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Heersink School of Medicine

Doxycycline as Post-Exposure Prophylaxis

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SOUTHEAST
STD/HIV PREVENTION
TRAINING CENTER
CONNECTING · PROVIDERS · PRACTICE · & PATIENTS

Disclosures

Merck, Sharpe, Dohme, Inc. – Research funds to UAB

ViiV – Ad hoc Advisor

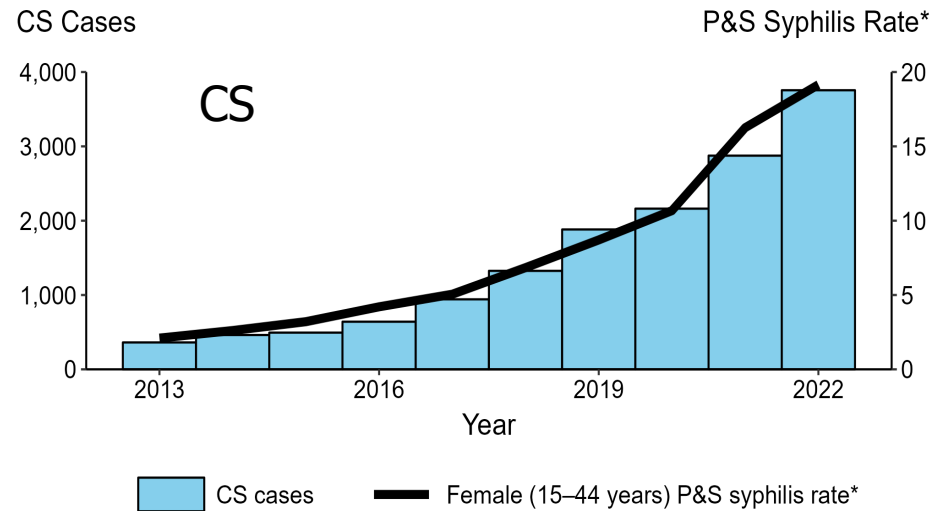
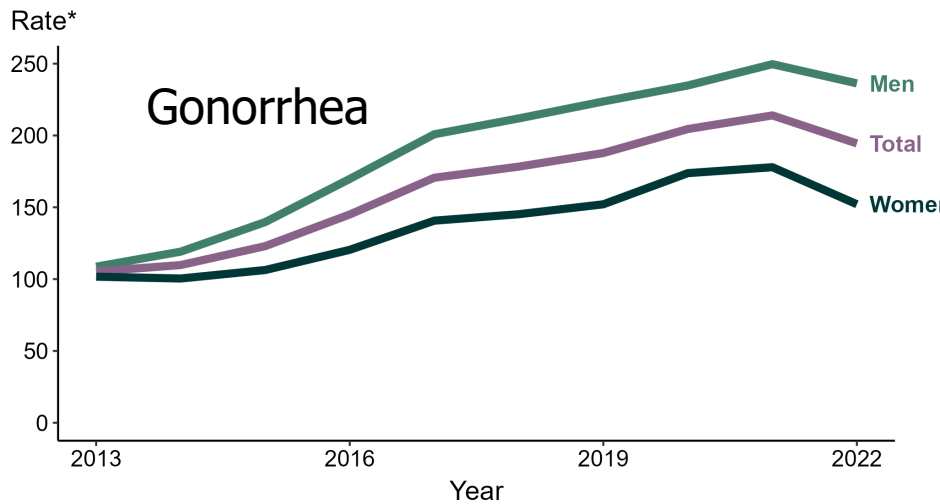
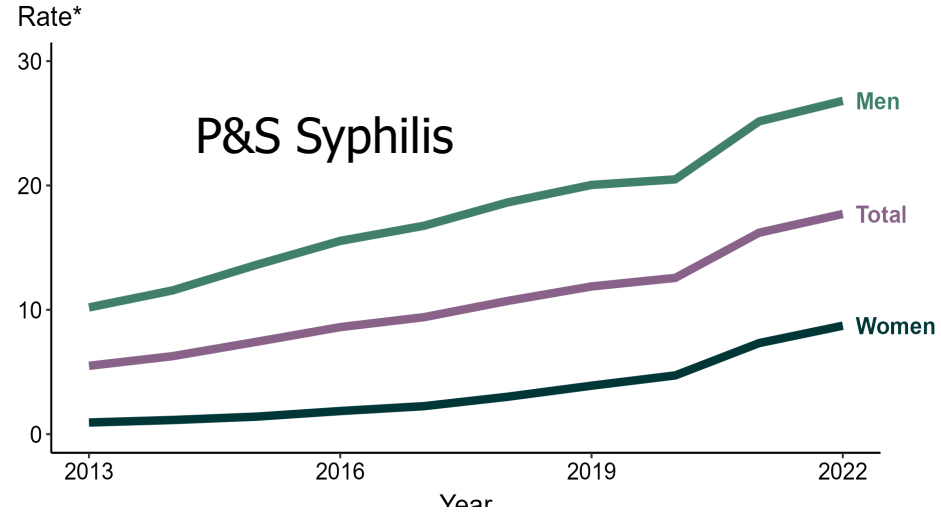
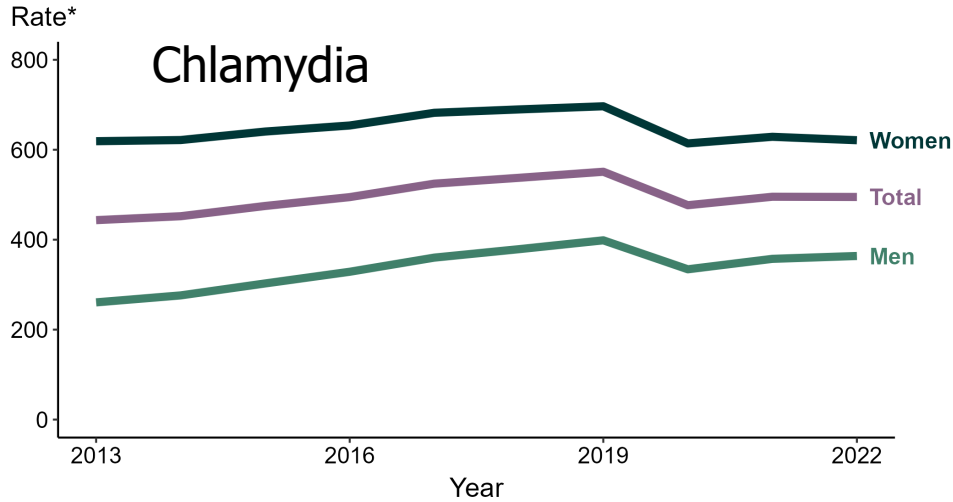
NIH/NIMH – K23MH126794

Objectives

- 1. Review recent STI epidemiology in the US**
- 2. Review doxycycline and its use for STIs**
- 3. Discuss data for doxycycline as post-exposure prophylaxis**
- 4. Discuss real-world applications and pending guidelines**

Polling at [menti.com](https://www.menti.com) CODE: 3259 2405

CDC Surveillance Data - 2022



Centers for Disease Control and Prevention. *Sexually Transmitted Infections Surveillance 2022*. Atlanta: U.S. Department of Health and Human Services; 2024

1967
Years of Safety

95% oral
absorption

20h half-life
QD or BID

Interrupted by
calcium,
aluminum,
magnesium,
and iron

Doxy

Common &
Affordable

FDA Class D
Potential for
"brown teeth"

GI Upset
Esophagitis
Skin Reactions
Photosensitivity

Few DDIs and
no dose change
in CKD

STI Treatment | 6

Chlamydia

Syphilis

Doxy

M.
genitalium

gonorrhea

Doxycycline Prophylax among HIV-Infected Men Who Continue to A Randomized,

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

Robert K. Bolan, MD,* Matthew R. Beyn Arleen A. Leibowitz, PhD,

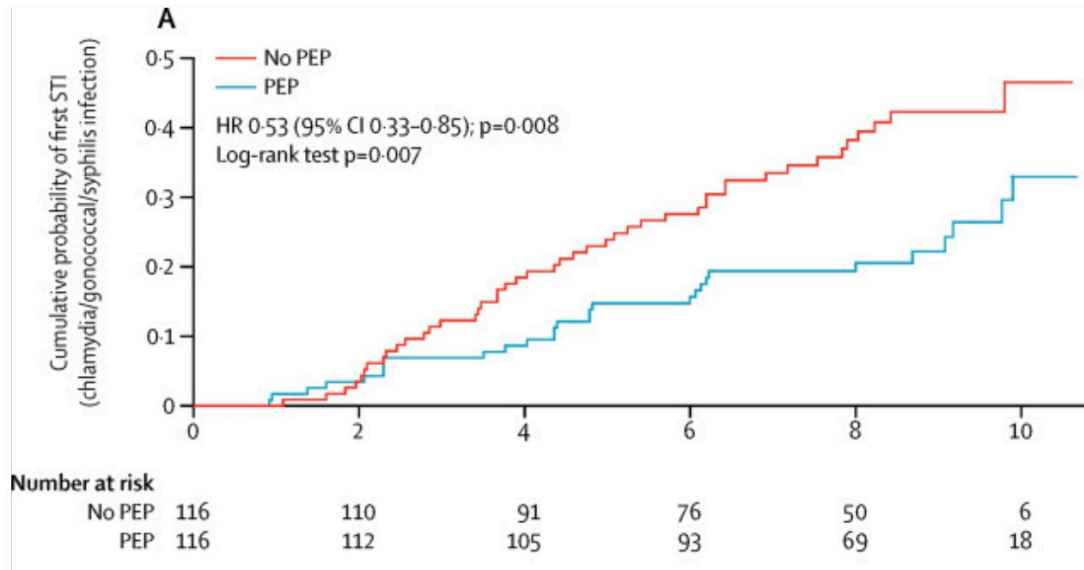
Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Bercot, Cécile Bébéar, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Charbonneau, Alexandre Aslan, Julie Chas, Laurence Niedbalski, Bruno Spire, Luis Sagon-Teysier, Diane Carette, Soizic Le Mestre, Veronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group*

2015



2018

2023



DoxyPEP (NEJM 2023)
DOXYVAC (CROI 2024)
dPEP (NEJM 2023)

DOXY
PEP

ORIGINAL ARTICLE

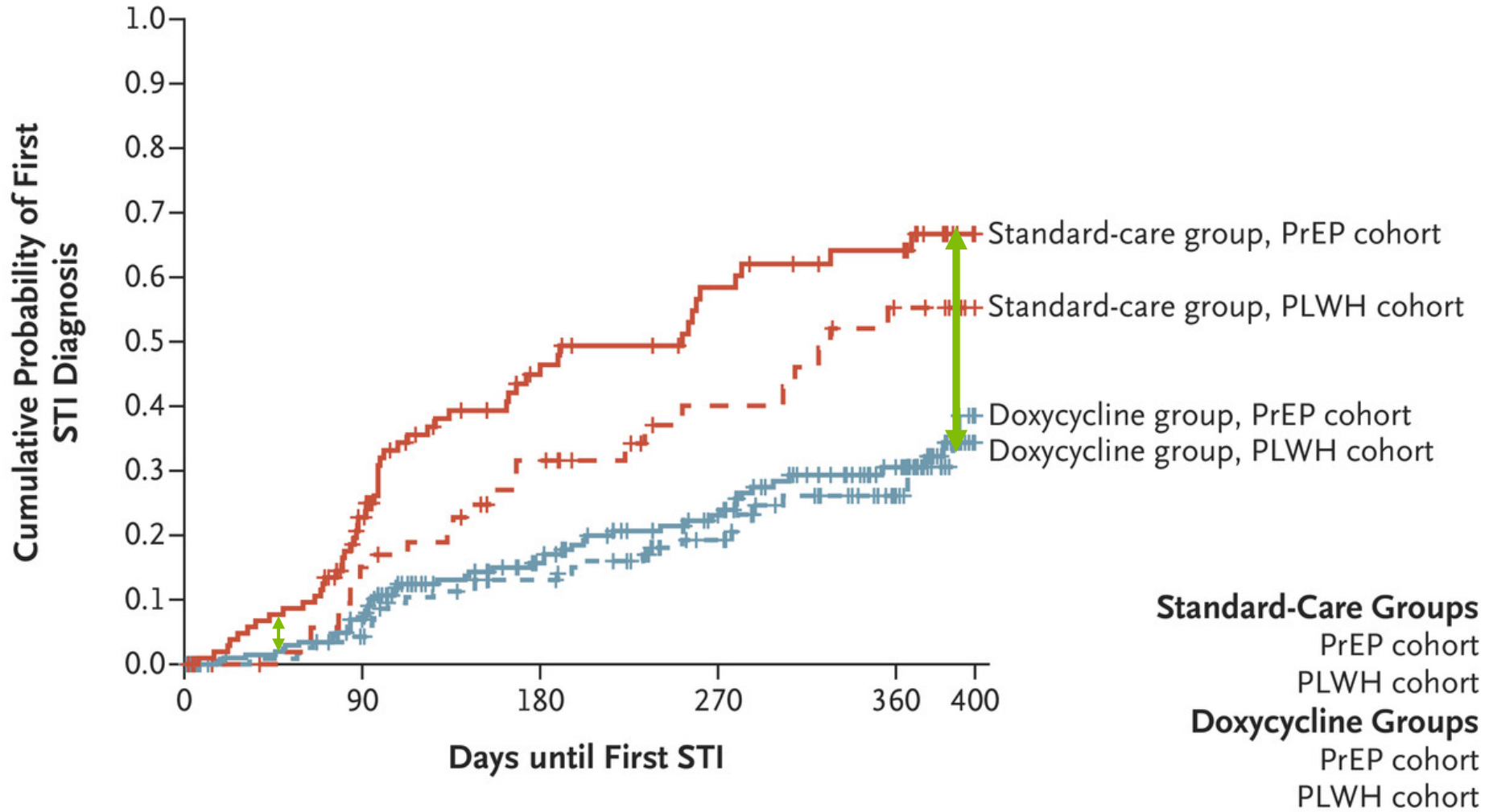
Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D.,
Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H.,
Cole Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S.,
Rodney Perkins, R.N., M.P.H., Melody Nasser, B.A., Carolina Lopez, B.A.,
Eric Vittinghoff, Ph.D., Susan P. Buchbinder, M.D., Hyman Scott, M.D., M.P.H.,
Edwin D. Charlebois, Ph.D., M.P.H., Diane V. Havlir, M.D., Olusegun O. Soge, Ph.D.,
and Connie Celum, M.D., M.P.H., for the DoxyPEP Study Team*

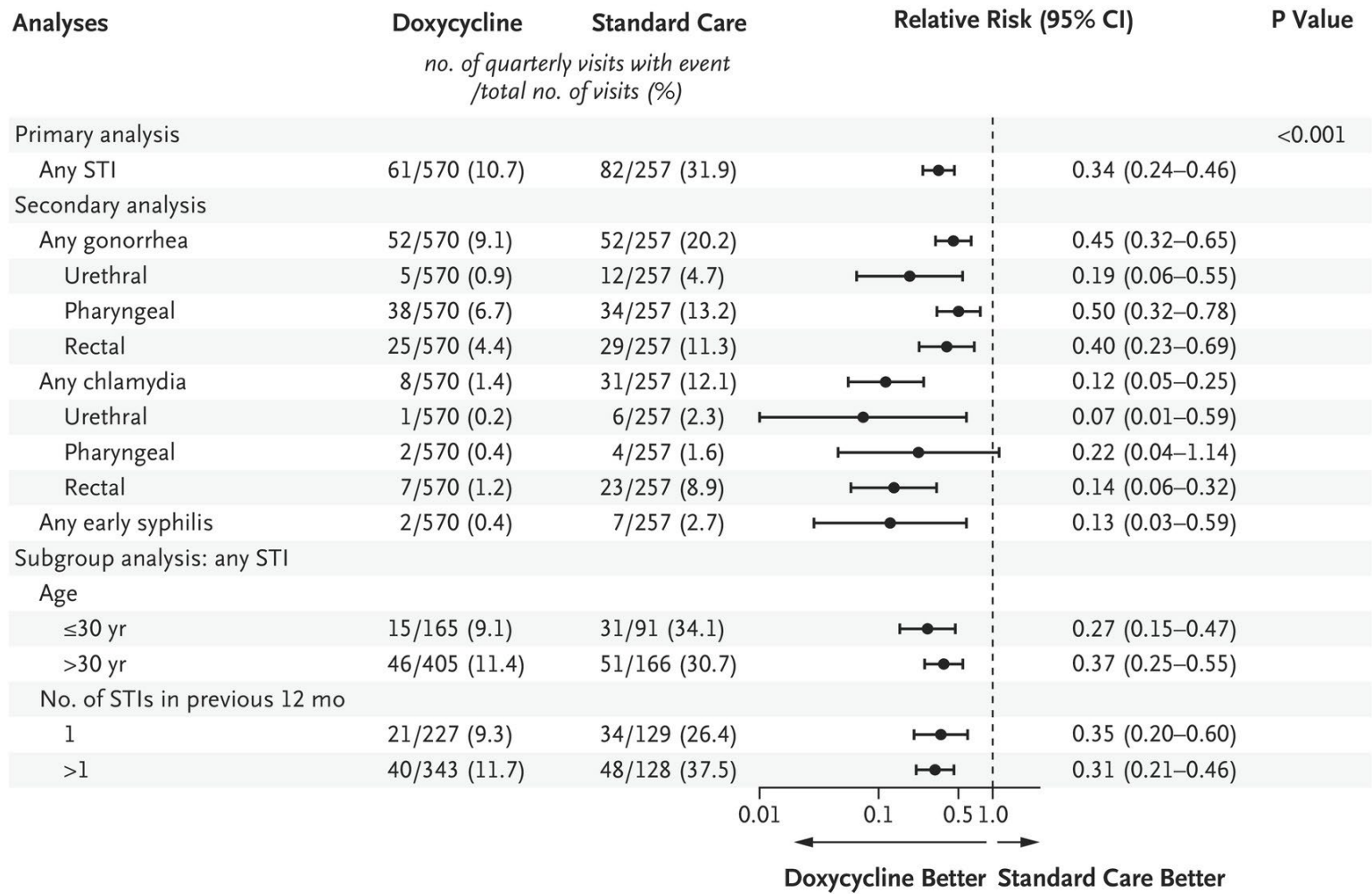
Open-Label, 2:1 RCT
MSM & Transgender wor
PLWH and PrEP
Recent Bacterial STI

Doxycycline 200mg once
< 24-72 hours / encounter
Quarterly STI testing

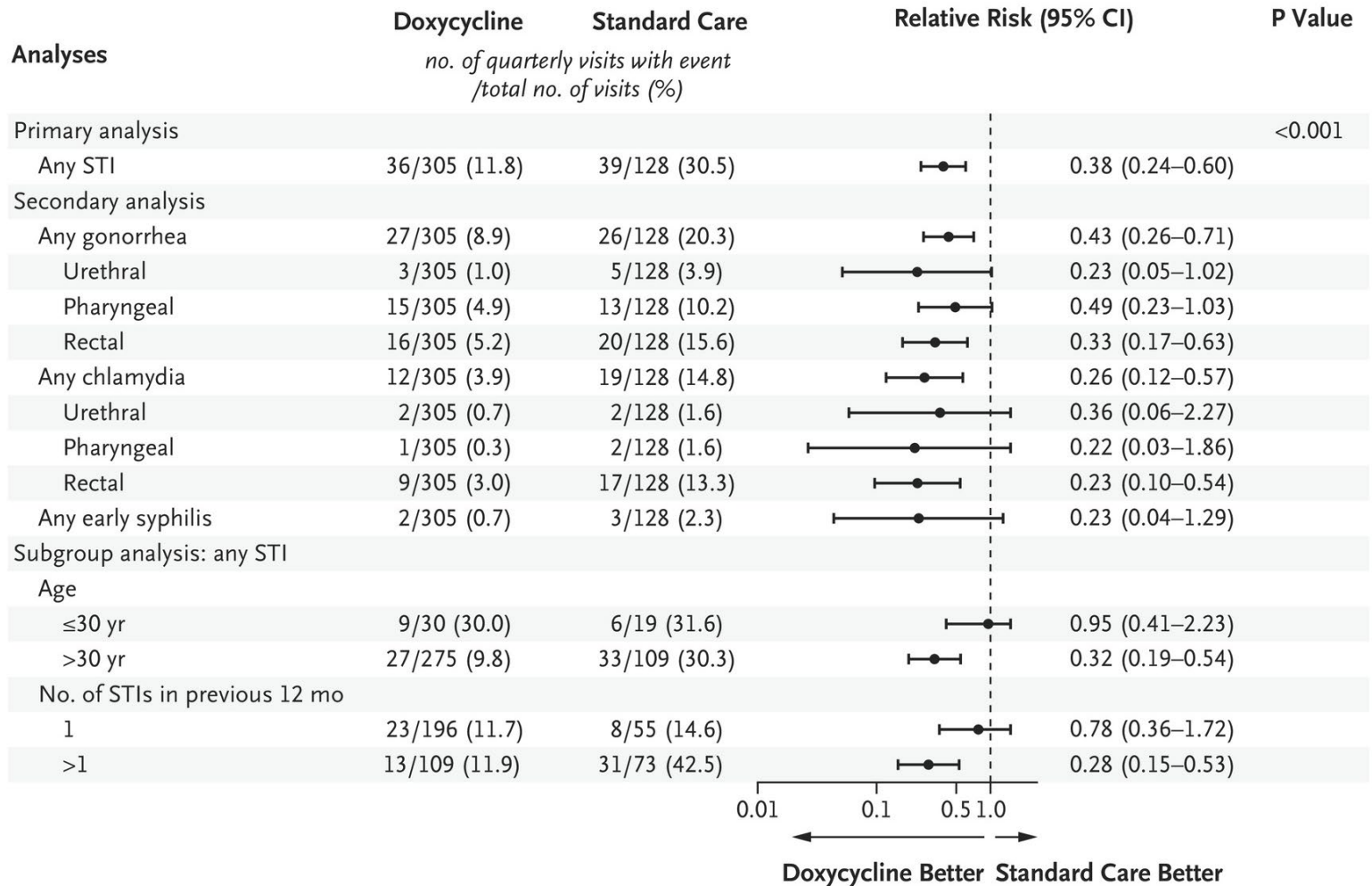
Characteristic	PrEP Cohort		PLWH Cohort		Total (N=501)
	Doxycycline Group (N=220)	Standard-Care Group (N=107)	Doxycycline Group (N=119)	Standard-Care Group (N=55)	
Median age (IQR) — yr	36 (31–42)	36 (31–42)	43 (36–54)	42 (37–50)	38 (32–47)
Race — no./total no. (%)†					
White	144/209 (69)	66/104 (63)	74/116 (64)	37/53 (70)	321/482 (67)
Black	9/209 (4)	5/104 (5)	15/116 (13)	7/53 (13)	36/482 (7)
Asian or Pacific Islander	33/209 (16)	12/104 (12)	7/116 (6)	1/53 (2)	53/482 (11)
Multiple races or other	23/209 (11)	21/104 (20)	20/116 (17)	8/53 (15)	72/482 (15)
Hispanic or Latino ethnic group — no. (%)†	55 (25)	41 (38)	41 (34)	14 (25)	151 (30)
Gender identity — no. (%)					
Man	212 (96)	107 (100)	109 (92)	54 (98)	482 (96)
Transgender woman or gender-diverse	8 (4)	0	10 (8)	1 (2)	19 (4)
Gender of sexual partners — no./total no. (%)					
Men only	191/220 (87)	90/107 (84)	105/118 (89)	48/55 (87)	434/500 (87)
Multiple genders	29/220 (13)	17/107 (16)	13/118 (11)	7/55 (13)	66/500 (13)
Annual income — no./total no. (%)					
<\$20,000	31/219 (14)	13/106 (12)	42/119 (35)	17/55 (31)	103/499 (21)
\$20,001–\$50,000	64/219 (29)	39/106 (37)	40/119 (34)	22/55 (40)	165/499 (33)
\$50,001–\$75,000	45/219 (21)	14/106 (13)	22/119 (18)	5/55 (9)	86/499 (17)
>\$75,000	79/219 (36)	40/106 (38)	15/119 (13)	11/55 (20)	145/499 (29)
STI in the past 12 mo — no. (%)					
Gonorrhea	155 (70)	78 (73)	71 (60)	39 (71)	343 (68)
Chlamydia	144 (65)	63 (59)	58 (49)	27 (49)	292 (58)
Syphilis‡	32 (15)	16 (1)	35 (29)	17 (31)	100 (20)
Two or more STIs in the past 12 mo — no. (%)	106 (48)	44 (41)	39 (33)	26 (47)	215 (43)
Any STI at baseline — no./total no. (%)	65/219 (30)	27/106 (25)	34/114 (30)	20/55 (36)	146/494 (30)
Gonorrhea	40/218 (18)	20/107 (19)	25/117 (21)	14/54 (26)	99/496 (20)
Chlamydia	31/219 (14)	11/107 (10)	11/117 (9)	8/54 (15)	61/497 (12)
Syphilis	5/219 (2)	1/107 (1)	11/117 (9)	4/55 (7)	21/498 (4)
Median no. of sexual partners in the past 3 mo (IQR)	8 (4–17)	10 (5–16.5)	7 (3–18.5)	10.5 (3–20)	9 (4–17)
Transactional sex during lifetime — no./total no. (%)§	47/219 (21)	28/107 (26)	47/116 (41)	21/49 (43)	143/491 (29)
Substance use in the past 3 mo — no./total no. (%)					
Stimulants: methamphetamine, cocaine, or crack	51/216 (24)	22/107 (21)	50/117 (43)	23/53 (43)	146/493 (30)
Heroin or other opioids	2/216 (1)	1/107 (1)	9/117 (8)	2/53 (4)	14/493 (3)
Ecstasy, GHB, or ketamine	63/216 (29)	34/107 (32)	39/117 (33)	21/53 (40)	157/493 (32)
Amyl nitrates, also known as poppers	93/216 (43)	47/107 (44)	56/117 (48)	28/53 (53)	224/493 (45)
Marijuana	96/216 (44)	56/107 (52)	60/117 (51)	27/53 (51)	239/493 (48)



A PrEP Cohort

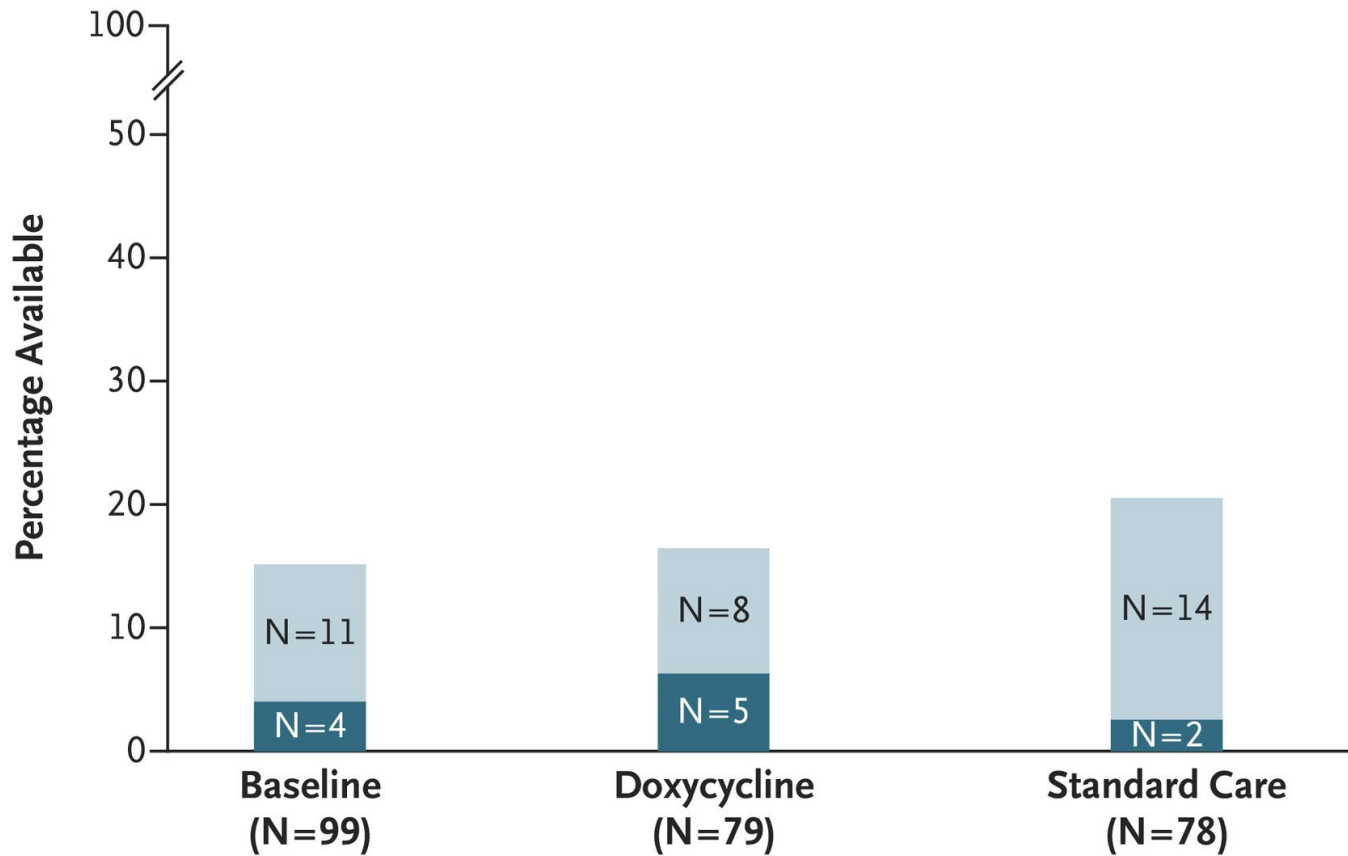


B PLWH Cohort

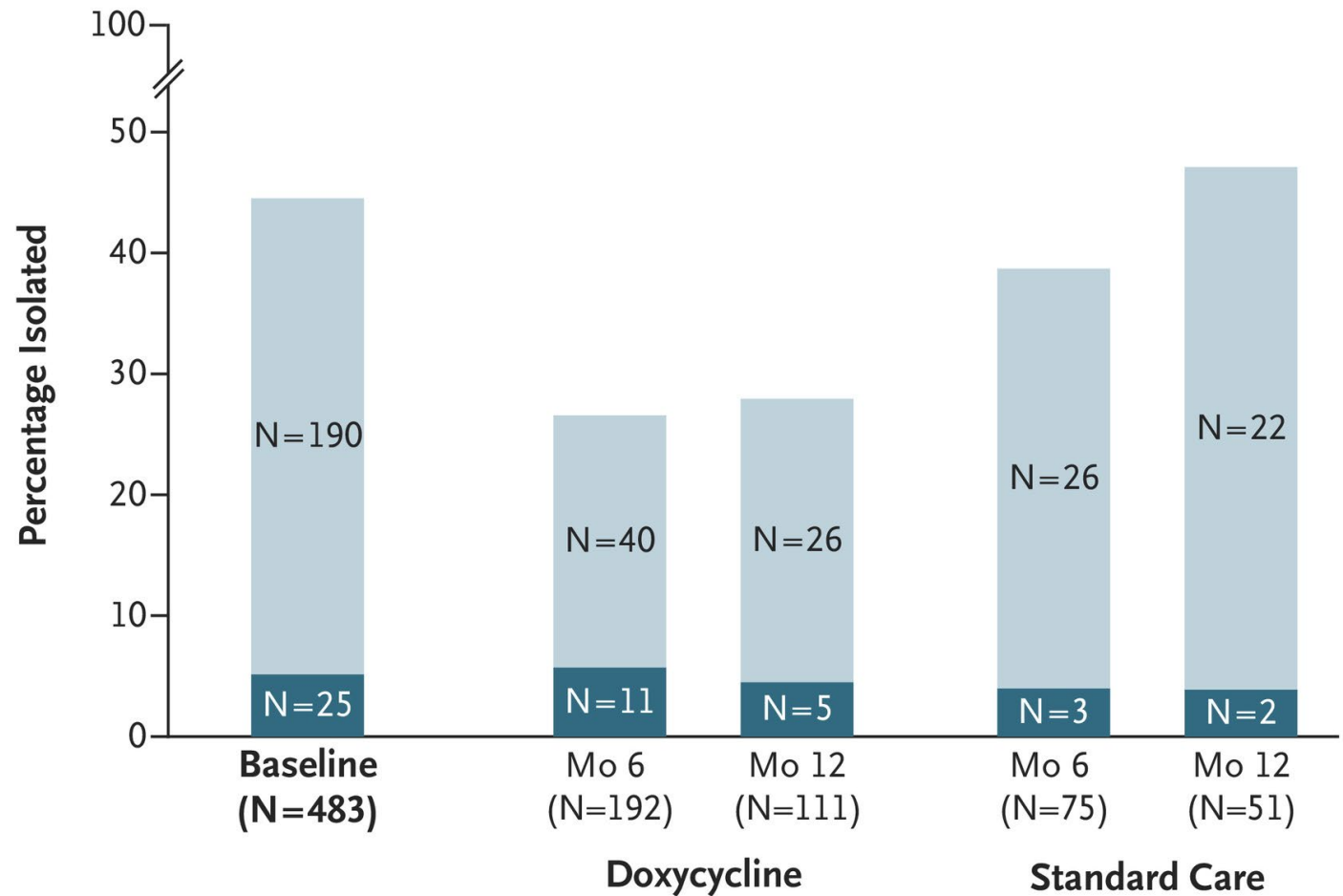


Resistant Not resistant

A *N. gonorrhoeae* Culture

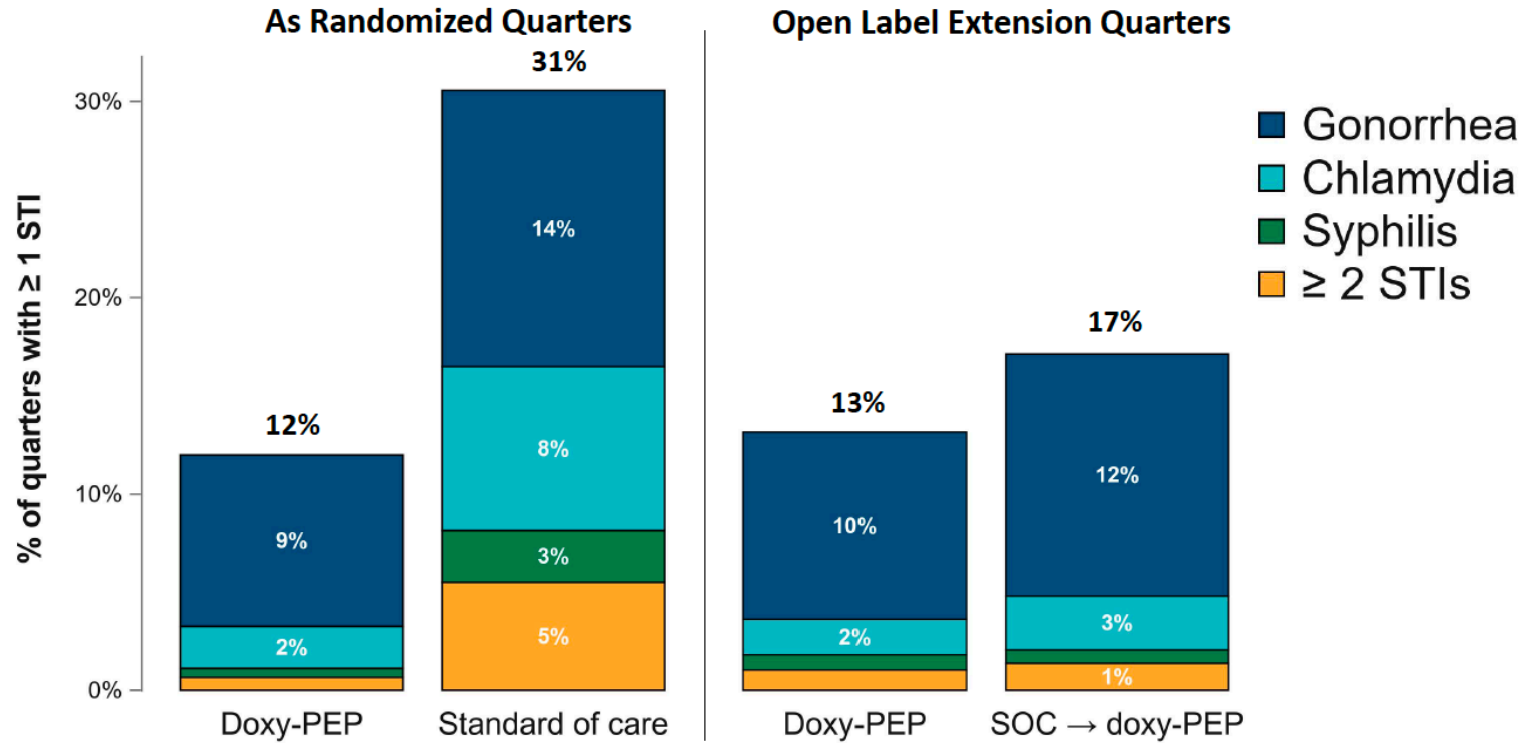


GC Resistance

S. aureus TCN resistance**B** *S. aureus* Culture

DoxyPEP Open Label Extension

Sustained reduction in STIs during OLE



Sexual behavior during OLE

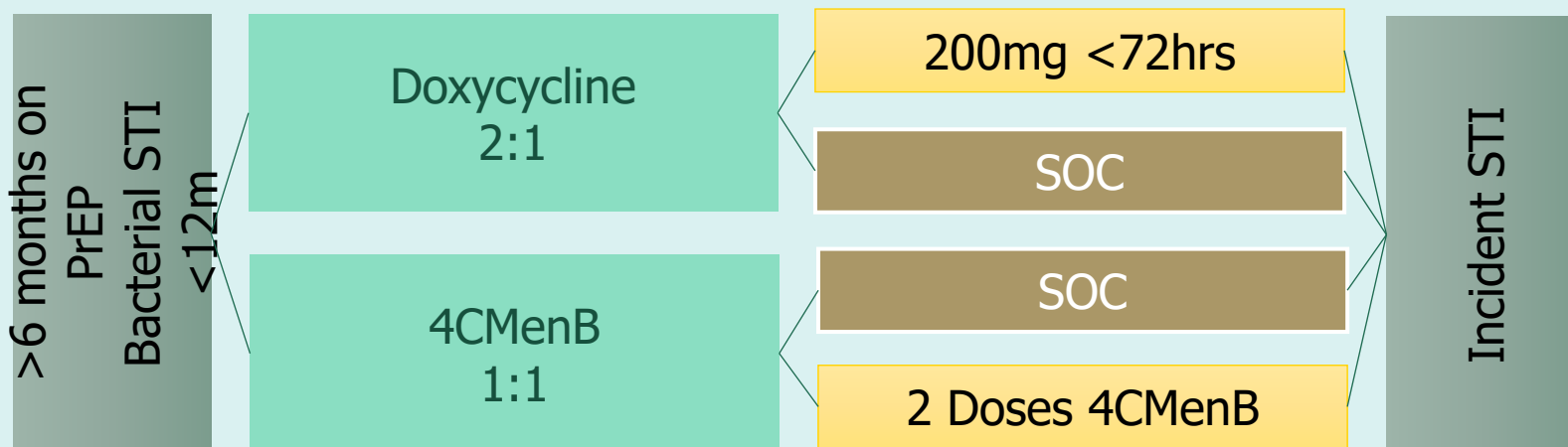
<i>median (IQR)</i>	As-randomized		AR→OLE	
	doxy-PEP N quarters = 1077	SOC N quarters = 455	doxy-PEP N quarters = 388	SOC → doxy-PEP N quarters = 146
Doxy doses/quarter	15 (4-30)	—	17 (7-32)	17 (5-30)
Sex partners/quarter	10 (4-25)	8 (4-15)	12 (6-25)	16.5 (5-31)
Condomless insertive sex acts/quarter	5 (1-20)	4 (2-12)	8 (2-20)	8 (3-25)
Condomless receptive sex acts/quarter	8 (2-20)	5 (1-15)	10 (2-23.5)	10 (2-25)
% of condomless sex acts covered by doxy-PEP per quarter	82.4%	—	77.3%	81.3%

- **Sexual partners & condomless sex:** ↑ during OLE in both groups; doubled in SOC → doxy-PEP
- **Reported doxy-PEP coverage of condomless sex:** High (> 75%) during OLE; comparable to doxy-PEP AR



DOXYVAC – Results

- ANRS – French PrEP study, on-demand PrEP
- Open-label, randomized trial
- MSM on PrEP

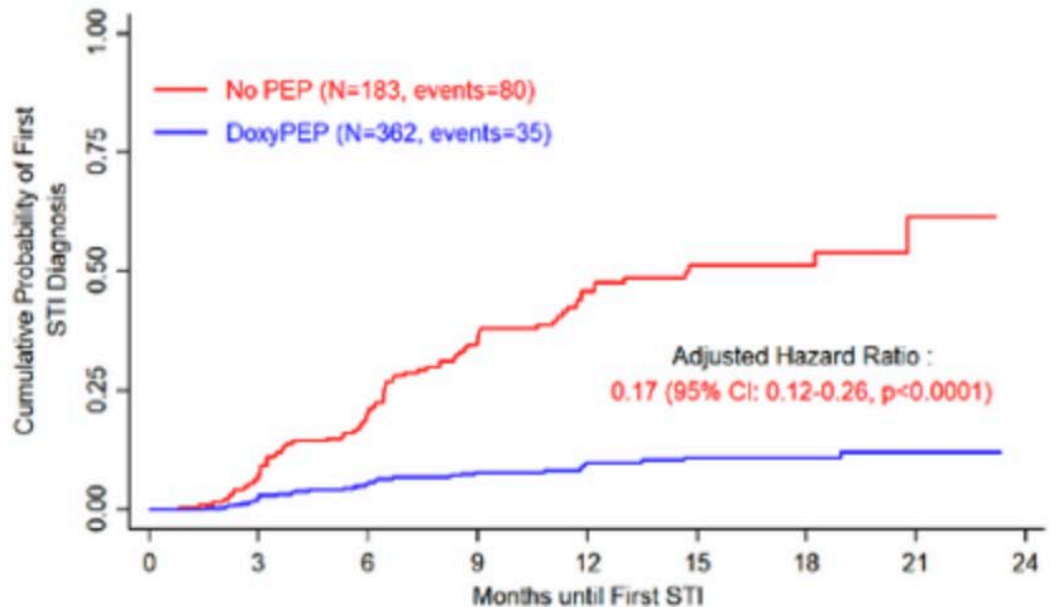


Doxycycline PEP Time to First CT or Syphilis Infection

No interaction between
Doxy PEP and 4CMenB
vaccine ($p=0.83$)

Median follow-up:
14 months (IQR: 9-18)

115 subjects infected
80 in No PEP arm
(incidence: 53.2/100 PY),
35 in Doxy PEP arm
(incidence: 8.8/100 PY)



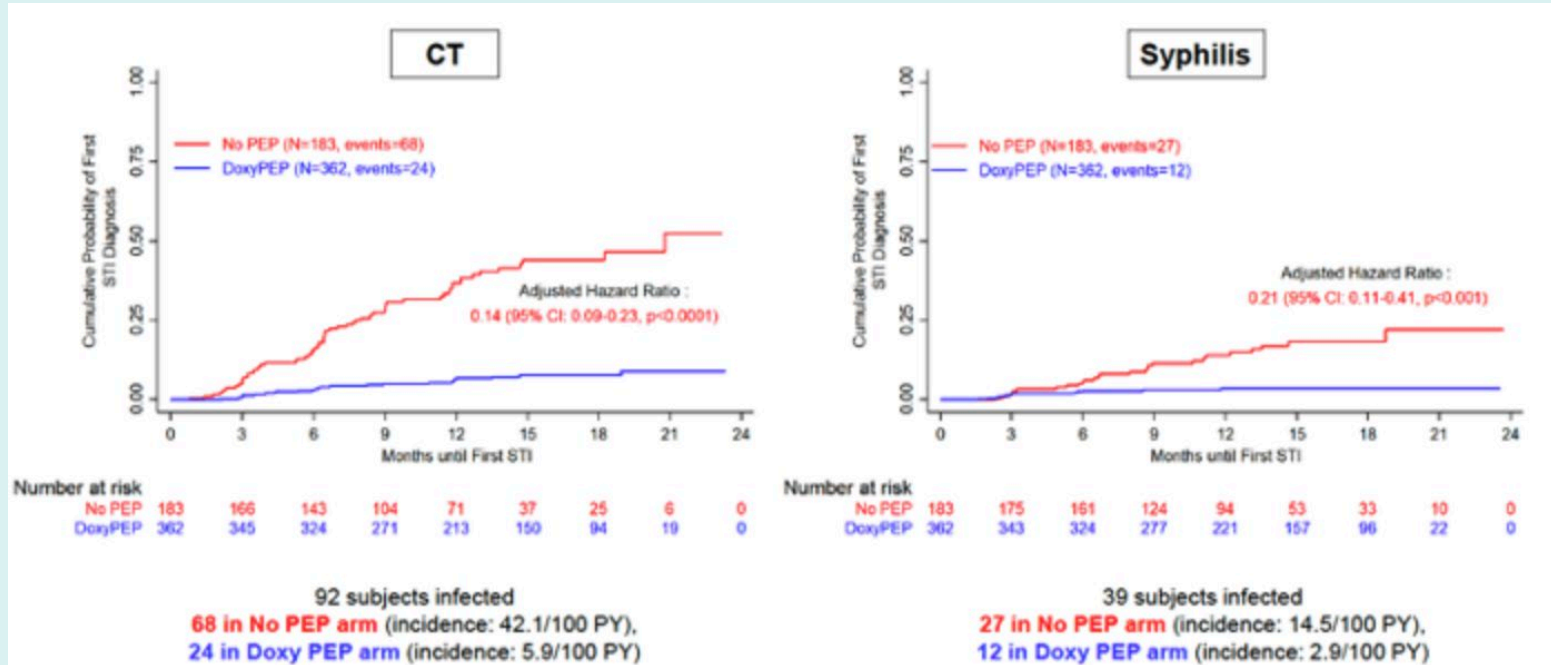
Number at risk

No PEP	183	164	135	92	60	32	20	4	0
DoxyPEP	362	339	316	264	206	146	90	19	0

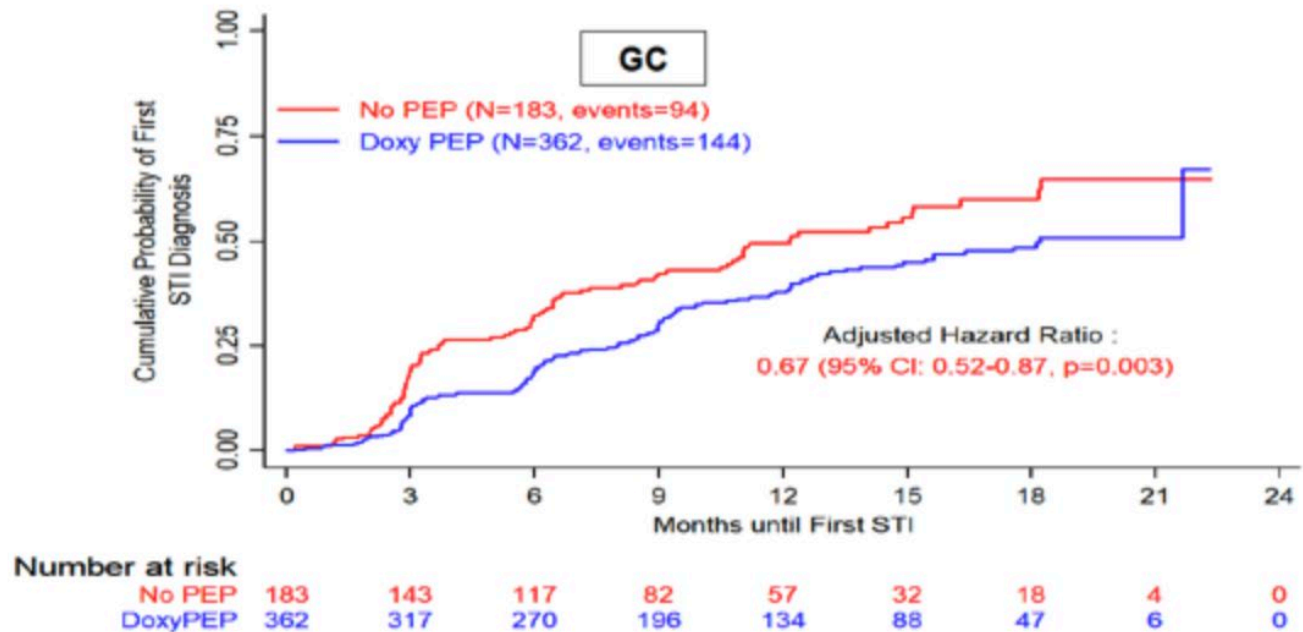
Interim analysis:
49 subjects infected, aHR: 0.16

For CT multi-sites infection = 1 single event

Significantly lower CT and syphilis each



Doxycycline PEP Time to First GC



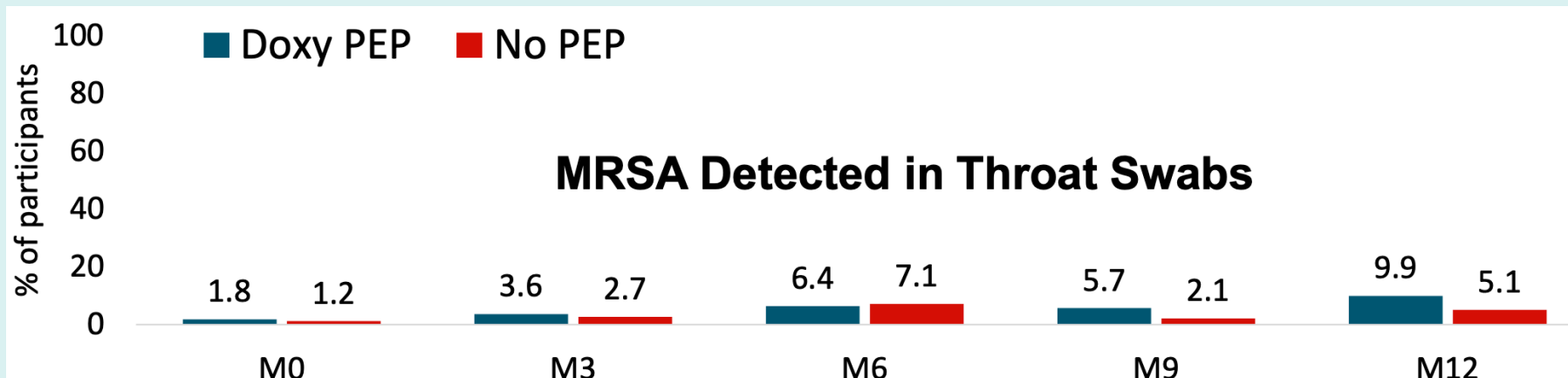
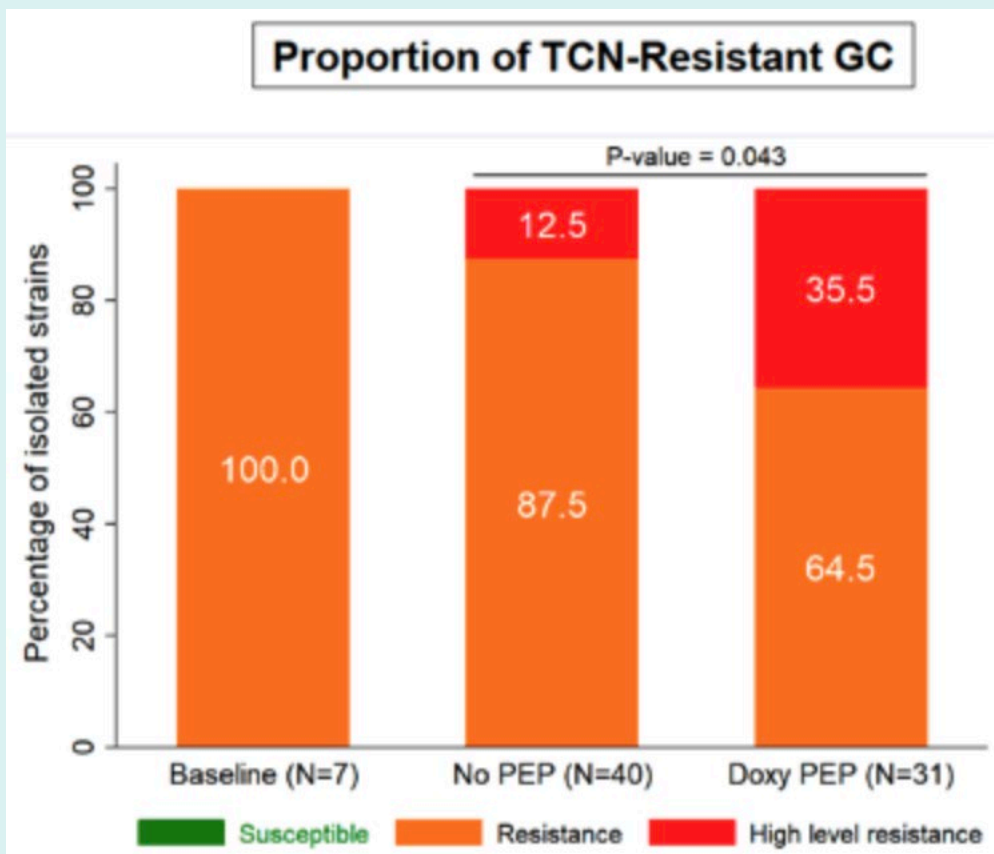
Interim analysis:
84 subjects infected, aHR: 0.49

238 subjects infected
94 in No PEP arm (incidence: 68.4/100 PY)
144 in Doxy PEP arm (incidence: 45.5 /100 PY)

78 positive GC cultures

No Susceptible GC

More "high level" (MIC >8mg/L) in DoxyPEP arm

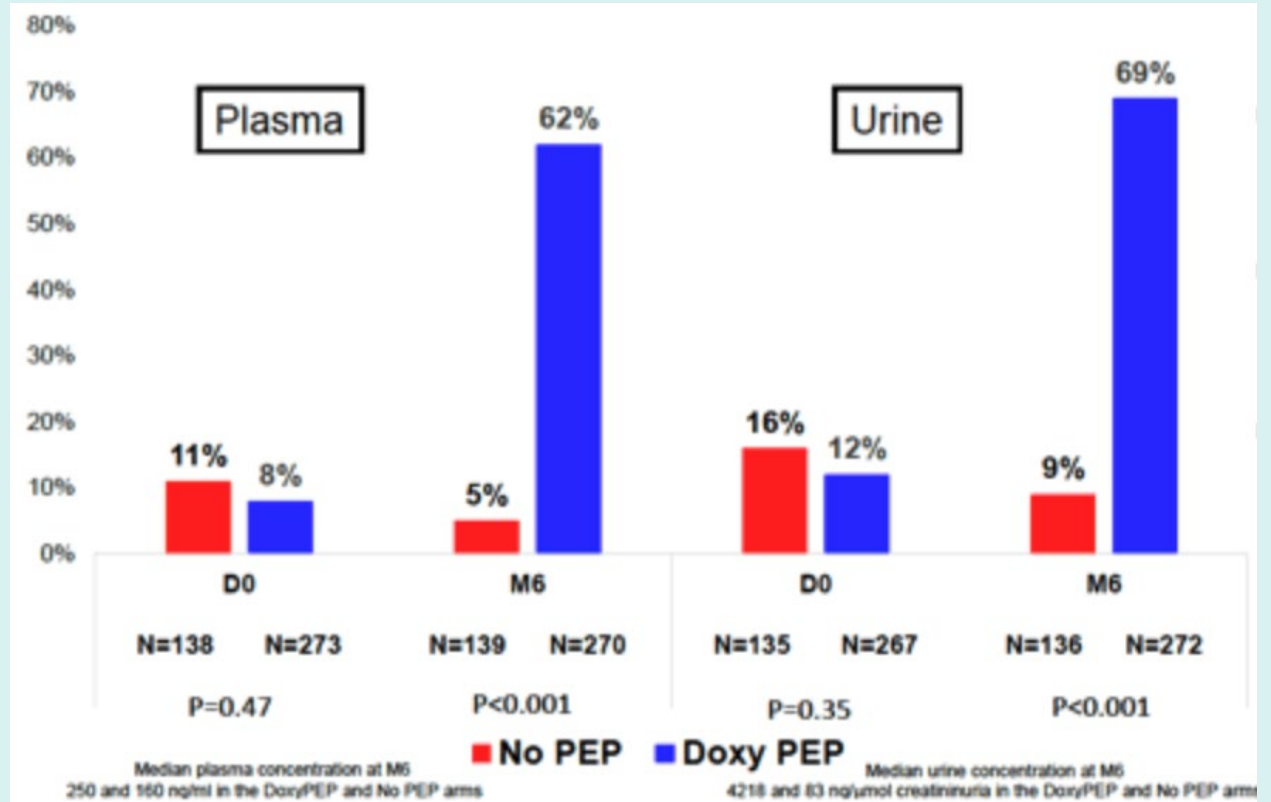


No significant difference in MRSA detection in throat swabs

Reasonably good adherence

Median time to PEP <24hrs

Median PEP at last sex act >70%



dPEP Kenya

- Open-Label 1:1 Randomized Control Trial
- ~450 Cisgender Kenyan Women on PrEP
- Primary outcome was incident STI
- Median Age 24 years, 18% have STI at baseline

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Doxycycline PEP (N = 224)	Standard Care (N = 225)
Median age (IQR) — yr	24 (22–27)	24 (22–27)
Highest level of education — no. (%)		
No schooling	1 (0.4)	0
Primary school	48 (21.4)	55 (24.4)
Secondary school	135 (60.3)	128 (56.9)
Postsecondary school	40 (17.9)	42 (18.7)
Earns own income — no. (%)	137 (61.2)	143 (63.6)
Marital status — no. (%)		
Never married	158 (70.5)	139 (61.8)
Married	39 (17.4)	53 (23.6)
Previously married	27 (12.1)	33 (14.7)
Has a primary sex partner — no. (%)	186 (83.0)	184 (81.8)
New sex partner in the previous 3 mo — no. (%)	77 (34.4)	72 (32.0)
Median no. of partners in the previous 3 mo (IQR)	2 (1–5)	2 (1–4)
History of transactional sex in the previous 3 mo — no. (%)	89 (39.7)	76 (33.8)
Condom use at last vaginal sex act — no./total no. (%)†	62/199 (31.2)	67/199 (33.7)
History of anal sex in the previous 3 mo — no. (%)	4 (1.8)	7 (3.1)
Median duration of HIV PrEP (IQR) — mo	7.5 (4.1–14.9)	7.2 (3.7–13.8)
Use of contraception — no. (%)‡	143 (63.8)	135 (60.0)
Parity — no. (%)		
None	72 (32.1)	65 (28.9)
1 live birth	89 (39.7)	83 (36.9)
≥2 live births	63 (28.1)	77 (34.2)
Presence of STI — no. (%)		
<i>Chlamydia trachomatis</i> §	30 (13.4)	33 (14.7)
<i>Neisseria gonorrhoeae</i> §	10 (4.5)	7 (3.1)
<i>Treponema pallidum</i>	0	2 (0.9)
Any STI§	40 (17.9)	40 (17.9)

* Percentages may not total 100 because of rounding. HIV PrEP denotes preexposure prophylaxis against human immunodeficiency virus, IQR denotes interquartile range, PEP postexposure prophylaxis, and STI sexually transmitted infection.

† A total of 51 participants did not have vaginal sex in the 3 months before enrollment.

‡ Contraception includes intrauterine device, implant, depot medroxyprogesterone acetate, and oral contraceptive pills.

§ One participant without an endocervical swab collected at baseline was enrolled.

dPEP-KE

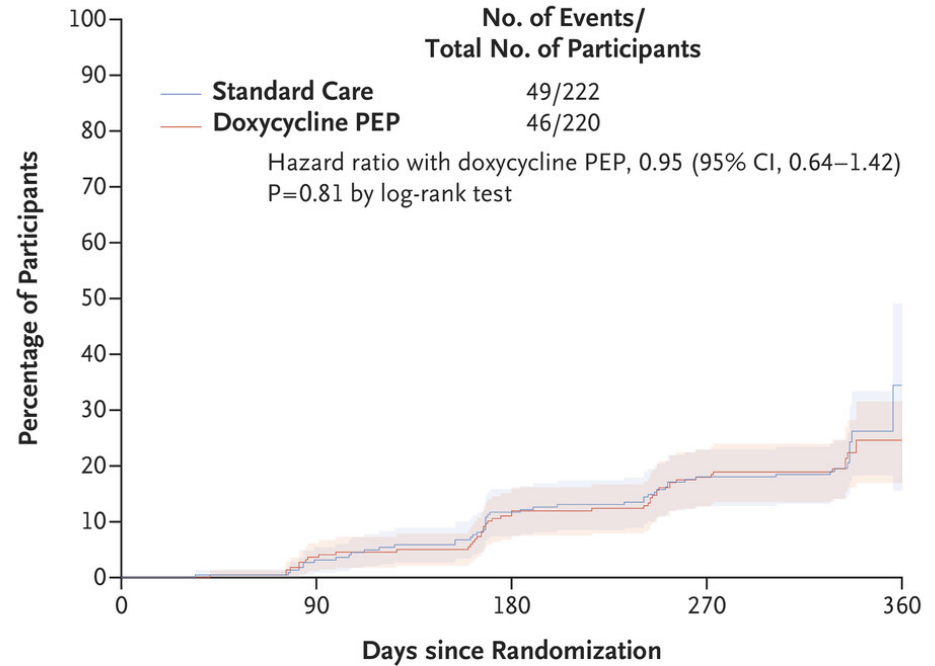
	dPEP N=224	SOC N=225	RR (95% CI)
Any	50/854	59/886	0.88 (0.60-1.29)
CT	35/854	50/886	0.73 (0.47-1.13)
GC	19/854	12/886	1.64 (0.78-3.47)

1 incident syphilis infection

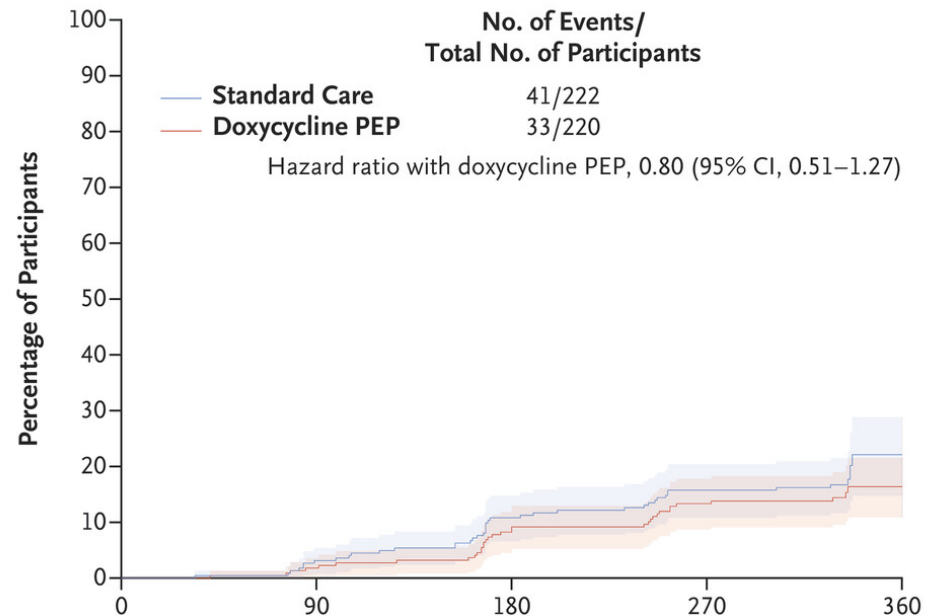
80 Pregnancies

10.1% visits with doxycycline on hold

A First Sexually Transmitted Infection



B First *C. trachomatis* Infection



Adherence

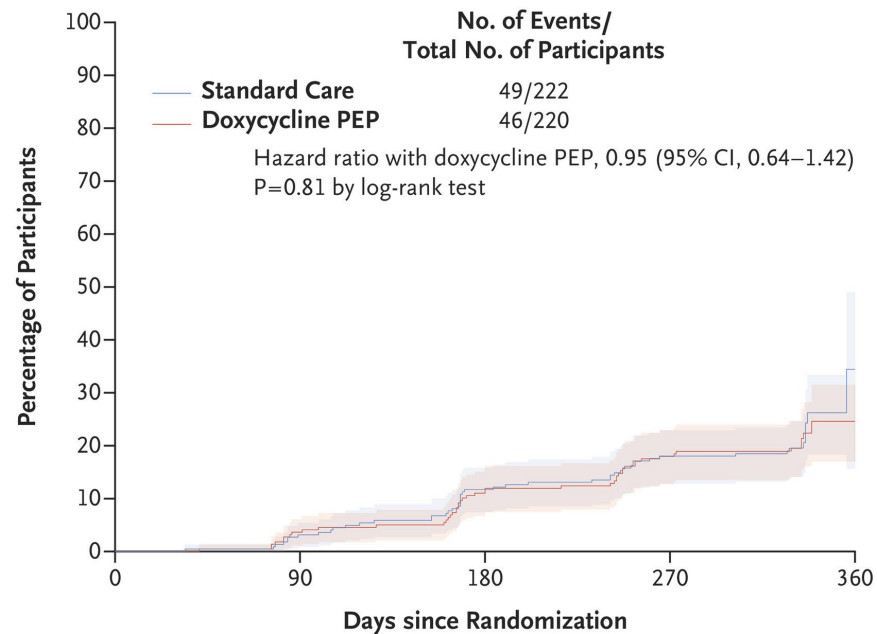
- 91% - completed quarterly timeline follow-back calendars
- 80% - Reported PEP event coverage in last 2 weeks
- 23.3% of visits reported not using PEP at last sex act

- 78% in dPEP group completed SMS surveys
- 55% reported taking PEP after their last sex act

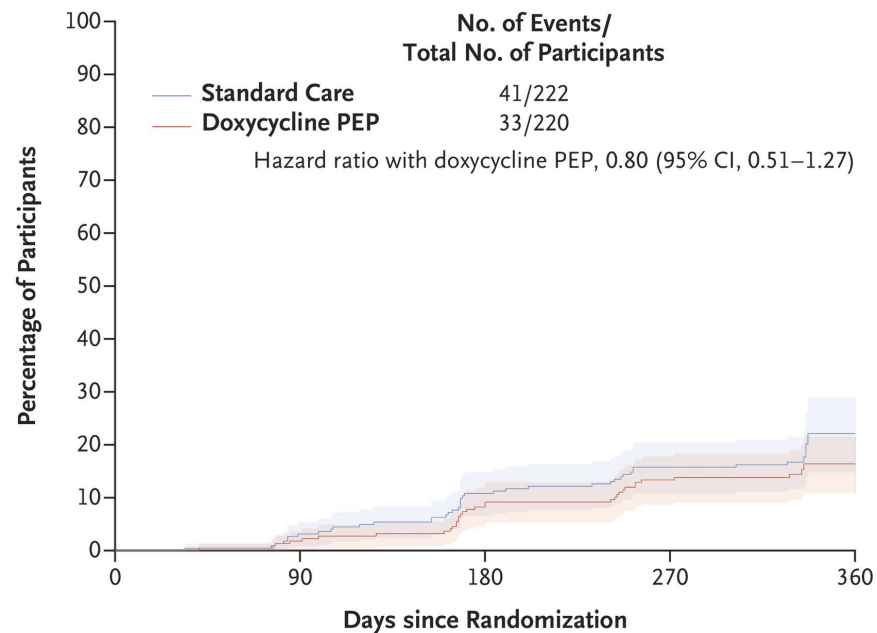
- Among 50 dPEP hair samples
- 29% had detectable doxycycline in all visit
 - 33% when accounting for pregnancy hold visits
 - 6.7% had detectable at baseline, 5.1% in SOC arm

Stewart et al., NEJM 2023

A First Sexually Transmitted Infection



B First *C. trachomatis* Infection



Kenya dPEP

Kenyan cisgender women on PrEP

No clear benefit yet

4 social harms (IPV)

Subjective adherence good

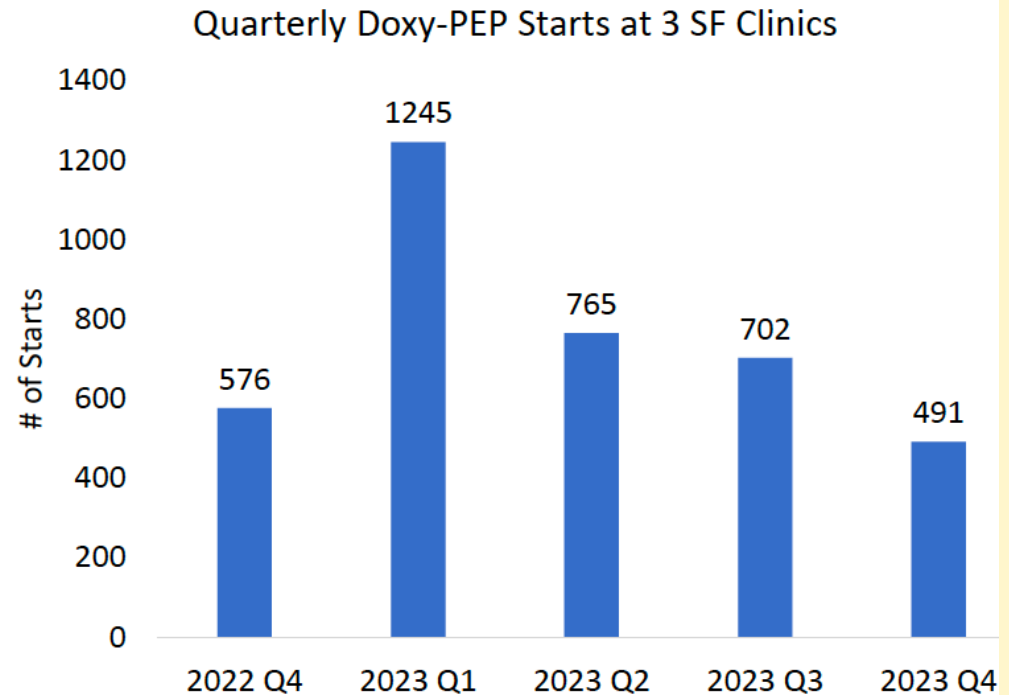
Objective adherence (doxy levels) were not adequate and not consistent with appropriate dosing.

Does it work? Don't know yet.

? Pregnancy concerns (44 pregnancies in PEP arm) outcomes not reported.

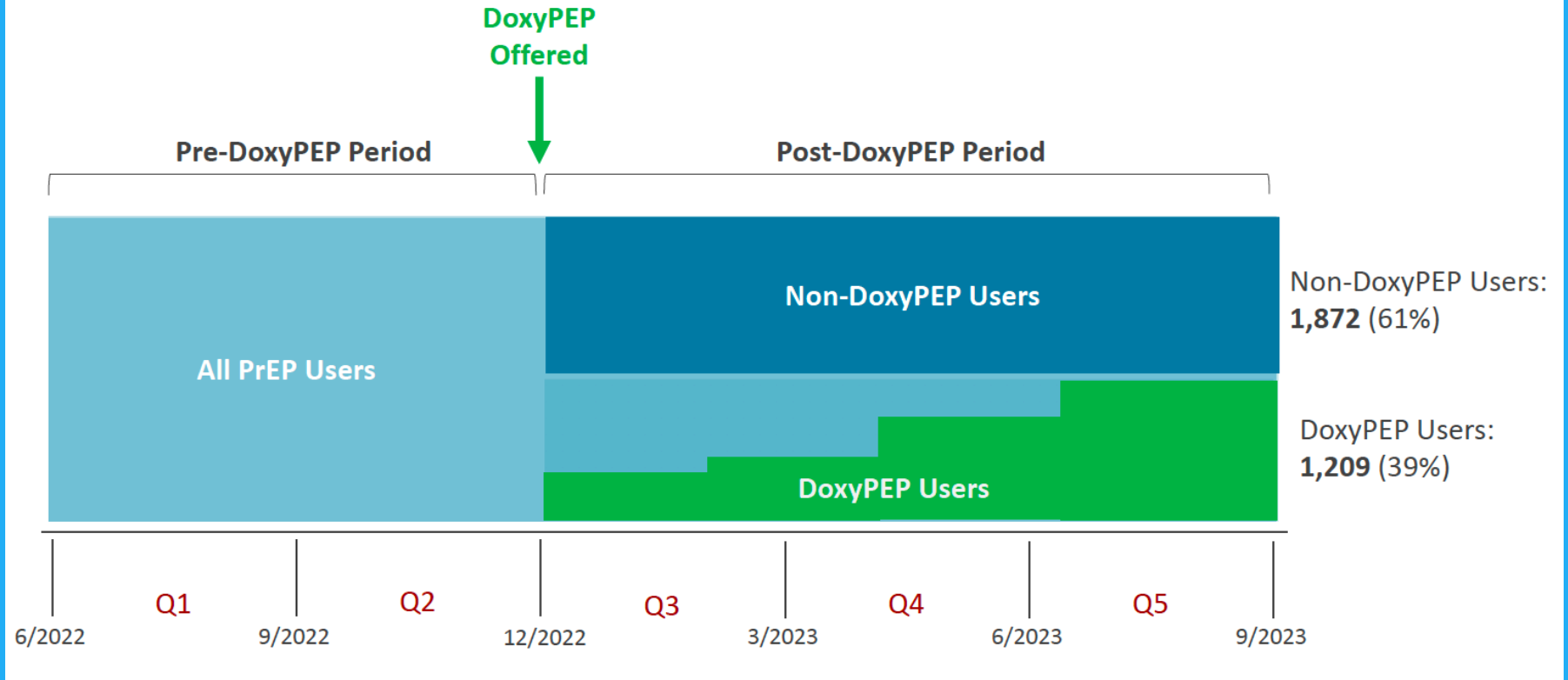
Background: Doxy-PEP Uptake at 3 SF Clinics

- 3 SF clinics provide sentinel surveillance data on uptake
- Rapid adoption of doxy-PEP
 - ~600 starts in first 2 months
- Starts through 2023:
 - >3,700
 - 20% of MSM and TGW



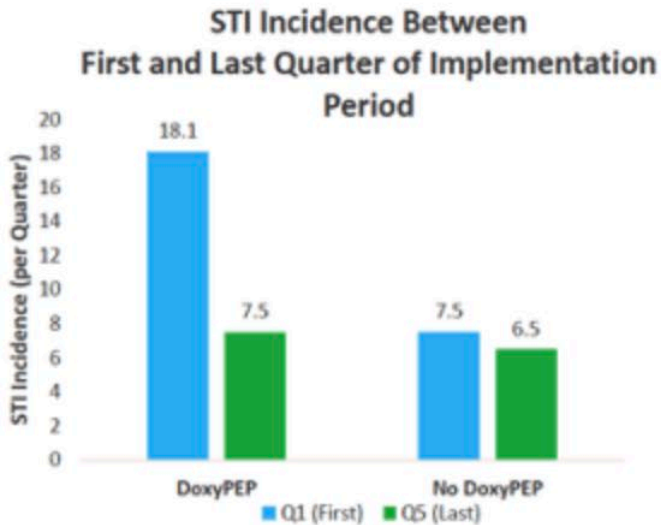
DoxyPEP uptake at San Francisco PrEP Clinic

DoxyPEP Timeline



Real world effectiveness

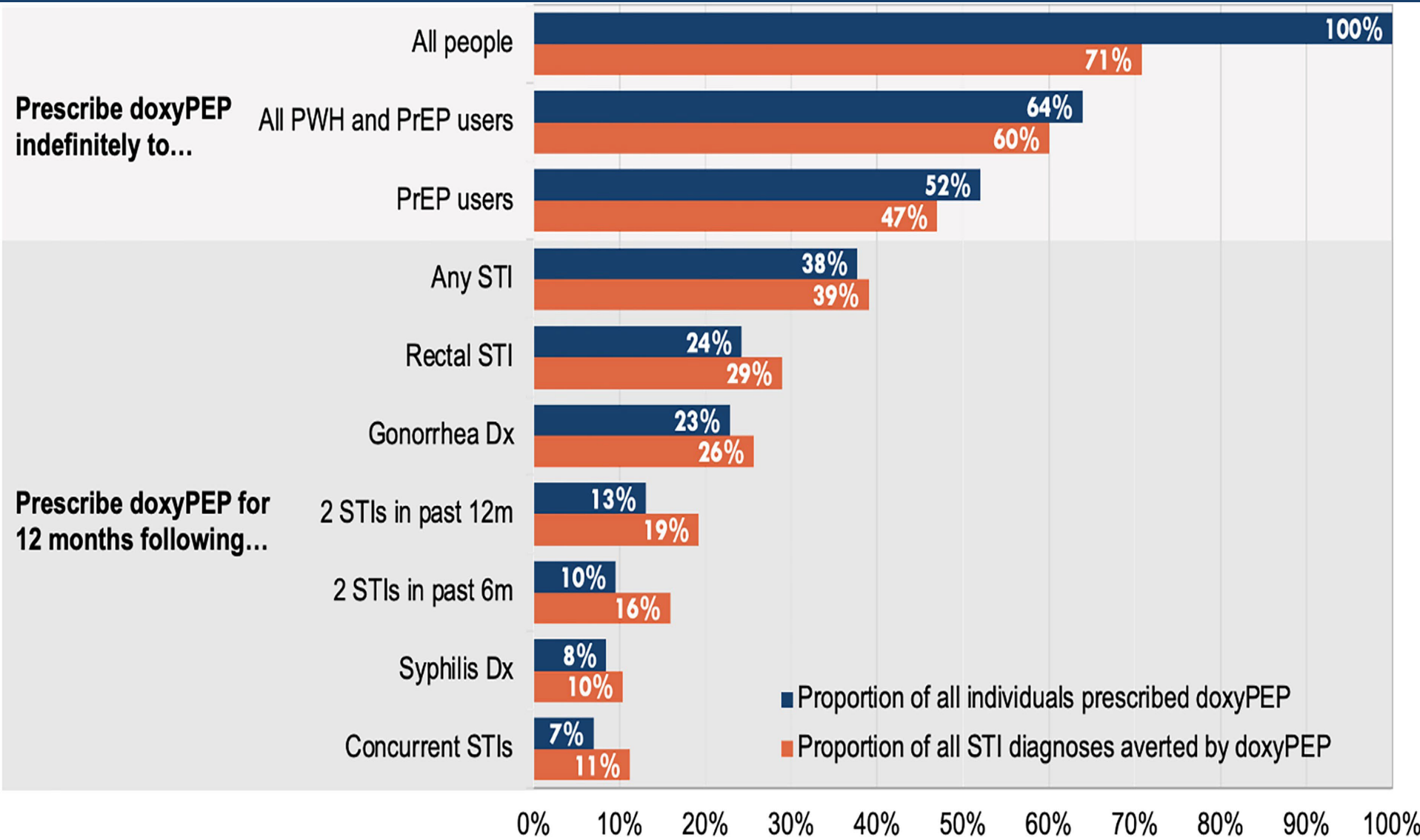
STI Incidence among DoxyPEP Users (Pre-Post Analysis)



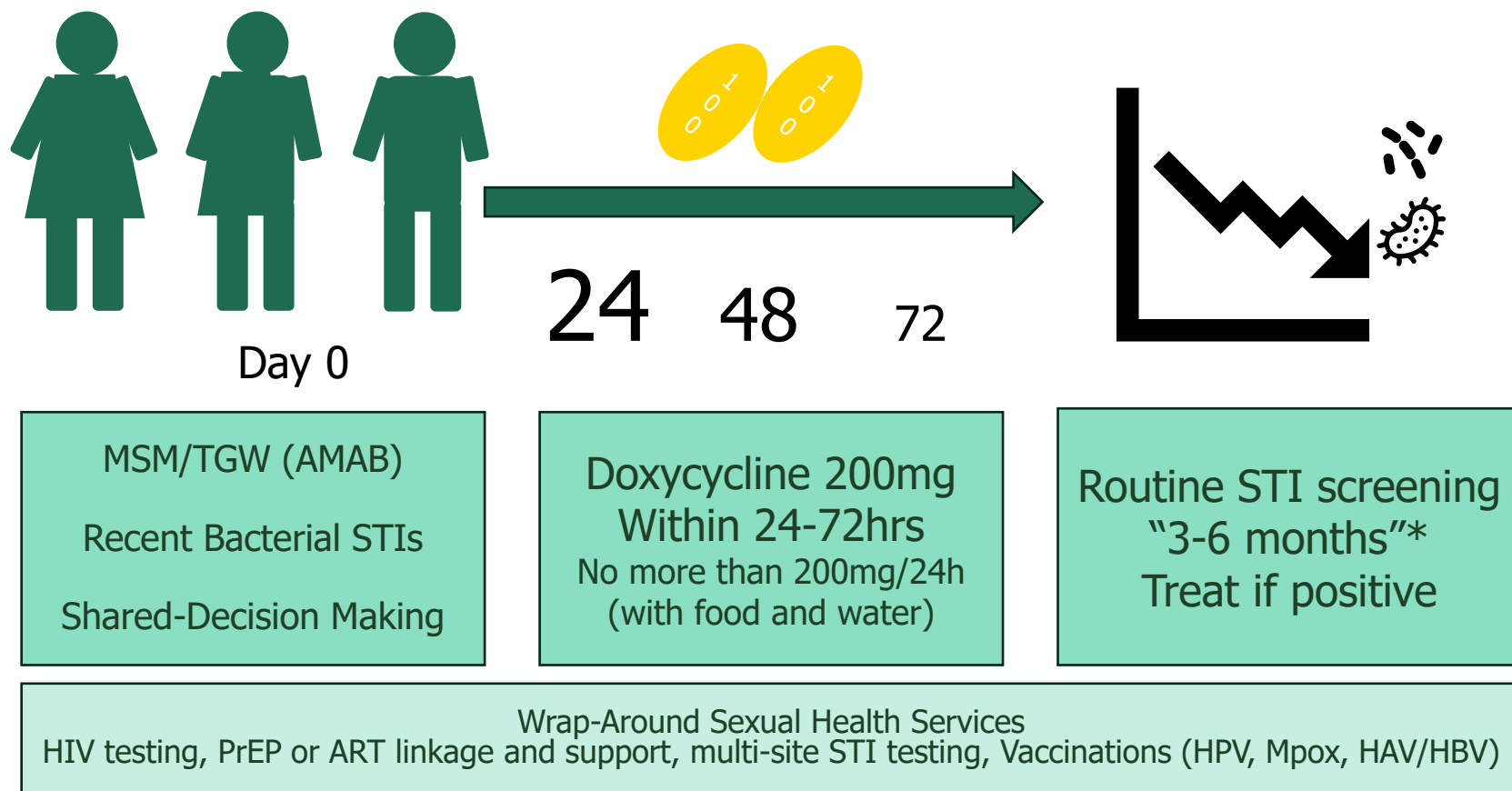
	IRR	95% CI	p-value
Any STI	0.42	0.24 - 0.74	0.003
Chlamydia	0.33	0.23 - 0.46	<0.001
Syphilis	0.22	0.09 - 0.54	0.001
Gonorrhea	0.89	0.69 - 1.15	0.383

Any STI: Chlamydia, Syphilis, or Gonorrhea at any site.

Modeling data to predict best coverage



DoxyPEP Provision



Template protocols available ncsd.org

<https://www.cdc.gov/std/treatment/guidelines-for-doxycycline.htm> (not published yet)

Polling Questions

Join at mentl.com | use code 3259 2405

Mentimeter

Do you have any questions or concerns regarding DoxyPEP?

All responses to your question will be shown here

Each response can be up to 200 characters long

Turn on voting in Interactivity to let participants vote for their favorites



JS

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Content



Design



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Help & Feedback

Doxycycline PEP Concerns

- Antimicrobial Resistance
 - Questionable increase in gonorrhea AMR but no increase in *Staphylococcus aureus* TCN-resistance in DOXYPEP.
 - High-level GC Resistance in DOXYVAC already but no increase in TCN-resistance in *S. aureus*
- Microbiome disruption
 - DOXYVAC without significant changes in *E. coli*, used as a marker for gut microbiome
- Long-term data are not yet available
- Safety in persons who are/can be pregnant unknown

Doxycycline PEP Summary

- Doxycycline as post-exposure prophylaxis is highly effective in GBM/TGW/AMAB but more data are needed in AFAB.
- DoxyPEP is safe
- Long term implications for antimicrobial resistance and microbiome are unknown, although short term data are reassuring
- More data are needed for effectiveness in persons assigned female sex at birth.

Gratitude

Participants & Patients

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Heersink School of Medicine

Thank you!

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