HPTN 2023 State of the Network

Myron S. Cohen, MD
Wafaa M. El-Sadr, MD, MPH, MPA
HPTN Principal Investigators

HPTN Annual Meeting

Network Structure – Leaders

Myron
S. Cohen

Wafaa
El-Sadr

Executive Committee (EC)

- Myron S. Cohen
- Wafaa El-Sadr
- Quarraisha Abdool Karim
- Chris Beyrer
- Sinead Delany-Moretlwe
- Deborah Donnell
- Susan Eshleman
- Sybil Hosek
- Raphael Landovitz
- Nyaradzo Mgodi
- David Serwadda
- Sten Vermund
- Nirupama Sista
- Melissa Turner
- Darrell Wheeler
- 2 NIH Representatives

Leadership and Operations Center (LOC) FHI 360

Nirupama
Sista

Statistical and Data Management Center (SDMC) SCHARP

Deborah
Donnell

Laboratory Center (LC) Johns Hopkins University

Susan
Eshleman

Mark
Marzinke

78 Trials

ongoing or completed

172,000+

Study participants enrolled

800+

Publications

History: HPTN Research Evolution

HPTN
HIV Prevention Trials Network

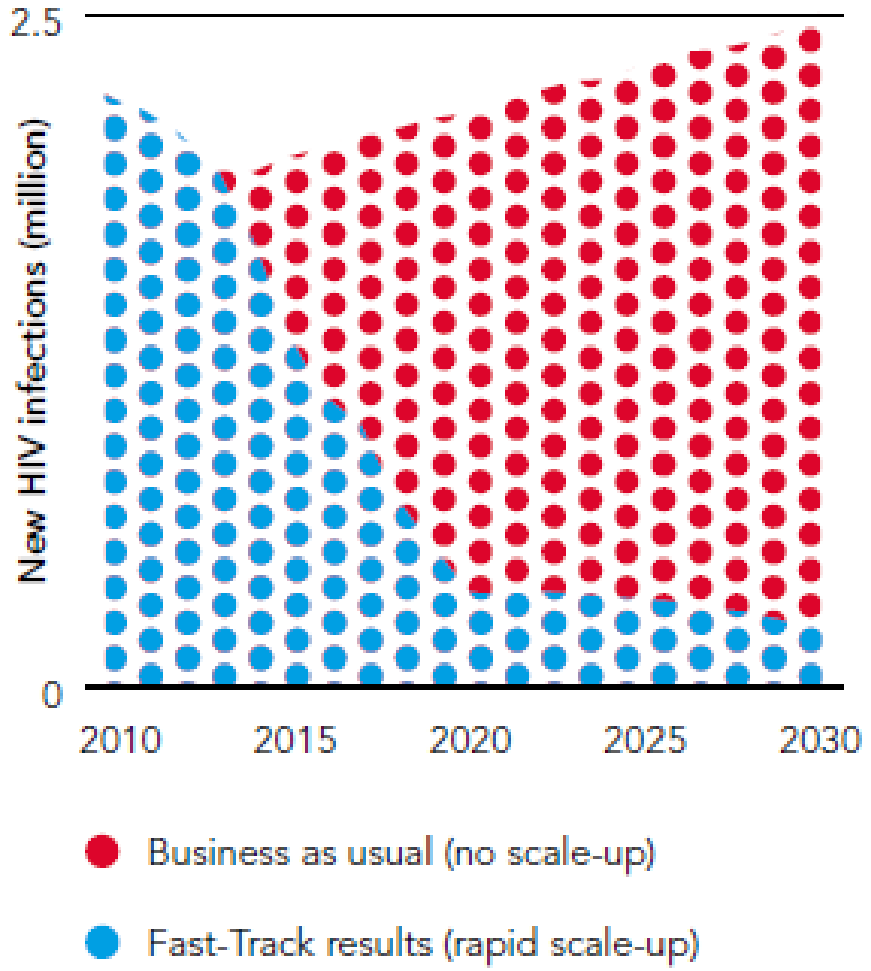
Cates & Self	Cates & Coates	Vermund & Abdool-Karim	El-Sadr & Cohen	El-Sadr & Cohen
Vaccines Microbicides MTCT ART Prevention **STI Treatment** Substance Use **Behavioral** Structural Intervention	~~Vaccines~~ **Microbicides** **MTCT!!** ART STI Treatment Substance Use Behavioral Structural Intervention	~~Vaccines~~ ~~Microbicides~~ ~~MTCT~~ **TaSP (052) !!!!** STI Treatment Substance Use Behavioral Structural Intervention	**Integrated Strategies**: Biomedical Behavioral Structural **Oral PrEP!!!** Alternate drugs, regimens, and formulations Phase I to III	**LA-PrEP!!** **Multipurpose technology** **Broadly-neutralizing antibodies as PrEP** **Integrated strategies** -Trans prevention! -PWID! *Heterosexeual men* *Pregnant women* *STI Vaccines ?*
1993 **IMC/HIVNET**	**1999** **HPTN I**	**2006** **HPTN II**	**2013** **HPTN III**	**2020** **HPTN IV**

UNDETECTABLE = UNTRANSMITTABLE

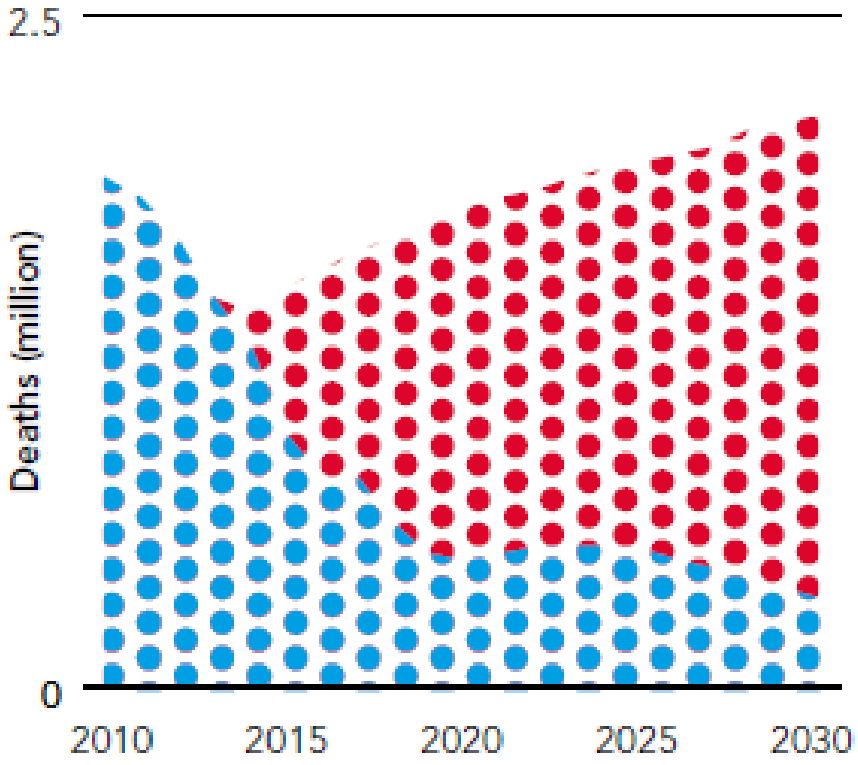
Prevention Access Campaign

The impact of Fast-Track

New HIV infections in low- and middle-income countries



AIDS-related deaths in low- and middle-income countries



UNN AIDS 05-895-95 01506_JC2743_Understanding_FastTrack_en

Two Points to Consider First

- **HPTN/HVTN = The COVID Prevention Network (CovPN)**

- Moderna, Astra Zeneca, J&J, Novavax vaccines
- mAbs from Lilly, Regeneron and Astra Zeneca

But.. Consider the HPTN/HVTN Opportunity Costs

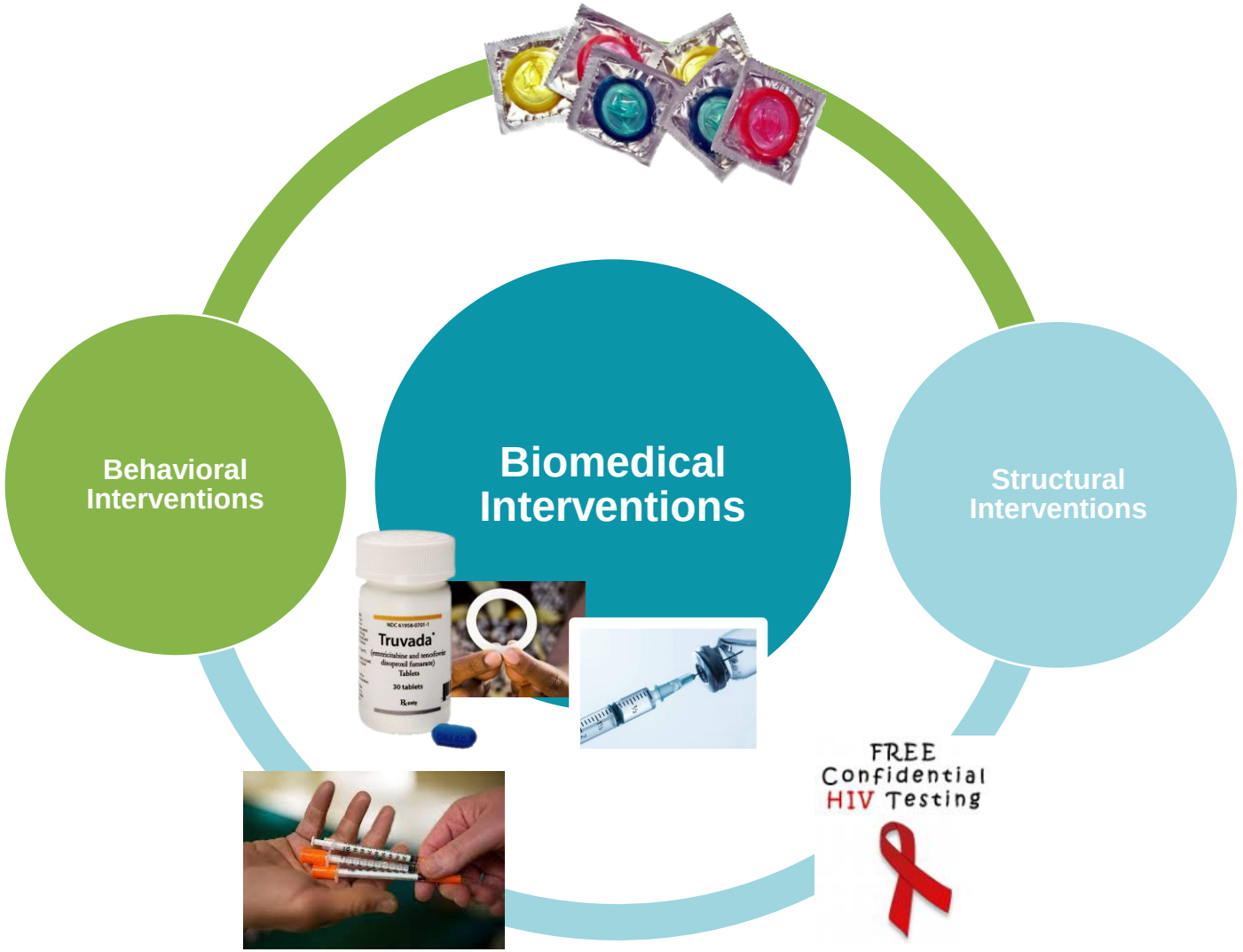
Recent HVTN Vaccine Trials

-HIV vaccine development continues to prove VERY challenging

-Collaborative HVTN/HPTN bnAb research for next PrEP

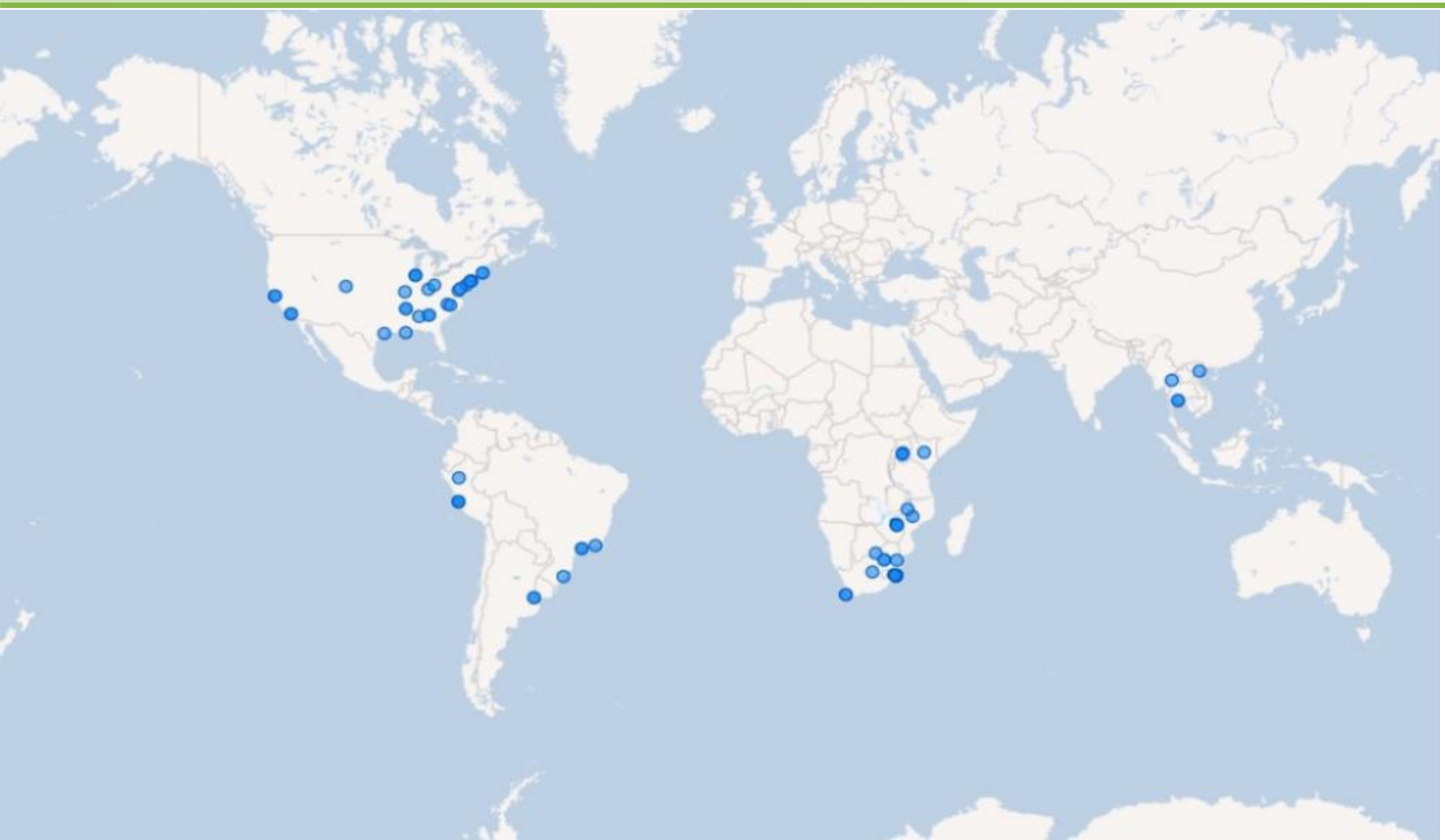
-bnAb research informs vaccine development, long-term

Achieving Population Impact



Forward: 2023 Clinical Research Sites

HPTN
HIV Prevention Trials Network



68
HPTN Sites

13
Countries

22
African Sites

5
Asian Sites

30
North American Sites

11
South American Sites

NEXT in PrEP

HPTN HIV Prevention Trials Network

CAB LA PrEP IS APPROVED in the U.S. – What's Next?

HPTN HIV Prevention Trials Network

- Open label extension (OLE) studies will estimate continued safety and protection, PK, resistance, and include pregnancy and adolescent substudies.
- ViiV is working to gain approval for PrEP in all HPTN 083 and HPTN 084 in participating countries; affordable access where it is awaiting approval BEYOND the U.S.
- New studies in development to examine effectiveness of CAB-LA among adolescents and PWID.
- New studies to explore different routes of administration (e.g., thigh). fewer injections/year and more.
- Combine cabotegravir-LA with contraceptives in future studies?

Pregnancy Sub-Study in HPTN 084 OLE

- Estimate the incidence of pregnancy among participants during the OLE period
- Evaluate safety and infant outcomes among pregnant participants
- Evaluate the PK of CAB LA among pregnant participants, combining blinded, unblinded and OLE periods
- Evaluate concentration in breastmilk and infants among women who receive CAB LA injections during pregnancy and/or the early post-partum period.

The HPTN/Gilead Collaboration: A New paradigm

- Lenacapavir, a first-in-class selective HIV capsid inhibitor, with sub-cutaneous injections every 6 months

- HPTN and Gilead will develop two companion studies in collaboration:

  - **HPTN 102/Purpose 3: A lenacapavir Phase 2 PK, safety, acceptability in cis-gender women in the US**

  - **HPTN 103/Purpose 4: A phase 2 PK, safety, acceptability of lenacapavir in people who inject drugs (PWID) in the US**

Rectal Douche: HPTN 106

Phase 2 Open-label comparative randomized (1:1) crossover study of two 8-week on-demand open label product sequences comparing rectal and oral tenofovir-based PrEP

Sample Size: ~150 participants in the US assigned male at birth with a history of receptive anal intercourse and experience with douching, ≥18 years of age

Study duration: 19 weeks per participant; participant accrual approximately 9 months

Regulatory Sponsor: NIH

Primary Objectives:

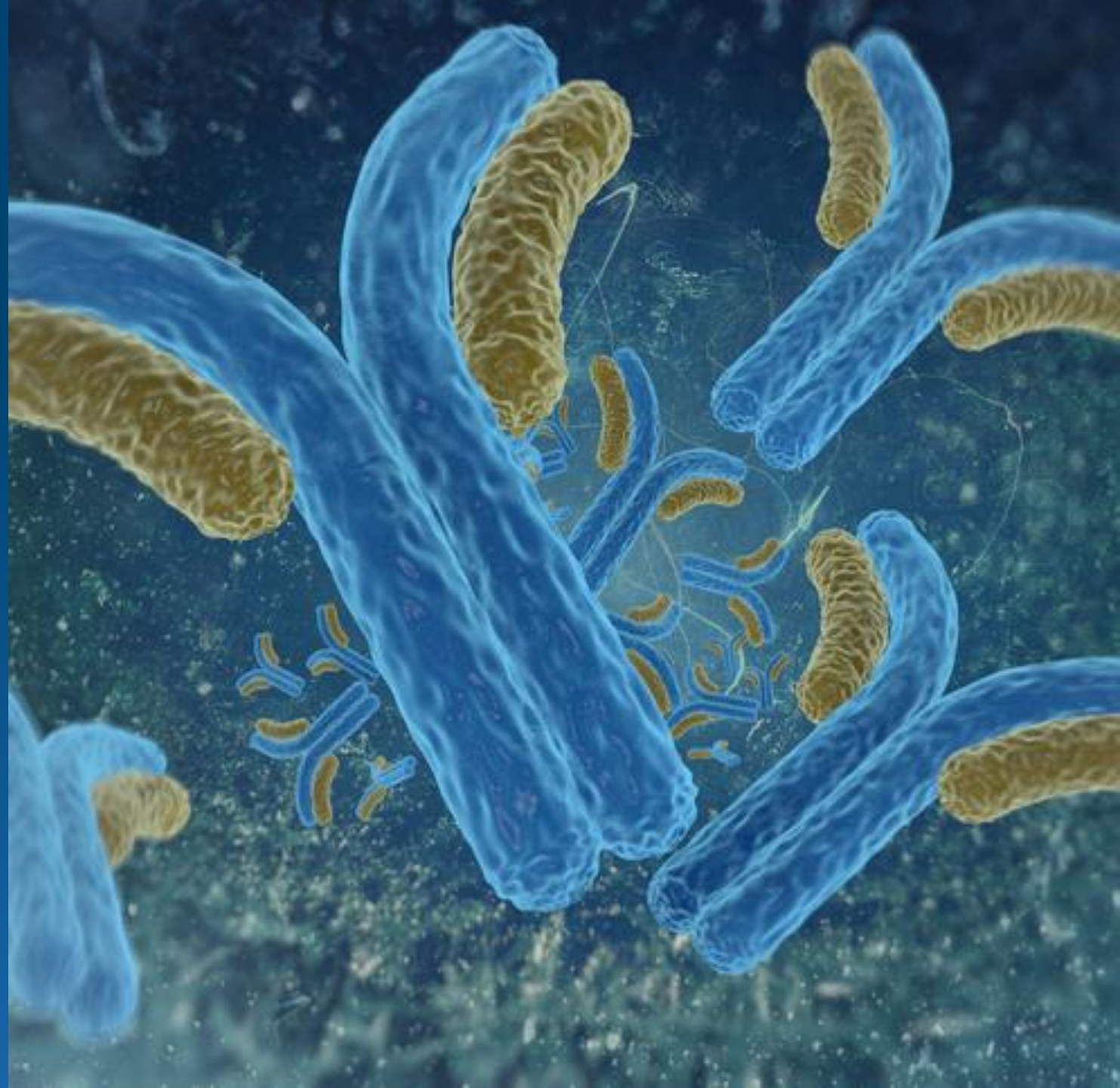
- Safety and acceptability of the on-demand rectal TFV douche vs oral F/TDF tablet
- Study enrollment begins: Q4 2023,

Challenges: drug manufacturing expected to be complete summer 2023, concurrent forward movement related to data management, labs and site preparedness

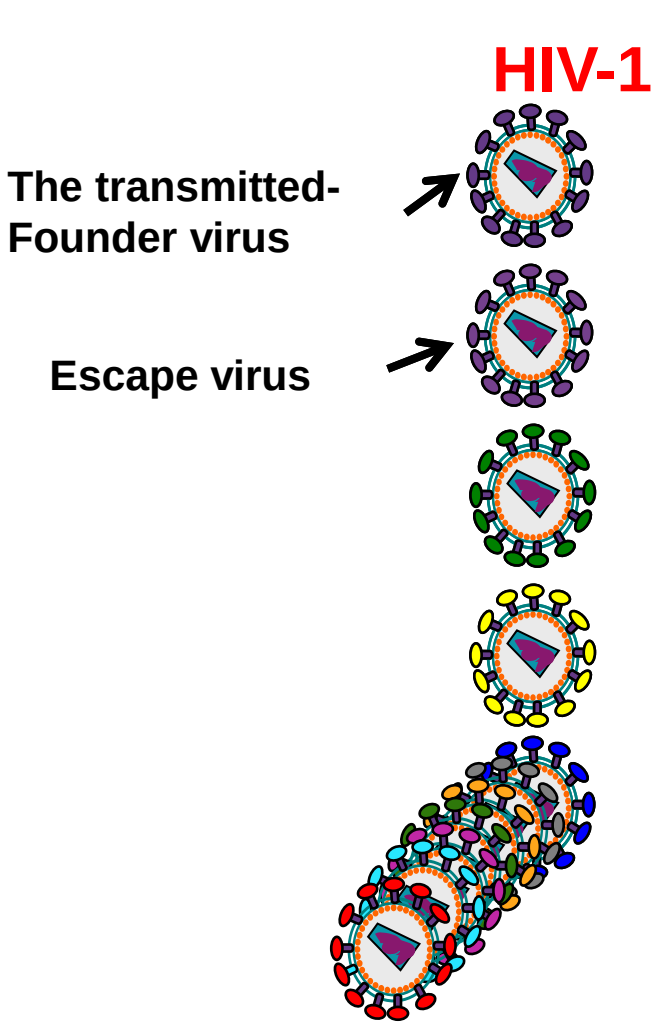
Speculation: phase 2 complete (data analyzed) Q4 2025, so will there be a phase 3?

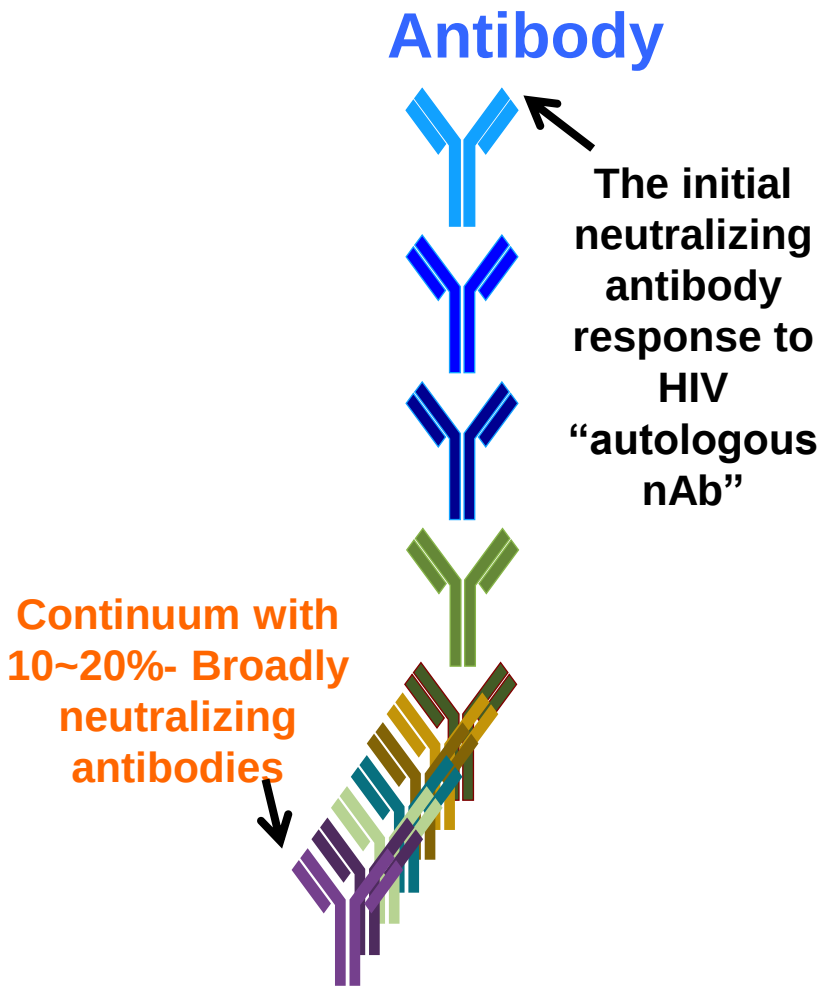
Broadly Neutralizing Antibodies for HIV Prevention

HPTN HIV Prevention Trials Network

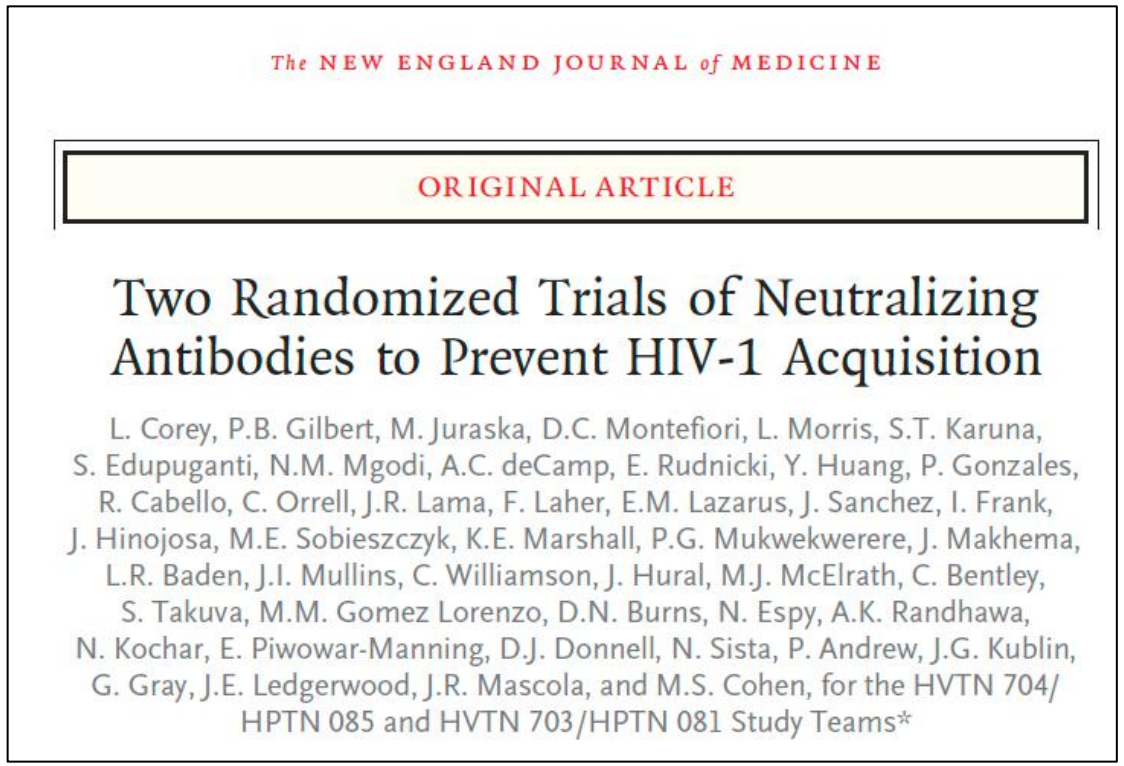


Broadly Neutralizing Antibodies





Antibody Mediated Prevention trials



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two Randomized Trials of Neutralizing Antibodies to Prevent HIV-1 Acquisition

L. Corey, P.B. Gilbert, M. Juraska, D.C. Montefiori, L. Morris, S.T. Karuna, S. Edupuganti, N.M. Mgodi, A.C. deCamp, E. Rudnicki, Y. Huang, P. Gonzales, R. Cabello, C. Orrell, J.R. Lama, F. Laher, E.M. Lazarus, J. Sanchez, I. Frank, J. Hinojosa, M.E. Sobieszczyk, K.E. Marshall, P.G. Mukwekwerere, J. Makhema, L.R. Baden, J.I. Mullins, C. Williamson, J. Hural, M.J. McElrath, C. Bentley, S. Takuva, M.M. Gomez Lorenzo, D.N. Burns, N. Espy, A.K. Randhawa, N. Kochar, E. Piwowar-Manning, D.J. Donnell, N. Sista, P. Andrew, J.G. Kublin, G. Gray, J.E. Ledgerwood, J.R. Mascola, and M.S. Cohen, for the HVTN 704/HPTN 085 and HVTN 703/HPTN 081 Study Teams*

- VRC01 is a broadly neutralizing antibody (bNAb) which blocks the CD4 binding site on the HIV envelope
- VRC01 was infused every 2 months x 10 to high-risk women (Africa) and MSM and transgender individuals (Americas) (n=4,600)
- Two doses of VRC01 were evaluated: 10 mg/kg and 30 mg/kg

VRCO1 neutralized highly sensitive viruses, no effect on others

N ENGL J MED 384;11 NEJM.ORG MARCH 18, 2021

bNAb PrEP Joint Studies

HPTN HIV Prevention Trials Network

Study (HVTN/HPTN)	Product (s)	Target	Route	Long-acting
703/081, 704/085	VRC01	CD4 binding site	IV	
127/087	VRC07-523LS	CD4 binding site	IV, SC, IM	√
130/089	PGT121, PGDM1400, 10-1074, VRC07-523LS	CD4 binding site	IV	√
136/092	PGT121.414.LS, VRC07-523LS	CD4-bs + V3	IV, SC	√
140/101	PGDM1400LS, VRC07-523LS, PGT121.414.LS	CD4-bs + V2+ V3	IV, SC	√
141/105	VRC01.23LS, ePGDM1400v9LS, ePGT121v1LS	CD4-bs +V2+ V3	IV, SC	√
143/109	VRC01.23LS, PGDM1400LS, PGT121.414LS	CD4-bs + V2+ V3	IV	√

NIH Criteria for a bNab PreP Trial

- **Pharmacology leads to a stable combination (i.e.no “tails”)**
- A product manufacturer
- A commercial partner
- An ethical trial design
- Feasible implementation

Dual Prevention Pill: HPTN 104

Phase 2b, open label, randomized crossover study of DPP (co-formulated F/TDF+ ethynyl estradiol/levonorgestrel oral contraceptive pill (OCP), compared with the two tablets with daily oral F/TDF + OCP (2PR) for PrEP and pregnancy prevention in HIV-uninfected women

Sample Size: ~300 women 16-39 years (100 adolescents) for 48 weeks per participant

Regulatory Sponsor: Viatris

Primary Objective:

- Compare PrEP adherence to the DPP versus 2PR during a randomized crossover period

Challenge: BE data is gatekeeper for availability of drug formulation

Approval of DPP is through 503B pathway (bioequivalence data is sufficient)

BE 4 pilot starts late May. Results expected late Aug 2023

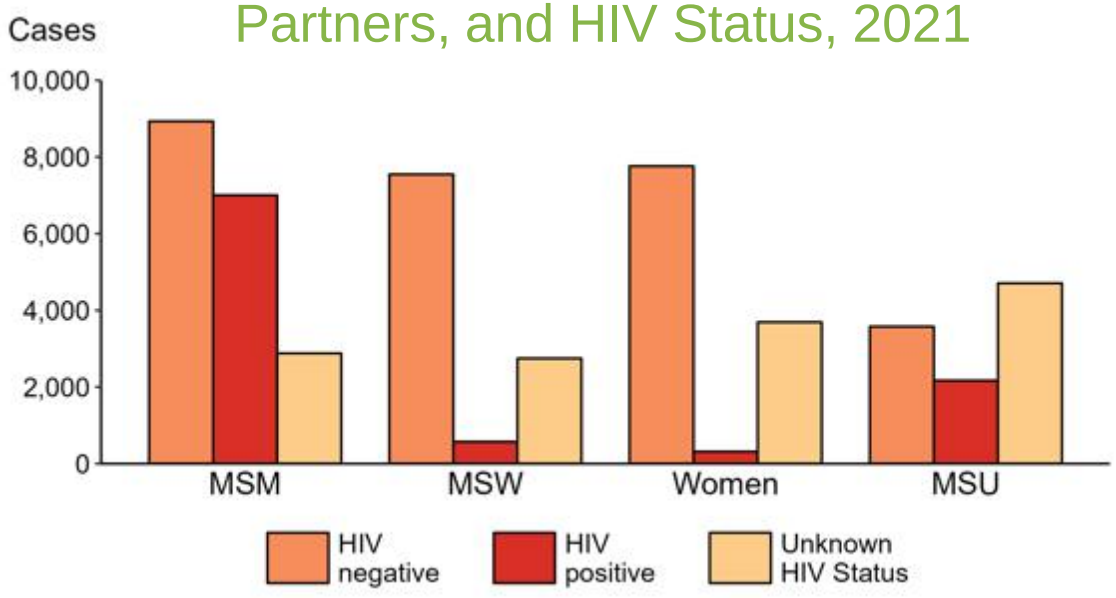
Pivotal BE: Results expected Q3 2024

Speculation: submissions (Q4 2024). Approval ; Q 4 2025?

Back to STIs and the HIV "Syndemic"

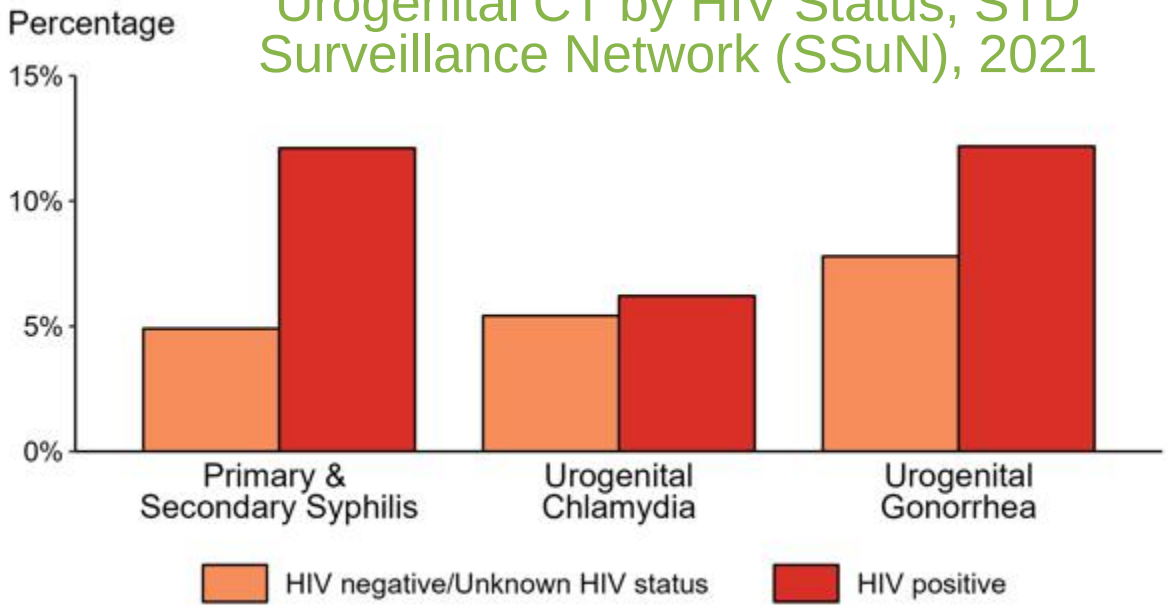
HPTN HIV Prevention Trials Network

Primary & Secondary Syphilis: Reported Cases by Sex, Sex of Sex Partners, and HIV Status, 2021



Among cases with reported HIV status, 44% among MSM were HIV+, compared with 38% among men with unknown sex of sex partners, 7.1% among men who have sex with women only, and 3.9% among women

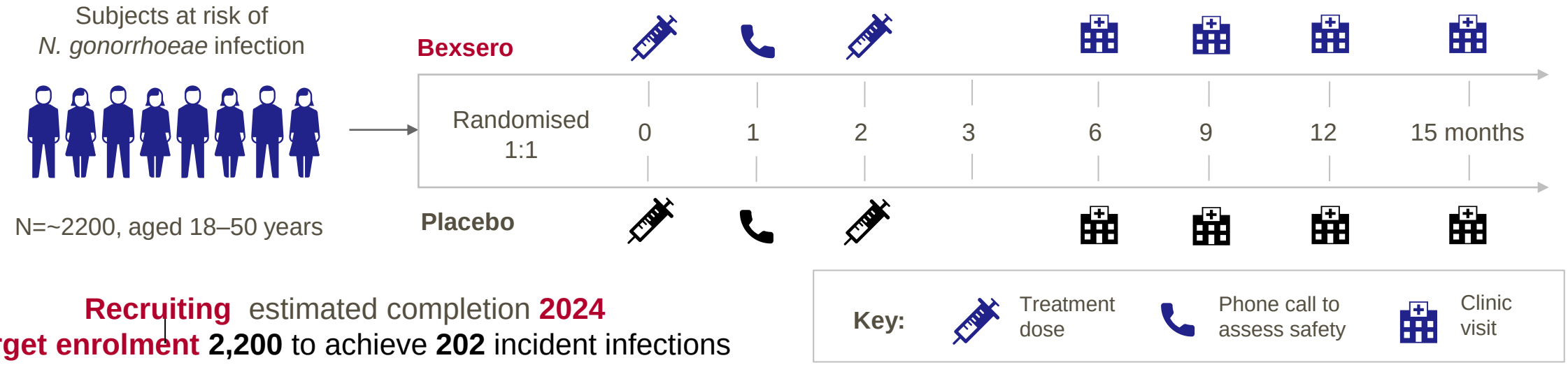
Proportion of MSM with Primary and Secondary Syphilis, Urogenital GC, or Urogenital CT by HIV Status, STD Surveillance Network (SSuN), 2021



Percent with primary and secondary syphilis was higher for HIV+ compared with those not (12% vs 4.9%), similar to urogenital chlamydia (6.2% vs 5.4%) and gonorrhea (12% vs 7.8%)

A Phase II randomized, observer-blind, placebo-controlled study to assess efficacy of meningococcal Group B vaccine MenB+OMV NZ (Bexsero) in preventing gonococcal infection (DMID Protocol 19-0004/HPTN 108)

Study design	Phase II, randomised, observer-blind, placebo-controlled trial (USA and Thailand)
Primary objective	Bexsero efficacy in preventing urogenital and/or anorectal gonococcal infection



Recruiting estimated completion **2024**
Target enrolment **2,200** to achieve **202** incident infections
Current enrolment **667** across 11 sites

3 HPTN Sites in the US and (soon) Malawi

Clinical trials.gov. NCT04350138. https://clinicaltrials.gov/ct2/show/NCT04350138 (accessed September 2022)

Integrated Strategies

HPTN HIV Prevention Trials Network

HPTN 091

Integrating HIV Prevention, Gender-Affirmative Medical Care, and Peer Health Navigation for Transgender Women in the Americas: A Vanguard Study

HPTN 091: Study Status

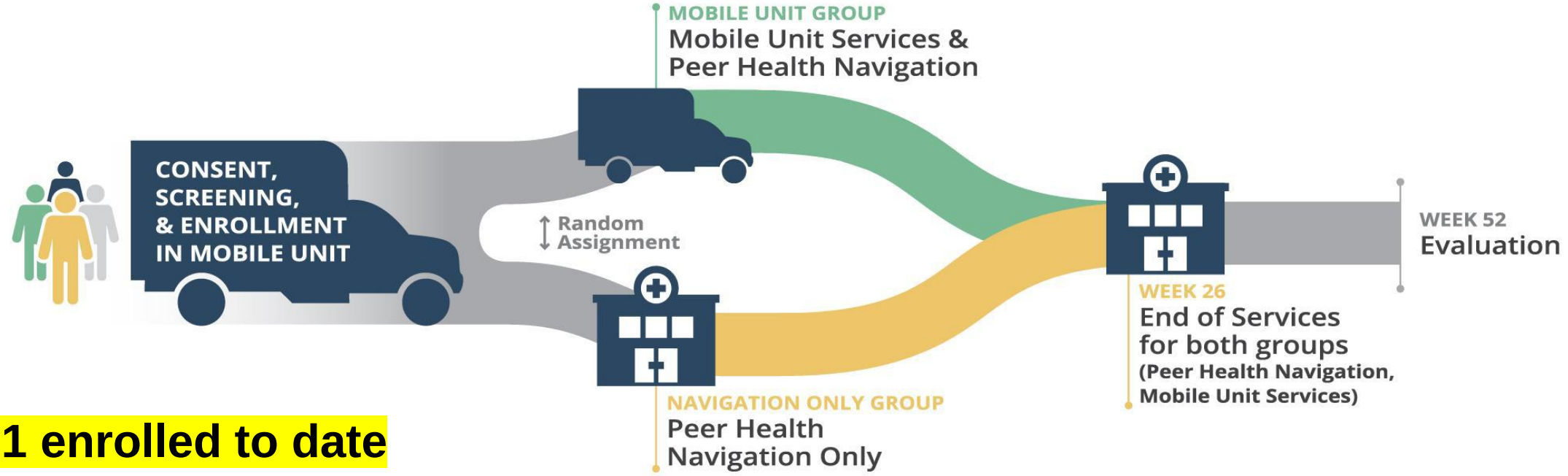
- Enrollment was completed on 16 December 2022. 307 (99%) participants were enrolled in the study. Follow up is anticipated to end Q2 2024.
- An immediate vs deferred intervention study design.
- Sites have a process transitioning participants off the study and to local resources.
- The study has experience exceptional (>90%) retention.

HPTN 094

INTEGRA: A Vanguard Study of Health Service Delivery in a Mobile Health Delivery Unit to Link Persons who Inject Drugs to Integrated Care and Prevention for Addiction, HIV, HCV and Primary Care

HPTN 094: Study Design

- A two-arm, individually randomized, controlled, open label study
- 450 participants (400 participants without HIV) allotted in 1:1 ratio to intervention and control arms, with a target of a minimum 25% women, a target of a minimum of 25% participants under 30 years of age and approximately 10% living with HIV



371 enrolled to date

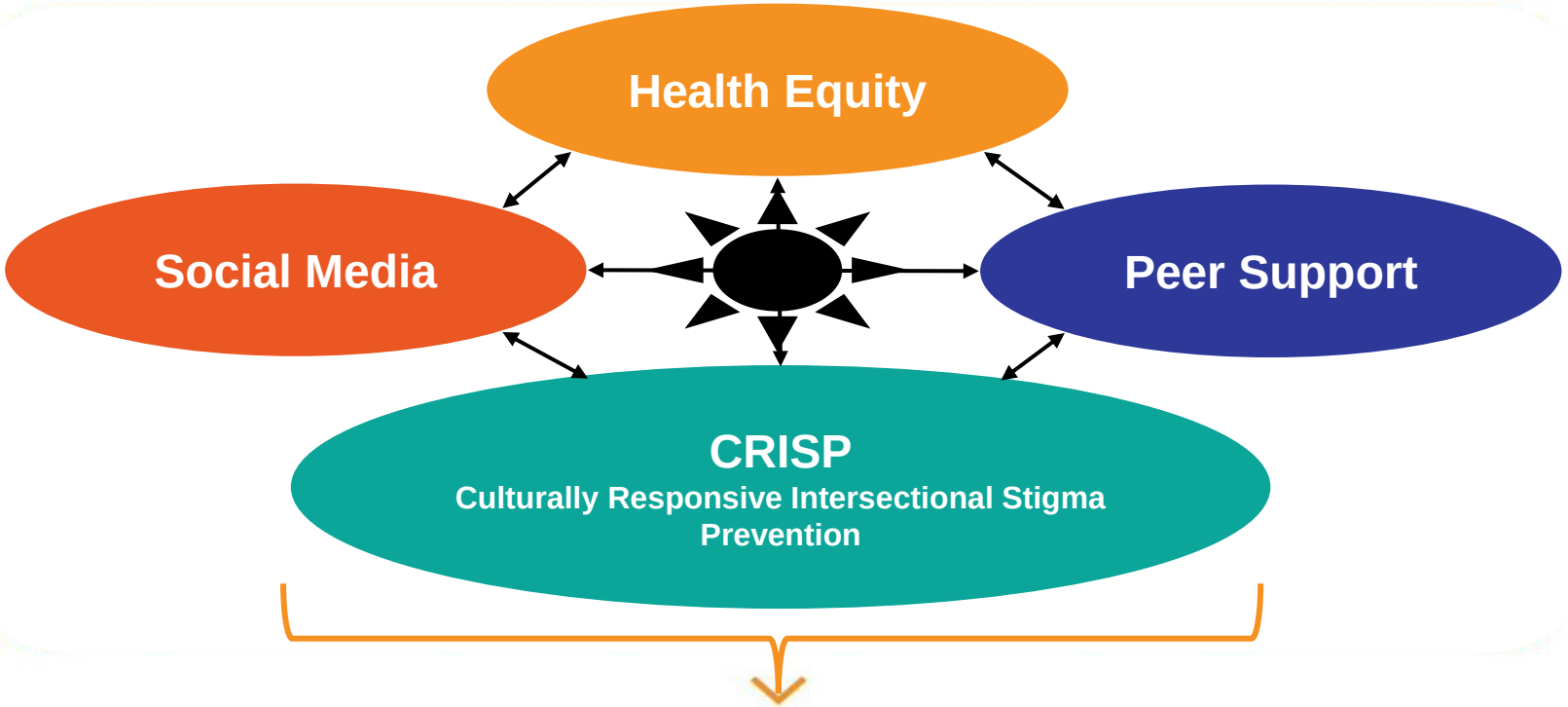
HPTN 096 Pilot

Getting to Zero among Black MSM in the American South: Testing the Efficacy of an Integrated Strategy

HPTN 096: An Evolving Experimental Strategy

HPTN HIV Prevention Trials Network

Integrated Strategy

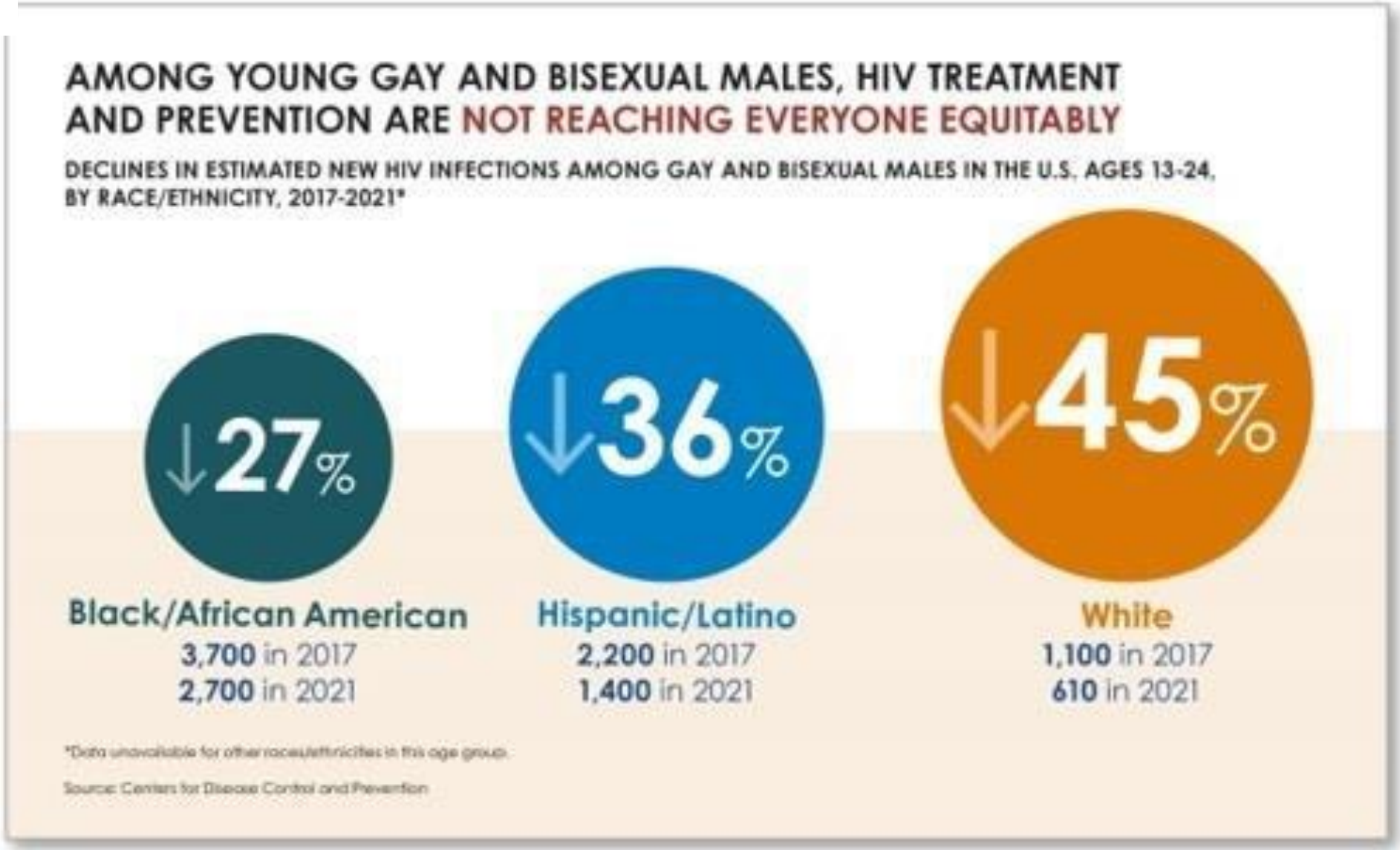


CRISP Facility-Level Outcomes

Increased Number of Black MSM Clients/Patients at CRISP healthcare facilities

- Increased Viral Suppression in Black MSM
- Increased PrEP Prescriptions in Black MSM

Newsroom https://www.cdc.gov/media/releases/2023/p0523-hiv-declines-among-young-people.html?



New Approved Concepts

- **HPTN 111:** Uptake of HIV Self-testing and Linkage to Prevention and Care among Heterosexual Men Attending Barbershops in Uganda: A Cluster Randomized Trial
- **HPTN 112:** Improving HIV Prevention Among Heterosexual Men Seeking STI Services in Sub-Saharan Africa: Examining the Feasibility, Acceptability, and Associated Costs of a Systems-Navigator-Delivered Integrated Prevention Package
- **HPTN 113:** Double Prevention: A Vanguard Study of an Integrated Strategy of HIV PrEP and STI PEP for Young Latino Sexual Minority Men (SMM) in the Americas

Community Engagement

HPTN HIV Prevention Trials Network

Community Engagement

Community Engagement is pivotal part of all HPTN studies.

A few examples:

- Advocacy for affordable post-trial access to CAB LA in countries where HPTN 083 and HPTN 084 are being conducted
- Participating in the development of all forthcoming HPTN research initiatives
- Authored “Including pregnant and breastfeeding people in trials of novel LAED PrEP agents – perspectives from sub-Saharan Africa community stakeholders” for JIAS Special Issue
- Community-led study branding HPTN 106 and the HPTN 096 “What I Want Most” campaign

HPTN Scholars Program

Domestic Program established in 2010

- 48 Scholars to date

International Program established in 2015

- 15 Scholars to date

60+ Scholars since 2010 (some were in multiple cohorts)

- 34% men; 66% women
- 20 datasets: HPTN 037-HPTN 082
- 50+ mentors

HPTN involvement

- Protocol Team Members (HPTN 073, 078, 094, 096)
- Protocol Team Leadership (HPTN 091, HPTN 096)
- Memberships/Observerships: Black Caucus, Scientific Committees, and Working Groups

HPTN HIV Prevention Trials Network

2022-2023 HPTN Scholars

Dr. Tina Herrera

Dr. David Zelaya

Dr. Donte Boyd

Dr. Waru Gichane

Dr. Sophia Zamudio-Haas

Dr. Victoria Ndyanabangi

Kudzai Hlahla

Acknowledgments

HPTN
HIV Prevention Trials Network

Thank you very much to all study participants, investigators and site staff, community groups, collaborators and funders

Overall support for the HIV Prevention Trials Network (HPTN) is provided by:

- National Institute of Allergy and Infectious Diseases (NIAID)
- Office of the Director (OD), National Institutes of Health (NIH)
- National Institute on Drug Abuse (NIDA)
- National Institute of Mental Health (NIMH)
- Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)
- ViiV Healthcare, Gilead Sciences, The Bill and Melinda Gates Foundation, and Viatris
- Collaborations with HVTN, ACTG, IAVI, AVAC and Rockefeller University

Award Numbers UM1AI068619 (HPTN Leadership and Operations Center), UM1AI068617 (HPTN Statistical and Data Management Center), and UM1AI068613 (HPTN Laboratory Center).

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