



HPTN
HIV Prevention
Trials Network

HPTN 2017

The Way Forward

Myron S. Cohen
Wafaa El-Sadr
on behalf of THE NETWORK



HPTN MISSION

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

- Develop integrated combination HIV prevention strategies
- Improve systemic pre-exposure prophylaxis (PrEP) and develop new PrEP agents and strategies
- Optimize application of new knowledge to key populations

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**

We Are Building Partnerships

- Across Networks (VTN)
- BMGF
- VIIV, Gilead, Merck, and others (?)
- USAID
- The PANGEA Phylogeny Consortium
- The Northwestern Implant Consortium
- NIH Vaccine Research Center



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, Many Magnus, Jason E. Farley, Albert Liu, Ian Frank, Ken Ho, Jorge Santana, Joanne D. Stekler, Marybeth McCauley, and Kenneth H. Mayer

HPTN 067/ADAPT



IAS 2015
vancouver, canada
8th IAS Conference on HIV Pathogenesis,
Treatment & Prevention 19-22 July 2015



- HPTN 067/ADAPT key results presented:
 - HPTN 067/ADAPT Cape Town: A comparison of daily and nondaily PrEP dosing in African women. L-G Bekker et al (CROI 2015)
 - HPTN 067/ADAPT Study: A comparison of daily and non-daily pre-exposure prophylaxis dosing Thai/NYC. T. Holtz/S. Mannheimer et al. (IAS 2015)

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

The NEW ENGLAND
JOURNAL *of* MEDICINE

Established in 1812

September 1, 2016

Vol. 375 No. 9

Antiretroviral Therapy for the Prevention
of HIV-1 Transmission

M.S. Cohen, Y.Q. Chen, M. McCauley, T. Gamble, M.C. Hosseinipour, N. Kumarasamy, J.G. Hakim, J. Kumwenda, B. Grinsztejn, J.H.S. Pilotto, S.V. Godbole, S. Chariyalertsak, B.R. Santos, K.H. Mayer, I.F. Hoffman, S.H. Eshleman, E. Piwowar-Manning, L. Cottle, X.C. Zhang, J. Makhema, L.A. Mills, R. Panchia, S. Faesen, J. Eron, J. Gallant, D. Havlir, S. Swindells, V. Elharrar, D. Burns, T.E. Taha, K. Nielsen-Saines, D.D. Celentano, M. Essex, S.E. Hudelson, A.D. Redd, and T.R. Fleming, for the HPTN 052 Study Team*

Cohen, et al.; N Engl J Med, 2016 Sep 1;375(9):830-9

UNAIDS Treatment Targets



90%

Diagnosed



90%

On Treatment



90%

Virally Suppressed

Treatment as Prevention Trials

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

...and many smaller studies

HPTN 071 (PopART) Study Design

PopART Intervention Package

- Annual rounds of home based voluntary HIV testing by Community HIV-care Providers (CHiPs)
- Health promotion, active referral and/or retention in care support by CHiPs for the following:
 - Voluntary Medical Male Circumcision (VMMC) for HIV negative men
 - Prevention of Mother to Child Transmission (PMTCT) for HIV positive women
 - HIV treatment and care for all HIV positive individuals
 - Promotion of sexual health and TB services
 - Condom provision
- ART irrespective of CD4-count or clinical stage provided at the local health centre

Population Cohort

- ~ 2,000 randomly selected adults (18-44) from each study community (N ~42,000)
- Annual household visits for blood collection and study survey completion for 3 years
- Study results will inform the primary outcome and some secondary outcomes



Primary Outcome: HIV Incidence

HPTN 074

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

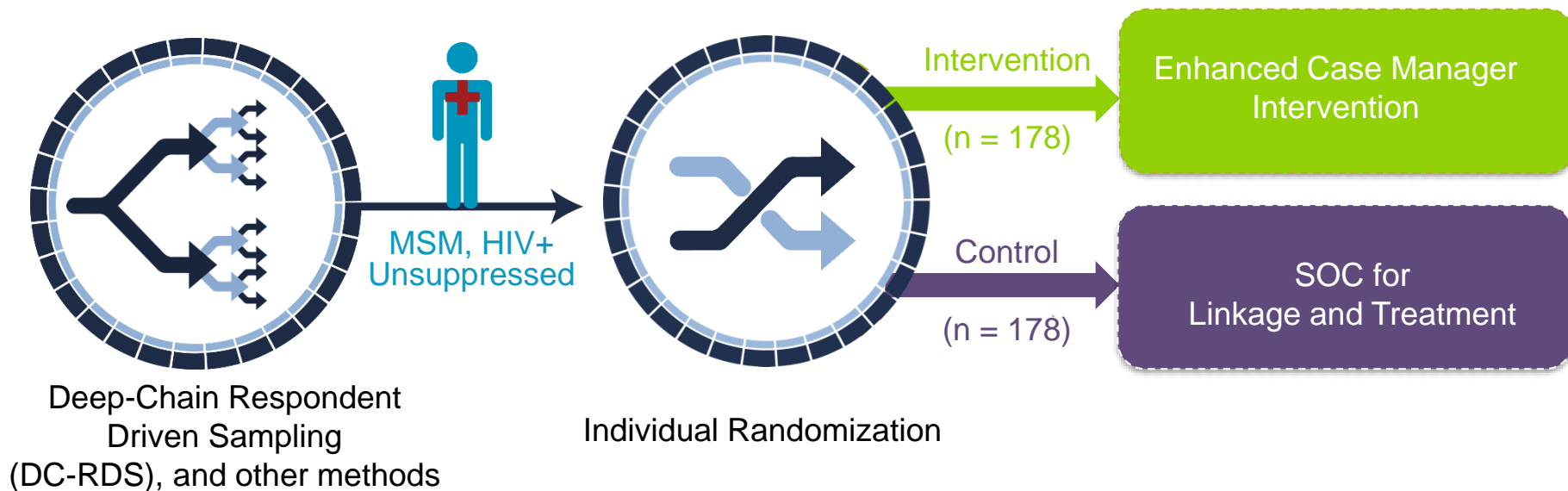
- Vietnam, Ukraine, Indonesia
- 504 HIV infected PWID
- 810 PWID “partners”
- Excellent retention
- Suppression results?
- **Durability extension?**
- **What’s NEXT?**

HPTN 078

Enhancing Recruitment, Linkage to Care and Treatment for HIV-Infected Men Who Have Sex with Men (MSM) in the United States

Screened population	Enrolled participants
2700	356
MSM \geq 16 yo	MSM HIV+, Unsuppressed
Study Duration: 24 M Follow-up	

Study Design



WHO IS MOST AT RISK OF HIV INFECTION

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



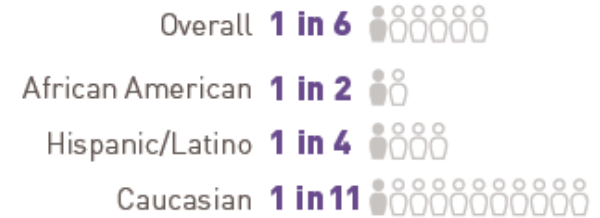
There are approximately **1.2 million** individuals in the United States living with HIV, with nearly **40,000** new cases diagnosed each year.^{1,2}

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 2010.¹

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.^{3,4}

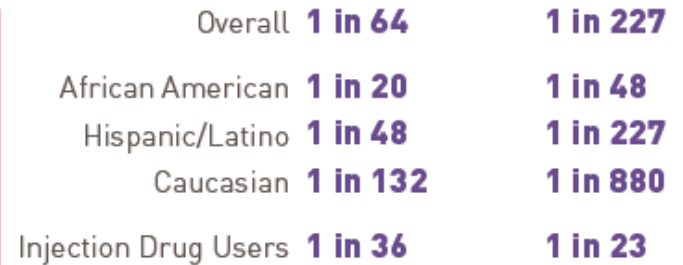
MEN WHO HAVE SEX WITH MEN (MSM)



HETEROSEXUAL

	MEN	WOMEN
Overall	1 in 473	1 in 241

OVERALL



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.⁴



22% OF TRANSGENDER WOMEN ARE HIV POSITIVE⁵

PrEP Research Summary

Optimize the use of TDF/FTC

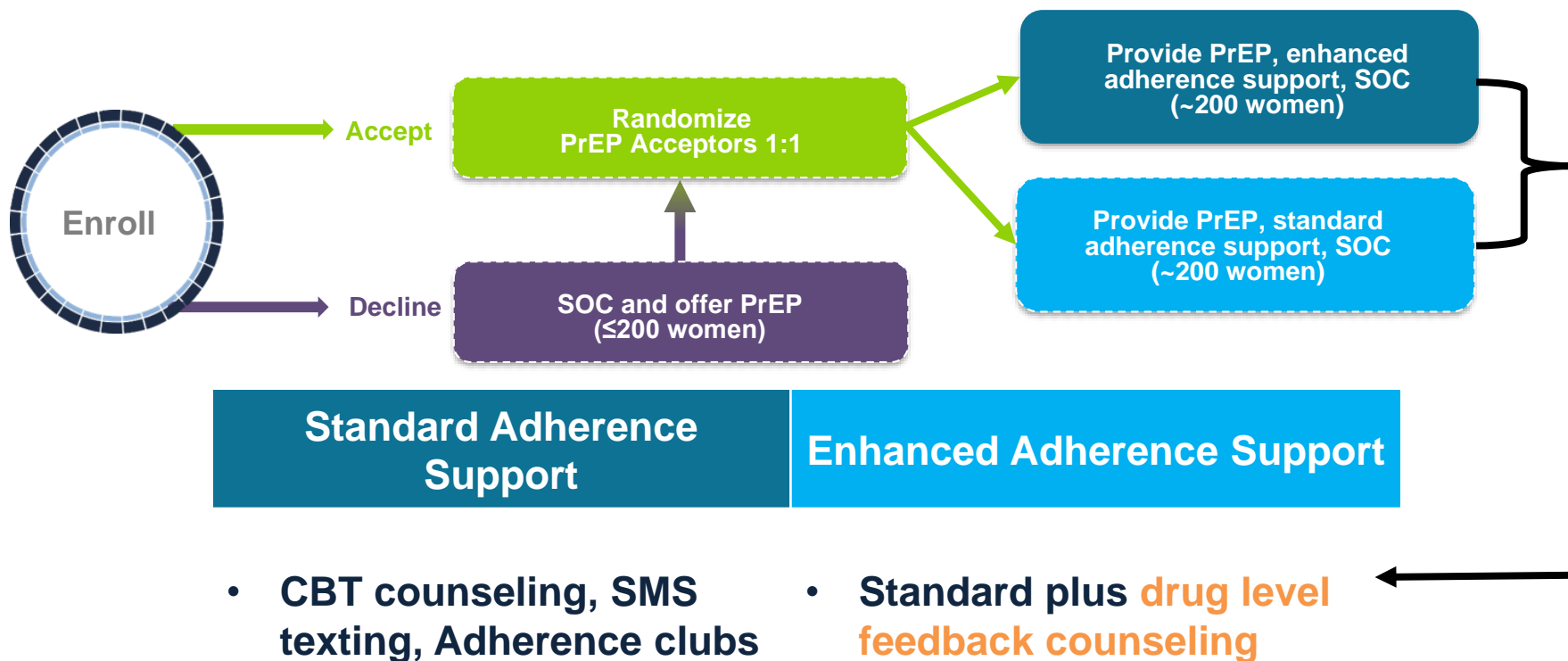
- Pharmacology and adherence (HPTN 066, 067)
- Vanguard (pilot) studies directed toward:
 - Acceptability in MSM in the US (HPTN 073)
 - Recruitment of MSM in Africa (HPTN 075)
 - PrEP uptake in women in Africa (HPTN 082)

Develop new PrEP/ drugs/delivery methods for PrEP

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

HPTN 082 Study Design

PrEP = Daily oral FTC/TDF



- CBT counseling, SMS texting, Adherence clubs

- Standard plus drug level feedback counseling

Primary objectives:

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

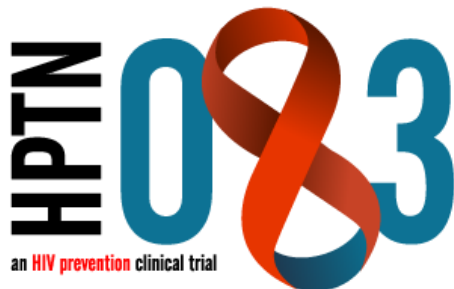
Enrolled participants
229

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)**

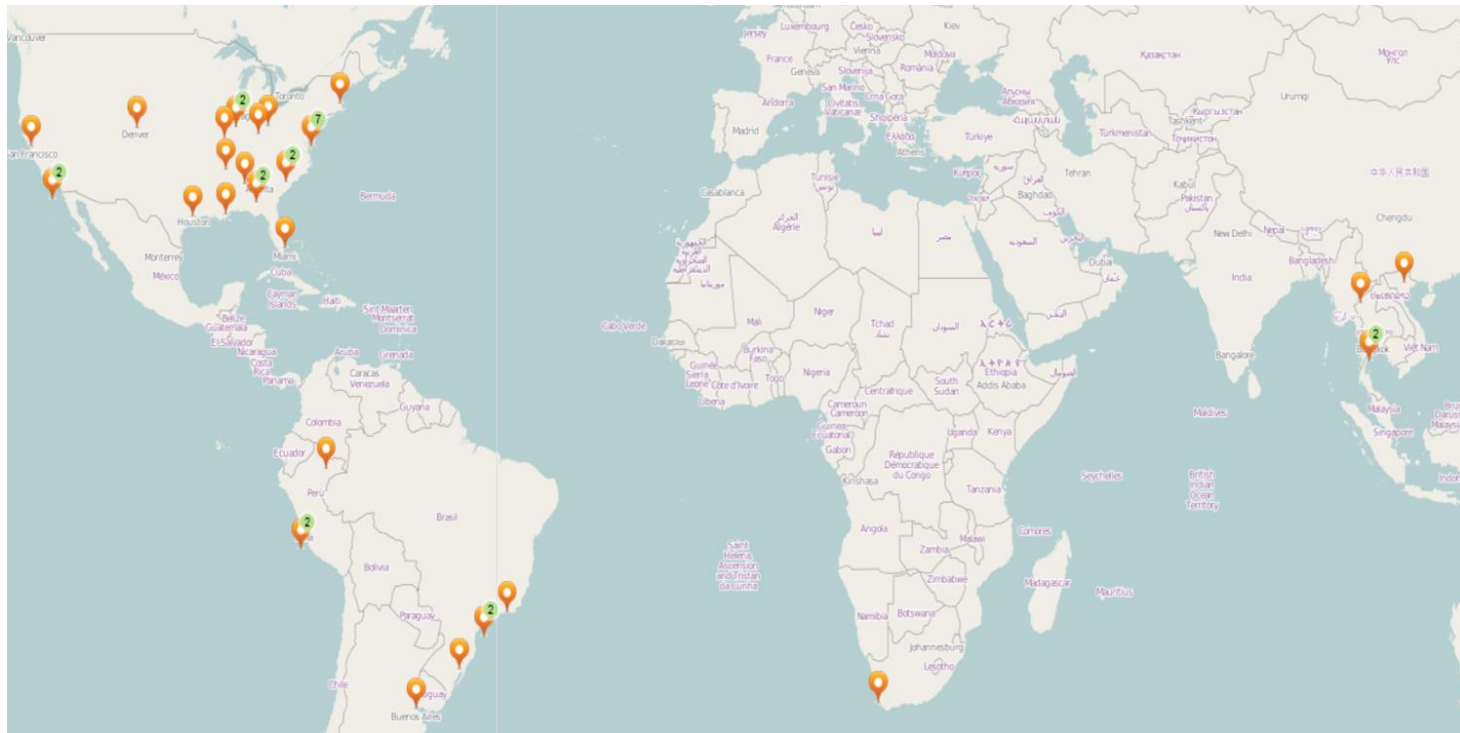
N=4500; Study duration: Enrollment 24-30 months; follow-up ~ 4.5 years

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.
122 Enrolled ! (as of April 5 2017)**

HPTN 084: CAB LA 600mg

To Prevent HIV Acquisition in Women
Delaney-Moretlwe and Hosseinipour, *Protocol Chairs*

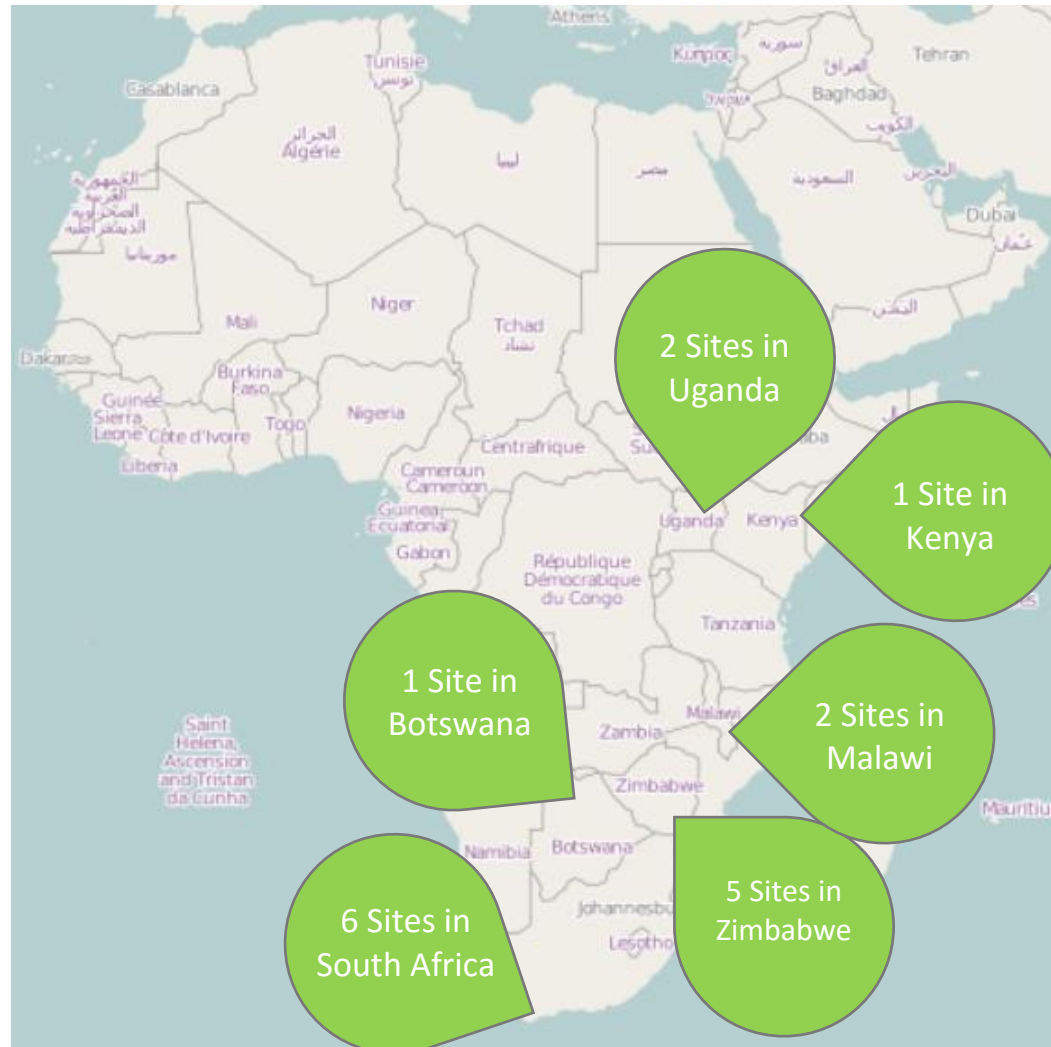
Step 1	Daily oral CAB and TDF/FTC placebo	Oral TDF/FTC and oral CAB placebo
Step 2	CAB LA and oral TDF/FTC placebo at two time points 4 weeks apart and every 8 weeks thereafter	Oral TDF/FTC and injectable placebo at two time points 4 weeks apart and every 8 weeks thereafter
Step 3	Open-label oral TDF/FTC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

HPTN 084 Research Sites

(to date)



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

Northwestern Receives \$17 Million Grant for HIV Prevention Research

Northwestern Medicine scientists have received a 5-year, \$17.5 million grant from the National Institutes of Health (NIH) for an interdisciplinary project that aims to invent, develop and test an implantable drug delivery system to protect high-risk individuals from HIV infection for up to a year at a time.

The Sustained Long-Acting Protection Against HIV (SLAP HIV) program, funded by the NIH's National Institute of Allergy and Infectious Diseases (NIAID), will bring together 15 basic scientists and clinical investigators from 15 departments across Northwestern University Feinberg School of Medicine, McCormick School of Engineering and Kellogg School of Management.

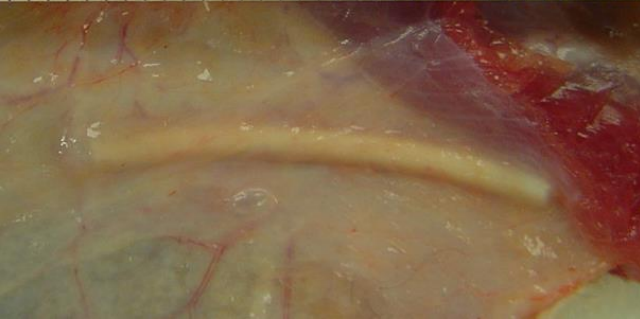
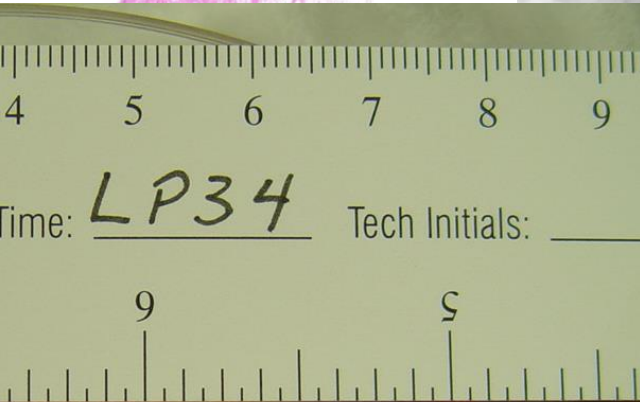


Patrick Kiser, PhD, associate professor in Obstetrics and Gynecology (left), and Thomas Hope, PhD, professor in Cell and Molecular Biology (right), are principal investigators of the new study.

Sustained Long-Acting Protection Against HIV

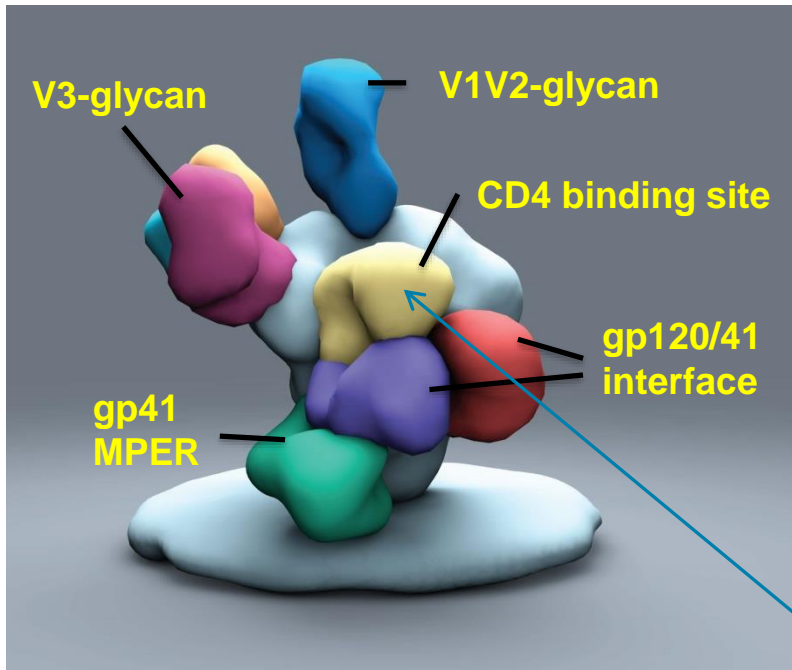
SLAP-HIV

- Northwestern University



Patrick Kiser and Tom Hope

Neutralizing Ab to HIV-1



- V1V2-Glycan – binds to trimer cap
- V3-glycan, N332 supersite
- gp41 MPER – near membrane
- gp120/41 interface – bind to parts of both gp120 and gp41
- CD4 binding site of gp120 – where the virus attaches to CD4

Antibodies (VRC01, 3BNC117) and others in early phase clinical trials

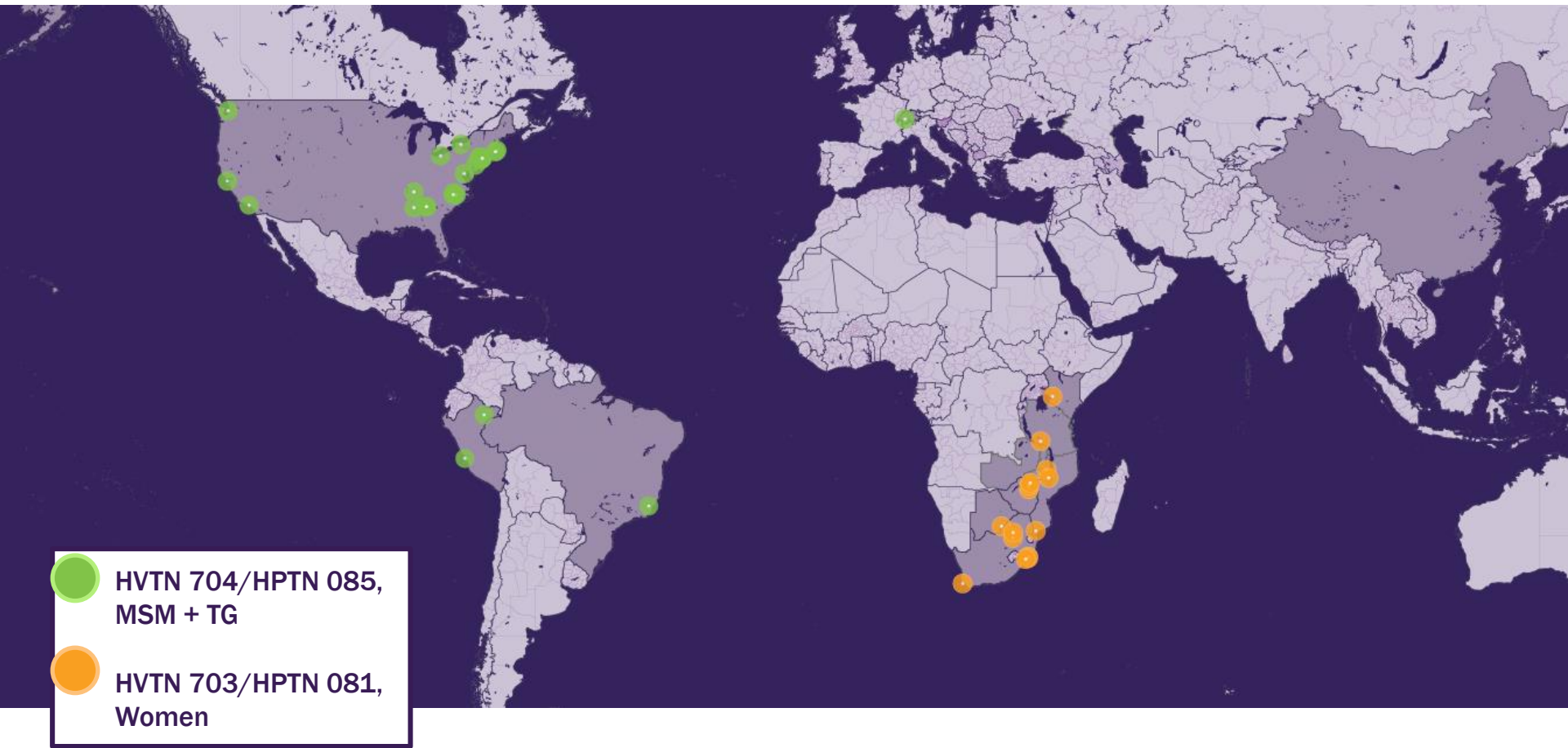
The AMP Studies: Highlights

Cohort	IV Treatment	n=	Schedule
North + South American MSM (2400) HVTN 704 / HPTN 085	VRC01 10 mg/kg	800	Every 8 wks x 10 doses
	VRC01 30 mg/kg	800	
	Placebo Control	800	
sub-Saharan African women (1500) HVTN 703 / HPTN 081	VRC01 10 mg/kg	500	Every 8 wks x 10 doses
	VRC01 30 mg/kg	500	
	Placebo Control	500	

- **Two different infusion doses: important to know if lower dose of 10 mg/kg can protect**
- **Powered to associate mAb serum level with protection**
- **All subjects provided an HIV “prevention package”**

AMP Research Sites

47 sites in 11 countries



AMP Enrollment Update

As of April 6, 2017



703/081
African Women

704/085
MSM + TG

557/1500
enrolled

978/2700
enrolled

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

- **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 partnerships**
 - Five, study-specific national stakeholder consultations
- **Social Media**
 - #GivePrEPaShot social marketing campaign and website for HPTN 083
- **Dissemination of Results**
 - Webinars, at sites, brochures, etc.

Cross Site Exchange of Best Practices



Building on Lessons Learned in the Community



Community Outreach/Education



Manuscript Writing

Curr HIV/AIDS Rep
DOI 10.1007/s11904-016-0322-z



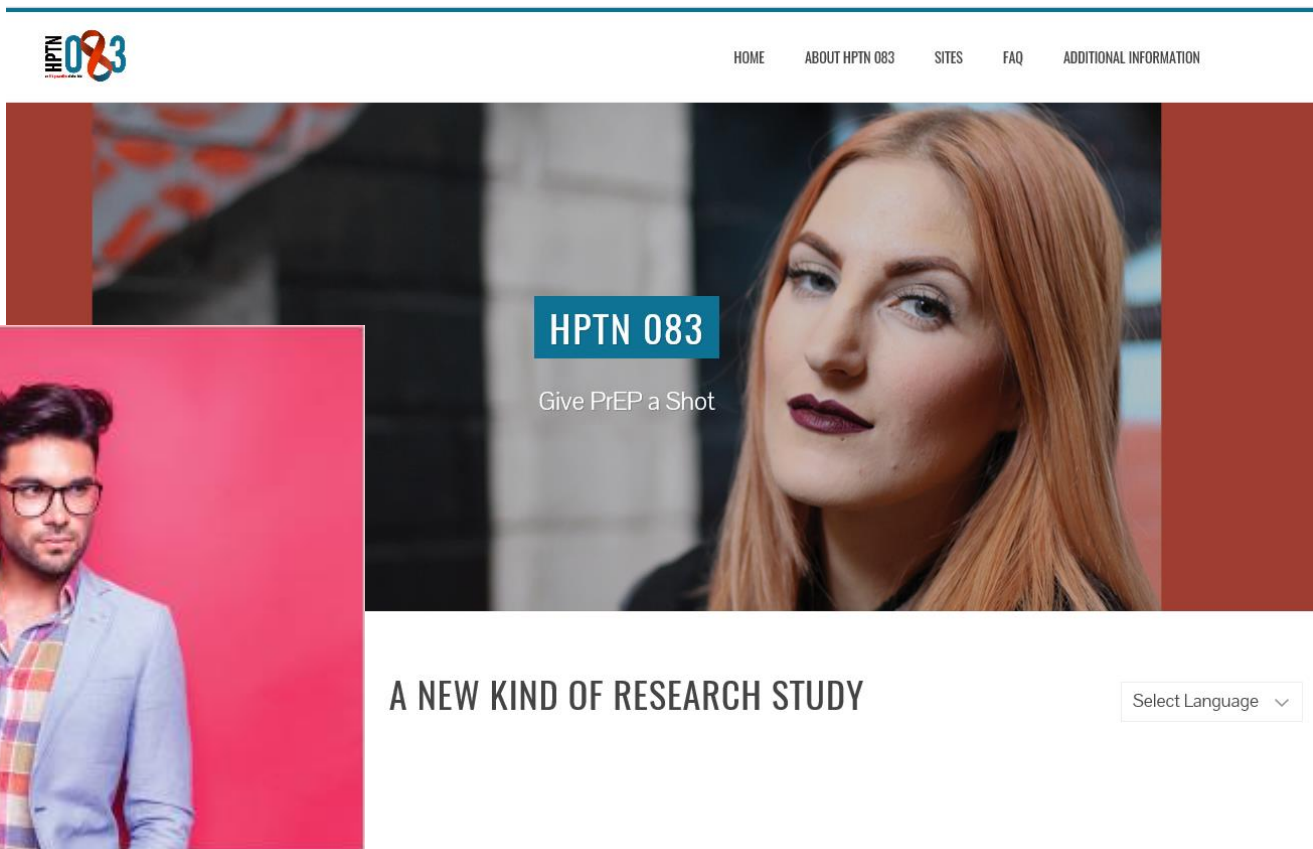
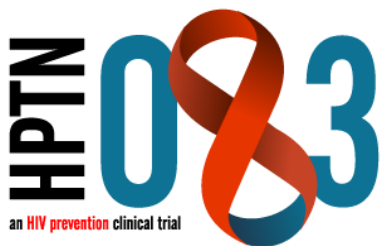
THE GLOBAL EPIDEMIC (S.H. VERMUND, SECTION EDITOR)

Implementing Community Engagement for Combination Prevention: Lessons Learnt From the First Year of the HPTN 071 (PopART) Community-Randomized Study

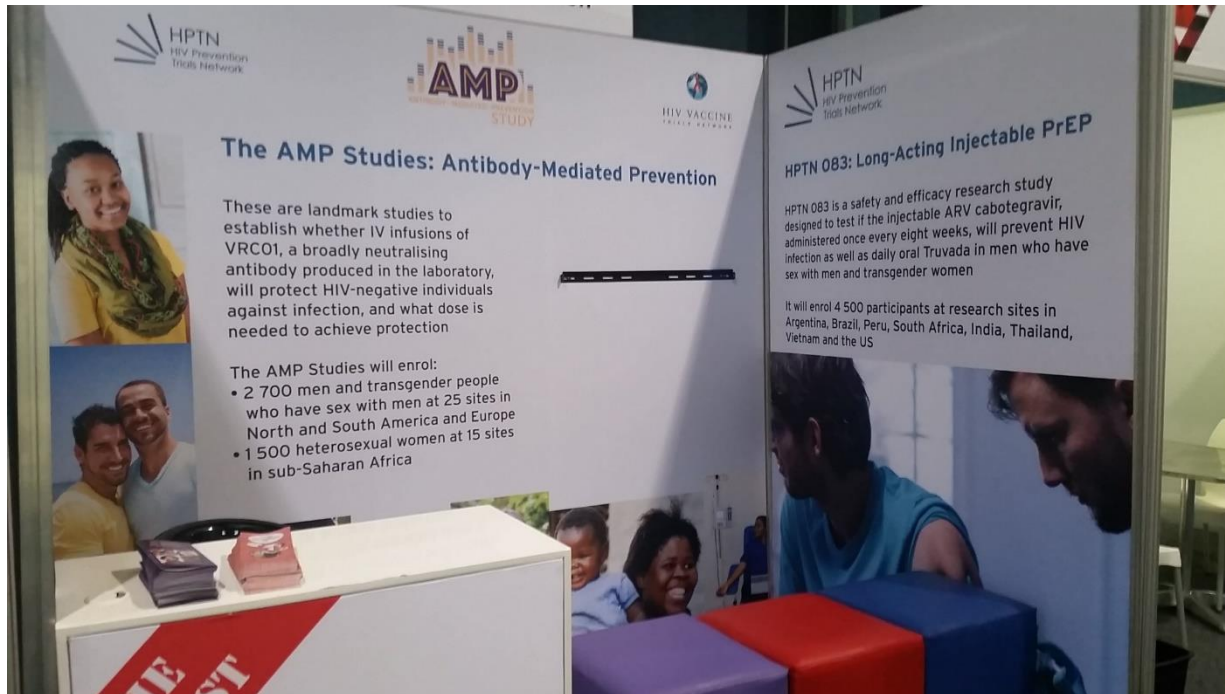

**Musonda Simwinga¹ · Virginia Bond^{1,3} · Nozizwe Makola² · Graeme Hoddinott² ·
Steve Belemu¹ · Rhonda White⁴ · Kwame Shanaube¹ · Janet Seeley^{3,5} · Ayana Moore⁴ ·
on behalf of the HPTN 071 (PopART) study team**



HPTN 083 “Give PrEP a Shot” website, social marketing, and materials



Dissemination - Cross Network Collaboration



We Love You. Love Yourself. BE HEALTHY

**PLEASE JOIN US FOR
AN EXCITING BREAKFAST
PLENARY AT THE
2017 NAESM MEETING!**

Saturday, January 21, 8:30-10 a.m. • Bent Tree 1-2
Dallas/Addison Marriott Quorum by the Galleria • Dallas, Texas

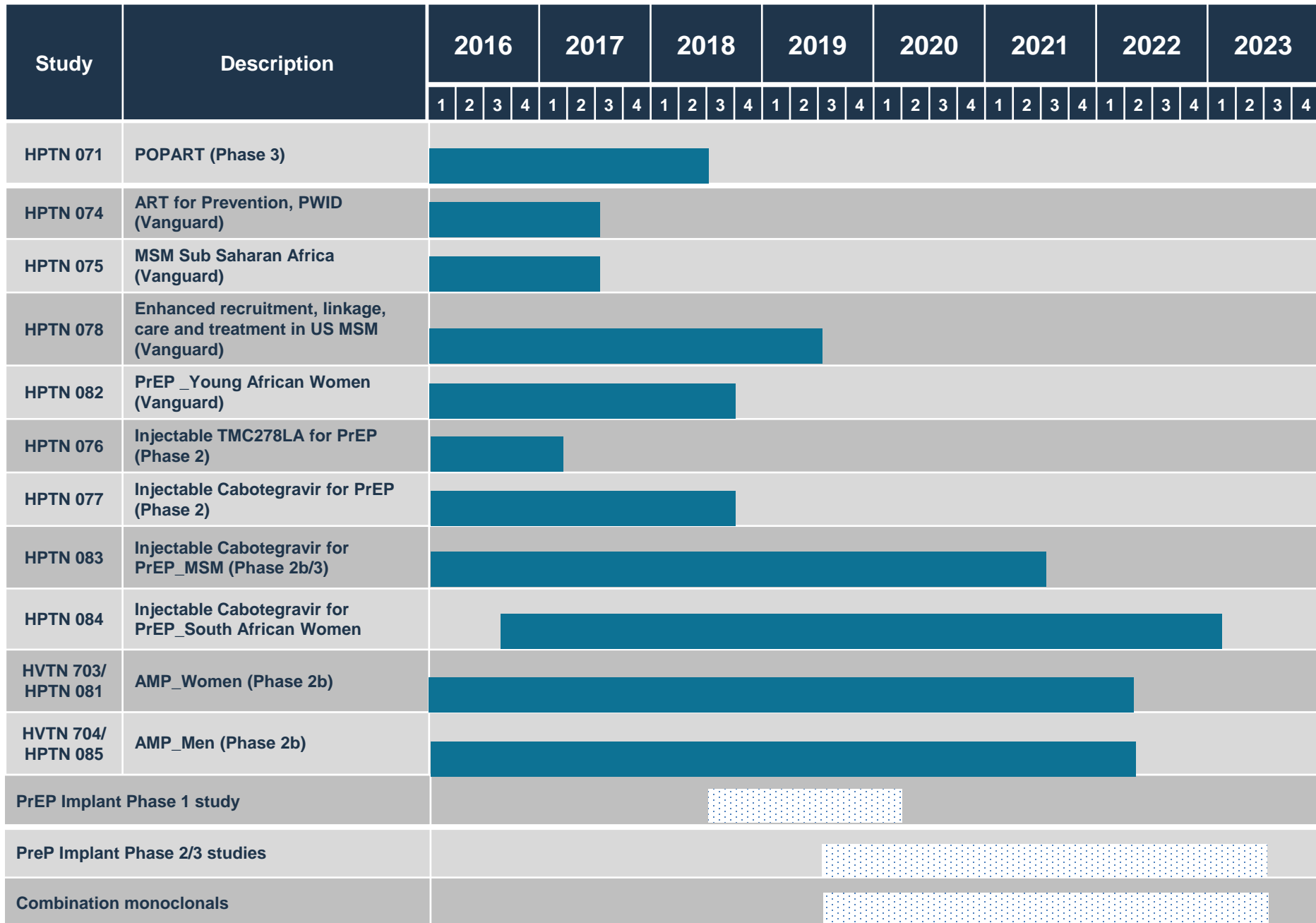
**HIV Prevention Research Studies Engaging
Black MSM and Transgender Persons**

Presenters will provide updates on two biomedical HIV prevention research studies that seek to advance HIV prevention options available for Black MSM, and transgender men and women who have sex with men, with the ultimate goal of reducing the HIV epidemic among these groups.

HPTN Research Portfolio Timeline

Study Development to Anticipated Last F/U Visit



The Way Forward

When we complete our current studies we will have:

- A long-acting PrEP agent ready for licensing as an alternative prevention product, if proven successful.
- Determined strategies to deliver HIV testing and universal access to ART to decrease HIV incidence
- Established methods for optimizing uptake of TDF/FTC in MSM in the U.S. and young women in Africa
- Advanced BnABS for prevention of HIV infection and

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

Acknowledgements

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