BIOMEDICAL STRATEGIES FOR HIV PREVENTION

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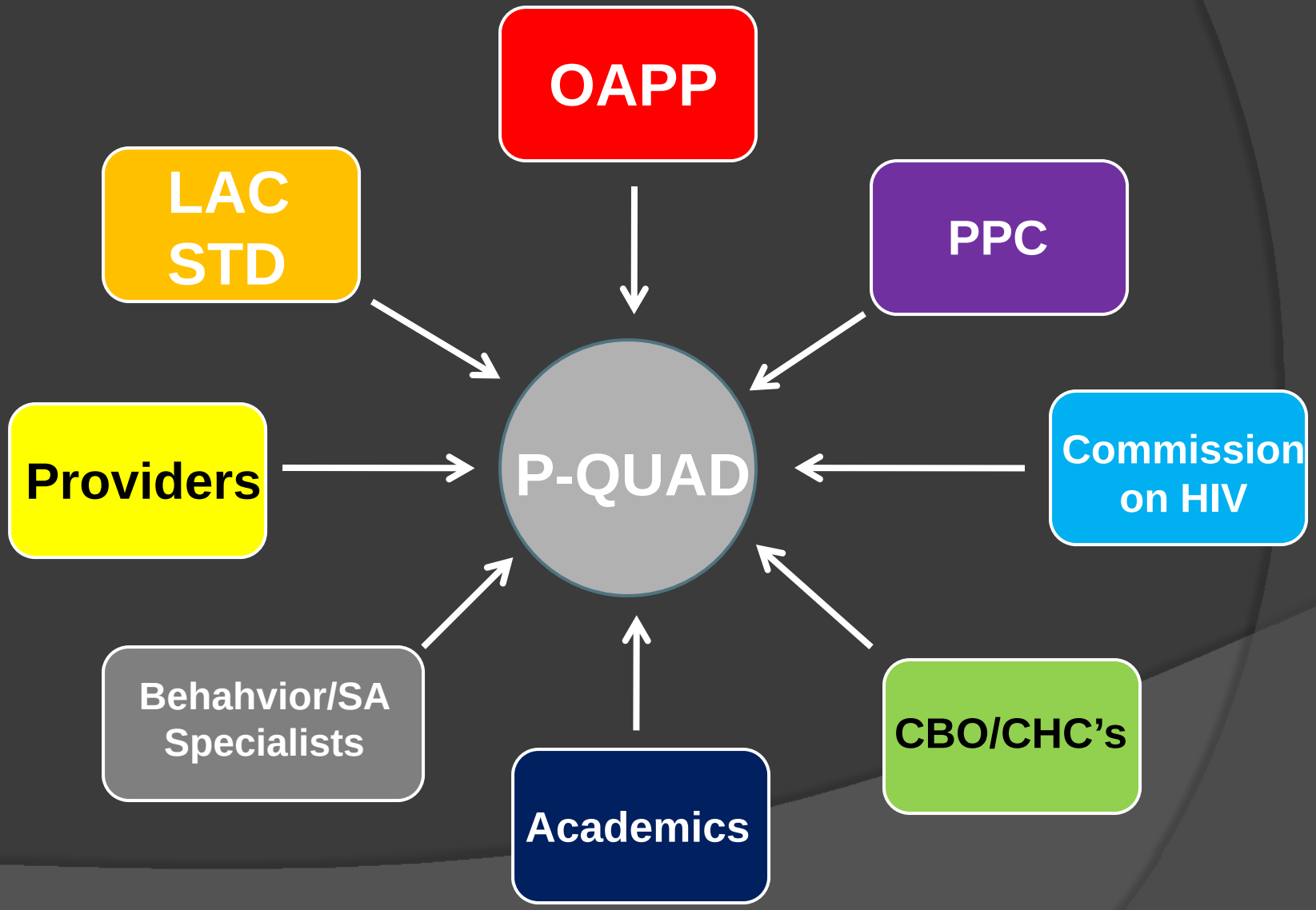
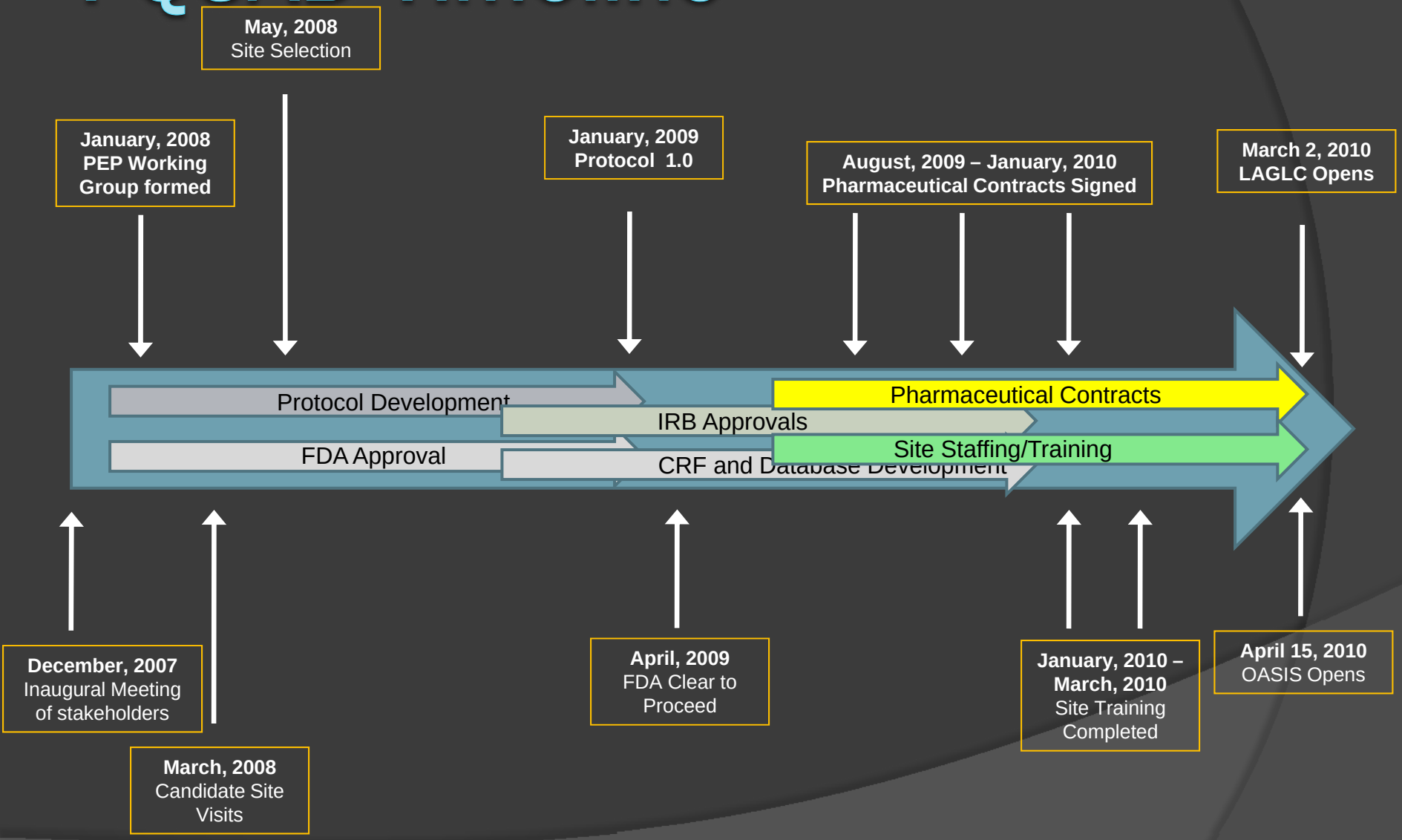
A Pilot Project to Operationalize Post-exposure Prophylaxis following Sexual Exposure to HIV in Los Angeles County

THE LOS ANGELES COUNTY P-QUAD PROJECT

P-QUAD Genesis



PQUAD Timeline



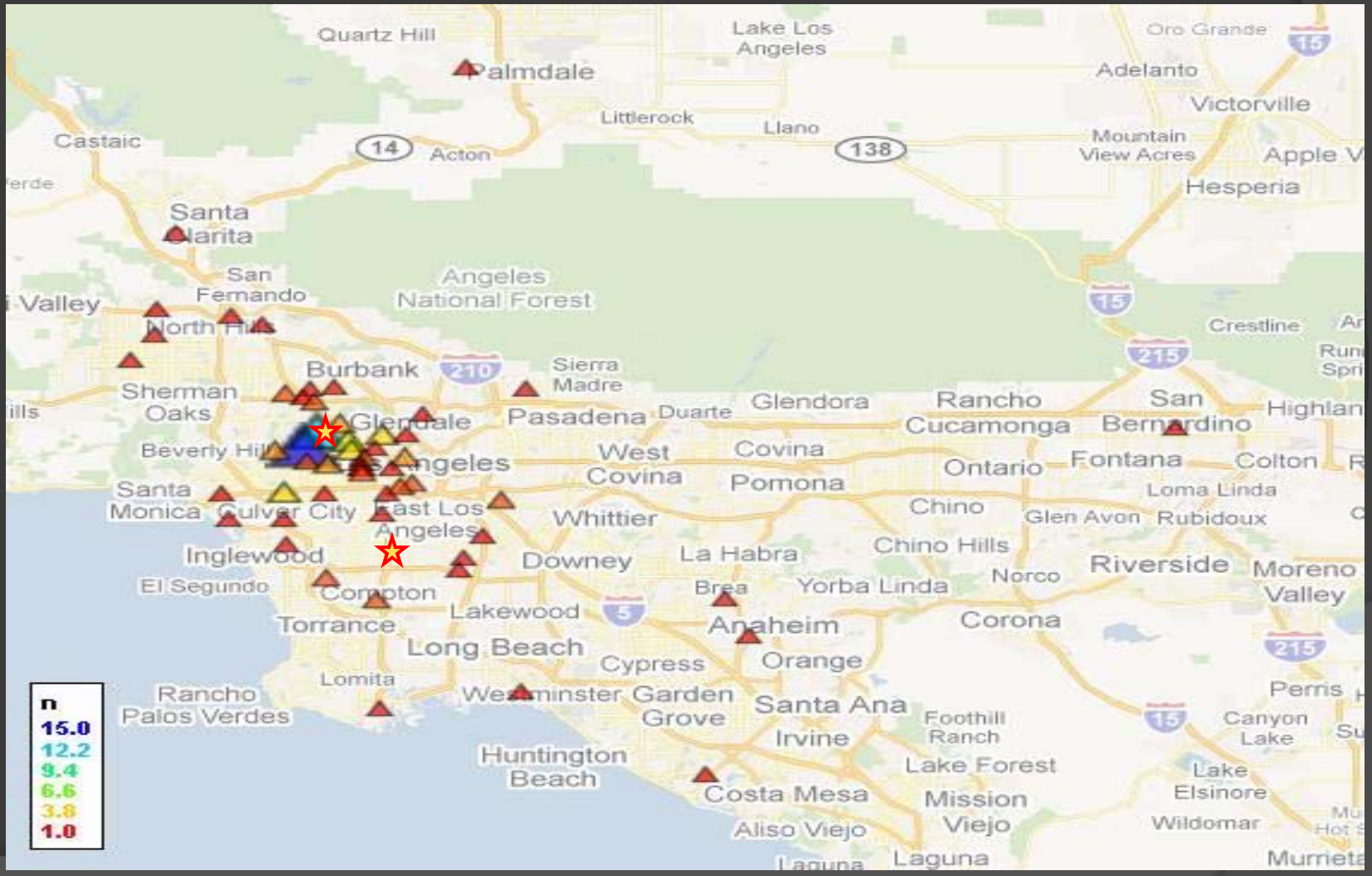
Planned enrollment

- 300 participants; 28 days of treatment
  - TDF/FTC or AZT/3TC
  - TDF/FTC + r/LPV or AZT/3TC + r/LPV
  - Additional option for TDF/FTC + RAL or AZT/3TC + RAL (option added after study initiation)
- Safety labs, serial HIV testing at 4-6 weeks, 3 months, and 6 months
- STI testing at baseline, repeat RPR at 3 months
- Substance use and behavioral assessments
- Planned transition to Public Health Service Delivery Model

As of 12/01/2010

- Totals
  - Screened 155, Enrolled 141
  - Data frozen at 112 (106 at LAGLC, 6 at OASIS)
  - 27 had already initiated PEP at another location (ED, Primary Care, AHF)
- LAGLC
  - Screened 142, enrolled 132
- OASIS
  - Screened 13, enrolled 9

Zip Codes of Residence



Demographics (N=112)

Variable	N (%)
Sex	
Male	103 (92)
Female	8 (7)
Transgender	1 (1)
Age, years	
<20	1 (1)
20-30	53 (48)
31-40	29 (26)
41-50	23 (20)
>50	6 (5)
Race/Ethnicity	
White/Caucasian	61 (54)
Black/African-American	9 (8)
Hispanic/Latino	33 (29)
Asian/Pacific Islander	4 (4)
Mixed Race/Other	5 (4)

Education and Income (N=112)

Education Level	N (%)
High School or less	24 (21)
Some College or Associates Degree	44 (39)
Bachelor's Degree	32 (28)
Advanced Degree	11 (10)
Missing	1 (1)
Family Income	
<$10,000	35 (31)
$10 – 30,000	37 (33)
$30 – 50,000	22 (20)
$50 – 75,000	10 (9)
$75 – 100,000	4 (4)
Missing	4 (4)

Insurance Status (N=112)

Health Insurance Type	N (%)
None	79 (70)
Private	26 (23)
MediCal	5 (4)
University Provided	1 (1)
COBRA	1 (1)

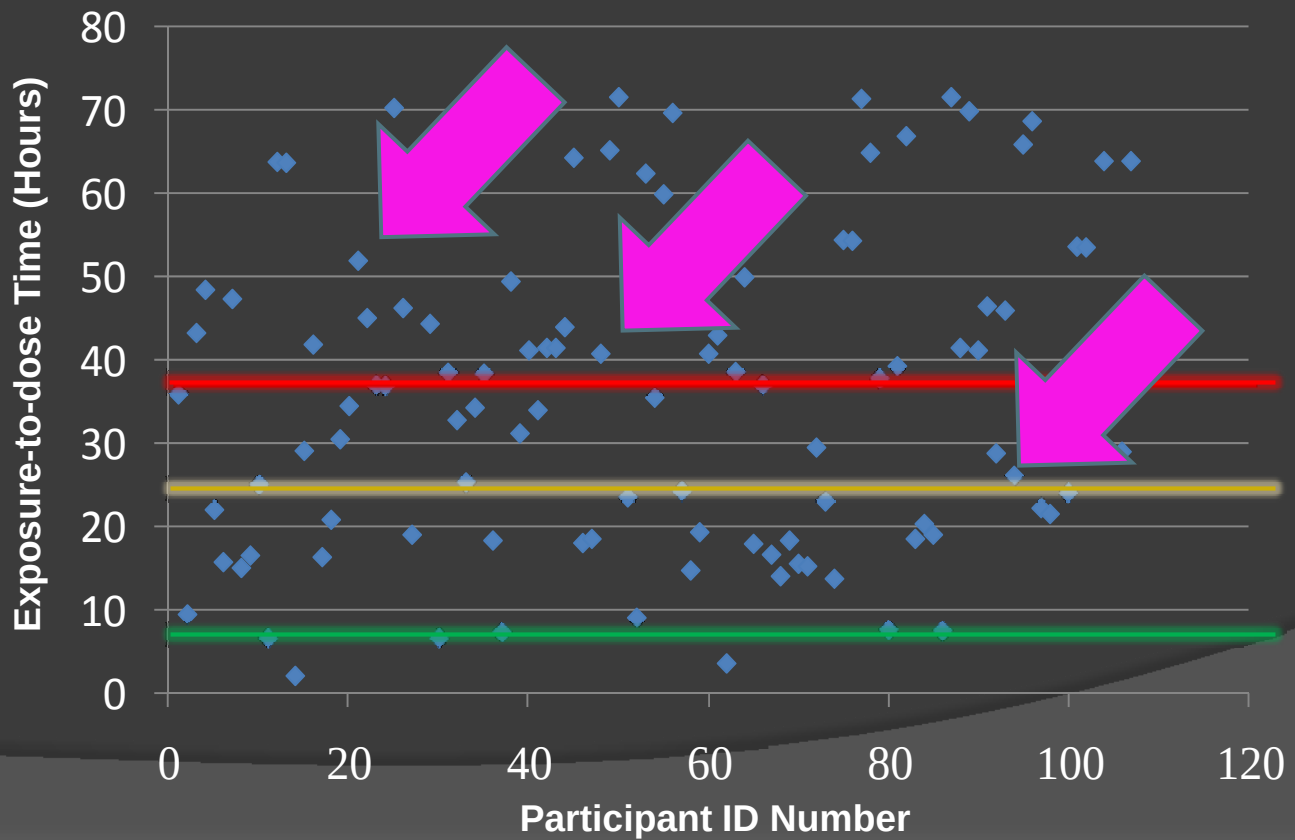
Type of Exposure

(Totals Sum to > 100% as multiple routes of exposure possible)

Exposure	N (%)
Receptive anal intercourse	67 (60)
Insertive anal intercourse	51 (45)
Receptive vaginal intercourse	8 (7)
Insertive vaginal intercourse	3 (3)
Receptive oral intercourse with ejaculation	1 (1)

Time Interval: Exposure to First Dose (n=112)

- Mean 35.63 hrs (SD 18.94)
- Range: 2 – 71.7 hrs



32 (29%) under 24 hrs

6 (5%) under 8 hrs

Regimens Prescribed (n=112)

- Nucleosides
  - Truvada (TDF/FTC) = 107(96%)
  - Combivir (AZT/3TC) = 5 (4%)

- Expanded Regimen was used in 111 cases
  - Kaletra (r/LPV) = 97 (87%)
  - Raltegravir = 14 (13%)

Baseline STI's (N=112)

All linked to treatment

Infection	N (%)
Gonorrhea*	
Urethra	2 (2)
Rectum	6 (5)
Pharynx	6 (5)
Chlamydia*	
Urethra	3 (3)
Rectum	5 (4)
Syphilis (Incident)	3 (3)
Hepatitis B	1† (1)

*In 15 unique participants: 10 mono infections, 3 dual-infections, 2 triple infections

†Particpant 4-days post-HBV vaccination – f/u HBsAg was negative, pt has not presented for HBV DNA testing due to cost

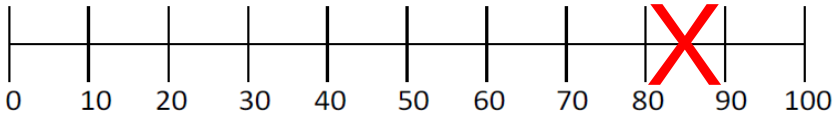
Follow up Rates: Clinical Evaluations, N = 112

Baseline	Day 14	Week 4-6	Week 12	Week 24
112/112 (100%)	101/112 (90%)	88/112 (79%)	44/86 (51%)	17/49 (35%)

Adherence by VAS

Put a mark on the line below at the point that shows your best guess about how much of your prescribed HIV medication you have taken in your first 2 weeks of treatment.

Example: 0% means you have taken no medication, 50% means you have taken half your medication, 100% means you have taken every single dose of your medication.



- 2 Week Visit
  - Mean self-reported adherence 97.7% (SD 10.92)
  - Range 10-100%
  - N=21 Missing
- 4 Week Visit
  - Mean self-reported adherence 96.4% (SD 12.8)
  - Range 0-100%
  - N=32 Missing

Discontinuation

- Six participants that have chosen to discontinue treatment
  - 4 participants reported treatment limiting AE's (fatigue, nausea, diarrhea)
  - 1 participant self-discontinued treatment when repeated HIV Elisa tests were negative
  - 1 participant never picked up 2nd set of 14 days of medication due to incarceration

Seroconversions (N=3)

- 1016 reported RAI with recently seroconverted HIV+ partner
- Interval of time from exposure to first dose = 64 hrs
- Baseline EIA negative*, week 4-6 EIA negative*, week 12 EIA positive with positive WB (p17/18, p24, gp41, p51, gp160)

- Baseline: 4/2/10 – Viral RNA not detected, <48
- Week 4: 4/30/10 – Viral RNA not detected, <48
- Week 12: 7/2/10 – 145,000 copies/mL

- Genotype with ONLY protease mutation L10I (wild type virus)
- No Baseline or 3-month STI's
- Denies repeat exposures
- 100% medication adherence reported
- Currently being linked to care

*Also NAAT negative via CDC program @ LAGLC

Seroconversions (cont'd)

- 1064 reported RAI with recently seroconverted HIV+ partner
- Interval of time from exposure to first dose = 41 hrs
- Baseline EIA negative*, week 4-6 EIA negative*, week 12 EIA positive with positive WB (p24, gp41, p55, gp120, gp160)

- Baseline: 7/13/10 – Viral RNA not detected, <48
- Week 4: 8/12/10 – Viral RNA not detected, <48
- Week 12: 10/1/10 – 32,500 copies/mL

- Genotype with A71V only (minor protease mutation)
- No Baseline or 3-month STI's
- Notes a series of exposures antecedent to sentinel exposure, outside of 72 hour window, and one IAI subsequent exposure
- 100% medication adherence reported
- Linked to subspecialty HIV care

Seroconversions (cont'd)

- 1101 reported RAI with partner who subsequent to intercourse disclosed HIV+ status
- Interval of time from exposure to first dose = 26 hrs
- Baseline EIA negative*, week 4-6 EIA negative*, week 12 EIA negative -> NAAT testing positive, repeat EIA/WB at week 14, positive

- Baseline: 9/21/10 – Viral RNA not detected, <48
- Week 4: 10/21/10 – Viral RNA not detected, <48
- Week 12: 10/1/10 – 1,370,000 copies/mL

- Genotype pending
- No Baseline or 3-month STI's
- Participant only admits oral intercourse with current (different) HIV+ partner – however partner reveals UAI
- 100% medication adherence reported at week 2, 90% at week 4
- Linked to subspecialty HIV care

Serious Adverse Events

- Two SAEs reported
  - Both involved overdoses of medicaiton
  - No clinical sequellae

EXPOSED to HIV?

WHAT IS POST PROPHYLAXIS

Post Exposure Prophylaxis (PEP) is a co
tions that can be taken after someone is
HIV infection. **PEP is NOT a "morning-a
not a cure for AIDS.** PEP is a combinatic
that **MAY** prevent HIV infection, if taken
time after possible HIV exposure. Availa
your risk of becoming HIV+ by approxin
prevent exposure to HIV in the first plac
using clean needles, reducing the numb
ner's HIV status before sex.

How does PEP work?

It takes several days for HIV infection to
drugs stop HIV from multiplying in the b
HIV-infected would then die naturally w
person who has been exposed to HIV b
hours after the exposure), this maximize
the virus from establishing itself in the b

When do I take PEP?

We think PEP is only effective if taken v
to HIV. The sooner you take PEP, the mc
becoming infected with HIV. If you wait
for PEP. Research has shown that PEP d
infection could already occur. However,

CALL: 213-351-7699

IF YOU THINK YOU MAY HAVE HAD AN EXPOSURE
WITHIN THE LAST 72 HOURS (3 DAYS)
YOU MAY BE ELIGIBLE FOR **PEP** (Post Exposure Prophylaxis)

PEP is available for people who have had a high risk exposure to HIV
(unprotected sex or needle sharing with a partner of unknown HIV status or known HIV+ status.)

PARTICIPATING SITES:

The L.A. Gay & Lesbian Center
1625 N. Schrader Blvd., L.A., CA 90028
(near Hollywood/West Hollywood)
CALL: 323-860-5880

OASIS Clinic
1807 E. 120th St., L.A., CA 90059
(near Downton/Compton)
CALL: 310-668-5131

APLA AIDS Project Los Angeles · CHIPTS · Gay & Lesbian Center · UCLA CARE

with generous support from: Abbott Labs, Gilead Sciences, GlaxoSmithKline and Merck

P-QUAD
Post-exposure Prophylaxis (PEP) Pilot Program

P-QUAD is a Pilot Project to Operationalize the Prevention Strategy of Post-exposure Prophylaxis following Sexual Exposure to HIV in combination with Educational Programming and Behavioral Risk Reduction Strategies in Los Angeles County

?

d needles with someone whose HIV
isk for being HIV infected) **OR** if you
les with someone who is HIV+, you may
der will ask you questions about your
o take an HIV test to make sure that
ou qualify, you will be prescribed 28

days and not miss any doses. If you miss
eatment may not work. Remember: no
% effective for preventing HIV infection.

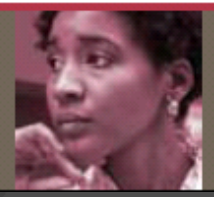
gue, vomiting, headaches and diarrhea.
EP experience side effects, however
le don't have to change or stop taking

tial will be tested for pregnancy. If you
ding immediately and transition to a
rogram.

e 28-day dose?

EP treatment, test for HIV again at 4-6
risk exposure to make sure you are not
tatus, and try not to expose yourself to

ed PEP,
7699



Slides courtesy of Bob Grant

PREP: THE iPrEx DATA

Some Thoughts on PrEP

- Strategy of administering antiretrovirals on a daily basis – regardless of exposure
  - Not entirely unlike OCPs to prevent pregnancy
- Might be particularly applicable to:
  - Serodiscordant relationships
  - Partners who cannot control condom use
  - Frequently exposed (CSW, some MSM)

Animal Models

- Suggest TDF + FTC offers better protection than TDF alone
- Effective protection from IV, rectal, and vaginal challenges
- Intermittent dosing may be possible

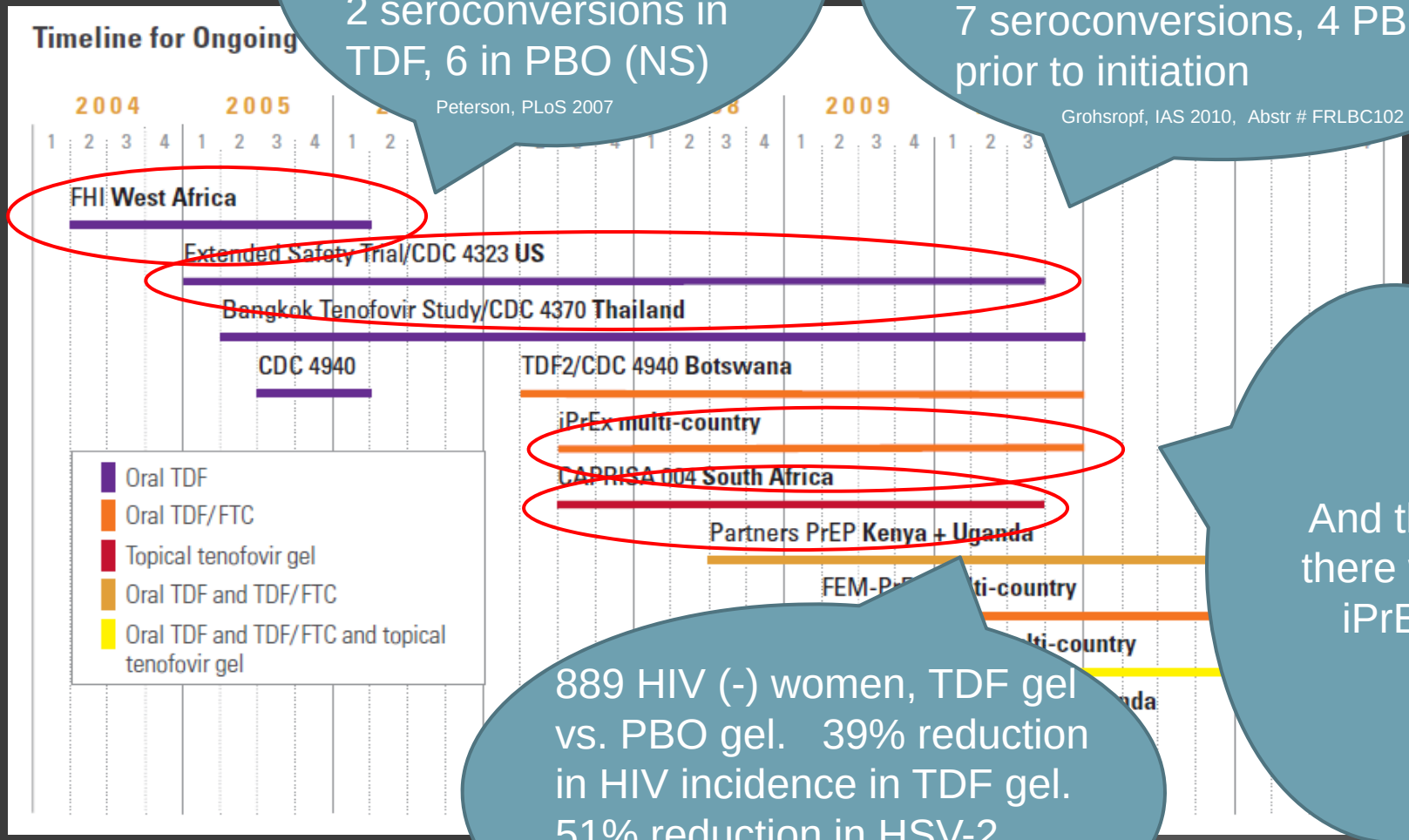
Humar

936 HIV (-) women, randomized to TDF vs. PBO daily.
2 seroconversions in TDF, 6 in PBO (NS)

Peterson, PLoS 2007

400 HIV (-) MSM, randomized to TDF vs. PBO daily, immed vs. deferred
7 seroconversions, 4 PBO, 3 prior to initiation

Grohsropf, IAS 2010, Abstr # FRLBC102



And then there was iPrEx

889 HIV (-) women, TDF gel vs. PBO gel. 39% reduction in HIV incidence in TDF gel. 51% reduction in HSV-2 acquisition.

Abdul-Karrem, Science, 2010

g/ht/d/sp/i/262/pid/262, October 6, 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

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iPrEx: Global Prevention Initiative

Enrolled	**2,499**
HIV Test and Counseling Visits	**39,613**
Baseline Partners (median, 12 wks)	**7**
Follow-up Partners (median, 12 wks)	**2**
Syphilis Cases Dx and Rx	**1,019**
Condoms distributed	**585,000**
HBV vaccine doses given	**4,533**

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Fully enrolled as of December 2009

Sites	11
Participants	2,499

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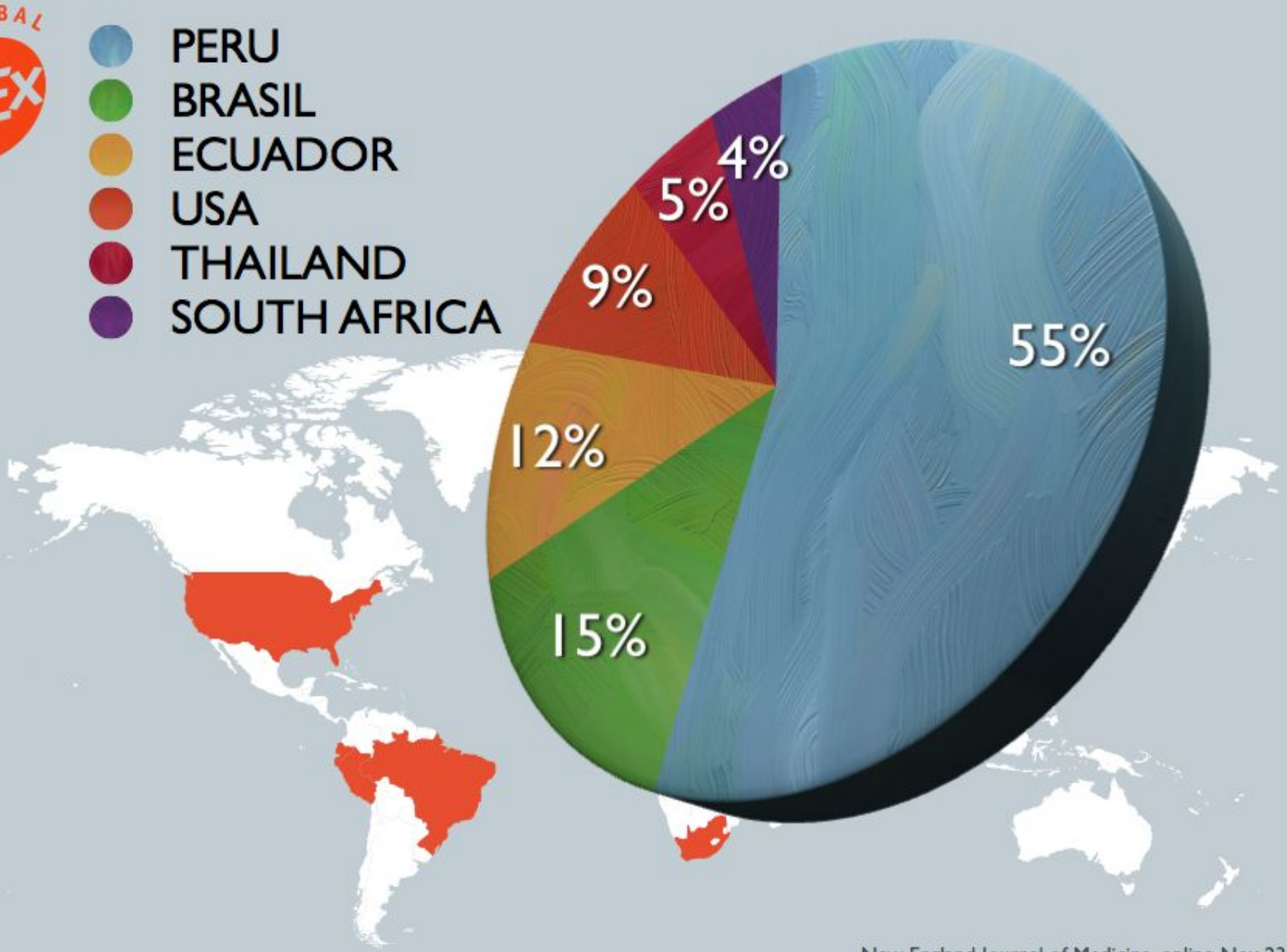
Participants	2,499



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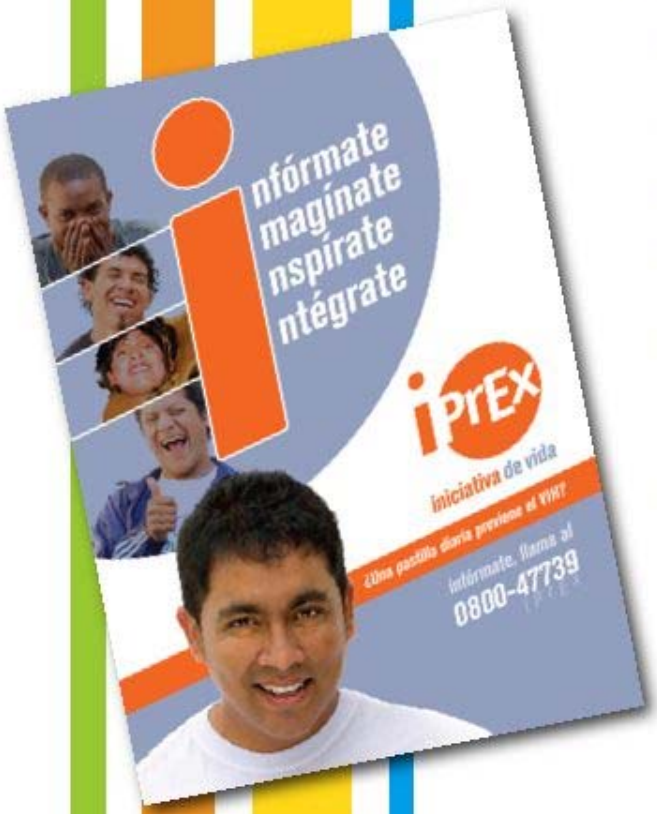
The iPrEx Study

- **High Risk MSM**
- **Randomized 1:1 Daily Oral PREP**
- **FTC/TDF vs Placebo**
- **Followed Monthly on Drug for:**
  - HIV seroconversion
  - Adverse Events
  - Metabolic Effects
  - HBV Flares among HBsAg+
  - Risk Behavior & STIs
  - Adherence
  - If Infected
    - *Drug Resistance*
    - *Viral Load*
    - *CD4+ T Cell Count*



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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 STI treatment
- PEP if requested and meet local criteria
- HBV vaccine

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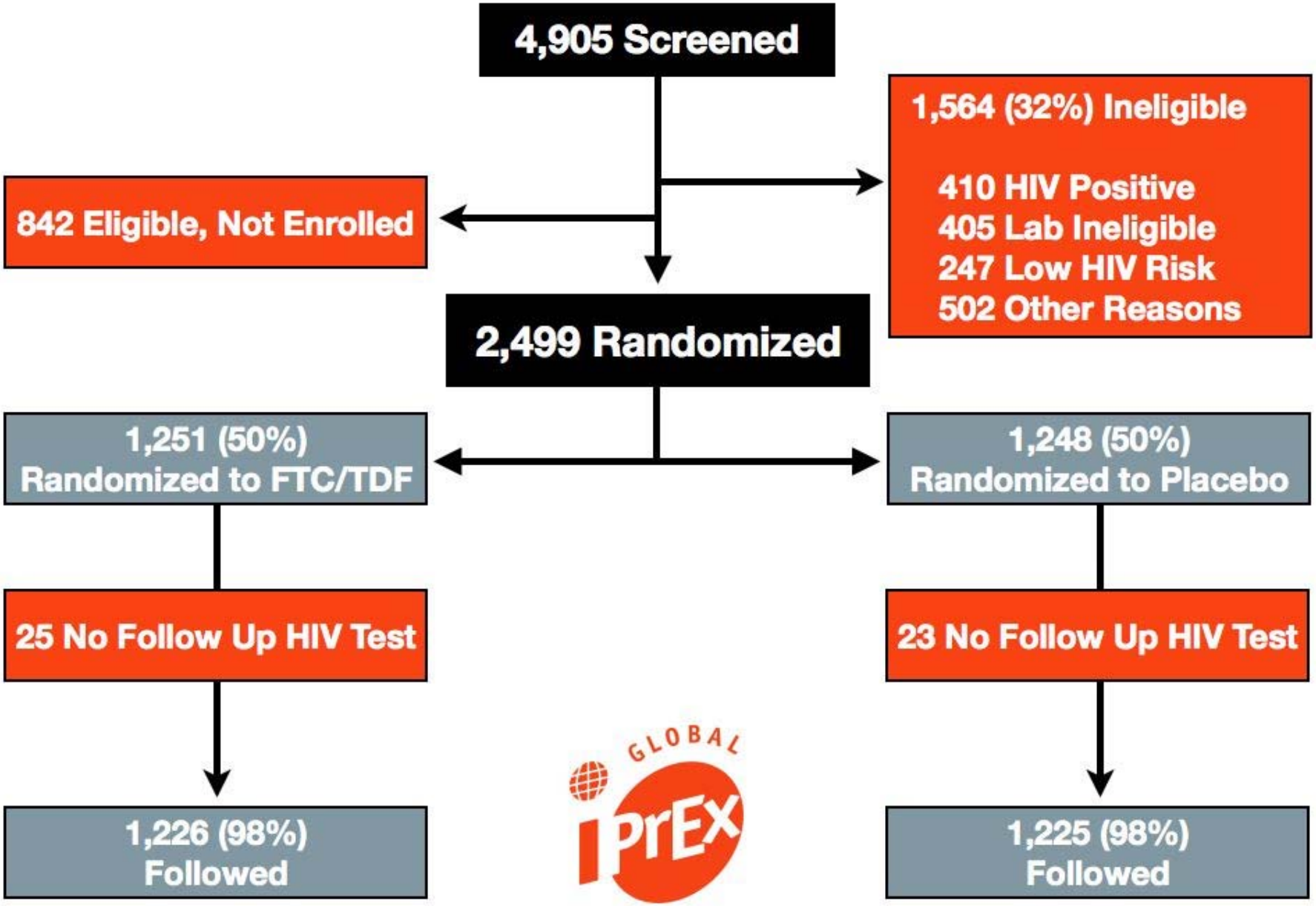

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FTC/TDF

1,226 (98%) Followed

Quarterly Visit Attendance

W12	1,075/1,194	90%
W24	984/1,116	88%
W36	882/1,019	87%
W48	759/880	86%
W60	642/719	89%
W72	516/582	89%
W84	415/646	89%
W96	343/384	89%
W108	258/283	91%
W120	147/157	94%
W132	70/75	93%
W144	6/8	75%

2 Infected at Enrollment

1,224 Followed for Seroconversion

GLOBAL iPrEx

PLACEBO

1,225 (98%) Followed

Quarterly Visit Attendance

W12	1,098/1,203	92%
W24	989/1,130	88%
W36	901/1,025	88%
W48	783/886	88%
W60	624/706	88%
W72	517/572	90%
W84	397/460	86%
W96	331/378	88%
W108	252/275	92%
W120	136/150	91%
W132	62/66	94%
W144	4/5	80%

8 Infected at Enrollment

1,217 Followed for Seroconversion

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2 Infected at Enrollment	8 Infected at Enrollment
1,224 Followed for Seroconversion	1,217 Followed for Seroconversion

Off Study During Follow -Up	199	16%
- Unable to contact	87	7%
- Participant relocated	51	4%
- Refused further participation	41	3%
- Investigator decision	11	1%
- Death	1	0%
- Other reasons	8	1%

Off Study During Follow -Up	182	15%
- Unable to contact	55	4%
- Participant relocated	59	5%
- Refused further participation	46	4%
- Investigator decision	5	0%
- Death	4	0%
- Other reasons	13	1%

FTC/TDF **PLACEBO**

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Baseline Characteristics of the Participants, According to Study Group

Characteristic	FTC/TDF	PLACEBO
Age - no. (%) P=0.04	**(n=1,251)**	**(n=1,248)**
18-24	591 (47)	662 (53)
25-29	274 (22)	241 (19)
30-39	249 (20)	224 (18)
≥40	137 (11)	121 (10)

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Baseline Characteristics of the Participants, According to Study Group

Characteristic	FTC/TDF	PLACEBO
Education Level - no. (%) P=0.26	(n=1,251)	(n=1,248)
Less than Secondary	279 (22)	244 (20)
Complete Secondary	430 (34)	453 (36)
Post-Secondary	525 (42)	539 (43)
No Answer / Missing	17 (1)	12 (1)

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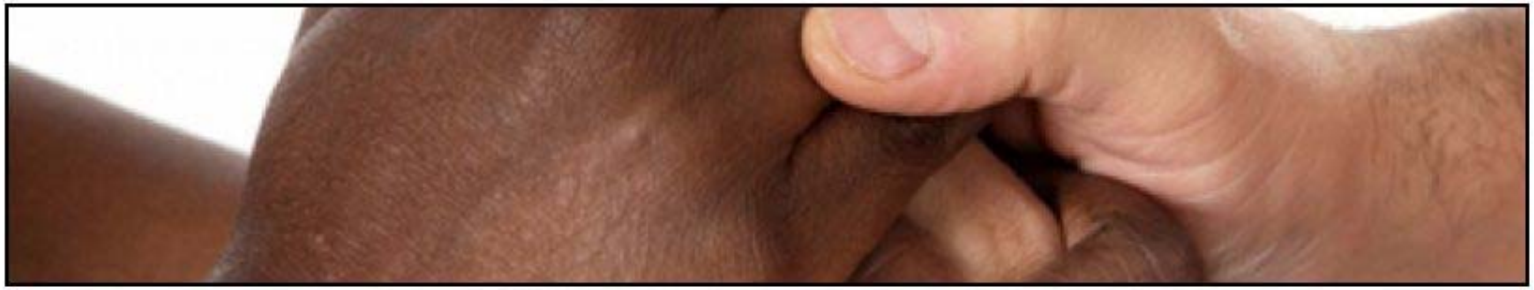
Baseline Characteristics of the Participants, According to Study Group



Characteristic	FTC/TDF	PLACEBO
Race/Ethnicity - no. (%) P=0.40	**(n=1,251)**	**(n=1,248)**
Black	117 (9)	97 (8)
White	223 (18)	208 (17)
Mixed/Other	849 (68)	878 (70)
Asian	62 (5)	65 (5)
Hispanic/Latino (any race)	900 (72)	906 (73)

iPrEx

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Baseline Characteristics of the Participants, According to Study Group

Characteristic	FTC/TDF	PLACEBO
Number of Alcoholic Drinks (on Days when Alcohol Consumed - no. (%) P=0.40	(n=1,251)	(n=1,248)
0 (in the past month)	206 (16)	184 (15)
1-4 per day	348 (28)	345 (28)
≥ 5 per day	666 (53)	687 (55)
Refused/Missing/Don't Know	31 (2)	32 (3)

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HIV Testing

39,613 visits with HIV testing

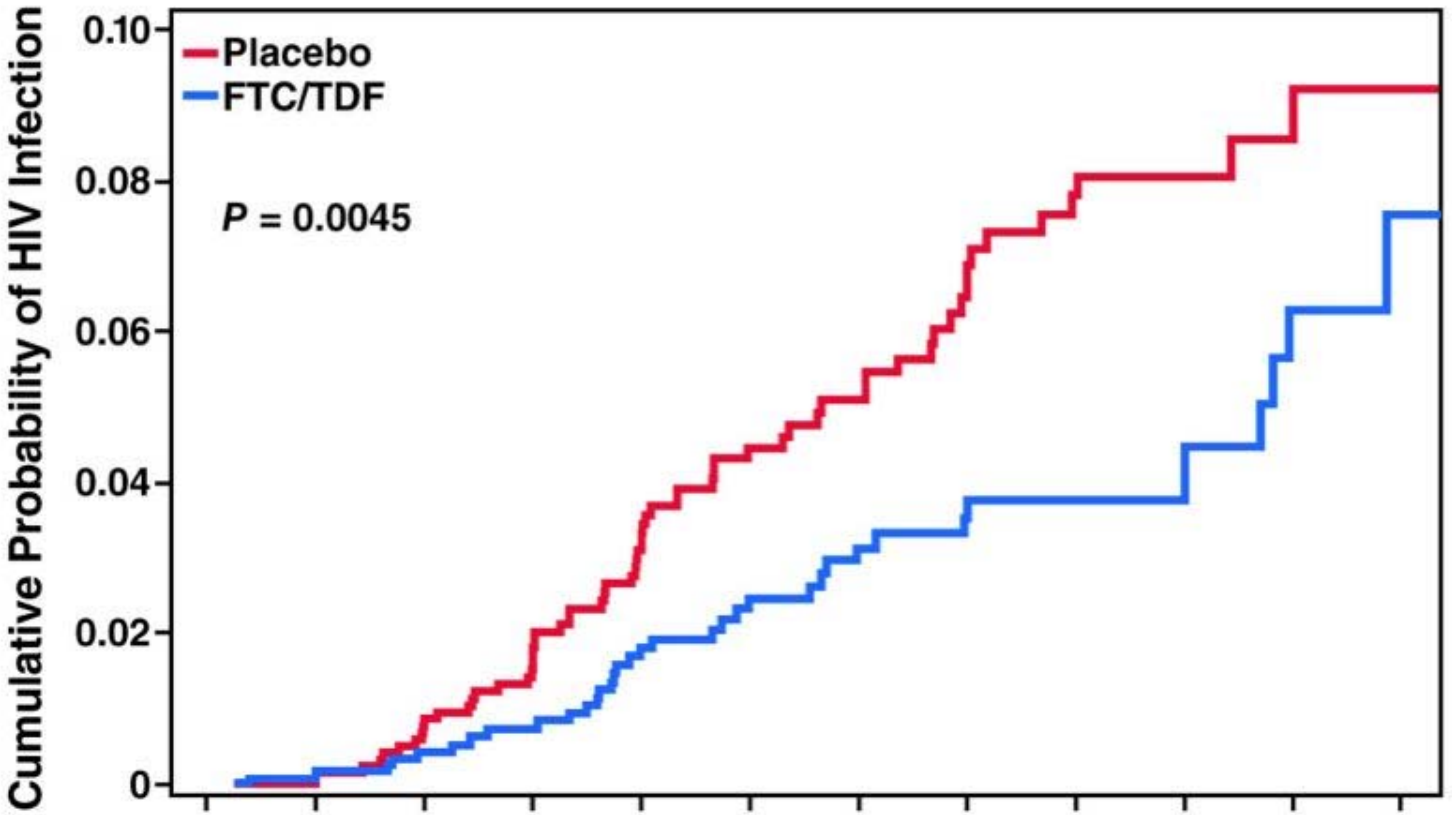
7 false positive tests in 3 people

HIV Infections

110 in total (100 incident, 10 at baseline)

At least on specimen with undetectable RNA for all incident seroconverters

Efficacy (MITT) 44% (15-63%)
Infection Numbers: 64 – 36 = 28 averted



N =												
Placebo:	1248	1194	1108	1005	852	674	546	444	370	258	137	60
FTC/TDF:	1251	1188	1097	988	848	693	558	447	367	267	147	65

10.200B2

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Summary
Efficacy of Oral FTC/TDF PrEP

	Efficacy	95% CI	P Value
Intention to Treat	47%	22-64	P=0.001
Modified Intention to Treat	44%	15-63	P=0.005
As Treated (50%)	50%	18-70	P=0.006
As Treated (90%)	73%	41-88	P<0.0006
Unprotected RAI at Baseline	58%	32-74	P<0.0006

GLOBAL PrEx

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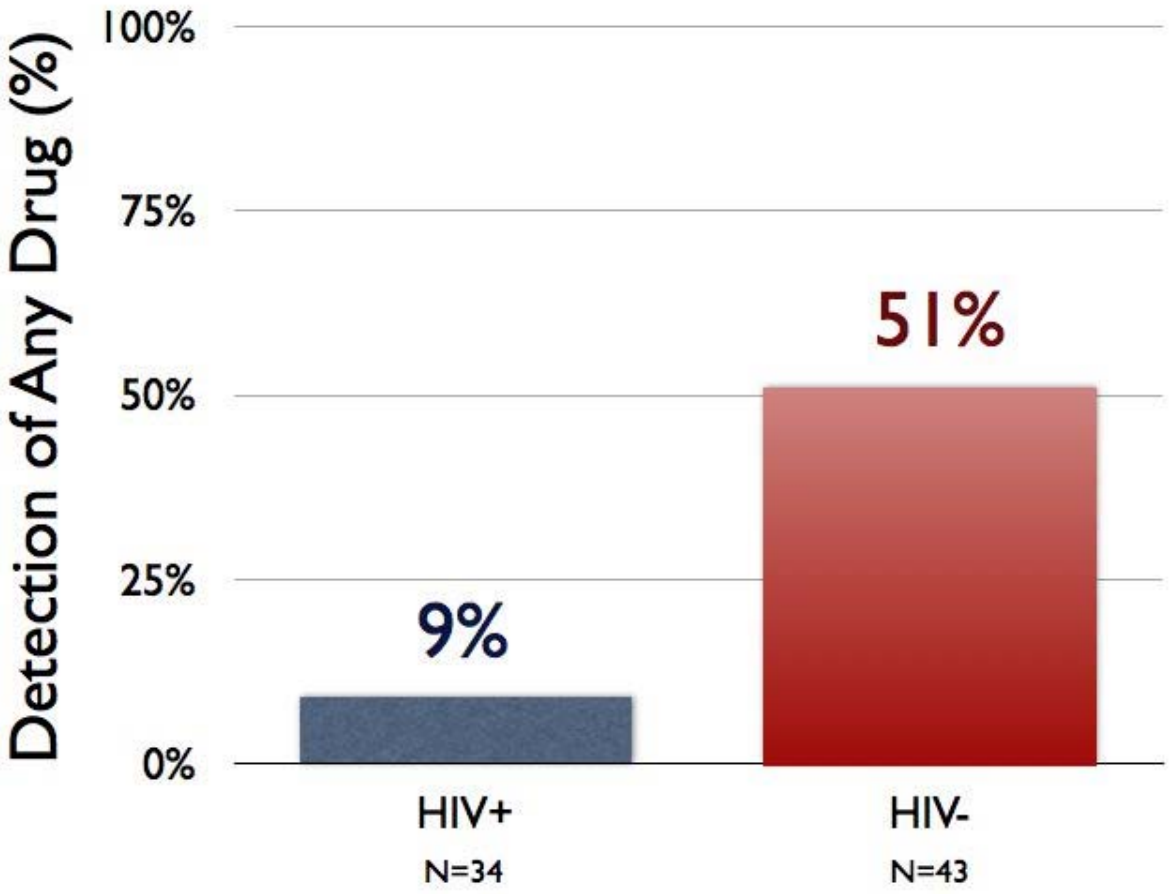
Drug Detection by HIV Status in the FTC/TDF Group



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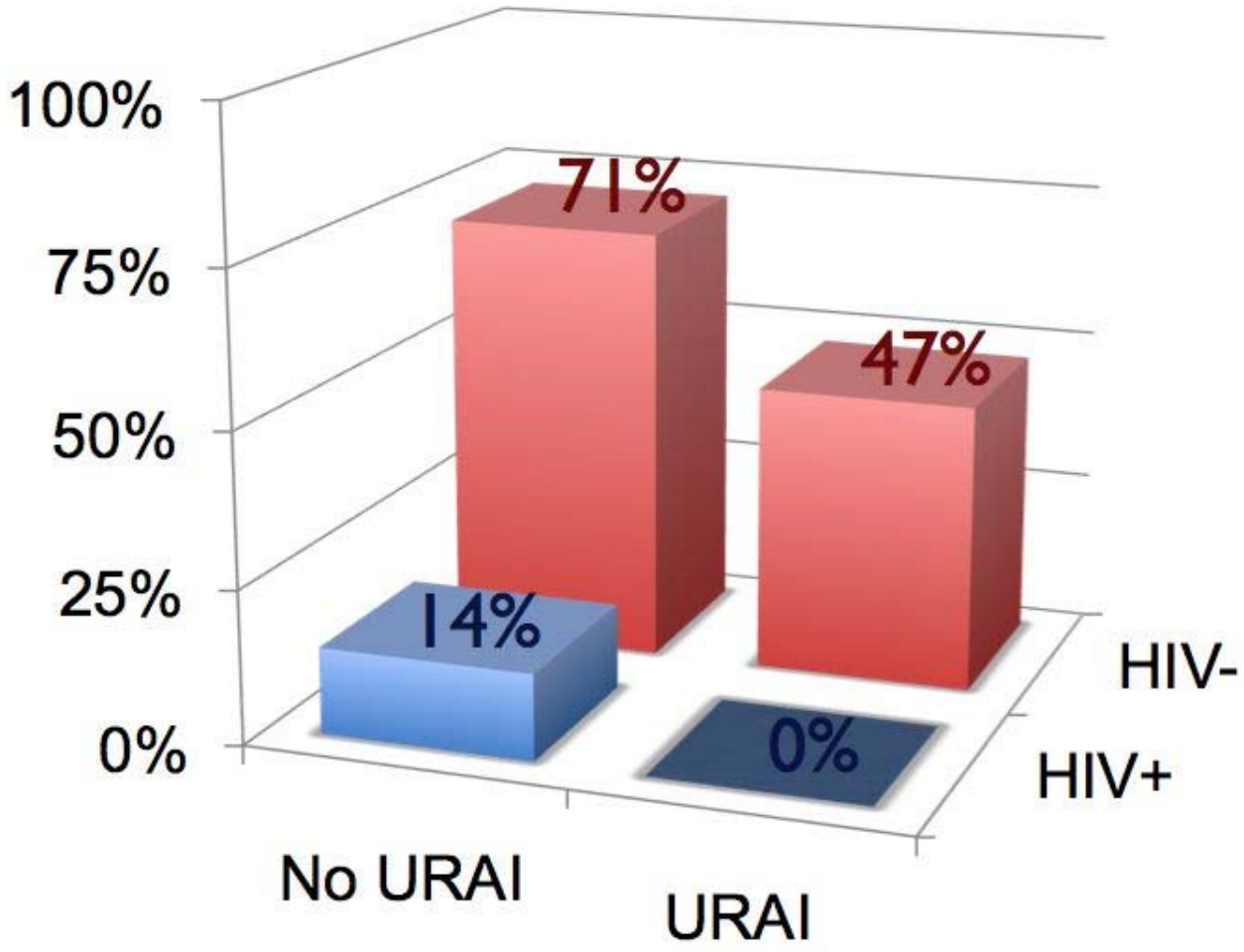
Drug Detection by HIV Status

by Unprotected Receptive Anal Intercourse (URAI)



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Drug Level And Decreased HIV Risk Ratio

- Case-control study is nested in a larger cohort
  - Matched for time on study and place
  - Conditional logistic regression used

- Strong Correlate of Protection
  - Odds ratio 12.9, P<0.001
  - **92%** reduction in HIV risk (95% CI 40-99%)

- If adjusted for URAI
  - **95%** reduction in HIV risk (95% CI 70-99%)

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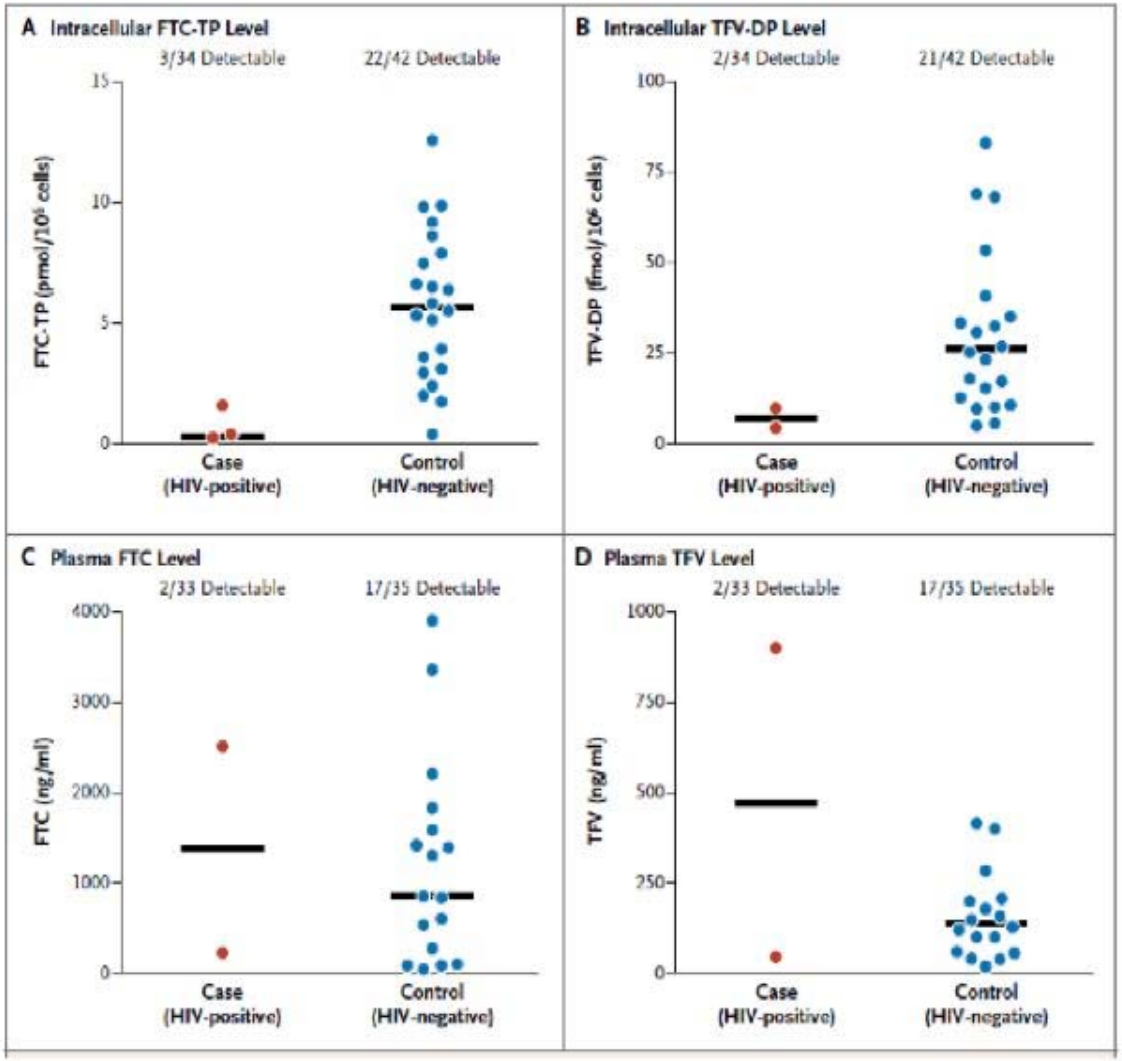
Drug Levels



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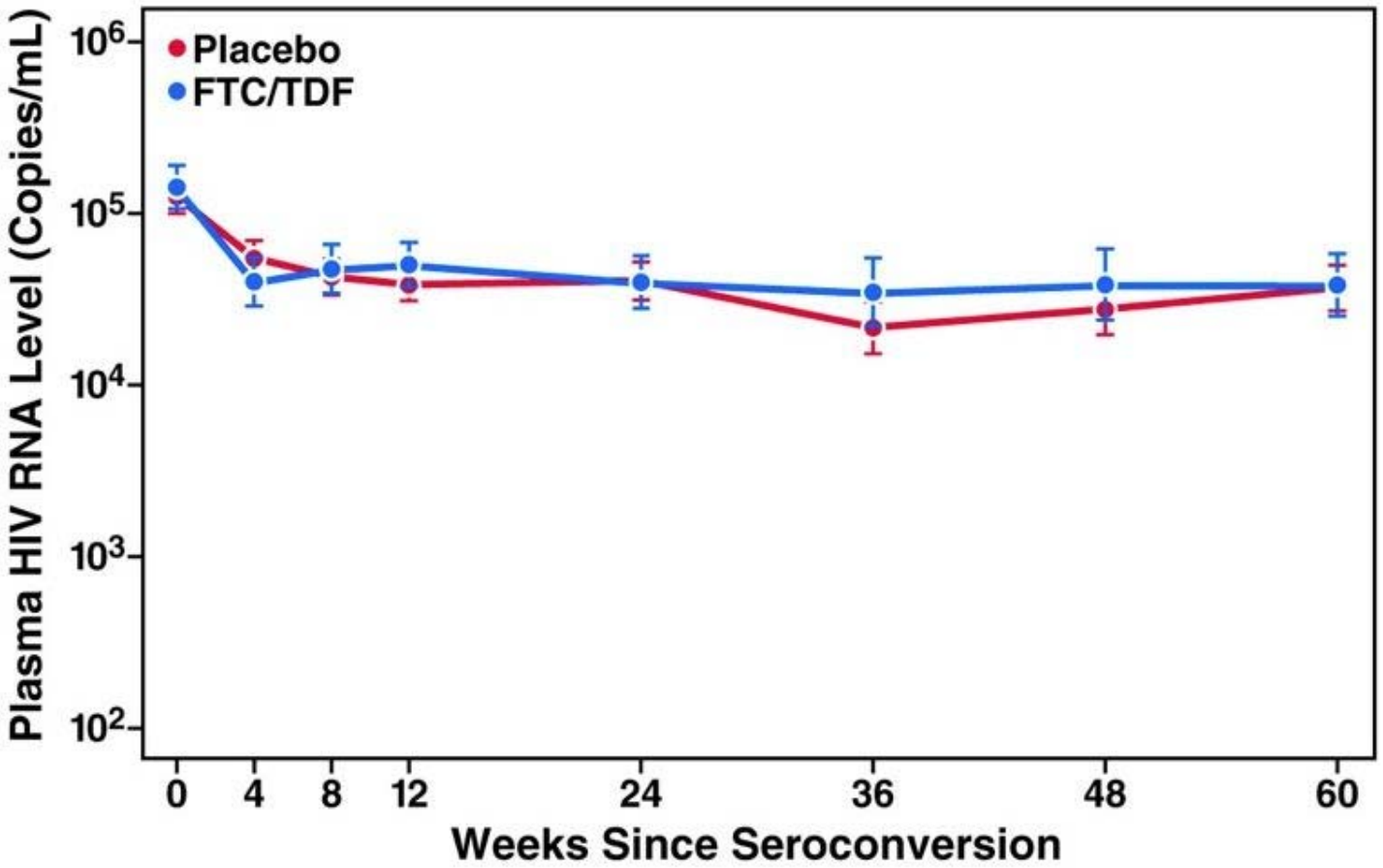
Plasma HIV Level



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REPEAT

FTC/TDF

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Drug Resistance

Genotypic Resistance	HIV Status at Enrollment			
	Infected		Uninfected	
	Placebo N=8	FTC/TDF N=2	Placebo N=64	FTC/TDF N=36
65R	0 (0%)	0 (0%)	0 (0%)	0 (0%)
70E	0 (0%)	0 (0%)	0 (0%)	0 (0%)
184I	0 (0%)	1 (50%)	0 (0%)	0 (0%)
184V	1 (13%)	1 (50%)	0 (0%)	0 (0%)
TDF Resistance	0 (0%)	0 (0%)	0 (0%)	0 (0%)
FTC Resistance	1 (13%)	2 (100%)	0 (0%)	0 (0%)

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Adverse events

Adverse Event	TDF/FTC		Placebo		P value
	n (%)	Events	n (%)	Events	
Grade 3 or Grade 4	151 (12%)	248	164 (13%)	285	p=0.51
Serious AE	60 (5%)	76	67 (5%)	87	p=0.57
Death	1 (<1%)	1*	4 (<1%)	4	p=0.18

*Motorcycle accident

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Adverse events

Adverse Event	TDF/FTC		Placebo		P value
	n (%)	Events	n (%)	Events	
Creatinine Elevated	25 (2%)	28	14 (1%)	15	p=0.08
Headache	56 (4%)	66	41 (3%)	55	p=0.10
Nausea	20 (2%)	22	9 (<1%)	10	p=0.04
Weight Decreased	27 (2%)	34	14 (1%)	19	p=0.04

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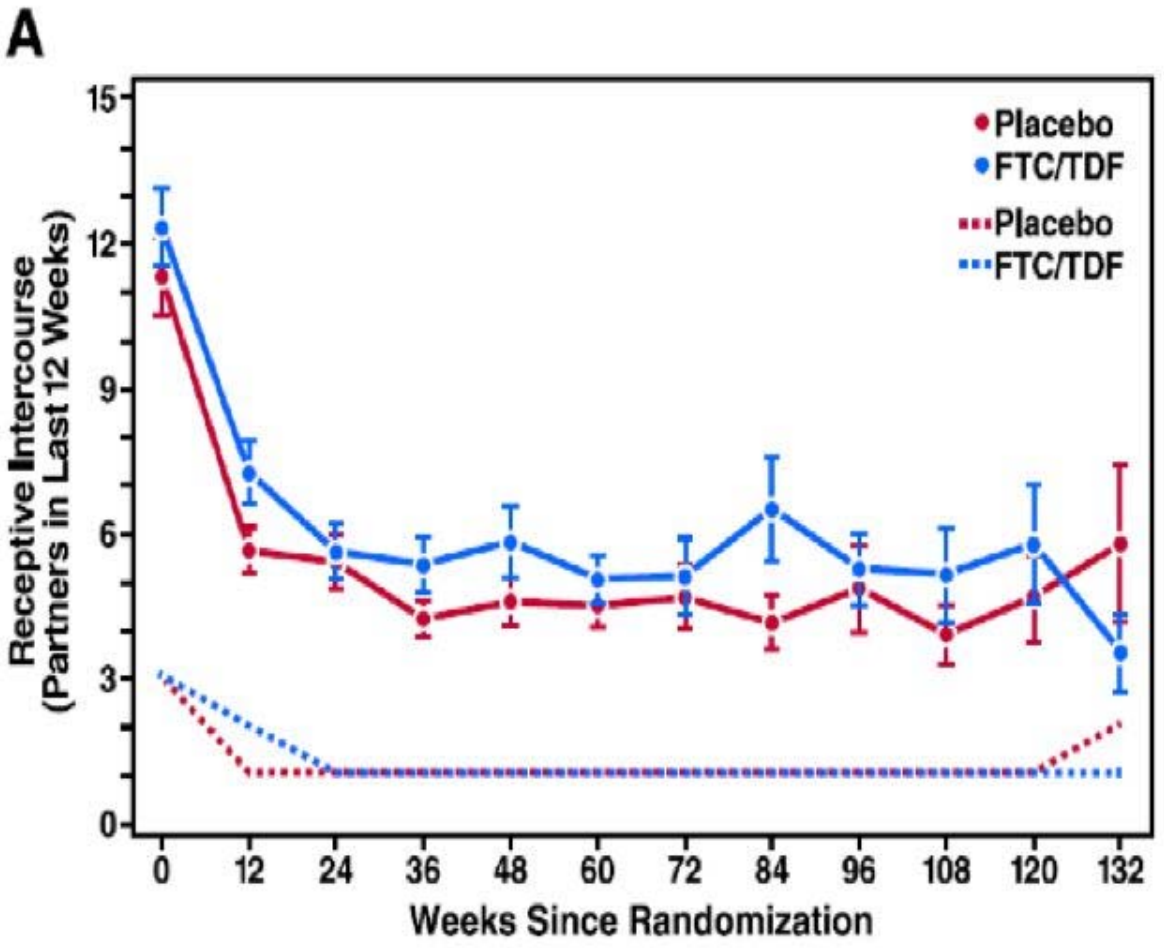
Sexual Partners



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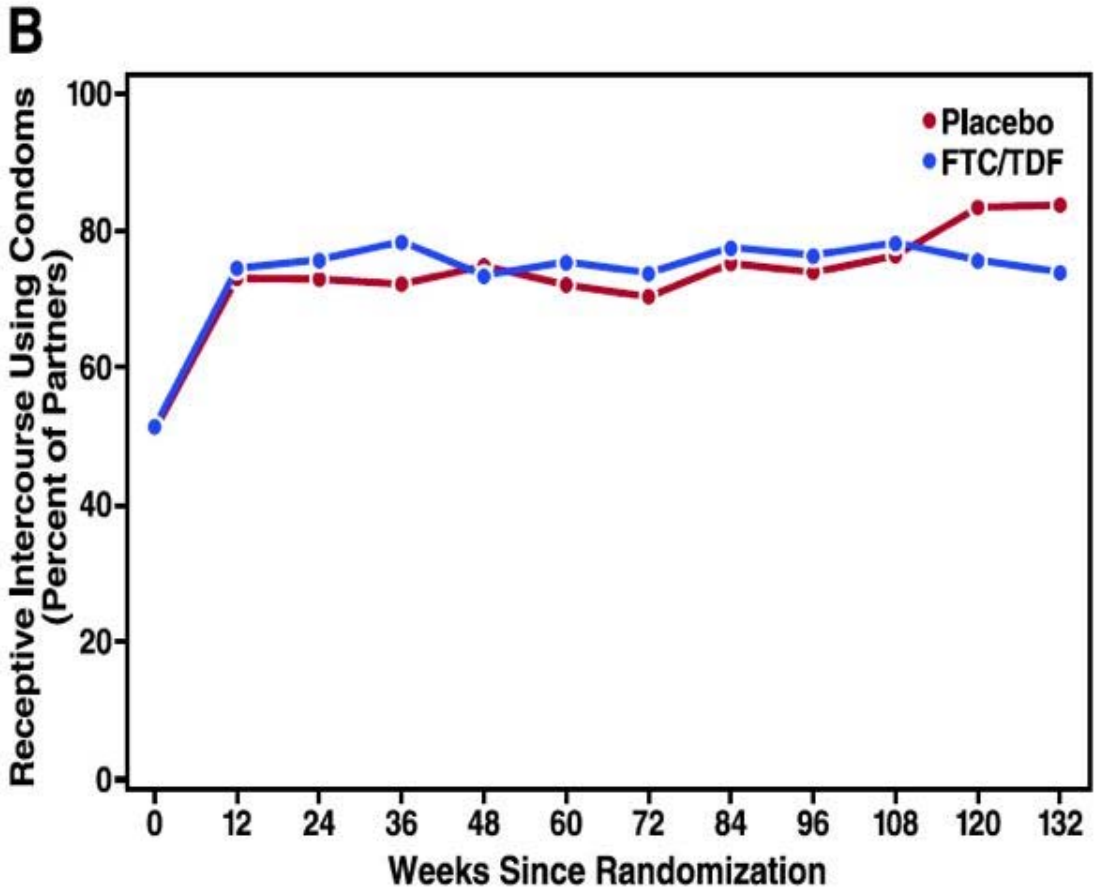
Condom Use with High Risk Sex



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Conclusions: Efficacy

Oral FTC/TDF PrEP provided additional protection against the acquisition of HIV infection among MSM receiving a comprehensive package of prevention services.

Detectable drug in blood strongly correlated with the prophylactic effect.

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Conclusions: Safety

There was no moderate or severe toxicity.

Nausea and unintentional weight loss were more common in the first few weeks of FTC/TDF use, occurring in less than 1 in 10.

FTC resistance occurred when FTC/TDF was started in people who were already HIV infected.

FTC and TDF resistance did not occur among those infected after PrEP started.

Open Label Extension

Sponsored by

NIH/NIAID/DAIDS

with drug donated by

Gilead Sciences

Premise

Sexual and pill taking behavior are significant determinants of PrEP effects in practice

Information about PrEP safety and efficacy could affect behavior

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GLOBAL iPrEX

The iPrEx Study: Safety, Efficacy, Behavior, and Biology

Questions/Comments?

THANK YOU!

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