

DOXYPEP

Current Evidence & Remaining Questions

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Some slides courtesy of Beatrice Berçot, Chase Cannon, Stephanie Cohen



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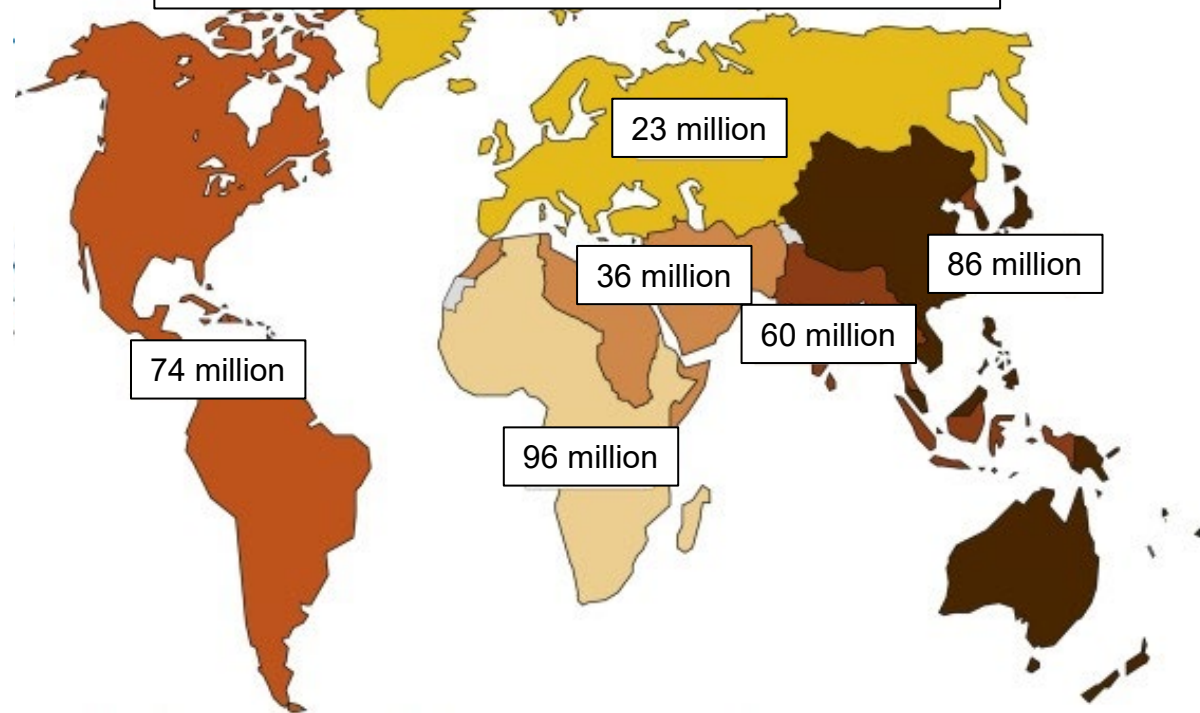


Disclosures

- Doxycycline provided by Mayne Pharmaceuticals
- Laboratory support from Cepheid & Hologic

Sustained Increases in Sexually Transmitted Infections in US and worldwide

WHO estimates more than 374 million new curable STIs each year



THE STATE OF STIs IN THE UNITED STATES, 2022

CDC's 2022 STI Surveillance Report underscores that STIs must be a public health priority

- 1.6 million** CASES OF CHLAMYDIA (6.2% decrease since 2018)
- 648,056** CASES OF GONORRHEA (11% increase since 2018)
- 207,255** CASES OF SYPHILIS (80% increase since 2018)
- 3,755** CASES OF SYPHILIS AMONG NEWBORNS (183% increase since 2018)

ANYONE WHO HAS SEX COULD GET AN STI, BUT SOME GROUPS ARE MORE AFFECTED

- YOUNG PEOPLE AGED 15-24
- GAY & BISEXUAL MEN
- PREGNANT PEOPLE
- RACIAL & ETHNIC MINORITY GROUPS

LEARN MORE AT: www.cdc.gov/std/

- **Gonorrhea:** threat of increasing incidence of antimicrobial resistance
- **Syphilis:** increase in heterosexual networks with congenital syphilis

Doxycycline Post-Exposure Prophylaxis (doxy-PEP)

- Why Doxycycline?
 - Safe, well tolerated, and inexpensive
 - Active against chlamydia (CT) & syphilis
 - Some resistance in gonorrhea (GC)- ≈20% of US isolates, higher in other settings
 - However:
 - Not used as 1st line treatment for GC
 - unknown how much activity needed for PEP
- Three recent RCTs:
 - Investigated doxy-PEP efficacy to reduce bacterial STI's
 - Impact of intermittent doxy use on drug resistance, in STIs and other bacteria)

Intervention: Open label doxycycline 200mg taken as PEP within 72 hours after condomless sexual contact
Maximum of 200 mg every 24 hours

Inclusion criteria:

- **Male sex at birth**
- **Living with HIV or on PrEP**
- **≥ 1 STI in past 12 months**
- **Condomless sex with ≥ 1 male partner in past 12 months**

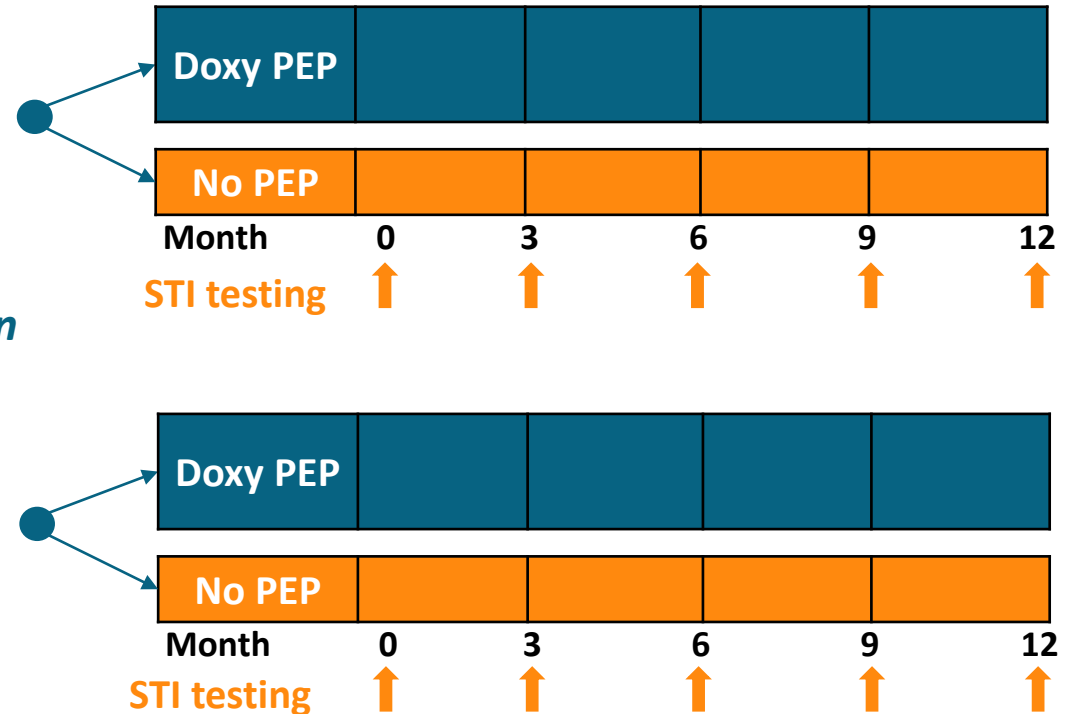
STI Testing: Quarterly 3 site GC/CT testing + RPR, GC culture before treatment

Sites: San Francisco & Seattle HIV & STI clinics

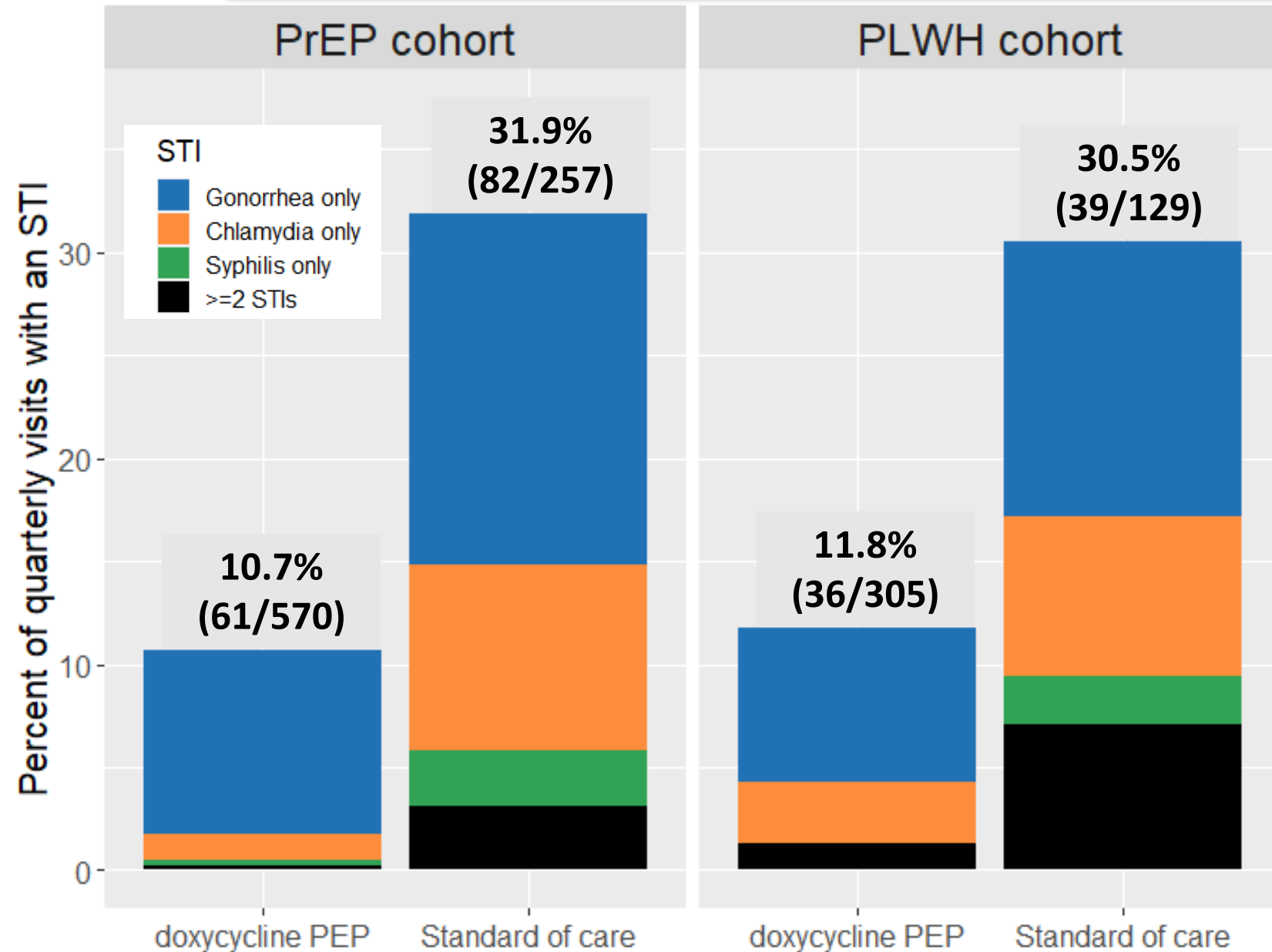
**MSM & TGW
living with HIV**
(planned n = 390)

2:1 randomization

**MSM & TGW
on HIV PrEP**
(planned n = 390)

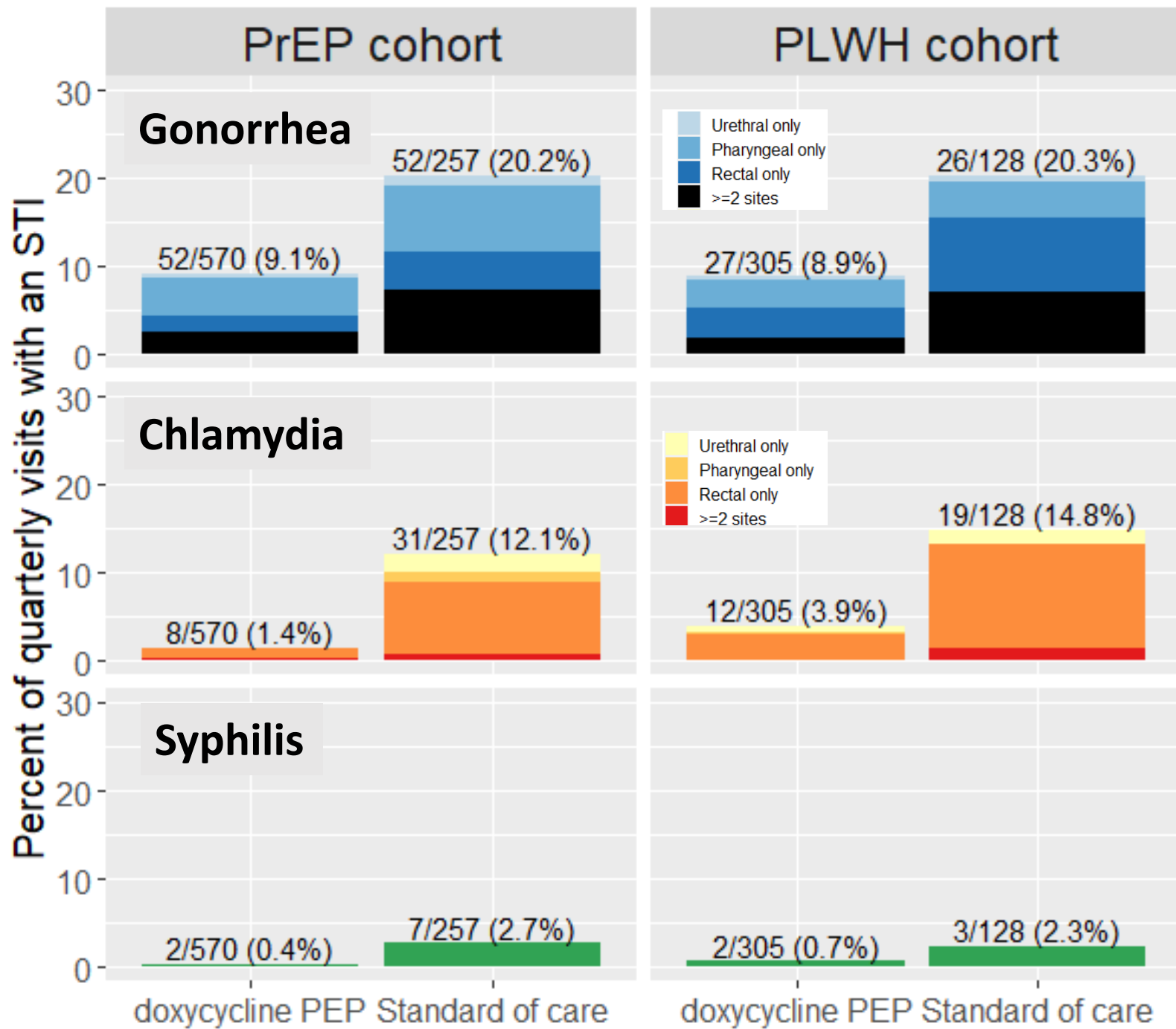


Primary Endpoint: STI incidence per quarter



Risk reduction in STI incidence/quarter (95% CI)	
PrEP	66% (54% - 76%)
Living with HIV	62% (40% - 76%)
Total	65% (54% - 73%)

all p < 0.0001



Individual quarterly STI incidence by study arm & cohort

Risk reduction in each STI per quarter (95% CI)

	PrEP	PLWH
GC	55% (35%-68%) <i>p</i> <0.0001	57% (29%-74%) <i>p</i> =0.001
CT	88% (75%-95%) <i>p</i> <0.0001	74% (43%-88%) <i>p</i> =0.0007
Syphilis	87% (41%-97%) <i>p</i> =0.0084	77% (-71%, 96%) <i>p</i> =0.095

Qualitative benefits of doxy-PEP



Emotionally...that confidence [due to doxy-PEP] counts for a lot in terms of my mood, and my positivity, and my... sex positivity...before, there would be this kind of cloud of shame come over [a sex act]. (Age 44, HIV-, Seattle)

Sex-positive and person-first intervention

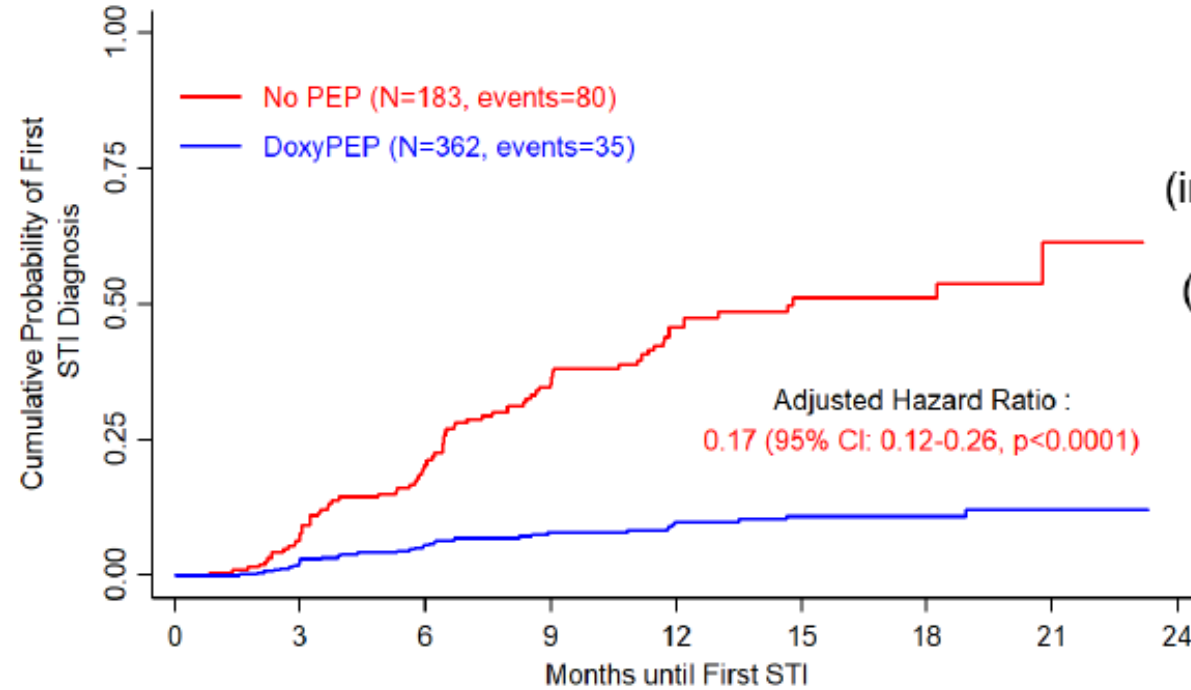
- Improved peace of mind & sexual pleasure
- Decreased stigma around STI diagnosis and disclosure
- Increased self-awareness about sexual behavior
- Facilitates communication with partners

DOXYVAC

Molina et al

Study design	Factorial: 2:1 dPEP vs none + Men B vax vs none
Inclusion criteria	Adult MSM with ≥ 1 recent STI, at least 6 mo on oral HIV PrEP
Participants	502; early stop for effectiveness
Primary outcome	Time to first syphilis or CT
Results	CT or syph \downarrow 83%* GC: \downarrow 33%*

Time to first CT or syphilis



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)

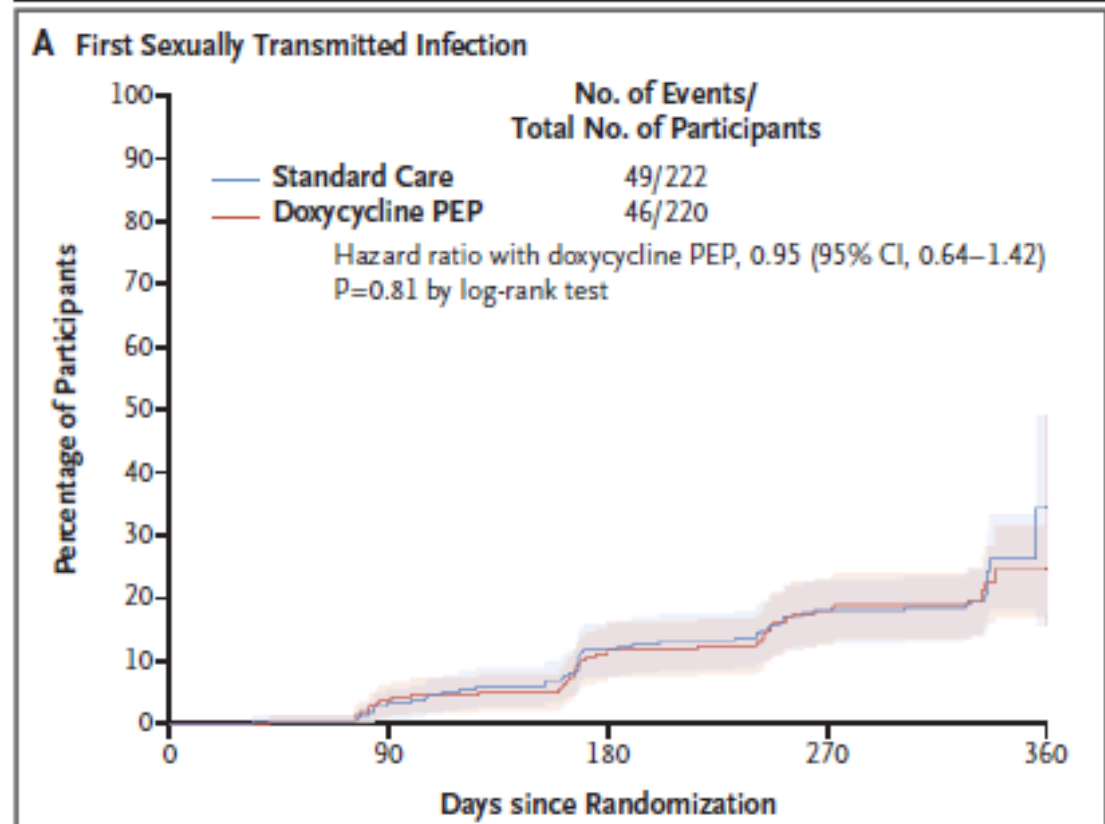
- Median 3.5 doses per month (IQR 2-5.5)
- Significant STI risk reduction for CT, syphilis & Mgen (aHR: 0.55, 95% CI: 0.34-0.89)
- Smaller decrease for GC (aHR: 0.67; 95% CI: 0.52-0.87)
- No significant change in sexual behavior during follow-up

dPEP = doxycycline post-exposure prophylaxis
MSM = men who have sex with men
PrEP = pre-exposure prophylaxis
*Statistically significant result

DPEP Kenya Trial



- 18% had an STI at enrollment
- 27% annual STI incidence
- 109 new STIs
 - 50 doxy-PEP
 - 59 standard of care
- 78% were C trachomatis
 - 35 doxy-PEP
 - 50 standard of care



NO difference in STI incidence between the two arms

Bottom line:

- Adherence likely an issue; high self-reported adherence but in a random sample of 50 participants assigned to doxy-PEP, only 29% had doxycycline detected in hair samples.
- Need more data to understand effectiveness and role of doxy-PEP in cis-gender women

What we know

DoxyPEP works very well to prevent STI's in MSM with consistent results in two RCTs

↓ *Each* bacterial STI – less effective against gonorrhea

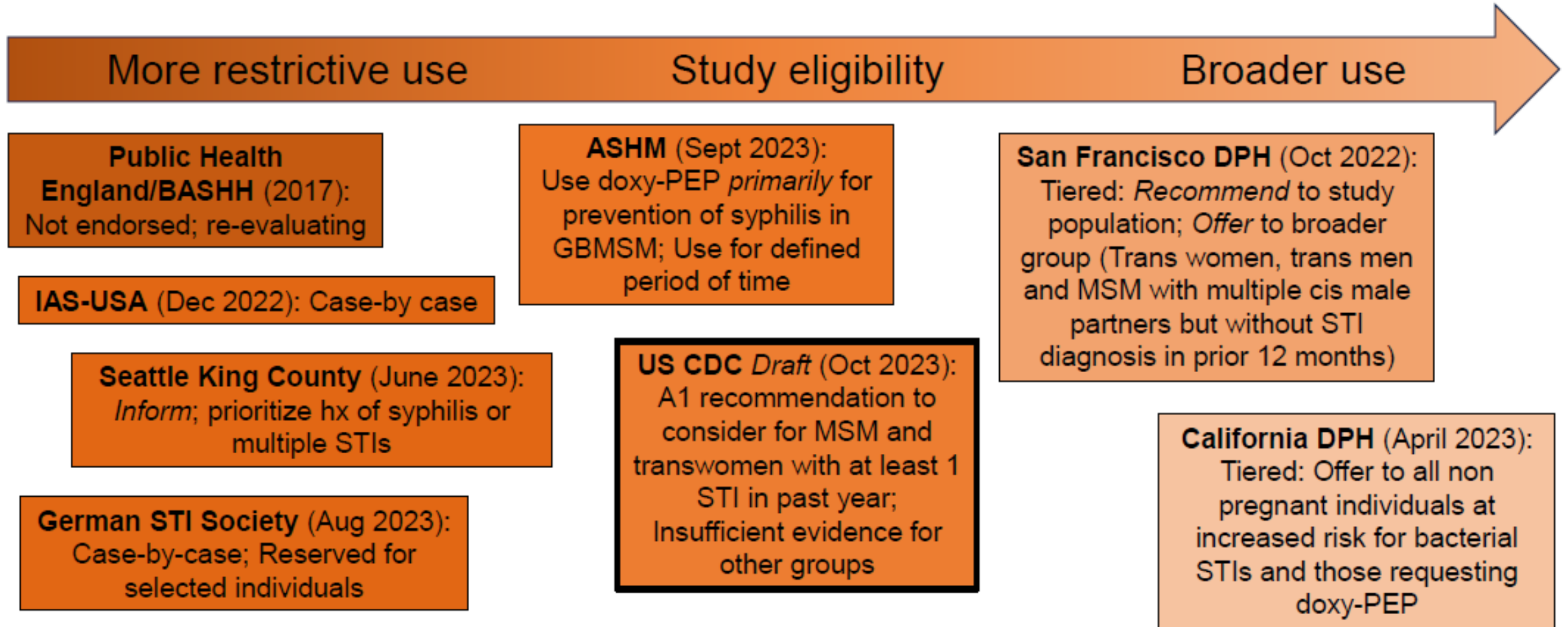
DoxyPEP : Need to treat about **5 people** to prevent a quarter with an STI, in a population with a high STI incidence (30% per quarter)

Safe & well tolerated

Low adherence in cis-gender women may explain lack of efficacy- need more data in this population

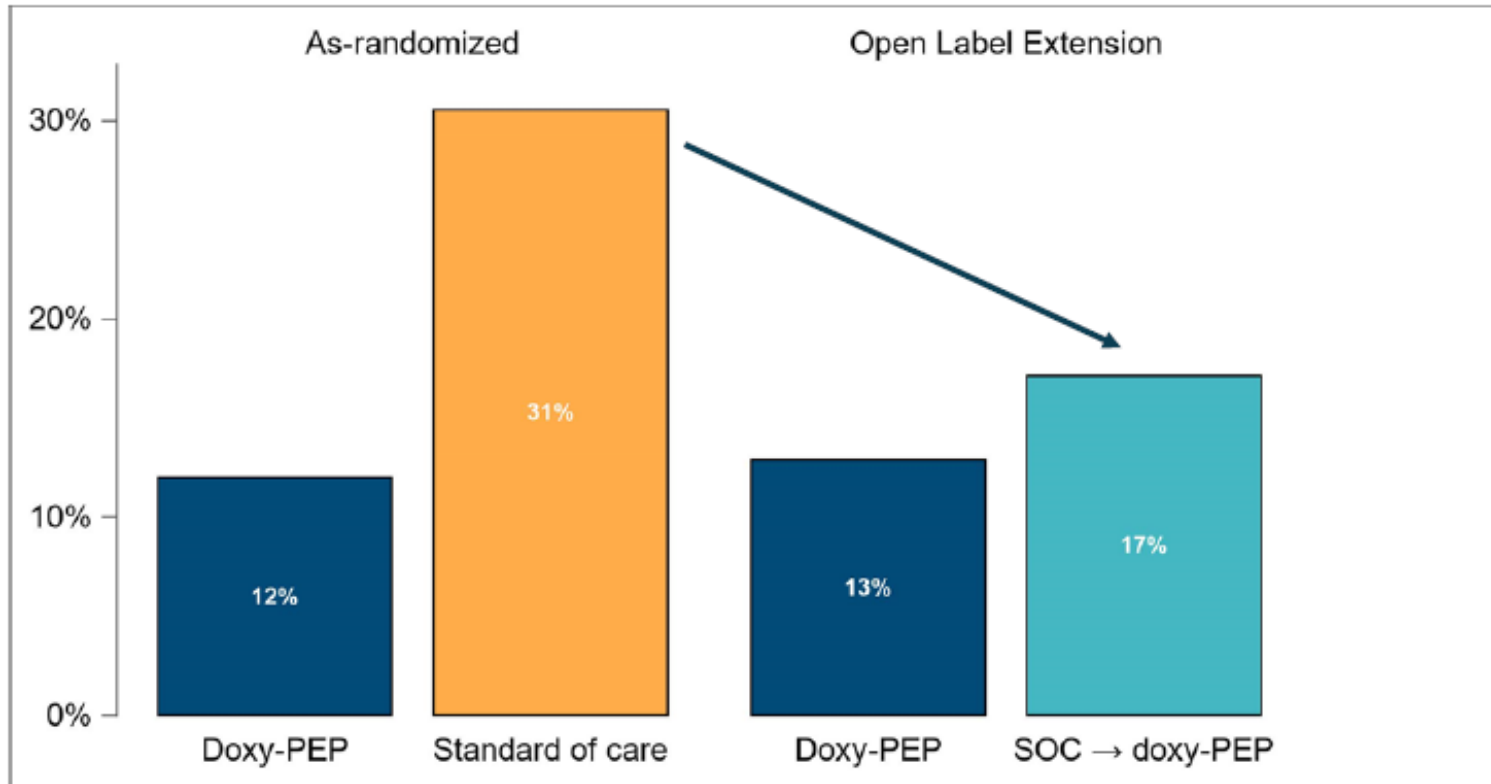
Who Should be Offered doxy-PEP?

Current guidelines do not agree



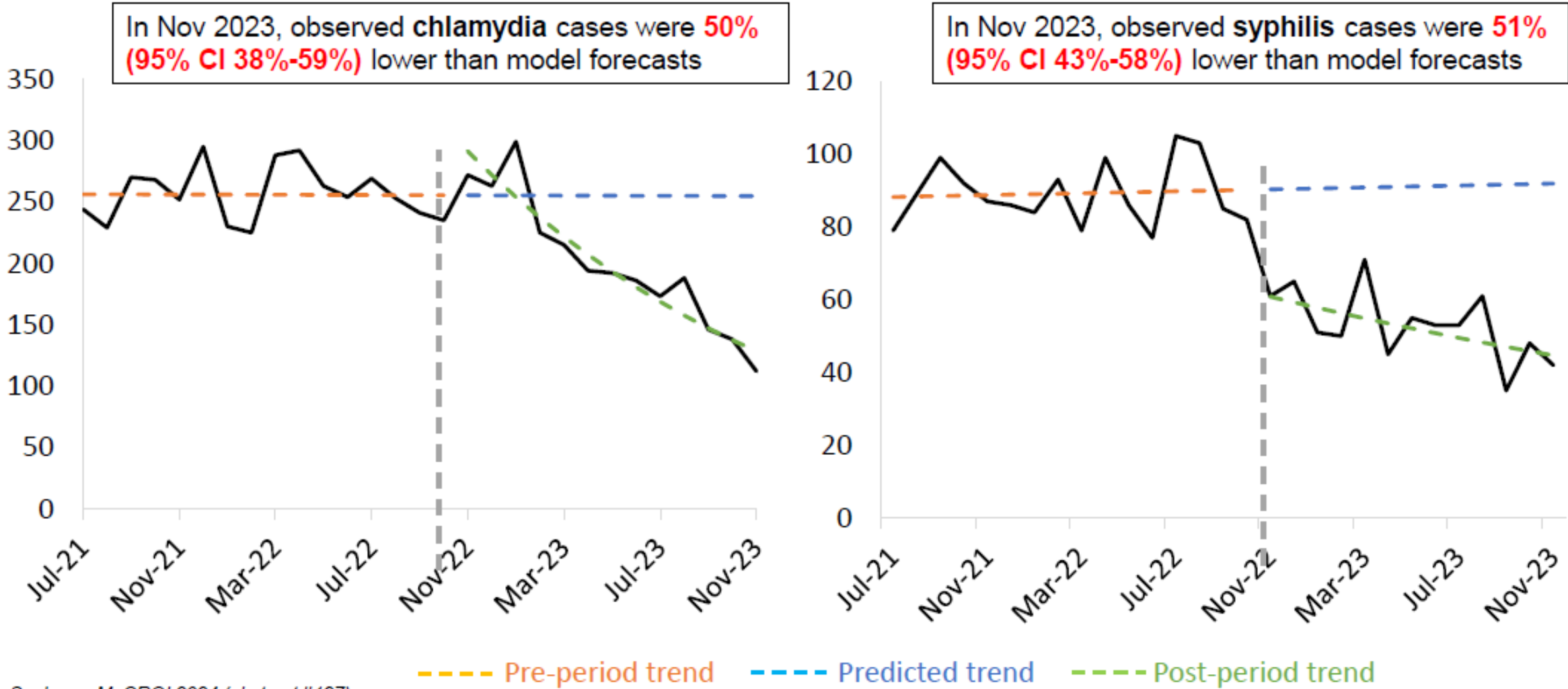
Sustained reduction of STIs during Open Label Extension of DoxyPEP study

Incidence of ≥ 1 STI per quarter



- Doxy-PEP offered to SOC pts after early stop due to efficacy; all but 1 SOC ppt accepted doxy-PEP
- Sustained decreased incidence in STI, comparable to during RCT despite modest increases in # of partners & condomless sex acts

Decline in **citywide** chlamydia and early syphilis cases in MSM in SF after release of doxy-PEP guidelines



Sankaran M, CROI 2024 (abstract #127)

What we are still learning

Antimicrobial resistance impact:

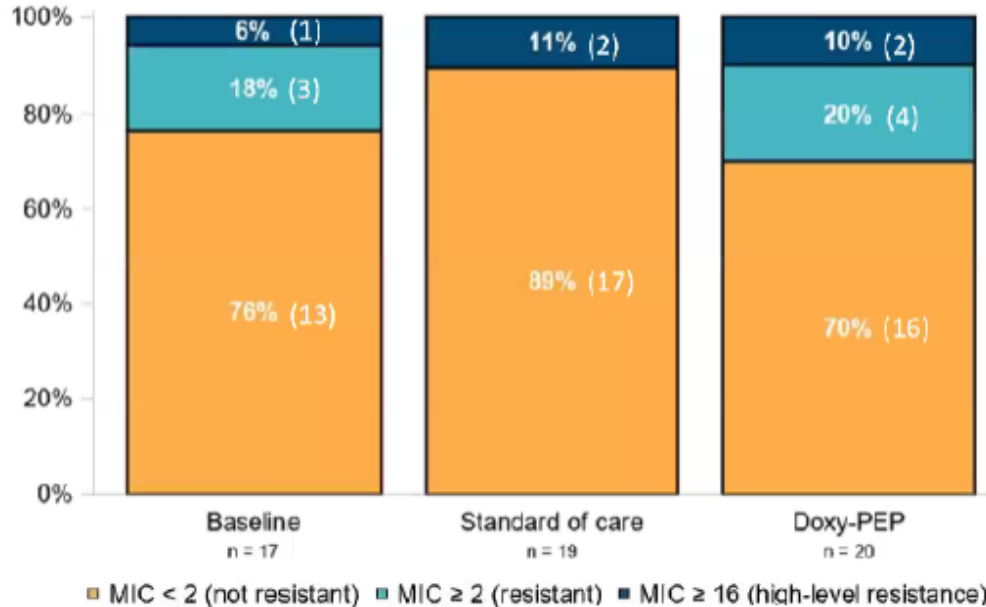
- > Will existing TCN-resistance affect doxy-PEP efficacy against GC?
- > Impact on off-target bacteria like Staph aureus, commensal Neisseria, and the gut microbiome
- > Impact on other STIs: CT, Syphilis, *M. gen*

GC: Impact in Doxyvac/DoxyPEP trials (2020-22)

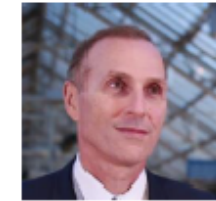
DOXYPEP



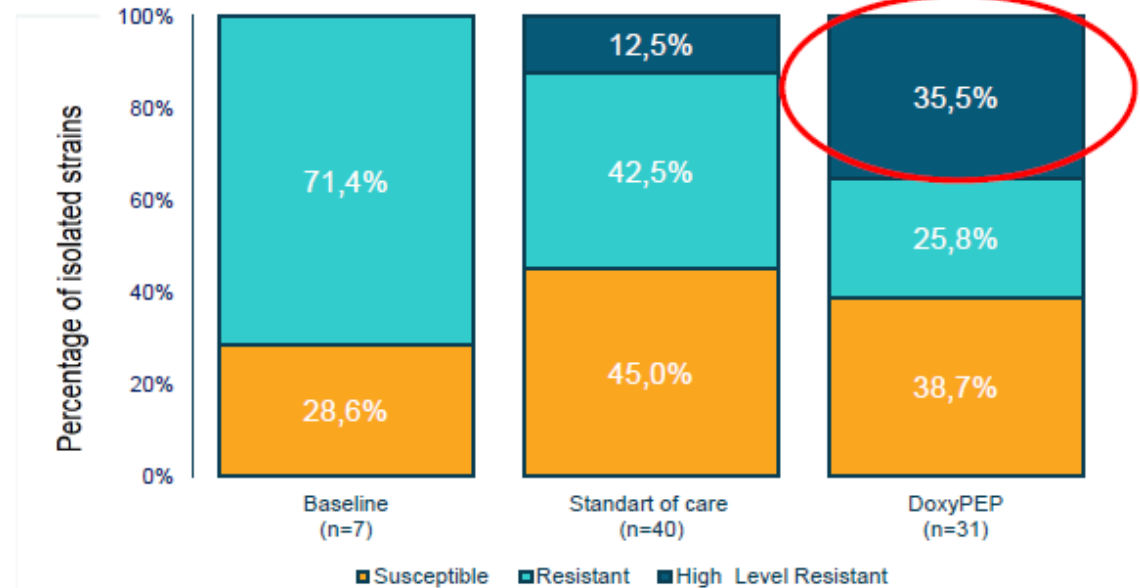
- GC: 56 cultures



Doxyvac



- GC: 78 cultures



Resistance defined by MIC ≥ 2 mg/L

Increased TCN-R in doxy-PEP vs. standard of care suggests doxy-PEP may be less protective against GC strains with existing TCN-R.

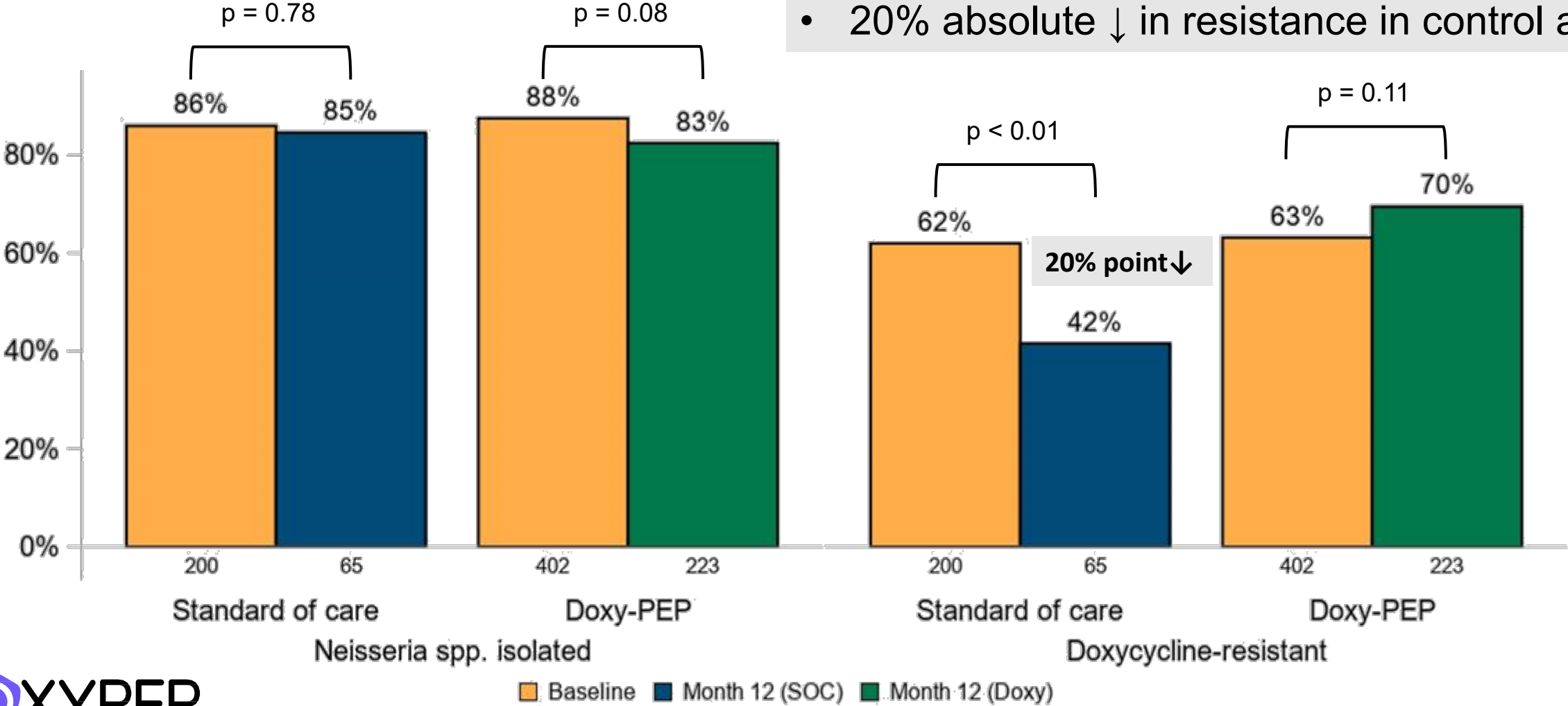
More high-level tetracycline-resistant isolates in the PEP group ($p=0.04$)

Does **NOT** address the potential impact of doxy-PEP use driving GC resistance; requires population based surveillance and longer follow-up

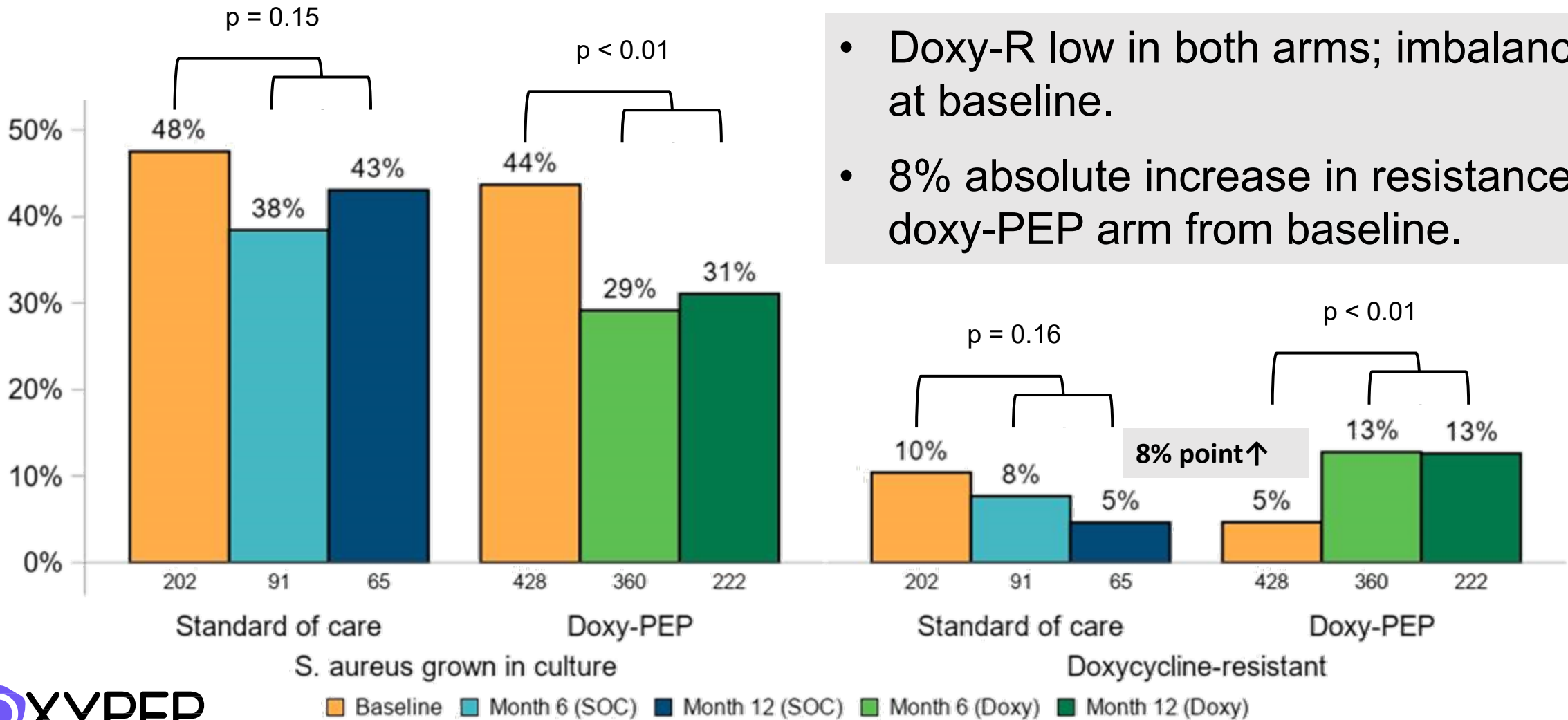
Slide adapted from Beatrice Berçot

Commensal *Neisseria*: >60% with baseline doxycycline resistance

- No change in resistance in doxy-PEP arm.
- 20% absolute ↓ in resistance in control arm.



S. aureus: 8% absolute increase in doxycycline resistance (doxy-R) in doxy-PEP arm



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

GUT RESISTOME

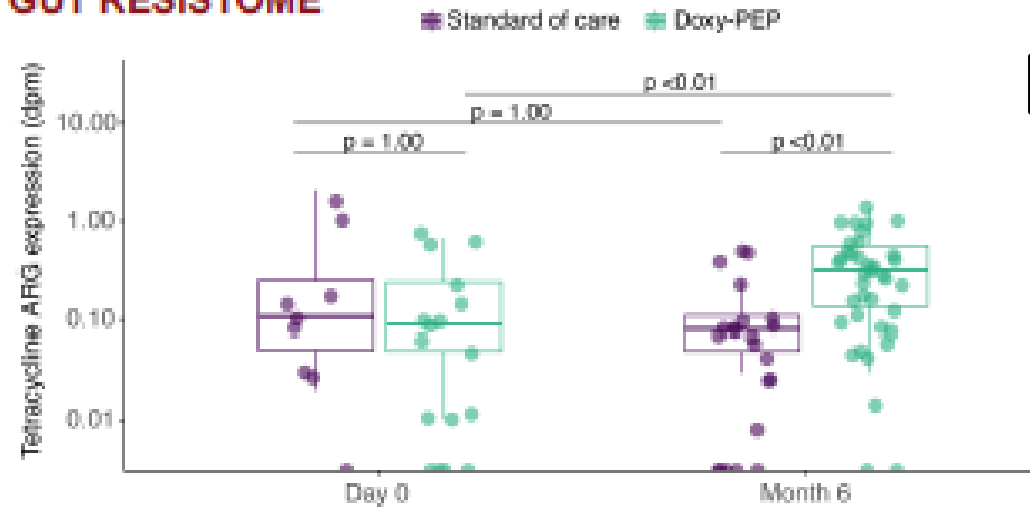


Figure 3. Tetracycline ARG expression by study arm and visit in the RNA-seq samples (n=86). Tetracycline ARG expression increased in the doxy-PEP Month 6 group compared

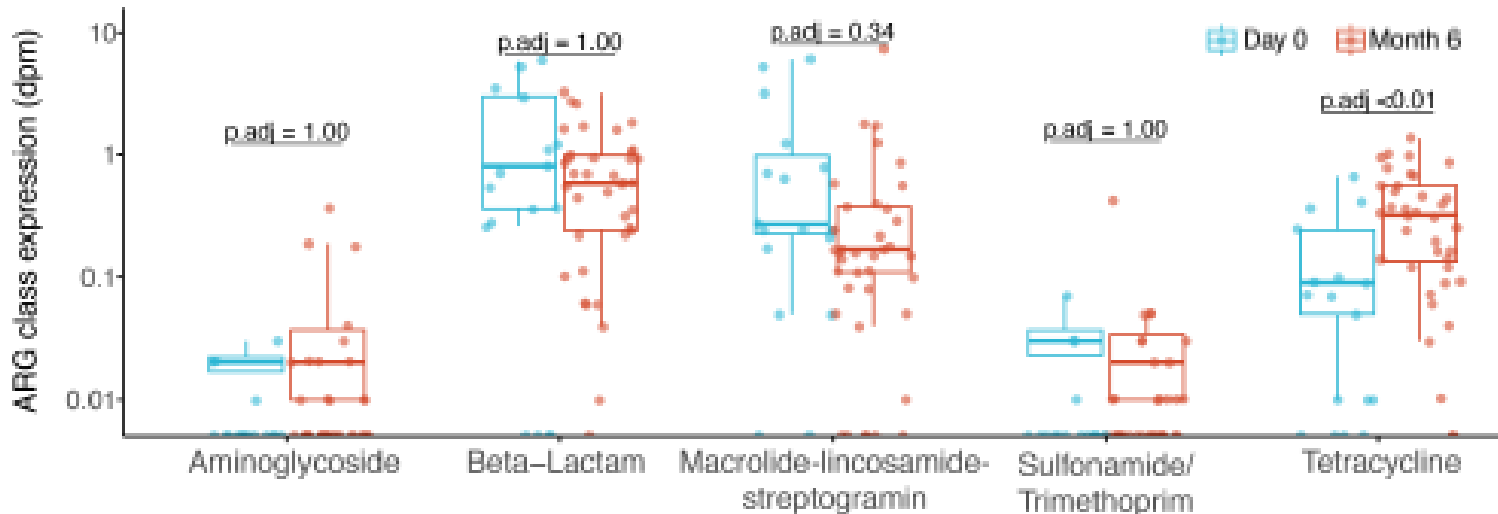


Figure 2. Impact of doxy-PEP use on ARG class expression, normalized by reads per million sequenced and gene length (depth per million, dpm) in the doxy-PEP RNA-seq samples (n=55). Tetracycline ARG expression significantly increased between Day 0 and Month 6, while no difference was observed among non-tetracycline ARG classes.

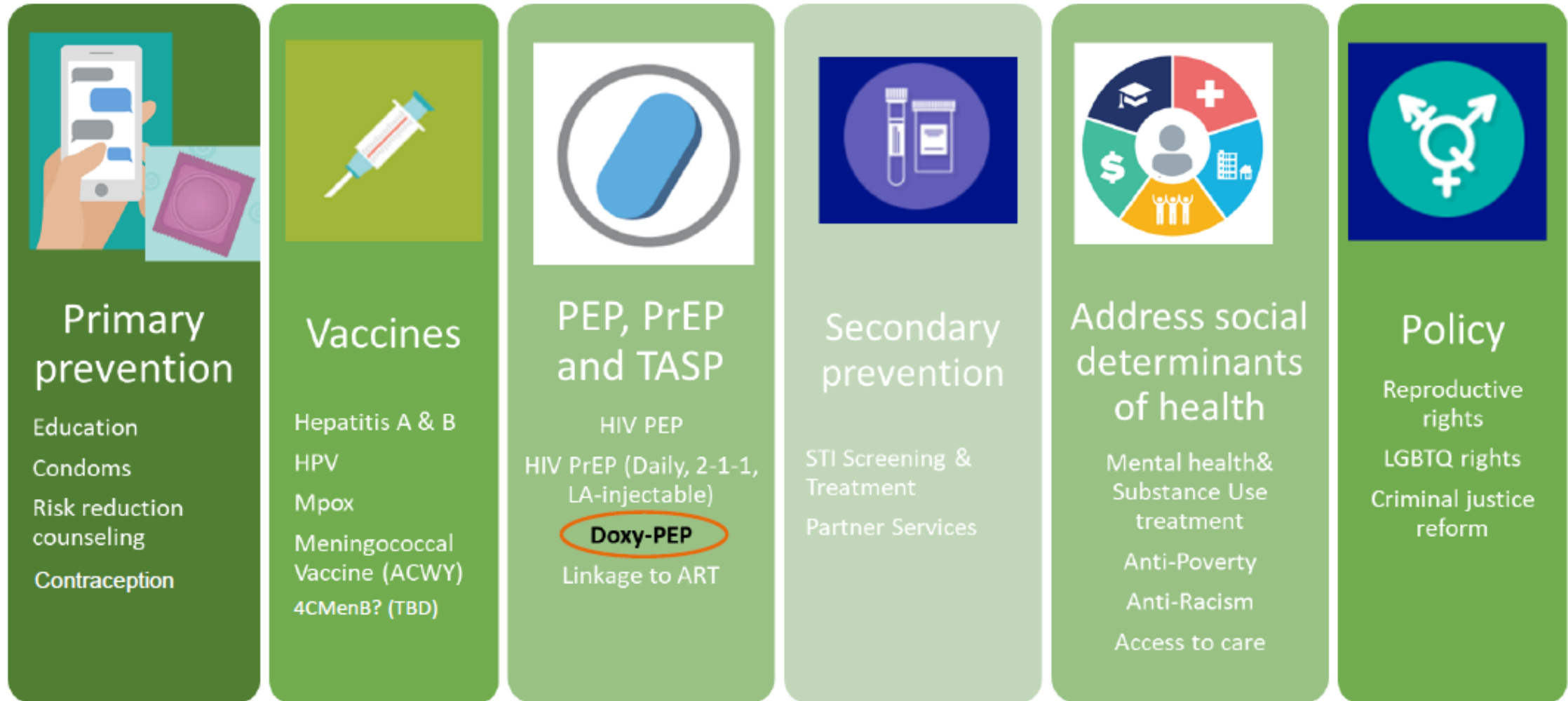
Doxy-PEP Impact on Gut Microbiome

- 45% of the antibiotic resistance genes by mass were *already* TCN-resistant genes at study entry
- Active TCN-resistant gene expression increased with doxy-PEP use
- No other antimicrobial class resistance genes increased
- Clinically significance of increased gene expression not clear

DoxyPEP Conclusions

- Doxy-PEP could be impactful in reducing STI rates while developing STI vaccines
- Not an intervention intended for all MSM & TW, rather a focused intervention for those at highest risk of STIs
 - Consistent, strong evidence that doxy-PEP is highly effective for MSM/TW for chlamydia and syphilis
 - Shared decision-making with MSM & TW about their need/risk, evidence about efficacy, what is known about AMR
 - Use over time may change as STI risk changes
 - Part of comprehensive STI/HIV prevention that is under the user's control

Doxy-PEP as part of a comprehensive package of sexual health services



Next steps

- Need better tools for GC reduction
- Need data to inform use in cis-gender women & men who have sex with women
- Important to balance the known efficacy of doxy-PEP for MSM & TW with unknowns about AMR
- Guidelines for use are important to avoid use of ineffective antibiotics, provide guidance on populations that will benefit most, and to provide a summary of the evidence.
- Critical to get additional data on AMR during doxy-PEP implementation
 - Monitor impact on AMR in STIs, bystander bacteria and microbiome
- Monitor access to doxy-PEP, uptake and persistence in sentinel cities and address equitable utilization during roll-out
 - Consider “doxy-PEP to need ratio” similar to PrEP to need ratio to ensure reaching those with highest need
 - Evaluate impact on population STI rates

Readable, concise, non-stigmatizing patient and provider facing education and social marketing tools, in multiple languages

About Doxy-PEP

What is doxy-PEP?

- Doxy-PEP means taking the antibiotic doxycycline after sex, to prevent getting an STI. It is like a morning-after pill but for STIs. Taking doxy-PEP reduces your chance of acquiring syphilis, gonorrhea, and chlamydia by about two-thirds.

When should I take doxy-PEP?

- Two 100 mg pills of doxycycline should be taken after condomless sex. Condomless sex means isn't used for the entire time.

What about when I have sex again?

- If you have sex again within 24 hours of taking last dose, you can take doxycycline as often as don't take more than 200 mg (two 100 mg pill).

How should I take doxy-PEP?

- Take doxycycline with plenty of water or soon you swallow, if your stomach is upset by dry.
- Some people are more sensitive to the sun.
- Please do not share doxycycline with others.
- Avoid dairy products, calcium, antacids, or iron.

What are we still learning about doxy-PEP?

- Does it affect normal ("good") bacteria in our body?
- Could it increase or decrease the bacteria that cause STIs?
- Will doxy-PEP increase doxycycline resistance?
- Although doxycycline has been used for chlamydia or syphilis.
- About 25% of gonorrhea in the US is these strains. The DoxyPEP study and other PEP changes resistance in gonorrhea.

Reminders

- Call us at 825-217-6932 if you ran out of doxy-PEP, think you may have an STI.
- Please continue to get tested for STIs every 3 months.
- Doxy-PEP doesn't protect against MPX (monkeypox).



Acerca de Doxy-PEP

¿Qué es doxy-PEP?

- El doxy-PEP significa tomar el antibiótico doxiciclina después de las relaciones para prevenir contraer una infección de transmisión sexual (ITS). Es como una píldora del día después pero para las ITS. Tomar doxy-PEP reduce la probabilidad de contraer sífilis, gonorrea y clamidia en aproximadamente dos tercios.

¿Cuándo debo tomar doxy-PEP?

- Se toma dos pastillas de doxiciclina de 100 mg dentro de las 24 horas, pero a más tardar 72 horas después de tener relaciones sexuales sin condón. Las relaciones sin condón significa las relaciones orales, anales o vaginales/con agujero dilatado, en las que no se usó un condón todo el rato.

¿Y qué pasa si vuelvo a tener relaciones?

- Si vuelve a tener relaciones dentro de las 24 horas después de tomar doxiciclina, tome otra dosis 24 horas después de la última dosis. Puede tomar doxiciclina tan frecuentemente como todos los días cuando está teniendo relaciones sin condón, pero no tome más de 200 mg (dos pastillas de 100 mg) cada 24 horas.

¿Cómo debo tomar doxy-PEP?

- Tomar la doxiciclina con abundante agua o algo más para beber para que no se ataquen al tragar. Si la doxiciclina le produce náuseas estomacales, puede ser útil tomarla con alimentos.
- Algunas personas son más sensibles al sol cuando toman doxiciclina, así que use protector solar.
- No comparta la doxiciclina con otras personas.
- Evite los productos lácteos, el calcio, los antácidos y los multivitamínicos dentro de las 2 horas antes o después de tomar doxiciclina para una absorción óptima de doxiciclina en el cuerpo.

¿Qué estamos aprendiendo todavía sobre doxy-PEP?

- ¿Afecta las bacterias normales ("buenas") en nuestros intestinos?
- ¿Podría aumentar o disminuir las bacterias que viven en nuestra piel, o hacerlas resistentes a la doxiciclina?
- ¿Doxy-PEP aumentará la resistencia a la doxiciclina en las bacterias que causan las ITS?
 - Aunque la doxiciclina se ha utilizado durante décadas, no parece haber resistencia a la doxiciclina en la clamidia ni en la sífilis.
 - Aproximadamente el 25% de la gonorrea en los EE. UU. ya es resistente a doxy-PEP puede no funcionar contra estas cepas. El estudio DoxyPEP, y otros estudios científicos, nos ayudan a comprender si el uso de doxy-PEP cambia la resistencia en la gonorrea.

Recordatorios

- Llámenos al 628-217-6932 si se le acabó la doxiciclina, si tiene algún efecto secundario o si cree que puede tener una ITS.
- El doxy-PEP reduce la posibilidad de contraer sífilis, gonorrea y clamidia, pero estas ITS aún pueden ocurrir. Continúe haciéndose la prueba a intervalos regulares y si tiene síntomas.
- Doxy-PEP no protege contra MPX (viruela del mono), VIH u otras infecciones virales.

DoxyPEP

Doxycycline Post-exposure Prophylaxis

Fact Sheet

What is DoxyPEP?

DoxyPEP is also known as Doxycycline Post-exposure Prophylaxis. Doxycycline is an antibiotic commonly used to treat bacterial infections. DoxyPEP can prevent bacterial STIs like syphilis, chlamydia, and gonorrhea when taken after condomless sex.

Who is DoxyPEP for?

DoxyPEP can be used by men who have sex with men who have sex with men who use DoxyPEP is not currently recommended.

Is DoxyPEP effective?

- DoxyPEP is effective
- Research showed it prevents chlamydia, and syphilis
- DoxyPEP is well tolerated

What are the benefits of DoxyPEP?

DoxyPEP prevents chlamydia, gonorrhea, and syphilis. Many people taking DoxyPEP do not get STIs. For some people, using DoxyPEP is a good option, and allow individuals to to

What are the risks of DoxyPEP?

DoxyPEP risks may include:

Side Effects



Sun Sensitivity



Esophagus & Stomach Irritation



Antibiotic Resistance

Other Possible Risks



Microbiome Changes

DoxyPEP may change your microbiome (the normal bacteria found on your stomach, and other parts of your body). Possible changes in your microbiome may have long-term health effects which are currently unknown.

How do I take DoxyPEP?

- Take 200mg of doxycycline within 24 hours - but no later than 72 hours - after condomless oral, anal, or vaginal sex.
- Do not take more than 200mg of doxycycline within a 24-hour period.
- DoxyPEP can be taken as often as every day, depending on sexual activity.

How else can I protect myself?

DoxyPEP is just one part of a comprehensive safer sex plan. Additional ways to protect yourself from HIV & STIs include using condoms, regularly testing for HIV/STIs, taking HIV PrEP, limiting your number of sex partners, and getting treated for HIV and STIs if you test positive.

How can I learn more about DoxyPEP?



Scan the QR code, or [click here](#), to view Public Health - Seattle & King County's DoxyPEP Guidelines.

The risks and benefits of DoxyPEP are complex. Talk to your medical provider if you're interested in taking DoxyPEP.

NOW OFFERING

A NEW TOOL TO HELP PREVENT SEXUALLY TRANSMITTED INFECTIONS

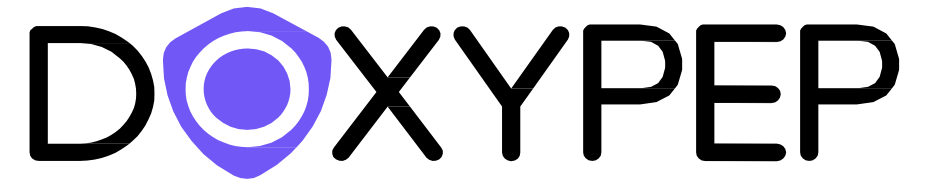
DOXYCYCLINE AS STI PEP

TALK TO YOUR HEALTHCARE PROVIDER TODAY TO SEE IF DOXYCYCLINE AS STI PEP IS RIGHT FOR YOU



Acknowledgments

- DoxyPEP participants
- Entire DoxyPEP team
- Beatrice Berçot
- Chase Cannon
- Stephanie Cohen
- Julie Dombrowski
- Jean-Michel Molina
- Funding from NIH DMID (R01 AI143439)

The logo for DoxyPEP features the word "DOXYPEP" in a bold, black, sans-serif font. The letter "O" is replaced by a stylized purple icon consisting of a central circle surrounded by a hexagonal shape with rounded corners. The background of the slide is white, with a large, abstract graphic on the right side composed of several overlapping, semi-transparent, curved bands in shades of light blue and light green, creating a sense of depth and movement.