

# PrEP Update



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**Forum for  
Collaborative HIV Research**



# Evidence for PrEP Efficacy with Tenofovir-Based Regimens, Oct 2012

Study	Population	N	Efficacy (%)
<b>CAPRISA 004</b> <i>South Africa</i>	Women	889	<b>39%</b> <b>Vaginal TFV gel</b> <b>Pericoital dosing</b>
<b>iPrEx</b> <i>Brazil, Ecuador, Peru, South Africa, Thailand, US</i>	Men Having Sex with Men	2499	<b>44%</b> <b>Daily oral FTC/TDF</b>
<b>TDF2 Study</b> <i>Botswana</i>	Young men & women	1200	<b>62%</b> <b>Daily oral FTC/TDF</b>
<b>Partners PrEP Study</b> <i>Kenya, Uganda</i>	Heterosexual couples	4758	<b>67% daily oral TDF</b> <b>75% daily oral FTC/TDF</b>

# Disappointing Results of PrEP in Women: FEM-PrEP and VOICE

- FEM-PrEP: Phase III study of oral TDF/FTC planned for 3900 high-risk women in Africa (2120 randomized)
  - Announced April 18, 2011, that study was ended early because of lack of efficacy
  - 35 vs 33 new HIV infections in the placebo and TDF/FTC arms<sup>[1]</sup>
  - TFV blood levels suggest that use was too low (< 40%) to assess efficacy
  - 4 vs 1 patient with M184V/I in the TDF/FTC and placebo arms
- VOICE: Phase IIB placebo-controlled trial of > 5000 women in South Africa, Uganda, and Zimbabwe<sup>[2]</sup>
  - Daily oral TDF; daily oral TDF/FTC; daily vaginal TFV 1% gel
  - DSMB stopped the **daily oral TDF arm** in September 2011 and the **daily vaginal gel arm** in November 2011, both for lack of efficacy
  - **Daily oral TDF/FTC arm** continues

1. Van Damme L, et al N Engl J Med. 2012 Jul 11. [Epub ahead of print]. 2. These data are available in press release format only, have not been peer reviewed, may be incomplete, and we await presentation or publication in a peer-reviewed format before conclusions should be made from these data.

# PrEP (Like ART) Works When Taken

	Blood Samples With Tenofovir Detected, %	HIV Protection Efficacy in Randomized Comparison,%
Partners PrEP*[1]	81	75
TDF2[2]	79	62
iPrEx[3]	51	44
FEM-PrEP[4]	26	6

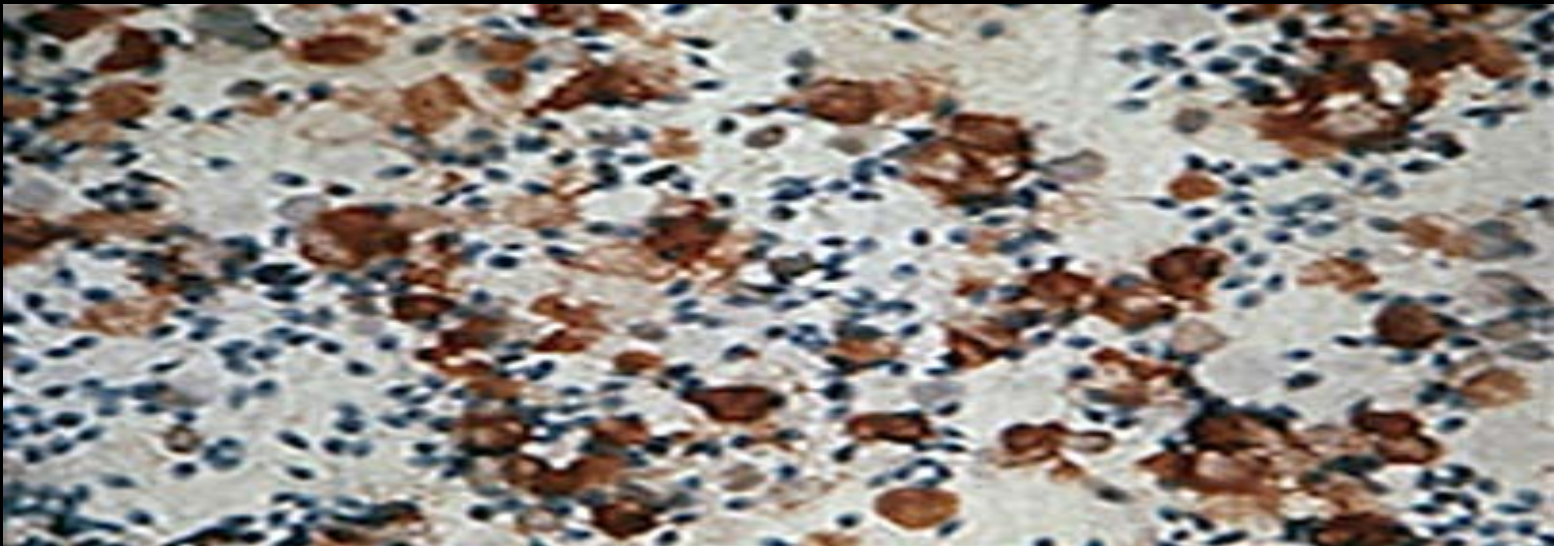
\*TDF/FTC arm

**There is a clear dose-response  
between evidence of PrEP use and efficacy**

1. Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print]. 2. Thigpen MC, et al N Engl J Med. 2012;[Epub ahead of print]. 3. Grant RM, et al. N Engl J Med. 2010;363:2587-2599. 4. Van Damme L, et al N Engl J Med. 2012;[Epub ahead of print].

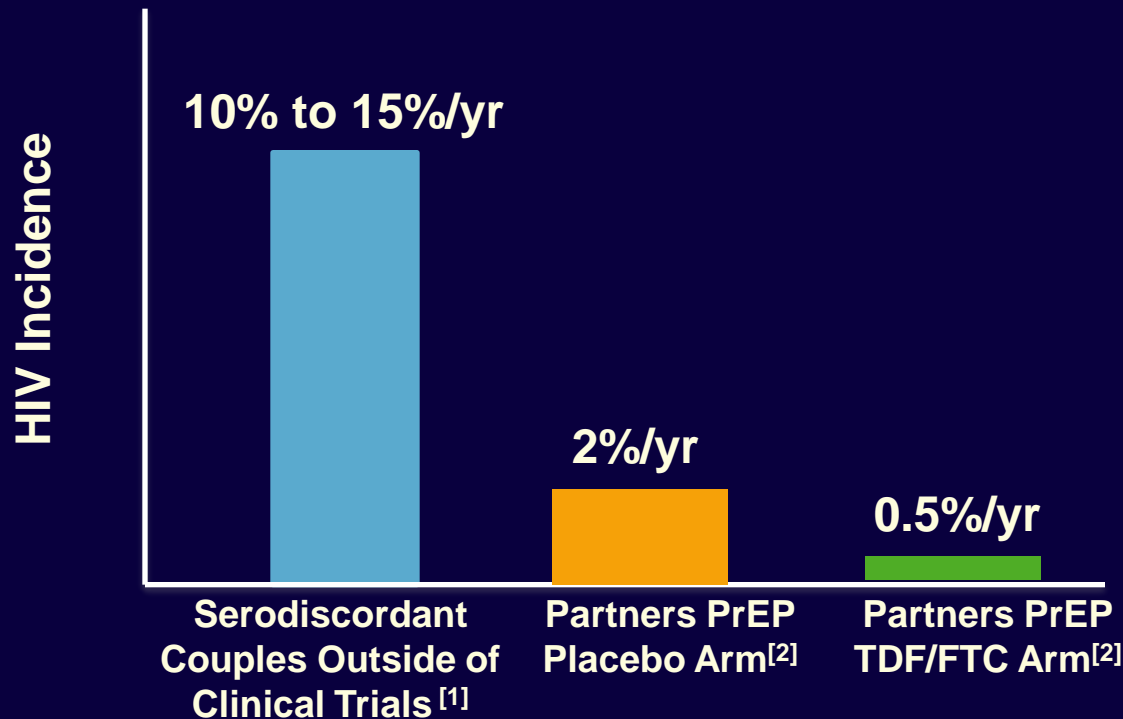
# Why was oral and topical PrEP ineffective for some women?

- Adherence?
- Pharmacology?
- Genital Tract Inflammation, STDs?
- Viral challenge from partners?



# PrEP Works Together With Other HIV Prevention Strategies

- Ongoing HIV counseling and testing, condoms, risk reduction, male circumcision, treatment of STIs *plus PrEP* synergize to maximally reduce HIV risk



1. Quinn TC, et al. N Engl J Med. 2000;342:921-929. 2. Baeten JM, et al. N Engl J Med. 2012;[Epub ahead of print]. .

# What's Next?

- ❑ VOICE TDF/TFC arm: Efficacy would suggest FEMPrEP's failure was adherence
- ❑ FACTS (pericoital gel) tie breaker?
- ❑ CAPRISA 004 vs. VOICE gel arms: could daily gel be worse than pericoital?
- ❑ MTN 007: Tenofovir daily rectal gel downregulated many genes. Is less more?
- ❑ Thai IDU (CDC) study



# NEXT-PrEP (HPTN 069)

- Maraviroc alone
- Maraviroc-FTC
- Maraviroc-TDF
- TDF-FTC
- 400 U.S. MSM, 200 women  
12 sites (ACTG+HPTN)
- Substudies to assess PK, co-receptor occupancy, immunohistology
- To start by early spring 2012
- Enrolling now at your neighborhood CRS



# Correlates of Drug Detectability

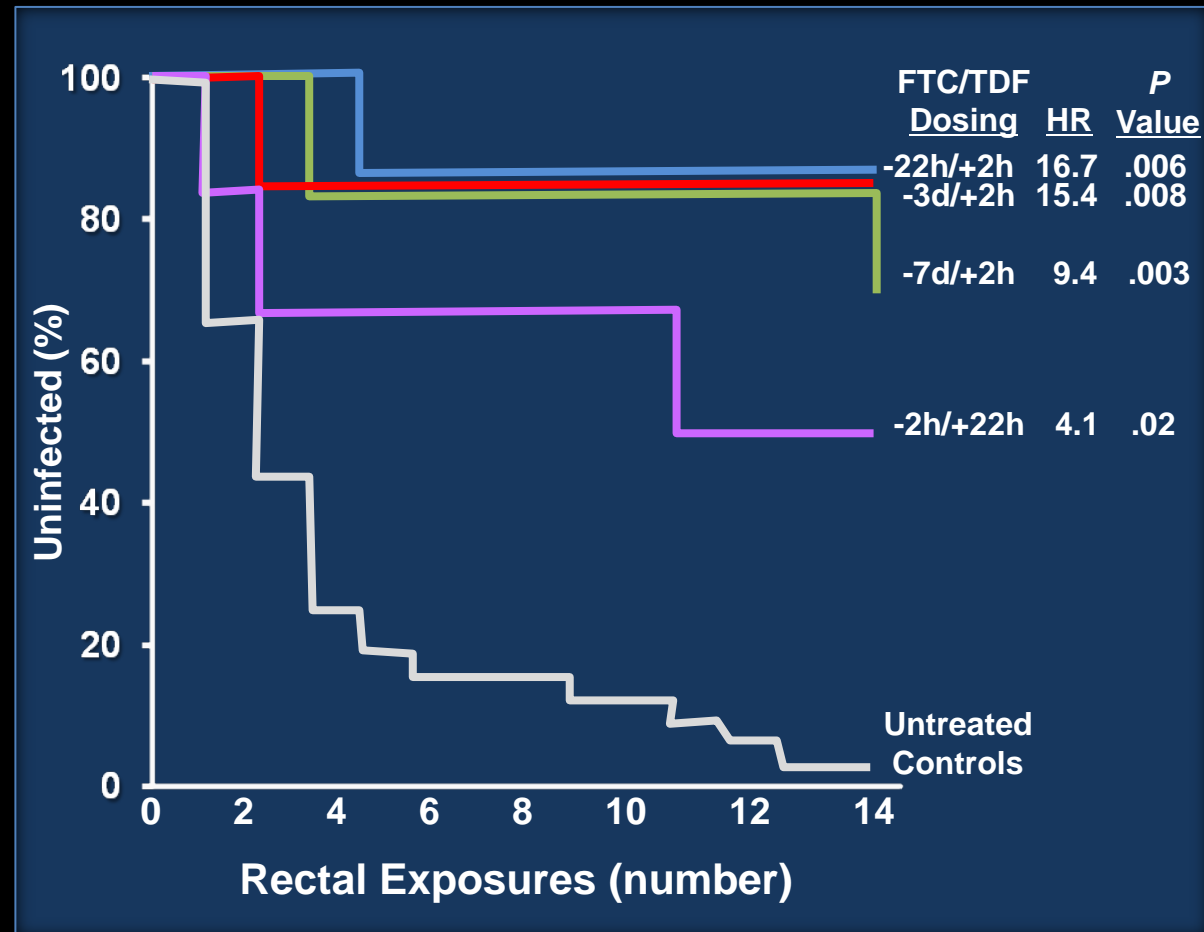
- 179 samples from 7 sites (2 US, 4 South America, 1 South Africa) were evaluated after Wk 24 visit
- Overall detection rate
  - TFV-DP: 50%
  - FTC-TP: 62%

Parameter	n	Drug Detected, %
<b>US vs non-US</b>		
▪ US	34	97
▪ Non-US	145	50
<b>Age</b>		
▪ ≥ 25 yrs	101	73
▪ < 25 yrs	78	44
<b>Recent reported sex</b>		
▪ URAI	49	76
▪ Sex, not URAI	107	59
▪ No sex	23	35

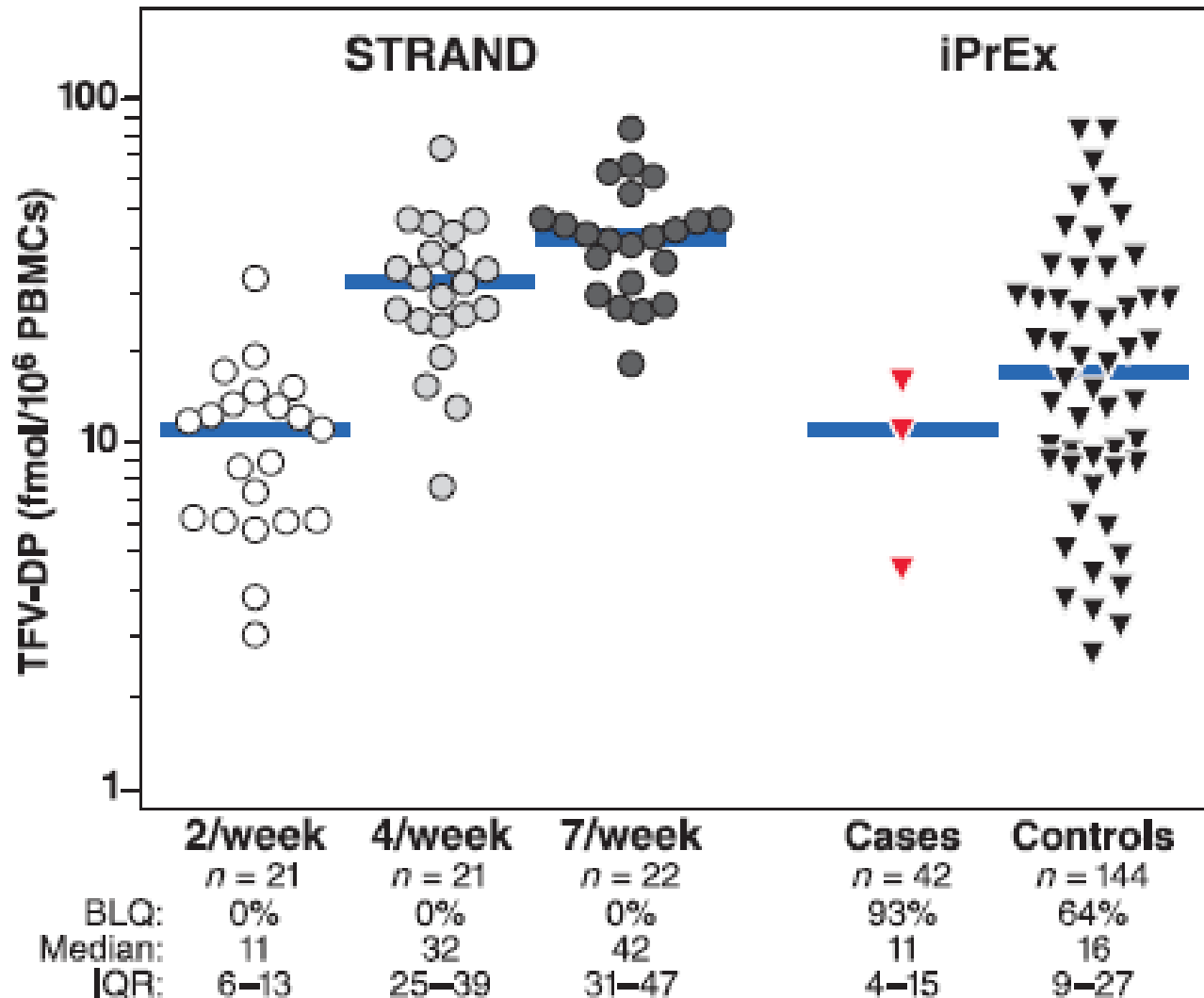
# Peri-Exposure Prophylaxis in Macaques With Oral FTC/TDF

- Macaque model of rectal transmission of HIV
  - Rectal exposure with R5 virus inoculum (10 TCID<sub>50</sub>)
- 2 doses of FTC/TDF
  - Before SHIV exposure (-)
  - After SHIV exposure (+)
- Extended window of protection
  - Associated with extended long intracellular persistence of drug
- No drug resistance in macaques failing PrEP

## Protection From SHIV



## Comparison of TDF/FTC Levels between Strand DOT Study and iPrEX Participants (Anderson, Sci Trans Med, 2012)



# What about intermittent PrEP?

- **IAVI** studies in East Africa: MSM and FSW, small size, but many missed post-coital doses
- **HPTN 066**: dose proportionality study of weekly TDF/FTC, twice weekly, and double dose twice weekly. DOT. Sampling blood, mucosal secretions and tissues.
- **HPTN 067**: MSM in Bangkok and NYC, and high risk women in Cape Town, comparing adherence to coitally dependent vs. fixed intermittent PrEP.
- **Ipergay**: getting underway, 2 pre/ 1post dose; placebo controversy



REVIEW |

Annals of Internal Medicine

## What Primary Care Providers Need to Know About Preexposure Prophylaxis for HIV Prevention

A Narrative Review

Douglas Krakower, MD, and Kenneth H. Mayer, MD

As HIV prevalence climbs globally, including more than 50 000 new infections per year in the United States, we need more effective HIV prevention strategies. The use of antiretrovirals for preexposure prophylaxis (PrEP) among high-risk persons without HIV is emerging as one such strategy. Randomized, controlled trials have demonstrated that once-daily oral PrEP decreased HIV incidence among at-risk men who have sex with men and African heterosexuals, including serodiscordant couples. An additional randomized, controlled trial of a topical pericoital antiretroviral microbicide gel decreased HIV incidence among at-risk heterosexual South African women. Two other studies in African women did not demonstrate the efficacy of oral or topical PrEP, raising concerns about adherence patterns and efficacy in this population.

The U.S. Food and Drug Administration (FDA) Antiviral Drugs Advisory Committee reviewed these studies and additional data in May 2012 and voted to advise the approval of oral tenofovir-emtricitabine for PrEP in high-risk populations. On 16 July 2012,

the FDA recommended that this combination medication be approved for use as PrEP in high-risk persons without HIV. Patients may seek PrEP from their primary care providers, and those receiving PrEP require monitoring. Thus, primary care providers should become familiar with PrEP. This review outlines current knowledge about PrEP as it pertains to primary care, including identifying persons likely to benefit from PrEP; counseling to maximize adherence and reduce potential increases in risky behavior; and monitoring for potential drug toxicities, HIV acquisition, and antiretroviral drug resistance. Issues related to cost and insurance coverage are also discussed. Recent data suggest that PrEP, combined with other prevention strategies, holds promise in helping to curtail the HIV epidemic.

*Ann Intern Med.* 2012;157:490-497.

For author affiliations, see end of text.

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[www.annals.org](http://www.annals.org)

[www.truvadapreprems.com](http://www.truvadapreprems.com)

# Youth

- ATN 082: 58 young MSM In Chicago randomized to PrEP vs placebo
- 46 enrolled in iPrEX OLE, 70% used PrEP
- Of PrEP users, blood levels indicate about 50% adherence, comparable to self-report
- Youth enjoyed integrated adherence counseling
- Lots of interim visits for social issues
- No seroconversions
- ATN 110: PrEP demo project for youth, 18-24.
- ATN 113: 16 and 17 y.o. under review

# Black MSM PrEP: HPTN 073(N=300, 3 cities)

- Writing Team led by Darrell Wheeler, PhD
- Cultural adaptation of PrEP with staff reflective of the community
- Assessment of willingness to use PrEP and of long term adherence
- Using lessons learned from peer navigation to build in nonprofessional supports
- DC, NC, LA

## Federal & Network Partners

HPTN Network  
Leadership

NIAID

NIMH

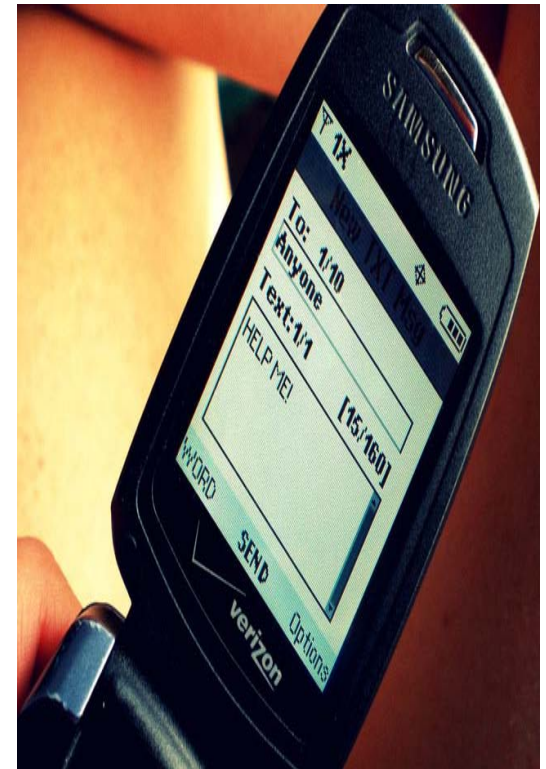
NIDA

CDC

HRSA

# Demostration and “Real World” Projects

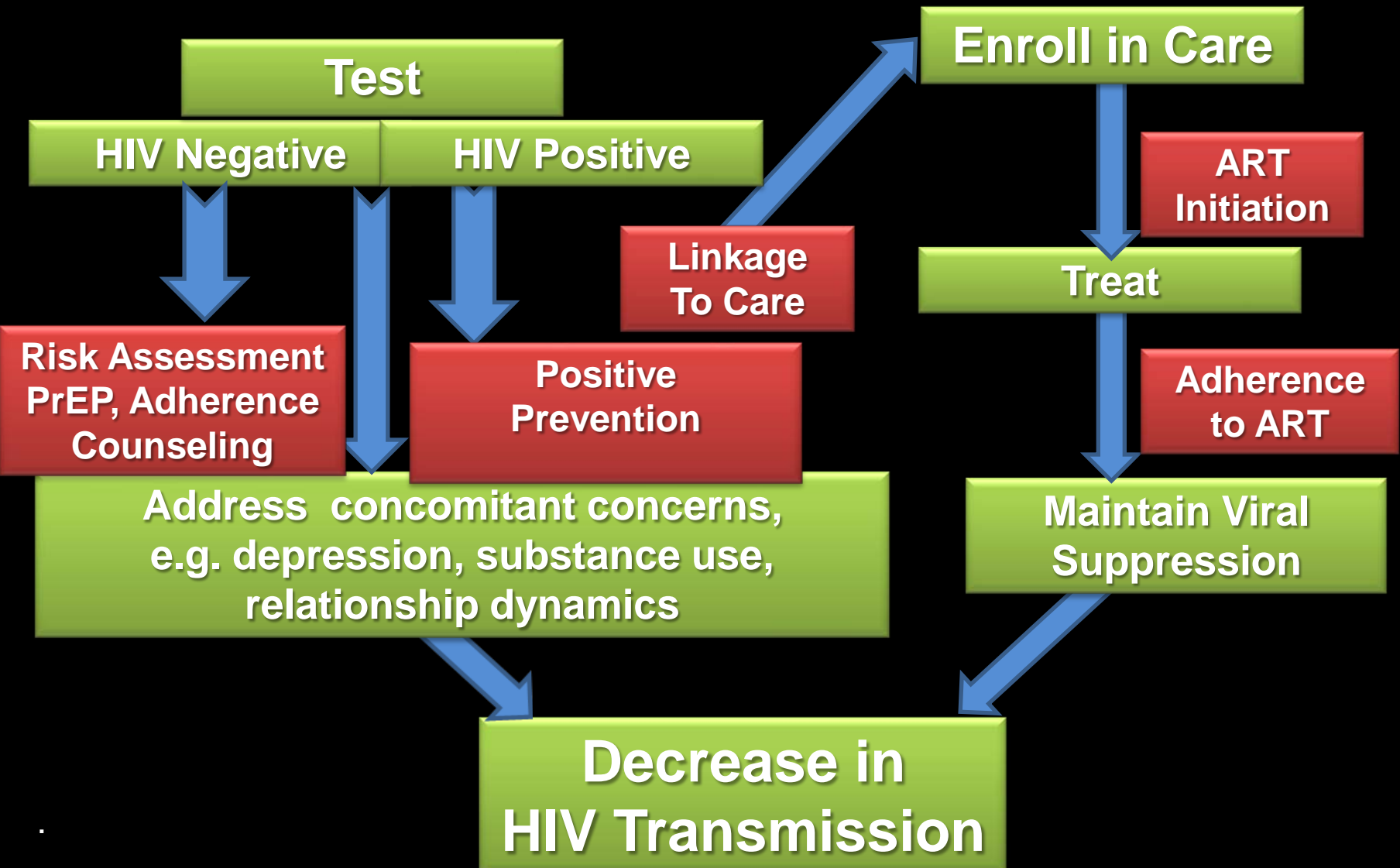
- Lester Lancet study (Kenya), weekly SMS messages → ↑adherence and ↓PVL in HIV+ pts
- SF adapting this for use in PrEP with weekly SMS messages, inc. Miami
- R34 (Mayer/Safren) to developing adherence intervention using SMS
- R21 (Mimiaga/Mitty) to study stimulant using MSM
- Southern California projects also studying ways to ↑adherence
- Other groups developing concepts. Whitman-Walker in DC, southern US





# Combination Antiretroviral Prevention

## Interventions to Increase Testing



# Thank You

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