Clinical characteristics of syphilis in MSM on Postexposure Prophylaxis with Doxycycline (Doxy-PEP)

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BACKGROUND

- In the last years, Doxycycline post-exposure prophylaxis (**Doxy-PEP**) has gained attention as an **effective** strategy to **prevent bacterial STIs** (syphilis, chlamydia, gonorrhea) among **high-risk** populations.
- Pivotal RCT demonstrated reductions of up to **70–87% in *C. trachomatis* and *T. pallidum*** infections, and **~50% in *N. gonorrhoeae*** incidence[1].
- Following these findings, **real-world implementation programs** report rapid uptake of Doxy-PEP among PrEP users and sexual health clinic attendees[2,3].
- One of the potencial **limitation** of Doxy-PEP use is **interference** with **syphilis serologic** diagnosis.
- **This study aimed to describe the characteristics of syphilis cases diagnosed in individuals enrolled in a Doxy-PEP program within a real-life cohort.**

METHODS

- Participants were recruited between March 2023 and April 2025 in a Doxy-PEP study (***PRIDOX study***, CROI 2025 Abstract 1275 and JAC 2025[3]).
- STI screening was performed every 3–6 months or upon symptoms.
- Syphilis diagnosis followed commonly accepted criteria.
- Doxycycline adherence was classified as **poor** (<4 doses/month), **moderate** (<8 doses/month), or **good** (>8 doses/month).

Table 1: Doxy-PEP population

Characteristics of the 313 participants	
Men who have sex with men (MSM)*	310 (99%)
Age in years (mean ± SD)	38.9 ± 8.5
Spanish	231 (73.8%)
High educational level	164 (52.4%)
Chemsex	121 (38.6%)
≥ 10 sexual partners per month	**111 (35.5%)**
Condom use	
- Never	34 (10.9%)
- Hardly ever	83 (26.5%)
- Sometimes	123 (39.3%)

*3TGW

In real-world conditions, **syphilis** incidence among **Doxy-PEP** users is **low** and comparable to clinical trials. Most cases were **asymptomatic**, with **minimal RPR increases.**

RESULTS

- **Nine cases** of syphilis were diagnosed among 313 participants (**prevalence 2.88%;** 95% CI: 1.02–4.73), with an **incidence of 1.92 episodes per 100 person-years** (95% CI: 0.67–3.17).
- Characteristics of people on Doxy-PEP are shown in **Table 1.**
- The **mean time** from Doxy-PEP initiation **to syphilis** diagnosis was **37.1 weeks** (± 23.2).
- All cases occurred in **MSM** (8 on PrEP and 1 PLHIV).
- Cases details are shown in **Table 2.**
- All patients responded **favorably** to a single dose of **benzathine penicillin G**, with **RPR negativization in all cases.**

Table 2: Cases of syphilis among Doxy-PEP users

Case	Age	Status	Previous Syphilis	Doxy-PEP initiation	Syphilis date	RPR at Doxy-PEP	RPR at Syphilis	Clinical	Other STIs	Adherence	Response
1	41	PrEP	yes	05/10/23	08/04/23	Neg	1/8	Latent	NG	regular	yes
2	34	PrEP	yes	05/18/23	08/10/23	1/4	1/32	Latent	no	poor	yes
3	37	PrEP	yes	06/28/23	08/08/24	Neg	1/4	Latent	no	regular	yes
4	44	PLHIV	yes	07/07/23	04/12/24	Neg	1/4	Secondary	NG	good	yes
5	49	PrEP	no	07/02/23	02/22/24	Neg	1/2	Primary*	no	good	yes
6	47	PrEP	yes	08/01/23	11/30/23	Neg	1/8	Latent	no	regular	yes
7	29	PrEP	yes	11/15/23	07/22/24	1/1	1/4	Secondary	no	regular	yes
8	28	PrEP	yes	07/07/23	03/26/25	1/1	1/4	Latent	no	regular	yes
9	27	PrEP	no	11/15/23	07/22/24	Neg	1/4	Latent	NG/CT	good	yes

*Cutaneus lesions and genital chancre with positive PCR assay for *Treponema pallidum*; NG= *Neisseria gonohrroeae*; CT= *Chlamydia trachomatis.*

CONCLUSIONS

- In real-world conditions, **syphilis incidence** among **Doxy-PEP** users **is low** and comparable to clinical trials.
- Most cases are **asymptomatic**, with **minimal RPR increases.**
- Treatment with **benzathine penicillin G** remains **effective**.
- **Adequate adherence** to Doxy-PEP may be **key** to reducing syphilis incidence.

DISCUSION

Expanding use of Doxycycline-PEP brings new challenges for syphilis management

Major uncertainties remain regarding its impact on:

- ✓ ***Diagnosis and serologic interpretation of syphilis****, due to potential partial suppression or delayed antibody response after intermittent doxycycline exposure.*
- ✓ ***RPR/VDRL titre kinetics****, potentially complicating distinction between reinfection and treatment response.*
- ✓ *Public health surveillance, given possible **"silent" or serologically atypical infections.***
- ✓ ***Antimicrobial resistance*** *and microbiome shifts.*

References:

1. Szondy I et al. Int J Infect Dis, 2024.
2. Osmundson J et al. Open Forum Infectious Diseases, 2025
3. Palacios R et al. JAC, 2025.

This study aimed to describe the characteristics of syphilis cases diagnosed in people on Doxy-PEP: Incidence is low, mostly asymptomatic and with minimal RPR increases.

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