

A pilot, randomized controlled trial of doxycycline pre-exposure prophylaxis versus placebo for prevention of bacterial sexually transmitted infections in men who have sex with men living with HIV

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In a pilot study of 52 men who have sex with men living with HIV, doxyPrEP was feasible, and yielded significant reductions in chlamydia, syphilis and gonorrhea compared to those on placebo, over one year of follow-up.

Background

- Doxycycline post-exposure prophylaxis (doxyPEP; 200mg within 72h of sexual exposure) is efficacious in reducing bacterial sexually transmitted infections (STI) in gay, bi, and other men who have sex with men (GBM) and transgender women (1-3).
- Doxycycline pre-exposure prophylaxis (doxyPrEP) has also shown promise (4), and may represent an alternate option for STI prevention.

Methods

- The Daily Doxycycline in HIV-positive GBM for STI prevention (DaDHS) study is a randomized, double-blind, placebo-controlled study of doxyPrEP vs. placebo.
- Participants from Vancouver and Toronto, Canada, were randomized 1:1 to 48 weeks of daily doxyPrEP (100mg doxycycline hyclate) or placebo, and followed quarterly with questionnaires (e.g. adherence, sexual history), pill counts, STI screens (syphilis serology; multi-site gonorrhea and chlamydia nucleic acid amplification testing) and routine labs. Nasal swabs for commensals were also collected.
- The primary outcome was doxyPrEP feasibility (adherence and tolerability); secondary outcomes were STI incidence, changes in sexual behaviour and antimicrobial resistance (AMR).
- STI rates were compared using Poisson regression.

Results

- Between 01/2020-01/2023, 52 participants were randomized.
- In total, 41 (78.8%) completed the protocol; 8 (15.4%) were lost to follow-up, 1 (1.9%) was withdrawn by the investigator, and 2 (3.8) withdrew consent.
- Participant characteristics are presented in Table 1, adherence data is presented in Table 2, and STI data is presented in Figure 1 and Table 3.
- There were no between-arm differences in sexual behaviours, adverse events (AEs) or tetracycline resistance to *S. aureus*.
- Most AEs (78.2%) were mild, and the proportion of AEs related to study drug did not differ by arm. There was one doxyPrEP-related discontinuation (worsening GERD) and one serious AE unrelated to doxyPrEP (i.e. mpox proctitis).

Table 1: Baseline sociodemographic and clinical characteristics

Characteristic	All (n=52)	DoxyPrEP (n=26)	Placebo (n=26)
Age, median (IQR)	43 (38, 54)	42 (37, 53)	48 (39, 57)
Ethnicity, n (%)			
White/Caucasian	31 (59.6)	15 (57.7)	16 (61.5)
Hispanic/Latinx	11 (21.2)	6 (23.1)	5 (19.2)
South Asian	3 (5.8)	1 (3.8)	2 (7.7)
Black	2 (3.8)	0 (0.0)	2 (7.7)
Southeast Asian	2 (3.8)	1 (3.8)	1 (3.8)
Middle Eastern	1 (1.9)	1 (3.8)	0 (0.0)
Years since HIV diagnosis			
Median (IQR)	8.0 (5.0, 14.0)	10.0 (6.0, 15.0)	6.0 (3.0, 12.0)
Range	1-33	1-33	1-25
Undetectable viral load, n (%)	40/46 (87.0)	22/23 (95.7)	18/23 (78.3)
STI at baseline, n (%)			
Syphilis	1 (1.9)	0 (0.0)	1 (3.8)
Chlamydia	5 (9.6)	3 (11.5)	2 (7.7)
Gonorrhea	3 (5.8)	0 (0.0)	3 (11.5)
Number of male sexual partners, last 3 months, median (IQR)	8 (5, 15)	10 (5, 15)	7 (4, 13)

Abbreviations: CI, confidence interval; doxyPrEP, doxycycline pre-exposure prophylaxis; IQR, interquartile range; STI, sexually transmitted infection.

Table 2: Adherence to study medications

Measure	DoxyPrEP	Placebo	P-value
Pill counts - Week 1-48			
Median (IQR)	0.95 (0.88, 0.98)	0.96 (0.87, 0.97)	0.90
≥85%, n (%)	13/17 (76.5)	14/18 (77.8)	1.00
≥90%, n (%)	12/17 (70.6)	13/18 (72.2)	0.92
≥95%, n (%)	8/17 (47.1)	10/18 (55.6)	0.62
Simplified Medication Adherence Questionnaire, n (%)			
Week 1-24	3/17 (17.6)	8/19 (42.1)	0.112
Week 25-48	2/14 (14.3)	8/17 (47.1)	0.052
Week 1-48	1/18 (5.6)	7/19 (36.8)	0.042

Figure 1: Number of participants with chlamydia and gonorrhea, by anatomic site

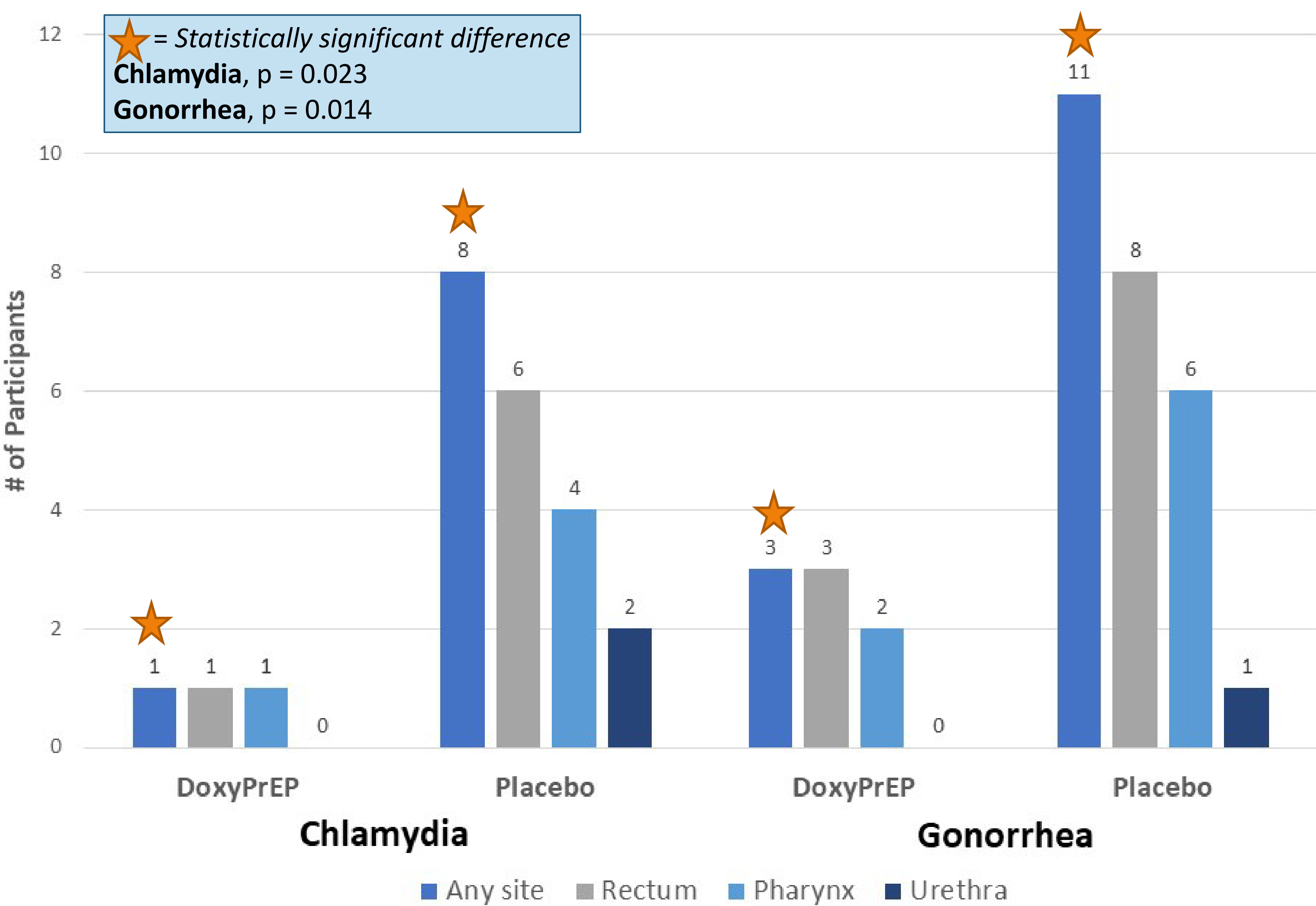


Table 3: Bacterial STI incidence at 48 weeks, by study arm

	Total STIs per arm		Incidence rate (95% CI), per 100 PY		Rate ratio* (95% CI)	p
	DoxyPrEP	Placebo	DoxyPrEP	Placebo		
Syphilis	1	5	3.95 (0.96, 16.28)	19.26 (10.23, 36.28)	0.21 (0.04, 0.97)	0.04
Chlamydia	1	13	3.97 (0.69, 22.77)	50.09 (30.86, 81.30)	0.08 (0.01, 0.49)	0.01
Gonorrhea	4	13	15.88 (6.61, 38.15)	50.09 (30.81, 81.44)	0.32 (0.12, 0.86)	0.02
TOTAL	6	31	23.71 (9.93, 56.66)	119.44 (81.42, 175.20)	0.20 (0.08, 0.51)	<0.001

Abbreviations: CI, confidence interval; doxyPrEP, doxycycline pre-exposure prophylaxis; PY, person-years; STI, sexually transmitted infection. *Rate ratio <1 suggests lower incidence rate in doxycycline arm.

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Conclusions

- In a study of 52 GBM living with HIV, the use of daily doxyPrEP was feasible, as measured through adherence and tolerability.
- DoxyPrEP led to significant reductions in bacterial STIs: 79% reduction in syphilis incidence, 92% reduction in chlamydia incidence, and 68% reduction in gonorrhea incidence.
- These pilot findings support the ongoing evaluation of doxyPrEP compared to doxyPEP in our ongoing **disco** trial.

Check out our DISCO study website:

