

Event-driven HIV and STI Prevention for People Assigned Female Sex at Birth

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Disclaimer

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Data Considerations

Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.



To Learn More:

<https://www.cdc.gov/minorityhealth/racism-disparities>

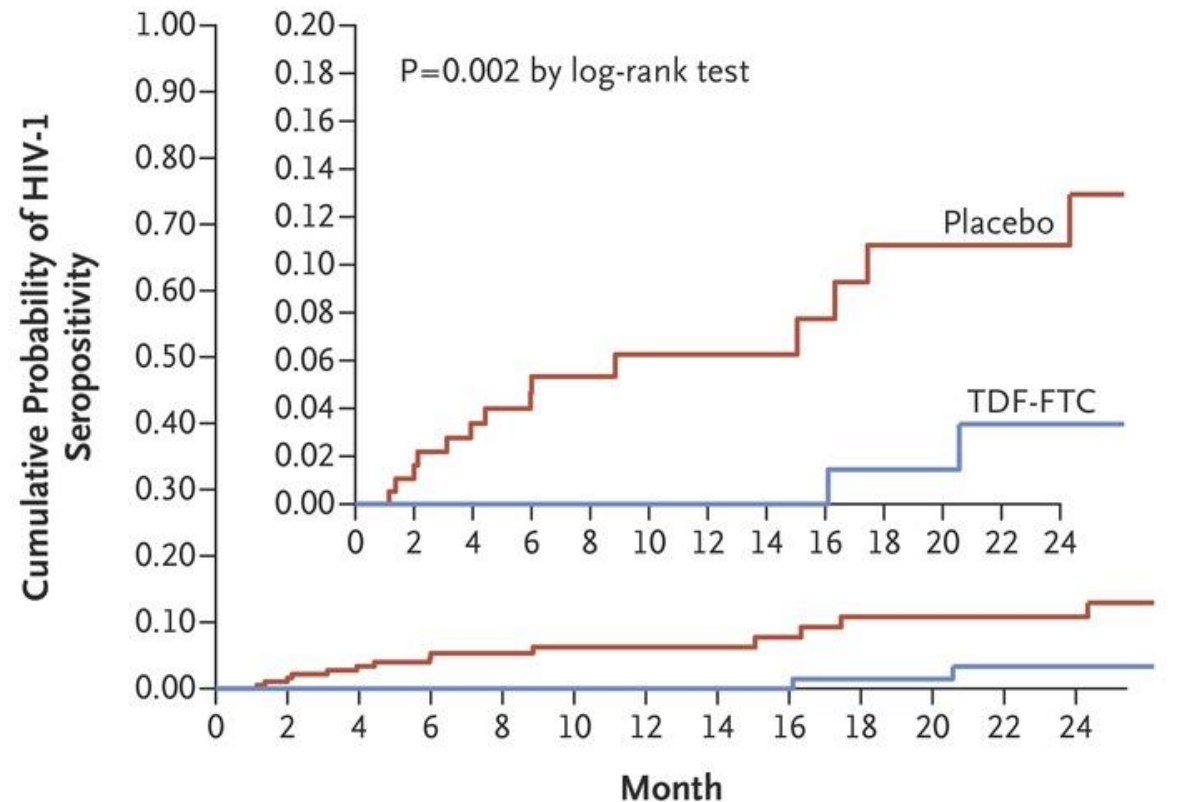
HIV PREVENTION

Event-Driven PrEP

Proven efficacy in placebo-controlled RCT

ORIGINAL ARTICLE

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection



No. at Risk

Placebo	201	141	74	55	42
TDF-FTC	199	141	82	58	43

400 MSM mostly in France (43 in Canada)

16 HIV infections with 2 assigned to event-driven PrEP for 86% reduction in HIV (P=0.002)

Breakthrough infections were due to nonuse

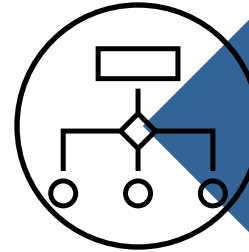
Median of 4 pills per week

ANRS IPERGAY
Molina et al, NEJM, 2015

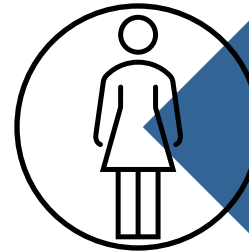


Decreased coverage with intermittent PrEP

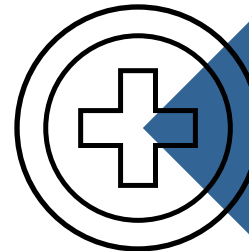
Decreased coverage with event-driven pre/post PrEP compared with daily PrEP (52% vs 75%)



Randomized, open-label 1:1:1 assigned to daily, weekly, or pre/post PrEP (2012-2014)



191 cisgender women in Cape Town, South Africa



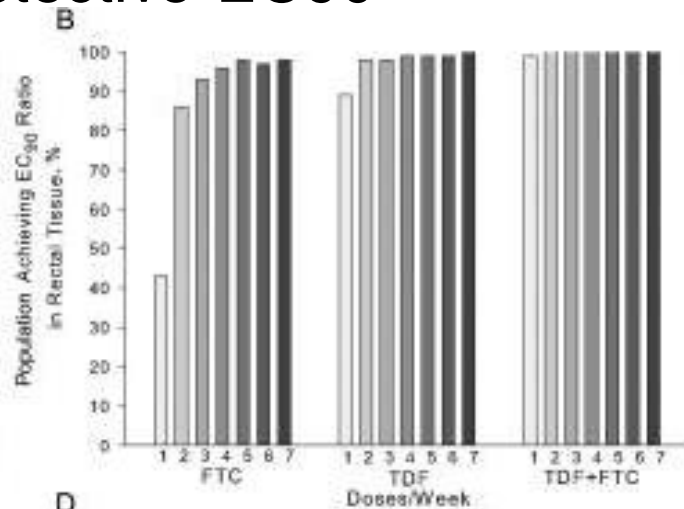
Women in Cape Town had 4 seroconversions

- 2 among weekly group and 2 among with pre/post use

TDF drug levels are higher in rectum than vagina

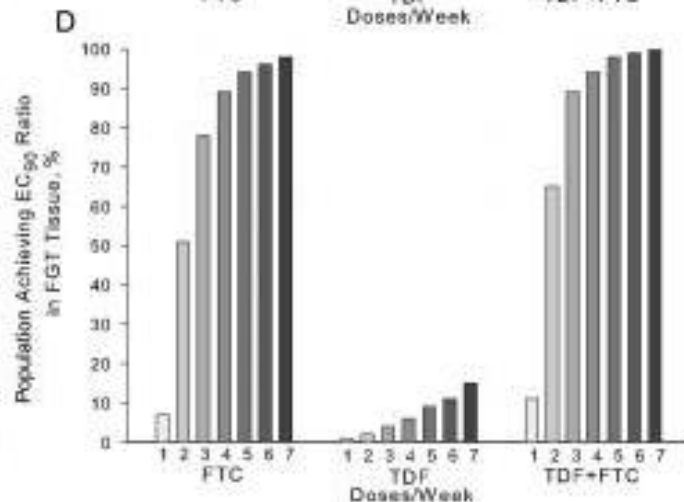
47 cisgender women given TDF/FTC to predict time to protective EC90

Rectal Tissue



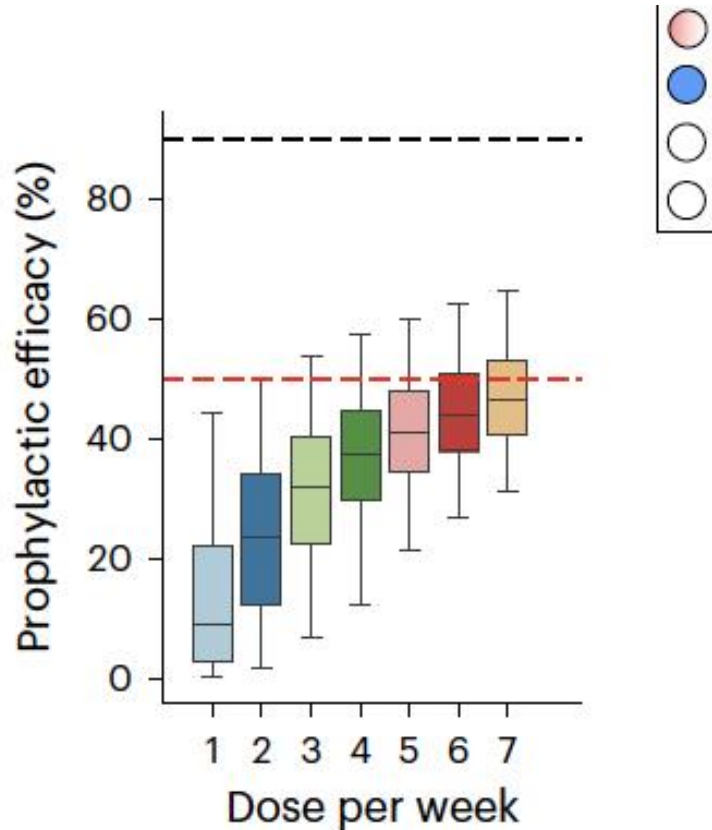
Daily TDF/FTC is proven to be protective for vaginal/front sex

Vaginal Tissue

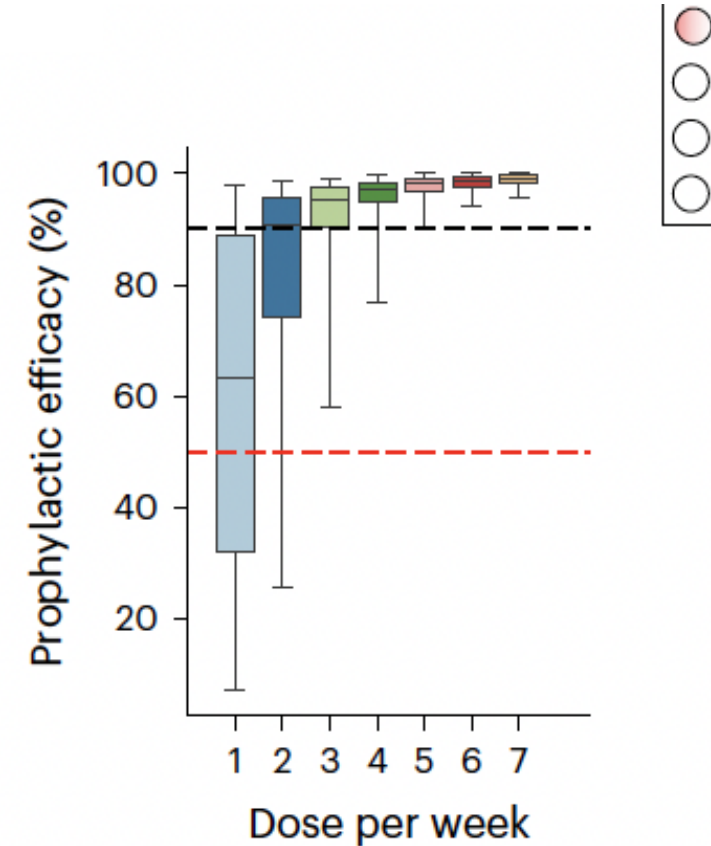


Clinical data incongruent with vaginal drug levels

Estimates of dose-dependent effectiveness based on vaginal PK data

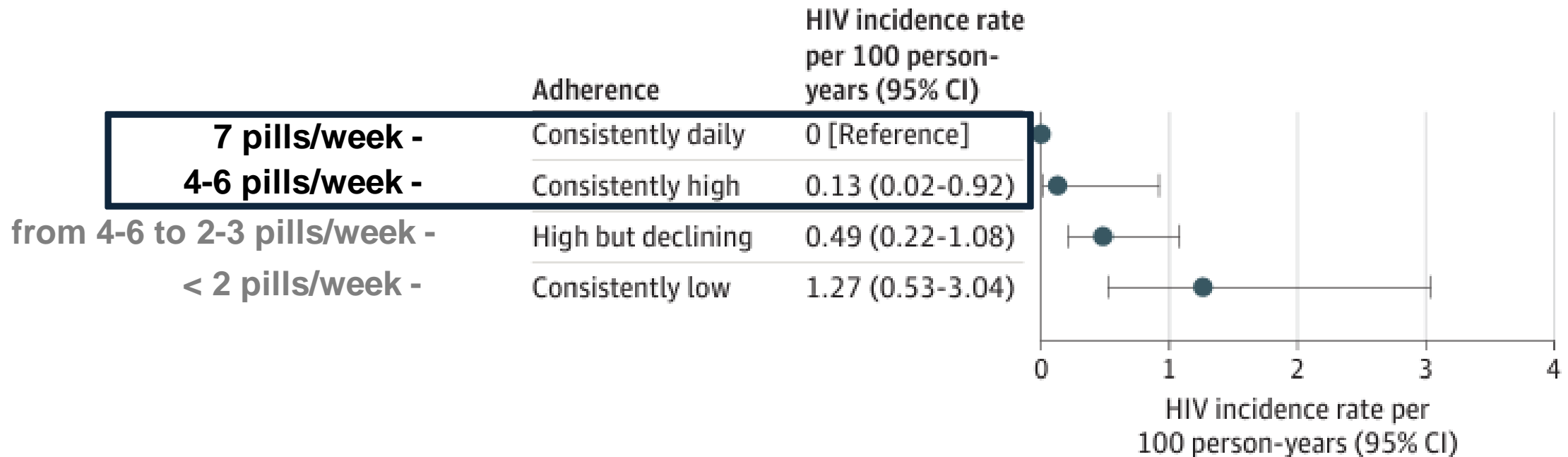


Estimates of dose-dependent effectiveness based on PBMC PK data



Do vaginas demand perfection?

Figure 4. HIV Incidence Rates Among Cisgender Women by Adherence Trajectory (n = 2954)



Pooled data from 11 F/TDF PrEP studies among cisgender women in 6 countries [2012 to 2020]

Imperfect adherence is protective so might event-driven PrEP

Imperfect adherence is protective for cisgender men

Event-driven PrEP works for cisgender men

Imperfect adherence is protective for women

**Event-driven PrEP
may work for women**

STI PREVENTION

DoxyPEP

Doxycycline Post-Exposure Prophylaxis for STI Prevention among Cisgender Women





Background

STIs are on the rise, notably among people who might benefit from PrEP regardless of sex or gender

Sequelae of bacterial STIs can be severe and chronic among cisgender women or in the uterus

Doxycycline PEP significantly reduced incident bacterial STIs by 60-70% in people assigned male sex at birth in France¹ and the USA²

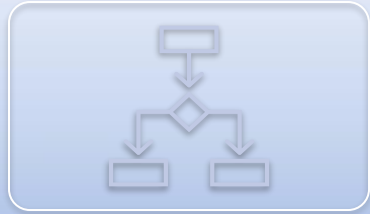
Doxycycline drug levels are more variable but high in vaginal secretions.³

¹Molina et al, Lancet ID, 2018

²Luetkemeyer et al, NEJM, 2023

³Haaland et al, EBioMedicine, 2024

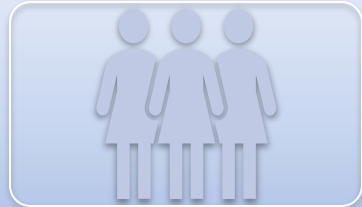
Methods



Design:

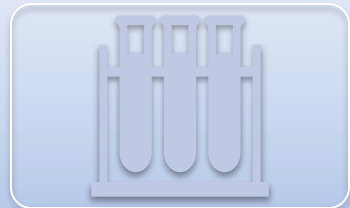
Open-label 1:1 randomized trial

Intervention: 200mg doxycycline hyclate within 72 hours of sex
Standard of Care: Quarterly STI testing and treatment



Population:

449 nonpregnant cisgender women, aged 18-30, taking HIV PrEP, in Kisumu, Kenya during 2020-2022



Approach:

Quarterly follow-up with STI (endocervical) NAAT testing and treatment and surveys.

Results: Baseline Characteristics

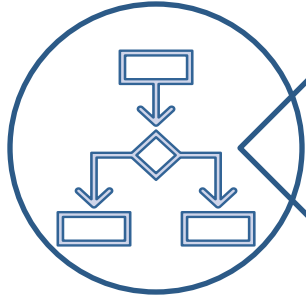


	Doxycycline PEP (N=224)	Standard of Care (N = 225)
Age, Median [IQR], years	24 [22-27]	24 [22-27]
Months on HIV PrEP, Median [IQR]	7.5 [4.1-14.9]	7.2 [3.7-13.8]
	% (n)	% (n)
Bacterial STI at baseline	18% (40)	18% (40)
<i>Chlamydia trachomatis</i>	13% (30)	15% (33)
<i>Neisseria gonorrhoeae</i>	5% (10)	3% (7)
<i>Treponema pallidum</i>	0% (0)	1% (2)

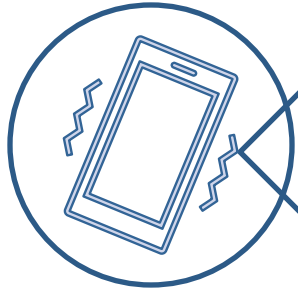
66% never married, 69% had prior pregnancies, 61% were using hormonal contraception, and 37% reported transactional sex



Results: Retention and Follow-up



97% of follow-up visits completed



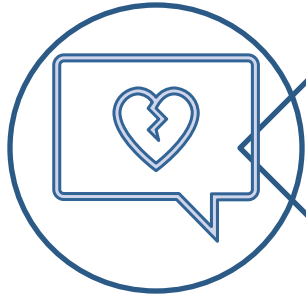
82% of weekly SMS surveys completed



44 pregnancies accounting for 10% of follow-up time
with other holds accounting for 5% in intervention group



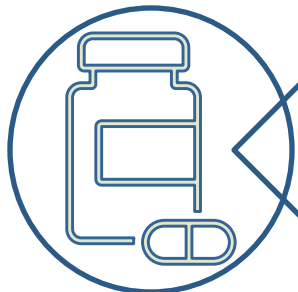
Results: Sexual Behavior & PrEP use



In weekly SMS surveys, zero sexual exposures reported in 28.4% (2222/7818) of weeks



>1 partner at 45.6% of the follow-up visits:
17.5% (305/1740) with 2 partners and 28.1% (489/1740) with ≥ 3



13% self-reported PrEP discontinuation. 0 incident HIV cases.

Results: Incident STIs

Overall STI incidence of 27 per 100 person-years

Analysis	Endpoint	Total	PEP (N=224)	SOC (N=225)	RR	95% CI	P-value
Intention to Treat	All STIs	109	50	59	0.88	0.60-1.29	0.51
	Chlamydia	85	35	50	0.73	0.47-1.13	0.16
	Gonorrhea	31	19	12	1.64	0.78-3.47	0.19

Relative risk calculated using generalized estimation equation (GEE) with modified Poisson regression.

Results: Incident STIs

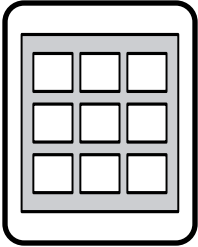
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Censoring Pregnancy Time	All STIs	105	48	57	0.91	0.62-1.35	0.65
	Chlamydia	82	33	49	0.73	0.46-1.15	0.18

Results: Incident STIs

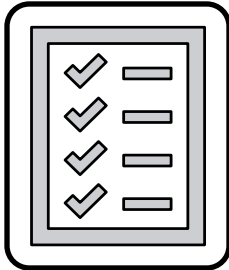
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Subgroup analyses of STI incidence by age, hormonal contraception use, transactional sex, and STI detected at baseline found similar results.

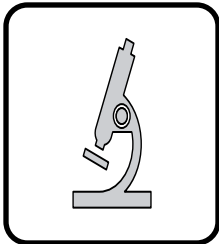
Results: Secondary Outcomes



No severe adverse reactions related to doxycycline.
4 participants reported social harms related to PEP use.



No incident HIV.



100% (n=6) tetracycline-resistant (*tetM*) *Neisseria gonorrhoeae* at baseline and 100% at follow-up (n=22).
0% (n=66) detection of *tetC* in *Chlamydia trachomatis*.

Results: Objective hair drug testing



- In a randomly selected subset of 50 participants assigned to doxycycline PEP
 - 56.0% (28/50) of participants had doxycycline detected at least once
 - 29.0% (58/200) of all quarterly visits had doxycycline detected,
 - 32.6% (58/178) when medication holds excluded
- 6.7% (3/45) of enrollment visits had doxycycline detected
- 5.1% (2/39) of follow up visits among SOC group had doxycycline detected

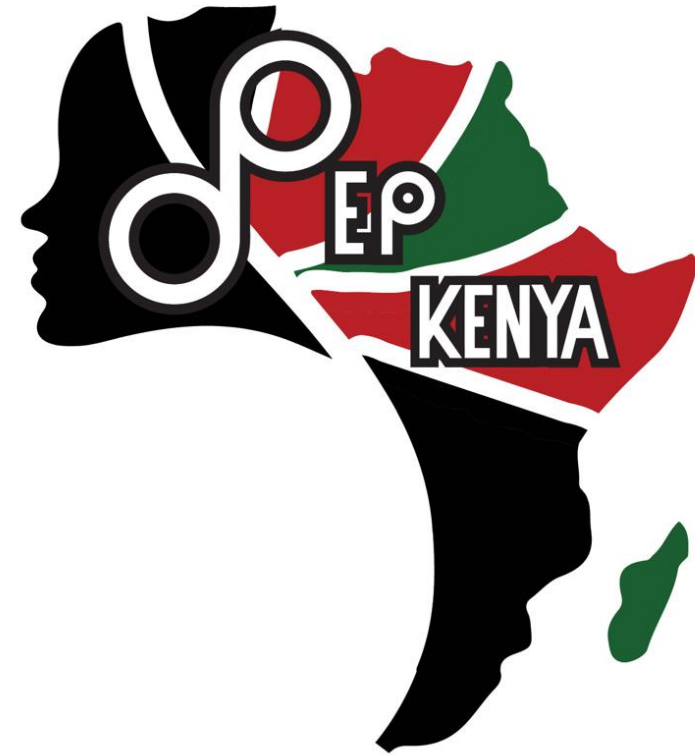
Conclusion

Our findings emphasize the need for STI preventive options for women that are effective and acceptable.

Adherence to preventive medicines needs to be better understood and supported for biomedical prevention to be effective.

Differing results between trials among MSM and this trial among cisgender women are likely explained by low use of doxycycline PEP.

Additional trials of doxycycline PEP for people AFAB regardless of gender are forthcoming.



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