AETC AIDS Education & Training Center Program

DoxyPEP: Translating studies into practice

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HRSA Acknowledgement Statement
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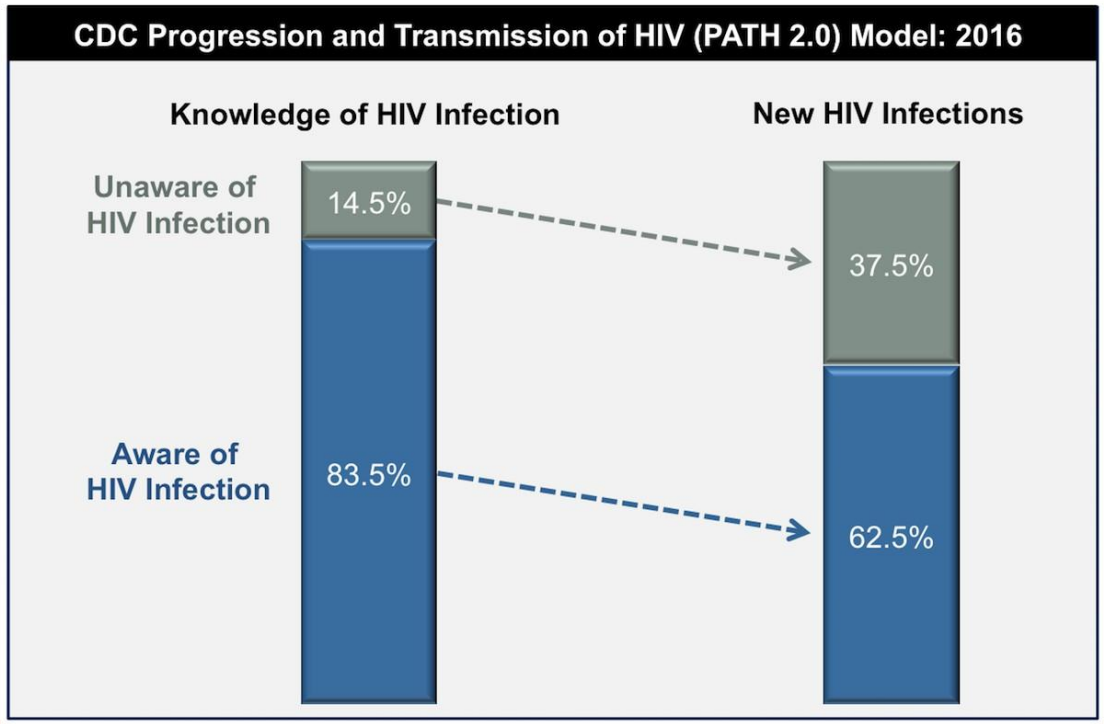
Disclosure

Speaker: Gilead Sciences, Speaker's Bureau (HIV Treatment)

Objectives

- Explain the doxyPEP study and its impact on sexually transmitted infections
- Explain when to use doxyPEP with persons at risk of aquiring HIV
- Describe chlamydia and gonorrhea management with doxyPEP
- Discuss the unknowns of doxyPEP

Integrating HIV and STI Prevention, WHY?



Li Z, et al., 2019

Screening for HIV

At least once

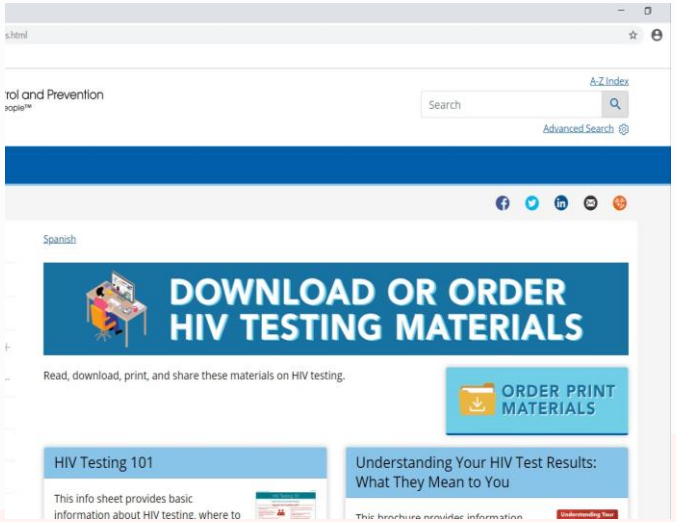
- ALL 13 to 64 years old (15 to 65 for USPSTF)

At least annually

- ALL sexually active MSM (along with syphilis, gonorrhea, chlamydia screen)
- Anyone who has unsafe sex or shares injection drug equipment (along with HCV screen)

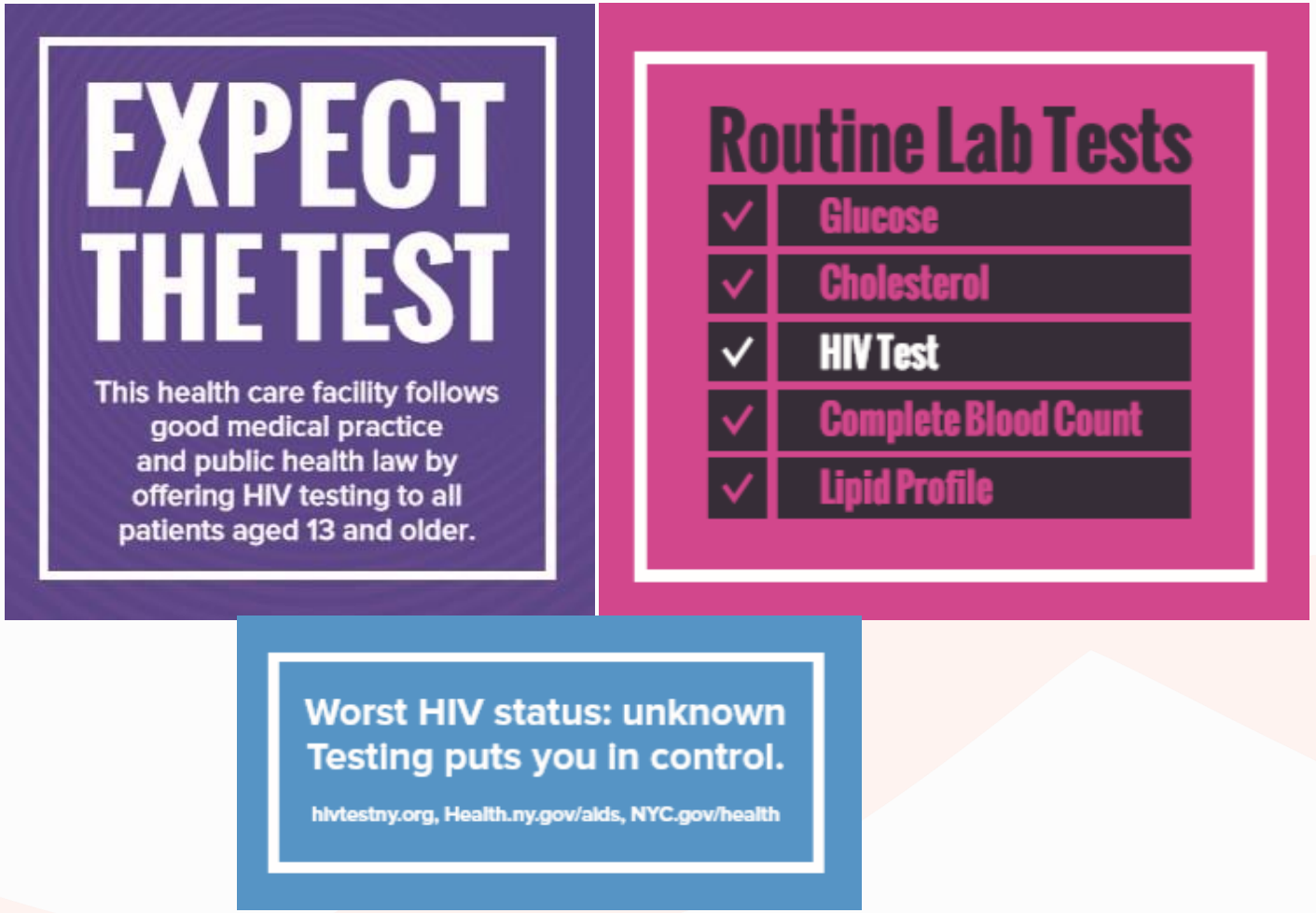
CDC, 2020

https://www.cdc.gov/hiv/basics/hiv-testing/resources.html



https://www.rethinkhivnevada.org/

Rethink HIV, 2022 & CDC 2022


EXPECT THE TEST
This health care facility follows good medical practice and public health law by offering HIV testing to all patients aged 13 and older.
Routine Lab Tests
Glucose
Cholesterol
HIV Test
Complete Blood Count
Lipid Profile
Worst HIV status: unknown
Testing puts you in control.
hivtestny.org, Health.ny.gov/aids, NYC.gov/health

NDPBH, 2021

Polling Question #1

ARS: 26 year old MSM on PrEP. Denies any symptoms. He has multiple condomless receptive and insertive oral and anal sexual encounters. Extragenital screening was reactive for pharyngeal chlamydia. What is the preferred treatment?

a) Azithromycin 1 gram orally x1
b) Doxycycline 100 mg BID orally x 7 days
c) No treatment as screening for pharyngeal chlamydia is not recommended and he is asymptomatic
d) A or B are both preferred

CDC 2021 Chlamydia (CT) and Gonorrhea (NG) screening

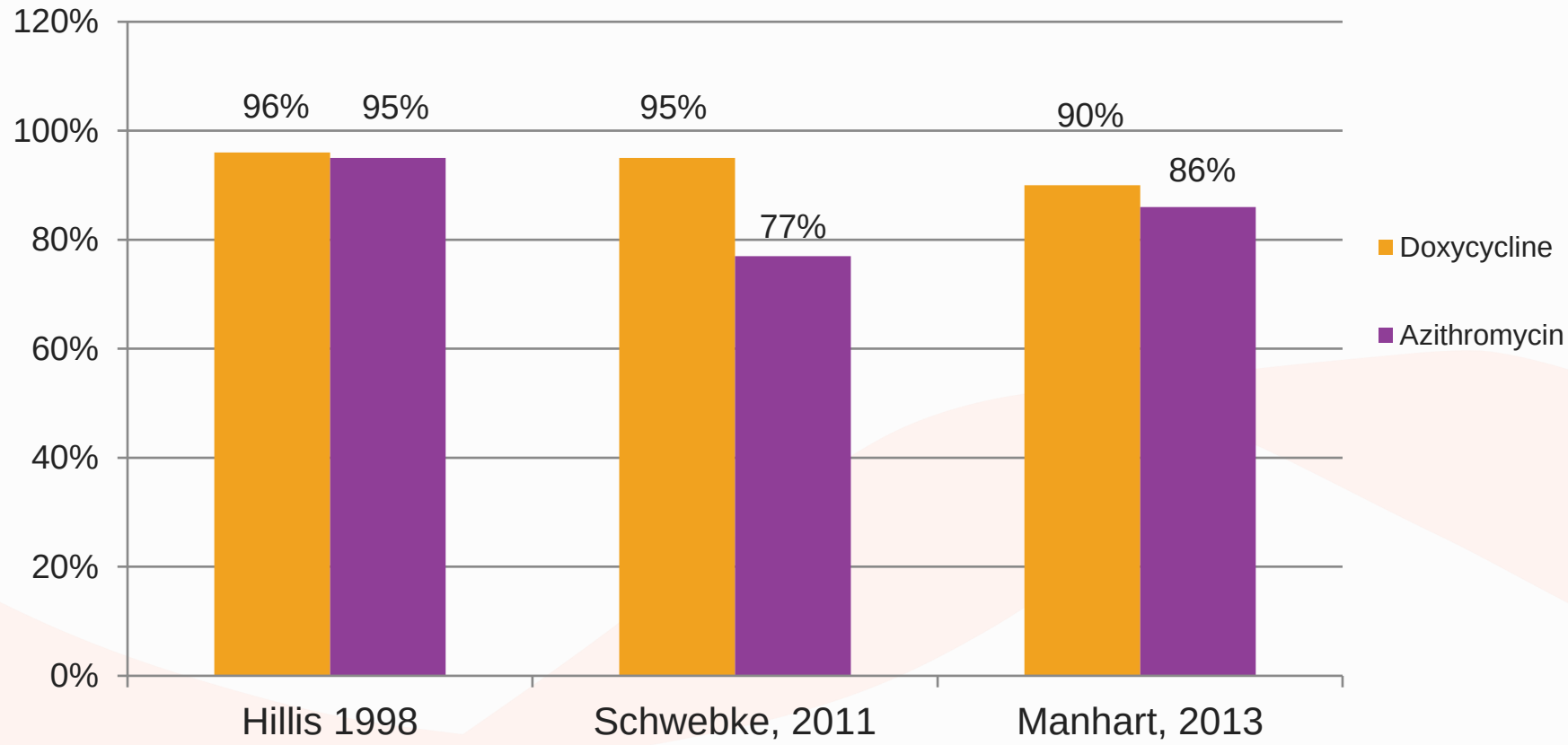
- Recommendations are for populations based on a mix of:
  - sexual orientation/practice (MSM, MSW)
  - gender identity (women, transgender, gender diverse)
  - associated co-morbidities (pregnancy, PWH, sexual assault)

- Extragenital site screening is recommended “at least annually for sexually active MSM at sites of contact” (urethra, rectum for CT and NG; throat NG)

CDC 2021 Chlamydia Treatment

- **PREFERRED**:
  - Doxycycline 100 mg BID oral x 7 days
- **ALTERNATIVE**:
  - Azithromycin 1g oral
  - Levofloxacin 500 mg daily oral x 7 days

Chlamydia Treatment: Azithromycin vs Doxycycline



SOURCE: slide 31 of 47 From KA Workowski. December 2019. Ryan White HIV/AIDS Program CLINICAL CONFERENCE, IAS–USA.

Chlamydia Treatment: Azithromycin vs Doxycycline

- Retrospective for rectal CT (Hathorn, et al., 2012; 2016)
  - Failure rate: 26% for azithromycin
  - Failure rate: 0.9% for doxycycline
- Meta-analysis for rectal CT (Kong, et al., 2015)
  - Pooled azithromycin efficacy – 82.9%
  - Pooled doxycycline efficacy – 99.6%
- Observational study for pharyngeal CT (Manavi, et al., 2016)
  - Failure rate: 10% for azithromycin
  - Failure rate: 2% for doxycycline

What about adherence?

- Low rates (16-25%) of complete adherence
  (Augenbraun, 1998; Bachmann, 1999)

BUT

- 94% microbial cure (Bachmann, 1999)
- 99.6% pooled efficacy (Kong, et al., 2015)
- 0.9% failure rate (Hathorn, et, al., 2016)

SOURCE: slide 32 of 47 From KA Workowski, MD. December 2019. Ryan White HIV/AIDS Program CLINICAL CONFERENCE, IAS–USA.

Polling Question #2

ARS: 26 year old MSM (same patient) now comes in with dysuria and urethritis. Vital signs are stable, afebrile, wt - 155 kg. What is the treatment?

a) No treatment, just test the patient first.
b) Ceftriaxone 500 mg IM and azithromycin 1 gram PO
c) Ceftriaxone 1000 mg IM and azithromycin 1 gram PO
d) Ceftriaxone 500 mg IM and doxycycline 100 mg PO BID x 7 days
e) Ceftriaxone 1000 mg IM and doxycycline 100 mg PO BID x 7 days
f) Ceftriaxone 500 mg IM
g) Ceftriaxone 1000 mg IM and

CDC 2021 Gonorrhea Treatment

- **PREFERRED**:
  - Ceftriaxone ***500 mg**** IM
    (*>150 kg use 1 g IM)

  ONLY IF unknown CT status:
  - ADD Doxycycline 100 mg BID oral x 7 days

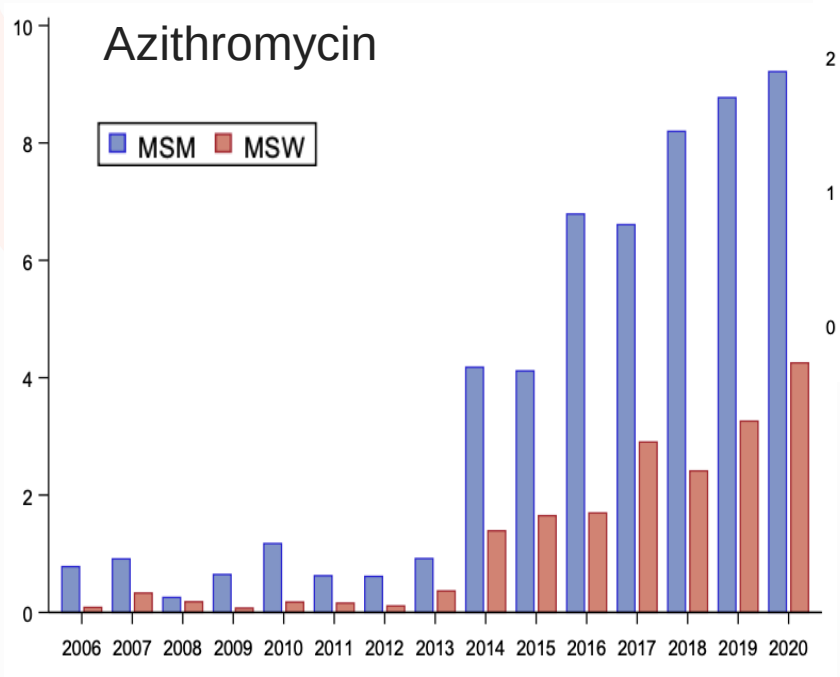
- **ALTERNATIVE**:
  - Gentamicin 240 mg IM ***PLUS***
  - Azithromycin 2g oral

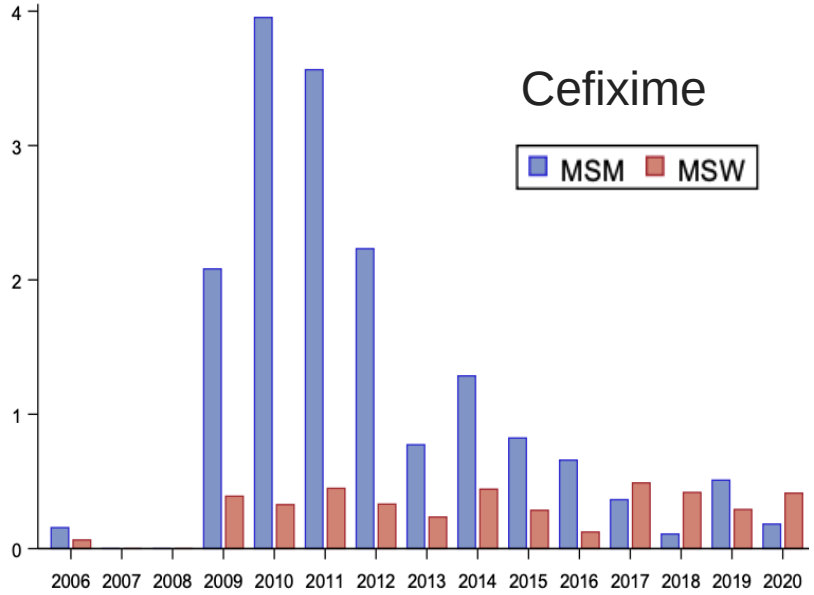
  - *Cefixime 800 mg IF unable to give ceftriaxone*

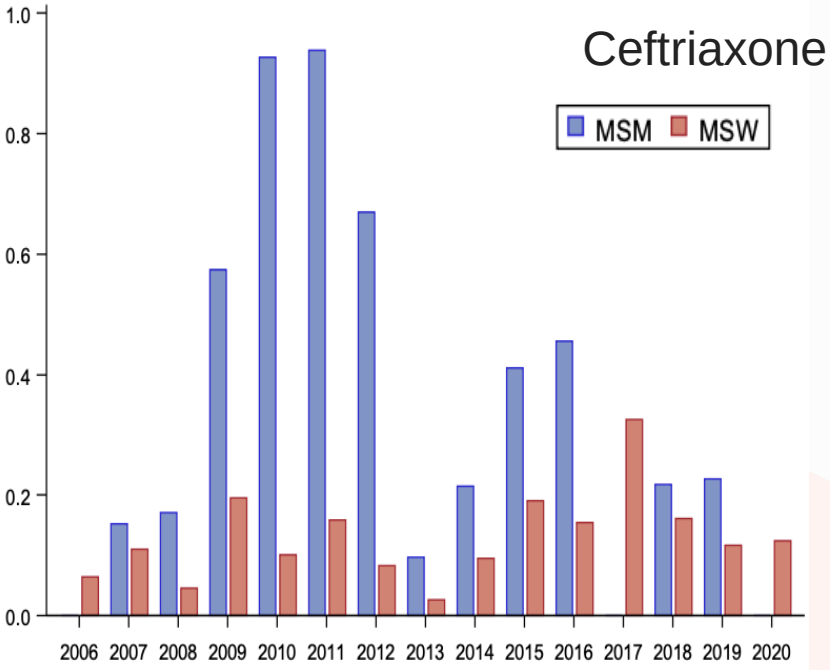
- *Europe*
  - Ceftriaxone ***500 mg*** IM ***PLUS***
  - Azithromycin 1 g oral
- *United Kingdom*
  - Ceftriaxone ***1 g*** IM
- *Japan*
  - Ceftriaxone ***1 g*** IM/IV

(1) CDC 2021 STI Treatment Guidelines
(2) slide 32 of 47 From KA Workowski, MD 2019, Ryan White CLINICAL CONFERENCE, IAS–USA.

CDC: Gonococcal Isolate Surveillance Program – Percentage of Isolates with Elevated MICs to Azithromycin, Cefixime, and Ceftriaxone by Sex and Sex of Partners, 2006-2020







NOTE: Elevated MIC: *Azithromycin: >/= 2.0 ug/mL, Cefixime: >/= 0.25 ug/mL, Ceftriaxone: >/= 0.125 ug/mL*

SOURCE: CDC GISP Profile 2020 (August 2022)

Polling Question #3

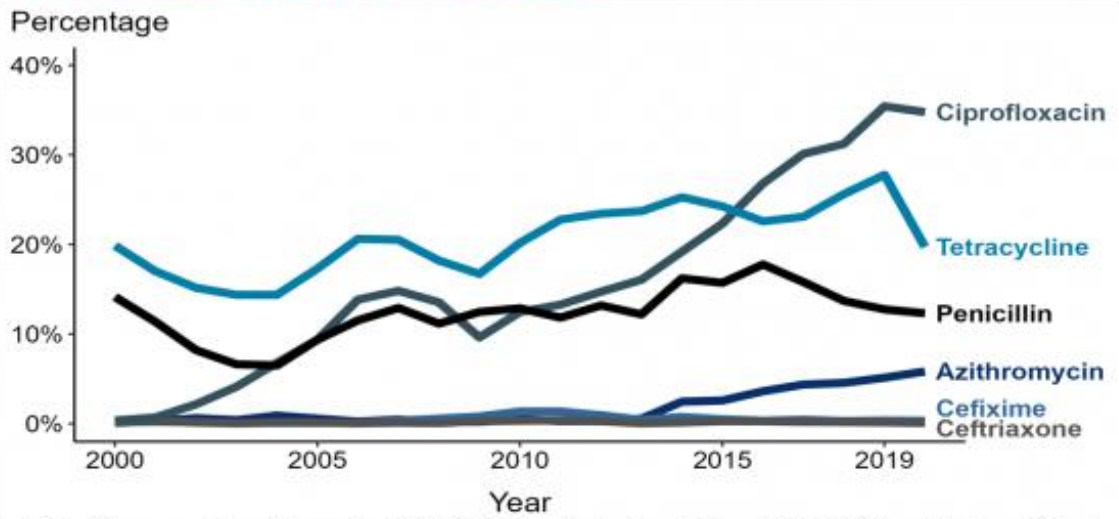
ARS: 26 year old MSM (same patient) treated empirically for urethritis and his results are now back and he is positive for urethral gonorrhea and syphilis. You treat him for his syphilis and he asks about doxyPEP. You say:

a) Sure.
b) What's that?
c) Let's discuss this.

Doxycycline for Post-exposure Prophylaxis

- Why doxycycline?
  - Treatment for chlamydia (1st line)
  - Treatment for syphilis (alternative)
  - Prior treatment for gonorrhea (~20% elevated MIC)
  - Known safety profile
  - Known tolerability
  - Inexpensive

***Neisseria gonorrhoeae* — Prevalence of Tetracycline, Penicillin, or Ciprofloxacin Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2020**



* Resistance: Ciprofloxacin: MIC ≥ 1.0 µg/mL; Penicillin: MIC ≥ 2.0 µg/mL or Beta-lactamase positive; Tetracycline: MIC ≥ 2.0 µg/mL

† Elevated MICs: Azithromycin: MIC ≥ 1.0 µg/mL 29 (2000–2004); ≥ 2.0 µg/mL (2005–2020); Ceftriaxone: MIC ≥ 0.125 µg/mL; Cefixime: MIC ≥ 0.25 µg/mL

SOURCE: https://www.cdc.gov/std/gisp/default.htm

#1 ANRS IPERGAY (Molina et al. Lancet. 2018)

Open Label, RCT: doxycycline hyclate 200 mg
as PEP within 24-72 hours after condomless sexual contact
(maximum of 6 pills per week = 3 doses)

Inclusion

- Male at birth
- On PrEP
- In past 6 months
  - >/= 2 condomless male partner

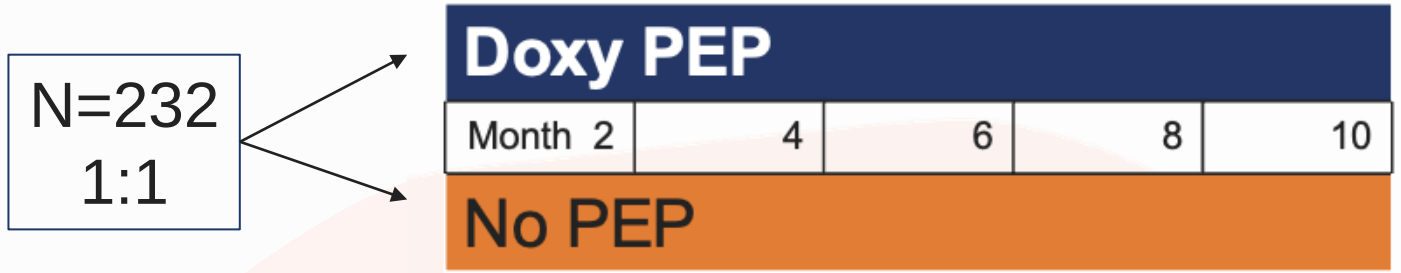
Exclusion

- STI at enrollment, use of retinoids or high dose vitamin A

Visits q2 months

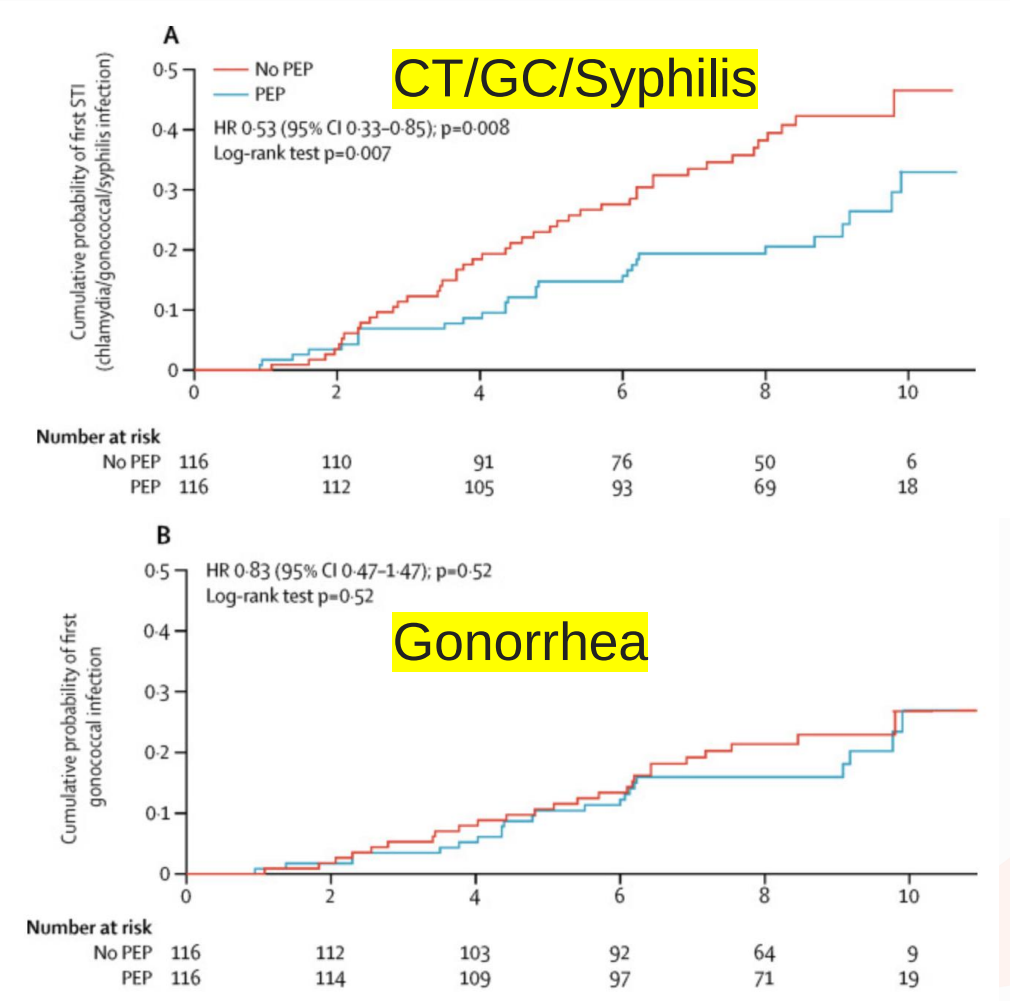
- EIA, RPR, 3 site GC/CT, GC cx if tx

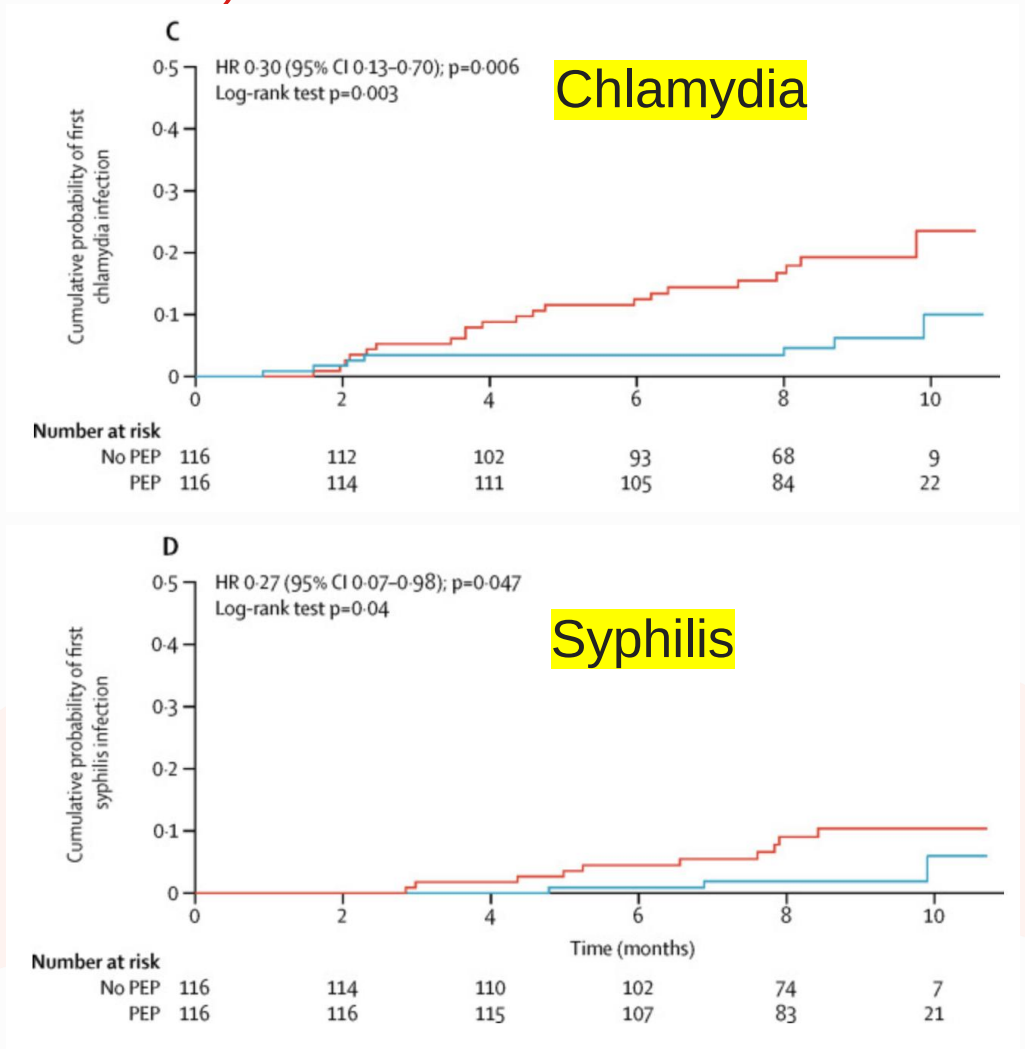
Study sites in France



SOURCE: Molina et al. Lancet 2018

#1 ANRS IPERGAY (Molina et al. Lancet. 2018)





#2 Doxy-PEP (Luetkemeyer et al. NEJM. 2023)

DOXYPEP

Open Label, RCT: doxycycline hyclate delayed release 200 mg as PEP within 72 hours after condomless sexual contact (maximum of 200 mg every 24 hours)

Inclusion

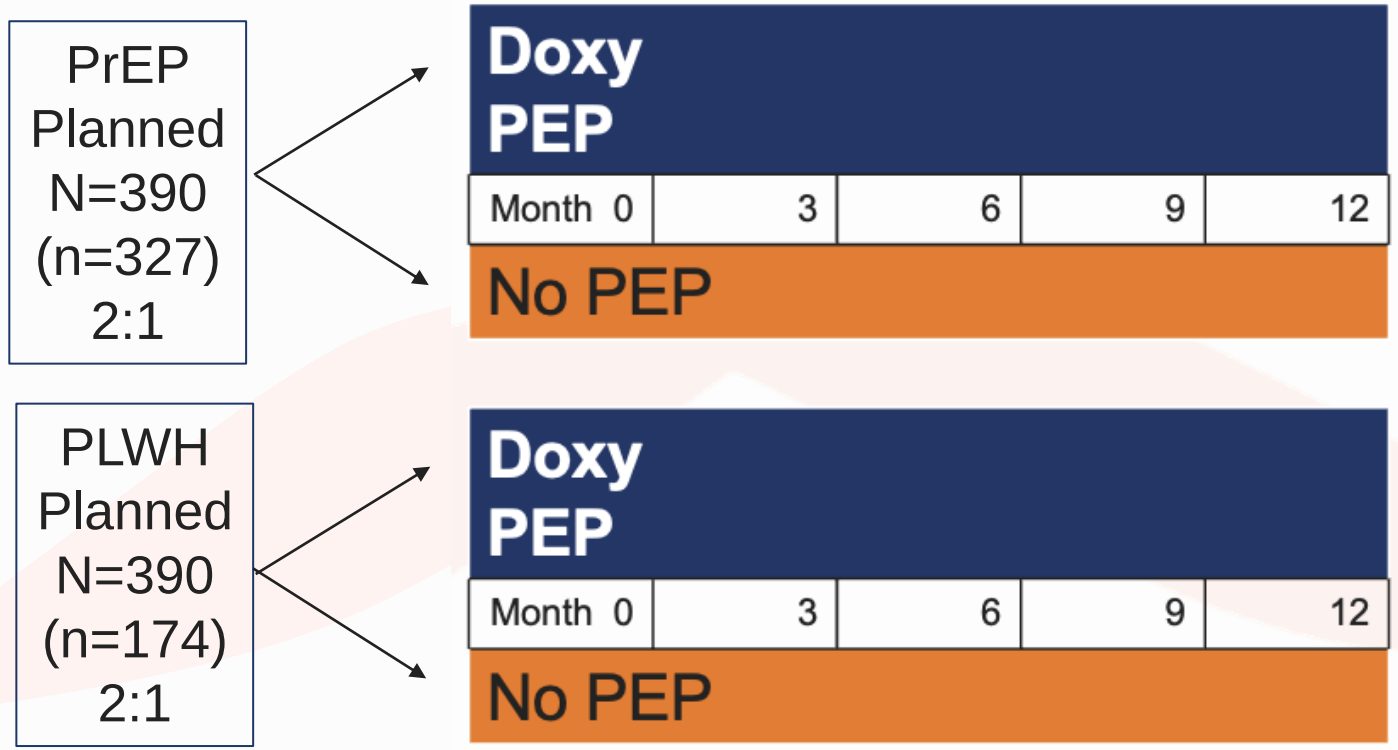
- Male at birth
- On PrEP or PWH
- In past 12 months
  - >/= 1 STI
  - >/= 1 condomless male partner

STI testing quarterly

- RPR, 3 site GC/CT, GC cx pre-tx

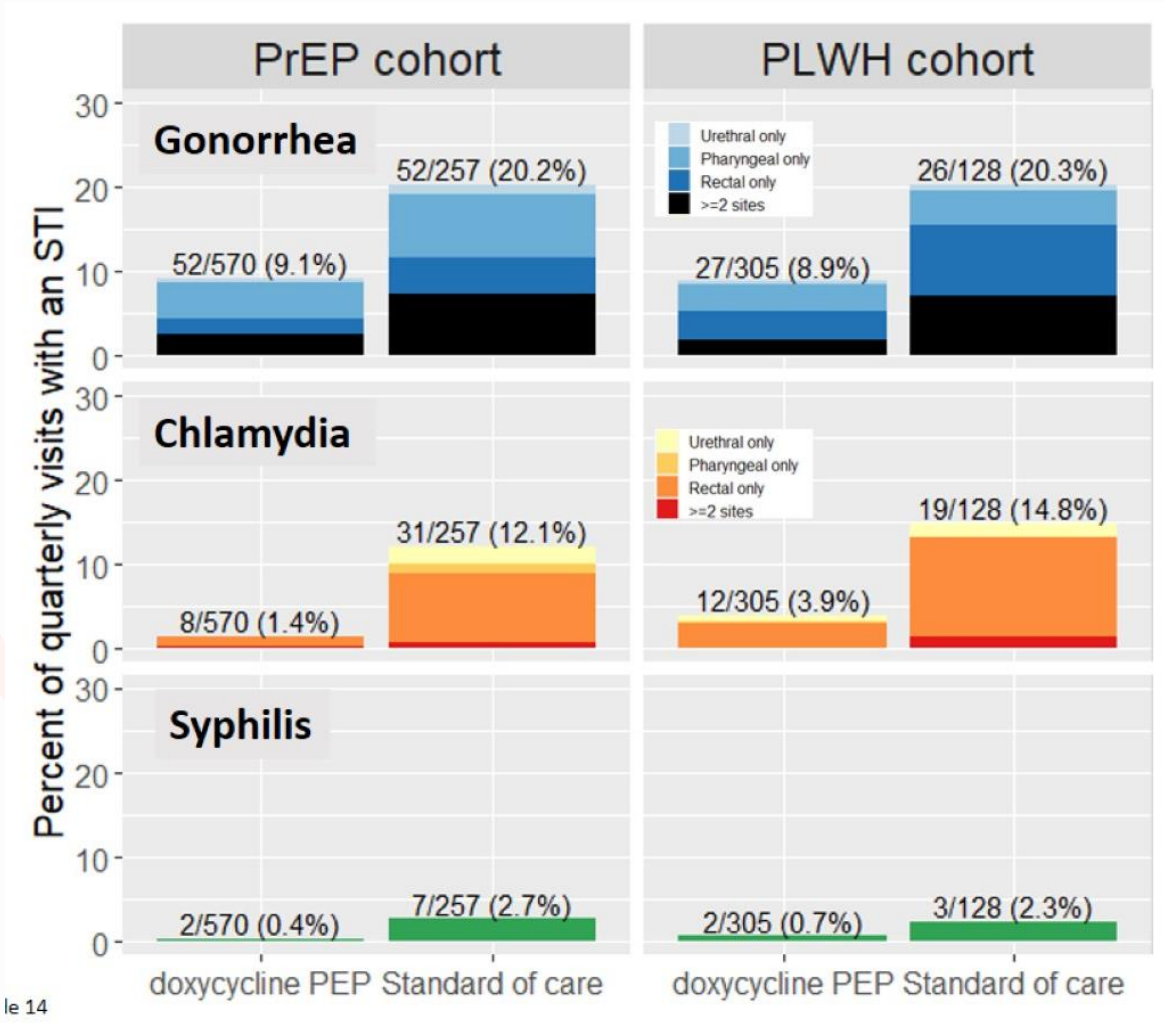
Study sites (HIV/STI clinics)

- San Francisco
- Seattle



SOURCE: Luetkemeyer, A. 2023. Webinar. IAS–USA.

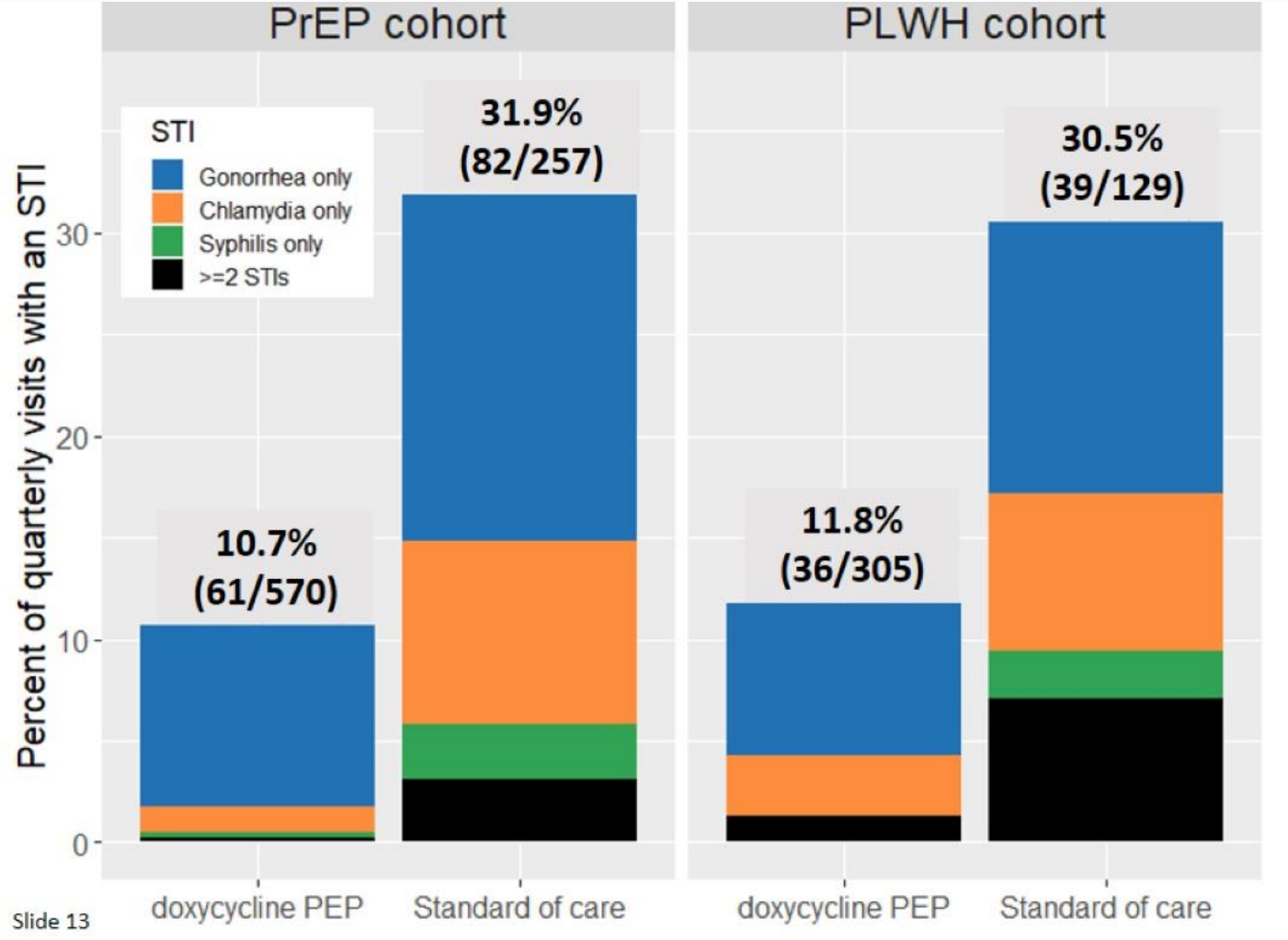
Primary Endpoint: STI incidence per quarter



Risk reduction in each STI incidence per quarter (95% CI)TOT		
	PrEP	PLWH
GC	55% (35%-68%) p<0.0001	57% (29%-74%) p<0.001
CT	88% (75%-95%) p<0.0001	74% (43%-88%) p<0.0007
Syphilis	87% (41%-97%) p<0.0084	77% (-71%,96%) p<0.095

SOURCE: Luetkemeyer, A. 2023. Webinar. IAS–USA.

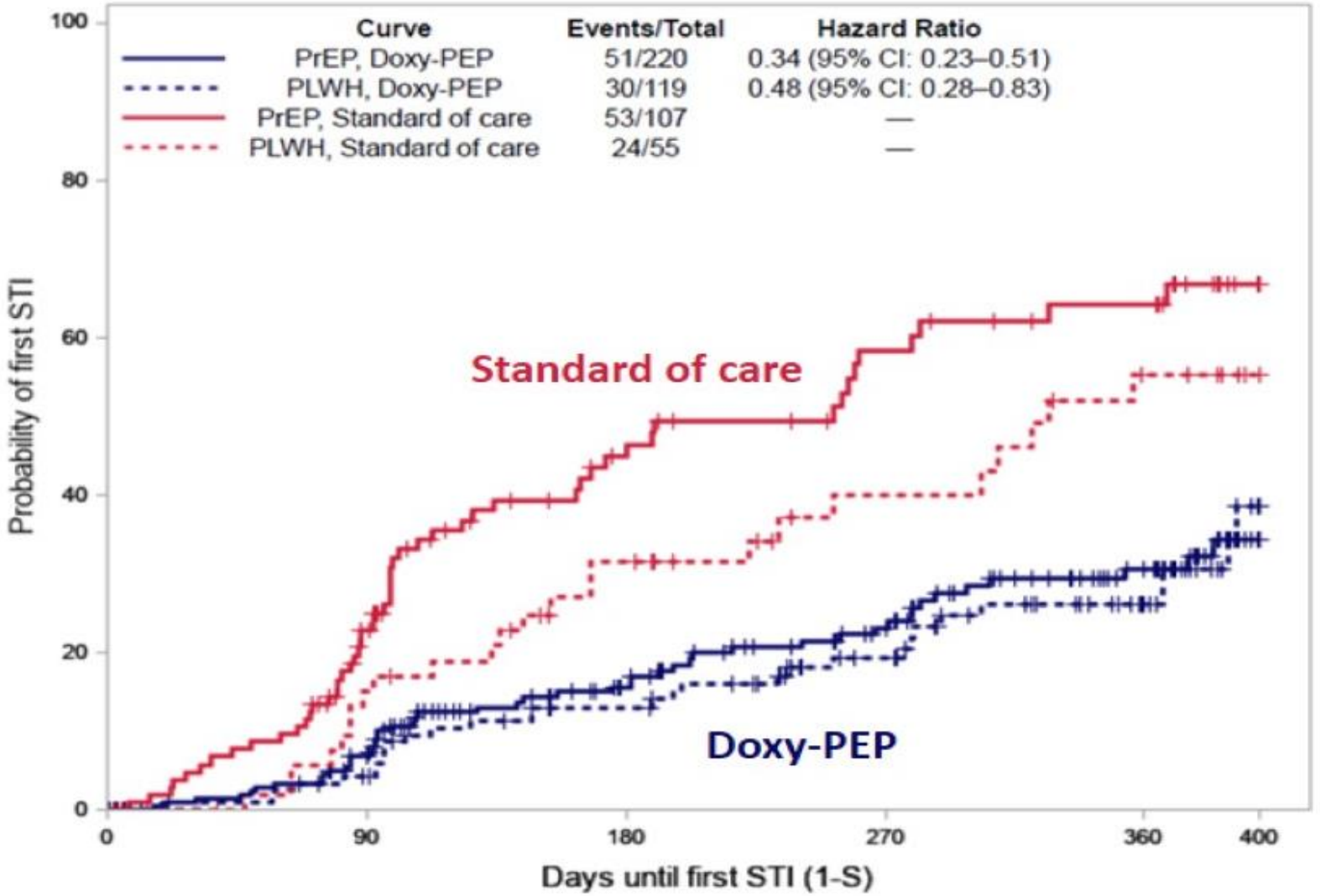
Primary Endpoint: STI incidence per quarter



Risk reduction in STI incidence per quarter (95% CI), p<0.0001	
PrEP	66% (54%-76%)
PLWH	62% (40%-76%)
Total	65% (54%-73%)

SOURCE: Luetkemeyer, A. 2023. Webinar. IAS–USA.

Doxy-PEP significantly reduces STI incidence (65% per quarter) among MSM and TGW with a history of recent STI.



SOURCE: Luetkemeyer, A. 2023. Webinar. IAS–USA.

#3 DOXYVAC (Molina et al. CROI. 2023)

Open Label, 2x2 factorial RCT:
doxycycline monohydrate 200 mg as PEP vs no PEP
4CMenB vaccine vs no vaccine

Inclusion

- MSM
- On PrEP >6 months (ANRS Prevenir)
- In past 12 months
  - >/= 1 STI

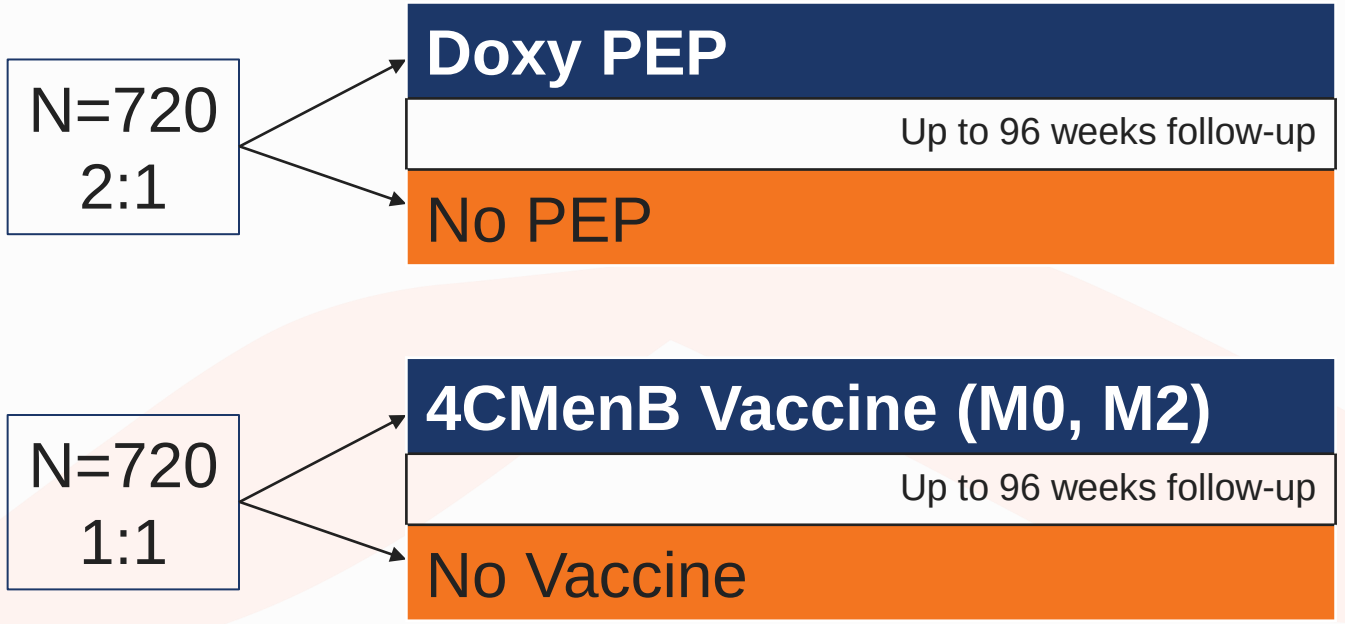
Exclusion

- No STI symptoms currently

STI testing quarterly

- Syphilis serology, 3 site GC/CT/MG

Study sites: multicenter France



#3 DOXYVAC (Molina et al. CROI. 2023)

Open Label, 2x2 factorial RCT:
doxycycline monohydrate 200 mg as PEP vs no PEP
4CMenB vaccine vs no vaccine

Gonorrhea Studies: vaccination

Retrospective case-control, New Zealand (Petousis-Harris, 2017)

- Group B outer membrane vesicle meningococcal vaccine (OMV)
- Effectiveness against gonorrhea (1/3 less likely to contract GC compared to CT)

NCT04350138

- Will an optimized Group B Meningococcal Vaccine Protect Against Gonorrhea?

Doxy PEP

Up to 96 weeks follow-up

No PEP

4CMenB Vaccine (M0, M2)

Up to 96 weeks follow-up

No Vaccine

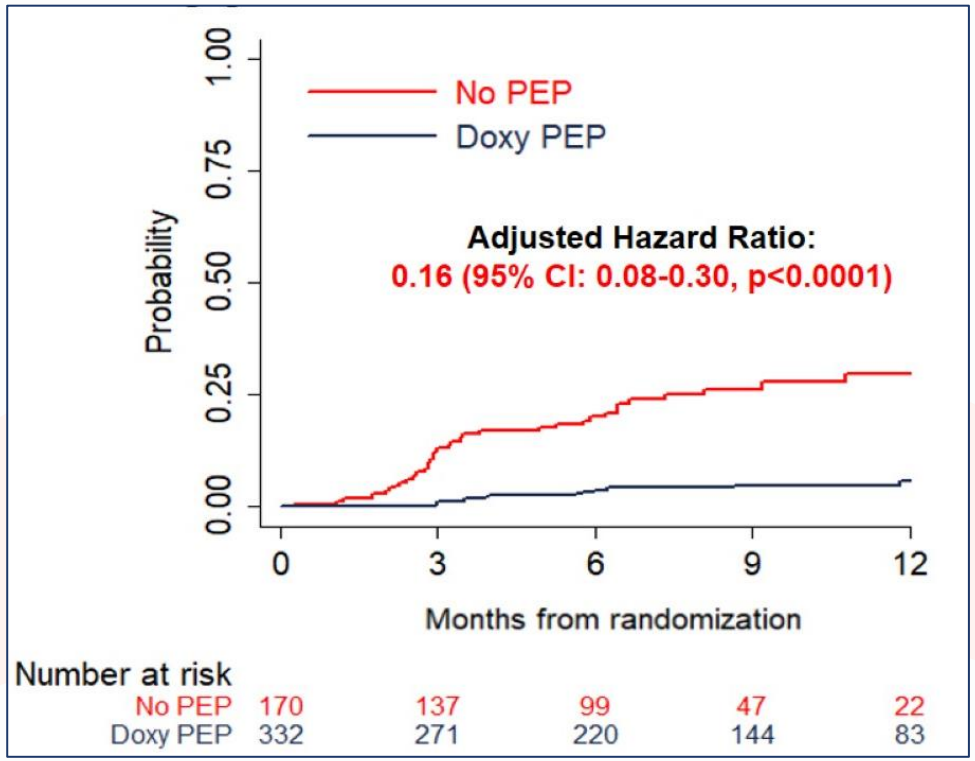
#3 DOXYVAC (Molina et al. CROI. 2023)

- Median follow-up:
  - 9 months
  - (IQR: 6 – 12 months)
- 49 STIs
  - 36 no PEP (35.4/100 PY)
  - 13 Doxy PEP (5.6/100 PY)
- Individual STI reduction
  - Syphilis: HR 0.21

  (95% CI: 0.09-0.47, p<0.001)
  - Chlamydia: HR 0.11

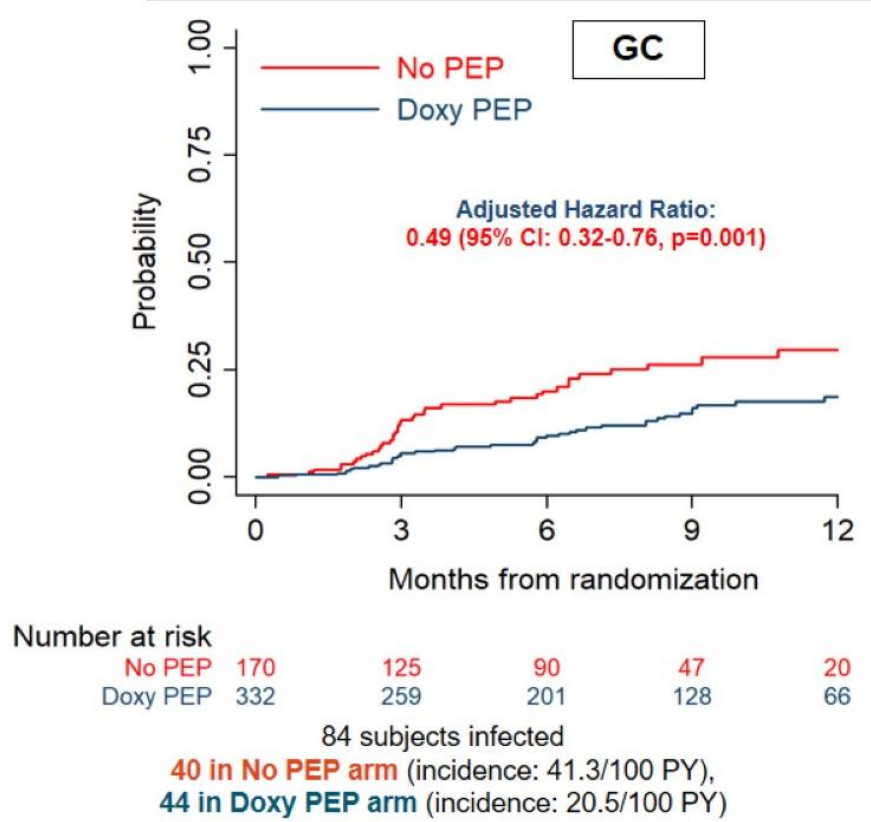
  (95% CI: 0.04-0.30, p<0.001)

Time to First CT or Syphilis

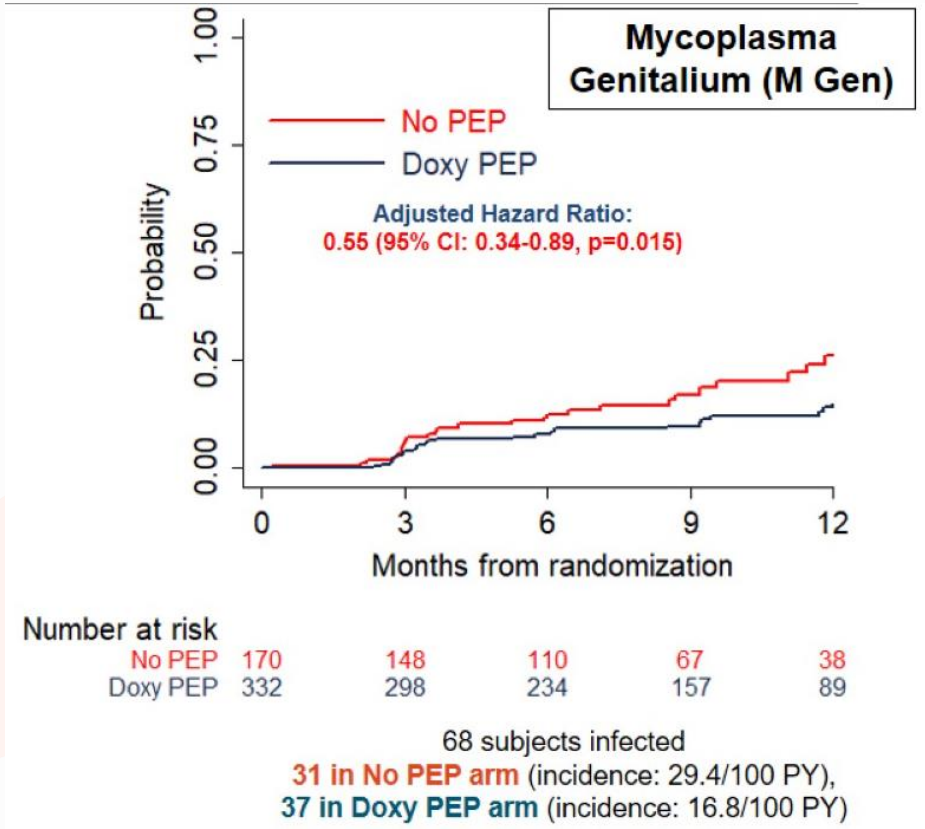


#3 DOXYVAC (Molina et al. CROI. 2023)

Time to First GC



Time to First M. gen



SOURCE: Molina et al. CROI. 2023

#4 D-PEP Kenya (Stewart. CROI. 2023)

Open Label, RCT: doxycycline hyclate 200 mg
as PEP within 72 hours after condomless sexual contact

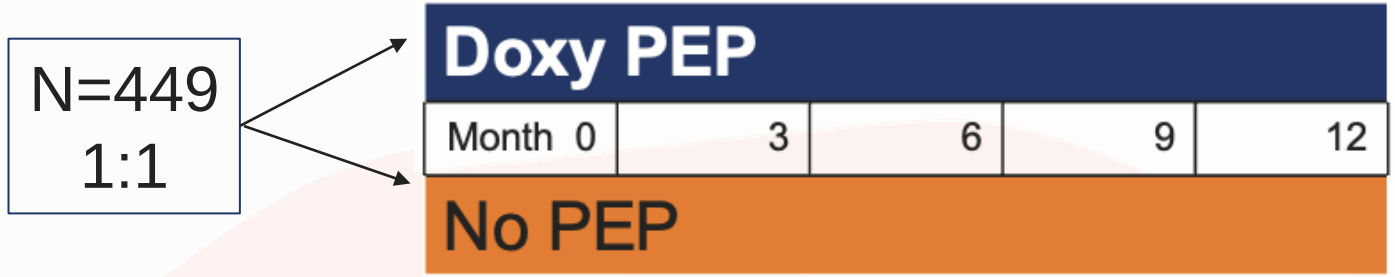
Inclusion

- FEMALE at birth, 18-30 years old
- On PrEP
- In past 6 months
  - >/= 2 condomless male partner

Visits quarterly x 12 months

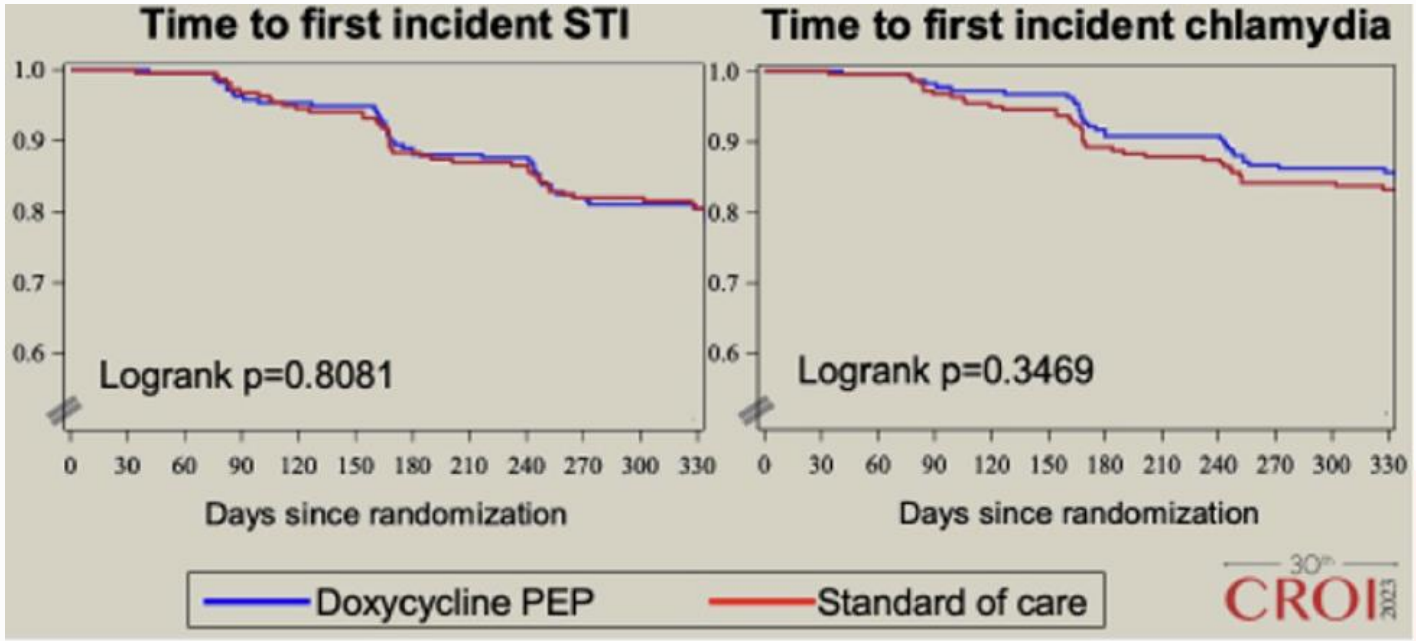
- GC/CT

Study site: Kisumu, Kenya



#4 D-PEP Kenya (Stewart. CROI. 2023)

- 18% had STI at enrollment
- Annual STI incidence 27%
- 109 new STIs
  - 50 doxy-PEP
  - 59 standard of care
- 78% of STIs were CT
  - 35 doxy-PEP
  - 50 standard of care



#4 D-PEP Kenya (Stewart et al. DPEP; ISSTDR 7.2023)

Self-Reported Adherence

- Quarterly Surveys
  - 77% (579/755) coverage of last sexual encounter
- Timeline follow-back calendar
  - In 72.8% of surveys >80% of sexual acts covered
- Weekly SMS
  - 64% full coverage at least 80% weeks
  - 78% of weekly SMS reported full coverage

Doxy Hair Testing

- Randomly selected subset, n=50

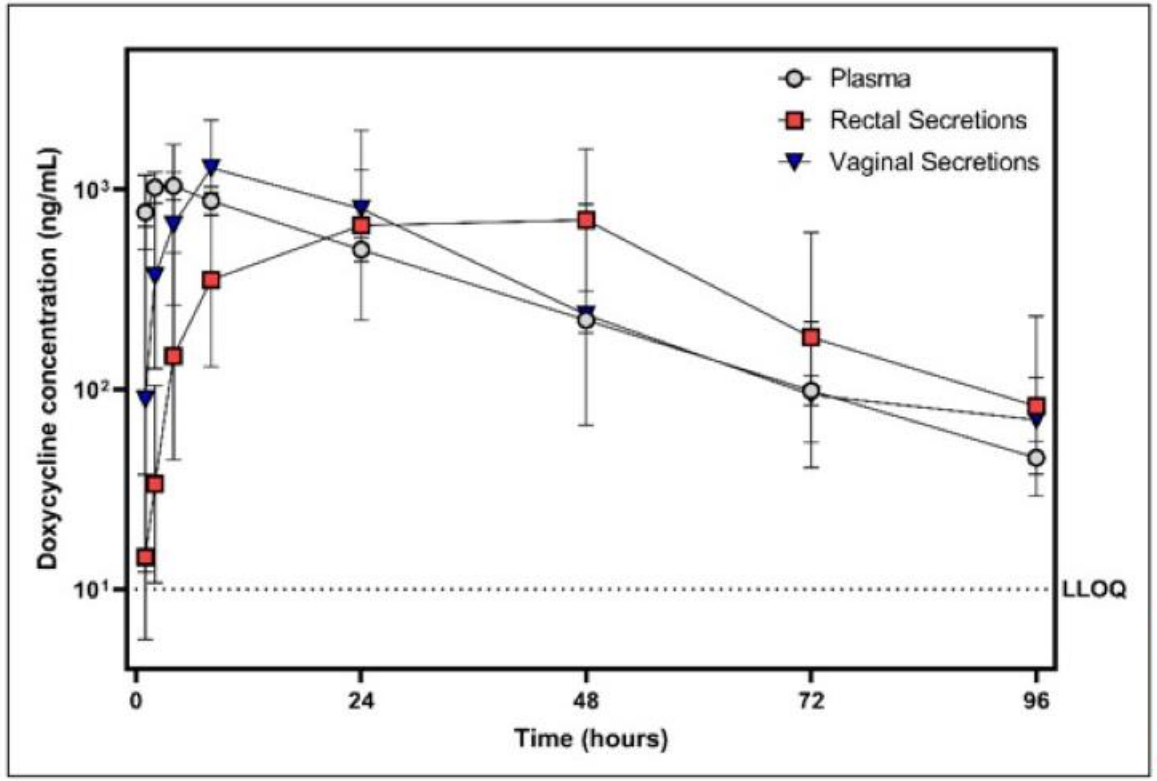
[%doxy detected]

  - 56% (28/50) at least once
  - 29% (58/200) of all quarterly visits
  - 6.7% (3/45) of enrollment visits

- 44% assigned to doxy-PEP never had doxycycline detected

SOURCE: Stewart et al. CROI 2023

Mucosal Doxycycline Concentrations



	C trachomatis		*T pallidum*		*N gonorrhoeae*	
	C_{max}*	Time >4x MIC	C_{max}*	Time >4x MIC	C_{max}*	Time >4x MIC
Plasma	16x	44h	10x	32h	4x	3h
Rectal Secretions	11x	62h	7x	51h	3x	NA
Vaginal Secretions	20x	45h	12x	38h	5x	11h

*Fold above MIC

Minimum Inhibitory Concentrations (MIC):

N gonorrhoeae (NG) MIC = 250 ng/mL CDC Antimicrob Resist Susc Test

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

C trachomatis (CT) MIC_{90} = 64 ng/mL Zheng *Sex Transm Dis* 2015

Haaland CROI 2023, abstract 118

Summary: Evidence for doxy-PEP in 2023

Study	Participating population		STI rate or outcome		Relative risk reduction	Absolute risk reduction
			Doxy-PEP	No doxy-PEP		
IPERGAY (France, 2015-2016)	232 MSM on HIV PrEP		37.7 per 100 person-years*	69.7 per 100 person-years*	47%* (15-67%)	32 per 100 person-years*
DoxyPEP (Seattle & SF, 2020-2022)	501 MSM & TGW with HIV or on HIV PrEP with recent bact. STI	**HIV (n=174)**	11.8% per quarter	30.5% per quarter	52% (17-72%)	18.7% per quarter
		PrEP (n=327)	10.7% per quarter	31.9% per quarter	66% (49-77%)	21.2% per quarter
DoxyVac (France, 2021-2022)	502 MSM on HIV PrEP with recent bact. STI		5.6 per 100 person-years*	35.4 per 100 person-years*	84%* (70-92%)	30 per 100 person-years*
dPEP *(Kenya, 2020-2022)*	*449 cis women on HIV PrEP*		*50 CT/GC infections total*	*59 CT/GC infections total*	*12% (P=0.51)*	*9 total infections at 12 months*

Molina JM et al, *Lancet Infect Dis* 2018; Luetkemeyer A et al, *NEJM* 2023; Molina JM CROI 2023, Stewart J CROI 2023

Slide courtesy of Chase Cannon

*Point estimates are for CT & syphilis only

Slide 27

Doxy-PEP: Few AEs and well-tolerated

RCT	Lab abnormalities	Adverse events	Discontinuation	Other effects
DoxyPEP (US)	1 (G2 transaminitis)	5 (G3 diarrhea or H/A)	2%	No weight gain compared to standard care
DOXYVAC (France)	None to date	2 (GI side effects)	6% (relocation, stable partnership)	*Pending final review*
dPEP (Kenya)	Not collected	~5% (GI side effects, acne)	5%	Social harms related to PEP use (n=4)

SOURCE: Luetkemeyer, A. 2023. Webinar. IAS–USA.

Doxy-PEP: What we know…

- It works to prevent STIs in MSM and TGW
- It works for CT, Syphilis, and even GC
- Number needed to treat is about 5 people to prevent an STI in a population with a high incidence of STIs (30% per quarter)
- Safe and well tolerated

SOURCE: Cellum, C. Ryan White Clinical Conference 2023

Doxy-PEP: What we are still studying…

- How does Doxy-PEP affect sexual behavior?
  - Does it change risk modification?
- What about antimicrobial resistance?
  - How will GC tetracycline resistance affect GC prevention?
  - What about other bacteria: S. aureus, gut microbiome?
  - Will it affect CT, Syphilis, M. genitalium?
- Who would benefit from DoxyPEP?

SOURCE: Cellum, C. Ryan White Clinical Conference 2023

Doxy-PEP: Sexual behavior and adherence

- Behavior at enrollment: median 9 partners (IQR 4,17) with 5 sex acts per month (IQR 1.7, 10.7) and 90.1% condomless
- During follow-up: no significant change in:
  - # partners, # condomless sex during follow-up in doxyPEP arm; also no difference between doxyPEP and standard of care
- Adherence (reported): 86% always/often [median 4 doses per month (IQR 1.0-10.0), 25% with >/= 10 doses per month

What about resistance?

S. aureus

- DoxyPEP associated with 14% reduction in colonization, 8% absolute increase in doxy-R compared to baseline
- MRSA prevalence was low (6%) and doxy-R MRSA was unchanged

N. gonorrhea

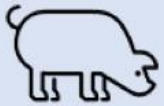
- DoxyPEP: TCN-R in 4 baseline GC isolates, 6 incident GC isolates in doxyPEP and 2 incident GC isolates in standard of care
- DOXYVAC: TCN-R – 30% DoxyPEP vs 19% SOC

SOURCE: Cellum, C. Ryan White Clinical Conference 2023

Impacts on other STIs

Chlamydia

- Doxy is now 1st line treatment for CT
- No clinical resistance to TCN class reported
- TCN resistance has been seen in *C.suis* (pig chlamydia) – could this be transferred to humans or acquired de novo?



Syphilis

- Doxy is an alternative therapy
- No clinical resistance to TCN class reported
- TCN resistance has been with single point mutation in other spirochetes
- Potential impact on syphilis serologies- delayed diagnosis or false negative?

M.genitalium

- Doxy not very effective - poor cure rate as monotherapy, but part of two-step therapy for *M. gen*
- Substantial resistance to macrolides & fluoroquinolones
- Clinical *M. gen* resistance not yet described

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Dugan 2004 AAC, Stamm AAC 2010

Antimicrobial resistance considerations

Doxy-PEP is not the only source of doxycycline exposure

- Many other sources including treatment for STIs, other infections, & food exposure
- Challenging to isolate the impact of doxy-PEP alone, particular with intermittent & variable use

Limits of STI surveillance

- CDC SURRG/ARLN testing for phenotypic TCN-R, not doxy-R; may overestimate ↓ susceptibility to doxycycline
- CT & Syphilis resistance: not well defined, expected to be rare, molecular & culture-based testing challenging & limited availability

Doxy-PEP impact on other bacteria

- Consider public health monitoring for doxy-R *S.aureus, Strep pneumoniae* based on available data, in areas of high doxy-PEP uptake. *Caveat- what is appropriate comparator?*
- Commensal *Neisseria* & gut microbiome more challenging

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Who would benefit from DoxyPEP?

Strut Clinic- San Francisco AIDS Foundation
≈ 1775 on doxy-PEP by 7/2023

BridgeHIV

Decline in GC/CT among PrEP Clients w/ DoxyPEP*

PrEP Clients	Non-DoxyPEP	Before DoxyPEP	After DoxyPEP	Total
Chlamydia Tests				
Indeterminate	3	5	1	9
Negative	12,924	5,927	3,283	22,134
Positive	262	348	32	642
Total	13,189	6,280	3,316	22,785
Positivity	2.0%	5.5%	1.0%	2.8%
Gonorrhea Tests				
Indeterminate	14	8	6	28
Negative	12,804	5,852	3171	21,827
Positive	371	421	146	938
Total	13,189	6,281	3,323	22,793
Positivity	2.8%	6.7%	4.4%	4.1%

Scott, 2023 ISSTDR

*Only clients on DoxPEP for 90 days or more

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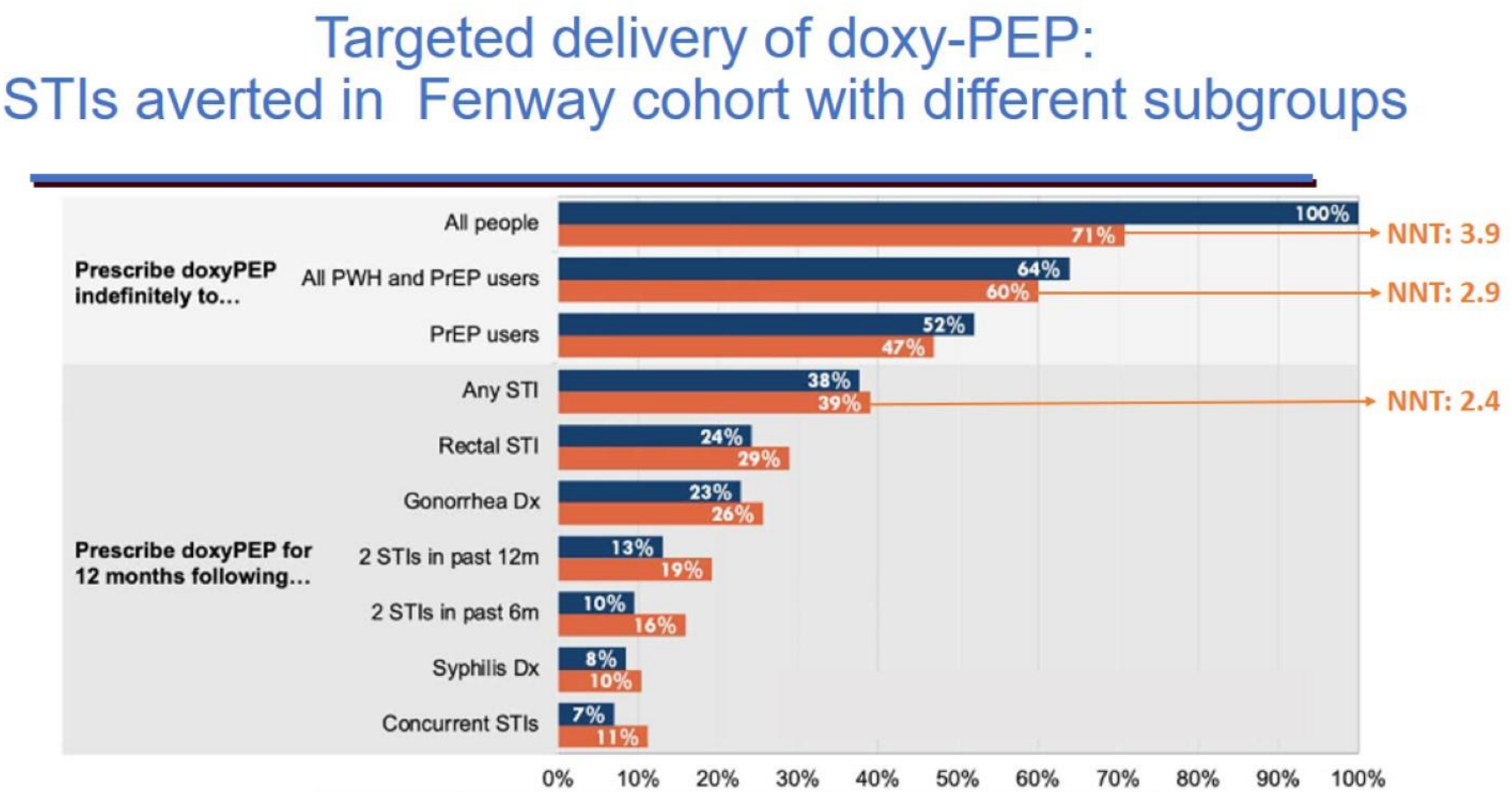
San Francisco City Clinic
≈ 828 on doxy-PEP by 6/2023

- Uptake
  - ≥1 sexual partners prior 3 months & ≥1 STI in prior year (GC,CT or syphilis): **74%**
  - ≥2 sexual partners and no STI in prior year: **60%**

  Increased uptake in each tier with the number of recent sexual partners
- No disparities thus far in doxy-PEP uptake by race/ethnicity or age
- Frequency of use similar to DoxyPEP RCT (4x-6x/month)
- People are using it "selectively" - after some encounters but not all

Bacon, 2023 ISSTDR

Who would benefit from DoxyPEP?



SOURCE: Cellum, C. Ryan White Clinical Conference 2023

Doxy-PEP: practical considerations

Who can get doxyPEP?

- MSM and TGW (? persons assigned female at birth)
- One bacterial STI in past 12 months, > 1 sex partner in 3 mos
- (?) self-identified risk, (?) reports plans of sexual risk

What do I prescribe?

- Doxycycline hyclate or monohydrate 100 mg tablets
- Take two tablets (200 mg) 24-72 hours after sex, may repeat once every 24 hours if with continued exposure.

What do I need to monitor?

- No serious lab abnormalities (package insert: LFTs, renal function, CBC “periodically” when taking prolonged period)
- Regular STI screening

Doxy-PEP: practical considerations

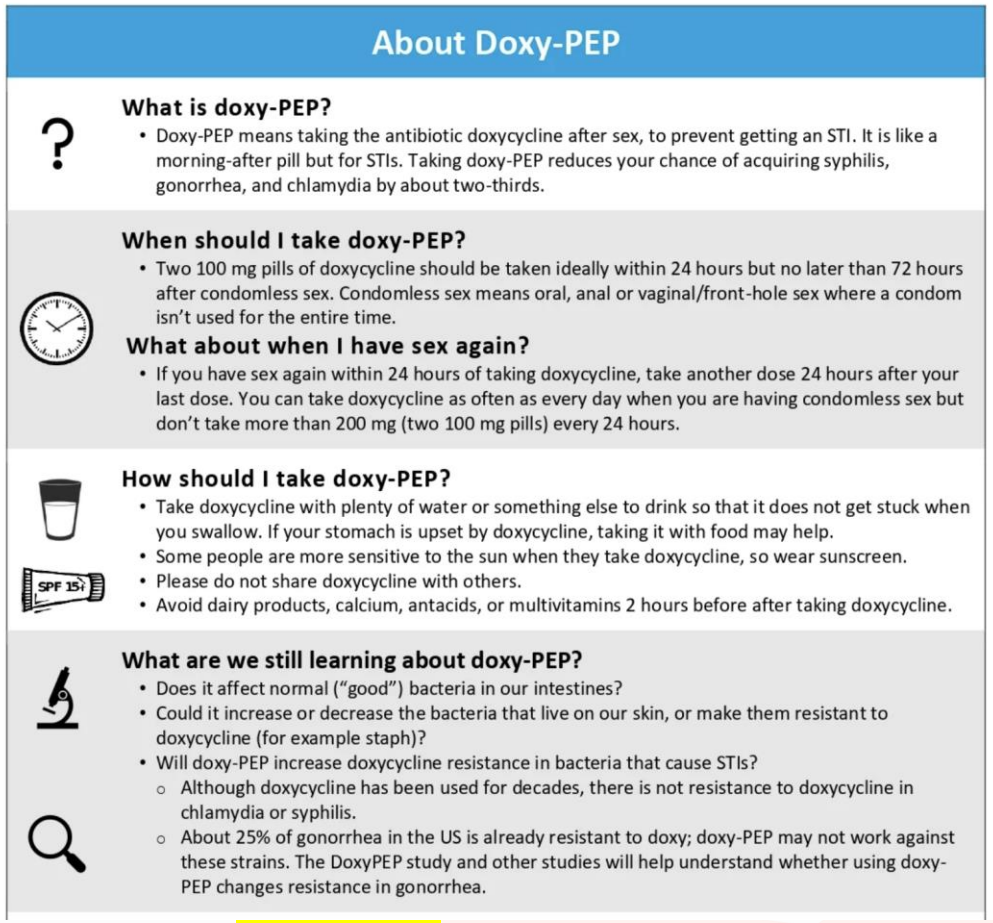
ICD-10 code

- Z20.2 Contact with and [suspected] exposure to infections with a predominantly sexual mode of transmission

Patient education on doxyPEP

- Do not use with polyvalent cations (iron, calcium carbonate)
- Full glass of water and stay upright for 30 minutes
- Avoid / limit sun exposure

Doxy-PEP: practical considerations



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 ideally within 24 hours but no later than 72 hours after condomless sex. Condomless sex means oral, anal or vaginal/front-hole sex where a condom isn't used for the entire time.

What about when I have sex again?

- If you have sex again within 24 hours of taking doxycycline, take another dose 24 hours after your last dose. You can take doxycycline as often as every day when you are having condomless sex but don't take more than 200 mg (two 100 mg pills) every 24 hours.

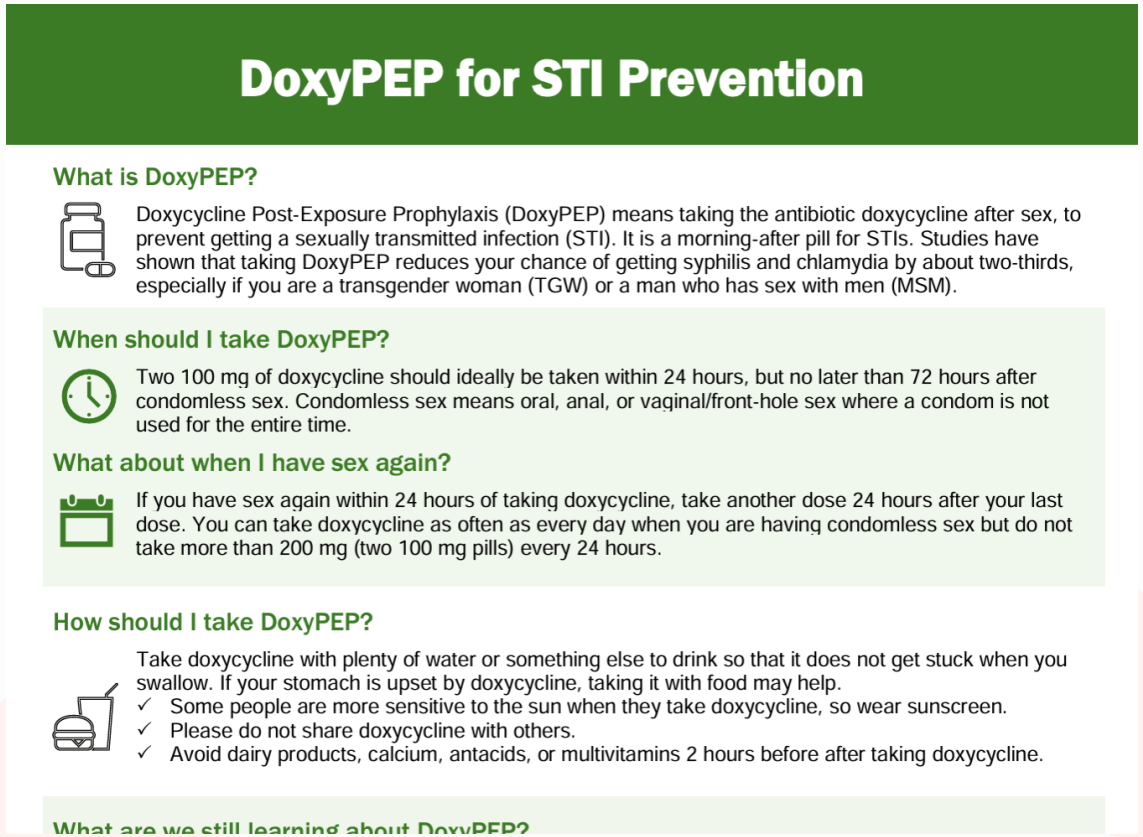
How should I take doxy-PEP?

- Take doxycycline with plenty of water or something else to drink so that it does not get stuck when you swallow. If your stomach is upset by doxycycline, taking it with food may help.
- Some people are more sensitive to the sun when they take doxycycline, so wear sunscreen.
- Please do not share doxycycline with others.
- Avoid dairy products, calcium, antacids, or multivitamins 2 hours before after taking doxycycline.

What are we still learning about doxy-PEP?

- Does it affect normal ("good") bacteria in our intestines?
- Could it increase or decrease the bacteria that live on our skin, or make them resistant to doxycycline (for example staph)?
- Will doxy-PEP increase doxycycline resistance in bacteria that cause STIs?
  - Although doxycycline has been used for decades, there is not resistance to doxycycline in chlamydia or syphilis.
  - About 25% of gonorrhea in the US is already resistant to doxy; doxy-PEP may not work against these strains. The DoxyPEP study and other studies will help understand whether using doxy-PEP changes resistance in gonorrhea.

https://www.sfcityclinic.org/services/sti-and-hiv-prevention/doxy-pep



DoxyPEP for STI Prevention

What is DoxyPEP?

Doxycycline Post-Exposure Prophylaxis (DoxyPEP) means taking the antibiotic doxycycline after sex, to prevent getting a sexually transmitted infection (STI). It is a morning-after pill for STIs. Studies have shown that taking DoxyPEP reduces your chance of getting syphilis and chlamydia by about two-thirds, especially if you are a transgender woman (TGW) or a man who has sex with men (MSM).

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Two 100 mg of doxycycline should ideally be taken within 24 hours, but no later than 72 hours after condomless sex. Condomless sex means oral, anal, or vaginal/front-hole sex where a condom is not used for the entire time.

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What are we still learning about DoxyPEP?

http://publichealth.lacounty.gov/dhsp/DPHSexualHealthClinics/HealthEducationLibrary/DoxyPEP/DoxyPEP_Factsheet-EN_FINAL_05.05.2023.pdf

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