



HIV Prevention: A Global Priority

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ICAP, Columbia University



CDC
CENTERS FOR DISEASE CONTROL
AND PREVENTION

June 5, 1981 / Vol

MMWRTM

MORBIDITY AND MORTALITY WEEKLY REPORT

- 249 Dengue Type 4
Travelers to the
- 250 *Pneumocystis* P
Los Angeles
- 252 Measles — Un
Weeks
- 253 Risk-Factor-P
- 259 Surveillance o
Poisoning —
- 261 Quarantine M

Pneumocystis Pneumonia — Los Angeles

In the period October 1980–May 1981, 5 young men, all active
treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at
California. Two of the patients died. All 5 patie
cytomegalovirus (CMV) infection and

RARE CANCER SEEN IN 41 HOMOSEXUALS

Outbreak Occurs Among Men
in New York and California
—8 Died Inside 2 Years

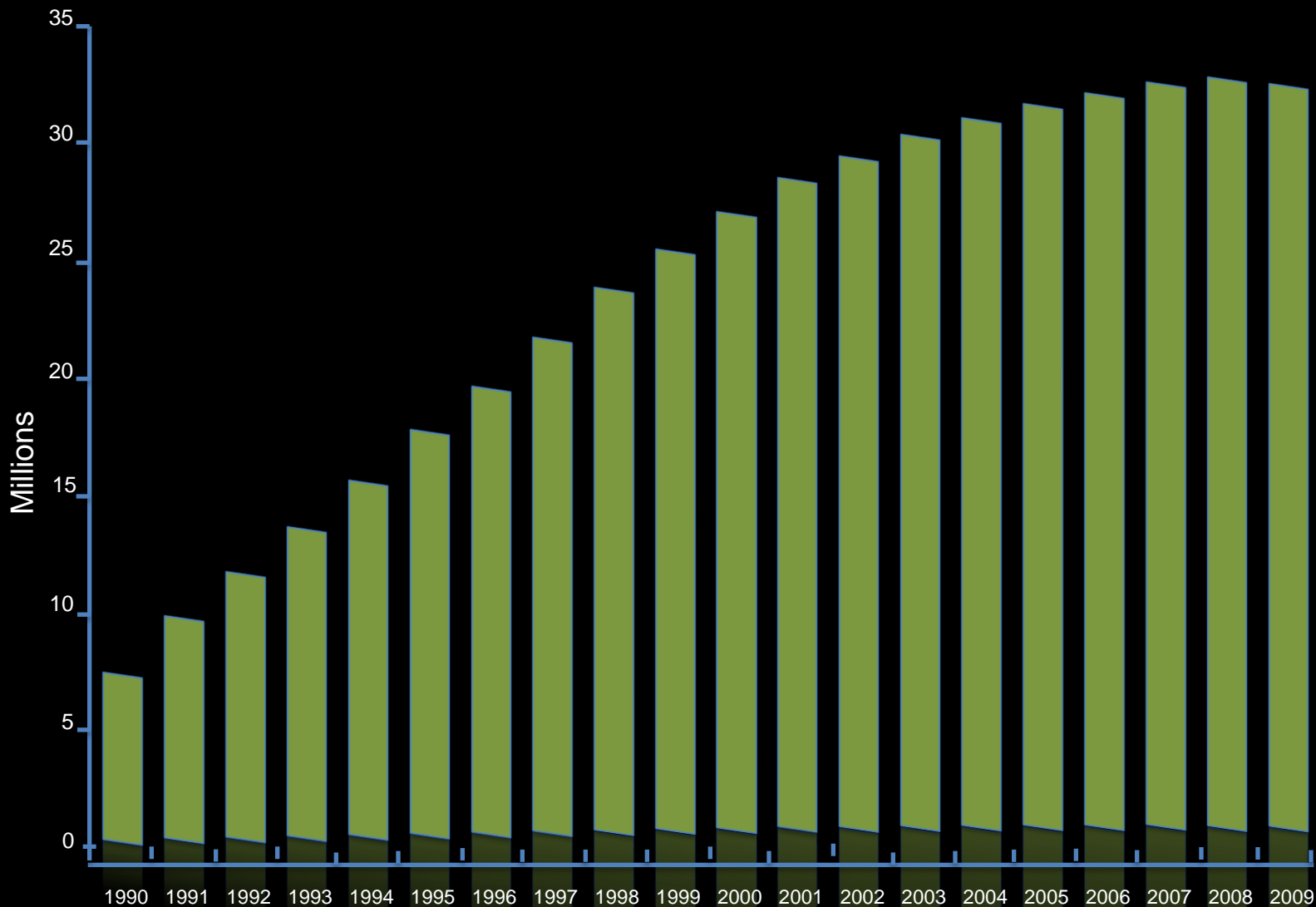
By LAWRENCE K. ALTMAN.

Doctors in New York and California have diagnosed among homosexual men 41 cases of a rare and often rapidly fatal form of cancer. Eight of the victims died less than 24 months after the diagnosis, ~~was made.~~

The cause of the outbreak is unknown, and there is as yet no evidence of contagion. But the doctors who have made the



Global Number of People Living with HIV, by year



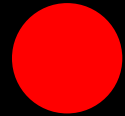
Caribbean
240,000



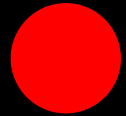
Middle East
& North Africa
460,000



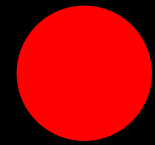
Eastern Europe
& Central Asia
1.4 million



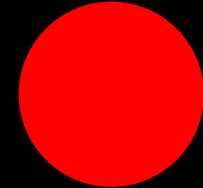
Central
& South America
1.4 million

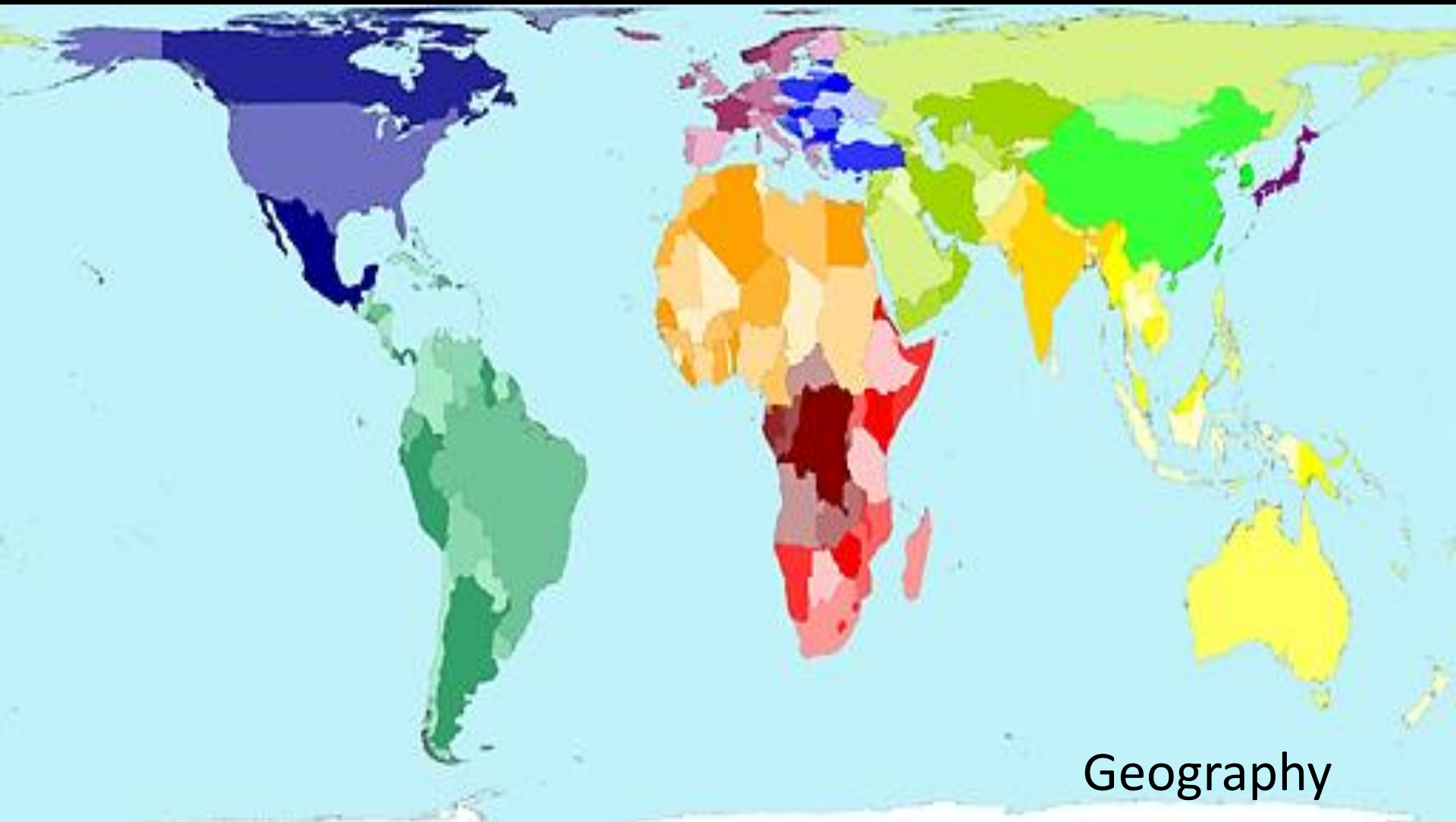


North America &
Western/
Central Europe
2.3 million

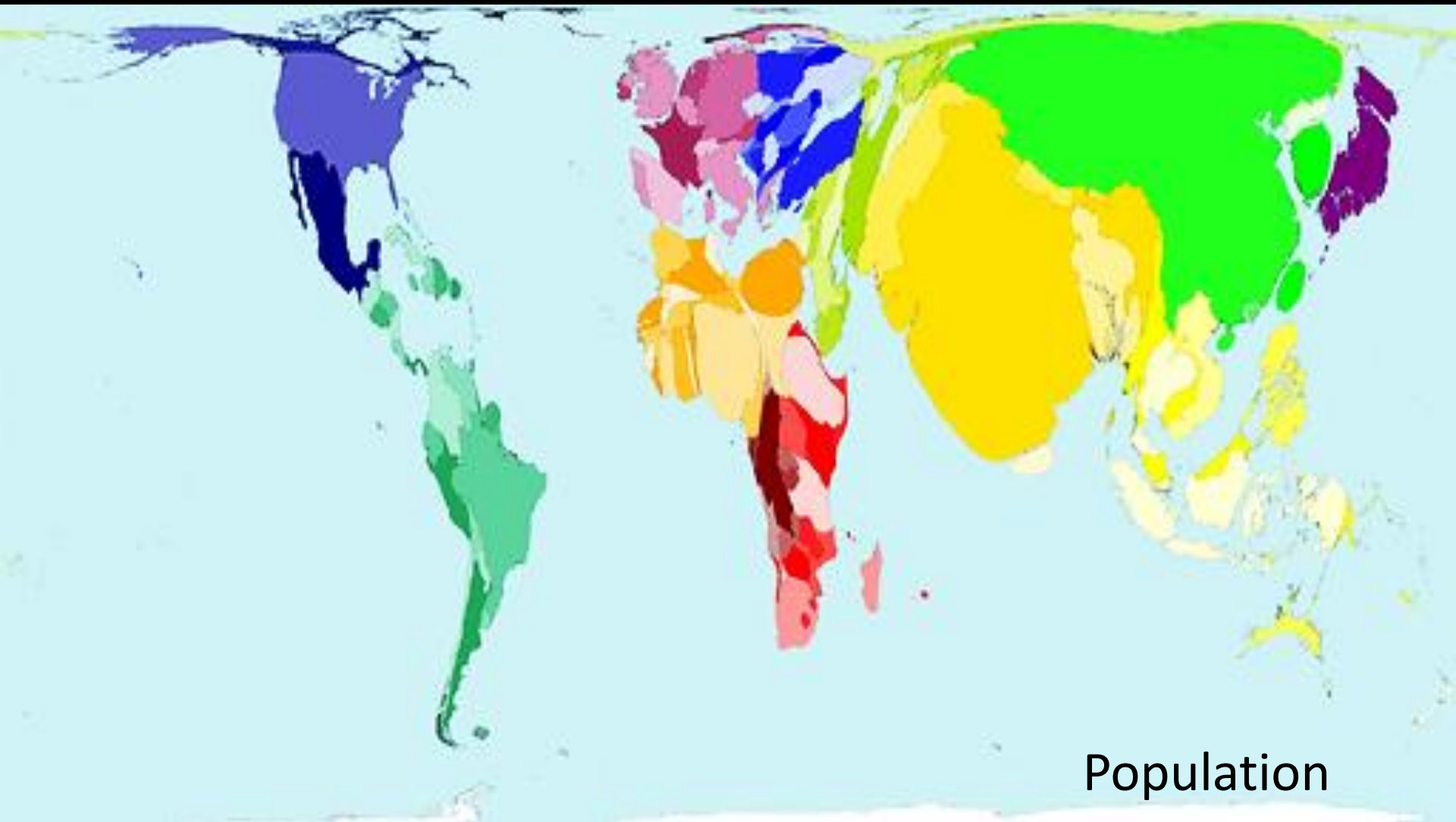


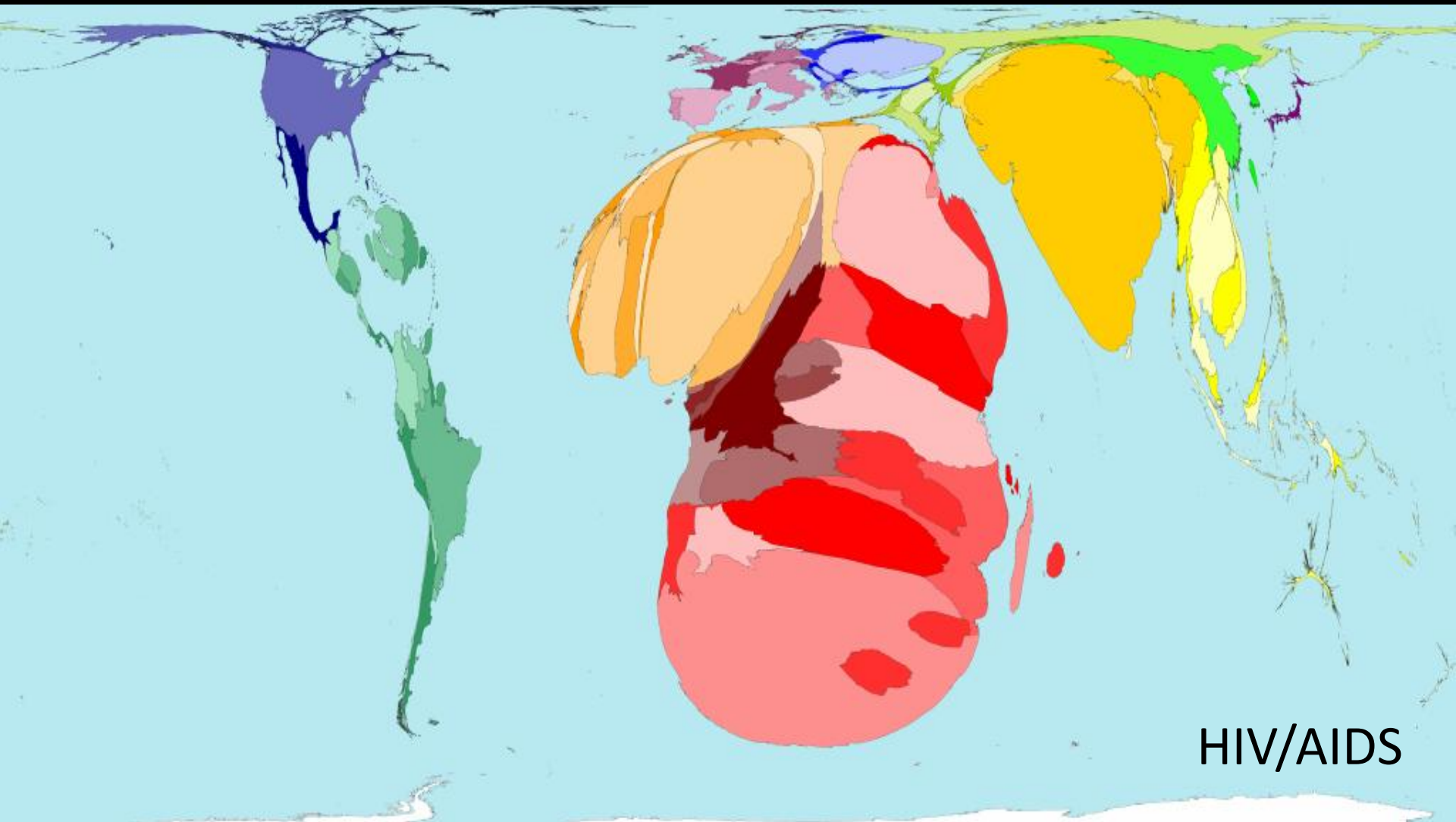
Asia
4.9 million





Geography

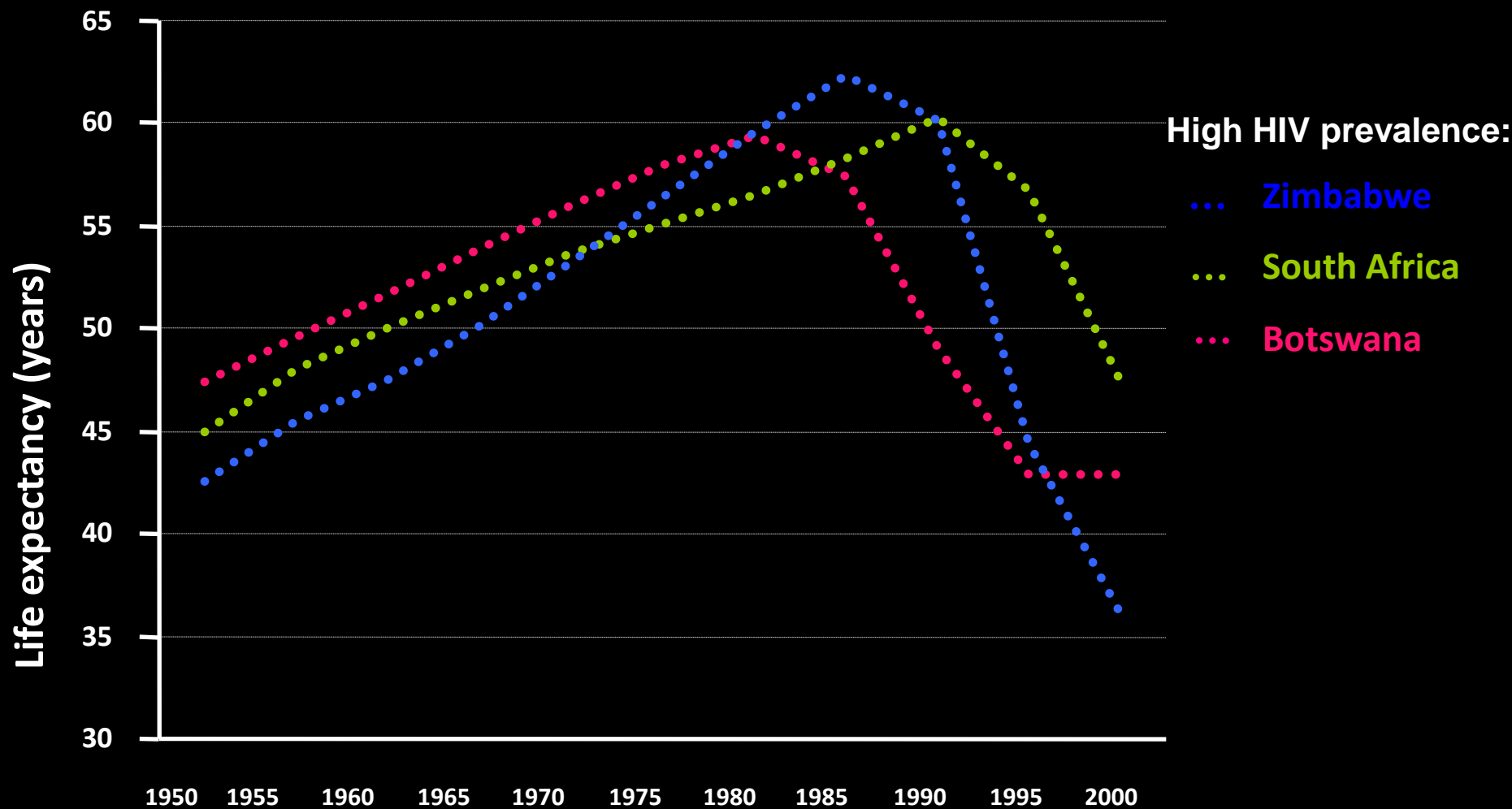




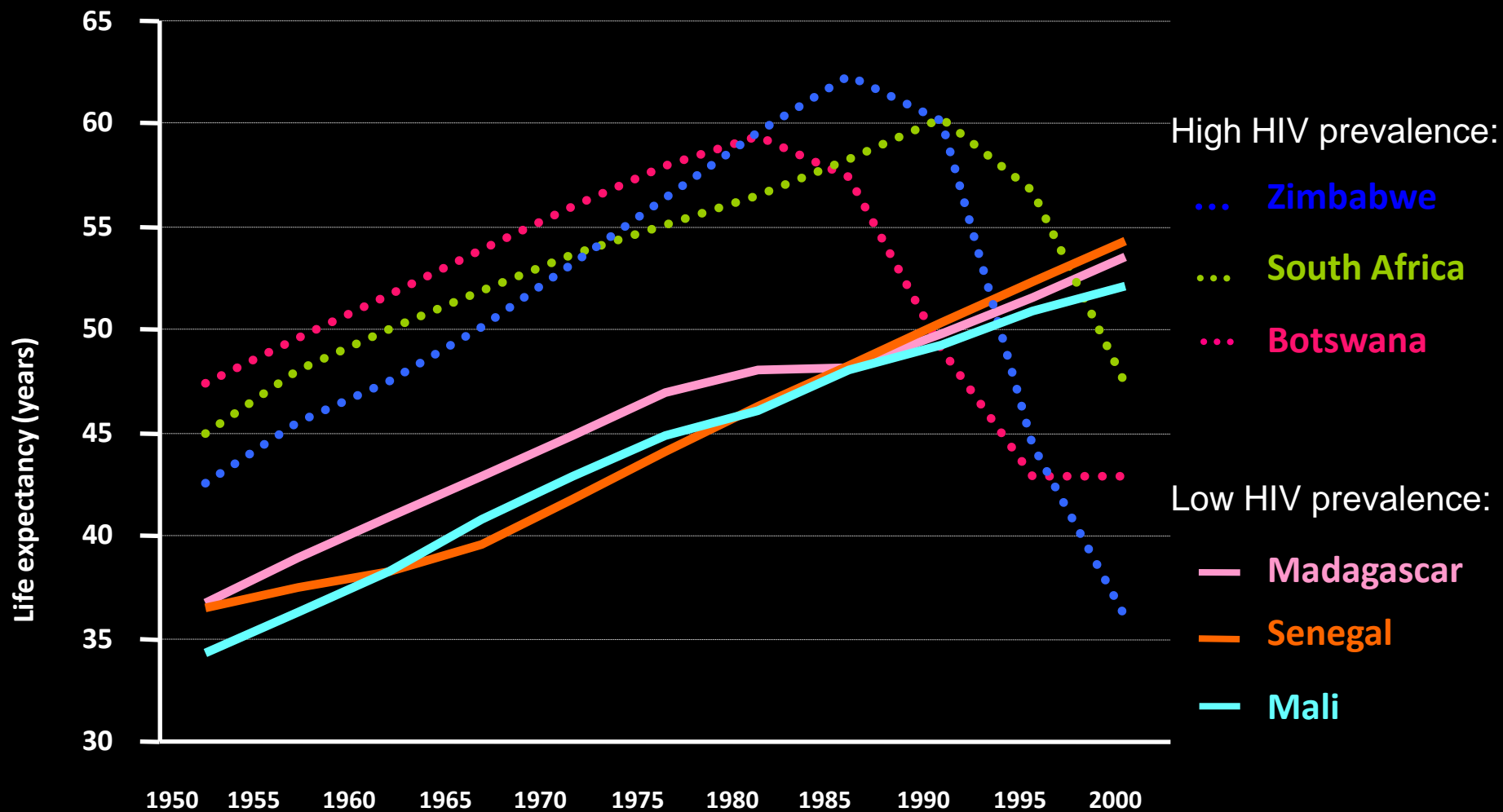
HIV/AIDS



Life Expectancy in Africa



Life Expectancy in Africa



One World One Hope

Vancouver 1996

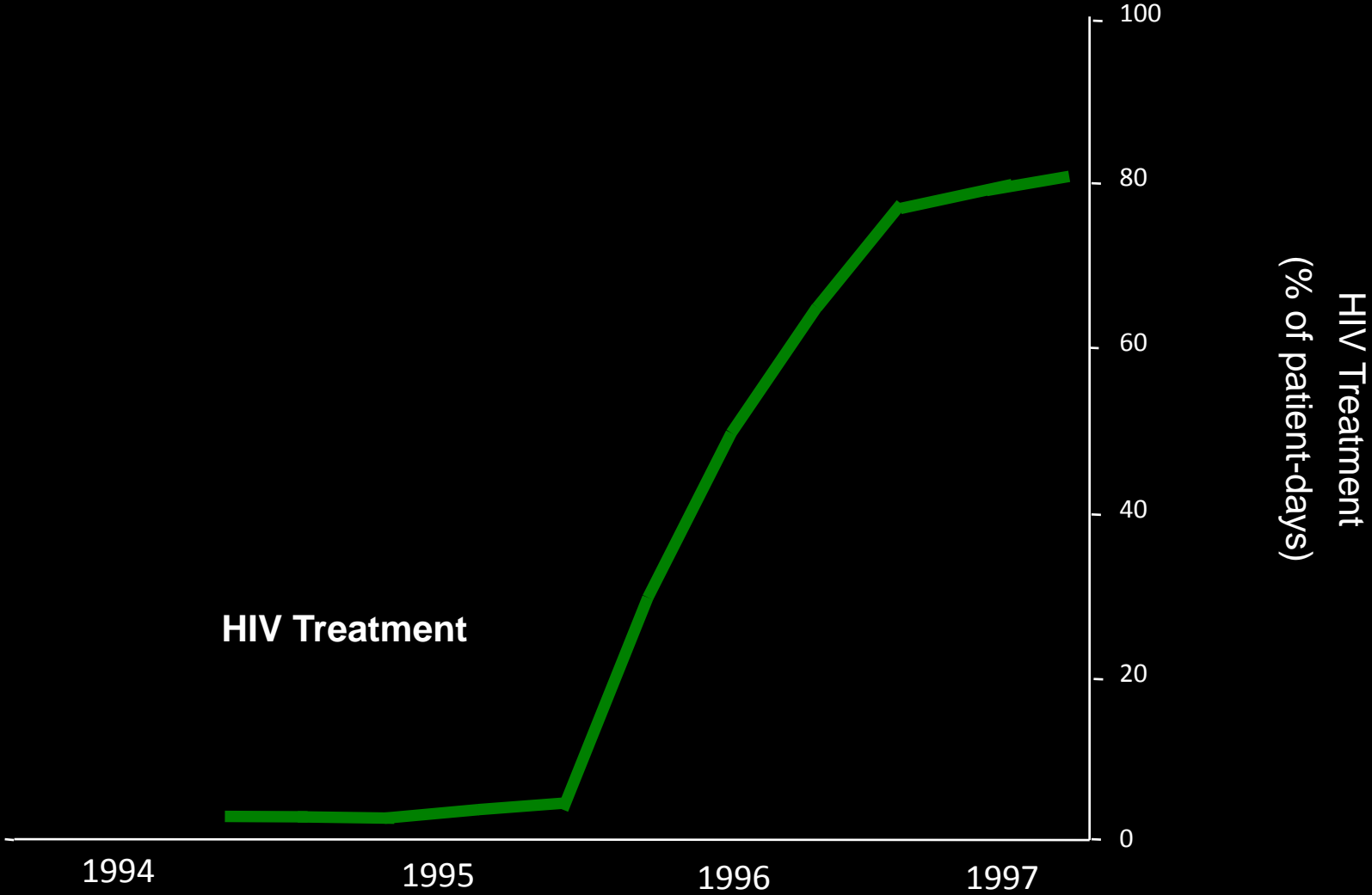


XI International
Conference
on AIDS
Vancouver, Canada
July 7-12, 1996

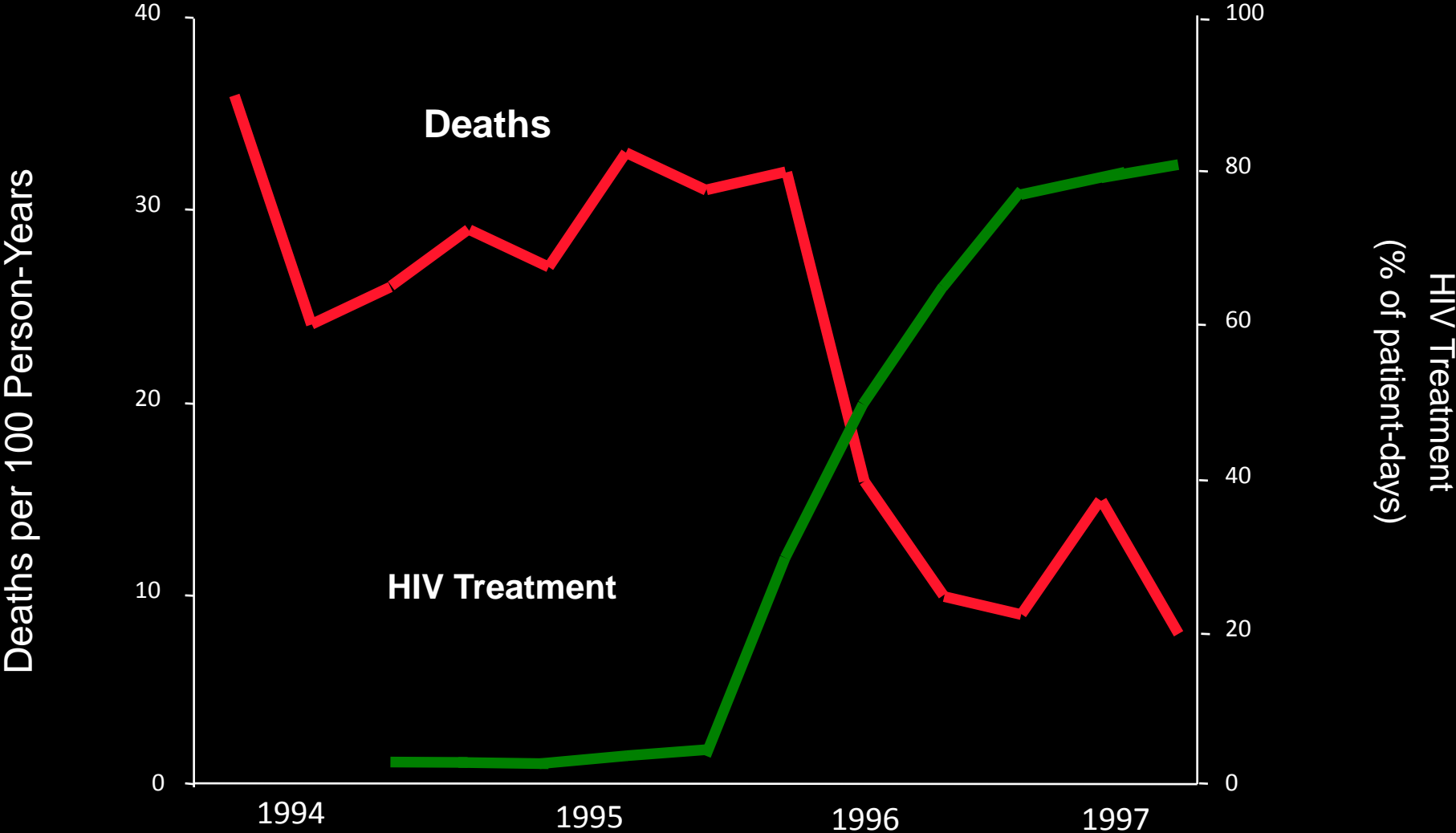
One World. **One Hope.**



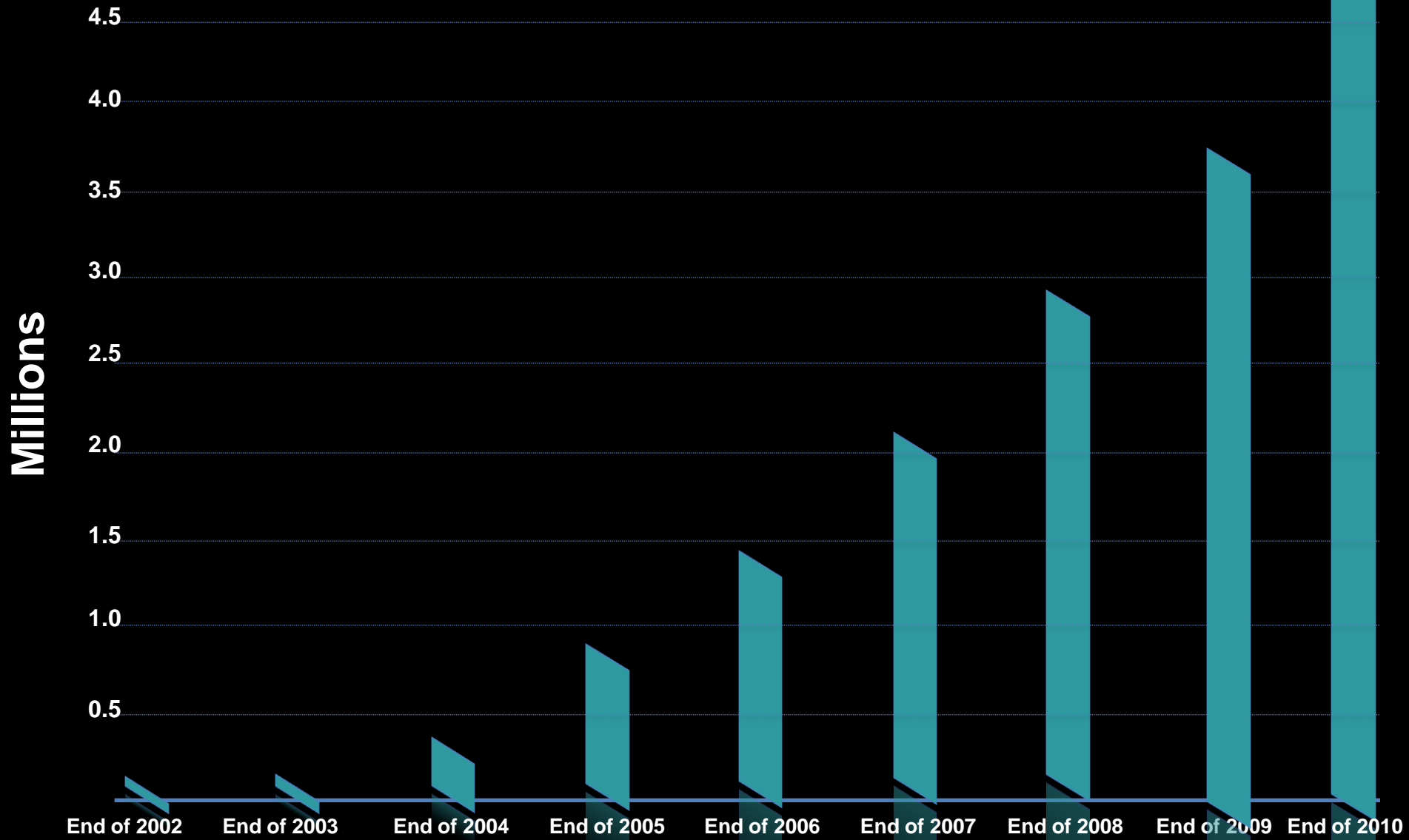
Expansion of Treatment and Deaths from HIV in the US



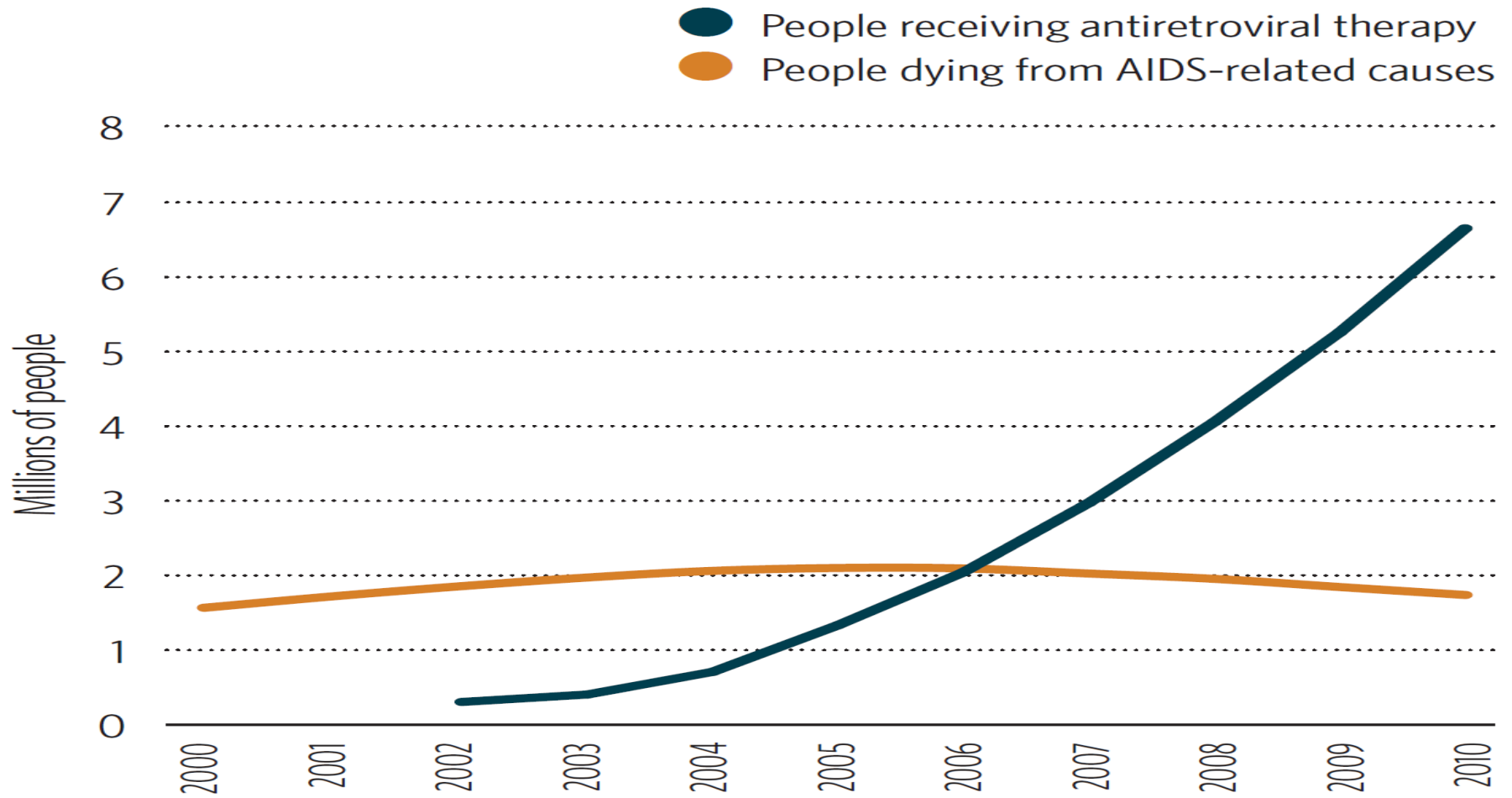
Expansion of Treatment and Deaths from HIV in the US



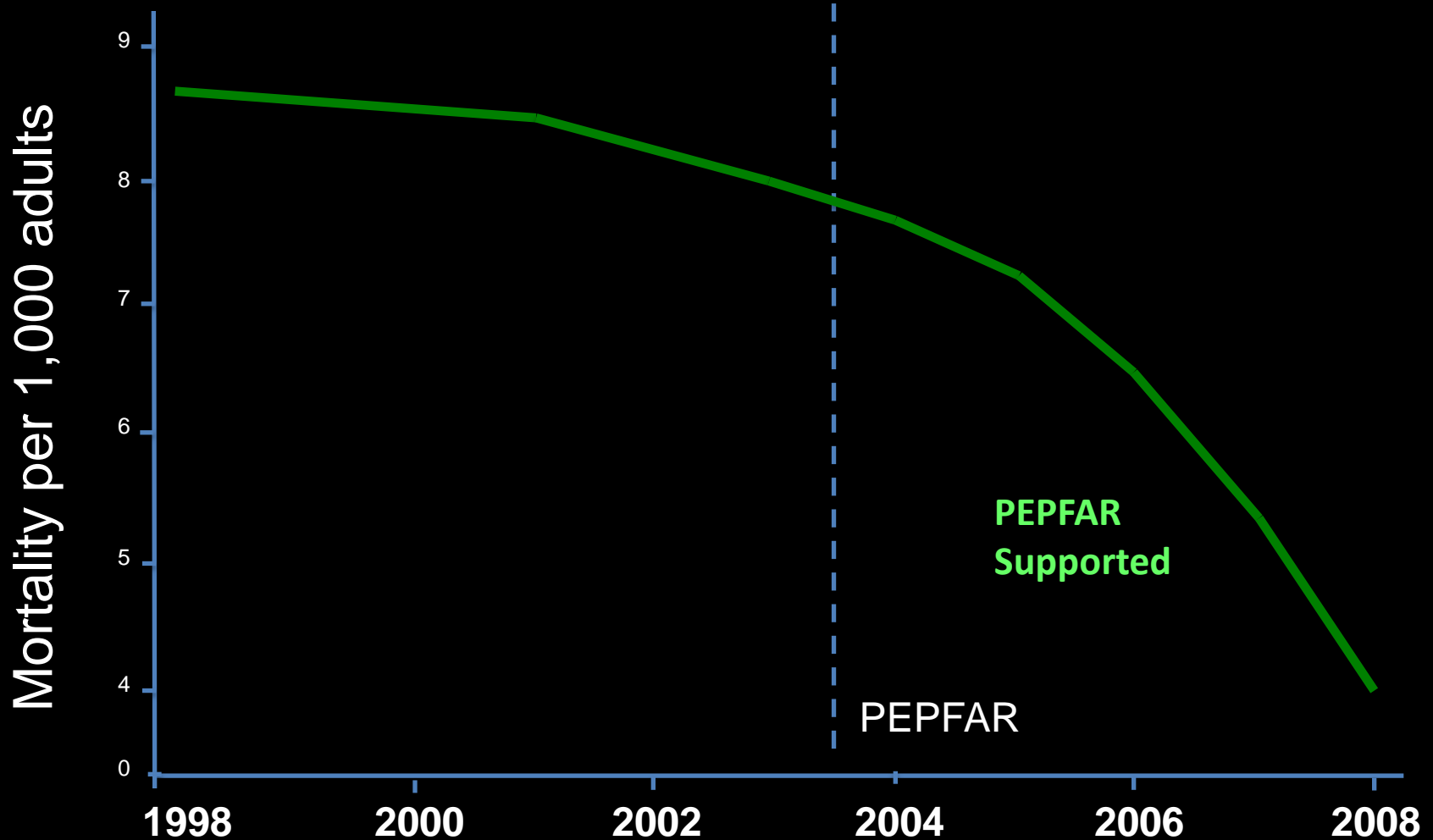
Global Scale-Up of HIV Treatment



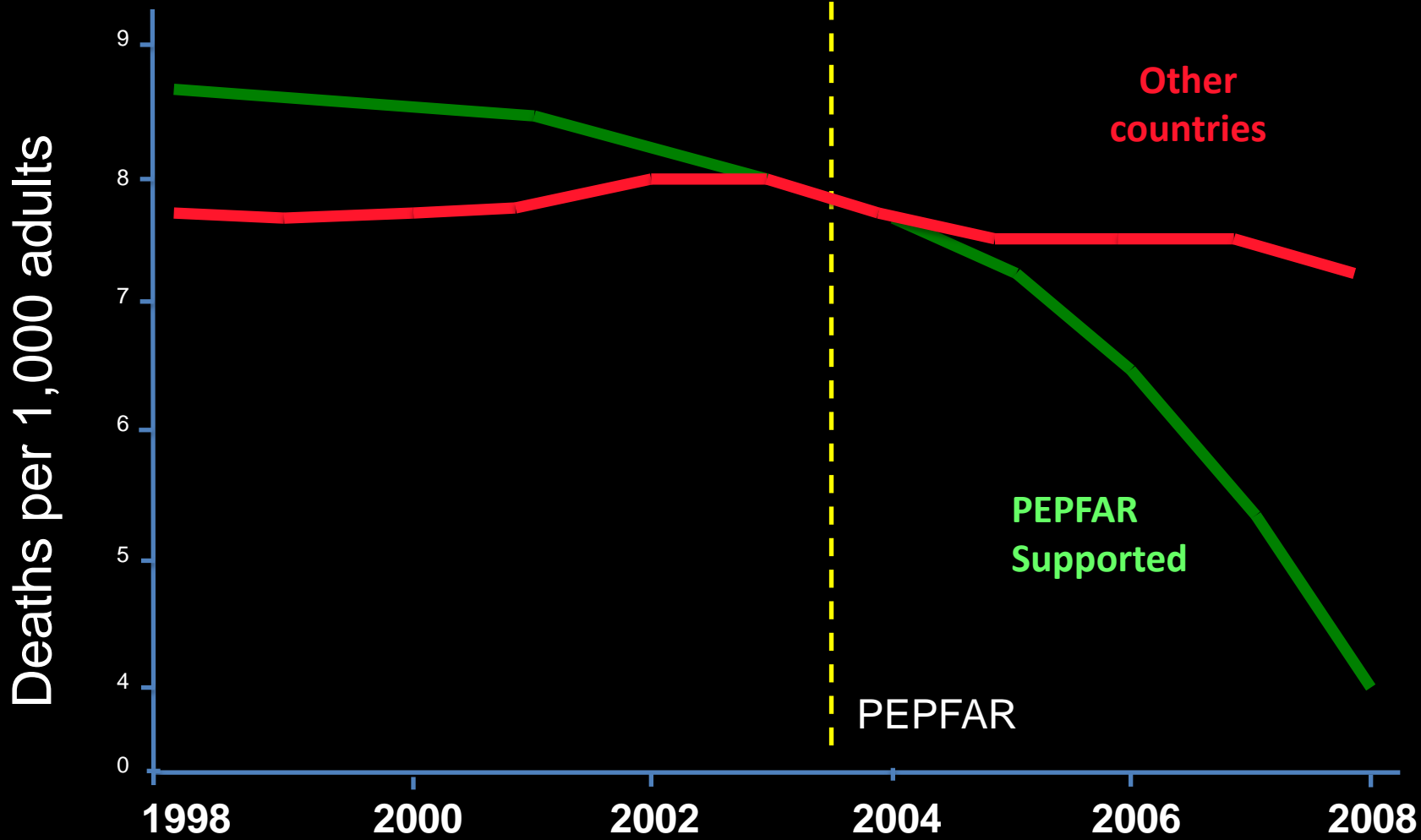
Scale-Up of ART & AIDS-Related Deaths



Deaths in PEPFAR-Supported Countries in Africa

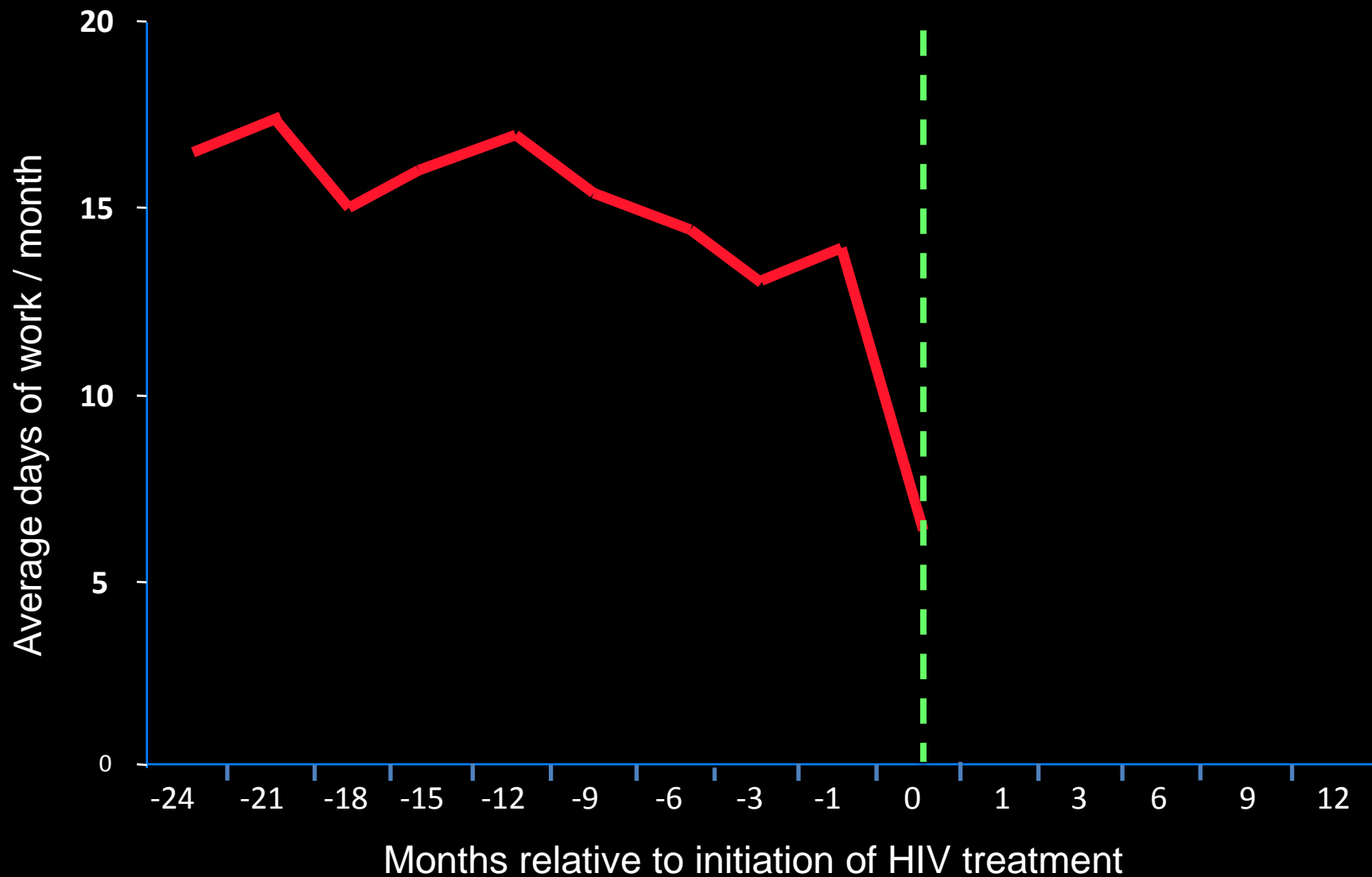


Deaths in PEPFAR-Supported Countries in Africa

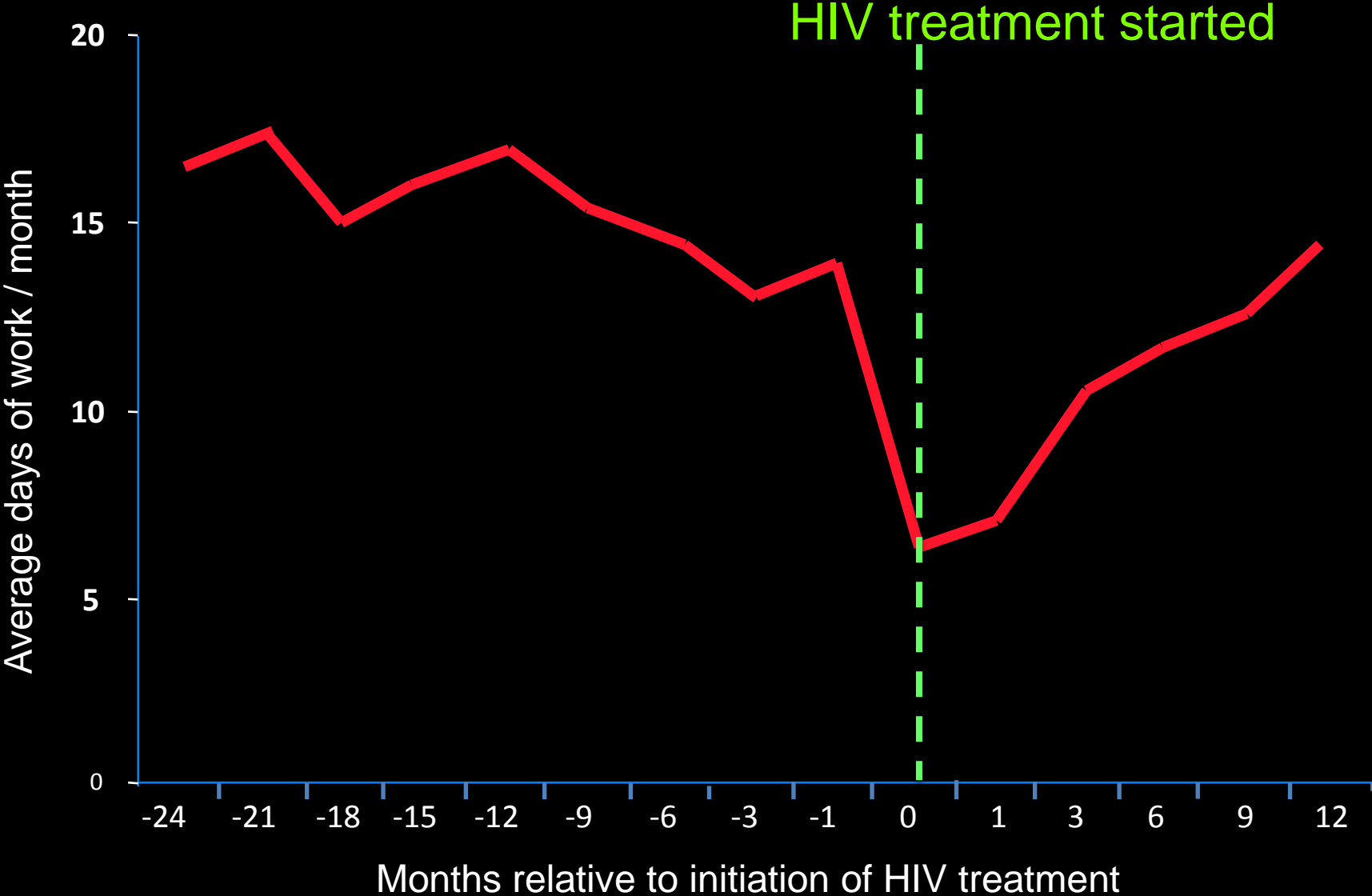


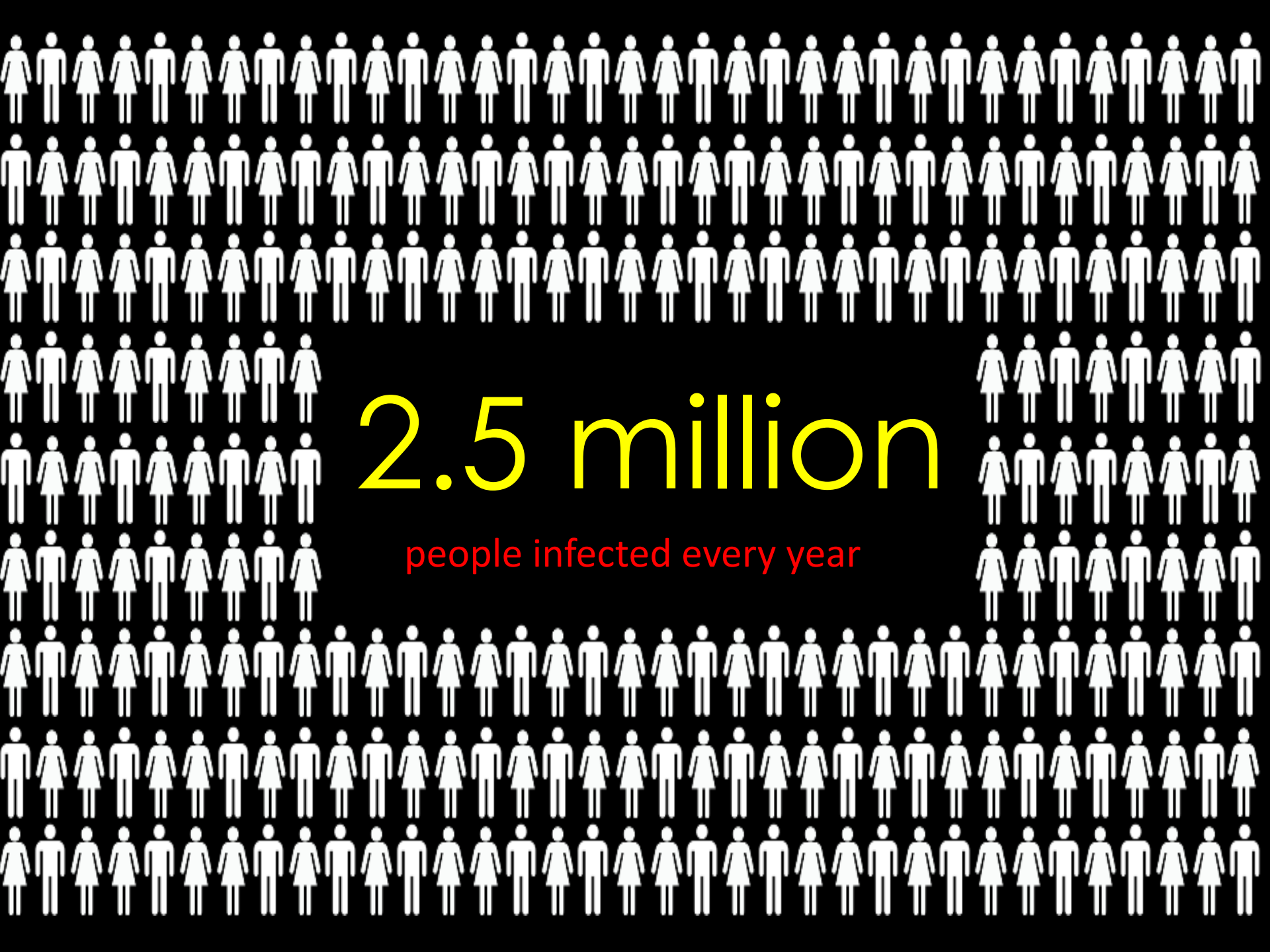
Adapted Bendavid et al. CROI 2012

HIV Treatment and Worker Productivity



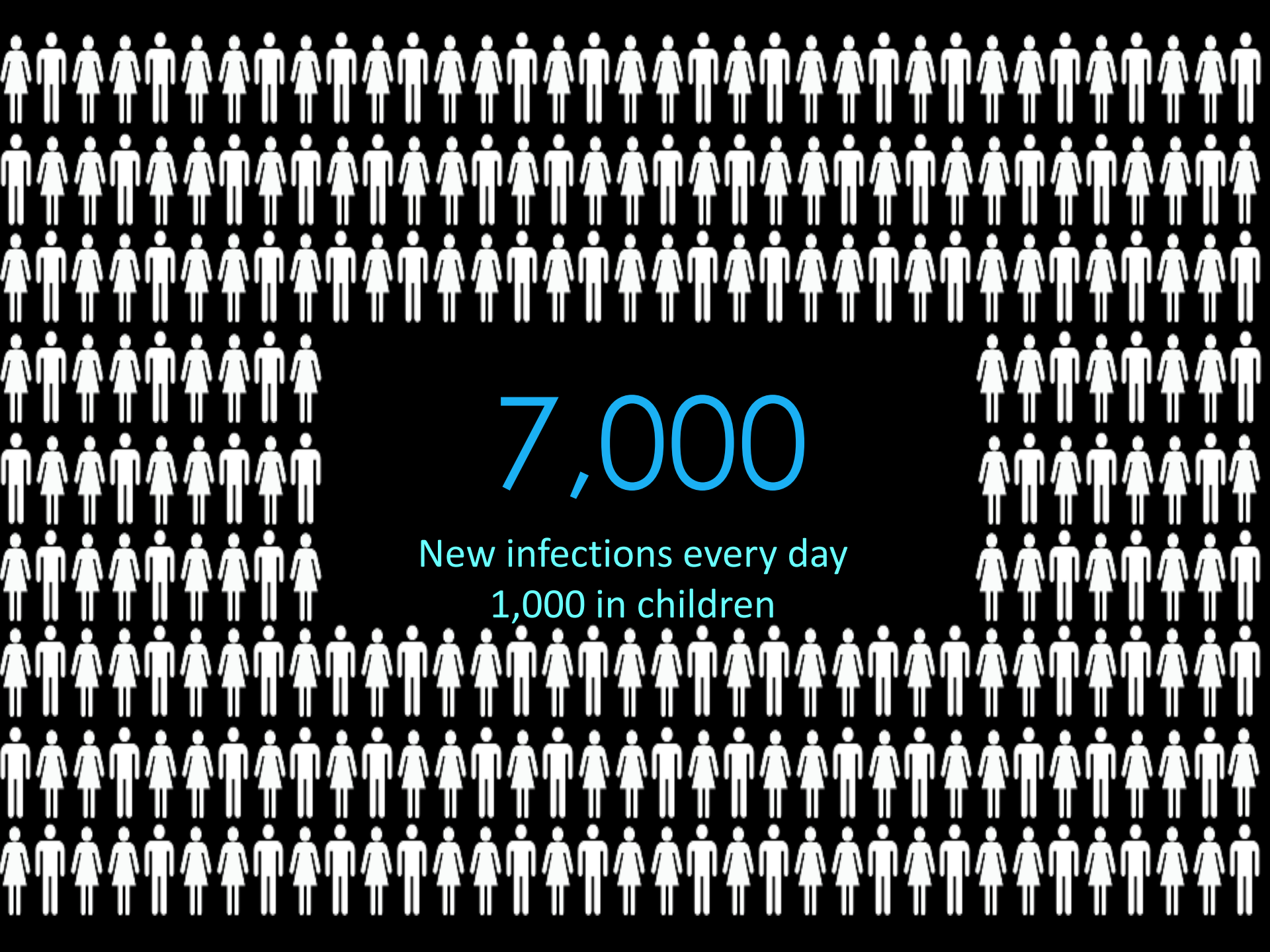
HIV Treatment and Worker Productivity





2.5 million

people infected every year

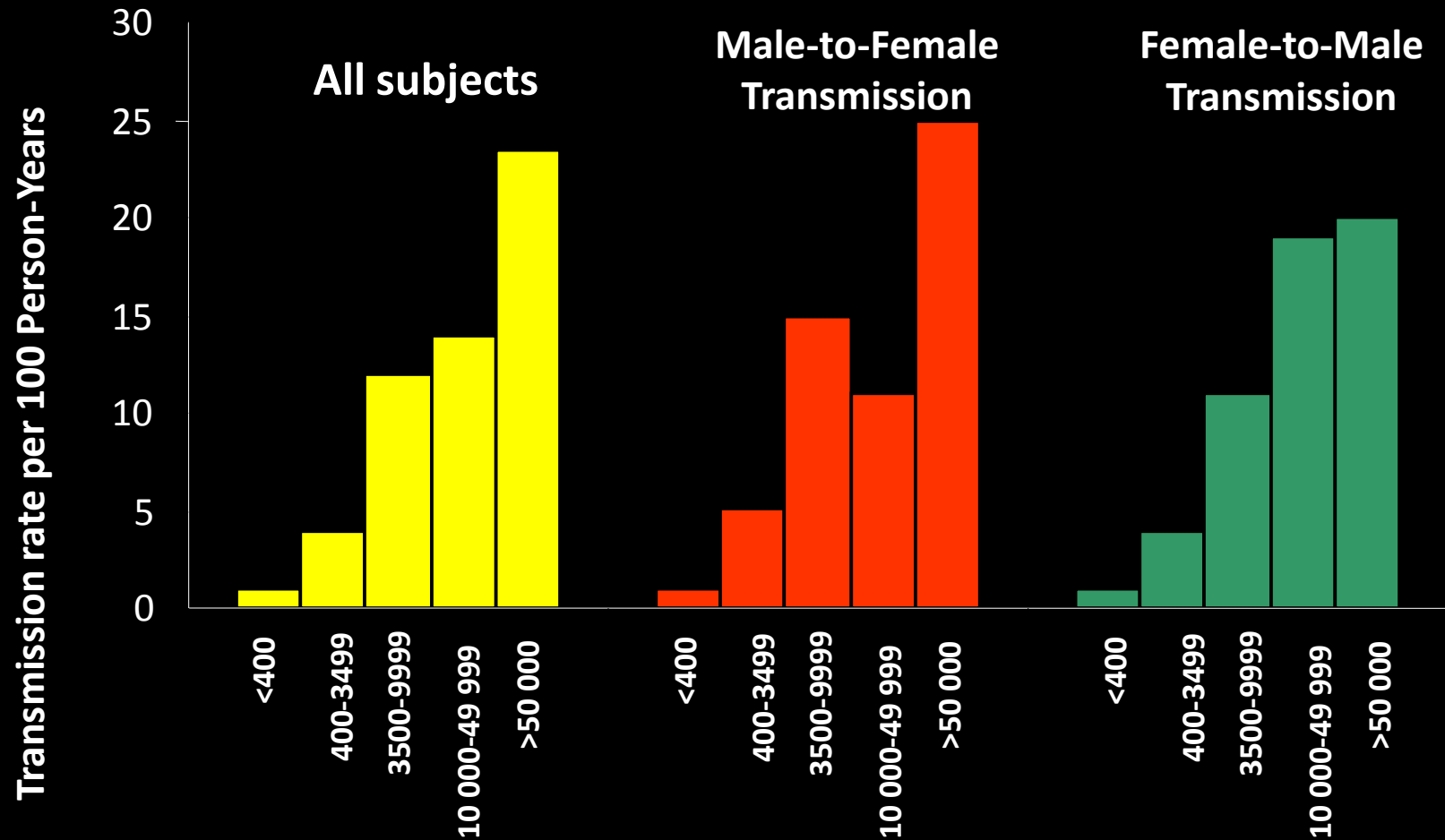


7,000

New infections every day
1,000 in children

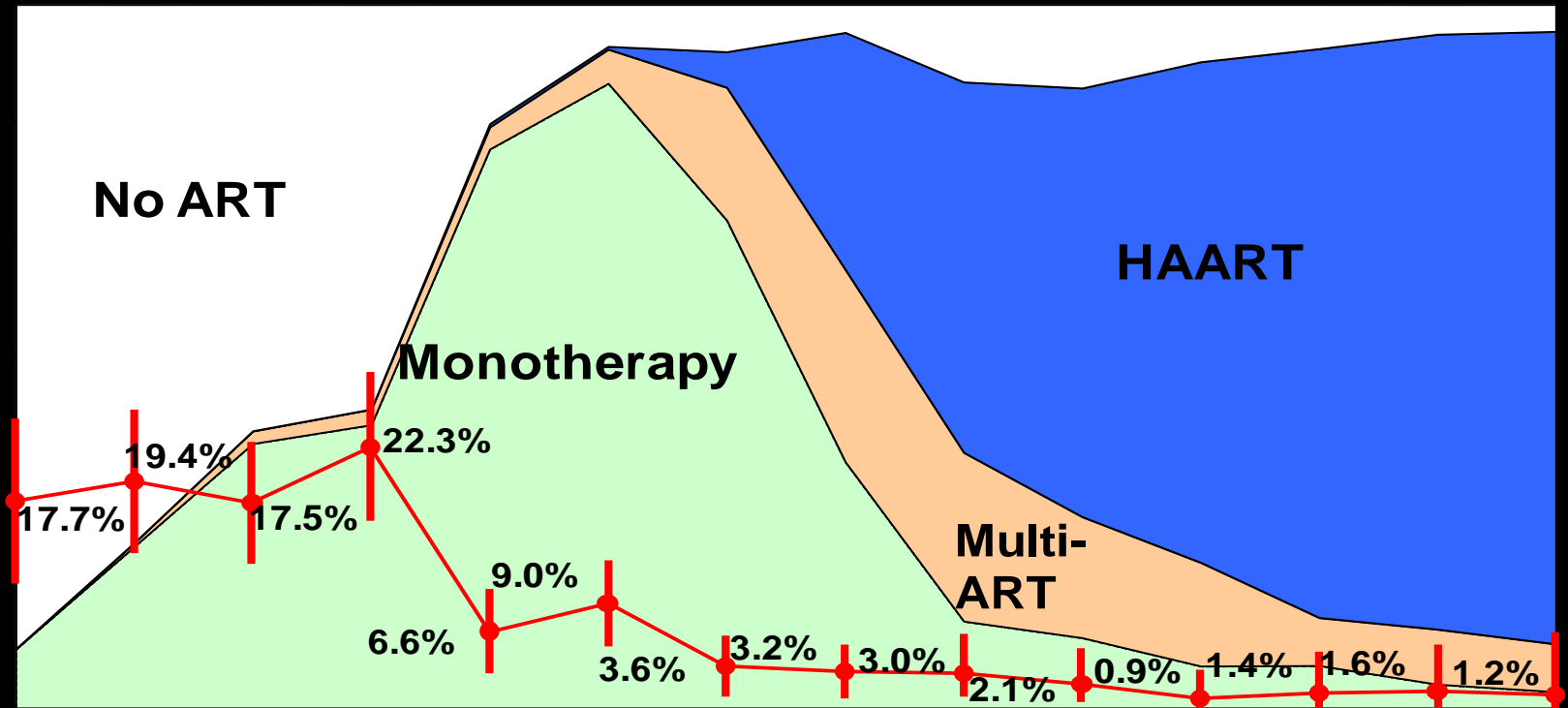
We can't treat our way out of this epidemic

Plasma HIV RNA Levels and HIV Rates in Discordant Couples

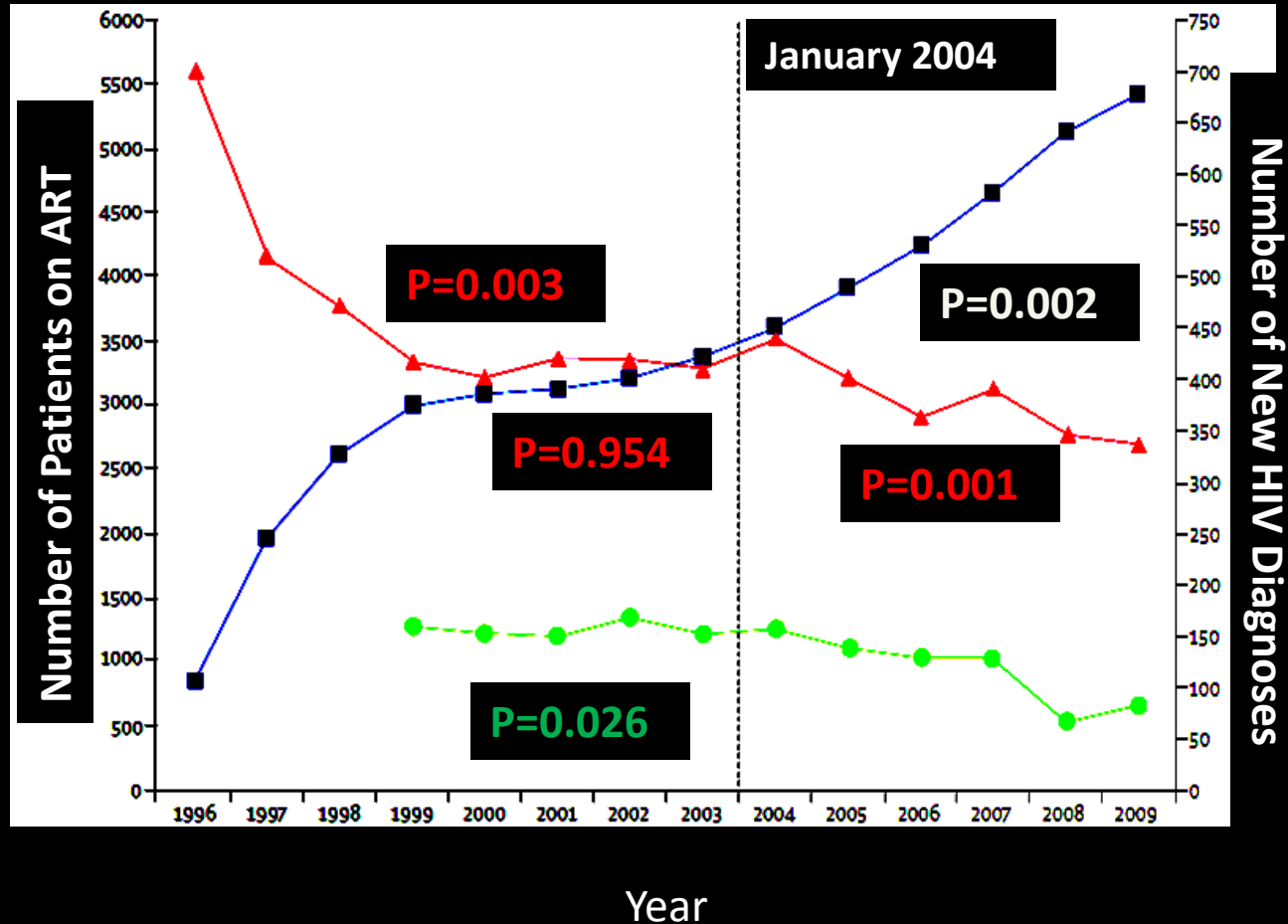


Viral load (HIV-1 RNA copies/ml) and HIV transmission

Maternal ART and Perinatal HIV Transmission--US WITS: 1990-2004



ART Use and New HIV Diagnoses-- British Columbia, Canada



New HIV Diagnoses (All)

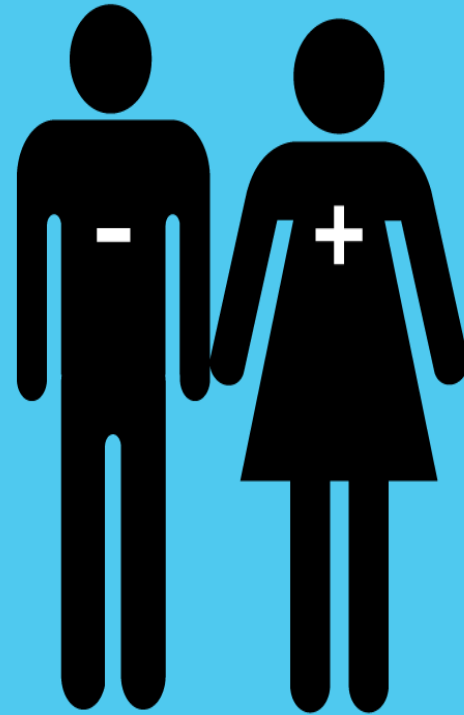
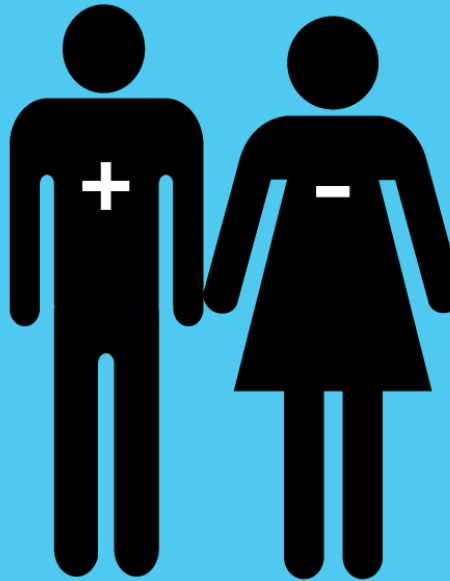


On ART



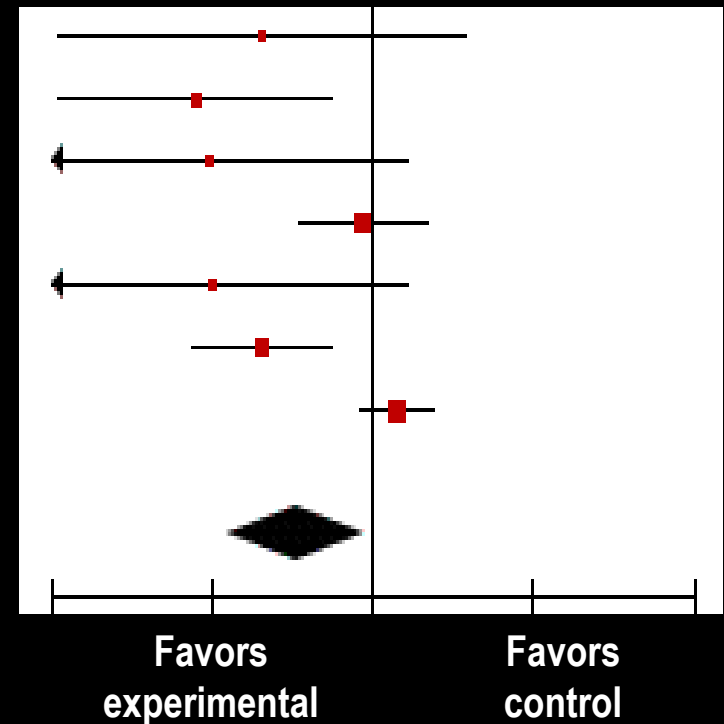
New HIV Diagnoses (ever IDU)

Sero-Discordant Couples



Use of ART and HIV Incidence: Observational Studies in Discordant Couples

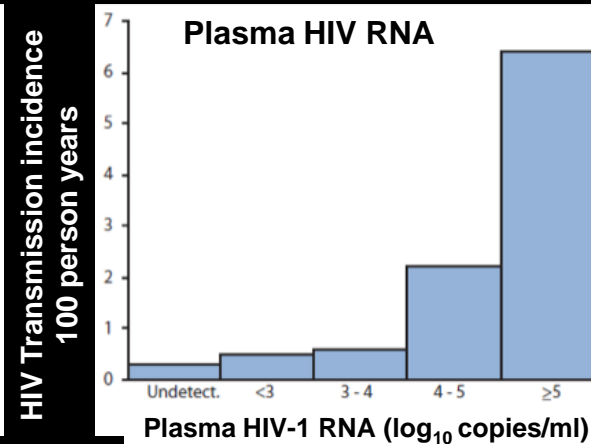
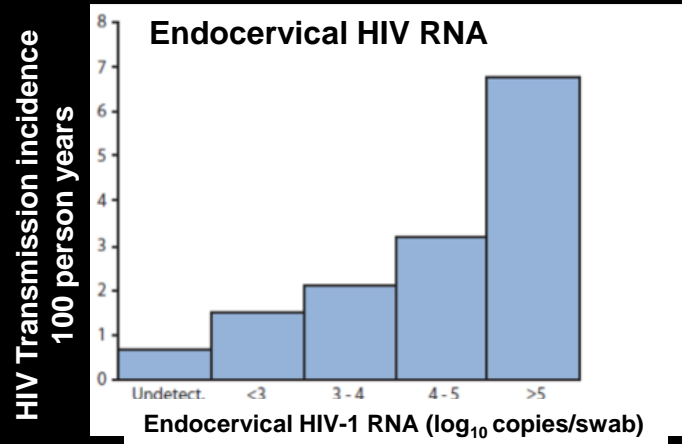
Study or Subgroup	Rate Ratio (95% CI)
Del Romero 2010	0.21 [0.01, 3.75]
Donnell 2010*	0.08 [0.01, 0.57]
Melo 2008	0.10 [0.01, 1.67]
Musicco 1994	0.88 [0.36, 2.16]
Reynolds 2011	0.10 [0.01, 1.64]
Sullivan 2009	0.21 [0.08, 0.56]
Wang 2010	1.44 [0.85, 2.44]
TOTAL	0.34 [0.13, 0.92]



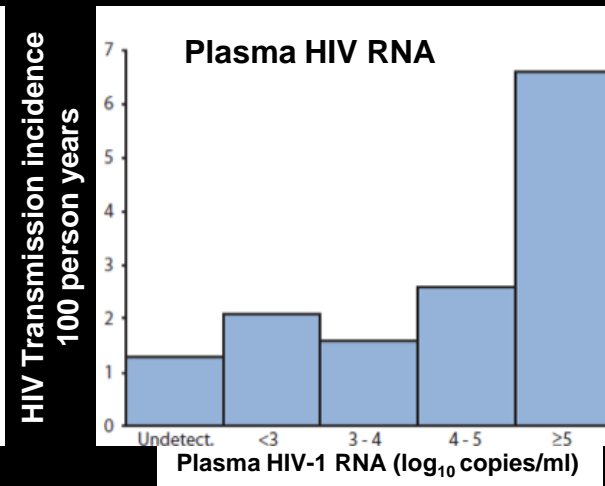
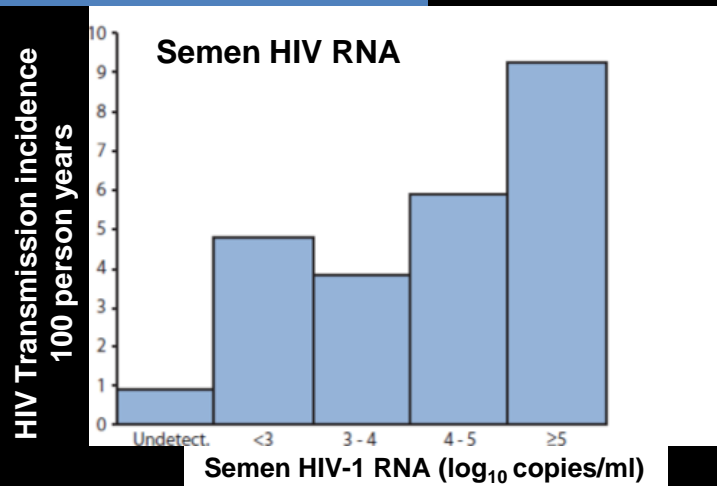
* Linked transmissions

Genital and Plasma HIV RNA and Risk of HIV Transmission

Female-Male HIV Transmission



Male-Female HIV Transmission



HPTN 052 Study: Design



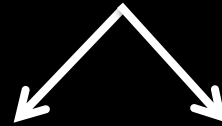
HIV-infected

CD4 350 to 550 cells/ μ L

HIV discordant partner



Randomization



Immediate ART
350-550 cells/ μ L

Deferred ART
CD4 <250>200

↓ Couples received intensive counseling
on risk reduction and use of condoms ↓

Primary Transmission Endpoint:

Linked transmissions

Primary Clinical Endpoint:

WHO stage 4, Pulmonary TB,
Severe bacterial infection or Death

HPTN 052 Study: Key Prevention Finding



1,763 sero-discordant couples (97% heterosexual) HIV infected partners: 890 men, 873 women

39 HIV Transmissions

28 linked HIV transmissions

11 unlinked

Immediate ART:
1 transmission

Deferred ART:
27 transmissions

✓ 96% Protection

The New York Times

Early H.I.V. Therapy Sharply Curbs Transmission

By DONALD G. McNEIL Jr.
Published: May 12, 2011

On Thursday, Dr. Fauci

from the
director
2005 he

EDITORIAL

When T

Published: May

The discovery
AIDS virus
and nations
troubling is

INSIDE THIS WEEK: TECHNOLOGY QUARTER

The Economist

JUNE 4TH-10TH 2011 Economist.com

- The trap for Turkey
- Wall Street's plumbing p
- Lady Gaga, Mother Teres
- 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

23 December 2011 | \$10

Science

BREAKTHROUGH OF THE YEAR

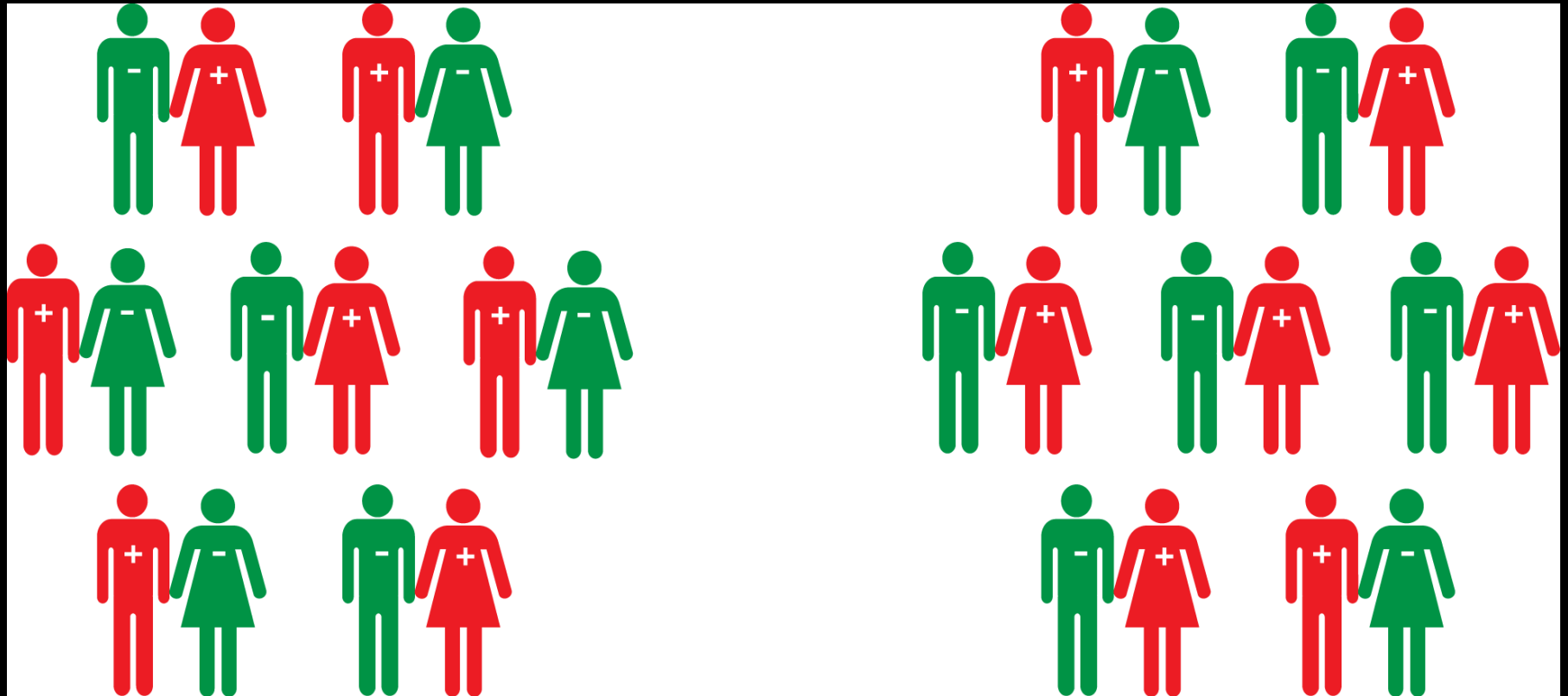
HIV Treatment as Prevention

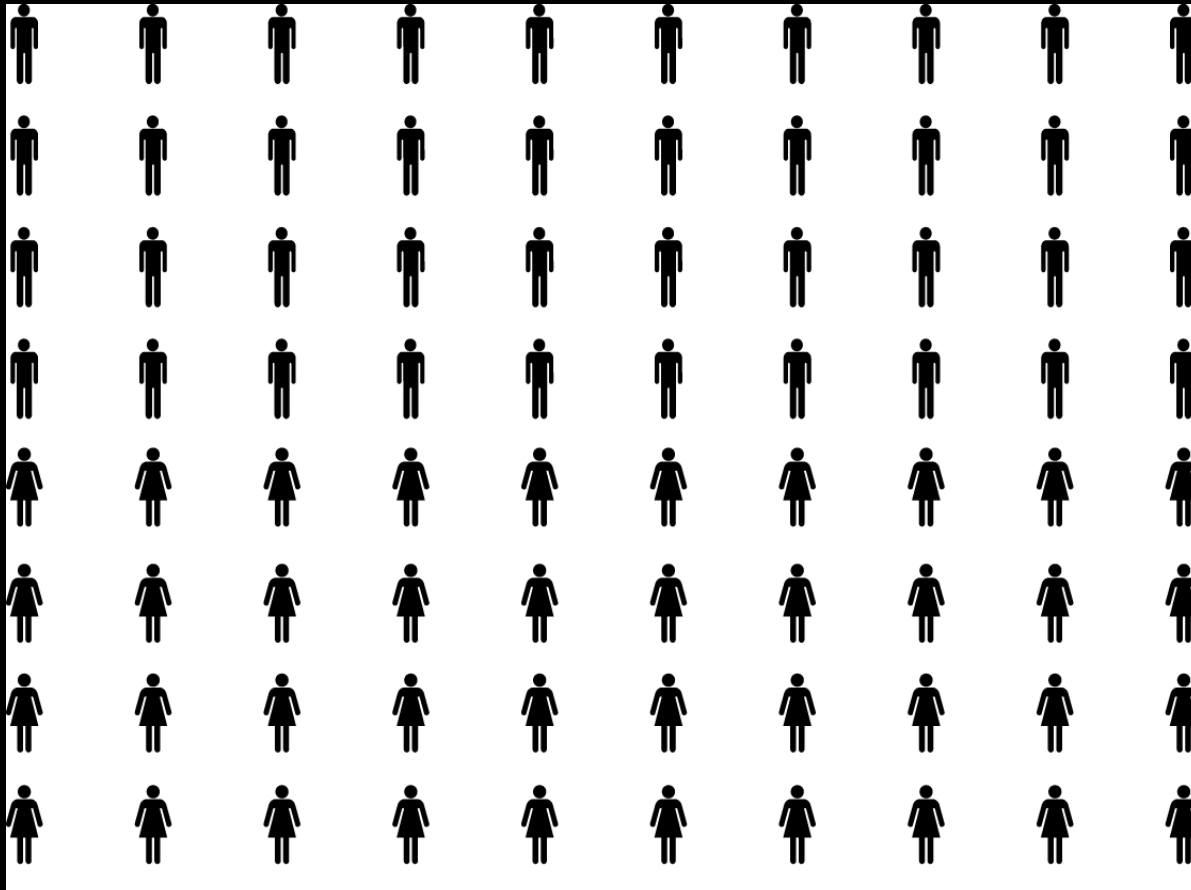


AAAS

We can treat our way out of this epidemic

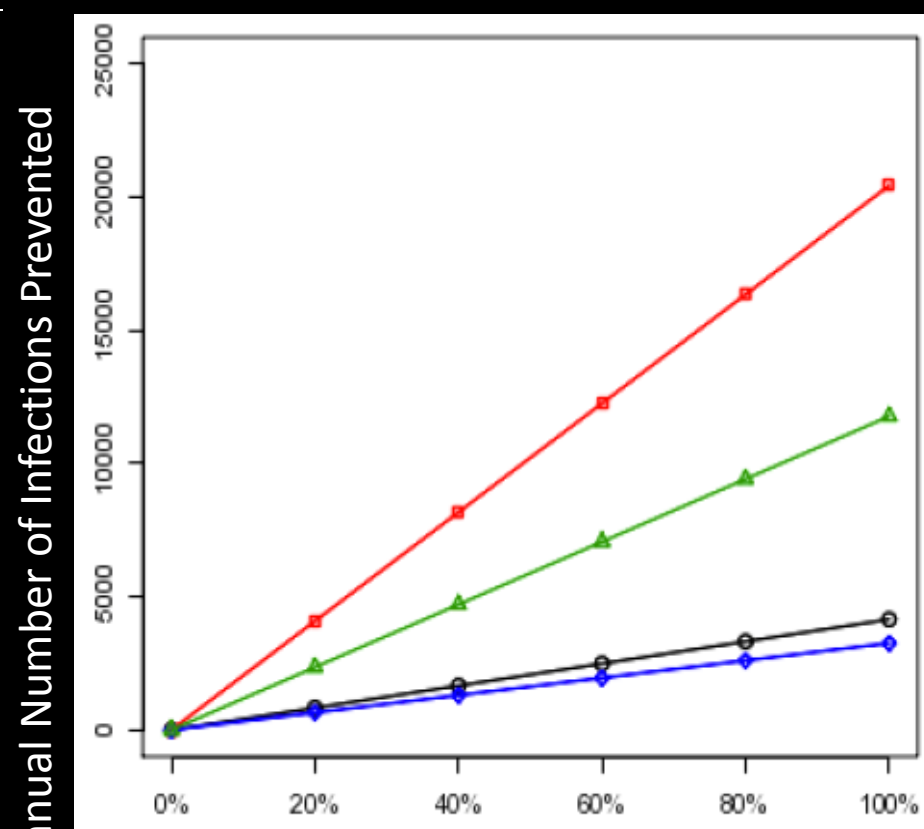
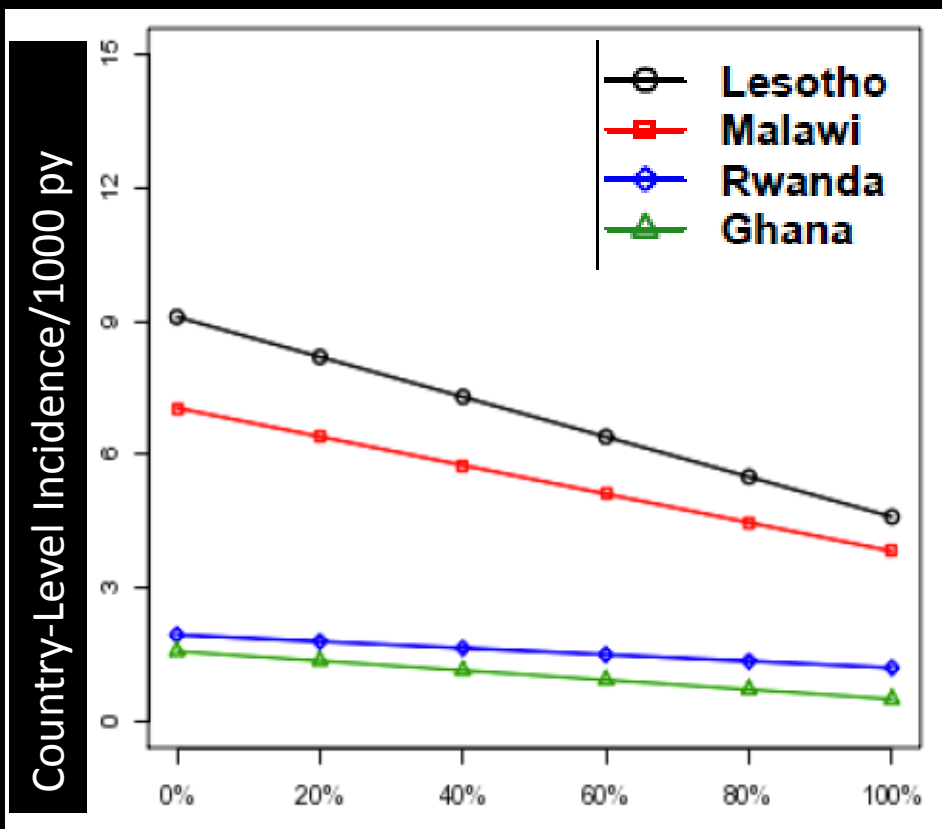
What would be the impact of treatment of discordant couples on the HIV Epidemic?





Country	Population	HIV prevalence	Percent discordant couples
Lesotho	2,067,000	19.5%	13.6%
Rwanda	9,998,000	1.7%	3.1%
Malawi	15,263,000	7.1%	9.7%
Ghana	23,837,000	0.9%	2%

Effect of ART for Discordant Couples on *HIV incidence* and *Number of Infections Prevented* at Population Level

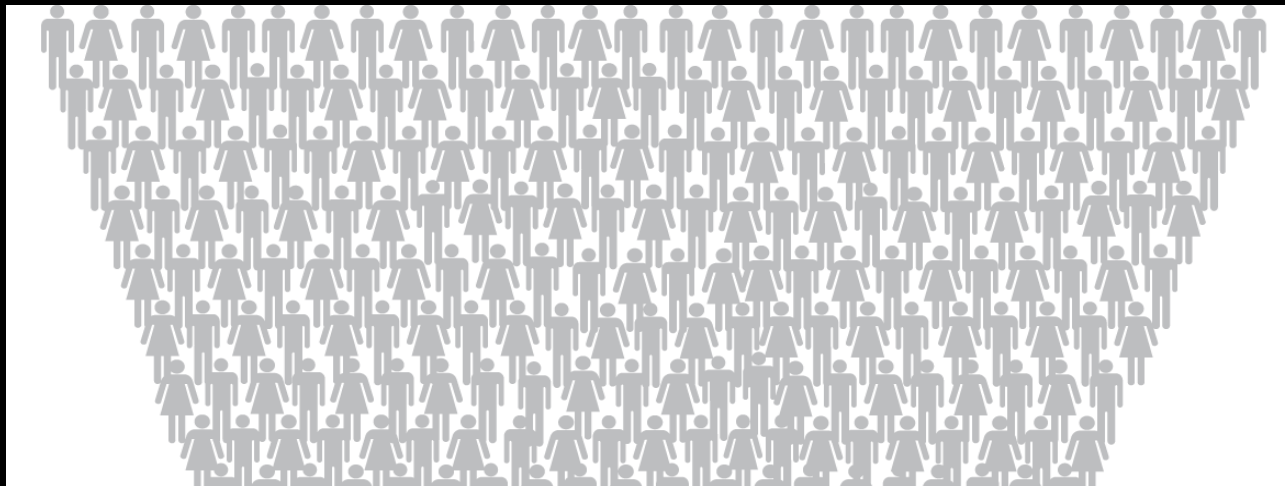


ART Coverage in Discordant Couples

ART Coverage in Discordant Couples

70% Stable Partners

What would be the effect of scale-up of HIV treatment on HIV epidemic?



Could widespread use of combination antiretroviral therapy eradicate HIV epidemics?

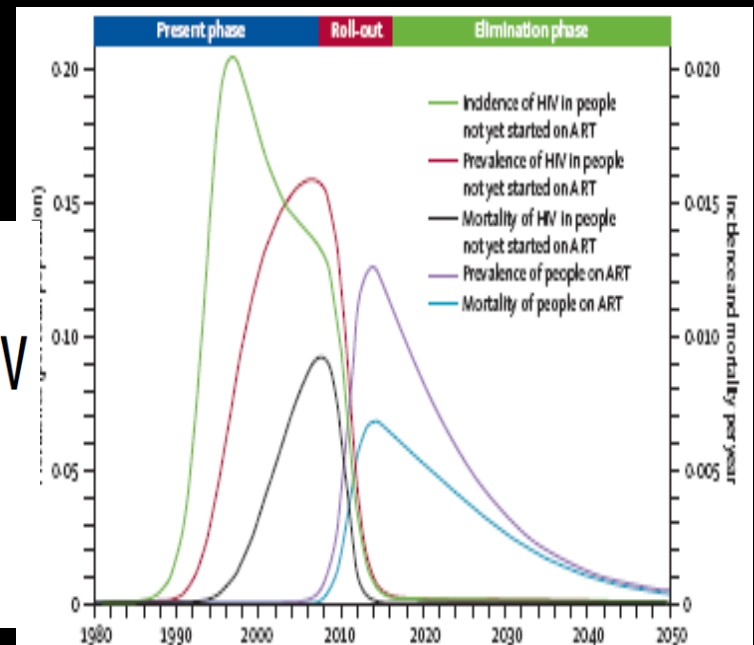
J X Velasco-Hernandez, H B Gershengorn, and S M Blower

Modelling the effect of combination antiretroviral treatments on HIV incidence

Matthew G. Law^a, Garrett Prestage^a, Andrew Grulich^a,
Paul Van de Ven^b and Susan Kippax^b

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

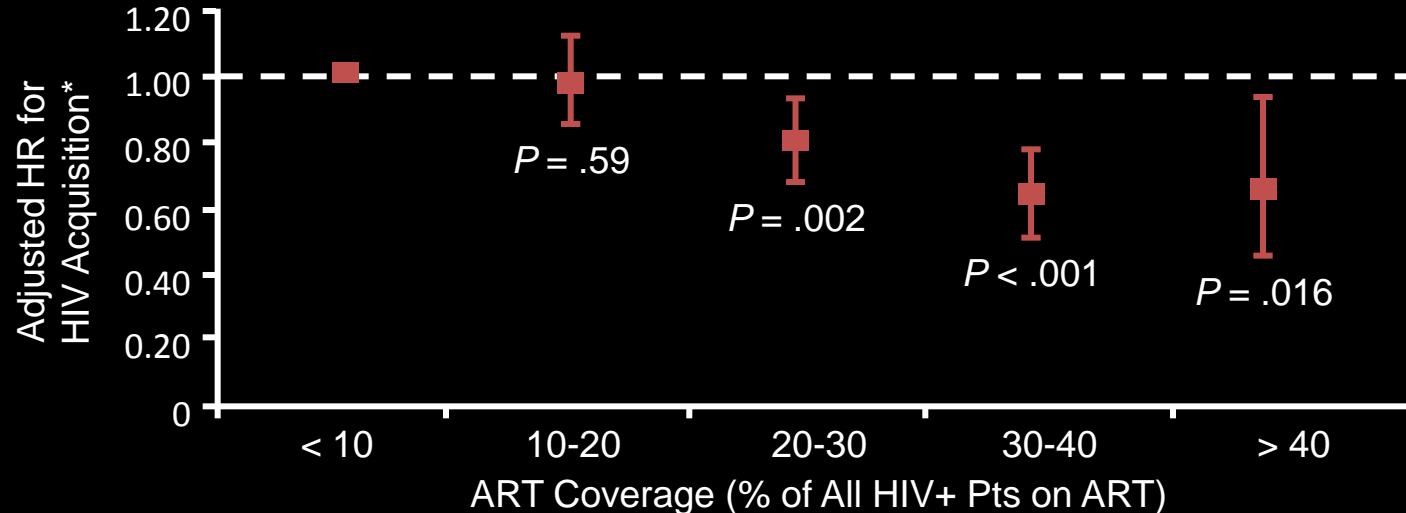


A Mathematical Model of Comprehensive Test-and-Treat Services and HIV Incidence among Men Who Have Sex with Men in the United States

Stephen W. Sorensen¹, Stephanie L. Sansom^{1*}, John T. Brooks¹, Gary Marks¹, Elizabeth M. Begier², Kate Buchacz¹, Elizabeth A. DiNenno¹, Jonathan H. Mermin¹, Peter H. Kilmarx¹

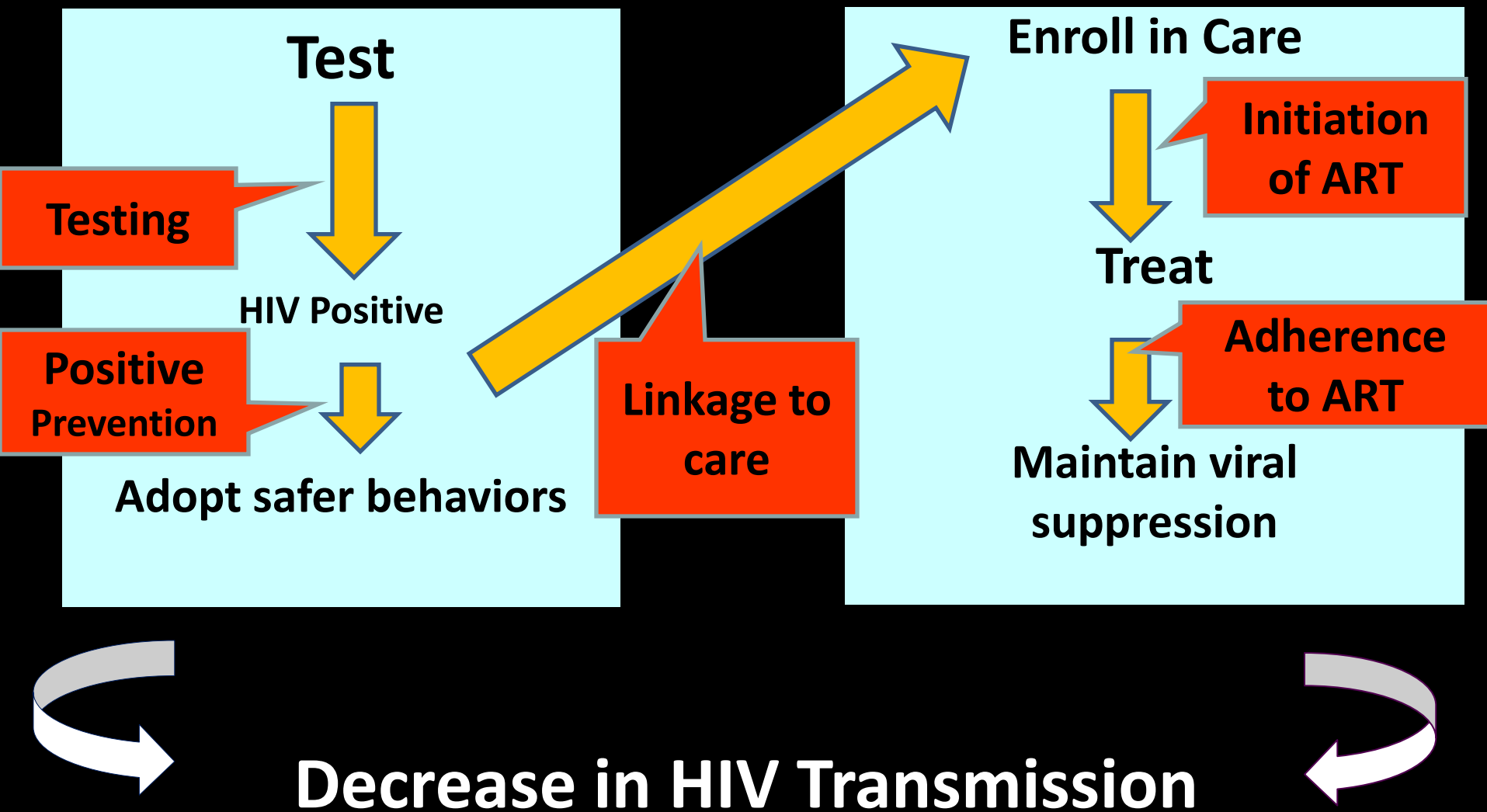
Lower Risk of HIV Acquisition With expanded ART Coverage

- Hlabisa, South Africa: rural community with 24% adult HIV prevalence
 - 20,000 pts started on ART since 2004
- 1413 seroconversions observed; HIV incidence estimated according to time-adjusted ART coverage in local community

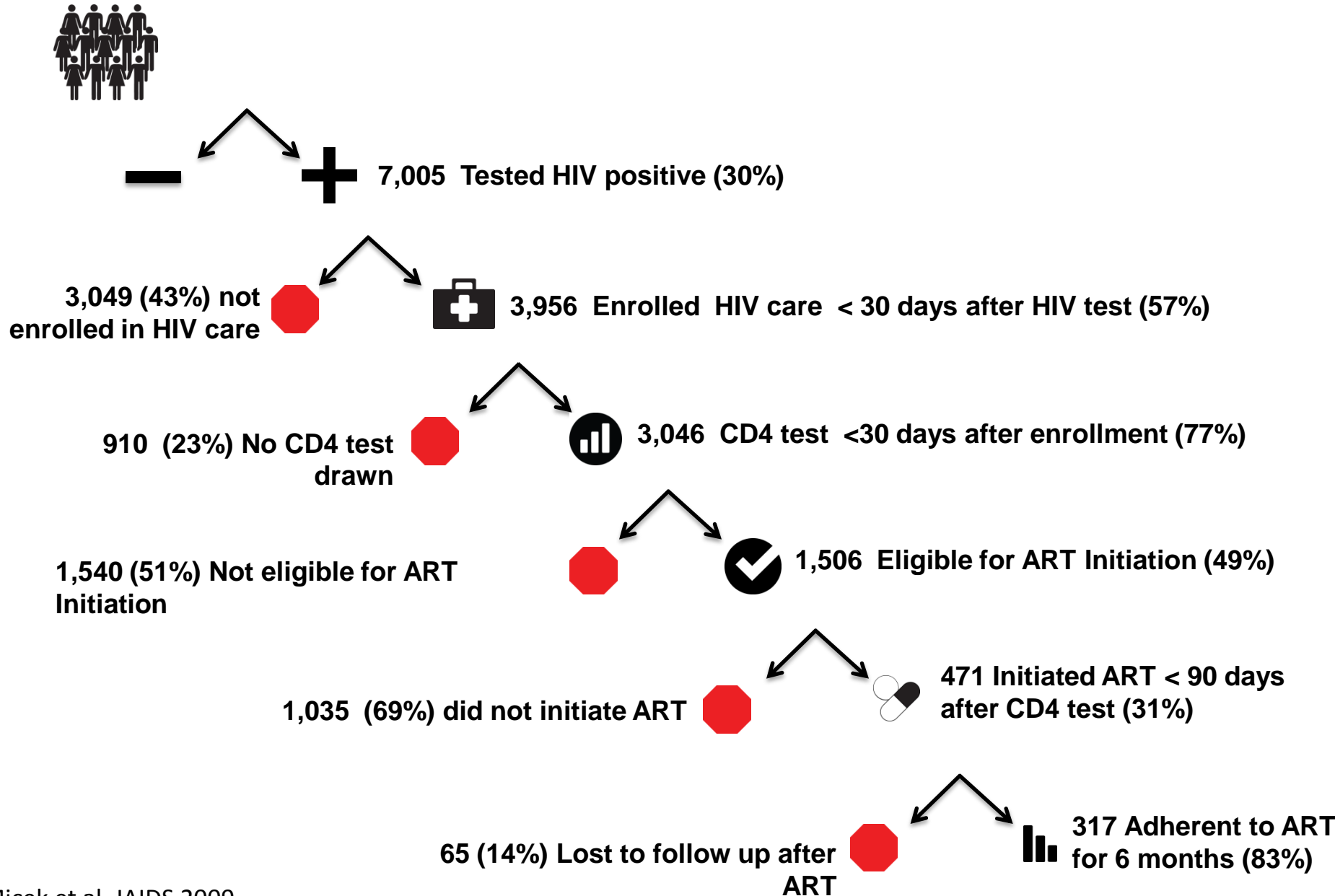


*Adjusted for age, sex, community-level HIV prevalence, urban vs rural locale, marital status, > 1 partner in last 12 mos, and household wealth index.

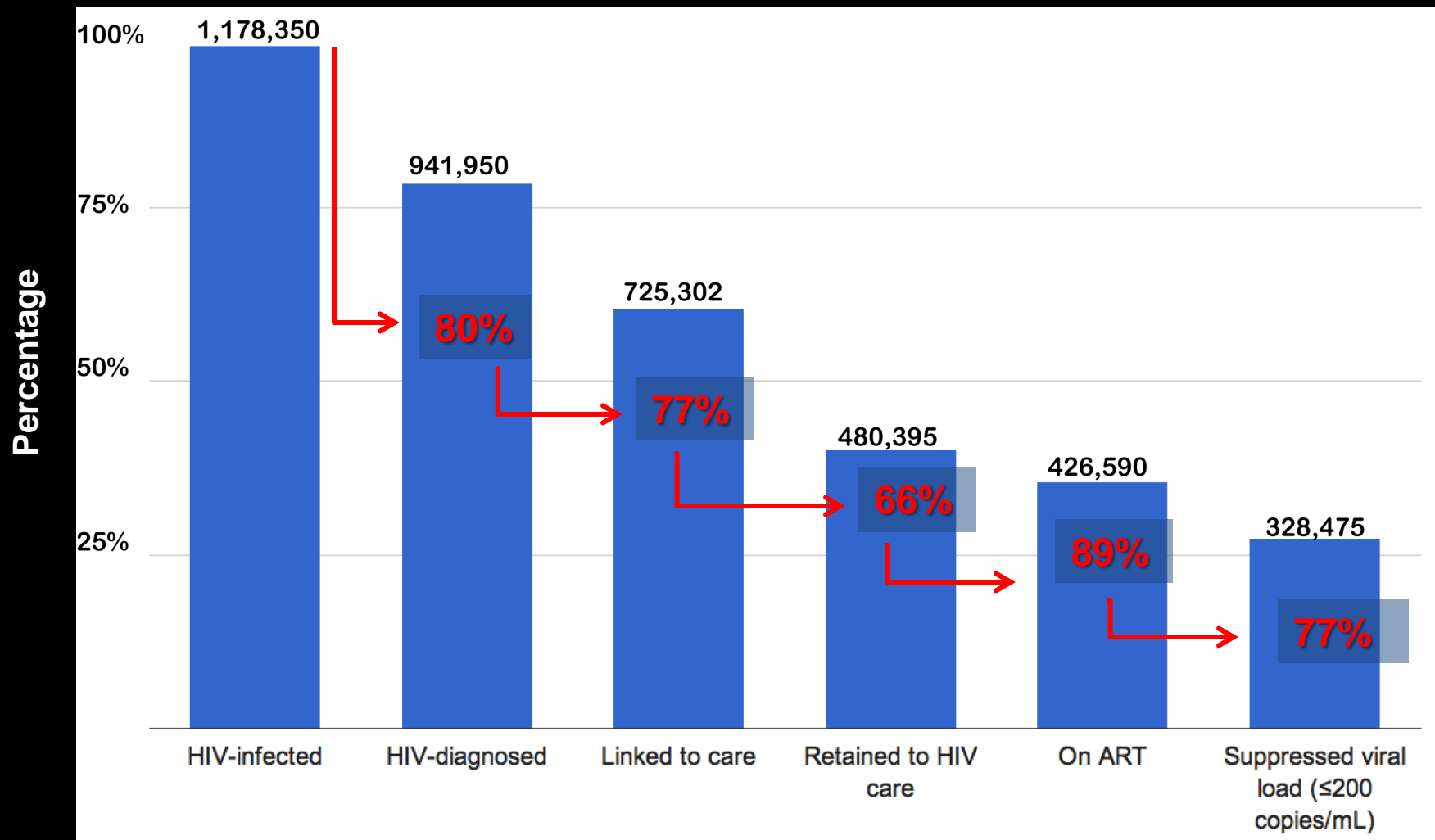
What is Needed to Achieve Population Impact of ART for Prevention



HIV to ART: Testing, Care, and Treatment-- Mozambique



The Continuum of HIV Care--US

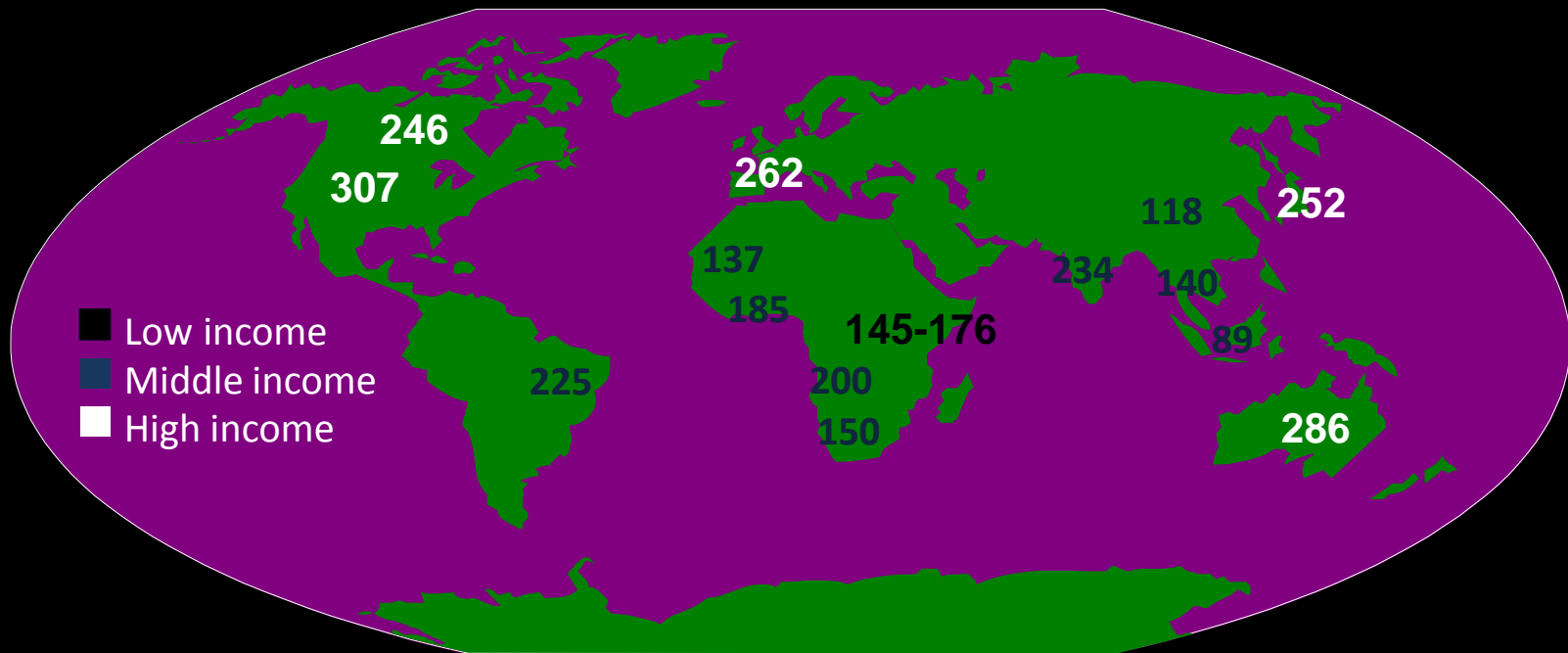


Of all with HIV infection, 850,000 individuals do not have suppressed HIV RNA (72%)

HPTN 043— Community HIV Testing

	Tanzania		Zimbabwe		Thailand	
	CBVCT Plus SVCT	SVCT	CBVCT Plus SVCT	SVCT	CBVCT Plus SVCT	SVCT
Population size	6250	6733	10,700	12,150	11,270	10.033
First time HIV test	37%	9%	52%	5%	69%	23%

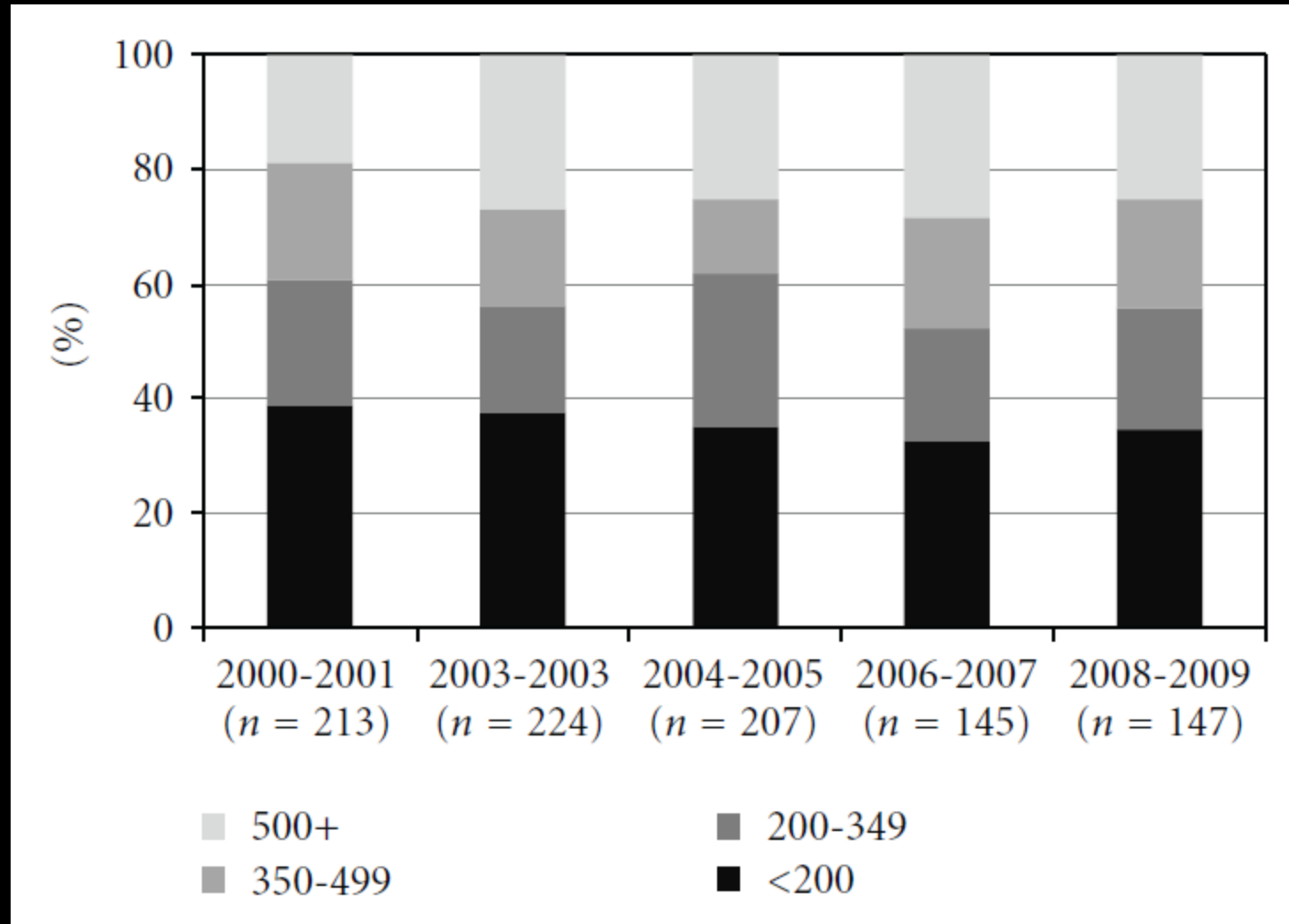
CD4+ Cell Count at Initiation of HIV Treatment



Source of HIV Testing and CD4+ Cell Count

	Home-based	VCT	PITC	TB
Number tested	946	10,261	8,073	272
Percent female	72%	66%	62%	50%
Mean CD4+ in HIV+ (cells/mm³) Missing data	323 (194-491) 23%	217 (87-404) 45%	190 (70-371) 52%	136 (59-266) 38%
WHO III or IV Missing data	14% 26%	38% 18%	46% 23%	79% 19%

CD4+ Count at Entry into Care --HOPS



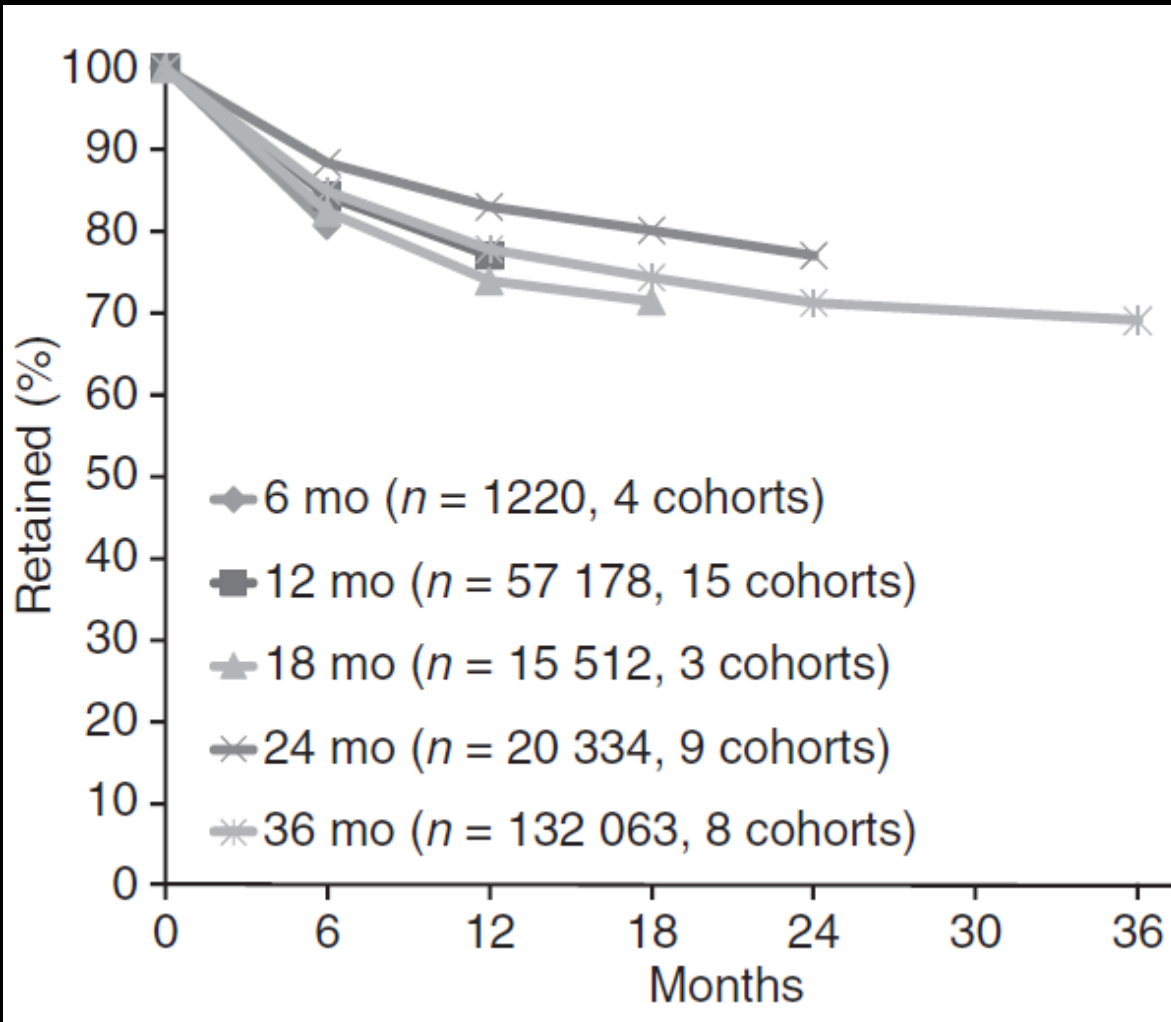
Factors associated with late diagnosis

- Not being MSM OR: 1.99
- Age ≥ 35 OR: 2.14
- Not white race/ethnicity OR: 1.45

Factors Associated with Initiation of ART at Higher CD4+ cell counts- San Francisco

At CD4>500 cells/mm³	P value
White	<0.001
MSM	0.003
Non poor	0.005
Diagnosed by private provider	<0.001
At CD4>350 cells/mm³	P value
Older	<0.001
White	<0.001
MSM	0.012
Non-poor	<0.001

Retention in ART Programs



36 cohorts

226, 307 patients

All losses except transfers

Retention:

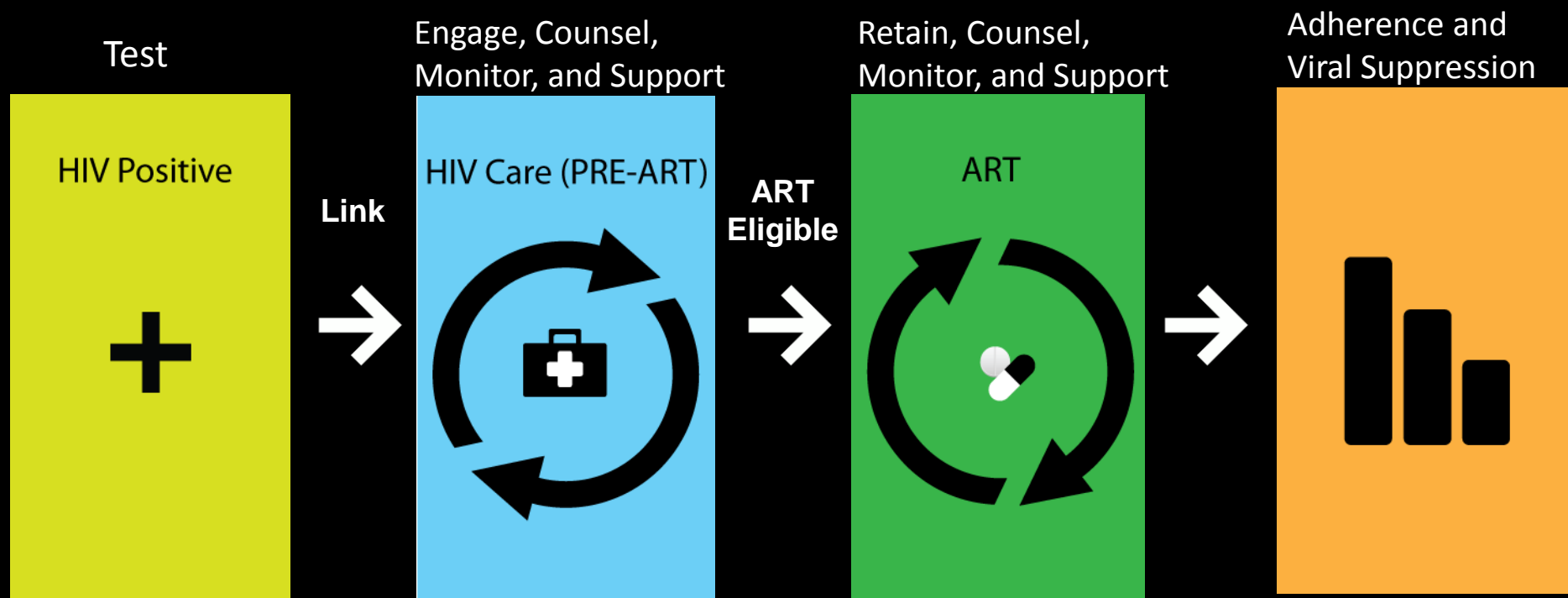
•6 months: 86.1%

•12 months: 80.2%

•24 months: 76.8%

•36 months: 72.3%

HIV Care/Prevention Continuum





HIV PREVENTION TRIALS NETWORK

Test, Link to Care Plus Treat HPTN 065 (TLC-Plus Study)

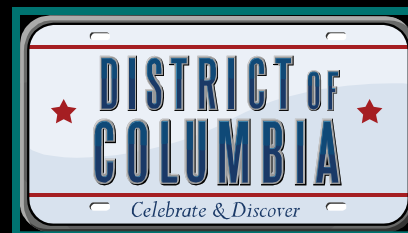


HPTN 065

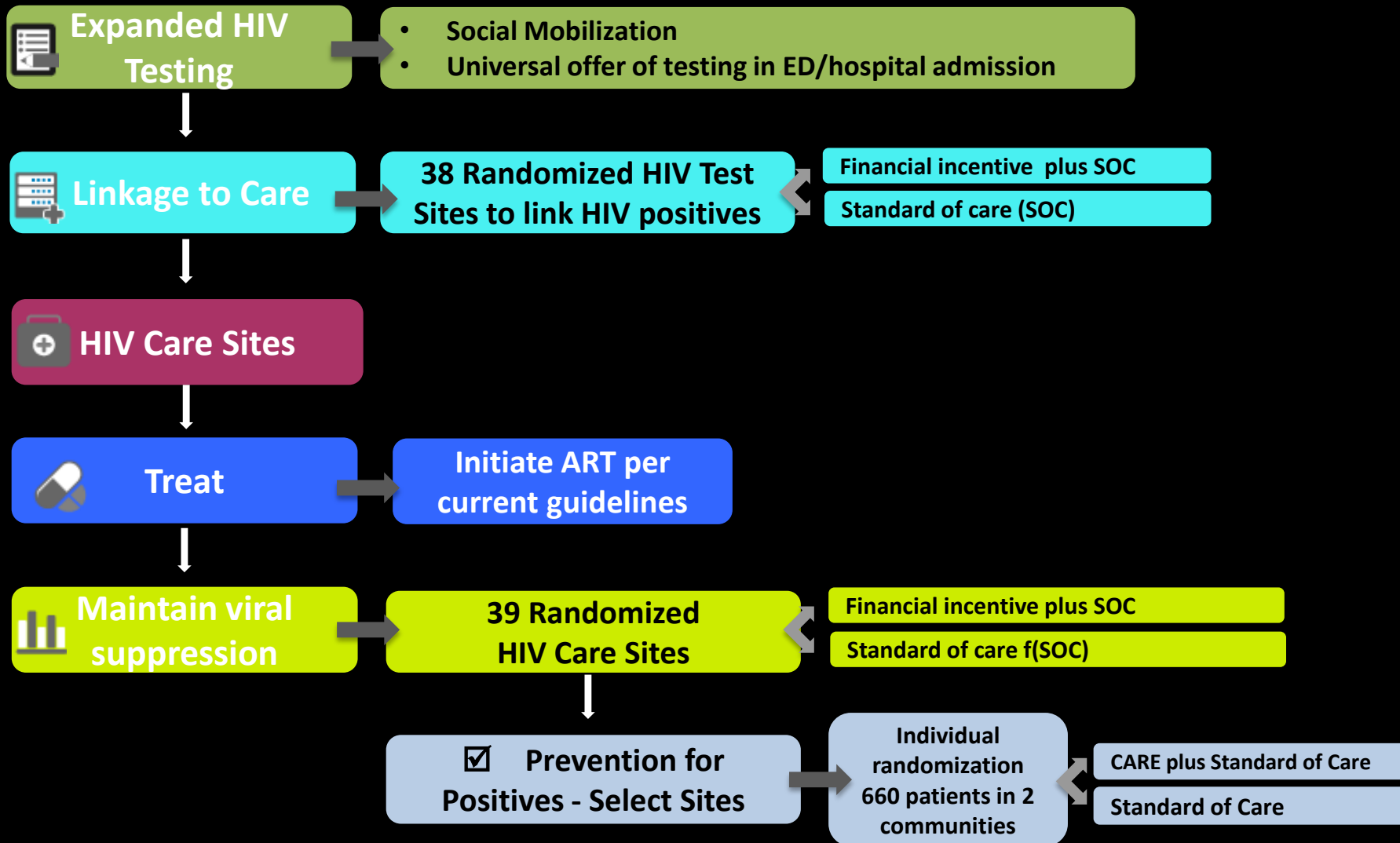
Test Link to Care Plus Treat (TLC-Plus)

PURPOSE

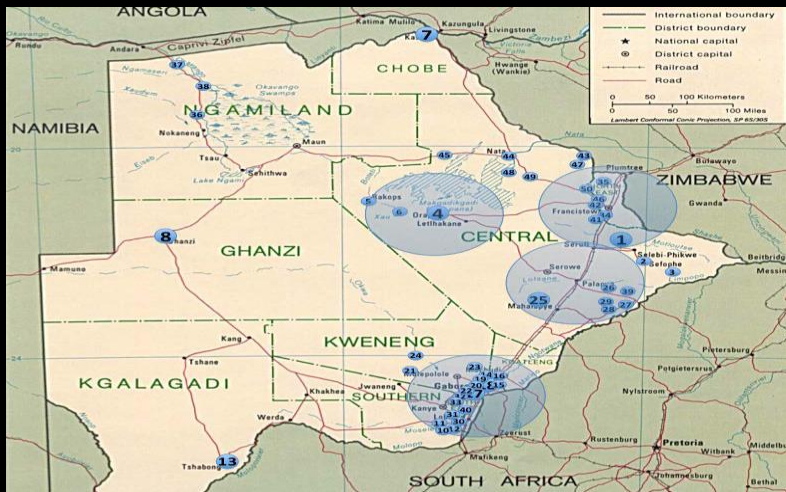
To evaluate the **feasibility** of an enhanced community-level HIV test, link-to-care plus treat strategy in the U.S.



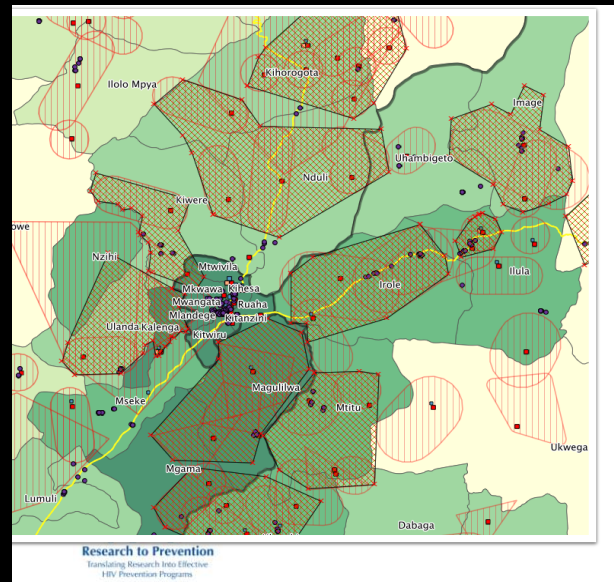
HPTN 065 (TLC Plus): Study Design



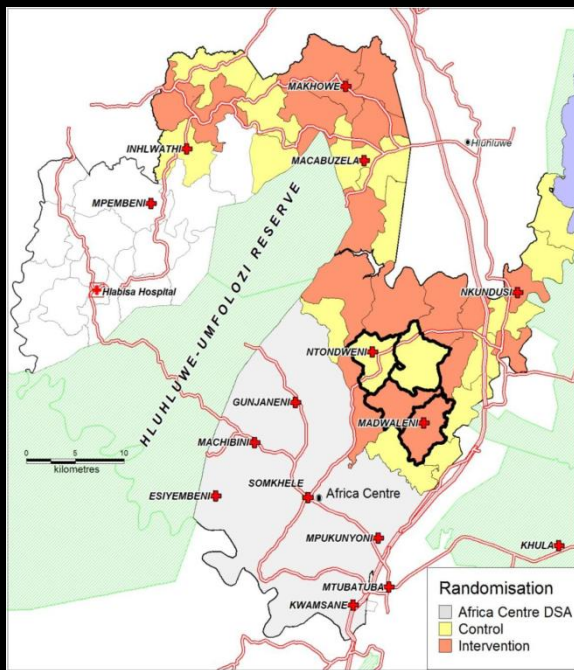
Study	HPTN 071 (PopART)	Iringa /JHU Study	TasP-ANRS	Botswana/HSPH
Principal investigator	<ul style="list-style-type: none"> • Richard Hayes (PI) • Sarah Fidler , Helen Ayles & Nulda Beyer (Co-PIs) 	<ul style="list-style-type: none"> • David D. Celentano (PI) • Jessie Mbwambo & Deanna Kerrigan (coPI) 	<ul style="list-style-type: none"> • Francois Dabis & Marie-Louise Newell PIs 	<ul style="list-style-type: none"> • Max Essex (PI)
Funder	• NIAID, NIMH, OGAC, BMGF	• USAID, OGAC	• ANRS	• CDC, OGAC
Country	Zambia & South Africa	Tanzania	South Africa	Botswana
Design	Cluster RCT	Cluster RCT	Cluster-RCT	Paired cluster-RCT
Clusters	<ul style="list-style-type: none"> • 24 (15 Zambia, 9 in SA) • ~55,000 per cluster 	<ul style="list-style-type: none"> • 24 total clusters • ~10,000 per cluster 	<ul style="list-style-type: none"> • 34 total clusters • 1,250 per cluster 	<ul style="list-style-type: none"> • 30 total clusters • 5,000 per cluster
Study arms	Three arm	Two arm	Two arm	Two arm
Interventions	<ul style="list-style-type: none"> • Home-based C&T, mobile & clinic-based C&T • Male circumcision • Risk reduction counseling & condom provision • Immediate ART to all HIV+ 	<ul style="list-style-type: none"> • HIV testing, care and ART for CD4< 350 • Male circumcision • Cash transfer - women • BCC • Key groups FSW, MSM) 	<ul style="list-style-type: none"> • Home-based C&T • Immediate ART initiation for all HIV+ 	<ul style="list-style-type: none"> • Home-based C&T • ART for CD4<350, WHO I/II or HIV RNA \geq10,000 • Male circumcision • PMTCT (option B)
Primary outcome	HIV incidence over 2 yrs	HIV incidence at 2 yrs	HIV incidence at 2 yrs	HIV incidence 2 yrs
How measured	Prospective cohort	Prospective cohort	Prospective cohort	Prospective cohort
Estimated annual HIV incidence	1.17% (Zambia) , 1.49% (SA)	1.0 per 100 py	2.5%	\pm 1.5% (15-49 yrs)



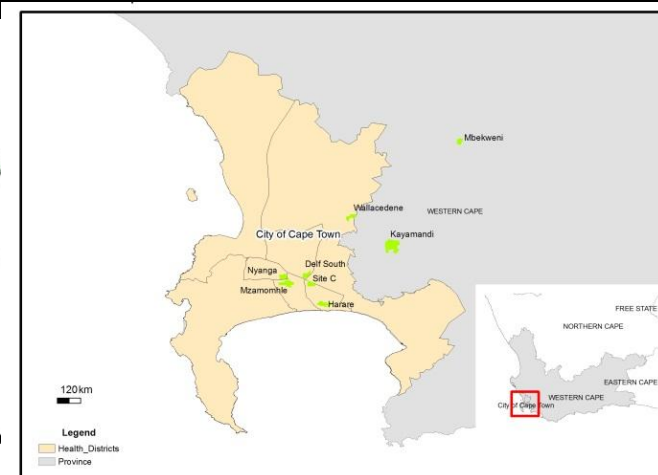
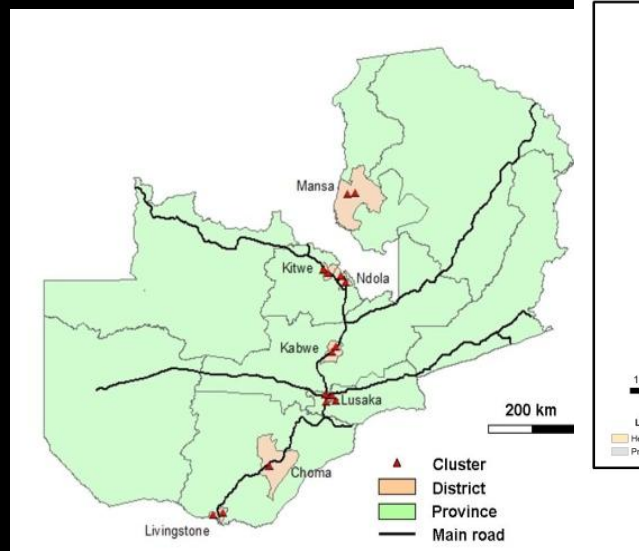
Botswana- CDC



Iringa Study- USAID

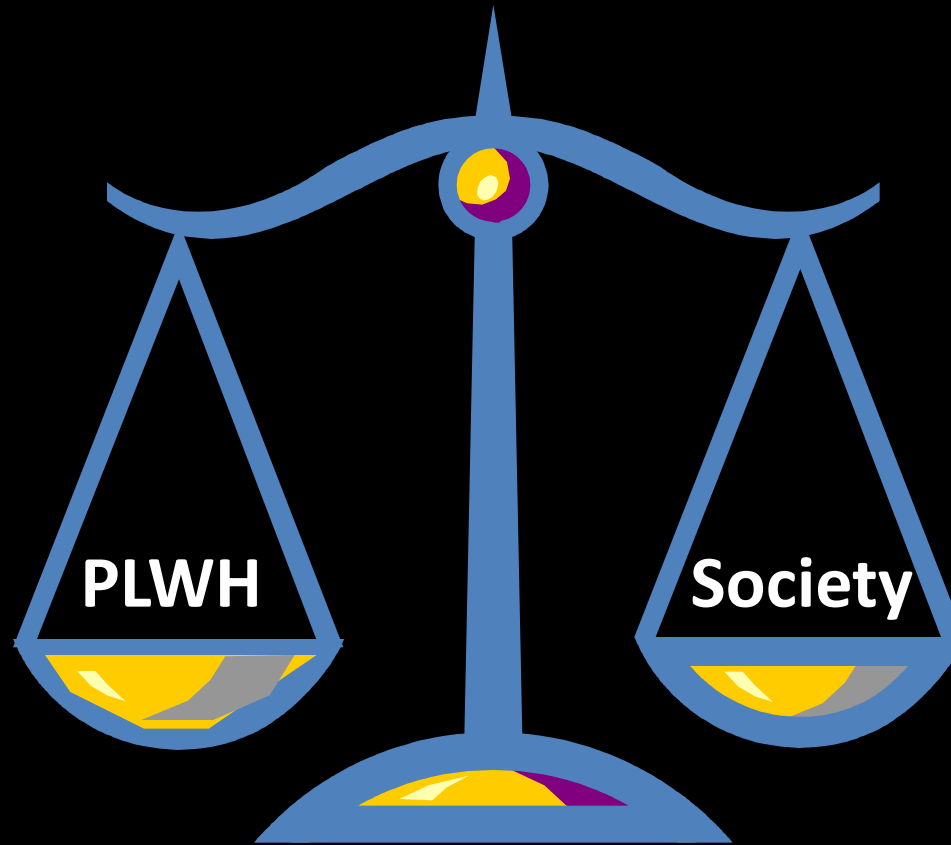


**TASP- Africa Centre
ANRS**



**HPTN 071 –NIH
PopART**

Balancing the Individual and Society



Health Systems
Ethics
Equity
Resources

Risks versus Benefits

Risks versus Benefits

DHHS Guidelines, 2012: When to Start

- ART recommended for all HIV-infected patients; *strength* of recommendation varies according to CD4+ cell count

CD4+ Cell Count	Recommendation
▪ < 350 cells/mm ³	▪ Start ART (AI)
▪ 350-500 cells/mm ³	▪ Start ART (AII)
▪ > 500 cells/mm ³	▪ Start ART (BIII)

Strength of recommendation:

A: Strong

B: Moderate

C: Optional

Quality of evidence:

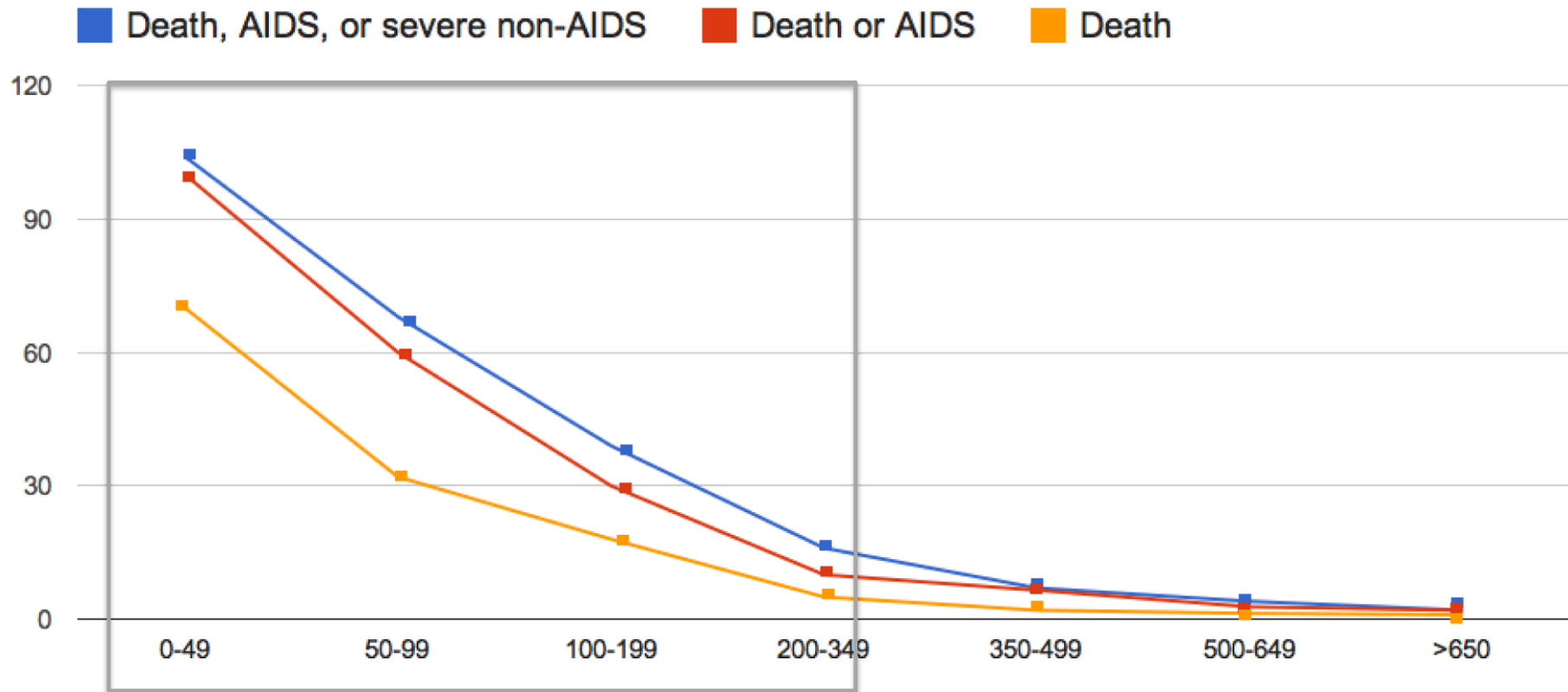
I: ≥1 randomized controlled trials

II: ≥1 well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes

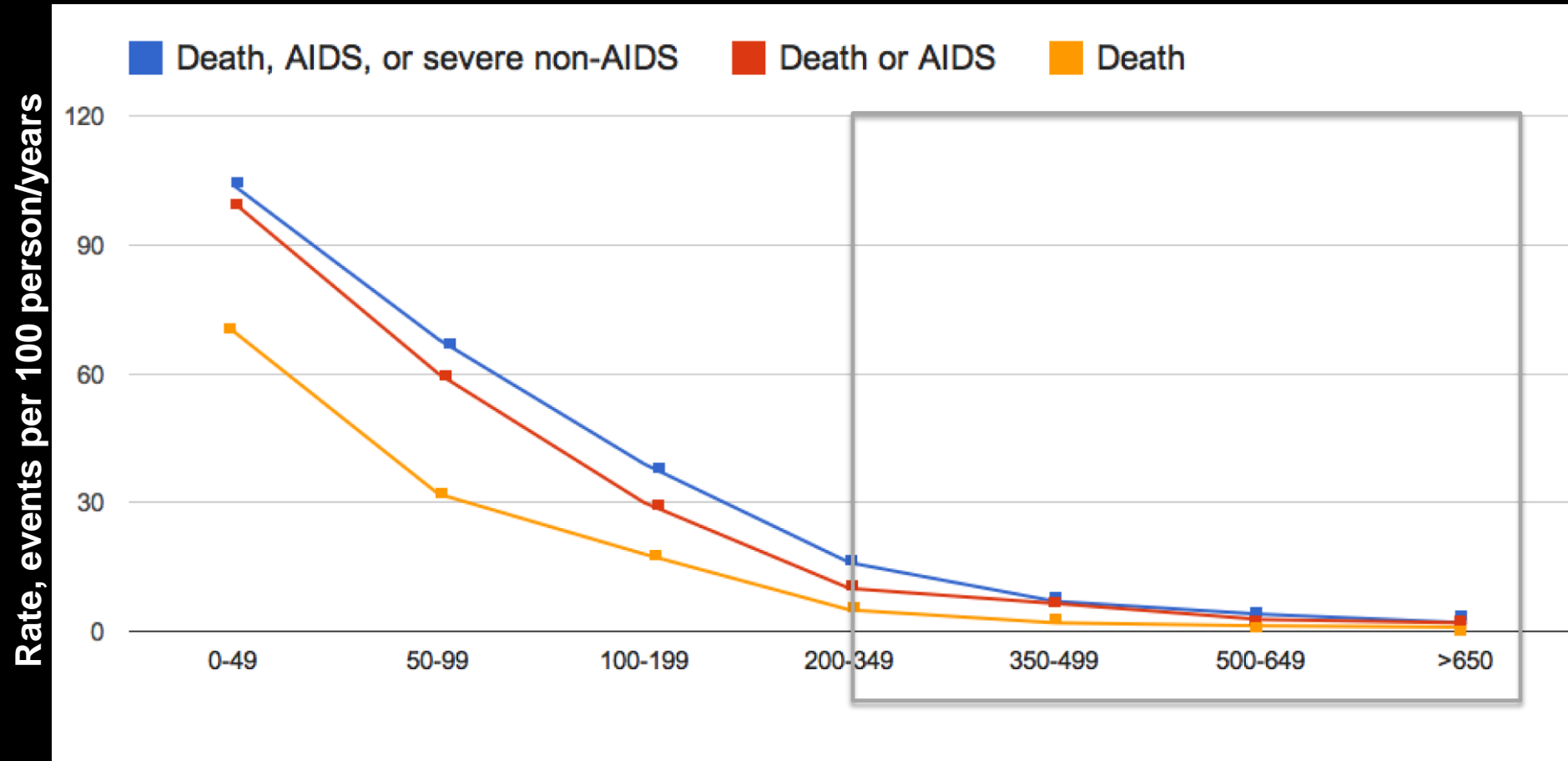
III: Expert opinion

HIV Disease Progression and Death by CD4+ cell Count

Rate, events per 100 person/years



HIV Disease Progression and Death by CD4+ cell Count

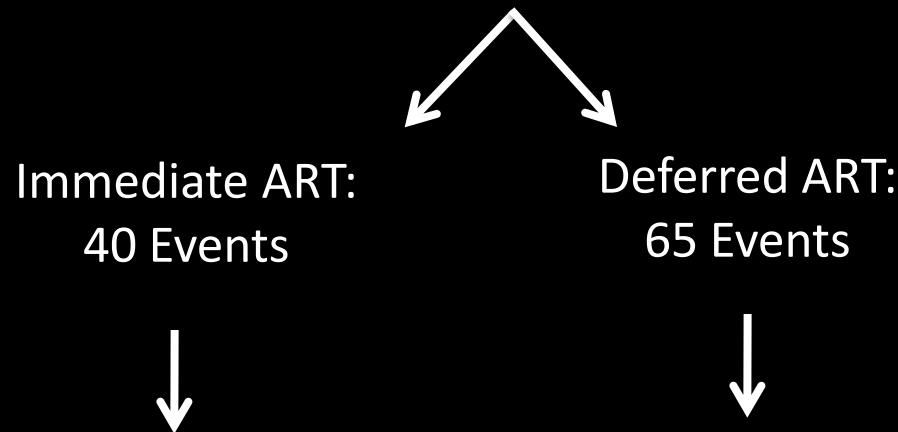


HPTN 052 Study: Key Finding



1,763 sero-discordant couples (97% heterosexual) HIV infected partners: 890 men, 873 women

■ ■ 105 Clinical Events



41% Reduction in Clinical Events

**TB (17 versus 33 cases)
Extrapulmonary TB (3 versus 17 cases) ($P = .002$)**

START Study



HIV-infected
ART-naïve
CD4+ count > 500 cells/mm³

Early ART Group

Initiate ART immediately
N=2,000

Deferred ART Group

Defer ART until the CD4+ count
declines to < 350 cells/mm³ or AIDS
N=2,000

Endpoints: Serious AIDS Event
Non-AIDS Events or
Death

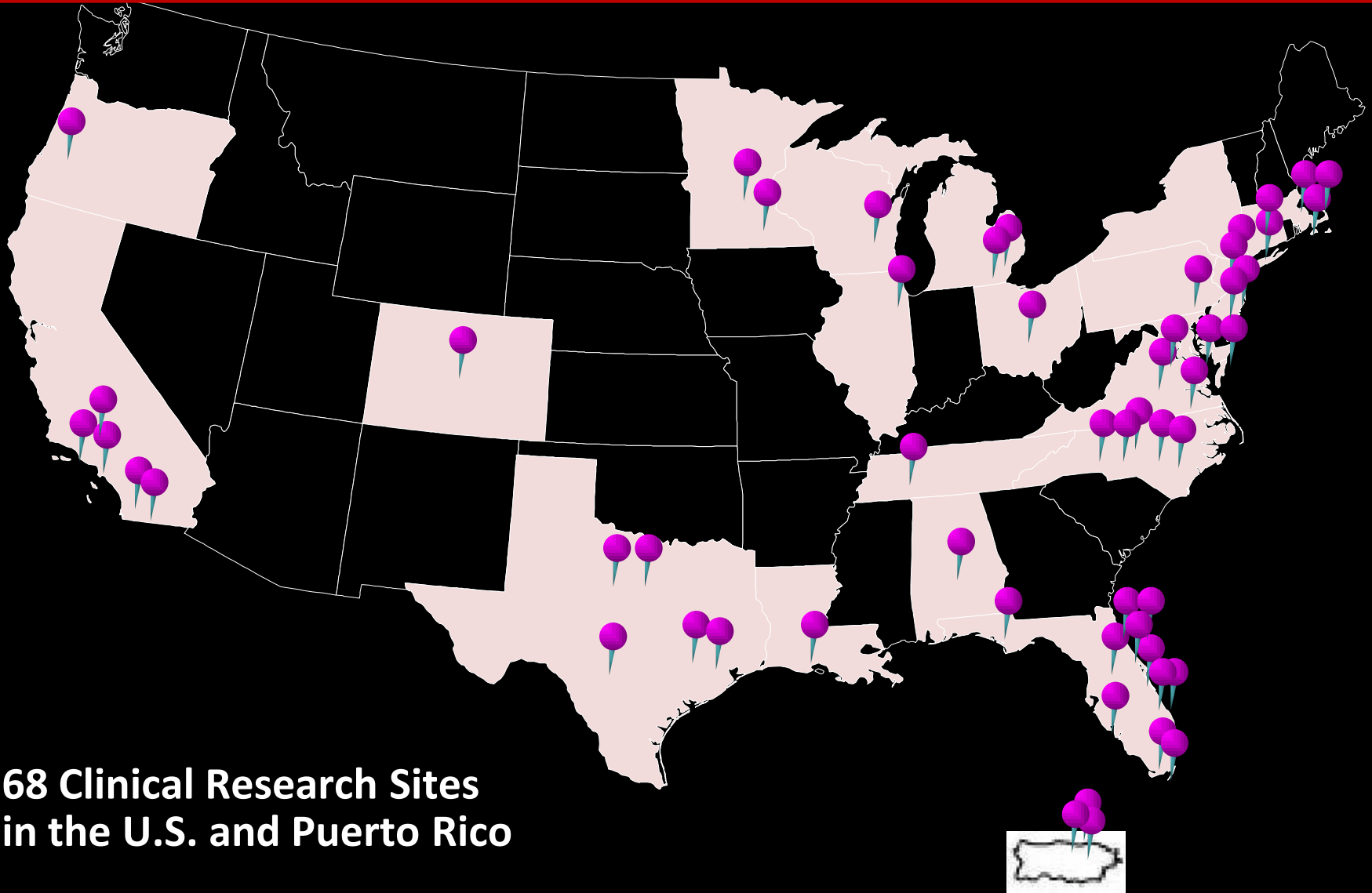
START Study



***In all, 238 Clinical Research Sites in 35 countries
With 68 sites in US and Puerto Rico***



START Study



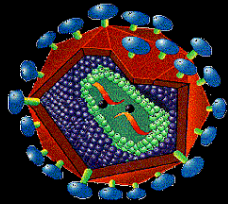
**68 Clinical Research Sites
in the U.S. and Puerto Rico**



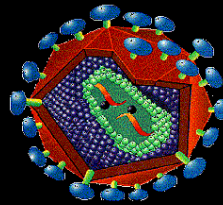
Clinical Trials for Prevention of Sexual Transmission of HIV

Intervention	Positive Effect	Adverse Effect	No Effect	Number of trials
Treatment	1		-	1
Behavioral	-		7	7
Structural	1		2	3
Male circumcision	3		1	4
STI treatment	1		8	9
Vaccine	1		3	4
PrEP (Topical microbicides)				
Non ARVs	-	1	11	12
ARVs	1		1	2
PrEP (Systemic, oral)	3		3	6

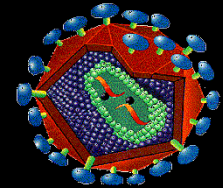
Pre-Exposure Prophylaxis (PrEP)



HIV Exposure



HIV Exposure

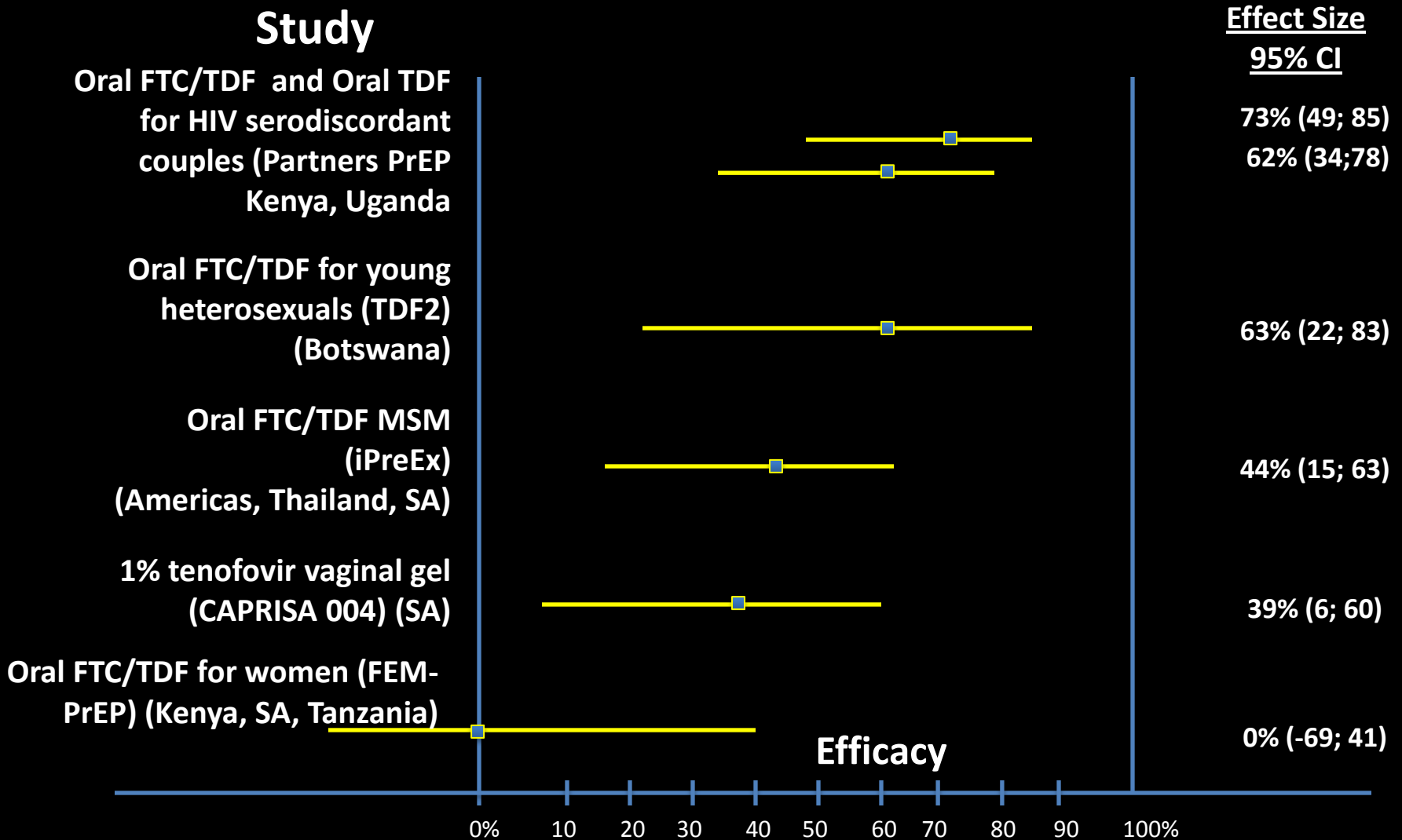


HIV Exposure



Pre-exposure
prophylaxis

Efficacy of Topical and Oral PrEP



The New York Times

FDA Advisory Committee Supports Approval of Gilead's Truvada® for Reducing the Risk of Acquiring HIV

Published: May 11, 2012



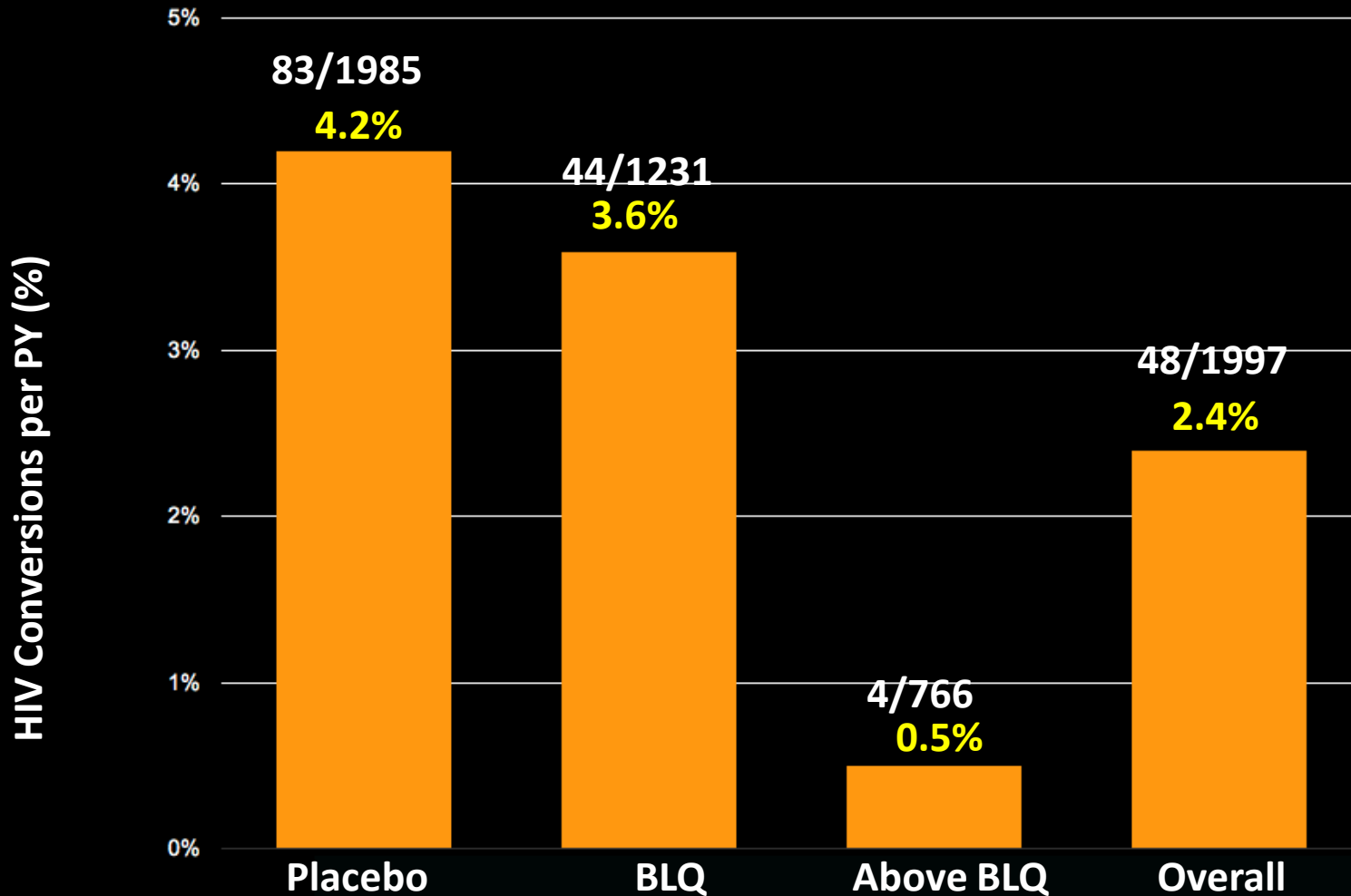
Taking Truvada to Prevent H.I.V. Also Comes With Risks

Published: May 14, 2012

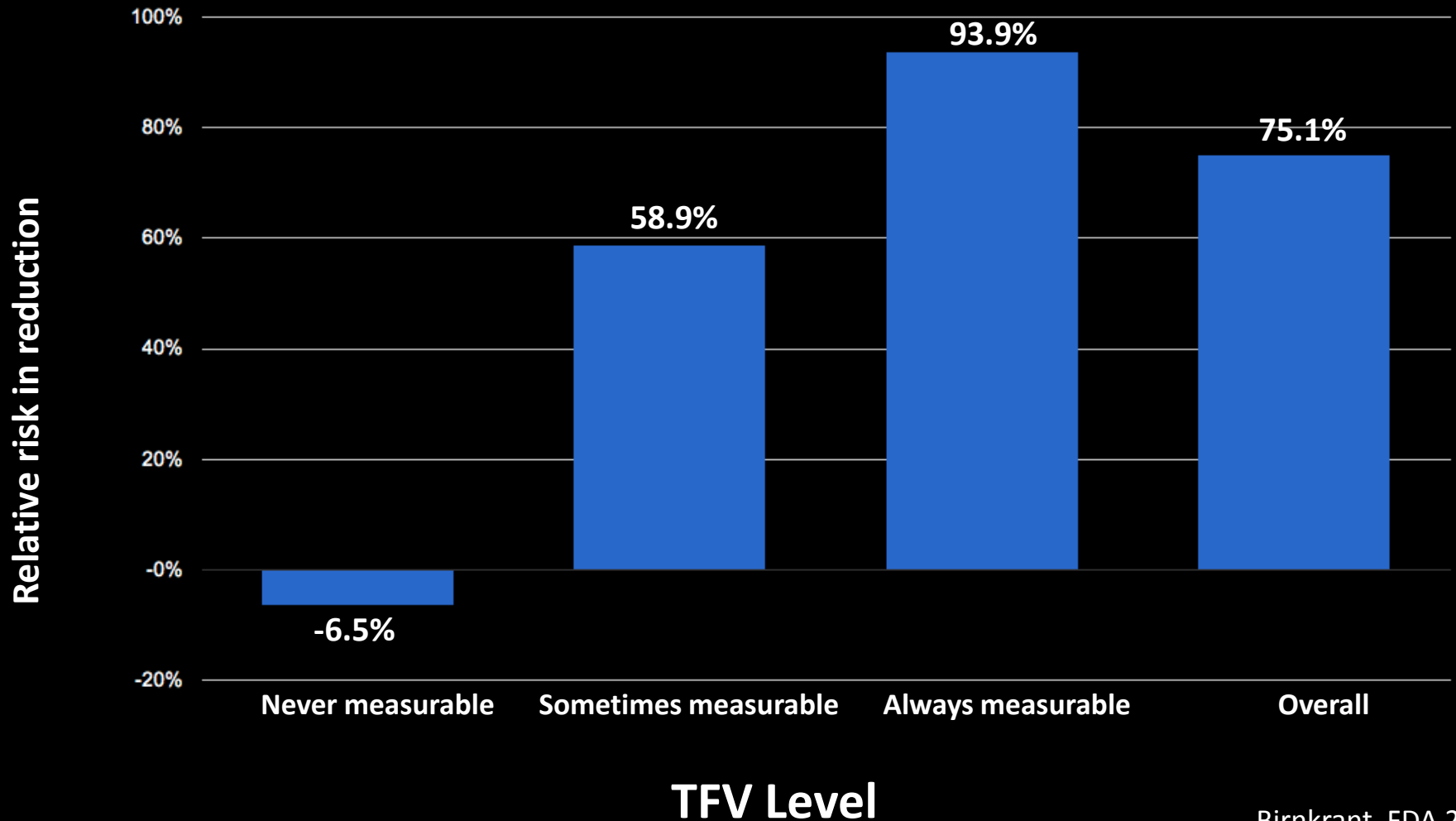


U.S. debates recommending drug for AIDS prevention

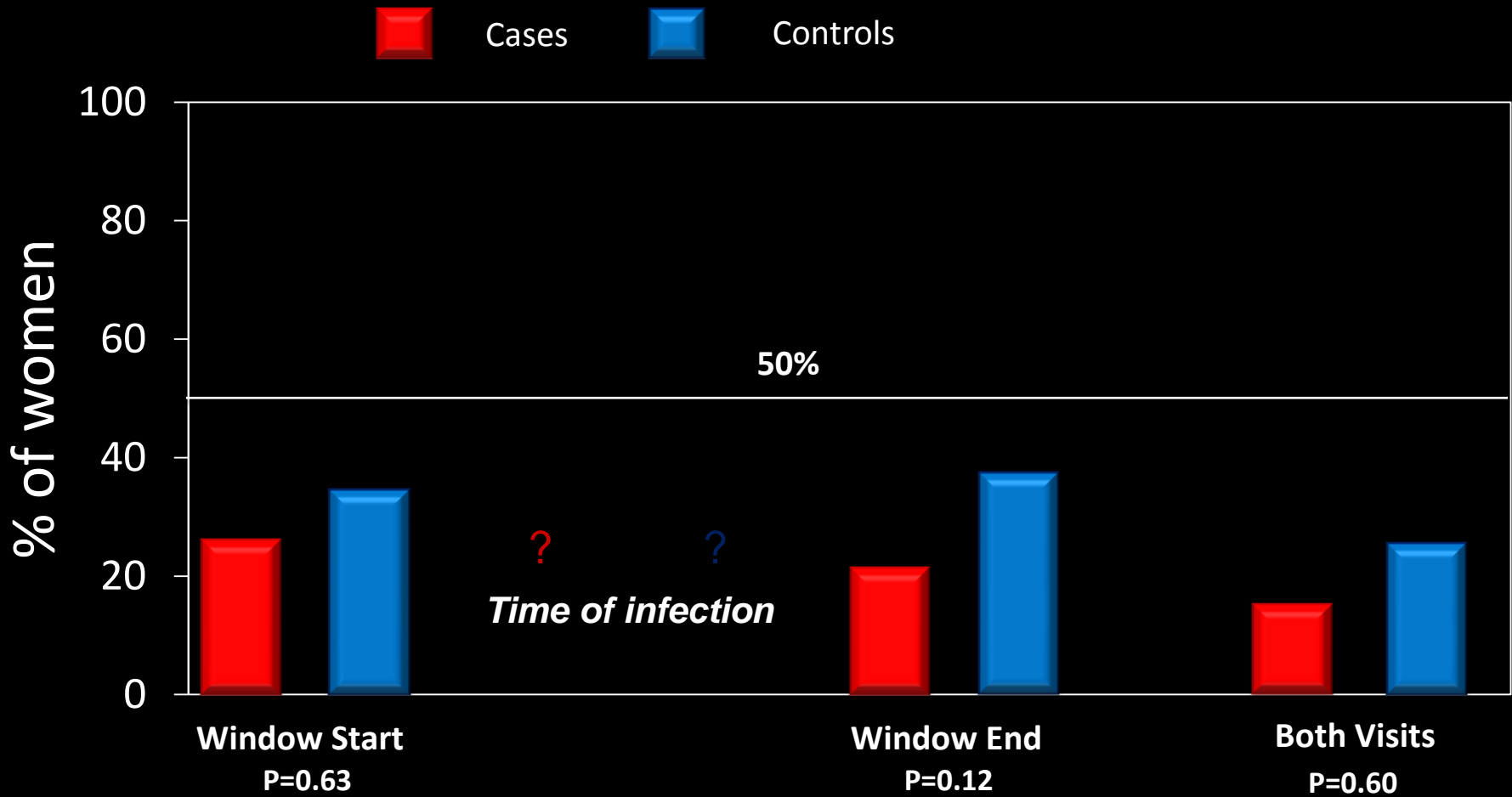
Adherence and HIV Acquisition-- iPrEx



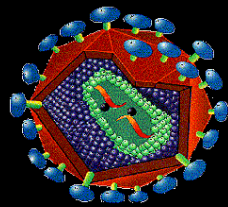
Adherence and HIV Acquisition— Partners PrEP Study



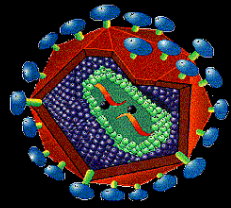
Infected *Cases* and Matched *Controls* with ≥ 10 ng/ml Tenofovir in Plasma at Visits Defining Infection Windows



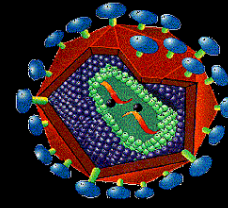
Pre-Exposure Prophylaxis (PrEP)



HIV
Exposure



HIV
Exposure



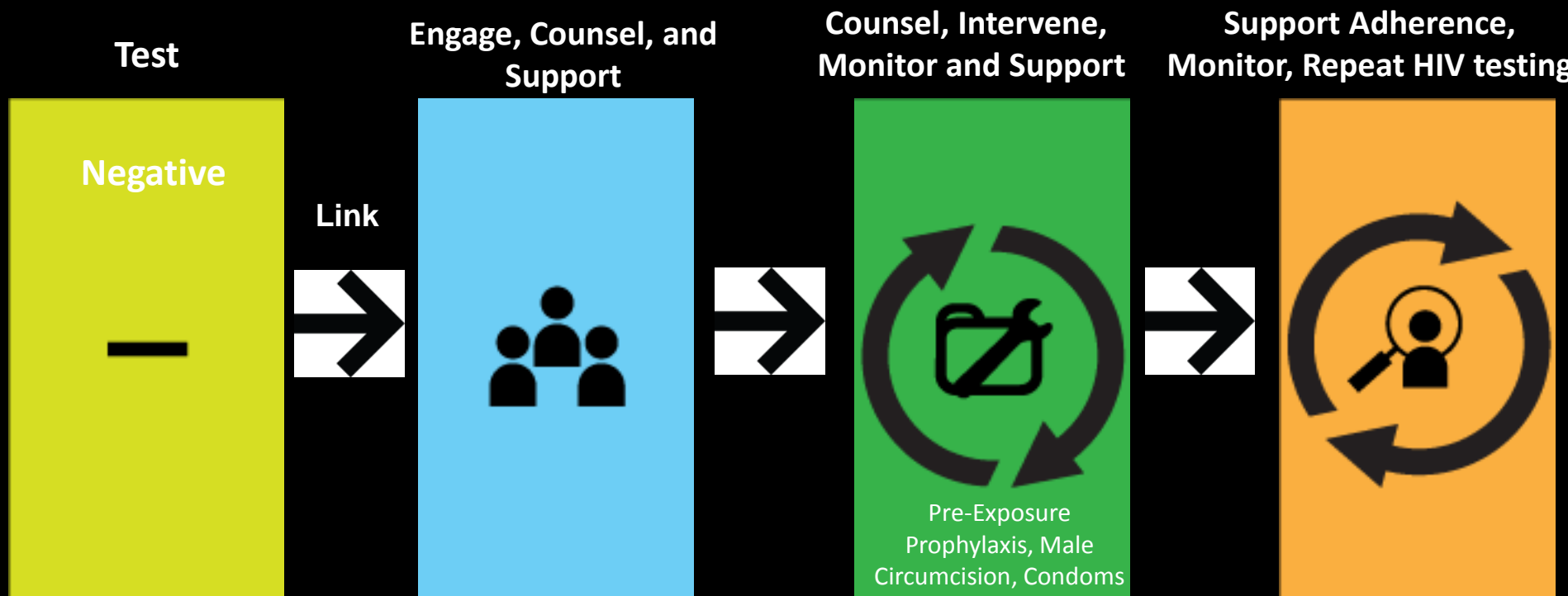
HIV
Infection



Pre-exposure
prophylaxis

HIV Prevention Continuum

HIV Negative Individuals



Efficacious Interventions



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

Effectiveness and Safety of Tenofovir Gel, an Antiretroviral Microbicide, for the Prevention of HIV Infection in Women

Quarraisha Abdool Karim,^{1,2,*} Salim S. Abdool Karim,^{1,2,3*} Janet A. Frohlich,³ Anneke C. Grobler,³ Cheryl Baxter,³ Leita E. Mansoor,³ Ayesha B. M. Kharsany,³ Sengeziwe Sibeko,³ Koleka P. Mlisana,³ Zabeen Omar,³ Tanuja N. Gengiah,³ Silvia Maarschalk,³ Natasha Arulappan,³ Muketisiwe Mlotshwa,³ Lynn Morris,³ Douglas Taylor,³ on behalf of the CAPRISA 004 Trial Group



PIVOTAL STUDY FINDS THAT HIV MEDICATIONS ARE HIGHLY EFFECTIVE AS PROPHYLAXIS AGAINST HIV INFECTION IN MEN AND WOMEN IN AFRICA

The NEW ENGLAND JOURNAL of MEDICINE

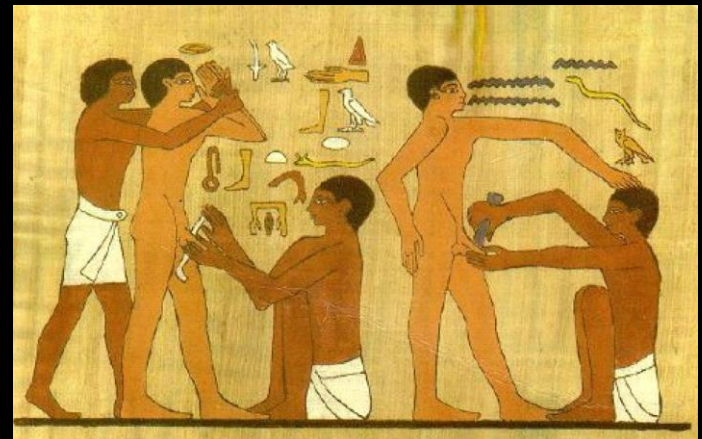
ESTABLISHED IN 1812

DECEMBER 30, 2010

VOL. 363 NO. 27

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

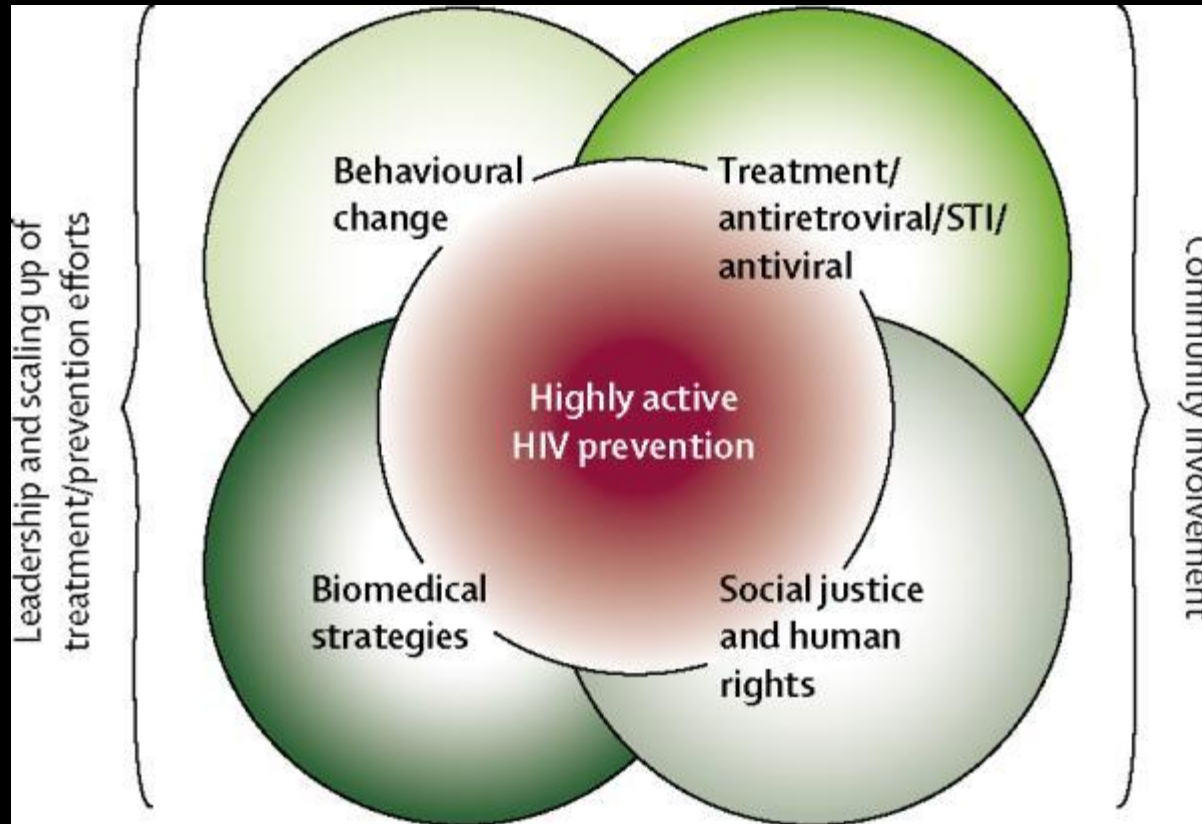
Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Felmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D.



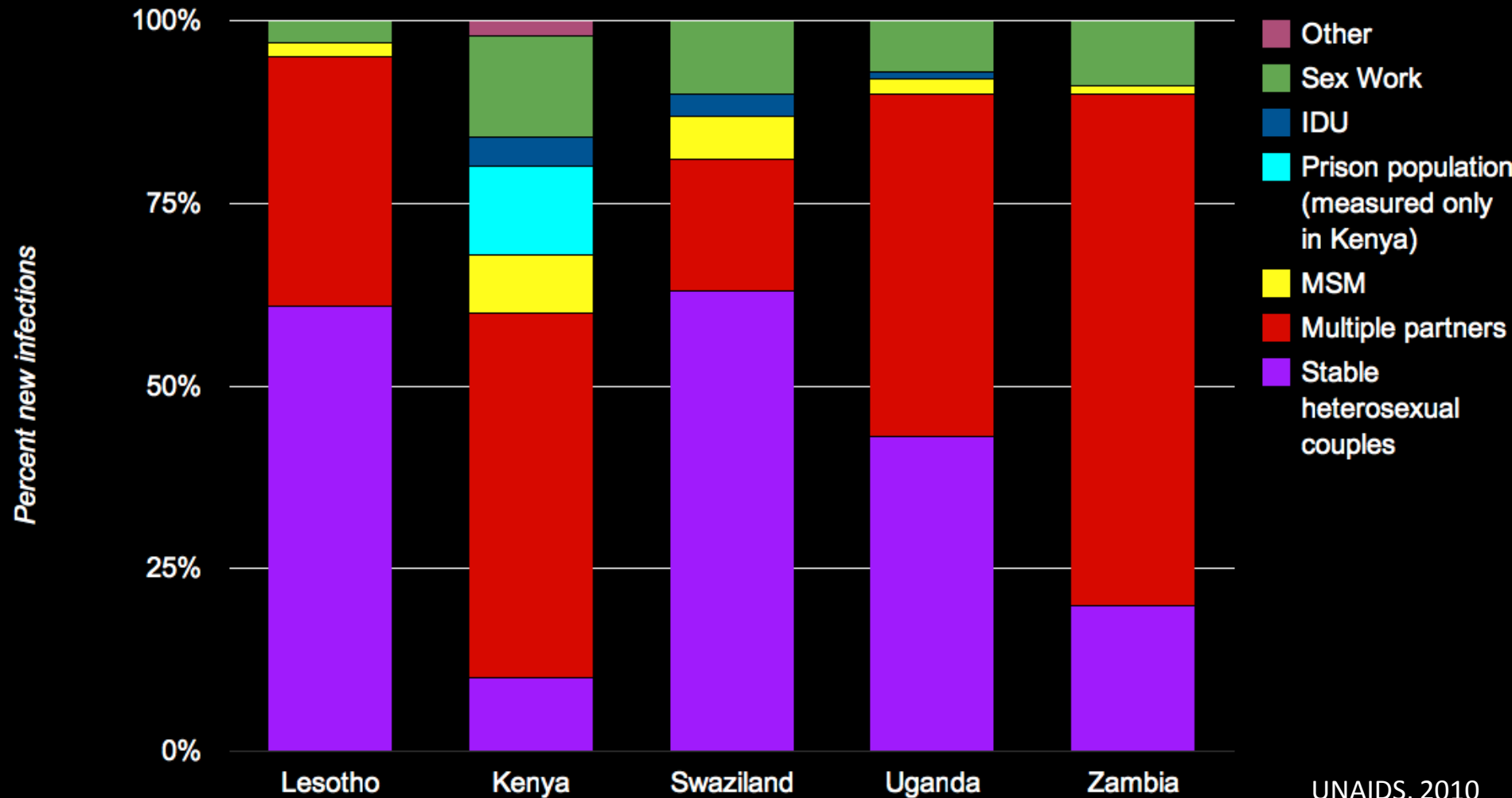
Prevention of HIV-1 Infection with Early Antiretroviral Therapy

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., Susan M. Muthya, M.D., Susan Chariyalertsak, M.D., Bruce R. Senter, M.D., Kenneth H. Mayer, M.D.

Combination Prevention



Contribution by Key Populations to the HIV Epidemic

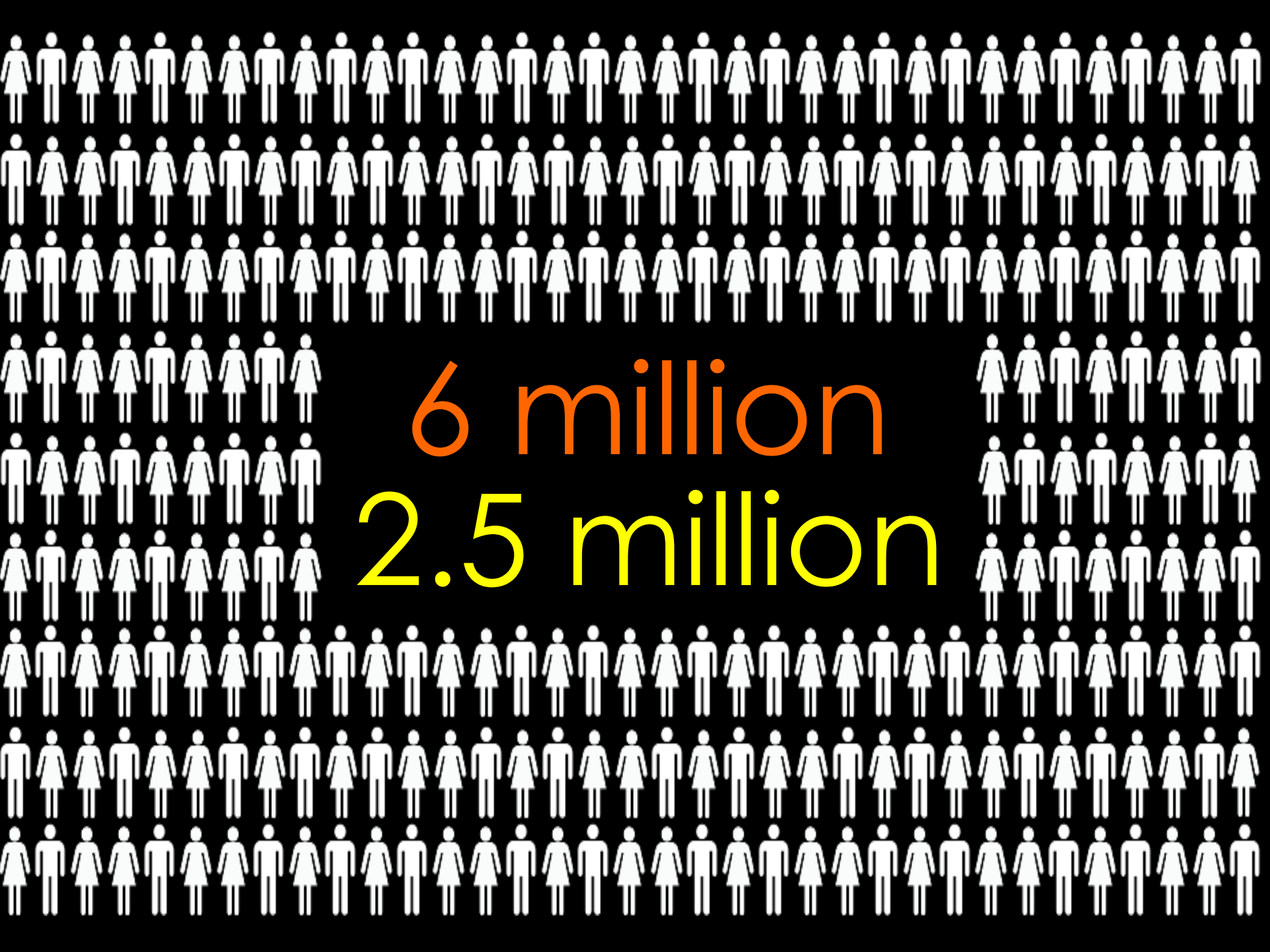


Conclusions-I

- Substantial achievements in the response to the HIV epidemic
- New prevention tools offer promise for control of HIV transmission
- Further efforts are needed to define how best to use these interventions:
 - Defining risks and benefits for individuals
 - Optimizing every step of the continuum of care and prevention
 - Determining efficacy of various interventions in specific populations

Conclusions-II

- Need for other efficacious interventions (vaccine, structural, behavioral)
- Research design challenges ahead
 - Design of studies in key hard to reach populations
 - Defining the population impact of various prevention interventions
 - Assessment of impact of combination strategies for prevention
 - Defining which interventions to be prioritized by various communities and countries
- Much remains to be done:
 - 6 million people need ART now for their own health
 - 2.5 million new infections annually



6 million
2.5 million

Thank you



ICAP

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COLUMBIA UNIVERSITY

Mailman School of Public Health