

CONTROLLING THE HIV EPIDEMIC WITH
ANTIRETROVIRALS



Having the Courage
of Our Convictions

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PrEP 2015: State of the Science

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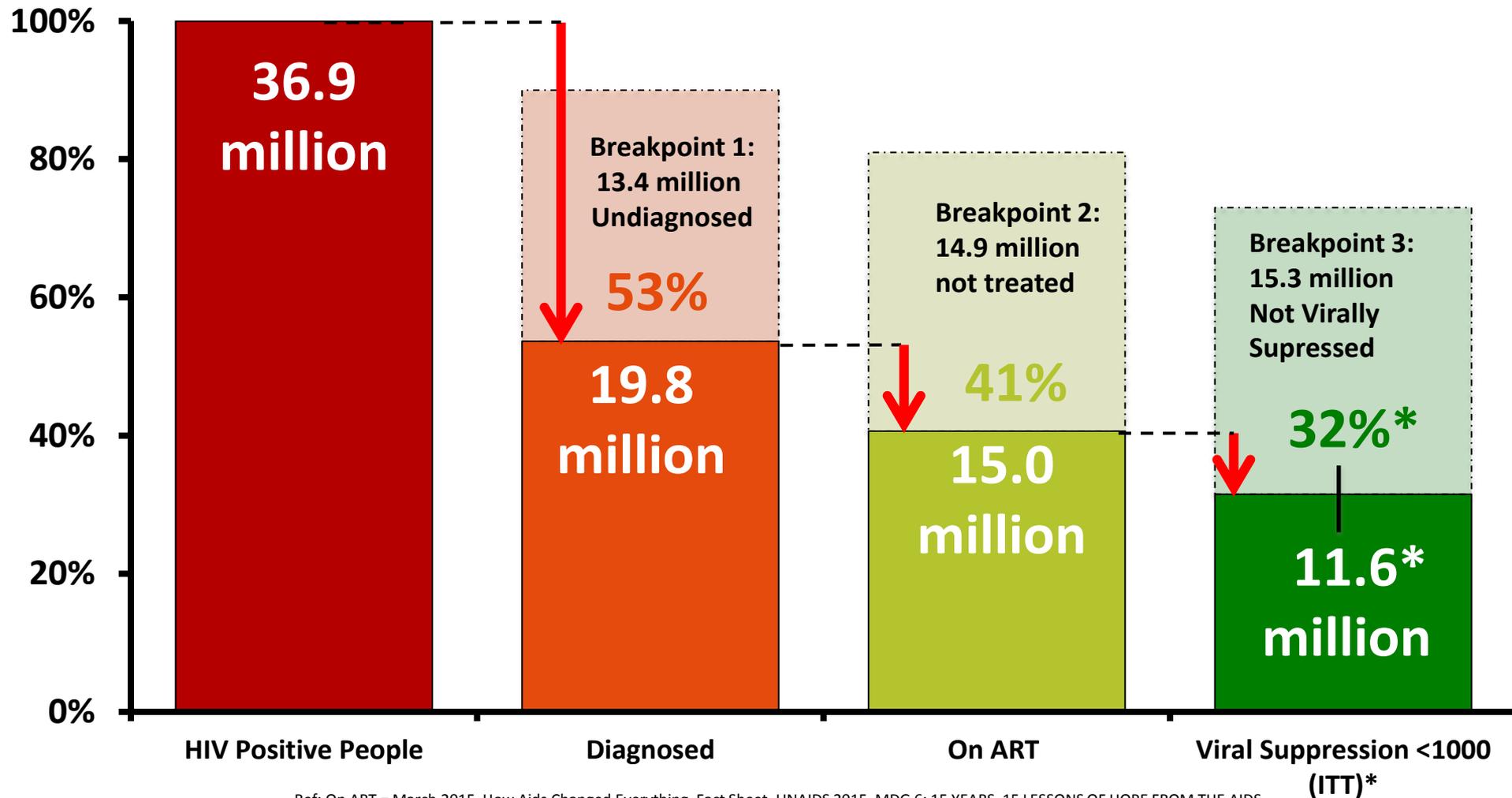


CONTROLLING THE HIV EPIDEMIC WITH ANTIRETROVIRALS

Having the Courage of Our Convictions

Why PrEP?

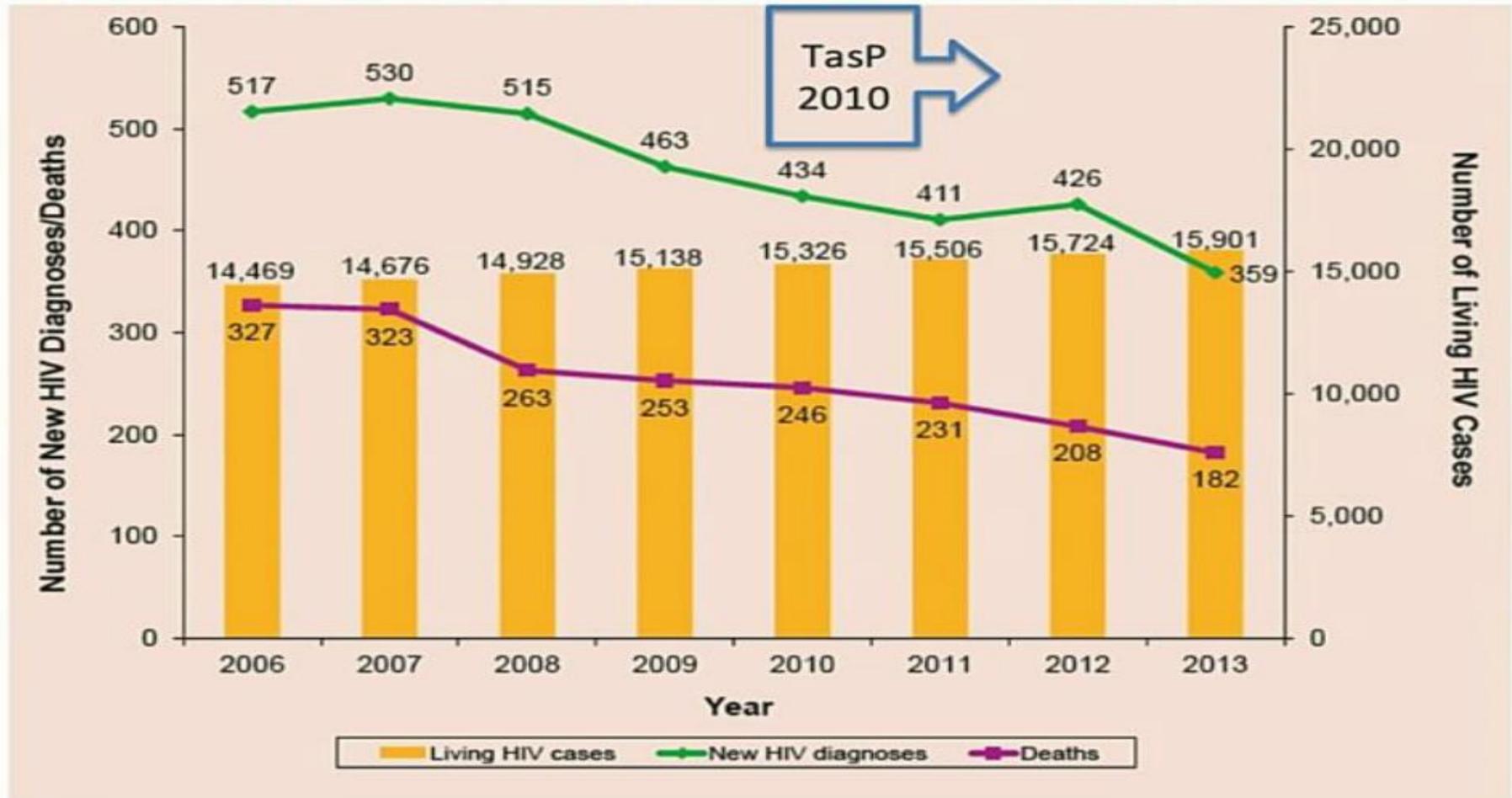
Gaps in reaching 90-90-90 Targets



Ref: On ART = March 2015. How Aids Changed Everything. Fact Sheet. UNAIDS 2015. MDG 6: 15 YEARS, 15 LESSONS OF HOPE FROM THE AIDS RESPONSE July 2015. * Average viral suppression% Intention to Treat LMIC rate from a Systematic Review by McMahon J. et al. Viral suppression after 12 months of antiretroviral therapy in low-and middle-income countries: a systematic review." *Bulletin of the World Health Organization* 91.5 (2013): 377-385.

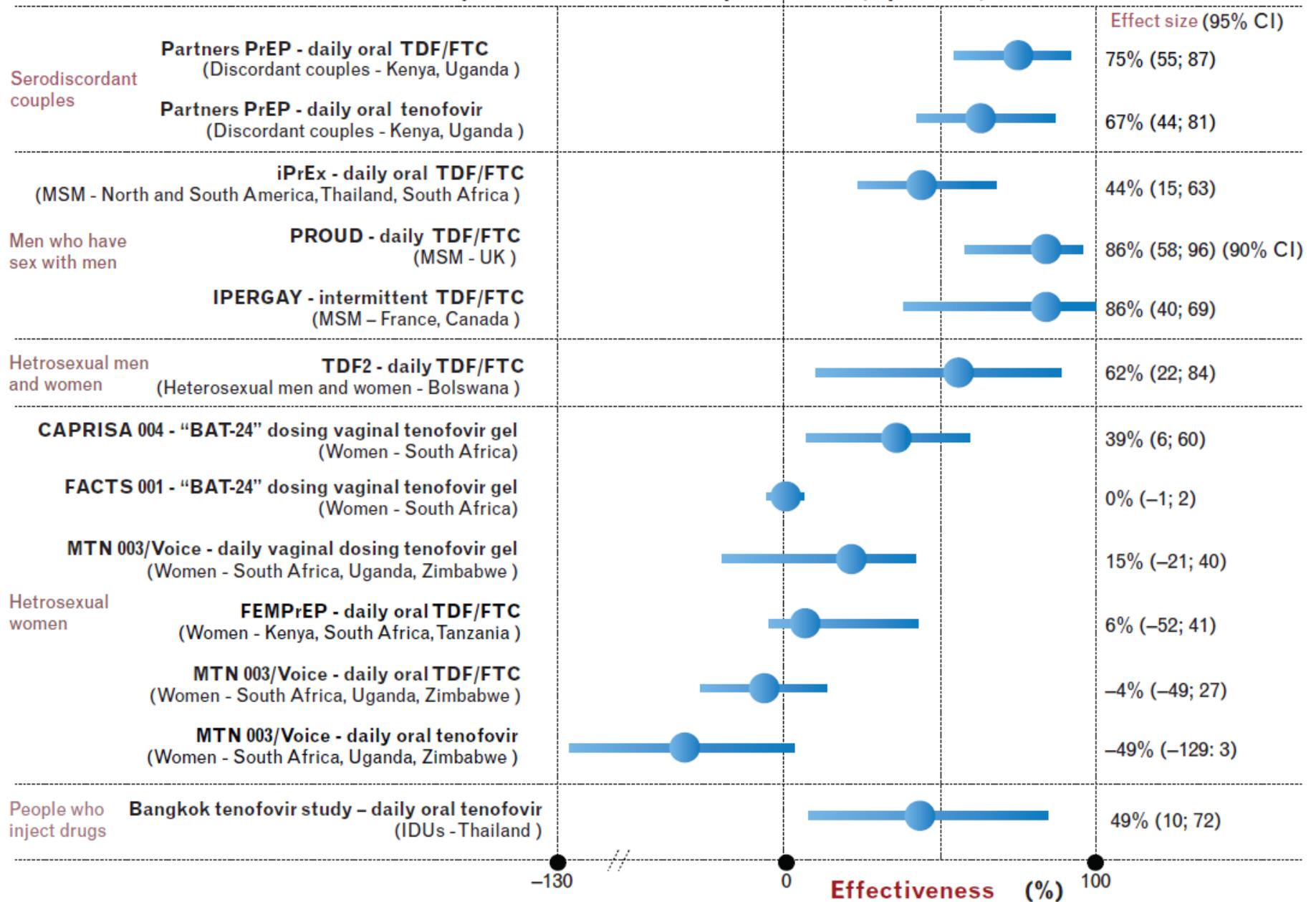
Leaks in the cascade may reduce TasP effectiveness: SF example (and Australian paradox, De Wit, AIDS Impact, 2015)

Figure 1.2 New HIV diagnoses, deaths, and prevalence, 2006-2013, San Francisco



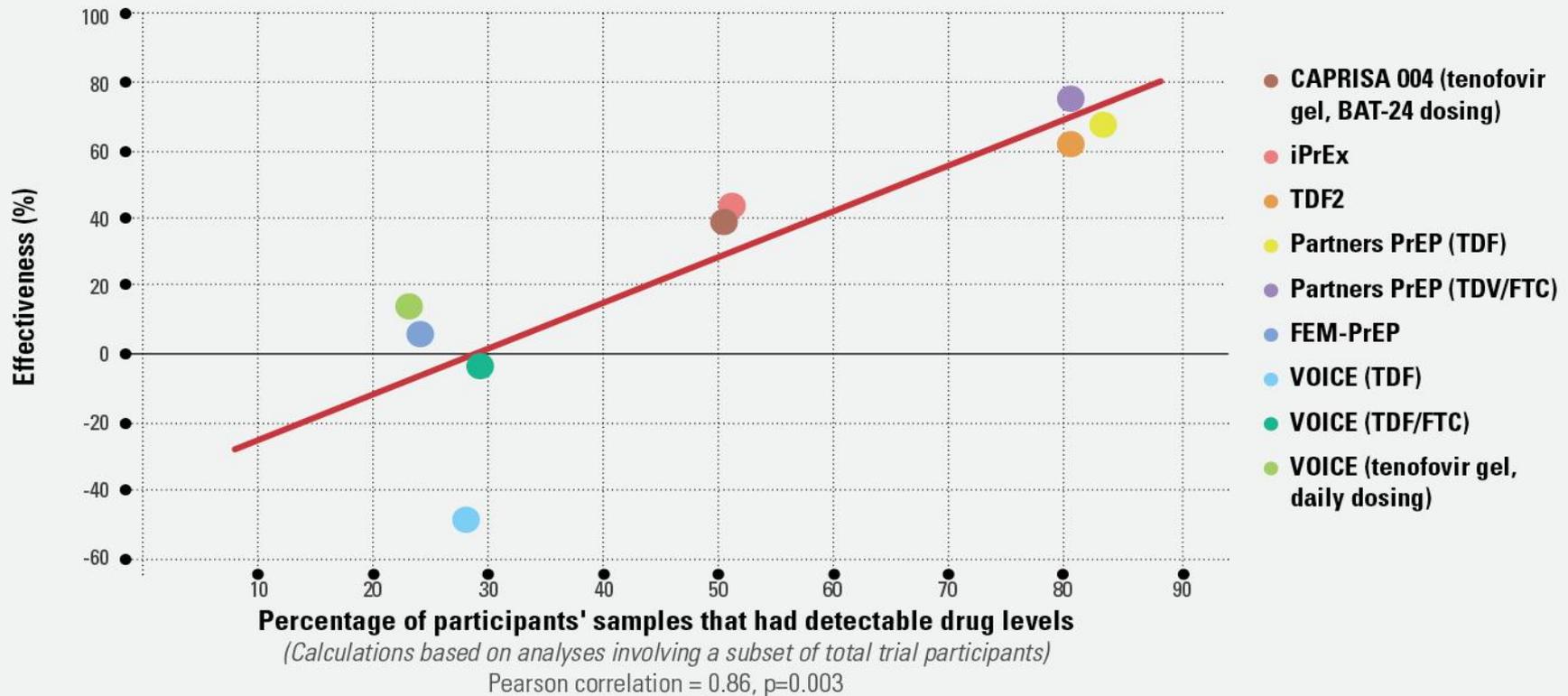
Adapted from SF DPH, 2013 HIV/AIDS Epidemiology Annual Report, August 2014.

Clinical trial evidence for oral and topical tenofovir-based prevention (April 2015)



PrEP works, but adherence is key

➔ Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention



Trials of oral and topical tenofovir-based PrEP show that these strategies reduce risk of HIV infection if they are used correctly and consistently. Higher adherence is directly linked to greater levels of protection.

Source: Salim S. Abdool Karim, CAPRISA

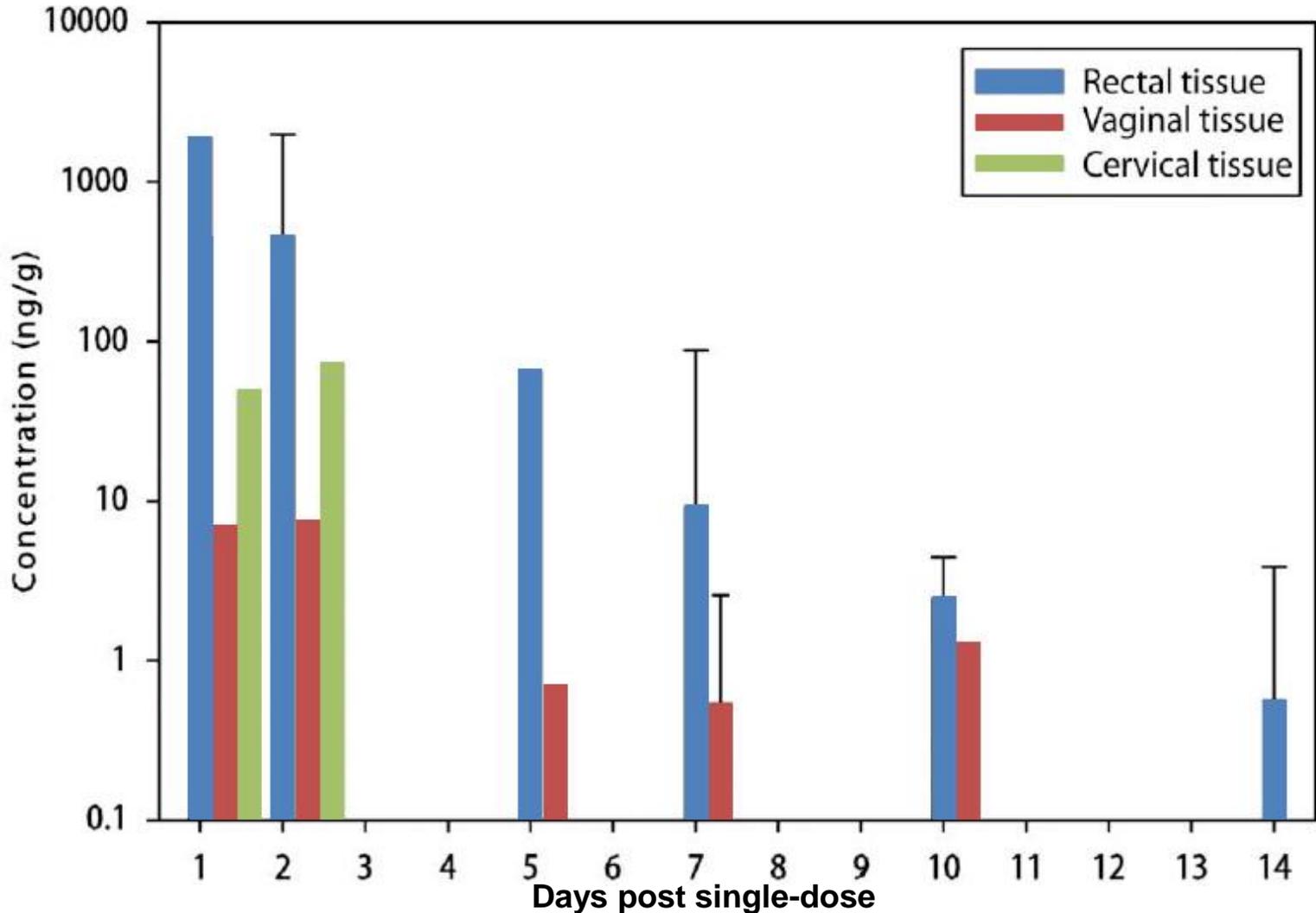
Influences on PrEP Adherence and Protection

- Trial (lots of stated negatives) vs. real world
- Self-perception of risk
- Medical trust/mistrust
- Biology (“forgiveness” when missing doses)
- Support for adherence
- Integrating behavioral health with PrEP
- Modality (Next Gen PreP)

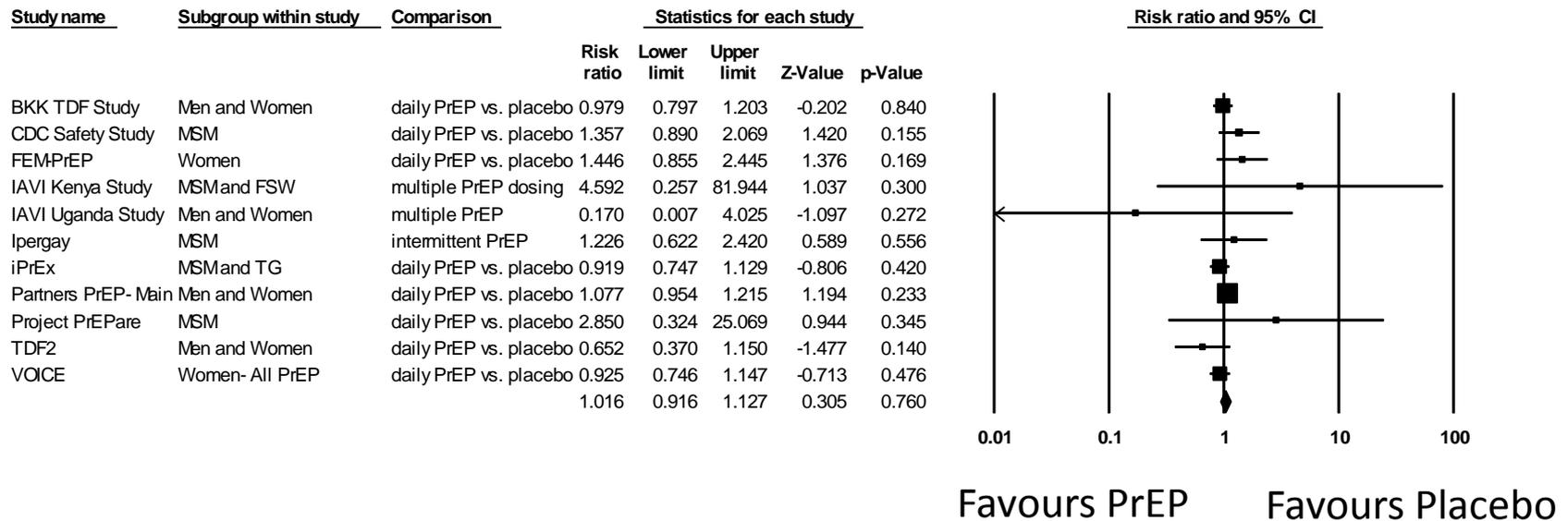
(Auerbach, MARRAZZO, VanDamme, Van der Straten, Stadler, Tolley, Hendrix, Abdool Karim, Saethre, Corneli)

“Forgiveness”

Tenofovir Concentration: Rectal > Cervical > Vaginal



PrEP is well-tolerated, discontinuations rare because of AEs



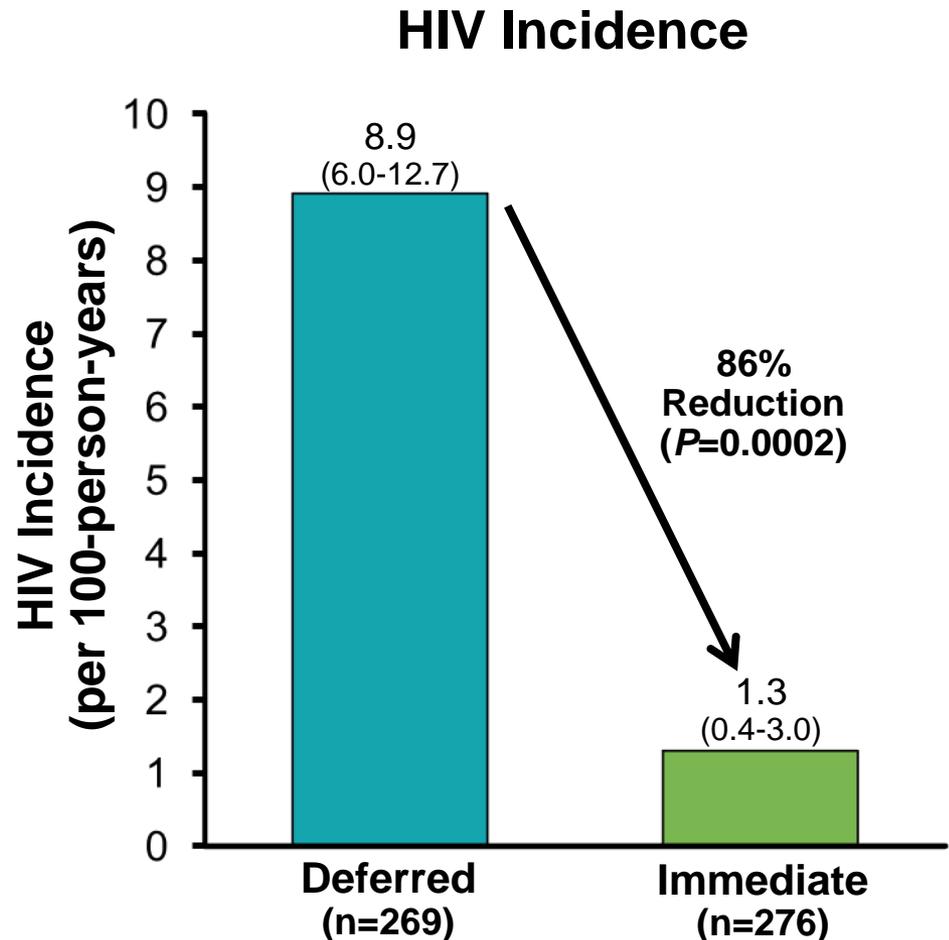
- No difference in proportion of participants reporting any adverse event (RR=1.01, 95% CI: 0.99-1.03, p=0.27) or any grade 3 or 4 adverse event comparing PrEP to placebo study arms.
- Several studies noted subclinical declines in renal functioning and bone mineral density among PrEP users.

PrEP: Risk, Compensation, Adherence, Coverage

- **Best Case: “risky” person is highly adherent (good coverage)** →→ **No HIV transmission**
- **Worst case: “risky” person is not adherent (poor coverage)** →→ **HIV Transmission; selection for resistance**
- **Risk compensation? Not often relevant**
 - Possible, not often seen in studies to date
 - But what if condoms are never used?
- **Match counseling messages and prevention intervention to risk** →→ **Requires discussion with clinician**

UK GU Med Clinics: PROUD Study

- Significantly fewer new HIV infections with immediate versus deferred PrEP (3 versus 19 cases)
 - 86% reduction ($P=0.0002$)
 - Number needed to treat to prevent 1 infection: 13
- PEP used by 31% in deferred arm
- Risk behaviors were similar between the 2 arms



PEP: post-exposure prophylaxis.

How To Improve Chemoprophylaxis Effectiveness?

New Oral PrEP Drugs and Dosing Strategies



Novel Adherence Strategies



Alternative Delivery Systems and Formulations



Vaginal & Rectal Microbicides



Intravaginal rings



**Injectables:
ARVs and mAbs**

CORRELATES OF PREP PROTECTION (GRANT ET AL, LANCET ID, 2014)

TABLE 2

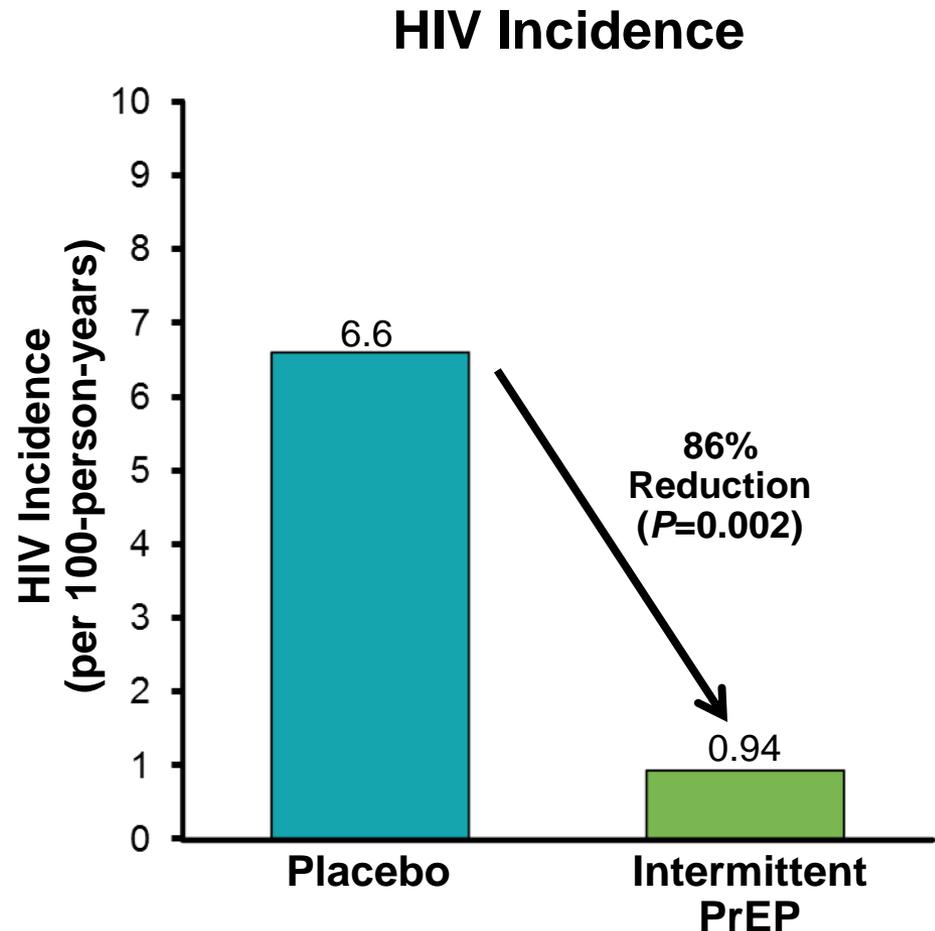
	BLQ	LLOQ to <350 fmol per punch	350-699 fmol per punch	700-1249 fmol per punch	≥1250 fmol per punch
Estimated dose (tablets per week)	None	<2	2-3	4-6	7
Follow-up (% of visits)	25%	26%	12%	21%	12%
HIV infections (n)	18	9	1	0	0
Person-years per infection	384	399	179	316	181
HIV incidence (95% CI)	4.70 (2.99-7.76)	2.25 (1.19-4.79)	0.56 (0.00-2.50)	0.00 (0.00-0.61)	0.00 (0.00-1.06)
HR vs previous placebo (95% CI)*	1.55 (0.88-2.56)	0.69 (0.32-1.32)	0.19 (0.01-0.88)	0.00 (0.00-0.25)	0.00 (0.00-0.50)
HR vs concurrent off-PrEP (95% CI)†	1.25 (0.60-2.64)	0.56 (0.23-1.31)	0.16 (0.01-0.79)	0.00 (0.00-0.21)	0.00 (0.00-0.43)

HR=hazard ratio. PrEP=pre-exposure prophylaxis. BLQ=below limit of quantification. LLOQ=lower limit of quantification. *Adjusted for study site. †Adjusted for study site, age, number of sexual partners, non-condom receptive anal intercourse, and syphilis. Drug concentration measurements were not available for 5% of visits.

Table 2: Effect of tenofovir diphosphate in dried blood spots on HIV infection

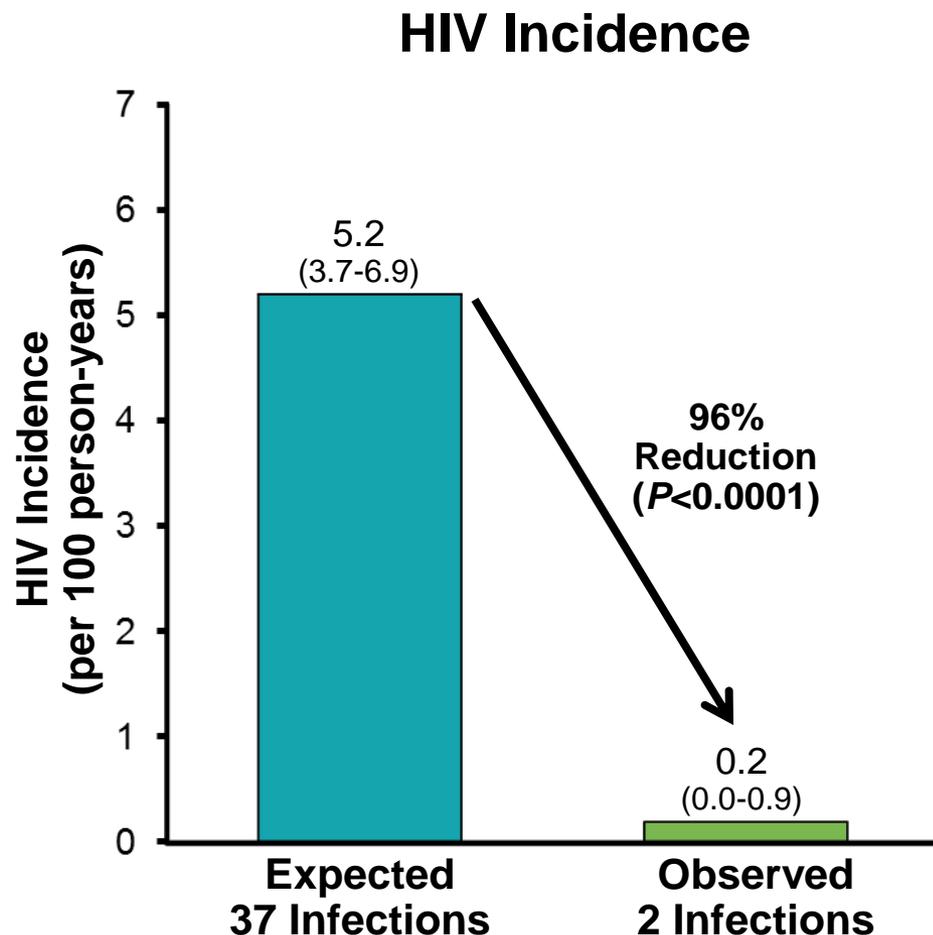
ANRS Ipergay Trial: Event-Driven PrEP

- Significantly fewer new HIV infections with intermittent PrEP versus placebo (2 versus 14 cases)
 - 86% reduction after a mean follow-up of 13 months ($P=0.002$)
- Safety of on-demand PrEP was similar to placebo except for GI adverse events
- Adherence to PrEP was good, supporting the acceptability of on-demand PrEP



Partners Demonstration Project: TasP and PrEP

- Open-label prospective study
 - Heterosexual discordant couples not using ART or PrEP in Kenya & Uganda
 - At high risk for HIV transmission based on risk scoring tool
 - ART per national guidelines (treat all seropositive partners in a discordant relationship)
 - PrEP (open-label emtricitabine/tenofovir DF) until HIV-positive partner is on therapy for 6 months as a 'bridge' to ART
- 858 person-years of follow-up
- 95% uptake of PrEP and 80% on ART



Tailoring PrEP for Key Populations

HPTN 073 Black MSM

Client-centered care
coordination (C4)

(Wheeler/Fields)

ATN 110/113

- ❑ YMSM 15-22 y.o.
- ❑ PreP + Individual vs. group EBI behavioral intervention (Hosek et al)



We've launched a new PrEP demonstration project for Black men who have sex with men.

Participate in the live Twitter chat on

#HPTN073

Wednesday, August 14

#PrEPChat

at 10 am PT / 1 pm ET

With our guests: @JonPaulLucas and @cchauncey

Be sure to follow @HIVptn

Join the HPTN 073 Webinar:

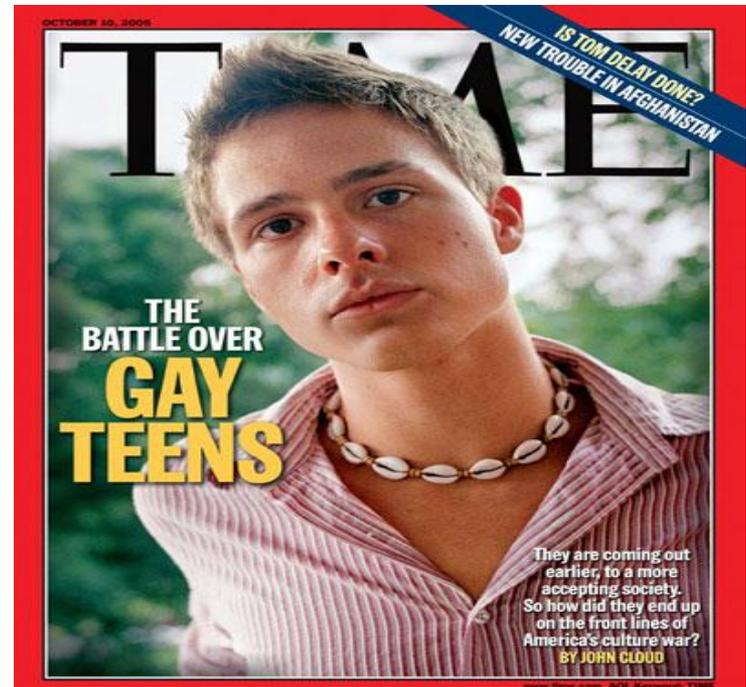
"Introducing HPTN 073: A BMSM PrEP Demonstration Study"

at 11 am PT / 2 pm ET

by registering at

<http://bit.ly/073Webinar>

Find out more about HPTN 073 at
www.HPTN.org and at Facebook/HIVptn



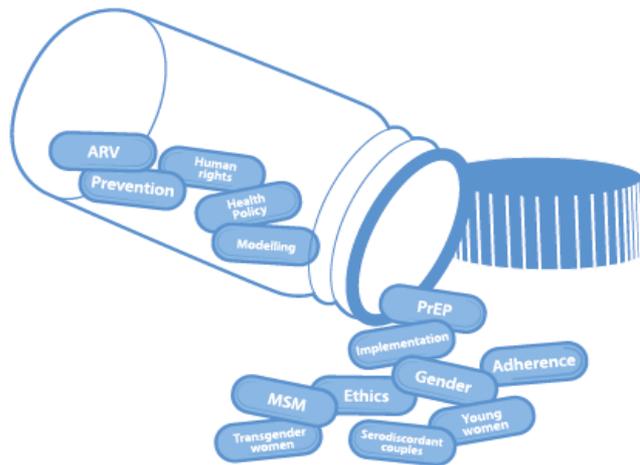
Global PrEP Scale-Up



The Network for Multi-disciplinary Studies on
ARV-based Prevention of the Sexual Transmission of HIV
NEMUS

PrEP Implementation Science: State-of-the-Art and Research Agenda

Guest Editors: Carlos F. Cáceres, Kenneth Mayer, Rachel Baggaley,
Kevin O'Reilly



Postcards from the field

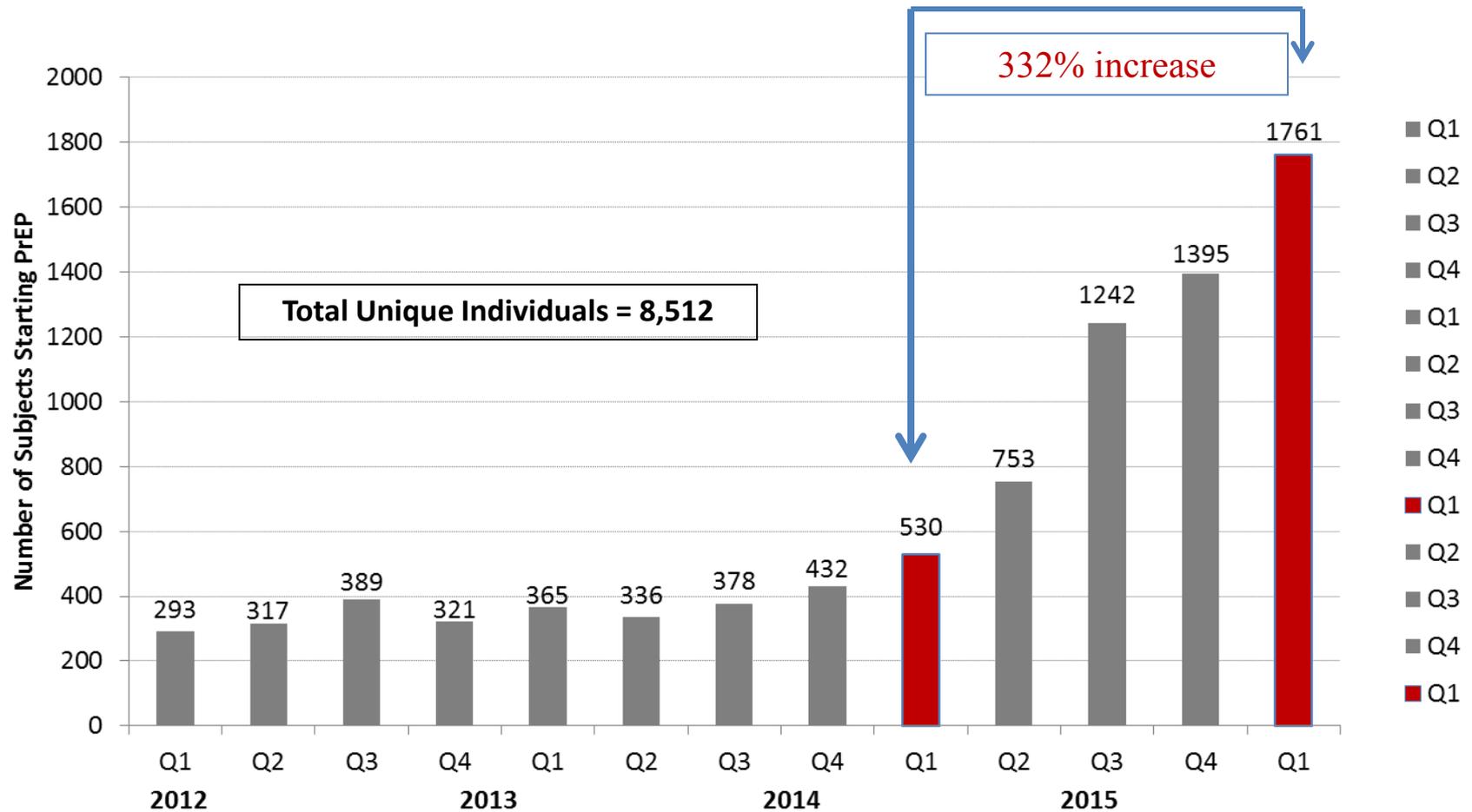
- Kenya
 - Southern Africa
 - Brazil
 - Australia
 - Thailand
 - US
- Programs being developed
in Peru, Canada, Europe



PrEP: Met and Unmet needs

- How many potential users in U.S.?
 - 275,000 MSM
 - 140,000 HIV-uninfected heterosexual partners(J. Mermin, Medscape, 5/14/2014)
<http://www.medscape.com/viewarticle/824770>
- What is the current uptake?

New PrEP Starts per Quarter



IMS National Prescription Database accounts for approx. 39% of all TVD prescriptions

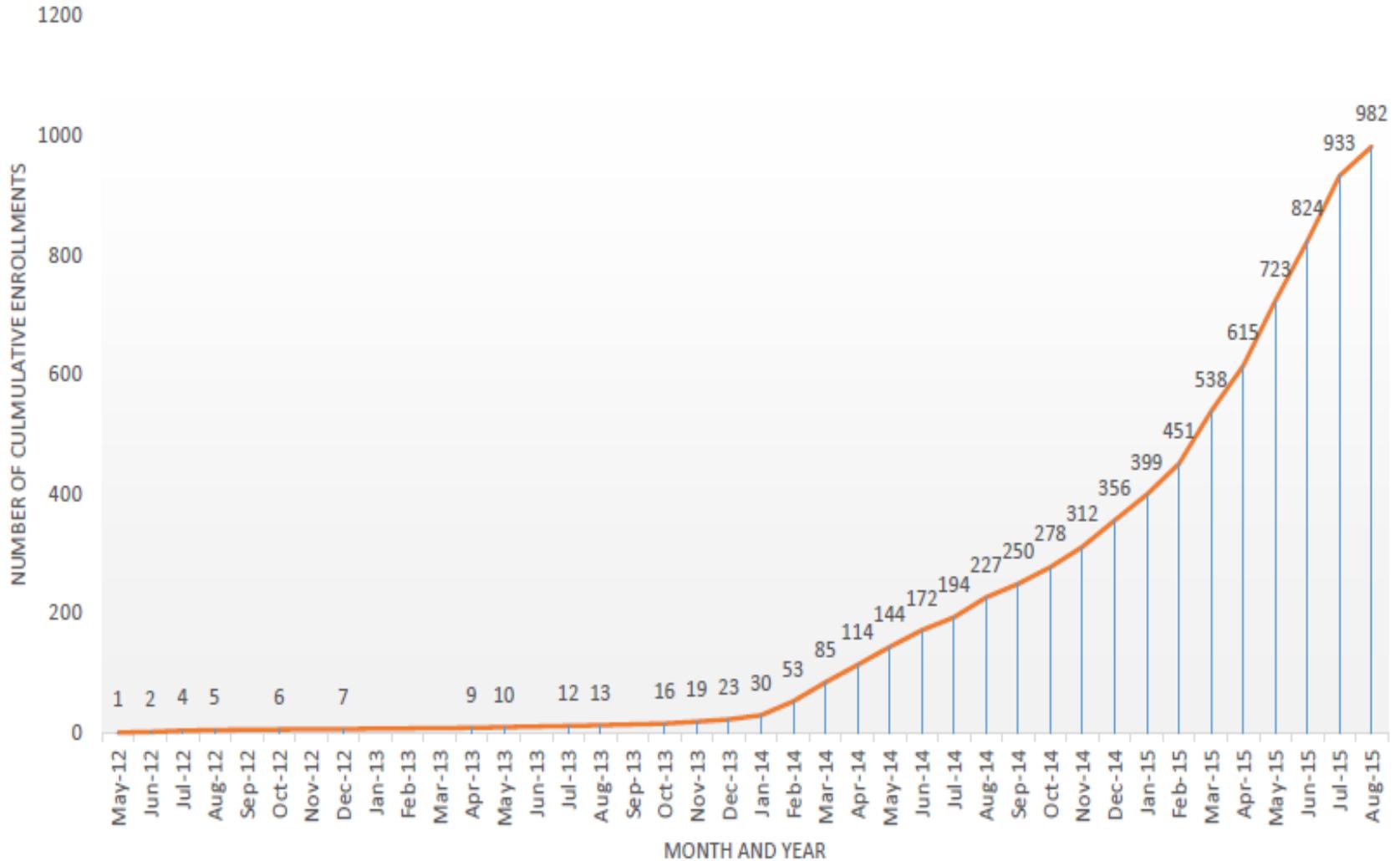
Examples of early adopters: U.S. Cities Involved in Demonstration Projects



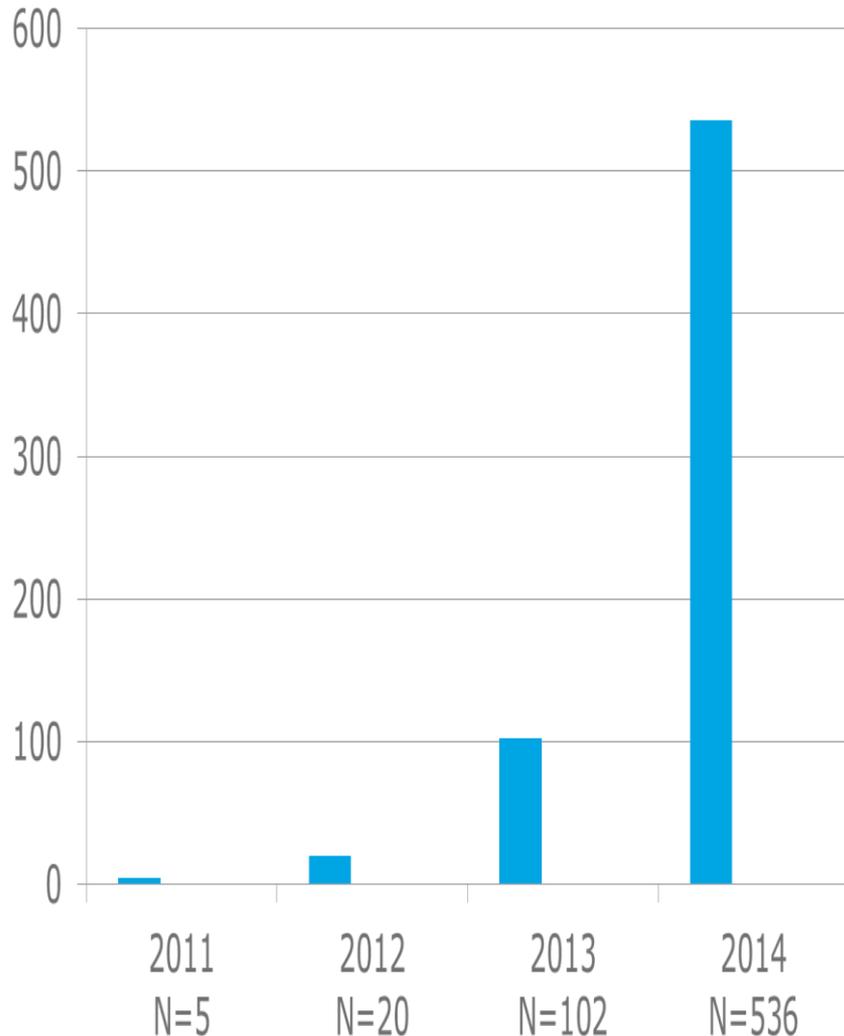
Demonstration and Implementation projects have a planned enrollment of approximately 8,000 participants.

* NYC = Manhattan, Harlem, Bronx and Brooklyn

Number of Cumulative Callen-Lorde Community Health Center PrEP Enrollments from May 2012-August 2015 By Month

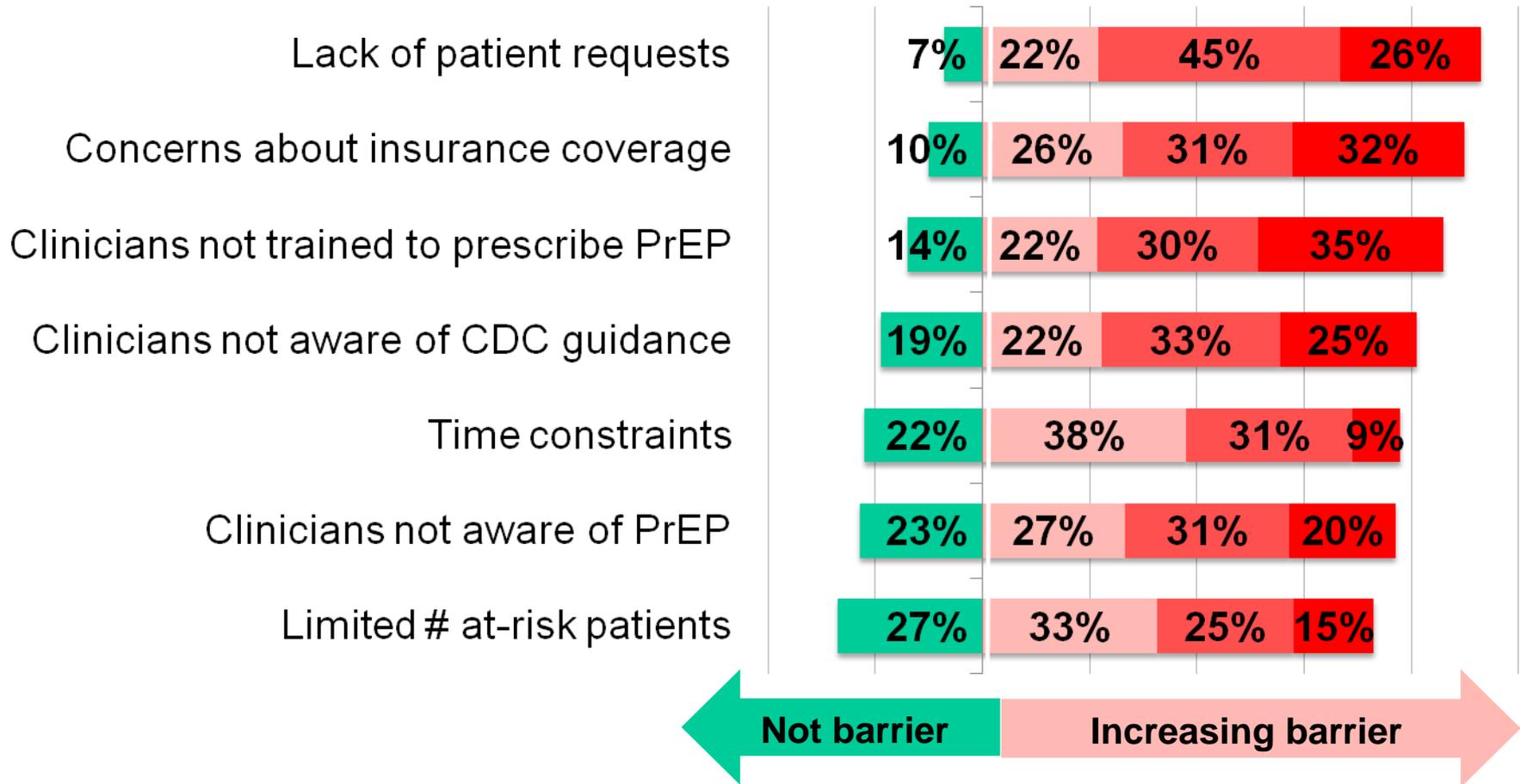


Fenway Health: PrEP Experience



- 85.5% of initiators still on PrEP; Longest: 3.8 years
- 79.7% White; 8% Black; 12.3% Latino
- 95.1% identified as gay
- 158 zip codes
- “Gayborhood” <10%
- Private Ins: 80.7%; Medicare: 9%; Medicaid: 8.7%
- 25.9% who d/c’ed PrEP, initiated again
- More than 30 prescribers

New England providers perceived numerous barriers to prescribing PrEP (Krakower, PLOS ONE, in press 2015)



BE SURE. PLAY SAFE.

PrEP + CONDOMS

Prevent HIV & Other STIs



TO HELP STOP HIV AND OTHER STIs, CHOOSE A COMBINATION THAT WORKS FOR YOU:

1. TAKE MEDICINES TO TREAT OR PREVENT HIV

If you have HIV, HIV medicines help keep you healthy and make it harder to pass HIV to your partners.

If you do not have HIV, daily PrEP and emergency PEP can help you stay HIV-negative.

(These medicines only stop HIV, not other STIs.)

2. USE CONDOMS AS OFTEN AS POSSIBLE

Consistent condom use helps prevent HIV and other STIs.

3. USE PLENTY OF WATER-BASED OR SILICONE-BASED LUBE

Either is safe on latex condoms.

YOU CAN ENJOY YOUR SEX LIFE AND STILL PROTECT YOURSELF FROM HIV AND STIs. BE SURE. PLAY SAFE.



BE SURE. PLAY SAFE.

HIV TREATMENT + CONDOMS

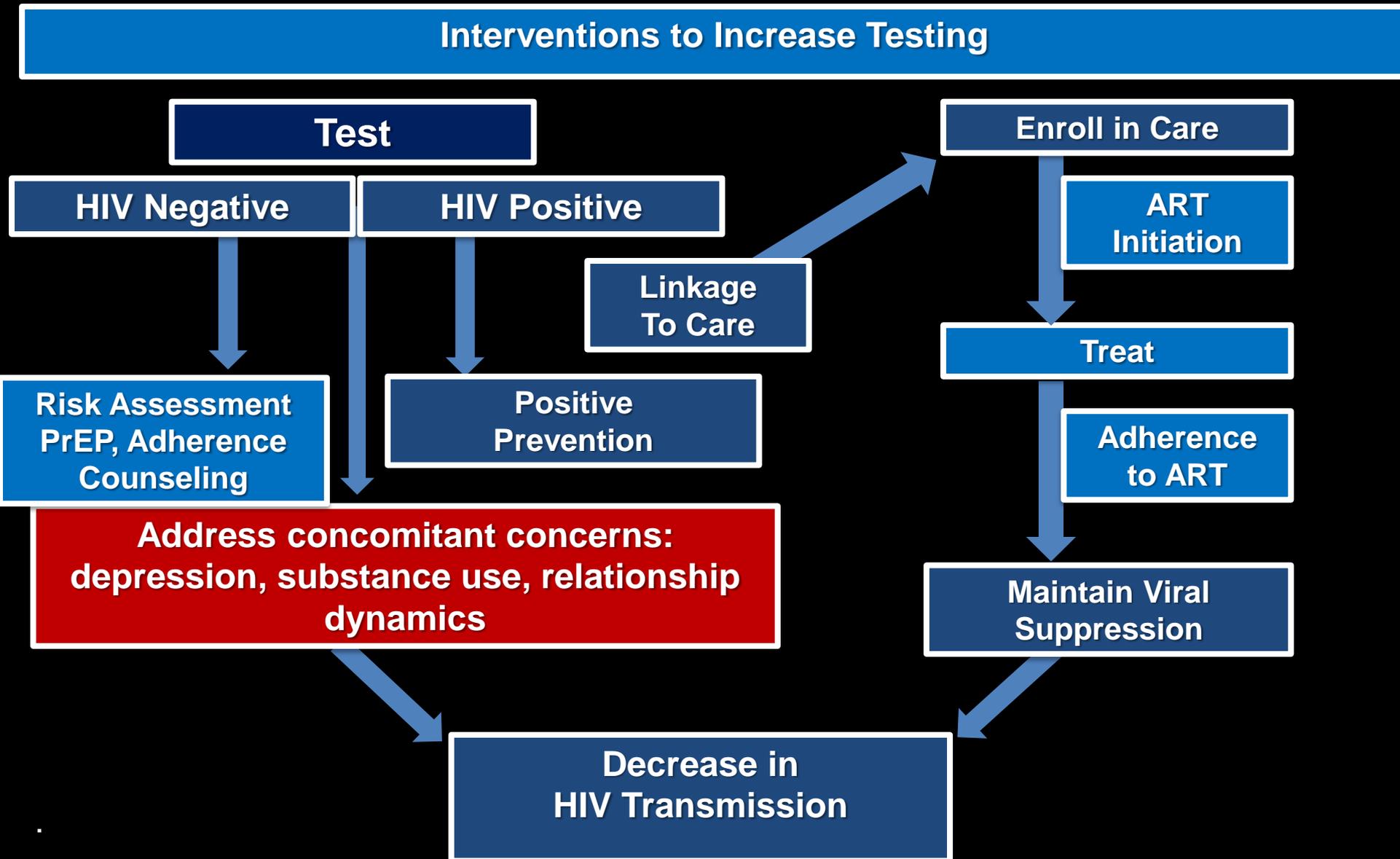
Prevent HIV & Other STIs



Protection against HIV, and other sexually transmitted infections (STIs) isn't **"ONE SIZE FITS ALL."**



Antiretrovirals alone are not sufficient



Many thanks

S. And Q. Abdool Karim
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Raphy Landovitz
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Rodney Vanderwarker
Mitchell Warren



TFI Biomed, Behavioral, Epi and Data Teams

Study Participants www.thefenwayinstitute.org

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