Cabotegravir Maintains Protective Efficacy in the Setting of Bacterial STIs: HPTN 083

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HPTN HIV Prevention Trials Network

CROI 2024

Background

- Bacterial sexually transmitted infections (STIs) facilitate HIV transmission and acquisition
- Mucosal inflammation and genital ulcers can lower the barrier to HIV infection
- It is important to determine whether STIs diminish efficacy of each pre-exposure prophylaxis (PrEP) agent

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Wasserheit JN. Sex Transm Dis. 1992; 19:61–77; Cohen, et al. Int AIDS Soc. 2019 Aug,22 Suppl 6:e25355.

Clement ME, et al. Abstract #131. March 4, 2024.

Background

- Prior studies: STIs do not attenuate the protection offered by tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) for HIV PrEP
- No such evaluations have been conducted for long-acting injectable cabotegravir (CAB-LA)

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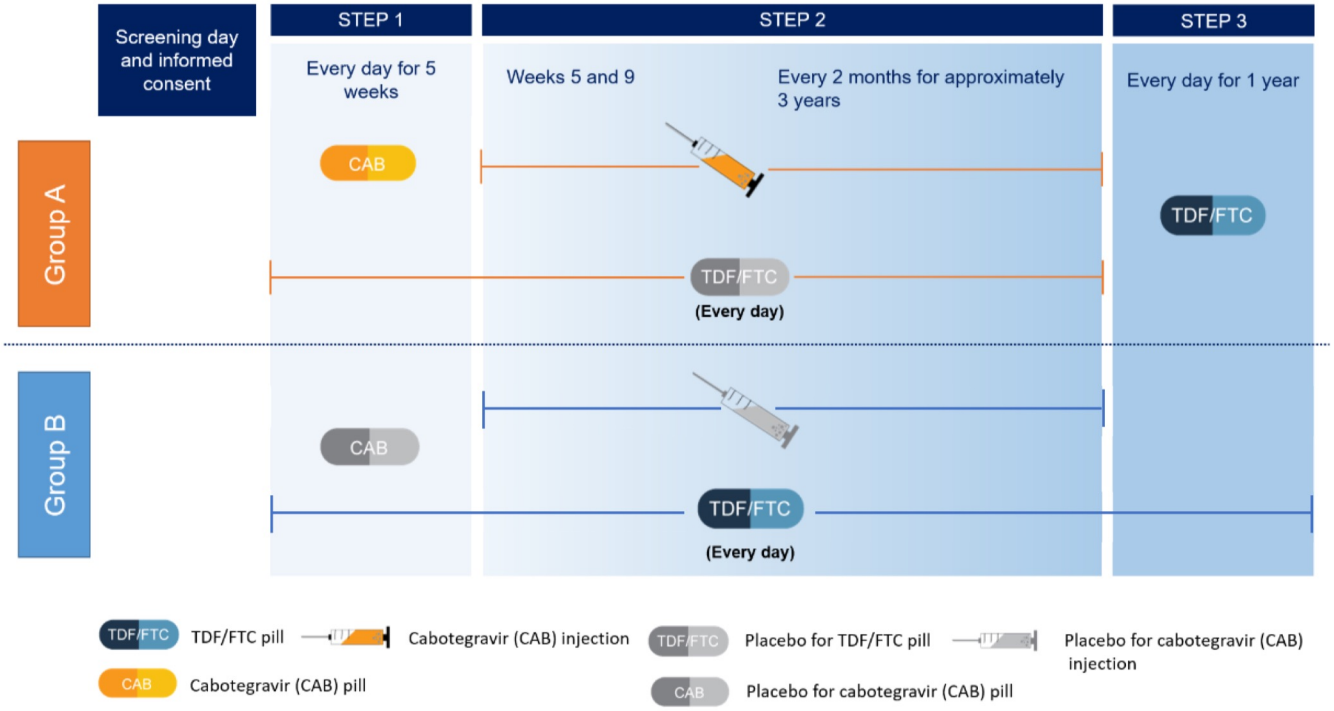
Solomon et al, Clin Infect Dis. 2014 Oct;59(7):1020-6; Murnane et al. AIDS. 2013 August 24; 27(13).

Clement ME, et al. Abstract #131. March 4, 2024.

Background



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Landovitz RJ, et al. N Engl J Med. 2021;385:595-608.

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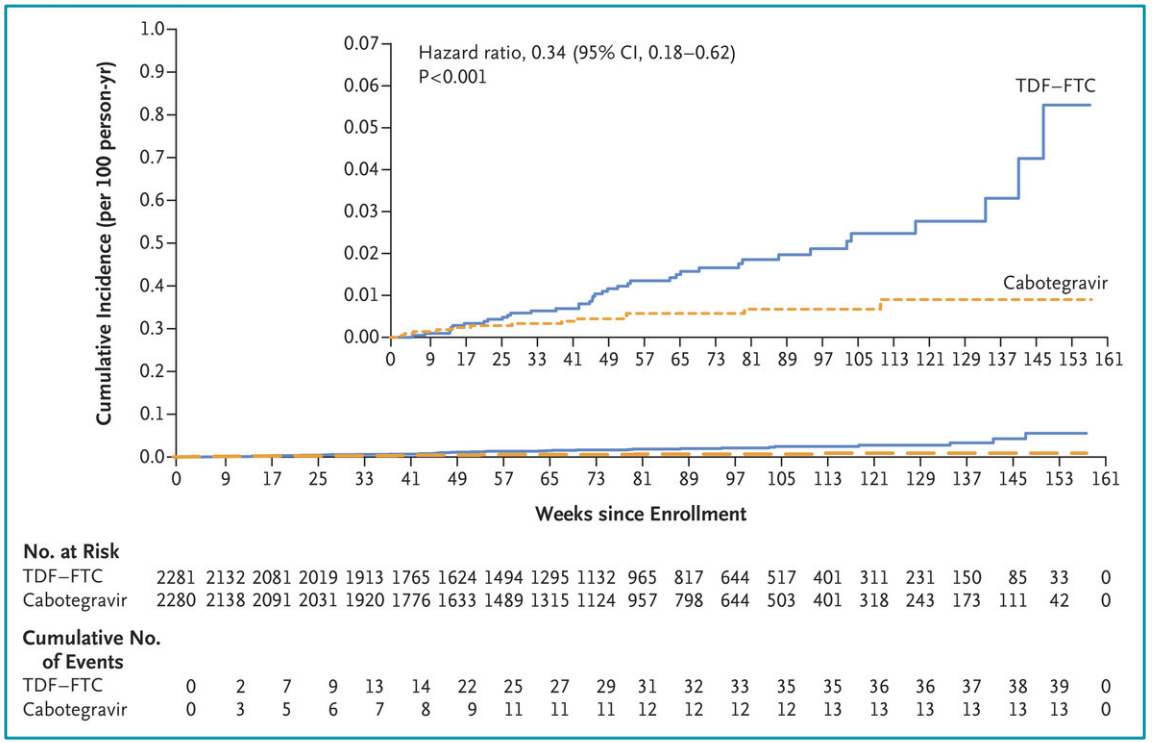

No. at Risk																					
TDF–FTC	2281	2132	2081	2019	1913	1765	1624	1494	1295	1132	965	817	644	517	401	311	231	150	85	33	0
Cabotegravir	2280	2138	2091	2031	1920	1776	1633	1489	1315	1124	957	798	644	503	401	318	243	173	111	42	0

Cumulative No. of Events																					
TDF–FTC	0	2	7	9	13	14	22	25	27	29	31	32	33	35	35	36	36	37	38	39	0
Cabotegravir	0	3	5	6	7	8	9	11	11	11	12	12	12	12	13	13	13	13	13	13	0

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Clement ME, et al. Abstract #131. March 4, 2024.

Methods

- Secondary analysis using data from HPTN 083 blinded period
- Serologic testing for syphilis and NAAT for rectal and urethral gonorrhea and chlamydia every 6 months, and with reported symptoms or exposures
- New syphilis infections were centrally adjudicated, as was date of first HIV diagnosis

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Methods

- Two analyses were conducted:
  - Association between baseline characteristics and STI incidence
  - CAB-LA maintenance of efficacy in the setting of bacterial STIs
- STI Incidence analysis: excluded those without follow-up STI testing
- Efficacy analysis: included those with baseline STI testing but without follow-up STI testing

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Methods: STI Incidence Analysis

- Incident STI infections per 100 person-years (PY), calculated from enrollment to last STI testing
- Rates were calculated by demographic characteristic:
  - Age, race, ethnicity, gender cohort, education, treatment arm, drug use, alcohol use, region, condom usage, partner number, marital status, and baseline STI.
- Poisson regression to model the association between baseline factors and STI incidence

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Methods: Maintenance of Efficacy

- Cox proportional hazards modeling with STI status as a time-varying covariate
    - Potential interactions between STI status and the relative efficacy of CAB-LA vs. TDF/FTC
- Each time interval between STI tests was classified as “STI-positive” or “STI-negative”

- We conducted a base case analysis and two sensitivity analyses

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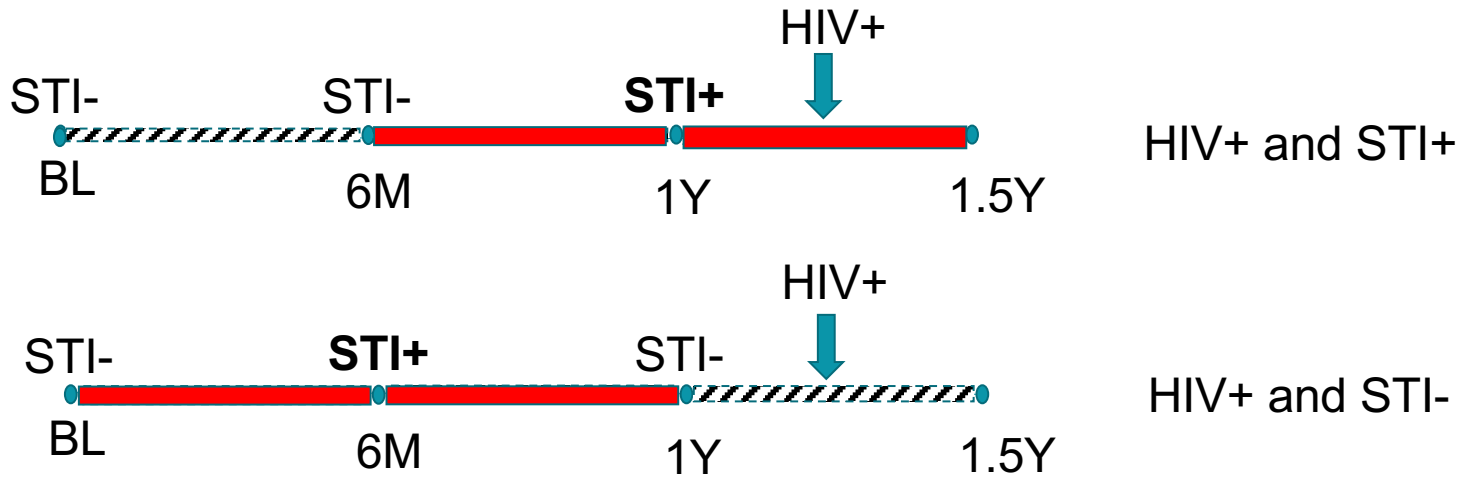
Methods: Maintenance of Efficacy

For the base case analysis, we considered intervals before and after each positive STI test as STI-positive



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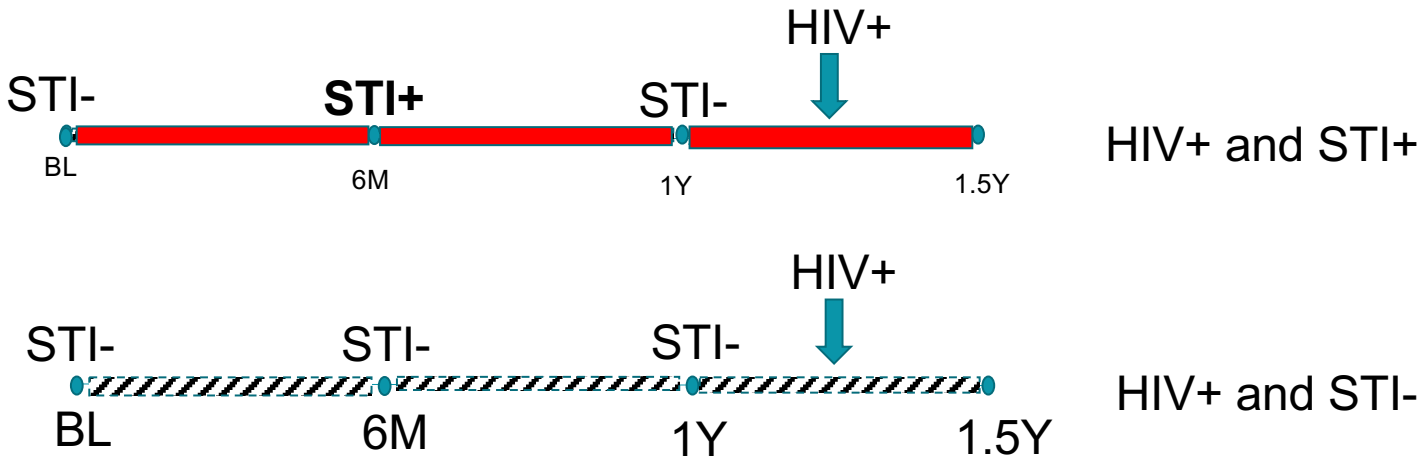
Methods: Maintenance of Efficacy

Sensitivity Analysis #1: Dichotomized participants as ever/never having an incident STI



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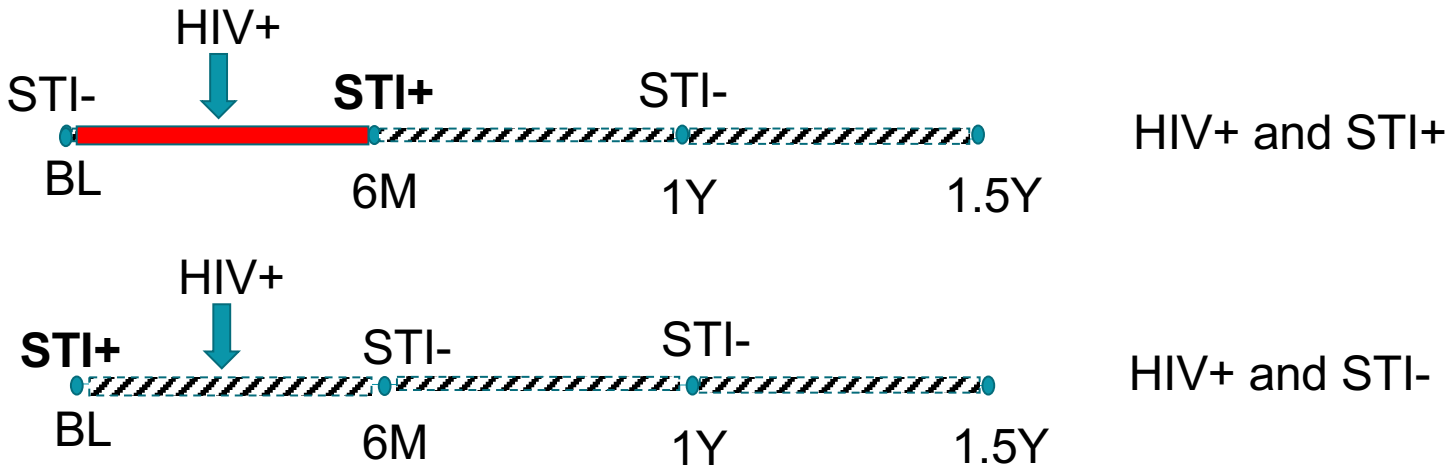
Methods: Maintenance of Efficacy

Sensitivity Analysis #2: Carried STI positive status backwards to the last STI negative test



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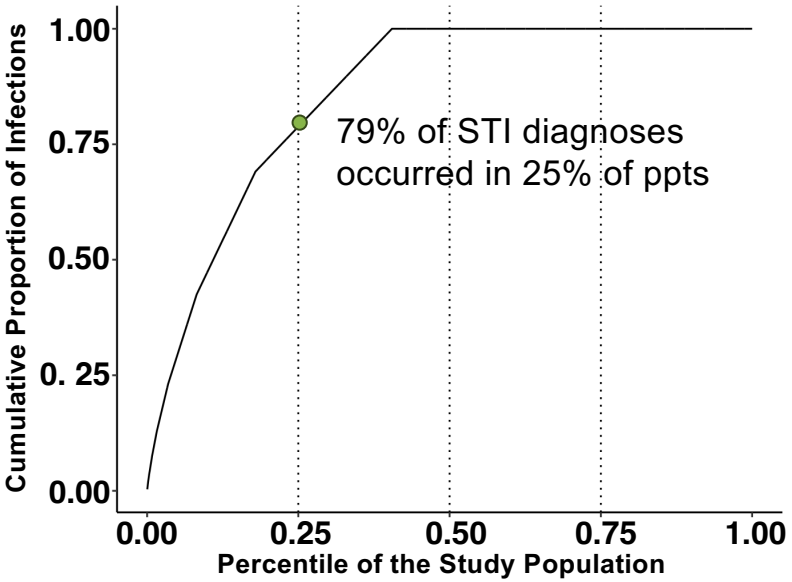
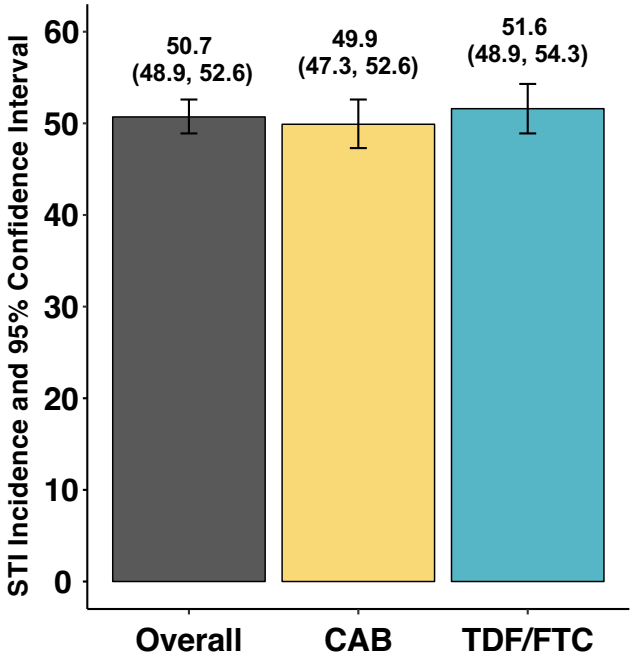
Results: STI incidence

Among 3859 participants, STIs were diagnosed in 1562 (40.5%), with multiple STIs reported for 691 (17.9%)





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Results: STI Incidence Rates, n= 3859 participants

	# Positive Tests	IR (per 100 PY)
Any STI	2819	50.7
Syphilis	923	16.7
Urogenital Gonorrhea	134	2.4
Urogenital Chlamydia	249	4.5
Rectal Gonorrhea	600	11.0
Rectal Chlamydia	913	16.7

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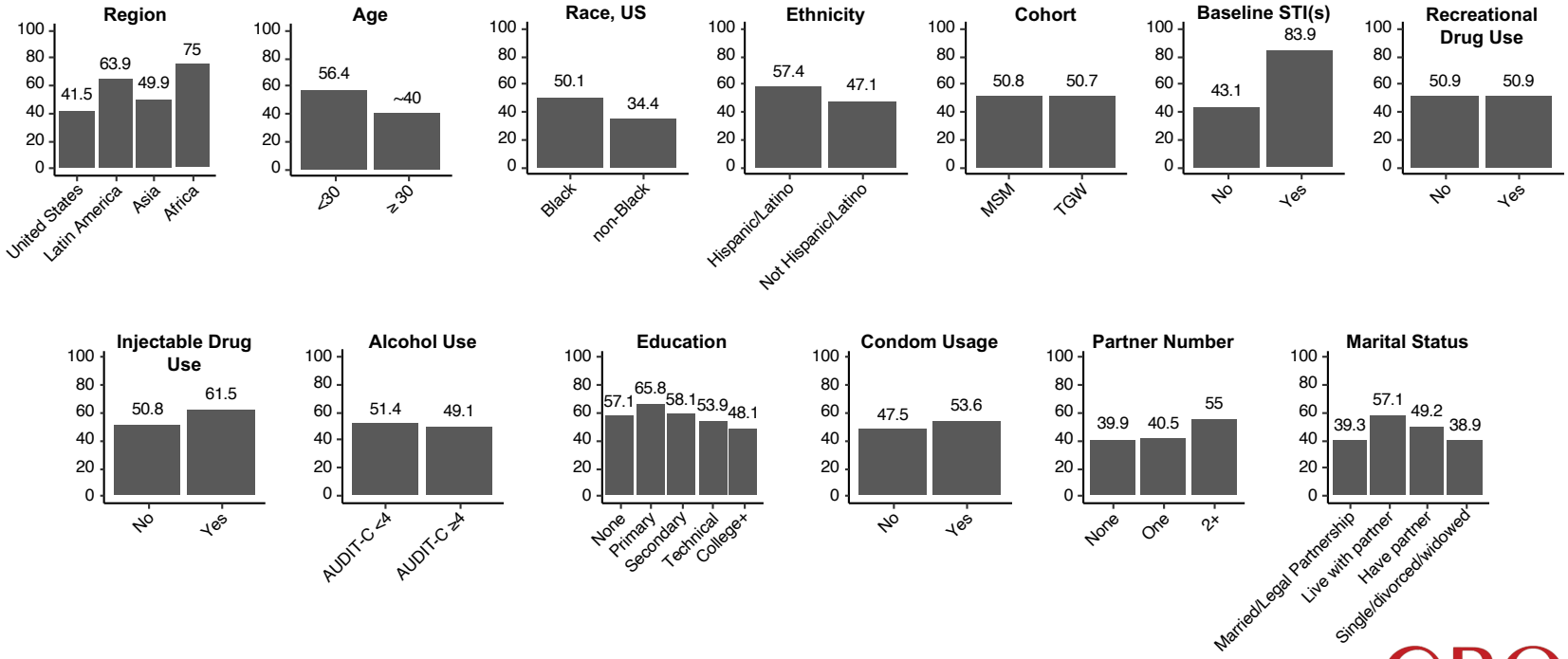
Results: STI Incidence Rate by Subgroup



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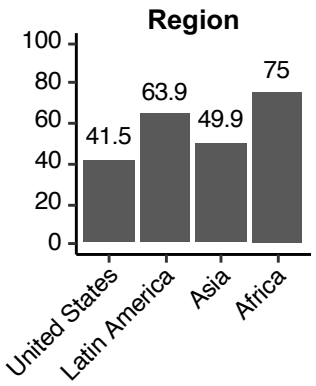

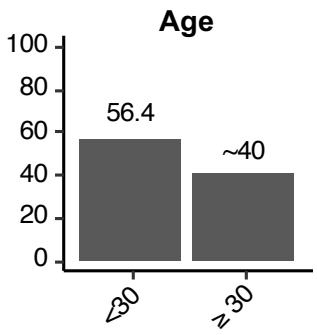

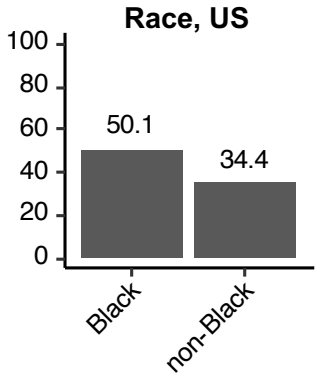

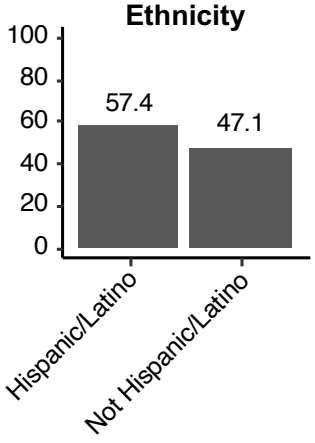

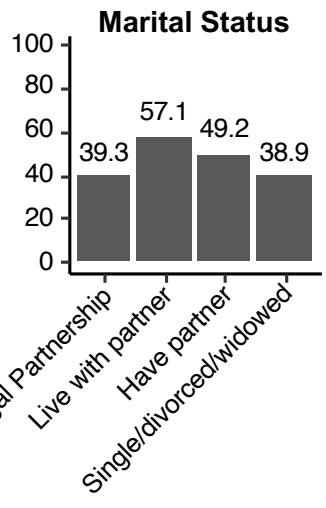

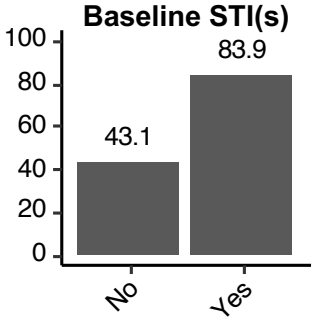

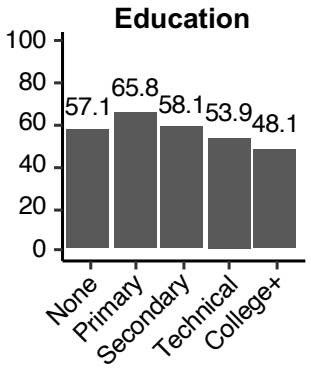

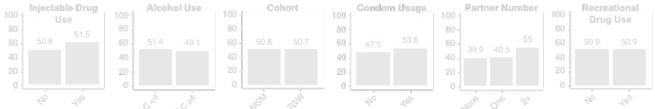

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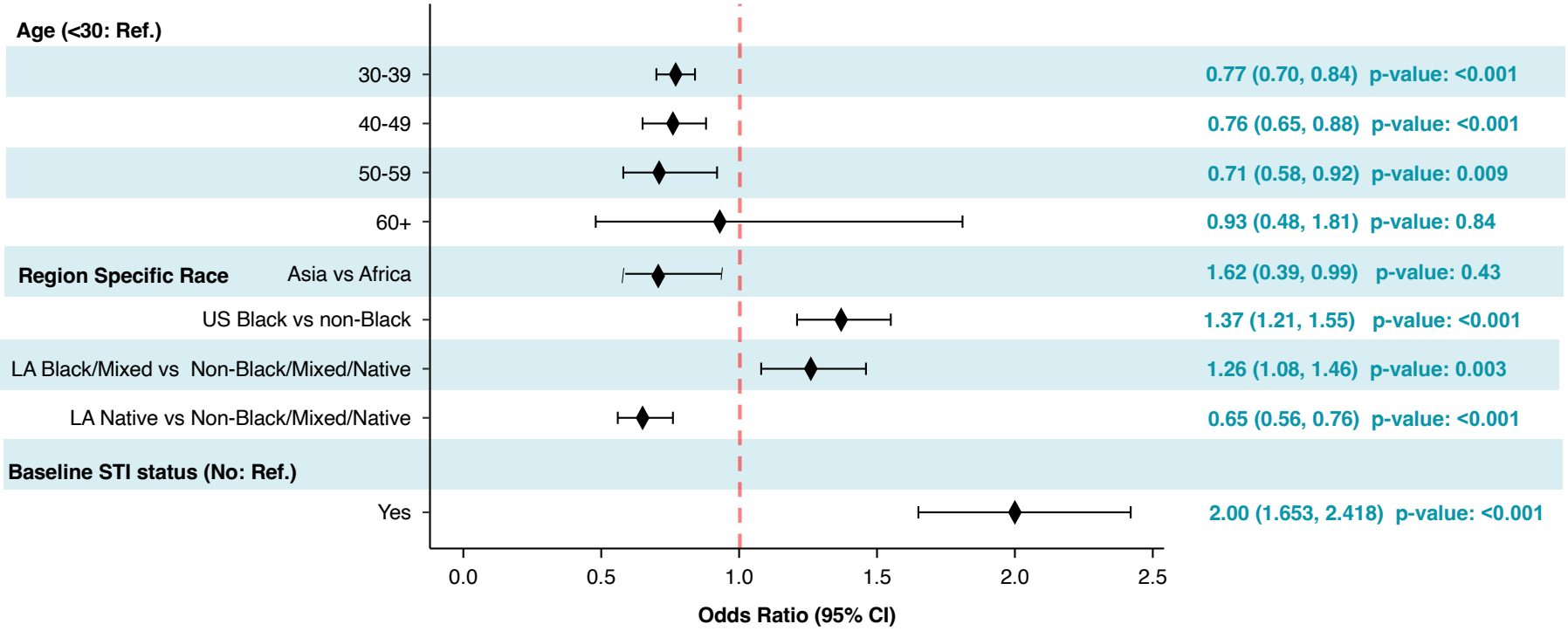
Results: STI incidence

In the final multivariable model: only age, race, and baseline STI status were statistically significant at p<0.05



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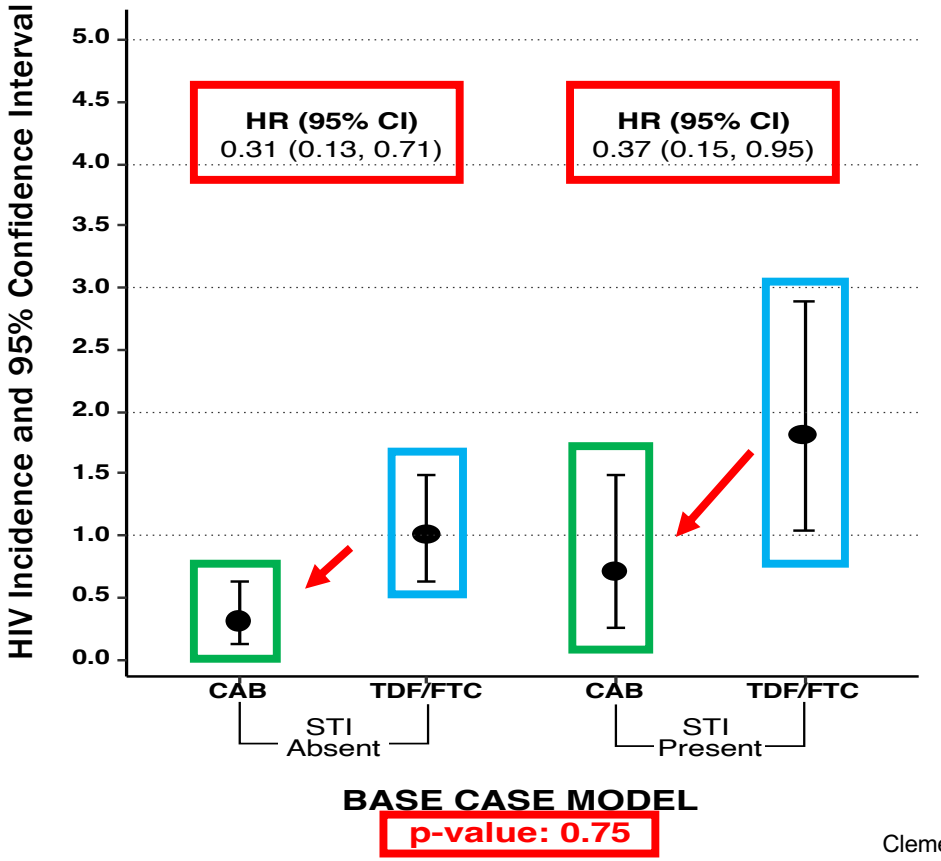
Results: Maintenance of Efficacy



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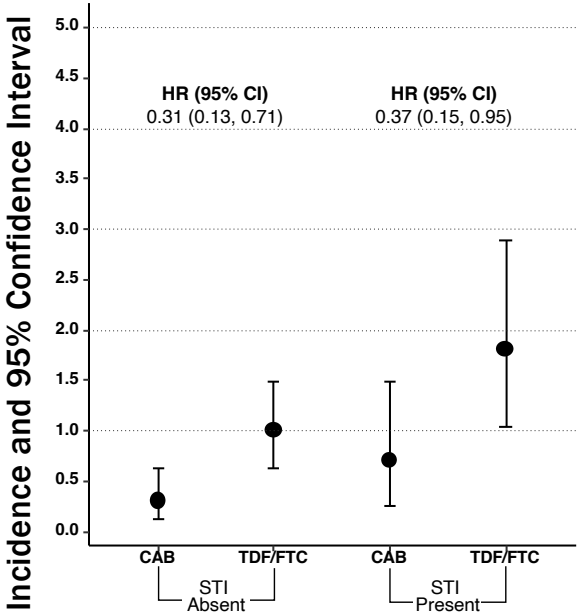
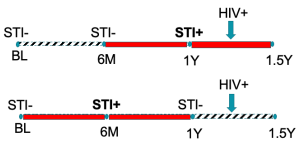
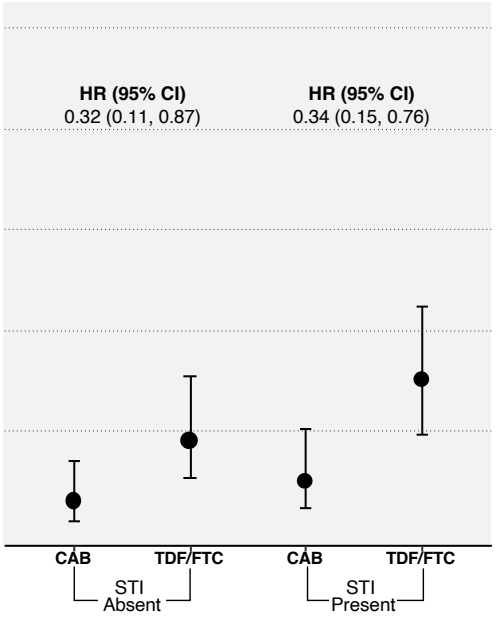
Results: Sensitivity Analyses



BASE CASE MODEL

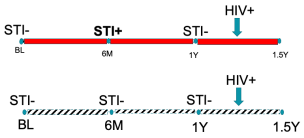
p-value: 0.75

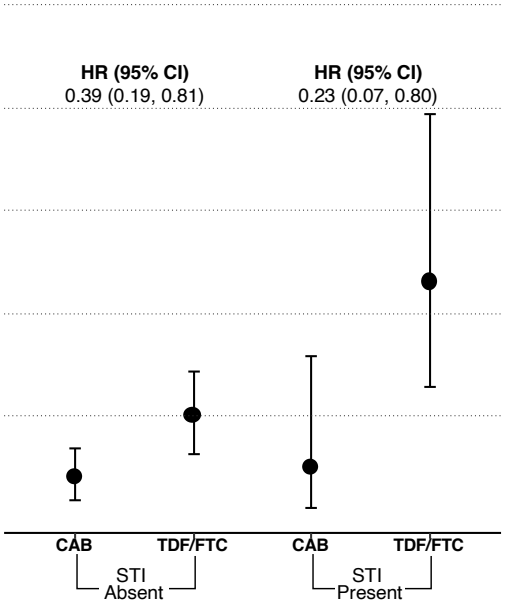




SENSITIVITY ANALYSIS #1

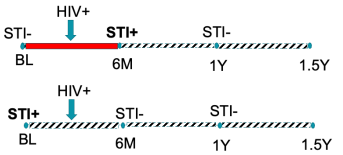
p-value: 0.90





SENSITIVITY ANALYSIS #2

p-value: 0.48



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Conclusions

- STI rates were high and concentrated among participants
- Factors associated with STIs were consistent with those reported in the literature, and not associated with study arm
- CAB-LA maintained robust protective efficacy in the setting of bacterial STIs

- These data may be helpful in guiding implementation of new biomedical STI prevention strategies
- CAB-LA maintained protective efficacy, and future PrEP agents should be similarly evaluated
- Continued innovation in STI prevention is critically needed

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Acknowledgements

Sponsors

- US National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), National Institute on Druga Abuse (NIDA), and the National Institute of Child Health and Human Development (NICHD), all components of U.S. National Institutes of Health

HIV Prevention Trials Network

- Laboratory Center (Johns Hopkins University)
- Statistical Center for HIV/AIDS Research and Prevention (SCHARP)
- Leadership and Operations Center, FHI360
- HPTN Leadership

Pharmaceutical Support

- ViiV Healthcare
- Gilead Sciences, Inc.

HPTN 083 Study Team

Ryan Kofron (UCLA)

Community Program Managers
Community Educators and Recruiters
CAB members

Our 43 sites in 7 countries

And especially, our HPTN Participants!

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