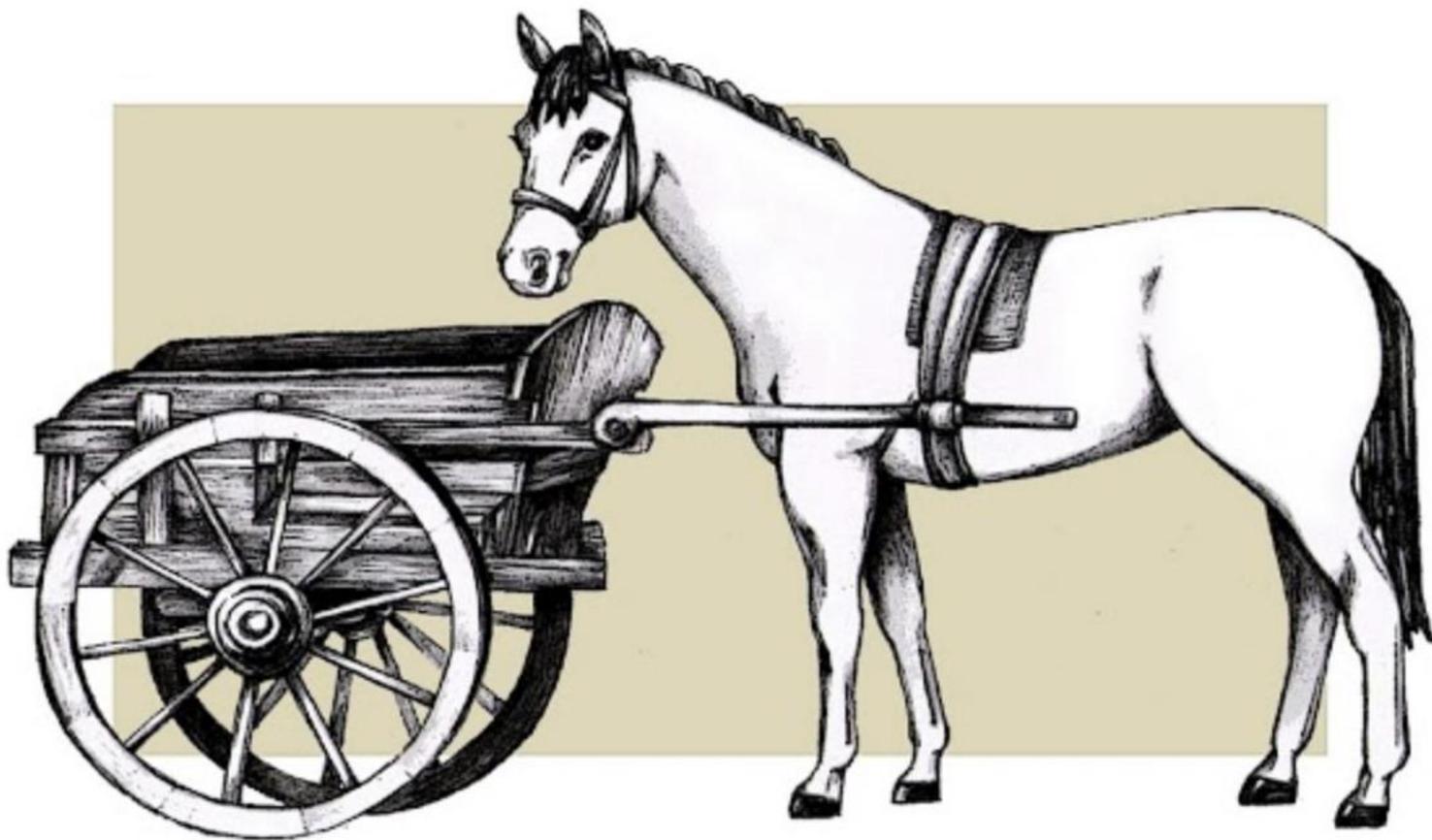
Mission:

To help our members, and the communities we serve, be healthy.

Vision:

To be the most highly regarded managed care plan in California.

Resources



<http://thecartbeforethehorse.blogspot.com>



Resources



Providers
Clinical Support
System



ASAM American Society of
Addiction Medicine



American Academy of
Addiction Psychiatry

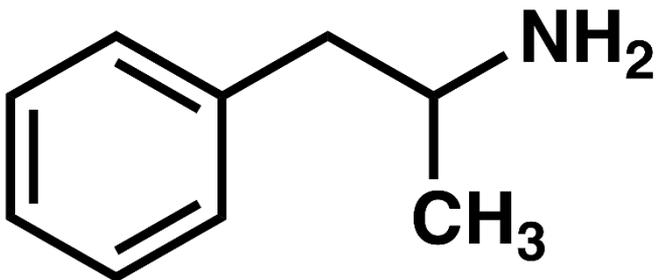
Translating Science. Transforming lives.



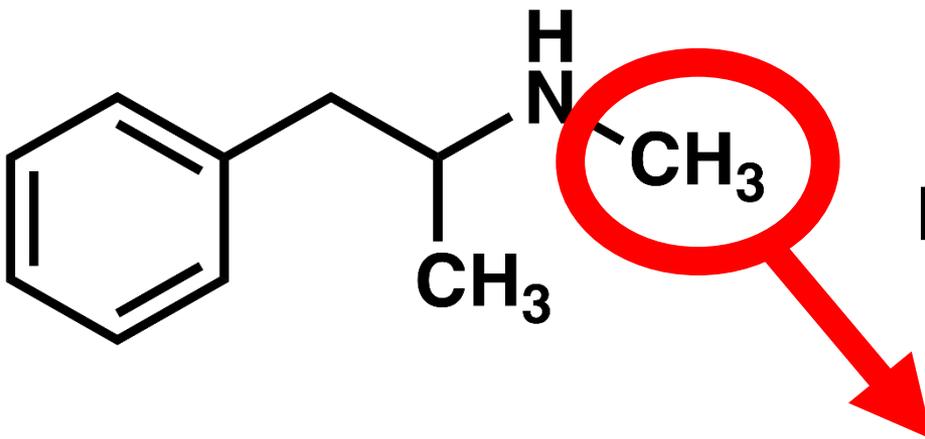
ATTC

Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

What is Methamphetamine



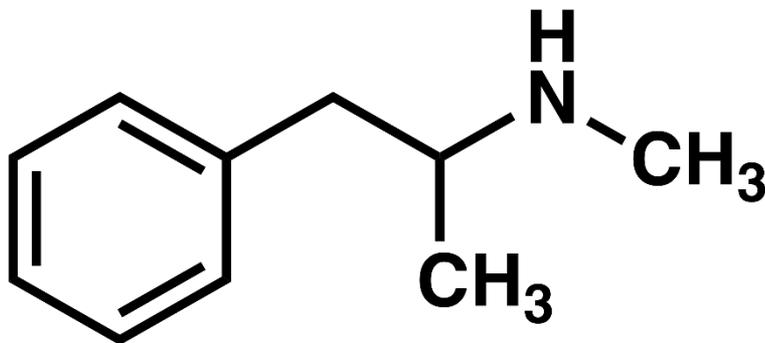
Amphetamine



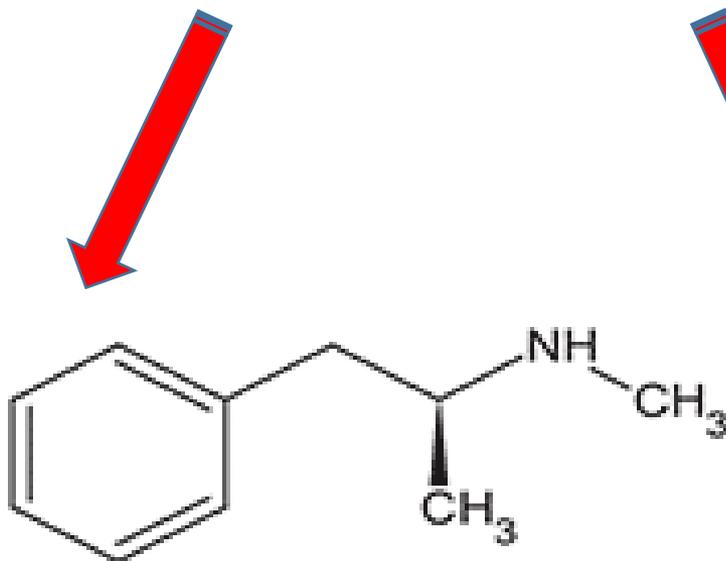
Methamphetamine

Prevents degradation in bloodstream

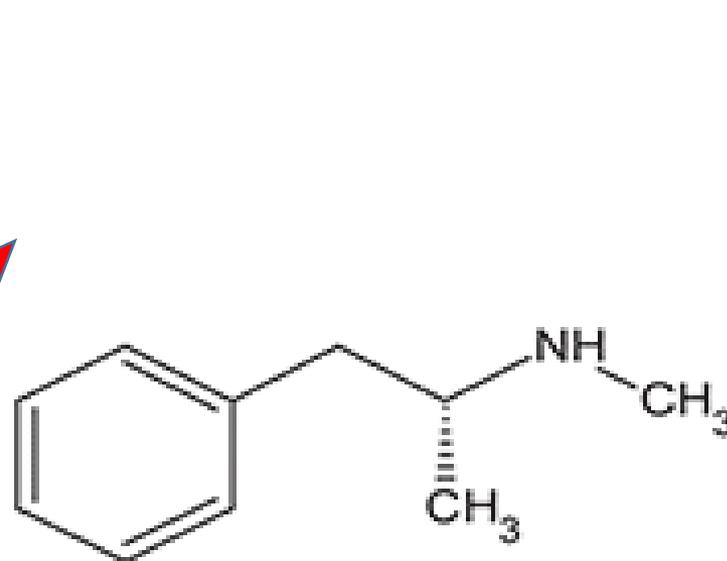
What is Methamphetamine



Methamphetamine

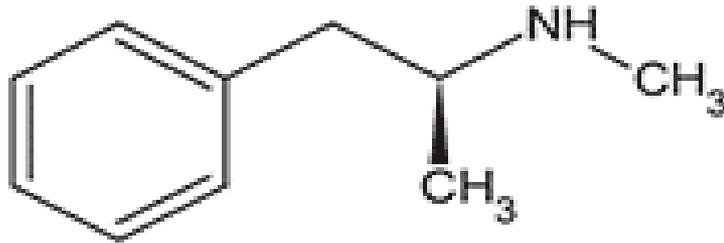


D-Methamphetamine
(dextro-Methamphetamine,
S(+)-Methamphetamine)

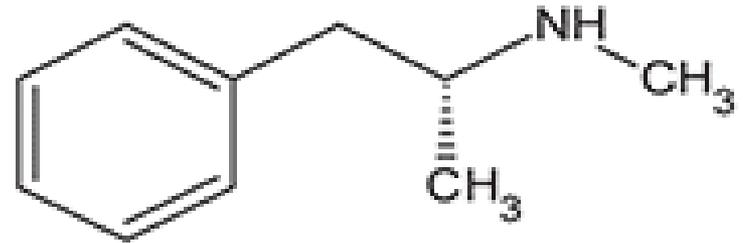


L-Methamphetamine
(levo-Methamphetamine,
R(-)-Methamphetamine)

What is Methamphetamine



D-Methamphetamine
 (dextro-Methamphetamine,
 S(+)-Methamphetamine)

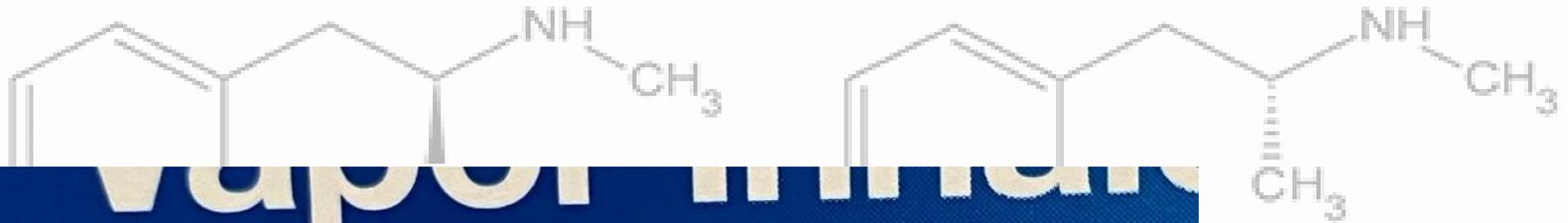


L-Methamphetamine
 (levo-Methamphetamine,
 R(-)-Methamphetamine)



Racemic mixture =
 “methamphetamine”
 Schedule 2:
 Desoxyn®
 Indications: ADHD,
 treatment refractory
 obesity

What is Methamphetamine

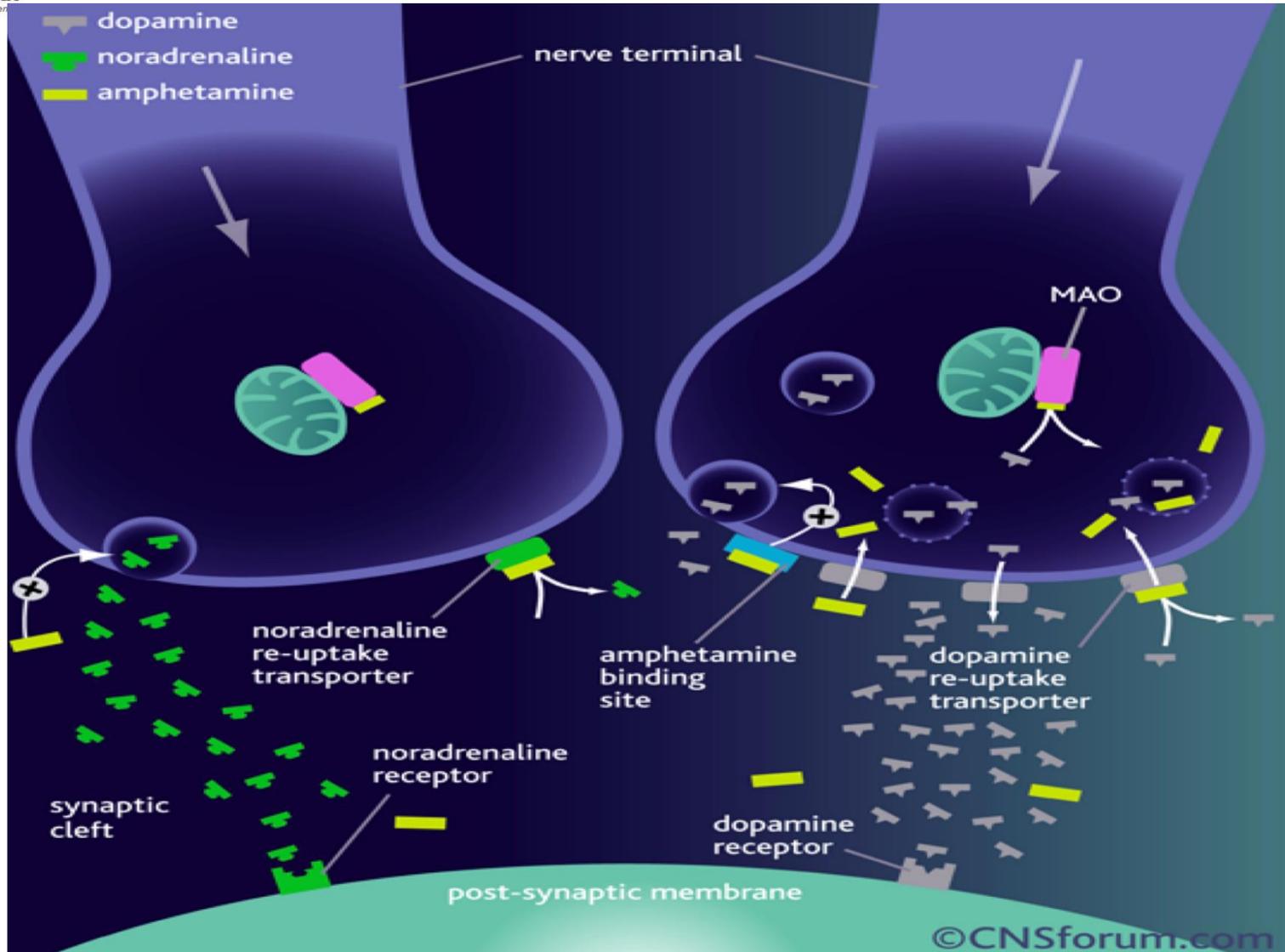


LEVMETAMFETAMINE
 Nasal decongestant

phetamine
 mphetamine,
 mphetamine)



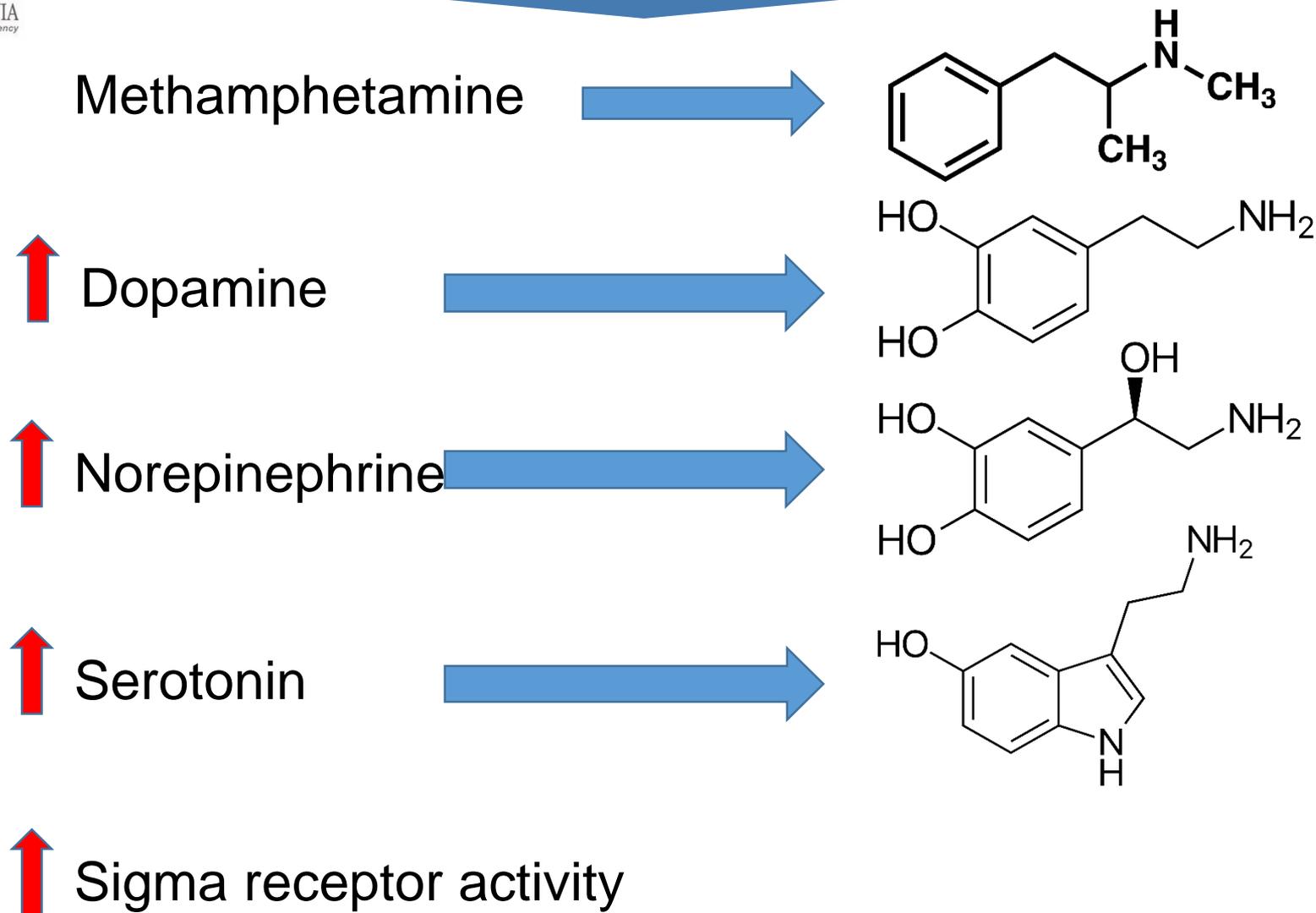
How does Methamphetamine work?



How does Methamphetamine work?

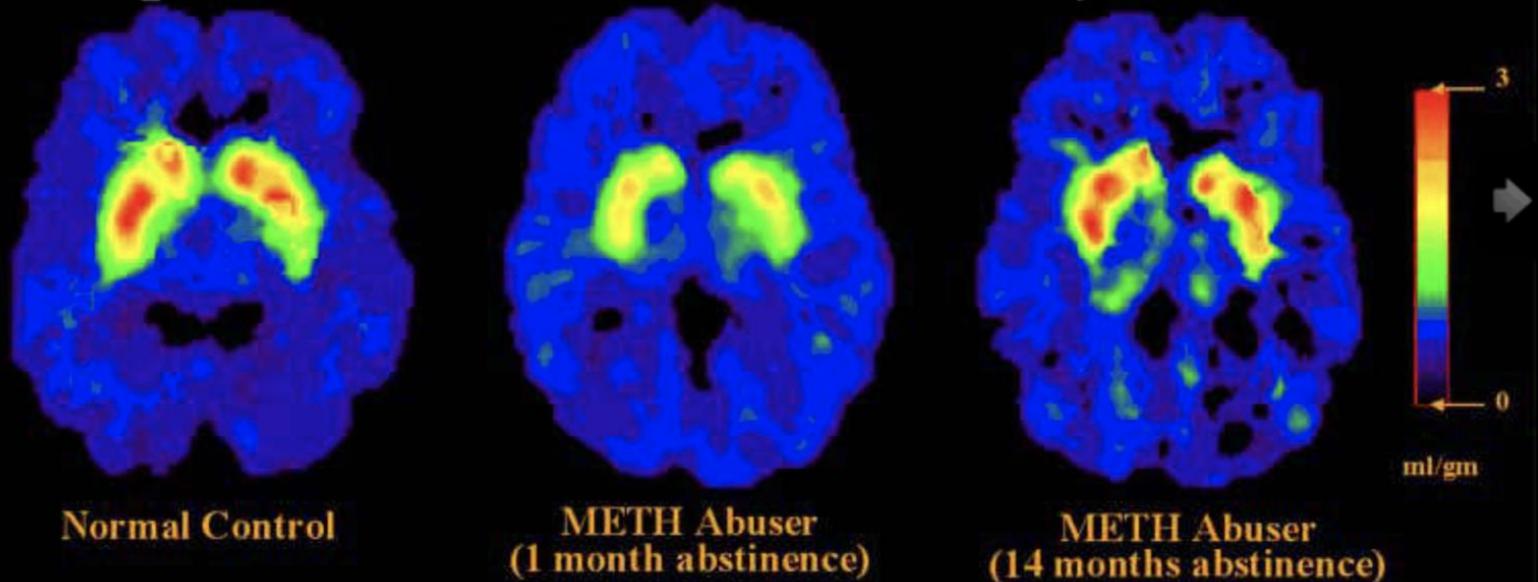


How does Methamphetamine work?



Methamphetamine

Figure 2. Partial Recovery of Brain Dopamine Transporters in Methamphetamine (METH) Abuser After Protracted Abstinence

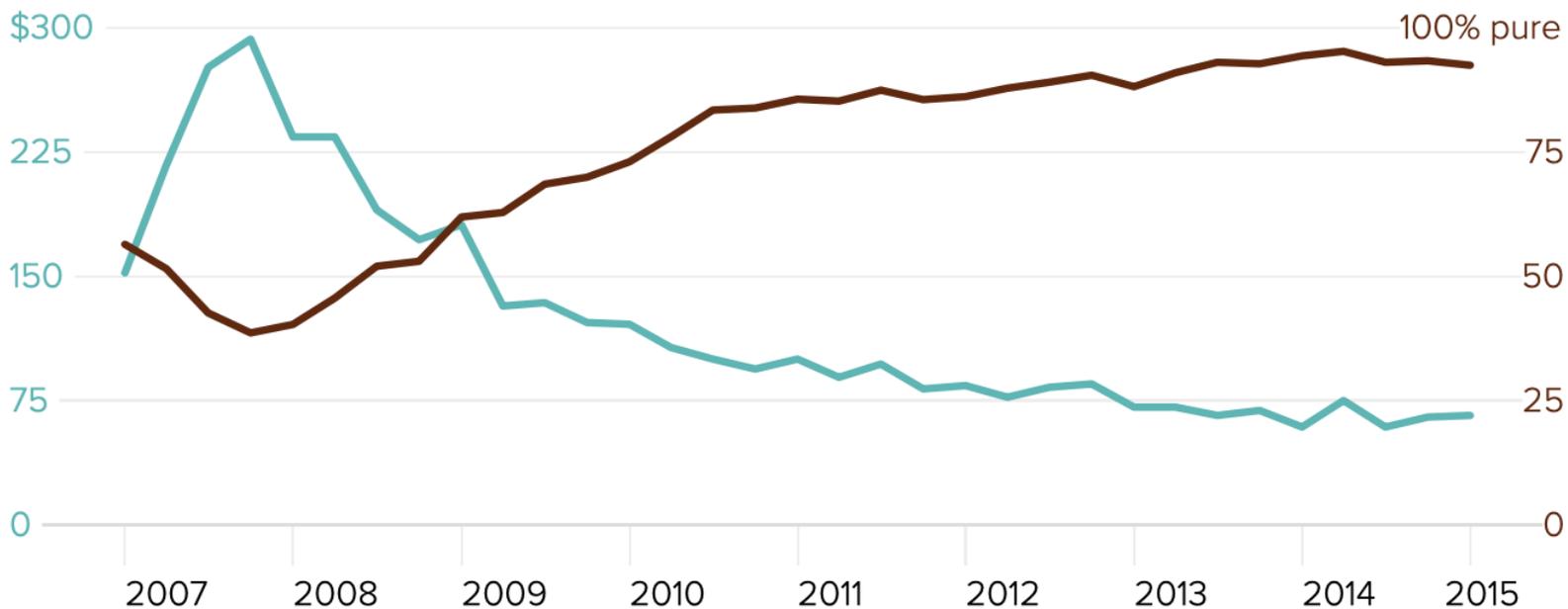


Source: Volkow, ND et al., Journal of Neuroscience 21, 9414-9418, 2001.

Methamphetamine

Price and Purity of U.S. Methamphetamine Purchases

■ Price (per pure gram)
 ■ Percent pure



Methamphetamine— Treatments

What do addiction studies normally assess?

- Negative urine toxicologies
- Decreased cravings
- Retention in treatment
- Frequency of use
- Amount used
- Abstinence at end of treatment

Methamphetamine— Behavioral Treatments

2018: systematic review and network meta-analysis

- 50 Clinical Studies; 6943 participants
- 12 different interventions
- Contingency Management + Community reinforcement approach best for efficacy and acceptability

De Crescenzo F, Ciabattini M, D'Alò GL, De Giorgi R, Del Giovane C, Cassar C, et al. (2018) Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. *PLoS Med* 15(12): e1002715.

Methamphetamine— Behavioral Treatments

San Francisco Chronicle

SF's Scott Wiener wants to fund financial rewards for meth addicts who stop using drugs



Alexei Koseff

| Feb. 26, 2020

| Updated: Feb. 26, 2020 7:16 p.m.

Democratic Sen. Scott Wiener introduced [SB888](#), which would expand the substance abuse treatment options that qualify for Medi-Cal, the state's health care program for the poor, to include [contingency management](#). These programs use vouchers or small cash prizes to motivate people to stay off drugs.

Methamphetamine— Behavioral Treatments

Exercise!?

- STRIDE: NIDA CTN
 - 9 residential SUD sites, 12 weeks
 - N = 302 (Stimulant abuse)
 - TAU + Exercise *or* health education
 - Exercise 3x/week
 - Outcome: abstinent days via Utox and self report during weeks 4-12

Trivedi MH, et al, Randomized Controlled Trial Comparing Exercise to Health Education for Stimulant Use Disorder: Results From the CTN-0037 STimulant Reduction Intervention Using Dosed Exercise (STRIDE) Study. J Clin Psychiatry 2017;78(8):1075–1082

Methamphetamine— Behavioral Treatments

Exercise!?

- **STRIDE: NIDA CTN**
 - No difference in primary outcome measure... BUT...
 - Those who actually adhered to the intervention had more abstinent days
 - ALSO, overall abstinence (75%) was higher for BOTH groups relative to most studies (50%)

Trivedi MH, et al, Randomized Controlled Trial Comparing Exercise to Health Education for Stimulant Use Disorder: Results From the CTN-0037 STimulant Reduction Intervention Using Dosed Exercise (STRIDE) Study. J Clin Psychiatry 2017;78(8):1075–1082

Methamphetamine— Behavioral Treatments

Exercise!?

- NIDA, inpatient methamphetamine specific
 - 8 weeks, exercise vs. health education
 - N = 135
 - 3x/week, structured 60 minutes exercise
 - 30” aerobic, 15” resistance
 - Outcomes: reduction in depression/anxiety

Rawson RA, et al, The Impact of Exercise On Depression and Anxiety Symptoms Among Abstinent Methamphetamine-Dependent Individuals in A Residential Treatment Setting

[Journal of Substance Abuse Treatment Volume 57](#), October 2015, Pages 36-40.

Methamphetamine— Behavioral Treatments

Exercise!?

- NIDA, inpatient methamphetamine specific
 - Dose effect observed (decrease in depression and anxiety severity)
 - No decrease in post-release meth use overall
 - Secondary analysis: lower severity of meth use at baseline → @ 1, 3, 6 months DID have reduction in use

Rawson RA, et al, The Impact of Exercise On Depression and Anxiety Symptoms Among Abstinent Methamphetamine-Dependent Individuals in A Residential Treatment Setting
[Journal of Substance Abuse Treatment Volume 57](#), October 2015, Pages 36-40.

Methamphetamine— Medication Treatments

Party Line = No FDA-Approved
medications for stimulant use
disorders

What should I do?



Studies have been small,
underpowered, design flaws
(adherence), high attrition, haven't
looked at combinations

Methamphetamine— Medication Treatments

- **Generally negative:**

- Sertraline (lower retention and more adverse effects)
- Aripiprazole (may make it worse—trial halted, INCREASE use))
- Imipramine
- Desipramine
- Ondansetron
- Tyrosine
- Fluoxetine
- Paroxetine
- Gabapentin
- N-acetylcysteine
- D-amphetamine (mixed—less effect on relapse, but perhaps effects on withdrawal and cravings)
- Modafinil (mixed, perhaps better in high severity users?)

Methamphetamine— Medication Treatments

- **Generally positive:**
 - Bupropion
 - Topiramate
 - Methylphenidate
 - Naltrexone
 - Mirtazapine

Methamphetamine— Medication Treatments

- **2018, Chan, et al:**
 - 14 RCTs, 1 Systematic Review
 - Low-strength evidence:
 - Topiramate (better for those who can produce negative Utox at baseline, reduction in use)
 - Bupropion (better for less severe at baseline, ?men)
 - Methylphenidate (reduction in use, severe)

Chan B, Kondo K, Ayers C, et al. **Pharmacotherapy for Stimulant Use Disorders: A Systematic Review [Internet]**. Washington (DC): [Department of Veterans Affairs \(US\)](#); 2018 Aug.

Methamphetamine— Medication Treatments

- **Methylphenidate:**
 - N = 110, DB, PC, RCT
 - 10 weeks active phase, 4 weeks placebo, 54mg/day MPH-SR
 - Outcome: self-reported days of MA use during the last 30 days of the active phase
 - Negative trial... BUT
 - HEAVY users at baseline, when taken out, DID have sig effect

Ling W, et al. Sustained-Release Methylphenidate in a Randomized Trial of Treatment of Methamphetamine Use Disorder.

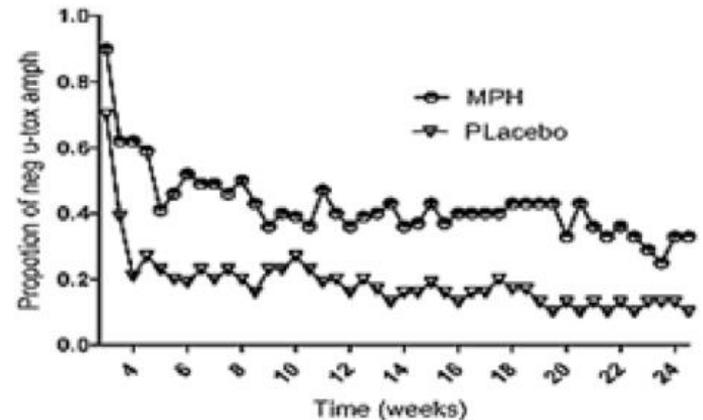
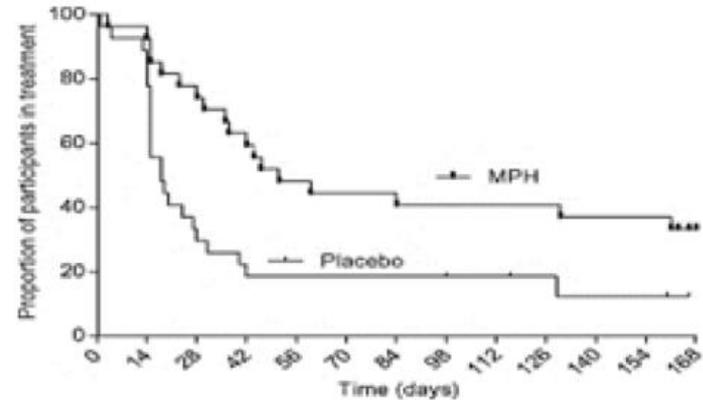
Methamphetamine— Medication Treatments

- **Methylphenidate:**
 - Criminal offenders with ADHD, amphetamine use disorder
 - N = 54; 72mg OROS MPH, then 180mg
 - In lower dose, no effect; higher dose saw effect in negative urines and retention in treatment

Konstenius M, et al. Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. [Addiction](#). 2014 Mar; 109(3): 440–449.

Methamphetamine— Medication Treatments

- **Methylphenidate:**



Konstenius M, et al. Methylphenidate for attention deficit hyperactivity disorder and drug relapse in criminal offenders with substance dependence: a 24-week randomized placebo-controlled trial. [Addiction](#). 2014 Mar; 109(3): 440–449.

Methamphetamine— Medication Treatments

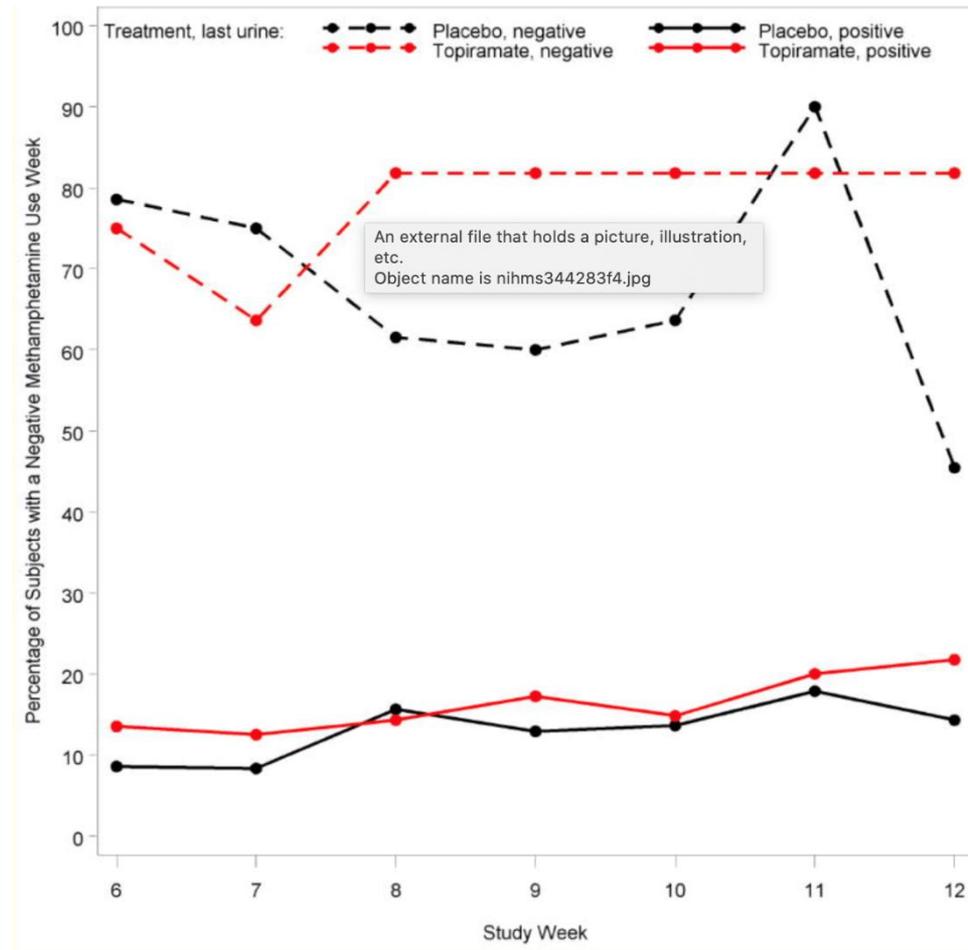
- **Bupropion:**
 - *“Lower severity” = <18days/month*
 - *SR 150mg BID*
 - *Overall, no effect, BUT...*
 - *Only 1/3rd adherent.*
 - *Of those:*
 - *Adherent (13) → 54% abstinent*
 - *Non-Adherent (28) → 18% abstinent*
 - *Replicated by Shoptaw, et al.*

Methamphetamine— Medication Treatments

- **Topiramate:**
 - N = 140, DB, PC, RCT
 - 13 weeks, 25mg start then escalated to 200mg/daily
 - Outcome: negative "methamphetamine use weeks" in weeks 6-12
 - Negative study, BUT... if urine was negative at baseline, then topiramate arm did have effect on increasing neg urines

Elkashef A, et al. Topiramate for the treatment of methamphetamine addiction: a multi-center placebo-controlled trial. [Addiction. 2012 Jul; 107\(7\): 1297–1306.](#)

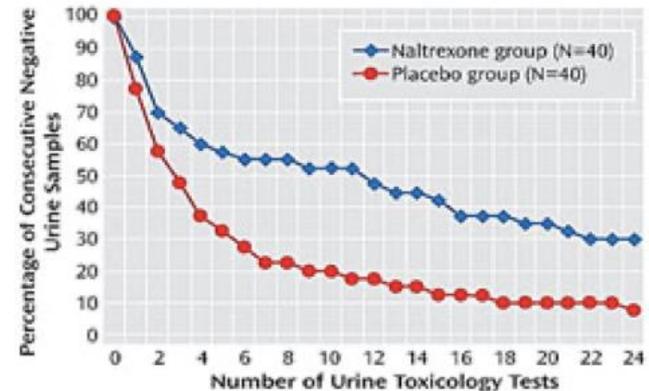
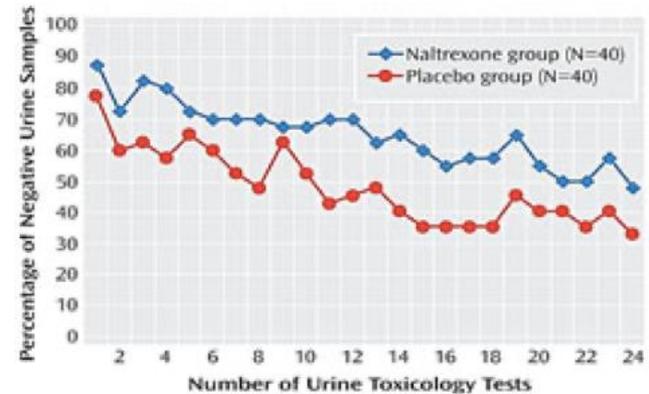
Methamphetamine— Medication Treatments



Elkashef A, et al. Topiramate for the treatment of methamphetamine addiction: a multi-center placebo-controlled trial. [Addiction. 2012 Jul; 107\(7\): 1297–1306.](#)

Methamphetamine— Medication Treatments

- **Naltrexone:**
 - N = 55, DB, PC, RCT
 - 12 weeks, 50mg daily
 - Outcome: negative urines (abstinence)



[Jayaram-Lindström N, et al. Naltrexone for the treatment of amphetamine dependence: a randomized, placebo-controlled trial. *Am J Psychiatry*. 2008 Nov;165\(11\):1442-8.](#)

Methamphetamine— Medication Treatments

- **Naltrexone:**
 - N = 100, DB, PC, RCT/active users/MSM
 - 12 weeks, LAI
 - Outcome: change in level of positive urines

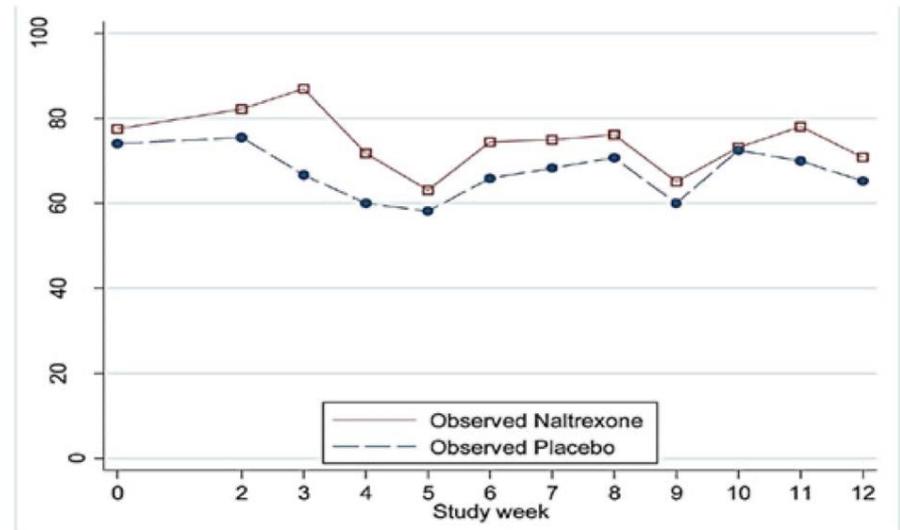


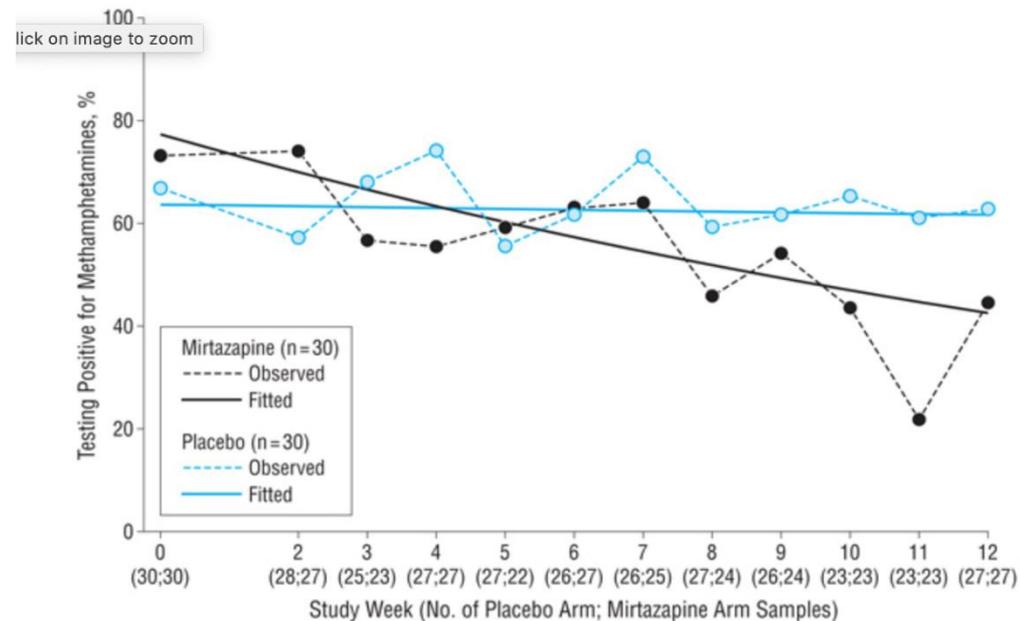
Figure 2. Weekly methamphetamine urine-positivity rates, by treatment arm

Coffin P, et al. **Extended-release naltrexone for methamphetamine dependence among men who have sex with men: a randomized placebo-controlled trial.**

[Addiction](#). 2018 Feb;113(2):268-278.

Methamphetamine— Medication Treatments

- **Mirtazapine:**
 - N = 60, DB, PC, RCT/active users/MSM
 - 12 weeks, 30mg Daily
 - Outcome: change in level of positive urines



[Colfax GN.](#) Mirtazapine to reduce methamphetamine use: a randomized controlled trial.
[Arch Gen Psychiatry.](#) 2011 Nov;68(11):1168-75.

Methamphetamine— Medication Treatments

- **Mirtazapine:**
 - N = 120, DB, PC, RCT/active users/MSM
 - 24 weeks + 12 follow up, 30mg Daily
 - Outcome: change in level of positive urines

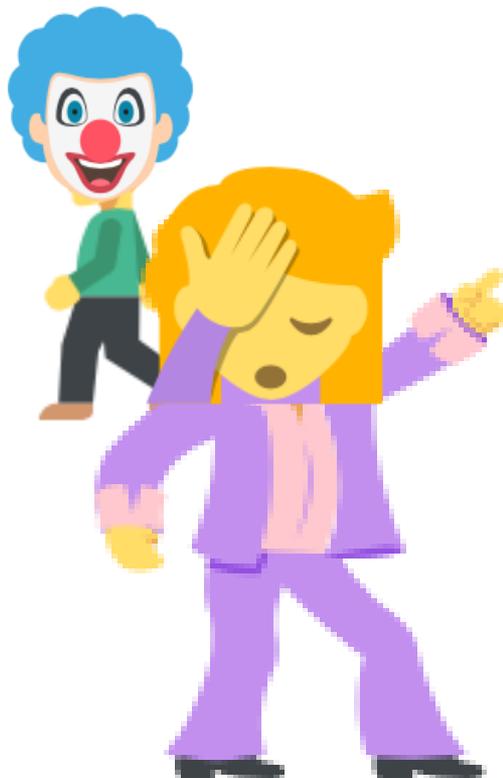
[Coffin PO](#), et al. **Effects of Mirtazapine for Methamphetamine Use Disorder Among Cisgender Men and Transgender Women Who Have Sex With Men: A Placebo-Controlled Randomized Clinical Trial.** [JAMA Psychiatry](#). 2019 Dec 11. doi: 10.1001/jamapsychiatry.2019.3655.

Methamphetamine— Medication Treatments

- **Biological approaches... not yet ready for prime time:**
 - Vaccines
 - Antibody-mediated sequestration
 - Have to mount big enough immune response
 - metabolism augmentation
 - Cholinesterase augmentation in cocaine users

On the shoulders of giants...

Francis Levin



Tom Kosten

John Mariani

Rick Rawson

Larissa Mooney

Tim Wilens

Resources

- <https://cme.csam-asam.org>
- <https://www.asam.org/education>
- <https://attcnetwork.org>
- <https://www.aaap.org/clinicians/education-training/>
- <https://pcssnow.org/education-training/>
- https://education.psychiatry.org/Users/ProductList.aspx?_ga=2.135620595.356069669.1583830631-1074198263.1583830631