

The Brown Bag Lunch webinar will begin shortly. Please call into the conference line using

Dial In Number:**1-857-232-0300**

Access Code: **3922402**

*Your line will be muted. When prompted, you can unmute your line by pressing \*6.*

This Training Was A Collaborative Effort of:



FENWAY  HEALTH



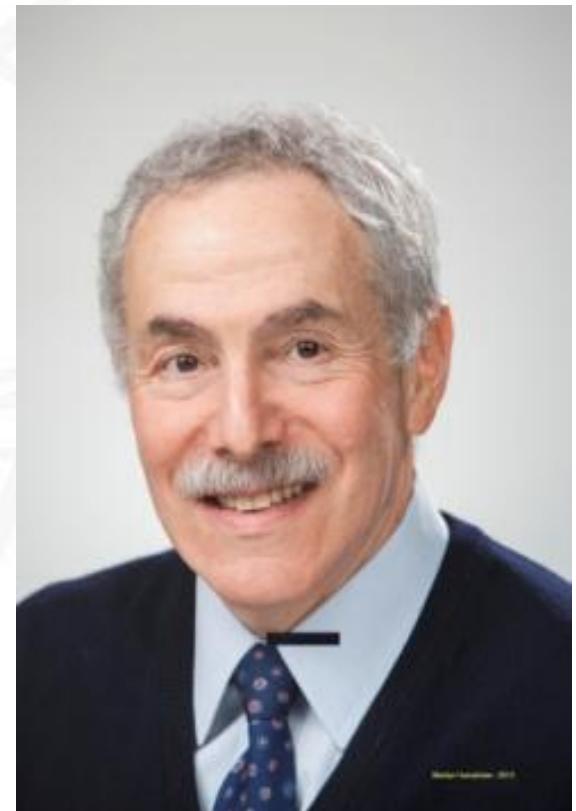
# Ice Breaker

- What do you find interesting and/or confusing about Biomedical and behavioral interventions?
- What do you want to learn?

# Facilitator: Kenneth Mayer, MD

**CURRENTLY:** *Medical Research Director, Co-Chair of The Fenway Institute,*

**Appointments:** Professor of Medicine, Harvard Medical School; Professor, Department of Global Health and Population, Harvard School of Public Health; Director of HIV Prevention Research and Attending Physician, Beth Israel Deaconess Medical Center; Adjunct Professor of Medicine and Community Health, Brown University, Program Advisory Committee, American Foundation for AIDS Research Chair, National Scientific Review Committee, HIV Prevention Trials Network Executive Committee and Chair, National Chair of the MSM Working Group for the Executive Committee of HIV Prevention Trials Network (HPTN)



**Areas of Research:** International HIV/AIDS, Gay and Bisexual Men's Health, HIV/AIDS Prevention, Microbicides, PrEP, PEP, Vaccines, and more

# Learning Objectives

- Understand the use, effect, and current research status of microbicides, pre-exposure prophylaxis (PrEP), post-exposure prophylaxis (PEP), vaccines, and treatment as prevention (TaP)
- Identify methods of integrating biomedical interventions with behavioral programs
- Learn the benefit of combination prevention
- Increase ability of local stakeholders to implement and monitor capacity building events that teach methods of integrating behavioral and biomedical interventions

# HIV Prevention Tool Box

**Male Circumcision**

**HIV Counseling and Testing**

**Treatment for Prevention**

**Treatment of STIs**

**Behavioral Interventions**

**Prevention for Positives**

**Needle Exchange**

**PrEP**

**Cash Incentives**

**Condoms**

**Microbicides**

**Vaccines**

# PrEP Background

# HIV Pandemic

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- The HIV epidemic is continuing to grow worldwide.
- Women and men need many different ways to prevent getting HIV through sex.

# HIV Prevention

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- Prior to PrEP and TasP research ways to prevent getting HIV were:
  - Abstaining from having sex,
  - Having sex with only one person who is not infected with HIV and who agrees not to have sex with anyone else, and
  - Using a condom correctly every time you have sex
  - Male circumcision (only protected males).
- New ways to prevent getting HIV are urgently needed.
- Recent research has shown that oral antiretroviral medications may prevent new HIV transmissions.

# What is PrEP?

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- PrEP (Pre-Exposure Prophylaxis) is a new approach that has shown the use of antiretroviral medications (ARVs) can reduce the risk of HIV infection in HIV-negative people.
- In mid-2012 the FDA approved Tenofovir/Emtricitabine (trade name: Truvada) to be used for prevention of HIV
- Used as part of a HIV prevention package (risk reduction counseling and condoms)

# Why the Interest in PrEP?

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- Data from numerous animal/human studies show protection from PrEP
- ARVs for PMTCT provides proof of concept in humans
- Success of Post-Exposure Prophylaxis (PEP) for needle stick exposure in observational data
- Intermittent PrEP – administration of PrEP at irregular intervals – may reduce costs and exposure of negative individuals to ART

# Why Tenofovir-Emtricitabine?

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- Limited side effects
- Strong safety profile as therapy among HIV positive people
- Relatively long duration of action in the body (product “half-life”)
- Less likelihood of promoting drug resistance compared to other ARVs
- First of many ARVs that may be used for PrEP

Study (reference)	Study population	Design	Results: Reduction in HIV Infection
<b>IPREX</b>	2499 Gay Men	TDF/FTC (Truvada) vs. placebo	TDF/FTC: <b>44%</b>  (92% if drug levels detectable)
<b>CDC – TDF-2</b>	1200 Adults in Botswana (45% women)	TDF/FTC (Truvada) vs. placebo	TDF/FTC: <b>62%</b>
<b>Partners PREP</b>	4758 discordant couples in Kenya and Uganda	TDF (Viread) vs. TDF/FTC (Truvada) vs. placebo	TDF: <b>67%</b> TDF/FTC: <b>75%</b>  (86-90% if drug levels detectable)

Study (reference)	Study population	Design	Results
<b>FEM-PrEP</b>	2120 Women in Kenya, South Africa and Tanzania	TDF/FTC (Truvada) vs. placebo	Product not proven effective in preventing HIV <b>due to low adherence</b> (approximately 33% adherent)
<b>MTN-003 (VOICE)</b>	5,029 Women in South Africa, Uganda, and Zimbabwe	TDF (Viread) vs. placebo TDF/FTC (Truvada) vs. placebo TDF gel vs. placebo	No product proven effective in preventing HIV <b>due to low adherence</b> (23%-29% adherent)

## PrEP Recommendations

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- PrEP should be targeted to individuals at very high risk for HIV infection
- PrEP should be taken daily medication consistently
- Women who are pregnant or trying to conceive should discuss potential risks and benefits PrEP with health care providers
- PrEP should be delivered as part of a comprehensive package of prevention services
- Individuals prescribed PrEP must be HIV negative

# HPTN 073: PrEP Adherence and Uptake Among BMSM in Three US Cities

# HPTN 073 Study Design

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- Demonstration project
- A total of 225 participants, 75 participants at three U.S. sites
- Once daily oral emtricitabine 200 mg / tenofovir disoproxil fumarate 300 mg (FTC/TDF) combined with Comprehensive Clinical Care Coordination (C4).

# HPTN 073 Main Study Questions

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- Will BMSM use PrEP?
- Is it safe for BMSM to use PrEP?
- Is it acceptable for local health care facilities to administer client-centered care coordination (C4) along with PrEP to BMSM?

# Clinical Research Sites for HPTN

## 073

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- Washington, DC
- Chapel Hill, NC
- Los Angeles, CA

# HPTN 067

## The ADAPT Study:

### Alternative Dosing to Augment PrEP pill-Taking



# HPTN 067: The ADAPT Study

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A Phase II, Randomized, Open-Label,  
Pharmacokinetic and Behavioral Study of the Use  
of Intermittent Oral Emtricitabine/Tenofovir  
Disoproxil Fumarate Pre-Exposure Prophylaxis  
(PrEP)

# Study Groups

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1. Daily
2. Event-driven (before and after sex)
3. Time-driven (2 times a week and a booster after sex)

Participants will be counseled to take no more than 2 tablets in a 24-hour period, or 7 tablets in a week.

# HPTN 067 Study Groups

Daily

120  
MSM

60  
Women

Time  
Driven

120  
MSM

60  
Women

Event  
Driven

120  
MSM

60  
Women

# Main Study Questions

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- How does taking oral Tenofovir-FTC tablets intermittently compare to taking the tablets daily? Will participants in the intermittent groups:
  - have the same coverage of sex events,
  - need fewer tablets for coverage, and
  - report fewer side effects compared to participants who take their tablets daily?

# Clinical Research Sites for HPTN 067

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- Cape Town, South Africa
- Bangkok, Thailand
- New York, United States

# HPTN 069/ACTG 5305

## NEXT-PREP: Novel Exploration of Therapeutics for PREP

**NEXT > PrEP**  
AN HPTN/ACTG STUDY



# HPTN 069/ACTG 5205: The NEXT PrEP Study

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A Phase II Randomized, Double-Blind, Study of the Safety and Tolerability of Maraviroc (MVC), Maraviroc + Emtricitabine (MVC+FTC), Maraviroc + Tenofovir disoproxil fumarate (MVC+TDF), or Tenofovir disoproxil fumarate + Emtricitabine (TDF+FTC) for Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Transmission in At-Risk Men Who Have Sex with Men and in At-Risk Women

# HPTN 069/ACTG 5305 Study Groups

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- There are 3 active drugs:
  - maraviroc (MVC)
  - emtricitabine (FTC)
  - tenofovir (TDF)
- Study Regimens (3 pills/arm):
  - **maraviroc + FTC placebo + TDF placebo**
  - **maraviroc + emtricitabine + TDF placebo**
  - **maraviroc + tenofovir + FTC placebo**
  - **tenofovir + emtricitabine + MVC placebo**

# HPTN 069/ACTG 5305 Study Groups

MVC

150

30 Tissue  
Subset

15 Drug  
Interaction  
Subset

MVC + FTC

150

30 Tissue  
Subset

15 Drug  
Interaction  
Subset

MVC + TDF

150

30 Tissue  
Subset

15 Drug  
Interaction  
Subset

FTC + TDF

150

30 Tissue  
Subset

15 Drug  
Interaction  
Subset



HIV PREVENTION TRIALS NETWORK

NEXT > PrEP  
AN HPTN/ACTG STUDY

# HPTN 069/ACTG 5305 Main Study Question

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Are the four different combinations of PrEP drugs maraviroc, emtricitabine, and tenofovir safe and tolerable for at-risk men who have sex with men (MSM), transgender, and at-risk women?

# Clinical Research Sites for HPTN 069/ACTG 5305

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- Baltimore, MD
- Boston, MA
- Chapel Hill, NC
- Cleveland, OH
- Los Angeles, CA
- Newark, NJ
- New York City, NY
- Philadelphia, PA
- Pittsburgh, PA
- San Francisco, CA
- San Juan, PR
- Seattle, WA
- Washington, DC

# BE PREPARED FOR THE FUTURE.

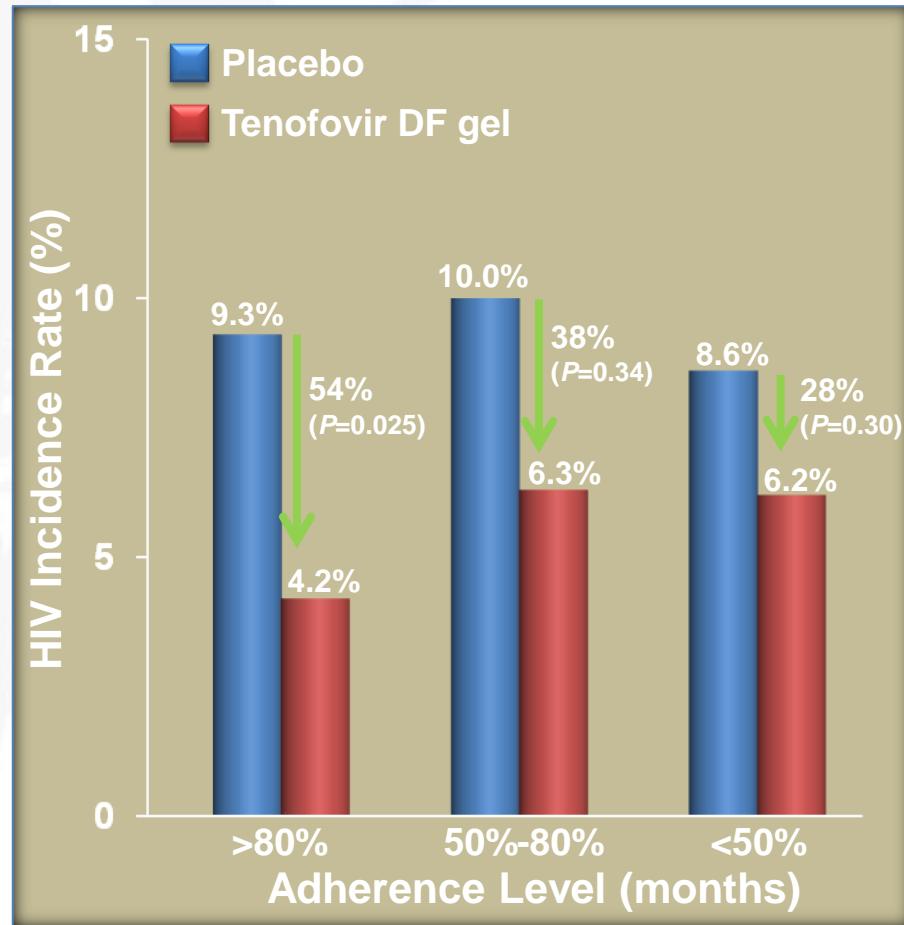
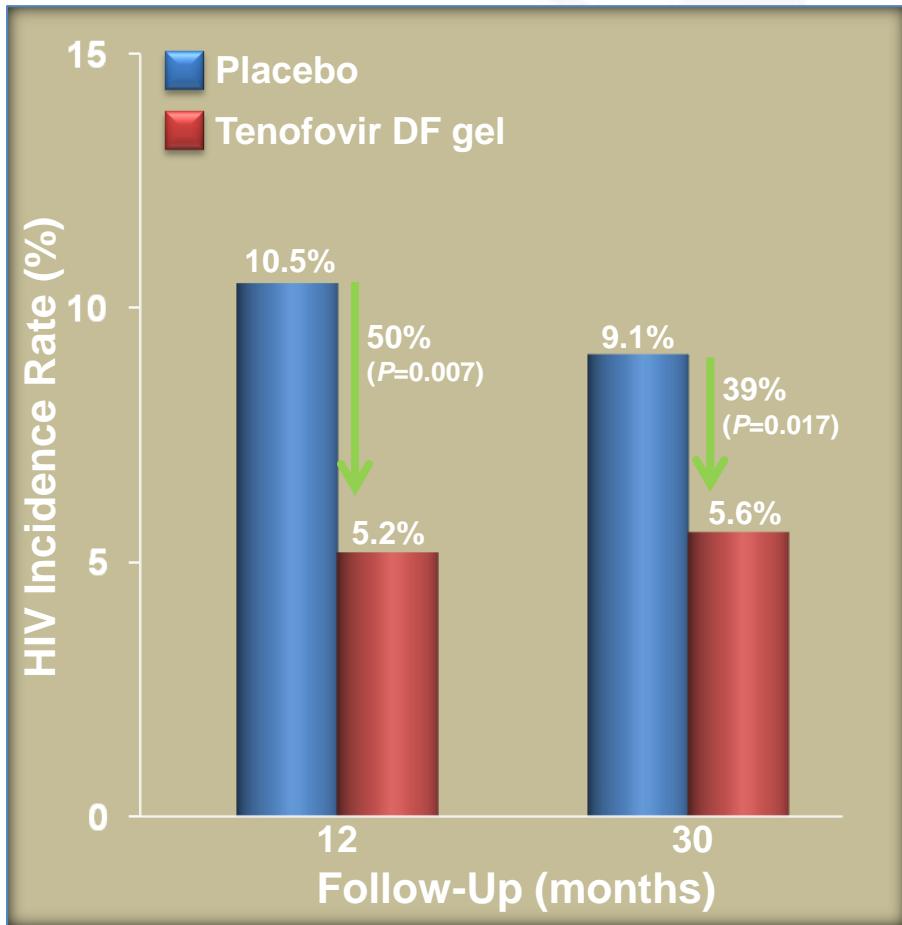
Volunteer for an HIV prevention study.

» Are you 18 or older and HIV negative?

Find out [how you can help](#) PrEP for the future and be reimbursed for your time and travel.

# Topical PrEP (Microbicides) and other new drugs and delivery systems

# CAPRISA 004 Results: Adherence is Key



# What about Topical Microbicides?

- Vaginal Gel: waiting for the tie breaker: the FACTS study
- Vaginal gel not tolerated rectally b/c glycerin (MTN 006)
- MTN 007: Phase 1 study of reformulated tenofovir 1% gel
  - Reduced glycerin tenofovir 1% gel
  - Reduced incidence and severity of GI adverse events
  - No significant changes in histology, inflammatory markers, and epithelial sloughing
  - Improved acceptability
- New studies focusing on younger MSM and MSW, and expanded safety, adherence

# New Antiretrovirals for Prevention

Agent	Mechanism	Status	Developers/ Sponsors
Dapivirine (gel and ring)	NNRTI	Phase 2/3 (ring)	Tibotec/IPM
UC-781 (gel)	NNRTI	Phase 1/2	CONRAD MTN
MIV-150 (gel)	NNRTI	Phase 1	Population Council
Maraviroc (oral and ring)	CCR5 inhibitor	Phase 1	ViiV/IPM HPTN/MTN
Rilpivirine/TMC278 (injectable)	NNRTI	Phase 1	Tibotec
GSK744	Integrase Inhibitor	Preclinical	Shinogi/GSK

# Treatment as Prevention (TasP) Background

# What is Treatment as Prevention

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- Treatment as prevention is the use of HIV treatment medications to reduce the risk that an HIV-positive person will pass the virus to their sexual partner.

# HPTN 052 Study Design

## Randomization

Stable, healthy, serodiscordant couples, sexually active  
CD4 count: 350 to 550 cells/mm<sup>3</sup>

Immediate ART

CD4 350-550

Delayed ART

CD4  $\leq$  250

**Primary Transmission Endpoint**  
Virally linked transmission events

**Primary Clinical Endpoint**

WHO stage 4 clinical events, pulmonary tuberculosis,  
severe bacterial infection and/or death

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Results of the  
on 12 May 2011  
HIV-positive per  
effective antiretroviral  
the risk of transmission  
uninfected seroconverting  
reduced by 96%

UNAIDS 2011 AIDS  
SMARTER, FASTER



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## Clinical Research Sites for HPTN 052

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- Brazil
- Botswana
- India
- Kenya
- Malawi
- South Africa
- Thailand
- United States
- Zimbabwe

# Revised HIV Treatment Guidelines



- DHHS revised their HIV Treatment Guidelines in March 2012
- ART recommended for all HIV-infected individuals, irrespective of CD4-cell count
- Changes based on
  - Growing body of evidence demonstrating harmful effects of ongoing HIV replication
  - HPTN 052 – ART significantly reduces the likelihood of HIV transmission

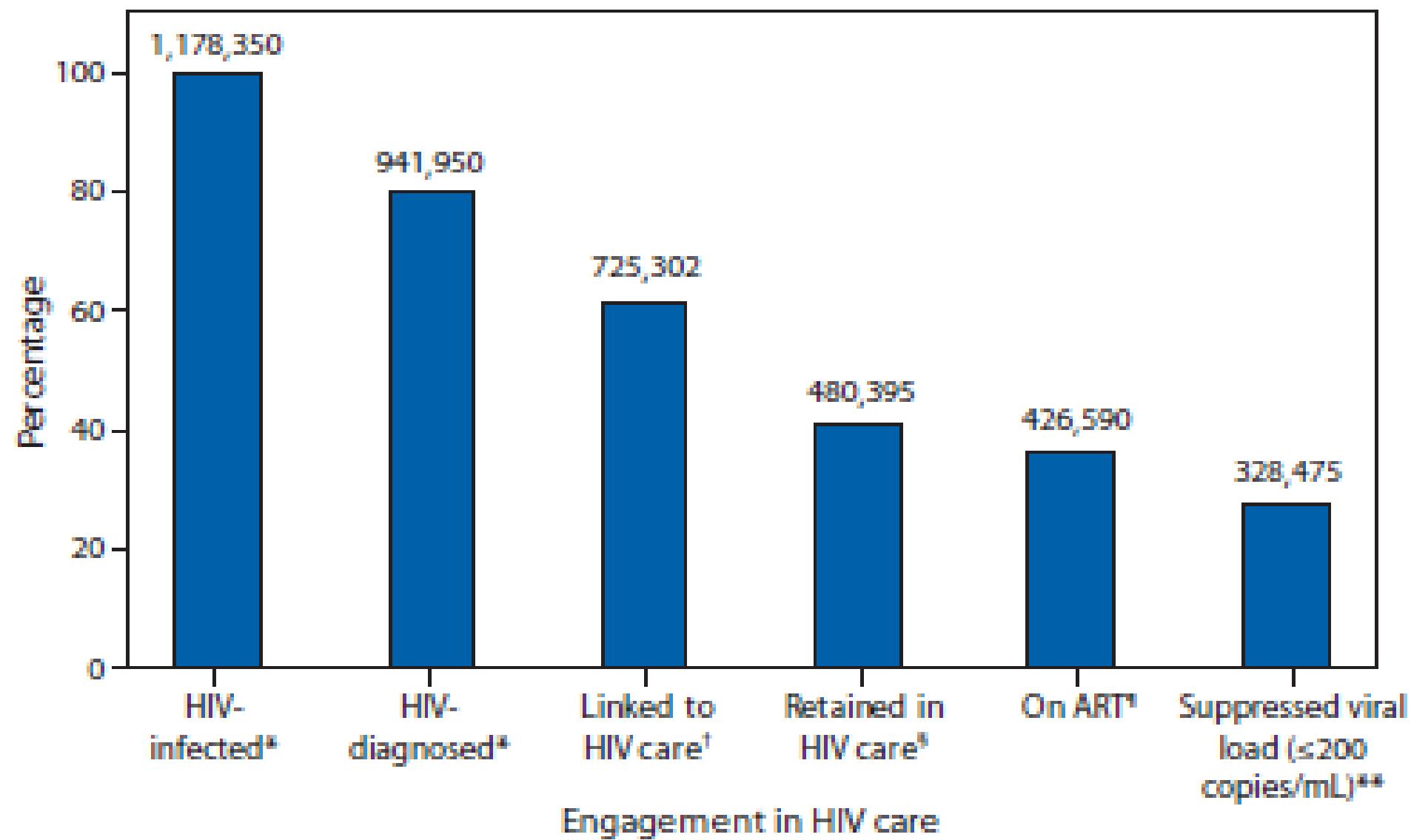
# Effective Implementation

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Effective implementation of TasP requires addressing barriers to:

- Expanded testing,
- Improved care linkage and engagement
- Earlier ART initiation and adherence

**FIGURE 3. Number and percentage of HIV-infected persons engaged in selected stages of the continuum of HIV care — United States**



# HPTN 065: TLC Plus

## Test, Link to Care Plus Treat

TLC-PLUS

# HPTN 065: TLC-Plus Study

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- A Study to Evaluate the Feasibility of an Enhanced Test, Link to Care, Plus Treat Approach for HIV Prevention in the United States
  - Duration of study will not permit evaluation of changes in HIV acquisition rates.
  - Study will use surveillance data, not individual participant-level data

# HPTN 065 Communities

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- Washington, DC
- New York, NY
- Chicago, IL
- Houston, TX
- Miami, FL
- Philadelphia, PN

# HPTN 065: Linkage-to-Care (L2C)

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- 37 HIV Test Sites were randomized for L2C
  - 18 in the Bronx, NY
  - 19 in Washington, DC
- Anyone newly found to be HIV-positive, or reconfirmed to be HIV-positive after having been out of care for at least one year, is eligible to receive a coupon at FI Test Sites
- \$25 gift card for getting lab work done (CD4 and VL)
- \$100 gift card for meeting with provider to review lab results and develop an individualized healthcare plan

# HPTN 065: Viral Suppression (VS)

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- 39 HIV Care Sites were randomized for VS
  - 20 in the Bronx, NY
  - 19 in Washington, DC
- To receive VS gift cards, patients must be **eligible** for the program and then **qualify** for each gift card
- Patients are **eligible** if they are on ART and an established patient
- Patients **qualify** for a gift card if they have a suppressed viral load (<400 copies/mL) and have not earned a gift card in the last 3 months

# HPTN 065 (TLC Plus) Study Design



## HIV Testing & Linkage to Care

Expanded HIV Testing

- Social Mobilization
- Universal offer of testing in ED/hospital admission

HIV Testing Sites

38 Randomized HIV Test Sites to link HIV positives

Financial incentive plus SOC  
Standard of care (SOC)



## HIV Treatment

Initiate ART per guidelines

39 Randomized HIV Care Sites

Financial incentive plus SOC  
Standard of care (SOC)



## Prevention for Positives

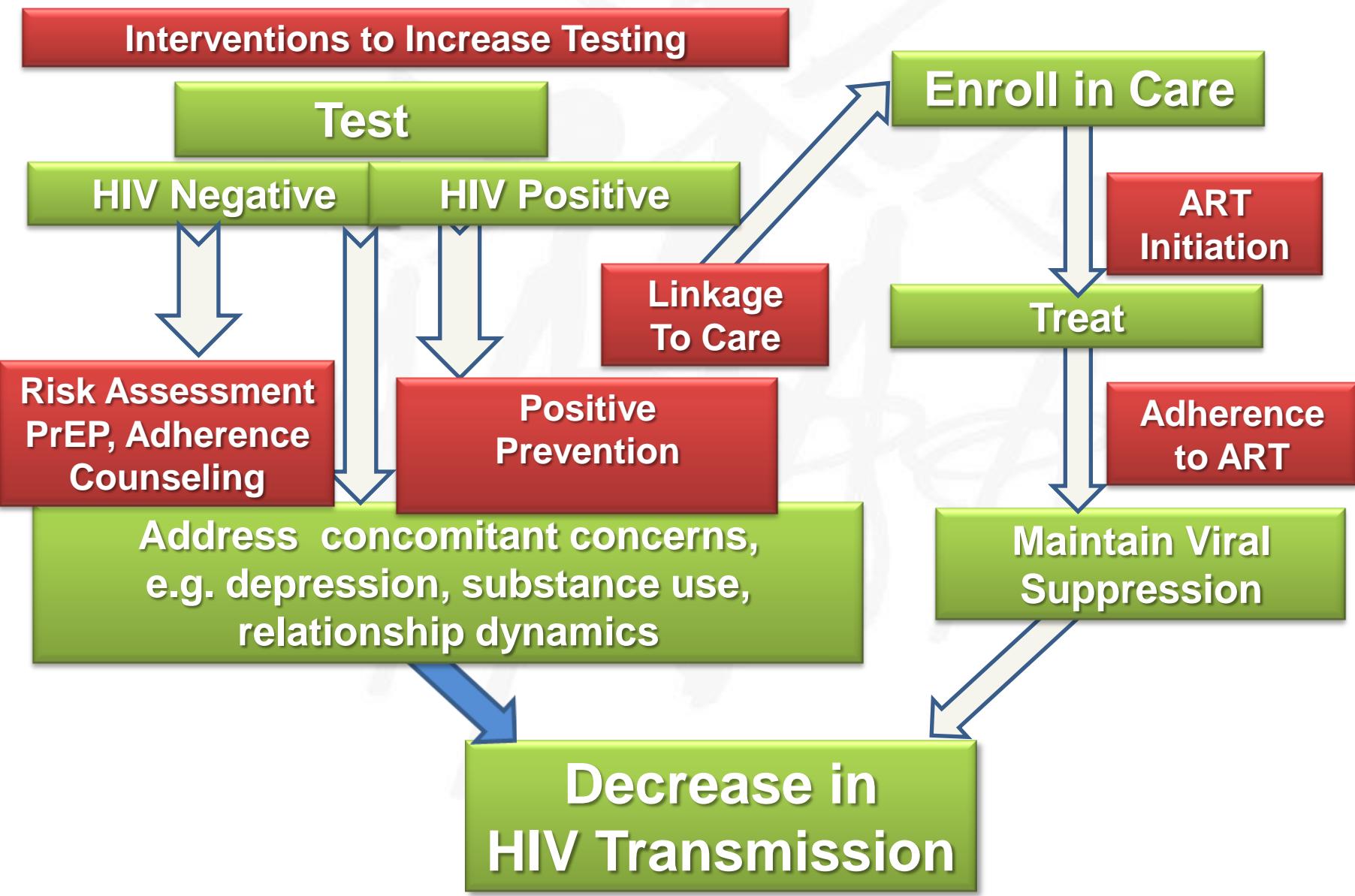
Select HIV Care Sites

Individual randomization of 660 patients in 2 communities

CARE plus Standard of Care  
Standard of Care

# Conclusions

# Combination Antiretroviral Prevention



# Additional Information

- [www.hptn.org](http://www.hptn.org)
  - [www.facebook.com/HIVptn](http://www.facebook.com/HIVptn)
  - [www.twitter.com/HIVptn](http://www.twitter.com/HIVptn)
- [www.nih.gov](http://www.nih.gov)
- [www.cdc.gov](http://www.cdc.gov)
- [www.thefenwayinstitute.org](http://www.thefenwayinstitute.org)

# ACKNOWLEDGEMENTS

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Thanks to Georgette King and Jonathan Lucas





WHAT ARE YOUR QUESTIONS?

# Discussion, Questions, and Answers

At this time, you can ask questions and share your ideas.

# Transforming Knowledge Into Educational and Mobilization Programming

- What types of event structure are you considering for your local Brown Bag event?
- What are 2 local needs that you already see this topic addressing (even in part) within African American communities?

# REMINDERS

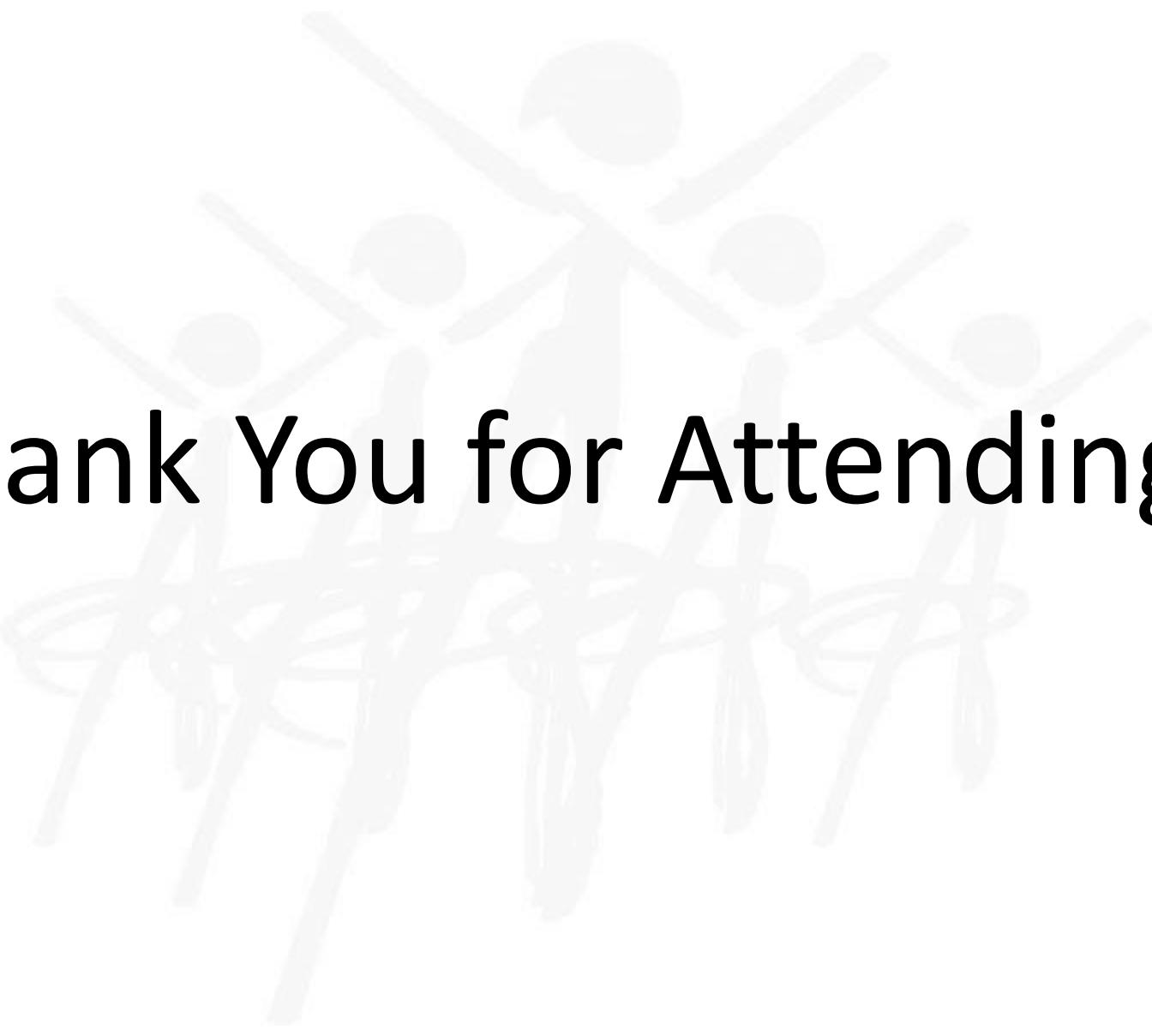
- Please fill out **evaluations** at  
<https://www.surveymonkey.com/s/BiomedicalBehavioralWebinar>
- Send your **organization's logo** to Josephine
- Email Josephine your **biography** and **picture** as soon as possible
- Please send you **Event Information Form** by Friday to get **fliers** for you Brown Bag Lunch

# UPCOMING EVENTS

- Upcoming Train-the-Trainer Webinars
  - May 15<sup>th</sup> – National Webinar on the Affordable Care Act
- Upcoming National Webinars
  - June 5<sup>th</sup> – Confronting Barriers to Black Leadership in HIV/AIDS Education and Advocacy
  - July 2<sup>nd</sup> – HIV and Co-Infections
- Join the Black AIDS Institute Programs
  - AAHU
  - Black Treatment Advocates Network (BTAN)
  - Knowledge, Attitude, and Behaviors (KAB) Survey of HIV workforce
  - Beyond the Quo



# ANNOUNCEMENTS FROM THE GROUP



**Thank You for Attending!!**