

# Methadone Maintenance Treatment and HIV Infection: From Harm Reduction to Addiction Treatment

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# Overview

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- **Substance use and the AIDS epidemic: history and current status**
- **Treatment of addiction is HIV prevention**
- **Addiction as a chronic medical problem**
- **Importance of access, acceptability, and sustainability**

## AN OUTBREAK OF COMMUNITY-ACQUIRED *PNEUMOCYSTIS CARINII* PNEUMONIA

### Initial Manifestation of Cellular Immune Dysfunction

HENRY MASUR, M.D., MARY ANN MICHELIS, M.D., JEFFREY B. GREENE, M.D., IDA ONORATO, M.D.,  
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LEE BRETTMAN, M.D., MICHAEL LANGE, M.D., HENRY W. MURRAY, M.D.,  
AND SUSANNA CUNNINGHAM-RUNDLES, PH.D.

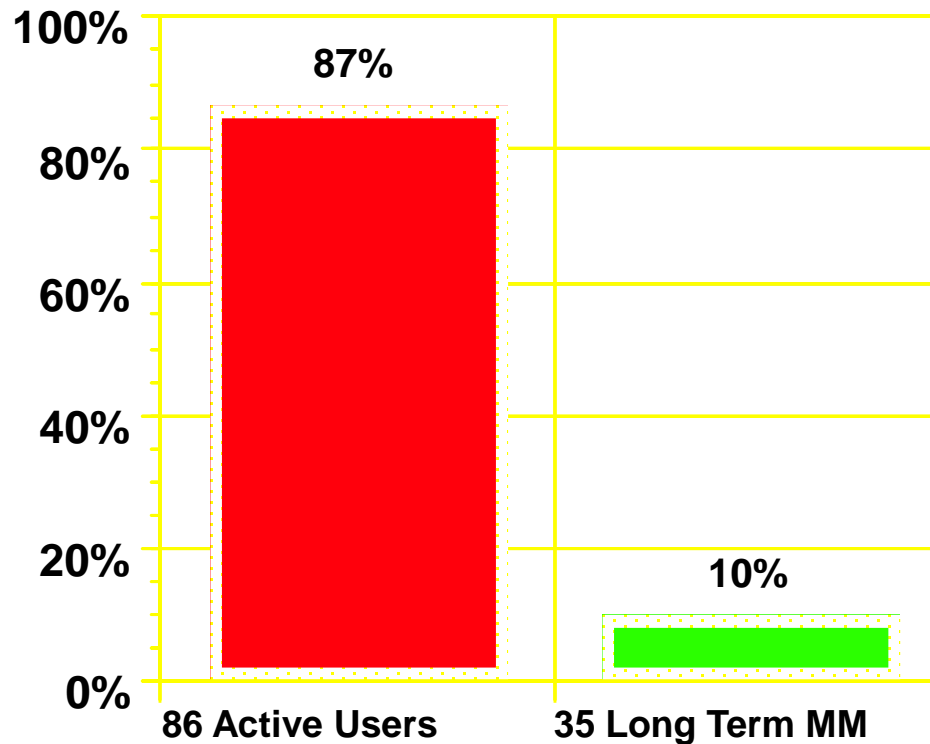
**Abstract** Eleven cases of community-acquired *Pneumocystis carinii* pneumonia occurred between 1979 and 1981 and prompted clinical and immunologic evaluation of the patients. Young men who were drug abusers (seven patients), homosexuals (six), or both (two) presented with pneumonia. Immunologic testing revealed that absolute lymphocyte counts, T-cell counts, and lymphocyte proliferation were depressed, and that humoral immunity was intact. Of the 11 patients, one was found to have Kaposi's sarcoma,

and another had angioimmunoblastic lymphadenopathy. Eight patients died. In the remaining three, no diagnosis of an immunosuppressive disease was established, despite persistence of immune defects. These cases of pneumocystosis suggest the importance of cell-mediated immune function in the defense against *P. carinii*. The occurrence of this infection among drug abusers and homosexuals indicates that these groups may be at high risk for this infection. (N Engl J Med. 1981; 305:1431-8.)

- 5 "drug abusers"
- 4 "homosexuals"
- 2 "both"

# HIV Prevalence Rates Among New York IDUs: 1984

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(MMRW, 1984)

# Adults and children estimated to be living with HIV | 2014



**Total: 36.9 million** [34.3 million – 41.4 million]

# Current global HIV epidemic

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- **Approximately 33,000,000 living with HIV/AIDS**
- **Over 3,000,000 IDUs living with HIV/AIDS**
- **Outside of sub-Saharan Africa, over 33% of all new infections are estimated to be attributable to injection drug use**
- **No estimates of the major role of alcohol and non-injection drug use**

# Predictors of sero-conversion in Project Explore: drug and alcohol use

<b>Drug</b>	<b>N at baseline</b>	<b>No. of infections</b>	<b>Hazard ratio*</b>	<b>95% CI</b>
<b>Heavy alcohol**</b>	<b>419</b>	<b>41</b>	<b>1.87</b>	<b>1.24, 2.81</b>
<b>Amphetamines</b>	<b>527</b>	<b>67</b>	<b>1.93</b>	<b>1.41, 2.64</b>
<b>Alcohol or drugs before sex</b>	<b>2952</b>	<b>205</b>	<b>1.57</b>	<b>1.08, 2.27</b>

\* REF = no, light or moderate use of alcohol; no speed use; no use before sex

\*\* Heavy alcohol = 4+ drinks every day or 6+ drinks on a typical day

# HIV epidemic in Asia

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## Asia and the Pacific (2016)

**5.1** million people living with HIV

**0.2%** adult HIV prevalence

**300,000** new HIV infections

**180,000** AIDS-related deaths

**64%** know their status

**41%** on antiretroviral treatment

**34%** virally suppressed

Source: UNAIDS Prevention Gap Report 2016



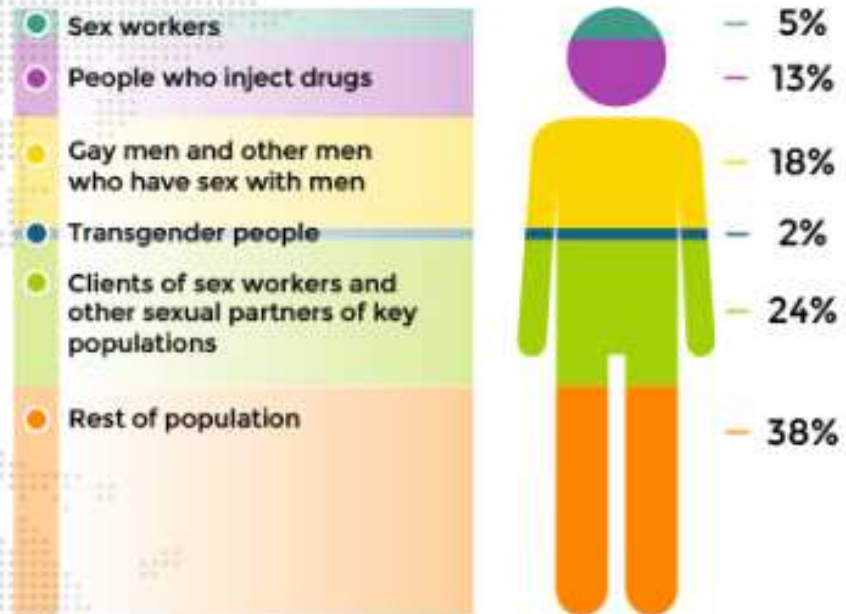
# Changing role of injection drug use

DISTRIBUTION OF NEW HIV INFECTIONS AMONG POPULATION GROUPS BY REGION

2014

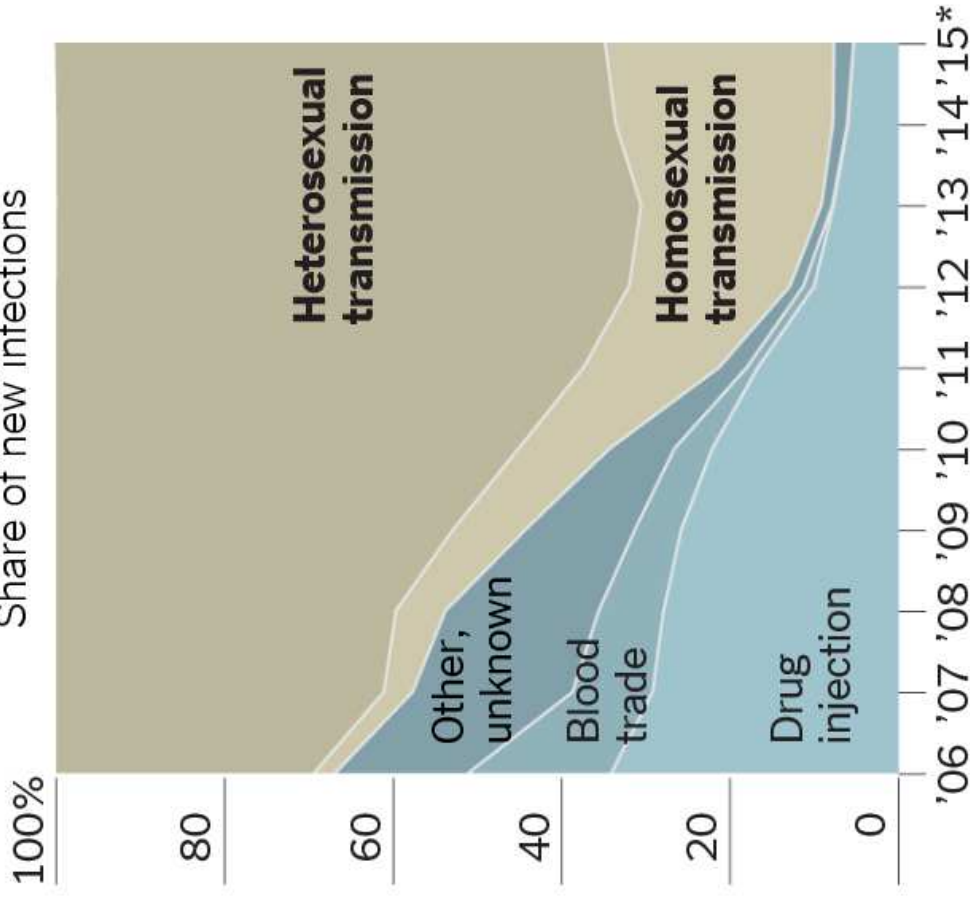
Source: UNAIDS special analysis, 2016

Asia and Pacific



## Reported incidence of H.I.V. transmission in China

Share of new infections

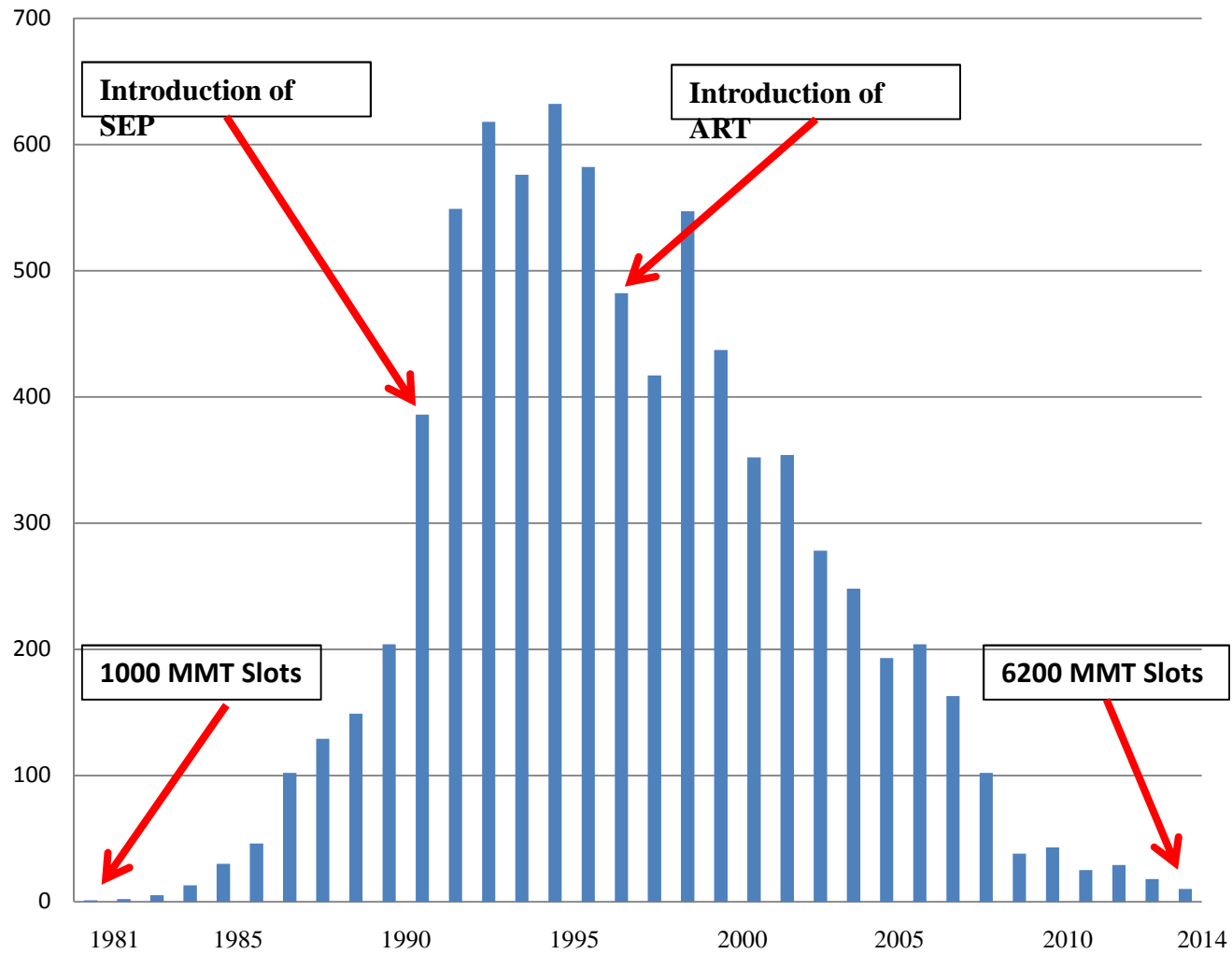


\*2015 figures through June.

Source: Chinese Journal of AIDS & STD, published by the Chinese Center for Disease Control and Prevention

# Number of new HIV/AIDS diagnoses among PWIDs in Philadelphia by year: 1981 to 2014

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# **Ineffective Responses to Drug Use Epidemics**

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ยาเสพติดให้โทษเป็นมหันตภัยร้ายแรงต่อมนุษย  
ทำลายชีวิต สังคม และประเทศชาติ  
ผู้ผลิต นำเข้า ส่งออก, จำหน่าย หรือมีไว้ใน  
ครอบครองเพื่อจำหน่ายซึ่งยาเสพติดให้โทษ อาจ  
ถูกจำคุกตลอดชีวิตหรือประหารชีวิต

## ANNOUNCEMENT

DRUGS CAUSE VERY SERIOUS EFFECTS  
TO HUMANS AS WELL AS DESTROY OUR LIFE,  
SOCIETY AND NATION. ANY PERSON WHO  
PRODUCES, IMPORTS, EXPORTS, SELLS OR  
HOLDS FOR SALE THOSE DRUGS SHALL BE  
PUNISHED WITH LIFE SENTENCE OR  
EXECUTION.

ตำรวจภูธรจังหวัด  
จังหวัดภูเก็ต  
ผู้ตรวจการ  
ผู้บังคับการ  
ผู้ช่วยผู้บัญชาการ  
ผู้บังคับการ  
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ผู้บังคับการ  
ผู้ช่วยผู้บัญชาการ

# Criminal justice responses to control drug use have not been effective

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## 武汉的强制戒毒中心





**THE U.S. STATE AND FEDERAL PRISON POPULATION HAS INCREASED OVER 800% IN JUST 40 YEARS**





1. A group of people at a dining table, with a woman in a white dress and a man in a white shirt.





# **Effective HIV prevention strategies for drug using populations**

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- **Education about HIV transmission**
- **HIV counseling and testing**
- **Increased access to sterile injection resources and condoms**
- **Drug treatment**
- **HIV treatment**

# Without interventions.....

**THE FRIDAY COVER**

## Welcome to the Red State HIV Epidemic

Republican governors face tough decisions as the disease spreads in middle America.

By ADAM WREN | May 28, 2015



### Indiana HIV outbreak has peaked, officials say

Chris Kenning, The Courier-Journal 3:31 p.m. EDT July 22, 2015



**f** 23 **t** 13 **in** **COMMENT** **EMAIL** **MORE**

At the height of Indiana's worst HIV outbreak, centered on the tiny rural town of Austin, health officials diagnosed as many as 22 new cases a week.

Fueled by a rural intravenous drug epidemic, the number of cases more than doubled to 153 between late March and mid-May. And many involved in combating the outbreak said they



Indiana University Health



**3.7K** SHARES

**f** 3088 Sha...

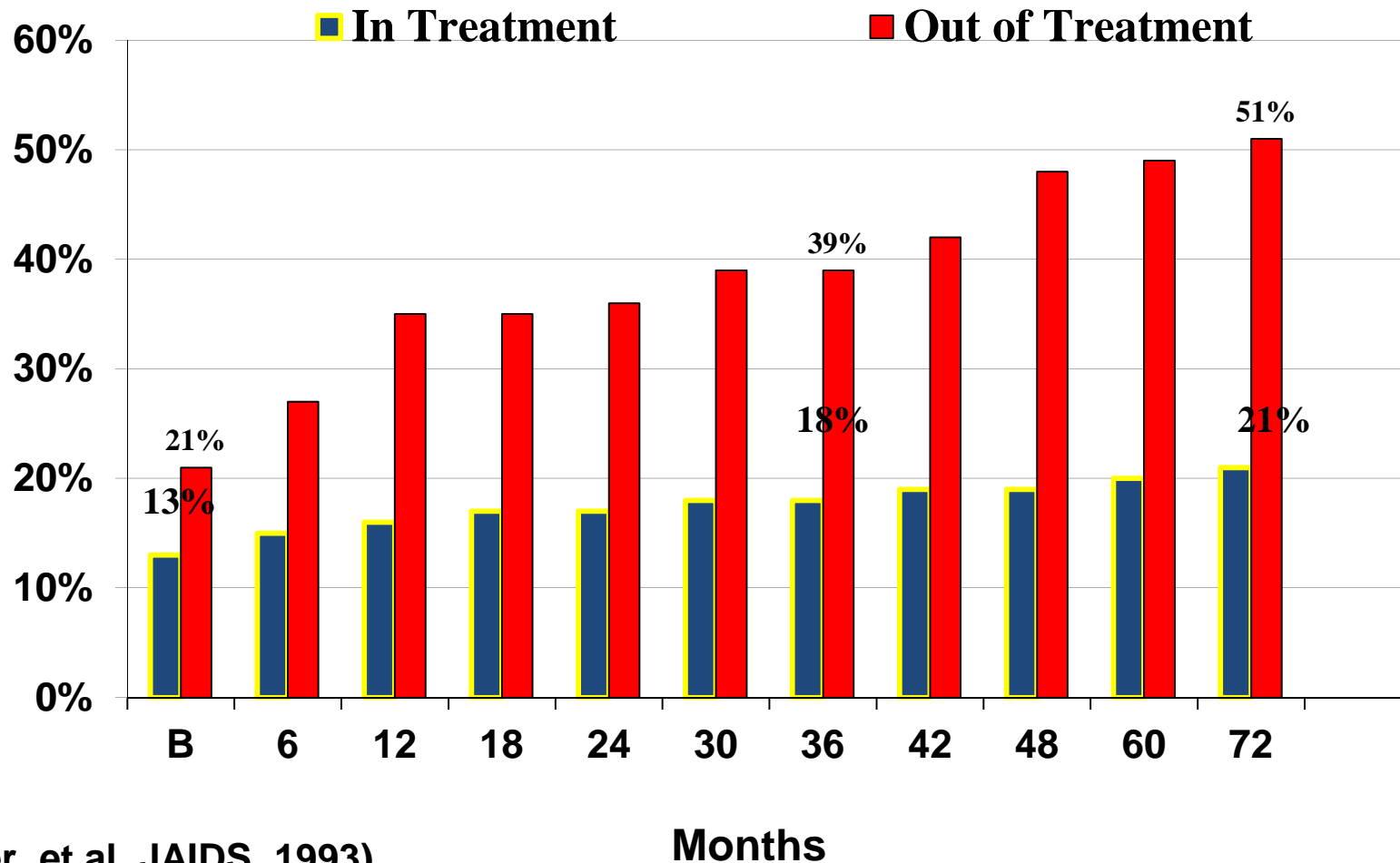
**I**t wasn't supposed to happen here. Not in Austin, an ice-cream-shop town of 4,200 in southeastern Indiana, off Interstate 65 on the road from Indianapolis to Louisville, where drug storefronts sit vacant and many residents, looking for a walk to the

## Indiana community's HIV outbreak a warning to rural America

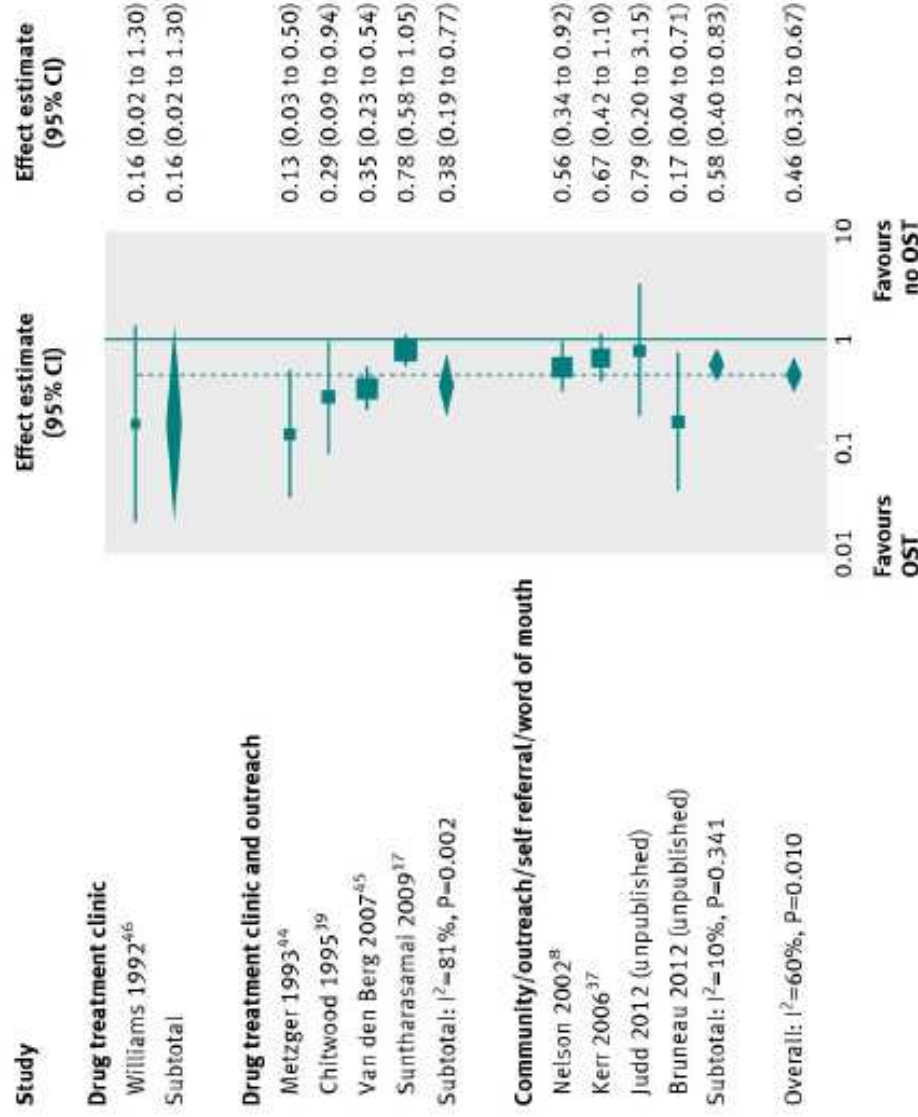
Laura Ungar and Chris Kenning, USA TODAY 7:25 p.m. EDT May 17, 2015

# Six year HIV infection rates by treatment status at time of enrollment

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(Metzger et al. JAIDS, 1993)



**Fig 5** Impact of opiate substitution treatment in relation to HIV incidence among people who inject drugs by site of recruitment of study participants

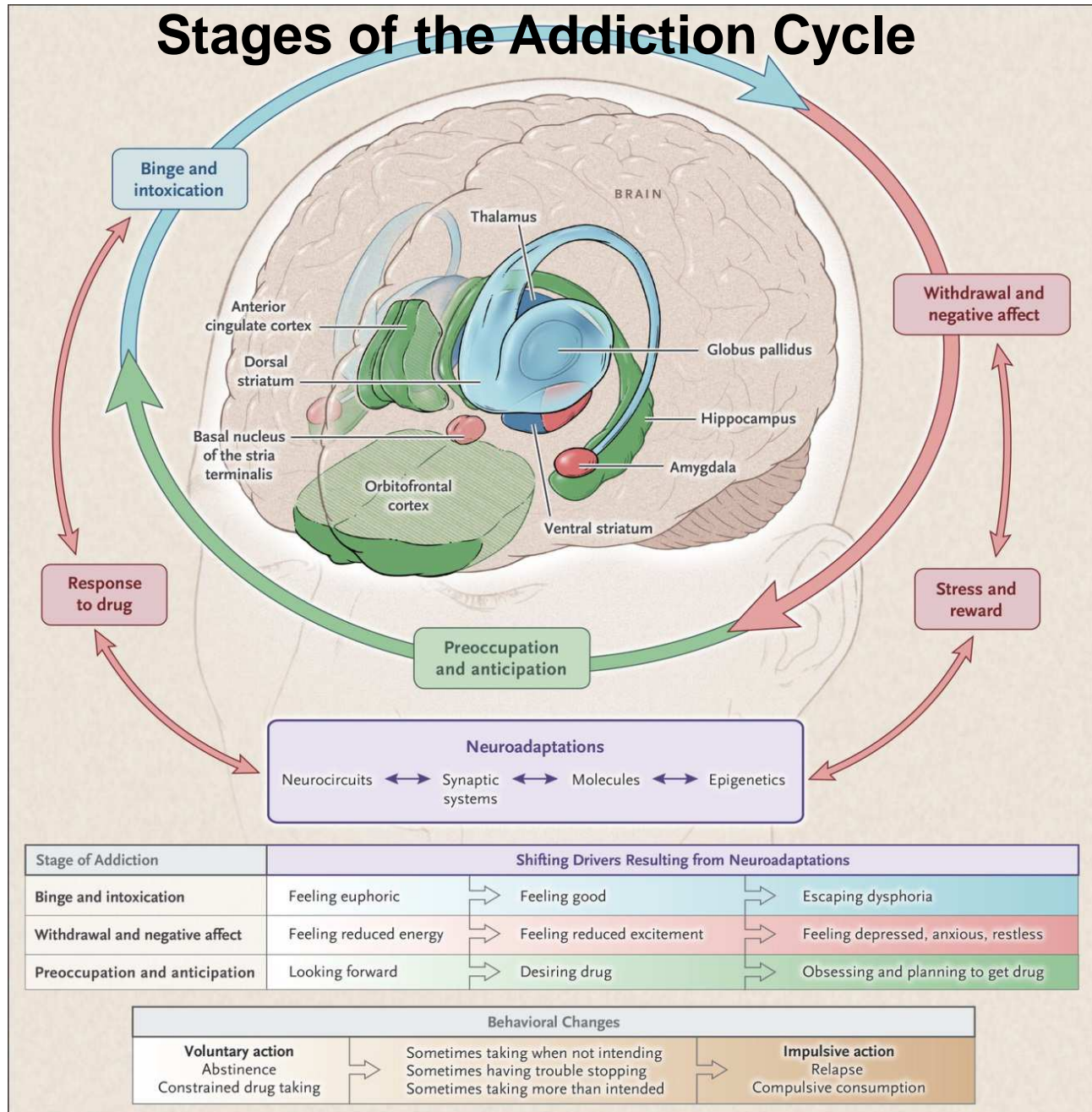
# Addiction is a chronic medical condition

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- **Biological features**  
CNS, genetics (susceptibility, medication response )
- **Behavioral features**  
behavioral patterns, conditioned association
- **Effective treatment requires attention to both--  
medication *assisted* treatment (MAT)**



# Stages of the Addiction Cycle



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

AUGUST 11, 2011

VOL. 365 NO. 6

## Prevention of HIV-1 Infection with Early Antiretroviral Therapy

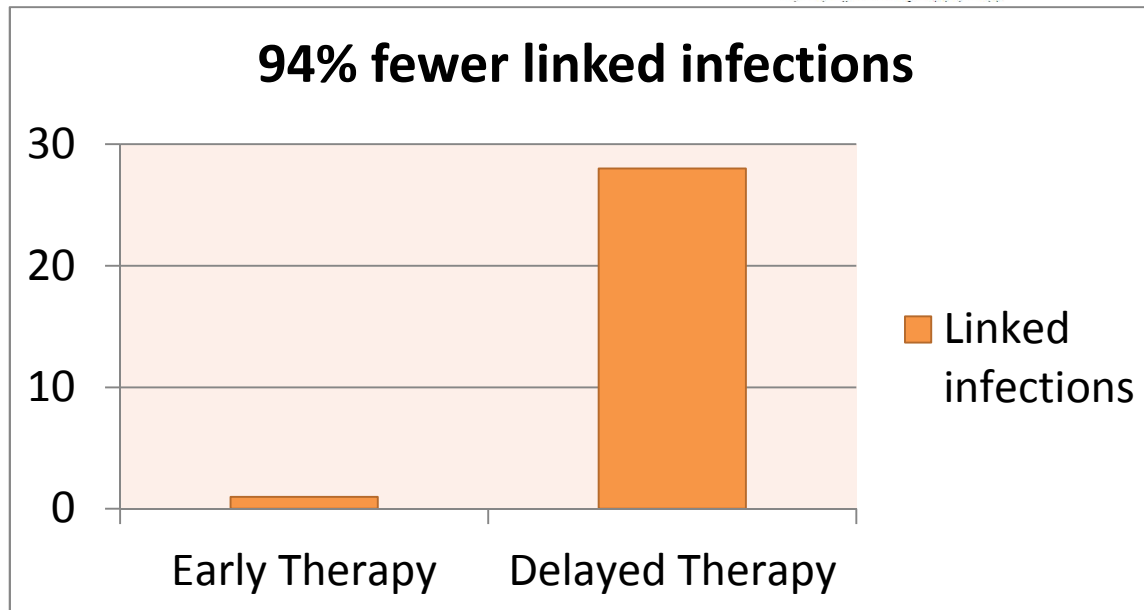
Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D.,  
Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D.,  
Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D.,  
Sanjay Mehendale, M.D., Suwat Chariyalertsak, M.D., Breno R. Santos, M.D., Kenneth H. Mayer, M.D.,  
Irving F. Hoffman, P.A., Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D.,  
Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch., Ian Sanne, M.B., B.Ch.,  
Joseph Eron, M.D., Joel Gallant, M.D., Diane Havlir, M.D., Susan Swindells, M.B., B.S., Heather Ribaudó, Ph.D.,  
Vanessa Elharrar, M.D., David Burns, M.D., Taha E. Taha, M.B., B.S., Karin Nielsen-Saines, M.D.,  
David Celentano, Sc.D., Max Essex, D.V.M., and Thomas R. Fleming, Ph.D., for the HPTN 052 Study Team\*

### ABSTRACT

#### BACKGROUND

Antiretroviral therapy that reduces viral replication could limit the transmission of human immunodeficiency virus type 1 (HIV-1) in serodiscordant couples.

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Cohen at the University of North Carolina



# Substance abuse treatment increases access and adherence to HIV treatment

## Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users

Sasha Uhlmann<sup>1,2</sup>, M.-J. Milloy<sup>1</sup>, Thomas Kerr<sup>1,2</sup>, Ruth Zhang<sup>1</sup>, Silvia Guillemi<sup>1</sup>, David Marsh<sup>3</sup>, Robert S. Hogg<sup>1,4</sup>, Julio S. G. Montaner<sup>1,2</sup> & Evan Wood<sup>1,2</sup>

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Available online at [www.sciencedirect.com](http://www.sciencedirect.com)



Commentary

Social and structural determinants of HAART access and adherence among injection drug users

Review

Andrea Krüsi<sup>a</sup>, Evan Wood<sup>a,b</sup>, Julio Montaner<sup>a,b</sup>, Thomas Kerr<sup>a,b,\*</sup>

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Adherence to HIV treatment among  
opioid substitution treatment (OST)

Bruno Spire<sup>a</sup>, Gregory M. Lucas<sup>b</sup>, M. Patrizia Carrieri<sup>a,\*</sup>

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Received 26 May 2006; received in revised form 19 October 2006; accepted 6 December 2006

Antiretroviral adherence and HIV treatment outcomes  
among HIV/HCV co-infected injection drug users:  
The role of methadone maintenance therapy

Anita Palepu<sup>a,b,\*</sup>, Mark W. Tyndall<sup>b,c</sup>, Ruth Joy<sup>c</sup>, Thomas Kerr<sup>b,c</sup>, Evan Wood<sup>b,c</sup>,  
Natasha Press<sup>b,c</sup>, Robert S. Hogg<sup>c,d</sup>, Julio S.G. Montaner<sup>b,c</sup>

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Received 15 November 2005; received in revised form 5 February 2006; accepted 7 February 2006





# Global need for more treatment coverage

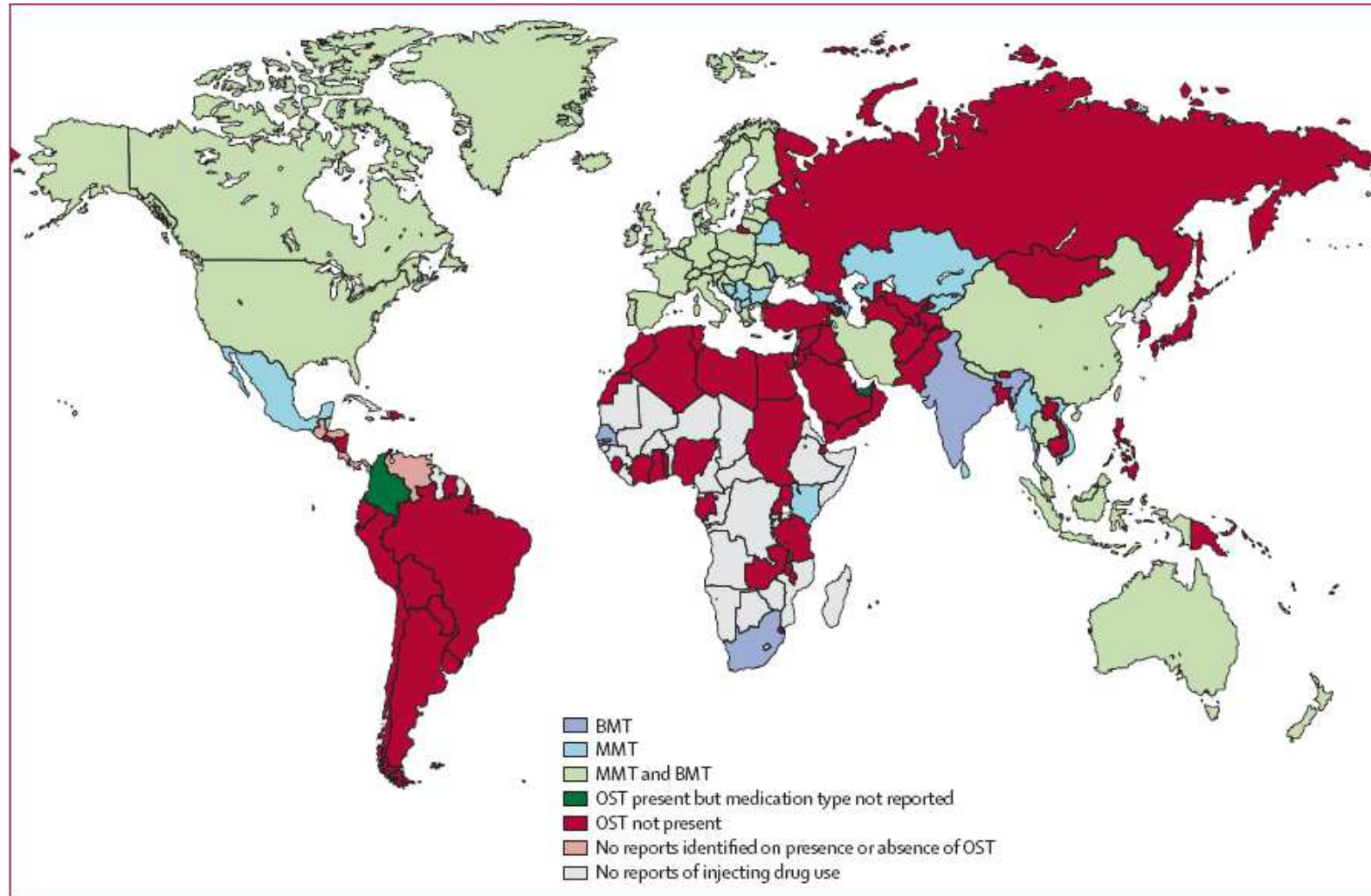


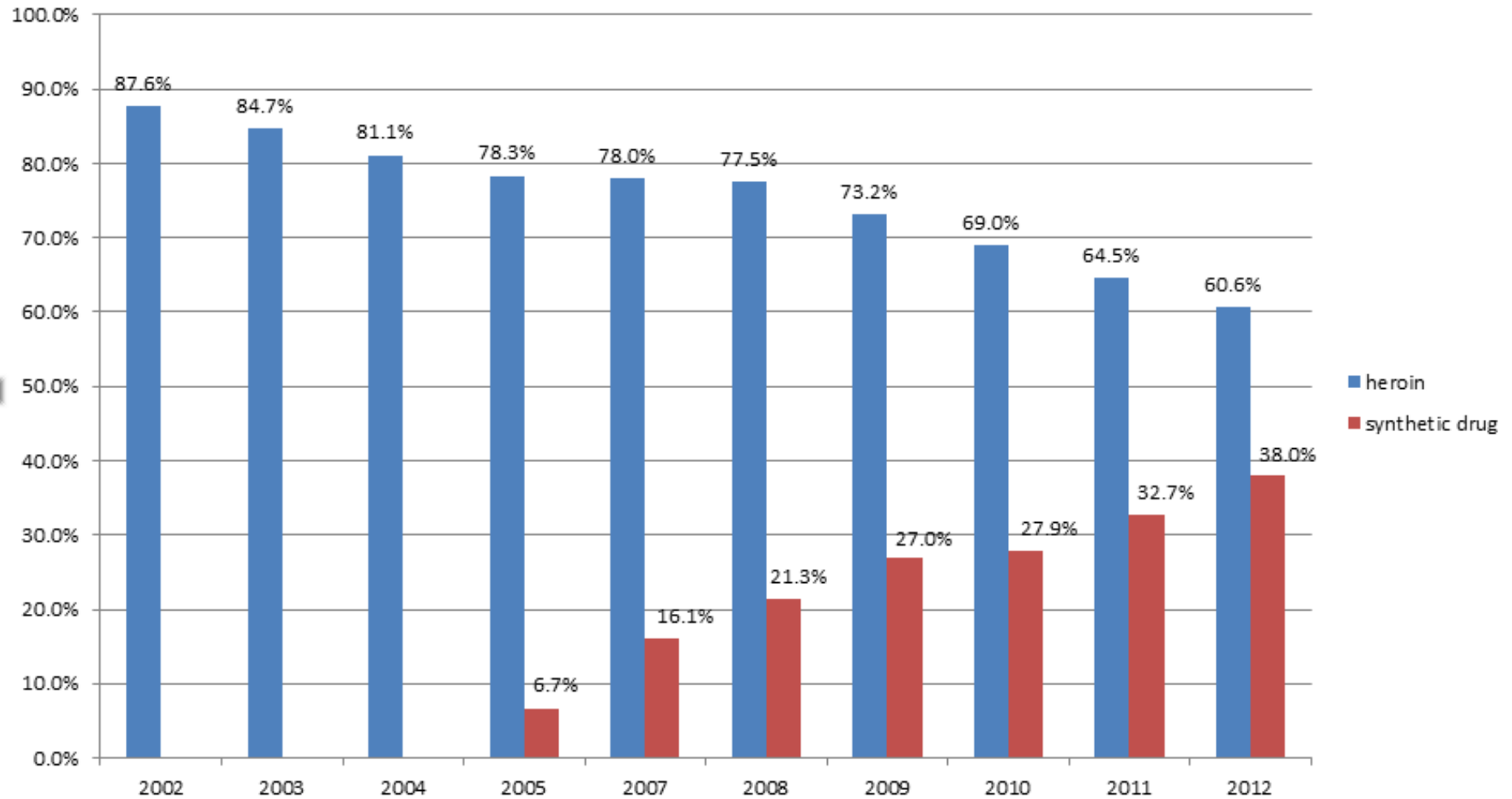
Figure 3: Availability of opioid substitution treatment

BMT=buprenorphine maintenance treatment. MMT= methadone maintenance treatment. OST=opioid substitution therapy.

Mathers et al., the Lancet , 2010

# Increasing variety of illicit drug use in China

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Need for additional medications and  
treatment strategies

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# Expanding Substance Use Treatment Options for HIV Prevention With Buprenorphine–Naloxone: HIV Prevention Trials Network 058

*David S. Metzger, PhD,\* Deborah Domell, PhD,† David D. Celentano, ScD,‡  
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Liping Fu, MD,\*\* Jun Ma, MD,\*\* Gregory M. Lucas, MD, PhD,†† Marek Chawarski, PhD,‡‡  
Yuhua Ruan, PhD,|| Paul Richardson, MSc,§§ Katherine Shin, PharmD,||| Ray Y. Chen, MD,¶¶  
Jeremy Sugarman, MD, MPH,## Bonnie J. Dye, MPH,\*\*\* Scott M. Rose, BS,\*\*\*  
Geetha Beauchamp, MS,††† and David N. Burns, MD, MPH,‡‡‡ for the HPTN 058 Protocol Team*

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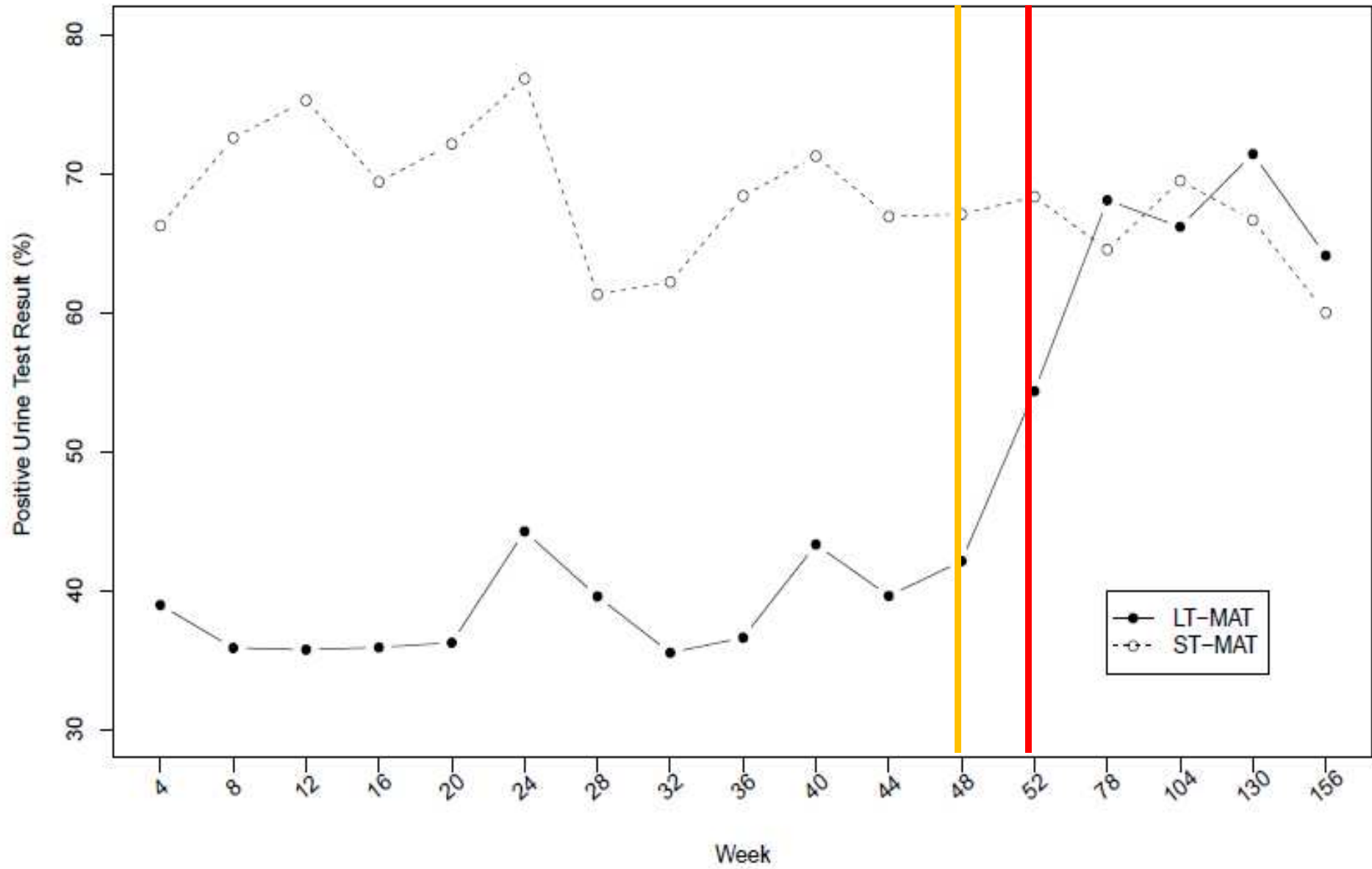
**Background:** Injection opioid use plays a significant role in the transmission of HIV infection in many communities and several regions of the world. Access to evidence-based treatments for opioid use disorders is extremely limited.

followed by dose tapering. All participants were followed for 52 weeks after treatment completion to assess durability of impact.

**Results:** Although the study was stopped early due to lower than expected occurrence of the primary end points, sufficient data were

# Positive Opiate Urine Drug Test

鸦片制剂尿检阳性结果





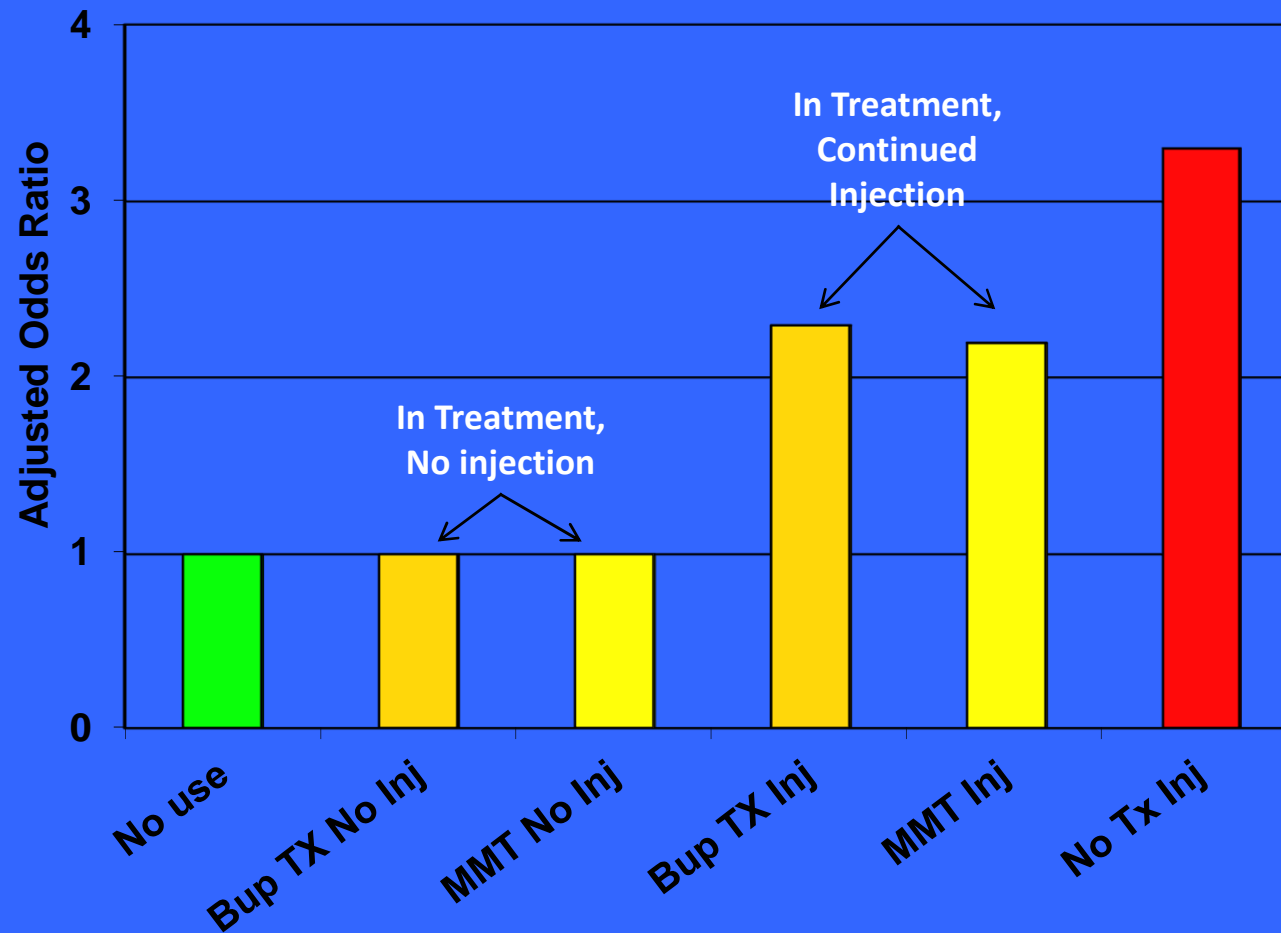
# How does drug treatment prevent HIV infection and transmission?

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- **Effective medication assisted treatments prevent withdrawal**
- **Reduce the frequency of drug use**
- **Fewer drug-related risk behaviors**
- **Fewer new infections**
- **Increased access to HIV treatment and primary care**
- **Increased adherence to HIV medications**

# MANIF 2000: Continued drug use regardless of substance use treatment status is associated with poor adherence

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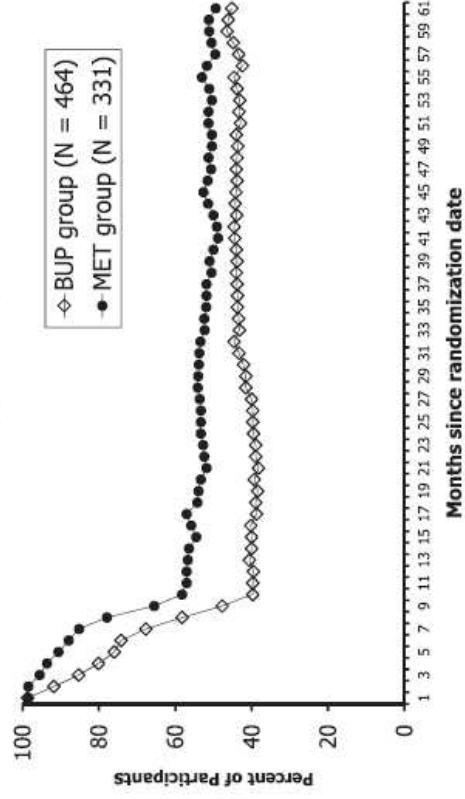
(Roux P et al 2008)

## Long-term outcomes after randomization to buprenorphine/naloxone versus methadone in a multi-site trial

Yih-Ing Hser<sup>1</sup>, Elizabeth Evans<sup>1</sup>, David Huang<sup>1</sup>, Robert Weiss<sup>1</sup>, Andrew Saxon<sup>2</sup>, Kathleen M. Carroll<sup>3</sup>, George Woody<sup>4</sup>, David Liu<sup>5</sup>, Paul Wakim<sup>5</sup>, Abigail G. Matthews<sup>6</sup>, Mary Hatch-Maillette<sup>7</sup>, Eve Jelstrom<sup>6</sup>, Katharina Wiest<sup>8</sup>, Paul McLaughlin<sup>9</sup> & Walter Ling<sup>1</sup>

University of California, Los Angeles, CA, USA,<sup>1</sup> Veterans Affairs Puget Sound Health Care System, Seattle, WA, USA,<sup>2</sup> Yale University School of Medicine, New Haven, CT, USA,<sup>3</sup> University of Pennsylvania, Philadelphia, PA, USA,<sup>4</sup> National Institute on Drug Abuse, Bethesda, MD, USA,<sup>5</sup> Emms Corporation, Rockville, MD, USA,<sup>6</sup> University of Washington, Seattle, WA, USA,<sup>7</sup> CODA, Inc., Portland, OR, USA,<sup>8</sup> and Hartford Dispensary, Hartford, CT, USA<sup>9</sup>

### Percent of Participants in Treatment<sup>†</sup> by the Two Randomized Groups (N = 795)



<sup>†</sup>Treatment is defined as received MET or BUP treatment medication

Figure 2 Percentage of participants in treatment<sup>†</sup> by the two randomized groups (n = 795). BUP: buprenorphine, MET: methadone.

Original Investigation

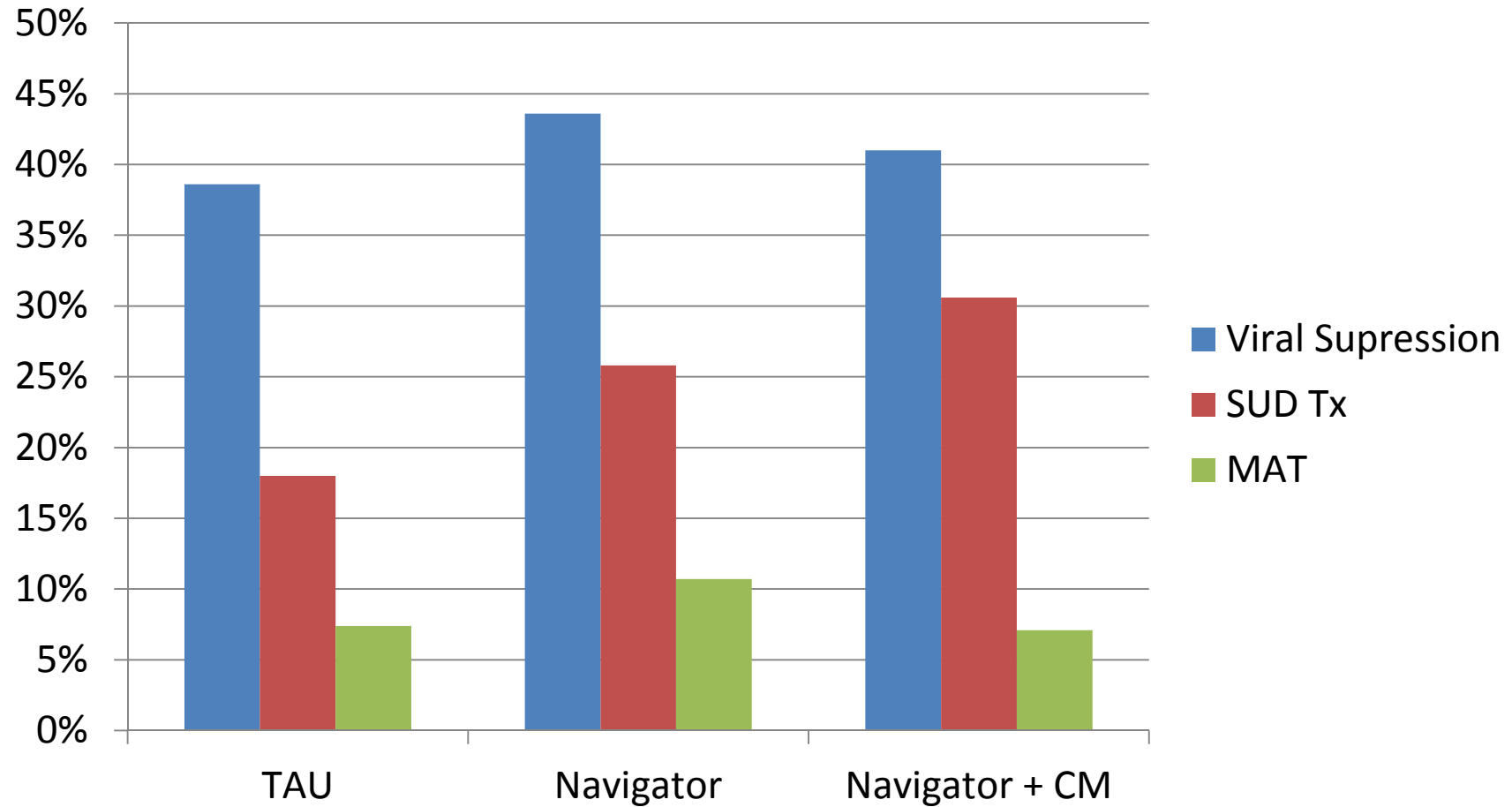
# Effect of Patient Navigation With or Without Financial Incentives on Viral Suppression Among Hospitalized Patients With HIV Infection and Substance Use A Randomized Clinical Trial

Lisa R. Metsch, PhD; Daniel J. Feaster, PhD; Lauren Gooden, PhD; Tim Matheson, PhD; Maxine Stitzer, PhD; Moupali Das, MD; Mamta K. Jain, MD; Allan E. Rodriguez, MD; Wendy S. Armstrong, MD; Gregory M. Lucas, MD, PhD; Ank E. Nijhawan, MD; Mari-Lynn Drainoni, PhD; Patricia Herrera, MD; Pamela Vergara-Rodriguez, MD; Jeffrey M. Jacobson, MD; Michael J. Mugavero, MD; Meg Sullivan, MD; Eric S. Daar, MD; Deborah K. McMahon, MD; David C. Ferris, MD; Robert Lindblad, MD; Paul VanVeldhuisen, PhD; Neal Oden, PhD; Pedro C. Castellón, MPH; Susan Tross, PhD; Louise F. Haynes, MSW; Antoine Douaihy, MD; James L. Sorensen, PhD; David S. Metzger, PhD; Raul N. Mandler, MD; Grant N. Colfax, MD; Carlos del Rio, MD

 Supplemental content at [jama.com](https://jama.com)

**IMPORTANCE** Substance use is a major driver of the HIV epidemic and is associated with poor HIV care outcomes. Patient navigation (care coordination with case management) and the use of financial incentives for achieving predetermined outcomes are interventions increasingly promoted to engage patients in substance use disorders treatment and HIV care, but there is little evidence for their efficacy in improving HIV-1 viral suppression rates.

# Support and incentives were not sufficient to improve rate of sustained viral suppression



Metsch et al, JAMA, 2016

# Requirements for treatments to impact public health

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- **Acceptable**
- **Accessible**
- **Affordable**

# Summary

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- When the health of even a small segment of the community is neglected, the public's health is threatened
- Addiction is a chronic medical condition with biological and behavioral components
- Medication in combination with behavioral interventions are most effective in sustaining behavior change
- Sustainability, acceptability and motivation remain major challenges

# Acknowledgements

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**Liying Ma, MD, PhD**

Chinese AIDS Prevention and Control  
China CDC

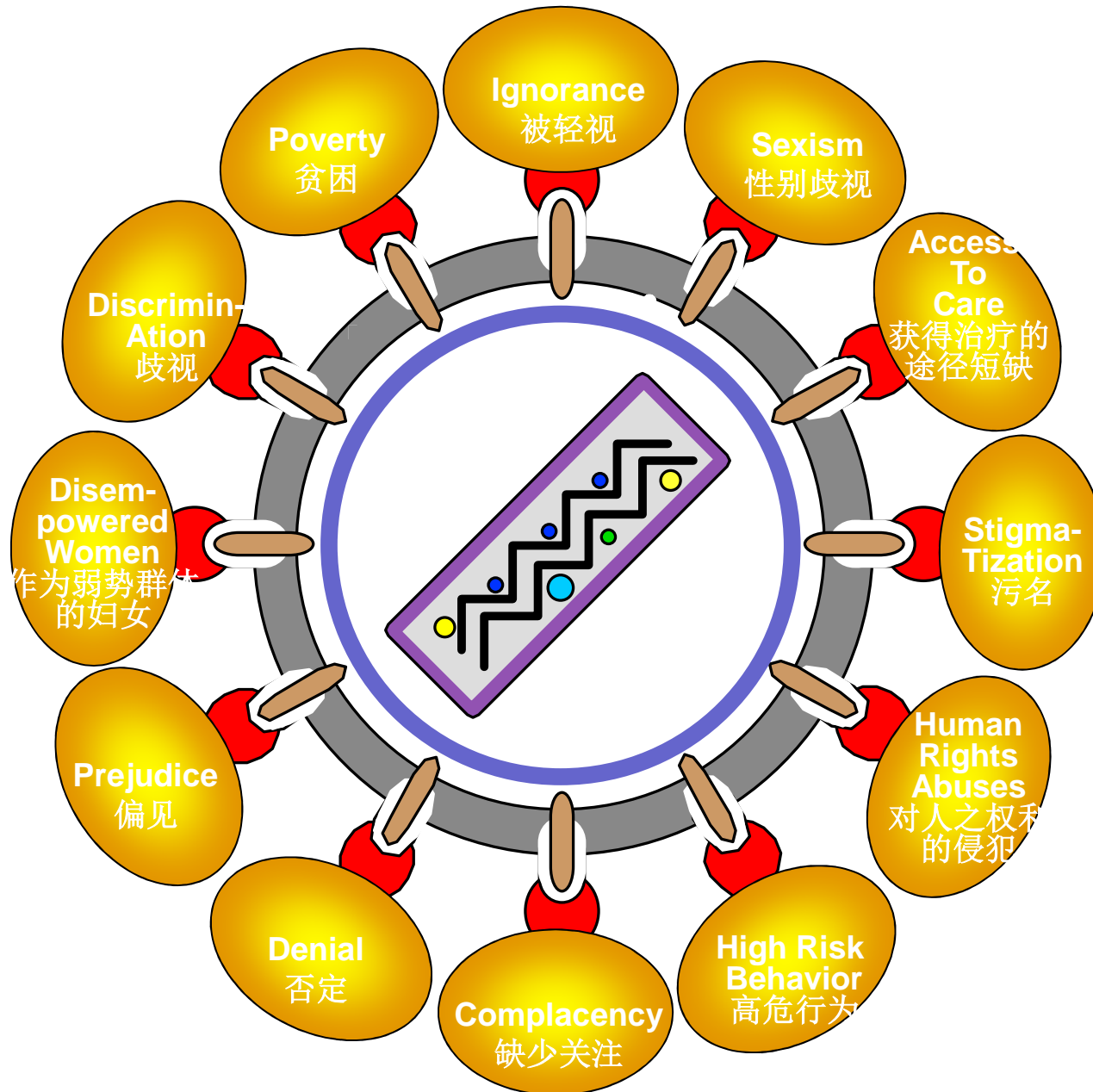
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鸣谢Jim Hoxie