HPTN
HIV Prevention Trials Network

HPTN
State of the Network

Achievements and Way Forward

June 2016

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HPTN Mission

To advance HIV prevention through the use of integrated strategies, centered on reducing HIV incidence in populations at greatest risk for infection.

Focus of the Research

- To identify new PrEP agents/regimens
- To design/implement integrated strategy studies

The Year in Review

- Four studies completed
- Four new studies launched and one to be launched shortly
- Completed enrollment of four studies:
  - First two studies of injectable long-acting ARVs for PrEP among women
  - Study among HIV+ PWID and their partners in Eastern Europe and southeast Asia
  - Study assessing feasibility of recruitment and retention of MSM in SSA (very, very close to complete enrollment)
- Launch of two monoclonal antibody studies (VRC 01) for HIV prevention in collaboration with HVTN

The Year in Review

- Progress in HPTN 071 (PopART), *the largest HIV prevention study to date!*
- Design of the *first non-inferiority phase 3 HIV prevention study (HPTN 083)*
- Findings from six studies presented at major conferences
- Expanded network reach and engaged in new collaborations around the world
- Expanded HPTN domestic scholars program to include international scholars

Studies Completed

- HPTN 068 (Financial incentives, conditional on school attendance, in young women SA)
- HPTN 052 (ART for prevention in discordant couples)
- HPTN 069/ACTG A5305 (Safety and tolerability of maraviroc-containing regimens for PrEP)
- HPTN 073 (Uptake and adherence with TDF/FTC PrEP among Black MSM)

HPTN 068: Effects of cash transfer for the prevention of HIV in young women in South Africa

Enrollment 2,537

- **Enrolled in grades 8, 9, 10 or 11 in participating high schools**
- **Age 13-20 years**

Follow Up: Completed March 2015

Intervention	Control
1,263	1,274
Cash transfer conditional on school attendance	No cash

Primary objective: HIV Incidence

HPTN 068: Key Findings

No difference in HIV incidence
HR 1.17 (95% CI 0.80-1.72, P=0.42)
No difference in HSV-2 incidence,
RR 0.92 (0.71- 1.18) (P=0.492)

- Overall HIV incidence: 1.8%,
  - 16 year olds: 1%
  - **≥ 20 years: 5%**
- High school attendance in both study arms
- School enrollment and attendance were protective for HIV acquisition irrespective of study arm.
  - **Three fold** higher risk of HIV infection in school drop out to non-drop outs [HR 3.21 (95% CI 1.81, 5.71, p<.0001)]

Insights from the study:

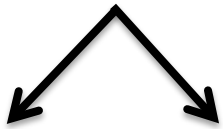
- Interventions should focus on 18-24 year olds and out of school youth
- Cash transfer may be efficacious in settings with low school enrollment

HPTN 052

1,763 sero-discordant couples
HIV-infected (CD4 350 to 550cells/µL)
HIV discordant partner

Randomization

Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, US, Zimbabwe



Immediate ART
350-550 cells/µl

Deferred ART
CD4 <250>200

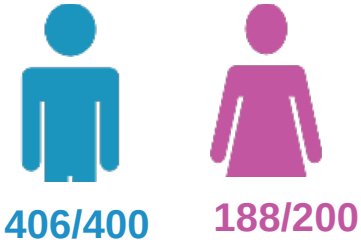
NEJM, August 2011

96% decrease in HIV transmission

IAS 2015 vancouver, canada

The benefit of early ART for HIV prevention among HIV-discordant couples is durable
Overall 93% risk reduction

HPTN 069/ACTG A5305– Safety and tolerability of Maraviroc for PrEP



Study Design	Phase 2 Double-blind Randomized
Location	13 sites – U.S. only

Study arms	
Arm 1	MVC
Arm 2	MVC+FTC/TDF
Arm 3	MVC+FTC
Arm 4	TDF

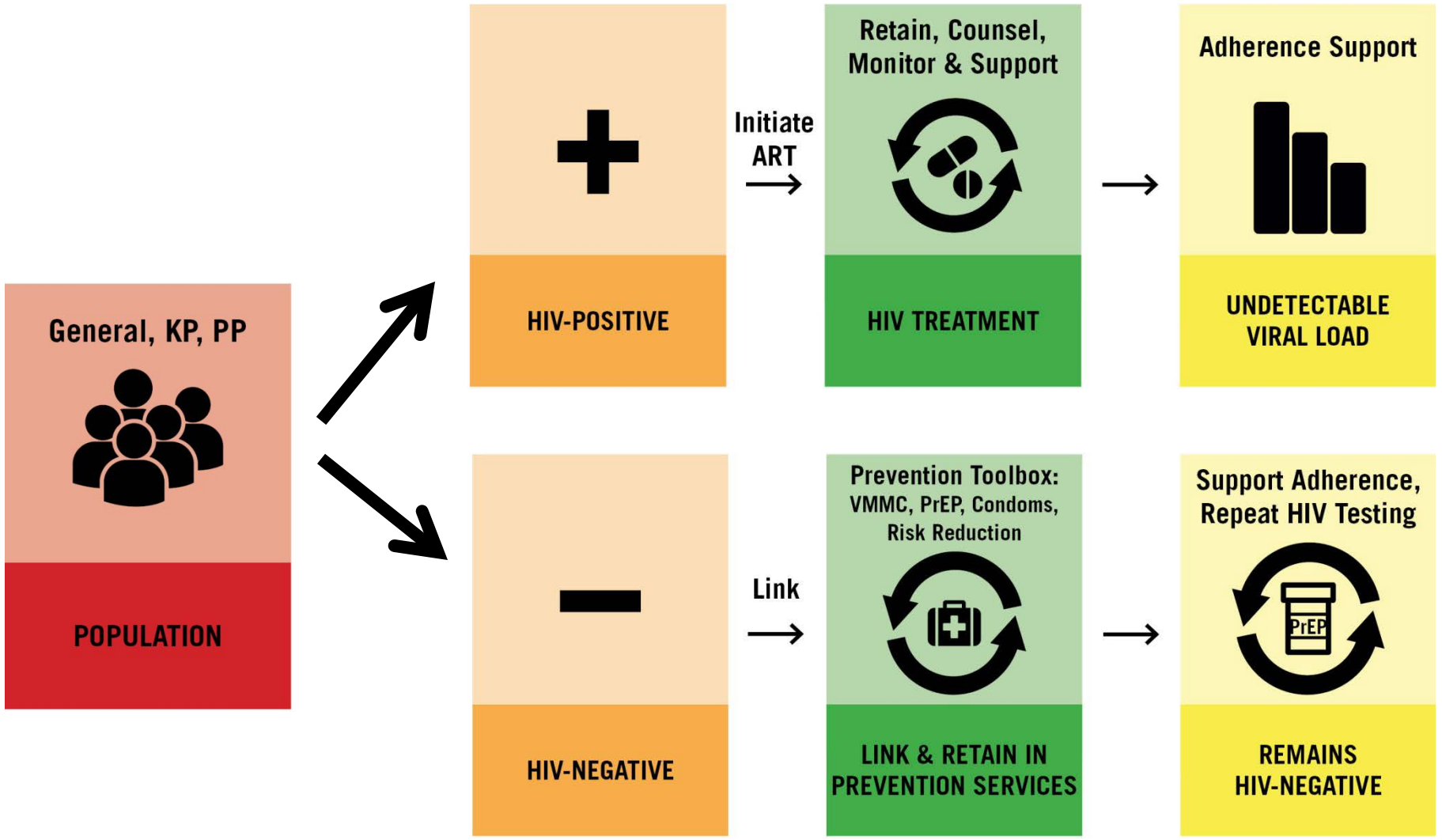
Study Status

Follow-up completed April 2015
Final results at CROI 2016

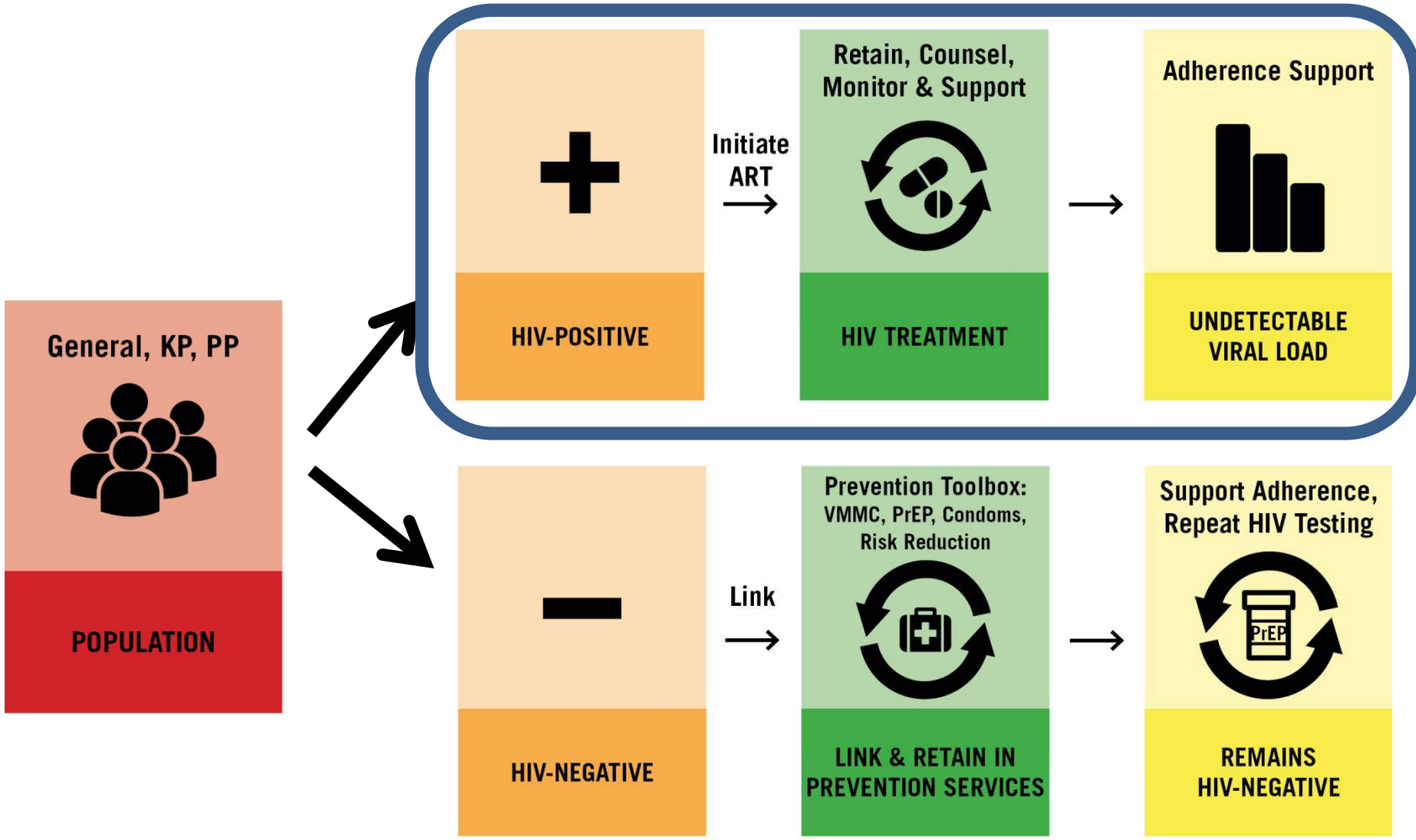
Follow-up completed November 2015
Final results to be presented at AIDS 2016

Maraviroc-containing regimens were comparably safe and well-tolerated to TDF+FTC

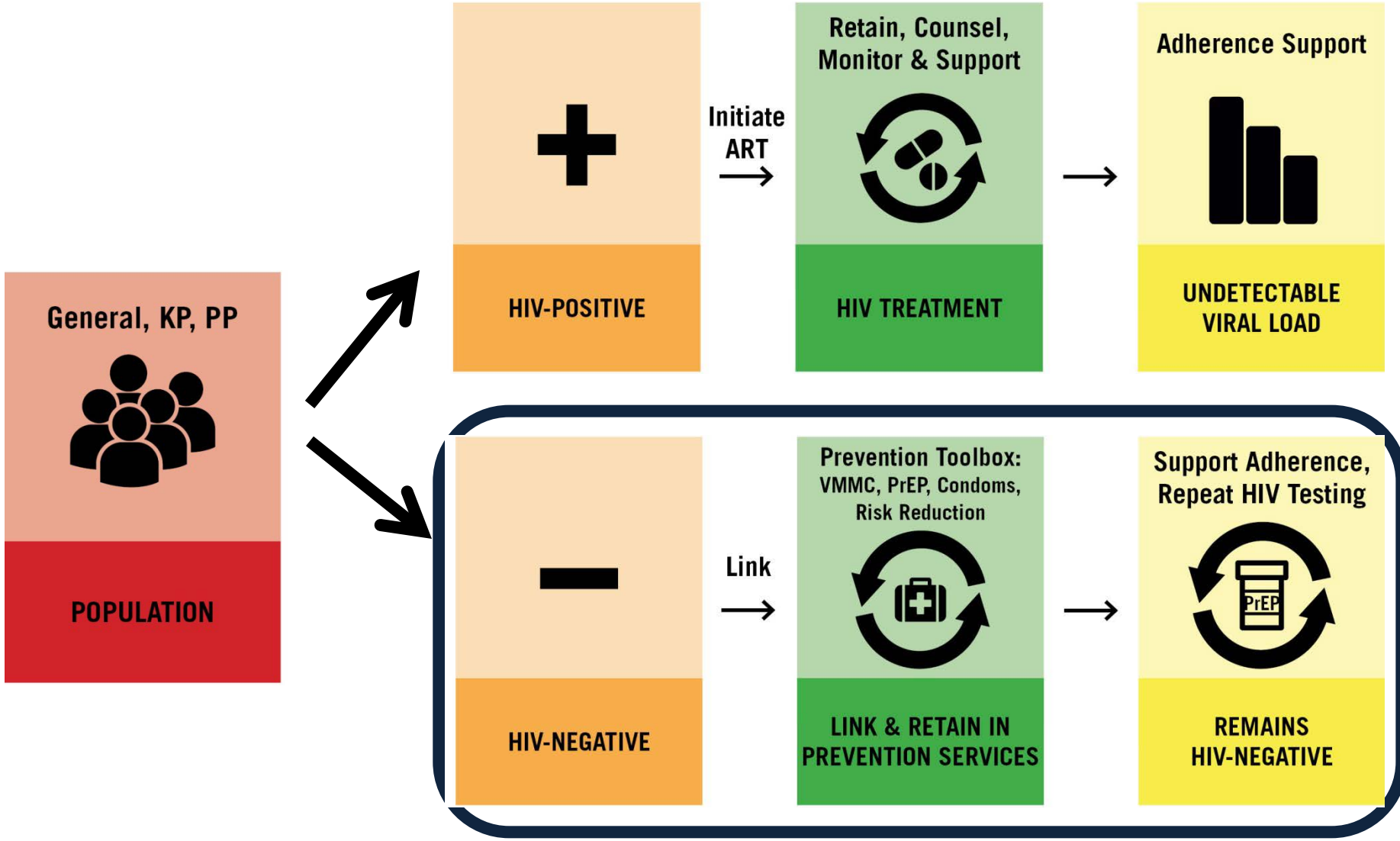
HPTN Prevention Strategy


General, KP, PP
POPULATION
HIV-POSITIVE
Initiate ART
Retain, Counsel, Monitor & Support
HIV TREATMENT
Adherence Support
UNDETECTABLE VIRAL LOAD
HIV-NEGATIVE
Link
Prevention Toolbox: VMMC, PrEP, Condoms, Risk Reduction
LINK & RETAIN IN PREVENTION SERVICES
Support Adherence, Repeat HIV Testing
PrEP
REMAINS HIV-NEGATIVE

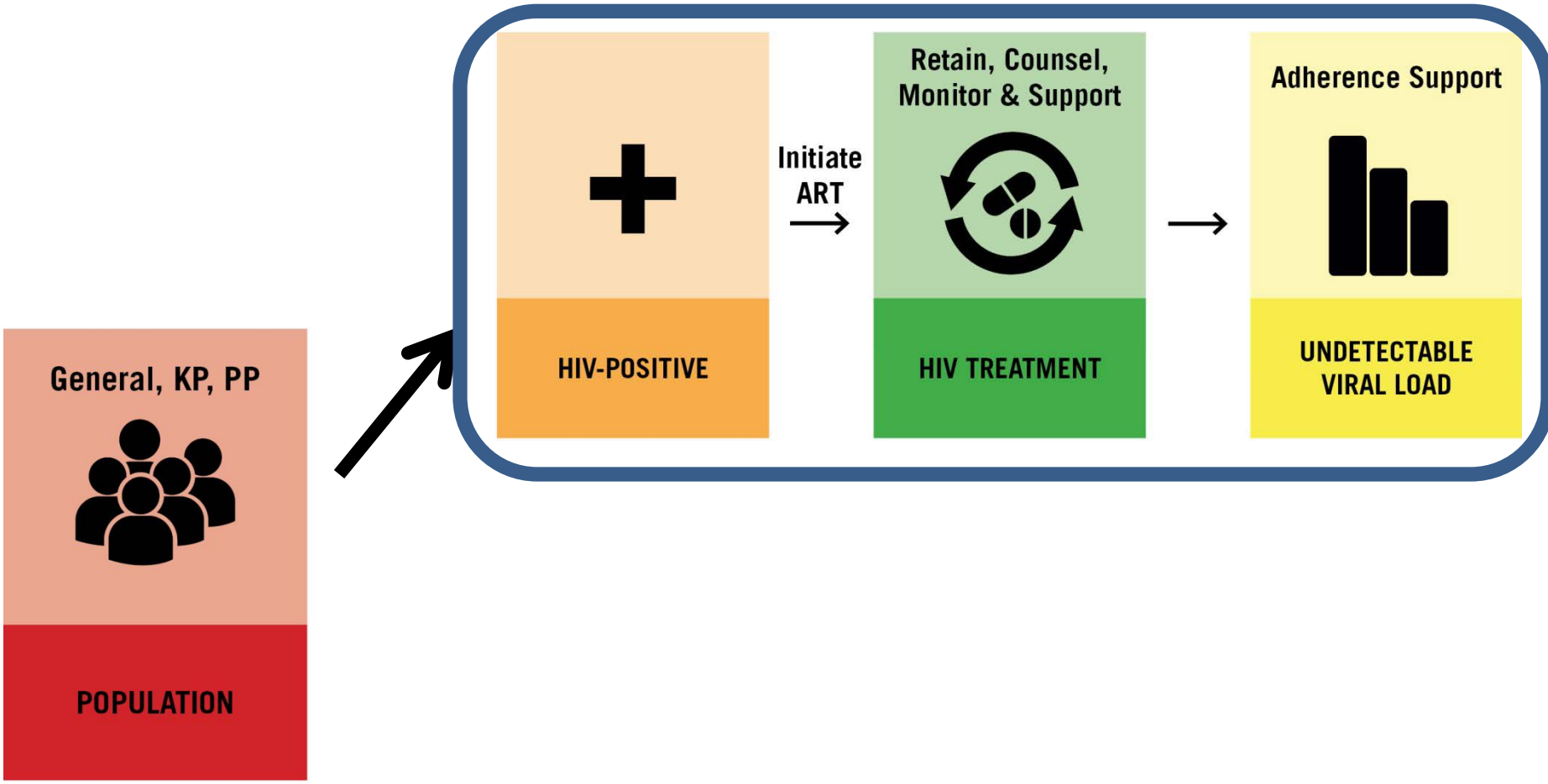
Prevention of HIV Transmission
ART for Prevention



Prevention of HIV Acquisition
Pre-exposure Prophylaxis



Prevention of HIV Transmission
ART for Prevention



UNAIDS Global Targets By 2020

90%

of all people living with HIV will know their HIV status

90%

of all people diagnosed with HIV will receive sustained antiretroviral therapy

90%

of all people receiving antiretroviral therapy will have durable suppression

UNAIDS 2014

Optimizing Use of ART for Prevention

Community-Level

HPTN
HIV Prevention
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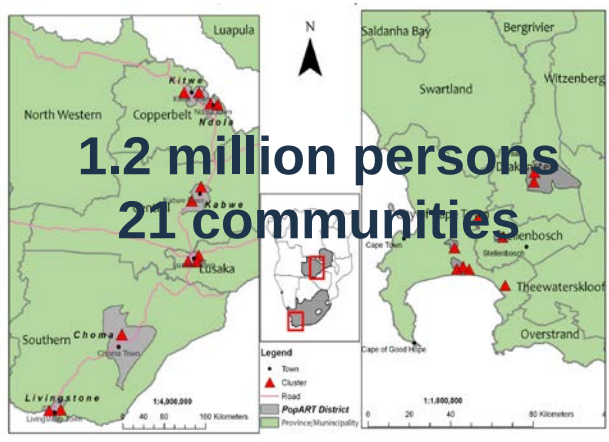
HPTN 071 (PopART)

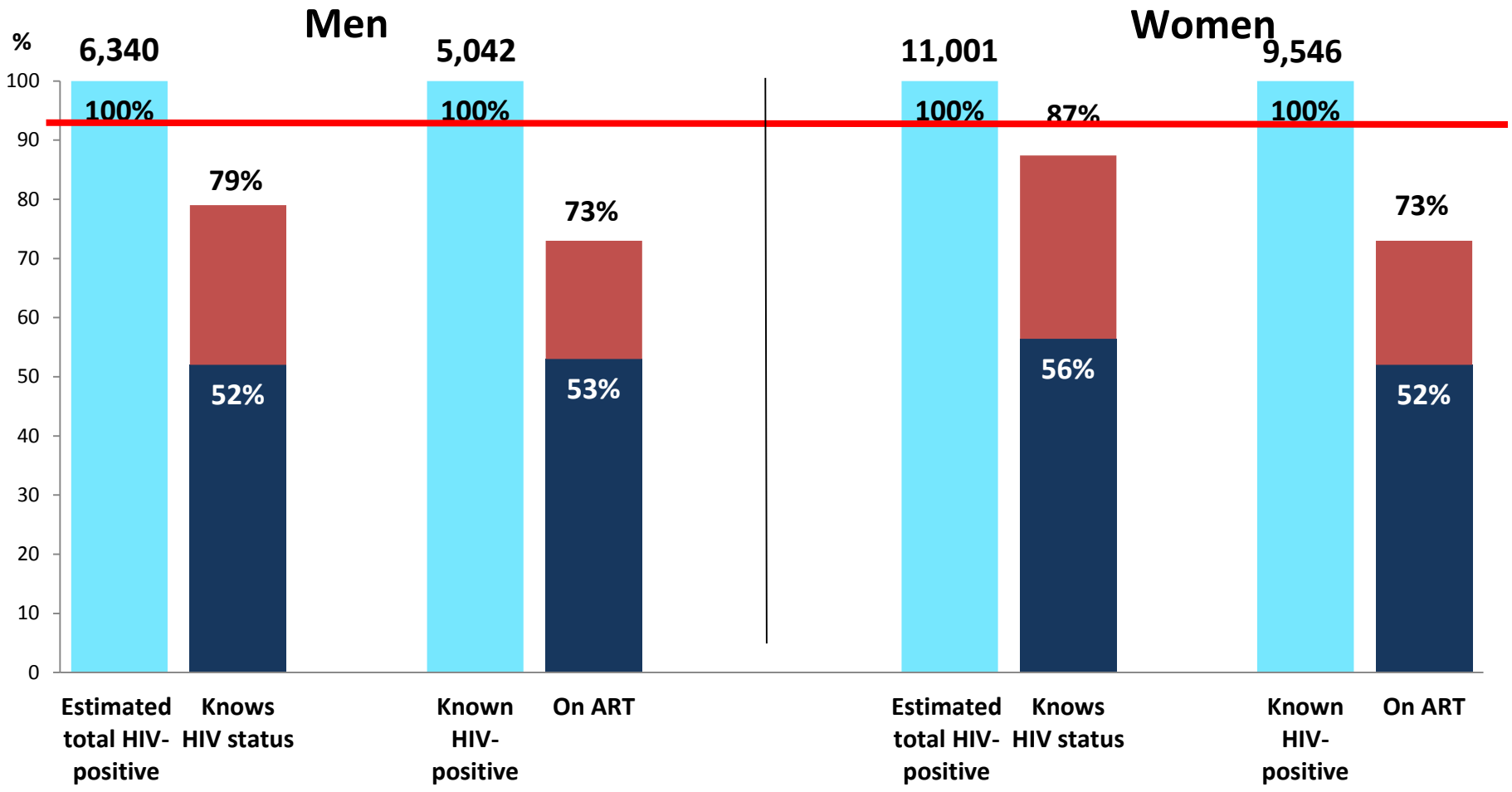
Interventions by CHiPs		
	Round 1	Round 2
Households Visited	161, 000	117, 486
Adults consented	317, 000+	220,634
Agreed to HIV test Or Reported HIV+	239, 000+	174,884



Study objective: To determine the impact of a community-level, combination HIV prevention package on community-level **HIV incidence.**

Population Cohort
>38,000 enrolled in PC0
>4600 new participants enrolled in PC12
>24,700 participants completed follow-up
>74,500 specimens collected and tested in-country and at HPTN LC

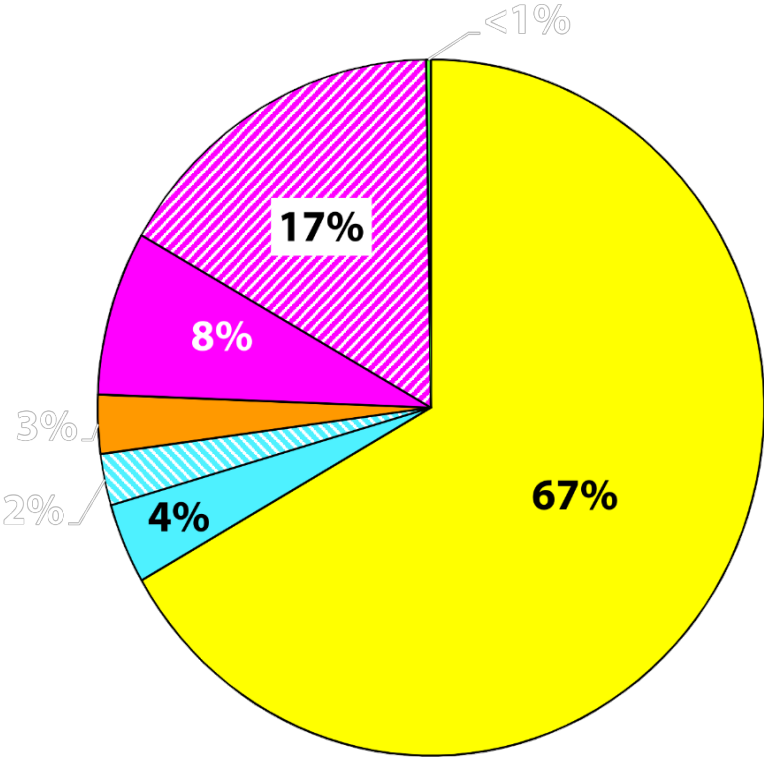
90-90: Estimated uptake, total HIV+ adult population Arm A - Zambia (R1)



Optimizing Use of ART for Prevention

MSM in the US

New HIV infections in the US, 2014

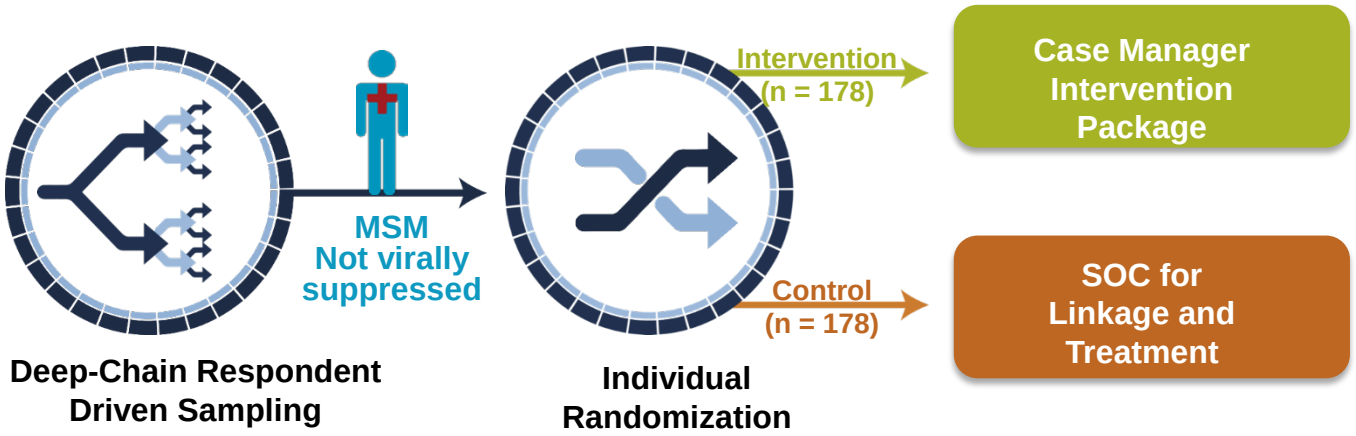


Two thirds of new HIV infections In the US occurred among MSM

CDC 2015

HPTN 078: Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected MSM in US

Screened population	Enrolled participants
2700	356
MSM ≥ 16 yo	MSM/ HIV+
Study Duration: 12 M Enrollment	24 M Follow-up



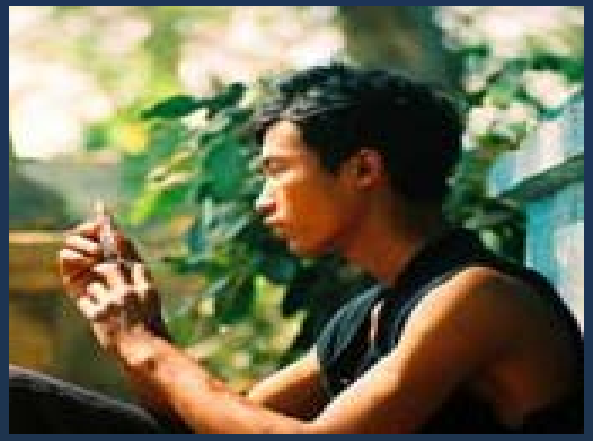
- Atlanta
- Baltimore
- Birmingham
- Boston

Primary objectives: Recruitment feasibility and viral suppression

All sites activated, enrollment started

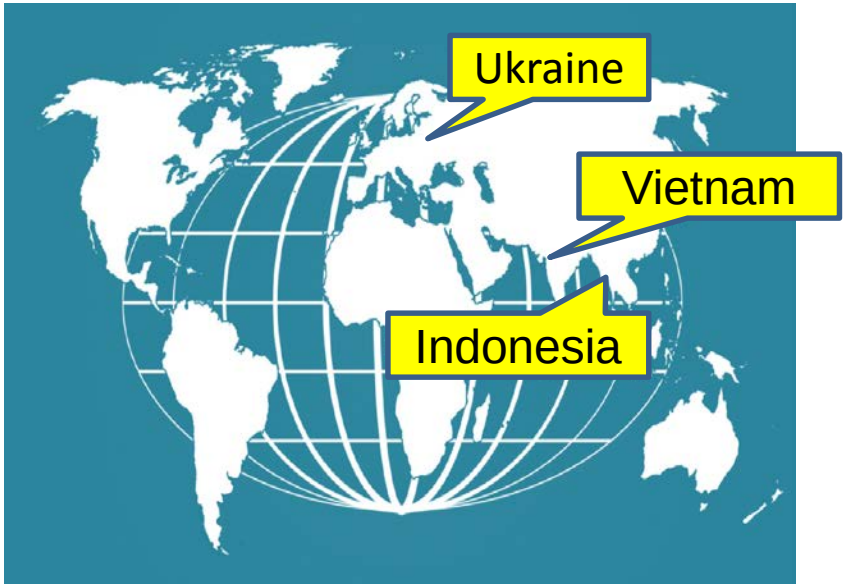
Optimizing Use of ART for Prevention

PWID in Eastern Europe and Southeast Asia

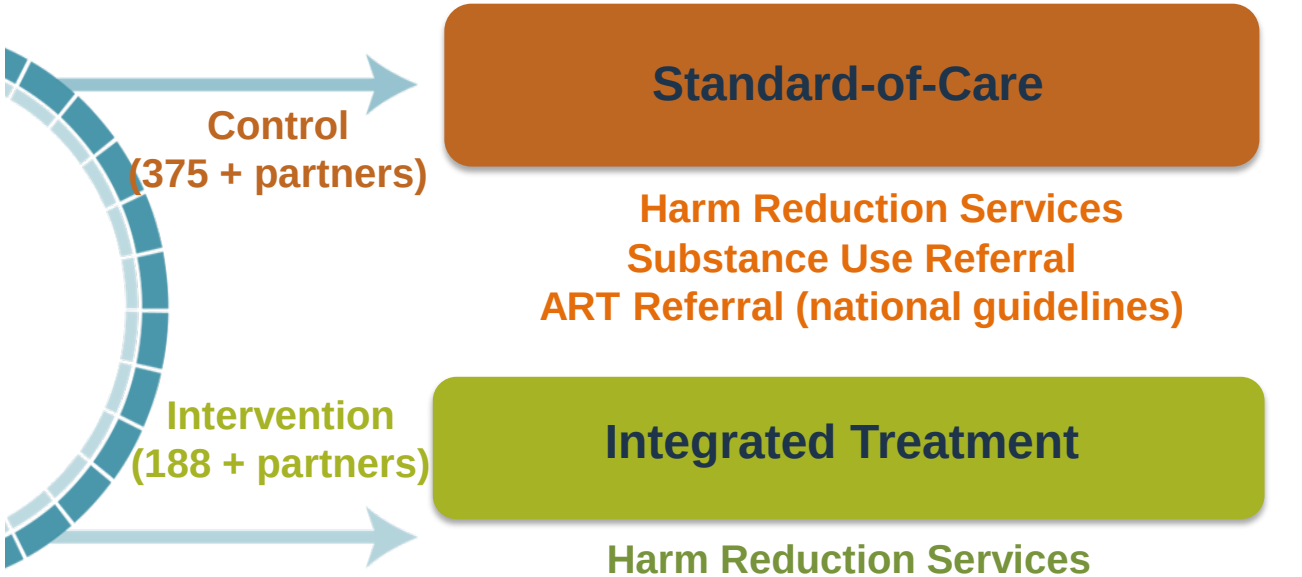


HPTN 074: A study comparing an integrated intervention including supported ART to standard of care for PWID

Intervention	Standard of Care
125 HIV +	375 HIV +
188 HIV – Partners	563 HIV – Partners
15 Months Recruitment 12 Months Follow-Up	



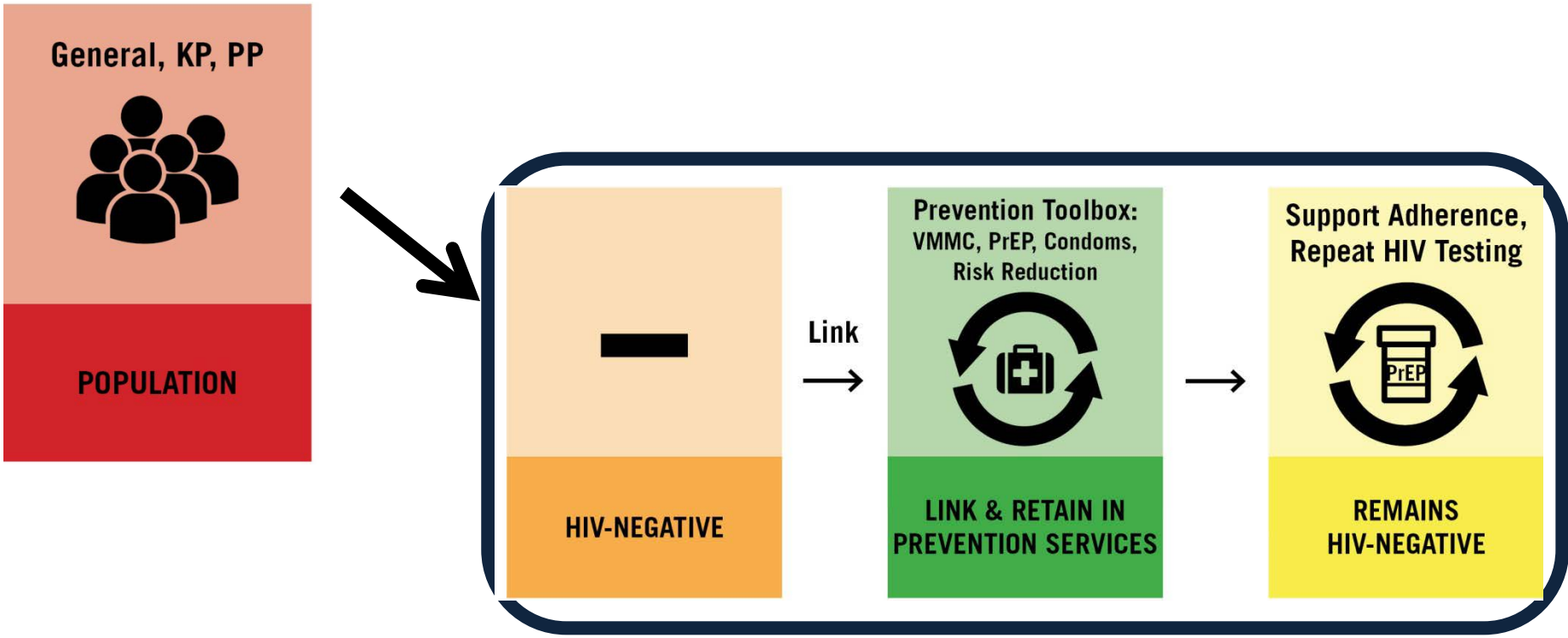
HPTN 074



Primary Objective: Assess HIV incidence, recruitment, retention, and feasibility and barriers of the intervention

Enrollment completed ahead of schedule!
484/500 Index Participants and 725/750 Partners

Prevention of HIV Acquisition
Pre-exposure Prophylaxis (PrEP)



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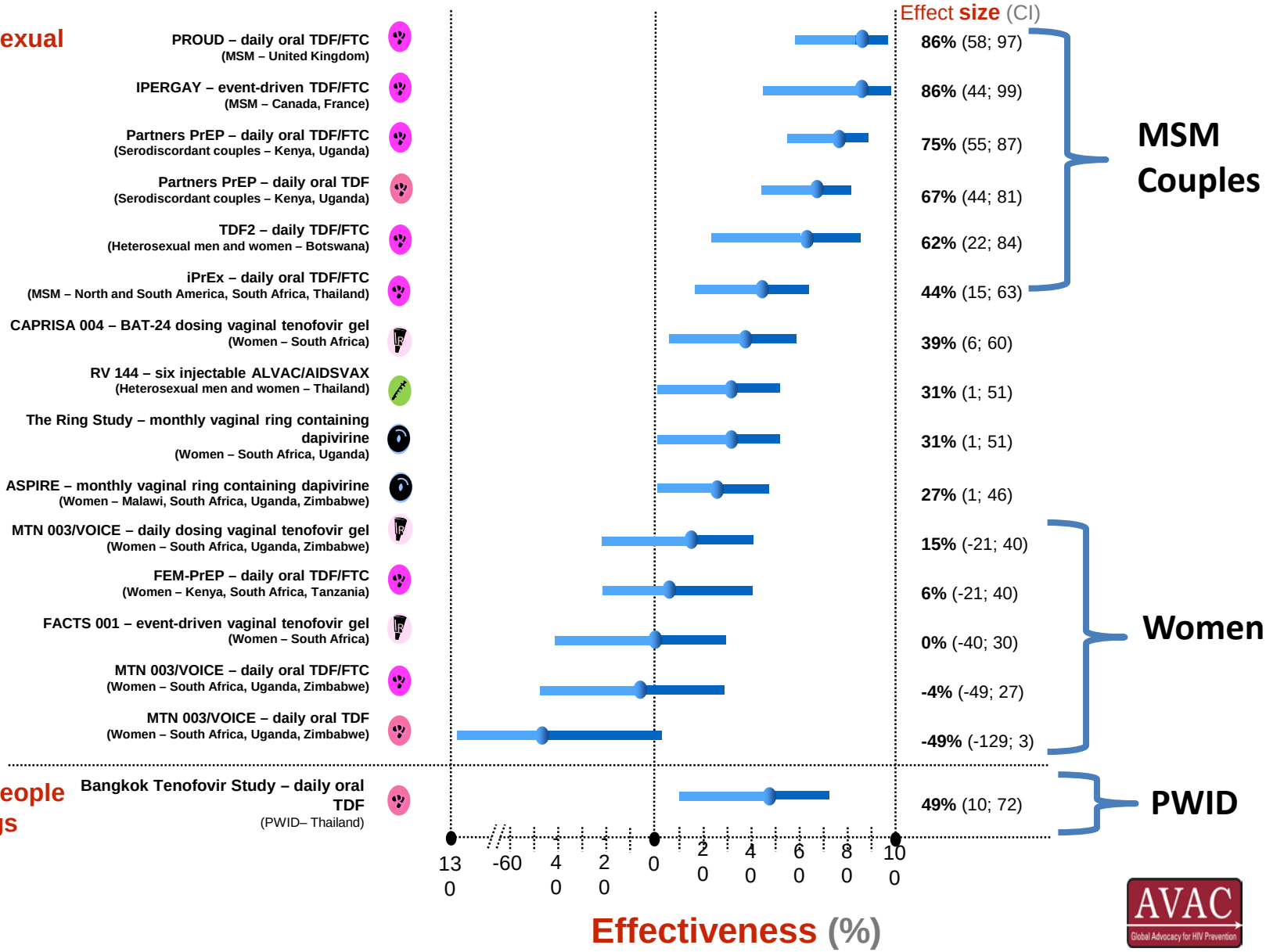
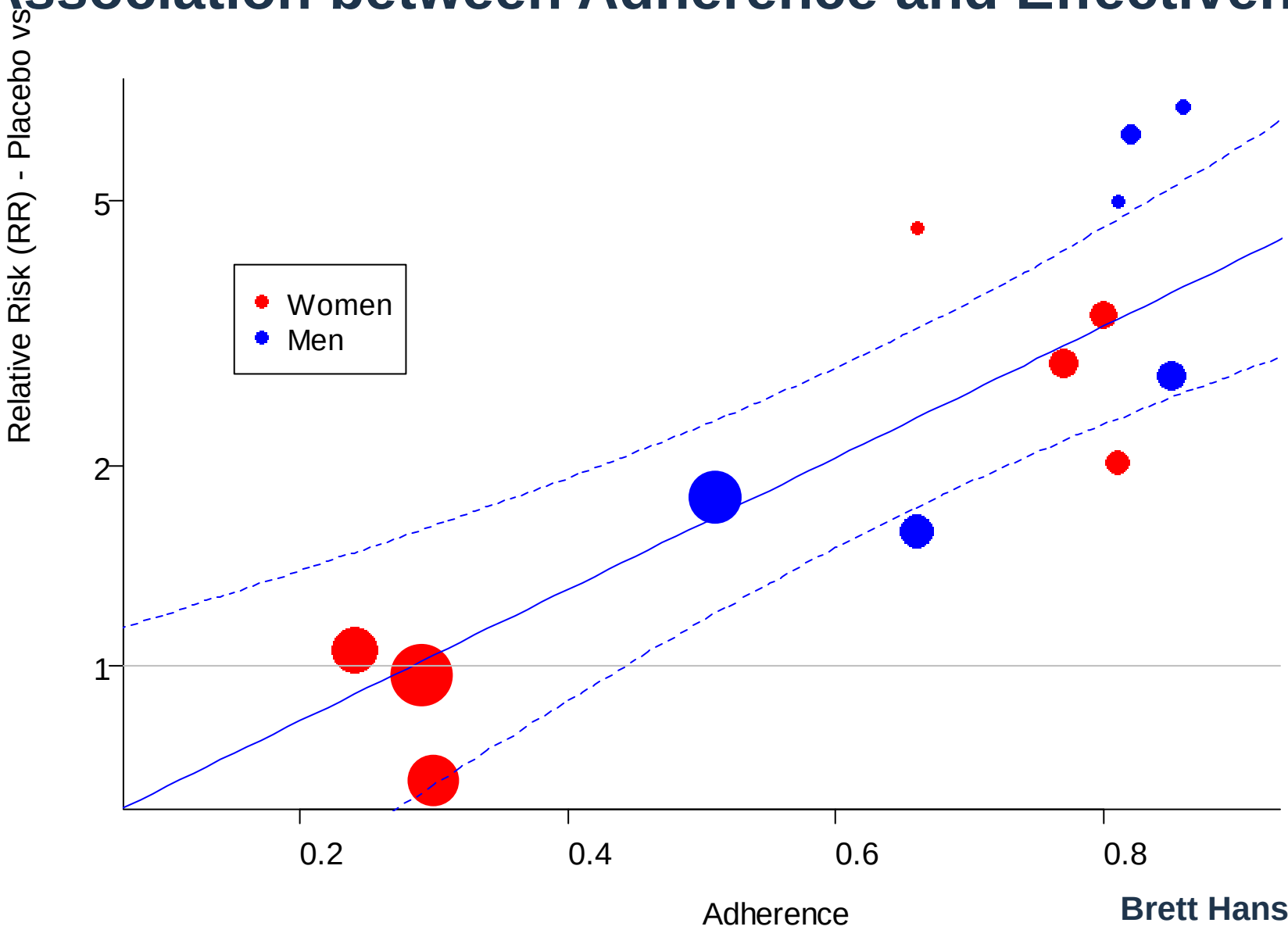
Clinical Trial Evidence for PrEP



AVAC
Global Advocacy for HIV Prevention

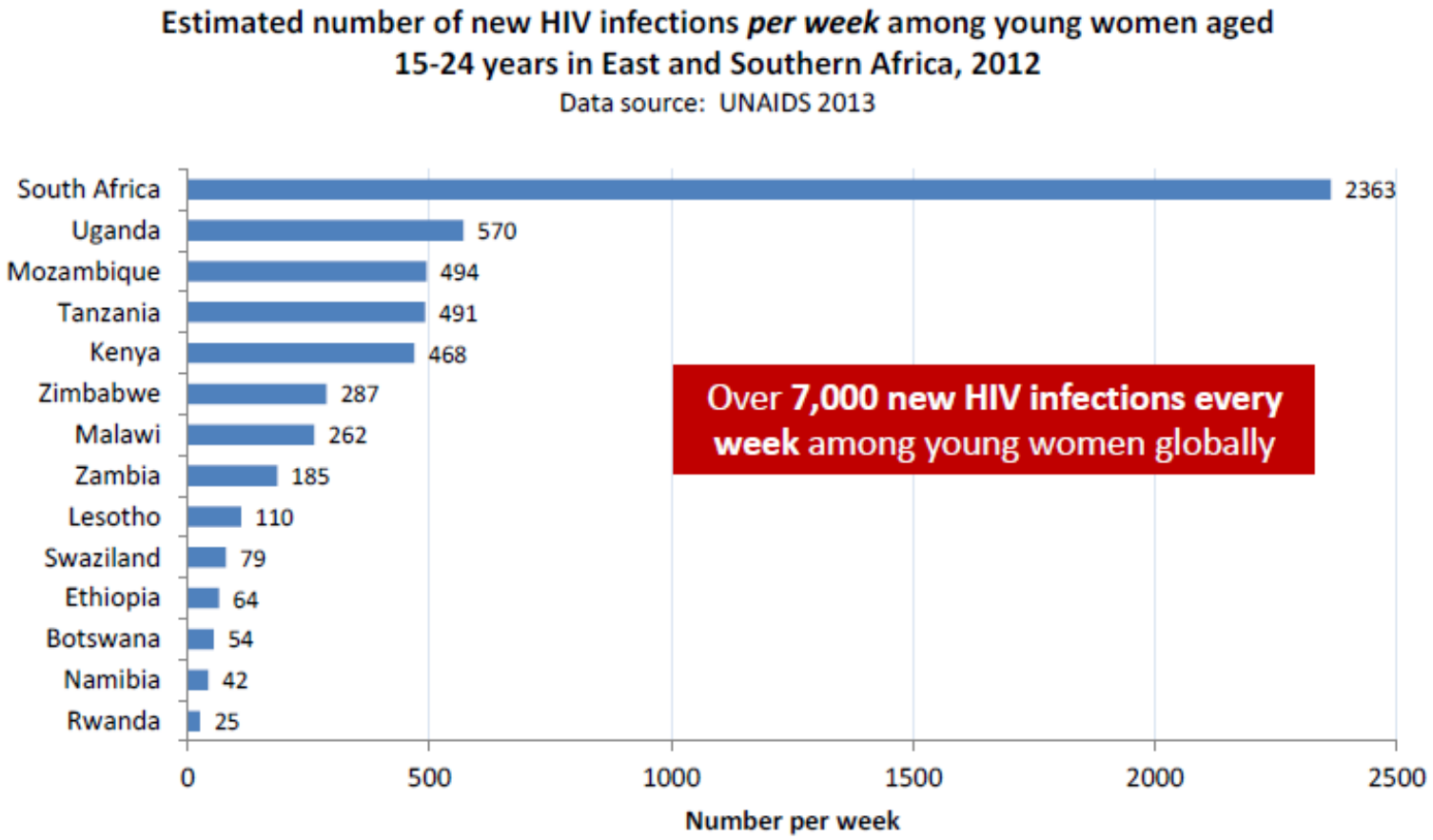
Adapted from: Salim S. Abdool Karim, CAPRISA

Association between Adherence and Effectiveness



Brett Hanscom

One-third of new HIV infections globally occur in young African women (15-24 yrs)



HPTN 082: Uptake and adherence to daily oral TDF/FTC PrEP in young (16-25 yrs) Southern African women

Study Population

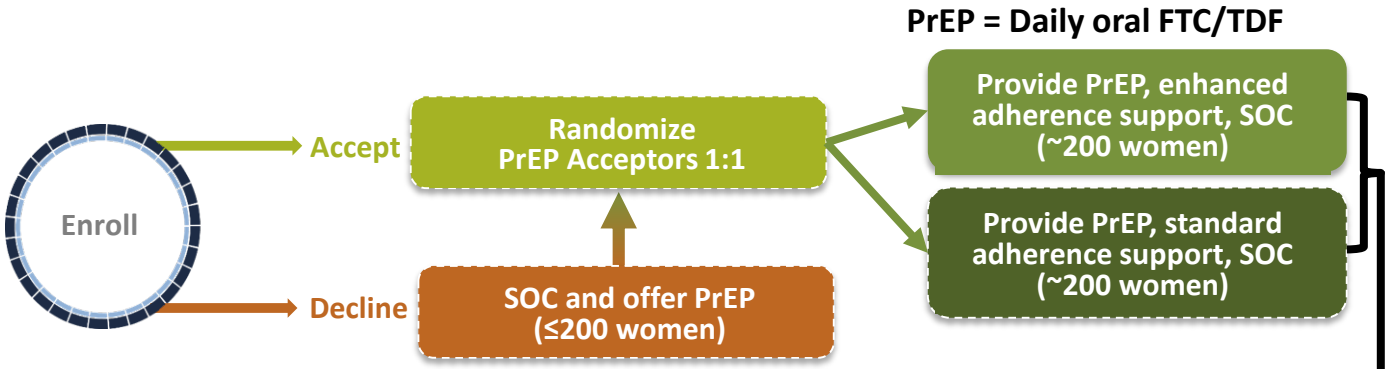
Uninfected women
Ages 16-25 yrs

South Africa
Zimbabwe

Target Enrollment

- 400 women who accept PrEP at enrollment
- ≤ 200 women who decline PrEP at enrollment

Study Design



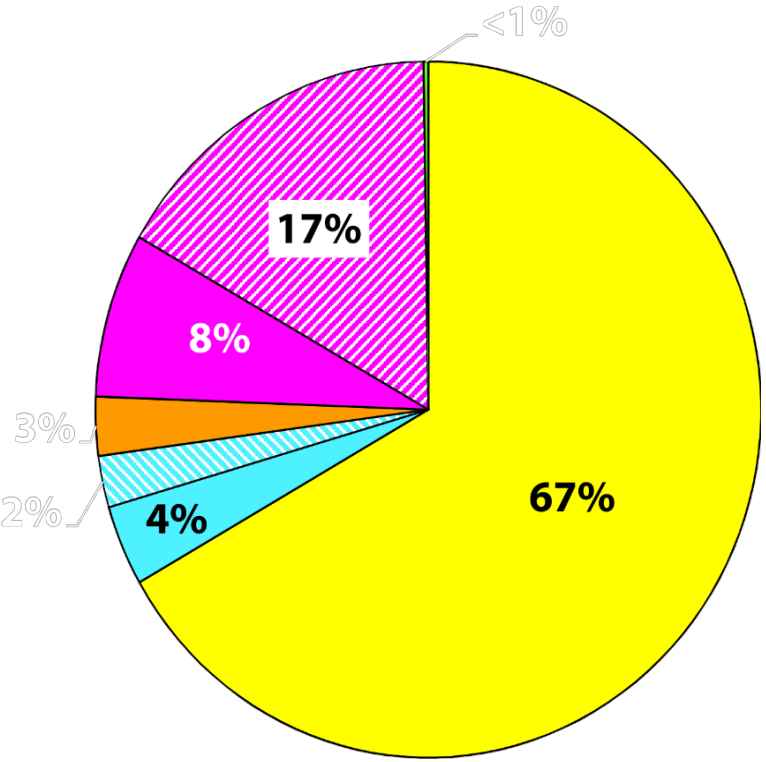
In-depth interviews exploring factors that influence women's decisions to use PrEP, to adhere to PrEP, and acceptability of PrEP in the first 3 months after PrEP acceptance. (~75 total, including acceptors and decliners)

Standard Adherence Support	Enhanced Adherence Support
• CBT counseling	• CBT counseling
• SMS texting	• SMS texting
• Adherence clubs	• Adherence clubs
	• Drug level feedback counseling

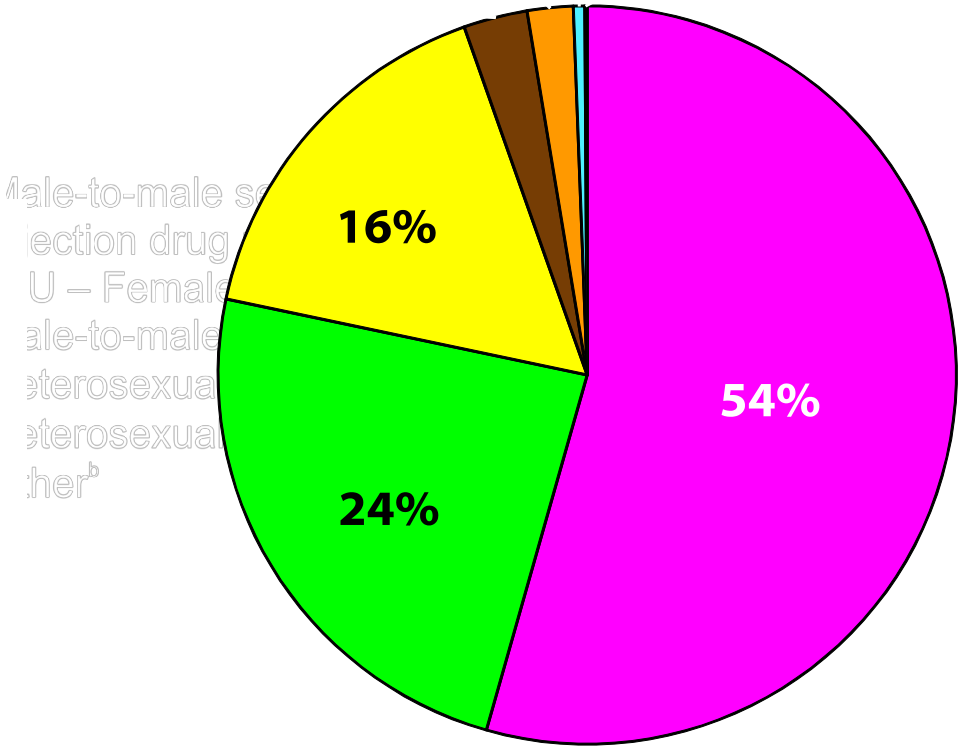
Primary objectives:
Assess the proportion and characteristics of women who accept versus decline PrEP

Training for study initiation in July 2016

New HIV infections in the US, 2014



Two thirds of new infections
In the US occured among MSM



More than half of new infection among MSM
In the US occured among Black MSM

HPTN 073: Uptake of and adherence to TDF/FTC PrEP among Black MSM in the US

Washington, DC
Los Angeles, CA
Chapel Hill, NC

Enrollment	226
Population	BMSM/HIV-
Study Duration: 12 M	

HIV negative BMSM

→ **Offer PrEP Daily Oral TDF/FTC** + **Client Centered Care Coordination (C4)**

Ongoing management of health & psychosocial needs

Study Status

Follow-up completed September 2015

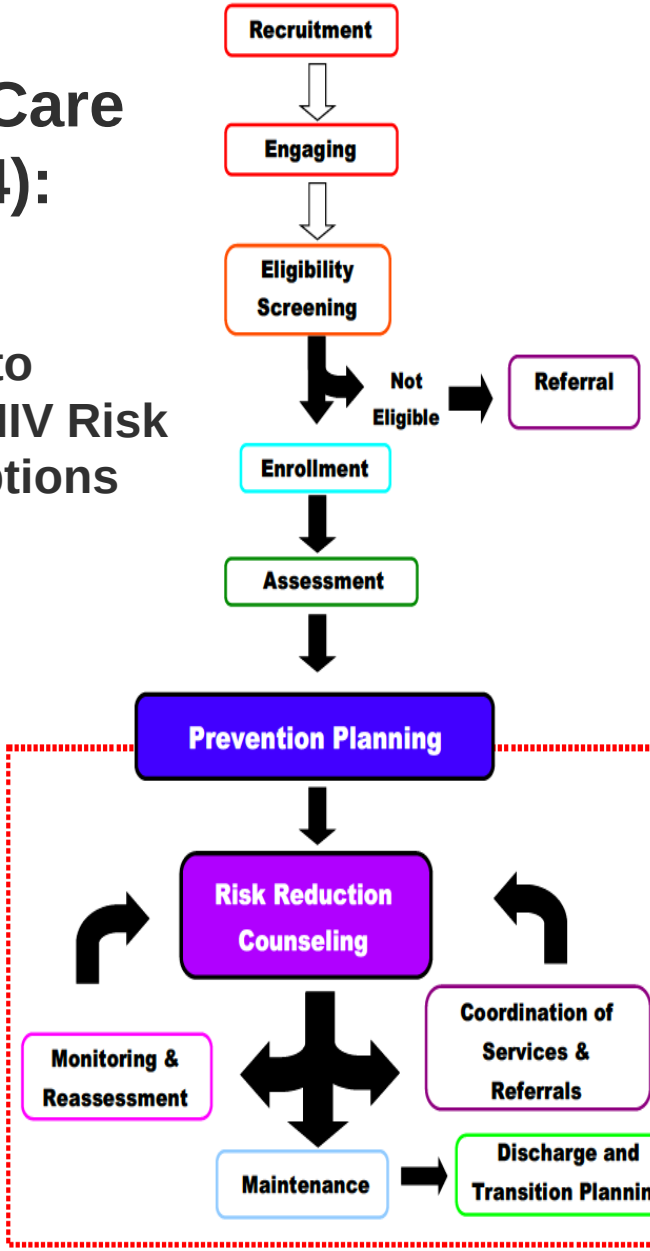
Self-reported uptake and adherence presented at CROI 2016

Additional results to be presented at AIDS 2016

HPTN 073

Client Centered Care Coordination (C4):

A Culturally Specific Intervention Package to Support PrEP Use in HIV Risk Reduction Menu of Options

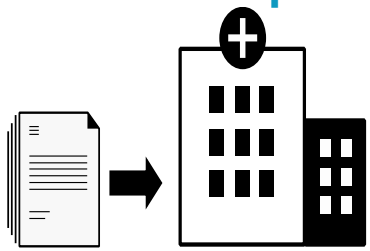


C4 Core Components

PrEP Uptake: 79%

12-Month Retention: 92%

Transition to Community Follow-Up



HPTN 075: Feasibility of recruitment and retention of African MSM

Observational study:

Kisumu, Kenya
Blantyre, Malawi
Soweto, SA
Cape Town, SA

400 MSM in 4 Sites

- Men 18-44 years living in sub-Saharan Africa who report anal sex with a man in the past 3 months

12 Months of Follow-Up

- 5 study visits with structured HIV behavioral assessments, medical examinations, and collection of biological samples

Primary Objective

To assess retention of a cohort of MSM to inform feasibility of an intervention study

Almost Completed enrollment!

389 of 400 men enrolled

Long-acting Agents for HIV Prevention

Two studies of safety of long-acting injectable PrEP initiated and enrollment completed

HPTN 076: Safety and acceptability of injectable rilpivirine (TMC278 LA) for PrEP

136

US Sites

Newark, NJ
Bronx, NY

International Sites

Cape Town, South Africa
Harare, Zimbabwe

HPTN 077: Safety, tolerability and pharmacokinetics of injectable cabotegravir (CAB) in men and women

194

International Sites

Soweto, South Africa
Vulindlela, South Africa
Lilongwe, Malawi
Rio de Janeiro, Brazil

US Sites

Los Angeles, California
San Francisco, California
Washington, DC
Chapel Hill, North Carolina

Primary objective: Evaluate the safety and tolerability of the product

Fully enrolled

HPTN 083: Phase 2B/3 Study of Efficacy of injectable cabotegravir for PrEP in MSM and transgender women

N = 4500 (10% TGW overall; 50% of US BMSM; 50% overall < 30 year old

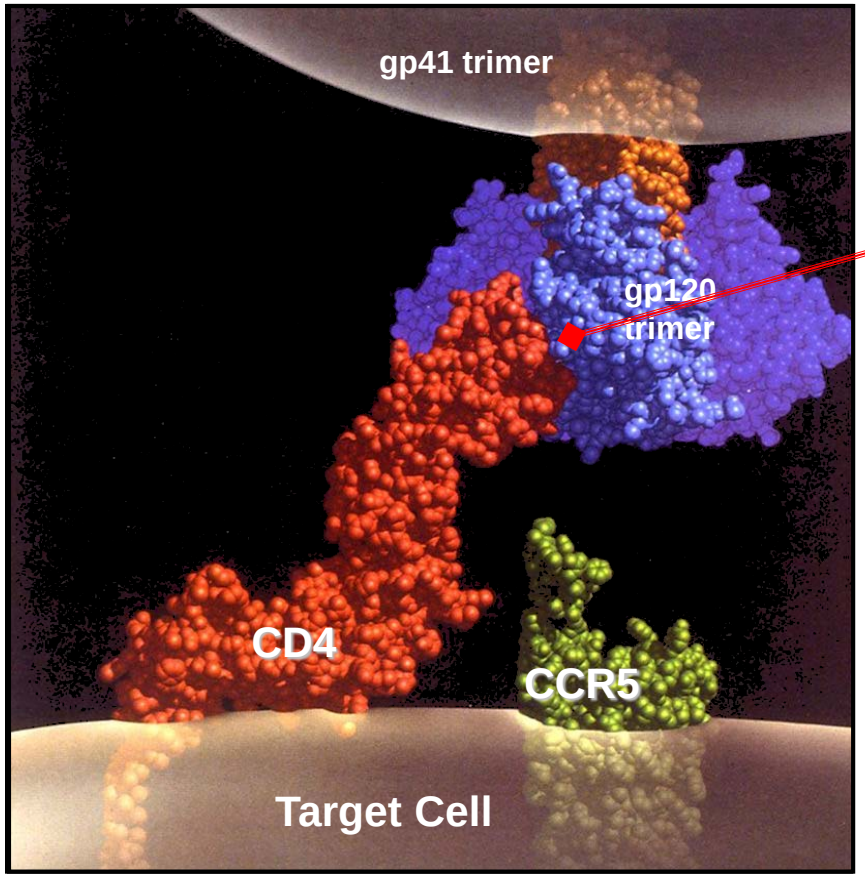
	CAB	TDF/FTC
Step 1	Daily oral CAB and oral TDF/FTC placebo	Daily oral TDF/FTC and oral CAB placebo
Step 2	Injectable CAB and daily oral TDF/FTC placebo	Daily oral TDF/FTC and injectable placebo
Step 3	Open-label daily oral TDF/FTC for up to 48 weeks	Open-label daily oral TDF/FTC for up to 48 weeks

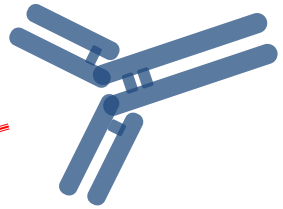
Primary objective: HIV Incidence

40+ sites chosen in the Americas (Argentina, Brazil, Peru, US) and Asia (Thailand, Vietnam; India pending)

HPTN 084: Phase 2B/3 Study of efficacy of injectable cabotegravir for PrEP in women (*under development*)

Monoclonal Antibodies for HIV Prevention





VRC01 MAb

VRC01 attaches to the CD4 binding site on gp120 envelope protein of HIV

VRC01 neutralize ~ 90% of diverse viral isolates

HIV VACCINE
TRIALS NETWORK

MSM+TG AMP: HVTN 704/HPTN 085

Enrolled participants
2700 MSM & TG in US
Study duration
92 weeks

Regimen	N*	
VRC01 10 mg/kg	900	Infusions every 8 weeks through Week 92
VRC01 30 mg/kg	900	
Control	900	
Total	**2700**	

Study opened 31 March, 2016

As of end of May,110 participants enrolled!

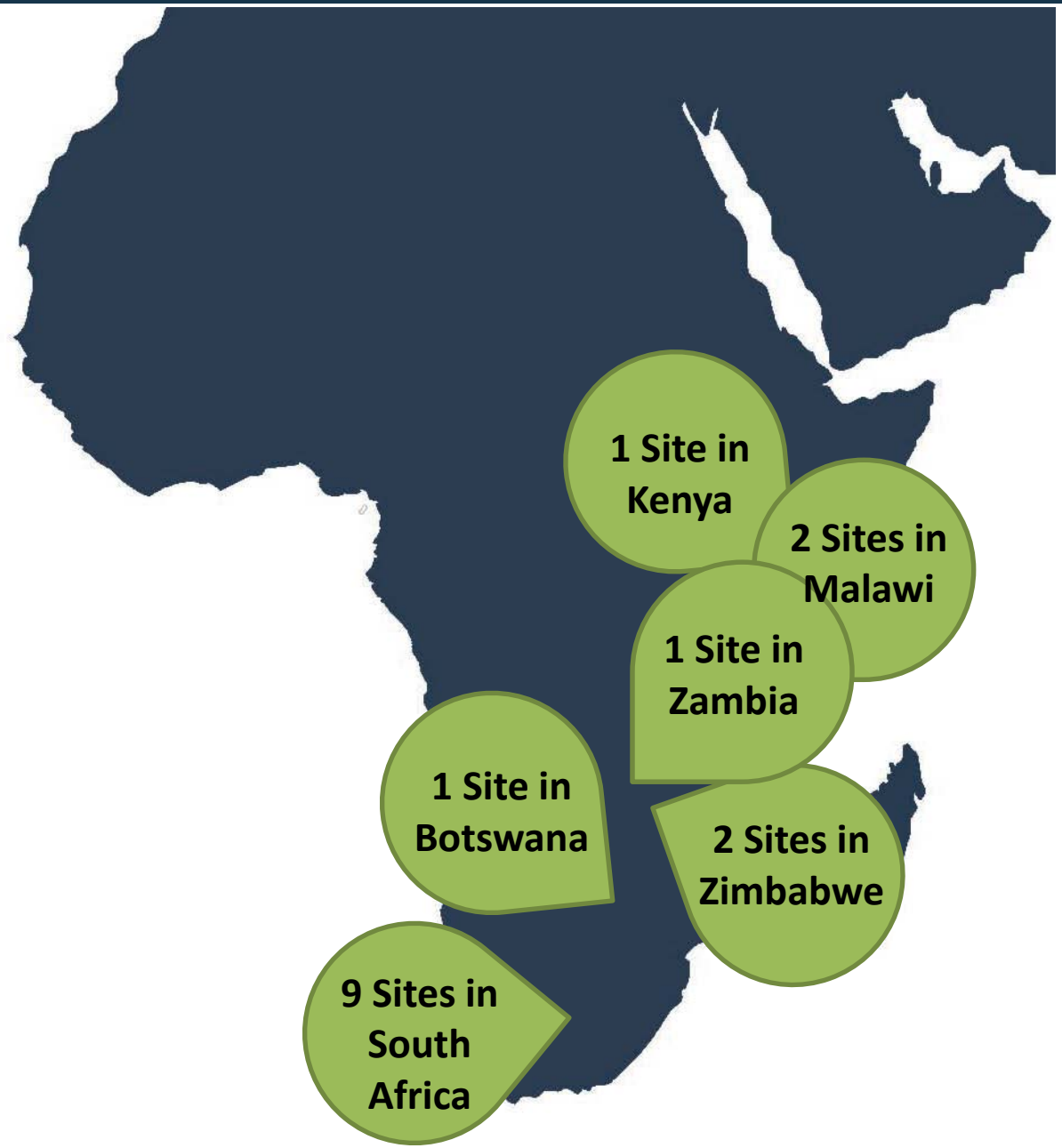
SSA Women AMP: HVTN 703/HPTN 081

Enrolled participants
1500 South African Women (First enrollments expected by mid-May)
Study duration
92 weeks

Regimen	N*	
VRC01 10 mg/kg	500	Infusions every 8 weeks through Week 92
VRC01 30 mg/kg	500	
Control	500	
Total	**1500**	

Study started enrollment


1 Site in Ukraine
1 Site in Puerto Rico
1 Site in China
34 Sites in the U.S.
4 Sites in Brazil
3 Sites in Thailand
1 Site in India
2 Sites in Vietnam
16 Sites in Africa
1 Site in Indonesia
5 Sites in Peru
2 Sites in Argentina


1 Site in Kenya
2 Sites in Malawi
1 Site in Zambia
1 Site in Botswana
2 Sites in Zimbabwe
9 Sites in South Africa

Community Engagement

- Eight capacity building community workshops for HVTN 703/HPTN 081, HVTN 704/HPTN 085 and HPTN 083
- In 1st quarter 2016, 31 CRSs provided education/outreach at 508 events
- Cross-network (HPTN & HVTN & MTN) biomedical research summit (NAESM Conference)
- Five-day science (HPTN & MTN) writing workshop
  - writing teams developed, several abstracts presented

HPTN Scholars Program

Goal: To develop the next generation of HIV prevention scientists

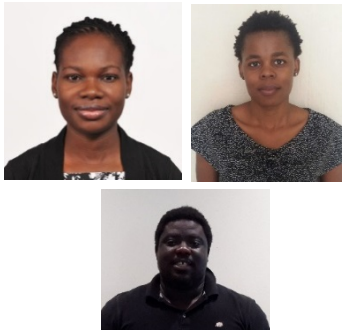
- Scholars utilize HPTN data to develop analytic skills, conduct reviews, give presentations, write publications

To date:
- 21 scholars completed program
- 31 mentors engaged
- K awards, R03, R21, faculty positions
- 12 presentations, 17 publications
  (+ 1 in press, 2 under review)

Sten Vermund
Darrell Wheeler
Ken Mayer
Quarraisha Abdool Karim
David Serwadda

Seventh Cohort of Scholars

Second Cohort of Int'l Scholars



HPTN Publications 2015-2016

- 46 Publications
- Presentations
  - IAS 2015 - 15
  - CROI 2015 – 7
  - CROI 2016 - 26
  - AIDS 2016 – 28

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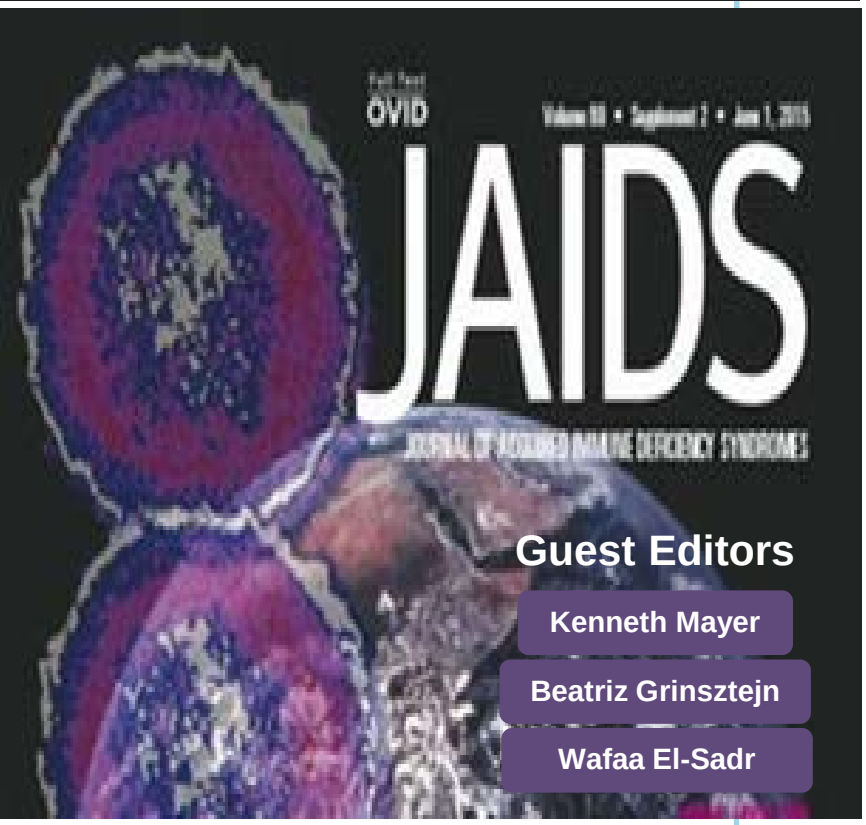
SPECIAL ISSUE:
HIV Prevention for Transgender Populations



JAIDS Supplement – online July 2016

Transgender People and HIV Prevention: What We Know and What We Need to Know
Kenneth Mayer, Beatriz Grinsztejn, and Wafaa M. El-Sadr

Global epidemiology of HIV infection and related syndemics affecting transgender people
Tonia Poteat, Ayden Scheim, Jessica Xavier, Sari L. Reisner, and Stefan Baral

Behavioral Interventions to Prevent HIV Transmission and Acquisition for Transgender Women: A Quick Review
Robert Garafalo, Lisa E. Kuhns, Sari L. Reisner, and Matthew J. Mimiaga

Transgender Women in Clinical Trials of Pre-Exposure Prophylaxis
Robert M. Grant, Jae Sevelius, Valdilea G. Veloso, and Madeline Deutsch

Pharmacologic considerations for Pre-Exposure Prophylaxis in Transgender Women
Peter Anderson

Integrated and Gender-Affirming Clinical Care and Research Programs for Transgender People to Address Disparities in HIV Infection
Sari L. Reisner, Asa Radix, and Madeline Deutsch

Engaging Transgender People in NIH-funded HIV/AIDS Clinical Trials Research
Rona L. Siskind, Michel Andrasik, Shelly T. Karuna, Gail B. Broder, Clare Collins, Albert Liu, Jonathan Paul Lucas, Gary W. Harper, and Philip Renzullo

Design Issues in Transgender Studies
Jim P. Hughes, Lynda Emel, Brett Hanscom, and Sahar Zangeneh

Ethical Issues to Consider in the Design of HIV Prevention Trials Involving Transgender People
Jerome Amir Singh

Conclusions

- Success in recruitment of important at risk populations, e.g., US Black MSM, PWID and their partners, MSM in SSA
- HPTN study results are informing future research by the network and other groups
- Suite of vanguard studies developed to identify how best
  - to recruit, engage specific populations and
  - to determine the uptake, adherence with and outcomes of key interventions
- New collaborations established, robust community engagement accomplished and continued commitment to a new generation of prevention researchers

Acknowledgements

- NIH Institutes (NIAID, NIMH, NIDA)
- PEPFAR; Bill and Melinda Gates Foundation; CDC; and pharmaceutical partners
- **Elsie Talavera and her team** ive
- Study participants and participating communities
- Investigators, staff and community representatives

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Thank you!