

# Test and Treat

A Prevention Strategy?

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# Persons Living with HIV/AIDS 2007

33.2 million (30.6-36.1 million) worldwide

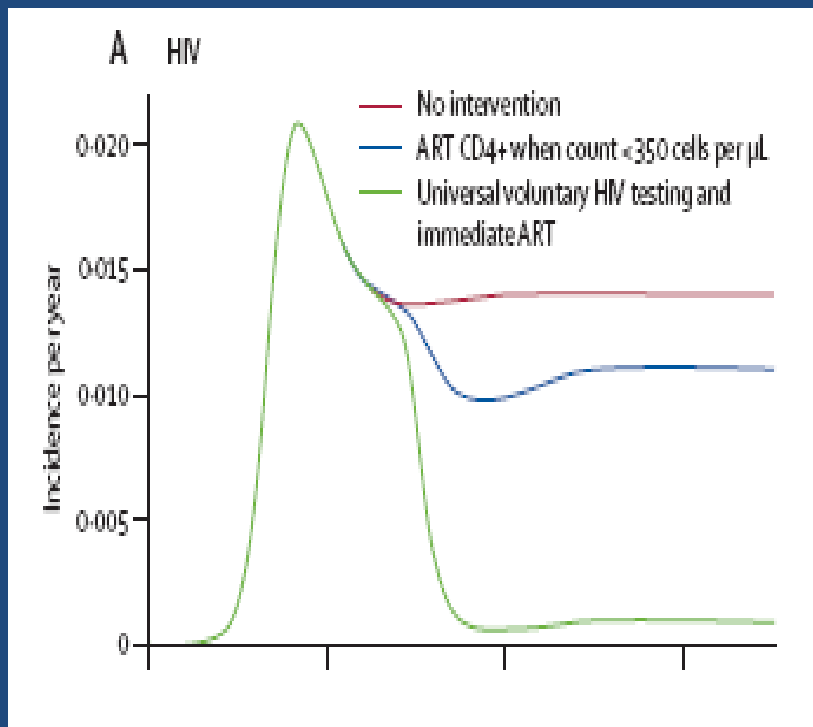


Source: UNAIDS, AIDS Epidemic Update, December 2007

# Modeling of Universal HIV Testing and Treatment

## Assumptions

- High uptake of annual testing by all >15 year old individuals
- Treat all HIV+
- 99% decrease in infectiousness
- High adherence and low failure with first line ART



# Limitations

- Assumptions
- Acute infection
- Resistance
- Logistics
- Results from one model:
  - Other models with different assumptions
  - Empiric data

# Testing and Treating Conceptual Framework

**Test**



Adoption of safer  
behaviors by  
HIV+ persons

+

**Treat with ART**

+

**Adherence**



Maintain viral  
suppression

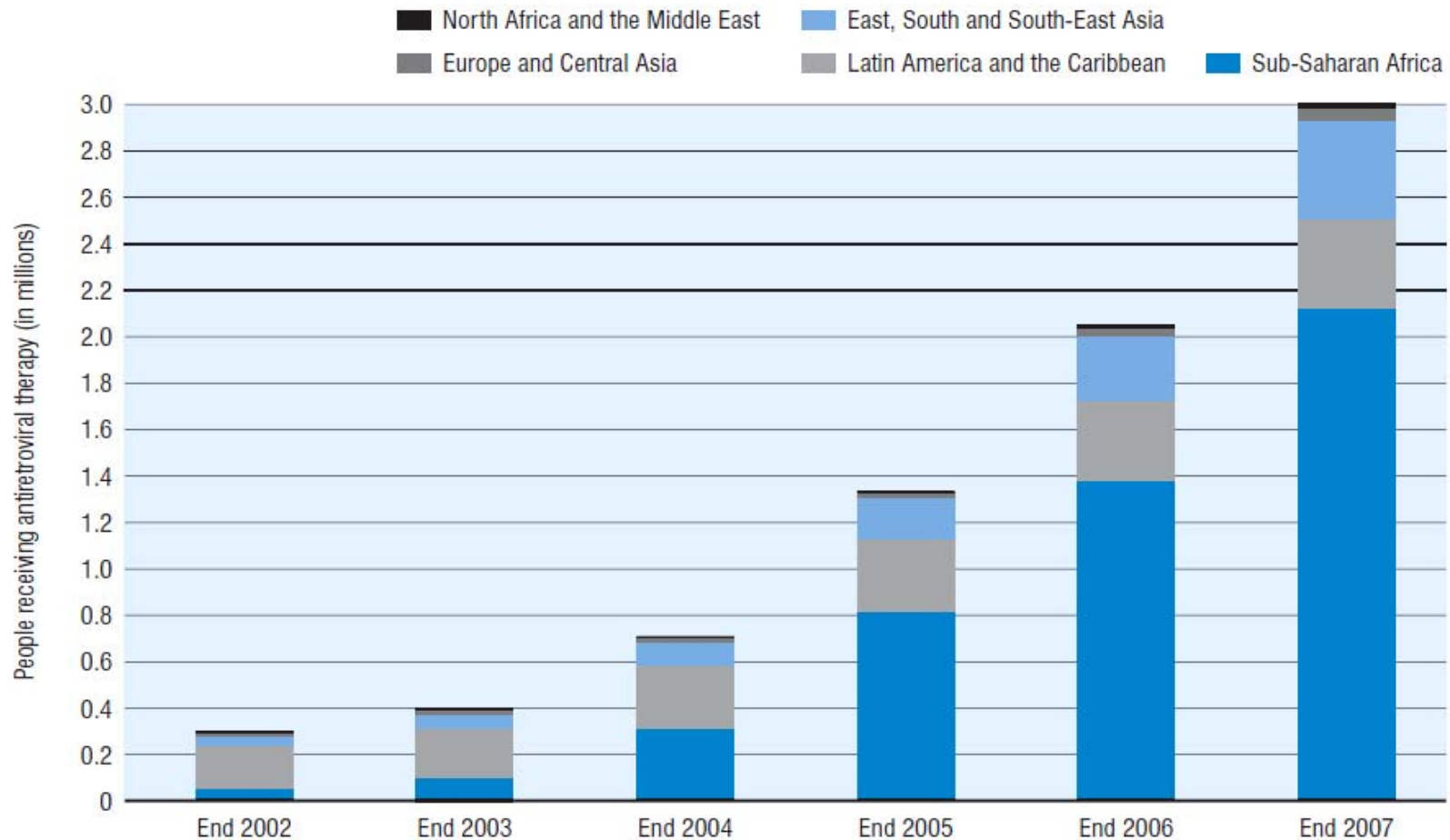
**Decrease in HIV Transmission**



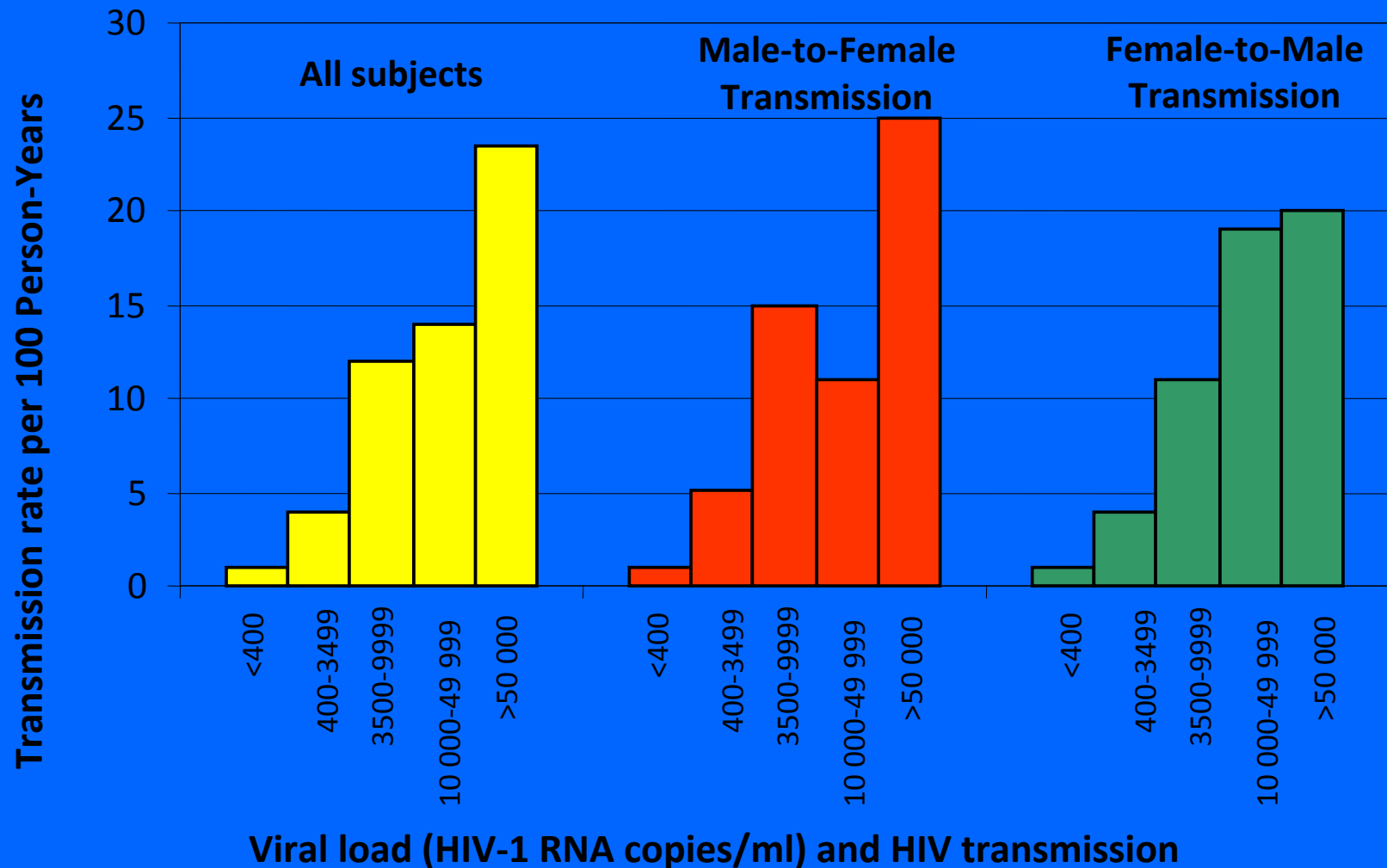
# Percentage HIV Tested

Country	Type of epidemic	Year	% of people who were tested in the 12 months preceding the survey and received the results (A)		% of people who were ever tested and received the results (B)		% of people ever tested who had been tested in the 12 months preceding the survey (A/B)	
			Women	Men	Women	Men	Women	Men
Benin	Generalized	2006	6.5	4.8	15.1	10.3	43	47
Congo	Generalized	2005	3.2	3.1	9.5	10.9	34	28
Côte d'Ivoire	Generalized	2005	3.7	3.2	10.9	7.9	34	41
Democratic Republic of the Congo	Generalized	2007	4.1	3.8	...	...	...	...
Ethiopia	Generalized	2005	2.3	2.3	3.8	4.9	61	47
Ghana <sup>a</sup>	Concentrated	2006	3.9	2.9	...	...	...	...
Guinea	Generalized	2005	1.0	3.0	2.1	6.0	48	50
Mali	Concentrated	2006	3.1	2.7	6.6	6.4	47	42
Namibia <sup>b</sup>	Generalized	2006	28.6	17.6	...	...	...	...
Niger	Concentrated	2006	0.9	1.6	1.9	3.9	47	41
Rwanda	Generalized	2005	12.0	11.0	21.2	20.1	57	55
Senegal	Concentrated	2005	1.0	2.0	2.7	4.2	37	47
Swaziland	Generalized	2007	21.9	8.9	...	...	...	...
Uganda	Generalized	2004–2005	4.0	3.8	12.7	10.8	37	35
Uganda	Generalized	2006	12.0	10.4	24.8	20.7	48	50
Zambia	Generalized	2007	18.5	11.7	...	...	...	...
Zimbabwe	Generalized	2005–2006	7.0	7.0	21.7	16.4	32	43

# Global Achievements in Access to ART in Low and Middle-income Countries



# Association of viral load and HIV transmission risk





# Impact of Antiretroviral Therapy (ART) on HIV Transmission

- Tororo, Uganda – prospective cohort study of home-based ART in a rural community
- 926 adults followed
- After starting ART
  - Risky sex *decreased* by 70% (P=0.002)
  - Median Viral Level *decreased* from 122,500 to <50 copies/mL
  - Estimated HIV transmission risk *reduced* by 98%
    - From 46 to 1 per 1000 PY

# Impact of ART on HIV Transmission

- Rwanda & Zambia – HIV discordant couples
- Followed 2,993 discordant couples
- HIV+ persons with CD4 <200 on ART
- HIV incidence by partner ART status:
  - On ART: 0.7 / 100 PY
  - Not on ART: 3.4 / 100 PY
    - OR, 0.2; 95% CI, 0.08-0.6

# **HIV Treatment as Prevention**

## **Strong Biological Plausability**

### **Retrospective Studies**

**Musicco et al. Archives Int Med 154: 1971; 1994**

**Castilla et al. JAIDS 40, 96, 2005**

### **Observational Studies**

**Kayitenkore et al. IAS, 2006**

**Bunnell et a. AIDS 20: 85-92, 2006**

**Reynolds et al. CROI 2009 Abstract 52a**

**Sullivan et al. CROI 2009 Abstract 52b**

### **Ecological Analysis**

**Katz et al. Am J. Public Health 92: 388, 2002 (-)**

**Duker et. al AIDS. 16:F19-24, 2002 (-)**

**Porco et al. AIDS 18:81, 2004 (+)**

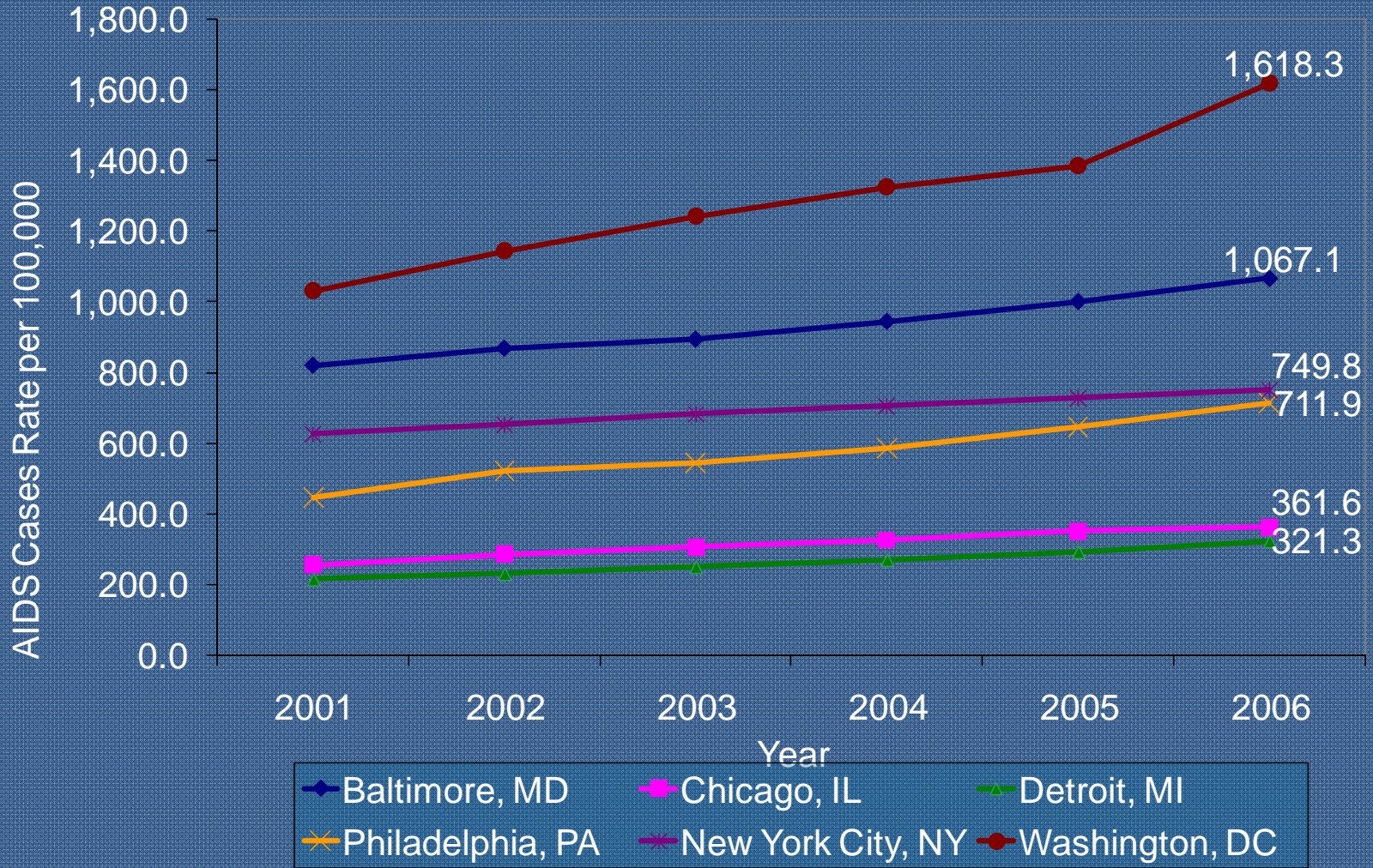
**Fang et al. JID 190: 879, 2004 (++)**

**Montaner et al. Lancet 368: 581, 2006 (??)**

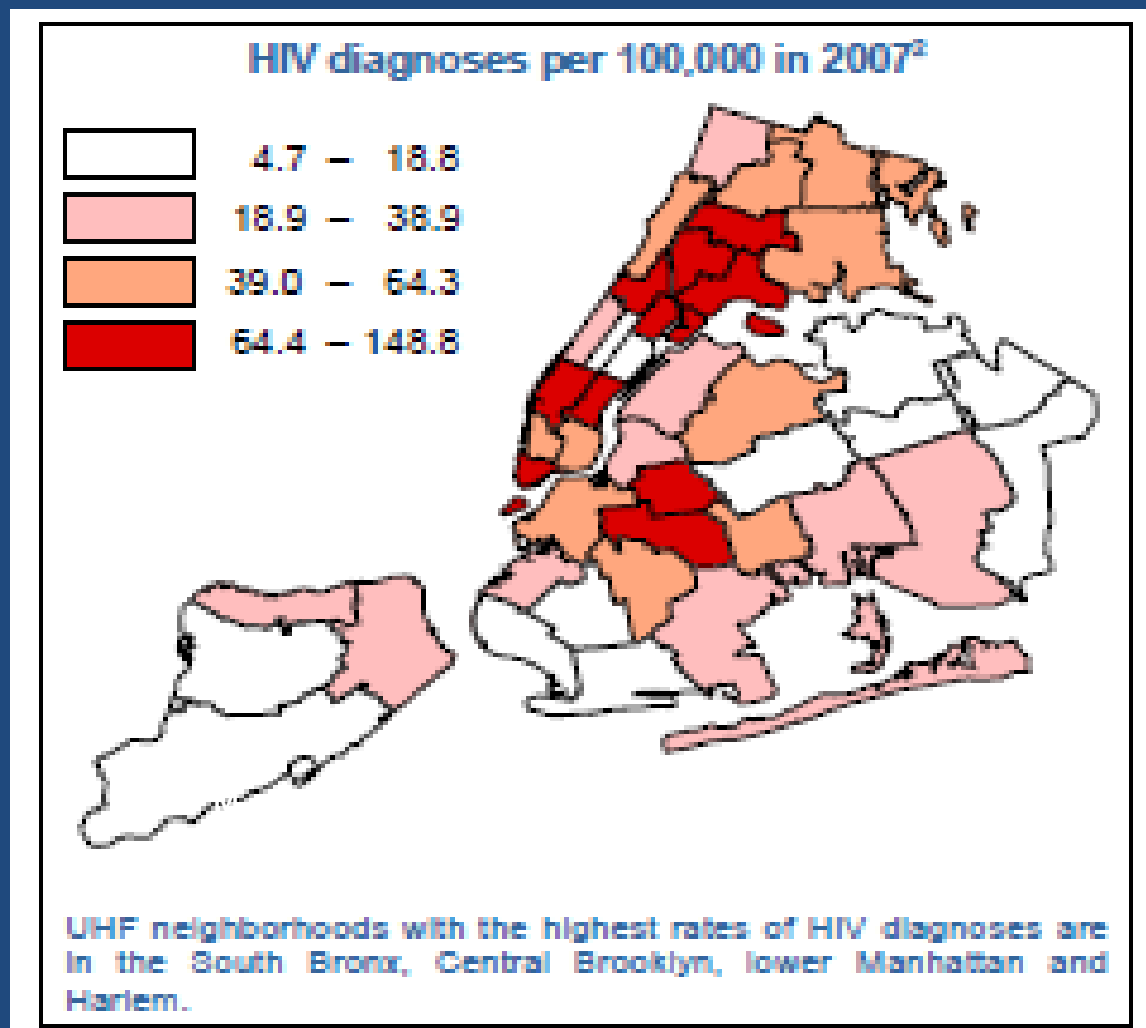
# What is the Relevance of Testing and Treating Strategy to the US HIV Epidemic

- Localized versus generalized epidemic
- Low prevalence and incidence in general but with *hotspots* of high prevalence and incidence
- Higher rates of awareness of HIV status
- Availability of testing and treatment but limitations of access
- Barriers to achievement of high rates of adherence and viral suppression

# The US Epidemic-1

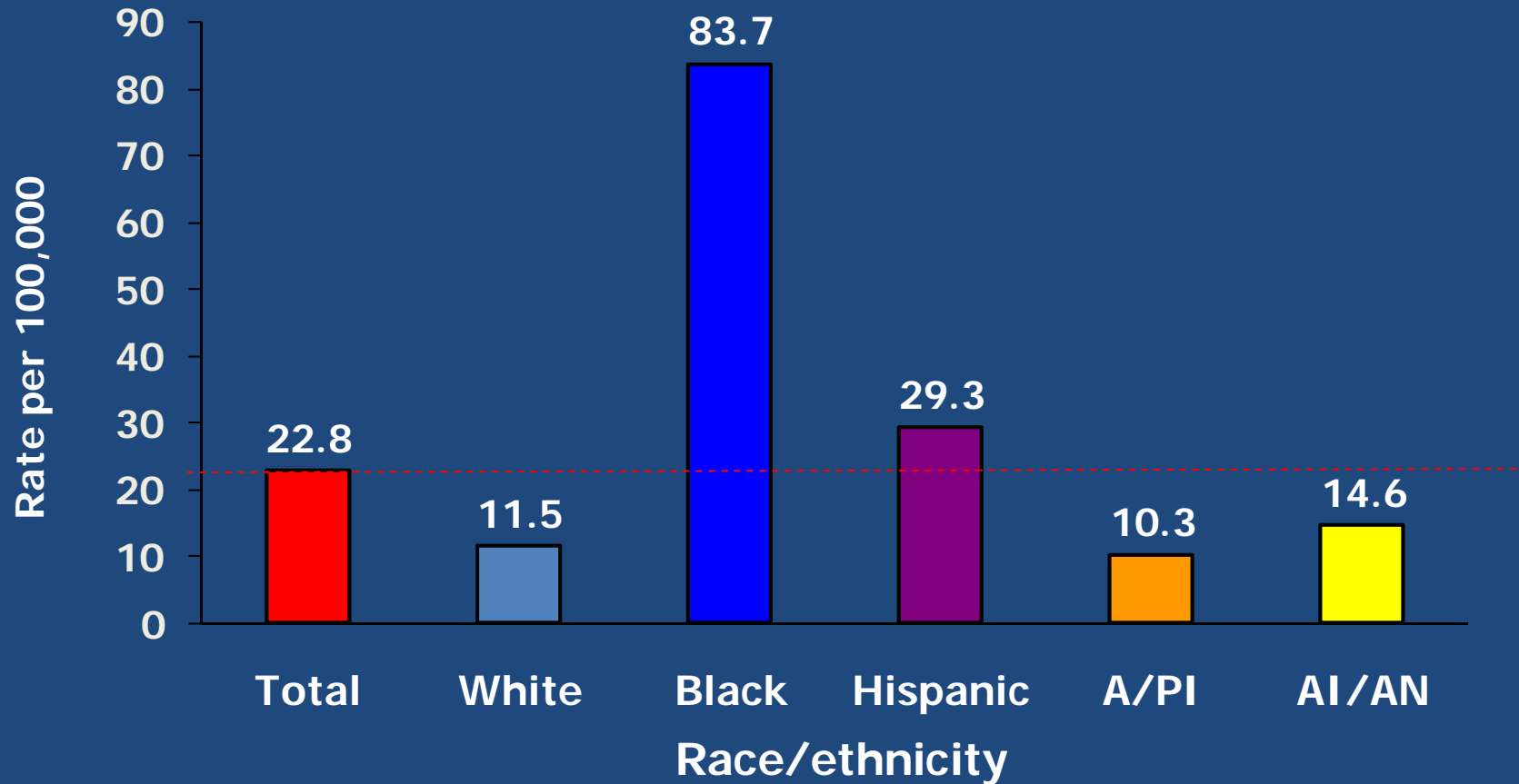


# “Hot spots”



# Estimated rates of new HIV Infections, by race/ethnicity, 2006\*

\*50 States and District of Columbia



Courtesy of Kevin Fenton, CDC

Total Male: 34.3 per 100,000

Total female: 11.9 per 100,000



# HIV Testing: National Health Interview Survey (NHIS), 2006

- U.S. adults have been tested for HIV
  - 40% (*71.5 million*) at least once
  - 10.4% (*17.8 million*) in preceding 12 mos
- Further efforts needed for expanded testing

REF: Duran et al, *MMWR* Aug. 2008



# HIV Testing in NYC

	CY '07	CY '08
• <b>City-Sponsored Tests:</b> (98-99% rapid tests)	<b>169,159</b>	<b>247,784</b>
• <b>Positive Tests</b>	<b>1,768</b>	<b>2,737</b>
• <b>Prevalence</b>	<b>1.0%</b>	<b>1.1%</b>

REF: NYC DOHMH BHIV Testing Unit, data reported: 4/9/2009



# “The Bronx Knows” Initiative

**EVERY BODY NEEDS TO KNOW**

Man, woman, gay or straight, you've gotta get tested for HIV. Found early, it's treatable. **Ignore it, and it's deadly.**

what's your status? **- stay safe** **+ get care** **? get tested**

For free testing sites, **call 311** or visit **[www.nyc.gov/bronxhivtesting](http://www.nyc.gov/bronxhivtesting)**

the **BRONX KNOWS**  
WHAT'S YOUR STATUS?  
- stay safe + get care ? get tested

NYC Health

- Test all Bronx residents ages 18-64 yrs who have never been tested before to identify undiagnosed HIV+ persons
- Link all HIV+ persons to high quality care and supportive services

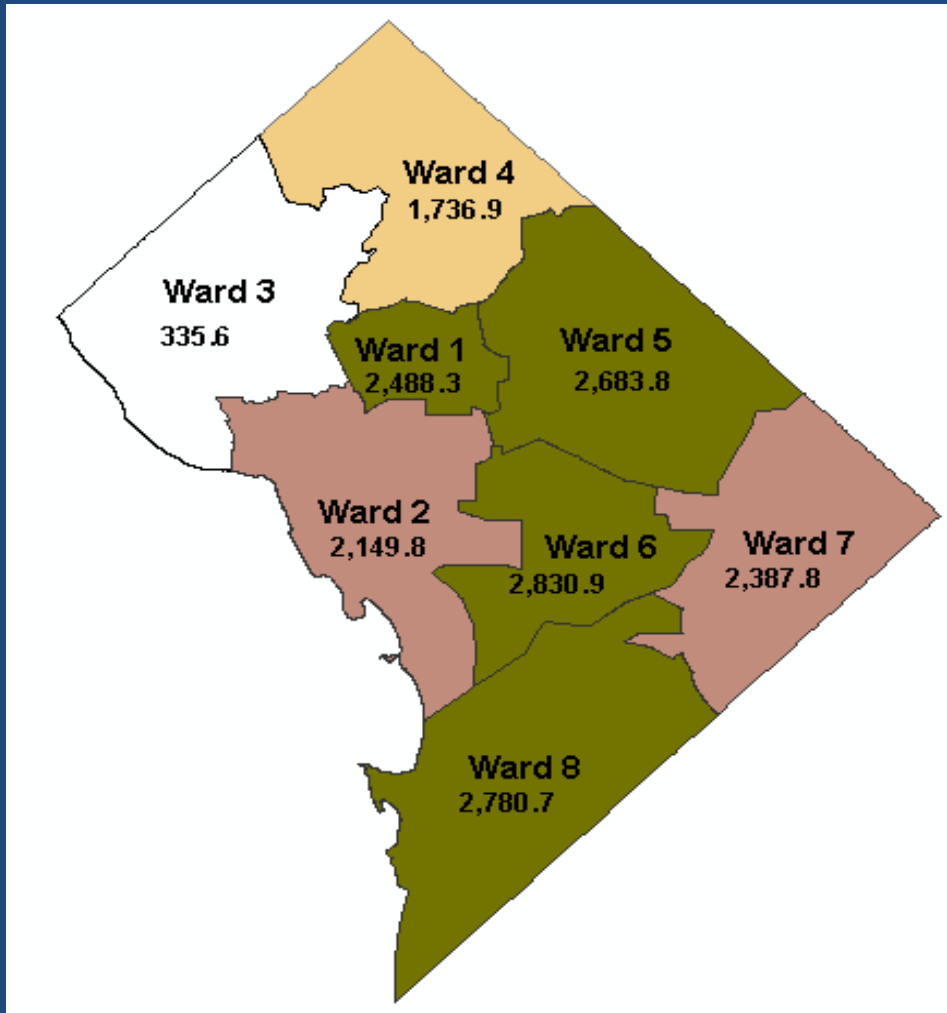
# HIV testing in the Bronx



Testing Locations

# Washington, D.C.:

## 7 of 8 wards with 1.7-2.8% prevalence



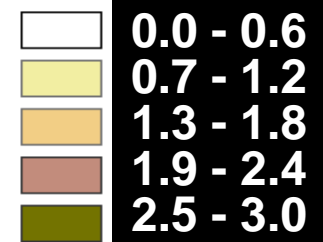
City-wide by  
race/ethnicity  
and sex

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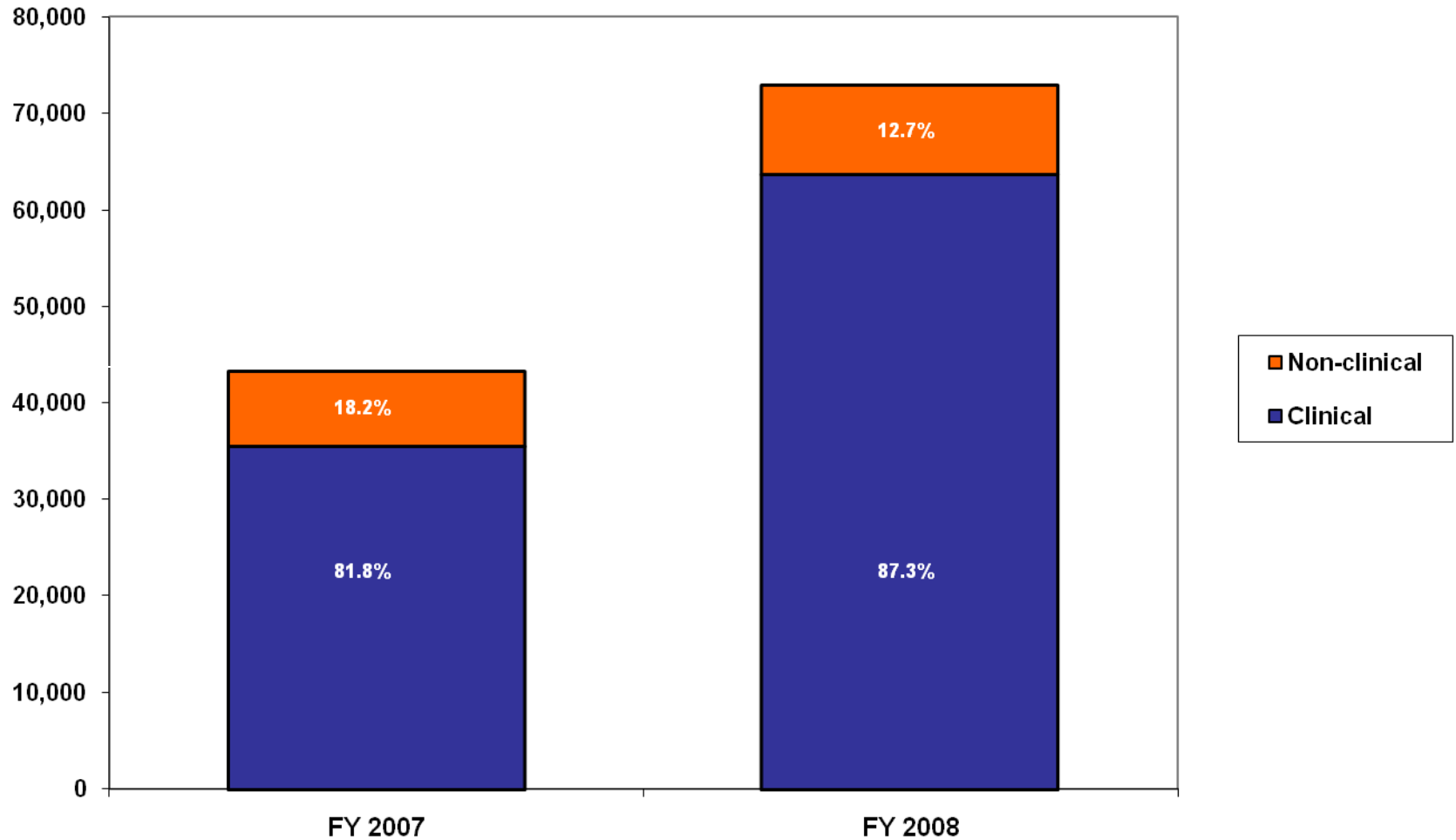
WF 0.2%  
HF 0.7%  
BF 2.6%  
WM 2.6%  
HM 3.0%  
BM 6.5%

**Population  
Prevalence**

**Rate per 100,000**



# HIV Testing Expansion in DC



2009

PREVIEW

# Elements of Intensive Testing and Treating Strategy

- Expansion of HIV testing
- Effective bridging to HIV care
- “Positive Prevention” counseling
- Prompt evaluation for ART eligibility and optimized ART initiation
- Adherence support for maintenance of viral suppression
- STI screening and treatment
- Supportive services: housing, substance use, mental hygiene



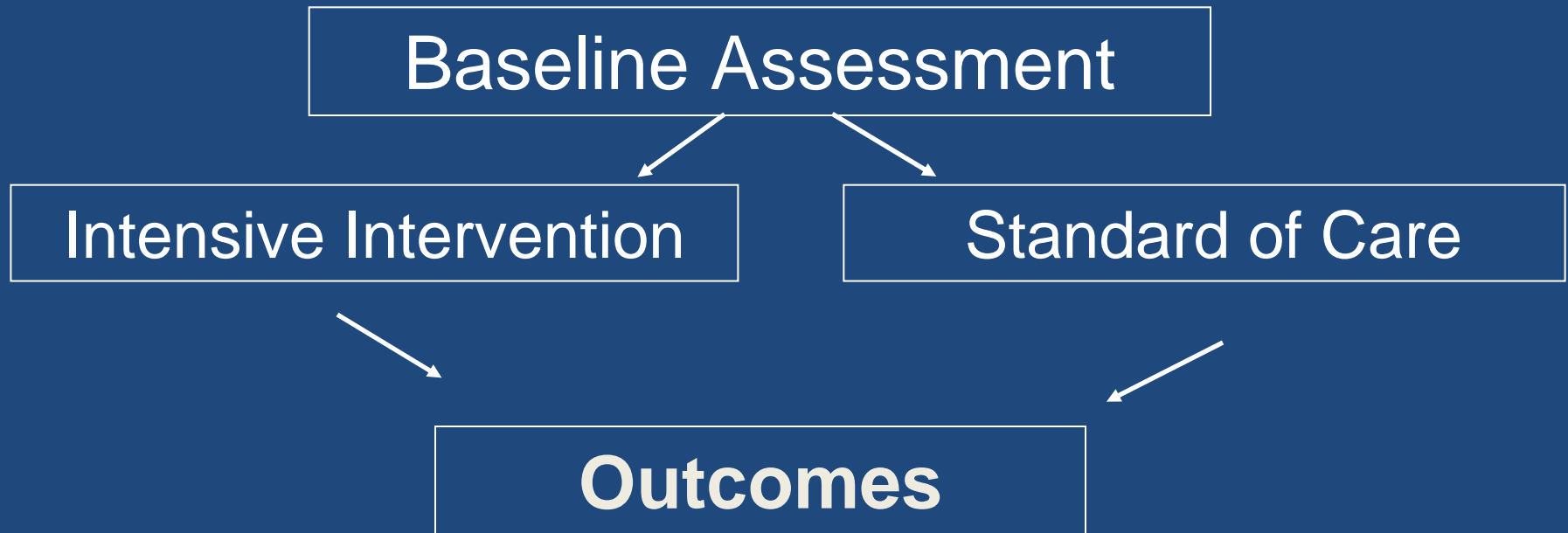
# A Focused Approach

- Identify HIV+ persons unaware of their HIV status
  - Risk reduction in HIV+ persons
- Link HIV+ to HIV care
  - Both newly diagnosed and those out-of-care
- Determine ART eligibility
  - Current guidelines
  - May evolve to earlier ART with results of current work
- Achieve & maintain of high ART adherence rates

Goal of maximal HIV RNA suppression  
with high coverage

# Proposed TNT Study Design

## Community-level comparison



Ultimate goal of wide Implementation of Intensive Intervention (if successful)



# Study Objectives

## Primary Objectives:

To determine the effectiveness of the TNT package interventions on change in community viral load among those known HIV+ (median HIV RNA or proportion with suppressed HIV RNA)

## Secondary Objectives

- Uptake of HIV testing
  - Change in proportion of individuals with prior HIV test within one year
  - Change in median first CD4 cell count after positive HIV test
  - Change in proportion with concomitant diagnosis of HIV and AIDS
- Enrolled in care
  - Change in the proportion of the known HIV+ community eligible for ART, but not on treatment
  - Change in the proportion of the known HIV+ community who have been evaluated for ART eligibility with ART initiation
- Estimated HIV incidence

# Routinely Collected Data

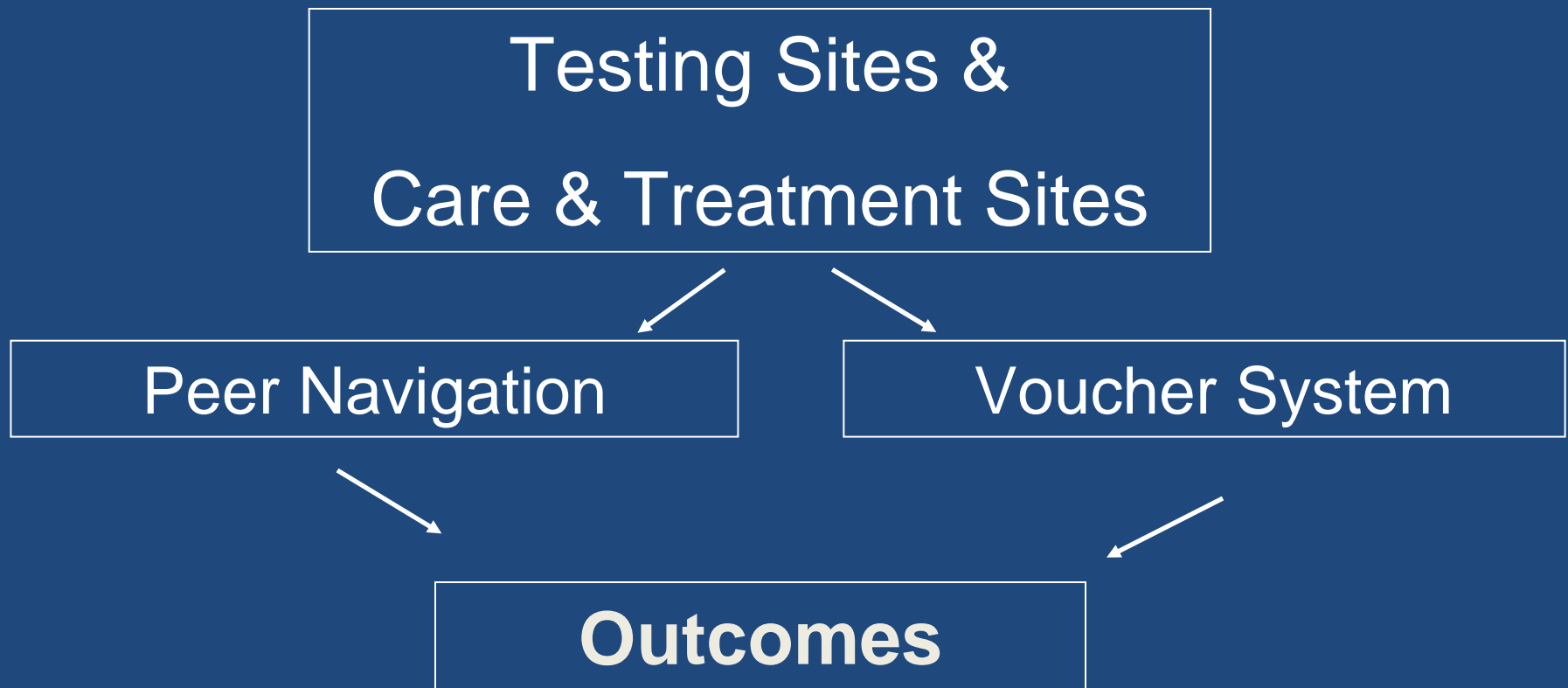
## For all persons tested (+/-)

- Total tests conducted
- Test result
- Previously Tested for HIV
- Self-reported HIV status
- Demographics of persons tested: Race, Ethnicity, Gender (including transgender), Age & zip code
- **Additional Data for HIV + Persons**
  - Risk Factor(s)
  - CD4, VL (every result for individual)
  - Concurrent AIDS diagnosis
  - STAHRS
- **Available aggregate data**
  - Index of community VL
  - Median, mean, range CD4 count
  - % linked to care within 3 months
  - % with concurrent diagnosis
  - % of new diagnoses that are recent infections

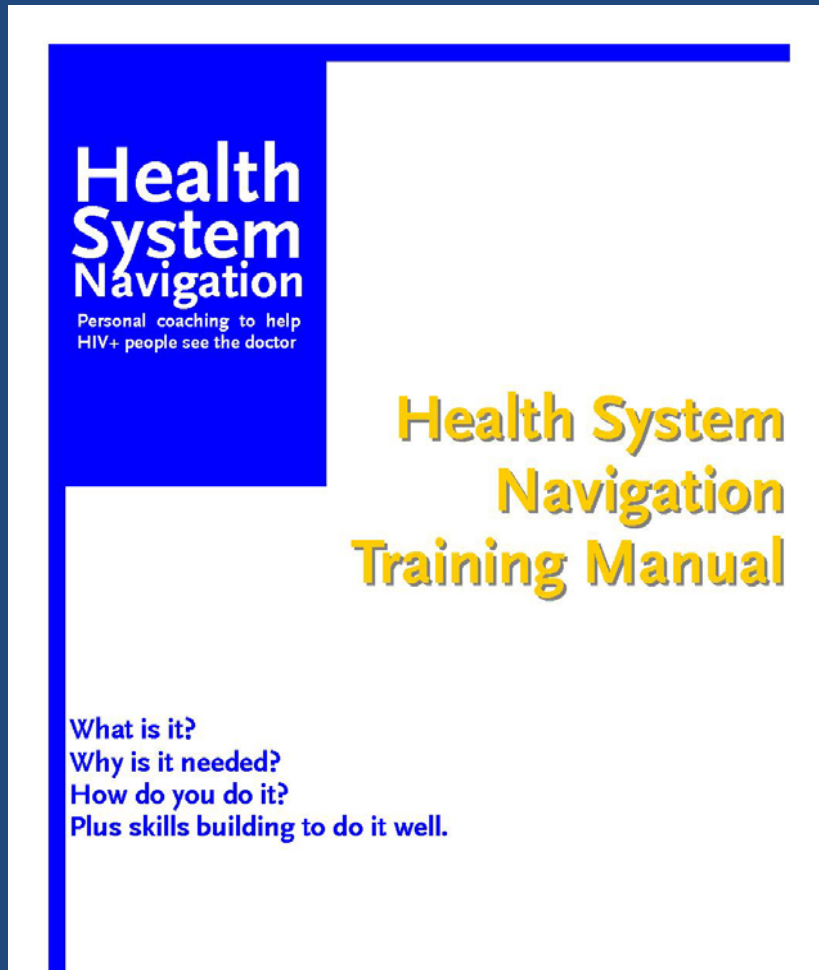
# Proposed Site Randomization

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# HIV System Navigation (HSN): An Emerging Model to Improve HIV Care Access



- Near Peers
- Structured training as per HRSA evaluation
- Finding at-risk persons for testing
- Engagement in testing, bridging to care, adherence to care, retention in care

# Financial Incentives (P4P4P)

- Smoking Cessation
- Weight Loss
- Other behaviors

**“Financial rewards to promote long-term changes in behavior could affect a wide range of health behavior.”**

Volpp et al, NEJM 2009  
Volpp et al, JAMA 2008

# Objectives from Randomized Comparison

- To determine the relative effectiveness of two strategies (peer educators versus vouchers) for engaging HIV+ persons in care:
  - Completion of referral from testing sites to care and treatment (completion of two visits at clinical site)
- To determine the relative effectiveness of two strategies (peer educators versus vouchers) for HIV+ persons taking ARTs
  - in achieving and maintaining suppressed HIV RNA

# Other Questions

- Cost effectiveness
- Perceptions of barriers and facilitators to linkage to care and maintenance in care
- Attitudes regarding ART initiation
- Others

# TNT for Prevention: Key Research Questions

1. Does expanded HIV testing reduce HIV transmission in a community? **HPTN 043**
2. Is an HIV-pos person on ART less likely to transmit to an HIV-neg sexual partner? **HPTN 052**
3. Should HIV therapy be started earlier than current SOC? **HPTN 052/ACTG 5245 & INSIGHT START**
4. Can we better engage hard-to-reach populations? **HPTN 061 (BROTHERS) & HPTN 064 (ISIS)**
5. Can combined testing expansion and bridging to good HIV care and treatment reduce HIV incidence? **“TNT”**



# Does expanded HIV testing reduce HIV transmission in a given community? HPTN 043

**Project  
accept**

**ACCEPT CHANGE!  
MAKE A DIFFERENCE IN LIFE!  
KNOW YOUR HIV STATUS!**

**WE OFFER:**

- Free Community-based voluntary counselling and testing for HIV (CBVCT)
- Same day results using rapid test
- Referral to existing support services in the community for people who have tested for HIV

**Look out for our caravan in your area!**



**Contact us at:**  
New Nurses' Home, First floor, East Wing, Chris Hani Baragwanath Hospital, Soweto  
Tel: 989-9700, 989-9895

A Phase III RCT of Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support for HIV in sub-Saharan Africa and Thailand (HPTN 043)

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# HPTN 052

**HIV-infected subjects with  
CD4 350 to 550cells/ $\mu$ L with discordant partner  
N=1750 couples**

**Randomization**

**Immediate ART  
350-550cells/uL**

**AZT+3TC+EFV**

**Deferred ART  
CD4 <250>200**

**Endpoints: i) Incidence in sexual partner  
ii) OIs and clinical Events  
iii) ART toxicity**

*Thailand, South Africa, Botswana,  
Kenya, Malawi, Brazil, India*

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# When to start ART ?

## Summary of current guidelines

	<i>symptoms or CD4 &lt;200</i>	<i>CD4 200-350</i>	<i>CD4 &gt;350</i>
<b>EACS, 2008</b>	<b>treat</b>	<b>treat</b>	<b>defer</b> W/ SPECIAL CONSIDERATIONS
<b>DHHS, 2008</b>	<b>treat</b>	<b>treat</b>	<b>defer</b> W/ SPECIAL CONSIDERATIONS
<b>WHO</b>	<b>treat</b>	<b>consider treat</b>	<b>defer</b>

# Effect of Early versus Deferred Antiretroviral Therapy on Survival

## NA-ACCORD Study, 1996-2005

Baseline CD4 Cell Count	<u>351-500</u>	<u>&gt;500</u>
No. in Group	8,362	9,155
% initiated ART above threshold	25%	24%
No. deaths, early/deferred	137/238	113/198
Relative risk of death	1.69 (1.26-2.26)	1.94 (1.37-2.79)

# INSIGHT START Design

HIV-infected individuals who are ART-naïve with  
CD4+ count > 500 cells/mm<sup>3</sup>

## Early ART Group

Initiate ART immediately  
following randomization  
N=2,000 for  
definitive trial

## Deferred ART Group

Defer ART until the CD4+ count  
declines to < 350 cells/mm<sup>3</sup> or  
AIDS develops  
N=2,000 for  
definitive trial

Serious AIDS, Non-AIDS Events or Death

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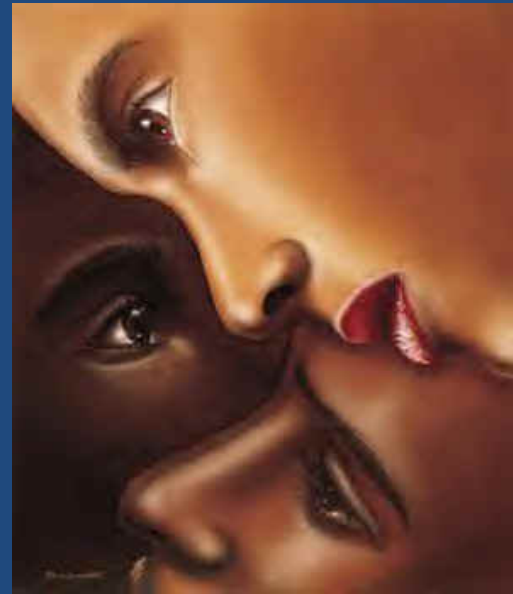


# HPTN 061 & HPTN 064

**BROTHERS: Community-Based,  
Multi-component  
HIV Prevention Intervention for Black  
MSM**



**ISIS**  
**HIV Seroincidence Study in Women**



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# Conclusions

- Intense interest in test and treat as a prevention strategy
- Success requires effective implementation of multiple interrelated steps on a large scale
- Test and treat study must include intensive community mobilization and partnerships
- Epidemic in US offers opportunity to evaluate the strategy in a unique situation
- Data are needed to determine the true benefits and risks of test and treat strategy

# Acknowledgement

- Members of the TNT concept team
- HPTN, CDC and departments of health
  
- Funding support by NIH