

# Stimulants and HIV: The Crisis Continues

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October 15, 2019



## **Disclosure**

**The information or content or conclusions are those of the author and should not be construed as the official position or policy of nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.**

# Objectives

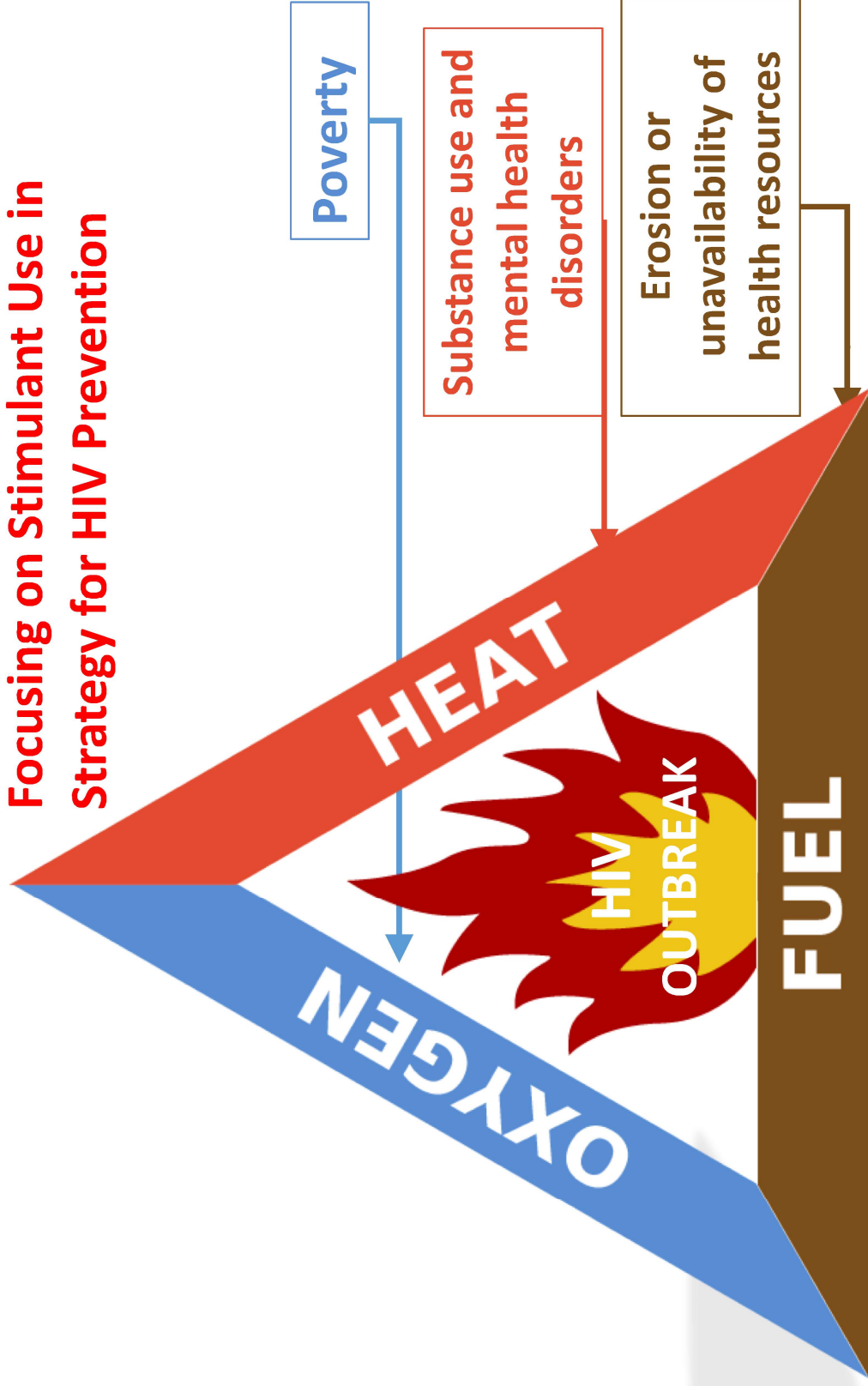


- **Understand the intersections of stimulant use, mental health disorders, and HIV especially for MSM**
- **Understand biological and behavioral impacts of stimulant use in the setting of HIV**
- **Understand advantages to reducing stimulant use, especially for MSM**
- **Understand treatment approaches, especially for MSM**

## Focusing on Stimulant Use in Strategy for HIV Prevention

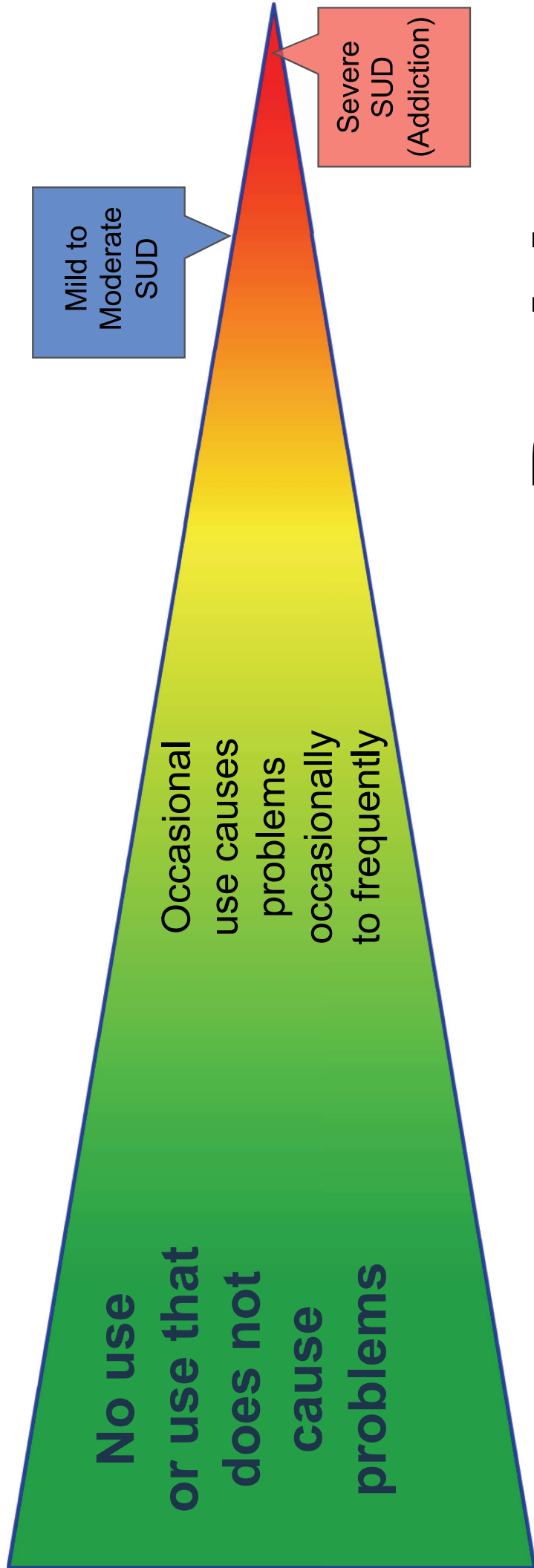
It's the remaining 20% we need to think about

For 80% of the population, standard biomedical, behavioral and risk reduction approaches to HIV prevention and care are effective



# Addiction: Definitional Constructs

# Definitions of a Spectrum: Drug Use to Drug Use Disorder, Mild to Moderate to Severe



Fun 

Fun with Problems 

Problems

# DSM-5 Definition: Substance Use Disorder

Maladaptive pattern of use, *clinically significant impairment or distress* and 2+ of the following in the same 12-month period:

1. Tolerance
2. Withdrawal
3. Used for longer periods than intended
4. Can't cut down or quit
5. Time spent getting, using or recovering
6. Give up social, work or fun activities
7. Craving or a strong desire or urge to use a substance
8. Continued use despite knowledge of negative consequences
9. Failure to fulfill major role obligations
10. Use in physically hazardous situations
11. Continued use despite social and interpersonal problems

Mild = 2-3 criteria; Moderate = 4-5 criteria; Severe = 6+ criteria

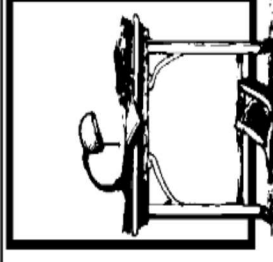
# Current Epidemiology





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*EDITORIAL*



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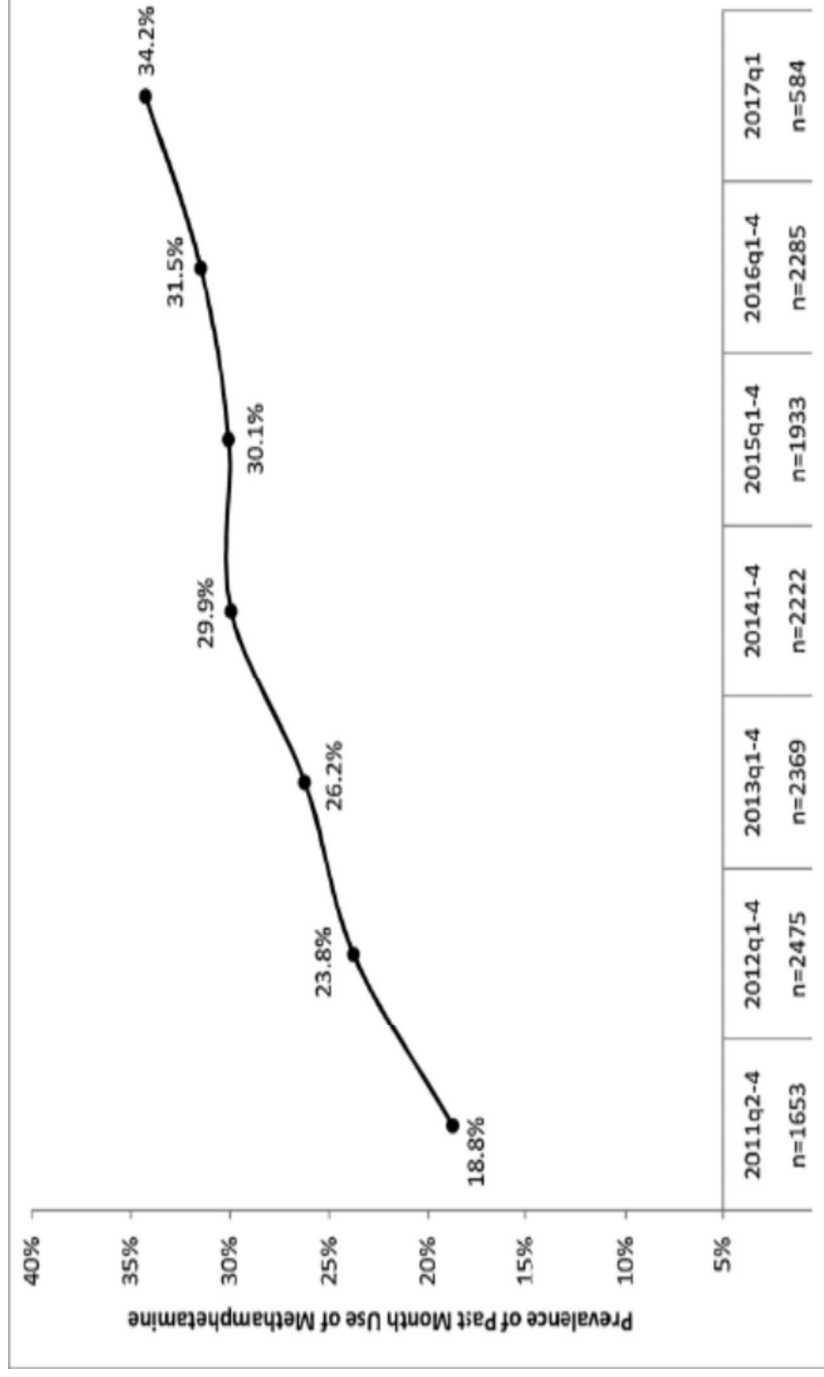
## **If a US Drug Abuse Epidemic Fails to Include a Major East Coast City, Can It Be Called an Epidemic?**

**Richard A. Rawson PhD , Sara L. Simon PhD & Walter Ling MD**

To cite this article: Richard A. Rawson PhD , Sara L. Simon PhD & Walter Ling MD (2001) If a US Drug Abuse Epidemic Fails to Include a Major East Coast City, Can It Be Called an Epidemic?, *Journal of Addictive Diseases*, 21:1, 1-4, DOI: [10.1300/J069v21n01\\_01](https://doi.org/10.1300/J069v21n01_01)

To link to this article: [https://doi.org/10.1300/J069v21n01\\_01](https://doi.org/10.1300/J069v21n01_01)

# News Flash: Meth is Coming to the East Coast



Ellis MS et al., *Drug Alc Depend.* 2018 193:14-20

# WV: Markers of a Growing Problem

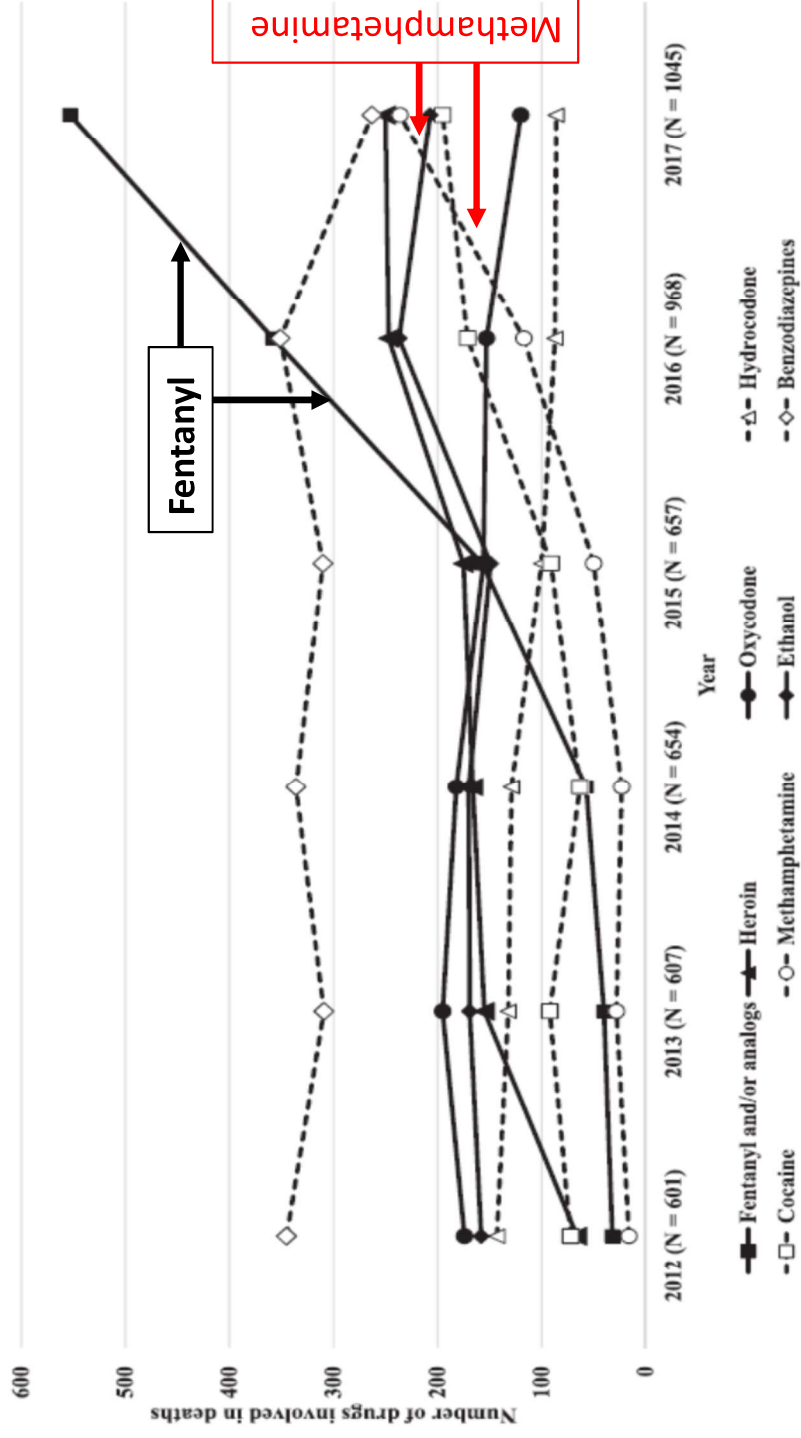


Fig. 1. Fentanyl ± FAs and other drug involvement in unintentional drug-related deaths in West Virginia, 2012–2017.

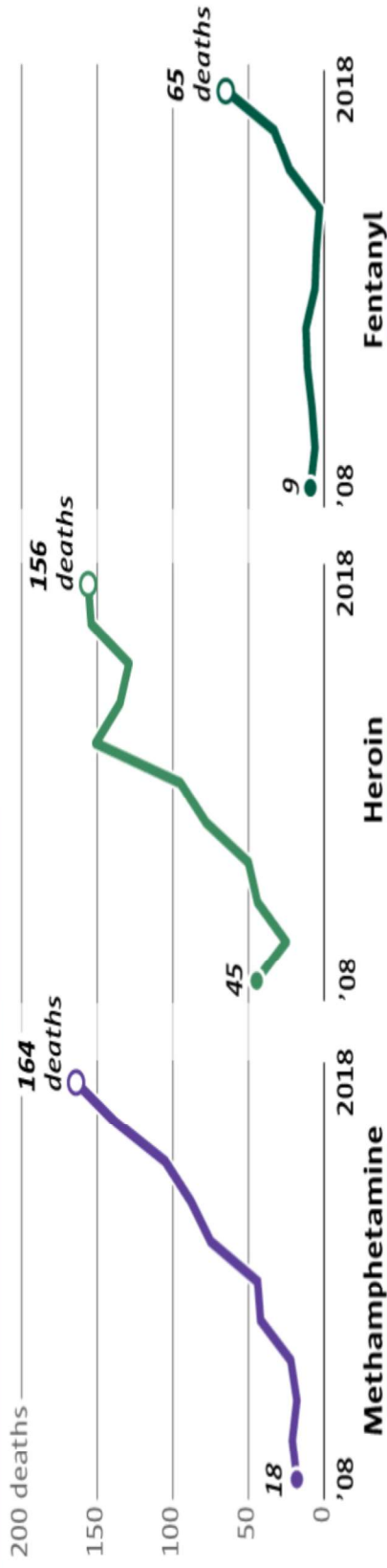
Dai Z et al. *Drug Alcohol Depend.* 2019,196:1-8.

# Meth is back in King County, bigger than it's been for decades

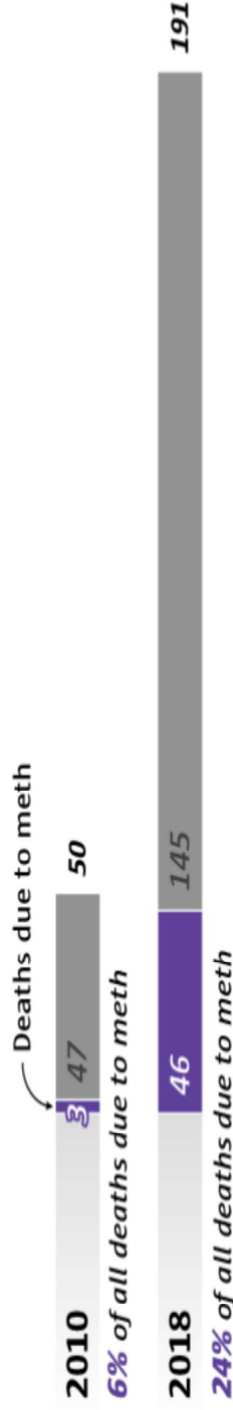
June 18, 2019 at 6:00 am | Updated June 19, 2019 at 9:20 am



## DRUG-INVOLVED OVERDOSE DEATHS IN KING COUNTY



## METH-INVOLVED DEATHS OF PEOPLE PRESUMED TO BE HOMELESS



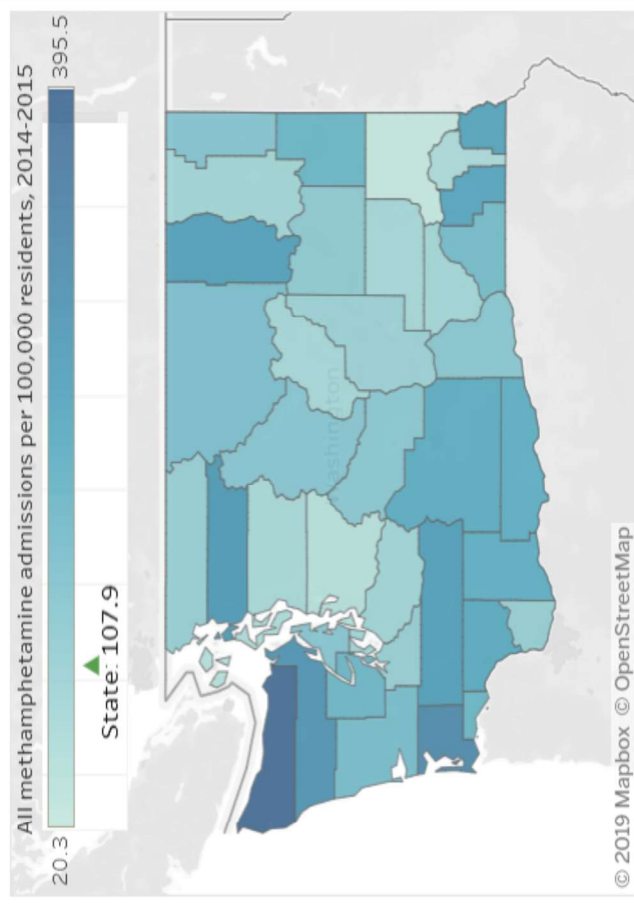
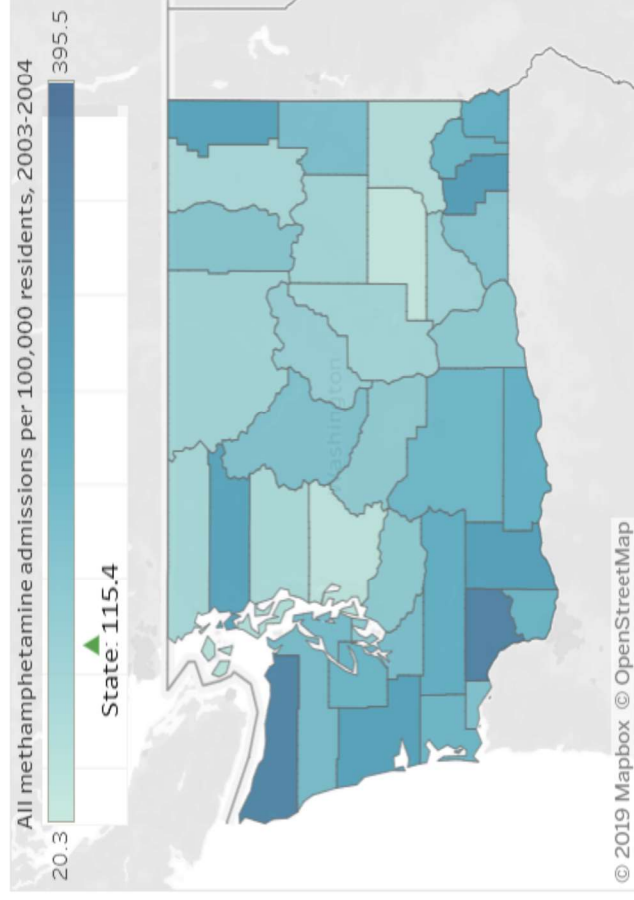
Source: King County medical examiner

EMILY M. ENG / THE SEATTLE TIMES



# Methamphetamine Treatment Admissions

**Publicly funded treatment admissions for which methamphetamine was reported as the primary drug, by county, 2014-2015 (latest available) versus 2003-2004**



t a b l e a u

Data sources: Division of Behavioral Health and Recovery, Washington State Department of Social and Health Services (admissions), state Office of Financial Management (population)

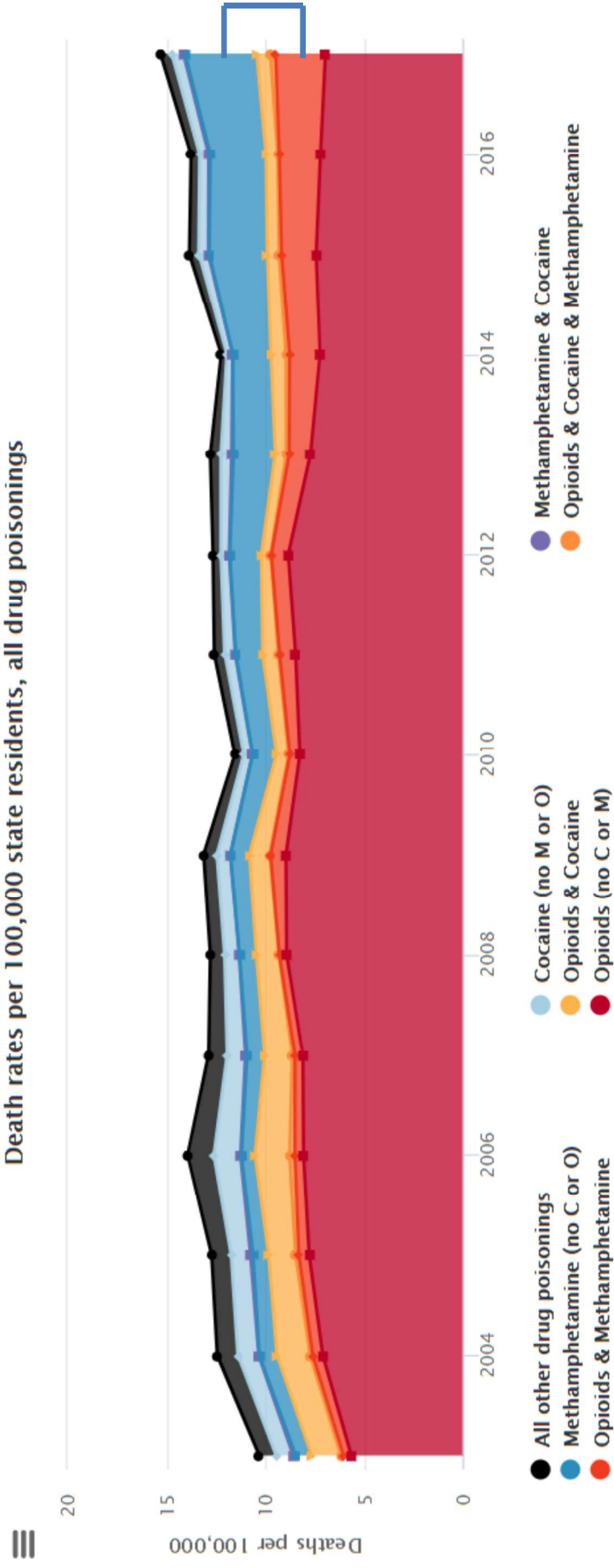
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<https://adai.washington.edu/WAdata/methamphetamine.htm>



# Drug Deaths

Death rates per 100,000 state residents, all drug poisonings



Analysis by UW ADAI. For data sources, see text or [adaai.uw.edu/WAdata](http://adaai.uw.edu/WAdata)

Data sources: Washington State Department of Health (deaths), state Office of Financial Management (population)



# Stimulant Links with HIV

- Methamphetamine links with incident HIV in Seattle MSM (Thiede et al. Am J Pub Health, 99(Suppl 1): S157–S164)

Figure 6-8c: HIV Prevalence among People who Inject Drugs (PWID), Seattle area National HIV Behavioral Surveillance, 2018

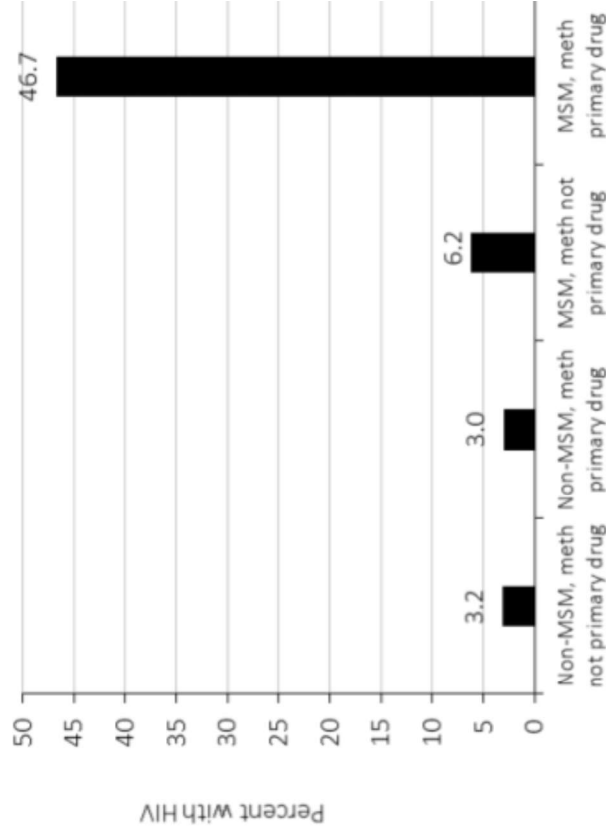
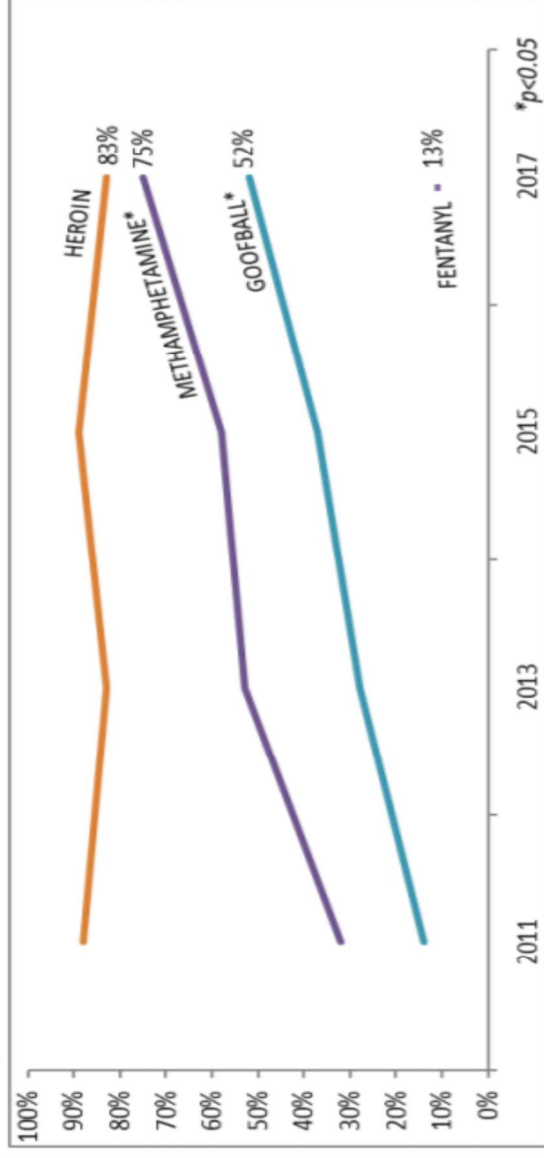


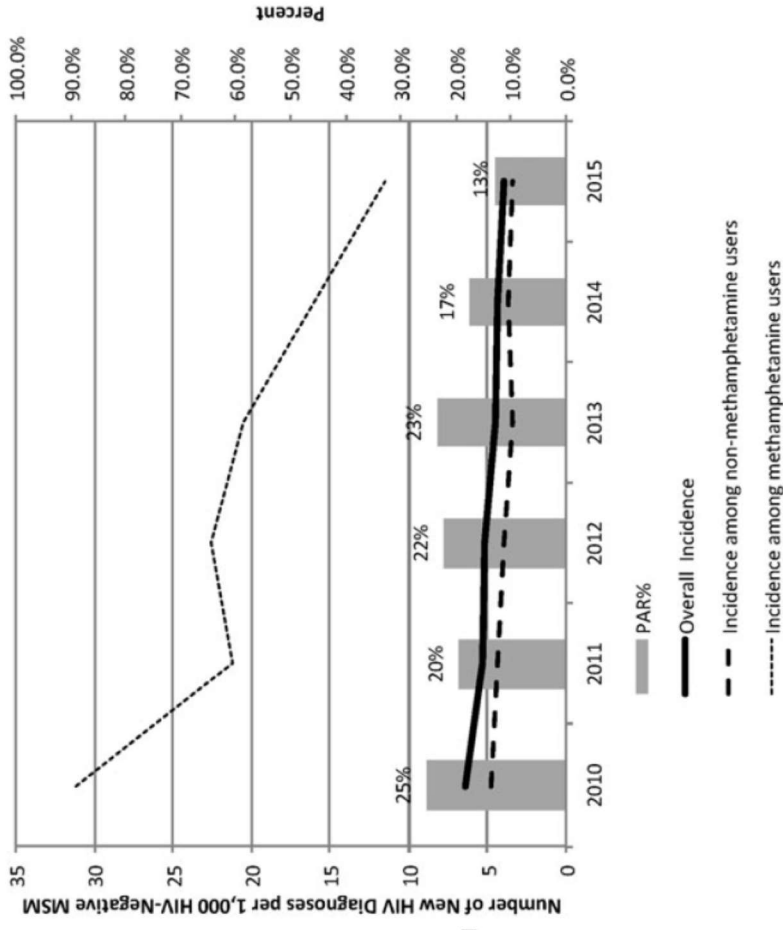
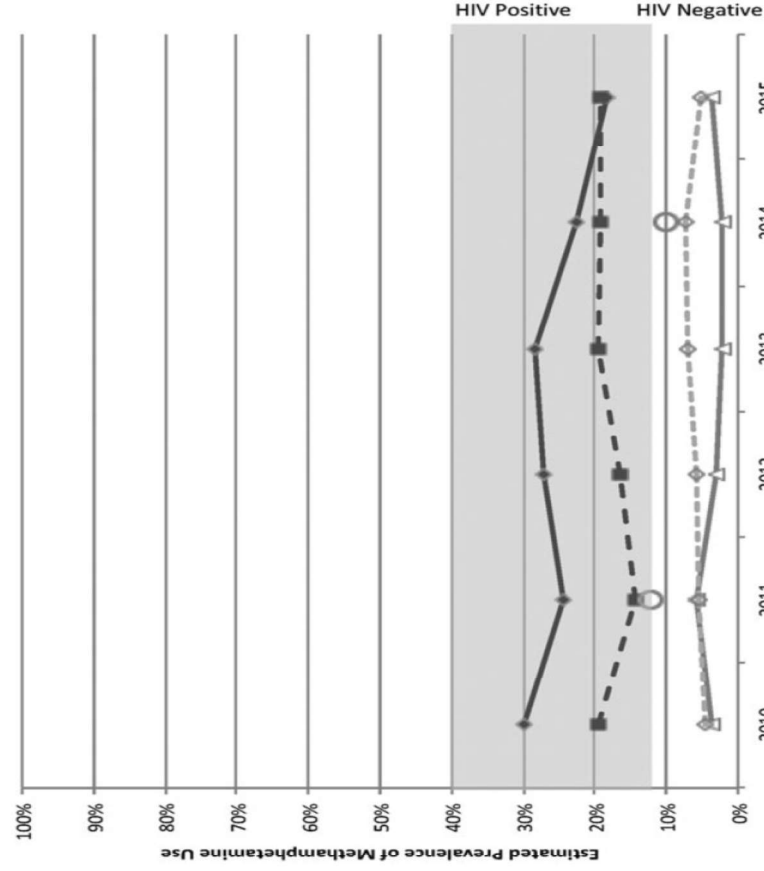
FIGURE 19-1. TRENDS IN REPORTED DRUG USE AMONG PUBLIC HEALTH – SEATTLE & KING COUNTY SYRINGE SERVICES PROGRAM (SSP) CLIENTS, 2011-2017



Note: Goofballs refer to injecting heroin and methamphetamine at the same time.



# HIV Incidence: MSM and Methamphetamine



Hood J., et al. 2018. *AIDS Pt Care & STDs*. 32:223-233.





# Substance Use and HIV





**mSTUDY**

MMSM And Substances Cohort at UCLA Linking Infections Noting Effects

## Annual Scientific Advisory Board Meeting

May 30, 2019

**Pamina Gorbach, DrPH & Steven Shoptaw, PhD**  
Departments of Epidemiology/  
Division of Infectious Diseases, Family Medicine  
NIDA U01DA036267 9/30/13-4/30/23



# Where Are We Now

**Men of Color who  
Have Sex With Men**  
544 enrolled at 6 years

## As of December 2018:

Currently enrolled

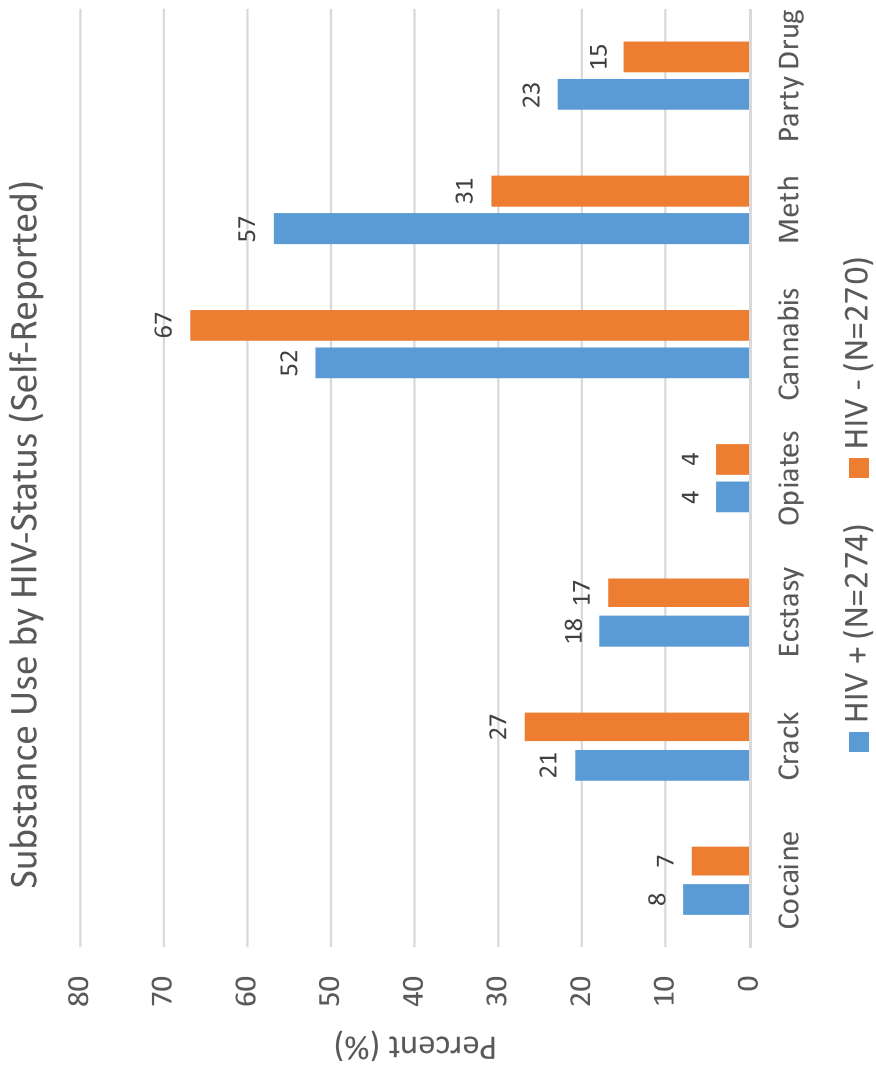
**274 HIV+**

**270 HIV-**

**11 seroconverters**

*Incidence 3.4%*

**8 known deaths**

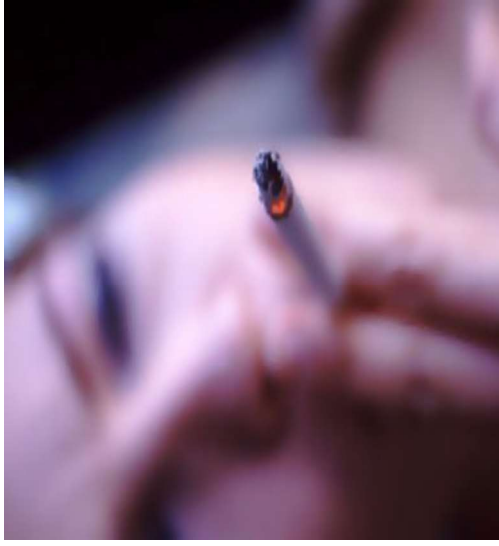


# Functions of Meth in MSM

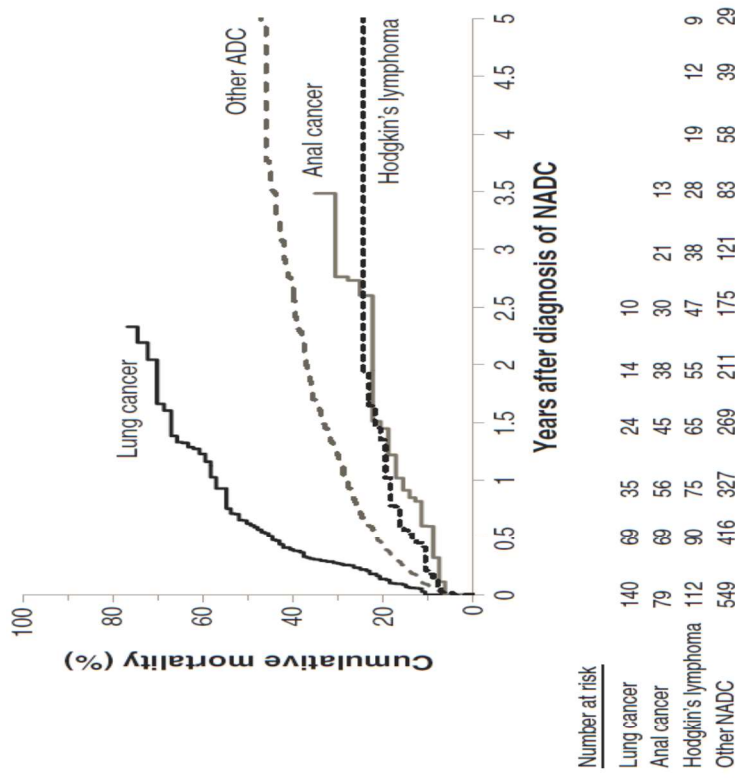
- Issues of identity (gay, drug user, HIV status)<sup>1</sup>
- Enhance sexual functioning <sup>2</sup>
- Boosts self confidence <sup>2</sup>
- Increases productivity <sup>2</sup>
- Weight loss/strong body experiences <sup>2</sup>
- Brightens mood <sup>2</sup>
- Aging/living with AIDS <sup>3</sup>

<sup>1</sup>Reback, 1997; <sup>2</sup>Halkitis et al., 2005a, b; <sup>3</sup>Kurtz 2005;

# The Most Devastating Drug is Licit



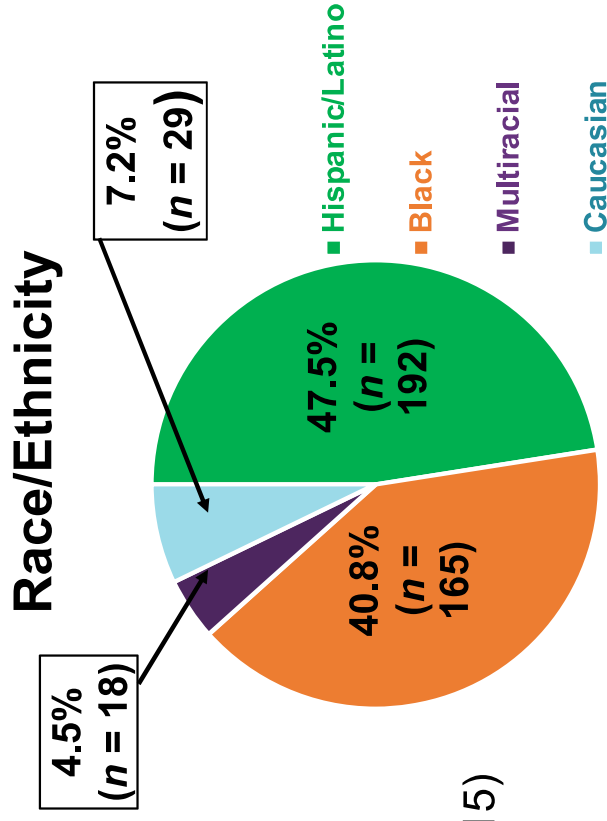
- Most preventable cause of morbidity and mortality
- 440,000+ premature deaths *annually*



Worm et al. 2013; *BMC Inf Dis*, 13:71

# mSTUDY: Cigarette/Nicotine Product Use

- 404 MSM
  - 48.0% ( $n = 194$ ) HIV+
  - 52.0% ( $n = 210$ ) HIV-
- 54.7% ( $n = 221$ ) of sample positive urine analysis for:
  - Marijuana 32.4% ( $n = 131$ )
  - Methamphetamine 28.5% ( $n = 115$ )
  - Cocaine 5.0% ( $n = 20$ )
- 48.8% reported cigarette and/or e-cigarette use



## mSTUDY: Nicotine Use Status and Other Drug Use

Nicotine Use with...	OR	95% CI	p-value
Cocaine	3.60	[1.09, 11.89]	0.036
Marijuana	2.17	[1.37, 3.46]	0.001
Methamphetamine	2.30	[1.23, 4.28]	0.009

Note: OR = odds ratio; CI = confidence interval; demographic variables: education, race, HIV status, age, and sexual history.

# Bivariate Analysis

Characteristic or behavior	All Participants (N=191)	Participants with HIV Infection (n=120)	Participants without HIV Infection (n=71)
	HR (95% CI)	aHR (95% CI)	HR (95% CI)
<i>Concurrent tobacco use</i>			
No	Ref	Ref	Ref
Yes	<b>3.47 (1.54, 7.82)</b>	<b>3.48 (1.54-7.89)</b>	<b>5.01 (1.76, 14.22)</b>
<i>Club drug use prior to starting meth*</i>			
No	Ref	Ref	Ref
Yes	<b>3.35 (1.49-7.54)</b>	<b>2.63 (1.15-6.00)</b>	<b>3.34 (1.27-8.78)</b>
<i>Any other clinical diagnoses†</i>			
No	Ref	Ref	Ref
Yes	<b>4.21 (1.25, 14.10)</b>	<b>3.89 (1.15-13.22)</b>	<b>4.11 (0.94, 17.98)</b>

**Bold text = p<0.05**

HR, hazard ratio; aHR, adjusted hazard ratio

\*Club drugs: cocaine, ecstasy, LSD, acid, PCP, ketamine

†Any other clinical diagnoses: bipolar disorder, depression, anxiety, suicidality, diabetes, cancer, attention deficit hyperactivity disorder (ADHD), obstructive sleep apnea (OSA), schizotypal disorder, post-traumatic stress disorder (PTSD), cardiovascular (CV) disease

Risk Group	Mortality Rate
<b>10-Year Standardized Mortality Ratio</b>	
GBM + Meth	3.95 (2.89-5.01)
<b>20-Year Standardized Mortality Ratio</b>	
GBM + Meth	3.39 (2.49-4.09)
<b>10-Year Crude Mortality Rate</b>	
GBM + Meth	2.3 per 1,000 PY
GBM + Meth + HIV	5.2 per 1,000 PY
<b>20-Year Crude Mortality Rate</b>	
GBM + Meth + HIV	3.4 per 1,000 PY
GBM + Meth + HIV + Tobacco use	16.9 per 1,000 PY



# Direct Links with HIV

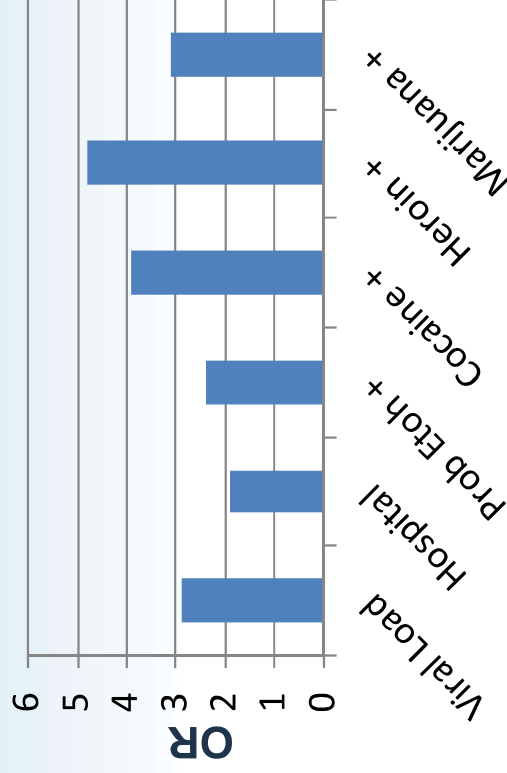
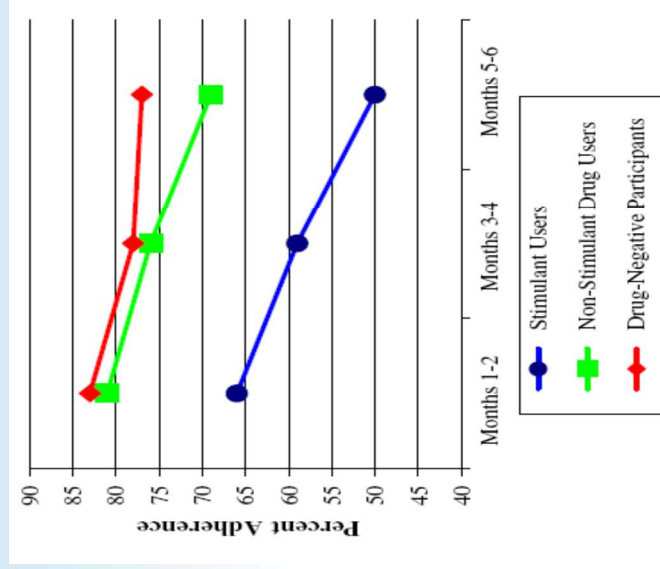


# Altering Infectiousness? Direct Effects of Substance Use on HIV

Substance	Effect	Reference
Methamphetamine	↓ host immunity by ↓ TLR-9 receptors	Cen et al., <i>AIDS Res &amp; Hum Retro</i> , 2013; 29:1129-37
Methamphetamine	↑ regulates anti-HIV microRNA	Mantri et al., <i>Am J Path</i> , 2013; 184:92-100
Cocaine	↑ HIV entry and replication in quiescent T-cells	Kim et al., <i>J Leuk Bio</i> , 2013; 94:835-43
Cocaine	↓ CD4+; ↑ VL; ↑ IL4, IL10	Parikh et al., <i>JAIDS</i> , 2014; 66:256-64
Alcohol	↑ TNF-α in hazardous drinkers PLWH	Miguez et al., <i>Alcohol</i> , 2012, 46:763-68
Marijuana	↓ PVL among PLWH and PWID	Milloy et al., <i>Drug Alc Rev</i> , 2015, 34:134-40

# Links Between Non-Injection Substance Use and ART Adherence, Viral Load

PLWH who Smoke Cigarettes have ↓ ART Adherence and ...



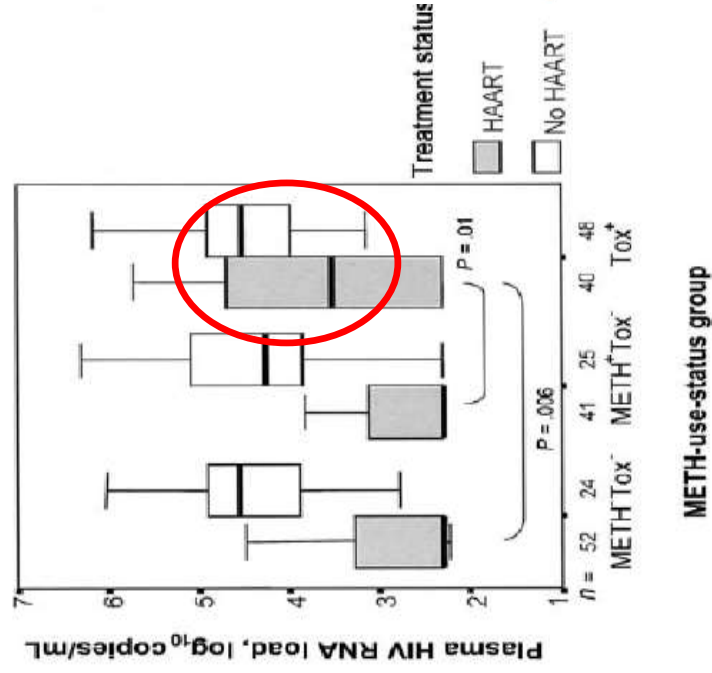
O’Cleirigh et al., AIDS & Beh, 2015, 19:178–185

Hinkin et al., 2007, AIDS & Behav 11:185–194;

Arnsten et al., 2002, J Gen Intern Med 17:377-381

## Methamphetamine: A Clear Signal

- A biological mechanism to explain a behavioral assumption



Recent Methamphetamine Use Is Associated With Increased Rectal Mucosal Inflammatory Cytokines, Regardless of HIV-1 Serostatus

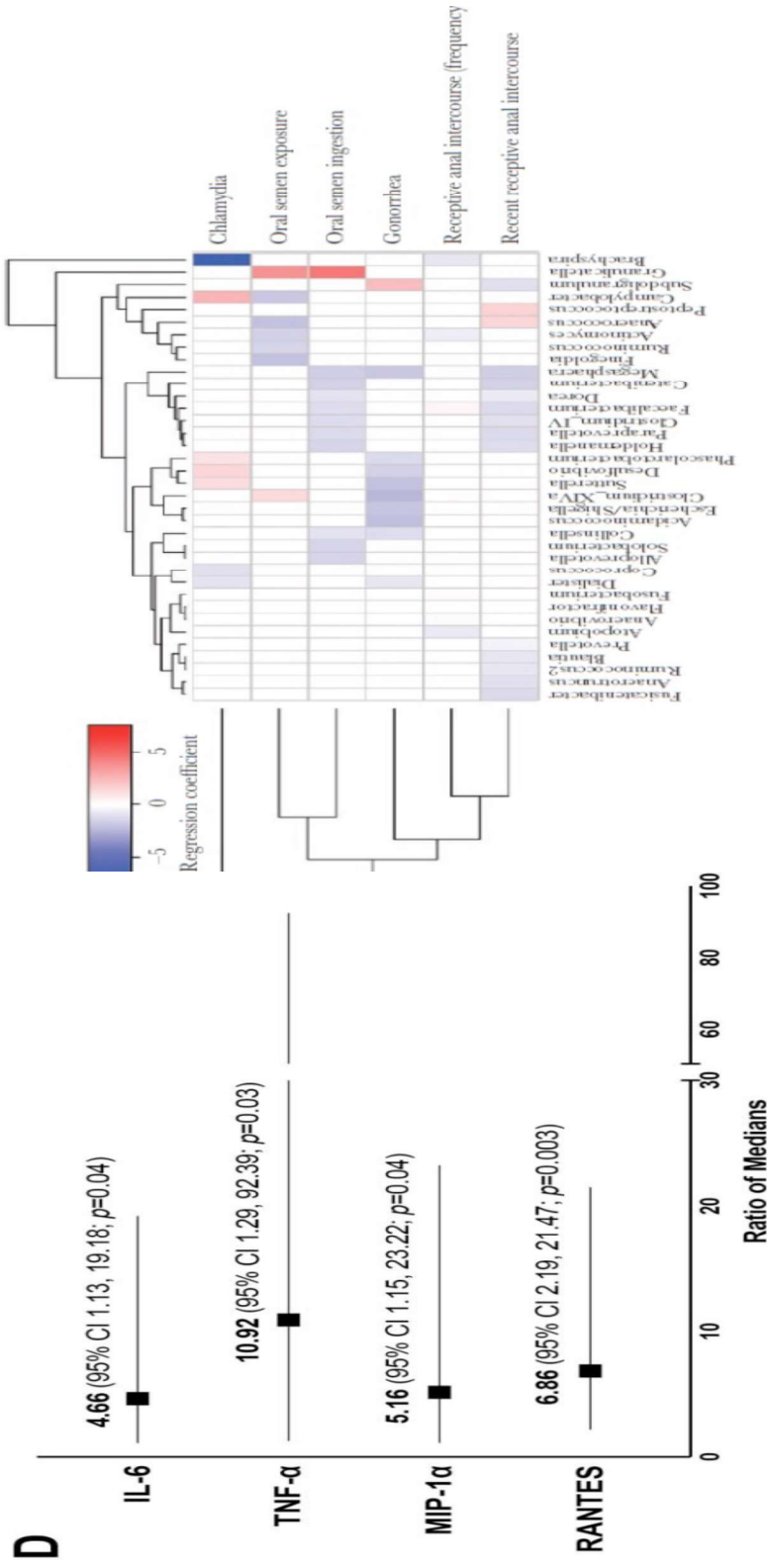
Jennifer A. Fulcher, MD, PhD,\*† Steven Shoptav, PhD,‡ Solomon B. Makgoeng, MS,§ Julie Elliott, MS,||  
F. Javier Ibarondo, PhD,\* Amy Ragsdale, MA,§ Ron Brookmeyer, PhD,¶ Peter A. Anton, MD,|| and  
Pamina M. Gorbach, MHS, DrPH\*§

# mSTUDY New Scientific Directions

**Direct Interactions of Drugs of Abuse and HIV Interactions of Drugs of Abuse, HIV, Behavior & Microbiome**

Recent Methamphetamine Use Is Associated With Increased Rectal Mucosal Inflammatory Cytokines, Regardless of HIV-1 Serostatus

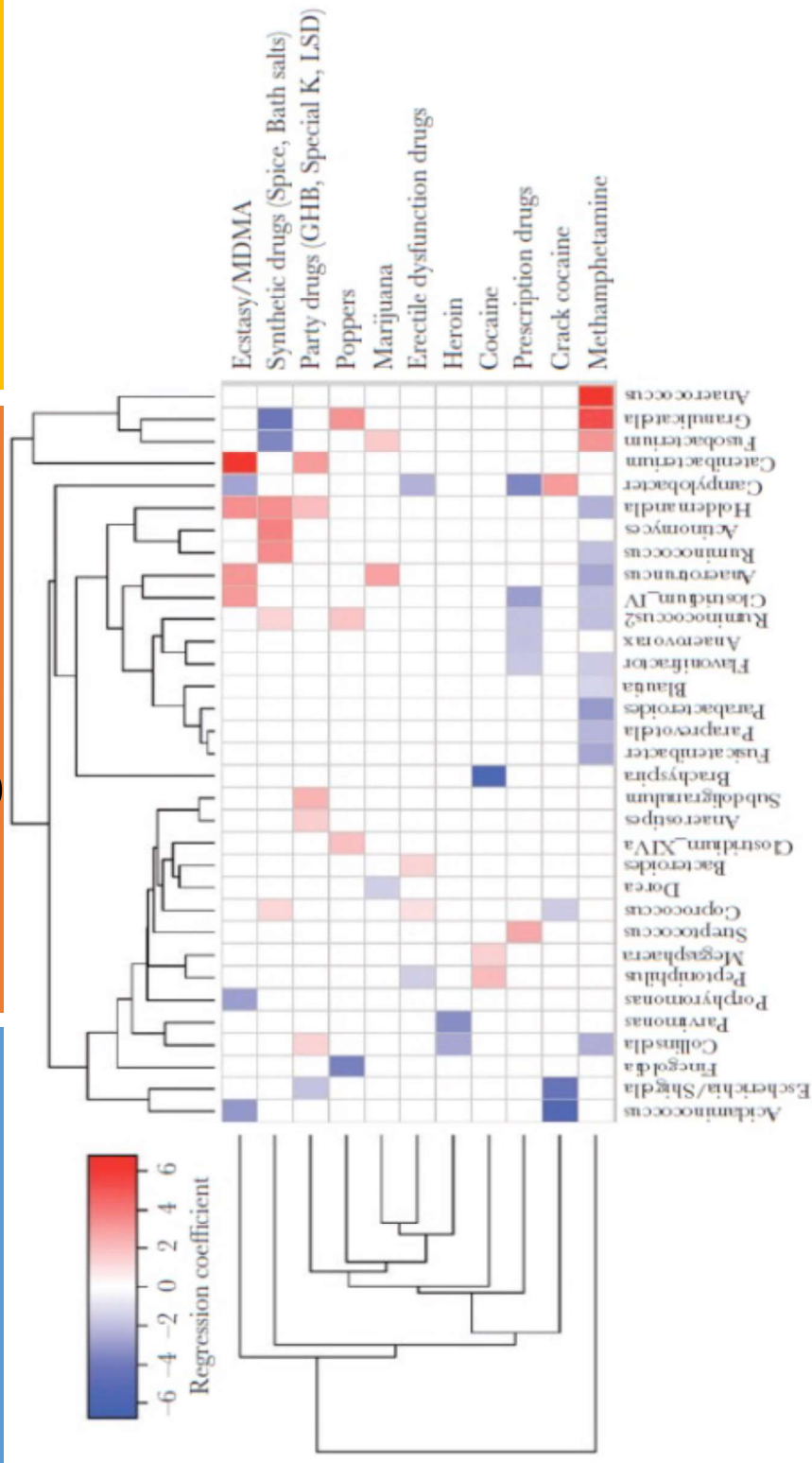
Effects of Substance Use and Sex Practices on the Intestinal Microbiome During HIV-1 Infection



Fulcher et al., 2018, *JAIDS*, 78:119-123

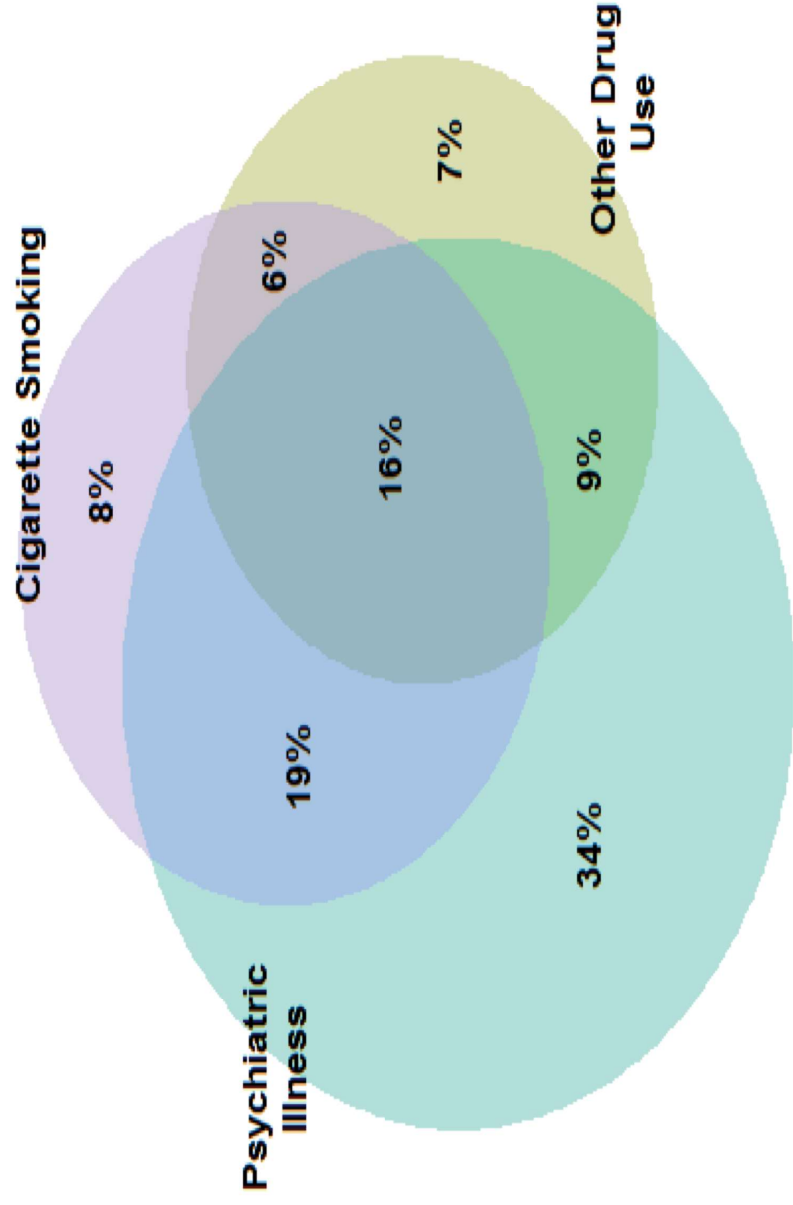
Fulcher et al., 2018, *JID*, July 2, 2018

# Microbiome and Drugs, mSTUDY 2018



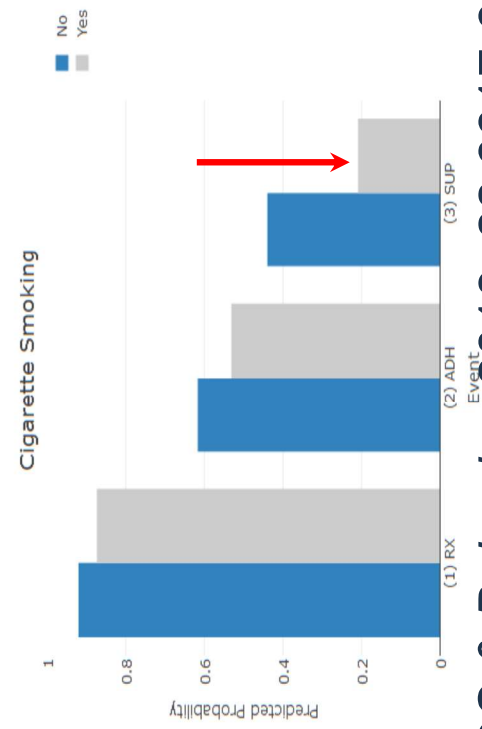
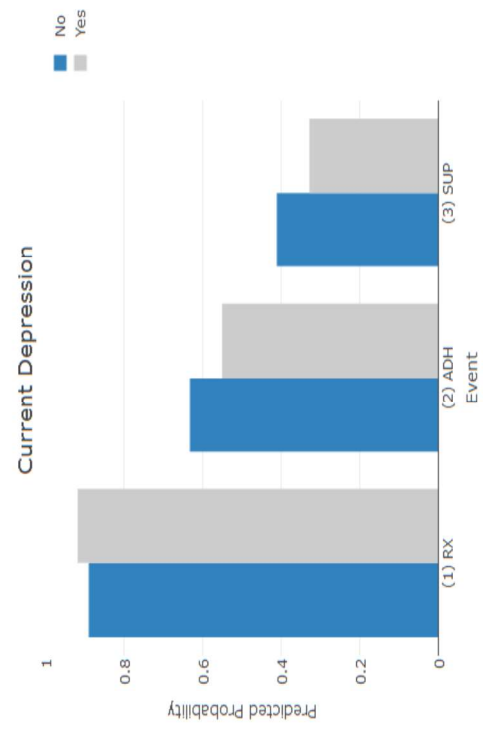
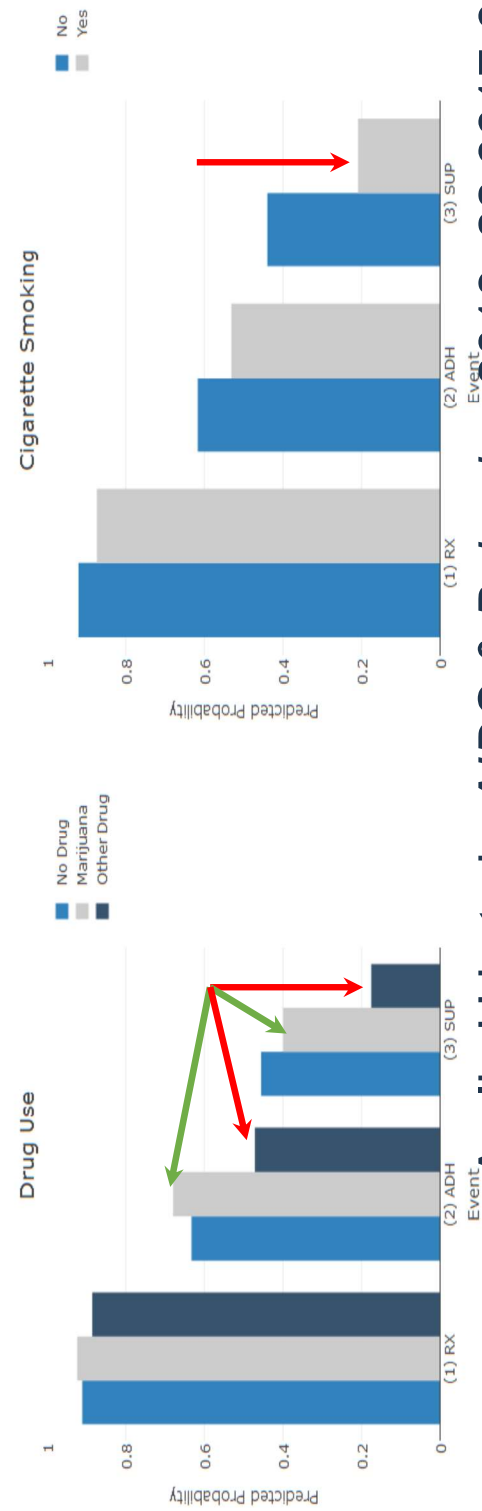
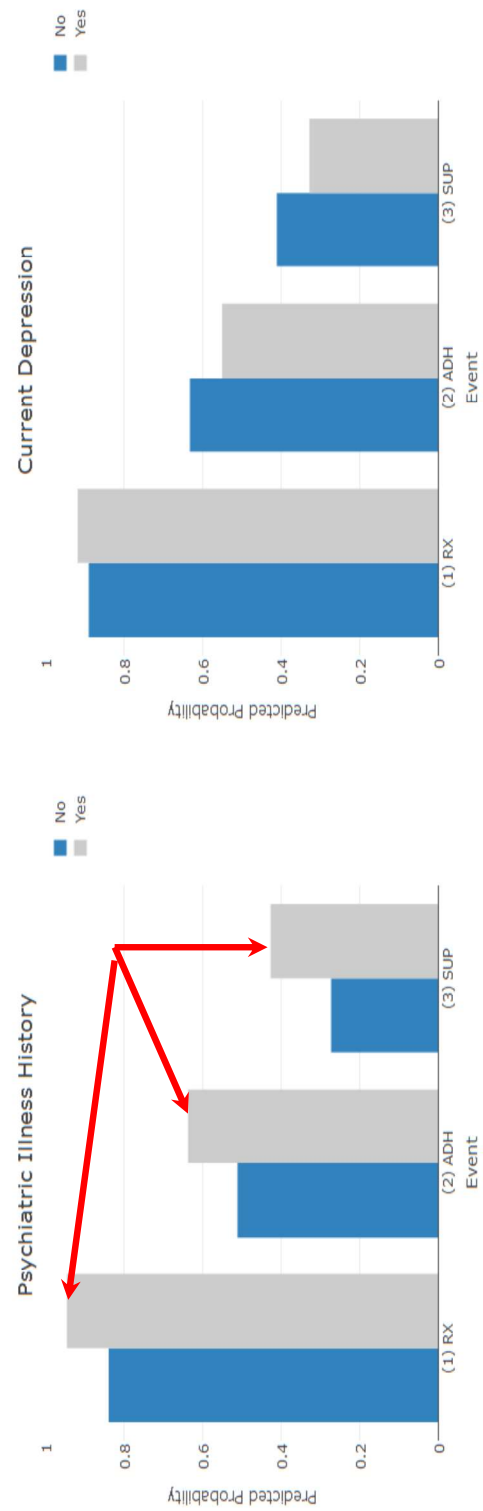
Fulcher et al., 2018, JID, July 2, 2018

# Psychiatric Illness, Drug use and Smoking in 155 HIV-Positive MoCSM



Aralis HJ et al., *AIDS & Behavior*, 2018. 22:3317-3129

# CARE CASCADE PROBABILITIES FOR (RX), (ADHERENCE) AND (SUPPRESSION) IN HIV+ (N=155)



Aralis HJ et al., AIDS & Behavior, 2018. 22:3317-3129



# Methamphetamine Phenotypes & Syndemics

Variable	Amount of Methamphetamine Past 6 Months (n=1,798 visits)			P value
	Weekly + (n=330 visits)	< Monthly (n=352 visits)	None (n=1,116 visits)	
Age	34.3	33.4	31.7	<.01
Unemployed	73.2%	57.2%	29.75	<.01
Unstable House	49.4%	35.5%	18.7%	<.01
Ever Jail?	61.8%	44.6%	28.5%	<.01
Smoker	51.5%	40.4%	23.6%	<.01
Binge drink 6 mo	35.2%	61.2%	50.5%	<.01
Cocaine 6 mo	23.3%	26.7%	15.6%	0.02
Heroin 6 mo	9.4%	4.6%	0.8%	<.01
Poppers 6 mo	50.6%	38.6%	24.6%	<.01
Concurrent Partnr	60.4%	42.3%	37.8%	<.01
HIV Positive	68.8%	66.2%	41.0%	<.01
Syphilis Positive	26.2%	19.4%	15.1%	<.01

## Summary

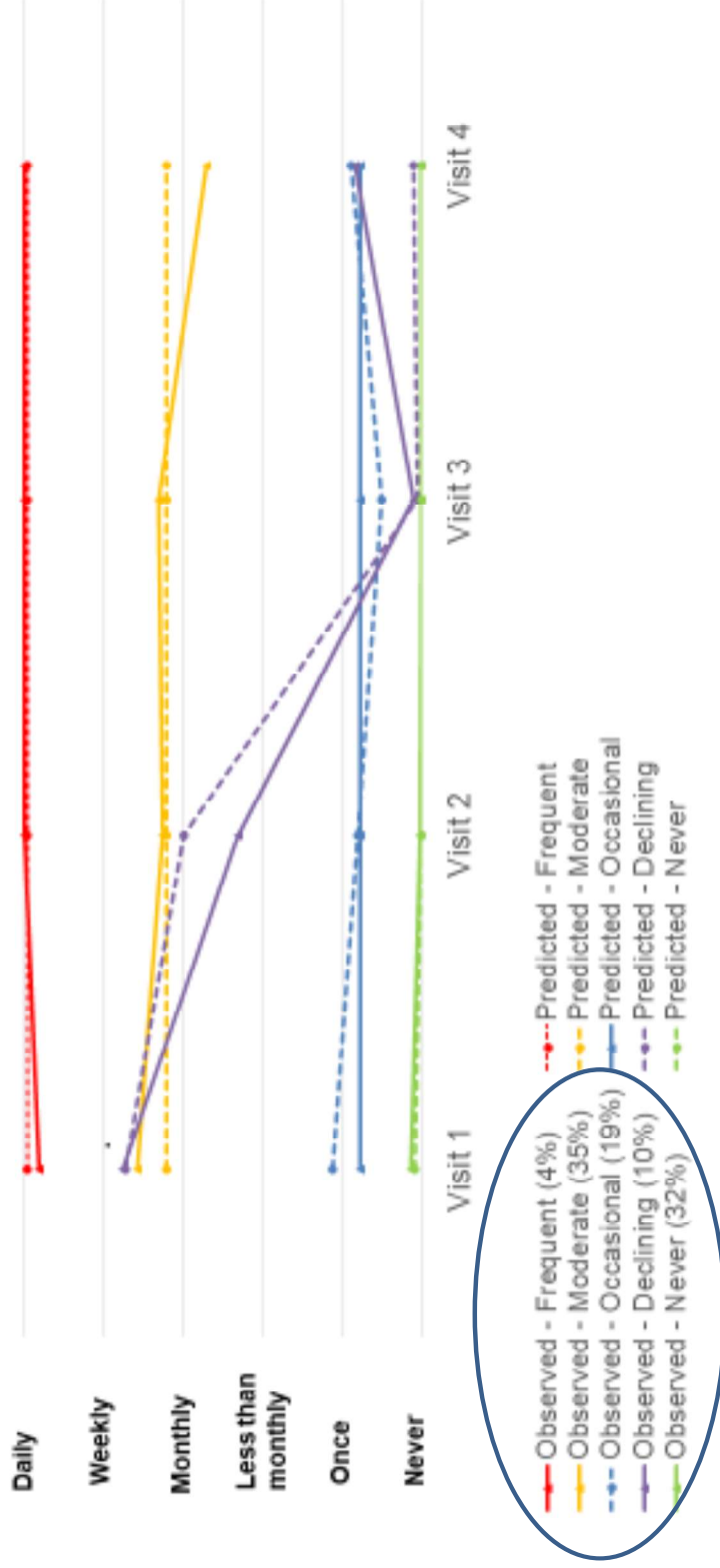
- Methamphetamine launches pro-inflammatory response in gut (and brain) that sensitizes to HIV infection; may release control of viral suppression in HIV+
- Gut flora disturbed by methamphetamine in opposite fashion to marijuana
- Smoking is bad for everyone, but especially for meth-using MSM living with HIV

# Stimulants and Interventions in the Setting of HIV

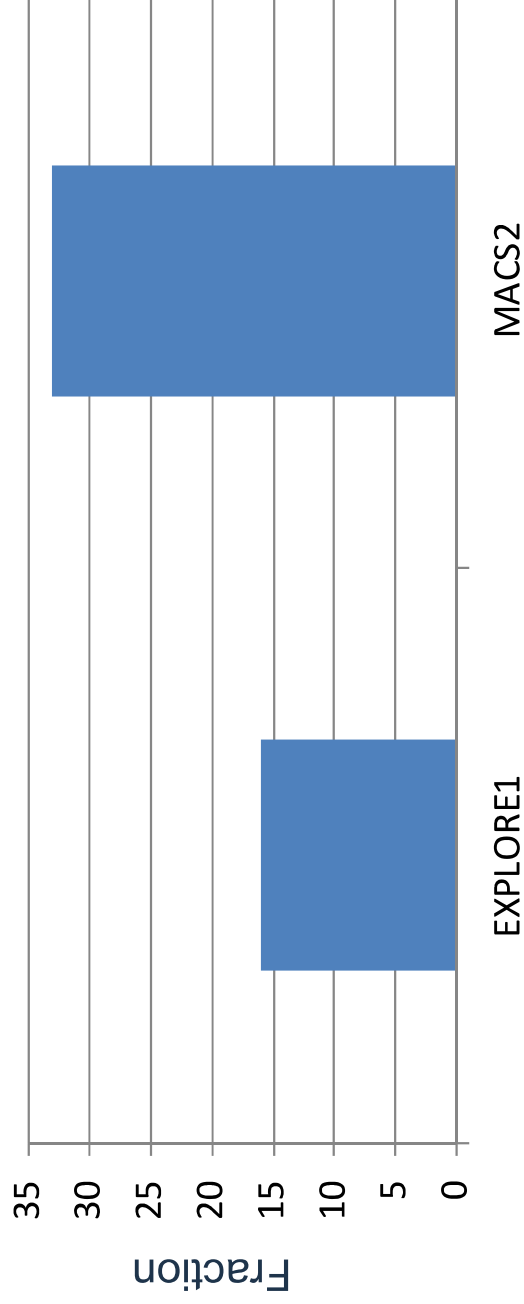


# Methamphetamine Use Trajectory

Figure 1. Methamphetamine Use Trajectories based on Self-Reported Use in the Past 6 Months



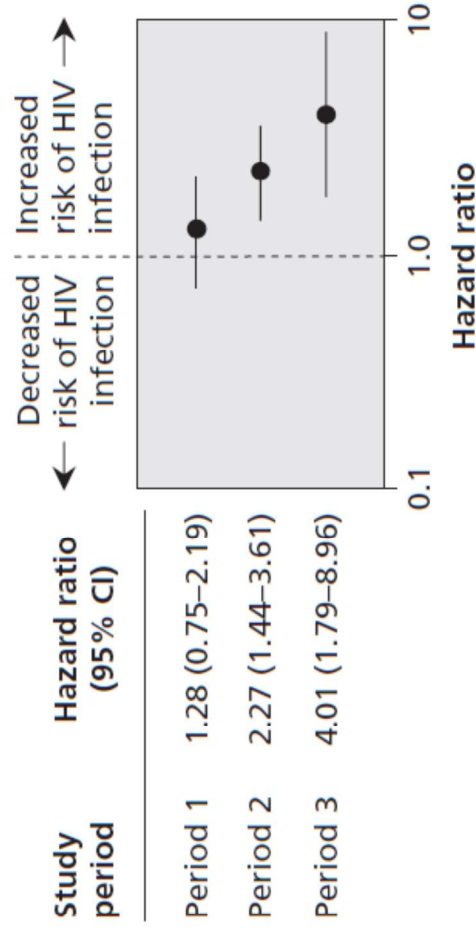
# Methamphetamine Use, HIV Incidence in MSM: Attributable Fraction



<sup>1</sup> Koblin et al., 2006, AIDS, 20: 731-739

<sup>2</sup> Ostrow et al., 2009, JAIDS, 51: 349-355

# Crack Cocaine Use and HIV Seroconversion among People Who Use Injection Drugs



**Figure 2:** Association between daily smoking of crack cocaine and HIV seroconversion. A hazard ratio above 1.0 indicates an increased risk of HIV seroconversion. Period 1 = May 1, 1996, to Nov. 30, 1999; period 2 = Dec. 1, 1999, to Nov. 30, 2002; period 3 = Dec. 1, 2002, to Dec. 31, 2005. CI = confidence interval.

# A SHAMELESS PLUG



**A Training Manual for Counselors**

[www.friendscommunitycenter.org/resources](http://www.friendscommunitycenter.org/resources)

# Contingency Management and Substance Use Disorders

- Operant conditioning (Skinner, 1938)
- Initial concepts derived from work with delinquent boys (Yates, 1970)
- Early work in MMT clinics to encourage opioid abstinence (Stitzer et al, 1977)
- Application to cocaine dependence by Higgins' group (1993, 1994)
- Original voucher-based CM now has alternative “fishbowl method” (Petry 2000)



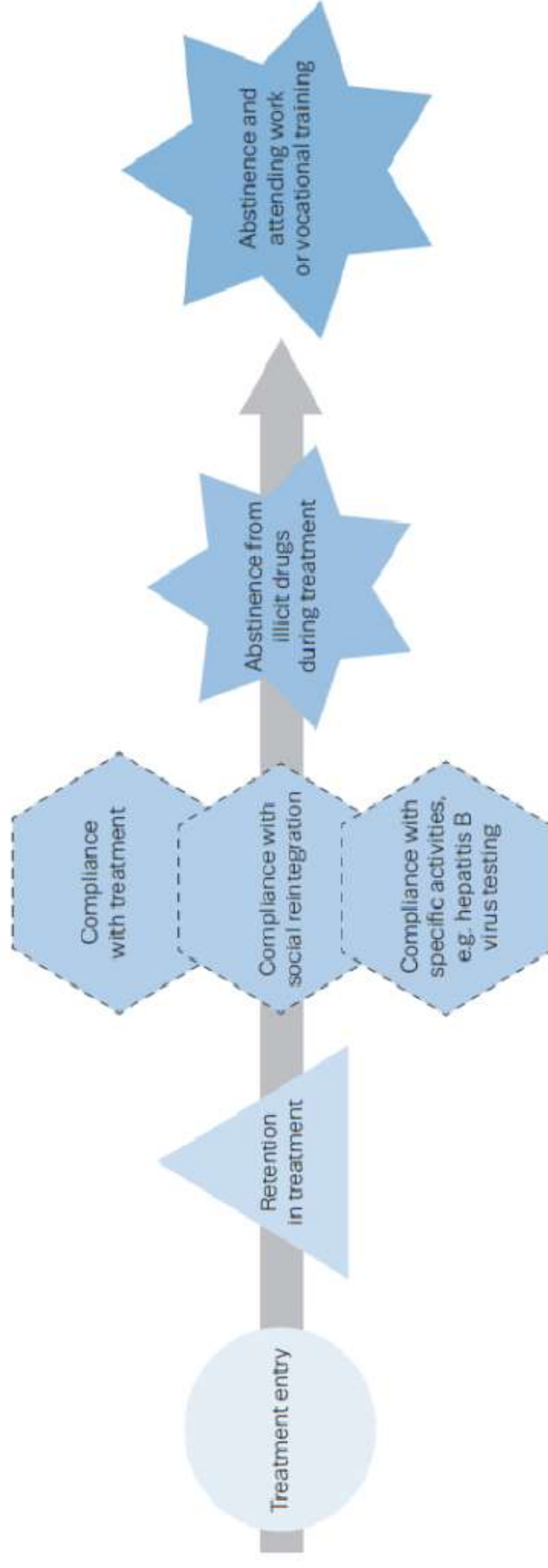
## Meta Analyses of CM

- $d=0.46$  (Benishek et al., 2014, 109:1426-1436) – Prize based only
- $d=0.58$  (Dutra et al., 2008, *Am J Psychiatry* 165:179-187)
- $d=0.52$  (Griffith et al., 2000, *Drug Alc Dep* 58:55-66)
- $d=0.40$  (Prendergast et al., 2006, *Addiction* 101:1546-1560)

# The “Place” for Contingency Management

FIGURE 1

Targets and possible use of contingency management along the treatment journey



European Monitoring Center for Drugs  
and Drug Addiction, 2016

# Methamphetamine treatment in MSM

Full trial: 162 methamphetamine dependent MSM in West Hollywood, CA



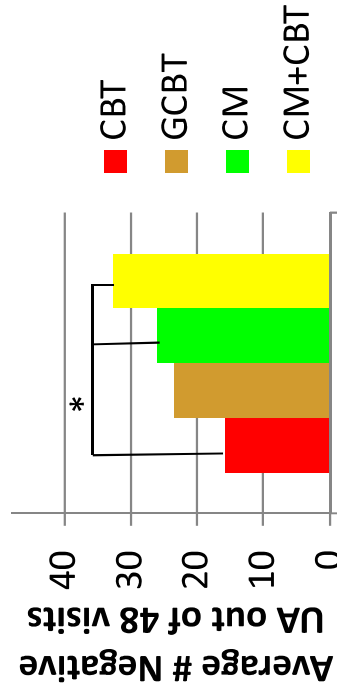
Duration: 16 weeks; 1 year follow-up evaluations

# Contingency management

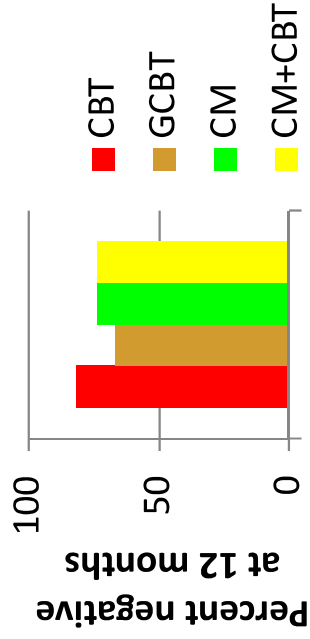
- Intensive outpatient treatment, 3x/week
- Subjects compensated on an escalating scale for consecutive clean urine samples
- Subjects can redeem their earnings at any time for various prizes, rewards, gift cards – generally rewards promote drug free lifestyle
- CM is effective at reducing drug use, increasing study attendance and adherence



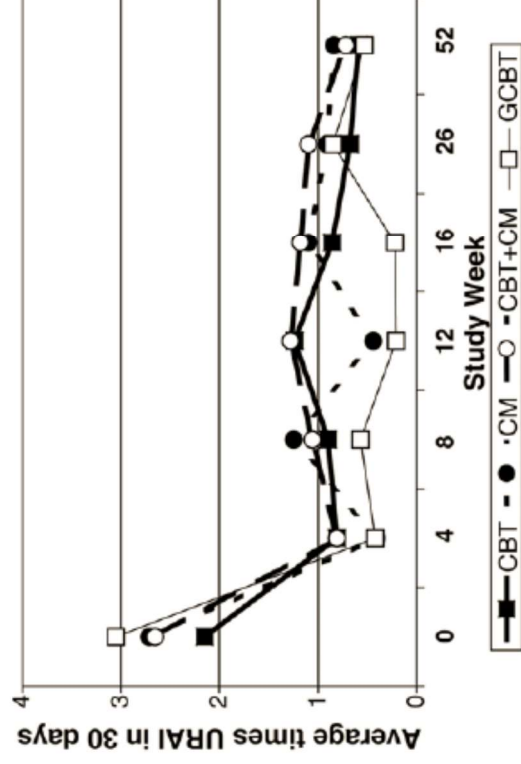
# Early Trial: CBT, CM, CM+CBT, GCBT in MA-Dependent MSM at risk for HIV



Assignment



Assignment



Shoptaw Reback et al. *Drug and Alcohol Dependence*, 2005. 78(2): 125-34.

# Contingency Management (CM) Boosts nPEP Outcomes in at-risk Stimulant Using MSM

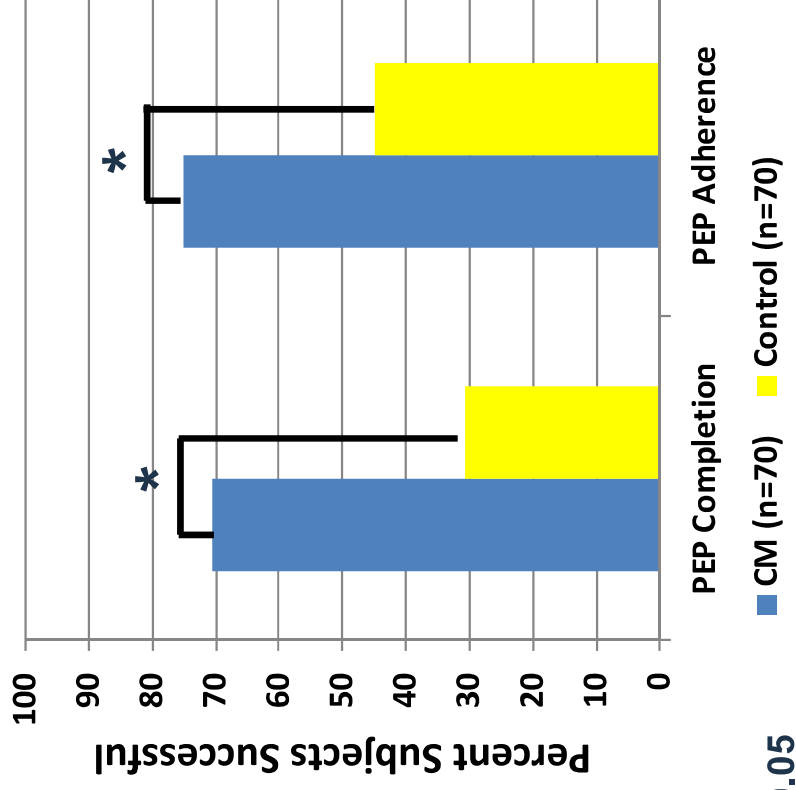
## Design:

- Escalating 8-week CM schedule with thrice-weekly visits based on drug-free urine samples
- \$430 maximum
- n=140

## Methamphetamine

### Outcomes:

- CM = 8.9 (SD=9)
- Control = 6.1 (SD=6) \*



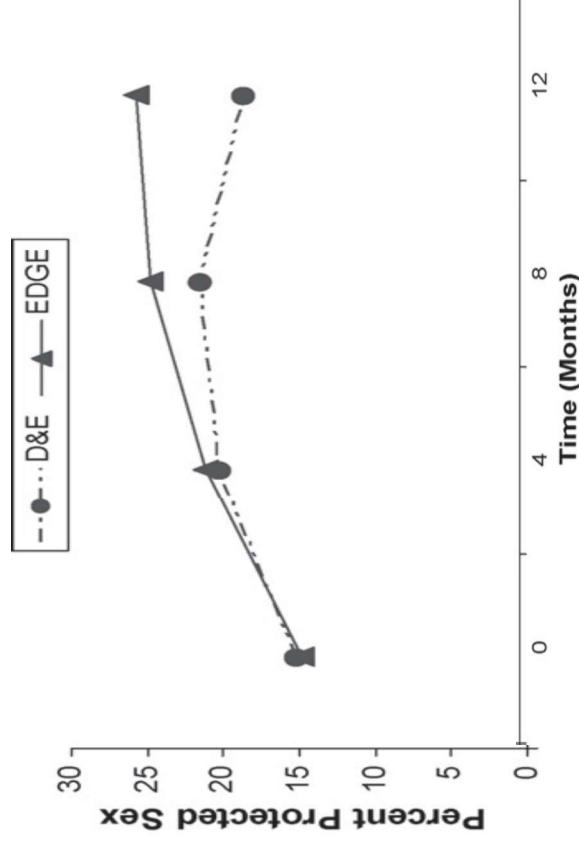
\* P<0.05



# Motivational Interviewing Reduces Risk Behaviors in Active MA-users

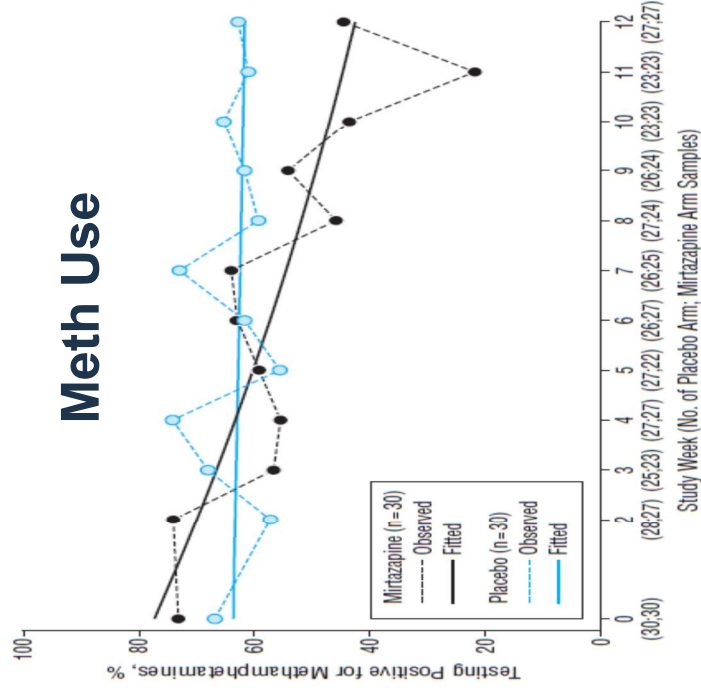
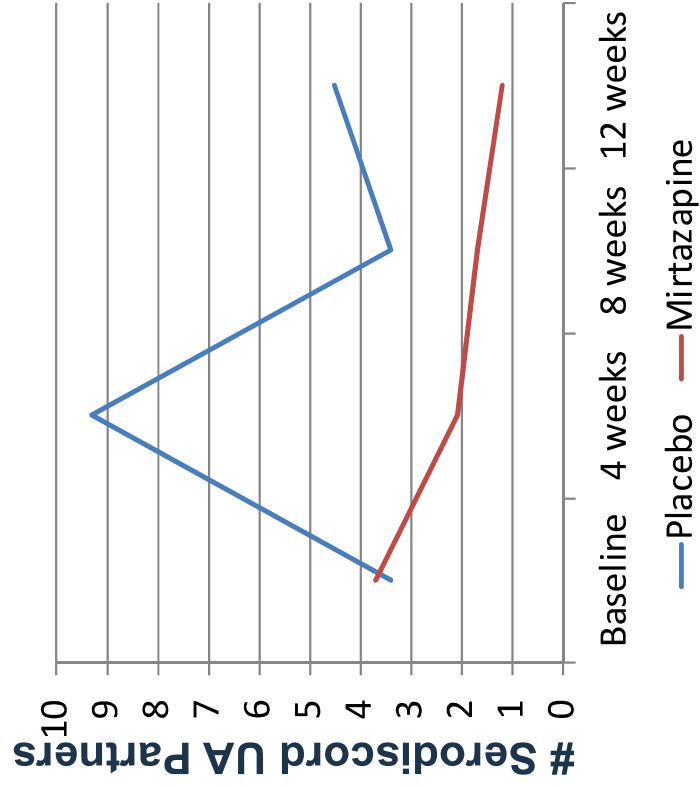
EDGE (HIV+ MSM)  
Fast Lane (HIV- Hetero)

1. Context of Unsafe Sex
2. Condom Use
3. Negotiation of Safer Sex
4. Social Support
5. EDGE: Disclosure of HIV status to sex partners



Mausbach, Strathdee, Patterson. *Drug Alc Dep.* 2007, 87:249-257  
Mausbach, Strathdee, Patterson. *Ann Beh Med.* 2007, 34:263-274

# Pharmacotherapy for Stimulant Use in MSM: Mirtazapine 30 mg/day



Colfax et al. *Archives Gen Psych*, 2011. 68(11): 1168-1175

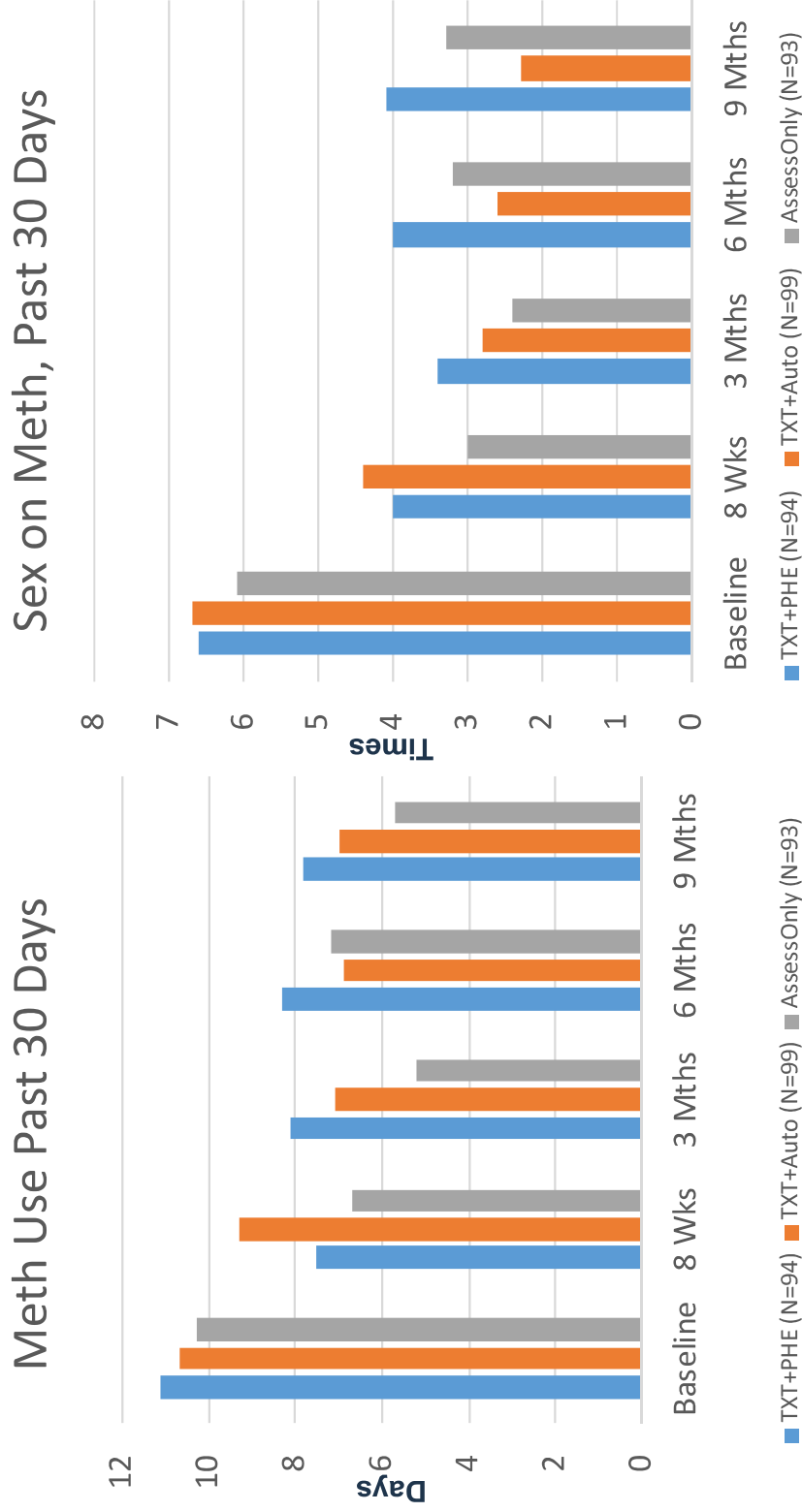


# Theory-based Text Msgs for Stimulant Use

Social Support	Informational Support	<p>“Did he give you a bug? Here’s where to go.”</p> <p>“Take care of your body, get vaccinated for hep A and B.”</p>
	Emotional Support	<p>“Screw your partner, not your life.”</p> <p>“You’re worth a new needle.”</p>
	Instrumental Support	<p>“Meth brings you down, meds bring you up.”</p> <p>“Pack your socks with condoms and lube.”</p>
	Health Threat	<p>“Is that precum or do you have a STD drip?”</p> <p>“Meth can take your teeth.”</p>
Health Belief	Health Behaviors to Reduce Risk	<p>“Dip it, don’t stick it.”</p> <p>“Inject clean, an abscess is a hot mess.”</p>
	Awareness of Health Risks	<p>“50% of men with Chlamydia have no symptoms.”</p> <p>“Using meth in public can be risky.”</p>
	Self-regulation Skills	<p>“Weekends getting longer and longer?”</p> <p>“Don’t have an open sores relationship.”</p>
Social Cognition	Self-Efficacy	<p>“Say 1<sup>st</sup> thing your poz, like you did last time. You can do it.”</p> <p>“You can take your meds, even when you party.”</p>

Reback et al., (2010). *Open AIDS Journal*. 4: 116-122

# Text Message Outcomes: Meth and Sex

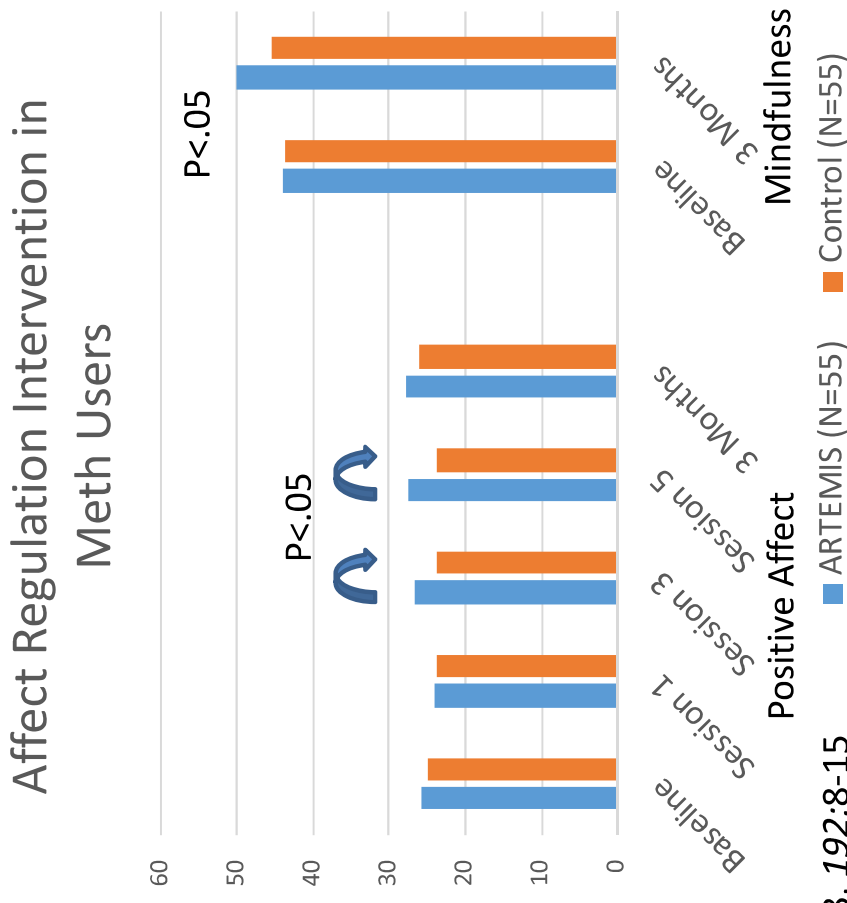


Reback CJ et al., AIDS Behav. 2019, 23:37-47

# ARTEMIS + CM in HIV+ Meth Users

## ARTEMIS Intervention

1. Positive event noting
2. Positive event capitalizing
3. Gratitude
4. Informal/formal mindfulness
5. Positive reappraisal
6. Personal strengths
7. Attainable goals
8. Acts of kindness (altruism)



# Strategy for Behavioral Responses

- CM WORKS: THE most effective tool on the shelf for reducing meth use among MSM
- Reducing meth use:
  - Reduces HIV transmission behaviors
  - Improves HIV-prevention medication adherence
- Affect regulation may boost CM outcomes for HIV-positive MSM
- Active meth users benefit from brief MI in reducing sex risk behaviors, both MSM and heterosexuals
- Mirtazapine reduces meth use (not abstinence) and sexual risk behaviors
- Remember to reinforce smoking cessation



**Thank You!**

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