

# Antiretrovirals for the Prevention of HIV infection: where are we in 2011?

Carlos del Rio, MD

Emory University Center for AIDS Research



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# Prevention goes Biological

# Behavioral interventions

- Until recently HIV prevention was based primarily on behavioral interventions.
- However, there is no RCT that has shown that any behavioral intervention can reduce HIV incidence although many have shown reductions in self-reported risk behavior or in surrogate markers like STIs.

# Biomedical HIV Prevention

- Vaccines – Thai RV144
- Microbicides – Caprisa 004
- Antiretrovirals for prevention:
  - PrEP – iPrEX, FEM-PrEP; Partners PrEP & TDF-2 (VOICE?)
  - HPTN 052
  - Test and Treat – HPTN 065

# Antiretrovirals for prevention

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1. Before exposure: PrEP
2. Treatment of infection

# Viral Load and HIV Transmission

- In individuals, suppressing HIV viral load reduces perinatal transmission

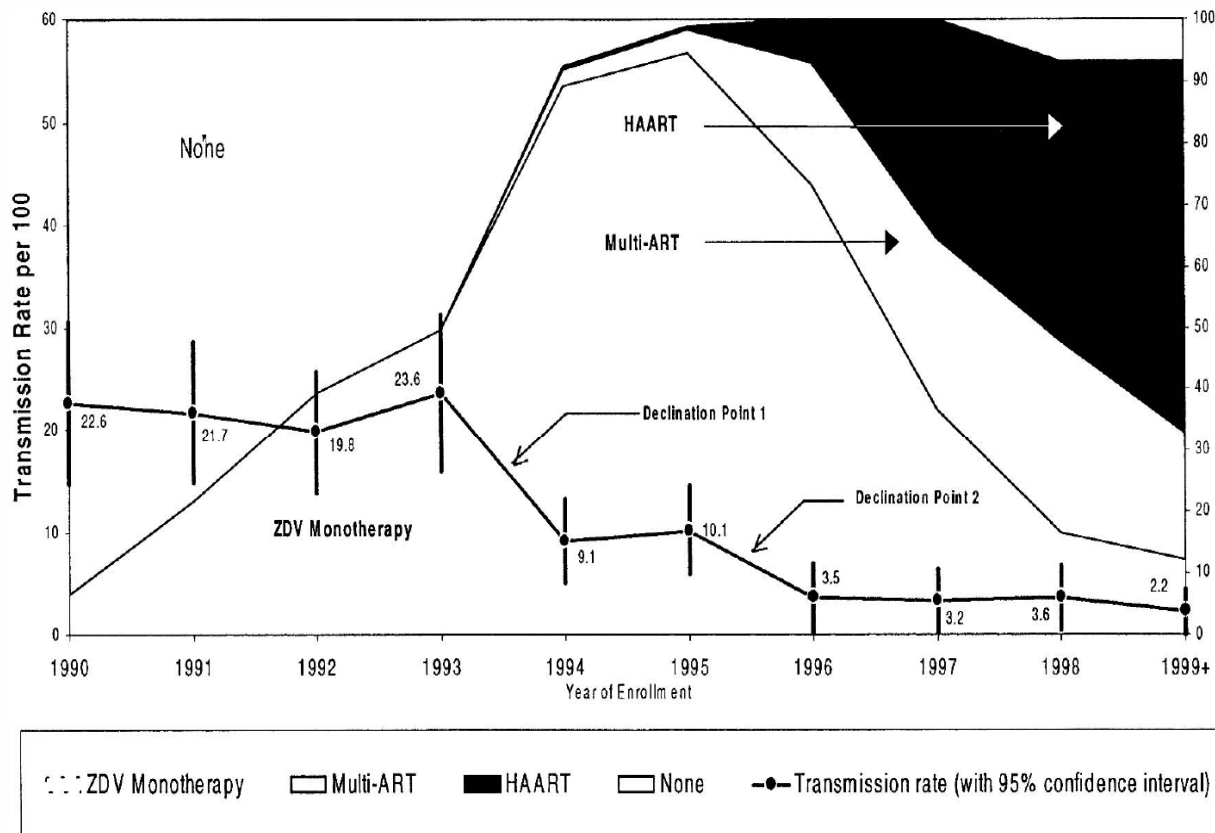


FIG. 1. Trends in mother-to-infant transmission rate and maternal antiretroviral therapy: 1990–1999+ (Women and Infants Transmission Study Group). Rates per 100 (95% confidence interval).

# iPrEx

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

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### Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S.,

#### **Conclusions:**

- 44% reduction in the incidence of HIV
- If pill use  $\geq 90\%$ , 73% reduction in incidence of HIV
- Risk compensation was not observed in either treatment group.

# Challenges for PrEP

- Intervention may be less effective in real world vs. clinical trial setting
- Potential for behavioral impact (disinhibition)
- Risk of resistance development in HIV+ individuals
- Risk of hepatic flares in HBV-infected individuals
- High cost relative to other prevention interventions; potential reimbursement barriers?
- Challenge of delivering appropriate education to healthcare providers and target populations; who will be prescribing it?
- Need to ensure no impact of ease of access to medication for HIV+ individuals



# ART for Prevention: Discordant Couples

- Evaluate effect of ART on HIV transmission among HIV serodiscordant, heterosexual couples (2993)
- ARV only if clinically indicated, negative partner tested q3 mo.
  - ▶ Not on ARV: 171 linked infections (3.4/100 CY)
  - ▶ On ARV: 4 linked infections (0.7/100 CY)
  - ▶ Sexual risk behavior lower in those on ARV (19% vs 25%;  $p < 0.05$ )
- Both ART and change in behavior independently reduced HIV transmission

Sullivan P, et al. CROI 2009; Abst# 52bLb

# ART for Prevention: Discordant Couples

ART in HIV+ve partner	Linked Transmission	Person-years of follow up	HIV sero-incidence
Post ART initiation	1	256	0.39 (95% CI: 0.09-2.18)
No ART	102	4851	2.23 (95% CI: 1.84-2.70)

*Donnell et al CROI 2010, session 40 # 136 & Lancet May 2010*

# Extending ART for prevention: clinical trial evaluation of strategy



## HPTN 052

**A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy Plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples**

### What is HPTN 052?

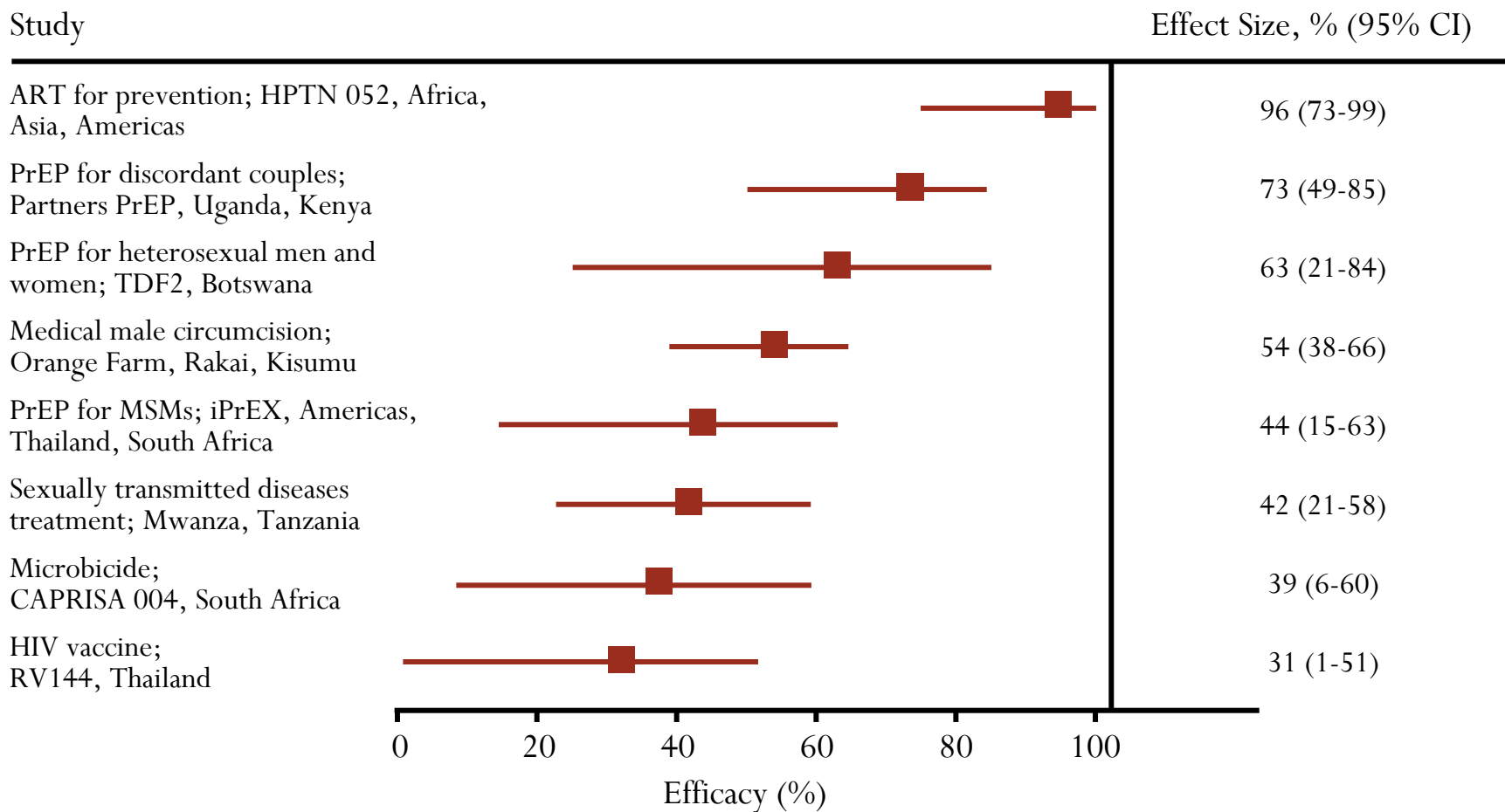
HPTN 052 is a Phase III, two-arm, multi-site, randomized trial to determine the effectiveness of two treatment strategies in preventing the sexual transmission of HIV in HIV-serodiscordant couples.

Based on data collected in Africa and Thailand, there is a correlation between HIV viral load (blood levels) and HIV transmission. Specifically, the higher the viral load in the blood, the more likely the chance for transmission. Antiretroviral therapy (ART) reduces the viral load in the blood, as well as in genital secretions (for both men and women), and the drugs can be detected in semen and vaginal and cervical secretions. All of this information strongly suggests that ART may make HIV-infected people less contagious. HPTN 052 compares the HIV-infection rates of two groups of HIV-serodiscordant couples. The index case of the first group starts taking ART as soon as the couple is enrolled in the study, while the index case of the second group starts taking ART when he or she has two consecutive measurements of a CD4+ cell count within or below the range of 200-250 cells/mm<sup>3</sup>, or when he or she develops an AIDS-defining illness. Both groups will receive HIV primary care and couples counseling sessions to teach them how to reduce their risk of transmission.

# HPTN 052

- DSMB interim analysis
- 1763 HIV serodiscordant couples (97% heterosexual)
- CD4 counts 350 – 550 cells/uL
- Randomized to ART or defer ART until CD4 < 250 cells/uL
- At the time of DSMB review: 39 cases of HIV infection with 28 confirmed as genetically linked
  - 27 among couples not on ART
  - 1 among couples on ART
- Thus 96% reduction in transmission with ART!

# Efficacy of HIV Prevention Strategies From Randomized Clinical Trials





# Testing and Transmission

Expand testing to as many as possible :

- People who know their status less likely to engage in high risk behavior
- Those found to be HIV infected can then be treated reducing their HIV viral load

# Testing and Transmission

- Couples Counseling and Testing is now more important than ever
- Discordant couples: Unprotected sex is high
- In Thailand, 74 % of incident infections in married discordant couples.
- In US, 68% of HIV among MSM: unprotected sex with main partners
- In Kenya, 84% don't know status: Of those infected with HIV, 75% had unprotected sex with partner of unknown or negative status
- Unsafe sex higher in those not knowing status

*Burnell, CROI 2010, Mwangi et al , CROI 2010*



# Can antiretrovirals decrease transmission at a population level?

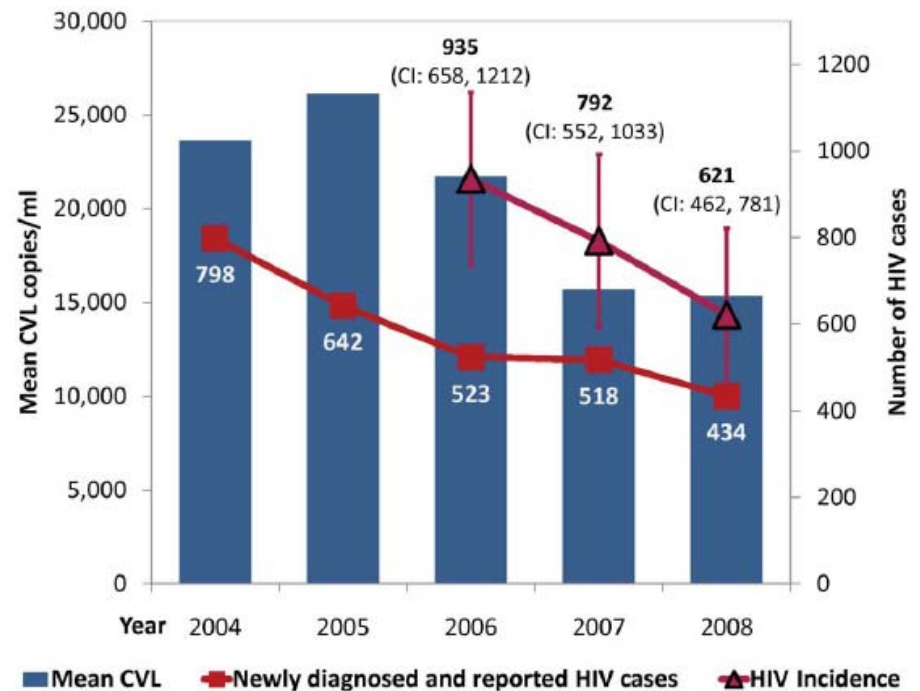
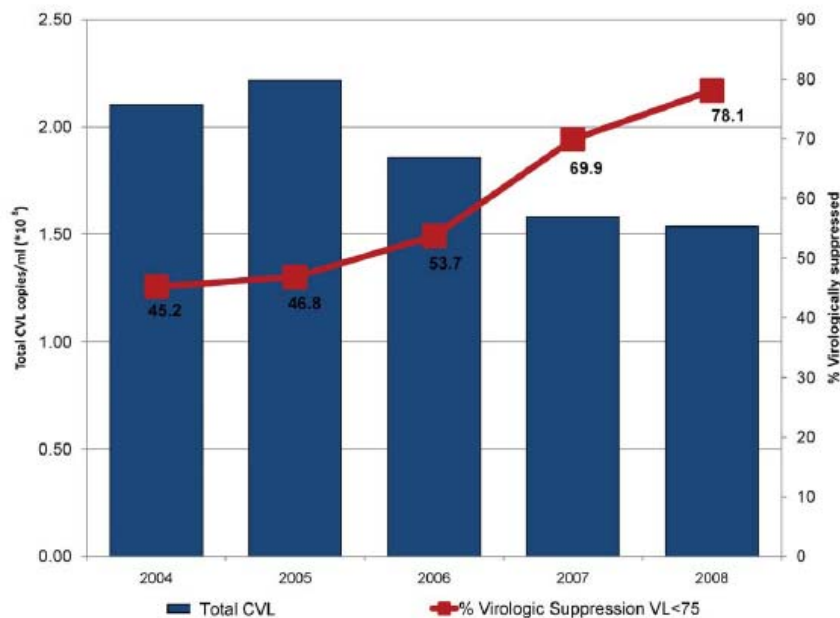
MSM: Increased ART options and coverage, increasing status awareness associated with decreased community VL and new infections- San Francisco from 2004 to 2008

*Das-Douglas et al, CROI 2010, Session 10 # 33*

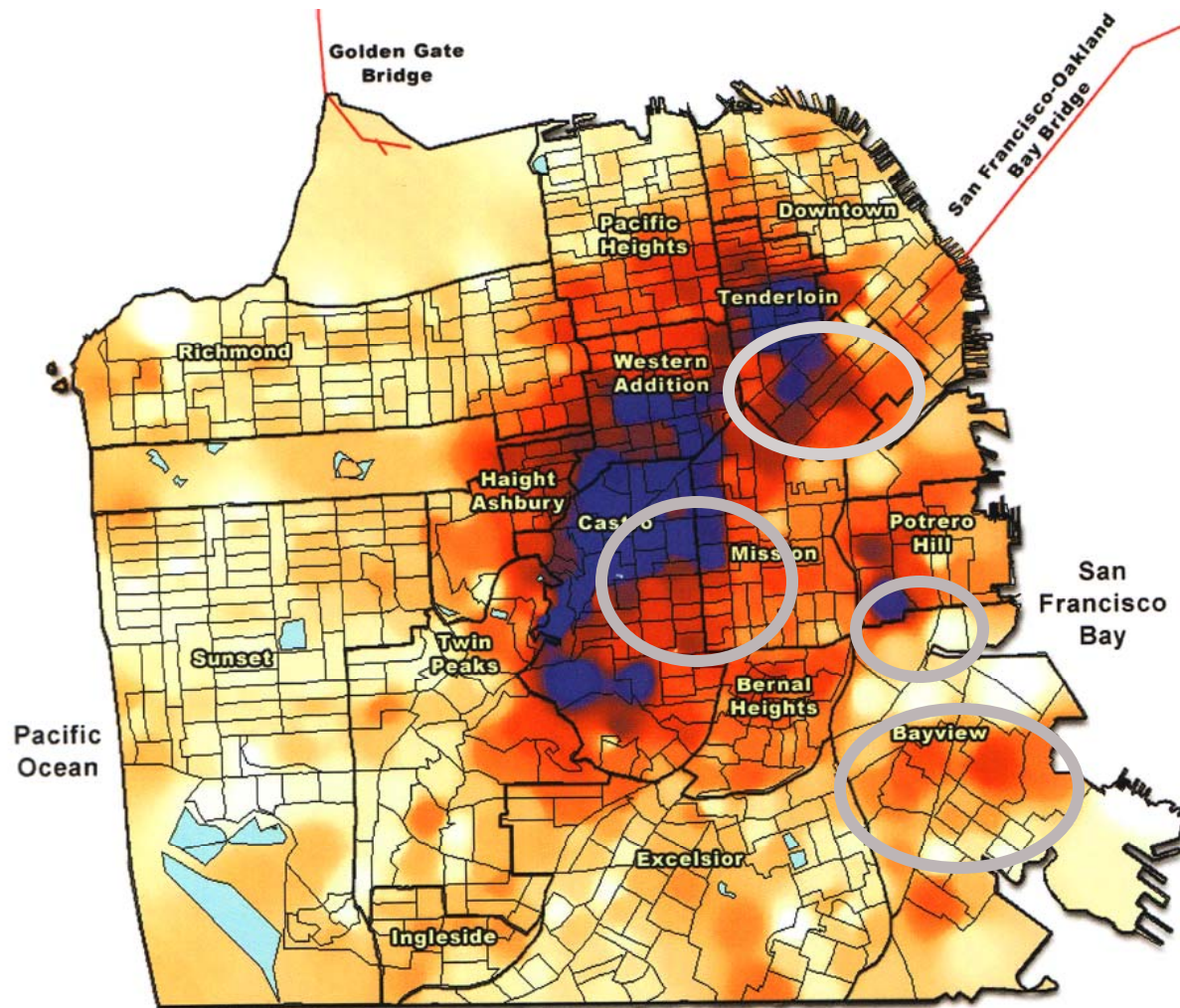
# Decreases in Community Viral Load Are Accompanied by Reductions in New HIV Infections in San Francisco

Moupali Das<sup>1,2\*</sup>, Priscilla Lee Chu<sup>1</sup>, Glenn-Milo Santos<sup>1</sup>, Susan Scheer<sup>1</sup>, Eric Vittinghoff<sup>2</sup>, Willi McFarland<sup>1,2</sup>, Grant N. Colfax<sup>1,2</sup>

**1** San Francisco Department of Public Health, San Francisco, California, United States of America, **2** University of California San Francisco, San Francisco, California, United States of America

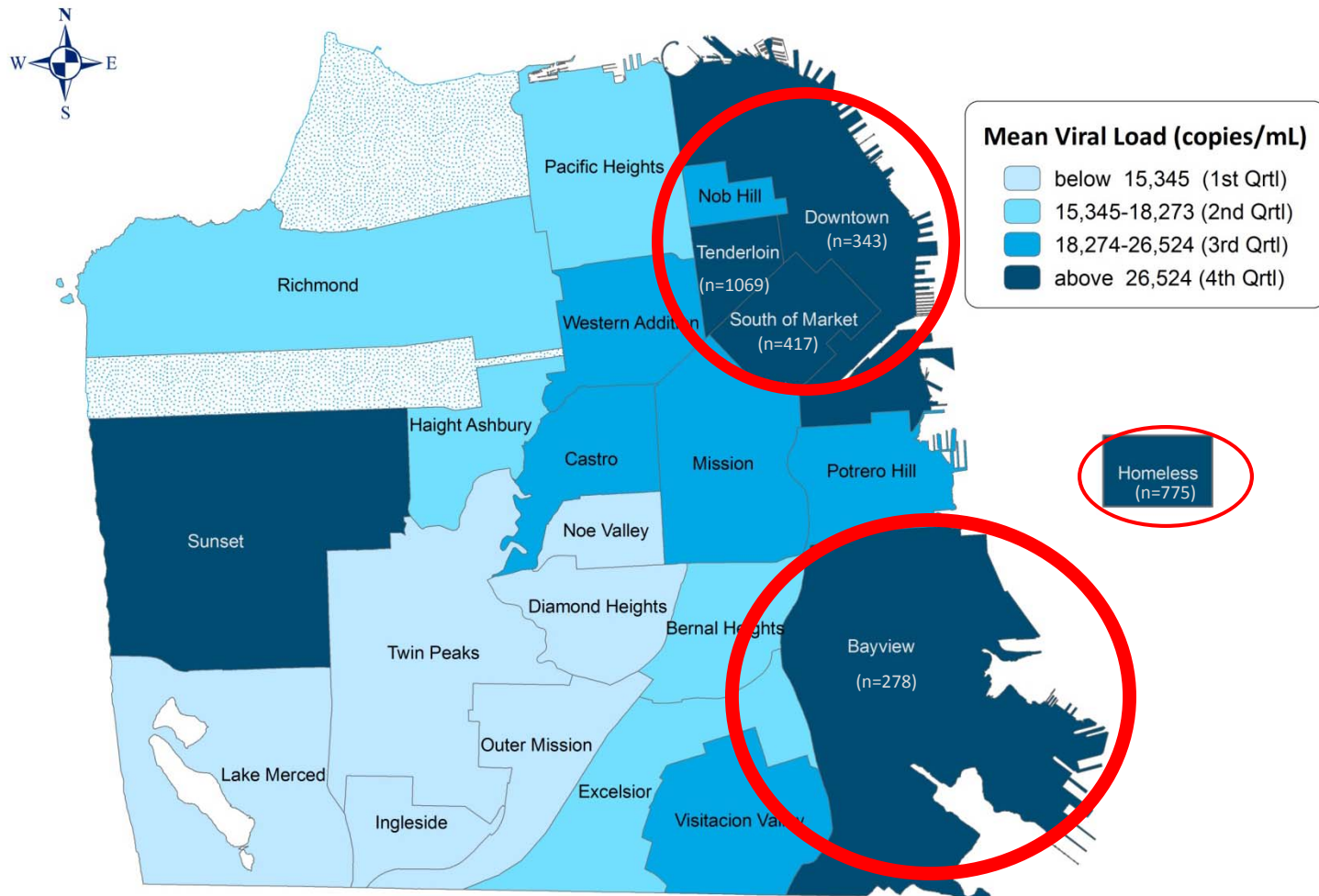


# Spatial distribution of AIDS in San Francisco



2000  
N=22,830

# Spatial Distribution of Mean CVL by Neighborhood, 2005-2008



Homeless persons had the highest mean viral load (38,974 copies/mL.)

# Can antiretrovirals decrease transmission at a population level?

Expanded HAART coverage associated with decrease in New HIV diagnosis, particularly in IDU in British Columbia.

Number of individuals on HAART increased from 2500 to 5000 from 2004 to 2009

50% decrease in new HIV diagnosis in IDU

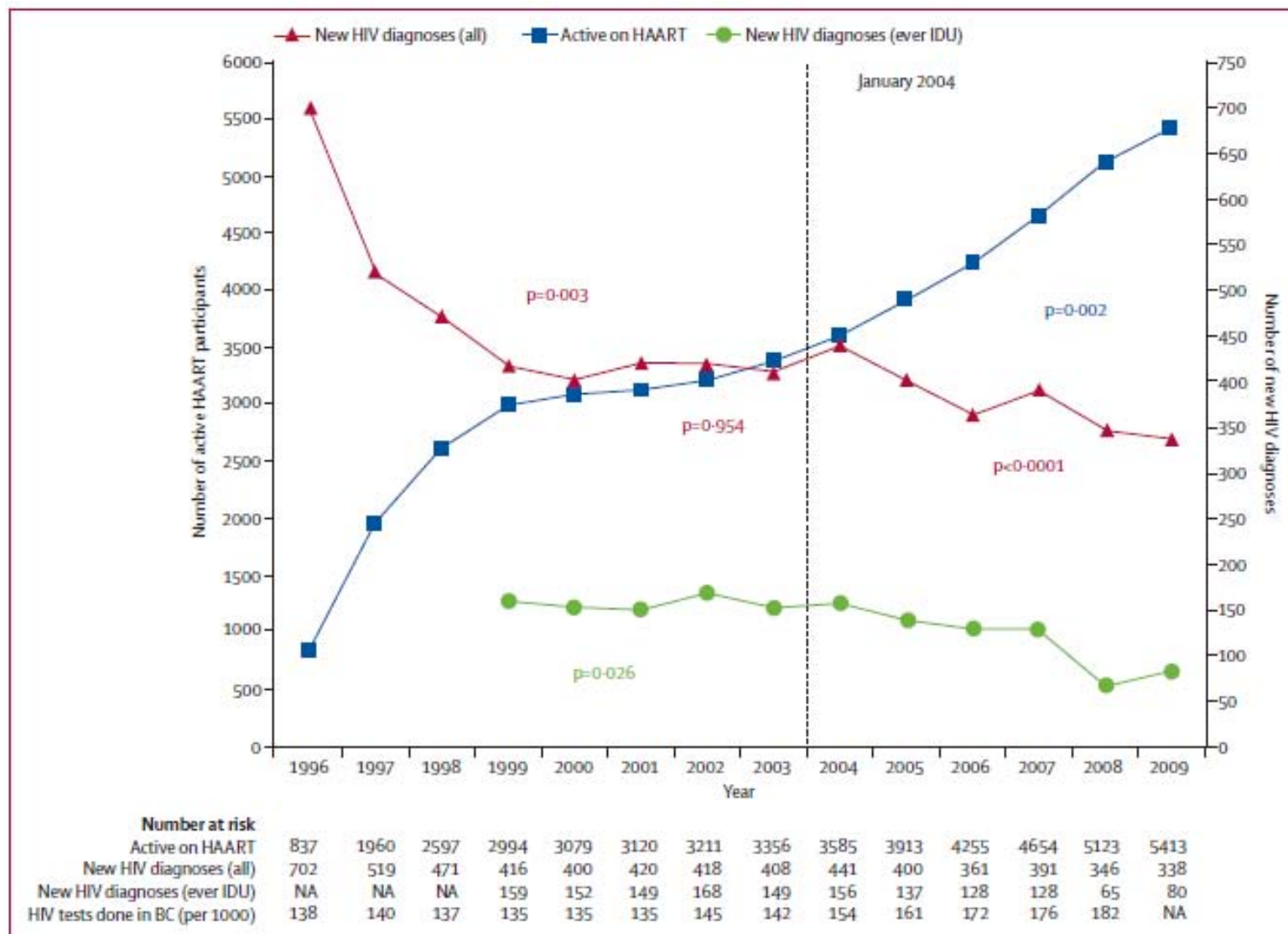
Proportion of HIV infected IDU with VL >1500 copies/mL decreased from 50% to 20%

*Montaner et al, CROI 2010, Session 24 # 88LB*

# Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study

*Julio S G Montaner, Viviane D Lima, Rolando Barrios, Benita Yip, Evan Wood, Thomas Kerr, Kate Shannon, P Richard Harrigan, Robert S Hogg, Patricia Daly, Perry Kendall*

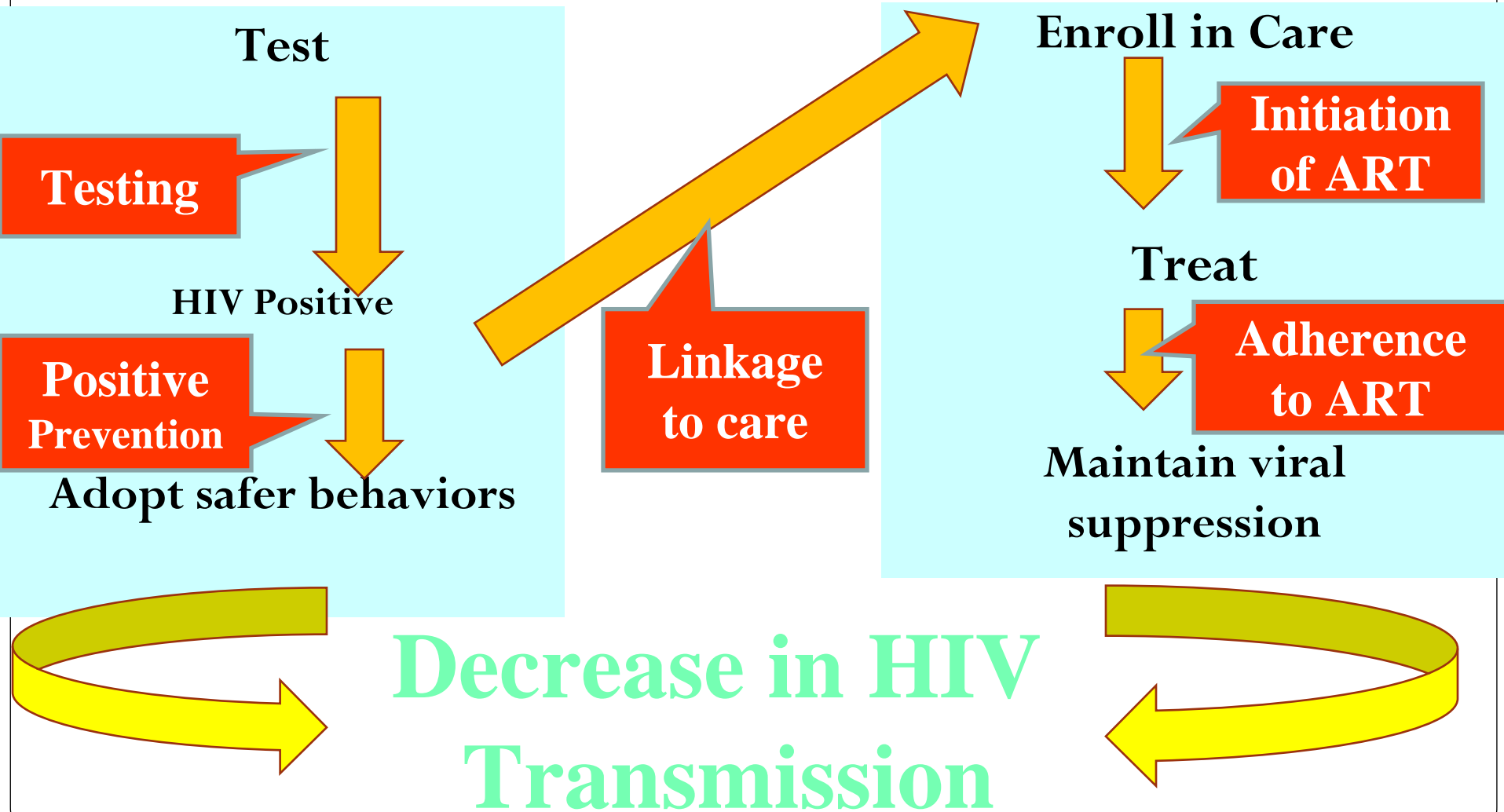
[www.thelancet.com](http://www.thelancet.com) Published online July 18, 2010 DOI:10.1016/S0140-6736(10)60936-1



**Figure 1: Number of active HAART participants and number of new HIV diagnoses per year in British Columbia, Canada, 1996–2009**

p values are for trend and were obtained from the generalised additive model. Injecting drug user (IDU) refers to individuals who have ever injected illicit drugs. HAART=highly active antiretroviral therapy. BC=British Columbia. NA=not available.

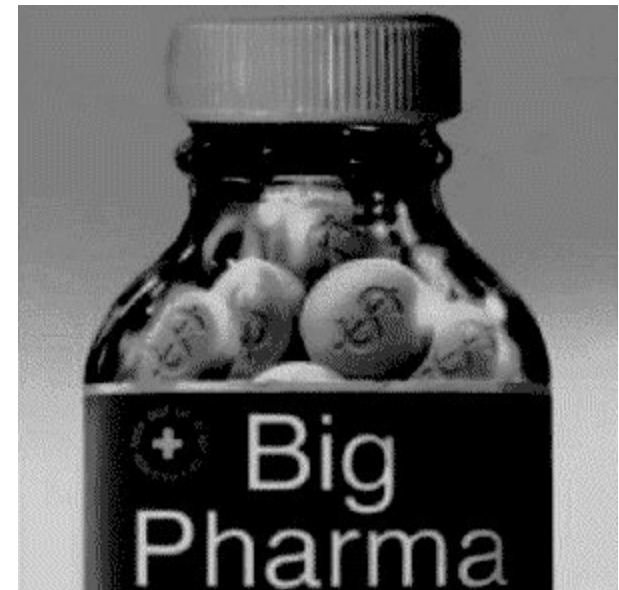
# HPTN 065 (TLC Plus): Testing, Linkage to Care, Plus Treatment





**POZ**

**“Medical Ethics and the Rights of People with HIV Under Assault” by Sean Strub**



*“Going too far to battle AIDS*

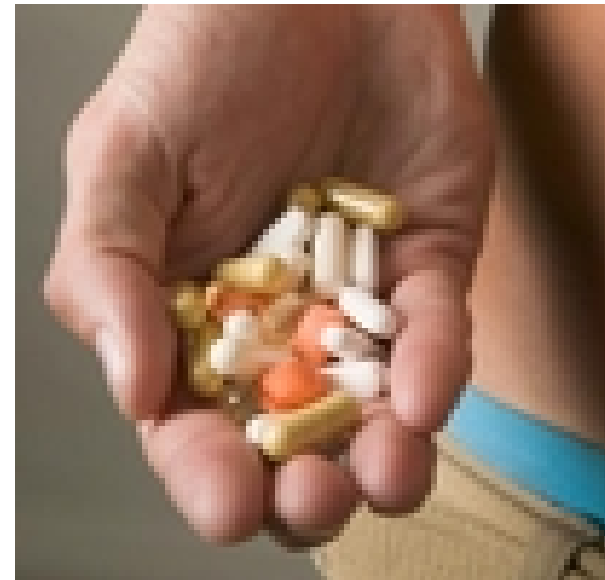
*Drug experiment on blacks looms in Washington” by Terry Michael Washington Post*

*March 17 2010*

# JAMA<sup>®</sup>

## Treat HIV-1 Infection Like Other Infections—Treat It

Bruce D. Walker, MD; Nesli Basqoz, MD



# The spectrum of engagement in care

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Not in HIV Care



Engaged in HIV Care

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Unaware of  
HIV infection

Aware of  
HIV infection  
(not in care)

Receiving some  
medical care but  
not HIV care

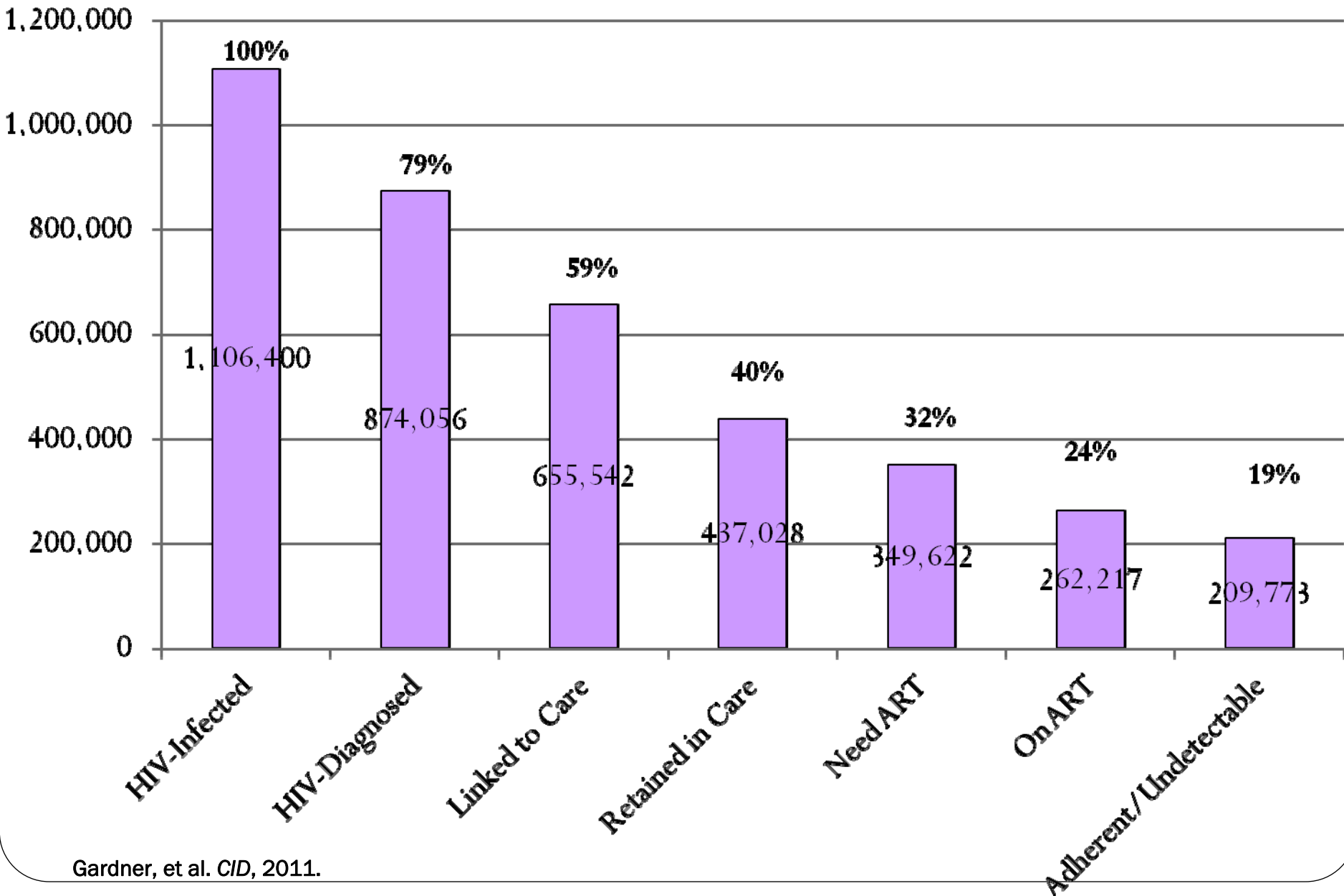
Entered HIV  
care but lost to  
follow-up

Cyclical or  
intermittent user  
of HIV care

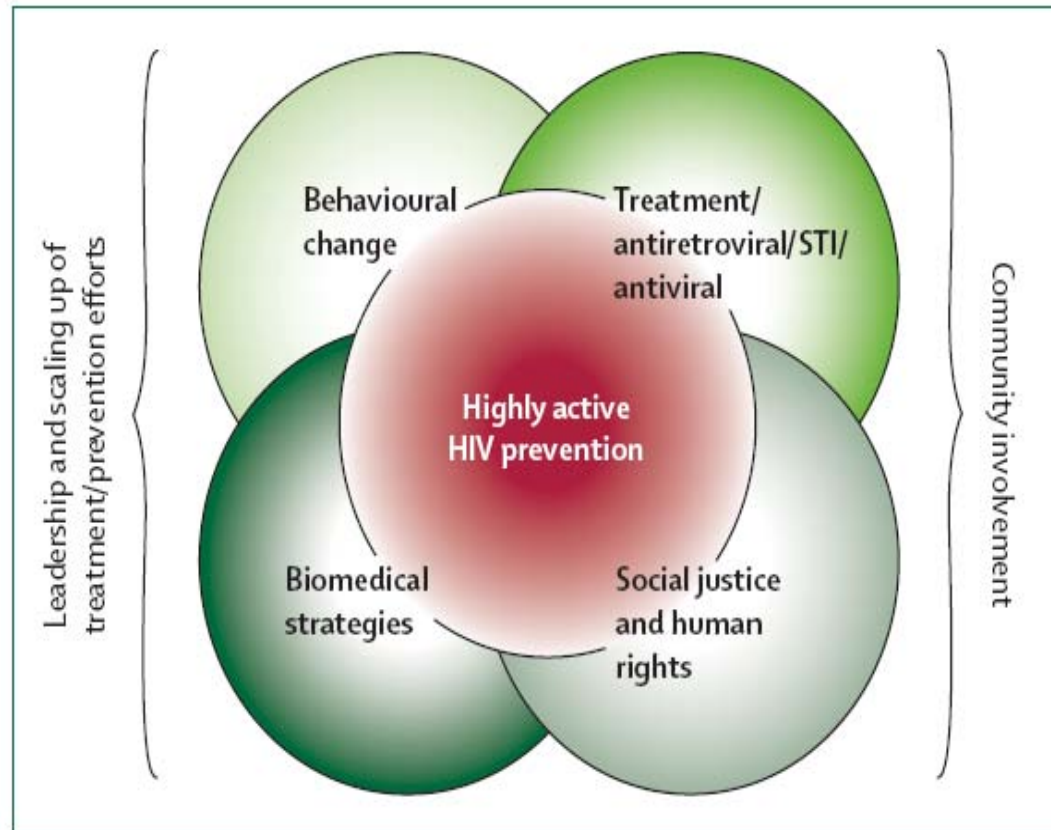
Fully engaged  
in HIV care

Eldred, *AIDS Patient Care and STD* 2007; 21 (suppl1)

# Major Gaps in the Implementation Cascade



# Not just TnT: Comprehensive Multi-level Highly Active HIV Prevention



**Figure 1: Highly active HIV prevention**

This term was coined by Prof K Holmes, University of Washington School of Medicine, Seattle, WA, USA.<sup>5</sup> STI=sexually transmitted infections.

# Treatment is Prevention



**Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women**  
Quarraisha Abdool Karim, *et al.*  
*Science* **329**, 1168 (2010);  
DOI: 10.1126/science.1193748



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Prevention of HIV-1 Infection with Early Antiretroviral Therapy

**But not all prevention is  
treatment...**

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# Substance Use Treatment is Prevention





# Mental Health Treatment is Prevention



# Housing is Prevention



# Food Security is Prevention



# Conclusions:

- HPTN 052 is a “game changer” study and offers tremendous opportunities to really impact the HIV epidemic in the US and abroad.
- With 96% reduction in risk of transmitting HIV and 40% reduction in risk of clinical events there are advantages to early therapy to both the individual and society.
- The epidemic in the US has changed dramatically, most new infections are now among young African-American MSM's.
  - How do we find them?; get them HIV tested and linked to care and prevention services?
- iPrEx results are encouraging and PrEP for high risk MSM need to be tested and found before they are infected so they can be offered PrEP.

# Policy implications:

- Need to scale up HIV testing including couples testing.
- Diagnosing HIV infection at a higher CD4 count should be a priority (current median CD4 at diagnosis in the US is 317 cells/ul).
- Case management at the time of diagnosis to ensure linkage to care is paramount.
- DHHS treatment guidelines should reflect the study findings and CD4 guided for “when to start” should be less important.
- Availability of antiretroviral therapy for those who need it should not be a problem (ADAP waiting lists should end).
- Engagement and retention into care must be priorities in all HIV clinical settings.
- Mental health and substance abuse treatment should be part of comprehensive HIV care.



“The arc of the moral universe is long but it bends toward justice.”

Martin Luther King, 1929-1968