Differential Risk Reduction of Gonorrhea and Chlamydia Among DoxyPEP Users Reporting High Adherence

1038

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Background

- Clinical trials and implementation studies demonstrate that doxyPEP reduces STI risk among people assigned male sex at birth.
- Population-level studies have documented diminished STI transmission in populations of cisgender men and transgender people who have sex with men (MTSM) where doxyPEP has been scaled.
- Reduced STI transmission may occur even when many individuals in a population do not consistently use doxyPEP.
- There are no studies to date that have evaluated whether consistent use (e.g. high adherence) of doxyPEP confers significantly different levels of protection from STIs compared to occasional or inconsistent use.

Objective: Quantify STI risk reduction associated with high adherence to doxyPEP compared to inconsistent use, using real-world clinical data.

Methods

Data source: Client data from San Francisco AIDS Foundation's Magnet program, a large sexual health clinic in San Francisco, September 2023-August 2025

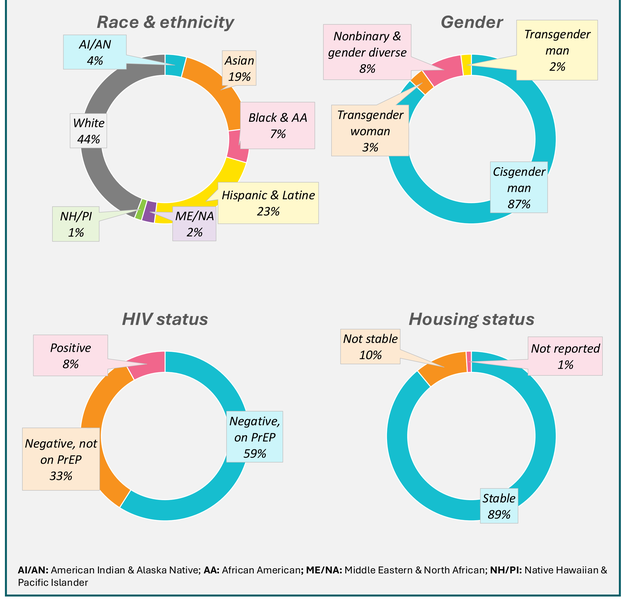
Study design: Retrospective cohort study

Key variables:

- **DoxyPEP use** among all clients, defined as "present" where the client record indicated an active doxyPEP prescription and "absent" otherwise.
- **DoxyPEP adherence** among doxyPEP users defined as "high" where clients reported always using doxyPEP as directed with 72 hours of a sexual encounter since their last visit or "inconsistent" where clients reported "often," "sometimes," "rarely," or "never" using doxyPEP as prescribed since their last visit.
- **Gonorrhea & chlamydia diagnoses** defined as "present" when ≥1 anatomical site tested positive for gonorrhea or chlamydia, respectively, and "absent" otherwise.
- **Syphilis diagnosis** defined as "present" when a client was diagnosed with new syphilis and "absent" otherwise.

This cohort study found that clients who reported **always using doxyPEP** following a sexual encounter had **reduced risk of gonorrhea or chlamydia diagnosis** compared to those who reported inconsistent use.

Figure 1: Demographic & Health Characteristics of Magnet Clinic Clients, 09/2023-08/2025 (N=8,188)



AI/AN: American Indian & Alaska Native; **AA:** African American; **ME/NA:** Middle Eastern & North African; **NH/PI:** Native Hawaiian & Pacific Islander

Analytic method: Multivariate Poisson log regression models using generalized estimating questions with robust standard errors, accounting for within-participant clustering, to **produce adjusted relative risks (aRR) for incident syphilis, gonorrhea, and chlamydia** associated with **any doxyPEP use** and, among users, **high doxyPEP adherence.** Each STI was treated as a dependent variable in separate models. All models were adjusted for number of sex partners reported in the last year; housing stability; and length of doxyPEP use.

Results

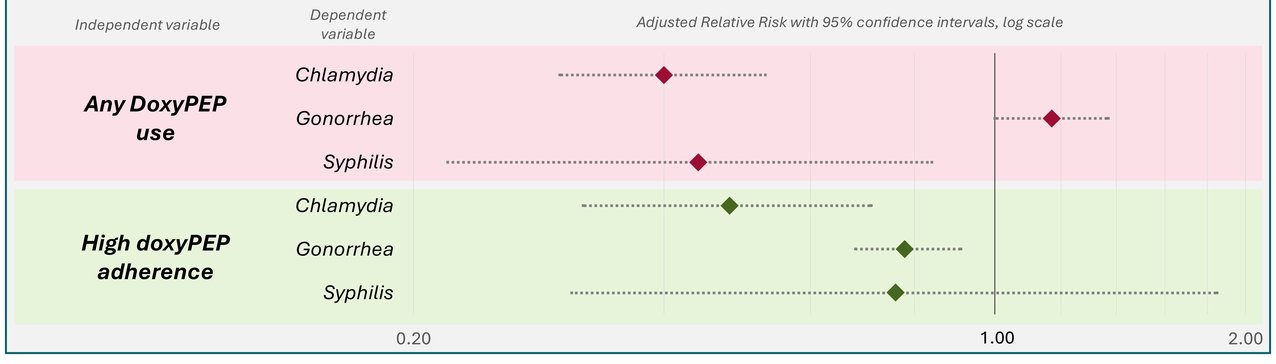
Descriptive results *(Figure 1)*

- Records of 8,188 unique clients seen over 22,992 visits during the study period were included in the analyses; 43% reported taking doxyPEP at their most recent visit.
- Clients were primarily (88%) cisgender men; 59% were HIV-negative PrEP users; and 89% reported stable housing at their last visit.
- Participants reported a median of 5 (IQR: 2, 10) sex partners in the past 12 months. Among those using doxyPEP, clients used it for a median of 9 months (IQR: 0, 22 months).

Inferential results *(Figure 2)*

- Any doxyPEP use was associated with **decreased risk of chlamydia** (aRR: 0.40 [95% CI: 0.30, 0.53]) **and syphilis** (0.44 [0.22, 0.84]) and with **higher risk of gonorrhea** (1.17 [1.00, 1.37]).
- Among doxyPEP users, high doxyPEP adherence was associated with **decreased risk of both chlamydia** (0.48 [0.32, 0.71]) **and gonorrhea** (0.78 [0.68, 0.91]) but **not syphilis** (0.76 [0.31, 1.85]).

Figure 2: Adjusted relative risks (aRR) for chlamydia, gonorrhea, and syphilis given any doxyPEP use and, among doxyPEP users, high adherence among Magnet Clinic Clients, 09/2023-08/2025 (N=8,188) – *log scale*



Conclusions

- We add to what is known by **disaggregating risk of incident STIs among doxyPEP users by self-reported adherence** over 3 years of clinical visits.
- Among doxyPEP users, the **consistent use of doxyPEP** – compared with inconsistent use – is associated with **a greater risk reduction of chlamydia and gonorrhea.**
- Additional adherence support may be needed to realize the greatest benefit of DoxyPEP on STI incidence, since consistent use may be required to reduce the risk of gonorrhea.
- Our analyses were limited by a small number of incident syphilis cases in the cohort (N=108), which may reflect the local impact of successful doxyPEP scale-up on syphilis incidence.

Implications for Further Study

- More formal and/or biological measurements of doxyPEP adherence may produce more precise, causal estimates of corresponding STI risk reduction.
- Studies with larger cohorts (e.g. more statistical power) and/or in populations with higher syphilis incidence may reveal more precise estimates of syphilis risk reduction due to high doxyPEP adherence.

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