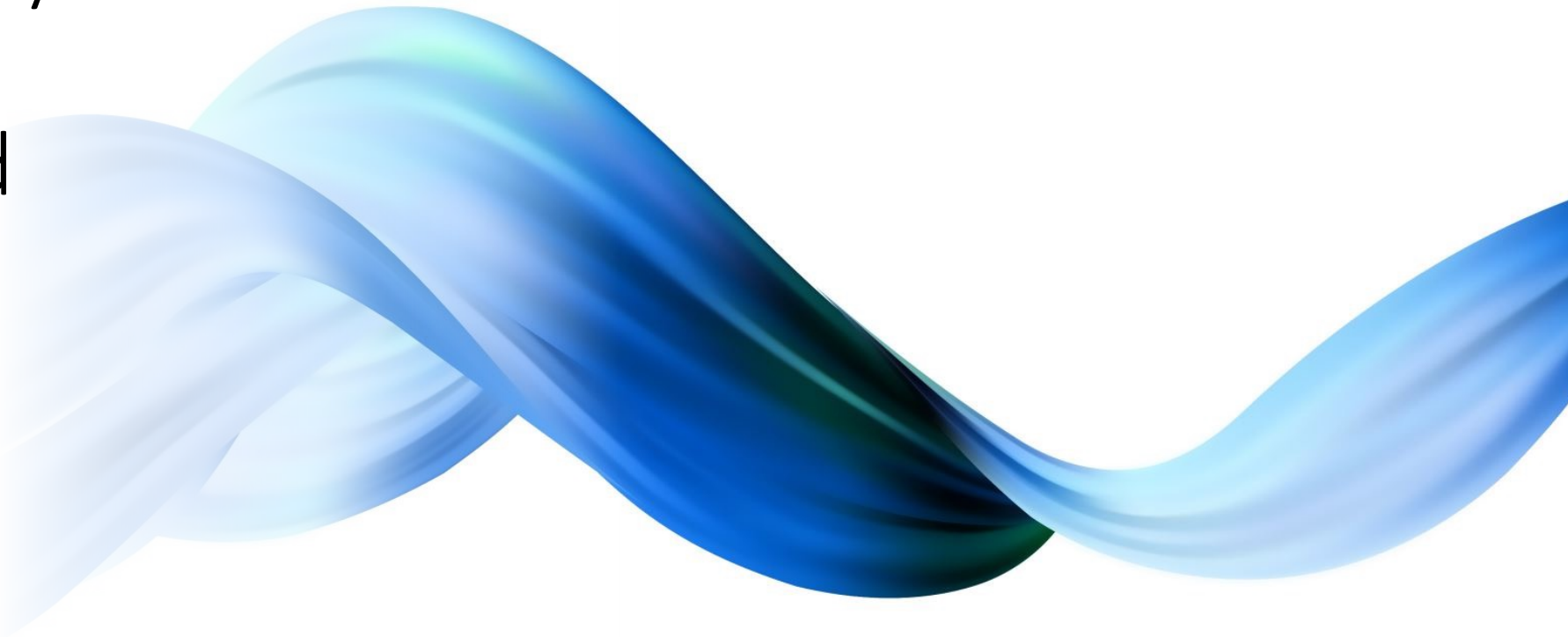
Doxycycline for Post-Exposure Prophylaxis (PEP): Efficacy, Guidelines, and Considerations



Amit (Mickey) Dhir, AGPCNP- C, MS, MBA, AAHIVS
PH.D. Student and Infectious Disease NP
Email – adhir1@jhmi.edu

Objectives

- To understand the efficacy of doxycycline as a post-exposure prophylaxis (PEP) agent.
- To familiarize the audience with the current guidelines and recommendations regarding the use of doxycycline for PEP.
- To understand clinical considerations for selecting doxycycline as a PEP option, including patient characteristics, and risk assessment.

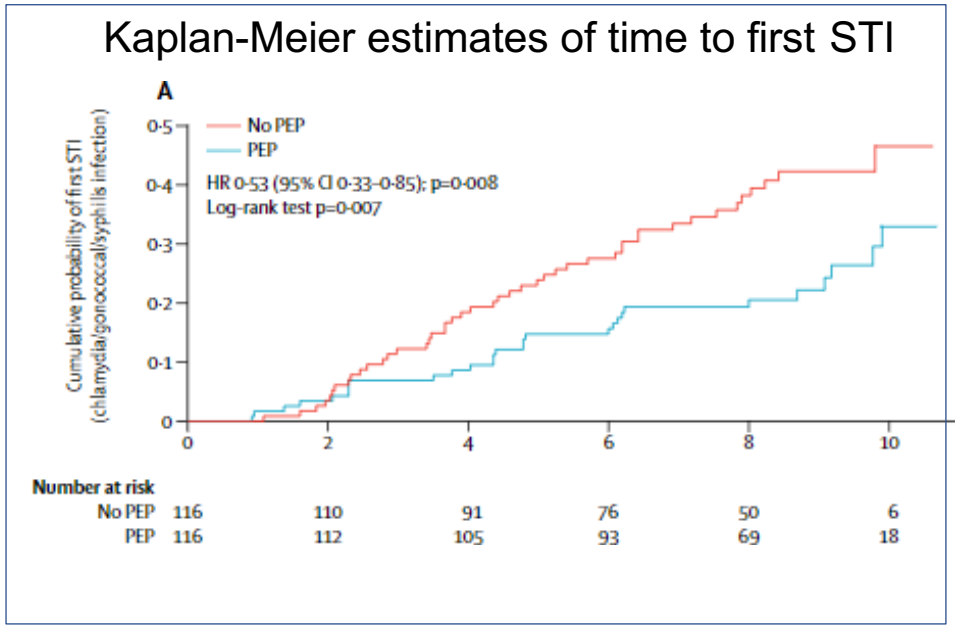
Background

- STI rates, including gonorrhea, chlamydia, and syphilis, are disproportionally high in MSM
- Intermittent doxycycline PEP has been shown to reduce occurrence of initial episode of a bacterial STI in MSM at high risk for STIs
  - ~70% and 63% reduction in chlamydia and syphilis, respectively
  - No prevention efficacy for gonorrhea observed
- Doxy as PEP trials are designed to assess efficacy of doxycycline PEP for prevention of STIs in MSM, Cis-women and TGW living with HIV or receiving PrEP

1. org/dph/files/reports/StudiesData/STD/SFSTDAnnlSum2018.pdf. 2. CDC. 2020 STI surveillance.
3. Molina. Lancet Infect Dis. 2018;18:308. 4. Luetkemeyer. AIDS 2022. Abstr OALBX0103.

Context of prior studies: IPERGAY

- RCT in open label extension of IPERGAY (N=232)
  - Event-driven (2-1-1) HIV PrEP study in France
  - Doxy PEP vs. usual care
- Doxy 200mg x1 ~24h after sex (≤72h)
- Targeting CT & syphilis
- Median 7 pills/month



47% ↓in STI
(69.7 vs 37.7/100 PY)

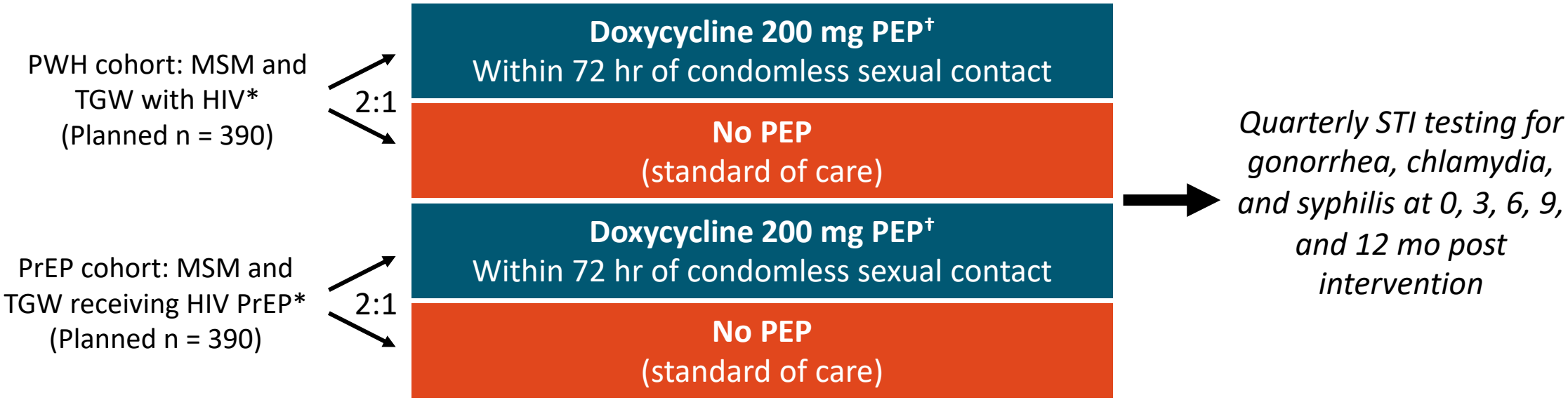
Molina JM et al. *Lancet Infect Dis* 2018

CROI 2023 & AIDS2022 on DoxyPEP and STI prevention

- A DoxyPEP PK study of vaginal and rectal tissues reported that a single 200 mg dose reaches levels >4x minimum inhibitory concentration (MIC) for chlamydia and syphilis for 2-4 days. However, levels of protection are lower for gonorrhoea and the 4x MIC threshold was not achieved in rectal tissue
- In a French study in gay men, DoxyPEP reduced the incidence rate of chlamydia and syphilis cases from 35.4 to 5.6/100 person-years. The same study also reported that the meningococcal vaccine (4CMenB) reduced the rates of gonorrhoea by 53%
- A US study reported that antibiotic resistance rose 8% for those on DoxyPEP but MRSA detection rates were unchanged
- A study of cisgender women in Kenya reported an overall decrease in the absolute number of bactErial STIs for those receiving DoxyPEP, however this was not statistically significant
- A retrospective study of DoxyPEP use in the US suggested that prescribing DoxyPEP for one year following an STI diagnosis may be more efficient than blanket prescribing of Doxy to all high-risk groups

DoxyPEP: Study Design

- Randomized, open-label study conducted at HIV and STI clinics in San Francisco and Seattle



*All participants were assigned male sex at birth, had ≥1 STI in past 12 mo, and had condomless sex with ≥1 partner in past 12 mo.
†Maximum dose of 200 mg/24 hr.

- **Primary endpoint:** ≥1 incident STI (gonorrhea, chlamydia, or syphilis) during quarterly STI test
- **5/13/2022:** Enrollment stopped early per DSMB after interim analysis showed significant effectiveness in both cohorts

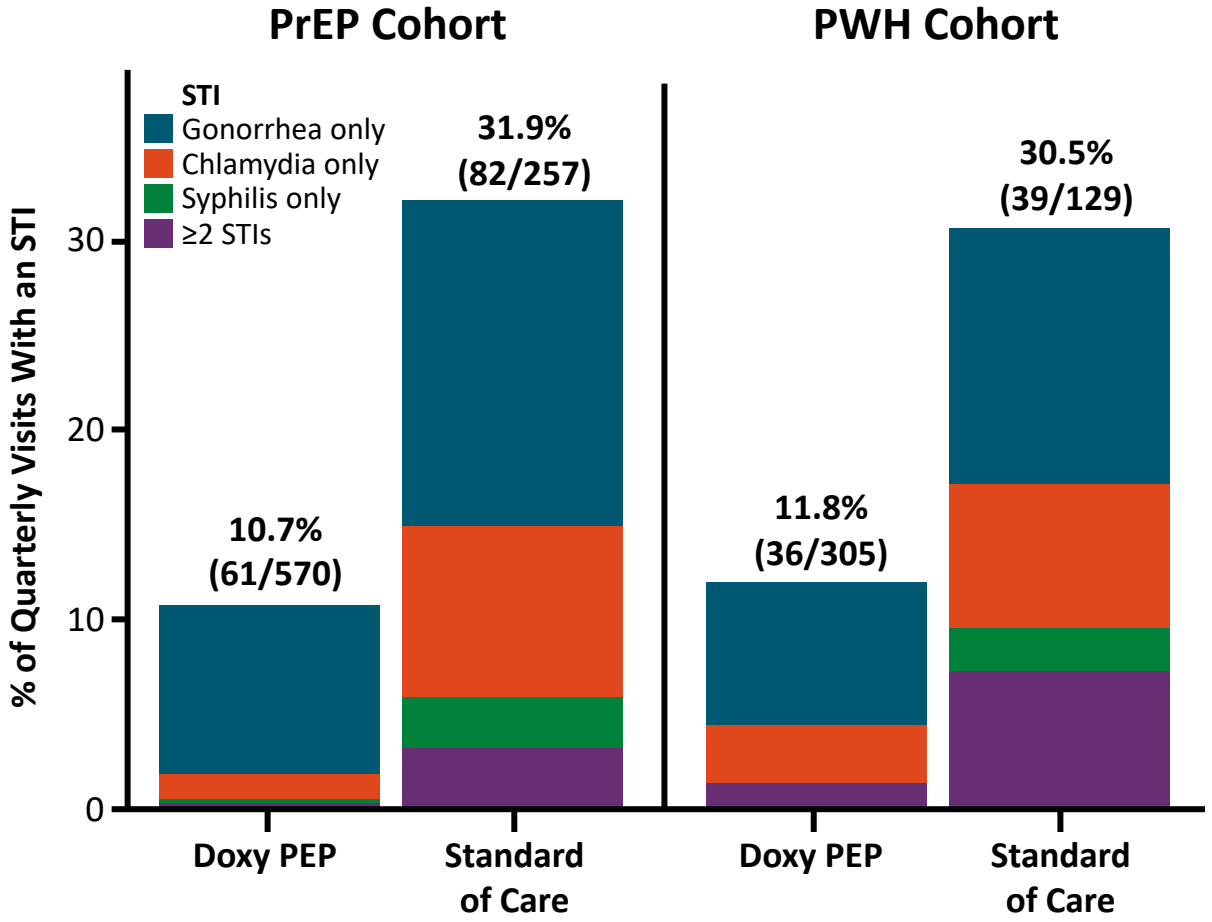
Luetkemeyer. AIDS 2022. Abstr OALBX0103.

DoxyPEP: Baseline Characteristics

Characteristic	PrEP Cohort (n = 327)	PWH Cohort (n = 174)	Total (N = 501)
Median age, yr (IQR)	36 (31-42)	43 (36-54)	38 (32-47)
Race, n (%)			
▪ White	210 (67)	111 (66)	321 (67)
▪ Black	14 (5)	22 (13)	36 (8)
▪ Asian/Pacific Islander	45 (14)	8 (5)	53 (11)
▪ Multiple races/other	44 (14)	28 (17)	72 (15)
Hispanic/Latinx, n (%)	96 (29)	55 (32)	151 (30)
Gender identity, n (%)			
▪ Man	319 (98)	163 (94)	482 (96)
▪ Trans woman/gender diverse	8 (2)	11 (6)	19 (4)
Male sexual partners only, n (%)	281 (86)	153 (88)	434 (87)
STI in prior 12 mo, n (%)			
▪ Gonorrhea	233 (71)	110 (63)	343 (69)
▪ Chlamydia	207 (63)	85 (49)	292 (58)
▪ Syphilis	48 (15)	52 (30)	100 (20)
Median no. of sexual partners in prior 3 mo (IQR)	9 (4-17)	8.5 (3-20)	9 (4-17)
Substance use in prior 3 mo, n (%)	178 (55)	115 (68)	293 (59)
▪ Stimulants (methamphetamine, cocaine, crack)	73 (23)	73 (43)	146 (30)
▪ Ecstasy, GHB, ketamine	97 (30)	60 (35)	157 (32)
▪ Amyl nitrate (poppers)	140 (43)	84 (49)	224 (45)

Luetkemeyer. AIDS 2022. Abstr OALBX0103.

DoxyPEP: Quarterly STI Incidence (Primary Endpoint)

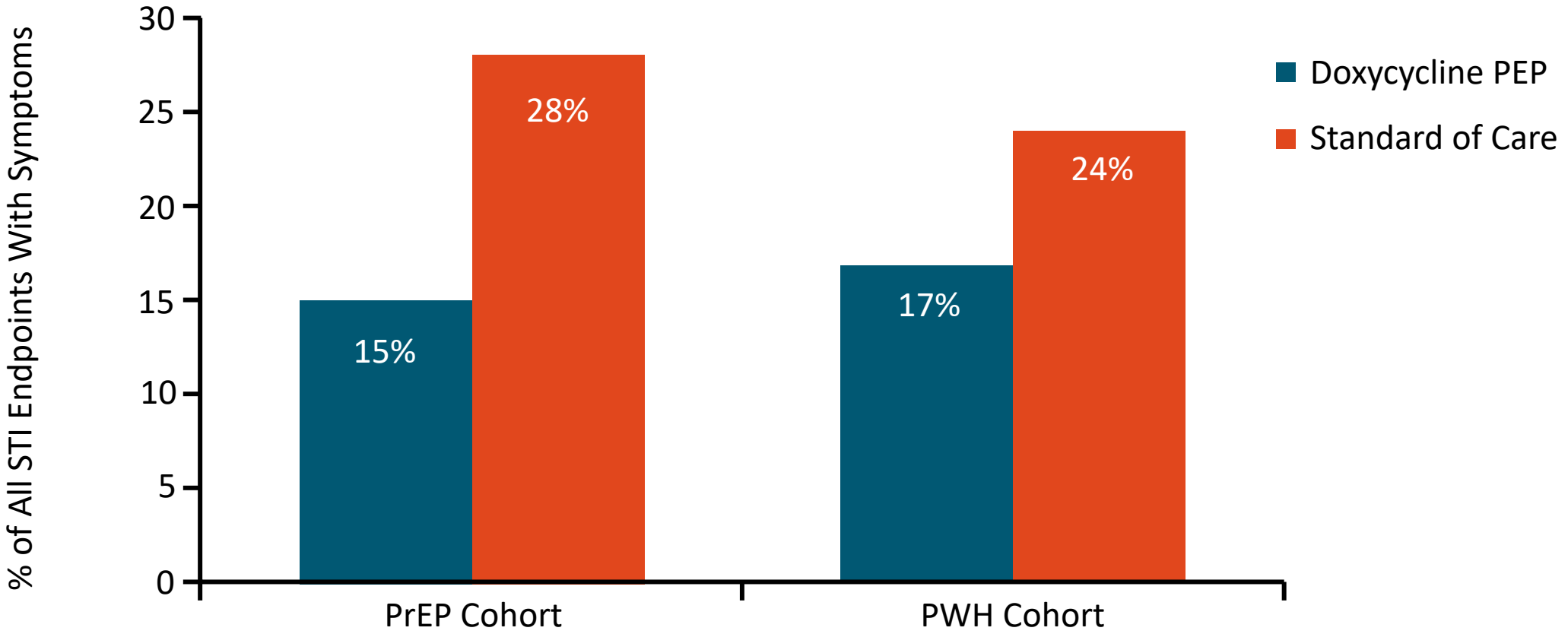


Risk Reduction in STI Incidence per Quarter (95% CI)	Doxy PEP vs Standard of Care*
PrEP	0.34 (0.24-0.46)
PWH	0.38 (0.24-0.60)
Total	0.35 (0.27-0.46)

*All *P* <.0001

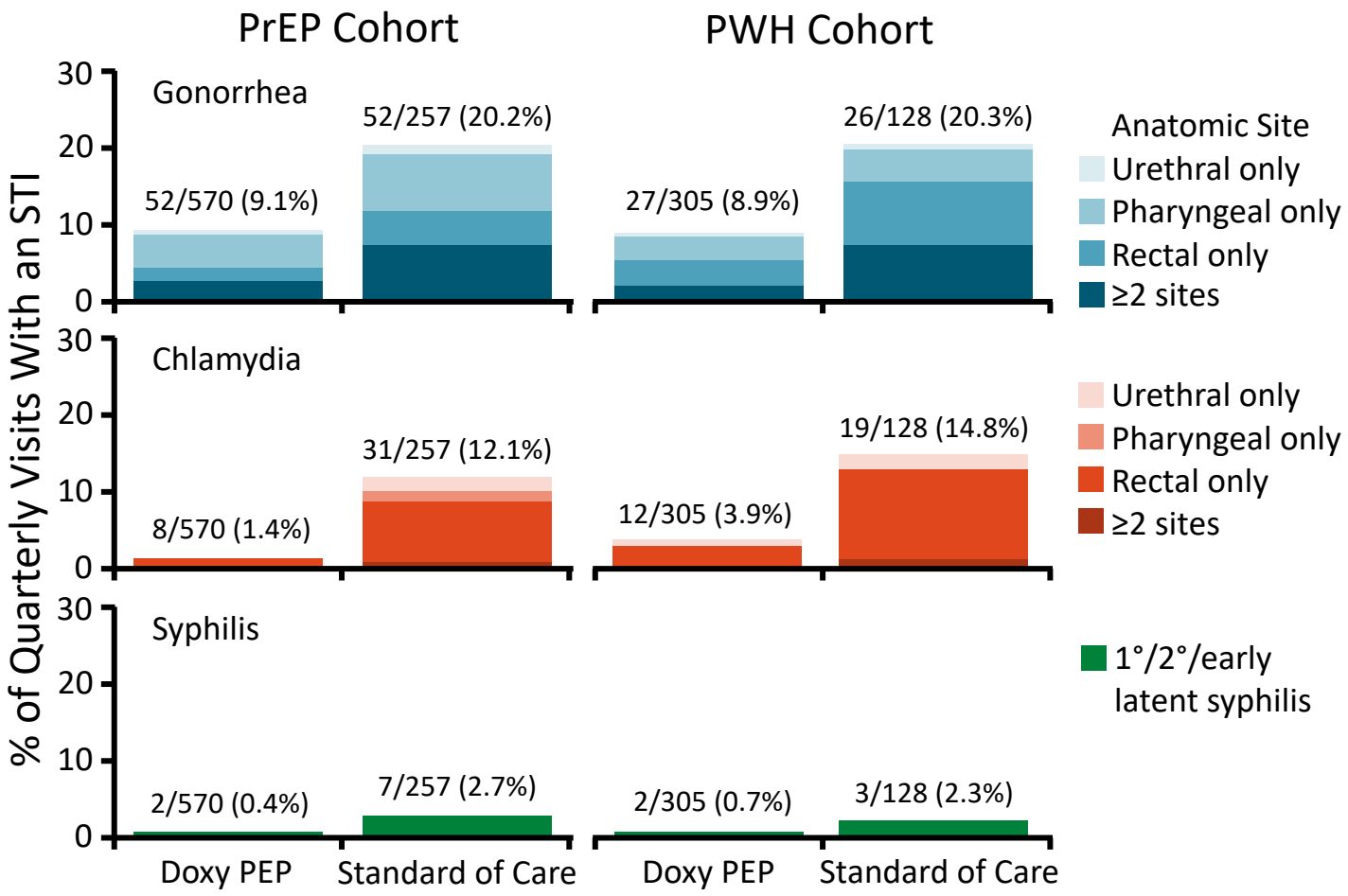
Luetkemeyer. AIDS 2022. Abstr OALBX0103. Reproduced with permission.

DoxyPEP: STI With Symptoms Reported at Diagnosis



Luetkemeyer. AIDS 2022. Abstr OALBX0103. Reproduced with permission.

DoxyPEP: STI Incidence By Anatomic Distribution and Study Arm and Cohort



Reduction in STI Incidence Per Quarter	Risk Reduction (95% CI) *P* Value	
	PrEP Cohort	PWH Cohort
Gonorrhea	0.45 (0.32-0.65) <.0001	0.43 (0.26-0.71) .001
Chlamydia	0.12 (0.05-0.25) <.0001	0.26 (0.12-0.57) .0007
Syphilis	0.13 (0.03-0.59) .0084	0.23 (0.04-1.29) .095

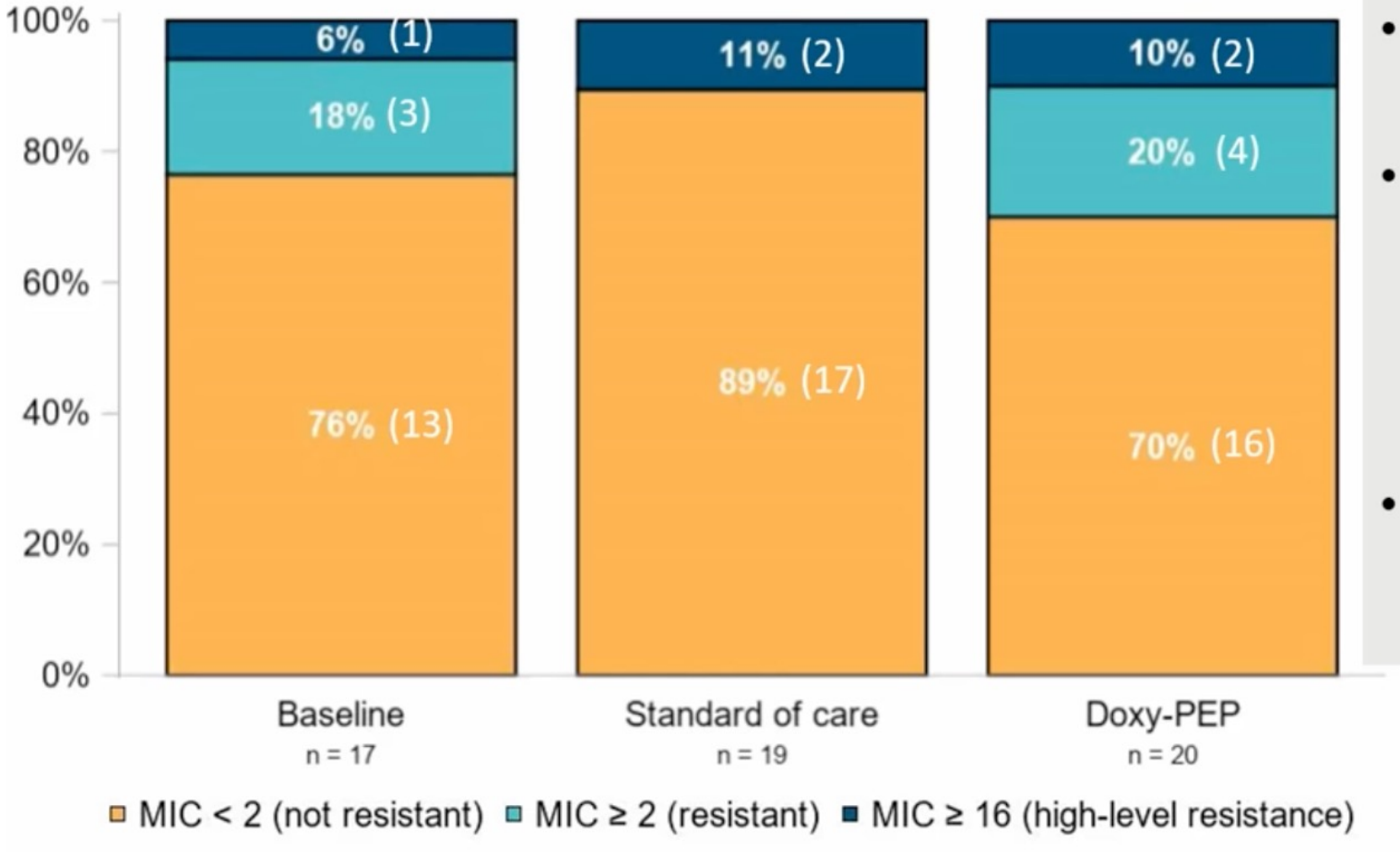
Luetkemeyer. AIDS 2022. Abstr OALBX0103.

DoxyPEP: Safety and Adherence

- No grade ≥3 AEs, grade ≥2 laboratory abnormalities, or SAEs observed
- Doxycycline PEP was well tolerated
  - Discontinuation due to intolerance or patient choice infrequent (1.5%)
  - 88% of participants described doxycycline PEP as acceptable/ very acceptable
- Median 7.3 (IQR: 1-10) sex acts/mo reported
  - 86% reported doxy-PEP always/often after anal/vaginal sex
  - Median doxyPEP doses: 4.0 per month (IQR 1.0- 10.0), 25% with ≥10 doses/month

Luetkemeyer. AIDS 2022. Abstr OALBX0103.

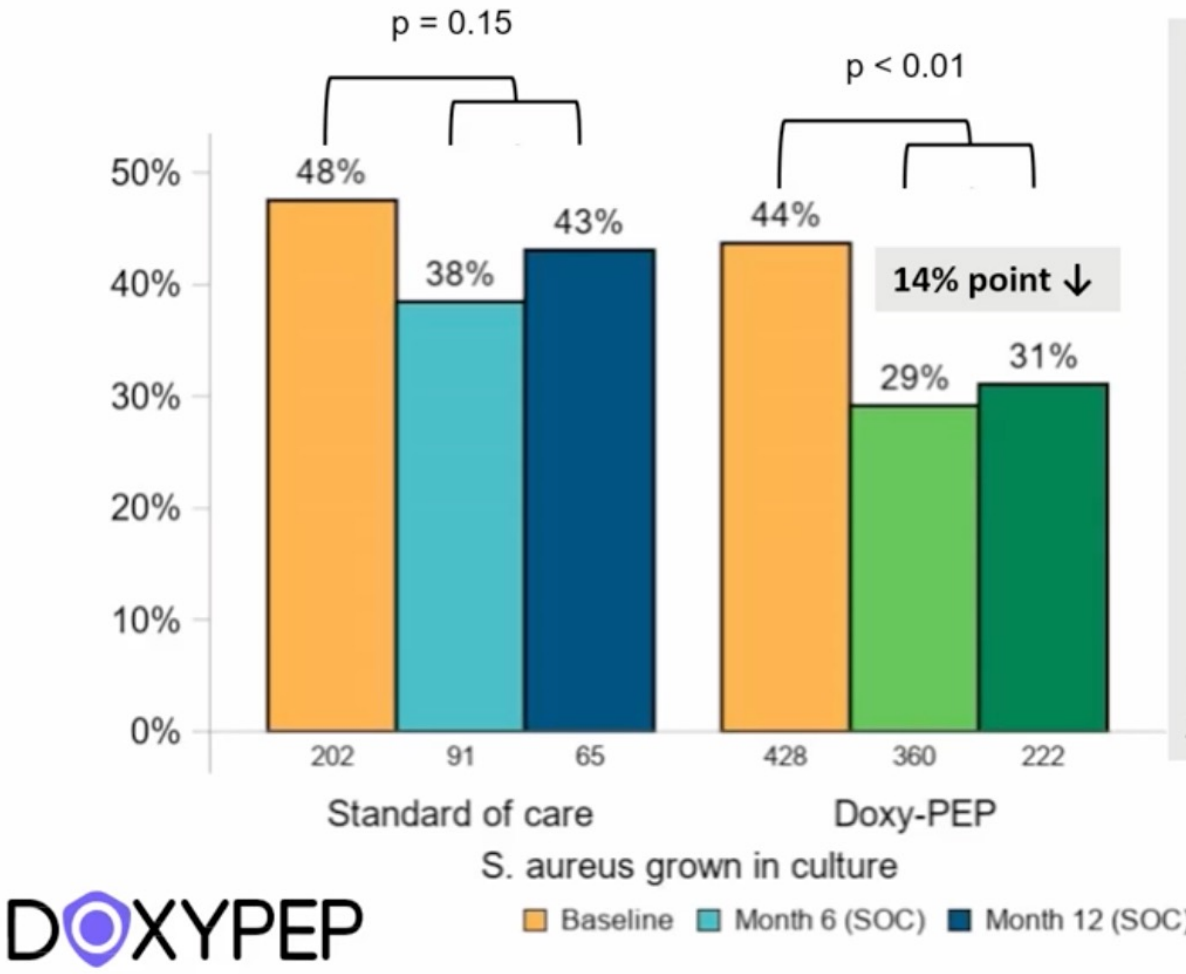
Tetracycline Resistance



- TCN-R similar in incident GC at baseline and on doxy-PEP
- Increased TCN-R in doxy-PEP vs. standard of care suggests doxy-PEP may be less protective against GC strains with existing TCN-R
- Limited by low number of GC samples with MIC results (56/320)

Luetkemeyer. CROI 2023

Staph Aureus



- *S. aureus* colonization is associated with subsequent clinical *Staph* infections, such as surgical infections and bacteremia.[1]
- DoxyPEP use associated with 14% absolute decrease in *S. aureus* colonization.

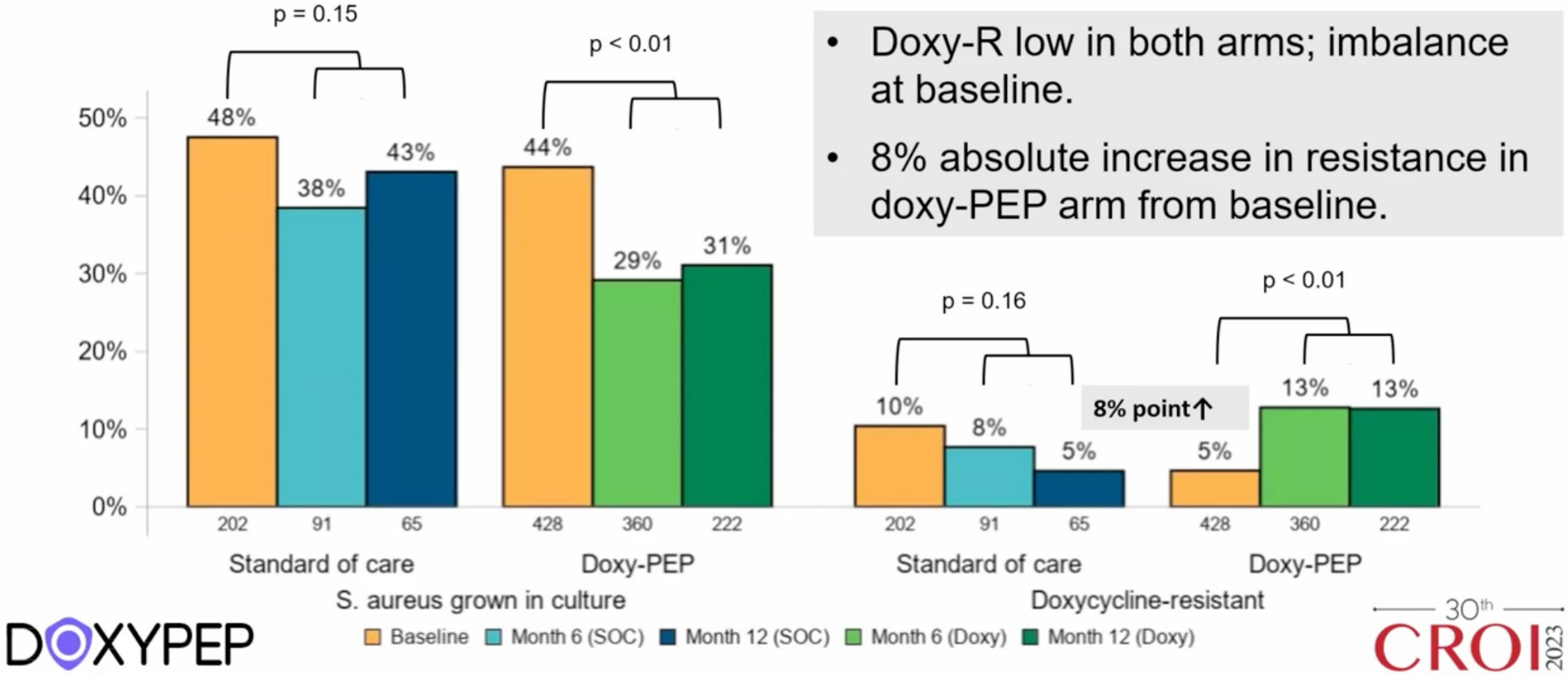
1. Oestergard *AIM* 2016; Jacobsson *Scand JID* 2008; Septimus *CID* 2016; Bode *NEJM* 2010

DOXYPEP

30th CROI 2023

Luetkemeyer. CROI 2023.

S. Aureus: 8% absolute increase in resistance in doxy-PEP arm



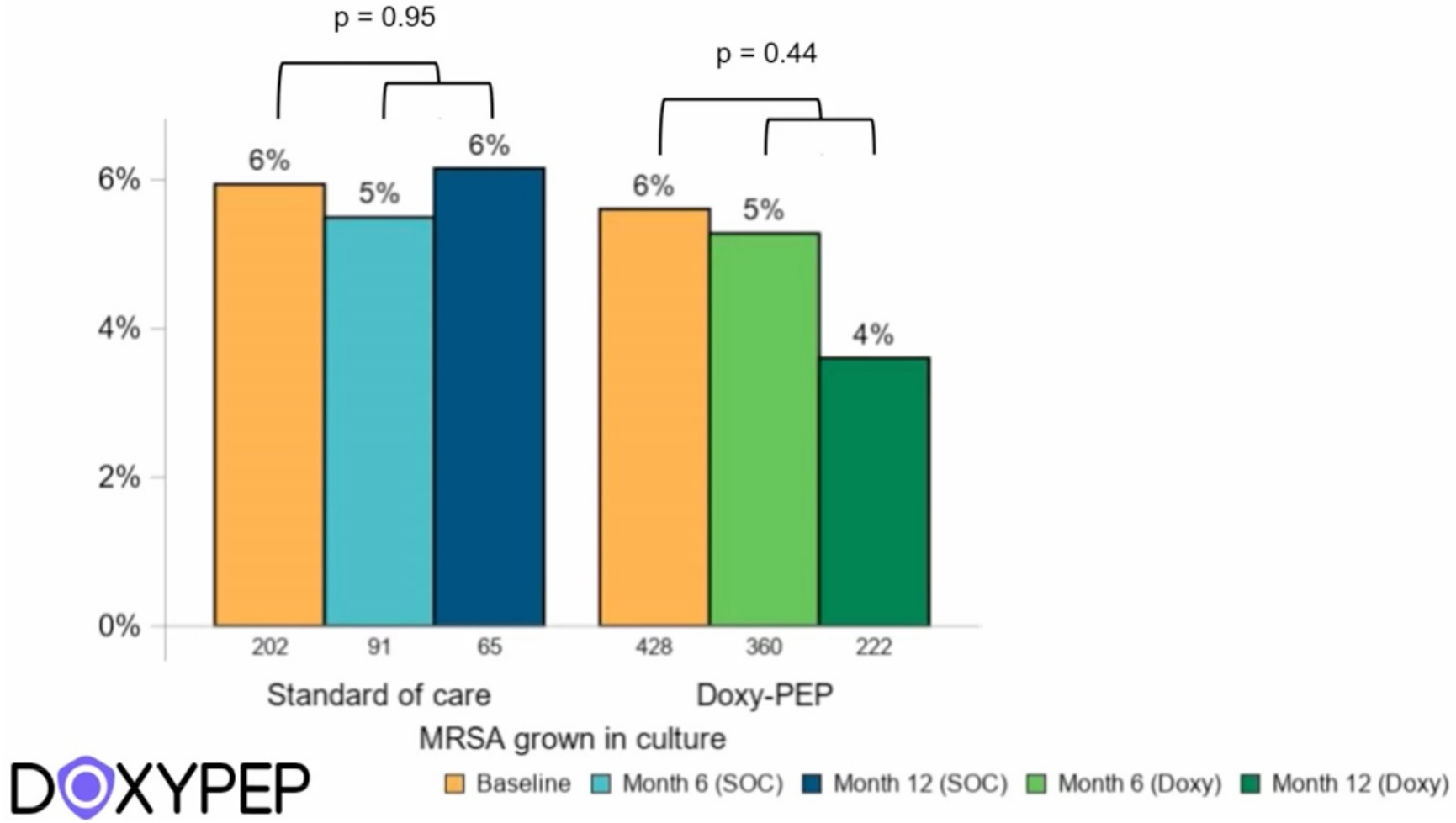
- Doxy-R low in both arms; imbalance at baseline.
- 8% absolute increase in resistance in doxy-PEP arm from baseline.

DOXYPEP

30th CROI 2023

Luetkemeyer. CROI 2023.

MRSA: Colonization low at 6%, no significant change with doxy-PEP

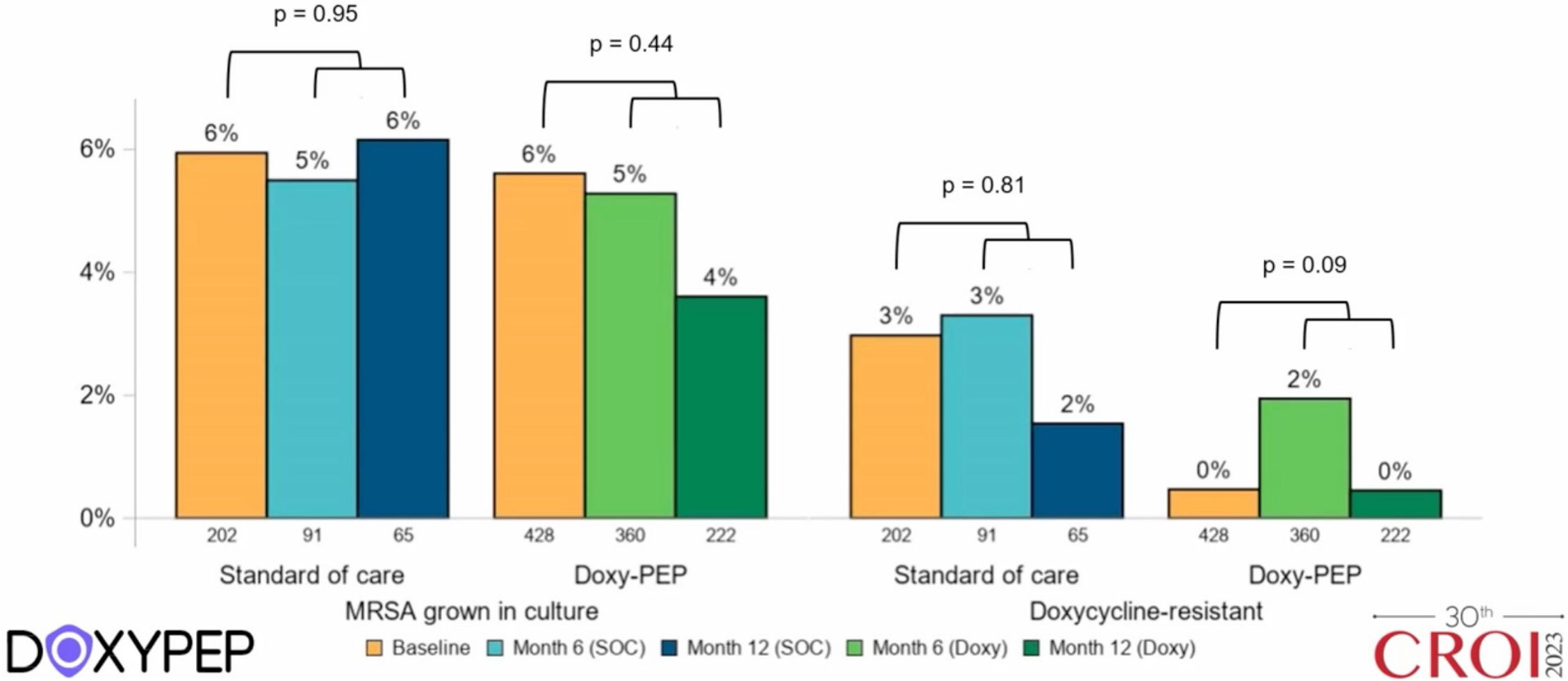


DOXYPEP

30th CROI 2023

Luetkemeyer. CROI 2023.

MRSA: No change in doxy resistance with doxy-PEP

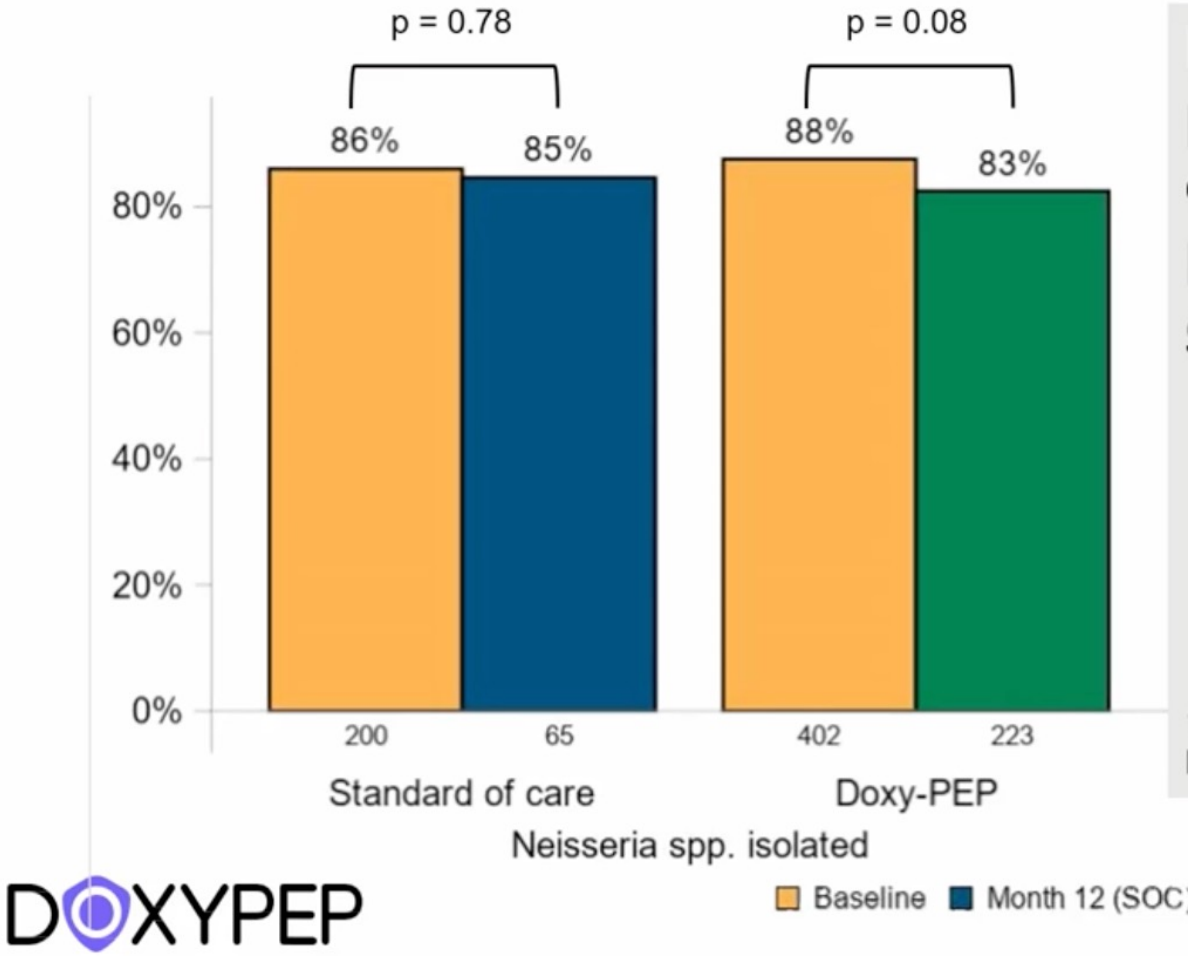


DOXYPEP

30th CROI 2023

Luetkemeyer. CROI 2023.

Commensal Neisseria: High rates of colonization & No change with doxy-PEP use



Non-pathogenic *Neisseria* colonizing the pharynx may serve as a reservoir for drug-resistant genes that can transmit to pathogenic bacteria including *N. gonorrhoeae*.[1]

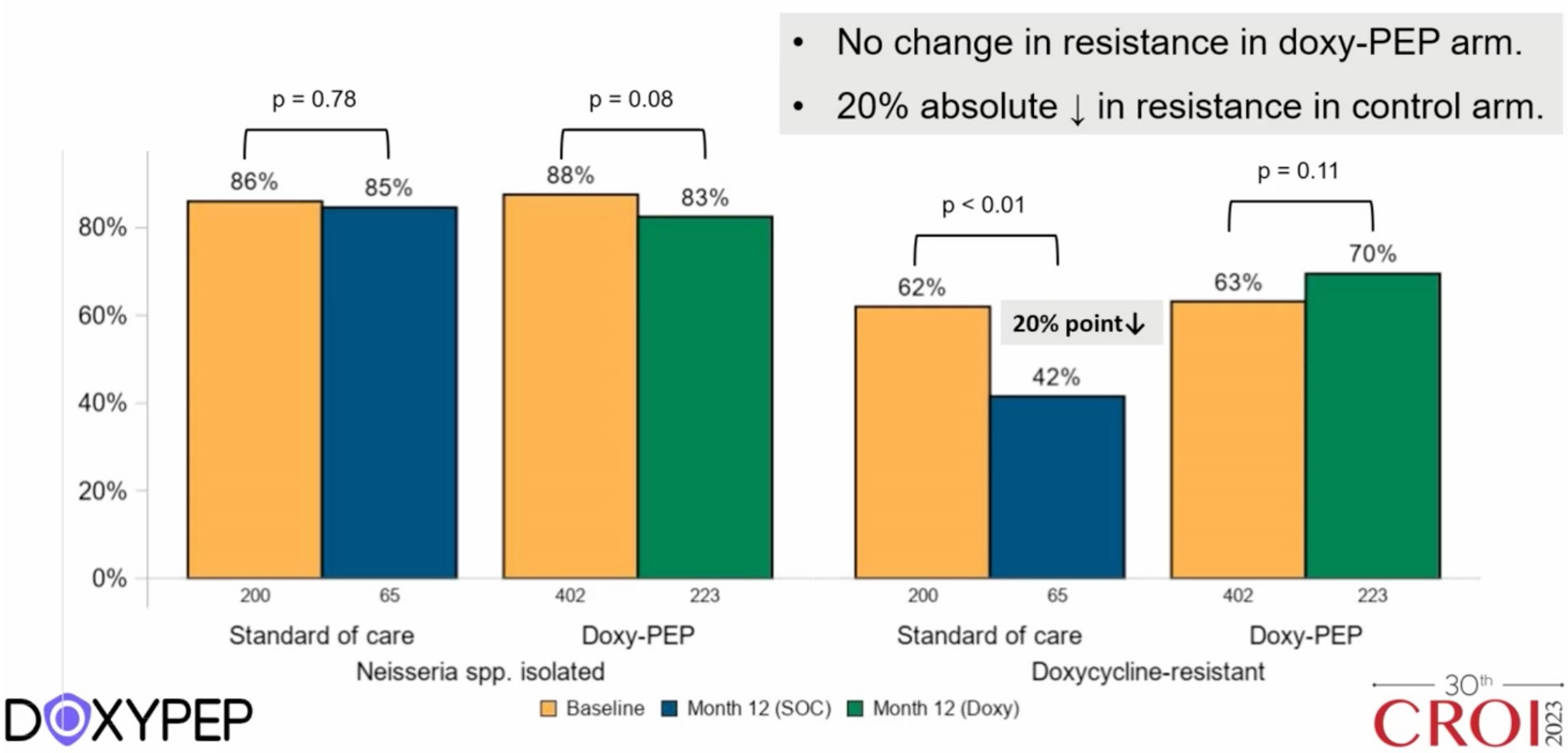
1. Chen *Antimicrob Agents Chemother* 2020; Fiore *Antibiotics* 2020; Rotman *Annu Rev Genet* 2014; Unemo *Clin Microbiol Rev* 2014

DOXYPEP

30th CROI 2023

Luetkemeyer. CROI 2023.

Commensal Neisseria: >60% baseline doxy resistance



Luetkemeyer. CROI 2023.

dPEP Kenya Study

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. Weekly SMS surveys on frequency of sex and doxycycline use.

Stewart. CROI 2023.

Methods

Primary endpoint: Any incident *C. trachomatis*, *N. gonorrhoeae*, or *T. pallidum* infection.

Power: Trial designed to accrue at least 66 primary endpoints for 80% power to detect 50% reduction in incident STIs between PEP and standard of care.

Primary analysis: Intention-to-treat analysis.

Analysis to censor pregnancy follow-up time.

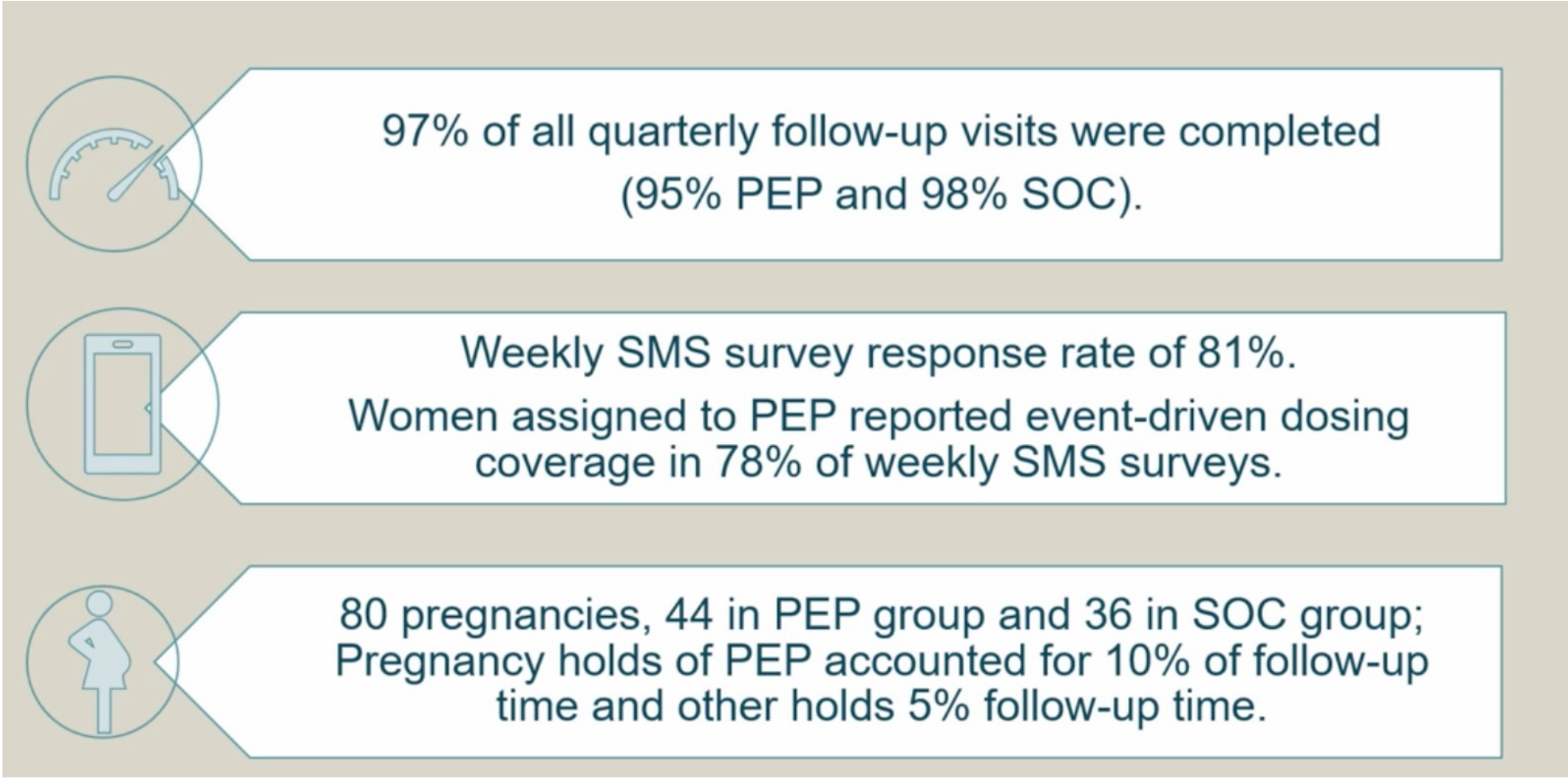
Stewart. CROI 2023.

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)
Chlamydia trachomatis	13% (30)	15% (33)
Neisseria gonorrhoeae	5% (10)	3% (7)
Treponema pallidum	0% (0)	1% (2)

Stewart. CROI 2023.

Results



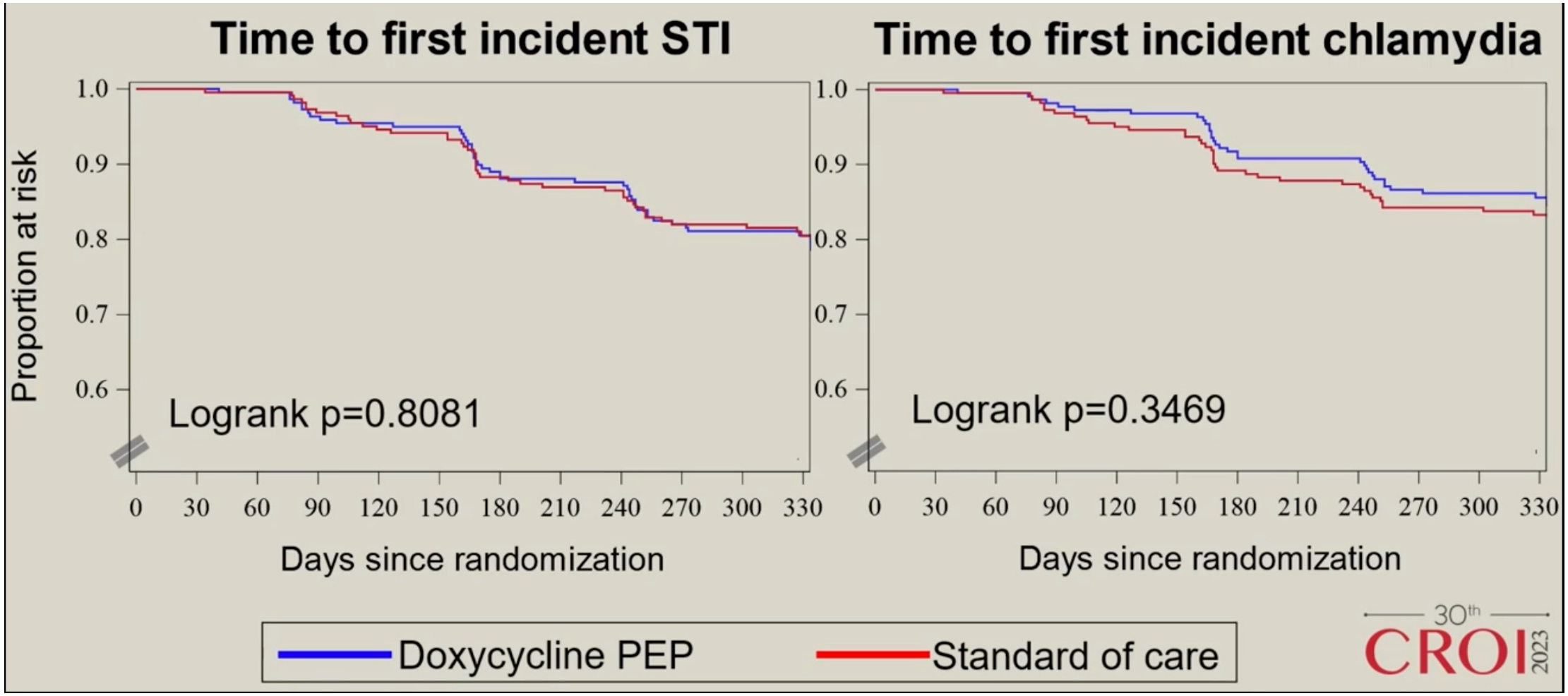
Stewart. CROI 2023.

Results – Incident STIs

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
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

Stewart. CROI 2023.

Time to 1st STI infection



Stewart. CROI 2023.

Adverse events

- No severe adverse events related to Doxy-PEP use
- No incident HIV infections
- TCN resistance
  - 100% Gonorrhea resistance at baseline (n=6) and 100% at follow up (n=22)
  - 0% resistance in Chlamydia (n=66)

Stewart. CROI 2023.

Summary

- Doxy PEP did not reduce incident STIs in cisgender women
- Endocervical tissue may differ from urethral, rectal or pharyngeal tissues
- High rates of gonorrhea resistance but none in chlamydia
- Self report adherence was high but imperfect
  - Recruitment
  - Adherence support
  - Open label design

Doxy PEP in Mucosal Tissues: Single dose study

(MUCOSAL PHARMACOLOGY OF DOXYCYCLINE FOR BACTERIAL STI PREVENTION IN MEN AND WOMEN)

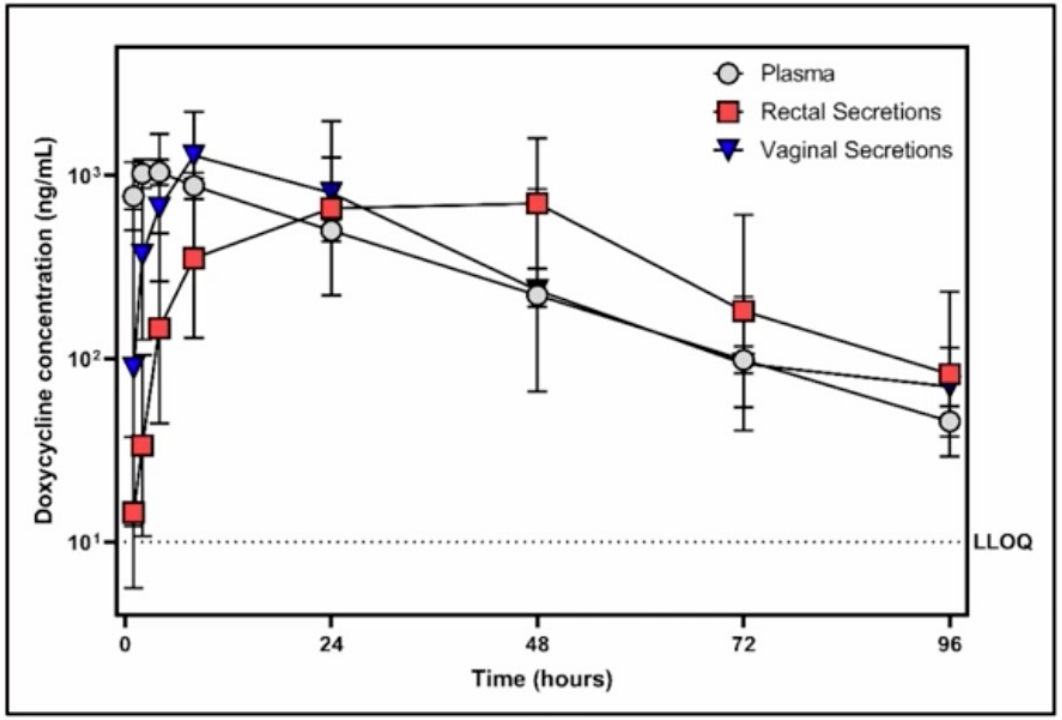
- Critical for dose selection and optimization to maximize efficacy and safety
- Define pharmacologic correlates of protection of each STI

Haaland. CROI 2023.

Methodology

- Conducted at Hope Clinic at Emory from June 2021-May 2022
  - 20 Participants; 50% black
  - 200 mg Doryx (Delayed released formulation)
  - BIKTARVY (BIC/TAF/FTC)
- Blood and Rectal or vaginal swabs 7 days after
  - 7 females provided rectal swabs
  - Rectal or vaginal and cervical biopsies and uretheral swabs collected at 24 hours
  - Doxy measured using liquid chromatography tandem mass spectrometry assays for plasma, mucosal swabs and biopsies
- Pharmacologic analysis
  - Doxy exposure and concentration
  - Time above MIC for C trachomatis, T Pallidum and N Gonorrhea

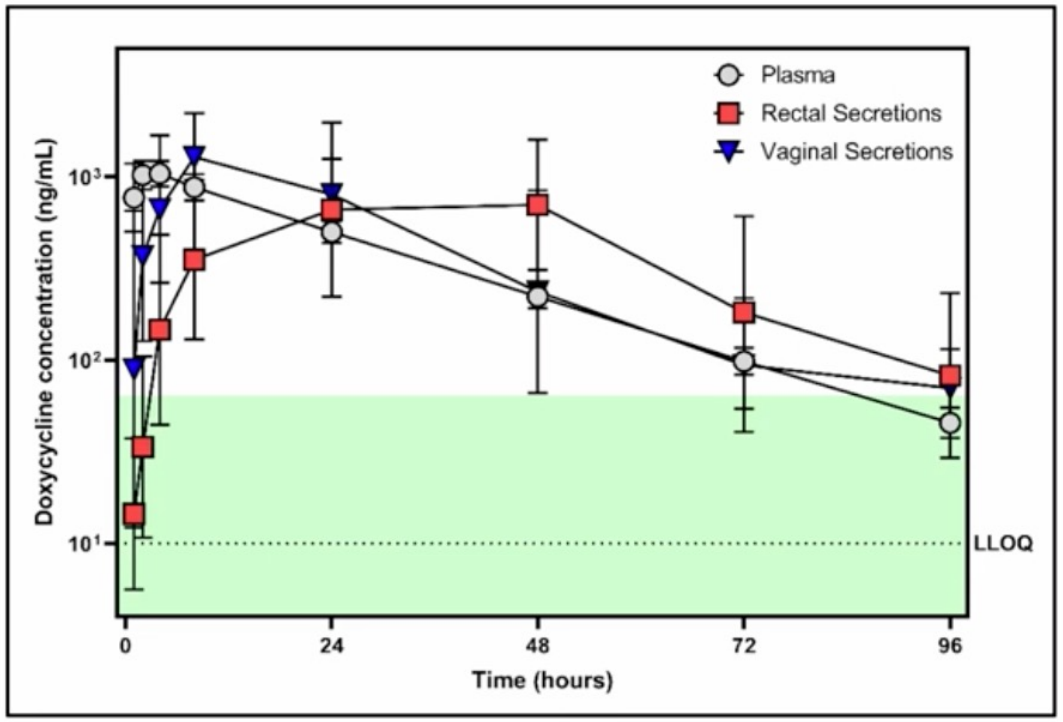
Mucosal Doxy Concentrations



	C_{max} (ng/mL) [95% CI]	T_{max}	$AUC_{0\text{-}96h}$ (ng*h/mL) [95% CI]	AUC Ratio (S:P)
Plasma	1042 [889 – 1222]	4 hr	33,951 [29,632 – 38,899]	
Rectal Secretions	704 [311 – 1596]	48 hr	73,511 [34,332 – 156,487]	2.17
Vaginal Secretions	1284 [742 – 2223]	8 hr	58,562 [32,719 – 104,816]	1.72

Haaland. CROI 2023.

Chlamydia

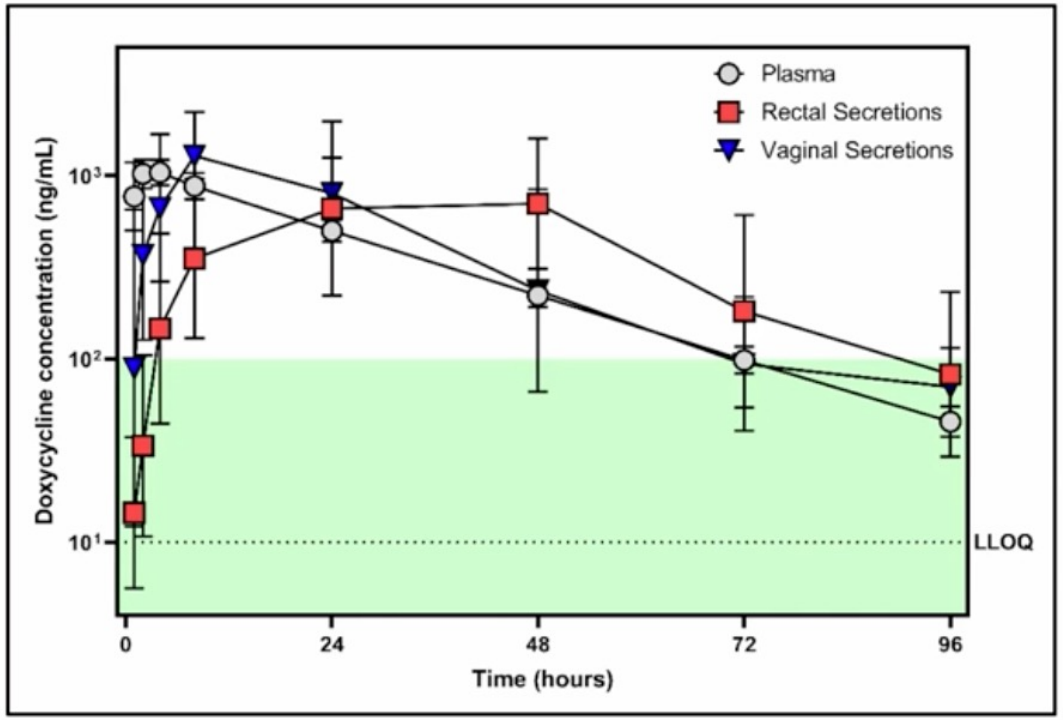


	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	16x	87 hr	44 hr
Rectal Secretions	11x	97 hr	62 hr
Vaginal Secretions	20x	101 hr	45 hr

Minimum Inhibitory Concentrations (MIC):
C trachomatis MIC_{90} = 64 ng/mL Zheng *Sex Transm Dis* 2015

Haaland. CROI 2023.

Syphilis



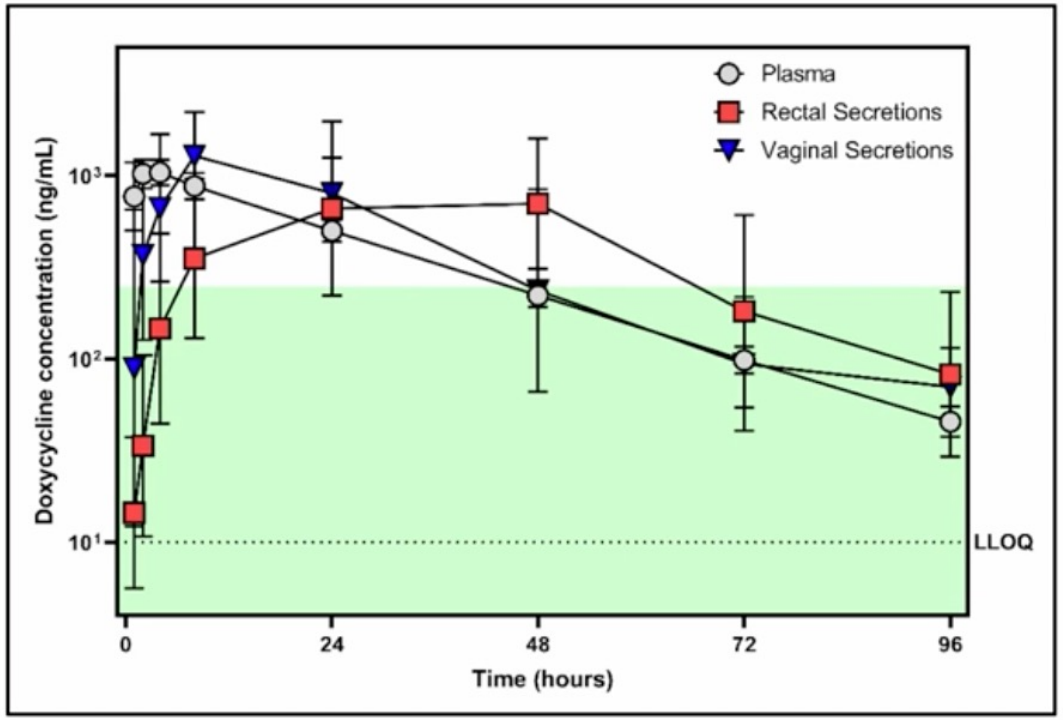
	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	10x	71 hr	32 hr
Rectal Secretions	7x	88 hr	51 hr
Vaginal Secretions	12x	70 hr	38 hr

Minimum Inhibitory Concentrations (MIC):

T pallidum MIC_{90} = 100 ng/mL Edmondson *Antimicrob Agents Chemother* 2020

Haaland. CROI 2023.

Gonorrhea



	Time above MIC value		
	C_{max}	MIC	4x MIC
Plasma	4x	45 hr	3 hr
Rectal Secretions	3x	62 hr	NA
Vaginal Secretions	5x	45 hr	11 hr

Minimum Inhibitory Concentrations (MIC):
N gonorrhoeae MIC = 250 ng/mL CDC Antimicrob Resist Susc Test

Haaland. CROI 2023.

Tissue and Urethral Doxy Concentrations

	C_{24} (ng/g or ng/mL) [95% CI]	Fold above MIC		
		C trachomatis	*T pallidum*	*N gonorrhoeae*
Rectal Tissue	616 [495 – 766]	9x	6x	2x
Vaginal Tissue	301 [130 – 698]	4x	3x	1x
Cervical Tissue	430 [220 – 840]	6x	4x	1x
Urethral Secretions	1166 [598 – 2394]	18x	11x	4x

- Tissue concentrations 24 hours after dose reach up to 9x MIC values
- Doxycycline detected on 9/11 male urethral swabs
  - Concentrations exceed 4x MIC values

Minimum Inhibitory Concentrations (MIC): Zheng *Sex Transm Dis* 2015; Edmondson *Antimicrob Agents Chemother* 2020; CDC Antimicrob Resist Susc Test

Haaland. CROI 2023.

Conclusions

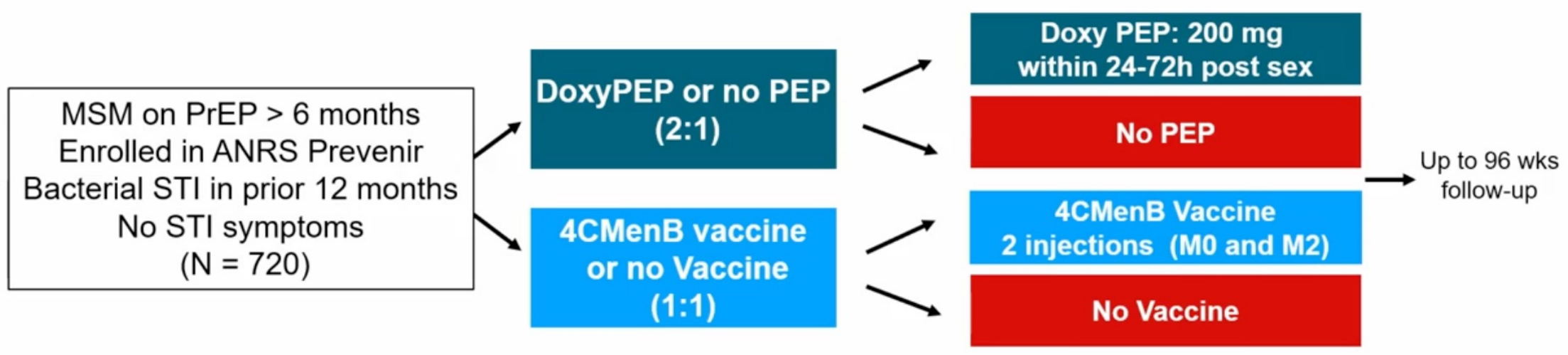
- Doxy efficiently distributes to mucosal sites of STI exposure and persists at concentrations exceeding reported MIC values
  - Helps explains efficacy against STIs observed among MSM
  - Predicts vaginal efficacy among women
  - Helps establish correlates of protection for each STI
- Mucosal doxy concentrations exceeded reported MIC values for Chlamydia and Syphilis to greater extent than for sensitive gonorrhea
  - Unclear how these differences affect prevention efficacy against each STI
  - Preclinical STI models may help evaluate dosing modalities and inform dose optimization

ANRS 174 DOXYVAC: AN OPEN-LABEL RANDOMIZED TRIAL TO PREVENT STIs IN MSM ON PrEP

- Incidence of STIs using DoxyPEP or 4CMenB vaccine
- Early discontinuation
  - Unblinded analysis
  - Significant effectiveness of both intervention
    - Stop new enrollments
    - offer DoxyPEP and 4CMenB to all

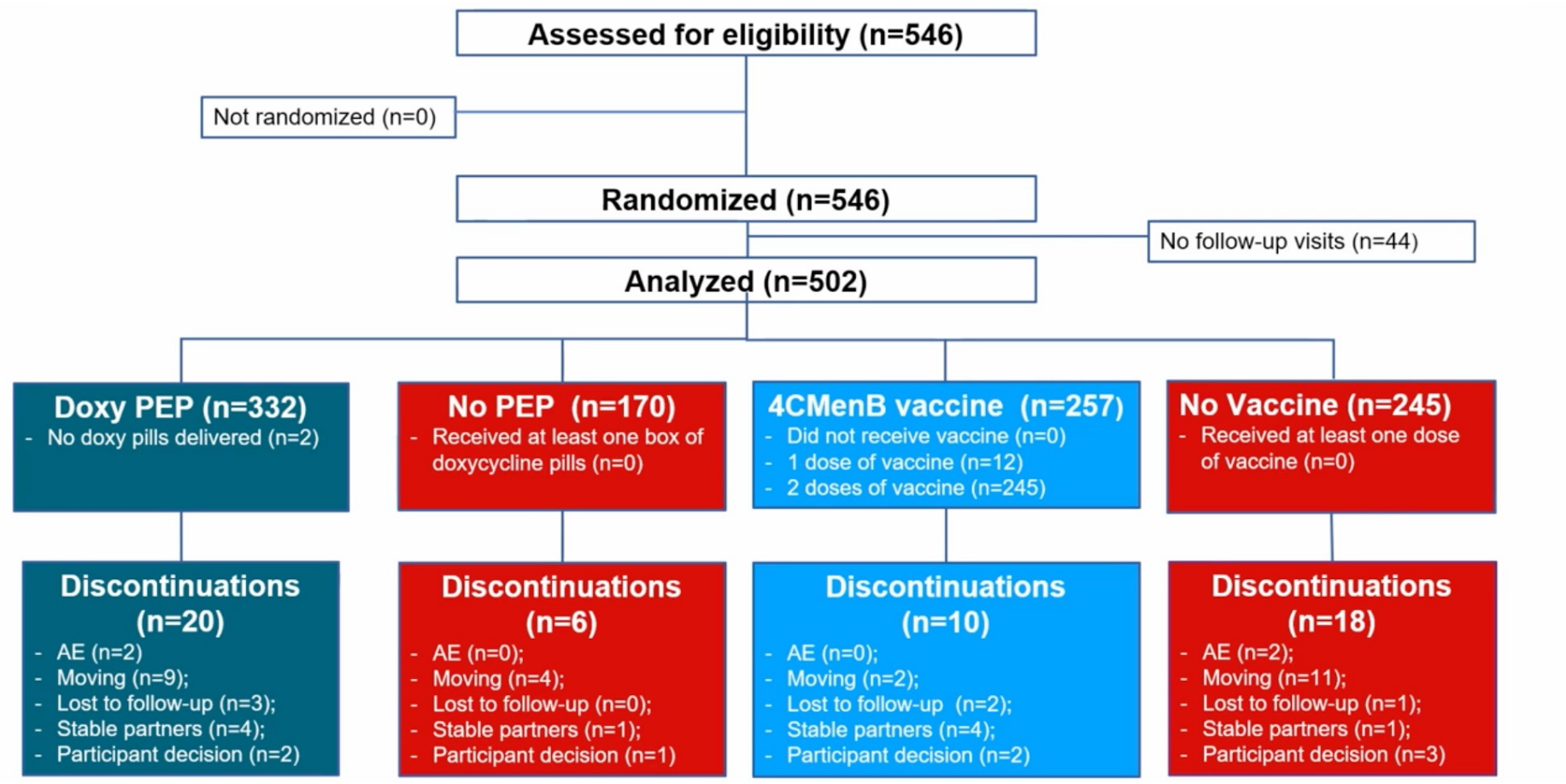
Molina. CROI 2023.

Study Design



Molina. CROI 2023.

Study flowchart



Molina. CROI 2023.

Baseline Characteristics

Median (IQR) or %	Doxy PEP (n = 332)	No PEP (n = 170)	4CMenB vaccine (n = 257)	No Vaccine (n = 245)	Total (n=502)
Age, years	40 (33-48)	39 (33-47)	40 (33-47)	39 (33-48)	**39 (33-47)**
White	79.2	82.9	75.9	85.3	**80.5**
Born in France	84.8	81.7	82.7	84.8	**83.8**
Secondary education	89.1	88.4	90.7	87.0	**88.9**
Employed	87.0	87.5	89.6	84.6	**87.2**
PrEP use, months	42 (32-55)	43 (35-55)	43 (32-55)	42 (33-54)	**42 (32-55)**
No. STIs in prior 12 months	2 (1-2)	2 (1-2)	2 (1-3)	2 (1-2)	**2 (1-2)**
Gonorrheae	67.3	70.1	67.5	69.0	**68.2**
Chlamydiae	50.3	47.9	52.5	46.3	**49.5**
Syphilis	21.5	17.4	20.4	19.8	**20.1**
M. genitalium	3.9	4.2	3.5	4.5	**4.0**
Condomless sex (4 weeks) no.	5 (3-10)	5 (2-10)	5 (2-10)	5 (3-10)	**5 (2-10)**
Partners (last 3 months) no.	10 (5-20)	10 (5-20)	10 (5-20)	10 (5-20)	**10 (5-20)**
Chemsex at last sex act	11.8	10.6	12.5	10.2	**11.4**

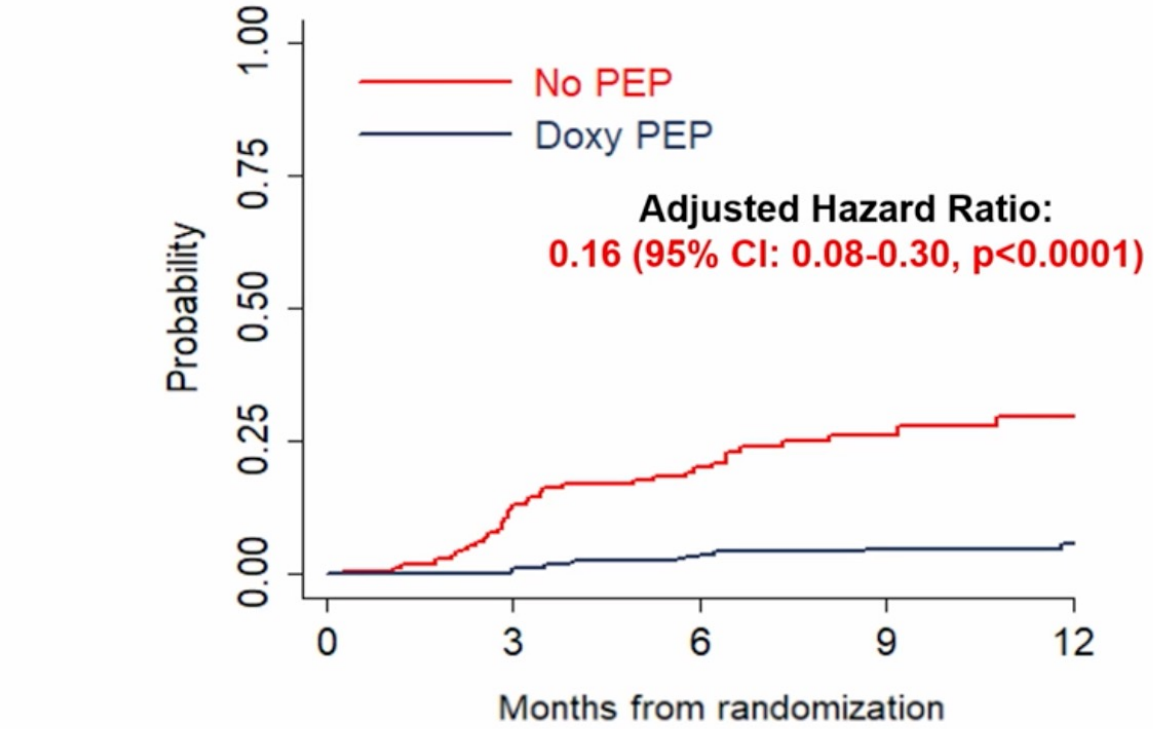
Molina. CROI 2023.

Primary Efficacy endpoint: Time to 1st CT or Syphilis Infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.99)

Median follow-up: **9 months**
(IQR: 6 to 12)

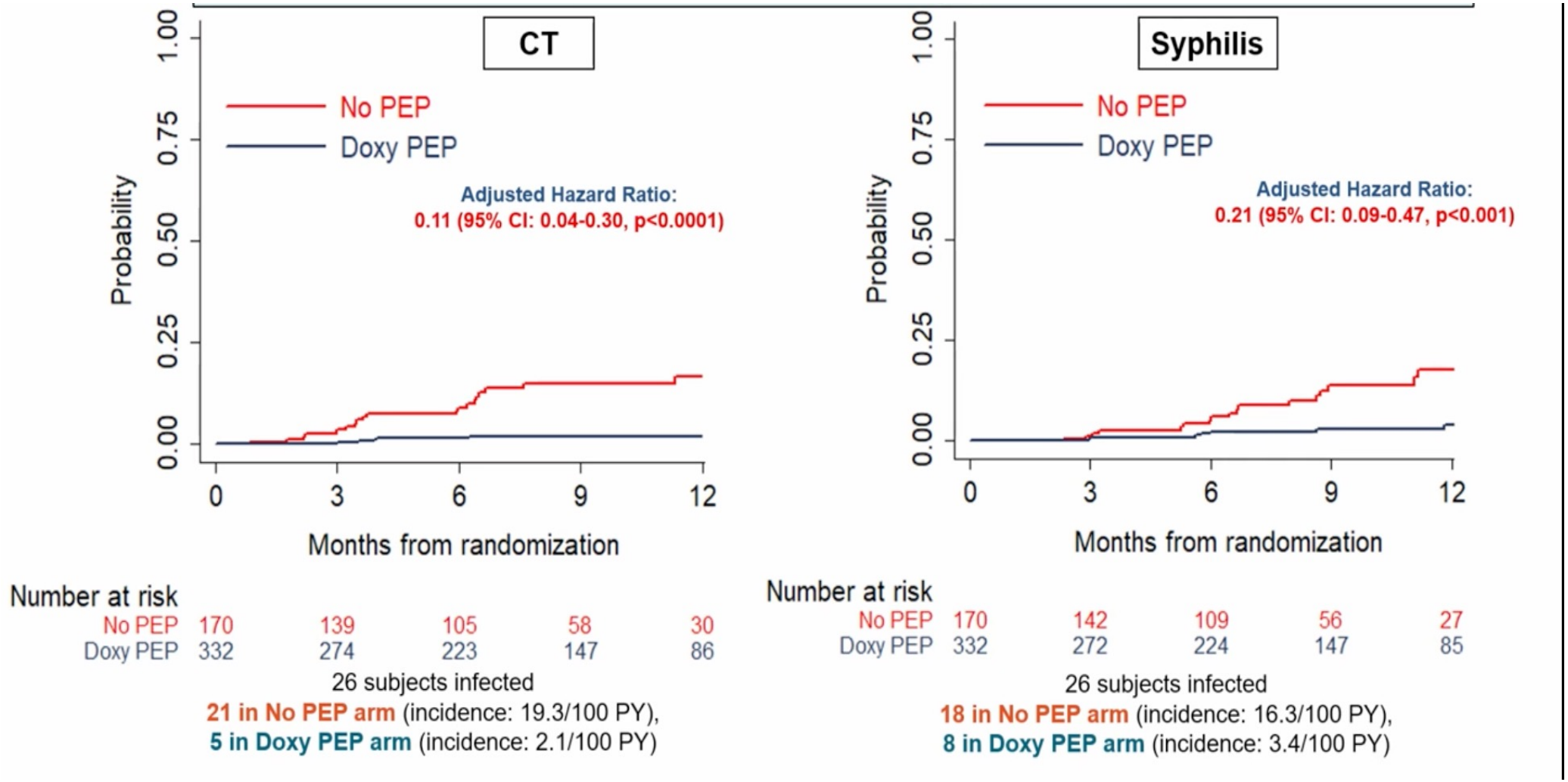
49 subjects infected
36 in No PEP arm
(incidence: 35.4/100 PY),
13 in Doxy PEP arm
(incidence: 5.6/100 PY)



Number at risk

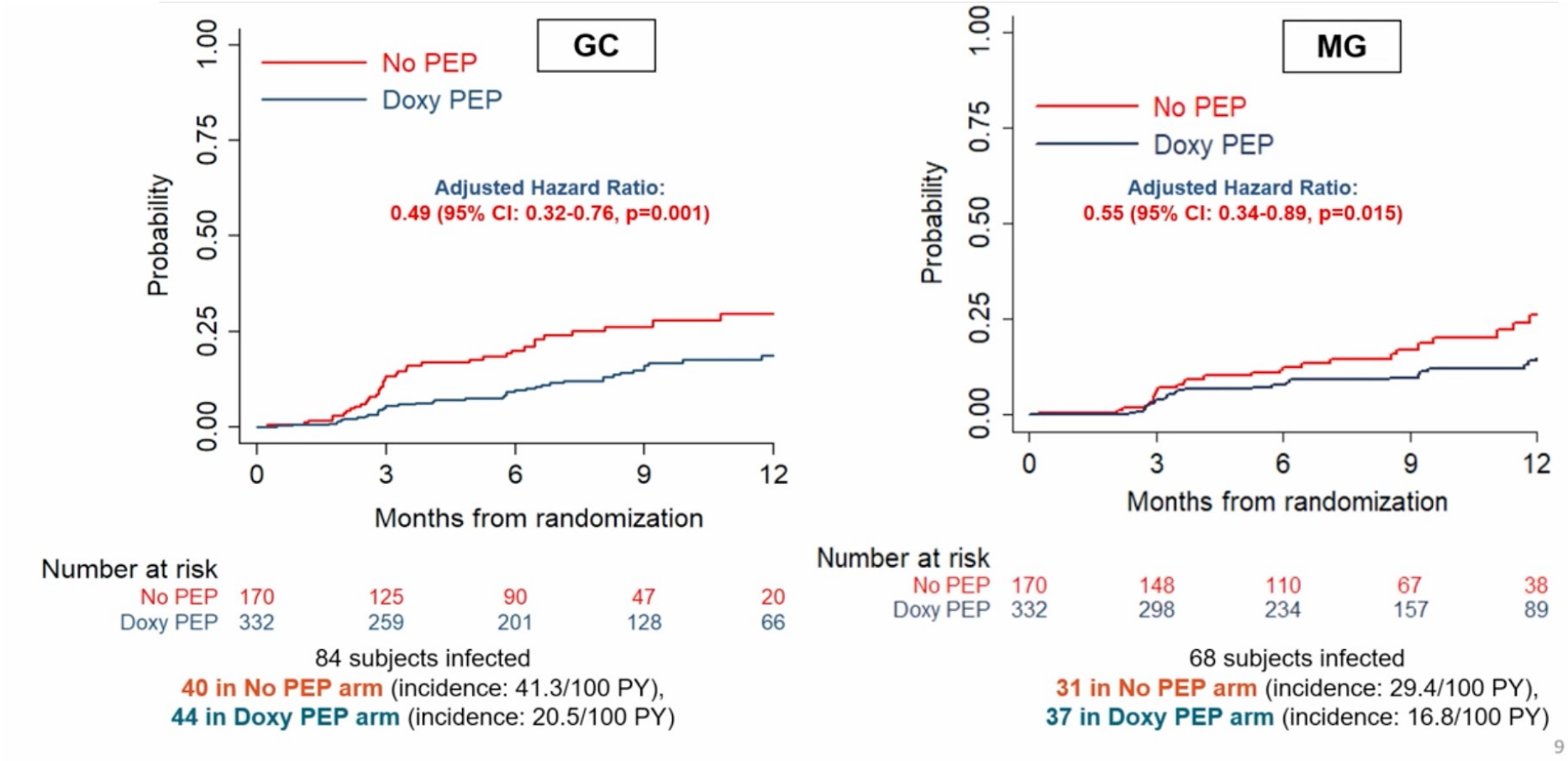
No PEP	170	137	99	47	22
Doxy PEP	332	271	220	144	83

Molina. CROI 2023.



Molina. CROI 2023.

Secondary Endpoint: Time to 1st GC and MG Infection



Molina. CROI 2023.

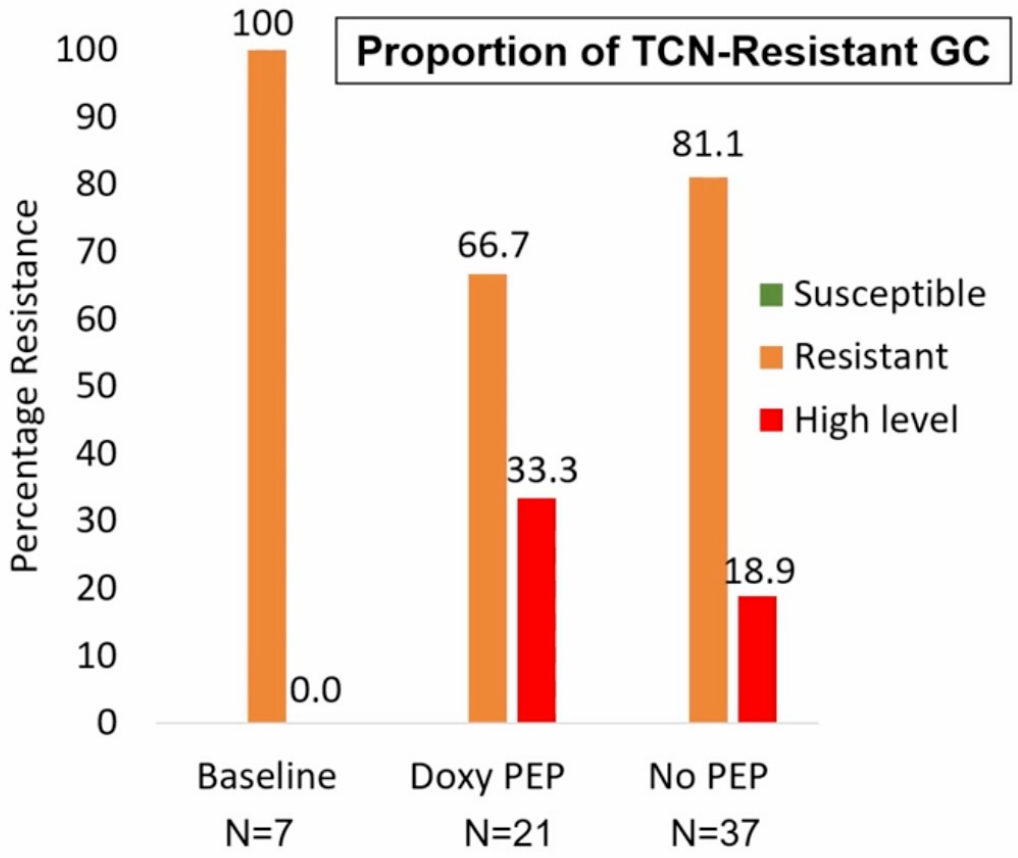
Tetracycline resistance

GC:

- 65 cultures available for resistance testing (15% of PCR positive samples)
- Tetracycline MICs determined by Etest
- Resistance using EUCAST 2023 breakpoints
  - Resistance: MIC > 0.5 mg/L
  - High level resistance: MIC > 8 mg/L

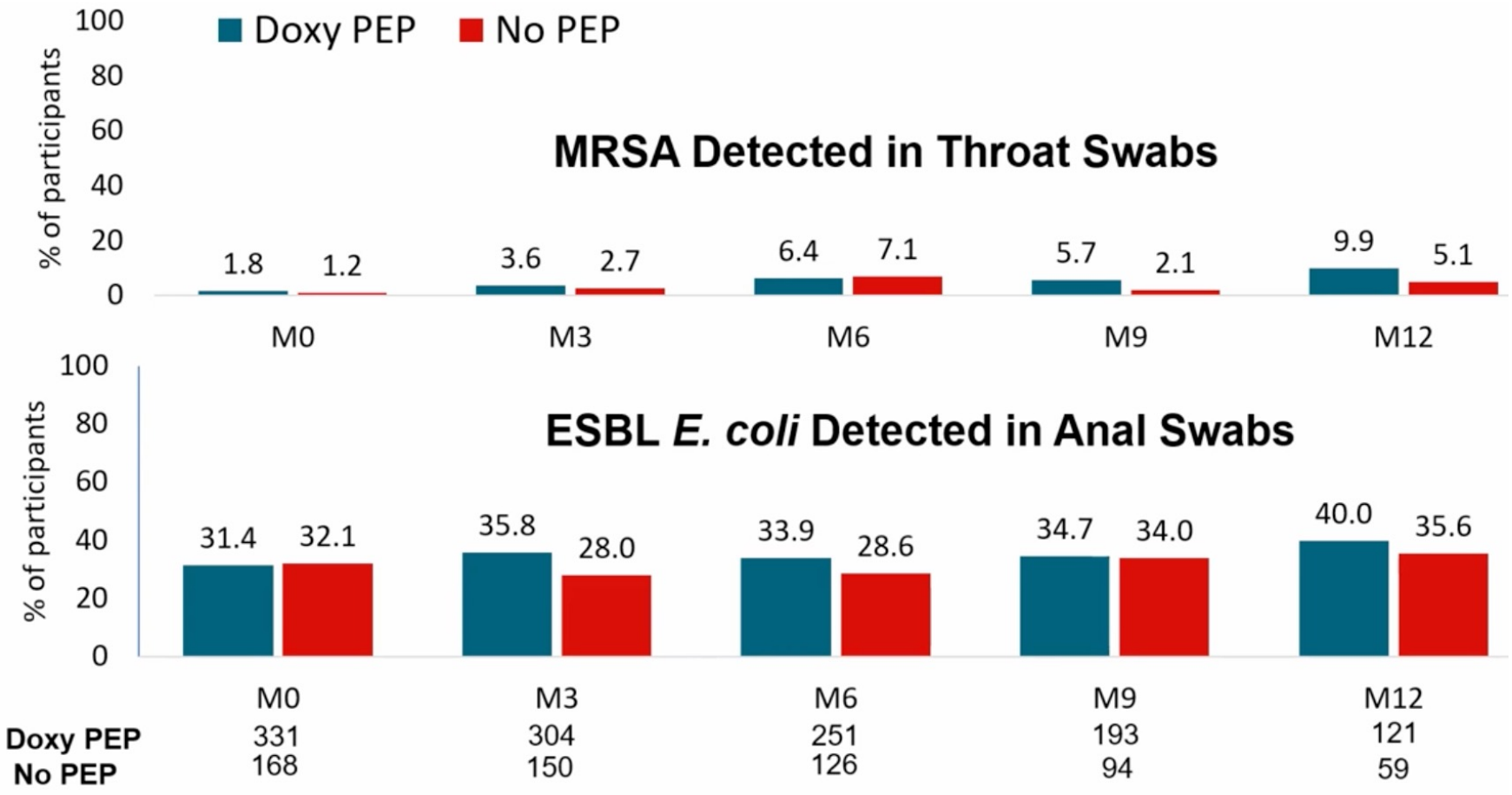
CT:

- 4/23 strains tested for TCN-R in culture: no resistance (but none from PEP arm)
- 53/65 PCR+ swabs with16S rRNA sequenced: no TCN-R mutation (only 3 from PEP arm)



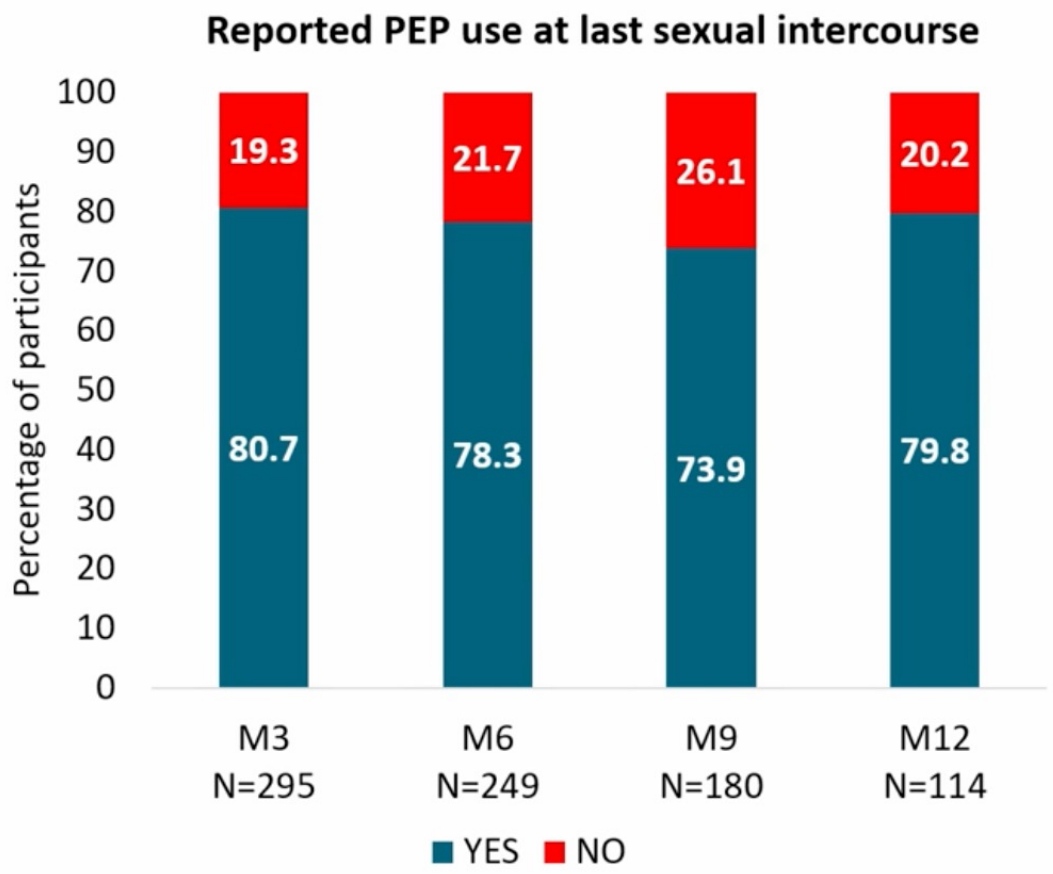
Molina. CROI 2023.

Microbiome Analysis



Molina. CROI 2023.

Self reported adherence



- **Median (IQR) time to PEP intake: 27h** (5-33) after sex
- **Median no. of pills/month (IQR): 7 pills** (4-11)
- **3 (0.9%) discontinued PEP:** GI AEs (n=2) and fear of AEs (n= 1)

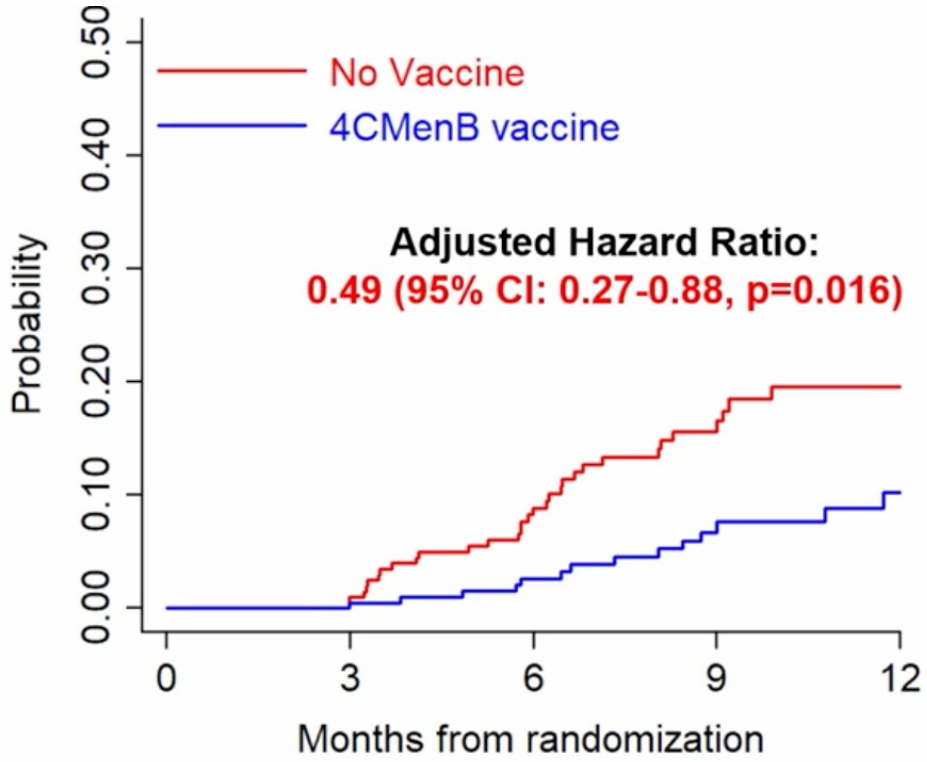
Molina. CROI 2023.

4CMENB vaccine: Time to 1st GC infection

No interaction between Doxy PEP and 4CMenB vaccine (p=0.41)

49 subjects infected
32 in No Vaccine arm
(incidence: 19.7/100 PY),
17 in 4CMenB vaccine arm
(incidence: 9.8/100 PY)

GC infections were considered from M3 visit (1 month after 2nd vaccine dose)

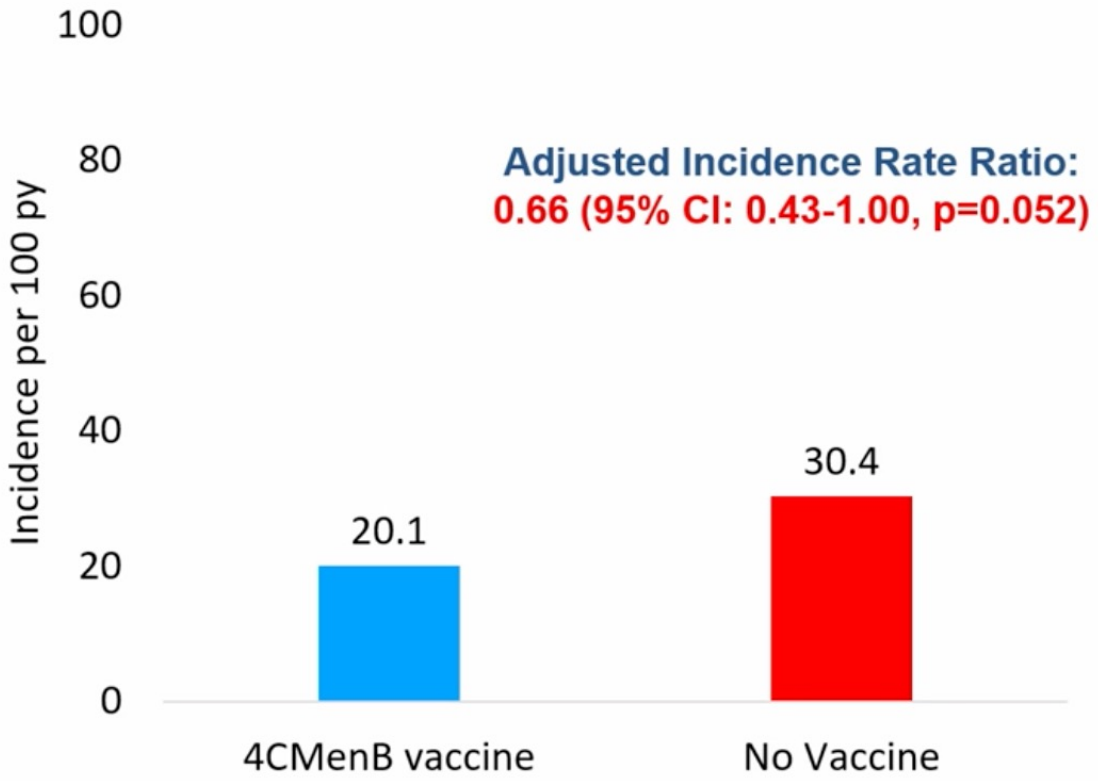


Number at risk					
No Vaccine	245	208	150	91	49
4CMenB vaccine	257	208	170	102	49

Molina. CROI 2023.

Cumulative Incidence of GC infections

90 GC infections
54 in No Vaccine arm,
36 in 4CMenB vaccine arm



GC infections were considered from M3 visit (1 month after 2nd vaccine dose)

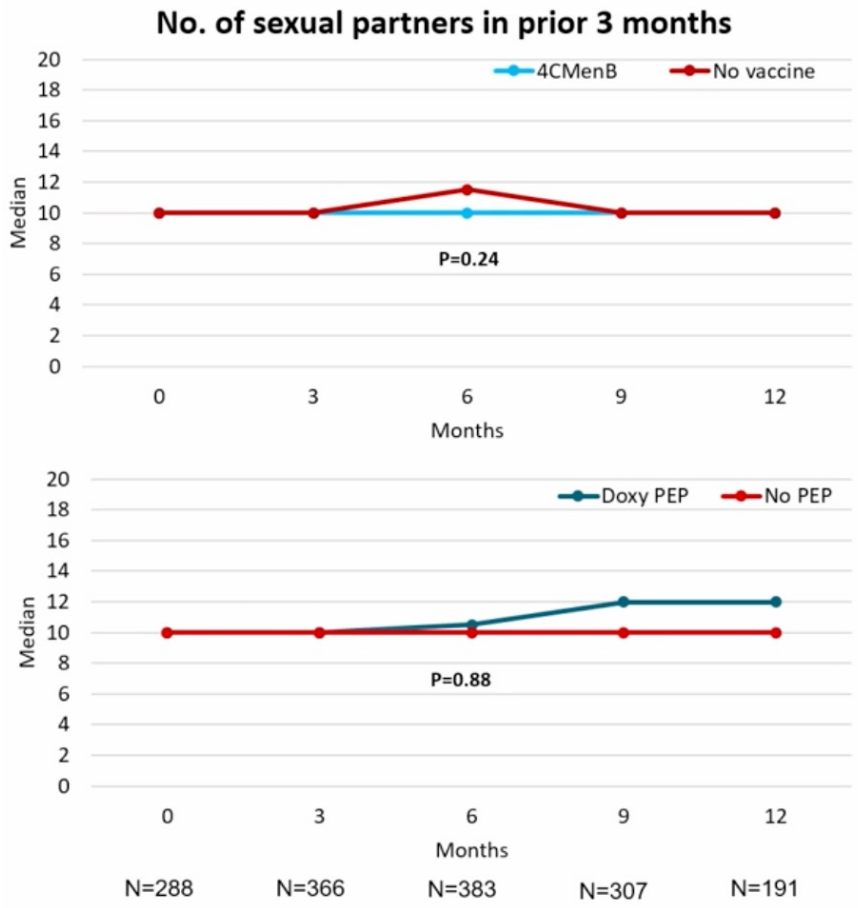
Molina. CROI 2023.

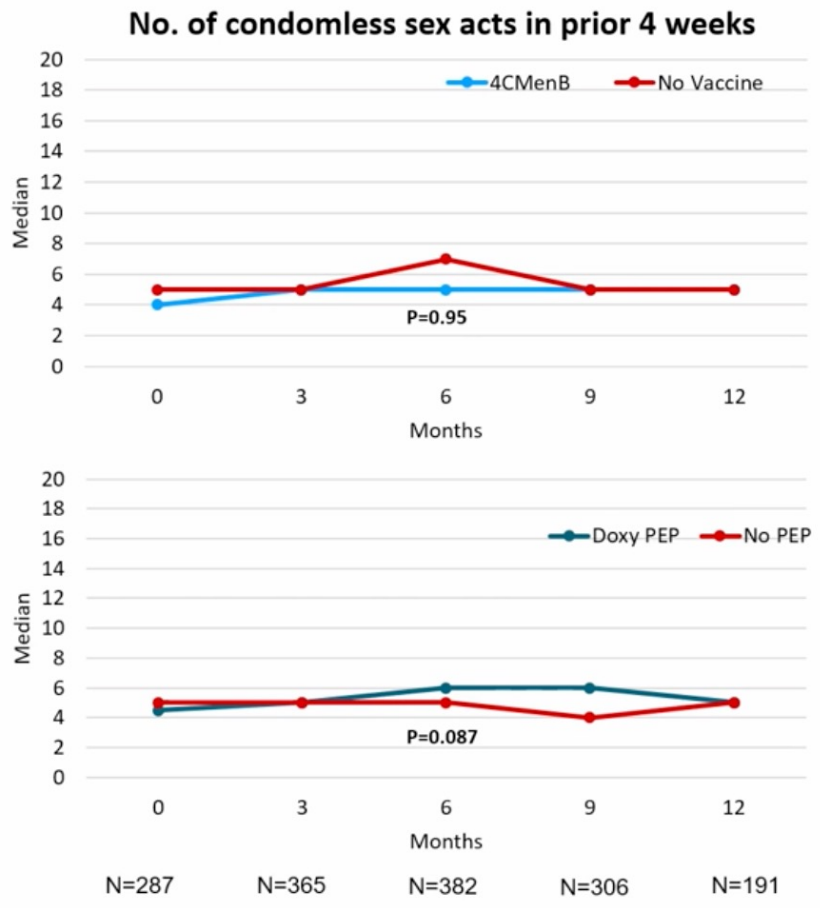
Adverse events

Nb of Participants (%)	PEP Doxy N=332	No PEP N=170	P value	4CMenB N=257	No Vaccine N=245	P value
Any Serious AE	26 (7.8)	10 (5.9)	0.58	23 (9.0)	13 (5.3)	0.16
Any drug-related SAE	0 (0)	0 (0.0)		0 (0)	0 (0.0)	
Any Grade 3 or 4 AE	10 (3.0)	6 (3.5)	0.75	10 (3.9)	6 (2.5)	0.36
Treatment D/C due to AE	3 (0.9)			0 (0.0)		
Drug-Related AEs	19 (5.7)			89 (34.6)		
Drug-Related AEs in > 3 pts						
Nausea/vomiting	7			1		
Abdominal pain	6			1		
Diarrhea	4			0		
Asthenia	0			9		
Fever	0			5		
Headache	0			5		
Nodule	0			6		
Oedema	0			8		
Pain	0			4		
Pain at injection site	0			77		
Redness	0			12		

Molina. CROI 2023.

Changes in Sexual Behavior





Molina. CROI 2023.

Summary

- Doxy PEP
  - Large studies shown significant reductions of STIs among MSM
  - Doxy PEP is well tolerated with high self reported adherence
  - Evaluation of full impact of antibiotic is underway (STIs, microbiome)
- 4CMenB vaccine
  - Reduced incidence of a first episode of GC infection
- No magic bullet: Interest for combined approaches
- Long term research is needed if doxyPEP is the driver of TCN resistance
- STI Research: A scientific priority to meet 2030 WHO/UNAIDS targets to reduce incidence of HIV and STI by 90%

POTENTIAL IMPACT AND EFFICIENCY OF DOXY-PEP AMONG PEOPLE WITH OR AT RISK OF HIV

- Through an EHR based cohort:
  - Estimate how many STIs could be averted using different doxy-PEP strategies
  - Identify prescribing strategies that minimize doxy-PEP use and maximize impact on STIs

Methods

- Through an EHR based cohort
    - Gay and bisexual men, transgender women and non-binary people assigned male sex at birth
    - >2 STI test events for Chlamydia, Gonorrhea and Syphilis from 2015-2020
    - People with HIV, PrEP use and HIV neg non-PrEP users

Potential doxy-PEP strategies

Prescribe doxy-PEP to patient groups

1. All patients accessing care
2. People with HIV & PrEP users
3. PrEP users only

Prescribe doxy-PEP for 12m after STI* diagnosis

4. Any STI diagnosis
5. Rectal STI diagnosis
6. STI at current visit + STI in past 12 months
7. STI at current visit + STI in past 6 months
8. Concurrent (2+) STIs at same visit
9. Syphilis diagnosis
10. Gonorrhea diagnosis

*STI = chlamydia, gonorrhea, syphilis

Traeger. CROI 2023.

Counterfactual scenarios - doxy-PEP

Doxy-PEP use

- Assumed doxy-PEP would have been prescribed to and used by patients who met criteria
- Could be prescribed multiple times per patient
- Calculated proportion of people who would be prescribed doxy-PEP using each strategy

STIs averted

- Assume STI incidence would have been reduced by clinical trial disease-specific efficacy estimates
- Calculated proportion of STIs that would have been averted by doxy-PEP

Number needed-to-treat (NNT)

- Calculated NNT for 1 year to avert 1 STI (person-years of doxy-PEP use / number of STIs averted)

Traeger. CROI 2023.

Results

Cohort

N=10,546

87% gay men
7% bisexual men
4% trans women
2% non-binary people

54% ever PrEP users
14% people with HIV

Race	
White	7355 (70.8%)
Black or African American	677 (6.5%)
Multiracial	646 (6.2%)
Asian	617 (5.9%)
American Indian or Alaska Native	56 (0.5%)
Native Hawaiian or Other Pacific Islander	25 (0.2%)
Other	193 (1.9%)
Not recorded	827 (8.0%)
Ethnicity	
Hispanic	1,517 (14.6%)
Not Hispanic	8,017 (77.1%)
Not recorded	862 (8.3%)

STI incidence

2015-2020:

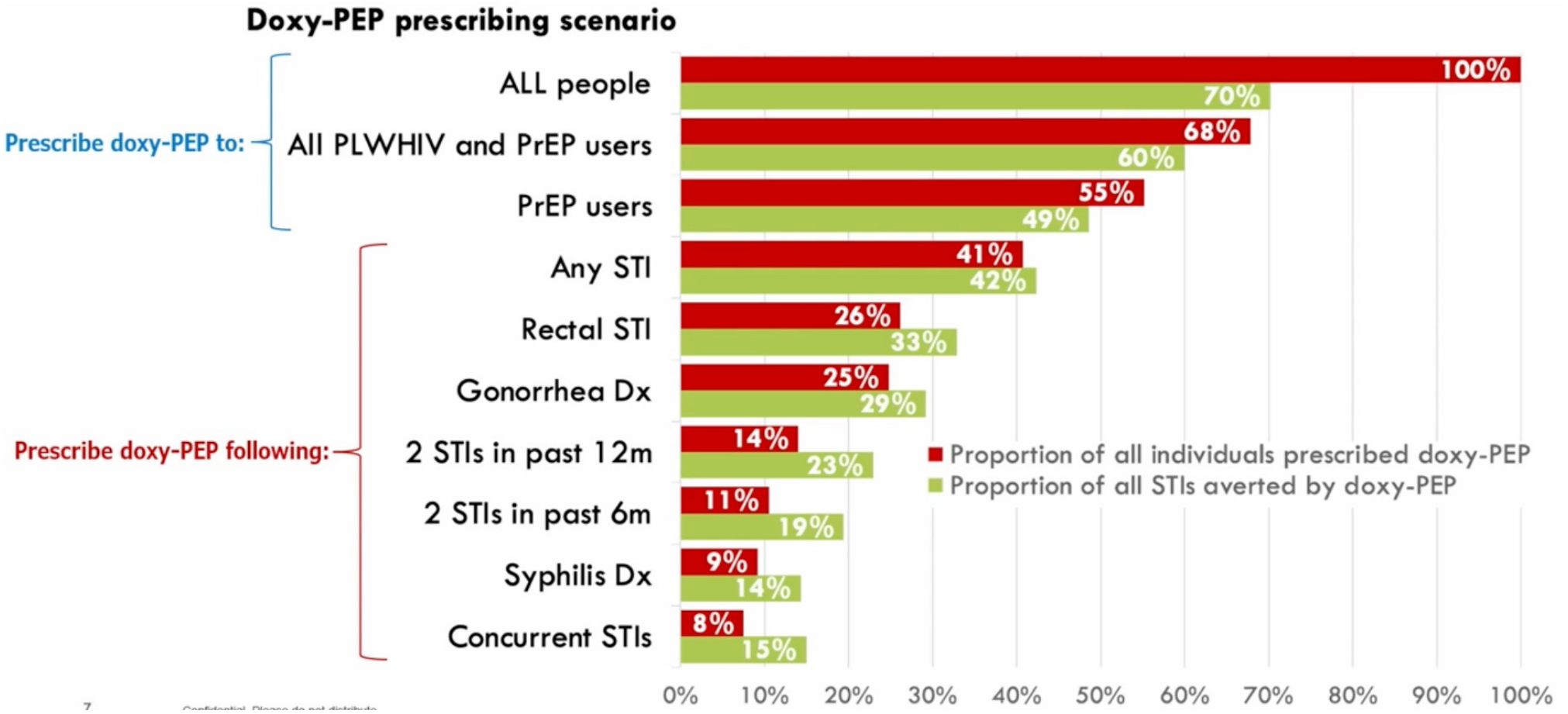
- 28,324 person-years of follow-up

	Number of diagnoses	Incidence rate / 100py
Chlamydia	5,673	21.6
Gonorrhoea	4,927	18.6
Syphilis	1,451	5.3
Any STI*	**10,582**	**37.4**

*Among people with >2 tests for each STI

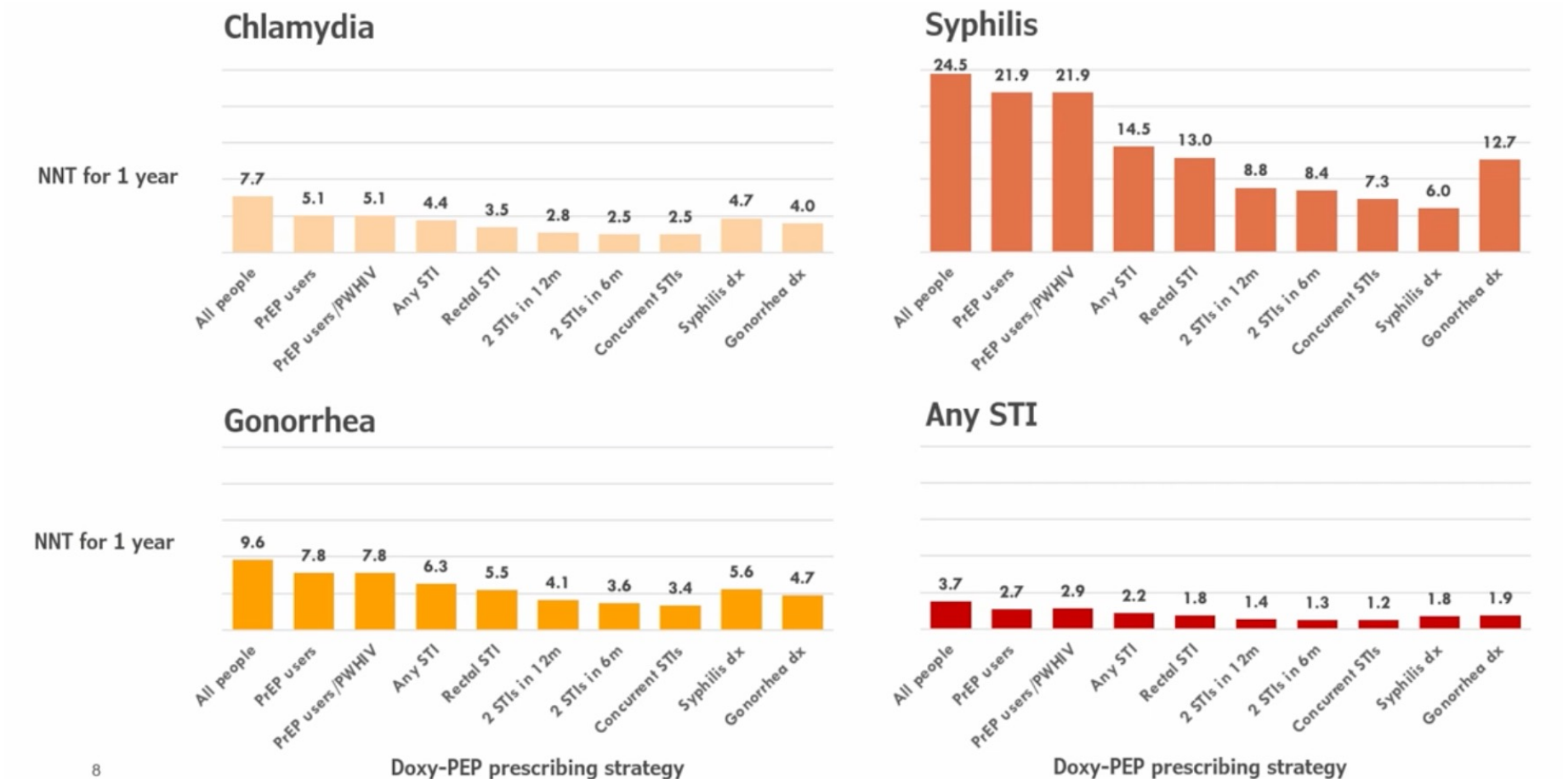
Traeger. CROI 2023.

Results: doxy-PEP use vs STIs averted



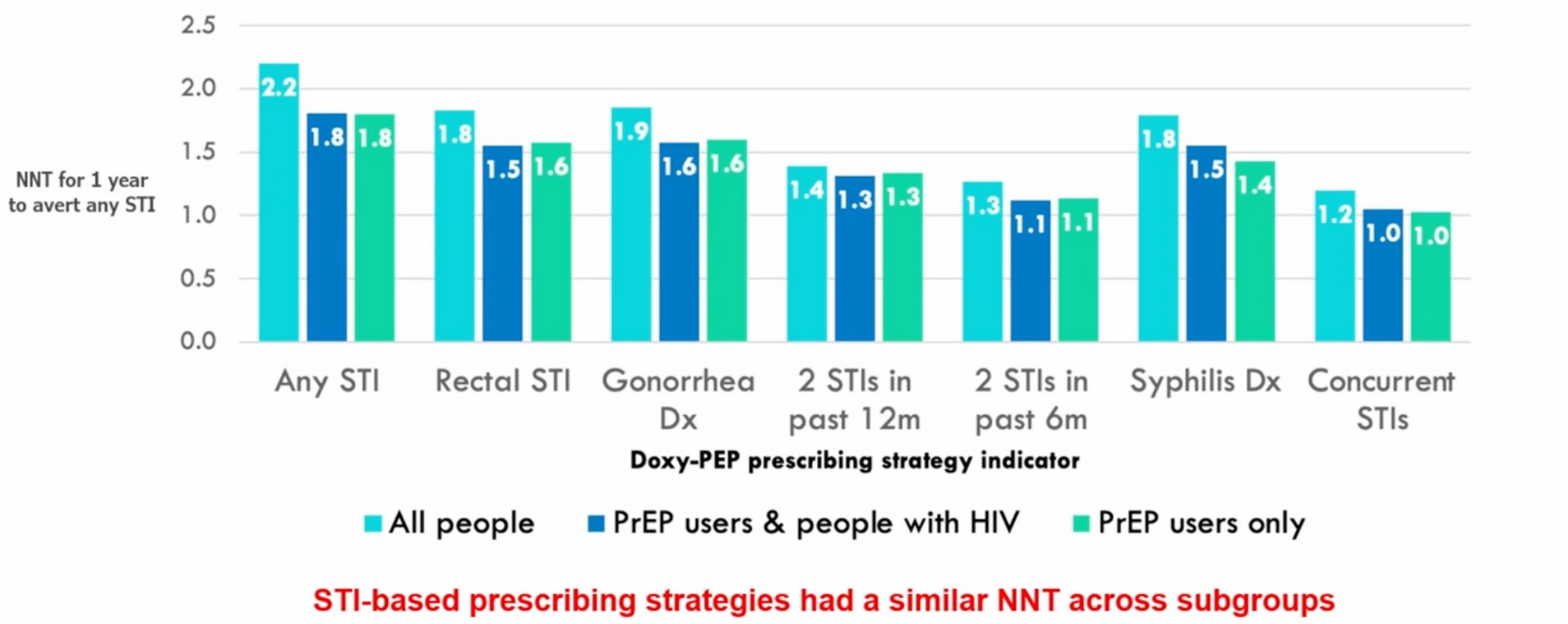
Traeger. CROI 2023.

Results: Efficiency of doxy-PEP



Traeger. CROI 2023.

Results: Restricting doxy-PEP to PrEP users and PLWHIV



Traeger. CROI 2023.

Limitations

- Generalizability
- Loss to follow up
- Impacts on onward transmission
- Real world assumptions

Implications

- Guidelines should incorporate recent diagnosis of STI as an indication for doxy-PEP
  - Prescribing for 12 months after STI diagnosis could avert ~ 42% of STIs
  - More efficient than prescribing to all people with HIV or PrEP users
  - Prescribing after multiple STIs reduces impact but improves efficiency
- Consider people not on PrEP with an STI for doxy-PEP
  - Following STI diagnosis, doxy PEP has similar efficiency for people with HIV, PrEP users and non-PrEP users
  - Restricting doxy-PEP to subgroups of people with STI (e.g., PrEP) may not be warranted
- Local epidemiology to target specific STIs
  - Prescribing after syphilis diagnosis could avert ~25% of infections, with only 9% of people on doxy-PEP
  - Background TCN resistance in gonorrhea is ~25% in the US (60-80% in Europe)

Other studies of DoxyPEP

Ongoing

- **DISCO study** – Canada - DoxyPEP vs Doxy PrEP among MSM
- **Syphiliaxis study** - Australia -observational cohort of DoxyPEP/PrEP in MSM & transgender women

CDCs Consideration – Doxy as STI-PEP

- **Doxy-PEP** is the first biomedical prevention tool that has been shown to be effective and well-tolerated, community awareness is growing, and many providers are already prescribing doxy-PEP to their patients at risk for STIs.

- Considerations (not guidelines)
  - Current efficacy data - AIDS2022 and CROI2023-1/CROI2023-2 only applies to gay and bisexual men and transgender women. Studies among heterosexual cis-gender women/vaginal sex – ongoing and need more data.

What is the recommendation?

- **Recommend doxy-PEP** to cis men and trans women who: 1) have had 1-2 bacterial STI in the past year and 2) report condomless anal or oral sexual contact with ≥ 1 cis male or trans female partner in the past year. These were the eligibility criteria used for the DoxyPEP study.
- **Offer doxy-PEP using shared decision making** to cis men, trans men and trans women who report having multiple cis male or trans female sex partners in the prior year, even if they have not previously been diagnosed with an STI.
- **At this time, there is insufficient evidence to recommend doxy-PEP for STI prevention for individuals who report receptive vaginal sex.**
    - Ongoing Trial in Kenya is assessing the safety and efficacy of Doxy PEP in cis women.

As a Provider, consider…

When initiating doxy-PEP, discuss the following key points with patients:

Efficacy:

1. In persons taking HIV PrEP, doxy-PEP reduced syphilis by 87%, chlamydia by 88% and gonorrhea by 55%.
2. In PLWH, doxy-PEP reduced syphilis by 77%, chlamydia by 74% and gonorrhea by 57%.
3. Consider people not on PrEP with an STI for doxy-PEP*
4. Efficacy against other bacterial STIs is not known, and doxy-PEP does not prevent HIV, monkeypox (MPX) or other viral infections, for example HPV and HSV.

Dosing and prescribing:

- 200 mg of doxycycline should be taken ideally **within 24 hours but no later than 72 hours** after condomless oral, anal or vaginal sex.
- Doxycycline can be taken as often as every day, depending on frequency of sexual activity, but individuals should not take more than 200 mg within a 24-hour period.
- Either doxycycline hyclate delayed release 200 mg (1 tab) OR doxycycline hyclate or monohydrate immediate release 100 mg (2 tabs taken simultaneously) are acceptable.
- Immediate release may be less expensive than delayed release and should be equivalently bioavailable.
- For ICD10 diagnosis code, use Z20.2 (Contact with and (suspected) exposure to infections with a predominantly sexual mode of transmission).

Counseling messages:

1. People taking doxycycline should be counseled about possible drug interactions, risk of sun sensitivity, remaining upright for 30 minutes after taking doxycycline to reduce the risk of pill esophagitis, and the rare risk of benign intracranial hypertension and other serious side effects.
2. Study data on the impact of doxy-PEP on antibiotic resistance and the gut microbiome are being collected and reviewed.
3. Impacts of long-term use of doxy-PEP for STI prevention for individual patients and for population-level rates of antimicrobial resistance are unknown.

Monitoring while taking doxycycline:

1. Per the doxycycline package insert, LFTs, renal function and a CBC should be checked periodically in patients taking doxycycline for a prolonged period. LFTs and CBCs were monitored in the DoxyPEP study, and there were no laboratory-related severe adverse events. Consider checking these laboratory parameters annually, particularly in individuals with a history of liver disease.
2. Persons taking doxy-PEP should be screened every three months for gonorrhea and chlamydia at all anatomic sites of exposure, syphilis, and HIV (if not known to be living with HIV).
3. If a patient is diagnosed with an STI while using doxy-PEP, they should be treated according to standard CDC STI treatment guidelines.

Don’t forget…

Offer patients a comprehensive sexual health package*

- Not Just Doxy PEP, as these patients are very likely eligible for **HIV PrEP**
- Regular sexual health/STI screenings – ALL site testing
- Recommend offer vaccines
- Ensure people living with HIV are in care and inform patients that maintaining an undetectable HIV viral load eliminates the risk of transmitting HIV to sexual partners.

Resources

- “Doxycycline post-exposure prophylaxis for STI prevention among MSM and transgender women on HIV PrEP or living with HIV: high efficacy to reduce incident STI's in a randomized trial.” AIDS 2022: https://programme.aids2022.org/Abstract/Abstract/?abstractid=13231

- CDC 2021 STI Treatment Guidelines: https://www.cdc.gov/std/treatment-guidelines/clinicalprimary.htm#CautionsForDoxyPEP

- Doxycycline use by pregnant and lactating people: Doxycycline Use by Pregnant and Lactating Women, FDA: https://www.fda.gov/drugs/bioterrorism-and-drug-preparedness/doxycycline-use-pregnant-and-lactating-women

- CROI 2023 Abstracts:
  1. Traeger MW, Mayer KH, Krakower DS, Gitin S, Jenness S, Marcus JL. Potential impact and efficiency of doxy-PEP among people with or at risk of HIV. 30th CROI, Conference on Retroviruses and Opportunistic Infections, February 19-22, 2023, Seattle. Abstract 122.
  2. Molina JM, Bercot B, Assoumou A, et al. ANRS 174 DOXYVAC: an open-label randomized trial to prevent STIs in MSM on PrEP. 30th CROI, Conference on Retroviruses and Opportunistic Infections, February 19-22, 2023, Seattle. Abstract 119.

Questions?