

# Evidence-Based Strategies to Address Substance Use: Gaps and Future Directions

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# TREATMENT AND HARM REDUCTION: Cheat Sheet

- Medications for opioid use disorder
  - Methadone
  - Buprenorphine (co-formulated with naloxone)
  - Extended release naltrexone
  - Others
    - Detoxification or medically assisted detoxification (i.e., clonidine, lofexidine)
- Harm-reduction services
  - Syringe services programs (formerly known as needle exchange)
  - Naloxone for overdose reversal
- Adjunctive services
  - 12-step programs
  - Mental health services / behavioral counseling
  - Housing services
  - Case management
- Other interventions
  - Prescription drug monitoring programs
  - Provider education
- Infectious diseases-related interventions
  - PrEP – Benefit likely highest in people who use stimulants
  - HIV treatment
  - HCV treatment
  - Vaccination – HAV, HBV, TDAP, pneumococcus
  - Screening – HIV, HBV, HCV, STIs

# TREATMENT AND HARM REDUCTION: Cheat Sheet

- Medications for opioid use disorder
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  - Buprenorphine (co-formulated with naloxone)
  - Extended release naltrexone
  - Others
    - Detoxification or medically assisted detoxification (i.e., clonidine, lofexidine)
    - Diacetylmorphine (heroin-based therapy)
    - Morphine sustained release or hydromorphone
- Harm-reduction services
  - Syringe services programs (formerly known as needle exchange)
  - Naloxone for overdose reversal
  - Safe injecting/consumption facilities } Not federally sanctioned
- Adjunctive services
  - 12-step programs
  - Mental health services / behavioral counseling
  - Housing services
  - Case management
- Other interventions
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} Not FDA approved

- Medications or interventions for stimulant use disorders

- Motivational interviewing
- Contingency management
- CBT

- Methamphetamine

- Mirtazapine

- Cocaine

- Topiramate
- Baclofen
- Buprenorphine

} Not FDA approved

# Methadone and Buprenorphine

- Agonist and partial agonist therapies work
- Multiple RCTs and meta-analyses
- Benefits:
  - Improved survival(1)
  - Improved HIV(2)/HCV(3) prevention
  - Improved HIV medication adherence and viral suppression(4)

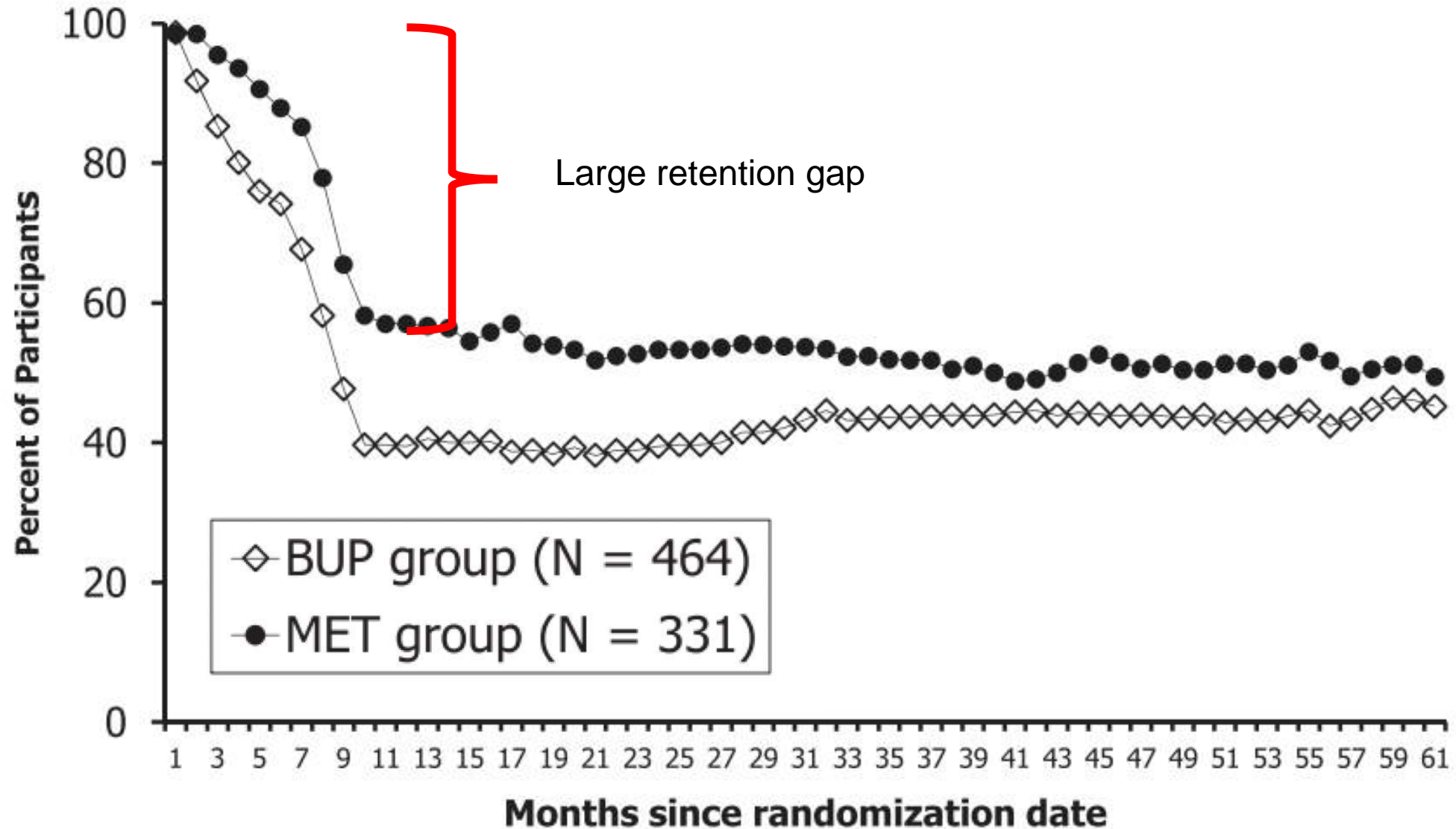
(1) Sordo, Luis et al. "Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies." *BMJ* vol. 357 j1550. 26 Apr. 2017, doi:10.1136/bmj.j1550

(2) MacArthur G. J., Minozzi S., Martin N., Vickerman P., Deren S., Bruneau J. et al Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. *BMJ* 2012; 345: e5945.

(3) Hagan, Holly et al. "A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs." *The Journal of infectious diseases* vol. 204,1 (2011): 74-83. doi:10.1093/infdis/jir196

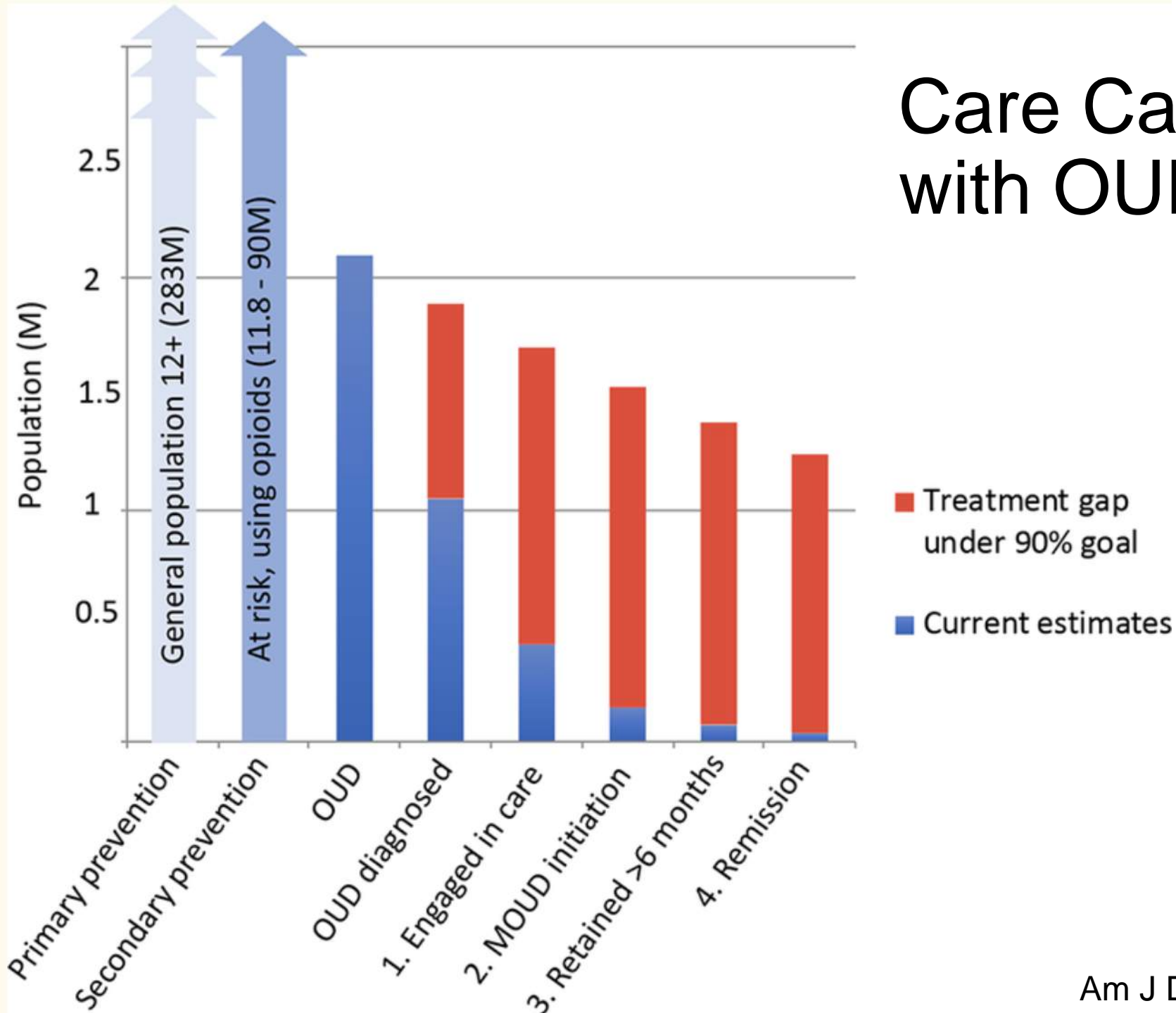
(4) Low A. J., Mburu G., Welton N. J., May M. T., Davies C. F., French C. *et al* impact of opioid substitution therapy on antiretroviral therapy outcomes: a systematic review and meta-analysis. *Clin Infect Dis* 2016; 63: 1094–1104.

# Gaps in Retention in Care: START Trial



†Treatment is defined as received MET or BUP treatment medication

# Care Cascade for People with OUD



# Methadone and Buprenorphine

- Agonist and partial agonist therapies work
- Multiple RCTs and meta-analyses
- Benefits:
  - Improved survival(1)
  - Improved HIV(2)/HCV(3) prevention
  - Improved HIV medication adherence and viral suppression(4)
- **Still many gaps: Interest, access, retention, stigma, side effects**

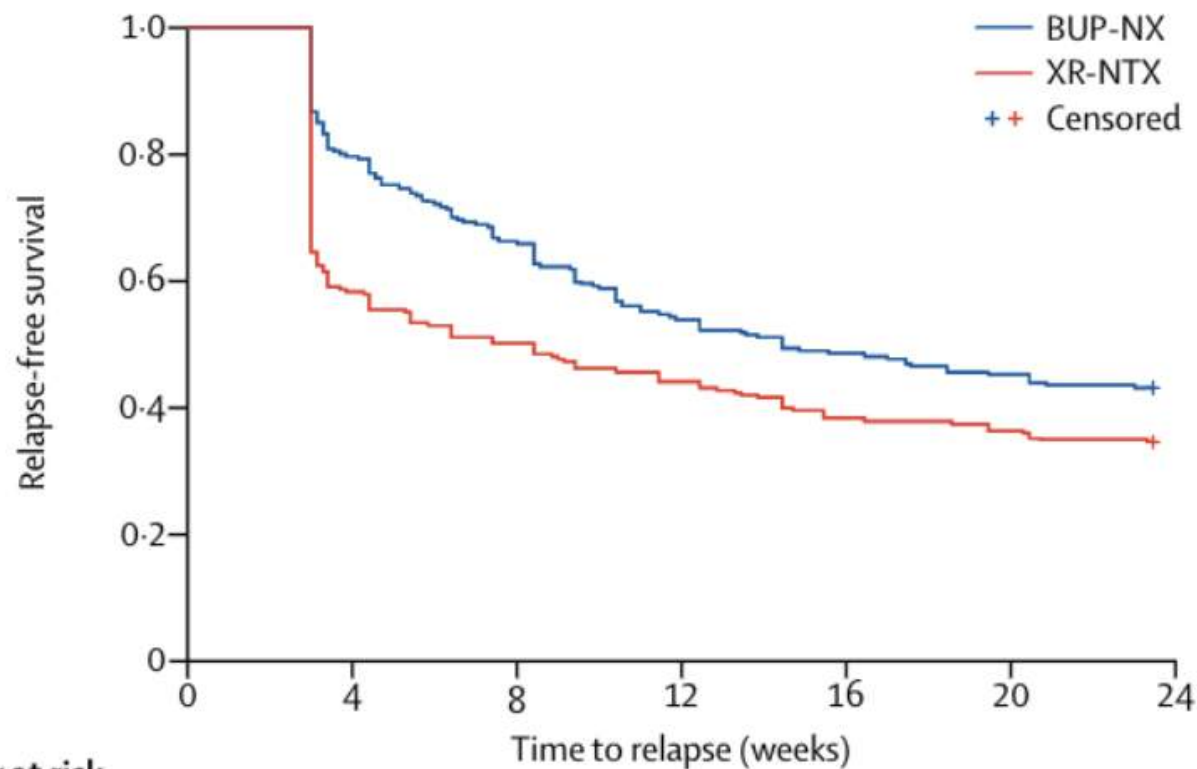
# Extended Release Naltrexone (XR-NTX)

- Opioid antagonist
- Given via injection once monthly
- Abstinence/"detoxification" (7-10 days) needed before induction
- Also has indication for treatment of alcohol use disorder
  
- No need for special license (x-wavier) or setting (OTP)
- Works really well in "America's drug free ethos"

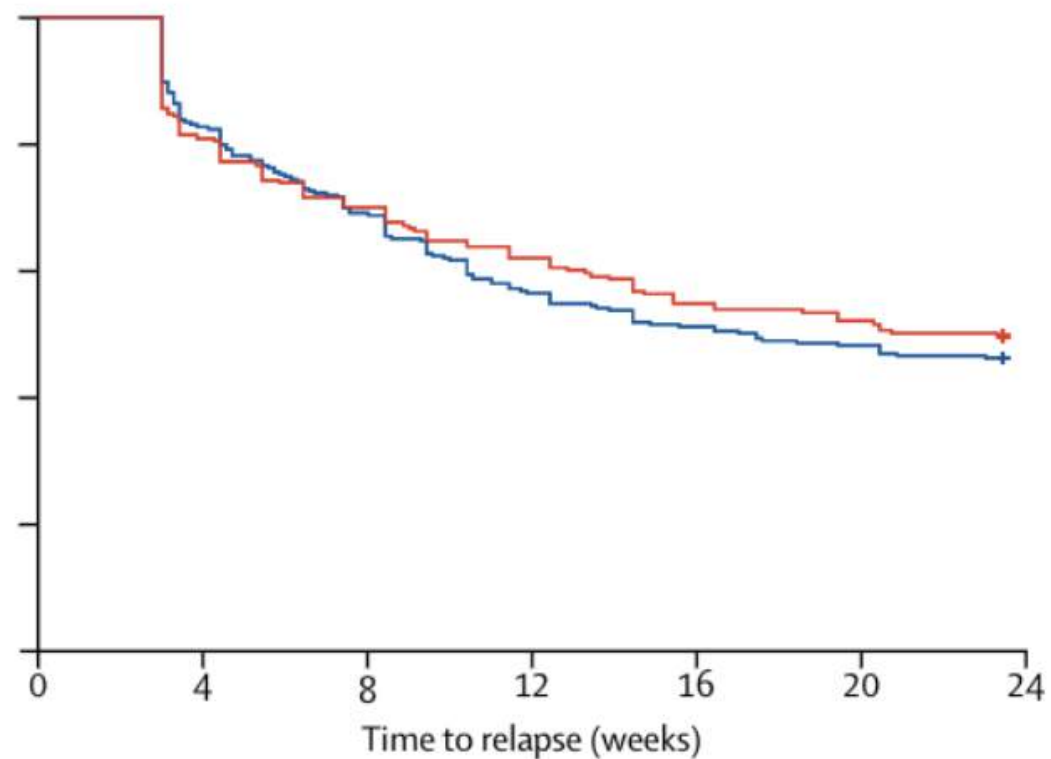


# Similar efficacy XR-NTX (if you can start it)

## Intent to treat analysis



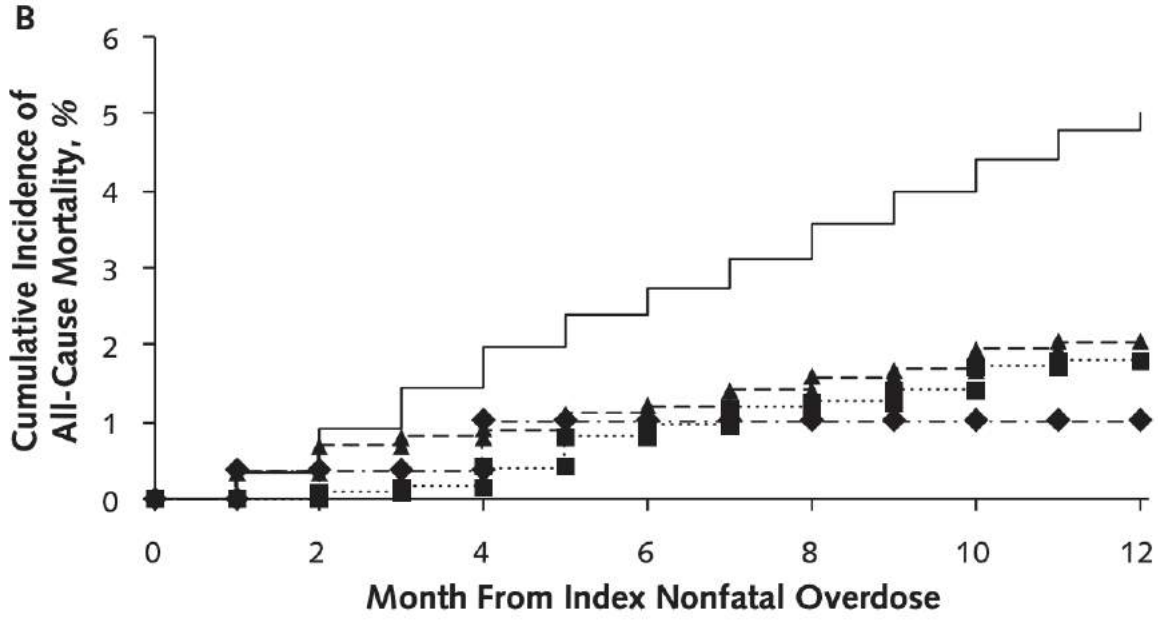
## Per protocol analysis



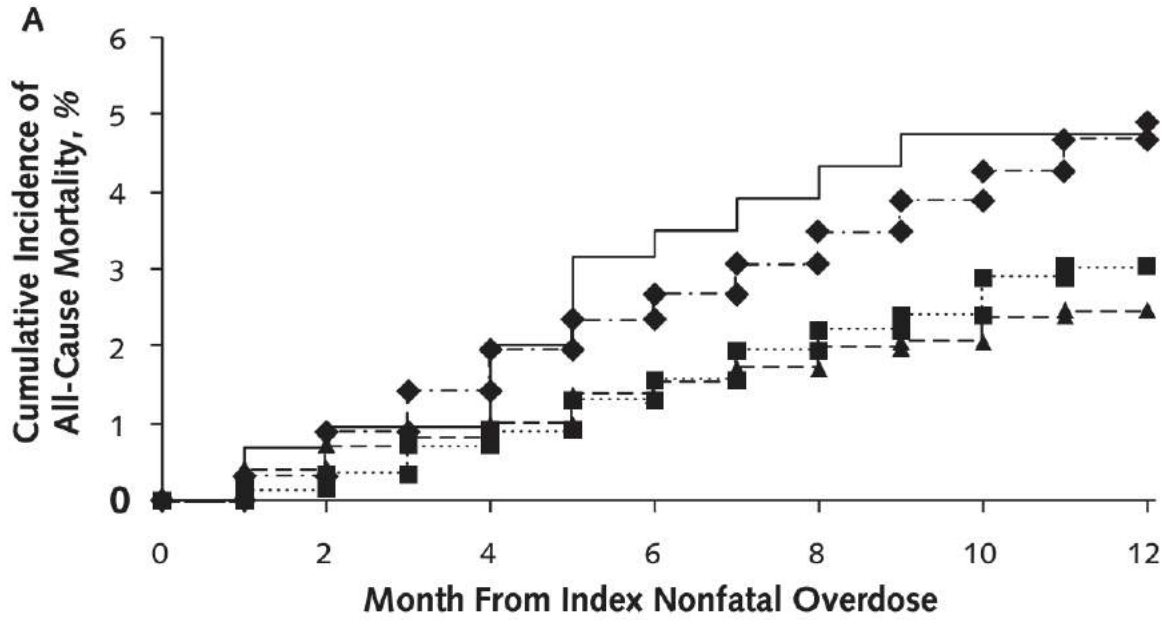
Number at risk		0	4	8	12	16	20	24			0	4	8	12	16	20	24
(censored)	BUP-NX	287	229	100	155	140	130	0 (124)	270	222	184	149	134	126	0 (120)		
	XR-NTX	283	165	142	125	109	103	0 (98)	204	164	141	124	109	103	0 (98)		

# Real World Example: Massachusetts

## On Treatment



## Off treatment

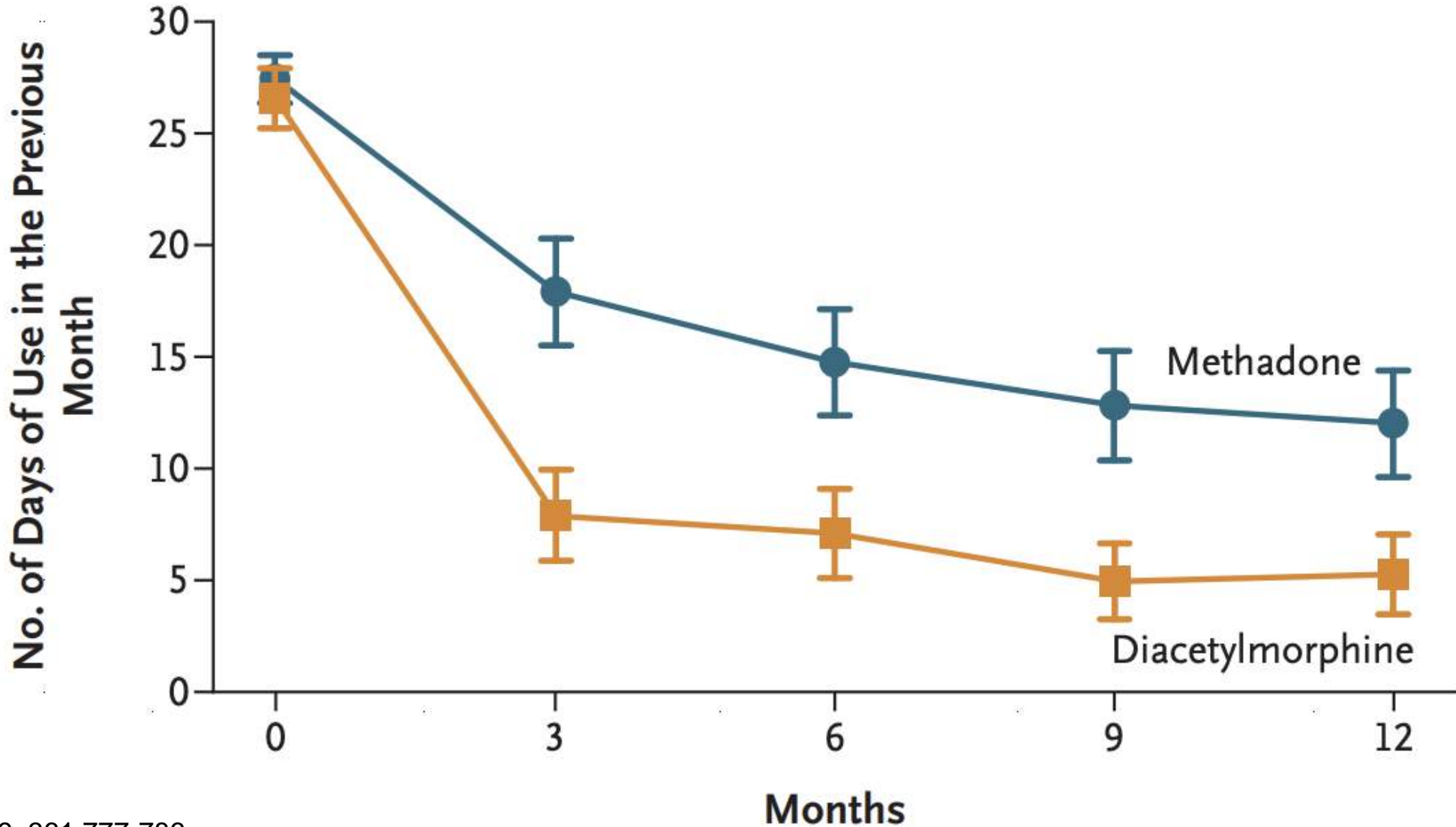


-▲- MMT 1,416 (8%)  
 -◆- Naltrexone 772 (4%)  
 -■- Buprenorphine 2,228 (13%)  
 — No MOUD 12,295 (70%)

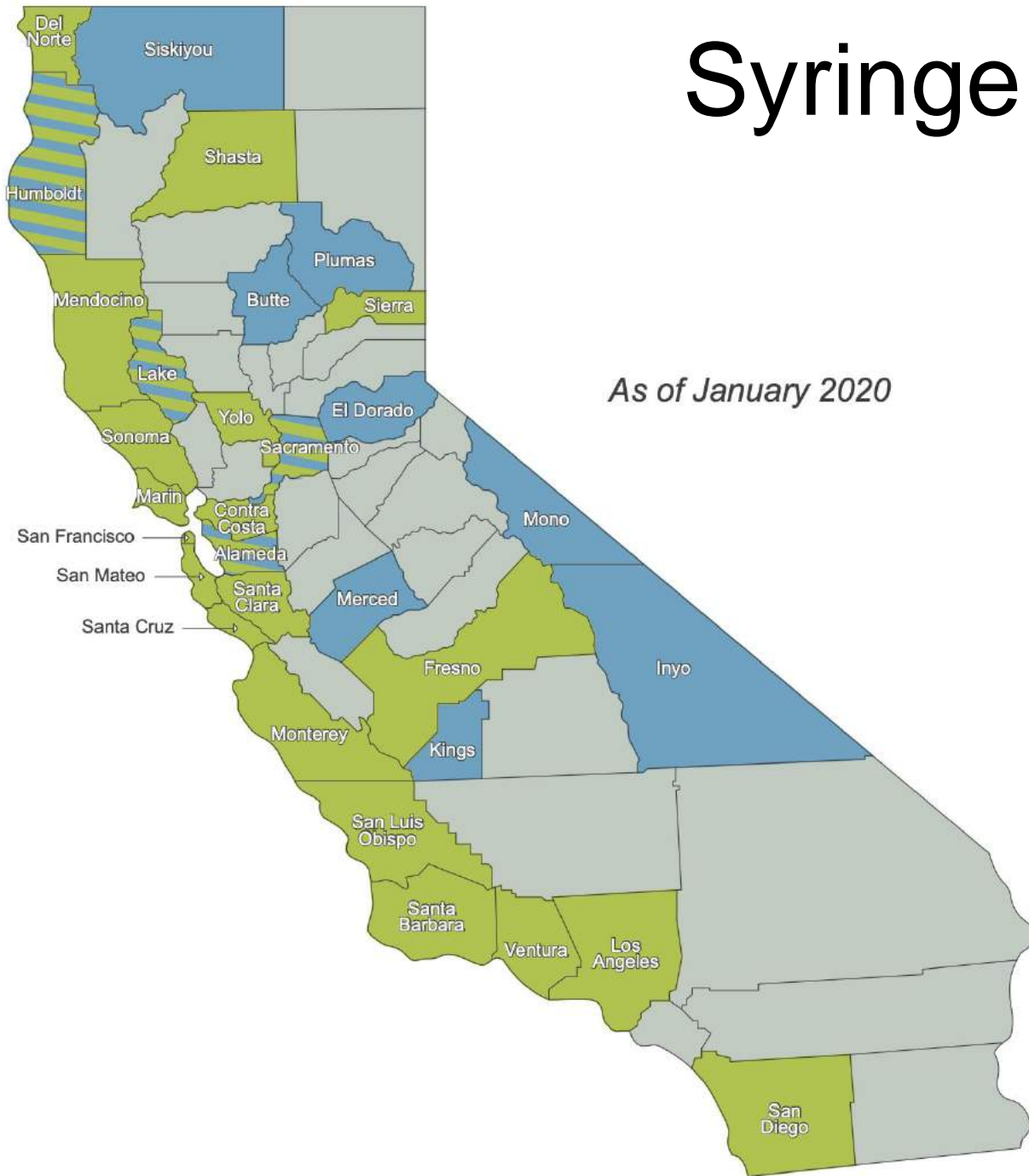
Larochelle MR, Bernson D, Land T, et al. Medication for Opioid Use Disorder After Nonfatal Opioid Overdose and Association With Mortality: A Cohort Study. *Ann Intern Med.* 2018;169(3):137-145. doi:10.7326/M17-3107

# Diacetylmorphine vs. Methadone: NAOMI trial

## A Street Heroin



# Syringe Services Programs

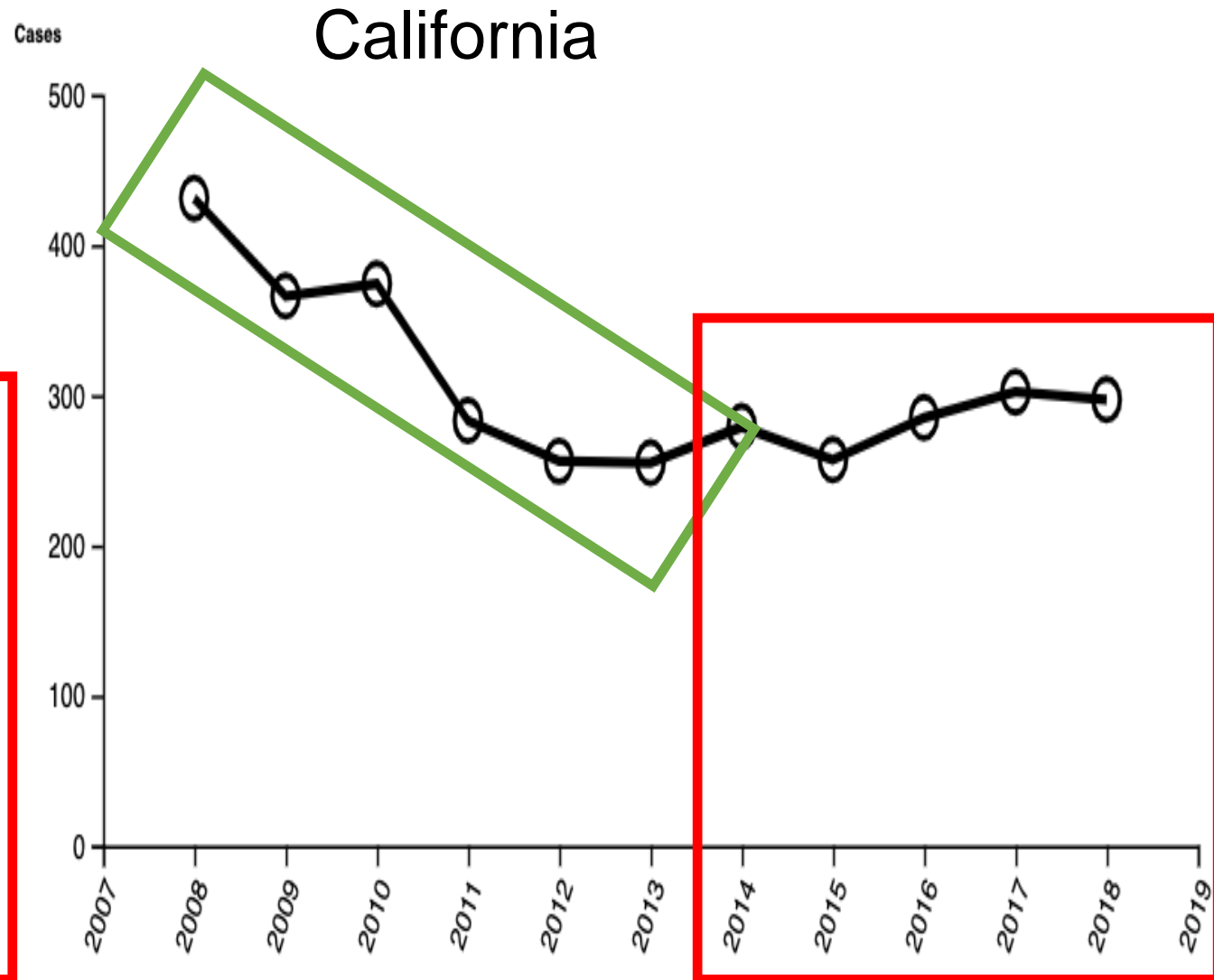
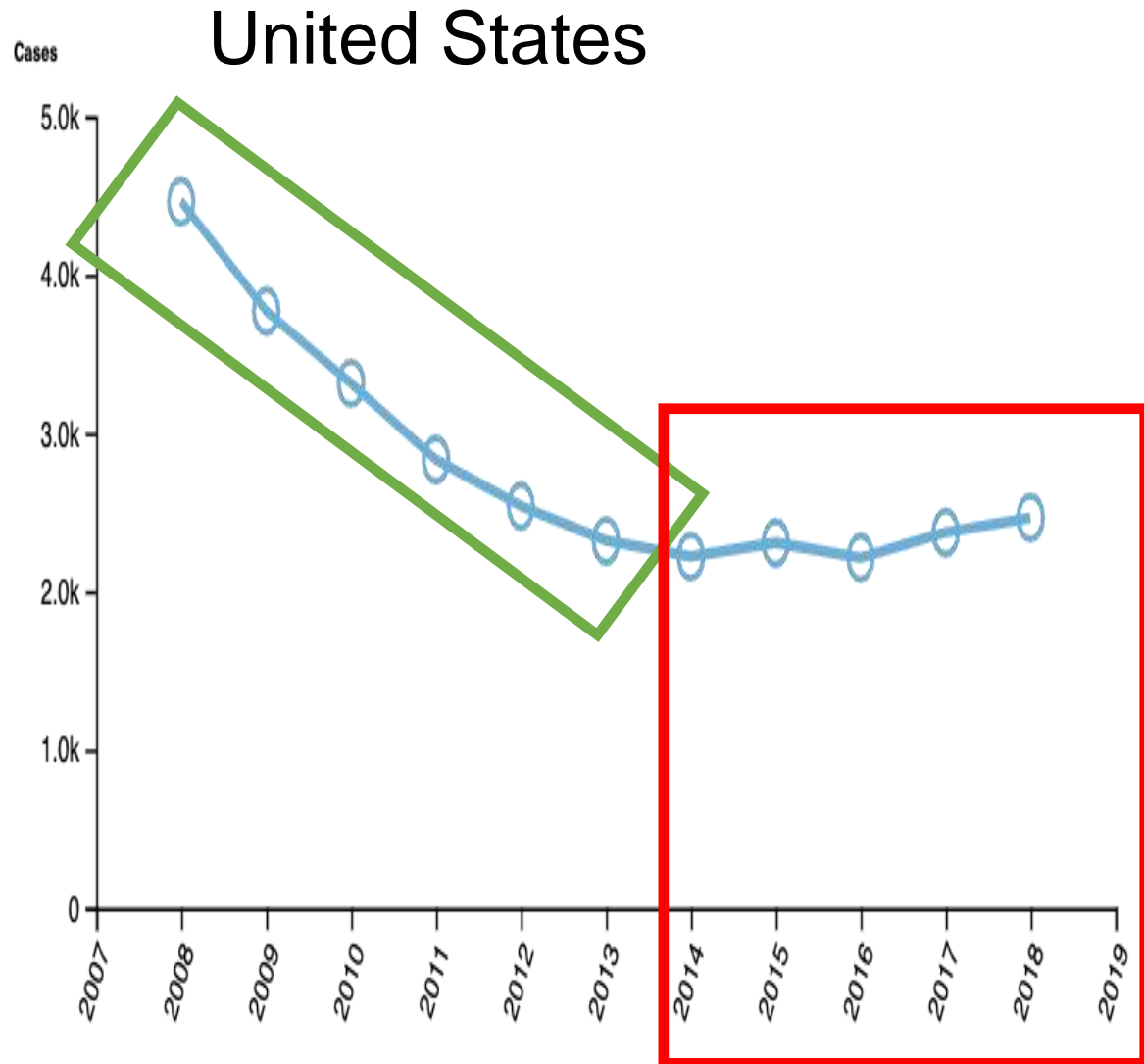


- Community-based prevention programs
- Provide a range of services:
  - Access to and disposal of sterile syringes and injection equipment
  - Naloxone distribution
  - Fentanyl test strip distribution
  - Vaccination
  - Testing and linkage to infectious disease care and substance use treatment
- List in California available at:
  - [https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OA\\_prev\\_sepdirectory.asp](https://www.cdph.ca.gov/Programs/CID/DOA/Pages/OA_prev_sepdirectory.asp)  
[X](#)

Jones L, Pickering L, Sumnall H, McVeigh J, Bellis MA. Optimal provision of needle and syringe programmes for injecting drug users: A systematic review. *Int J Drug Policy*. 2010;21(5):335-342.

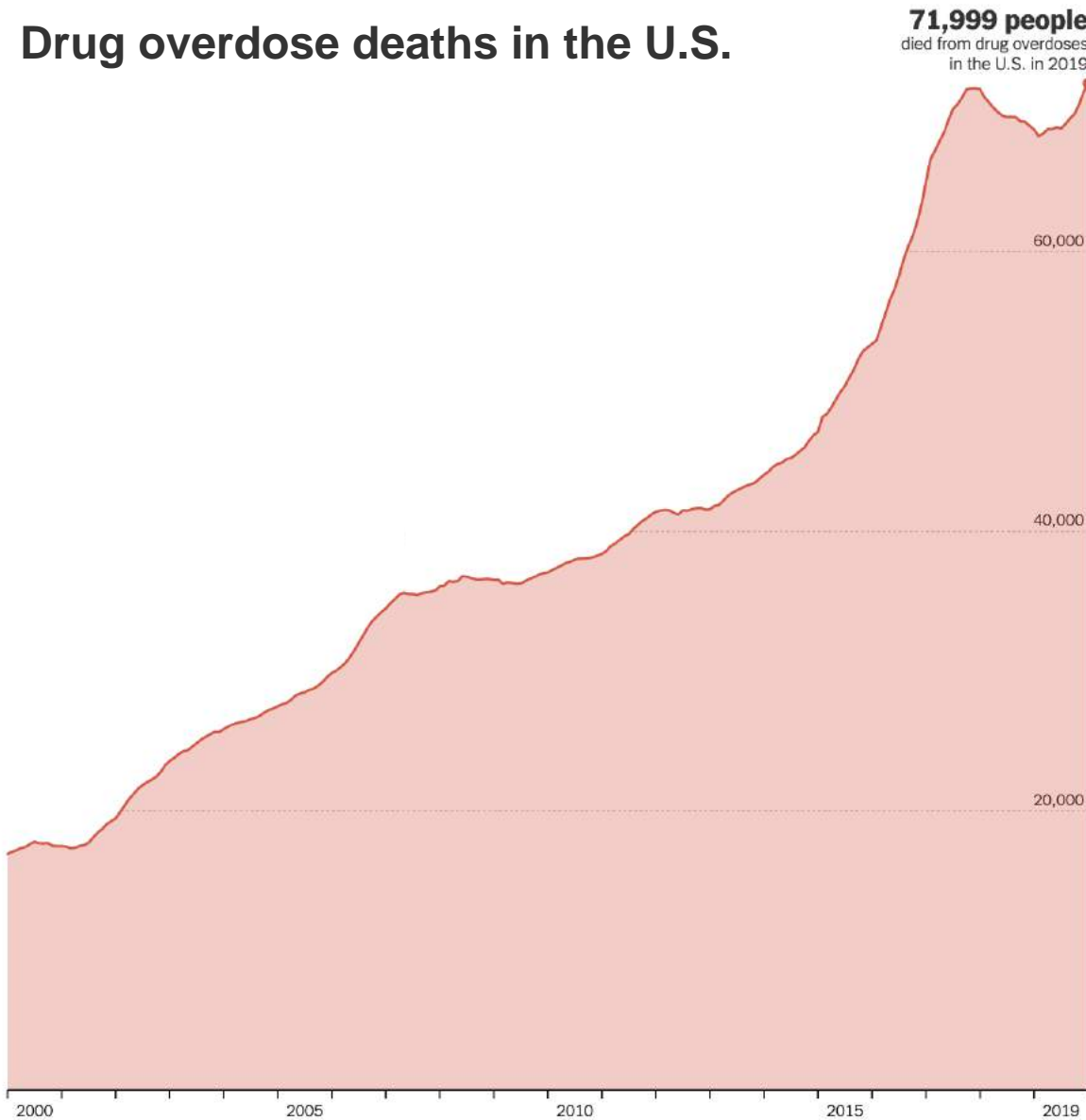
doi:10.1016/j.drugpo.2010.02.001

# New HIV Cases in PWID



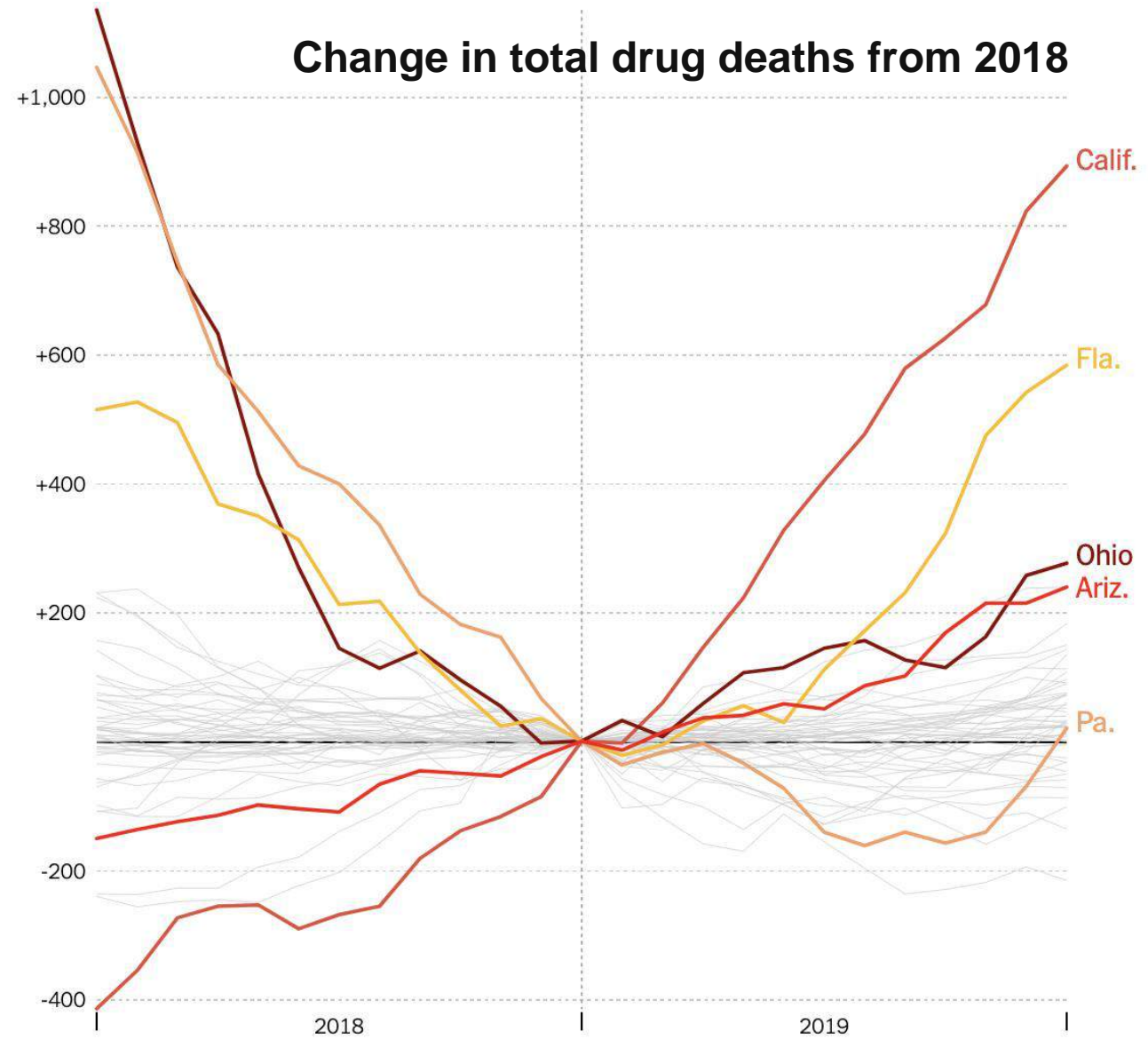
# Overdose Crisis in the United States

Drug overdose deaths in the U.S.



Source: Centers for Disease Control and Prevention

Change in total drug deaths from 2018



Katz et al. In Shadow of Pandemic, U.S. Drug Overdose Deaths Resurge to Record. NY Times (7/15/2020)



# Safe Consumption Sites

- Many names: Safe injection facilities, overdose preventions sites
- Exist since 1980s
- >100 worldwide
- INSITE (Vancouver, BC) best studied:
  - Lower overdose mortality (88 fewer overdose deaths per 100 000 person-years [PYs])
  - 67% fewer ambulance calls for treating overdoses
  - Modelled decreased HIV infections.



US – Unsanctioned site  
Am J Prev Med 2017;53(6):919–922

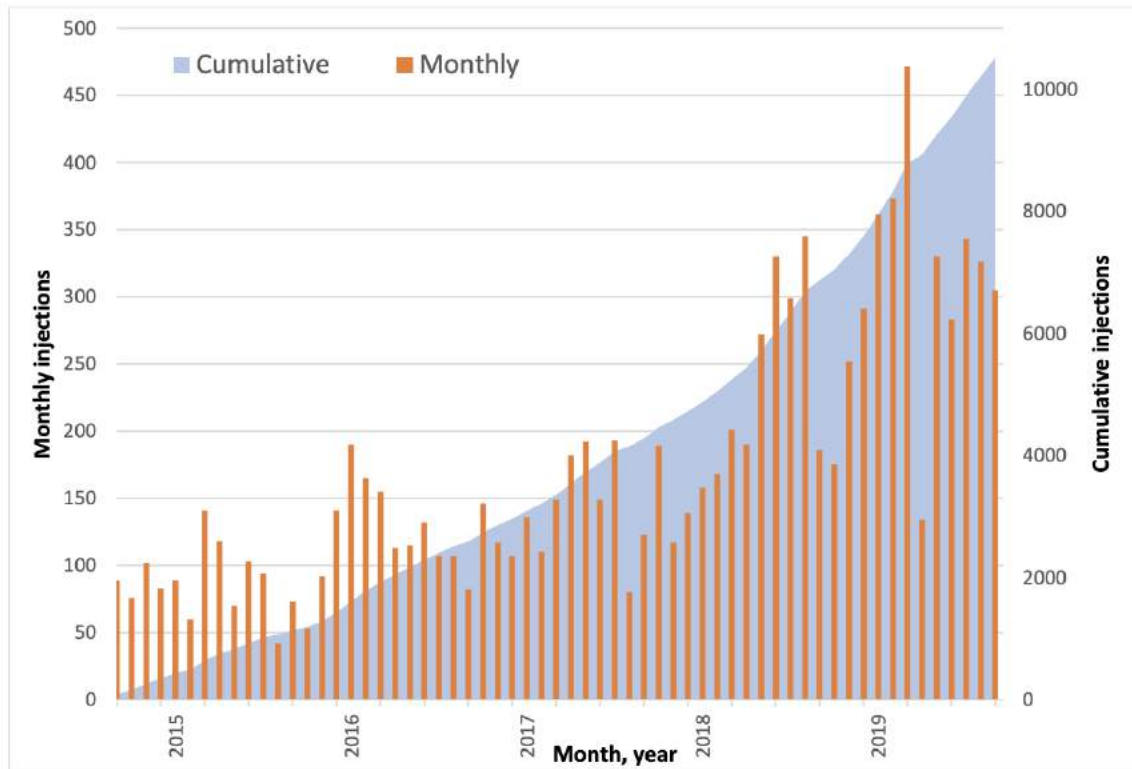


INSITE - Vancouver

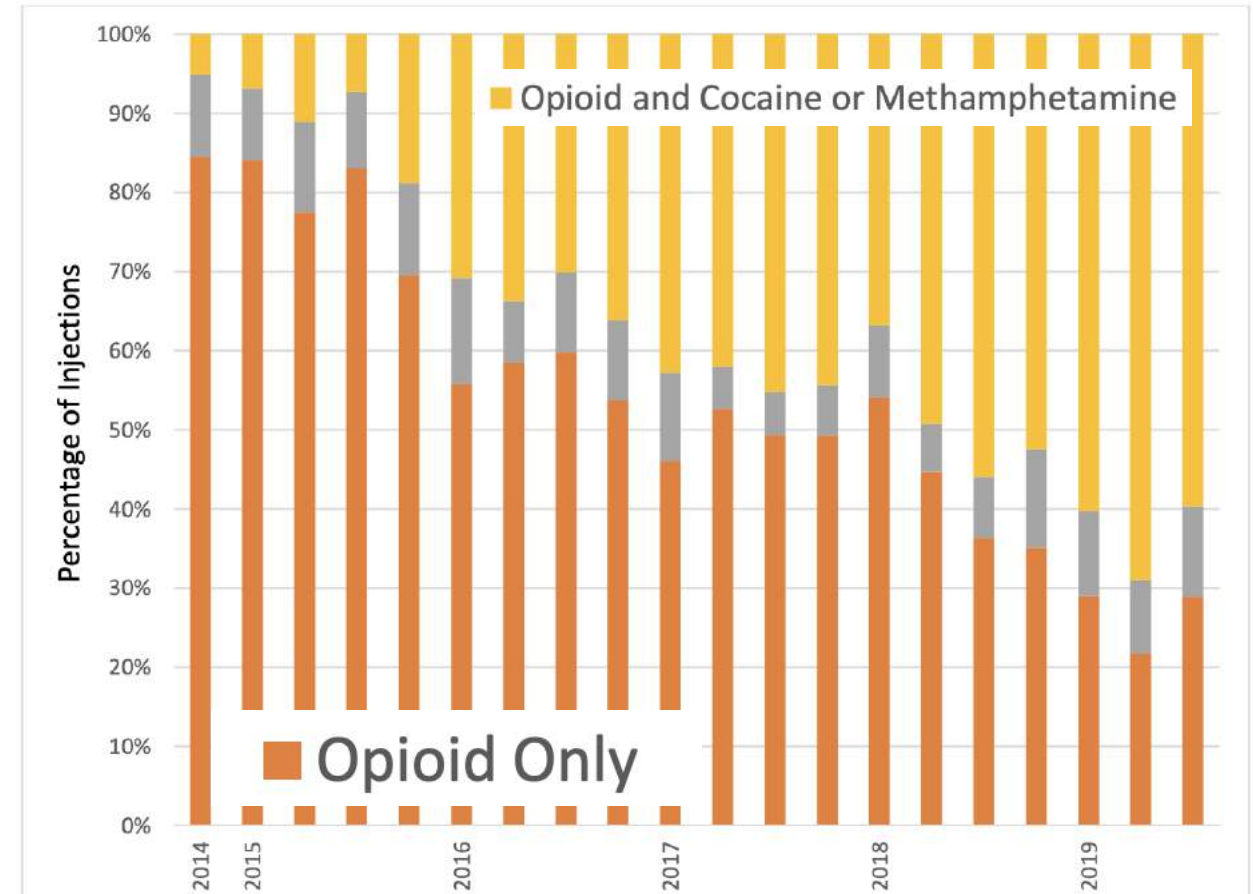


# Safe Consumption Sites: US Site - Unsanctioned

10,514 Injections – 33 Overdoses – 0 Deaths

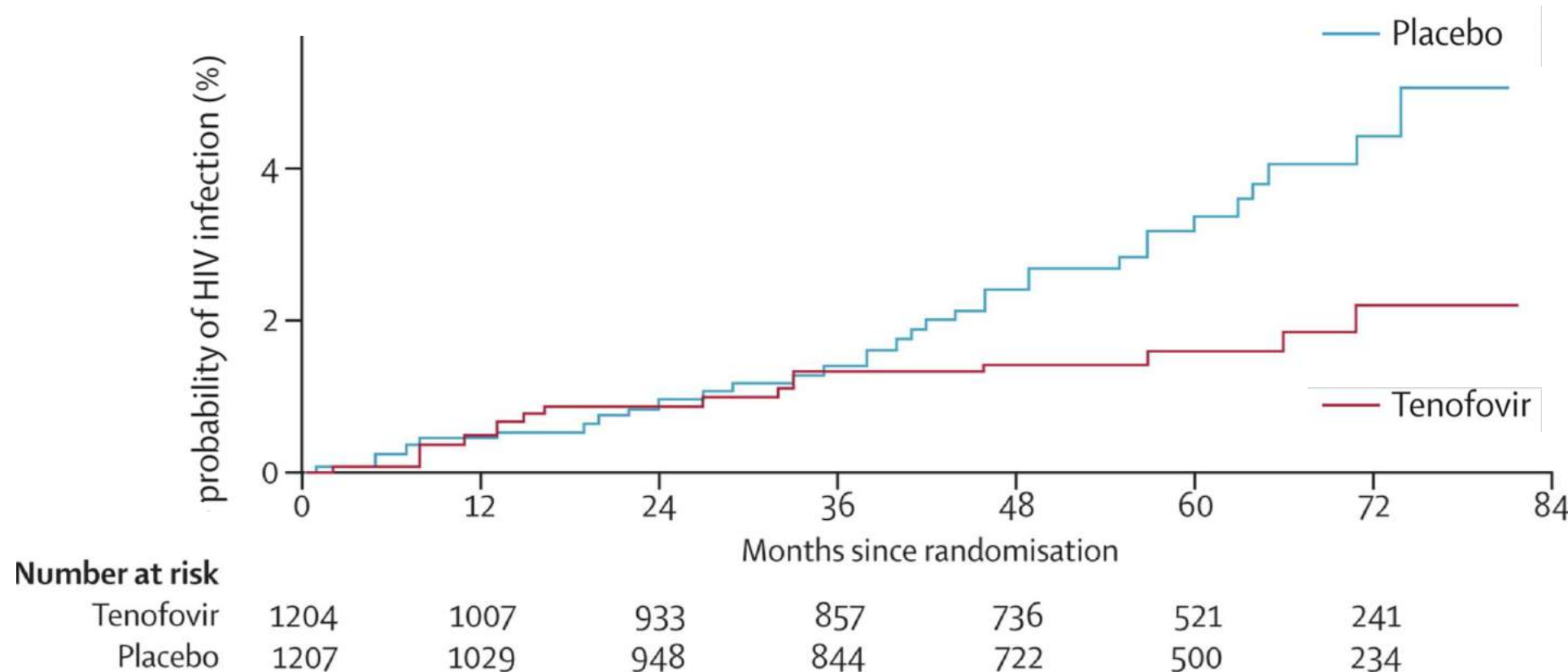


**Figure 1.** Number of Injections Per Month and Cumulative at an Unsanctioned Safe Consumption Site in the United States, 2014–2019



# PrEP for PWID

- Evidence of efficacy from the Bangkok trial
- 48.9% reduction in HIV incidence
- CDC recommended intervention for PWID



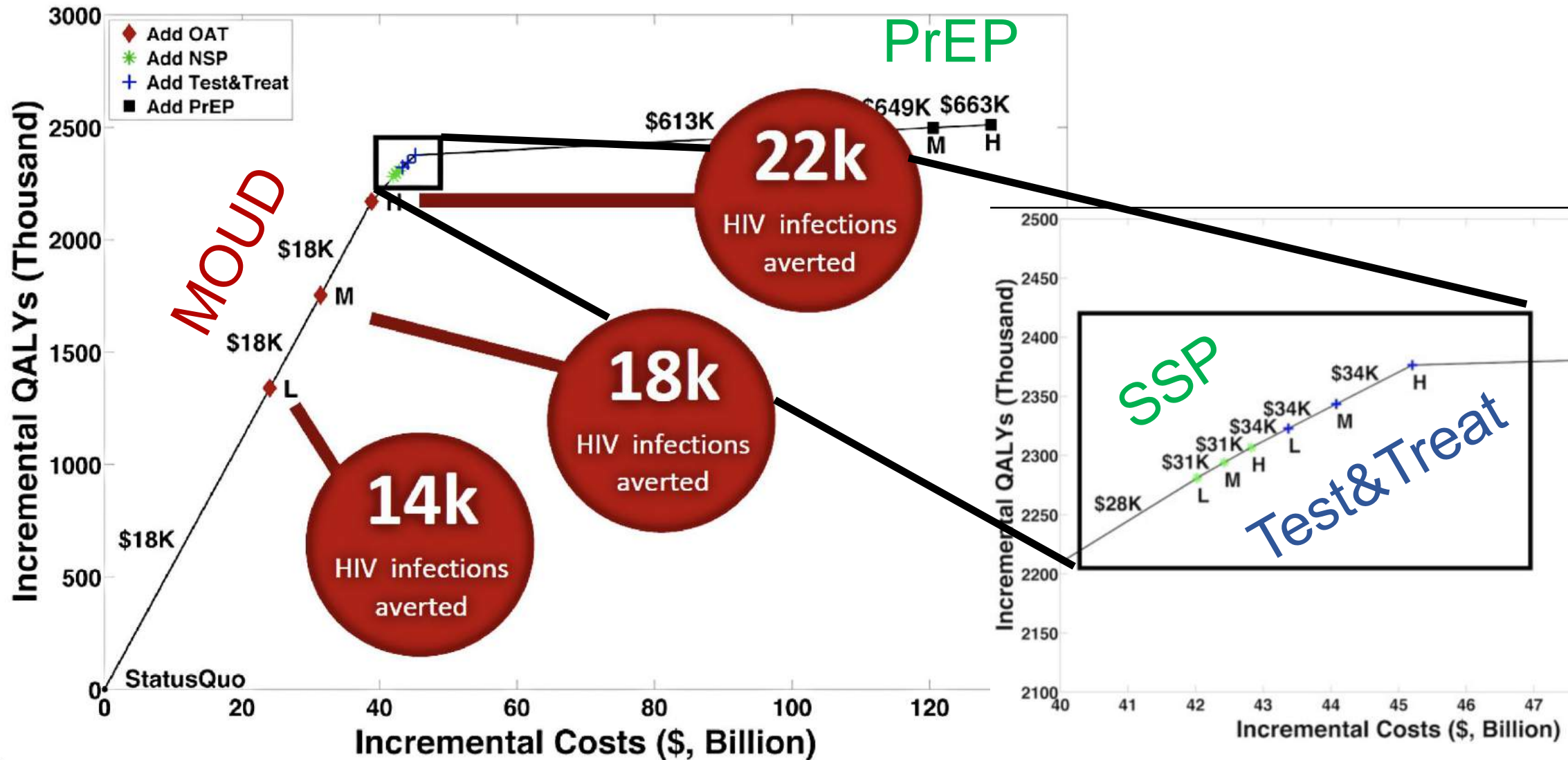
# PrEP for PWID

- PrEP awareness in PWID 13 to 57% in PWID vs >80% in MSM
  - 40% in Los Angeles/San Francisco
- PWID taking PrEP 1-3%
  - 2% in LA/SF

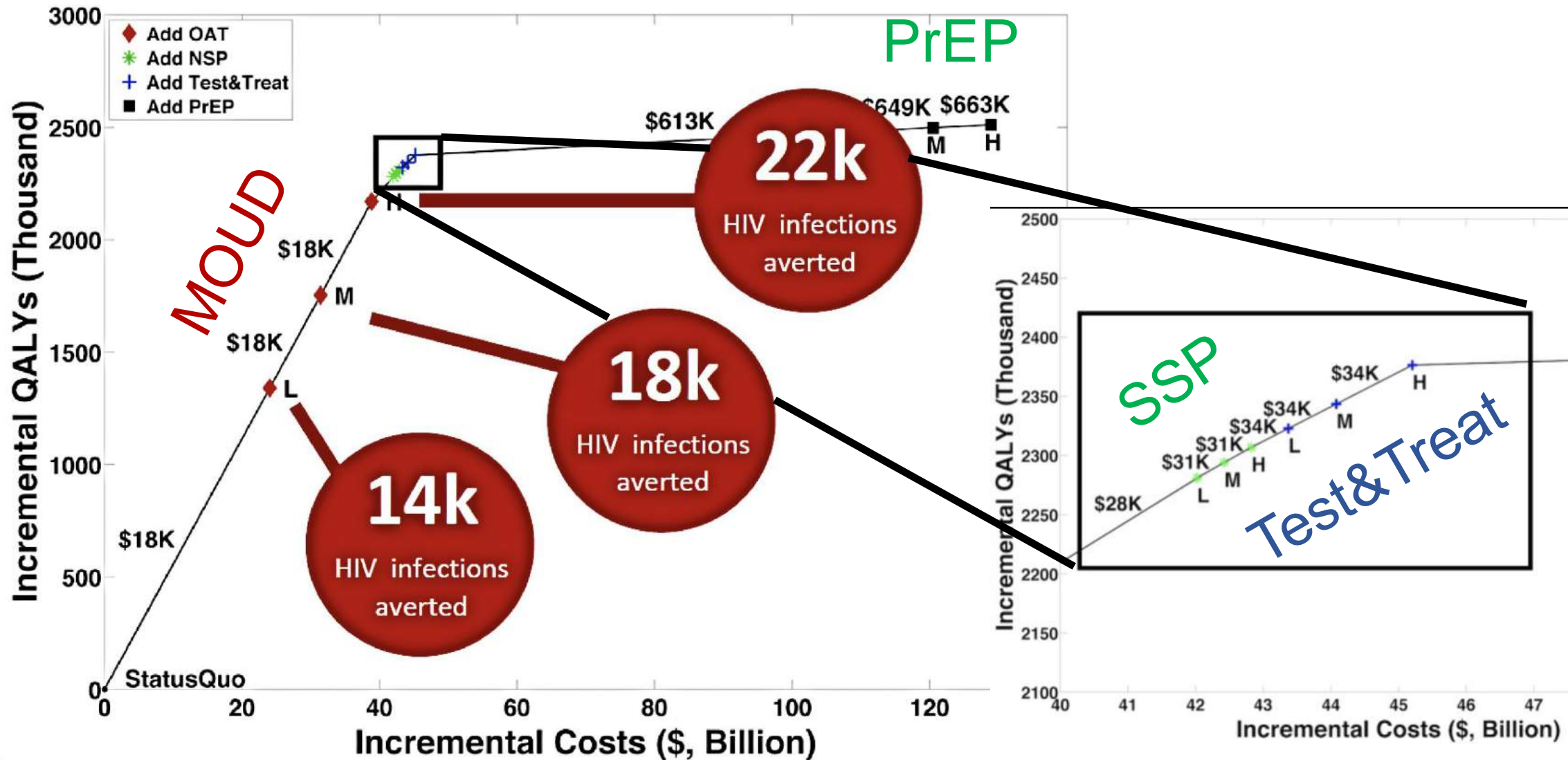
Mistler CB, Copenhaver MM, Shrestha R. The Pre-exposure Prophylaxis (PrEP) Care Cascade in People Who Inject Drugs: A Systematic Review. *AIDS Behav.* 2020;10.1007/s10461-020-02988-x. doi:10.1007/s10461-020-02988-x

Walters SM, Kral AH, Simpson KA, Wenger L, Bluthenthal RN. HIV Pre-Exposure Prophylaxis Prevention Awareness, Willingness, and Perceived Barriers among People Who Inject Drugs in Los Angeles and San Francisco, CA, 2016-2018. *Subst Use Misuse.* 2020;1-11. doi:10.1080/10826084.2020.1823419

# MOUD > NSP > Test&Treat > PrEP



# MOUD > NSP > Test&Treat > PrEP

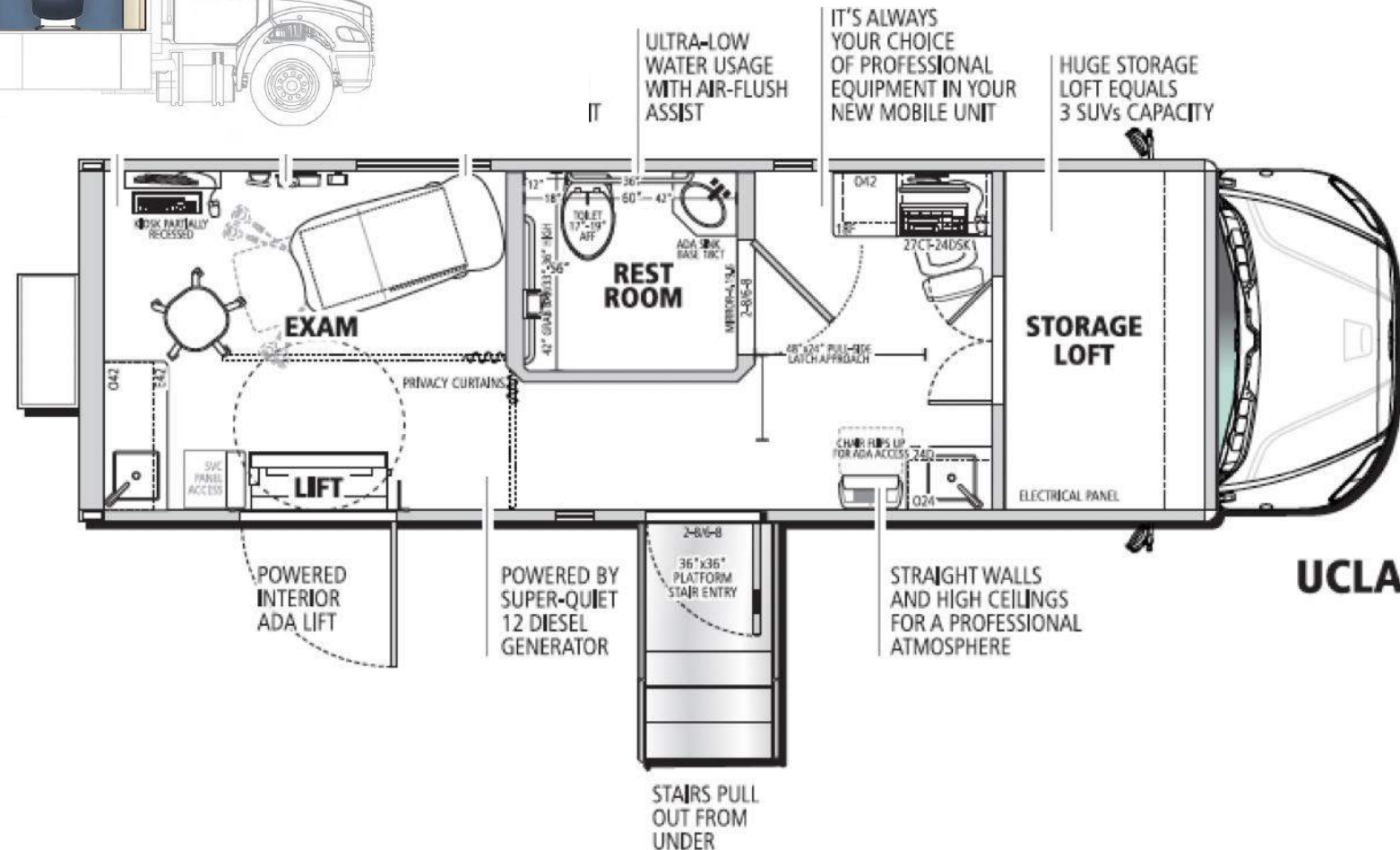




# Shameless Plug for HPTN 094



Informational Webinar on Monday 10/26 @ 4 PM, ask Elena or Me for details

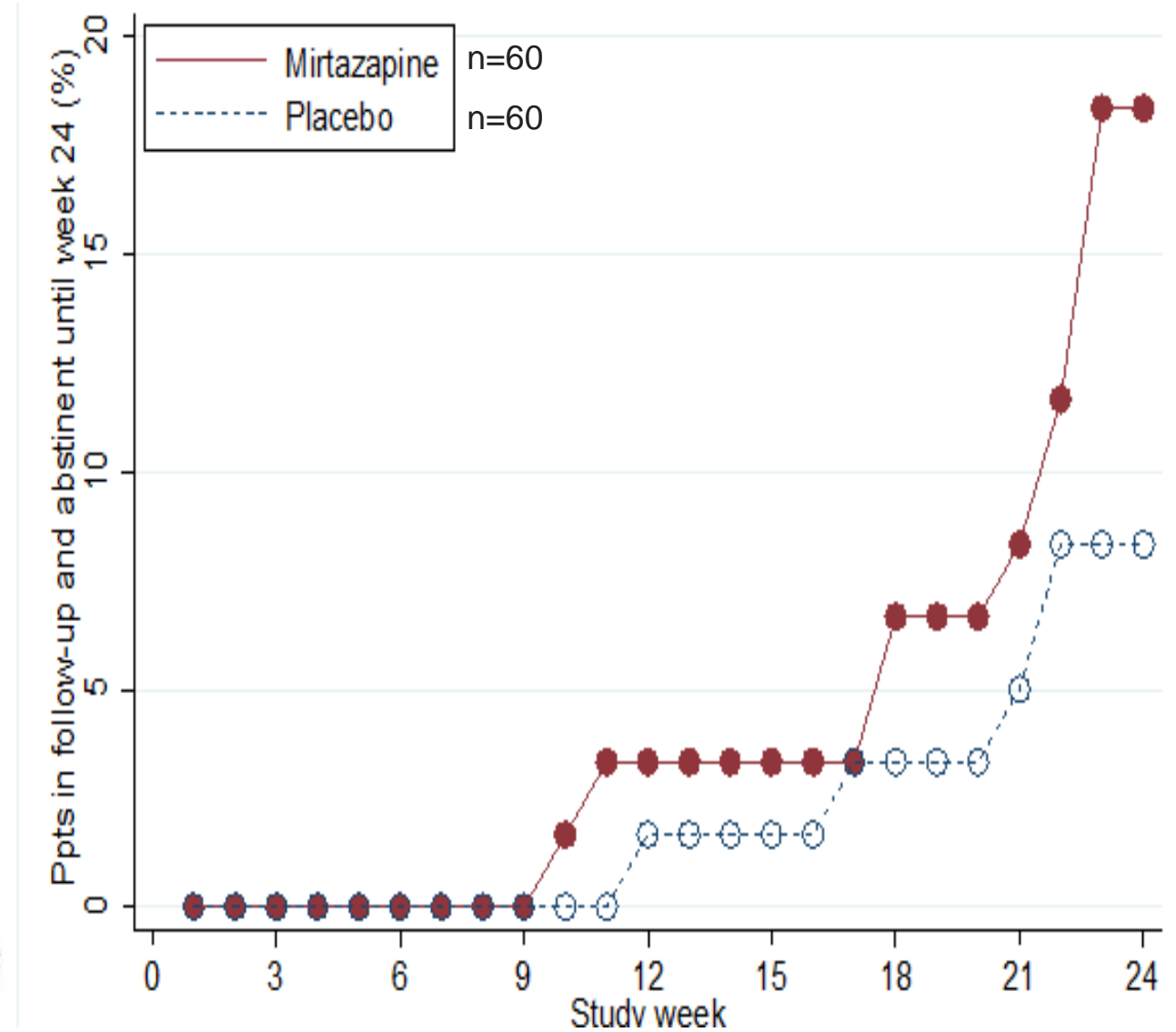
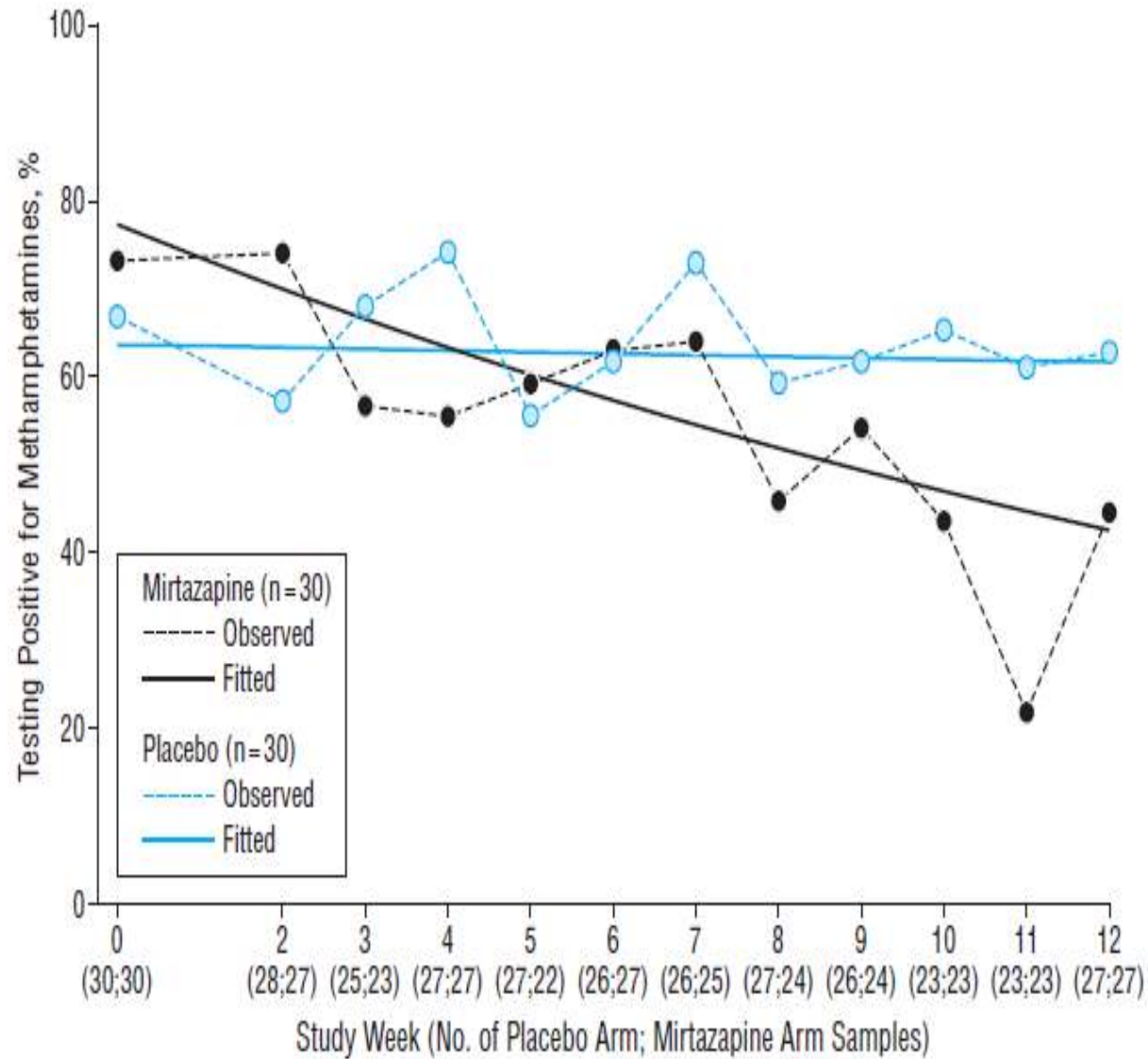


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# Pharmacologic Interventions for Methamphetamine Use

<b>Failed</b>	<b>Some Promise</b>	<b>Positive Outcome</b>
<b>Tricyclic Antidepressants</b>	Bupropion	Mirtazapine (treatment, in MSM)
<b>Serotonin Re-uptake Inhibitors</b>	Methylphenidate	
<b>Aripiprazole</b>	Modafinil	
<b>Extended-Release Naltrexone</b>	Dextroamphetamine	
<b>Ondansetron</b>	Oral Naltrexone	
<b>Mirtazapine (withdrawal)</b>		
<b>Varenicline</b>		
<b>Ibudilast</b>		
<b>Gamma-Vinyl-GABA</b>		
<b>Rivastigmine</b>		

# Mirtazapine for Methamphetamine (not FDA approved)





# TAKE HOME POINTS

- The US is experiencing a public health emergency in regards to substance use, injection drug use and drug overdose
- MAT for OUD WORKS <- for some
- SSP works, but more innovative strategies are need to tackle overdose epidemic
- Sadly, no effective pharmacotherapy for stimulant use (yet?)