

HIV National Summit

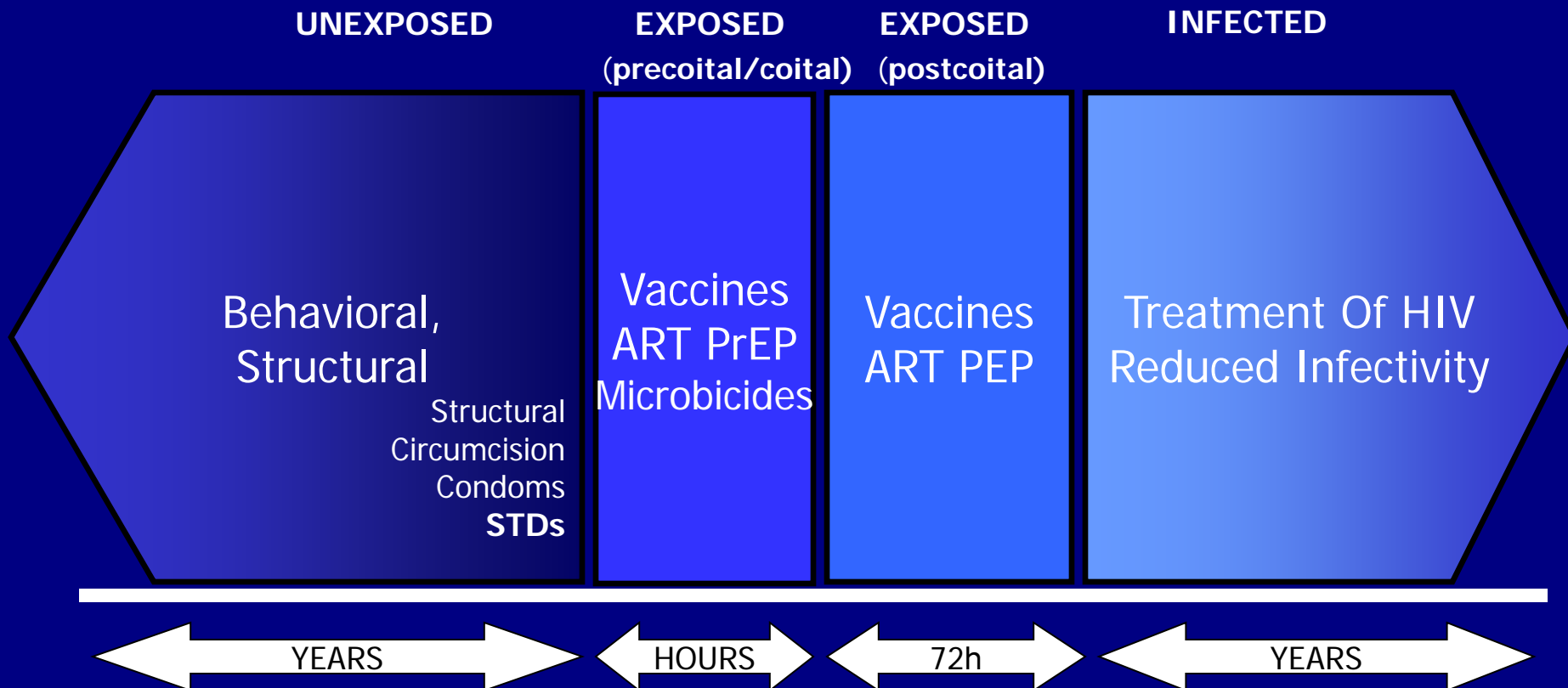
Working to End the HIV Pandemic

Myron S. Cohen, MD
Director, Institute for Global Health
The University of North Carolina



Four Prevention Opportunities

Cohen et al, JCI, 2008
Cohen IAS 2008



Behavioral Interventions?

- No single tool to reduce HIV incidence

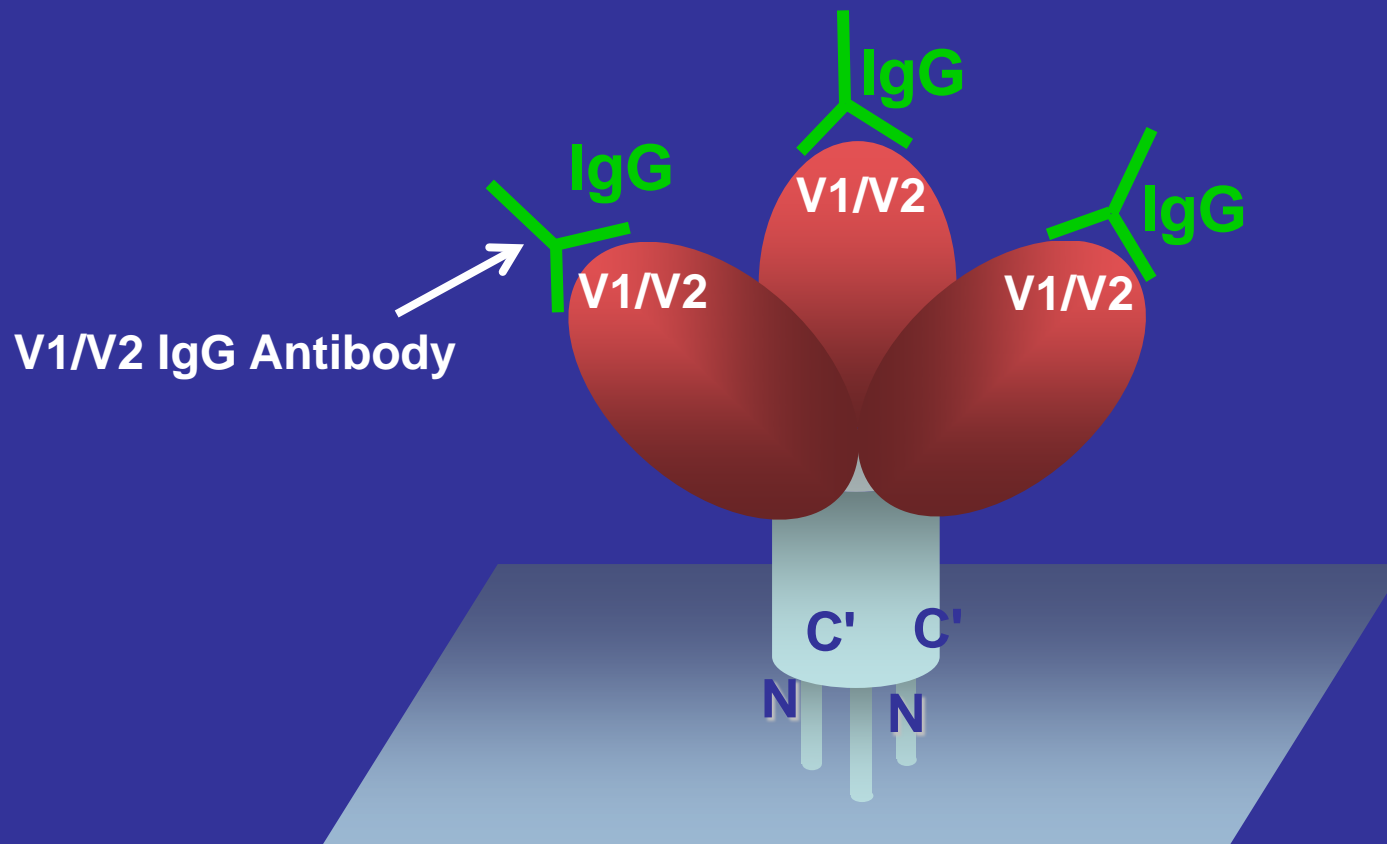
Padian, AIDS 2010

... But HIV incidence has fallen !

- HPTN 043..Effects of mobile VCT
 - A new HIV incidence assay algorithm
- *Laeyendecker et. al J Infect Dis. epub*

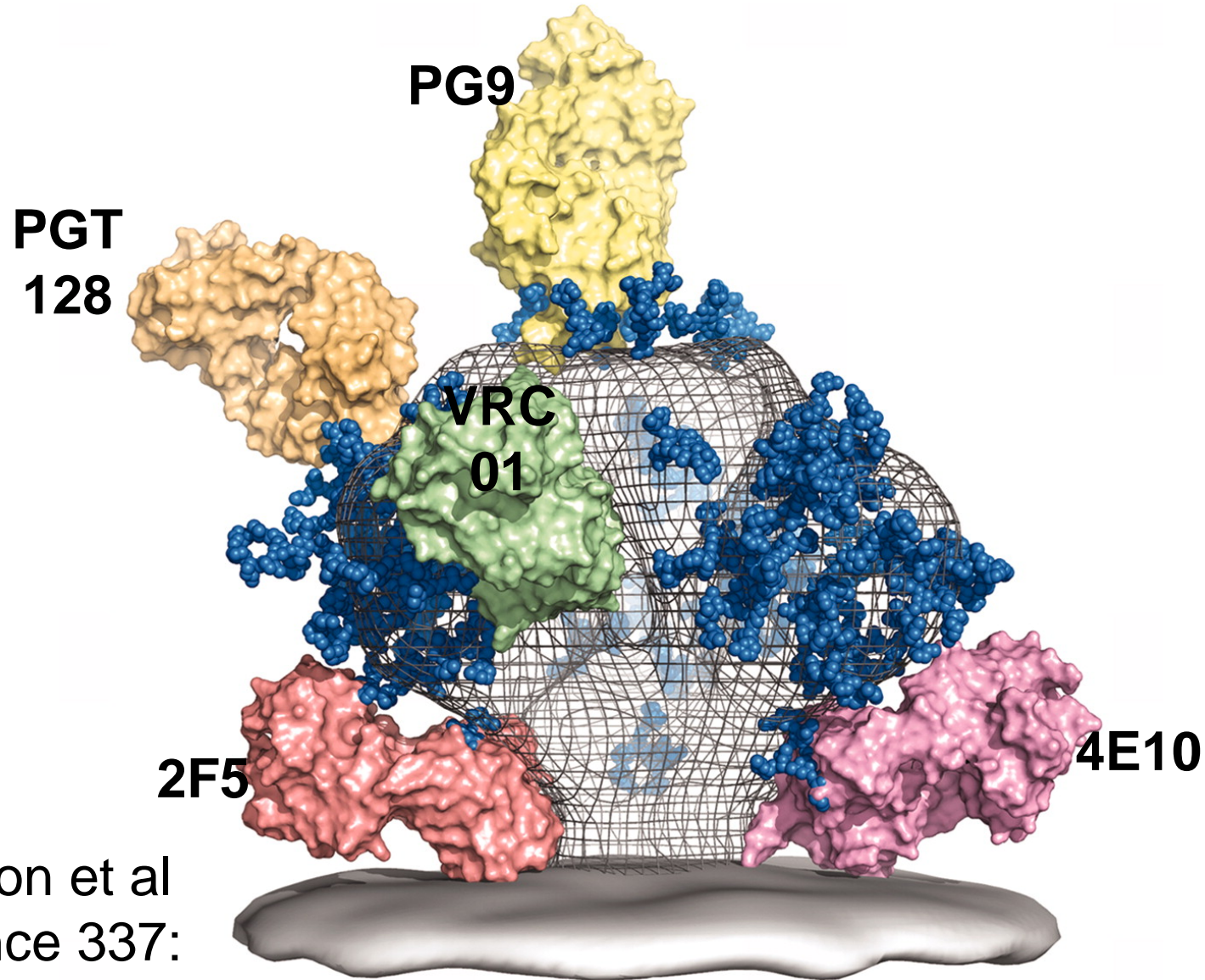
STAY TUNED

RV144 Idea: IgG Antibodies to V1/V2 Can Protect Against HIV-1 Infection



Envelope on HIV-1 Infected Cell

Antibody Fab Binding to HIV Envelope an Achilles' Heels



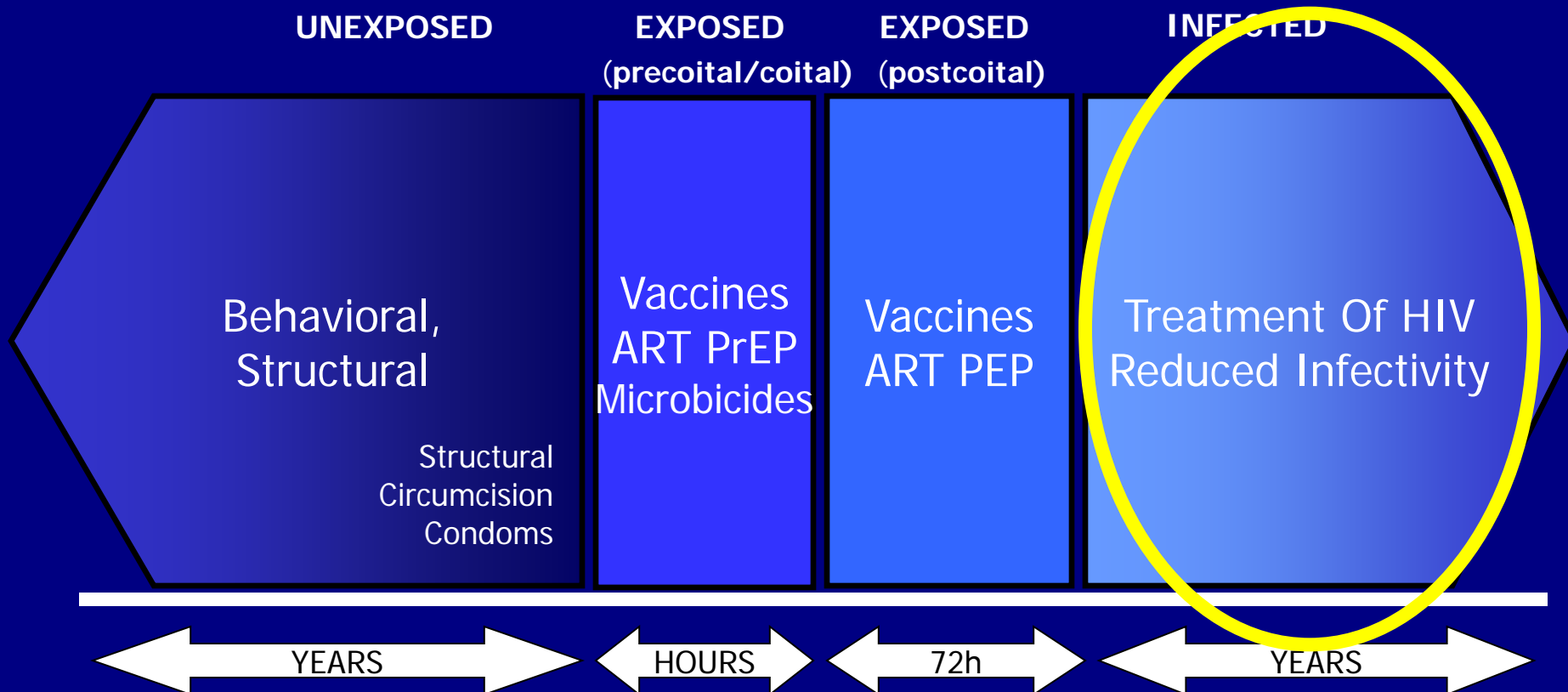
Burton et al
Science 337:
183, 2012

The Next Generation of PrEP

- **A maraviroc based regimen (HPTN 069)**
- **An injectable long acting ART**
 - TMC 278LA (rilpivirine)
 - S-GSK1265744LA (an integrase inhibitor)
- **Monoclonal antibodies**
 - Ibaluzimab (TMB-355)
 - VRC01-7
- **Vectored immunoprophylaxis (VIP),**

Four Prevention Opportunities

Cohen et al, JCI, 2008
Cohen IAS 2008



Treatment as Prevention

“The Four Questions”

- **Can ART prevent HIV transmission ?**
 - magnitude and durability
- **What do we tell infected people?**
- **Can we reduce HIV incidence with ART?**
- **Barriers to “Treatment as Prevention”?**

HPTN 052 Study Design

Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³



Primary Transmission Endpoint

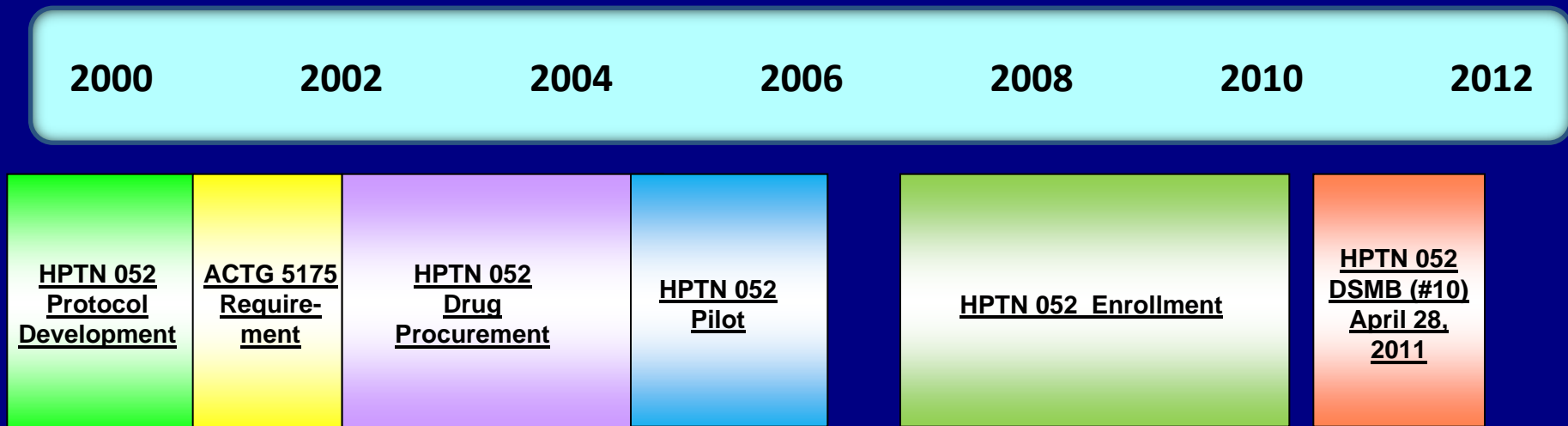
Virally linked transmission events

Primary Clinical Endpoint

WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

HPTN 052 Timeline: The Fast Track?

- ART for prevention of HIV 1993- THE PRESENT



HPTN 052 Enrollment

(Total Enrollment: 1763 couples)



96%

Results of the HPTN052 trial announced on 12 May 2011 show that if an HIV-positive person adheres to an effective antiretroviral therapy regimen, the risk of transmitting the virus to their uninfected sexual partner can be reduced by 96%

“Treatment for prevention is a game changer”.

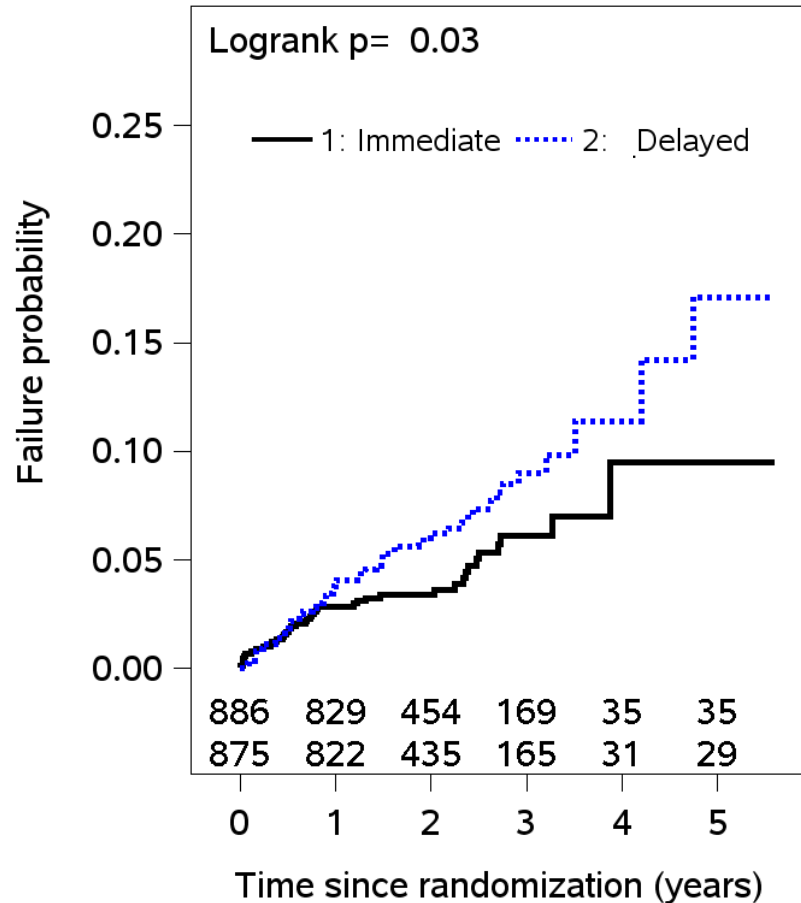
Michel Sidibe
Executive
Director of
UNAIDS

UNAIDS 2011 *AIDS at 30*
SMARTER , FASTER , BETTER CAMPAIGN

AIDS Events

Time to first AIDS defining disease

Logrank p= 0.03



Number of subjects experiencing ≥ 1 event

	Delayed	Immediate
Tuberculosis	34 (4%)	17 (2%)
Serious bacterial infection	13 (1%)	20 (2%)
WHO Stage 4 event	19 (2%)	9 (1%)
Oesophageal candidiasis	2	2
Cervical carcinoma	2	0
Cryptococcosis	0	1
HIV-related encephalopathy	1	0
Herpes simplex, chronic	8	2
Kaposi's sarcoma	1	1
CNS Lymphoma	1	0
Pneumocystis pneumonia	1	0
Septicemia	0	1
HIV Wasting	2	0
Bacterial pneumonia	1	2

Most Prevalent Secondary Events

Number of subjects experiencing ≥ 1 event

	Delayed (N=317)	Immediate (N=298)
Upper respiratory tract infection	87	72
Moderate unexplained weight loss*	61	76
Popular puritic eruption	52	33
Herpes zoster	53	17
Smear positive malaria	49	49
Oral Candidiasis, persistent	47	22
Unexplained severe weight loss	21	37
Dyslipidemia	7	23
Peripheral neuropathy	14	15
Seborrhoeic dermatitis	18	7
Hypertension	8	12
Oral ulcerations	9	10

HPTN 052: What Happened Next

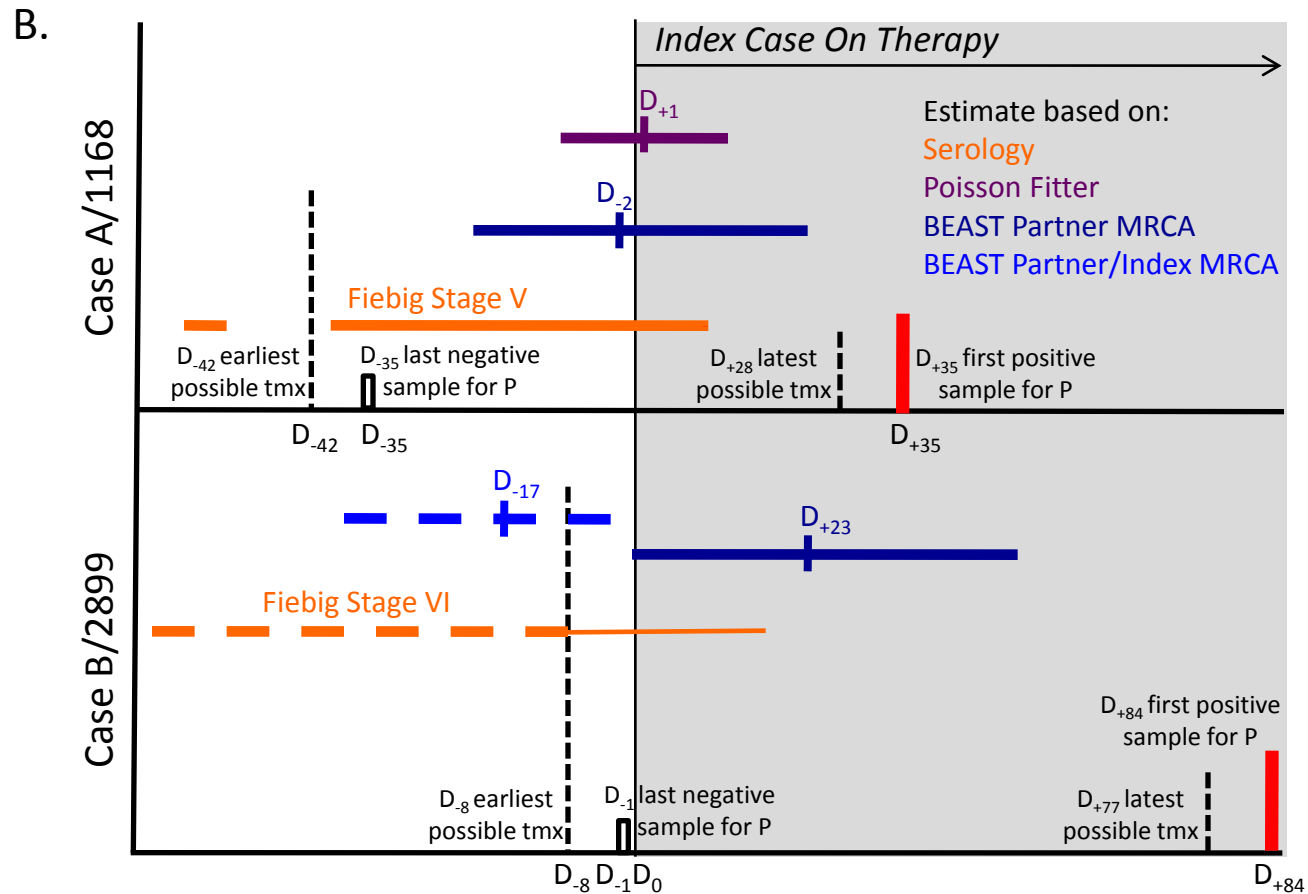
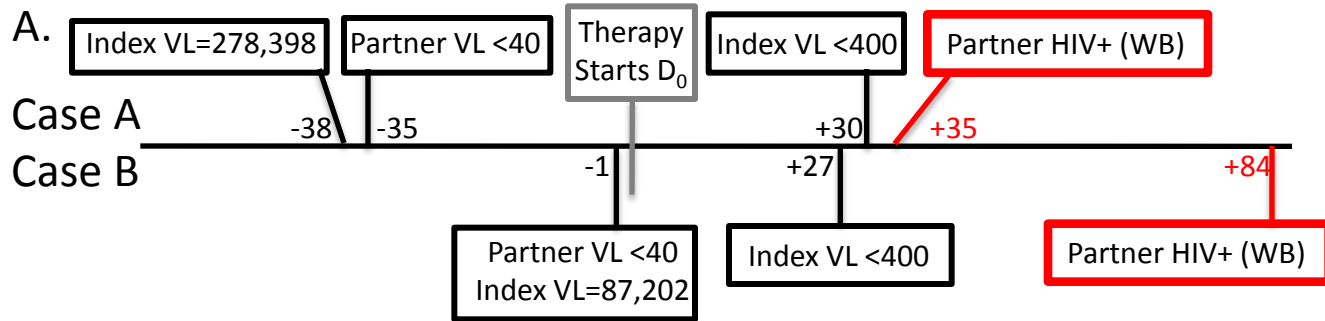
NIH DSMB Nov 9, 2012

- All HIV infected subjects offered ART
 - 1682 index cases/1763 (96% retention)
 - 1502 discordant couples (85% retention)
 - 1561/1682 index cases are NOW on ART

DURABILITY OF PREVENTION?

ADVERSE EVENTS?

DELAYED ART & CLINICAL OUTCOMES



HPTN 052 Cost Effectiveness

Walensky et al. IAS 2012

HPTN 052 results for India, South Africa used
Treatment/Prevention benefits both considered

- i) In South Africa, over the short term, early ART is “**cost-saving**”
- ii) Over time ART in INDIA and South Africa proves “**very cost effective**”

WHEN SHOULD ART BE STARTED?

Significantly higher employment at **CD4 \geq 500** among adults

- **Compared to CD4<200, CD4 \geq 500 associated with**

- 5.8 more days/month
- 2.2 more hours/day (40% more than ref. mean of 5.5)

Those with CD4 \geq 500 worked nearly 1 week/month more than those with CD4<200, and as much as HIV-uninfected adults

Regression model coefficients		
	(1)	(2)
Outcome:	Days worked in the past month	Hours worked on usual day in past
CD4<200	Reference	Reference
CD4 200-349	2.7	1.8
CD4 350-499	4.8	0.9
CD4 \geq 500	5.8**	2.2*
Observations	107	107

- Linear regression model with age, age-squared, and sex included as controls
- ** p<0.05, * p<0.10
- Reference group has CD4<200

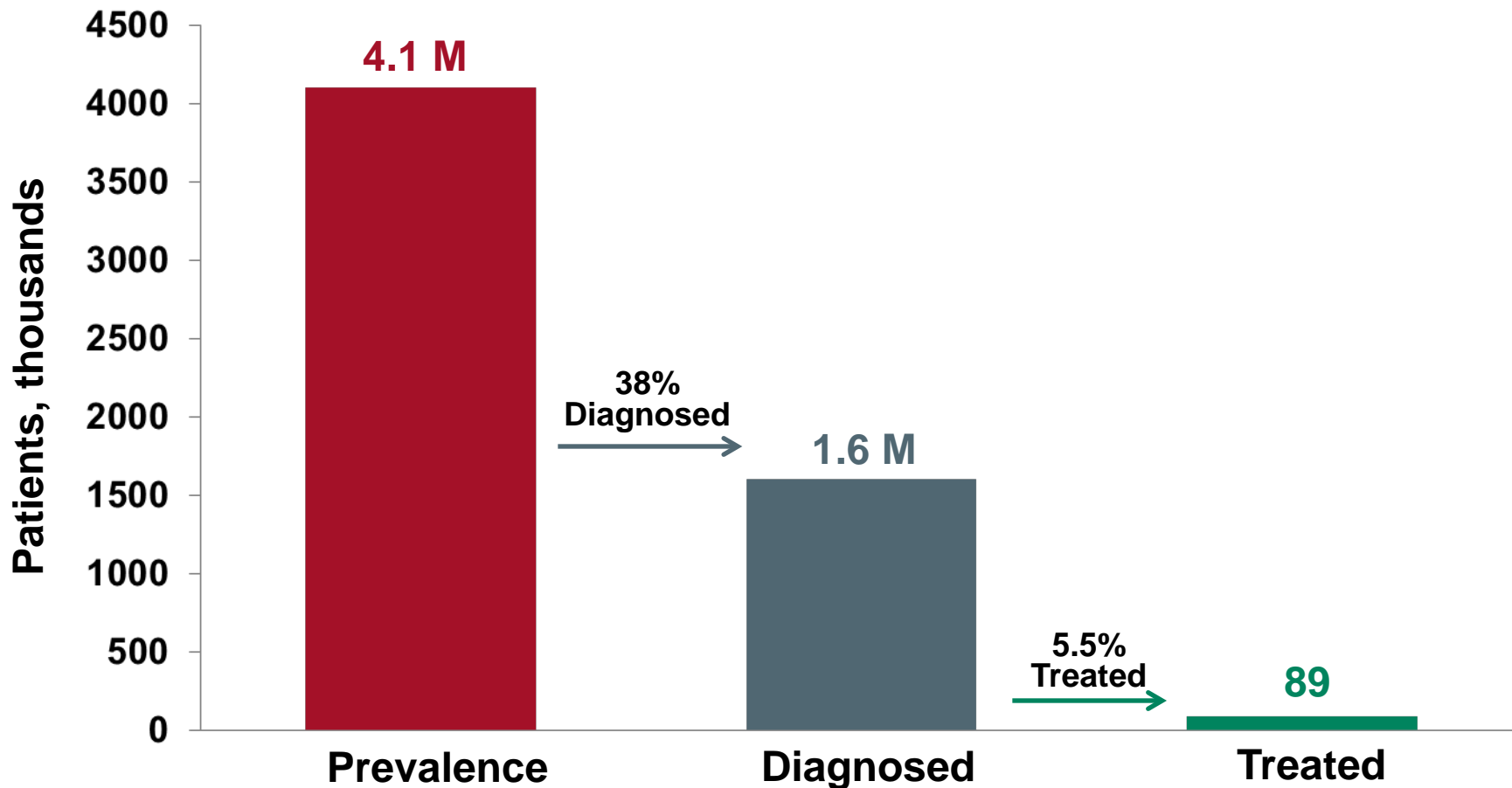
By Myron S. Cohen, Charles Holmes, Nancy Padian, Megan Wolf, Gottfried Hirnschall, Ying-Ru Lo, and Eric Goosby

HIV Treatment As Prevention: How Scientific Discovery Occurred And Translated Rapidly Into Policy For The Global Response

ABSTRACT In 2011 interim results of HIV Prevention Trials Network study 052, a National Institutes of Health study designed to test the effectiveness of antiretroviral treatment against the spread of HIV, were reported. These results showed that in a stable relationship in which one member of the couple was infected with HIV, treatment of the infected partner with antiretroviral drugs, combined with couples counseling and condom use, resulted in a 96 percent reduction in sexual transmission of HIV-1. This finding led to the use of antiretroviral treatment as a cornerstone of HIV prevention. Independent advisory committees of the President's Emergency Plan for AIDS Relief (PEPFAR) and the World Health Organization (WHO) have since issued analyses that set the stage for broader use of antiretroviral agents in treatment and prevention. This article describes the separate PEPFAR and WHO recommendations and outlines the design of prospective new trials to test how best to maximize the benefits of early treatment for prevention.

Chronic HCV Landscape in the United States

Currently, HCV HCPs Treat Only 5.5% of Diagnosed Patients



1. NHANES (1988-1994, 1999-2000, 2007-2010), Chak, Liver Int'l 2011 [ex-NHANES populations], and epidemiology modeling. Viremic excludes cured HCV patients.
2. NHANES diagnosis rate 42%. Assumed 5% diagnosis rate for incarcerated and homeless and 42% for all other ex-NHANES populations.
3. Wolters Kluwer Rx data and pegylated IFN sales, Vertex reported patients treated with Incivek, and Synovate Q2 and Q4 2011.
4. Other populations included in total prevalence are: healthcare workers, nursing home residents, chronic haemodialysis, haemophiliacs with transfusions.

The Economist

INSIDE THIS WEEK: TECHNOLOGY QUARTERLY

The
Economist

JUNE 4TH-10TH 2011

Economist.com

The trap for Turkey

Wall Street's plumbing problem

Lady Gaga, Mother Teresa and profits

Brazil's boiling economy

The farce that is FIFA

The end of AIDS?



How 5 million lives have
been saved, and a plague
could now be defeated

TnT: Aspiration Meets Reality

Smith, Cohen et al. PLOS MED, July 2012

1. When to Start?

2. Acute Infection?

2. The “CASCADE”?

3. Messages from Ecological Studies

Why START ART NOW?

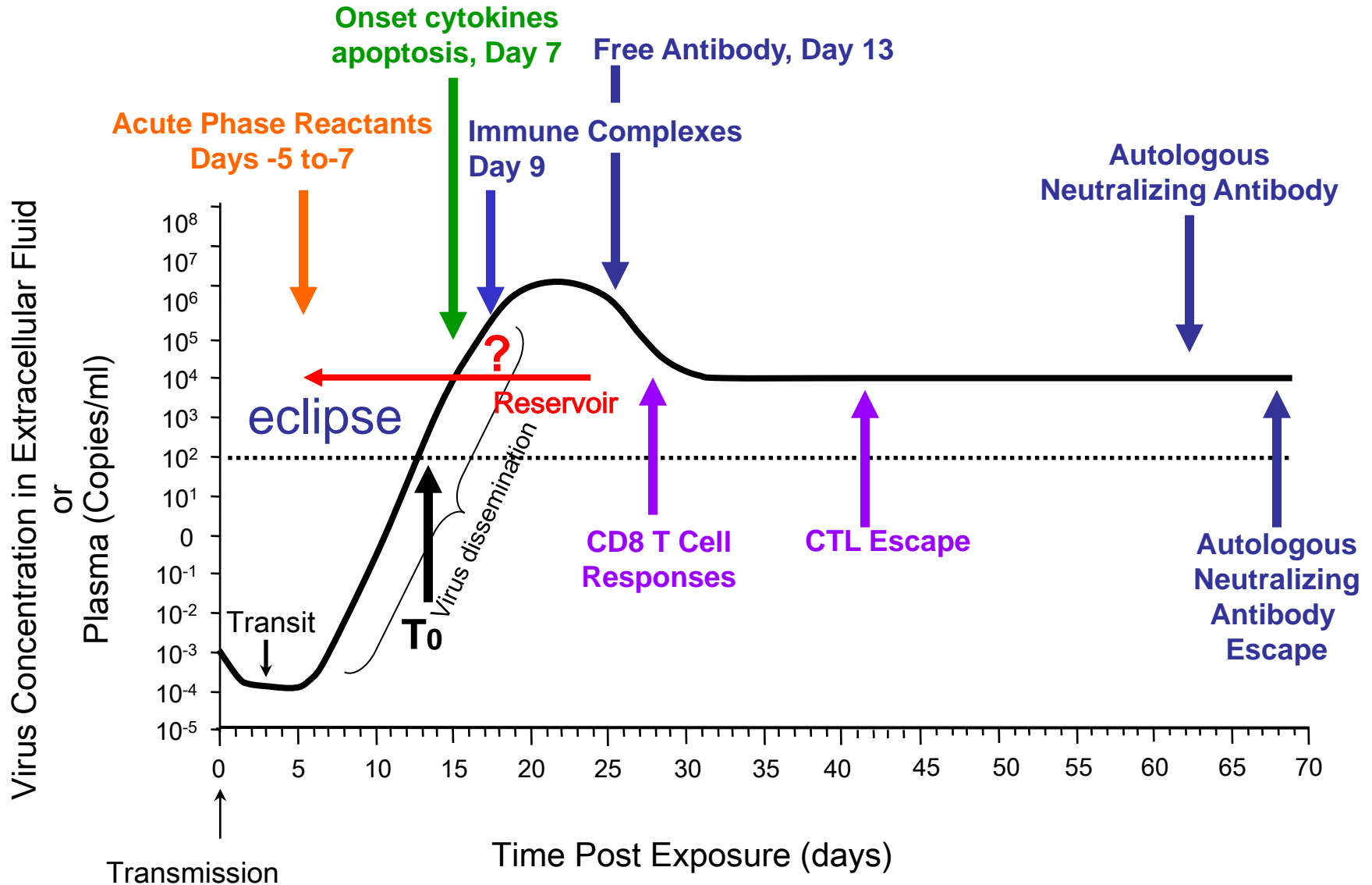
- The consequences of replication
- Reduced long-term survival
- Ongoing HIV transmission
- Cost /benefit and economic analysis

The arguments for delay include

- Anticipated detection of novel “harm”
- Ongoing search for “benefit”
- Intense focus on logistical challenges

Acute HIV-1 Infection

Cohen et al, NEJM, 2011



Black MSM

OR, 6.38 (4.33-9.39)

HIV
Detection

Diagnosed HIV+
OR, 3.00 (2.06-4.40)

Health insurance
coverage
OR, 0.47 (0.29-0.77)

ART utilization/ access
OR, 0.56 (0.41-0.76)

ART initiation
OR, 0.40 (0.26-0.62)

ART adherence
OR, 0.50 (0.33-0.76)

HIV suppression
OR, 0.51 (0.31-0.83)

Viral
Suppression

Lower income (<\$20k)
OR, 3.42 (1.94-6.01)

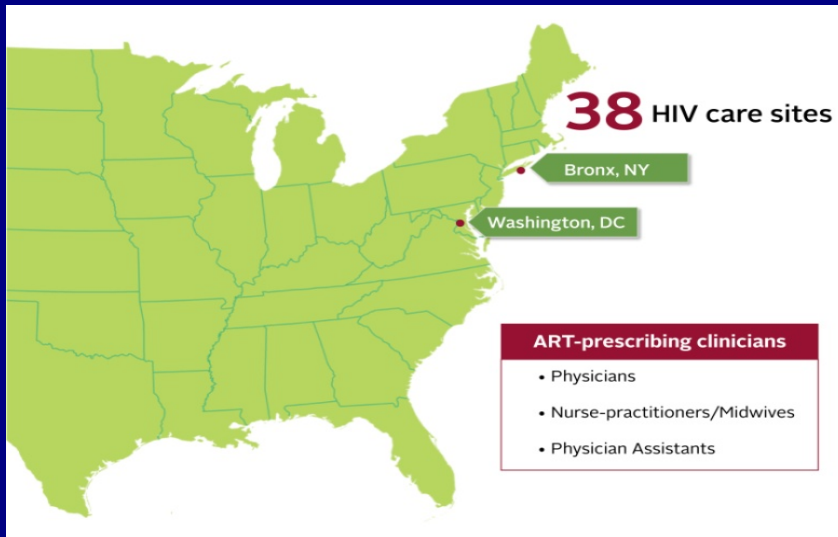
Healthcare visits
OR, 0.61 (0.42-0.90)

- 15 X risk for HIV
- Policies that criminalize homosexuality associated with increased HIV prevalence
- Safe and culturally competent access to care lacking for black MSM

HPTN 065 (TLC-Plus) Provider Survey

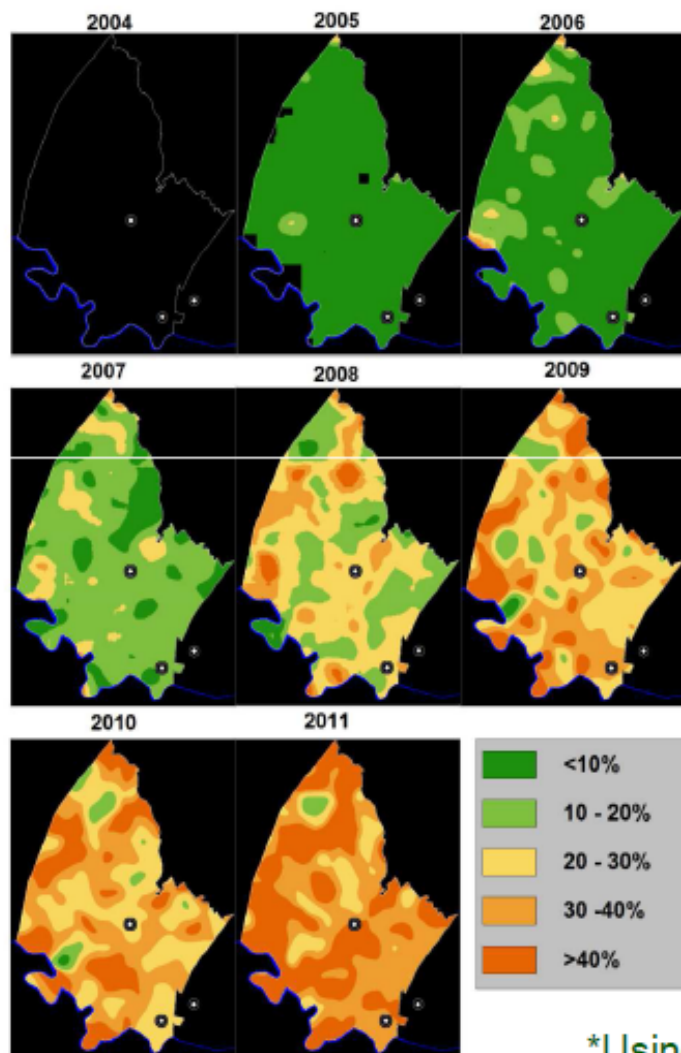
Study Population and Participants

- ART-prescribing providers at 38 participating HPTN 065 care sites in Bronx, NY and Washington, DC
- Internet-based survey (anonymous)



Glimmers of Hope

ART coverage 2004-2011



- **ART coverage** = proportion of the total HIV-infected population receiving ART
- **Patients on treatment:** Individual, geo-located DOH programme adult patients actively on treatment in June (2004-2011)
- **HIV-infected:** Individual, geo-located, HIV positive adults identified through population-based HIV surveillance data (2004-2011)

*Using a standard Gaussian kernel of radius 3km

The “Test and Treat” Movement

- ANRS PILOT in South Africa (KZN)
- THE PEPFAR Combination Prevention Trials:
 - CDC- BOTSWANA
 - NIH HPTN 071 -South Africa, Zambia
 - USAID JHU-Tanzania

Early ART, Circumcision, Counseling, OTHER

Measurement of HIV incidence

Increased use of viral phylogeny



Personal Conclusions

- 34,000,000 people with HIV to treat
 - for health, and transmission prevention
- Mass treatment of HIV is a “bridge”
 - to simpler, modified intervention
 - to a “cure”
 - to a vaccine

Wishful , magical or aspirational thinking?

HIV Prevention 2012

