

Pre-Exposure Prophylaxis

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November 2011

PREVENT HIV

FOR INFORMATION ON THIS NEW
EXCITING HIV PREVENTION

SMS "Info" at no cost to 30060 or
e-mail MCMHP@hiv-research.org.za

All participants will be compensated for their time and



The HIV Pandemic

2.6 Million

New HIV Infections in 2009

41% in Young People (ages 15-24)

The HIV Pandemic

One New Infection...

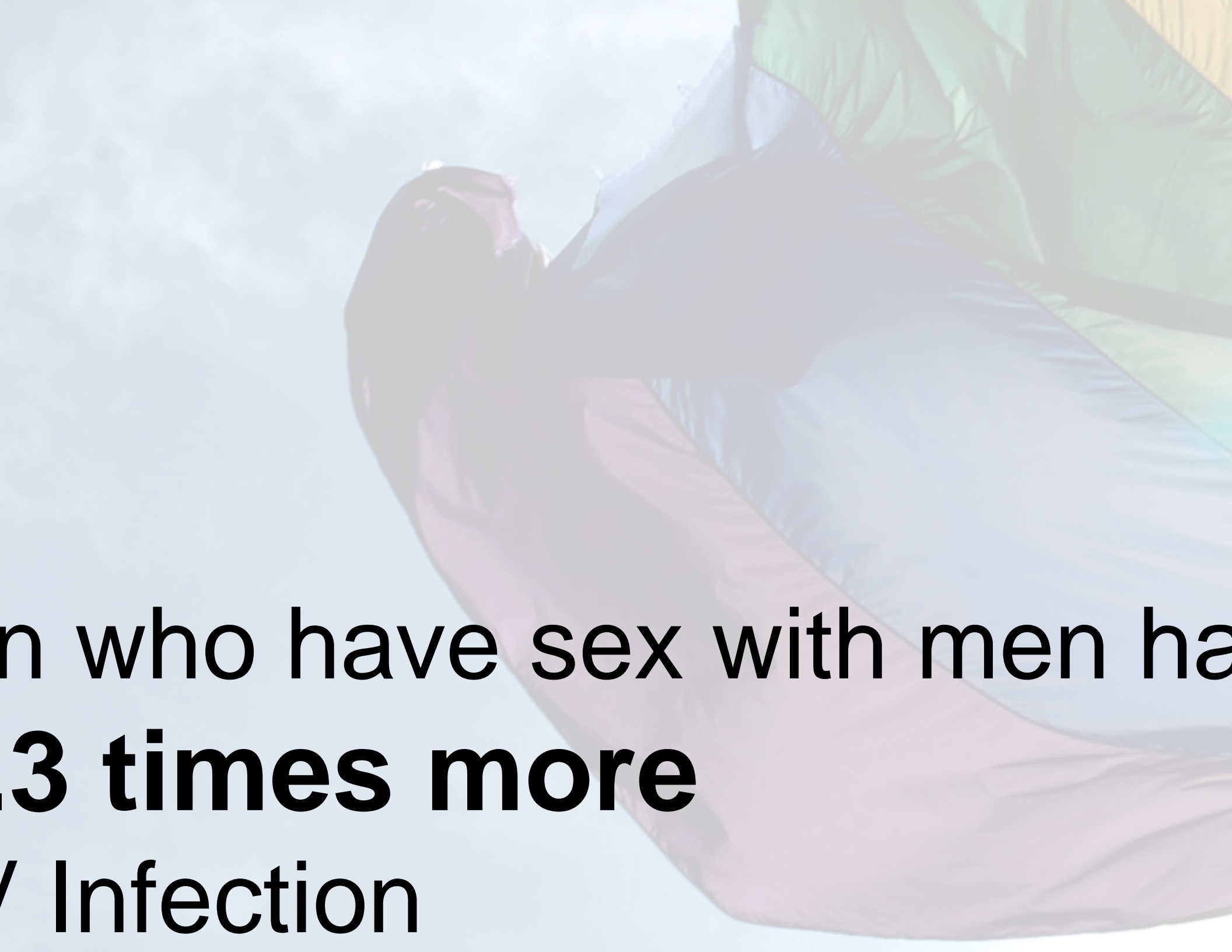
- Every 12 Seconds in the World
- Every 8 hours in Peru

The HIV Pandemic

1.2 Million

Started Therapy in 2009

2 New Infections For Everyone Starting Therapy



n who have sex with men ha
3 times more
/ Infection

Overall Odds Ratio

Aggregate Sample

Interval Plot

Americas

Ecuador
Peru
Bolivia
Uruguay
Argentina
Colombia
Paraguay
Brazil
Honduras
Panama
Guatemala
El Salvador
Nicaragua
Mexico
Trinidad/Tobago

Africa

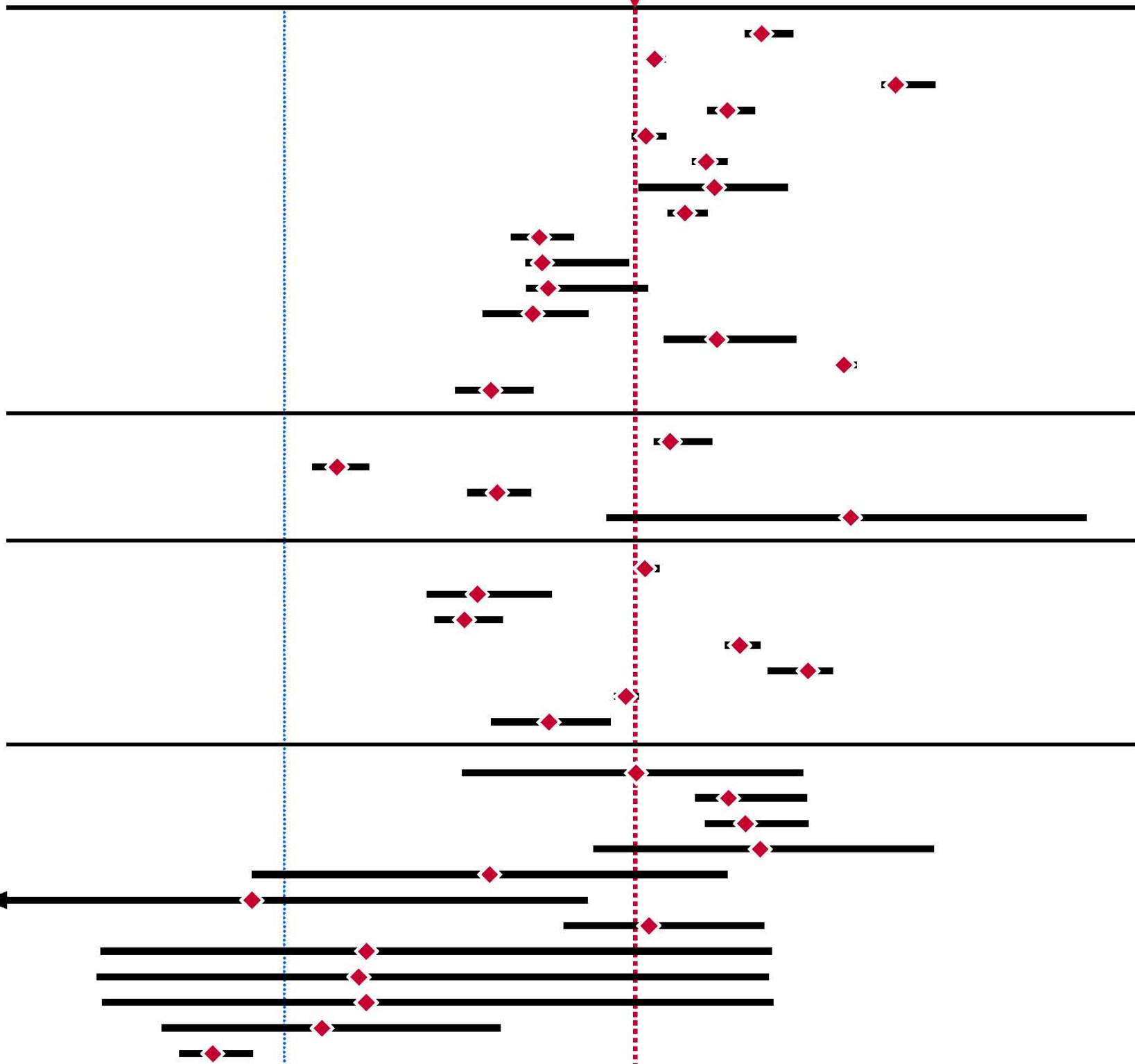
Senegal
Kenya
Sudan
Egypt

Asia

Thailand
Vietnam
Cambodia
China
Indonesia
India
Nepal

Europe

Czech Republic
Poland
Serbia
Slovenia
Armenia
Belarus
Georgia
Kazakhstan
Kyrgyzstan
Lithuania
Moldova
Russia

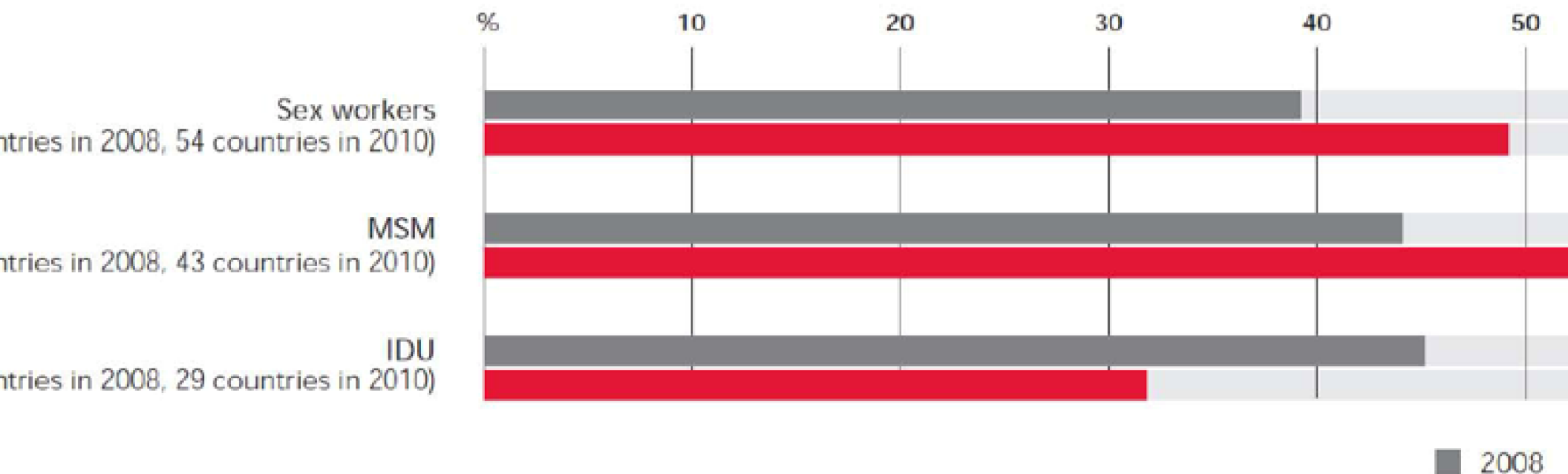


Prevention Trial Disappointments

- Trials showing no efficacy or harm...
 - Intensive counseling in MSM (Koblin *Lancet* 2004)
 - An adenovirus-vectored vaccine (Buchbinder *CROI* 2009)
 - Microbicides: N-9/Savvy/Cellulose Sulfate
 - Diaphragms (Padian *Lancet* 2007)
 - Mass STI treatment (Wawer *Lancet* 1999)
 - Herpes suppression (Celum *NEJM* 2009)

Prevention programmes for selected populations

Coverage of HIV prevention programmes for selected population groups, 2008 and 2010.



PrEP Initiative / Iniciativa PrEx

Sponsored by

NIH/NIAID/DAIDS

with co-funding by the

Bill & Melinda Gates Foundation

and drug donated by

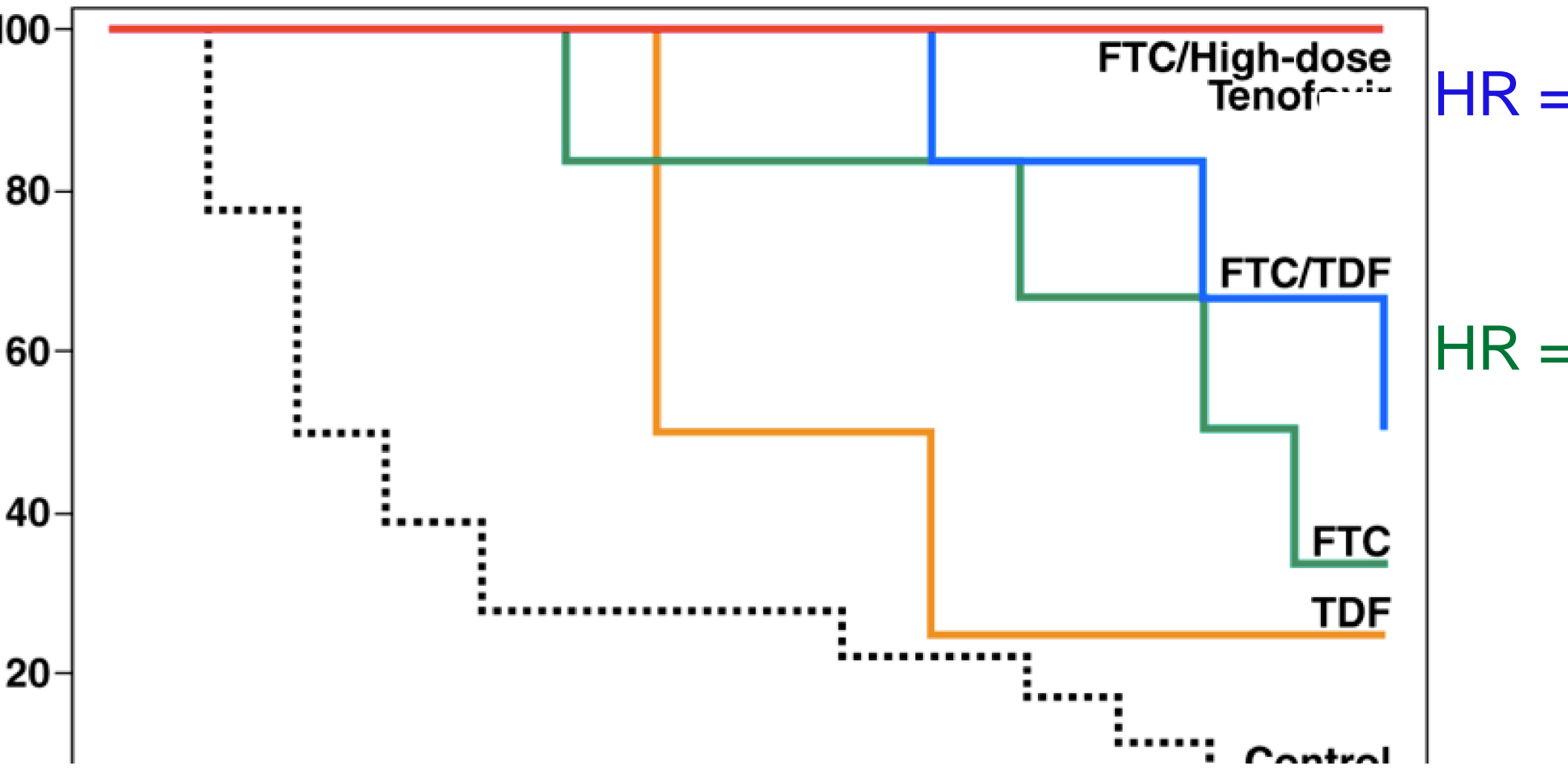
Gilead Sciences

Why Tenofovir and Emtricitabine

Protective in Animals
Licensed for Human Use
Excellent Safety Record
Long Time in Body (>48h)
Concentrated in Rectum
No TB Interactions



Reduction of Rectal SHIV Transmission by Chemoprophylaxis with ARVs



PrEP Initiative / Iniciativa PrEx

Auspiciado por

NIH/NIAID/DAIDS

con el co-auspicio de

Bill & Melinda Gates Foundation

y medicamento donado por

Gilead Sciences

Plamamiento completado en Diciembre

Sedes	11
Participantes	2499

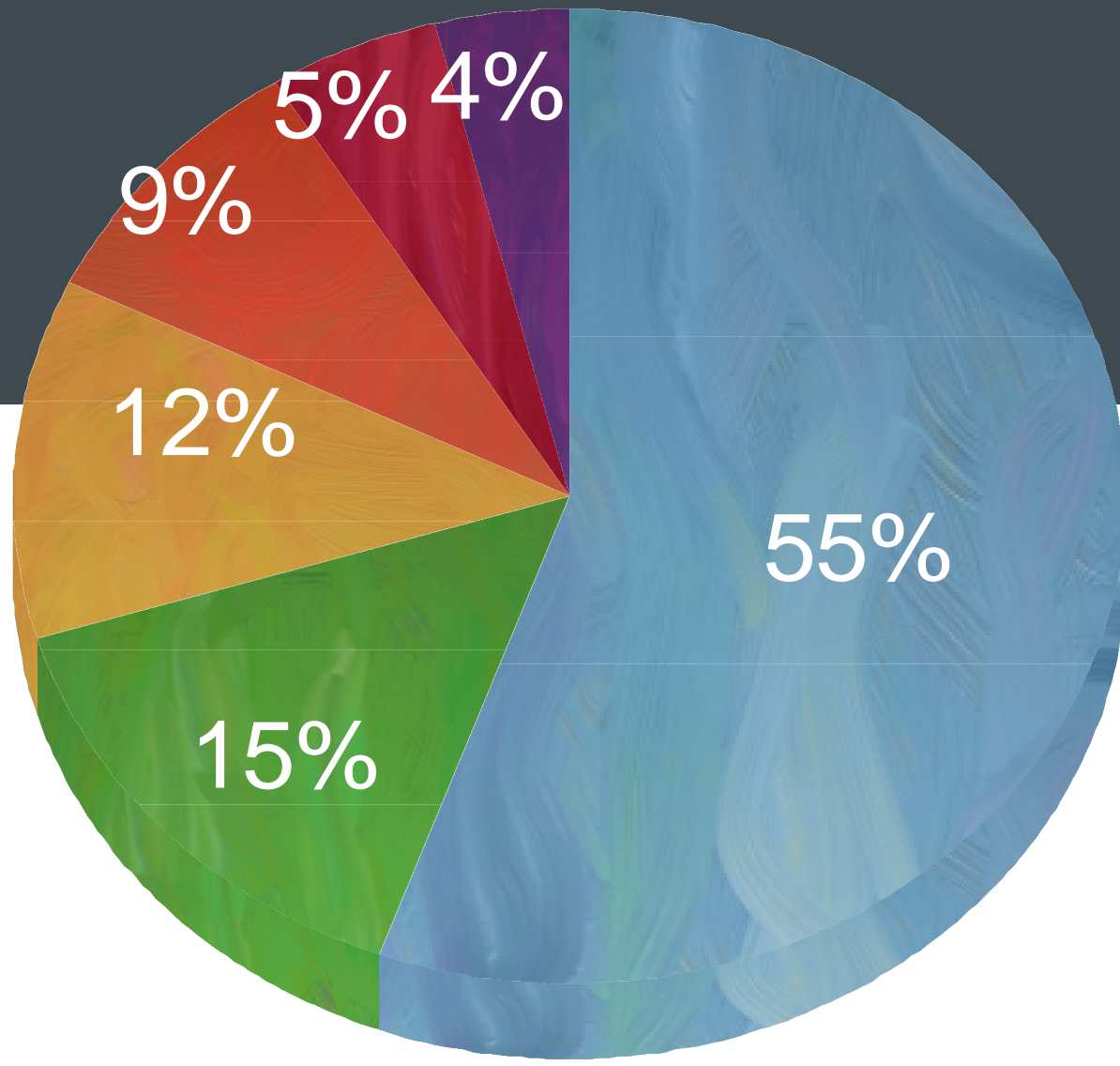
Francisco



participantes 2499



- PERU
- BRASIL
- ECUADOR
- EEUU
- TAILANDIA
- SUDAFRICA



Comprehensive Prevention Services Given to All

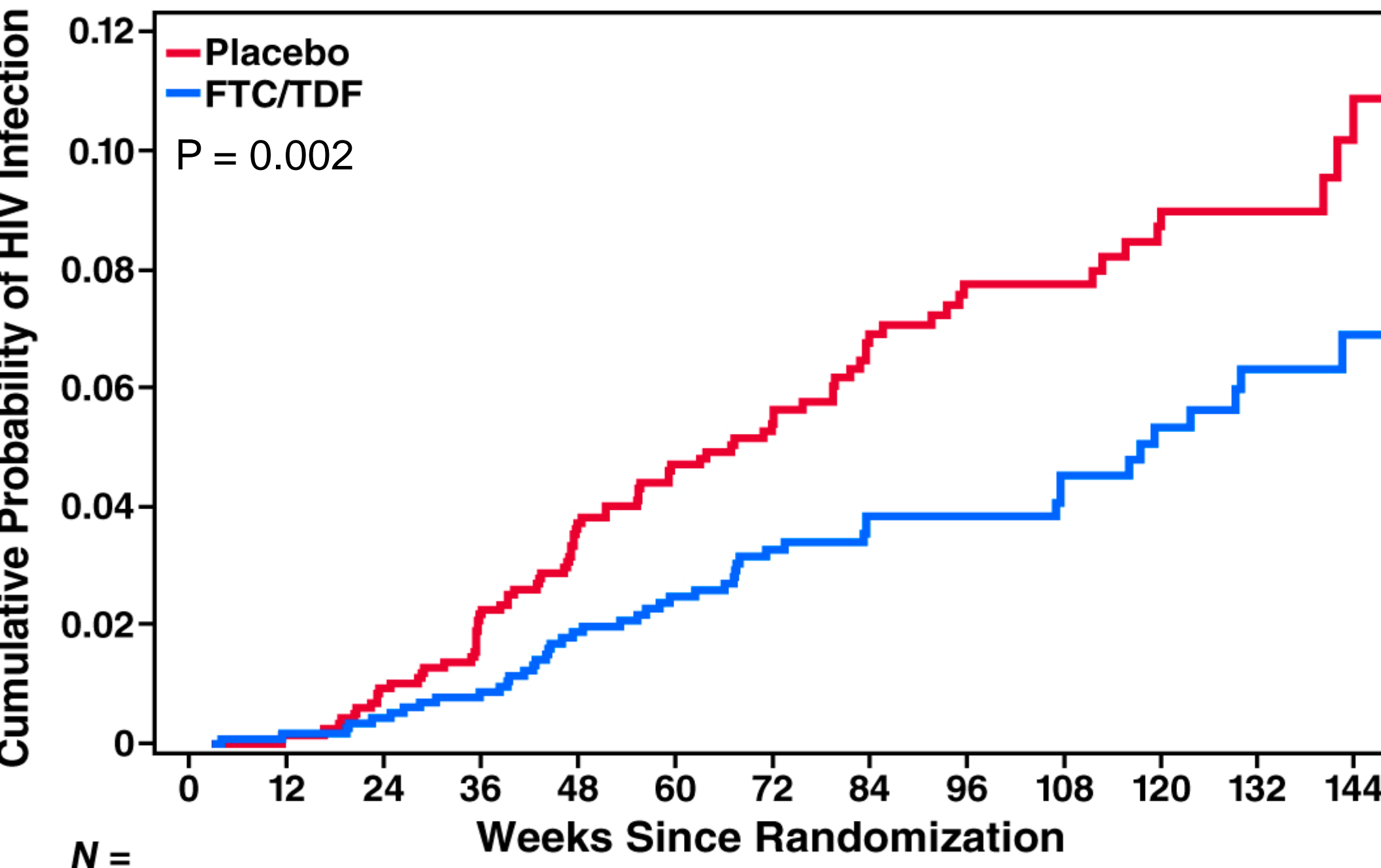
- HIV Testing Monthly
- Risk Reduction Counseling
- Condoms (15 or more)
- STI testing if any symptoms, monthly
- STI screening for all every 24 weeks
- Partner treatment
- PEP if recently exposed
- HBV vaccine

Objetivos del Estudio iPrEx

- Determinar si FTC/TDF es seguro en relación a eventos adversos
- Determinar si FTC/TDF es eficaz en prevenir infección por VIH

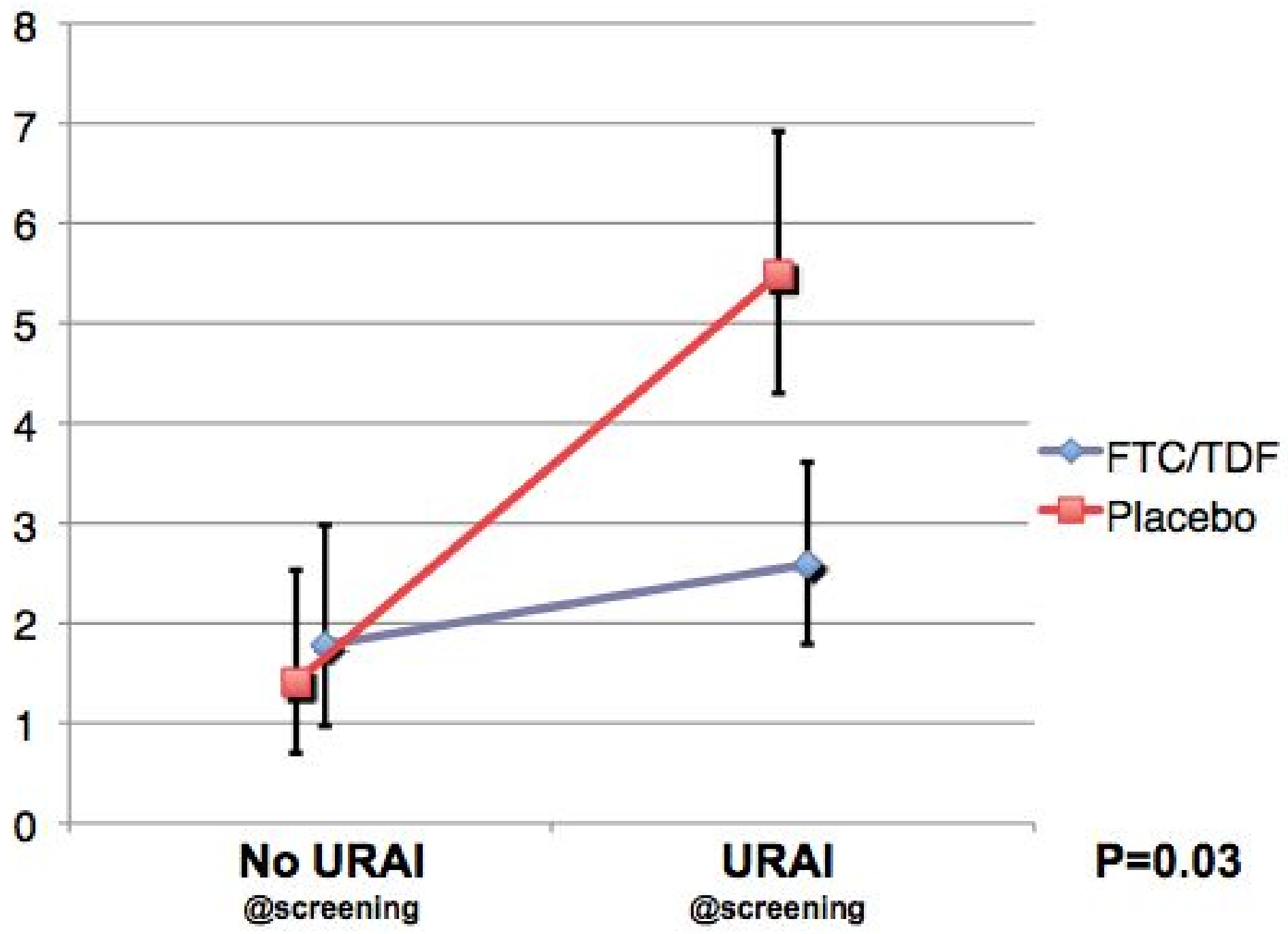
Efficacy (MIRI) 42% (16-66%) Through End of Study

Infection Numbers: $83 - 48 = 35$ averted



Bars are Standard Error of the Incidence Estimate

HIV incidence / 100 person years



P=0.03

1
FTC/TDF

1014
25%

1485
52%

In the Active Arm of iPrEx

Cases matched to controls by site and time on study

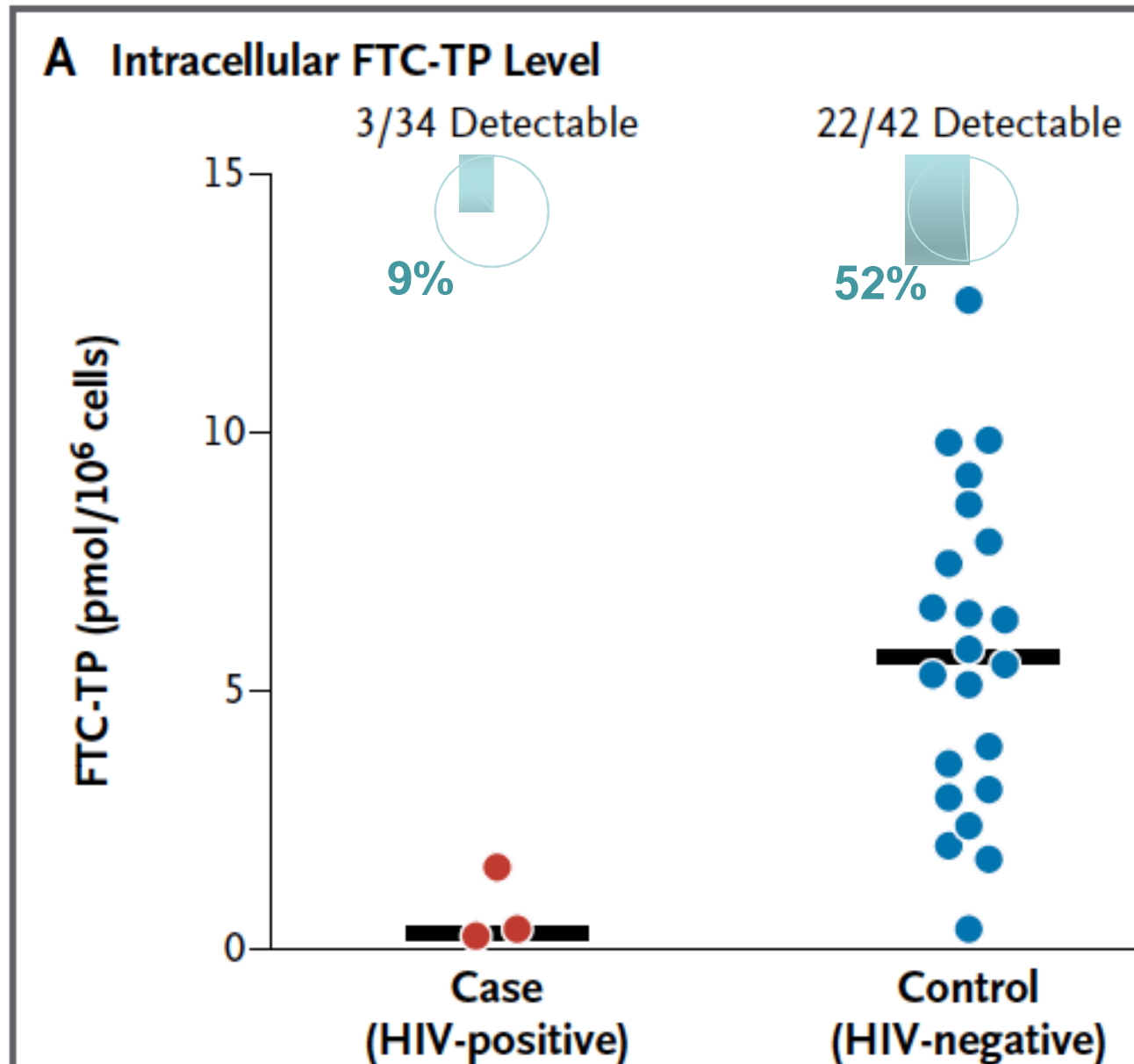
High Detection

Correlated with seronegative Status (OR 12.9, $P < 0.001$)

92% reduction in HIV risk

95% CI 71-99%

After controlling for Age, Risk Behavior.

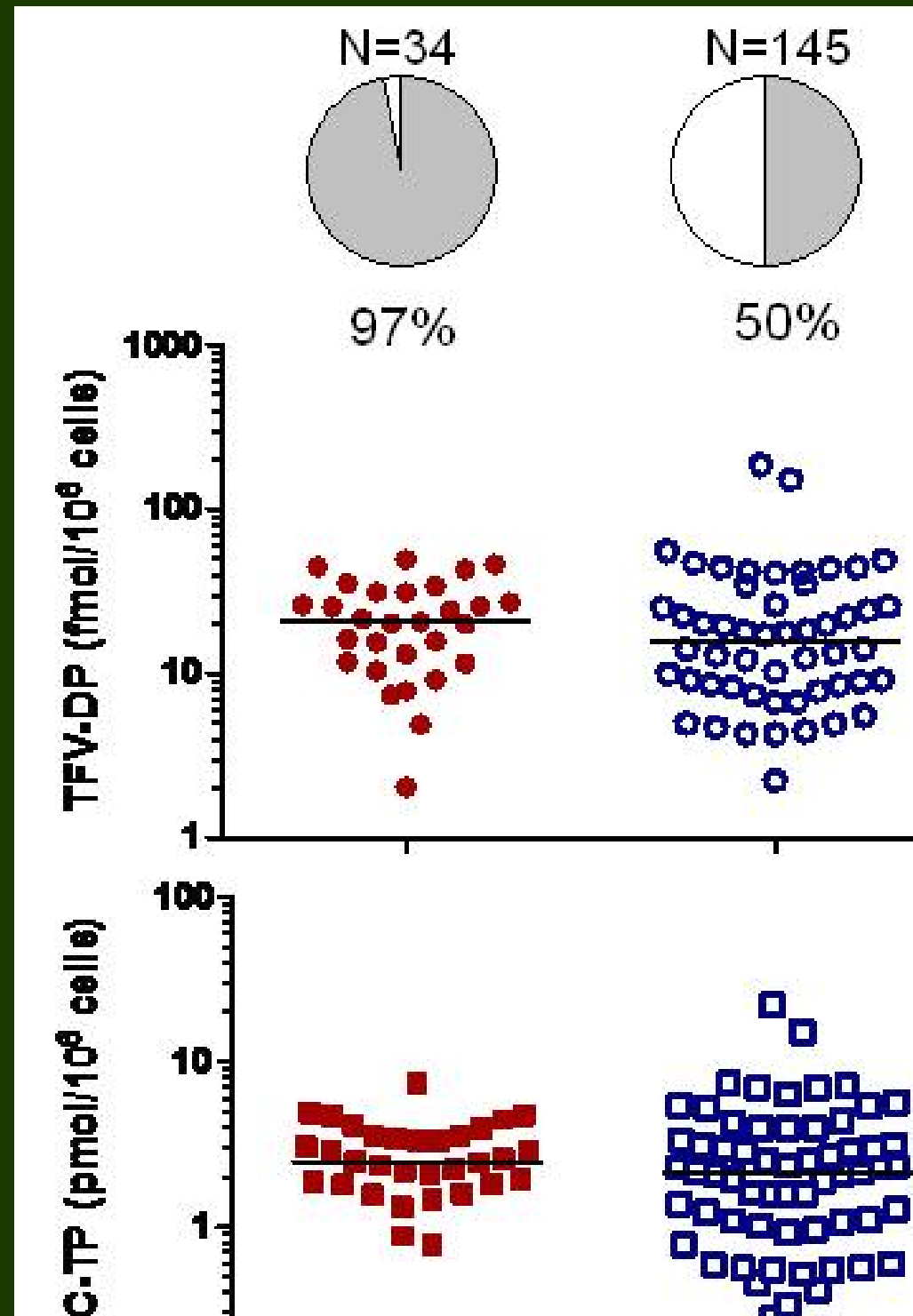


Predictors of detection - Site

The detection rate for either drug was 97% (US vs 50% non-US participants ($P < 0.0001$)).

Site viability at site was not a predictor of detection rate ($P > 0.9$).

Age, height, creatinine clearance did not explain US vs



In The USA

On PrEP **Off PrEP**

CDC Safety Study (US sites) 0 6

Daily Oral TDF vs Placebo

3 in placebo arm,

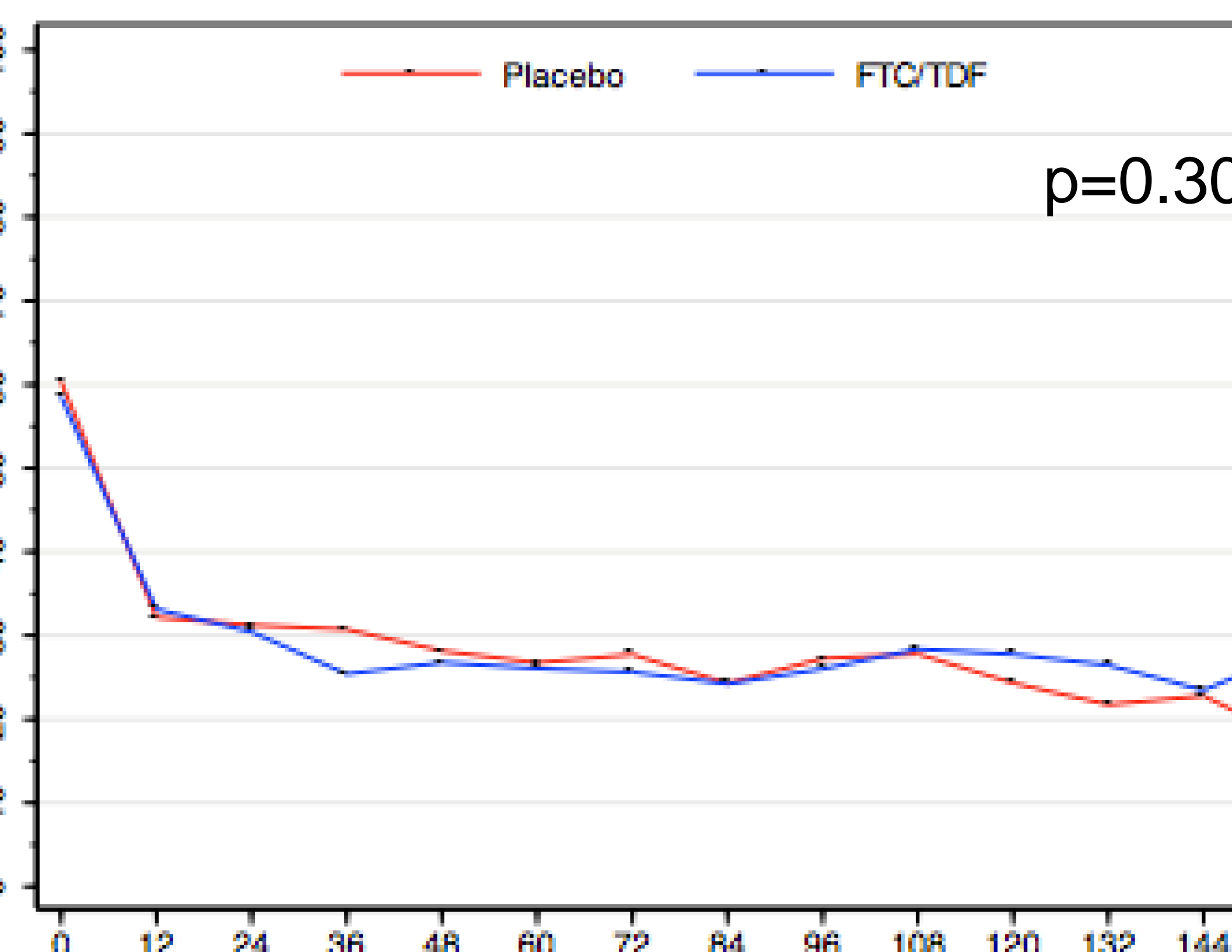
3 in deferred arm.

NIH iPrEx (US Sites) 0 3

Daily Oral FTC/TDF vs. Placebo

2 in placebo arm

1 in active arm 9 weeks after stopped drug

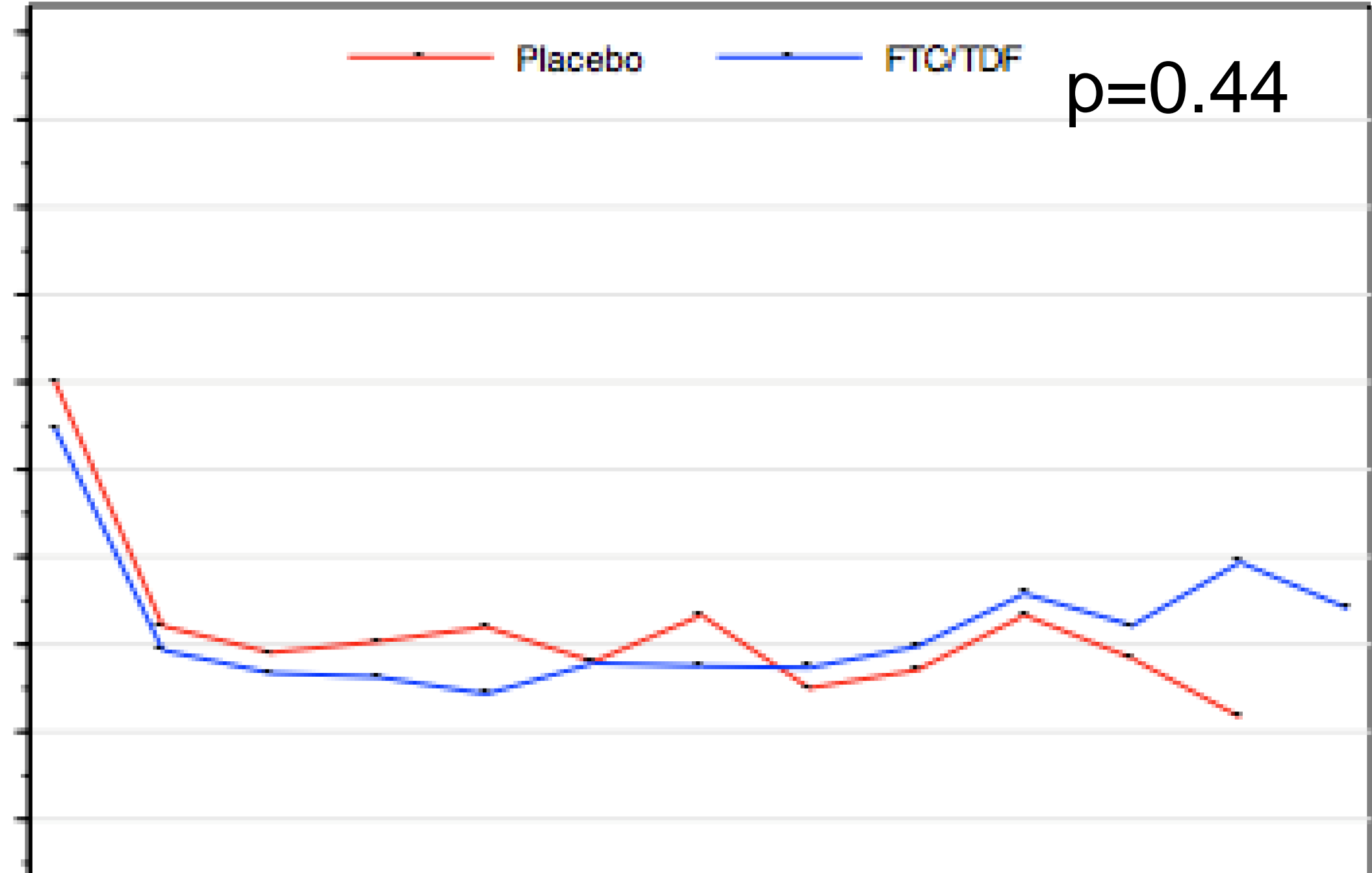


Perceived Drug Assignment

Based on Week 12 C.A.S.I.

Believe they are on...	Randomized to	
	FTC/TDF	Placebo
Placebo	115 (9%)	108 (9%)
Don't Know	791 (63%)	784 (63%)
Truvada	275 (22%)	278 (22%)
No CASI	67 (5%)	81 (7%)

Those who believed they were taking FTC/TDF



Acute HIV Infections

	Tests with RNA	Ab-,RNA+	Prevalence	Fold Change (95% CI)
Enrollment	2,499	10	0.4%	Reference
Follow-up: Placebo	11,322	12	0.1%	3.8 (1.5 to 9.5)
Follow-up: TDF	11,407	7	0.06%	6.5 (2.2 to 20.0)

Drug Resistance

Genotypic Resistance	HIV Status at Enrollment			
	Infected		Uninfected	
	Placebo N=8	FTC/TDF N=2	Placebo N=83	FTC/TDF N=48
R	0 (0%)	0 (0%)	0 (0%)	0 (0%)
E	0 (0%)	0 (0%)	0 (0%)	0 (0%)
I	0 (0%)	1 (50%)	0 (0%)	0 (0%)
V	1 (13%)	1 (50%)	0 (0%)	0 (0%)
F Resistance	0 (0%)	0 (0%)	0 (0%)	0 (0%)
C Resistance	1 (13%)	2 (100%)	0 (0%)	0 (0%)

N=10

- 5 symptomatic at enrollment
- 2 symptomatic within 1 week
- 1 anal sore
- 2 had Leukopenia

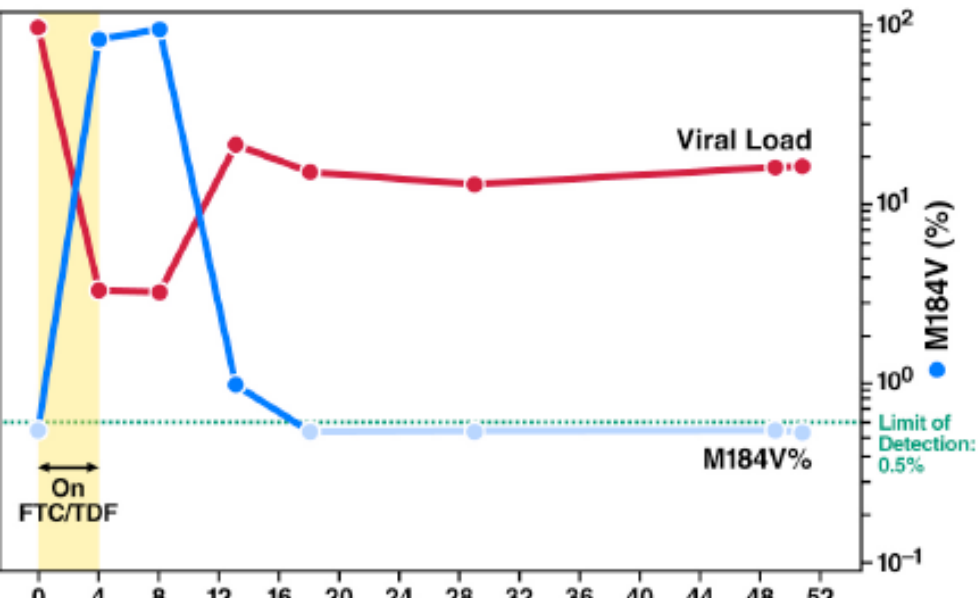
New HIV infections (91 samples tested with allele specific PCR)

- No drug resistance in participants on FTC/TDF
- 2 with minor variant drug resistance on placebo (1 to tenofovir, 1 to emtricitabine)

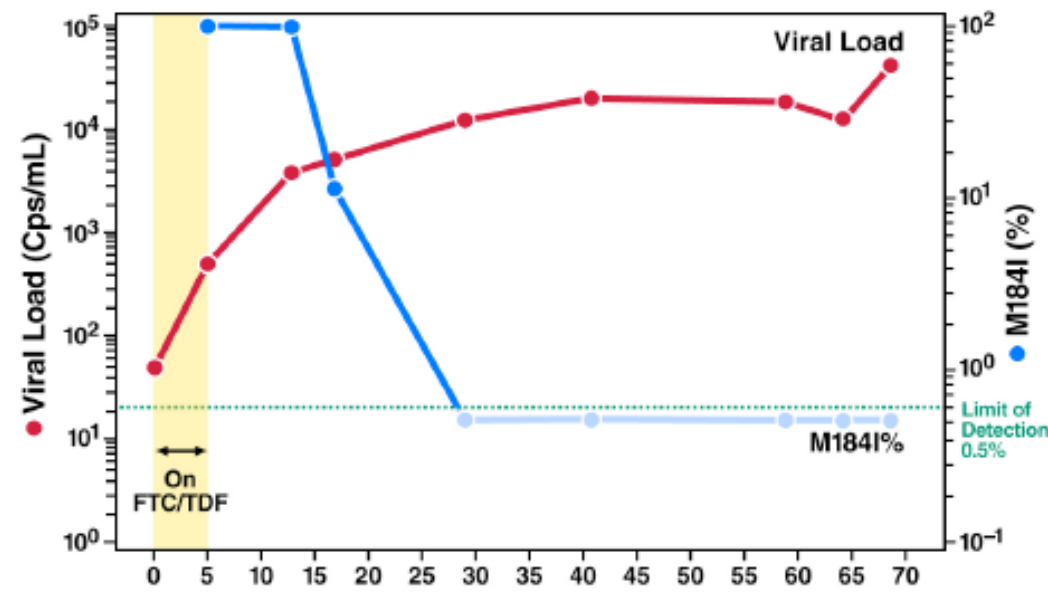
HIV infections already present at enrollment

- 2 cases of emtricitabine resistance
- Resistance dropped to $<0.5\%$ within 6 months after

FTC/TDF #1



FTC/TDF #2



With or Without PrEP

PrEP

- 2 Cases of FTC Resistance in iPrEx
- Wanes to below 0.5% within 6 months

No PrEP

- 35 HIV Infections were averted in iPrEx
- 3 to 4 would have had primary resistance
- 3 to 4 would eventually have secondary resistance

Conclusion: Not giving PrEP would allow more drug resistance than giving PrEP

10 Medical Breakthroughs

AIDS Drugs Lower the Risk of HIV Infection

191 of 500 | [View](#)

ICE PARK Thursday, Dec. 09, 2010



Antiretroviral drugs have turned the AIDS epidemic around, by thwarting virus in HIV-positive patients. But new research suggests that this powerful treatment may have another benefit - a weapon against infection in healthy individuals.

In a trial involving nearly 2,500 HIV-

Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men

- Condoms are first line of protection
 - Protect against HIV, STIs, and pregnancy
- Before Starting PrEP
 - Confirm that risk for HIV is “substantial and ongoing”
 - HIV test immediately before starting
 - Screen for Hepatitis B infection; vaccinate if susceptible
 - Verify adequate kidney function
- Prescribe
 - Daily oral FTC/TDF
- Monitor
 - Test HIV every 2 to 3 months with HIV testing
 - Test blood creatinine (kidney function) every 3 months
 - Provide risk reduction and adherence counseling
 - Check for STI symptoms, test and treat as needed
 - Test for STIs every 6 months even if asymptomatic

The Aims:

Provide Post-Trial Access in Accordance with the Declaration of Helsinki and Good Participatory Practices

Listen to PrEP users about Implementation Issues.

Learn if PrEP Use Increases When People Know The Tablet is Safe and Effective and Not a Placebo.

Learn What Happens With Sexual Practices.



Status on November 1, 2011

Site

Status

San Francisco

Enrolling

Boston

Enrolling

Cape Town

Enrolling

Chicago

Enrolling

Brazil x 3

Enrolling

Chiang Mai

Enrolling

Ecuador

Enrolling



Strategies for Improving PrEP Use

- Stop Using a Placebo
- Provide New Information
 - About Efficacy
 - About Safety
- Decide to Use PrEP
 - Everyone welcome
- “Next Step” Counseling
 - Neutral assessment,
 - Client defines the problem,
 - Problem solving,
 - Focus on barriers and facilitators
- Monitor and Discuss Drug Lev

Trials of Oral TC/TDF in Women

Sponsored by CDC, Gates, NIH, USAID (>8000 women)

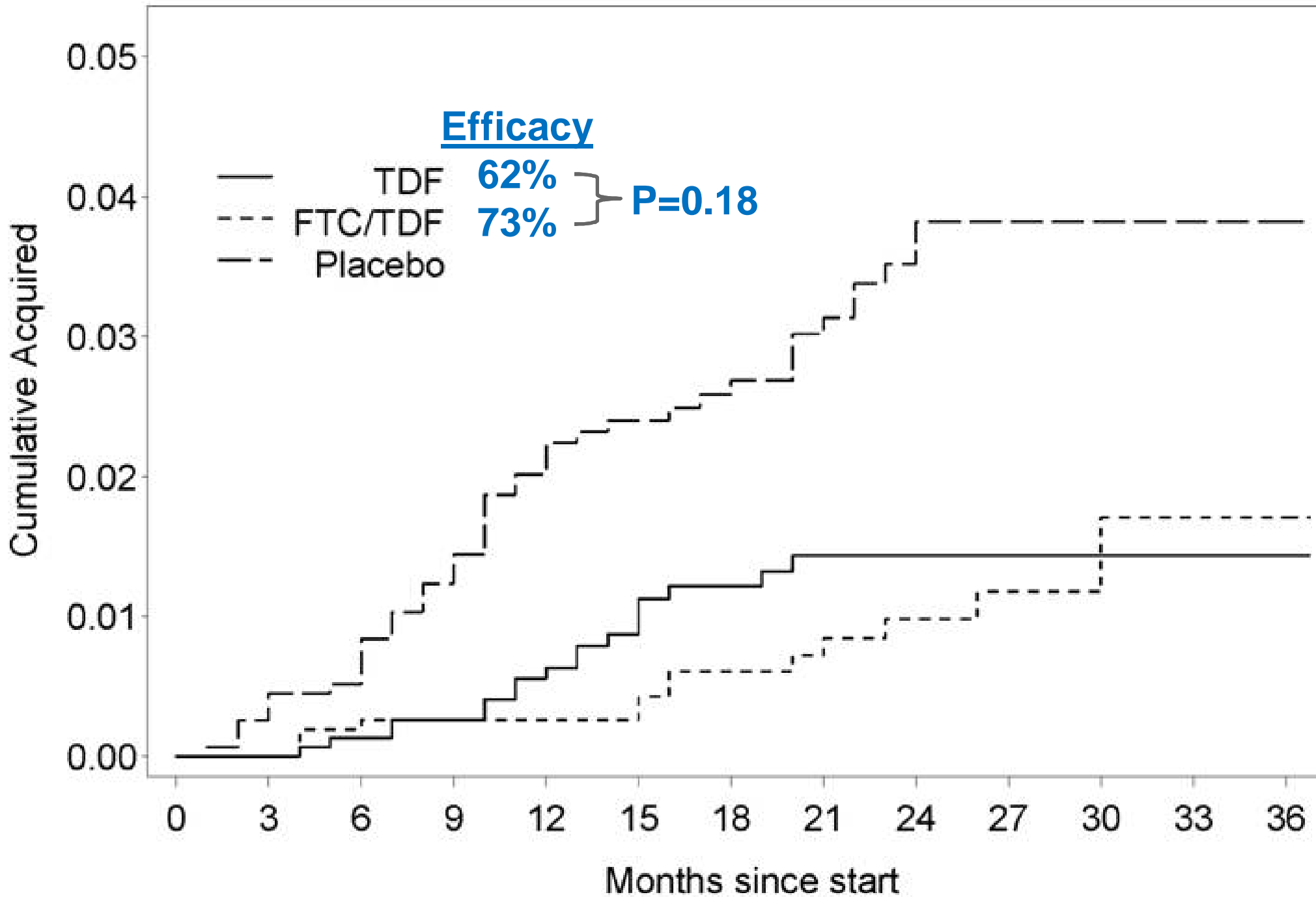


Efficacy of Daily Oral FTC/TDF/TDF

Trial	Pop.	Efficacy	95% CI
PrEx	MSM	42%	18 to 60%
Partners PrEP	Men	83%	49 to 94%
	Women	62%	19 to 82%
TDF2	Men	80%	25 to 97%
	Women	49%	-22 to 81%
TemPREP	Women	*	
VOICE	Women	**	

DSMB recommended discontinuation for futility; drug testing is in progress

*DSMB recommended stopping oral TDF; oral FTC/TDF continues



No. at risk:

	0	3	6	9	12	15	18	21	24	27	30	33	36
TDF	1573	1560	1546	1443	1292	1176	966	827	638	406	185	58	5

Better Places



From	To
Fear and stigma	HIV test
Negative HIV Test	Protective behavior
Multiple partners	Intimacy
Concordant couples	Viral suppression on treatment
Stigma and Loss to Follow-up	Retention in care
Don't ask (about sex), don't tell	Prevention for positives
Complacency	Hope and Action

Stop Spread to Let Treatment Catch Up

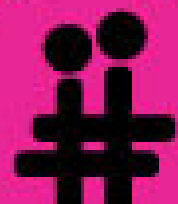
<i>Exposure</i>	<i>Intervention</i>
Discordant Couples	Early Therapy
Gestational	Suppressive Therapy
Needle	Clean Needles
Penile	Male Circumcision
Vaginal	TDF 1% Gel
Rectal	Oral FTC/TDF

THIS VALENTINE'S DAY

#LoveSafely

TWITTER.COM/UNAIDS

HIV PREVENTION



Question of Money...

is still a long haul. But AIDS can be beaten. A plague that years ago was blamed on man's promiscuity has ended up showing him in a new, more inventive and generous light."

The Economist

JUNE 4TH-10TH 2011

Economist.com

Wall Street's plumbing problem
Lady Gaga, Mother Teresa and
Brazil's boiling economy
The farce that is FIFA

The end of AIDS?



How 5 million lives
been saved, and