Uso della doxiPEP pro e contro

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Aggiornamenti infettivologici: HIV, epatiti &...
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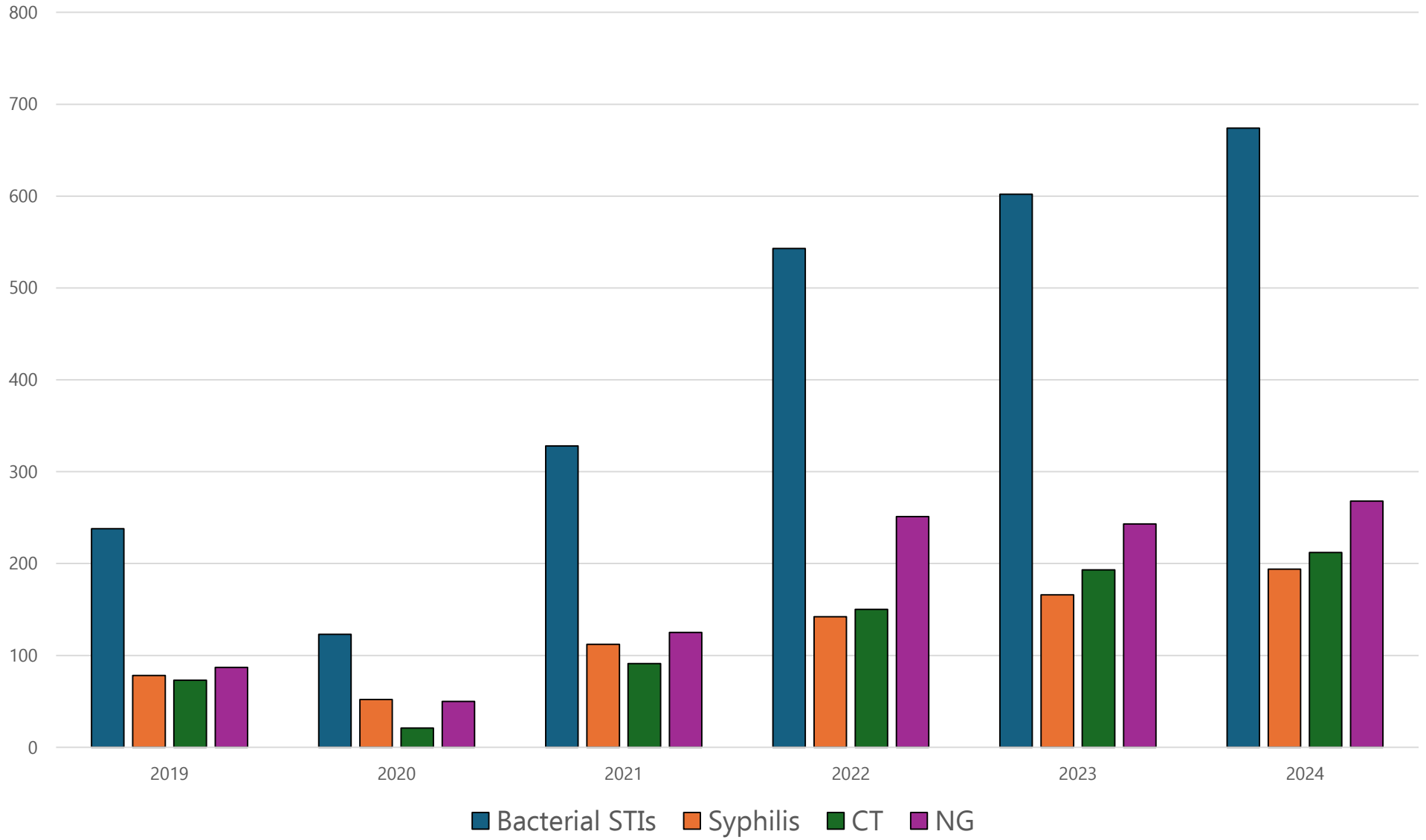
Conflict of interests

- No conflict of interests to declare.

STIs at Niguarda Hospital



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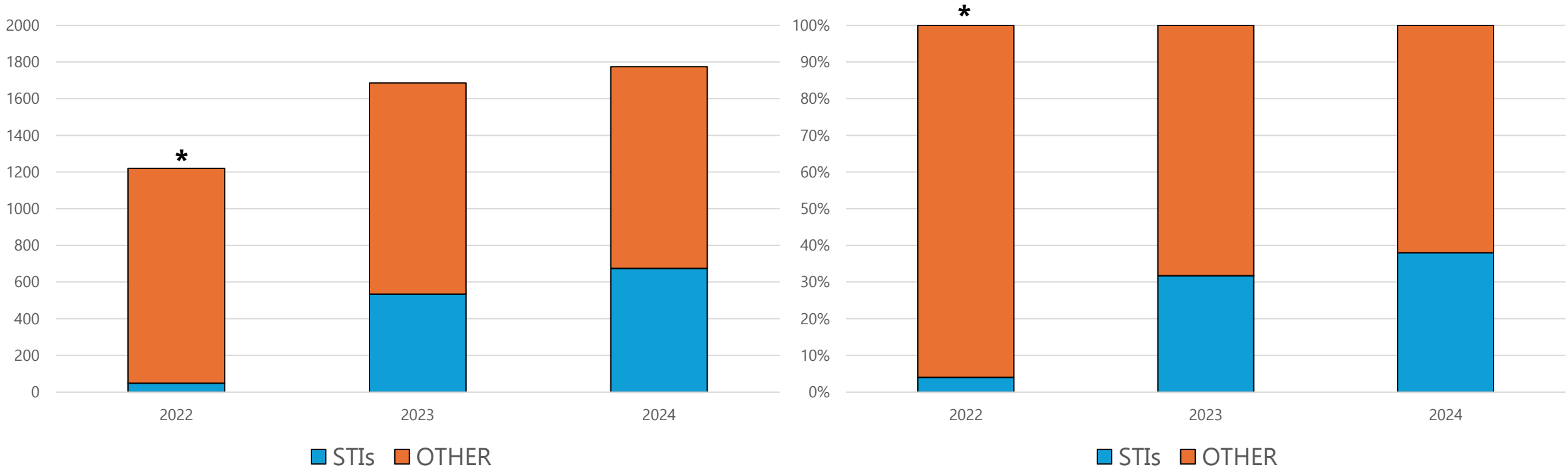
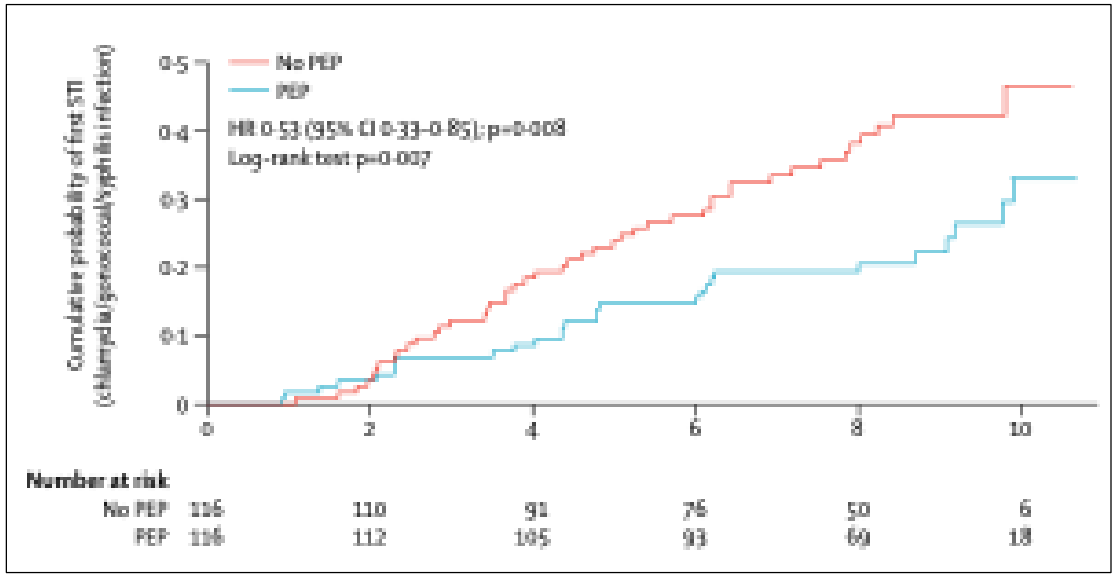
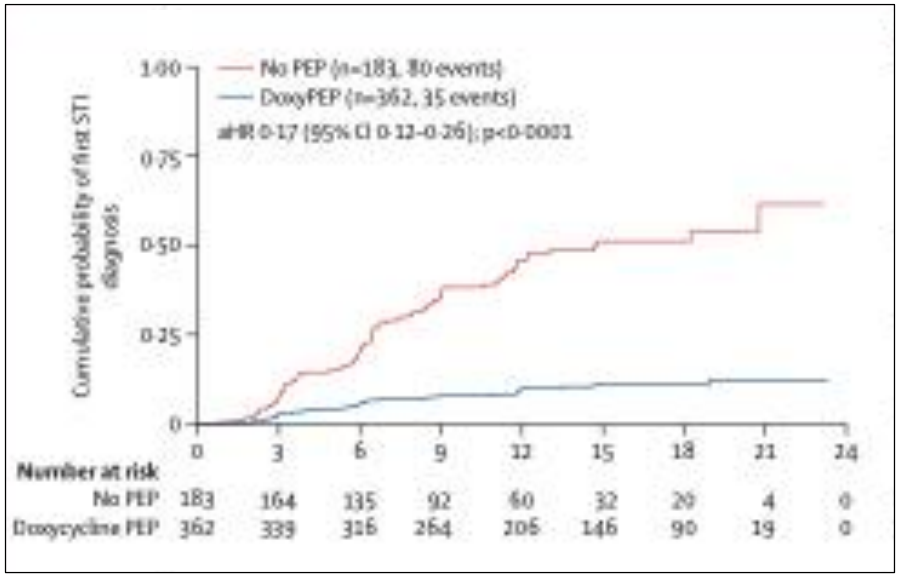
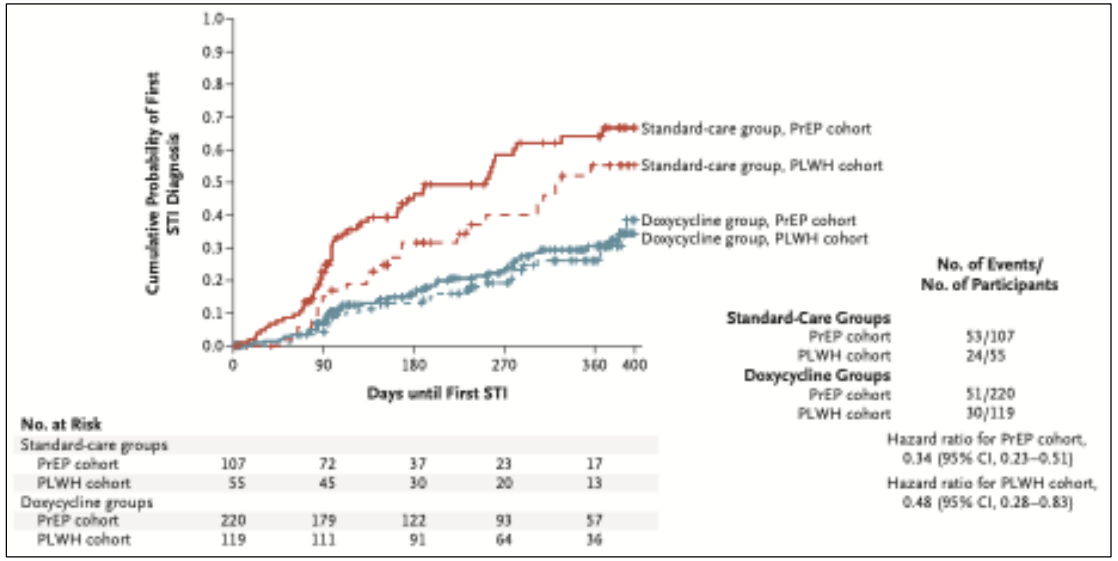


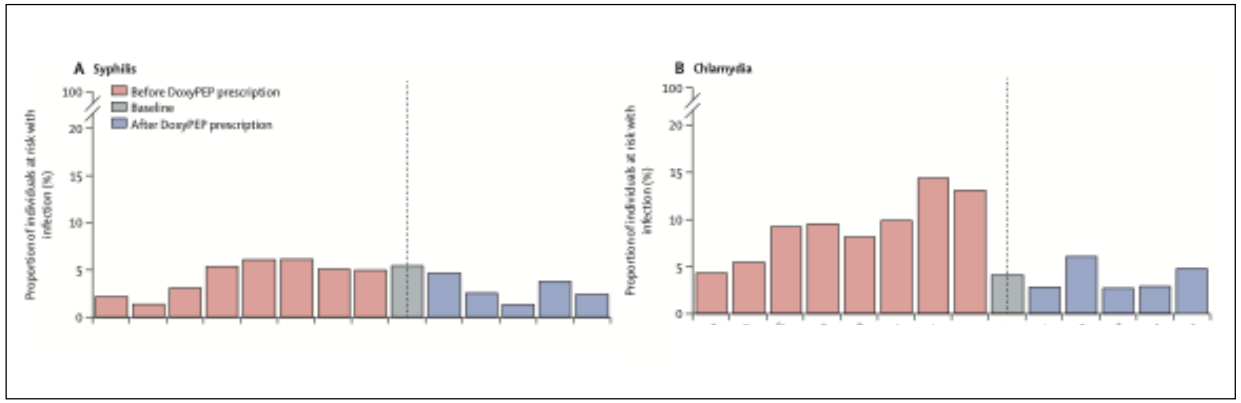

Partner Notification
dPEP
Behavioral change
Condom
Vaccines

DoxyPEP efficacy studies









Molina JM, Lancet Infect Dis 2018; Luetkemeyer AF, N Engl J Med 2023; Molina JM, Lancet Infect Dis 2024; Raccagni AR, Lancet Infect Dis 2025.

DoxyPEP efficacy: PK considerations

	C_{max} (µg/mL)[a]	T_{max} (hours)[b]	$T_{1/2}$ (hours)[a]	AUC_{0-96h} (µg*h/mL)[a]
Male (n = 11)	0.925 [0.768–1.112]	4 [1–4]	22 [19–25]	31.295 [25.231–38.815]
Female (n = 9)	1.319 [1.028–1.692]	2 [1–4]	18 [16–21]	37.264 [30.662–45.288]
Combined (n = 20)	1.042 [0.889–1.222]	2 [1–4]	20 [19–22]	33.951 [29.632–38.899]

[a]Values presented as geometric mean [95% confidence interval]. [b]Values presented as median [interquartile range].

Table 2: Mean plasma pharmacokinetic parameters among male and female participants receiving a single dose of doxycycline.

	C_{max} (µg/mL)[a]	T_{max} (hours)[b]	$T_{1/2}$ (hours)[a]	AUC_{0-96} (µg*h/mL)[a]	Secretion: plasma ratio
Male (n = 11)					
Plasma	0.925 [0.768–1.112]	4 [1–8]	22 [19–25]	33.295 [25.231–38.815]	
Rectal secretions	0.882 [0.233–3.334]	48 [2–72]	11 [6–19]	94.936 [29.875–301.692]	3.03 [1.03–8.93]
Female (n = 9)					
Plasma	1.319 [1.028–1.692]	2 [1–4]	18 [16–21]	37.264 [30.662–45.288]	
Vaginal secretions	1.284 [742–2223]	8 [1–8]	20 [16–24]	58.562 [32.719–104.816]	3.14 [1.62–4.77]
Rectal secretions	0.614 [0.077–4.846]	24 [2–48]	19 [8–42]	51.915 [14.004–192.462]	1.46 [0.35–6.14]
Combined (n = 18)					
Plasma	1.041 [0.902–1.202]	4 [2–8]	20 [19–22]	33.020 [28.927–37.692]	
Rectal secretions	0.704 [0.311–1.596]	48 [2–72]	14 [9–23]	73.511 [34.513–156.572]	2.22 [1.03–6.09]

[a]Values presented as geometric mean [95% confidence interval]. [b]Values presented as median [interquartile range].

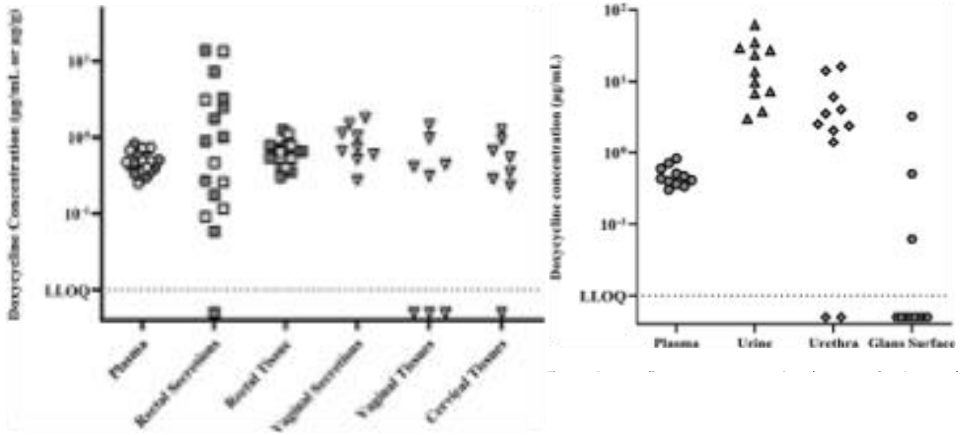
Table 3: Estimated pharmacokinetic parameters in plasma, rectal and vaginal secretions among male and female participants receiving a single dose of doxycycline.

	C. trachomatis[a]		*T. pallidum*[a]		*N. gonorrhoeae*[b]	
	1× MIC	4× MIC	1× MIC	4× MIC	1× MIC	4× MIC
Male (n = 11)						
Plasma	91 [82–98]	45 [38–54]	76 [67–79]	30 [21–39]	46 [38–55]	<0 [<0–8]
Rectal secretions	95 [63–103]	74 [<0–99]	91 [52–102]	61 [<0–96]	75 [<0–99]	<0 [<0–84]
Female (n = 9)						
Plasma	84 [75–91]	45 [40–48]	70 [65–76]	34 [28–39]	45 [41–49]	7 [1–15]
Vaginal secretions	101 [49–108]	46 [34–70]	70 [44–99]	38 [25–64]	45 [34–70]	11 [<0–37]
Rectal secretions[c]	102 [61–108]	59 [<0–92]	69 [56–105]	50 [<0–81]	60 [<0–93]	<0 [<0–54]
Combined (n = 20)						
Plasma	87 [82–93]	45 [41–48]	71 [68–79]	32 [27–37]	45 [42–50]	4 [<0–8]
Rectal secretions[c]	97 [66–105]	63 [20–92]	88 [61–102]	52 [<0–82]	62 [22–92]	<0 [<0–54]

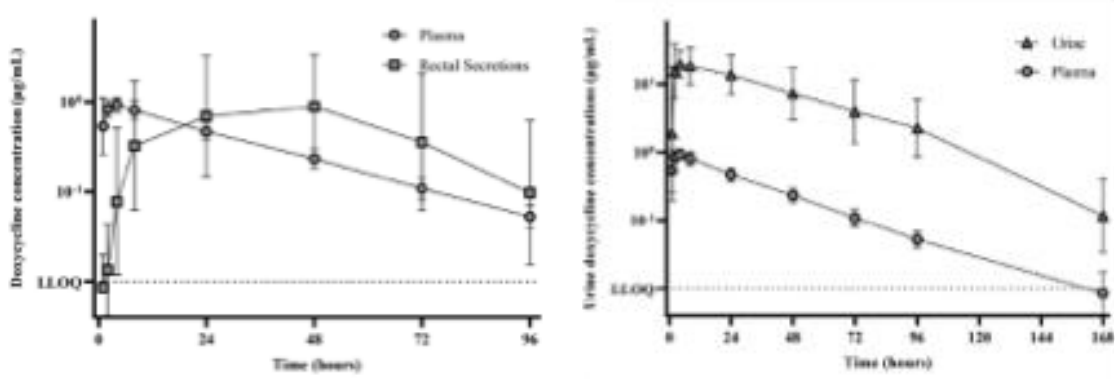
[a]Values presented as time geometric mean concentrations remain above 90% minimum inhibitory concentration (MIC) or 4 times MIC (hours) [95% confidence interval]. [b]Values presented as time geometric mean concentrations remain above minimum inhibitory concentration (MIC) or 4 times MIC (hours) [95% confidence interval]. [c]Seven female participants provided rectal secretions.

Table 4: Time estimated geometric mean concentrations remain above minimum inhibitory concentrations in hours in plasma, rectal and vaginal secretions among male and female participants receiving a single dose of doxycycline.

Doxycycline concentrations in plasma, rectal, vaginal, cervical tissues, and urine and estimated rectal, vaginal secretions, urethral and glans surface secretions concentrations collected 24 h after a single oral dose.



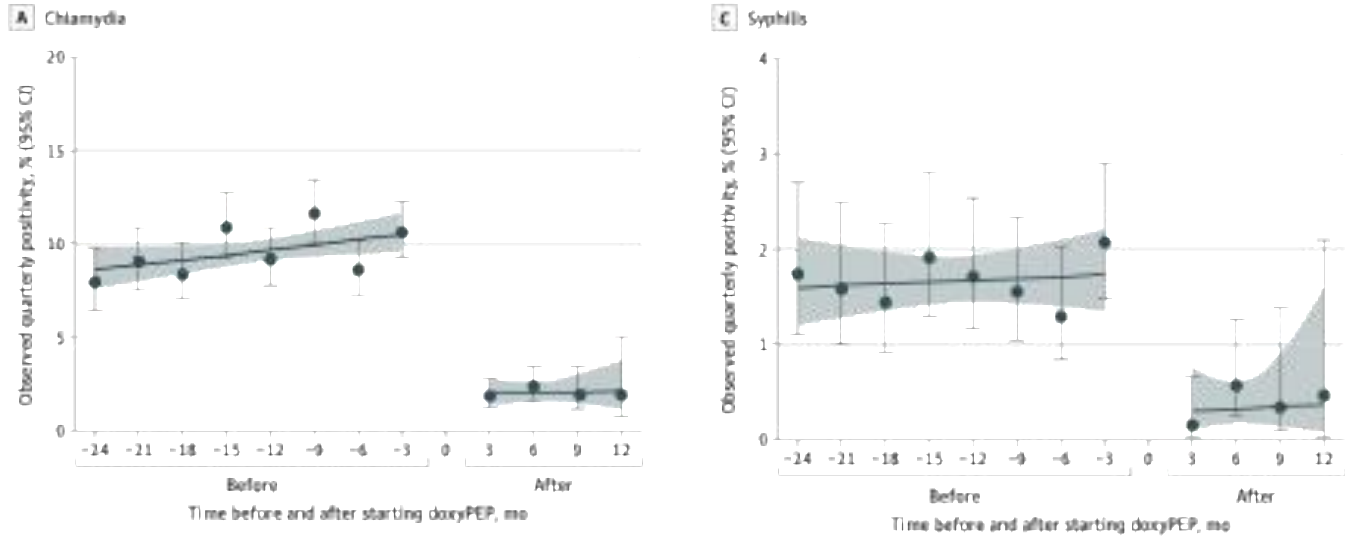
Mean plasma doxycycline concentrations and estimated mean rectal and urine concentrations collected following a single oral dose (geometric mean concentrations and 95% confidence intervals are presented from 1 to 96 h following dosing).



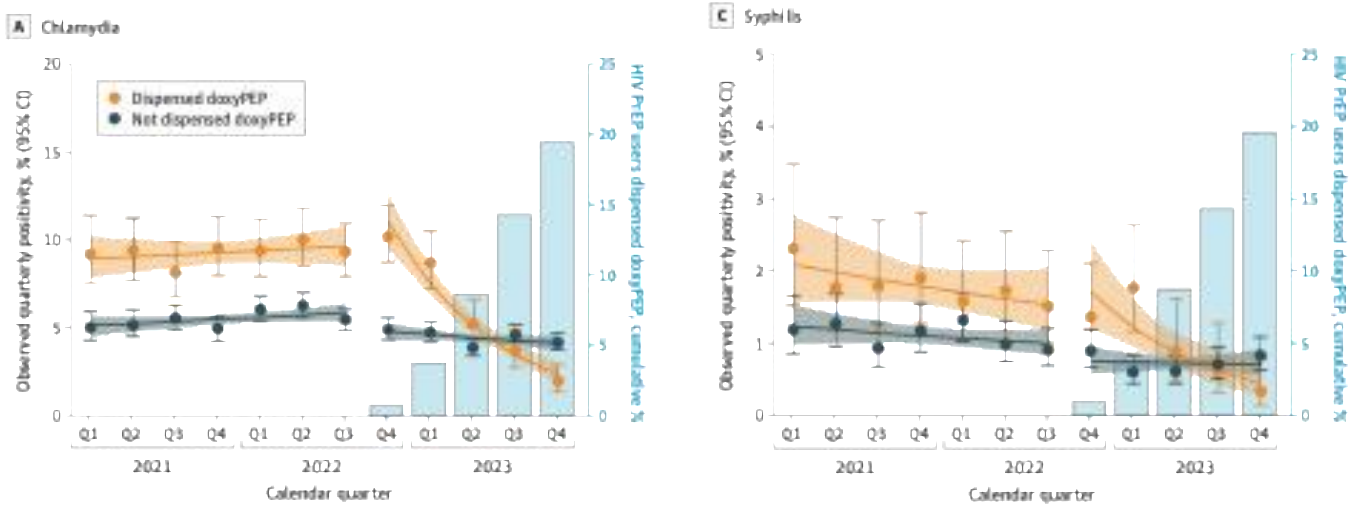
Haaland RE, eBioMed 2024.

DoxyPEP efficacy in real life

Quarterly sexually transmitted infection positivity from 24 months before to 12 months after starting DoxyPEP among PrEP users dispensed DoxyPEP at least once (N=2,253). Lines represent trends (mean quarterly positivity) for pre-doxyPEP and post-doxyPEP initiation; shaded areas, 95% CIs for trend. A baseline window from 90 days before to 14 days after starting doxyPEP was excluded.



Trends in quarterly sexually transmitted infection positivity From January 1, 2021, to December 31, 2023, among PrEP users dispensed and not dispensed DoxyPEP during the study period (N=11,551). Solid lines are 95% CIs for trend in the pre-doxyPEP implementation period and post-doxyPEP implementation period. Chlamydia positivity is at any anatomic site of infection.



Traeger MW, JAMA Internal Med 2025.

Received: 2 August 2023 | Accepted: 22 September 2023

DOI: 10.1111/ddg.15282

GUIDELINE

Position statement of the German STI Society on the prophylactic use of doxycycline to prevent STIs (Doxy-PEP, Doxy-PrEP)

Ricardo Niklas Werner[1] | Axel Jeremias Schmidt[2,3] | Anja Potthoff[4,5] | Petra Spornraft-Ragaller[6] | Norbert Hermann Brockmeyer[7] | for the German STI Society (DSTIG)

At present, however, unresolved questions remain, particularly regarding implications of a broad implementation of prophylactic doxycycline to prevent STIs on tetracycline and other antimicrobial resistance in bacterial STIs, non-STI-related bacterial pathogens, and the microbiome.
In response to the increasing demand and the challenge of balancing effectiveness, safety, and the risk of promoting antibiotic resistance, the German STI Society (DSTIG) has issued a position statement, providing specific recommendations regarding potential indications, criteria, and occasions for the use of doxycycline in STI prevention. These recommendations are based on current evidence and expert opinion.

MJA 220 (7) • 15 April 2024

Consensus statement

Australian consensus statement on doxycycline post-exposure prophylaxis (doxy-PEP) for the prevention of syphilis, chlamydia and gonorrhoea among gay, bisexual and other men who have sex with men

Vincent J Cornelisse[1,2], Benjamin Riley[3], Nicholas A Medland[2]

At the end of the consensus process, there remained some disagreement, as some stakeholders felt strongly that doxy-PEP should be considered *only* for the prevention of syphilis in GBMSM, and that the risk of increasing antimicrobial resistance outweighed any potential benefit from reductions in other bacterial STIs in the target population. The national roundtable made several other recommendations for clinicians, community, researchers and policy makers, as detailed in this article. ASHM will support the development of detailed clinical guidelines and education materials on doxy-PEP (www.ashm.org.au/doxy-pep).

Changes in management as a result of this consensus statement: For GBMSM at high risk of syphilis, and perhaps other bacterial STIs, clinicians may consider prescribing doxy-PEP for a limited period of time, followed by a review of ongoing need. Unlike human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP), doxy-PEP may not be suitable as a population-level intervention and should instead be used more selectively.

BASHH column

BASHH updated position statement on doxycycline as prophylaxis for sexually transmitted infections

Manik Kohli [1,2] Nicholas Medland,[3,4] Helen Fifer [5] John Saunders [1,5]

BMJ Kohli M, *et al. Sex Transm Infect* May 2022 Vol 98 No 3

Also of major concern is the potential for selection of resistance among potentially pathogenic bacterial flora such as *Staphylococcus aureus* and respiratory tract pathogens. Consideration also needs to be given to the impact on community prevalence of resistance determinants within commensal organisms, with higher prevalence purported among MSM populations.[12]

There remain key gaps in understanding the risk of AMR emergence with prophylactic doxycycline for STIs, as well as some of the facilitators and drivers that lead of the facilitators and drivers that lead to individuals' decisions to self-source antibiotics. In addition to addressing the question of efficacy, some current trials examining doxycycline as STI prophylaxis will attempt to address aspects of AMR. In the interim, it is important clinicians ask about antibiotic STI prophylaxis use and discuss the limited benefits and potential risks. This position statement provides an update on the current available evidence and practical guidance for clinicians providing care to individuals reporting antibiotic STI prophylaxis use.

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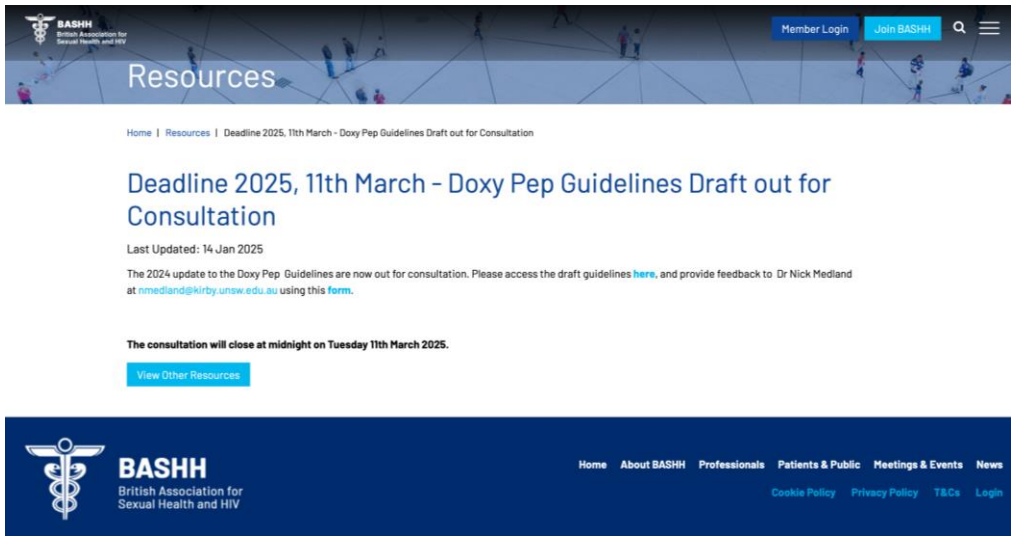


Italian ID Specialists' attitude towards doxyPEP

Attitudine alla DoxyPEP (0-100): 69 (IQR 34-81)
Maggiore in chi ha già prescritto la DoxyPEP [80, IQR=64-90 vs 50, IQR=25-75, p<0.001]

Motivi di prescrizione: 55/128 (43%)
ha già prescritto la DoxyPEP.

Motivi di prescrizione, n=55 (%)	
IST multiple	19 (35.9%)
Alto numero di partners	13 (24.5%)
Esposizioni ad alto rischio	11 (20.8%)
Group sex	10 (18.9%)
GBMSM	9 (17.0%)
Locali di cruising	7 (13.2%)
Chemsex	7 (13.2%)
Richiesta dell'utente	6 (11.3%)
HIV PEP	5 (9.4%)
HIV PrEP	4 (7.6%)
Violenza sessuale	3 (5.7%)
Sex worker	1 (1.9%)

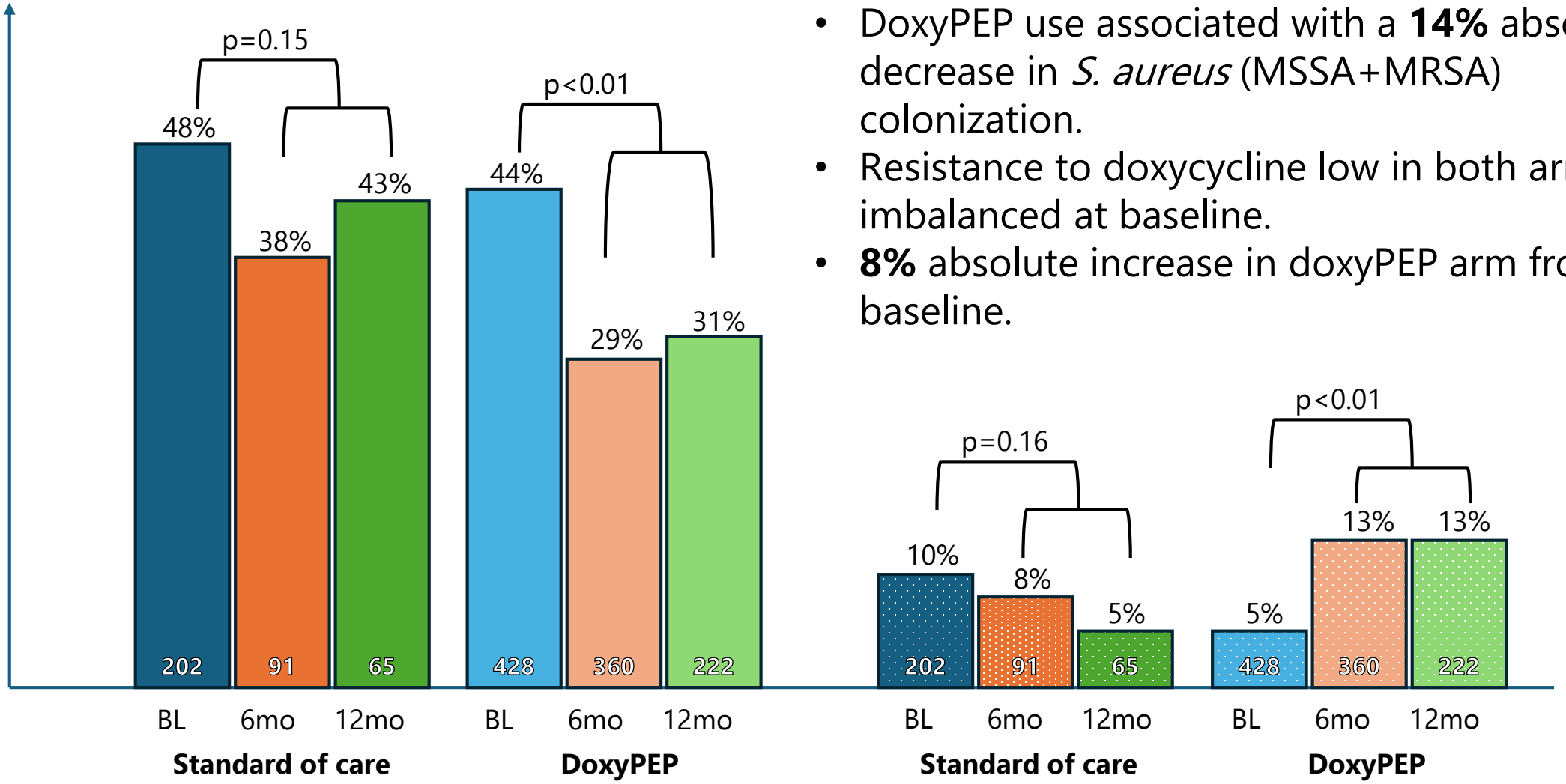
Maggiori preoccupazioni:

	Totale (n=128)	**Mai prescritto doxyPEP (n=73)**	**Prescritto doxyPEP (n=55)**	**p-value**
Antibioticoresistenza	110 (95.7%)	61 (96.8%)	49 (94.2%)	0.657
Superiorità del condom	27 (23.5%)	18 (28.6%)	9 (17.3%)	0.188
Tossicità	22 (19.1%)	17 (27.0%)	5 (9.6%)	**0.030**
Costi	11 (9.6%)	7 (11.1%)	4 (7.7%)	0.752
*Altro**	12 (10.4%)	5 (7.9%)	7 (13.5%)	0.372
Più di 2 preoccupazioni	58 (45.3%)	41 (56.2%)	17 (30.9%)	**0.007**

* **Altro:** Compensazione del rischio (5); Aderenza (3); Logistica (2); Inefficacia (2); Criteri di selezione degli utenti potenzialmente eleggibili (2).

Raccagni AR, XXIII Congresso Nazionale SIMIT 2024.

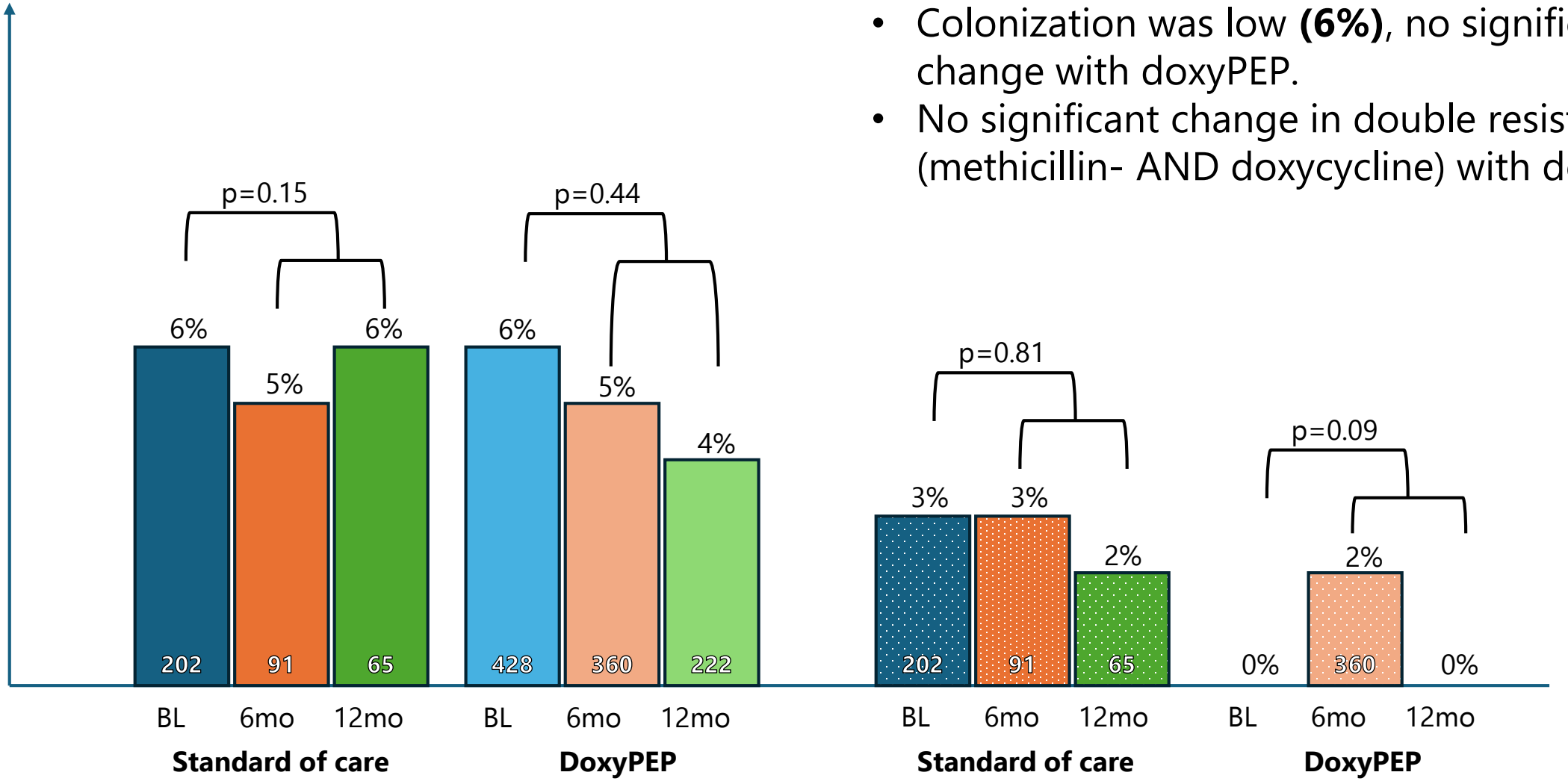
Antimicrobial resistance: SA colonization



- DoxyPEP use associated with a **14%** absolute decrease in *S. aureus* (MSSA+MRSA) colonization.
- Resistance to doxycycline low in both arms and imbalanced at baseline.
- **8%** absolute increase in doxyPEP arm from baseline.

Luetkemeyer AF, N Engl J Med 2023.

Antimicrobial resistance: MRSA colonization

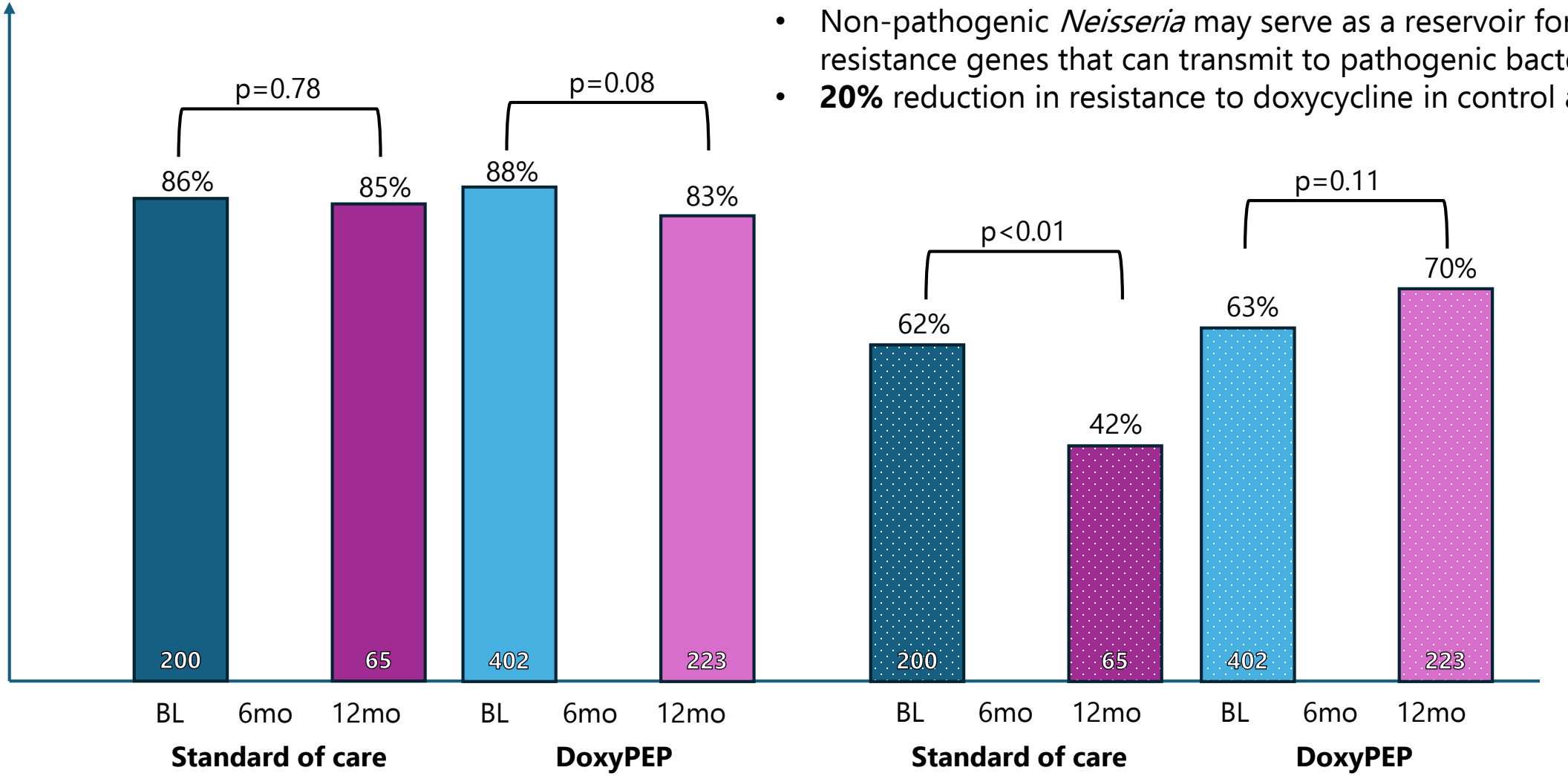


- Colonization was low **(6%)**, no significant change with doxyPEP.
- No significant change in double resistance (methicillin- AND doxycycline) with doxyPEP.

Luetkemeyer AF, N Engl J Med 2023.

Antimicrobial resistance: commensal pharyngeal non-pathogenic *Neisseria spp*

- Non-pathogenic *Neisseria* may serve as a reservoir for drug-resistance genes that can transmit to pathogenic bacteria.
- **20%** reduction in resistance to doxycycline in control arm.



Fiore MA, Antibiotics 2020; Luetkemeyer AF, N Engl J Med 2023.

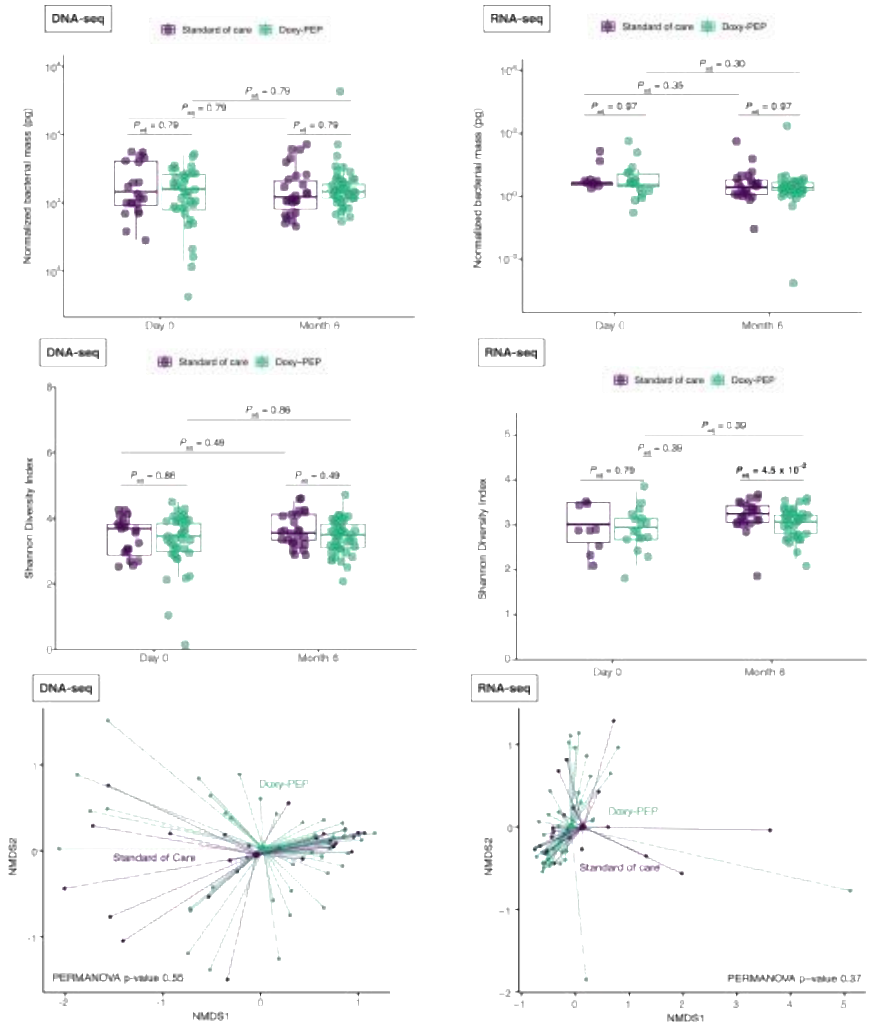
Antimicrobial resistance: gut microbiota

- DOXYPEP sub study assessing gut microbiota DNA (47 SOC vs 80 dPEP) and RNA (31 SOC vs 55 dPEP) sequencing.

Normalized bacterial microbiome mass.

Shannon Diversity Index to measure alpha diversity: observed richness (number of taxa) or evenness (the relative abundances of those taxa) of the sample within the gut habitat.

Bray-Curtis Index to measure beta diversity: the variability in community composition (the identity of taxa observed) among samples within the gut habitat.



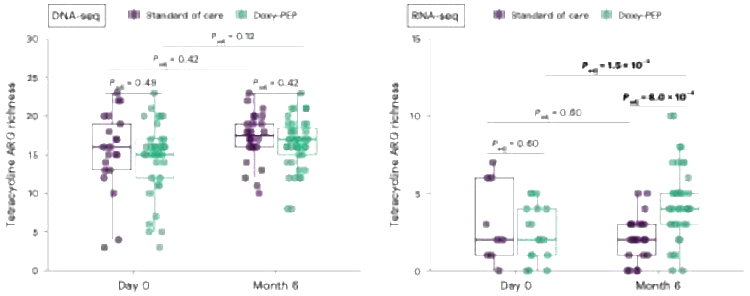
p-values for bacterial microbiome mass and alpha diversity were calculated using the two-sided Wilcoxon rank-sum test and adjusted for multiple comparisons; boxplot elements include a center line (median), box limits (upper and lower quartiles), whiskers (1.5x interquartile range). p-values for beta diversity were calculated using the two-sided PERMANOVA test and adjusted for multiple comparisons.
Significant p-values (<0.05) are bolded. Abbreviations: Padj, adjusted p-value; NMDS, non- metric multidimensional scaling.

Chu V, Nature Med 2024.

Antimicrobial resistance: gut microbiota

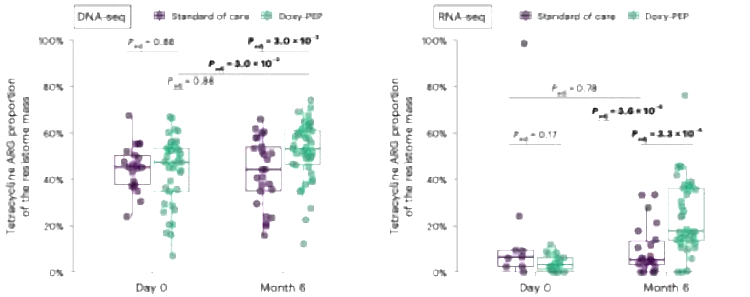
- DOXYPEP sub study assessing gut microbiota DNA (47 SOC vs 80 dPEP) and RNA (31 SOC vs 55 dPEP) sequencing.

Tetracycline antimicrobial resistance genes richness



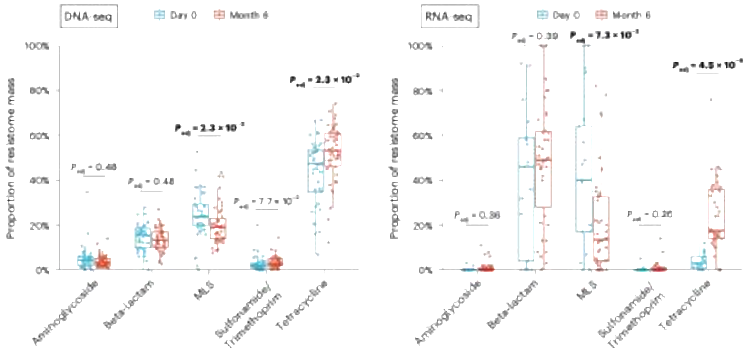
Although tetracycline antimicrobial resistance genes richness was not found to differ over time by DNA-seq, the number of detectably expressed tetracycline antimicrobial resistance genes increased by RNA-seq.

Tetracycline antimicrobial resistance genes proportion of resistome mass



Among participants in the dP arm, the proportion of tetracycline antimicrobial resistance genes in the resistome identified by DNA-seq increased over the 6-month study period (**46% to 51%**) as did the proportion of expressed tetracycline antimicrobial resistance genes identified by RNA-seq (**4% to 15%**). The most common mechanism of tetracycline resistance observed was **ribosomal target protection**.

The proportion of the resistome mass by antimicrobial resistance genes classes.



No proportional increases were noted in other non-tetracycline ARG classes, suggesting specificity of dP use for tetracycline ARGs. A sensitivity analysis adjusting for HIV status and cephalosporin exposure days showed statistically significant increases in proportional mass of tetracycline ARGs and decreases in proportional mass of MLS ARGs in the dP arm for both DNA-seq and RNA-seq data.

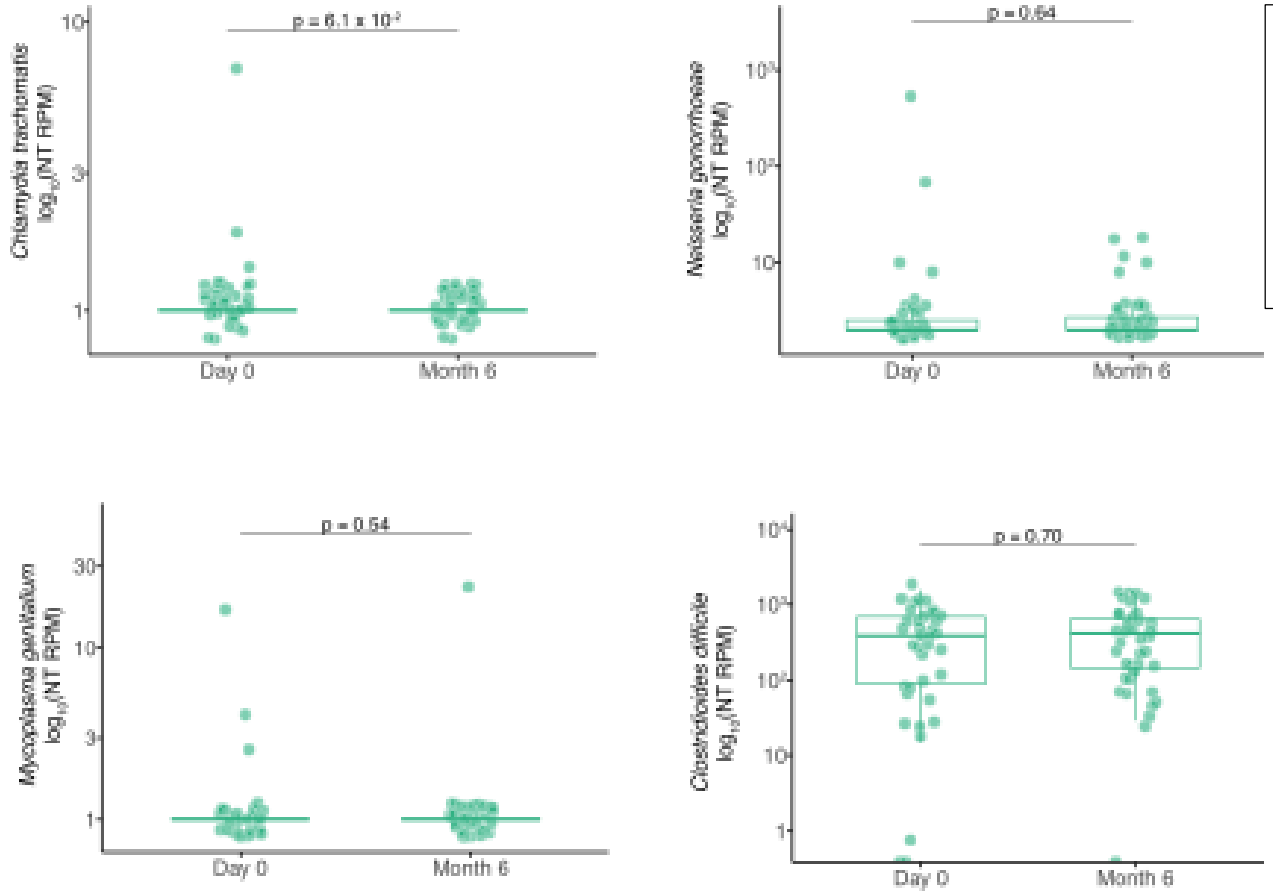
ARG: antimicrobial resistance genes; MLS: macrolide-lincosamide-streptogramin.

Chu V, Nature Med 2024.

Antimicrobial resistance: gut microbiota
(pathogens of special interest)

- DOXYPEP sub study assessing gut microbiota DNA (47 SOC vs 80 dPEP) and RNA (31 SOC vs 55 dPEP) sequencing.

Differential abundance comparison of specific pathogens of interest between time points in the in DNA-seq samples of the doxy-PEP arm (n = 80).



No differences in the relative abundance of enteric and STI pathogens *Clostridium difficile, N. gonorrheae* or *M. genitalium* existed between enrollment and month 6 in dP participants . A trend in *Chlamydia trachomatis* abundance reduction was observed (p=0.06).

p-values were calculated using the Wilcoxon rank-sum test and adjusted for multiple comparisons. Boxplot elements include a center line (median), box limits (upper and lower quartiles), whiskers (1.5x interquartile range).
Abbreviation: NT RPM, nucleotide reads per million.

Chu V, Nature Med 2024.

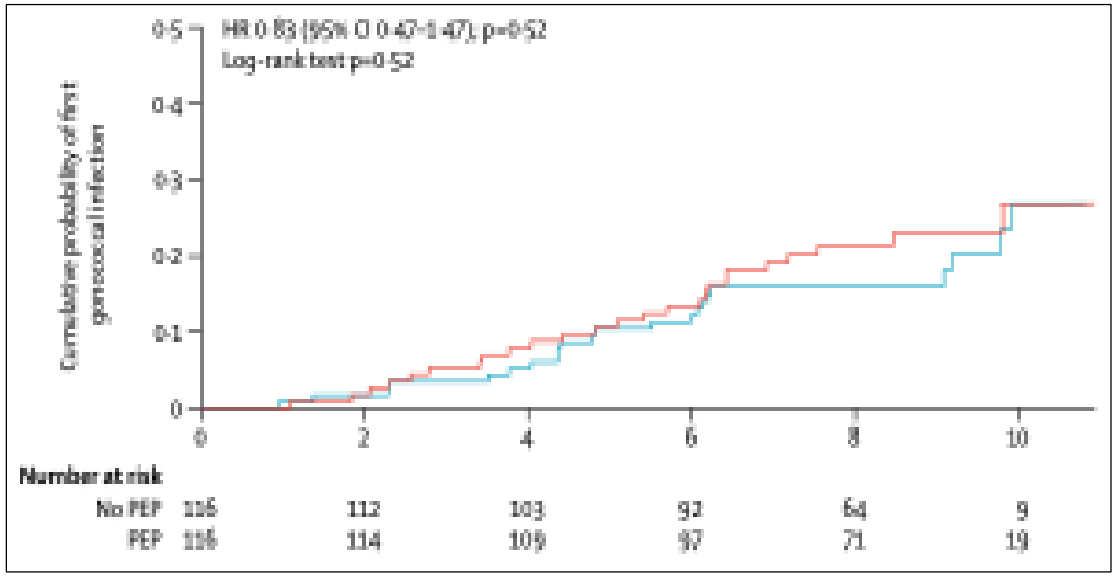
Antimicrobial resistance: C. trachomatis

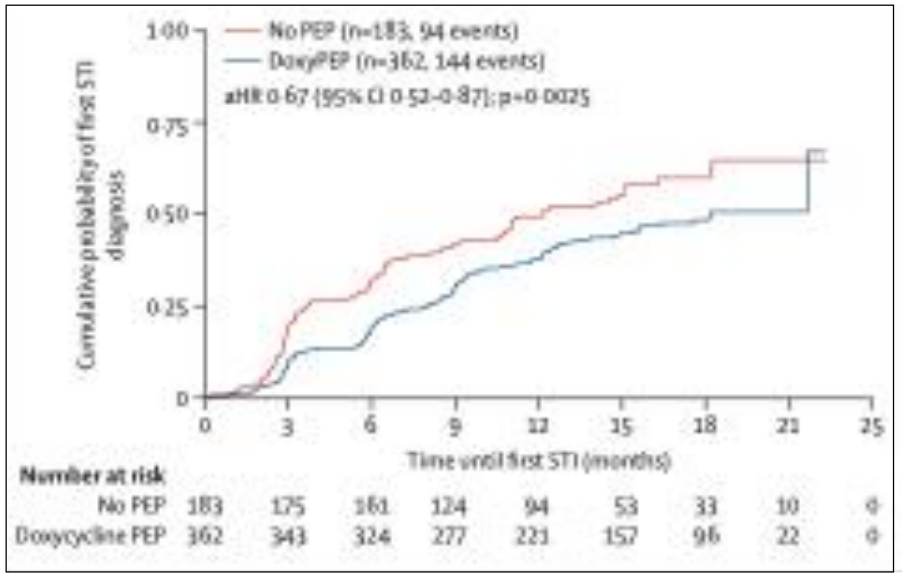
Standard of Care	2	Resistant strains	0
DoxyPEP	2	Resistant strains	0
Standard of Care	4	Resistant strains	0
DoxyPEP	0	Resistant strains	0

Standard of Care	5	Substitutions in 16S rRNA	0
DoxyPEP	5	Substitutions in 16S rRNA	0
Standard of Care	60	Substitutions in 16S rRNA	0
DoxyPEP	8	Substitutions in 16S rRNA	0
Standard of Care	31	Substitutions in 16S rRNA	0
DoxyPEP	25	Substitutions in 16S rRNA	0

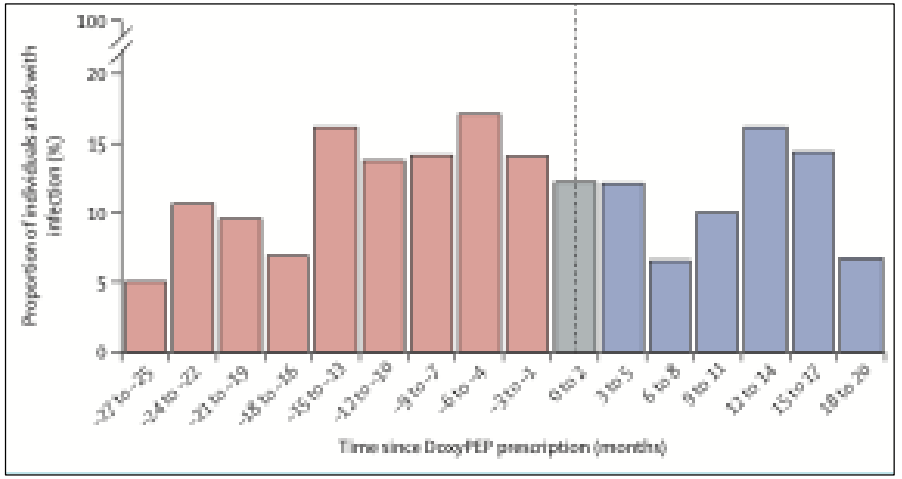
Molina JM, Lancet Infect Dis 2018; Molina JM, Lancet Infect Dis 2024; Stewart J, N Engl J Med 2023.

Antimicrobial resistance: N. gonorrhoeae





		PrEP		PLWH		Total	
		Doxy PEP	SOC	Doxy PEP	SOC	Doxy PEP	SOC
Baseline	GC infections	40	20	25	14	65	34
	GC cultures with resistance testing available	5	4	2	4	7	8
	Tetracycline-resistant	2 (40.0%)	1 (25.0%)	0 (0%)	1 (25.0%)	2 (28.6%)	2 (25.0%)
On Study	GC infections	52	52	27	26	79	78
	GC cultures with resistance testing available	7	10	6	6	13	16
	Tetracycline-resistant	3 (42.9%)	1 (10.0%)	2 (33.3%)	1 (16.7%)	5 (38.5%)	2 (12.5%)



Molina JM, Lancet Infect Dis 2018; Luetkemeyer AF, N Engl J Med 2023; Molina JM, Lancet Infect Dis 2024; Raccagni AR, Lancet Infect Dis 2025.

DoxyPEP efficacy: PK considerations

	C_{max} (µg/mL)[a]	T_{max} (hours)[b]	$T_{1/2}$ (hours)[a]	AUC_{0-96h} (µg*h/mL)[a]
Male (n = 11)	0.925 [0.768–1.112]	4 [1–4]	22 [19–25]	31.295 [25.231–38.815]
Female (n = 9)	1.319 [1.028–1.692]	2 [1–4]	18 [16–21]	37.264 [30.662–45.288]
Combined (n = 20)	1.042 [0.889–1.222]	2 [1–4]	20 [19–22]	33.951 [29.632–38.899]

[a]Values presented as geometric mean [95% confidence interval]. [b]Values presented as median [interquartile range].

Table 2: Mean plasma pharmacokinetic parameters among male and female participants receiving a single dose of doxycycline.

	C_{max} (µg/mL)[a]	T_{max} (hours)[b]	$T_{1/2}$ (hours)[a]	AUC_{0-96} (µg*h/mL)[a]	Secretion: plasma ratio
Male (n = 11)					
Plasma	0.925 [0.768–1.112]	4 [1–8]	22 [19–25]	33.295 [25.231–38.815]	
Rectal secretions	0.882 [0.233–3.334]	48 [2–72]	11 [6–19]	94.936 [29.875–301.692]	3.03 [1.03–8.93]
Female (n = 9)					
Plasma	1.319 [1.028–1.692]	2 [1–4]	18 [16–21]	37.264 [30.662–45.288]	
Vaginal secretions	1.284 [742–2223]	8 [1–8]	20 [16–24]	58.562 [32.719–104.816]	3.14 [1.62–4.77]
Rectal secretions	0.614 [0.077–4.846]	24 [2–48]	19 [8–42]	51.915 [14.004–192.462]	1.46 [0.35–6.14]
Combined (n = 18)					
Plasma	1.041 [0.902–1.202]	4 [2–8]	20 [19–22]	33.020 [28.927–37.692]	
Rectal secretions	0.704 [0.311–1.596]	48 [2–72]	14 [9–23]	73.511 [34.513–156.572]	2.22 [1.03–6.09]

[a]Values presented as geometric mean [95% confidence interval]. [b]Values presented as median [interquartile range].

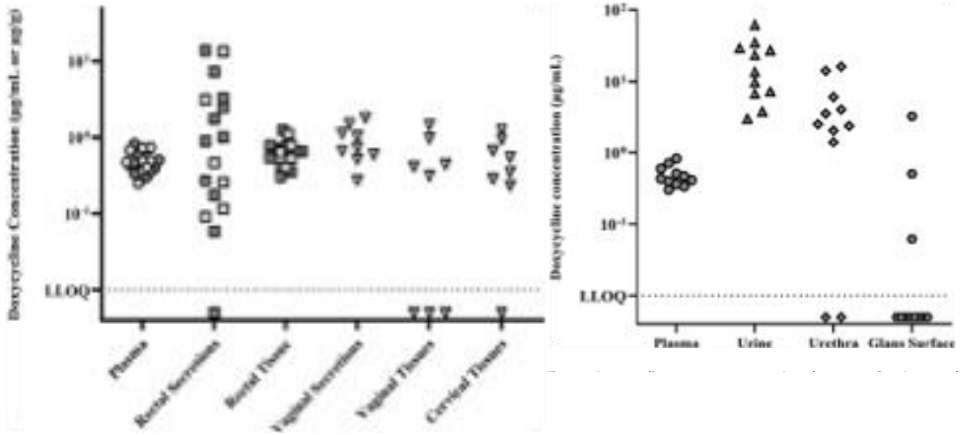
Table 3: Estimated pharmacokinetic parameters in plasma, rectal and vaginal secretions among male and female participants receiving a single dose of doxycycline.

	C. trachomatis[a]		*T. pallidum*[a]		*N. gonorrhoeae*[b]	
	1× MIC	4× MIC	1× MIC	4× MIC	1× MIC	4× MIC
Male (n = 11)						
Plasma	91 [82–98]	45 [38–54]	76 [67–79]	30 [21–39]	46 [38–55]	<0 [<0–8]
Rectal secretions	95 [63–103]	74 [<0–99]	91 [52–102]	61 [<0–96]	75 [<0–99]	<0 [<0–84]
Female (n = 9)						
Plasma	84 [75–91]	45 [40–48]	70 [65–76]	34 [28–39]	45 [41–49]	7 [1–15]
Vaginal secretions	101 [49–108]	46 [34–70]	70 [44–99]	38 [25–64]	45 [34–70]	11 [<0–37]
Rectal secretions[c]	102 [61–108]	59 [<0–92]	69 [56–105]	50 [<0–81]	60 [<0–93]	<0 [<0–54]
Combined (n = 20)						
Plasma	87 [82–93]	45 [41–48]	71 [68–79]	32 [27–37]	45 [42–50]	4 [<0–8]
Rectal secretions[c]	97 [66–105]	63 [20–92]	88 [61–102]	52 [<0–82]	62 [22–92]	<0 [<0–54]

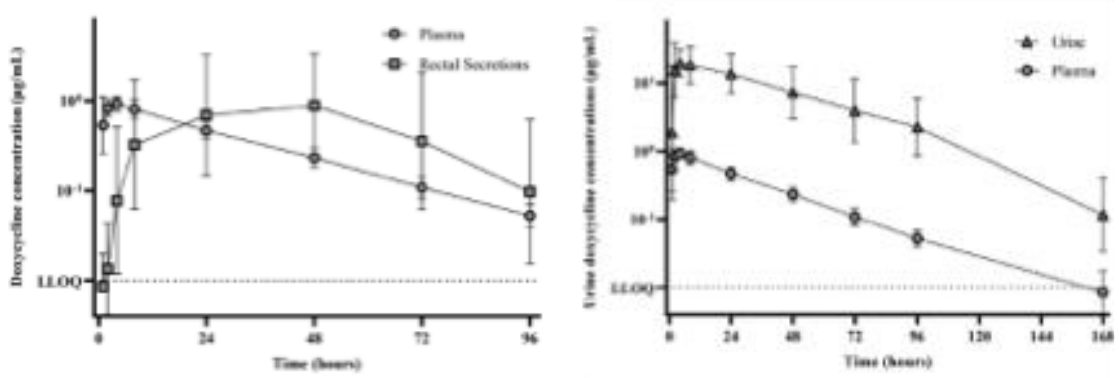
[a]Values presented as time geometric mean concentrations remain above 90% minimum inhibitory concentration (MIC) or 4 times MIC (hours) [95% confidence interval]. [b]Values presented as time geometric mean concentrations remain above minimum inhibitory concentration (MIC) or 4 times MIC (hours) [95% confidence interval]. [c]Seven female participants provided rectal secretions.

Table 4: Time estimated geometric mean concentrations remain above minimum inhibitory concentrations in hours in plasma, rectal and vaginal secretions among male and female participants receiving a single dose of doxycycline.

Doxycycline concentrations in plasma, rectal, vaginal, cervical tissues, and urine and estimated rectal, vaginal secretions, urethral and glans surface secretions concentrations collected 24 h after a single oral dose.



Mean plasma doxycycline concentrations and estimated mean rectal and urine concentrations collected following a single oral dose (geometric mean concentrations and 95% confidence intervals are presented from 1 to 96 h following dosing).



Haaland RE, eBioMed 2024.

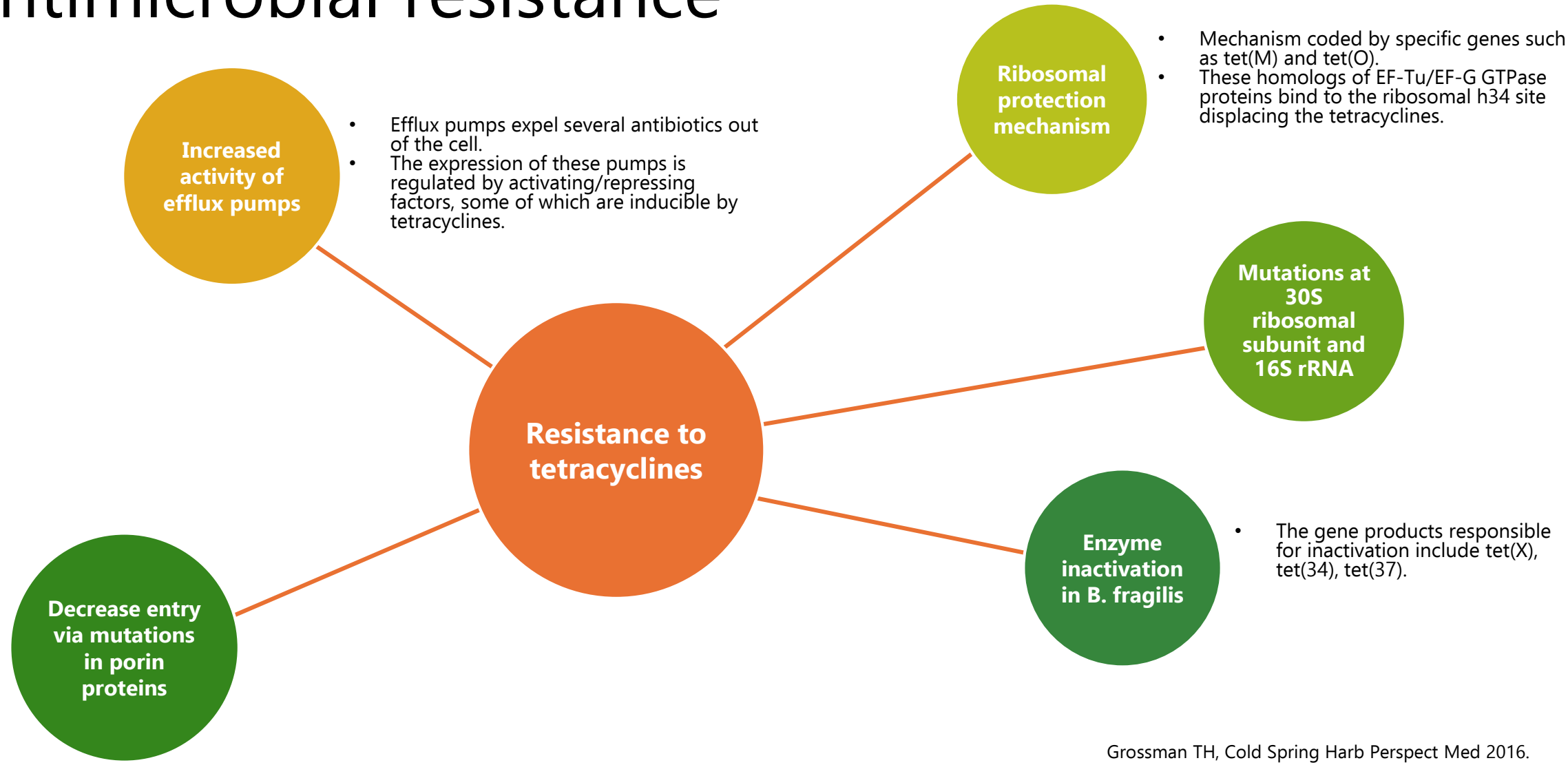
Tetracycline resistance in N. gonorrhoeae isolates (N=4,787) cultured in 19 EU/EEA countries in 2022

Countries (no. of isolates)	MIC range (mg/L)	MIC_{50} (mg/L)	MIC_{90} (mg/L)	EUCAST-no. of resistant isolates (%)[a]	CLSI-no. of resistant isolates (%)[b]	Tetracycline susceptibility testing method[c]
Austria (n = 379)	0.125–128	1	32	278 (73.4)	178 (47.0)	Decentralised, MGST
Belgium (n = 669)	≤0.125–≥128	1	32	516 (77.1)	253 (37.8)	Decentralised, AD
Bulgaria (n = 12)	0.25–32	1	16	9 (75.0)	2 (16.7)	Centralised, MGST
Czechia (n = 112)	0.125–64	1	32	57 (50.9)	24 (21.4)	Centralised, MGST
Estonia (n = 7)	0.064–16	0.5	16	1 (14.3)	1 (14.3)	Decentralised, MGST
France (n = 220)	0.25–>256	2	32	203 (92.3)	126 (57.3)	Decentralised, MGST
Germany (n = 200)	0.25–256	2	32	173 (86.5)	158 (79.0)	Decentralised, MGST
Greece (n = 100)	0.032–16	0.5	1	33 (33.0)	7 (7.0)	Decentralised, MGST
Hungary (n = 122)	0.125–128	1	16	73 (59.8)	26 (21.3)	Centralised, MGST
Ireland (n = 248)	0.125–32	0.5	1	114 (46.0)	20 (8.1)	Decentralised, MGST
Malta (n = 61)	0.064–32	0.5	8	20 (32.8)	16 (26.2)	Decentralised, MGST
The Netherlands (n = 196)	0.125–64	1	16	128 (65.3)	39 (19.9)	Centralised, MGST
Norway (n = 827)	0.032–64	0.5	16	324 (39.2)	170 (20.6)	Decentralised, MGST
Poland (n = 15)	0.5–16	1	4	8 (53.3)	2 (13.3)	Centralised, MGST
Portugal (n = 841)	0.25–>256	2	64	788 (93.7)	693 (82.4)	Decentralised, MGST
Slovakia (n = 80)	0.125–32	0.5	16	37 (46.3)	19 (23.8)	Centralised, MGST
Slovenia (n = 285)	0.032–32	0.5	1	71 (24.9)	14 (4.9)	Decentralised, MGST
Spain (n = 213)	0.064–32	0.25	2	39 (18.3)	22 (10.3)	Decentralised, MGST
Sweden (n = 200)	0.125–>256	1	32	162 (81.0)	80 (40.0)	Decentralised, MGST
Total = 4787	**0.032–>256**	**1**	**16**	**3034 (63.4%)**	**1850 (38.6%)**	

[a]Based on the clinical tetracycline resistance breakpoint (MIC>0.5 mg/L) stated by EUCAST. [b]Based on the clinical tetracycline resistance breakpoint (MIC>1.0 mg/L) stated by the US CLSI. [c]Tetracycline MICs (mg/L) were determined either by MIC gradient strip test, according to manufacturer's instructions, or agar dilution.

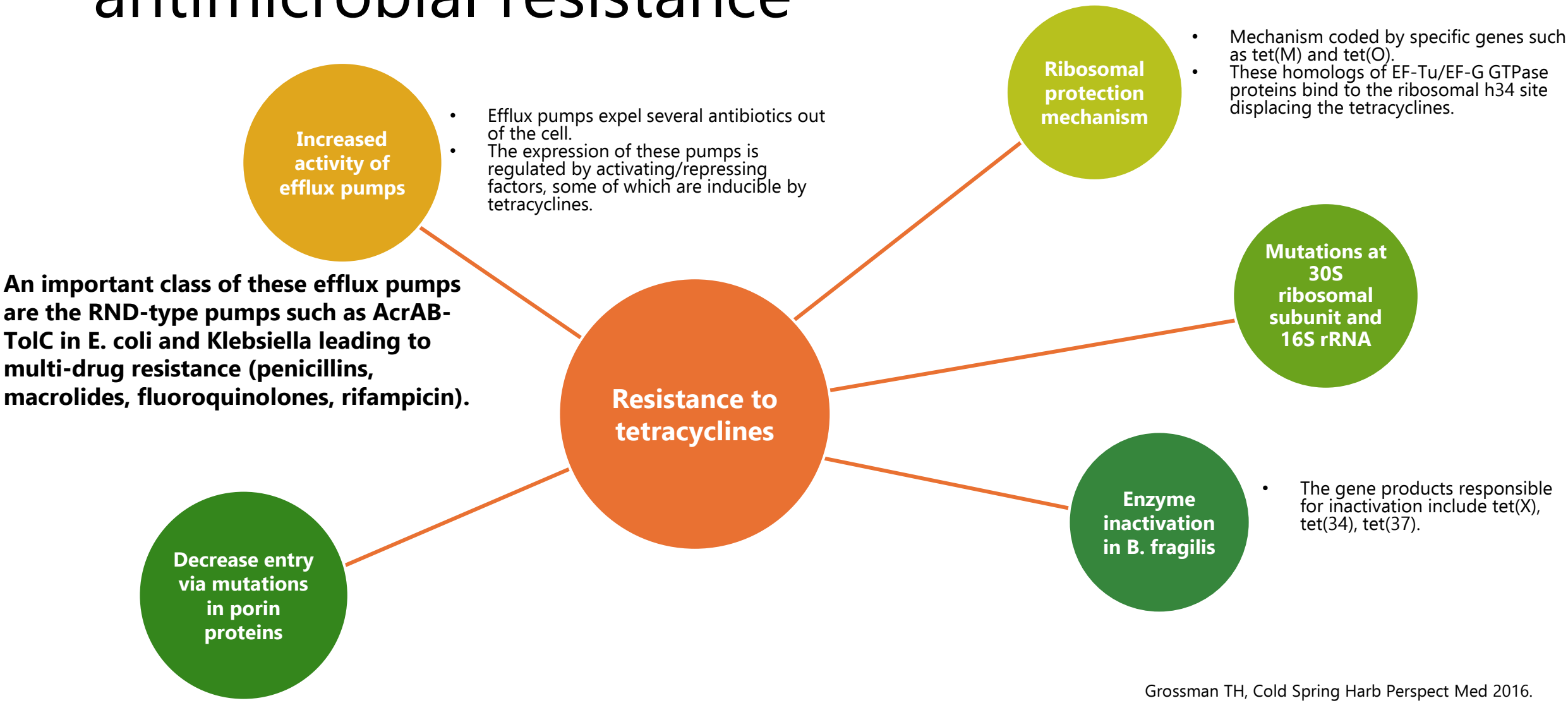
Unemo M, Lancet Reg Health 2024

Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance



Grossman TH, Cold Spring Harb Perspect Med 2016.

Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance



Grossman TH, Cold Spring Harb Perspect Med 2016.

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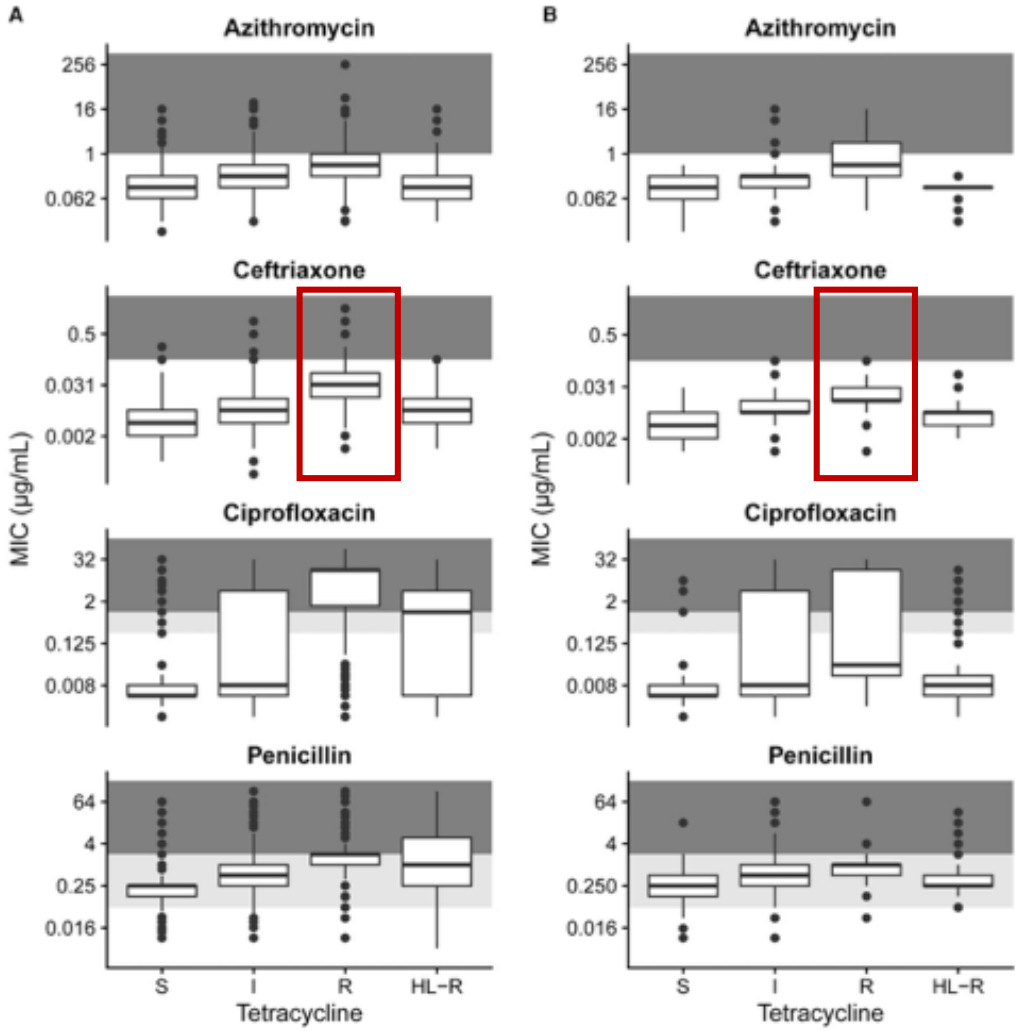
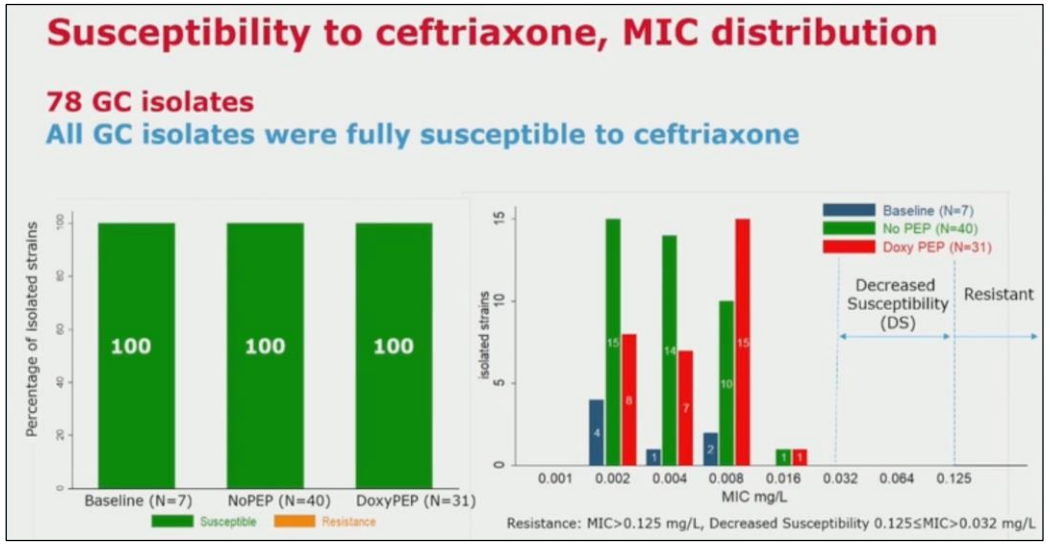
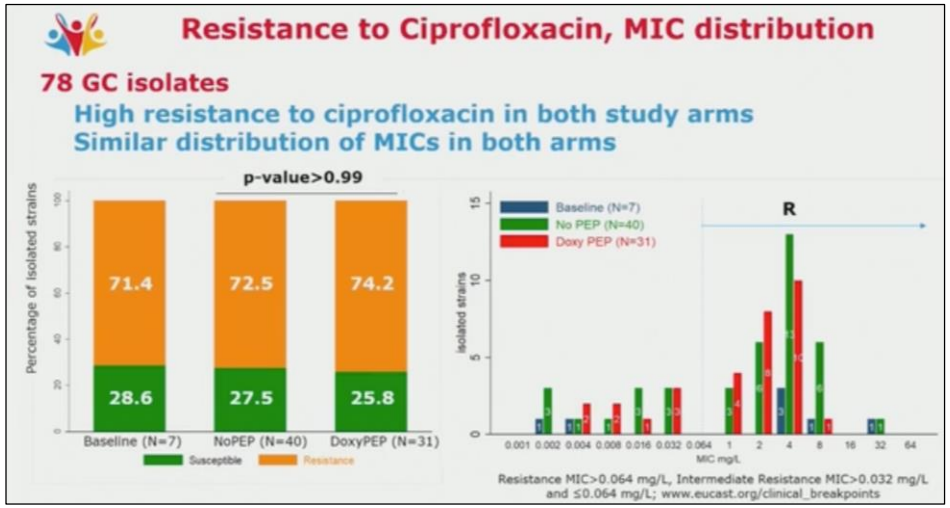


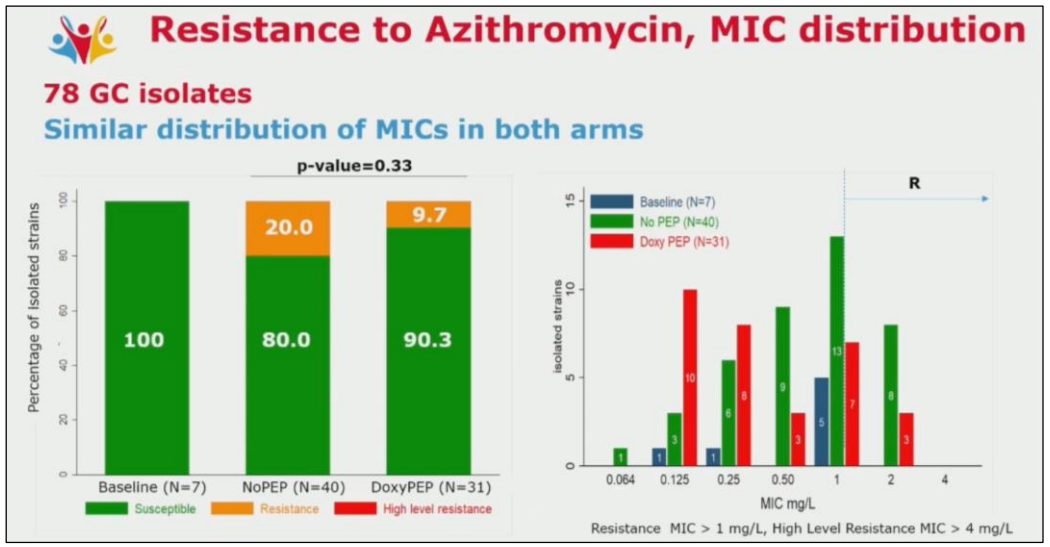
- Co-resistance with other antimicrobials is highest among isolates with chromosomally encoded resistance to tetracyclines.
- Isolates were classified as susceptible (MIC≤0.25 µg/mL), intermediate (0.25< MIC<2 µg/mL), resistant (2≤MIC≤8 µg/mL), or high-level resistant (MIC>8 µg/mL) in 5,644 global N. gonorrhoeae isolates (A) and 1,041 isolates collected in the United States in 2018 (B).
- Background shading corresponds to susceptible (white), intermediate (light gray), and resistant/non-susceptible (dark gray) MICs for each antimicrobial.

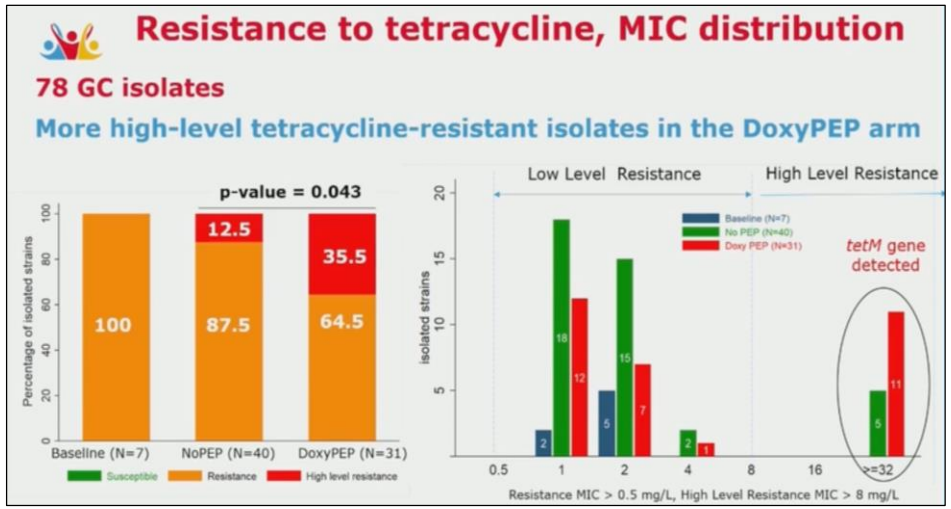
Mortimer TD, Clin Infect Dis 2023.

Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance



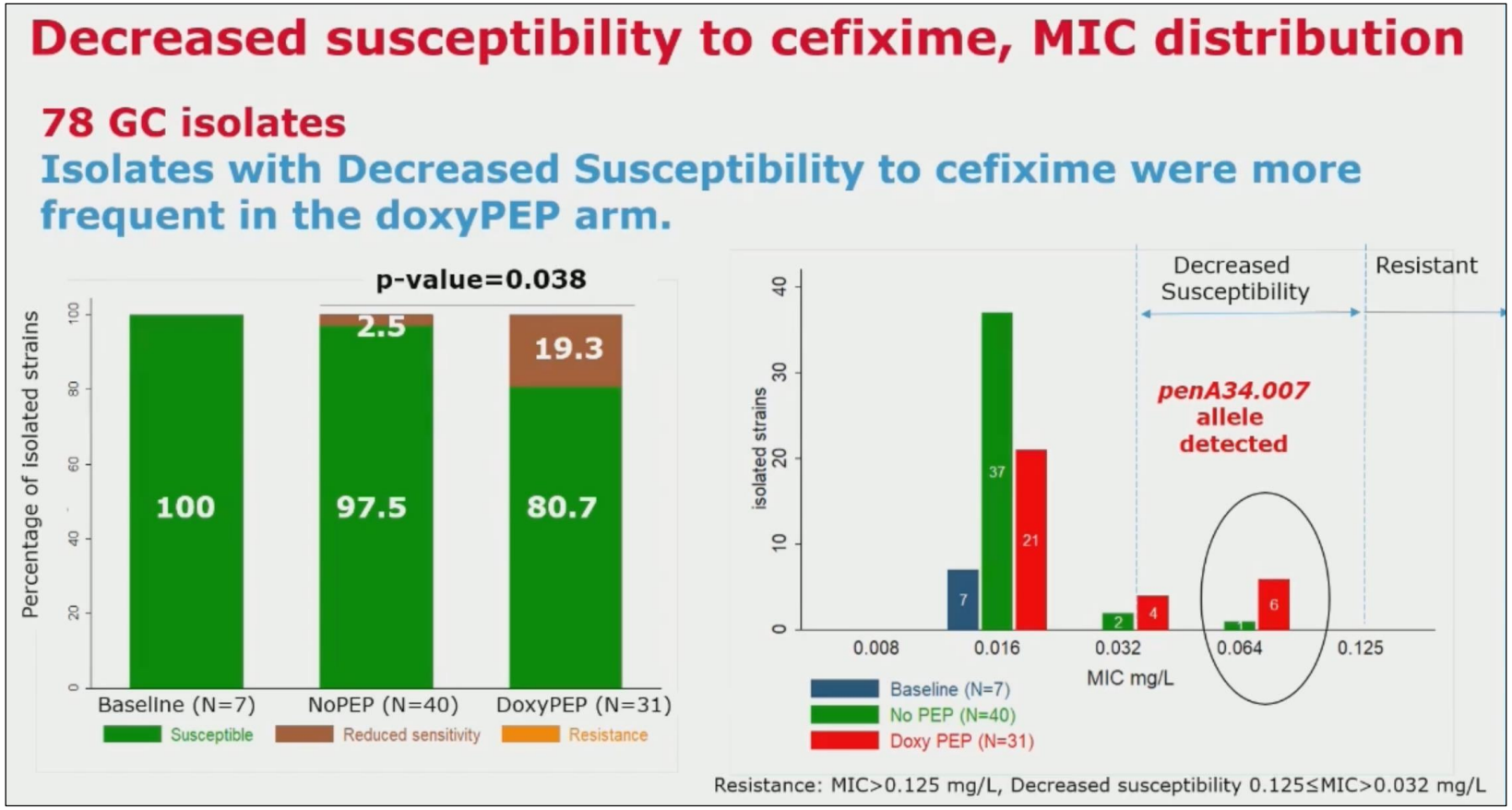






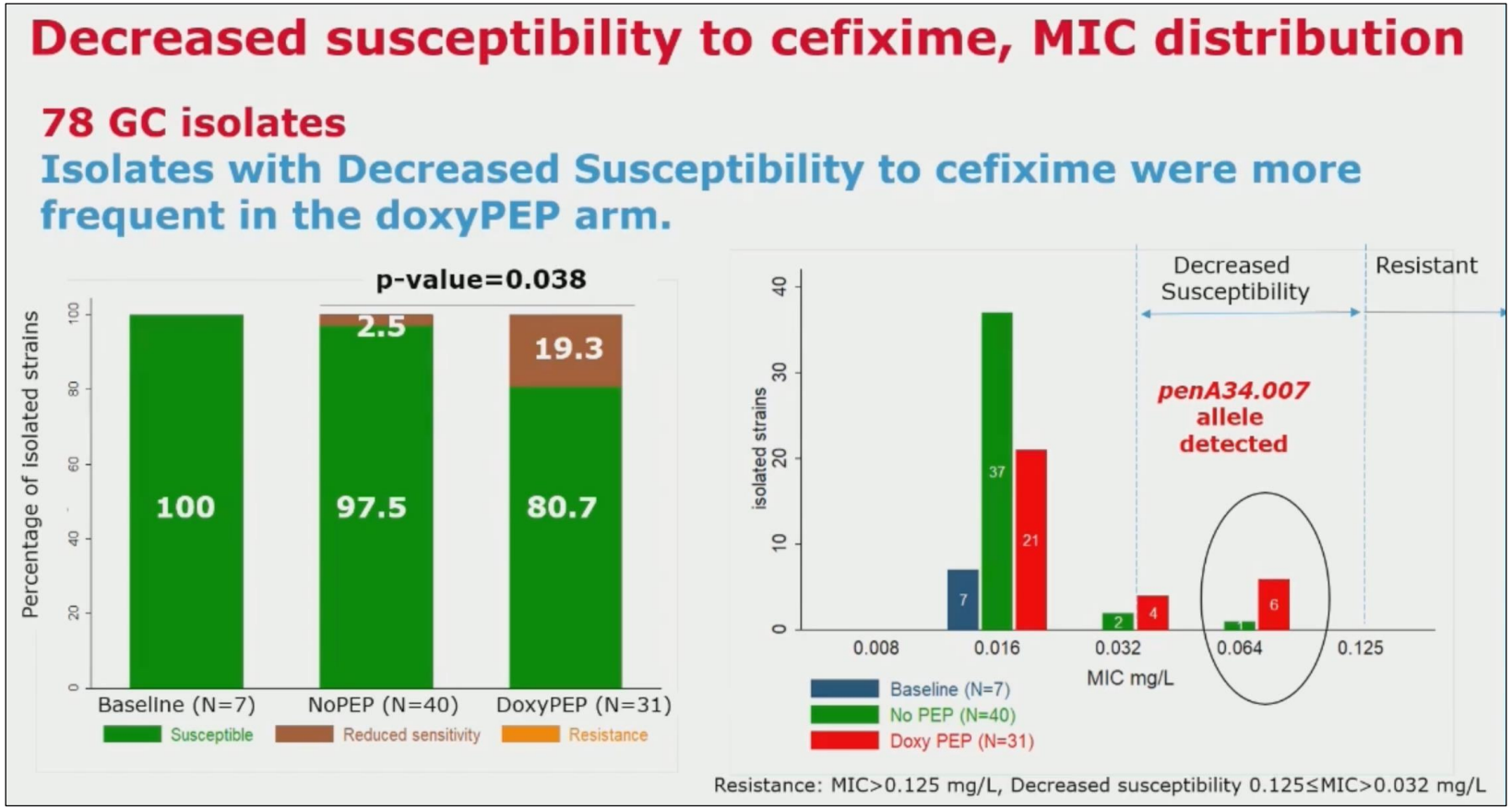
Berçot B, International AIDS Conference 2024.

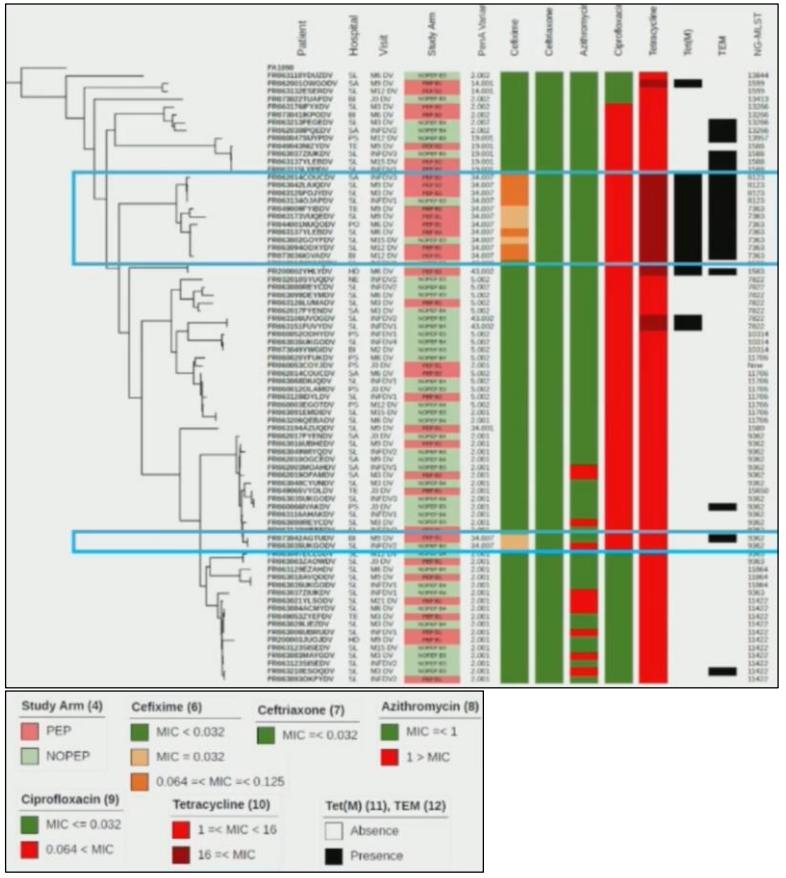
Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance



Berçot B, International AIDS Conference 2024.

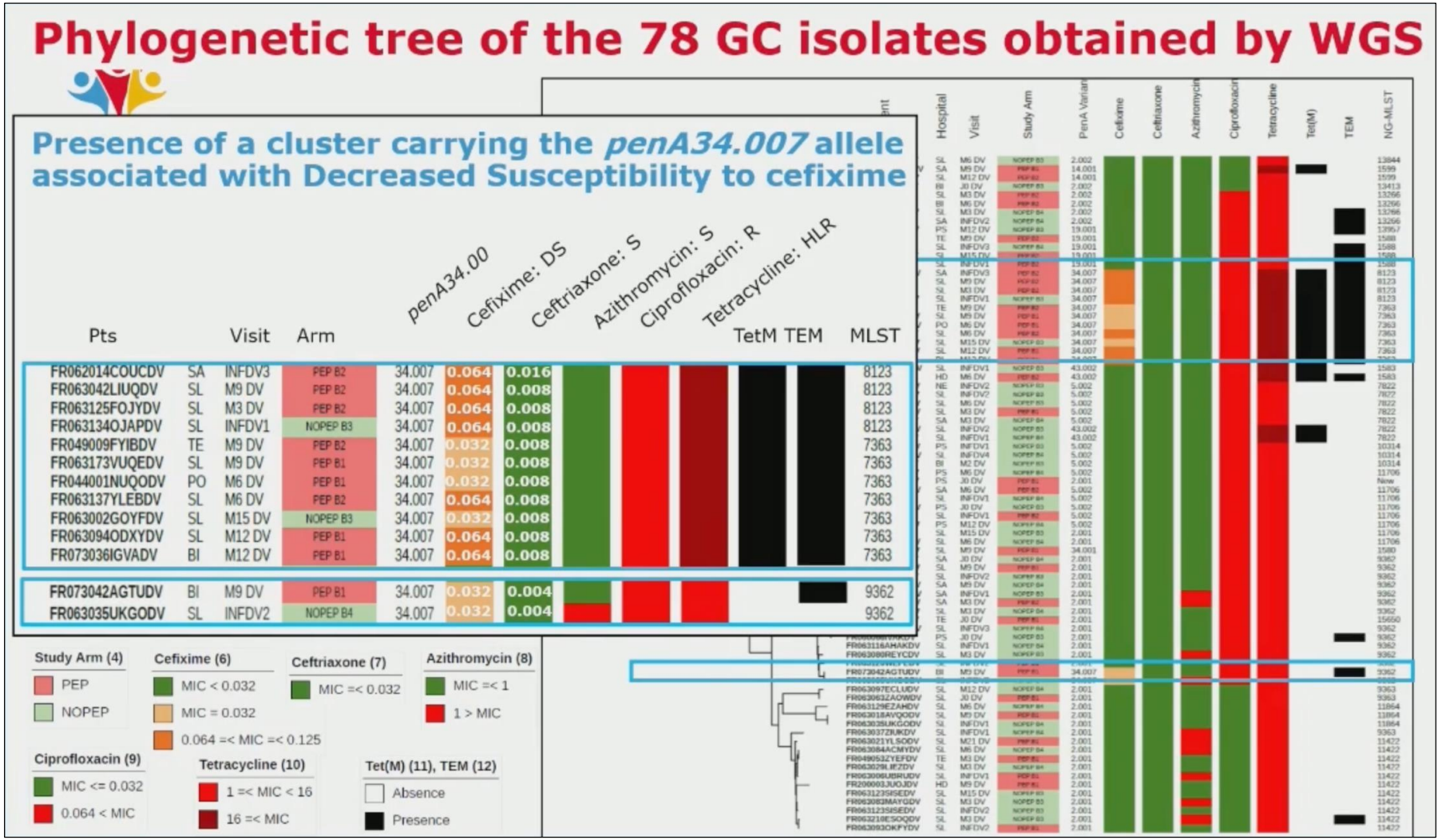
Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance





Berçot B, International AIDS Conference 2024.

Impact of DoxyPEP on N. gonorrhoeae antimicrobial resistance



Berçot B, International AIDS Conference 2024.

Users' DoxyPEP uptake

- A small German online survey showed that more than **one quarter** of the respondents employed doxyPEP using pills left over from previous doxycycline treatments. Self-prescribed doxyPEP use was reported by **54%** participants in a similar Spanish online investigation.
- According to the Italian SIMIT survey, **46.1%** of ID specialists have the perception that doxyPEP *sauvage* is occurring.

Source of information about doxyPEP.

		DoxyPEP aware (N=198)	Never used doxyPEP (N=136)	DoxyPEP users (N=62)	p
Source of doxyPEP information, n (%)	Friends	77 (41.0)	57 (41.9)	23 (20.4)	0.841
	Sexual partner	9 (4.8)	4 (2.9)	5 (8.8)	0.080
	General Practitioner	**9 (4.8)**	**6 (4.4)**	**3 (5.3)**	**0.798**
	PrEP staff	**36 (19.2)**	**18 (13.2)**	**19 (33.3)**	**0.001**
	NGO volunteers	**7 (3.7)**	**5 (3.7)**	**2 (3.5)**	**0.955**
	Internet	69 (36.7)	50 (36.8)	20 (35.1)	0.825
	Other	14 (7.5)	11 (8.1)	3 (5.3)	0.490

Hornuss D, Infection 2023; Sergio VB, Infection 2024;
Raccagni AR, XXIII Congresso Nazionale SIMIT 2024; Rossotti R, Sex Transm Dis 2025

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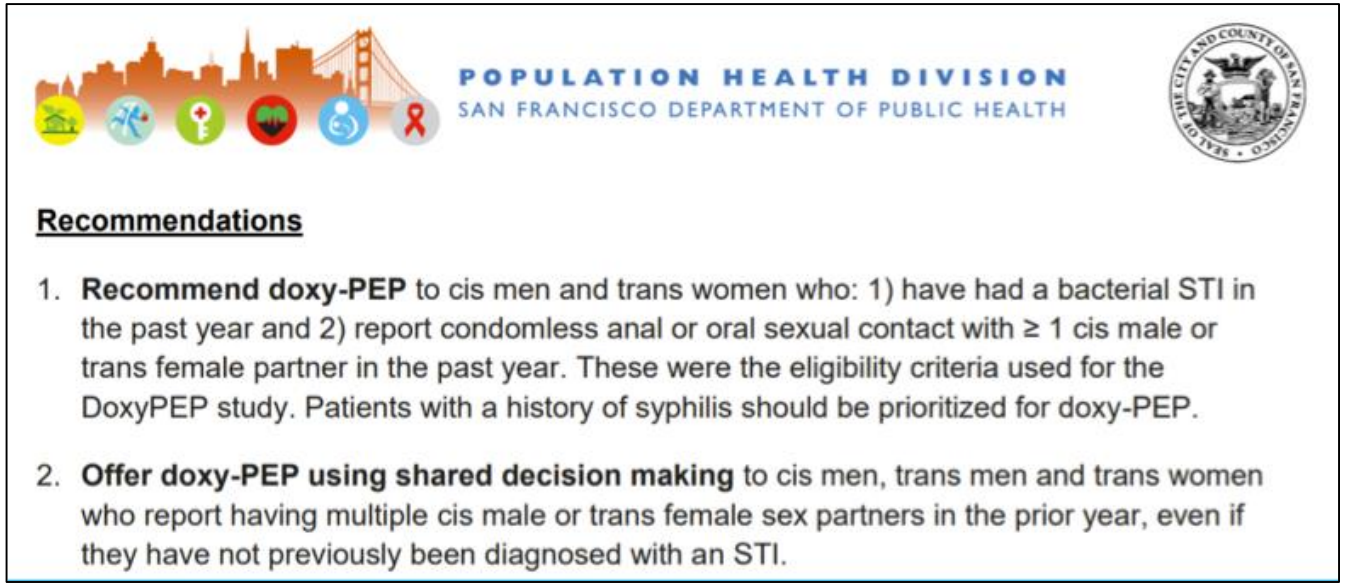
Features of doxyPEP use.			**SD, 95%CI**
Number of doxyPEP courses used in the previous 3 months, median (IQR)		1 (1-3)	1.84
Reason to use doxyPEP, n (%)	Exposure considered at major risk	17 (27.4)	5.7, 16.8-40.2
	STIs concerns	13 (21.0)	5.2, 11.7-33.2
	Sex concerns	10 (16.1)	4.7, 8.0-27.7
	Missing	22 (35.5)	6.1, 23.7-48.7
DoxyPEP taken following the right schedule, n (%)		**32 (51.6)**	**6.3, 35.6-64.5**
Errors declared while taking doxyPEP, n (%)	Wrong dose	13 (21.0)	5.2, 11.7-33.2
	Wrong timing	3 (4.8)	2.7, 1.0-13.5
	Other	14 (22.6)	5.3, 12.9-35.0

Hornuss D, Infection 2023; Sergio VB, Infection 2024;
Raccagni AR, XXIII Congresso Nazionale SIMIT 2024; Rossotti R, Sex Transm Dis 2025

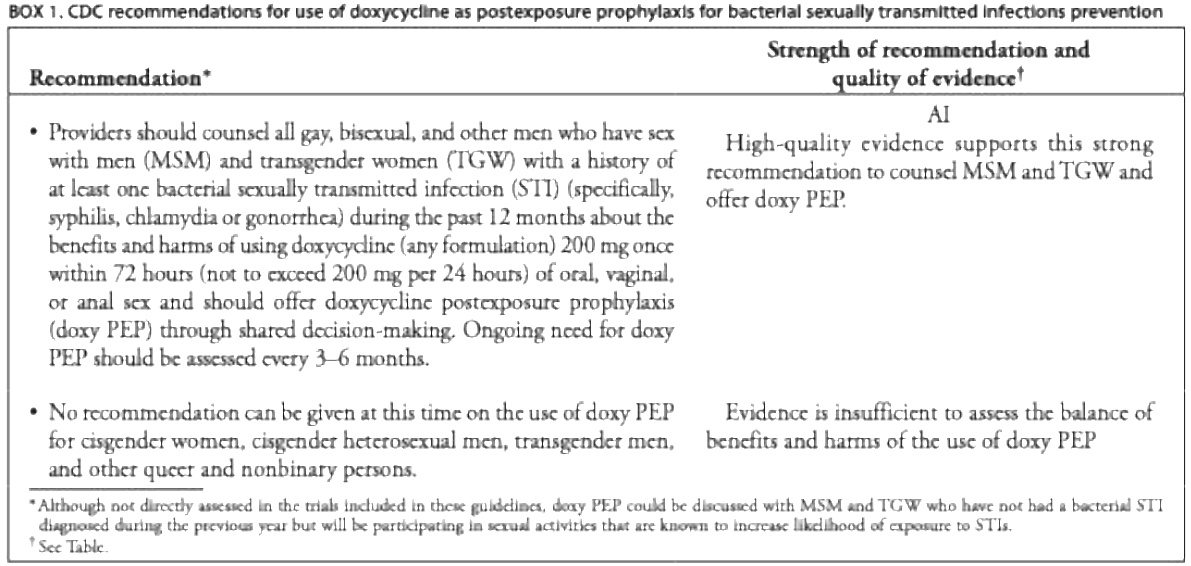
Users' DoxyPEP selection



POPULATION HEALTH DIVISION
SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

Recommendations

1. **Recommend doxy-PEP** to cis men and trans women who: 1) have had a 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. Patients with a history of syphilis should be prioritized for doxy-PEP.
2. **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.



BOX 1. CDC recommendations for use of doxycycline as postexposure prophylaxis for bacterial sexually transmitted infections prevention

Recommendation*	Strength of recommendation and quality of evidence†
• Providers should counsel all gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) with a history of at least one bacterial sexually transmitted infection (STI) (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months about the benefits and harms of using doxycycline (any formulation) 200 mg once within 72 hours (not to exceed 200 mg per 24 hours) of oral, vaginal, or anal sex and should offer doxycycline postexposure prophylaxis (doxy PEP) through shared decision-making. Ongoing need for doxy PEP should be assessed every 3–6 months.	AI High-quality evidence supports this strong recommendation to counsel MSM and TGW and offer doxy PEP.
• No recommendation can be given at this time on the use of doxy PEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons.	Evidence is insufficient to assess the balance of benefits and harms of the use of doxy PEP

*Although not directly assessed in the trials included in these guidelines, doxy PEP could be discussed with MSM and TGW who have not had a bacterial STI diagnosed during the previous year but will be participating in sexual activities that are known to increase likelihood of exposure to STIs.
†See Table.

- The draft of French guidelines suggests to offer doxyPEP to GBMSM and TGW who had at least 2 STIs in the previous years.
- DoxyPEP use was recommended for intensive sexual activity (more than five partners in 72 hours).

San Francisco Disease Prevention & Control, 2022; Bachmann LH, MMWR Recomm Rep 2024; Raccagni AR, Lancet Infect Dis 2025.

Users' DoxyPEP selection

251
- Individuals with at least one STI in the previous year.

129
- STIs registered in the same individuals in the following year.

85
- Number of infections (95%CI 70-98) that would be averted if doxyPEP was taken.

162
- Number of individuals without STIs in the following year (**64.5%**) who would have had antibiotic overuse if they had taken doxyPEP.

Rossotti R, CROI 2025.

Other DoxyPEP issues

- The efficacy in cis women is low.
  - A small study on Japanese SW showed good efficacy.
- Doxycycline has a well-known toxicity profile: **6.1% skin rash**, **4.2% more readily sunburned**, 8.2% headache, 12.1% diarrhea, **2.2% pain with swallowing**.
- DoxyPEP might be cost-effective if used for syphilis and Chlamydia (but not for gonorrhea) with a more targeted selection of users.
- Delayed serologic syphilis diagnosis is fascinating but no data so far.

Stewart J, N Engl J Med 2023; Abe S, IAS 2025; Luetkemeyer AF, N Engl J Med 2023;
Lai H, medRxiv 2024; Ard KL, ID Week 2023

Take home messages

- DoxyPEP is safe and greatly works for syphilis and Chlamydia.
  - Its role against gonorrhea is limited.
- Data on colonizing bacteria ecology seem reassuring (at least within a short term).
  - The risk of resistance development in C. trachomatis and N. gonorrhoeae is still under investigation.
- Criteria for users' selection need a better tailoring.
  - Education and counselling about doxyPEP are essential.
- Data about cis women and cost-effectiveness need additional evaluations.

THANK YOU!

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