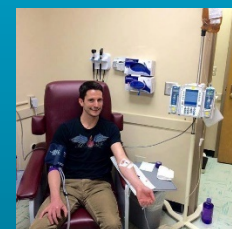


# HPTN 2017-8

## The Way Forward

**Myron S. Cohen**  
**Wafaa El-Sadr**  
on behalf of the HPTN



# HPTN MISSION

The HIV Prevention Trials Network (HPTN) advances HIV prevention through research:

- Integrated HIV prevention strategies
- Improve pre-exposure prophylaxis (PrEP)
- New strategies for key populations

# What Does this Really Mean?

- We are trying to develop tools/strategies
  - That improve public health policy/practice
  - That improve medical care
  - In a timely fashion (FAST)

# Highlights

- Where have we been?
- Where are we going?
- **WE NEED YOU (!!!) to go anywhere**

# The Year in Review: Metrics

- 9 ongoing studies including the HPTN 071 (PopART), the largest HIV prevention study to date
  - 6 new studies initiated/planned
- 78 sites are active (22 HPTN sites)
  - >25 new protocol-specific sites launched in the last year
- Successful scholars program
- 65 presentations, 47 publications
- Robust engagement of communities
- **Expanded global partnerships**
- **5 studies completed**



# The Effect of a Conditional Cash Transfer on HIV Incidence in Young Women in Rural South Africa (HPTN 068): a Phase 3, Randomised Controlled Trial

*Audrey Pettifor, Catherine MacPhail, James P Hughes, Amanda Selin, Jing Wang, F Xavier Gómez-Olivé, Susan H Eshleman, Ryan G Wagner, Wonderful Mabuza, Nomhle Khoza, Chirayath Suchindran, Immitrude Mokoena, Rhian Twine, Philip Andrew, Ellen Townley, Oliver Laeyendecker, Yaw Agyei, Stephen Tollman, Kathleen Kahn*

*Pettifor, et al.; Lancet Glob Health Dec 2016;4(12):e978-88*



## Phase 2 Study of the Safety and Tolerability of Maraviroc-Containing Regimens to Prevent HIV Infection in Men Who Have Sex With Men (HPTN 069/ACTG A5305)

Roy M. Gulick, Timothy J. Wilkin, Ying Q. Chen, Raphael J. Landovitz, K. Rivet Amico, Alicia M. Young, Paul Richardson, Mark A. Marzinke, Craig W. Hendrix, Susan H. Eshleman, Ian McGowan, Leslie M. Cottle, Adriana Andrade, Cheryl Marcus, Karin L. Klingman, Wairimu Chege, Alex R. Rinehart, James F. Rooney, Philip Andrew, Robert A. Salata, Manya Magnus, Jason E. Farley, Albert Liu, Ian Frank, Ken Ho, Jorge Santana, Joanne D. Stekler, Marybeth McCauley, and Kenneth H. Mayer



## Daily and non-daily pre-exposure prophylaxis in African women (HPTN 067/ADAPT Cape Town Trial): a randomised, open-label, phase 2 trial

*Prof Linda-Gail Bekker, MD, Surita Roux, MBChB, Elaine Sebastien, RNRM, Ntando Yola, PgDPH, K Rivet Amico, PhD, Prof James P Hughes, PhD, Mark A Marzinke, PhD, Craig W Hendrix, MD, Prof Peter L Anderson, PharmD, Vanessa Elharrar, MD, Michael Stirratt, PhD, James F Rooney, MD, Estelle Piwovar-Manning, MT(ASCP), Prof Susan H Eshleman, MD, Laura McKinstry, MPH, Maoji Li, MMath, Bonnie J Dye, MPH, Robert M Grant, MD, on behalf of the HPTN 067 (ADAPT) study team*

### Articles

A network meta-analysis of second-line therapies

See page e433

### Articles

Effect of vaginal microbiota on oral PrEP efficacy

See page e449

### Articles

A household survey of HIV incidence in Rwanda

See page e457



# WHO IS MOST AT RISK OF HIV INFECTION

HELPING TO PREVENT HIV STARTS WITH UNDERSTANDING WHICH POPULATIONS ARE AT HIGHER RISK



There are approximately **1.2 million** individuals in the United States living with HIV, with nearly **40,000** new cases diagnosed each year.<sup>1,2</sup>

The Centers for Disease Control and Prevention estimated over **60%** of new HIV infections in the United States were attributed to men who have sex with men (MSM), while **25%** of new HIV infections occurred from heterosexual sex in 2010.<sup>1</sup>

## CERTAIN POPULATIONS ARE AT HIGHER RISK OF CONTRACTING HIV THAN OTHERS

The Centers for Disease Control and Prevention report these statistics estimating the number of people in the United States who will contract HIV in their lifetime.<sup>3,4</sup>

### MEN WHO HAVE SEX WITH MEN (MSM)

Overall **1 in 6** 

African American **1 in 2** 

Hispanic/Latino **1 in 4** 

Caucasian **1 in 11** 

### HETEROSEXUAL

Overall **1 in 473** **1 in 241**

### OVERALL

Overall **1 in 64** **1 in 227**

African American **1 in 20** **1 in 48**

Hispanic/Latino **1 in 48** **1 in 227**

Caucasian **1 in 132** **1 in 880**

Injection Drug Users **1 in 36** **1 in 23**

## THE TRANSGENDER COMMUNITY IN THE UNITED STATES IS ONE OF THE HIGHEST-RISK GROUPS FOR HIV INFECTION

HIV prevalence in transgender women was estimated at nearly **50 times** higher than in all adults of reproductive age.<sup>6</sup>



**OF TRANSGENDER WOMEN ARE HIV POSITIVE<sup>5</sup>**

# HPTN 073

## PrEP Uptake and Use by Black Men Who Have Sex With Men in Three U.S. Cities



*Darrell P. Wheeler; Sheldon Fields; LaRon E. Nelson; Leo Wilton; Lisa Hightow-Weidman; Steven Shoptaw; Manya Magnus; Geetha Beauchamp; Phaedrea Watkins; Kenneth H. Mayer for the HPTN 073 Study*

# MSM: HPTN 075 and 078

Studies designed to better inform our ability to prevent HIV in hard to reach MSM ...worldwide

# HPTN 076

## Safety and Acceptability of TMC278 LA for PrEP



### **HPTN 076: TMC278 LA Safe, Tolerable, And Acceptable for HIV Pre-exposure Prophylaxis**

*Linda-Gail Bekker, Shuying S. Li, Betsy Tolley, Mark A. Marzinke, Nyaradzo Mgodzi, Jessica E. Justman, Shobha Swaminathan, Adeola Adeyeye, Jennifer H. Farrior, Nirupama Sista*

### **HPTN 076: Safety and Pharmacokinetics of Rilpivirine LA Through Week 76 in HIV-uninfected Women**

*N.D. Sista, S. Li, M. Marzinke, N. Mgodzi, J. Justman, S. Swaminathan, A. Adeyeye, E. Piwowar-Manning, S. Pathak, J. Farrior, L.-G. Bekker, and the HPTN Study Team*

# UNAIDS Treatment Targets



90%

Diagnosed



90%

On Treatment



90%

Virally Suppressed

# HPTN 052

Bruce Alberts, Editor of Science explains the choice of this work:

“The results have galvanized efforts to end the world’s AIDS epidemic in a way that would been inconceivable even a year ago”



# Treatment as Prevention Trials

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- **HPTN 071 (PopART)**
- CDC Botswana
- ANRS Africa Center
- SEARCH Uganda

...and many smaller studies

*Cohen et al. Lancet, 2013*



# HPTN 074

## Integrated intervention including supported ART compared to the standard of care for PWID

- Vietnam, Ukraine, Indonesia
- 504 HIV infected PWID
- 810 PWID “partners”
- Excellent retention
- Suppression results?
- **Durability extension?**
- **What’s NEXT?**

# PrEP Research Summary

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## **Optimize the use of TDF/FTC**

- Pharmacology and adherence (HPTN 066, 067)
- Vanguard (pilot) studies directed toward:
  - Acceptability in MSM in the US (HPTN 073)
  - Recruitment of MSM in Africa (HPTN 075)
  - PrEP uptake in women in Africa (HPTN 082)

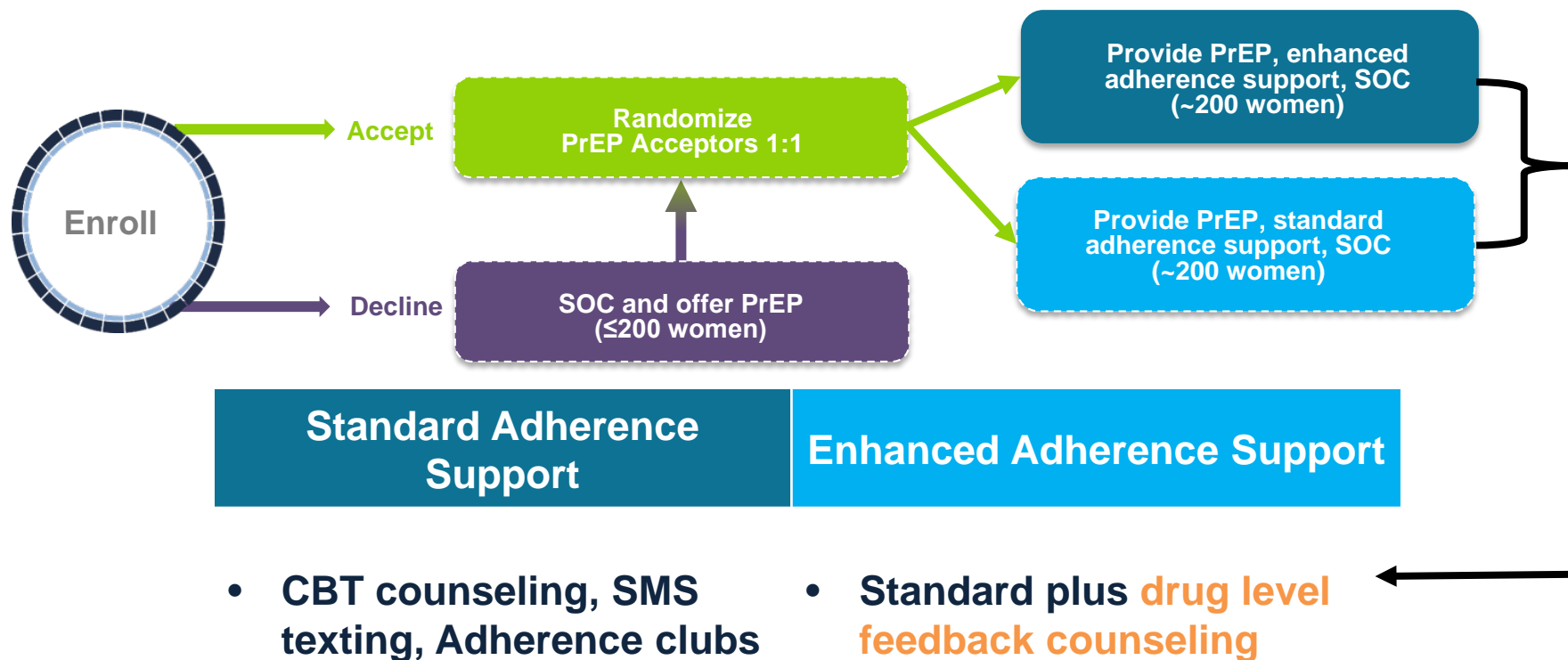
## **Develop new PrEP/ drugs/delivery methods for PrEP**

- Long-acting ART (HPTN 076, 077, 083, 084, 086)
- Broadly neutralizing antibodies (HPTN 081, 085, 087, 088)

# HPTN 082 Study Design

**HPTN** <sup>Q82</sup>  
HERS

PrEP = Daily oral FTC/TDF



## Primary objectives:

- Assess the proportion and characteristics women who accept versus decline PrEP
- Assess PrEP adherence using drug levels in young women

Enrolled  
participants

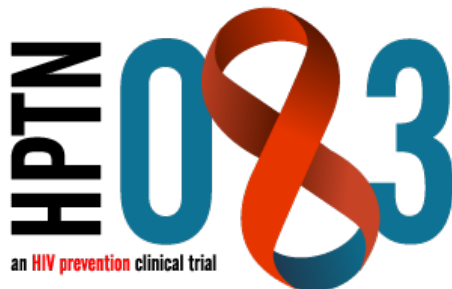
229

# HPTN 083: CAB LA 600mg

To Prevent HIV Acquisition in MSM and TGW

Landovitz and Grinsztejn, *Protocol Chairs*

Step 1	Daily oral CAB and TDF/FTC placebo	TDF/FTC and oral CAB placebo
Step 2	CAB LA at two time points 4 weeks apart and every 8 weeks thereafter and TDF/FTC placebo	TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter
Step 3	Open-label TDF/FTC to cover the PK tail	Open-label TDF/FTC to Cover the PK tail



**Primary Objective: Reduce HIV Incidence (**non-inferiority**, double blind, double dummy design)**

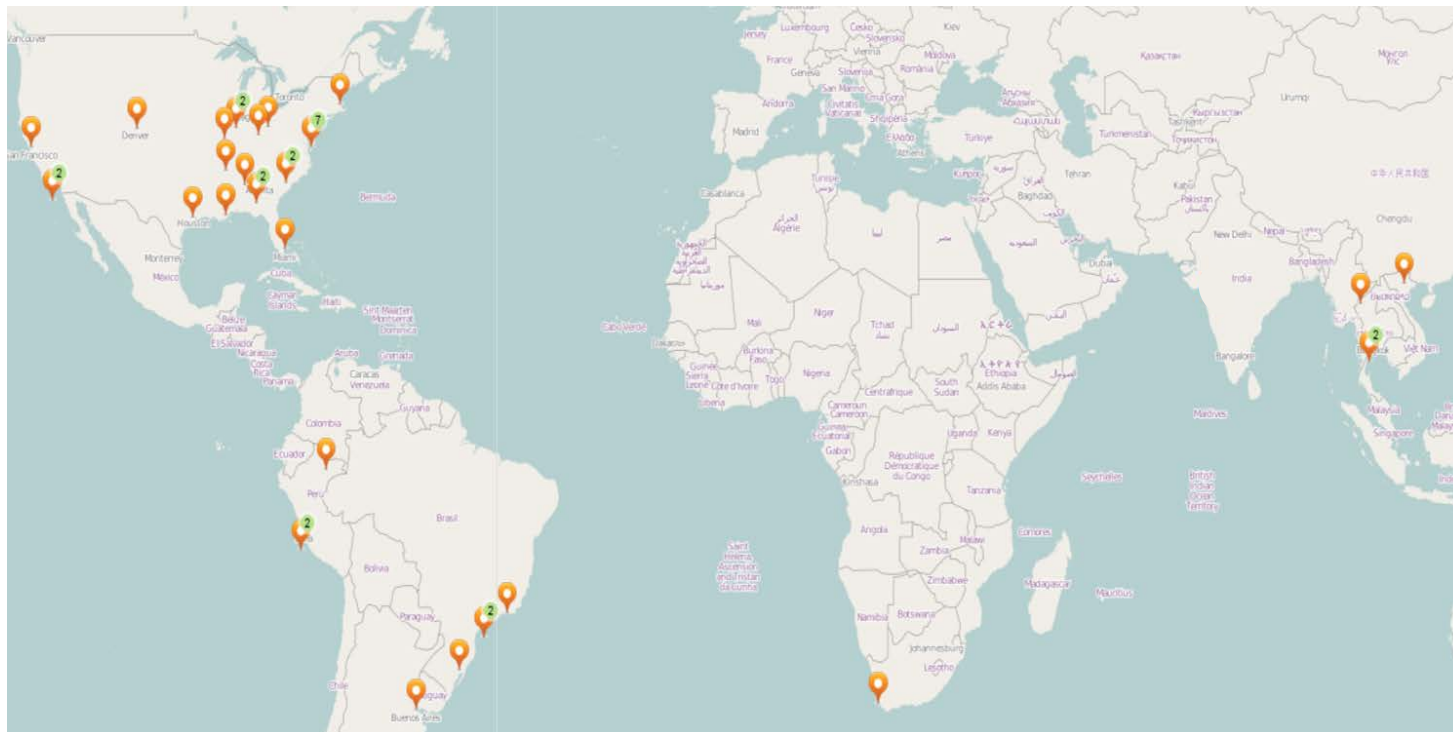
N=4500; Study duration: Enrollment 24-30 months; follow-up ~ 4.5 years

Enrollment goals:

- *Minimum* 50% of US enrollment Black MSM (~ 950)
- Overall minimum 10% TGW (~ 450)
- Overall > 50% under age 30

# HPTN 083 Research Sites

## 44 Sites in 7 Countries



**Study started in December 2016 in U.S.  
651 Enrolled! (as of October 12 2017)**

# HPTN 084: CAB LA 600mg

To Prevent HIV Acquisition in Women

Delaney-Moretlwe and Hosseinipour, *Protocol Chairs*

Step 1	Daily oral CAB and TDF/FTC placebo	Oral TDF/FTC and oral CAB placebo
Step 2	CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter	Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter
Step 3	Open-label oral TDF/FTC to cover the PK tail	Open-label oral TDF/FTC to cover the PK tail

**Primary Objective: Reduce HIV Incidence (**superiority**, double blind, double dummy design)**

Study duration: Enrollment 24 months; follow-up up to 4.5 years, N=3200

# Study Population

- 20 research sites in 7 countries in Sub-Saharan Africa
- 3,200 women who have sex with men
- Expected HIV incidence  $>3/100$  person years





# Subcutaneous PrEP Implants?

## Like Implanon/Nexplanon Contraception



- Simple insertion AND removal
- Long-acting (months to years)
- PrEP + contraception?
- Current development:
  - TAF, EFdA (MK-8591), Cabotegravir

**Partnerships established!**  
**Phase 1 2019**

# Passive Antibody Prevention Phase IIB Efficacy Studies

AMP = Antibody Mediated Prevention

Can a passively infused monoclonal antibody  
prevent HIV-1 infection in high risk adults:  
MSM in Americas & Heterosexual Women in sub-Saharan Africa?

Chairs: Lawrence Corey, HVTN  
Myron S. Cohen, HPTN

Co-chairs: Srilatha Edupuganti  
Nyaradzo Mgodhi

# The AMP Studies: Highlights

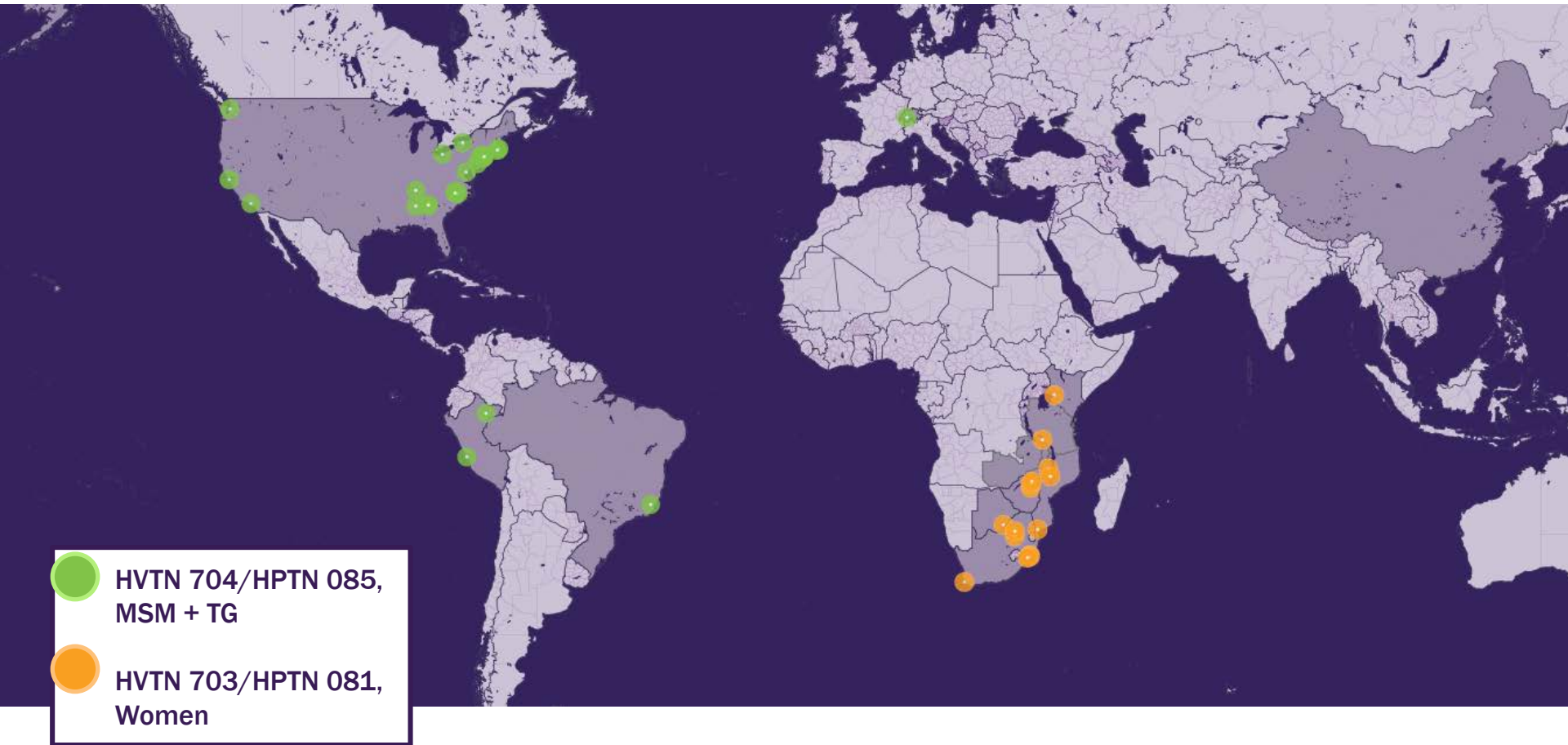
**HVTN 704/HPTN 085**

**HVTN 703/HPTN 081**

- Placebo controlled trial of VRC01 mAb (IV), given on q2 month schedule
- Two cohorts:
  - 2,400 MSM + TG in North & South America
  - 1,500 Women in sub-Saharan Africa
- Powered to detect 60% efficacy; and to associate VRC01 plasma level with protection
- Both trials opened in April/May 2016

# AMP Research Sites

47 sites in 11 countries



# AMP Enrollment Update

As of October 12, 2017



703/081  
African Women

1213/1500  
enrolled

704/085  
MSM + TG

1748/2700  
enrolled

The tree hugger who now  
embraces logging p. 24

Piecing together the proton  
size puzzle pgs. 39 & 79

Price tags influence pain  
perception pgs. 44 & 105

# Science

\$15  
6 OCTOBER 2017  
scienceemag.org

AAAS

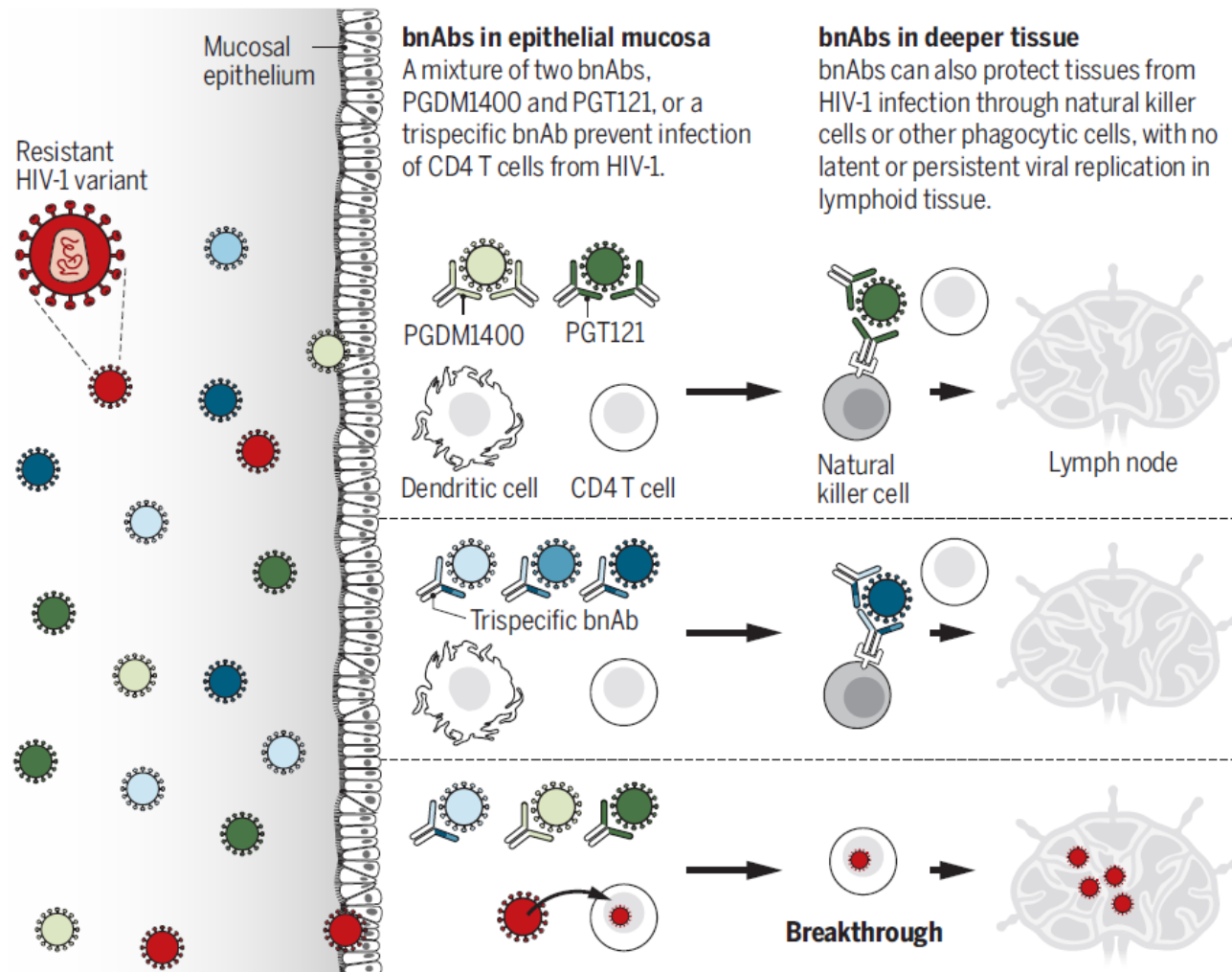
## *Broadly neutralizing antibodies to prevent HIV-1*

Studies show the potential of synthetic and  
Combinations of broadly neutralizing antibodies.

By Myron S. Cohen *and* Lawrence Corey

## bnAbs prevent HIV-1

Combinations of bnAbs and a trispecific antibody can bind to virions and prevent HIV-1 mucosal infection and elicit antiviral responses in deeper tissue. It is hoped this multitarget approach will prevent resistant breakthrough.





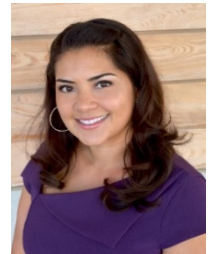
# HPTN Scholars Program

**Goal:** To develop the next generation of HIV prevention scientists from under-represented racial/ethnic communities

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

**To date:**

- 26 scholars completed program
- 31 mentors engaged
- K & U awards, R01, R03s, R21s, faculty positions
- 18 publications  
(+ 2 in press, 1 under review)



## Second Cohort of Int'l Scholars



# Community Engagement Activities

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- **Good Participatory Process**
  - Five HPTN 083 presentations at national conferences engaging community advocates, CBOs, ASOs, MSM & TG-specific service providers, and health departments
  - One HPTN 083 community webinar engaging U.S. national community advocates and providers
- **Scientific Literacy**
  - “Understanding Clinical Research Process and Principles of Clinical Research” workshop for the HPTN 071/PopART Zambia National CAB

# Community Engagement Activities

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- **Community partnerships**
  - Five, study-specific national stakeholder consultations (including HPTN 081 and HPTN 084)
  - SA AIDS booth, photo campaigns
- **Social Media**
  - #GivePrEPaShot social marketing campaign and website for HPTN 083
- **Dissemination of Results**
  - Webinars, at sites, brochures, posters, presentations, etc.

# Cross Site Exchange of Best Practices





# Community Outreach/Education







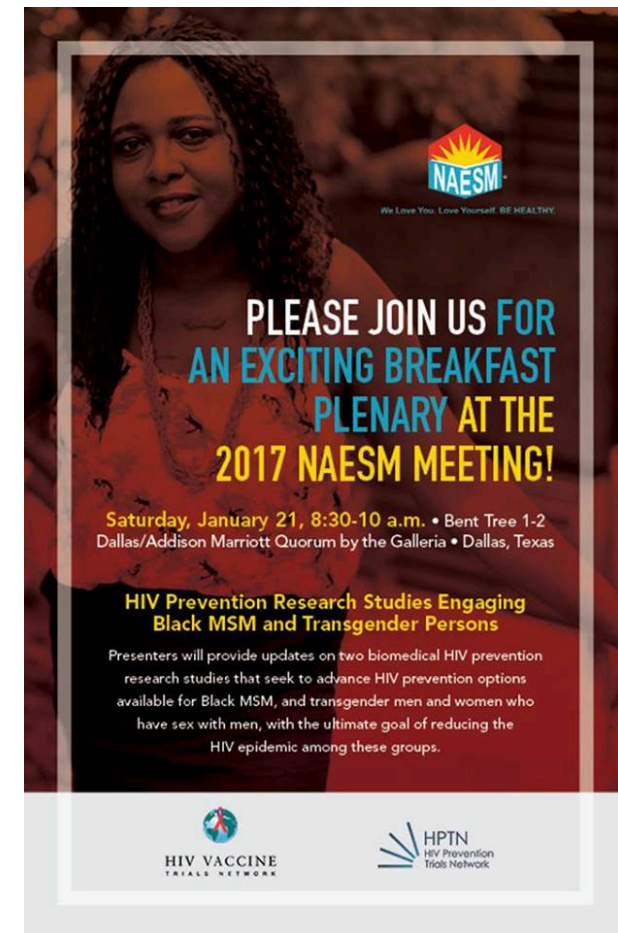
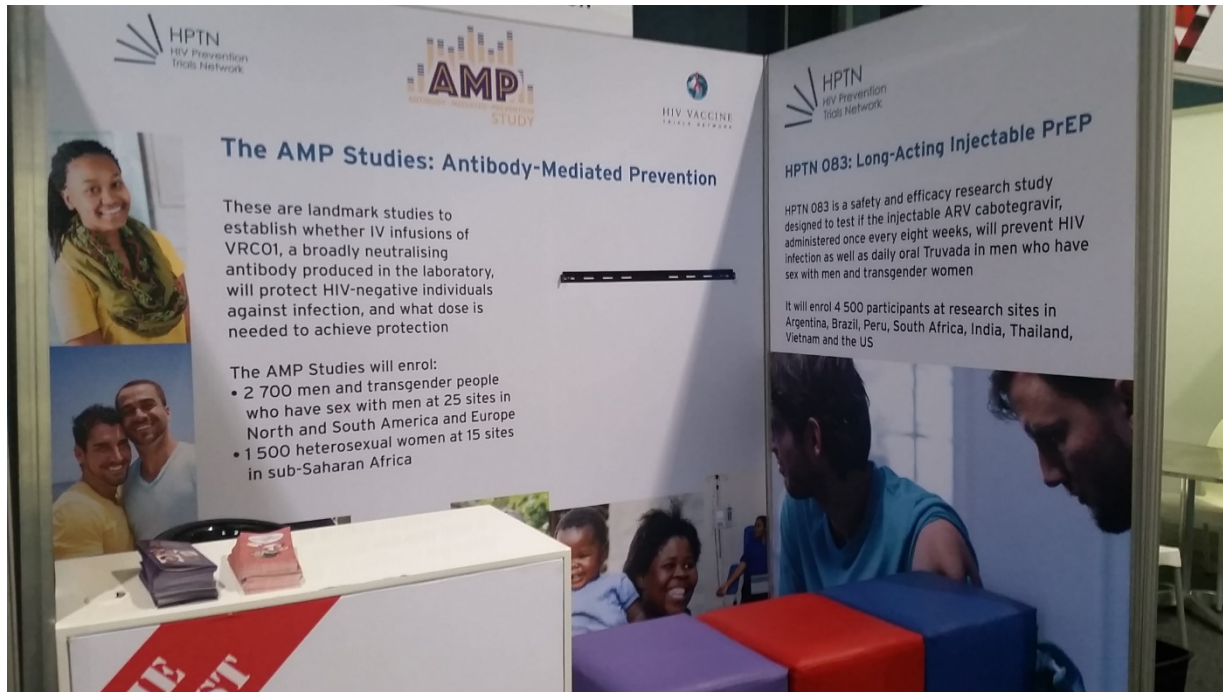


# Community Outreach/Education





# Dissemination - Cross Network Collaboration



# Dissemination – Best Practices



# Women and Adolescent Subjects

- ~40,000 women in HPTN clinical trials
- A rapidly growing and exciting adolescent research agenda team
- Consideration of ethical bridging studies

# The Way Forward

**When we complete our current studies we will have:**

- A long-acting PrEP agent
- Strategies to deliver HIV testing and universal access to ART to decrease HIV incidence
- Methods for optimizing uptake of TDF/FTC
- Advanced BnABS for prevention of HIV infection

**THE HPTN IS DETERMINED TO GENERATE RESEARCH RESULTS THAT INFORM AND GUIDE HIV PREVENTION STRATEGIES WORLDWIDE**

# The Team

- **Study participants and participating communities**
- **Site investigators, staff, and community representatives**
- BMGF, USAID, PEPFAR/OGAC, ViiV, Gilead, VRC, PANGEA, and many other partners
- NIH Institutes (NIAID, NIMH, NIDA) and OAR
- HPTN Scientific Committees, Working Groups, Executive Committee, and Scientific Advisory Group