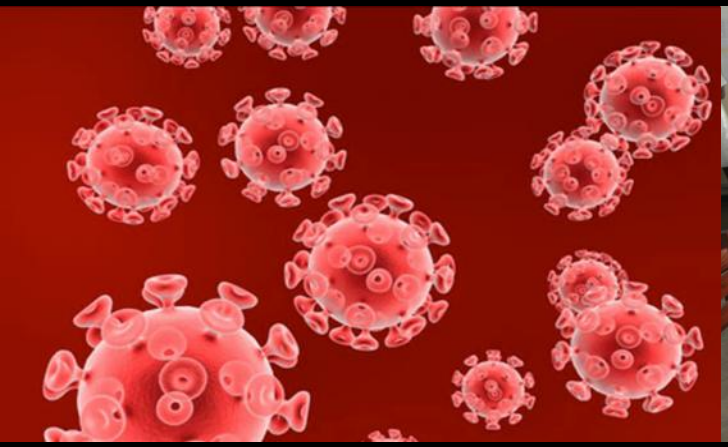
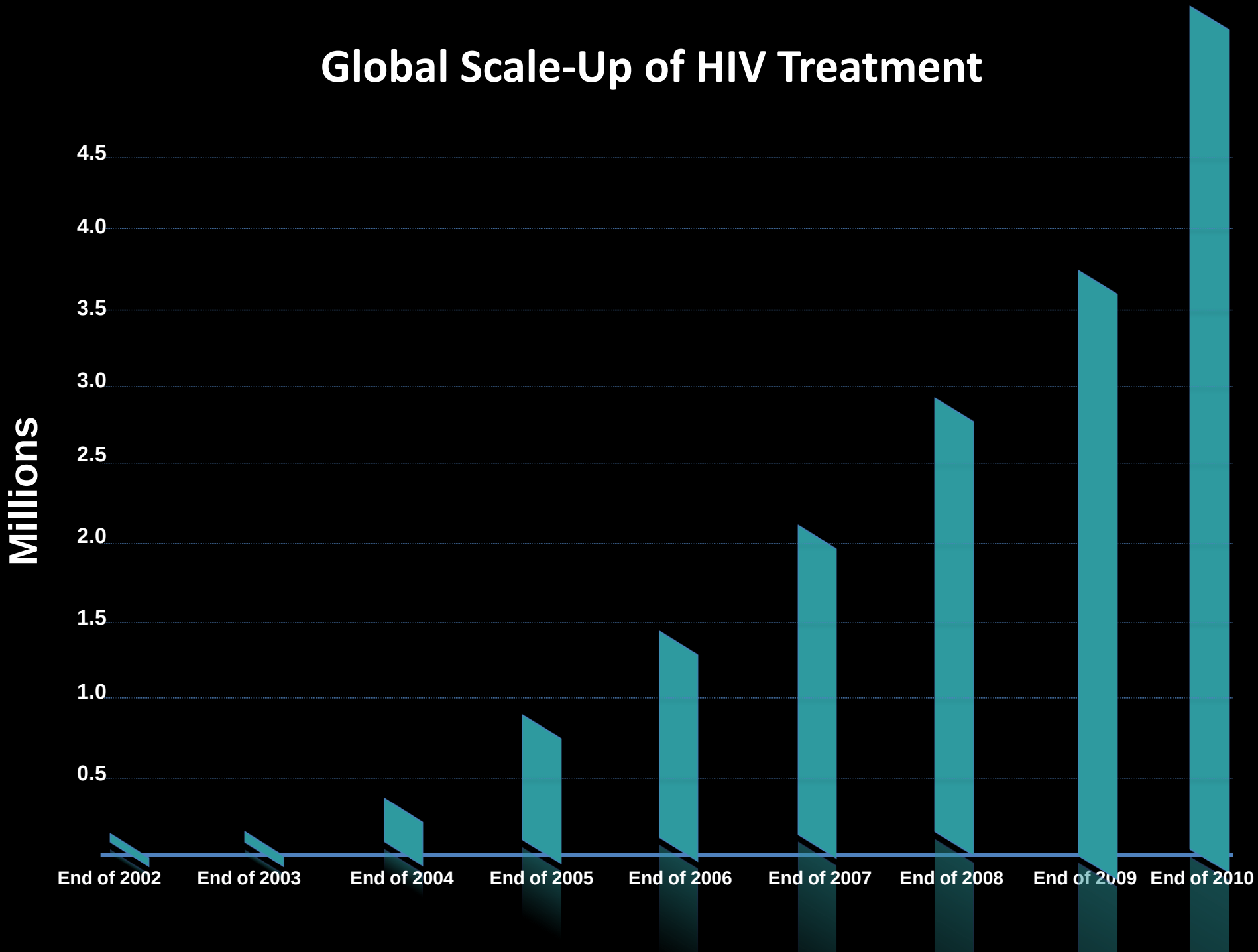


State of the Art for ART for Prevention

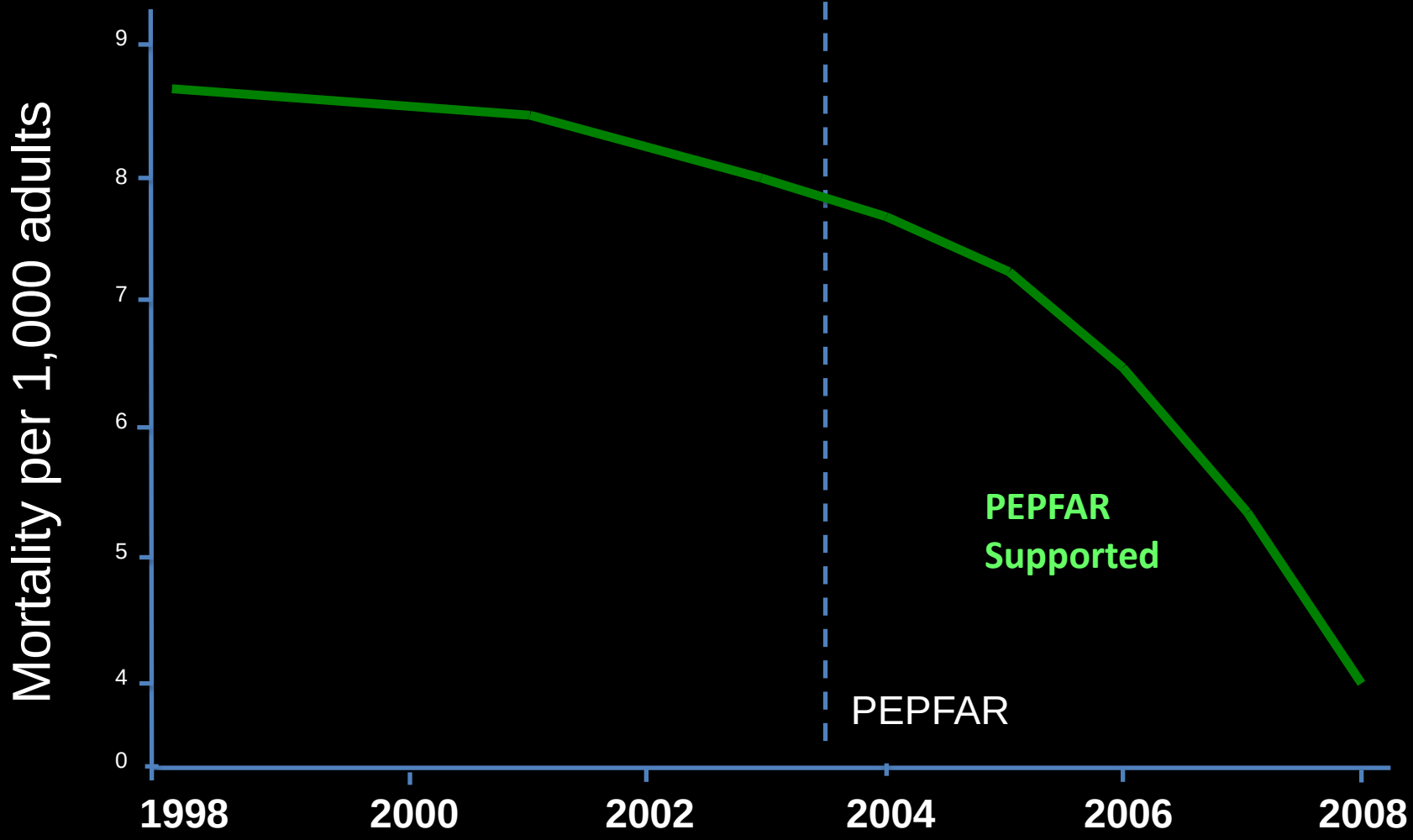
Wafaa El-Sadr, MD, MPH
ICAP-Columbia University

ICAP
Global. Health. Action.
COLUMBIA UNIVERSITY
Mailman School of Public Health

Global Scale-Up of HIV Treatment

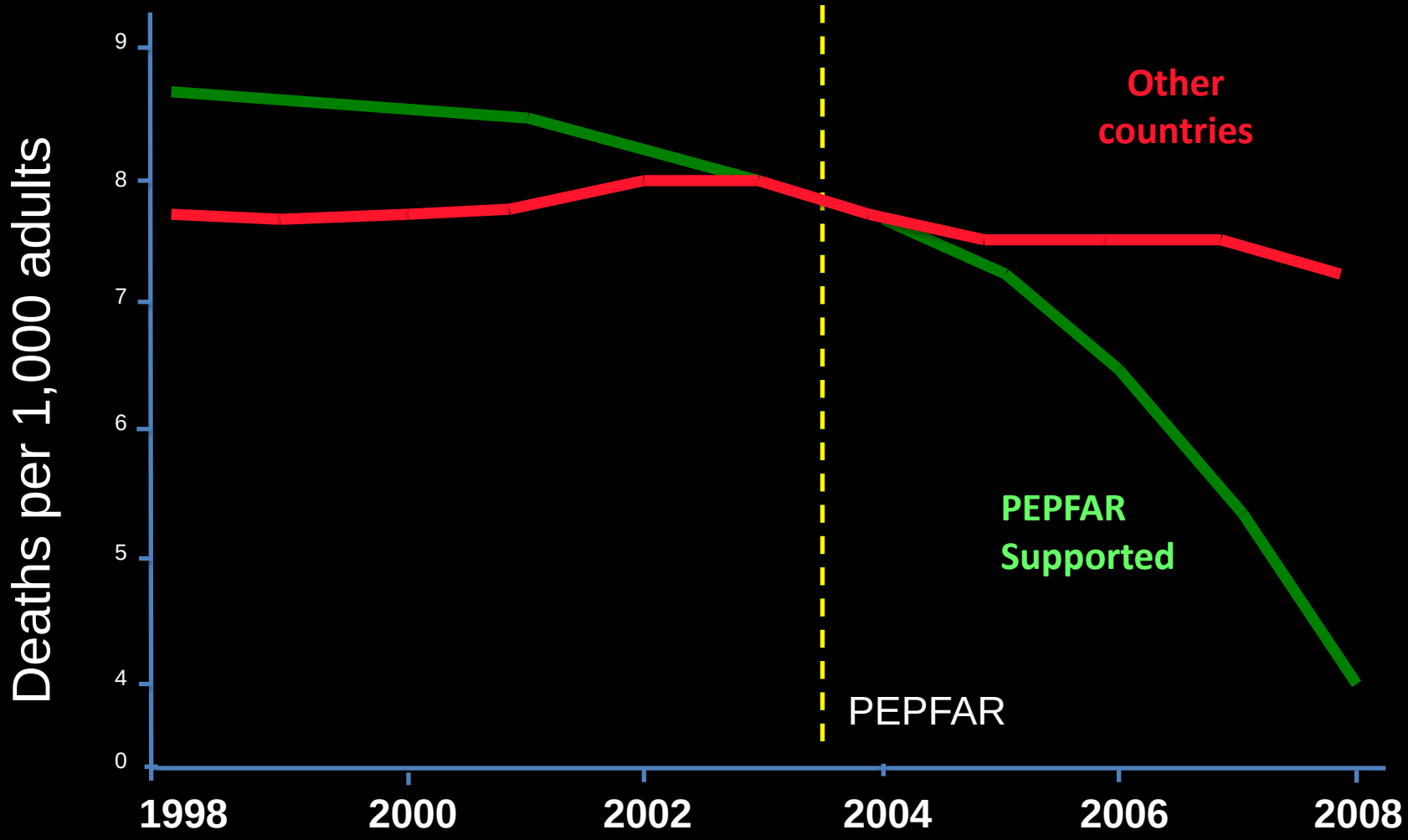


Deaths in PEPFAR-Supported Countries in Africa

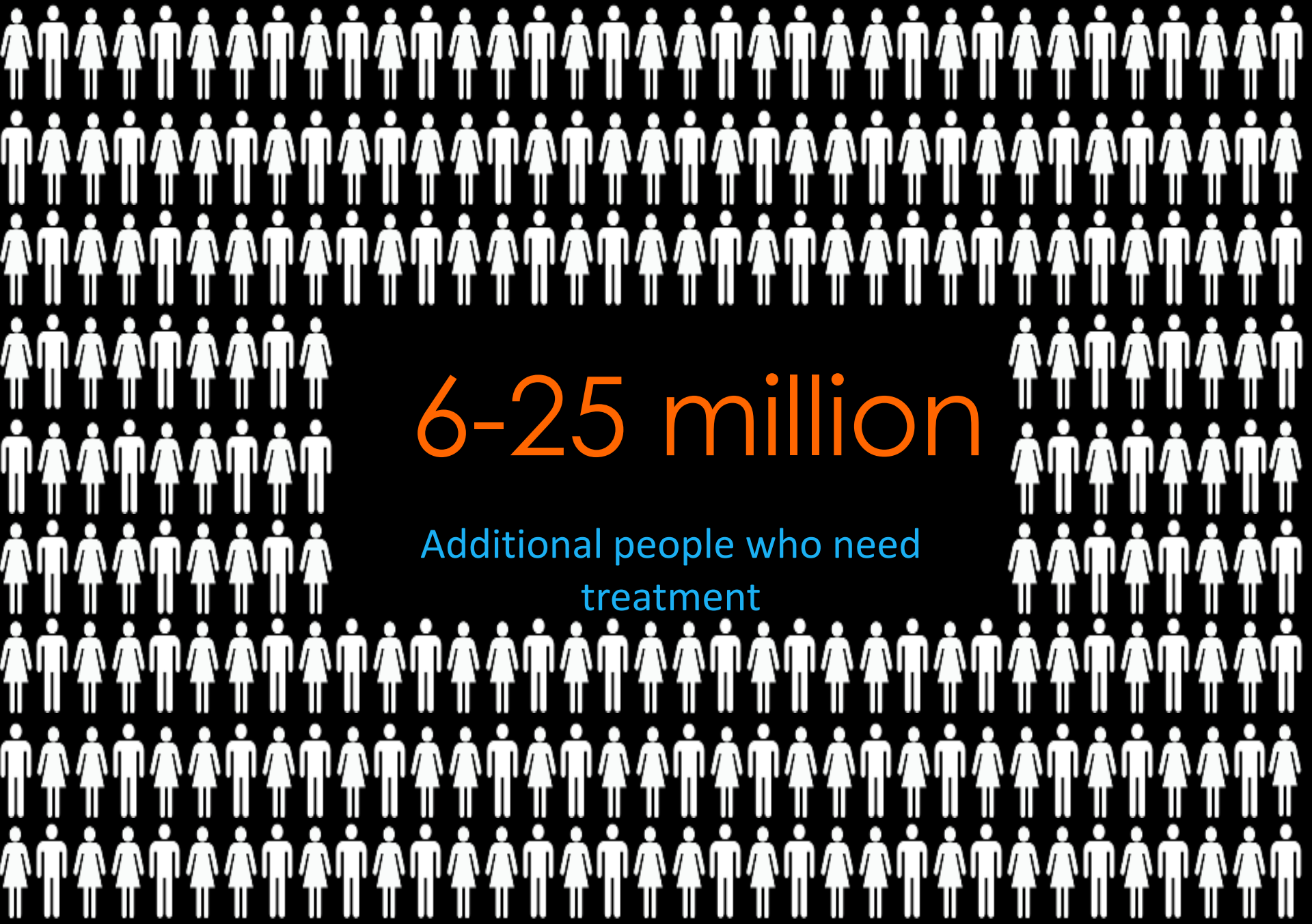


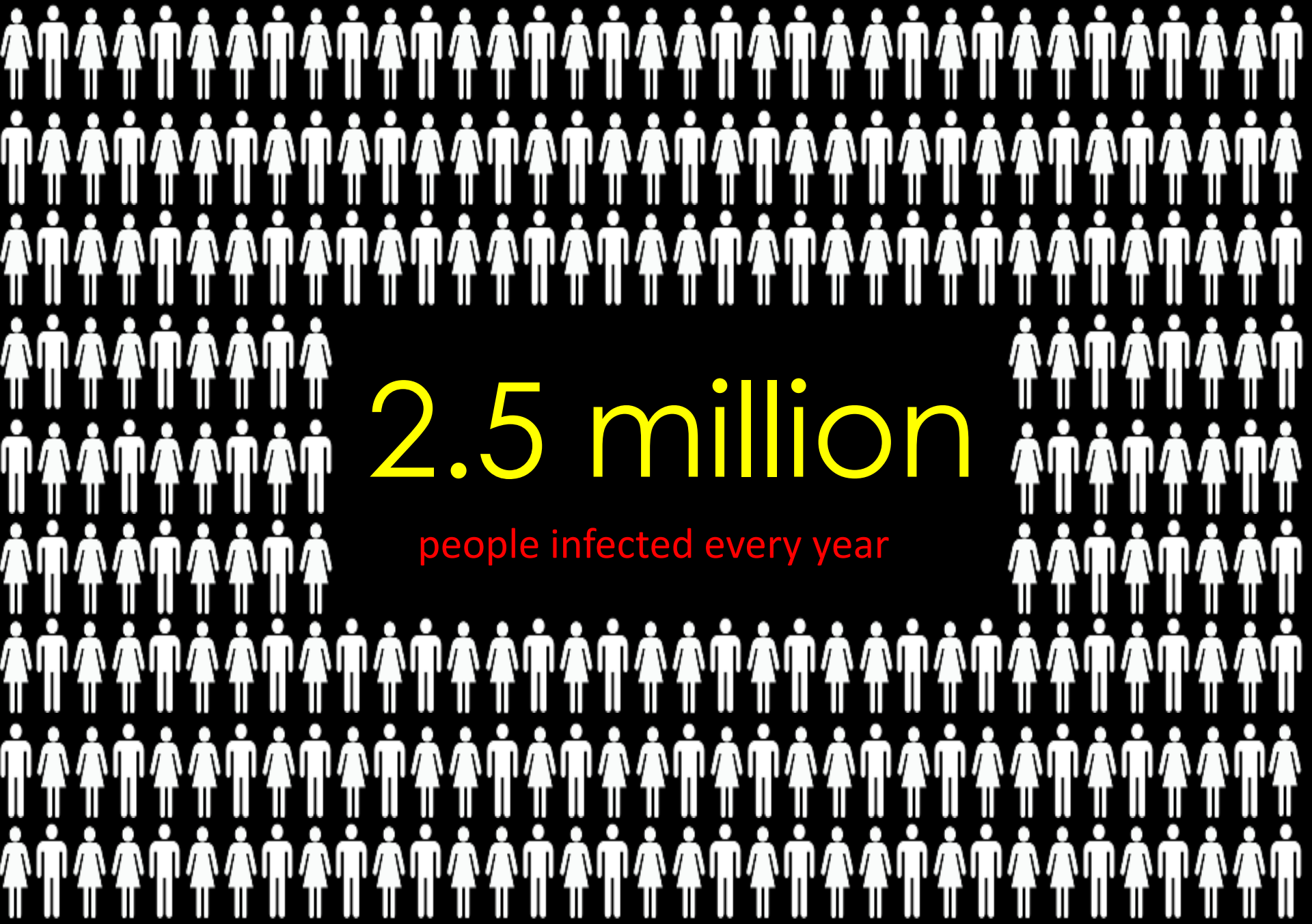
Adapted Bendavid et al. CROI2012

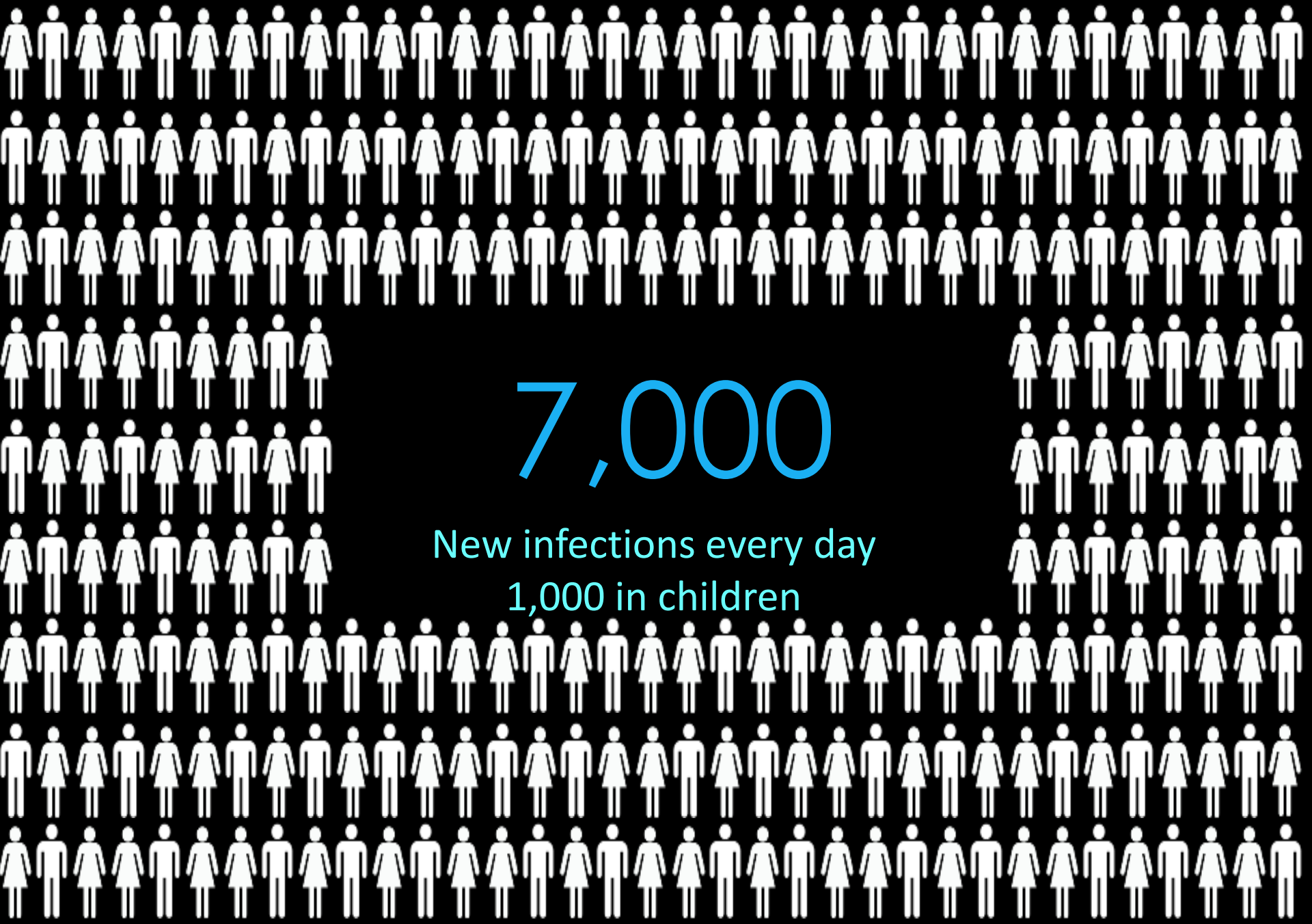
Deaths in PEPFAR-Supported Countries in Africa



Adapted Bendavid et al. CROI 2012

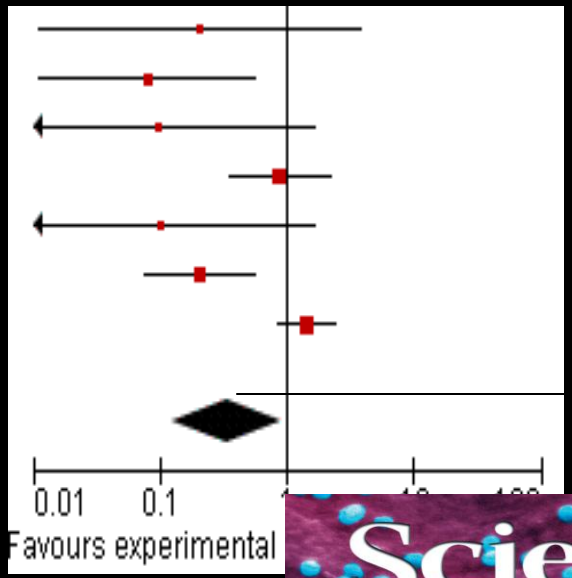

6-25 million
Additional people who need treatment

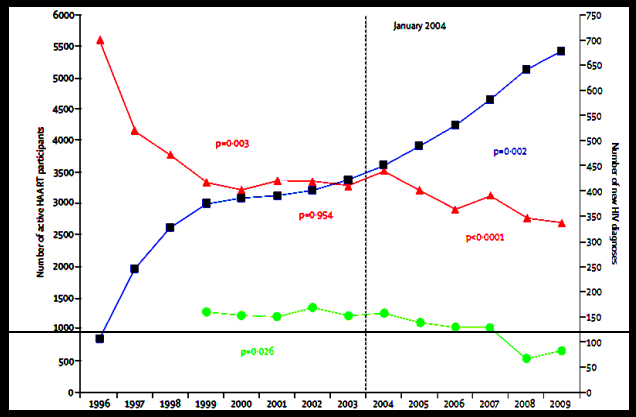

2.5 million
people infected every year

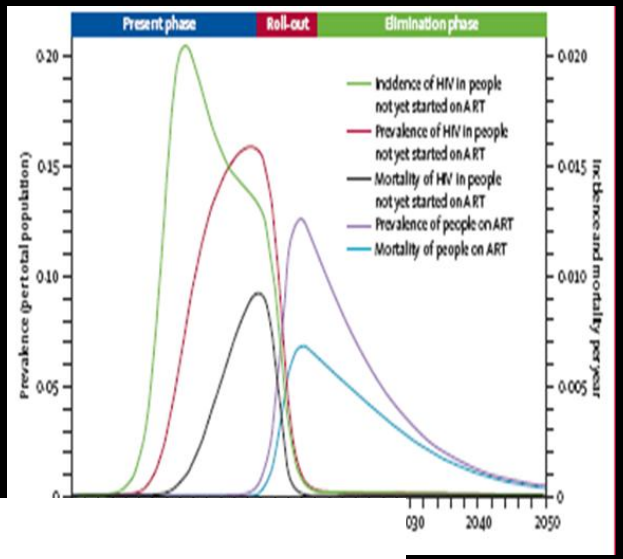

7,000
New infections every day
1,000 in children

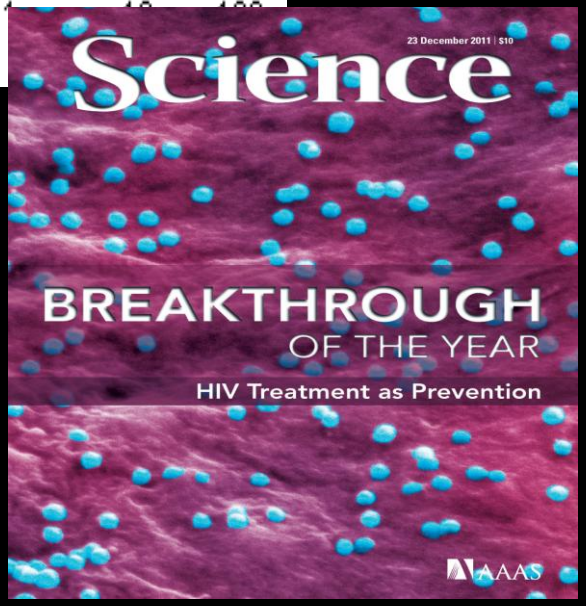
We can’t treat our way out of this epidemic

ART for Prevention: The Evidence









HPTN 052 Study

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

+ 39 HIV Transmissions

28 linked HIV transmissions

11 unlinked

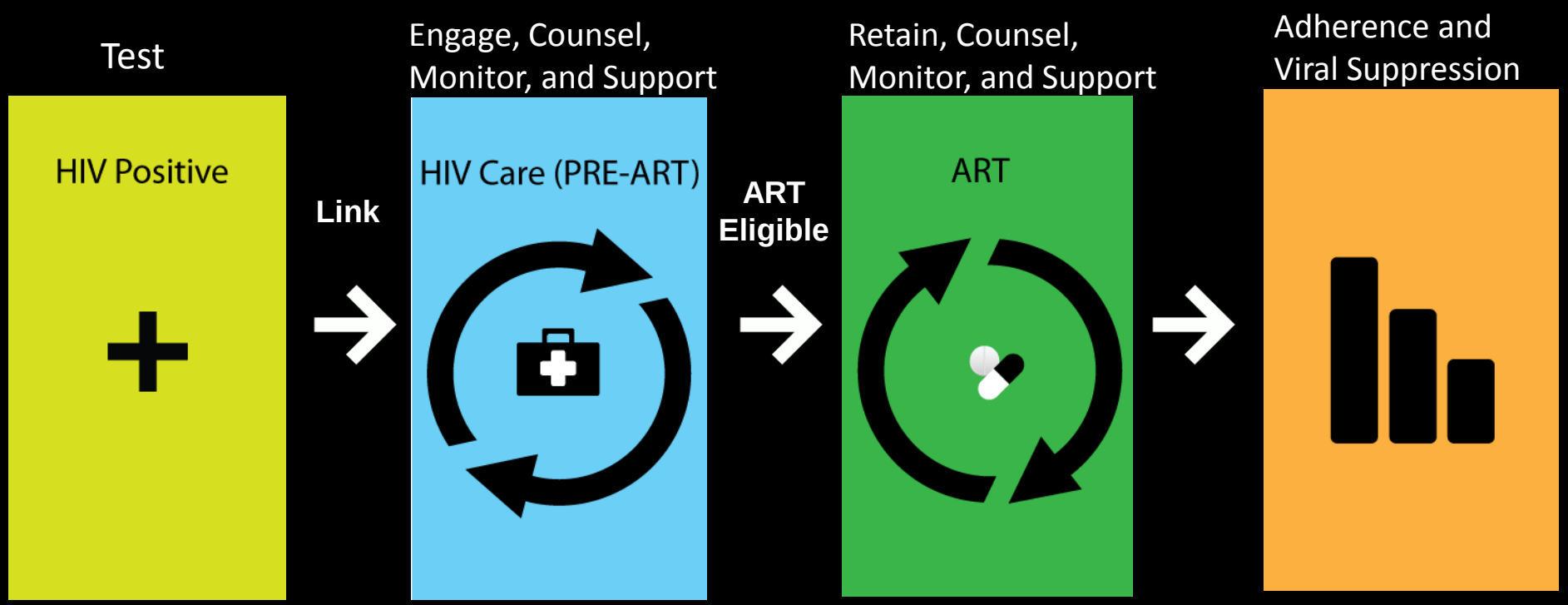
Immediate ART: 1 transmission

Deferred ART: 27 transmissions

☑ **96% Protection**

We can treat our way out of this epidemic

HIV Continuum

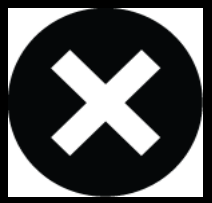


McNairy et al, AIDS 2012

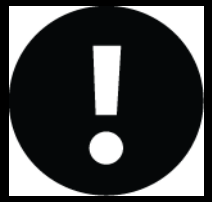
Challenges in Achieving Potential of ART for Prevention

Unaware of HIV Status

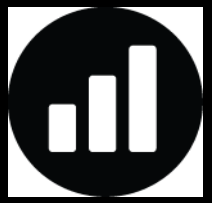
Late Diagnosis of HIV Disease



Failures in Linkage and Retention in Care

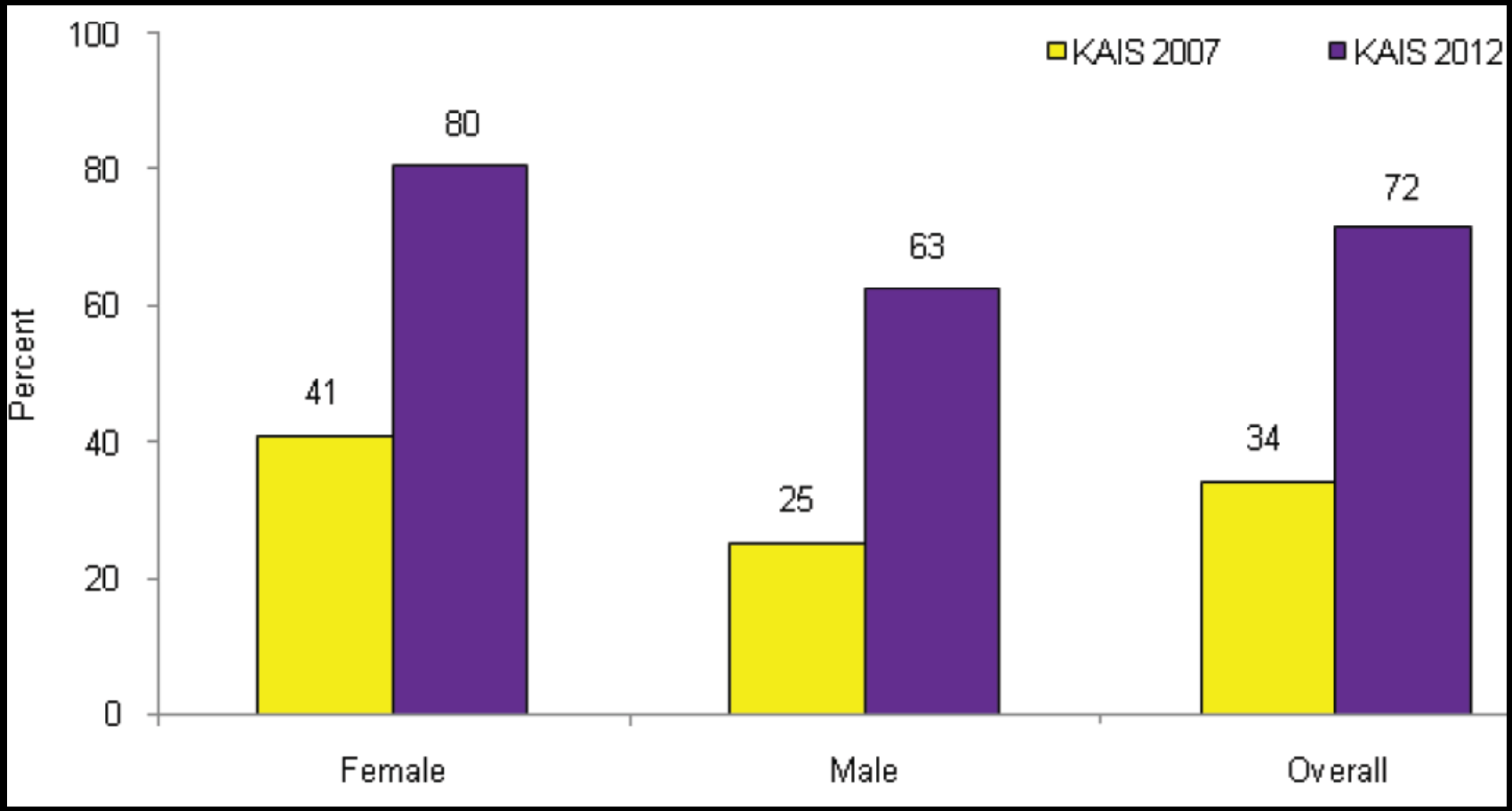


Late Initiation of ART



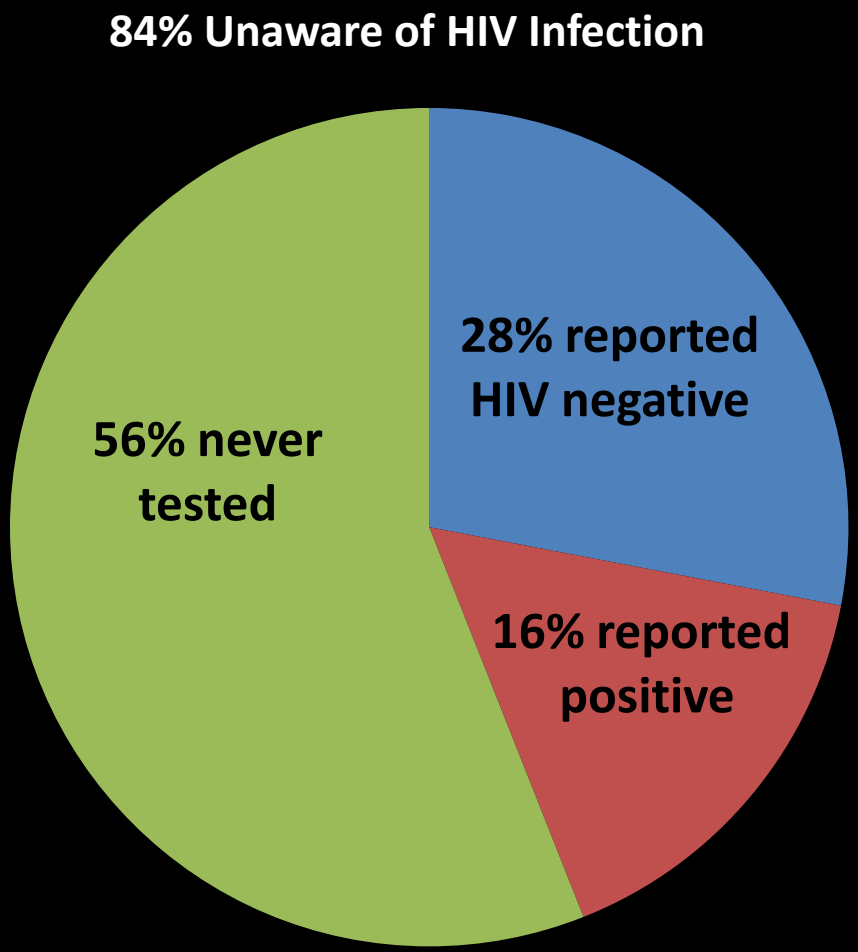
Inability to Achieve and Maintain Viral Suppression

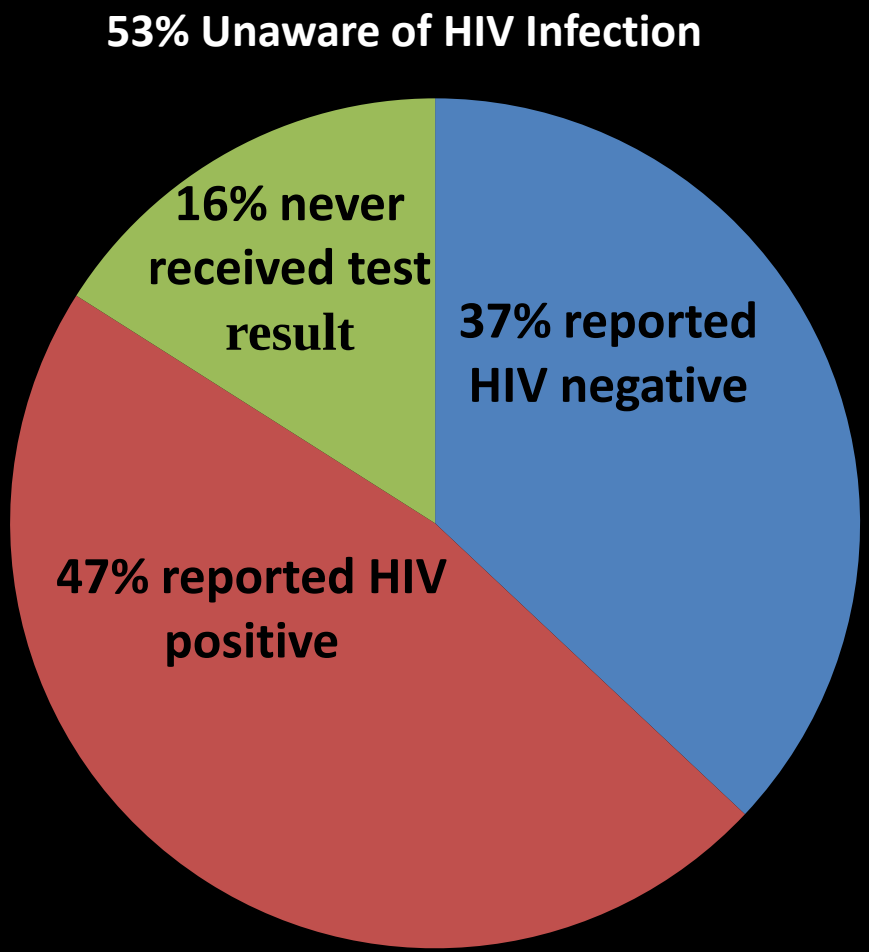
HIV Testing-Kenya (15-64 yrs) 2007 & 2012



KAIS Preliminary Findings 2012

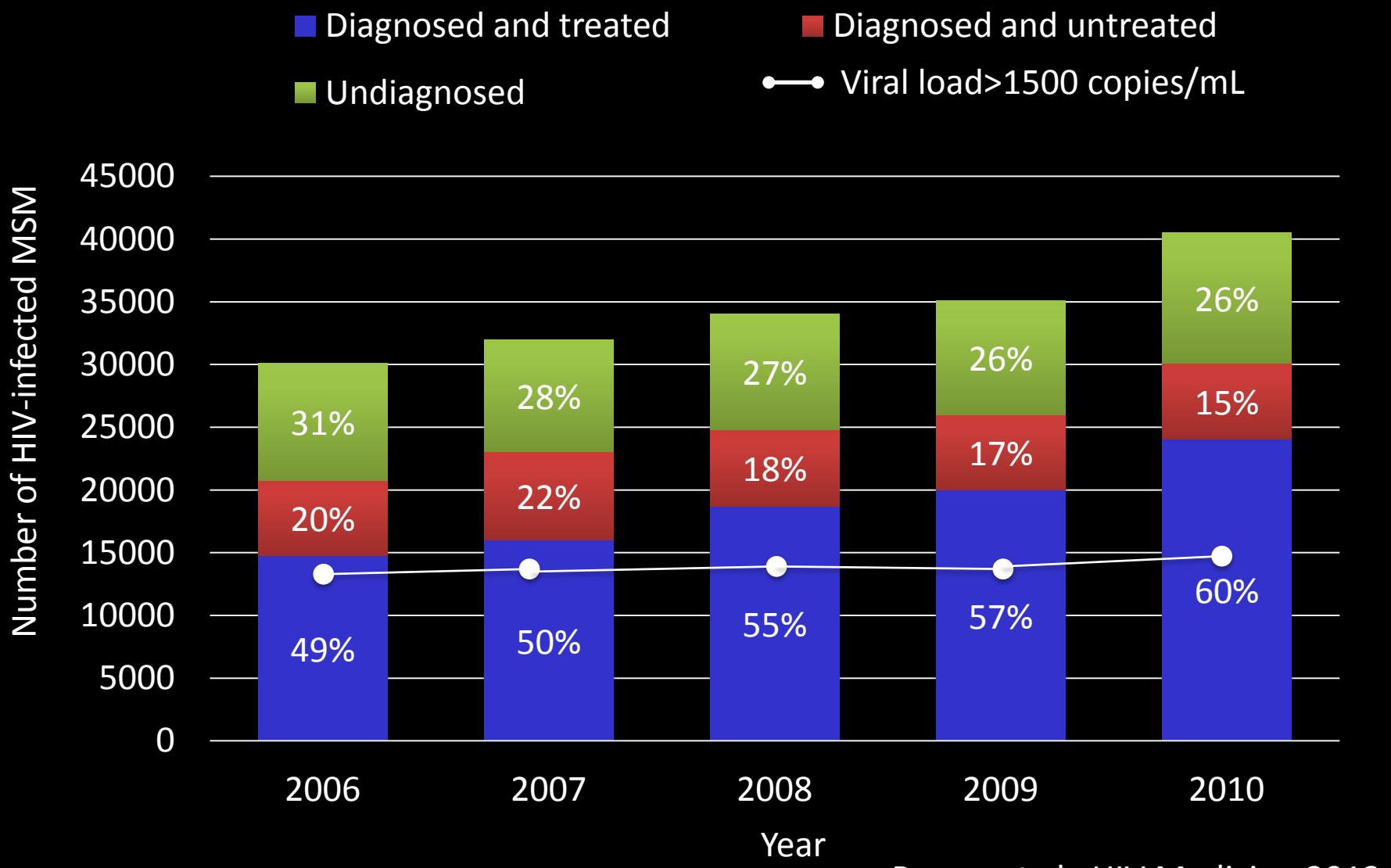
Awareness of HIV Positive Status-- Kenya (15-64 yrs)





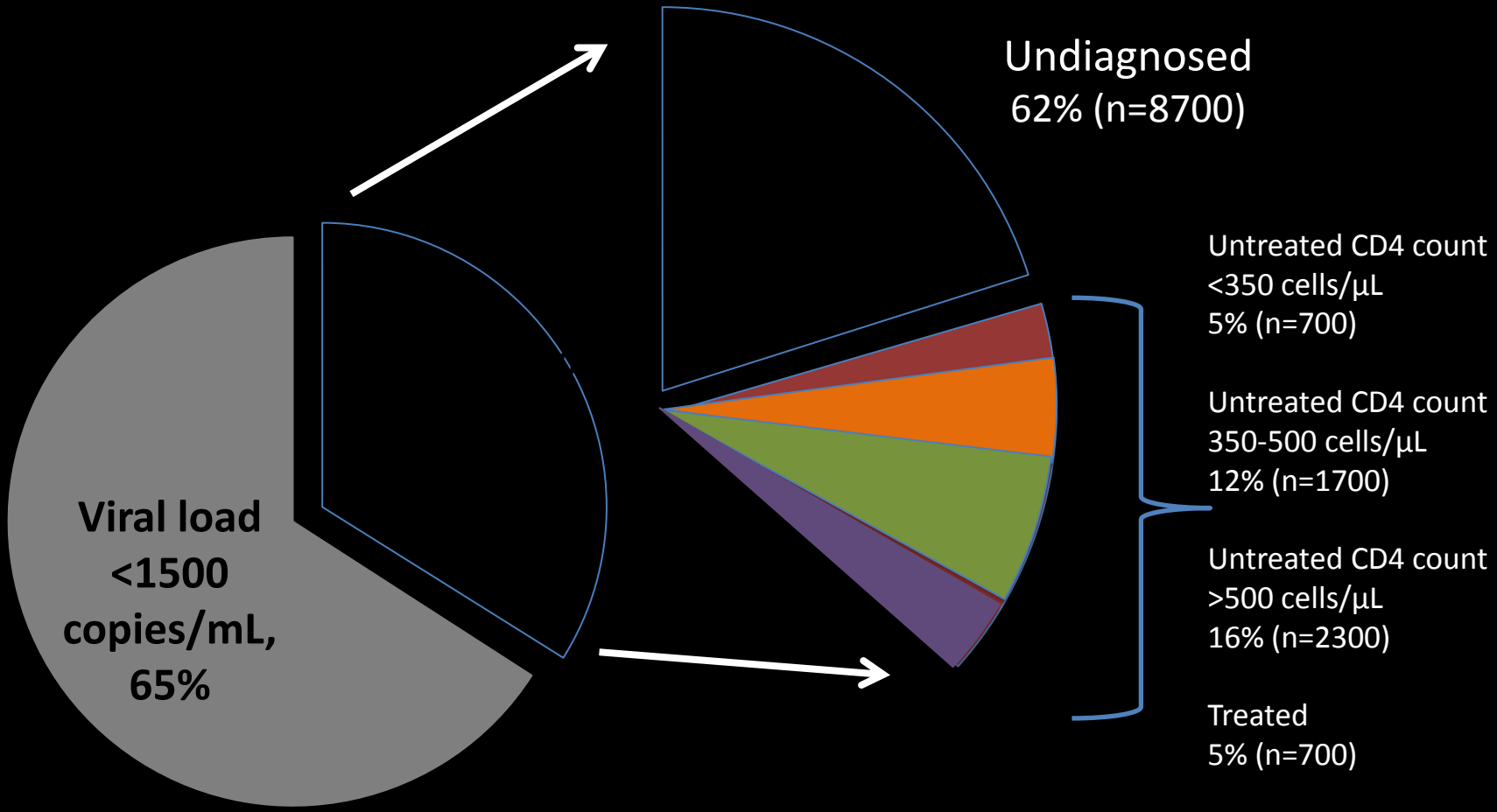
Kais 2012

HIV Diagnosis, ART Coverage and Viral Suppression– MSM in UK



Brown et al. HIV Medicine 2013

Distribution of Viral Load among MSM 2010-- UK



Brown et al. HIV Medicine 2013

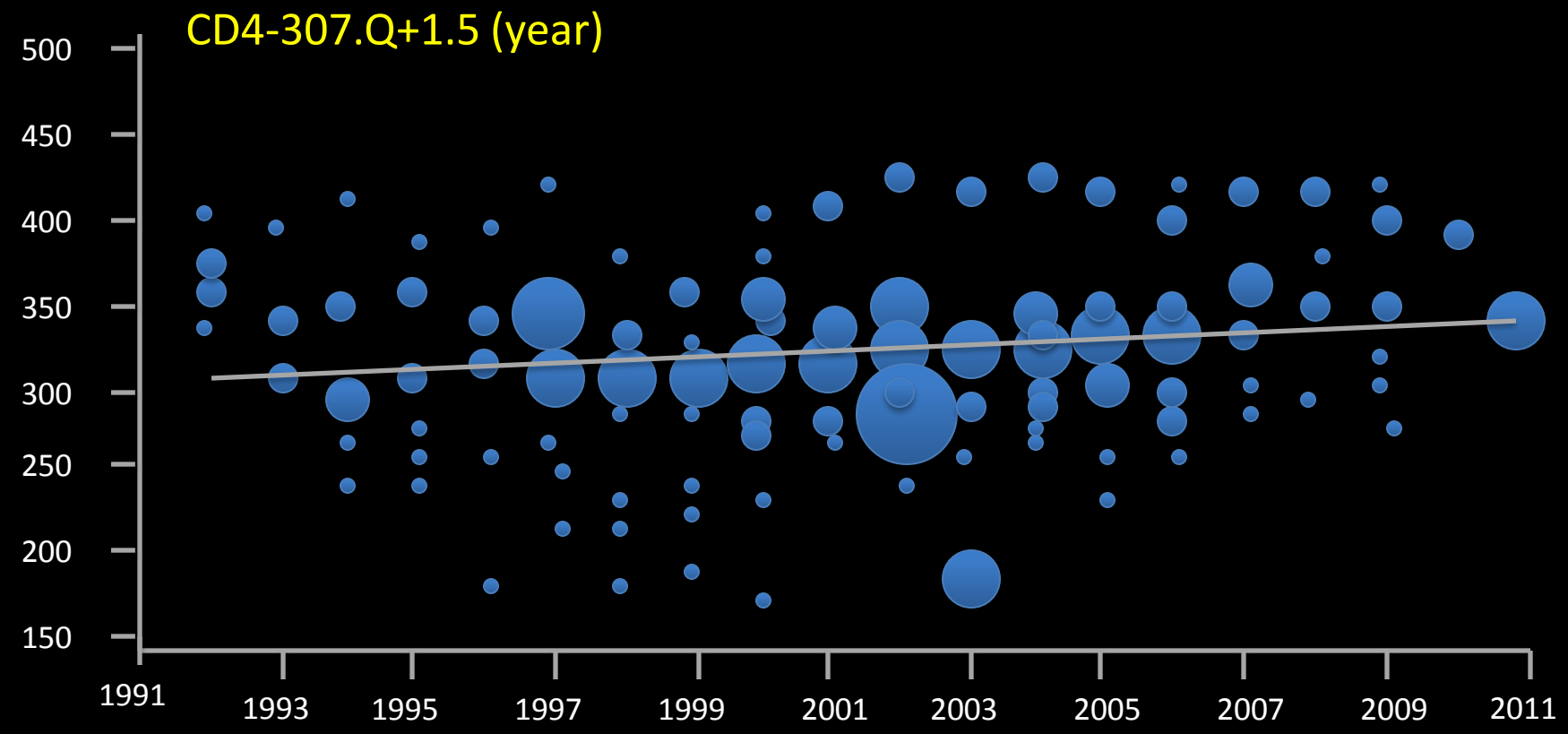
Lack of Awareness of HIV Infection: US MSM tested, by race/ethnicity

21 U.S. cities, 2008

Race/ethnicity	Total Number	HIV-infected and unaware
Asian/Pacific Islander	140	2.9%
Black, non-Hispanic	1,674	14.5%
Hispanic	1,850	6.7%
White, non-Hispanic	3,163	3.0%
Other	33	10.2%

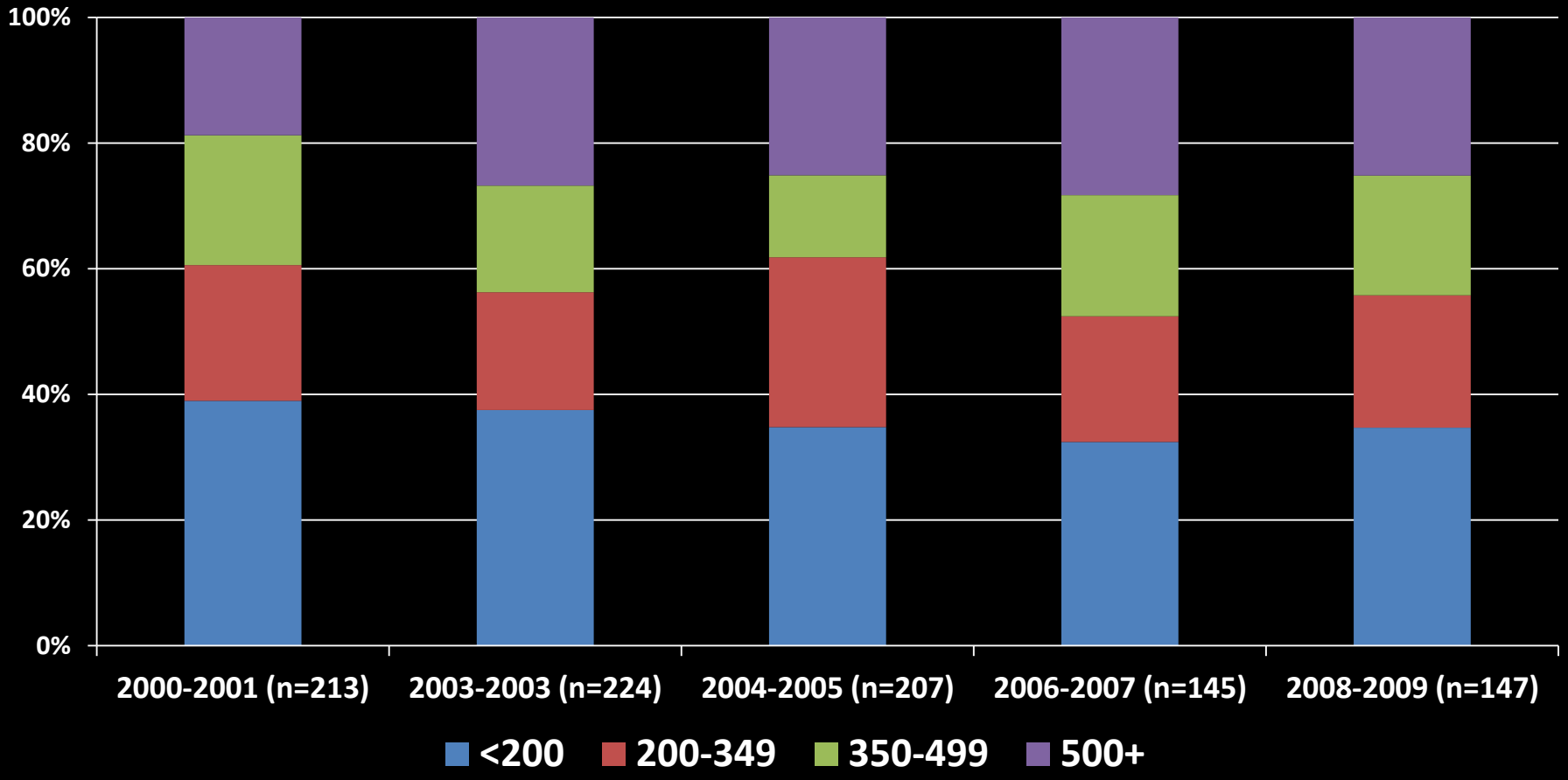
CDC. National HIV Behavioral Surveillance. *MMWR 2011; 60:694-699*

Mean CD4+ Cell Count Over Time in Developed Countries N= 44 studies



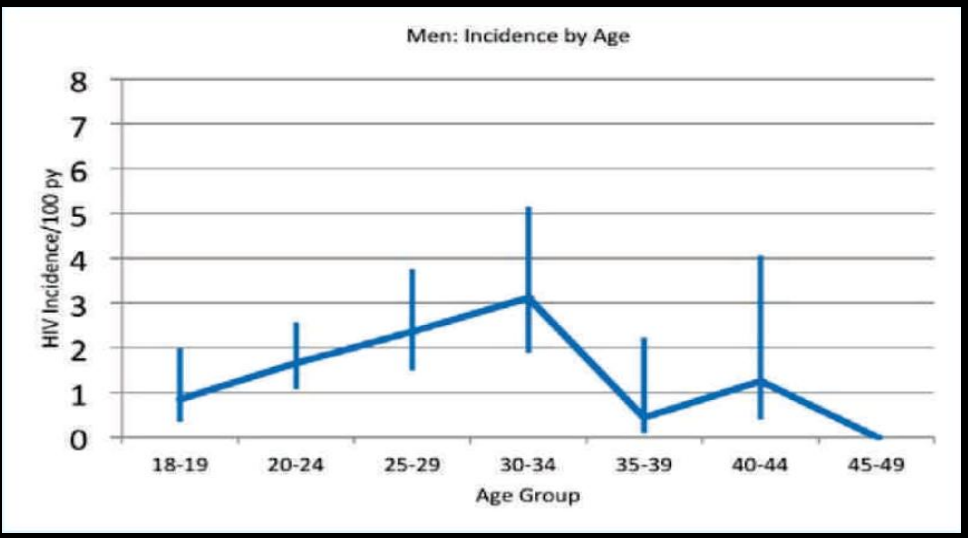
Lesko et al Clin Infec Dis 2013

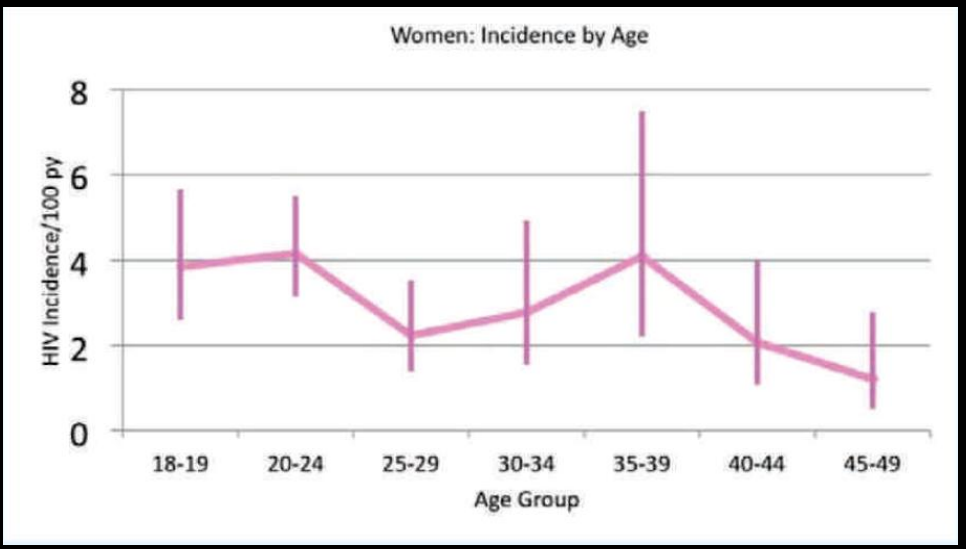
CD4 + Cell Counts at HIV Diagnosis—US HIV Outpatient Study (HOPS), 2000-2009



Buchacz K, Armon C, Palella F, et al. *AIDS Research and Treatment*, vol. 2012, 1-7.

Nationally representative sample of 18,169 adults (18-49 yrs)





Shims
Swaziland HIV Incidence Measurement Survey

Population HIV Viral Load in Swaziland: Assessing ART Program Effectiveness and Transmission Potential

Jessica Justman[1], Tanya M. Ellman[2], Deborah Donnell[3], Yen T. Duong[4], Jason Reed[4], George Bicego[5], Peter Ehrenkranz[5], Joy Chang[4], Lei Wang[3], Naomi Bock[4] and Rejoice Nkambule[6] for the SHIMS Study Team

[1]Columbia University, ICAP, Mailman School of Public Health, New York, United States, [2]Columbia University Medical Center, Medicine, New York, United States, [3]Fred Hutchinson Cancer Research Center, Seattle, United States, [4]Centers for Disease Control and Prevention, Atlanta, United States, [5]Centers for Disease Control and Prevention, Mbabane, Swaziland, [6]Ministry of Health - Swaziland, Mbabane, Swaziland

Abstract # 96
CROI, March 5, 2013

Estimating HIV Prevalence from the Swaziland HIV Incidence Measurement Survey

Rejoice Nkambule, Henry Ginindza, George Bicego, Deborah Donnell, Jessica Justman, Jason Reed, Ingrid Peterson and the SHIMS team

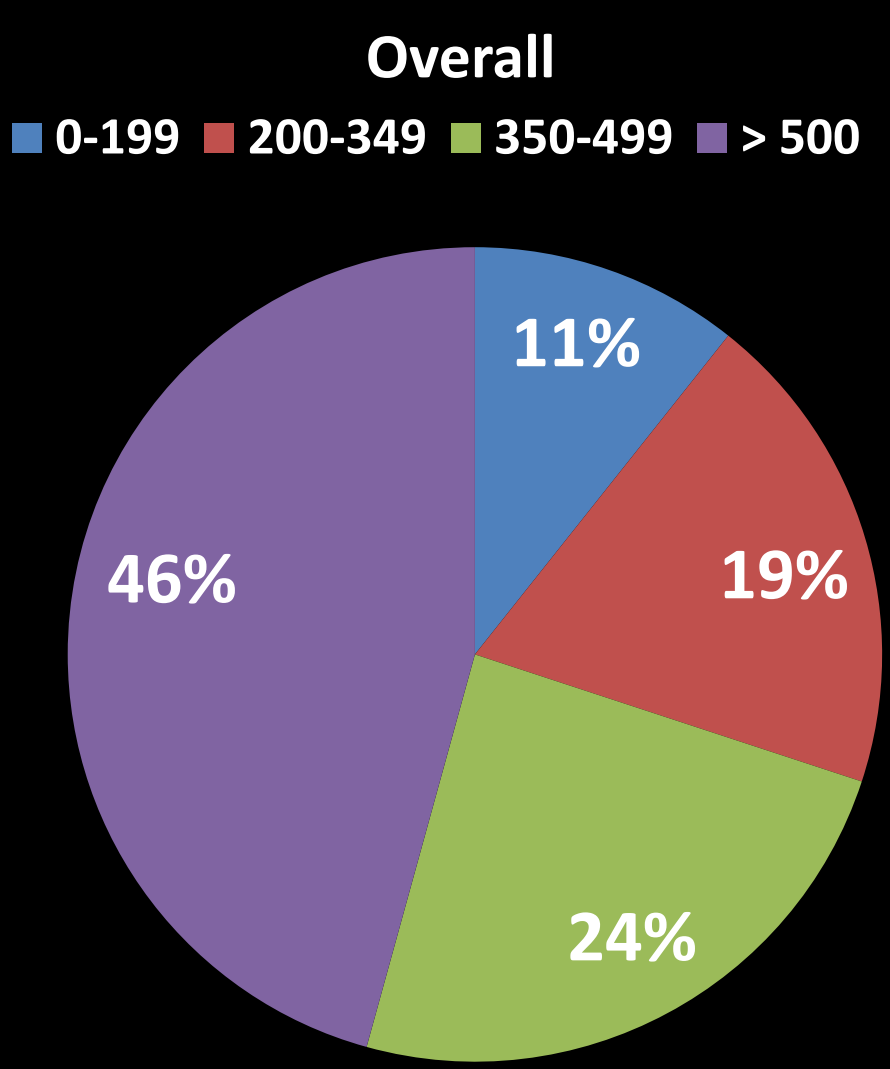
Abstract # 142
March 8, 2012

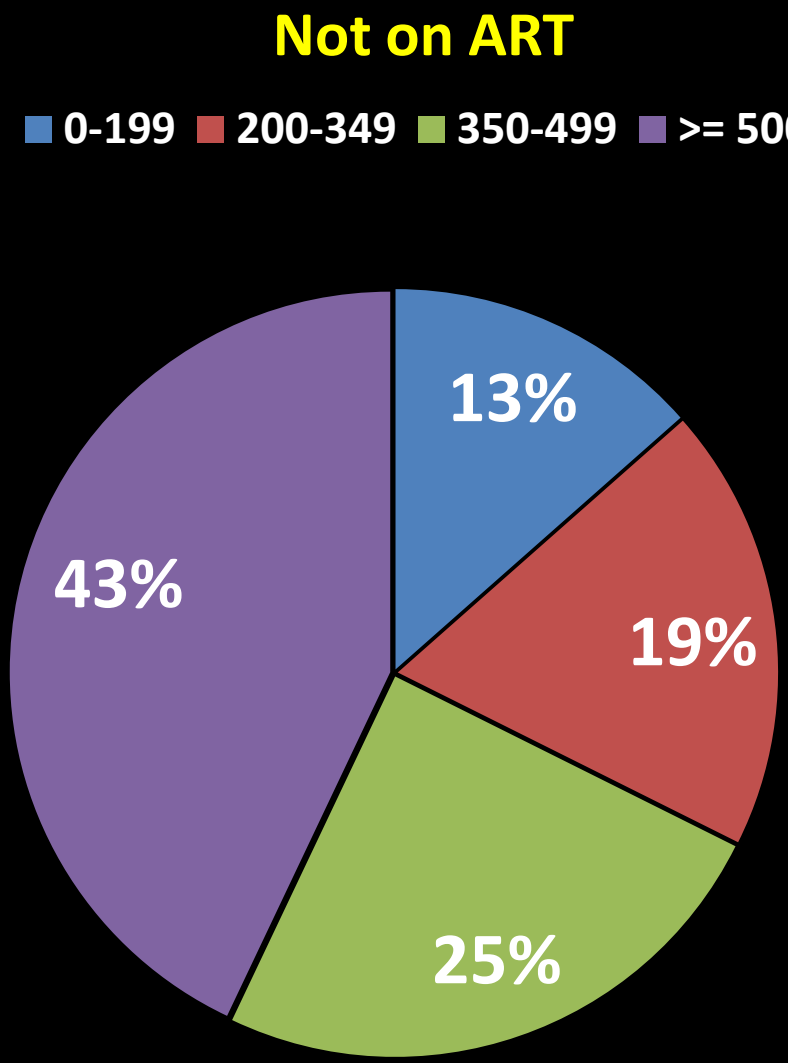
Estimating National HIV Incidence from Directly Observed Seroconversions in the Swaziland HIV Incidence Measurement Survey

Jason Reed, Jessica Justman, George Bicego, Deborah Donnell, Naomi Bock, Henry Ginindza, Alison Koler, Neena Philip, Makhosazna Makhanya, Khudzie Mlambo, Bharat S. Parekh, Yen T. Duong, Dennis L. Ellenberger, Connie Sexton, Rejoice Nkambule and the SHIMS Team

Abstract # FRLBX02
July 27, 2012

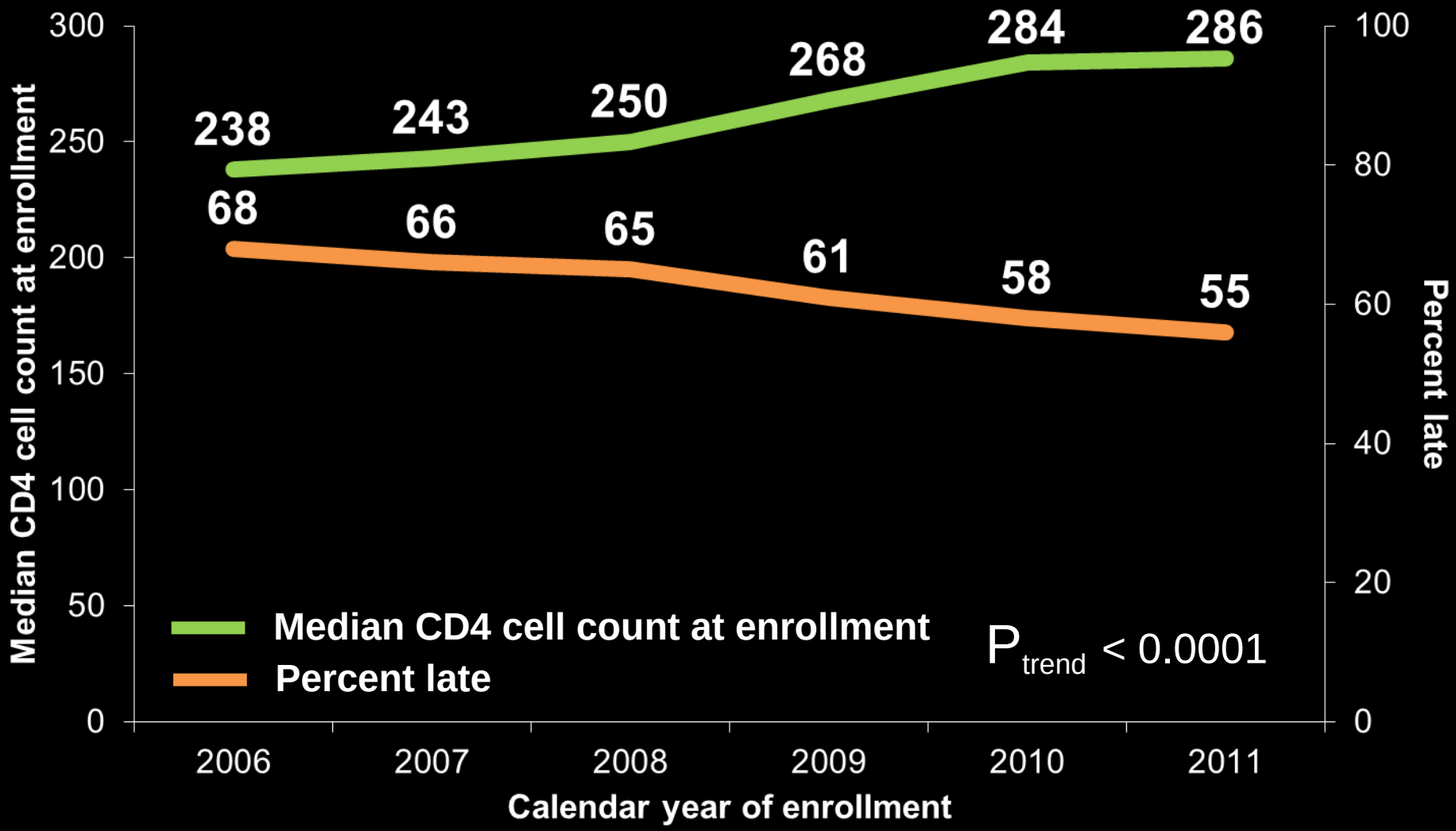
Population CD4+ Count Distribution—Swaziland





Azih et al. CROI 2013

Median CD4+ Count and Late Enrollment in Care Over Time

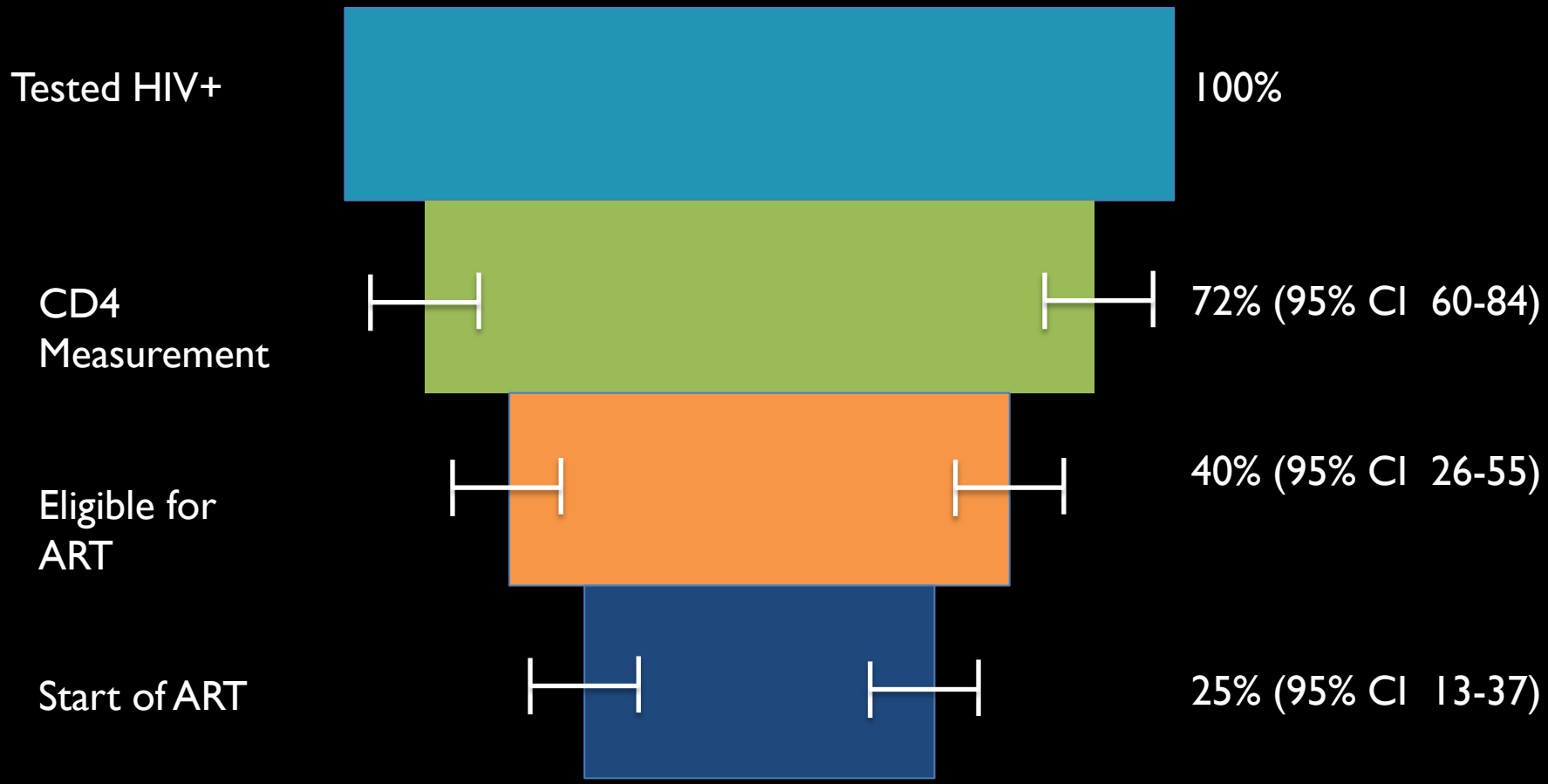


CD4<350 or WHO 3/4

Hoffman et al, CROI 2013

HIV Care Cascade in Sub Saharan Africa

29 studies included



Of 100 HIV+ patients, on average, 25 started ART.
Of ART-eligible patients 62% (95% CI 55.2-70.7%) started ART.

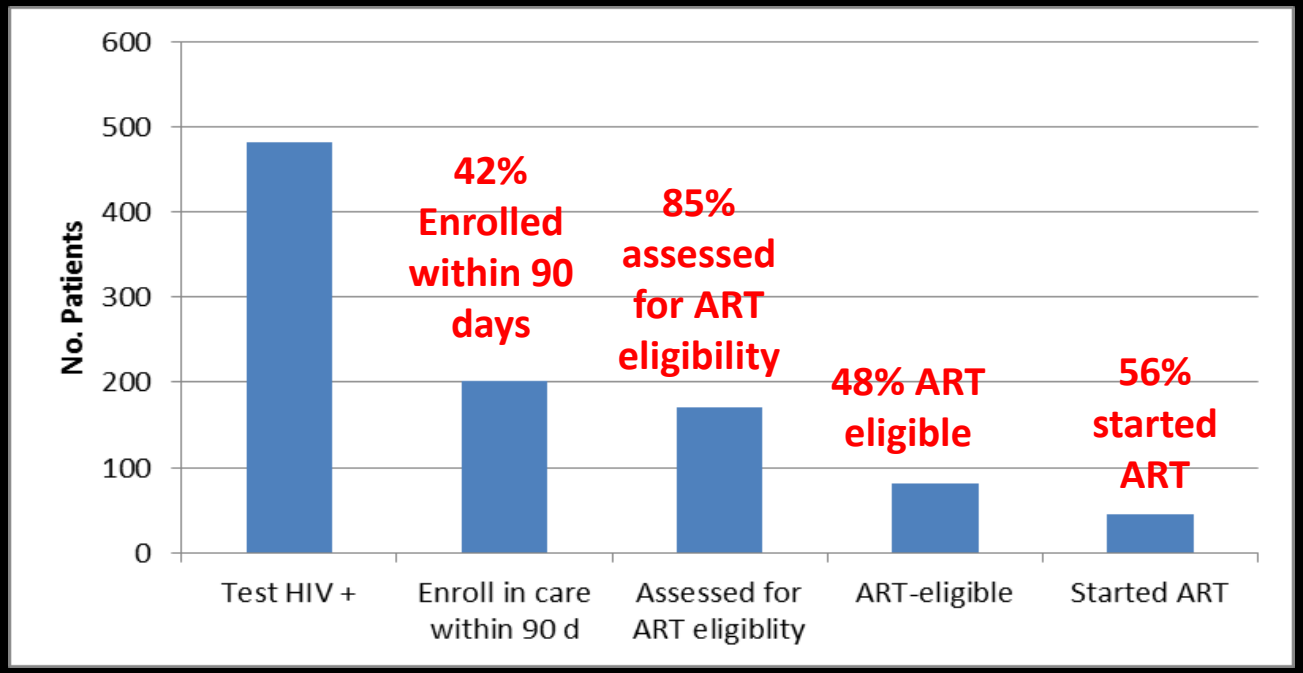
Mugglin et al. CROI 2012,

OPEN ACCESS Freely available online

PLoS one

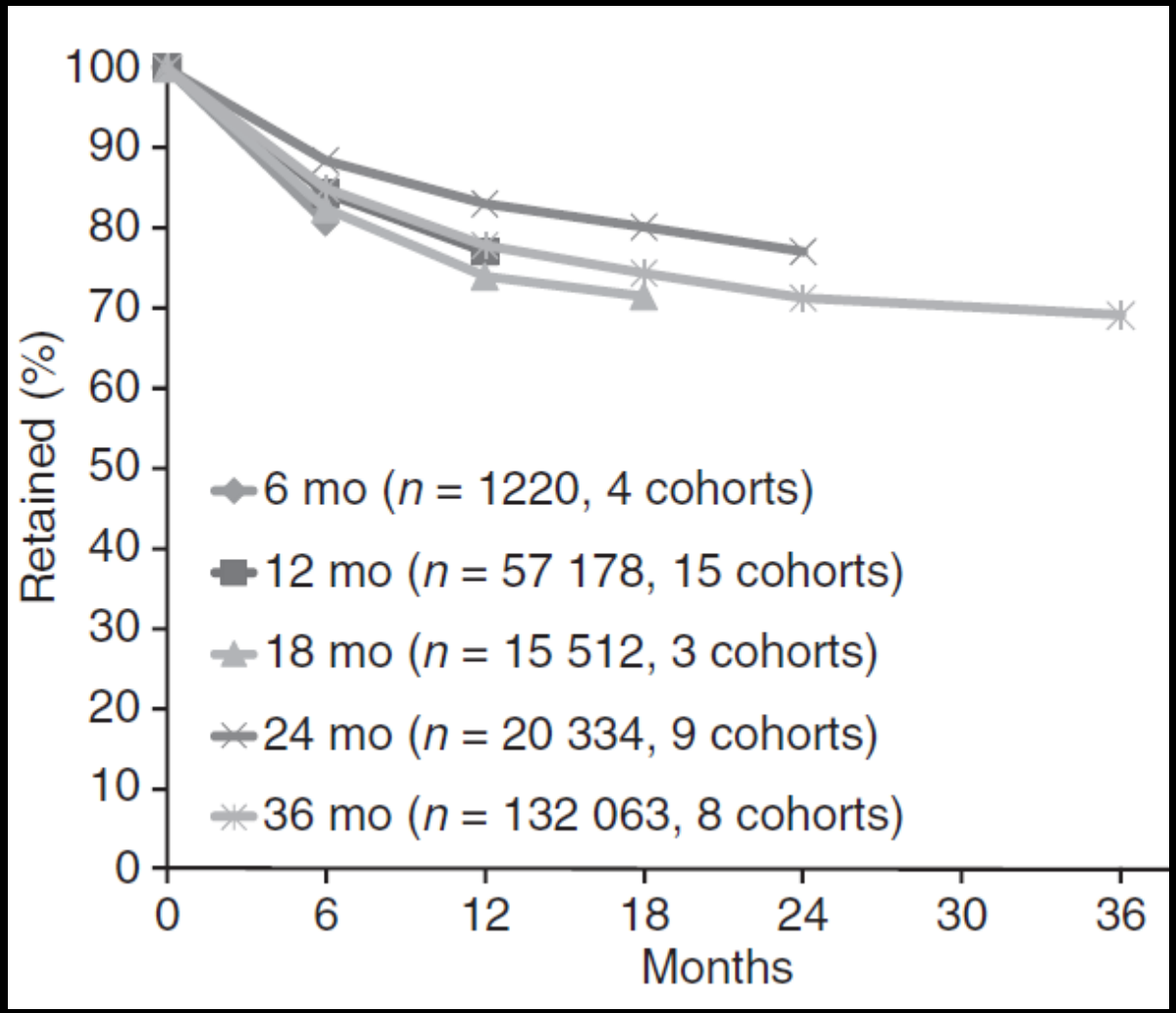
Patient Enrolment into HIV Care and Treatment within 90 Days of HIV Diagnosis in Eight Rwandan Health Facilities: A Review of Facility-Based Registers

- 8 health clinics
- 492 patients testing HIV+ from March-May 2009
- Testing sites: ANC, VCT, TB, OPD
- Median age 29 years, median CD4+ 387 cells/uL



Kaygamba et alPlos One, May 2012

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%

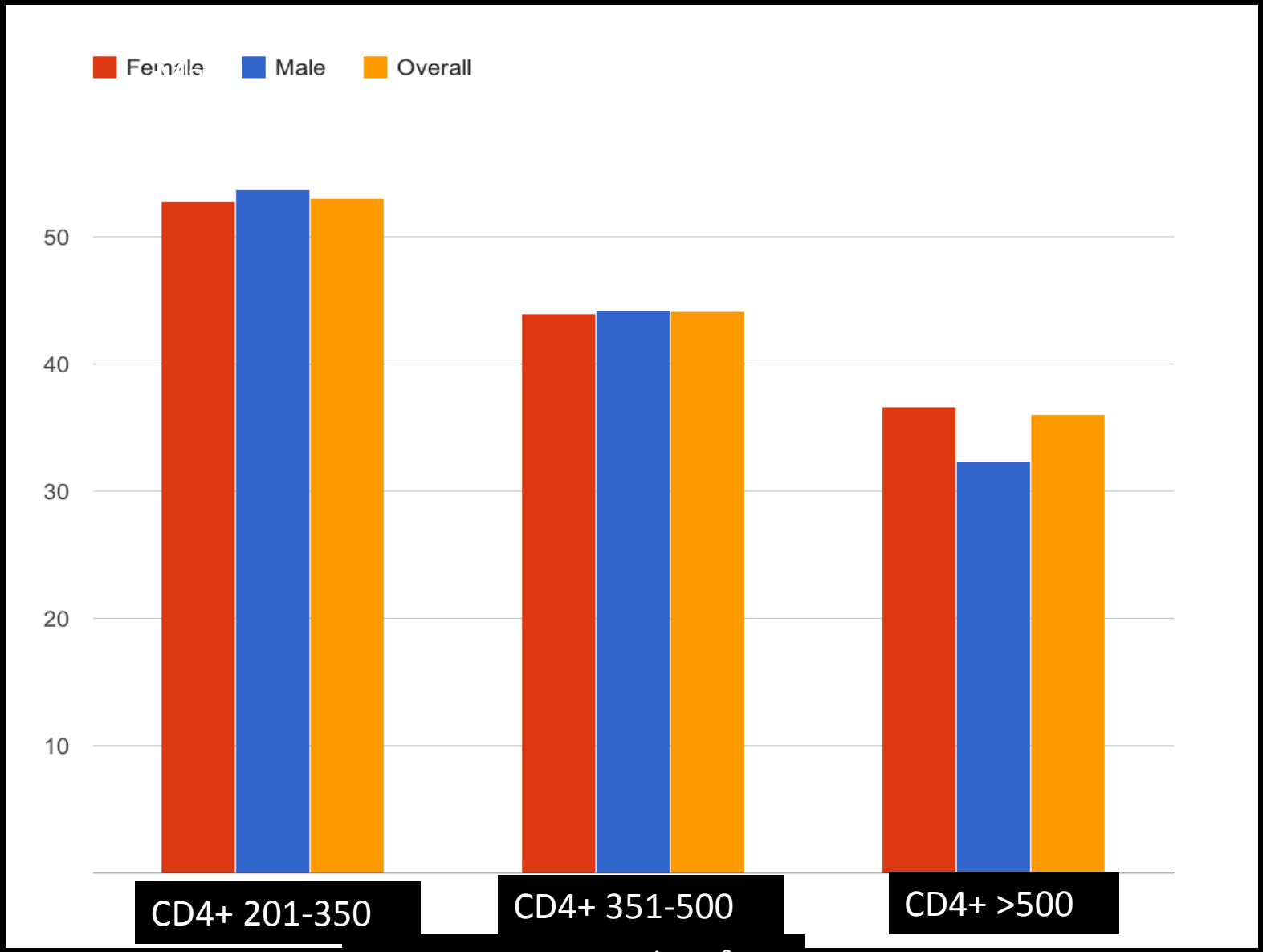
Fox and Rosen, Trop Med Int Health 2010

Barriers to Care and Predictor of Attrition: Systematic Review

Adapted Govindasamy et al. AIDS

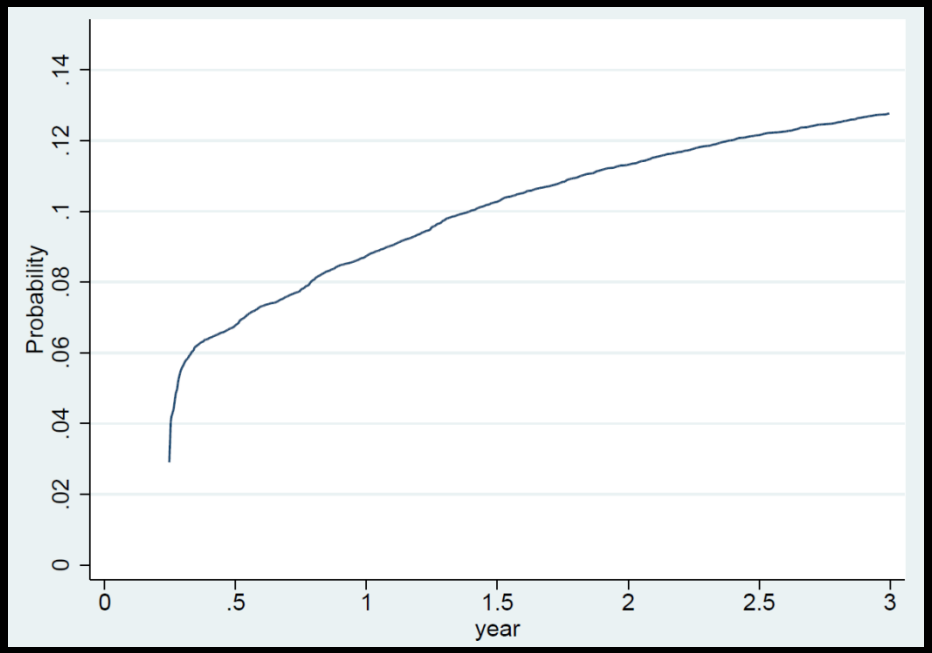
Factor	Predictor of Attrition	Barrier to Care
Economical		
Transport costs	✓	✓
Distance	✓	✓
Unable to make time (work)		✓
Food Shortage		✓
Patient time constraints		✓
Psycho-Social		
Stigma/fear of disclosure		✓
Fear of drug toxicities		✓
Perceived good health		✓
Health Systems		
Long clinic waiting times		✓
Poor service from HCWs		✓
Shortage of HCWs	✓	✓
Inconvenient clinic hours		✓

Retention in HIV Care (pre-ART) by Initial CD4+ Cell Count

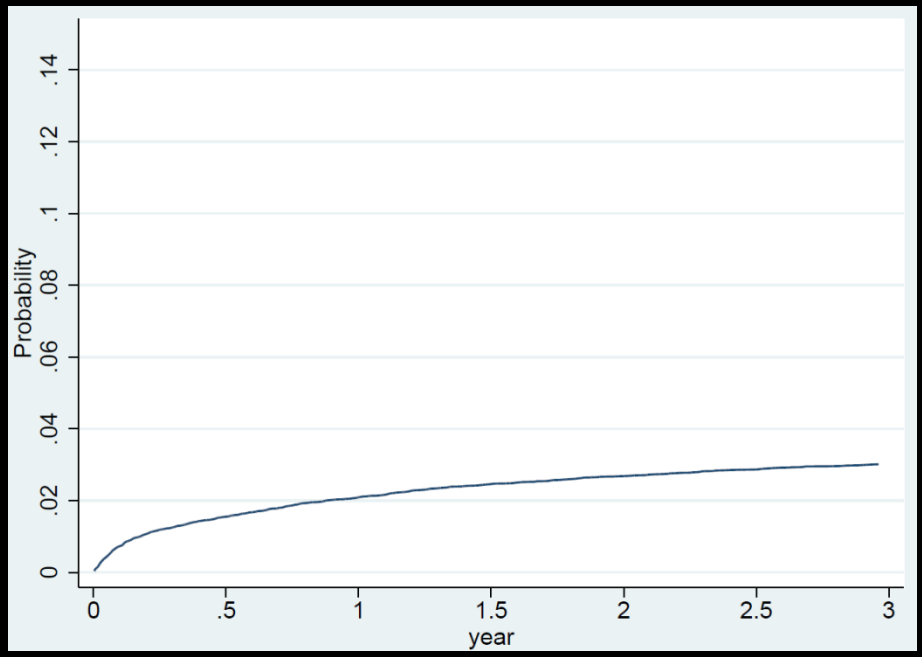


Adapted--Lessells et al, JAIDS 2011

LTF and mortality among pre-ART adult patients at 41 facilities in Rwanda (N=31,027)



Loss to follow-up in Pre-ART patients



Mortality in Pre-ART patients

	6 months	12 months	24 months
LTF	**6.6% (95%CI 6.3-6.9)**	**8.6% (95% CI 8.3-9.0)**	**11.2% (95%CI 10.9-11.6)**
Mortality	**1.5% (95%CI 1.4-1.7)**	**2.1% (95%CI 1.9-2.2)**	**2.7% (95%CI 2.5-2.8)**

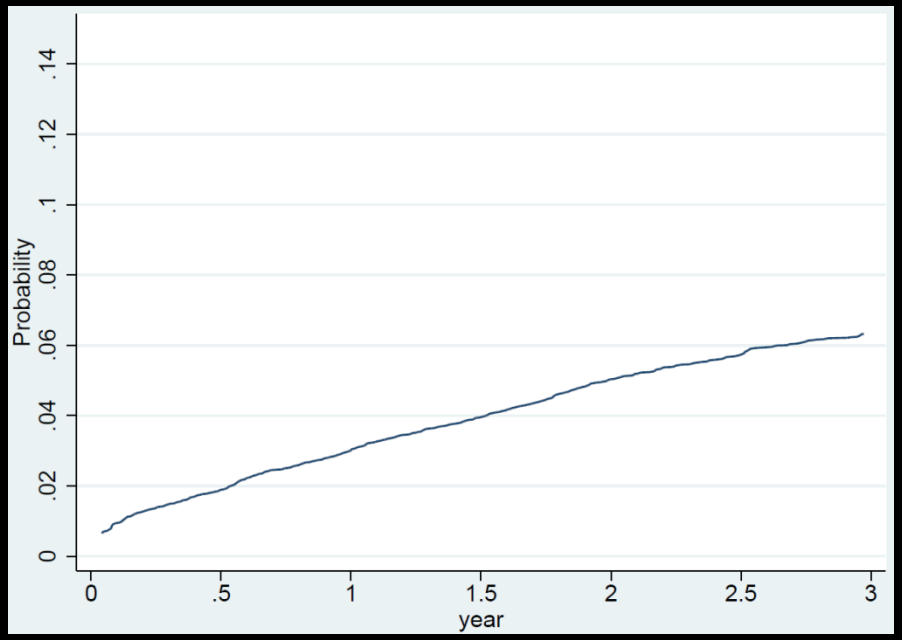
Teasdale et al, CROI 2013

Selected demographic and clinical characteristics and pre-ART LTF (N=31,027)

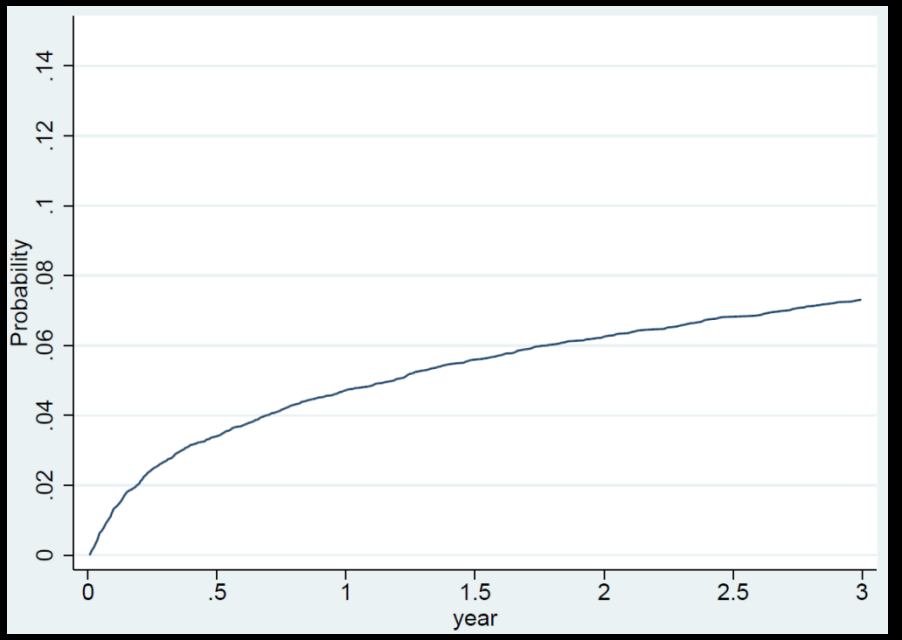
		aSHR*	95% CI
Male sex		1.27	1.08-1.51
Age	21-30	1.46	1.30-1.64
	31-40	1	Ref.
	41-50	0.84	0.73-0.95
Single vs. married		1.30	1.09-1.56
WHO Stage	I	1	Ref.
	II	0.69	0.55-0.87
	III	0.64	0.48-0.85
	IV	0.35	0.20-0.59
CD4+ count	<100	0.19	0.13-0.30
	100-199	0.20	0.15-0.27
	200-349	0.35	0.28-0.45
	≥350	1	Ref.

Teasdale et al, CROI 2013

LTF and mortality among adults on ART at 41 facilities in Rwanda (N=17,212)



Loss to follow-up in ART patients



Mortality in ART patients

	6 months	12 months	24 months
LTF	**1.9% (95%CI 1.8-1.9)**	**2.9% (95%CI 2.8-2.9)**	**4.4% (95%CI 4.4-4.5)**
Mortality	**3.4% (95%CI 3.4-3.5)**	**4.7% (95%CI 4.7-4.8)**	**6.3% (95%CI 6.2-6.4)**

Teasdale et al, CROI 2013

Selected demographic and clinical characteristics and LTF among adults on ART (N=17,212)

Characteristic		aHR†	95% CI
Male sex		1.39	1.17-1.67
Age	21-30	1.4	1.16-1.67
	31-40	1	Ref.
	41-50	0.81	0.72-0.92
Single vs. married		1.65	1.2-2.3
CD4 count	<100	0.64	0.44-0.92
	100-199	0.68	0.51-0.91
	200-349	0.63	0.51-0.79
	≥350	1	reference

†adjusted hazard ratio from Cox proportional hazards risk models

Teasdale et al, CROI 2013

Willingness to Initiate ART--SA

- 7287 adult patients HIV tested
  - 2,562 (35%) HIV-infected
    - 743 (29%) eligible for ART
  - 148 (20%) refused referral to initiate ART,
    - most (92%) refused again two months later
  - Characteristics of those who refused:
    - Median CD4+ count: 110 cells/mm^3
    - Factors associated with refusal:
      - Single: AOR: 1.8 (1.06-3.06)
      - TB: AOR: 3.5 (1.55-6.61)
  - Most common reason for refusal was feeling well (35%)

Katz et al AIDS 2011

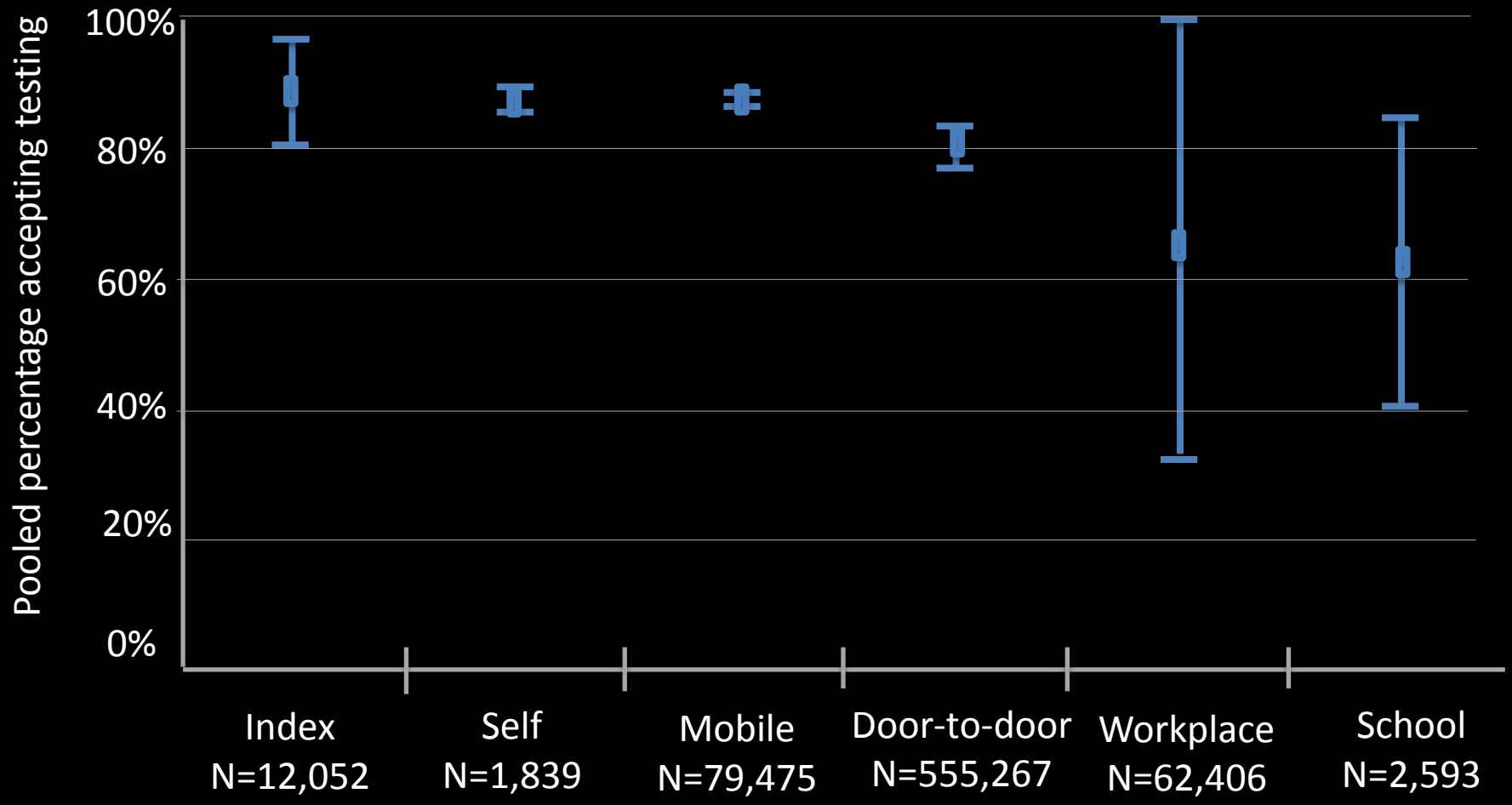
HPTN 052: Reasons for Declining ART at 1 Year and 1.5 Years of Follow-up

Reasons for Decline	N = 101 30 Jun 2012 (1 Year of Follow-up) [N (%)]	N = 73 31 Dec 2012 (1.5 Years of Follow-up) [N (%)]
Believes CD4 is too high	58 (57%)	42 (58%)
Not ready to begin ART (including) • Feels healthy • Doesn't want to take/commit to ART • Fear of side effects • Family problems • Mentally unprepared • Mobile lifestyle • In denial	28 (28%)	20 (27%)
Wants to discuss decision with family/friends	5 (5%)	3 (4%)
Plans to begin at a later date	3 (3%)	2 (3%)
Still deciding	1 (1%)	1 (1%)
Other/unknown reasons (including) • Lost-to-follow-up • Religious belief • Wants guaranteed drug supply after study • Spouse did not allow	6 (6%)	5 (7%)

Gamble et al, CROI 2013


HOW?

Uptake of Community HIV Testing and Counseling



Suthar et al PLoS 2013

Novel Approaches for Linkage & Retention

- **Novel Interventions**: POC CD4[1-2], case manager[3], SMS, care bags, financial/transport incentive[4]
- **Need for combination interventions:**
  - Use of multiple biomedical, structural and psychosocial barriers to testing and care

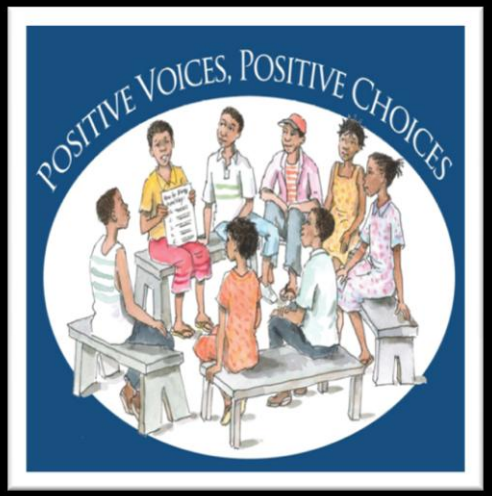
1. Jani et al. Lancet 2011
2. Faal et al. JAIDS 2011
3. Gardner et al. AIDS 2005
4. Emenyonu et al. CROI 2010
5. Kurth et al.. Curr HIV/AIDS Rep 2011
6. Merson et al. Lancet 2008
7. Piot et al. Lancet 2008
8. Van Rooyan CROI 2012

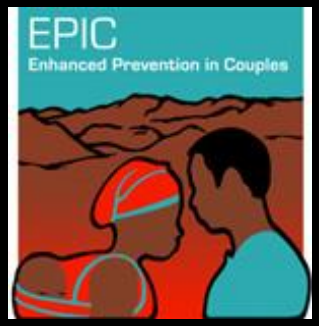
Link4Health

Swaziland combination strategy for linkange and retention

ENGAGE4HEALTH

LIGAÇÕES PELA SAÚDE



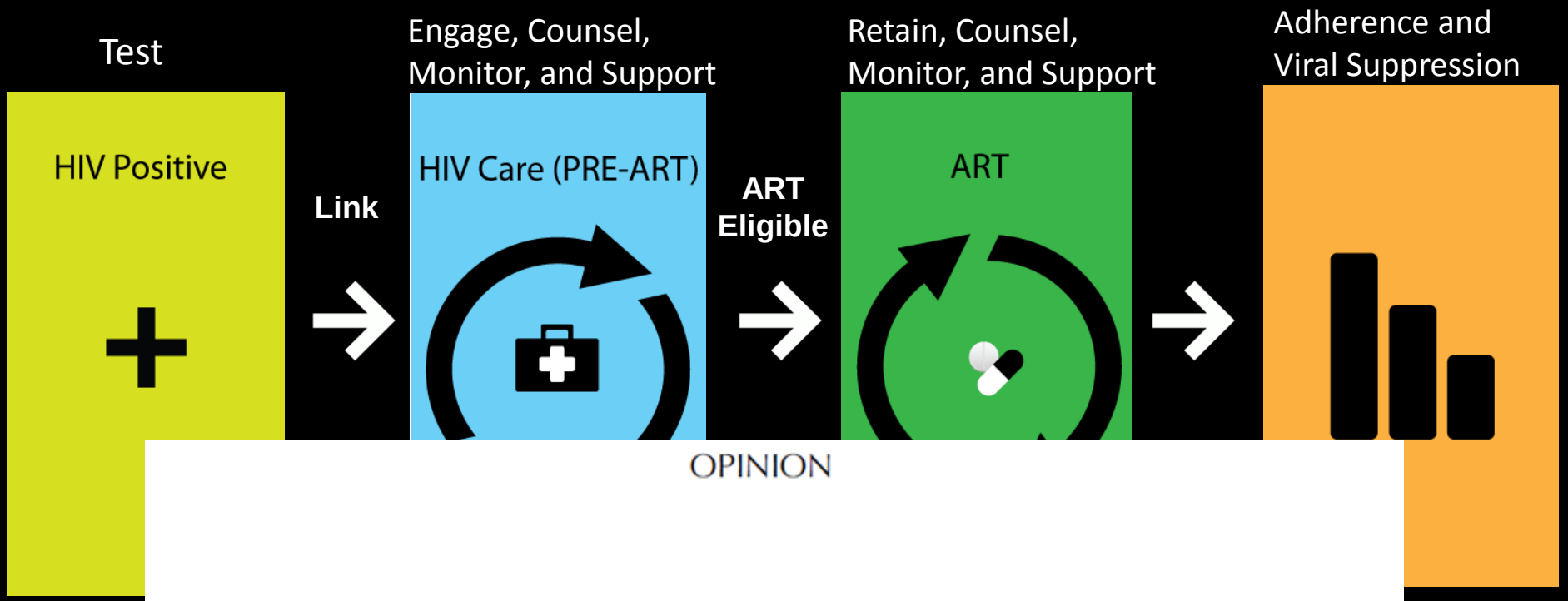


MIR4HEALTH

Mother and Infant Retention for Health

Start
TB patients on
ART and
Retain on
Treatment

HIV Continuum

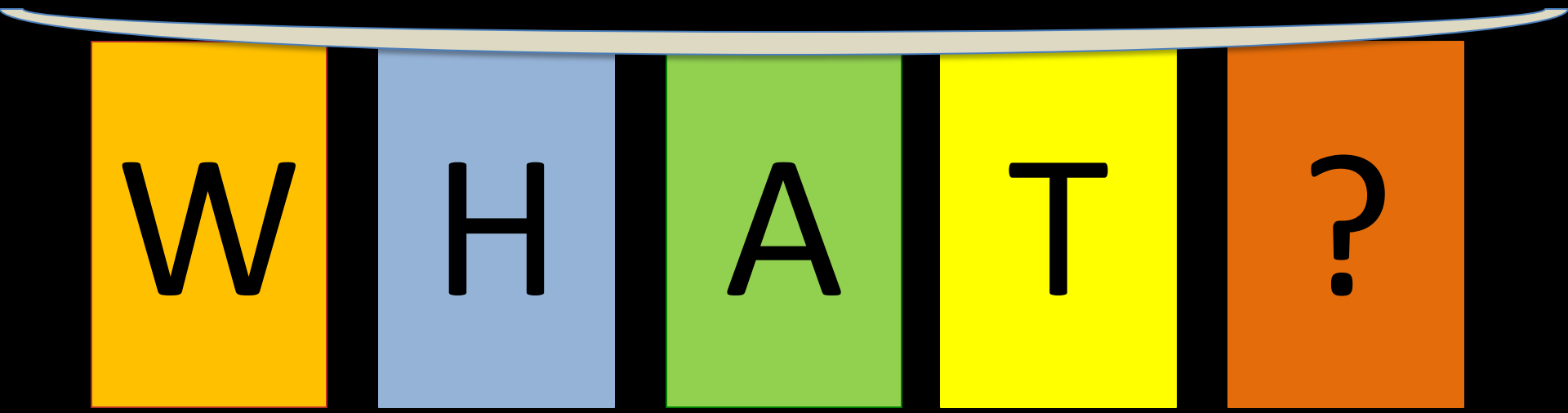


OPINION

The HIV care continuum: no partial credit given

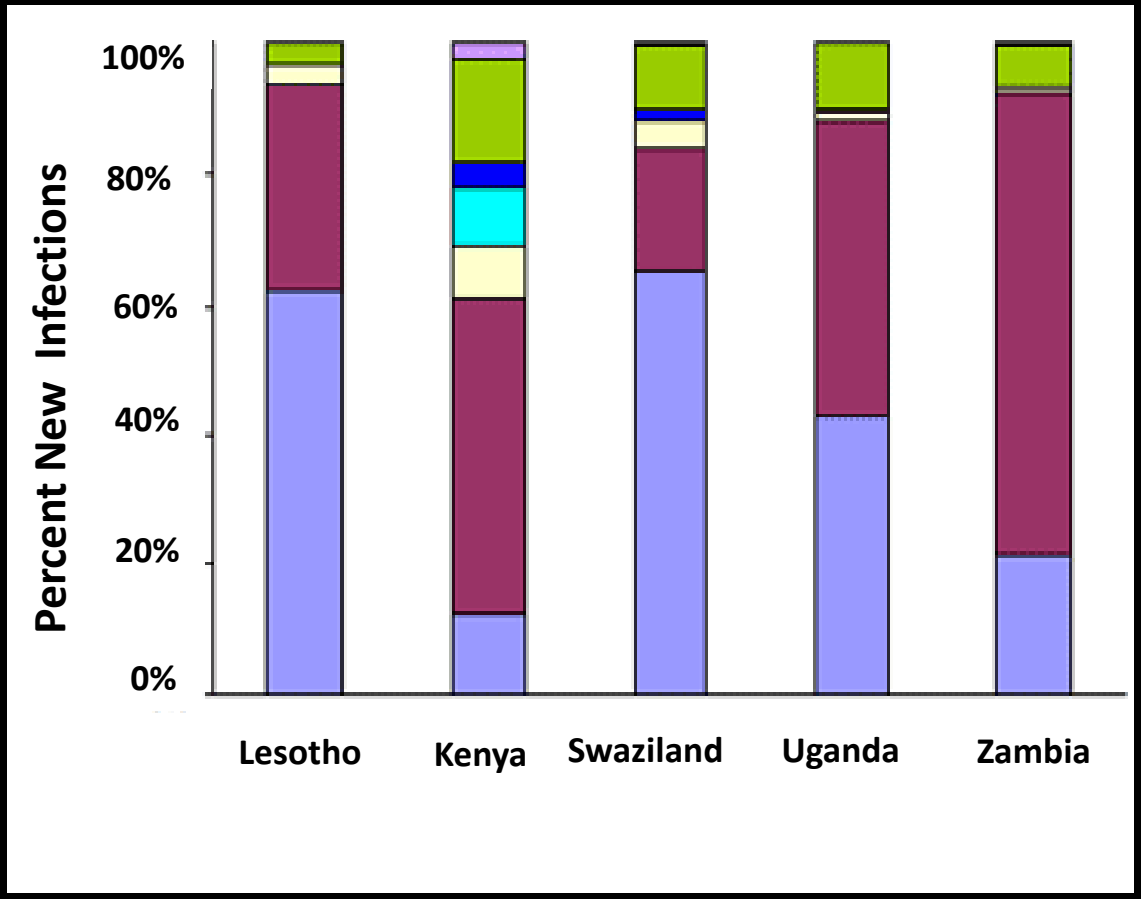
Margaret L. McNairy[a,b,c] and Wafaa M. El-Sadr[a,b]

McNairy et al, AIDS 2012


WHAT?

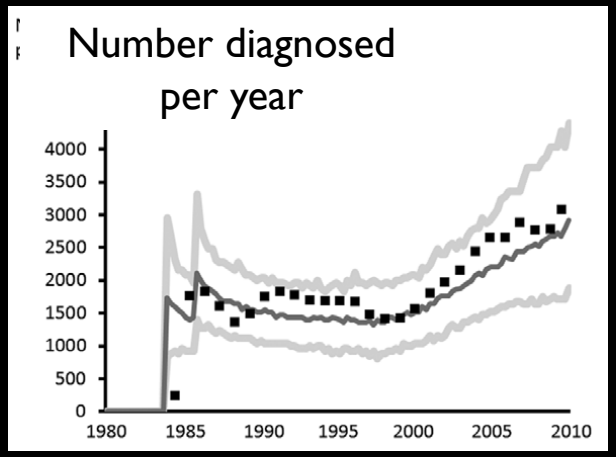
Efficacy to Effectiveness

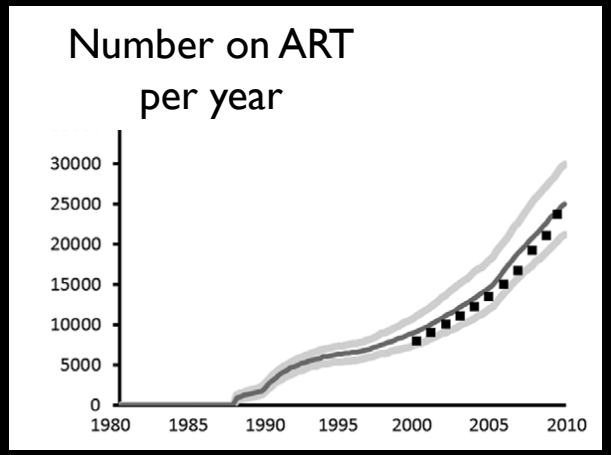
Contribution by Key Populations to the HIV Epidemic

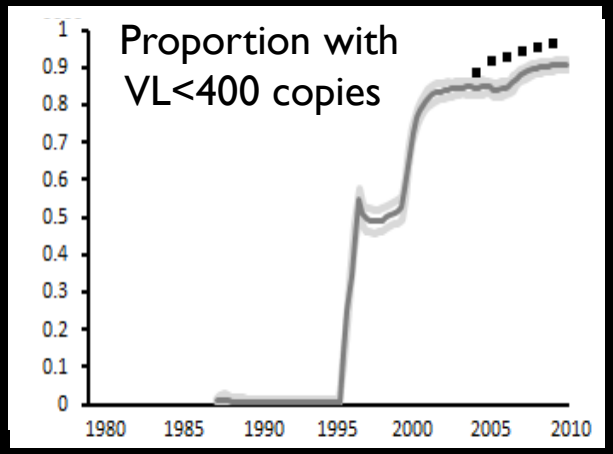


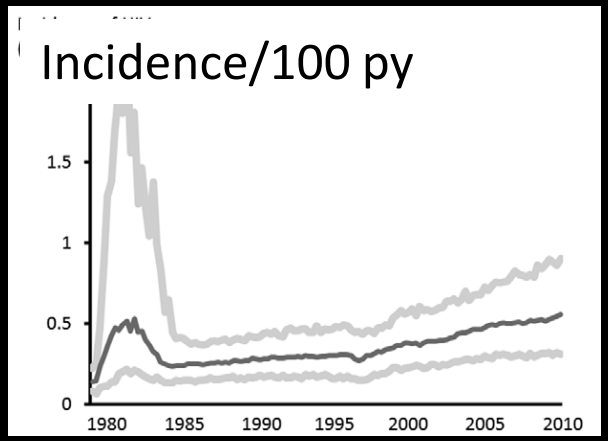
Proportion of new infections by group

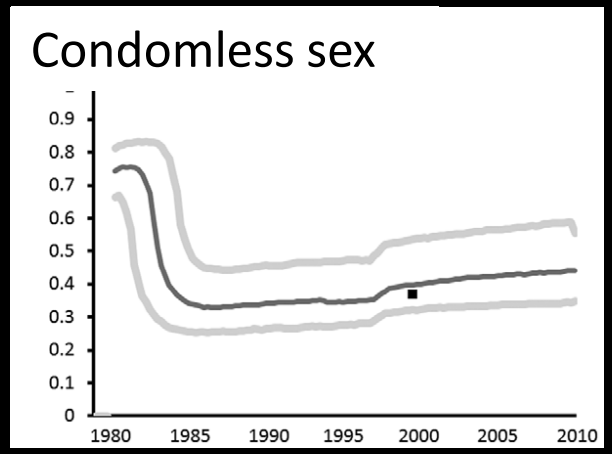
UNAIDS, 2010







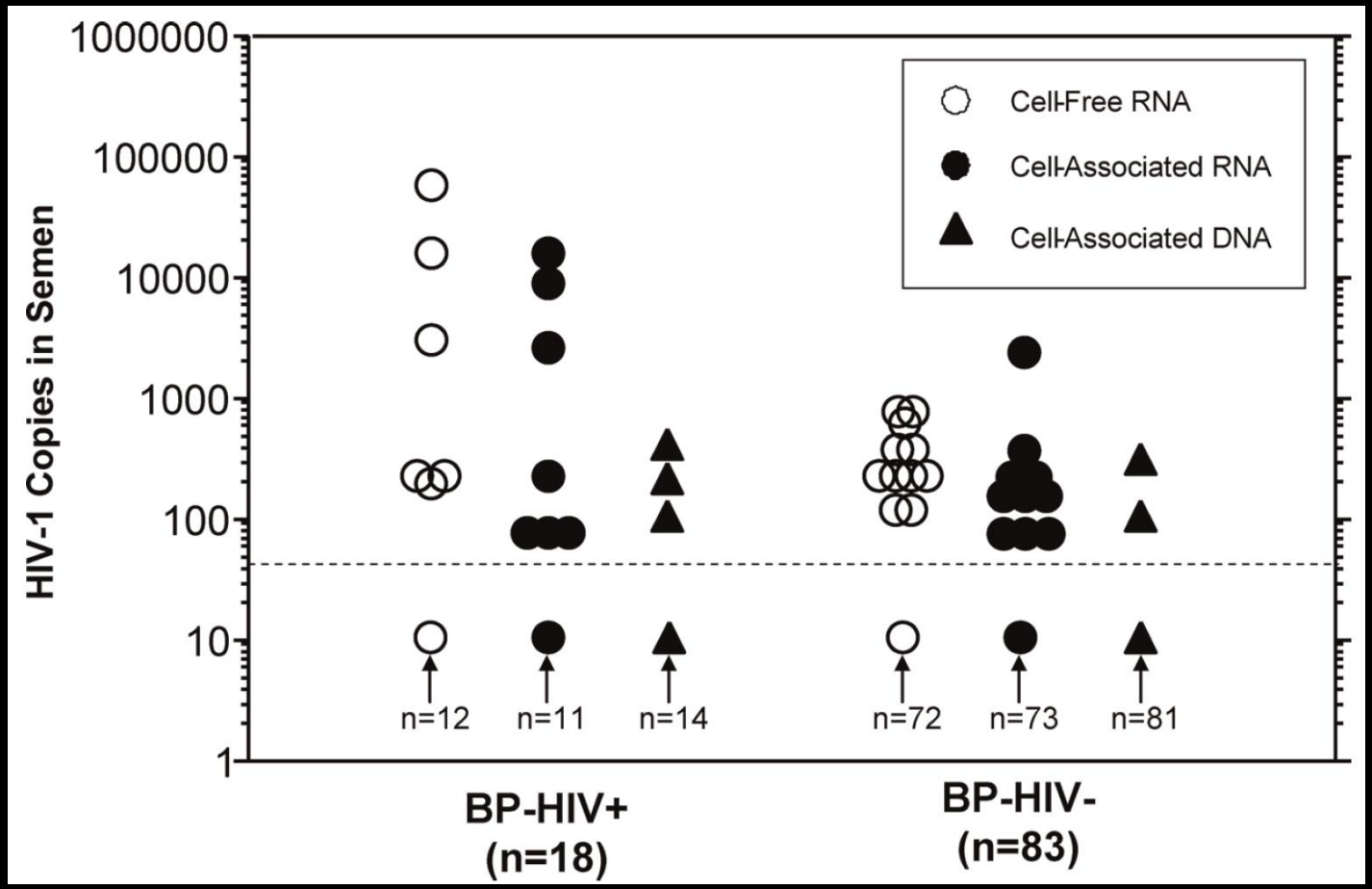




Scenario	Mean Incidence 2006-2010/100pyr	% difference Versus actual
Actual	0.53	---
No ART	0.89	+68%
No condoms	2.78	+425%
ART at diagnosis	0.36	-32%
Higher test rate	0.40	-25%
Higher test rate & ART at diagnosis	0.20	-62%

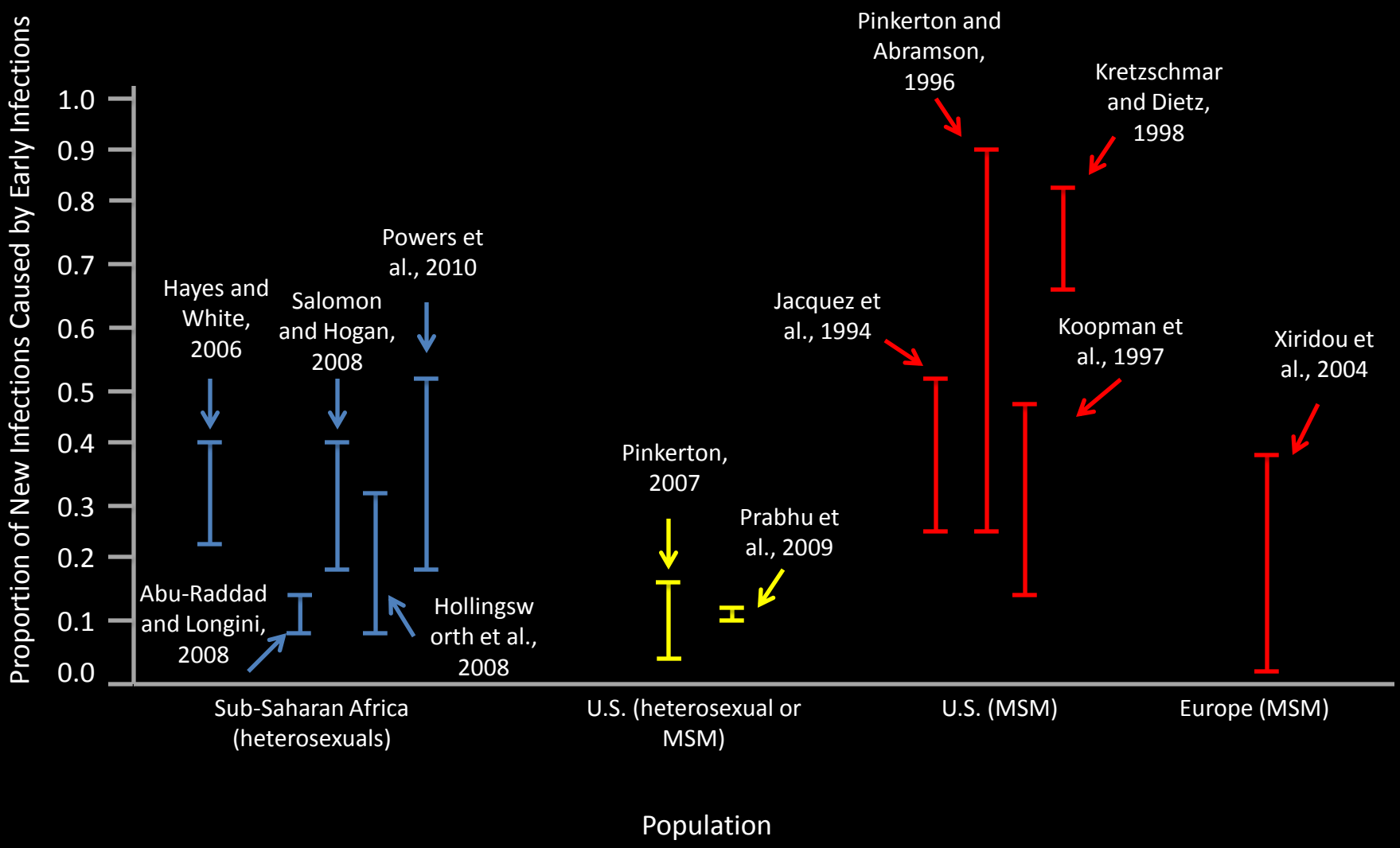
Phillips et al. PLOS One, 2013

Discordancy between Plasma and Seminal HIV Levels



Politch et al. AIDS 2012

Proportion of New Infections Caused by Early Infections



Cohen et al. NEJM 2011

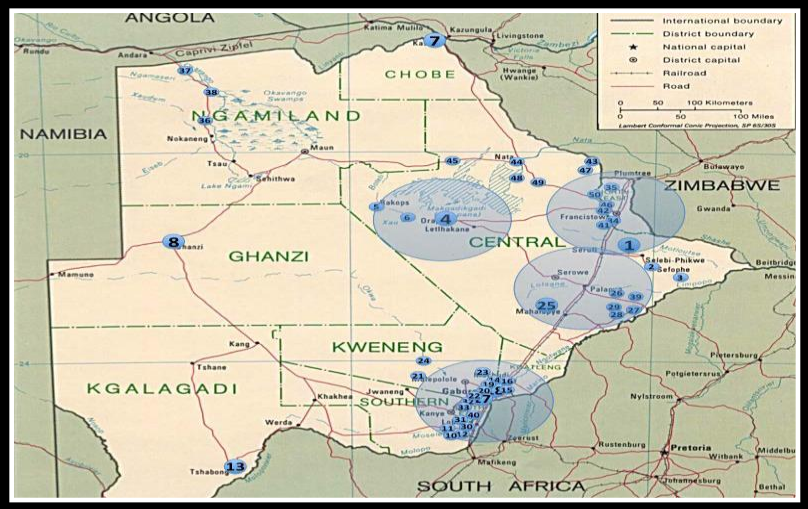
Studies in Key Populations

PARTNER Study (MSM)

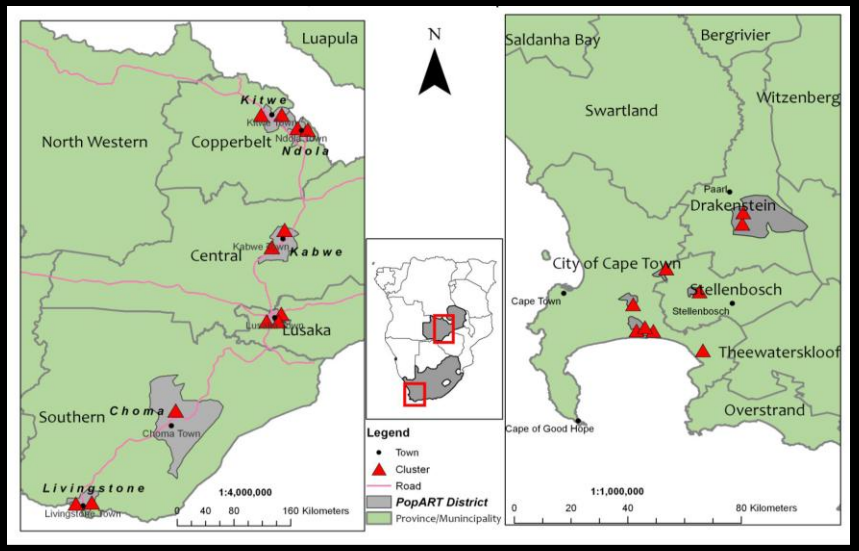
- International, observational multi-center study in 75 European sites from 2010 to 2014 (Phase 1) and 2014-2017 (Phase 2)
- Sero-different MSM partnerships (+ve partner on ART) who had condomless penetrative sex in the past 4 weeks in order to study:
  - risk of HIV transmission to partners, in partnerships that do not use condoms consistently and the HIV--positive partner on ART with viral load < 50 copies/mL
  - Reasons for lack of condom use and adoption of consistent condom use
- > 1000 couples enrolled so far

HPTN 074

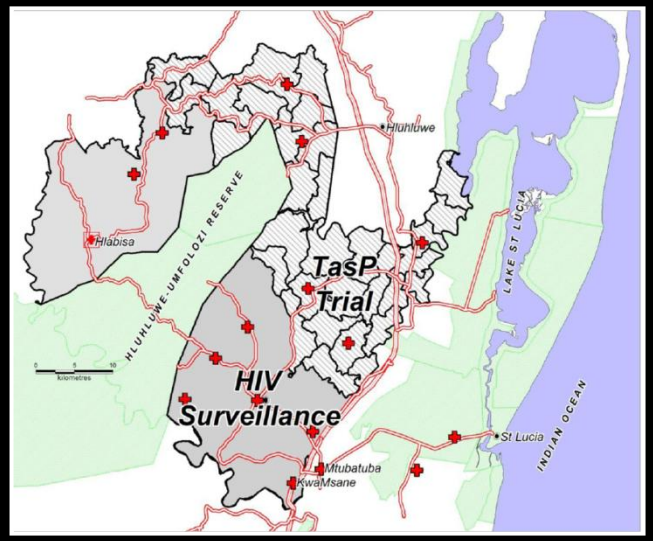
- Vanguard study
- Network-based randomized trial PWID and partners
- Integrated treatment and prevention
  - Facilitated ART
  - Substance use treatment
  - Behavioral counseling
- Sites under consideration: Eastern Europe and Asia



Botswana- CDC



HPTN 071 (PopART)
NIH



TASP- Africa Centre
ANRS

SEARCH Study

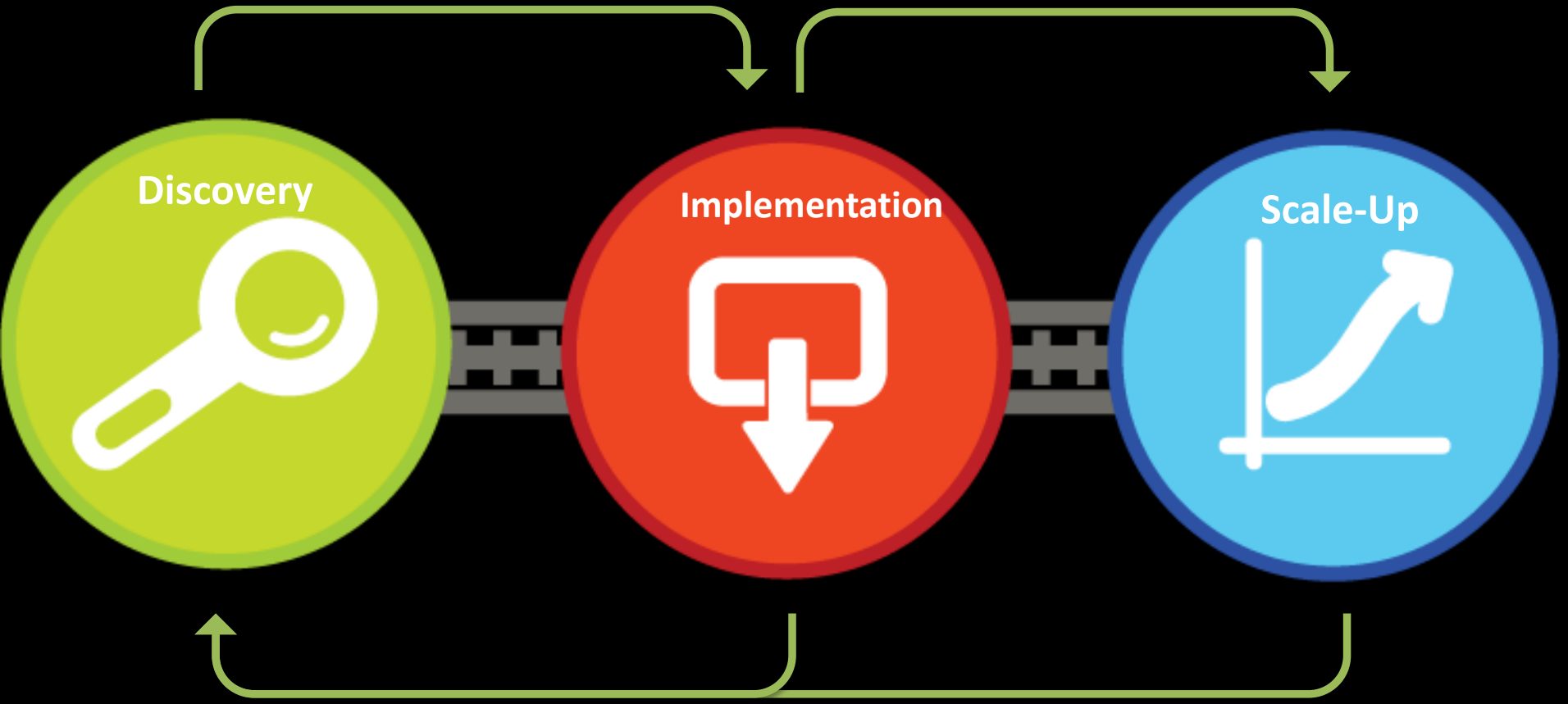
Bukoba Bila
BBM2
Mambukizi Mapya

Combination Prevention Bukoba
CDC

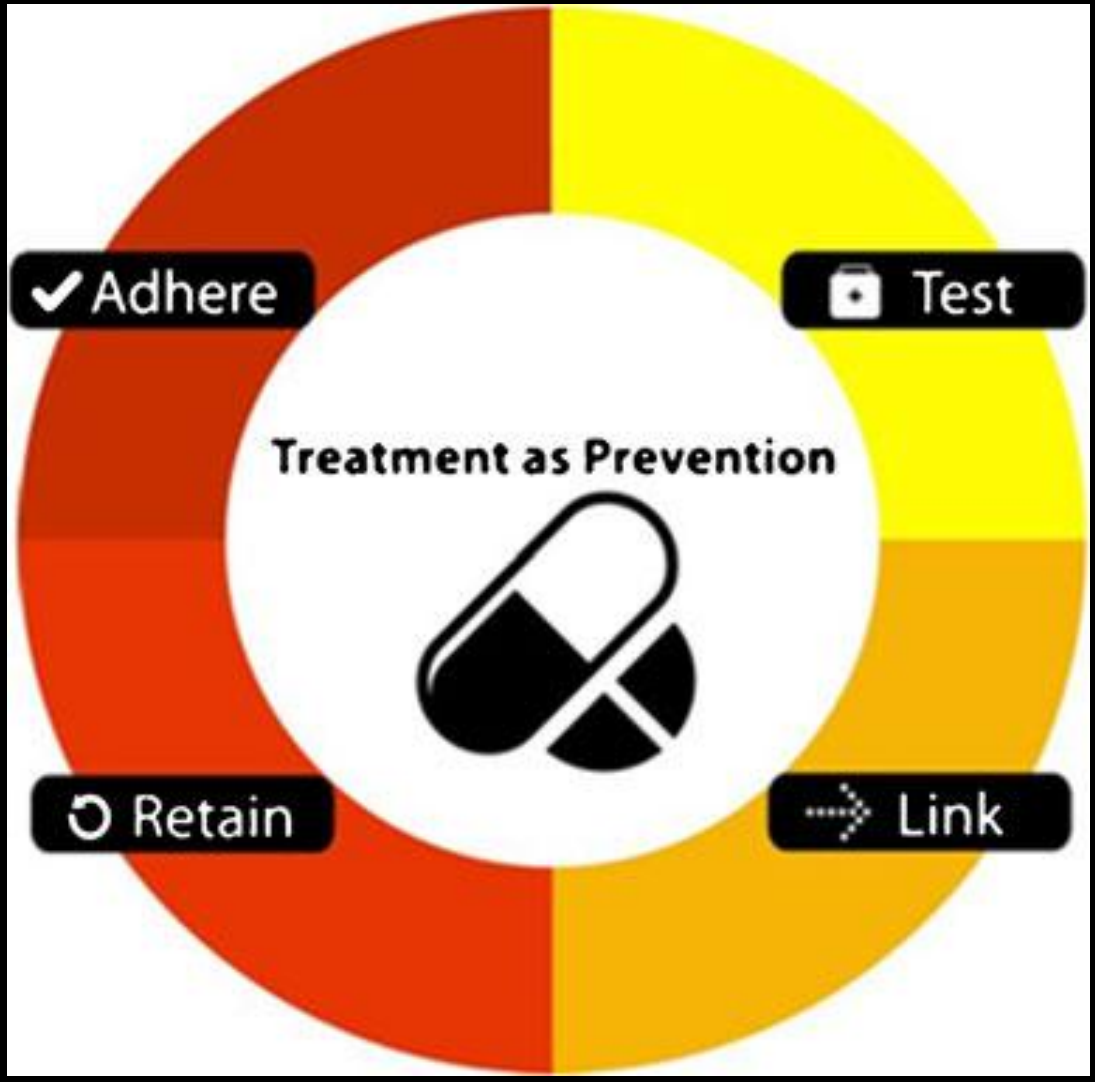
HPTN 065

TLC-PLUS


Silver Bullet
Just Ahead


Discovery
Implementation
Scale-Up

ART for Prevention is a Multi-component Integrated Strategy or Prevention *and Treatment*



McNairy et al. Curr HIV/AIDS Rep 2013

Conclusions

Access

Acceptability

Quality

Coverage

Effectiveness

Thank you

ICAP
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Mailman School of Public Health