Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Sex Transm Dis. Author manuscript; available in PMC 2025 July 31.

Published in final edited form as:

Sex Transm Dis. 2025 December 01; 52(12): 734–738. doi:10.1097/OLQ.0000000000002224.

Doxycycline post-exposure prophylaxis is effective and highly acceptable in an urban public sexually transmitted disease clinic: Philadelphia, 2019–2023

Felicia M. T. Lewis, MD[1,2], **Anna B. Cope, PhD**[1], **Kelly Clark, MPH**[2], **Robbie Madera, MPH**[2], **Lenore Asbel, MD**[2], **Daniel R. Newman, MPH**[1], **Nicole L. Davis, PhD**[1]

[1.]Division of STD Prevention, Centers for Disease Control and Prevention

[2.]STD Control Program, Philadelphia Department of Public Health

Abstract

Background: We sought to determine real-world effectiveness of doxycycline post-exposure prophylaxis (doxy PEP) in reducing sexually transmitted infections (STI) among men who have sex with men attending an HIV pre-exposure prophylaxis (HIV PrEP) clinic in Philadelphia.

Methods: Data from eligible HIV PrEP patients who did and did not receive doxy PEP from September 1, 2019-December 31, 2023 were analyzed. We used a cohort study design and Cox models to estimate associations between doxy PEP receipt and incident gonorrhea (GC), chlamydia (CT), and/or syphilis. We also used a crossover design and Poisson models to estimate incidence rate ratios (IRR) for any STI and each STI separately among individuals in the year before and after doxy PEP initiation.

Results: Among the 508 eligible men, most were young men of color and 416 (82%) opted to receive doxy PEP. Receiving doxy PEP was associated with a reduction in any incident STI (hazard ratio [HR] 0.61, 95% confidence interval 0.40–0.93) and any incident CT (HR 0.40, 95% CI 0.21–0.78). Participants experienced a 62% relative reduction in STI rates while taking doxy PEP (IRR 0.38 (95% CI 0.29–0.50), including a reduction in CT (IRR 0.28, 95% CI 0.20–0.39) and GC (IRR 0.49, 95% CI 0.37–0.65).

Conclusions: We observed a significant reduction in any STI and CT in both analytic arms, suggesting that doxy PEP is effective in real-world settings. Enhancing doxy PEP implementation would likely reduce community STI transmission.

Short summary:

Doxycycline post-exposure prophylaxis significantly reduced bacterial STI generally, and *Chlamydia trachomatis* specifically, in a diverse group of young men who have sex with men attending a real-world HIV PrEP clinic.

Corresponding author: Felicia Lewis, MD, 1930 S. Broad Street, Philadelphia PA 19145 bwe1@cdc.gov.

No authors report any conflicts of interest for this study.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Background

Doxycycline post-exposure prophylaxis (doxy PEP) is a strategy where patients may choose to take one dose of 200 mg of doxycycline within 72 hours of condomless sex to prevent bacterial sexually transmitted infections (STI), particularly chlamydia (CT) and syphilis. Based on its efficacy in clinical trials among gay, bisexual, and other men who have sex with men (MSM)[1–3], public health authorities, including the Centers for Disease Control and Prevention (CDC), have issued guidelines for doxy PEP use among MSM and other specific populations[4,5]. Evidence from San Francisco has demonstrated declines in bacterial STI following issuance of local doxy PEP guidelines[6,7] and among individuals taking doxy PEP in a large integrated health system[8] and a Federally Qualified Health Center[9]; however, data on effectiveness of doxy PEP outside of clinical trials remains limited.

Similar to many US jurisdictions, in 2015, Philadelphia began experiencing steep increases in syphilis rates[10], with limited means of stopping transmission. In 2019, following the publication of the IPERGAY trial that demonstrated doxy PEP efficacy for reducing syphilis and CT among MSM taking event-driven HIV PrEP[1], the Philadelphia Department of Public Health (PDPH) began offering doxy PEP to patients attending its HIV pre-exposure prophylaxis (HIV PrEP) clinic, Health Center #1. Most PDPH HIV PrEP patients are uninsured, and the majority identify as Black or Hispanic. We sought to evaluate the effectiveness of doxy PEP at preventing bacterial STI among these patients. Specifically, we used PDPH clinic and surveillance data to compare STI incidence among those receiving versus not receiving doxy PEP; to compare incidence of bacterial STI among doxy PEP recipients before and after initiation of doxy PEP; and to describe usage patterns of doxy PEP among the clinic population.

Methods

Clinical protocols:

Health Center #1 (HC#1) is the larger of 2 dedicated public STI clinics run by PDPH. All care is free of charge to all Philadelphia residents and most medications are dispensed on site. Any patient can enroll in the HIV PrEP program if they feel they are at increased risk for HIV acquisition and some patients are referred from other providers. HIV PrEP visits are scheduled every 3 months; at each visit, patients see a provider, have a thorough sexual history and counseling including provision of condoms, and are screened for HIV and syphilis. Patients are screened for CT and gonorrhea (GC) at all exposure sites using dual nucleic acid amplification tests. A new syphilis infection is defined as a reactive rapid plasma reagin (RPR) and/or treponemal-specific test in an individual with a prior non-reactive test, or a fourfold increase in RPR titer in a previously treated individual. Diagnoses are reported to the patient; any treatment is either provided by or verified by clinical staff. Beginning September 1, 2019, all MSM and a sample of female HIV PrEP patients ≥18 years old were offered doxy PEP treatment during routine HIV PrEP visits. Those who accepted received additional counseling to take 200 mg within 72 hours of any condomless sex and to report any adverse events to clinic. Due to pharmacy dispensing limitations, patients who accepted doxy PEP were given 12 doses (1 bottle, 24 100 mg pills) of doxycycline per 3-month period, but patients were able to receive another 12 doses

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

prior to their next routine visit if needed. All provisions of doxycycline are documented in the electronic medical record (EMR). The EMR is shared between clinic and PDPH STI surveillance; all positive reportable STI test results from Philadelphia residents are available, as are both positive and negative test results from HC#1 and other venues funded by PDPH.

Cohort analysis methods

Eligible participants included MSM who attended ≥2 HIV PrEP clinic visits between September 1, 2019 and December 31, 2023. Participants who received doxy PEP at ≥1 of those visits were included in the doxy PEP group; those that did not were included in the HIV PrEP-only group (Table 1). Descriptive statistics were used to compare selected demographic and behavioral characteristics of those who did and did not receive doxy PEP; race/ethnicity, sex of sex partners, number of sex partners in last 90 days and number of doxy PEP doses taken were self-reported. Any STI in the past 12 months was defined as any reported positive CT, GC, or syphilis test in the 12 months prior to the date of the first visit included in this analysis (i.e., doxy PEP group: 12 months prior to doxy PEP initiation; HIV PrEP-only group: 12 months prior to first included PrEP clinic visit). Non-reactive syphilis test results were not included in the dataset. We assumed any positive tests for the same STI within 30 days to be one infection. Lab results within 14 days of doxy PEP initiation and/or >90 days after the last HIV PrEP visits were excluded. For calculation of person-time, participants were considered lost to follow-up 90 days after a HIV PrEP visit to account for missed visits but could re-enter the analysis at their next attended HIV PrEP visit within the study period (Supplementary Table). Cox models were used to calculate hazard ratios [HR] to estimate associations between doxy PEP use and any STI (incident GC, CT, and/or syphilis, primary endpoint) and each STI separately (secondary endpoint). Participants were right-censored at the first STI occurrence. Models were not adjusted for covariates as no demographic characteristics were found to be confounders.

Crossover analysis methods

Participants from the cohort analysis who had ≥1 HIV PrEP visit in the year prior to and after first receipt of doxy PEP, and who began doxy PEP between 9/1/2019 and 12/31/2022 to ensure at least 365 days of follow-up after initiation, were included (Table 1). All positive GC, CT, and/or syphilis test results from one year before and after first doxy PEP receipt were included except for those that occurred within 14 days of doxy PEP initiation (one person could have >1 positive test result contribute to the incidence rates). Person-time before doxy PEP was calculated as time from first STI specimen collection date in the year prior to doxy PEP initiation to the date of first doxy PEP receipt; person-time after doxy PEP was calculated as the number of days from doxy PEP initiation to the date of the last specimen collection (up to 365 days). We assessed all demographic and behavioral characteristics described in the cohort analysis. We calculated median number of partners in the past 90 days and number of participants with any STI in the past 12 months, starting from the first visit included in the before-doxy PEP period. We used Poisson models to estimate incidence rate ratios (IRR) and robust 95% confidence intervals (CI) for any STI and for each STI separately, comparing incidence rates in the year after doxy PEP initiation to those the year before doxy PEP initiation. Generalized estimating equations (GEE) were

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

used to account for correlation within individuals. Models were not adjusted for covariates as no demographic variables were found to be confounders.

Usage

At each visit, providers documented the number of doxy PEP doses taken by patients in a free-text EMR field. Because a large proportion of visits were missing dose information, we approximated doxy PEP usage as the proportion of visits where a bottle containing 12 doxycycline doses was dispensed either at the visit or within 90 days prior to the visit. If a bottle was dispensed at <25% of visits, usage was categorized as low; medium and high usage were defined as doxy PEP being given at 26–74% and ≥75% of visits, respectively. The maximum number of doxy PEP doses dispensed per any 90-day period was 24 (3.75 doses/month).

This study was approved by the PDPH Institutional Review Board (study 2023–35). All data analyses were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina).

Results

Overall, 508 participants were eligible for the analysis and 416 (82%) opted to receive at least one bottle of doxy PEP during an HIV PrEP visit. There were no documented reports of serious adverse events (using FDA definition) to doxy PEP[11] (FDA definition; available at and very few recorded discontinuations due to side effects (<10, including one fixed drug eruption). Of the 416 participants who received doxy PEP, 350 were included in the crossover analysis.

Select demographic and clinical characteristics of participants are presented in Table 1. All participants were MSM and most were young men of color (doxy PEP cohort: 26.4% Black, 23.8% Hispanic, median age 28; crossover: 36.3% Black, 20.9% Hispanic, median age 28). Age, race/ethnicity, sex of sex partners, and median number of sex partners during the previous 90 days were similar in those who did and did not receive doxy PEP. Doxy PEP recipients in the cohort analysis attended more HIV PrEP clinic visits (median 3; IQR 2–6) than did HIV PrEP-only participants (median 1.5; IQR 1–2), though number of clinic visits were similar during both periods of the case-crossover analysis. A larger proportion of doxy PEP participants than HIV PrEP-only participants had a reported STI within the prior 12 months in the cohort [223 (53.6%) vs. 32 (34.8%)]. In the crossover analysis, 26.9% (n=94) participants had an STI in the 12 months prior to their before-doxy PEP period (i.e., 12–24 months before initiating doxy PEP).

Cohort

Doxy PEP recipients experienced 238 incident STIs during 314.38 person-years of follow-up for an incidence rate of 0.76 (95% CI 0.66–0.87); HIV PrEP-only participants had 27 STIs during 25.43 person-years of follow-up and an incidence rate of 1.06 (95% CI 0.70–1.55). Receiving doxy PEP was associated with a reduced rate of any incident STI (HR 0.61, 95% CI 0.40–0.93) and incident chlamydia specifically (HR 0.40, 95% CI 0.21–0.78). Doxy PEP receipt was also associated with a reduced rate of incident GC (HR 0.75, 95%

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

CI 0.45–1.24) and incident syphilis (HR 0.51, 95% CI 0.17–1.54), though these differences were not statistically significant (Table 2).

Crossover

Among the 350 patients included in the crossover analysis, 204 were diagnosed with at least 1 STI in the year before they initiated doxy PEP (58%) and 140 (40%) received a STI diagnosis in the year following doxy PEP initiation. In the year before doxy PEP initiation, patients were positive for any STI at 300 of 1065 visits (28% positivity); in the year after doxy PEP initiation, patients were positive for any STI at 188 of 947 visits (20%). Positivity for GC alone and CT alone also decreased between the before- and after-doxy PEP periods (GC: 19% to 15%; CT 11% to 5%). Negative syphilis tests were not available to calculate changes in syphilis positivity during the two time periods.

Participants experienced a 62% relative reduction in the rate of STIs while taking doxy PEP; 300 STIs were diagnosed during 173.91 person-years in their HIV PrEP-only period versus 188 STIs during 251.93 person-years in their doxy PEP period, for an incidence rate ratio (IRR) of 0.38 (95% CI 0.29–0.50). While on doxy PEP, participants also experienced relative reductions in rates of CT (IRR 0.28, 95% CI 0.20–0.39) and GC (IRR 0.49, 95% CI 0.37–0.65). Only 2 participants were diagnosed with syphilis during each study period (Table 3).

Usage patterns

Most participants were characterized as having low (n=88, 21.2%) or medium (n=226, 54.3%) usage; these proportions were consistent from 2020 through 2023 (Table 4). The doxy PEP program began in September 2019, and most patients only had 1 visit that year, resulting in a large proportion of high usage for 2019. Participants categorized as having low or medium usage attended a median of 3 HIV PrEP visits (IQR 1–6 and 3–6, respectively); those with high usage attended a median of 2 HIV PrEP visits (IQR 1–3). Median number of self-reported doses taken in the previous 90 days was missing for over one-third of participants in each usage category (low 33.2%, medium 44.3%, high 46.1%). Among those with known self-reported number of doses taken, a median of 0 doses were self-reported for those in the low (IQR 0–1) and medium (IQR 0–2) usage categories and a median of 4 doses (IQR 1–9.5) were self-reported in the high dosage category.

Conclusions

In this population of mostly non-White MSM attending a public STI clinic for HIV PrEP, doxy PEP was highly acceptable, safe, and associated with statistically significant declines in bacterial STI. Despite low reported doxy PEP usage, we observed a reduction in any STI and CT when 1) comparing patients who received doxy PEP to those who did not, and 2) comparing the year before to the year after a patient initiated doxy PEP. In the cohort analysis, doxy PEP was associated with a 39% relative reduction in the rate of incident STI (composite endpoint) and a 60% relative reduction in the rate of CT specifically. In the crossover, doxy PEP was associated with a 51–72% relative reduction in the rate of any STI (62%), GC (51%), and CT (72%). Our results suggest that doxy PEP is effective

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

in real-world settings, and that public health efforts to increase or enhance doxy PEP implementation would likely reduce STI transmission in the community.

Our findings of reduced occurrence of a first STI, and first occurrence of CT specifically, among those who received doxy PEP are similar to results reported in the IPERGAY substudy[1]. Although we did not observe a statistically significant decrease in incident GC or syphilis in the cohort analysis, the incidence of both diseases was lower in doxy PEP than HIV PrEP-only recipients. This aligns somewhat with a meta-analysis of randomized clinical trials[12] that observed a non-statistical decrease in GC among doxy PEP users compared to non-users, but differs from a large recent cohort study that observed a statistical decrease in both GC and syphilis[8]. In our crossover analysis, however, we noted a significant reduction in the rate of GC during the doxy PEP period compared with the HIV PrEP-only period. Differences in the magnitude of STI reductions between the cohort and crossover analyses may in part be due to censoring at the time of first STI in the cohort, whereas the crossover design counted all STIs in participants during each period. Studies that only include first incident STI may underestimate effectiveness of doxy PEP over time. Additionally, it is possible that at least some of the reduction in rate of the 3 outcomes (any STI, CT, GC) seen in the crossover analysis could be partially due to behavior change during the doxy PEP period, such as fewer sex partners or increased condom usage. Between-period differences in GC rates could also potentially be related to differences in specific sexual behaviors that result in different incidence of pharyngeal infection (which is more resistant to antibiotic therapy)[2].

Importantly, the number of doxy PEP doses reportedly taken by our patients appears much smaller than in clinical trials. Our clinic patients were prescribed a maximum of 3.75 doses per month, which was already fewer than reported in the IPERGAY trial (median dose taken per month 6.8, IQR 2.8–14.5)[1] and the DOXYPEP trial (median 4.0; IQR 1–10)[2] and similar to the DOXYVAC trial (median 3; IQR 3–13)[3]. Receiving fewer doses of doxy PEP may have resulted in patients conserving doses for higher-risk encounters. However, the median number of self-reported doses taken per month in our cohort was zero, and the 102 patients in our high usage group reported a median of only 4 doses in the 90-day period between visits. Unfortunately, our EMR could not make self-reported dose information a mandatory field, resulting in a high proportion of visits with missing dose information. It is possible that patients who took more doxy PEP were reluctant to disclose this to providers. However, it seems unlikely that participants routinely under-reported number of doses taken, or that those with missing dose information would considerably differ from other participants, given the typical exchange of extremely sensitive, personal information between patients and staff in HIV PrEP clinic. Additionally, reported dose counts may have been affected by recall bias, but even if all participants took all doses that we provided, it was still fewer than reported in clinical trials.

Our lower usage of doxy PEP may be related to differences in sexual behavior and number of partners between our population and trial participants in Paris, San Francisco, and Seattle. We did not record the number of sexual events that our patients experienced or the frequency with which they took doxy PEP after sex; it is possible that the number of sexual events may have been higher in clinical trials and/or trial participants may have taken doxy PEP more

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

frequently after sex than PDPH HIV PrEP clinic patients. However, the median number of sex partners in past 3 months reported by our participants (2–3) was substantially lower than the 9 in 3 months reported by Luetkemeyer[2] and the 10 in either 2[1] or 3[3] months reported by Molina. Doxy PEP intake has been associated with patients' perception of their personal risk of STI acquisition[13]. Consequently, people who have more sex partners may use doxy PEP more frequently than those with fewer sex partners. Furthermore, participants in clinical trials may have other unmeasured characteristics that are fundamentally different from a community cohort of MSM presenting for routine preventative care[14]. While we did not have direct measures of doxy PEP adherence, participants who received doxy PEP had lower STI incidence compared to those who were not prescribed doxy PEP. Our results may suggest that, at a population level, doxy PEP can be effective at lower frequency than previously noted. If true, this may allay some concerns over the development of antimicrobial resistance with the wider adoption of doxy PEP[15], though the ability to draw conclusions about antimicrobial resistance in the absence of data on long-term, intermittent doxycycline use is limited and requires further study[16].

Participants in our study were substantially younger and more likely to be Black than participants in other studies[1–3,8]. This is important, given the disproportionately high rates of bacterial STI among MSM, younger persons and Black persons in the US[17,18] and the medical mistrust engendered among Black Americans by the history of medical abuse performed upon them[19]. Uptake of doxy PEP was high among all racial and ethnic groups though a slightly higher proportion of eligible non-Hispanic White participants (84%) accepted doxy PEP compared with eligible non-Hispanic Black and Hispanic participants (80%). Effective measures to reduce STI are sorely needed for these populations, and our data suggest that, for some STIs, doxy PEP may be one. Additionally, our study began in 2019 and continued throughout both the COVID-19 pandemic and the 2022 clade II mpox outbreak; though we know that sexual behavior changed in many MSM during this time[20–22], we were unable to measure potential changes among our participants. However, our doxy PEP usage over time stayed steady, indicating a continuing need, and demonstrating that doxy PEP is feasible for continuation of STI care during disruptions of medical systems or for those with limited access to care.

The accuracy of our estimates was likely improved through the incorporation of positive tests among participants from surveillance data of all GC, CT, and syphilis case reports to the health department; however, surveillance data do not include negative tests, and unreported non-reactive syphilis tests prevented us from calculating syphilis positivity. Our methods for measuring doxycycline use were limited; estimates were based on a small number of visits and therefore may be unstable. Patients may also have been able to obtain doxycycline from elsewhere and not reported it to clinic, which may have biased results. Due to cost concerns, we were unable to alter our EMR to systematically collect pill counts and the specific number and type of sexual behaviors associated with doxy PEP use. Though differences in sexual behavior between doxy PEP recipients and non-recipients (such as consistent use of condoms in response to perceived STI risk) could potentially alter disease transmission, it is plausible that those who chose not to take doxy PEP might have perceived themselves to be at lower risk of STI, which if true, would favor a smaller intervention effect between groups than we observed.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

This analysis supports the growing body of evidence that, when offered as part of comprehensive sexual health interventions for MSM, doxy PEP is an effective tool for the reduction of bacterial STI in a real-world setting, even among populations who may be underinsured and minoritized. Furthermore, if validated, our finding of doxy PEP effectiveness at lower doses than in trials may allay some concerns about potential development of antimicrobial resistance. Further research on effectiveness of doxy PEP among other populations with substantial STI burden, and how to best deliver doxy PEP to the populations who need it most, may help expand its use as a novel, effective intervention for STI prevention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

Program implementation (FL, LA), study design (FL, DN, AC, ND), statistical analysis (KC, RM, AC, ND), writing (FL), editing (FL, AC, RM, LA, DN, ND); many thanks to the staff of PDPH Health Center #1 and most of all, our patients, without whom none of this is possible.

Funding and conflicts of interest:

This study did not receive any external or intramural funding.

References

1. Molina JM, Charreau I, Chidiac C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. Lancet Infect Dis. 2018;18(3):308–317. doi:10.1016/S1473-3099(17)30725-9 [PubMed: 29229440]
2. Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med. 2023;388(14):1296–1306. doi:10.1056/NEJMoa2211934 [PubMed: 37018493]
3. Molina JM, Bercot B, Assoumou L, et al. Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2 × 2 factorial design. Lancet Infect Dis. 2024;24(10):1093–1104. doi:10.1016/S1473-3099(24)00236-6 [PubMed: 38797183]
4. Updated Recommendations for Prescribing Doxycycline Post-Exposure Prophylaxis (DoxyPEP). San Francisco Department of Public Health; 2024. Accessed December 13, 2024. https://www.sf.gov/sites/default/files/2024-09/Update-Updated-Recommendations-Prescribing-Doxy-PEP-SFDPH-FINAL-9.12.24.pdf
5. Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep. 2024;73(2):1–8. doi:10.15585/mmwr.rr7302a1
6. Liu A, Hao J, Pickering TA, Klausner JD. Trends in Sexually Transmitted Infections Associated With the Doxycycline Postexposure Prophylaxis Guidelines in San Francisco. Sex Transm Dis. 2024;51(11):e46–e48. doi:10.1097/OLQ.0000000000001996 [PubMed: 38860659]
7. Sankaran M, Glidden DV, Kohn RP, et al. Doxycycline Postexposure Prophylaxis and Sexually Transmitted Infection Trends. JAMA Intern Med. 2025;185(3):266. doi:10.1001/jamainternmed.2024.7178 [PubMed: 39761052]
8. Traeger MW, Leyden WA, Volk JE, et al. Doxycycline Postexposure Prophylaxis and Bacterial Sexually Transmitted Infections Among Individuals Using HIV Preexposure Prophylaxis. JAMA Intern Med. Published online January 6, 2025. doi:10.1001/jamainternmed.2024.7186

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

9. Osmundson J, Holloway IW, Macias Gil R, Jann JT, Hong C, Bolan RK. Doxycycline Postexposure Prophylaxis for Bacterial STIs: Prescribing Patterns, Use, Short-term Outcomes Among 2083 Patients in a Los Angeles Federally Qualified Health Care Program, and Implications for Widespread Use. Open Forum Infect Dis. 2025;12(3):ofaf089. doi:10.1093/ofid/ofaf089 [PubMed: 40046893]
10. Philadelphia Department of Public Health. Syphilis Cases by Stage, 1990–2020. Accessed January 28, 2025. hip.phila.gov/data-reports-statistics/syphilis/
11. US Food & Drug Administration. What is a serious adverse event? Accessed June 3, 2025. https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event
12. Szondy I, Meznerics FA, Lőrincz K, et al. Doxycycline prophylaxis for the prevention of sexually transmitted infections: A systematic review and meta-analysis of randomized controlled trials. Int J Infect Dis. 2024;147:107186. doi:10.1016/j.ijid.2024.107186 [PubMed: 39122208]
13. Zucker J, Flanagan M, Li J, et al. The impact of doxy-PEP: effective use and changes in prevention behaviors. In:; 2024. https://stipreventionconference.org/wp-content/uploads/2024/11/2024-STI-Prevention-Conference_Abstract-Book_Final.pdf
14. Gouveia R, Cruz VT, Almeida L. Sociodemographic and psychological characteristics influencing patients' willingness to participate in clinical trials. BMJ Open Qual. 2022;11(4):e002044. doi:10.1136/bmjoq-2022-002044
15. Chu VT, Glascock A, Donnell D, et al. Impact of doxycycline post-exposure prophylaxis for sexually transmitted infections on the gut microbiome and antimicrobial resistome. Nat Med. 2025;31(1):207–217. doi:10.1038/s41591-024-03274-2 [PubMed: 39363100]
16. Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep. 2024;73(2):1–8. doi:10.15585/mmwr.rr7302a1
17. Centers for Disease Control and Prevention. Sexually Transmitted Infections Surveillance, 2023. Centers for Disease Control and Prevention; 2024. Accessed January 13, 2025. http://cdc.gov/sti-statistics/annual/index.html
18. Centers for Disease Control and Prevention. Sexually Transmitted Infections Treatment Guidelines, 2021. Centers for Disease Control and Prevention Accessed January 13, 2025. http://cdc.gov/std/treatment-guidelines/default.htm
19. Jaiswal J Whose Responsibility Is It to Dismantle Medical Mistrust? Future Directions for Researchers and Health Care Providers. Behav Med. 2019;45(2):188–196. doi:10.1080/08964289.2019.1630357 [PubMed: 31343959]
20. Copen CE, Delaney KP, Agnew-Brune C, et al. Modifications to Sexual Behaviors Associated With Mpox (Monkeypox) Virus Transmission Among Persons Presenting for mpox Vaccination, Washington, DC, August–October, 2022. Sex Transm Dis. 2024;51(1):54–60. doi:10.1097/OLQ.0000000000001889 [PubMed: 37889944]
21. Delaney KP, Sanchez T, Hannah M, et al. Strategies Adopted by Gay, Bisexual, and Other Men Who Have Sex with Men to Prevent *Monkeypox virus* Transmission — United States, August 2022. MMWR Morb Mortal Wkly Rep. 2022;71(35). doi:10.15585/mmwr.mm7135e1
22. Sanchez TH, Zlotorzynska M, Rai M, Baral SD. Characterizing the Impact of COVID-19 on Men Who Have Sex with Men Across the United States in April, 2020. AIDS Behav. 2020;24(7):2024–2032. doi:10.1007/s10461-020-02894-2 [PubMed: 32350773]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

TABLE 1.

Demographic and clinical characteristics of men who have sex with men receiving HIV PrEP, by doxy PEP and study design status, Philadelphia, 2019–2023

	Cohort		Crossover
	PrEP only (N=92)	PrEP and Doxy PEP (N=416)	(N=350)
Median age at first PrEP visit (IQR), years	26 (23, 31)	28 (25, 34)	28 (25, 34)
Race/ethnicity, n (%)			
Black NH	27 (29.3)	110 (26.4)	127 (36.3)
White NH	27 (29.3)	144 (34.6)	96 (27.4)
Hispanic	24 (26.1)	99 (23.8)	73 (20.9)
Other	14 (15.2)	63 (15.1)	54 (15.4)
Sex of sex partners, n (%)			
Male only	79 (85.9)	350 (84.1)	294 (84.0)
Multiple sexes	13 (14.1)	66 (15.9)	56 (16.0)
Median number of PrEP visits (IQR)	1.5 (1.0, 2.0)	3 (2.0, 6.0)	3 (1, 4) [Before doxy PEP Period] 3 (1, 3) [After doxy PEP Period]
Median number of sex partners in past 90 days (IQR)	2 (1, 4)	2 (1, 3)	3 (1, 4)
Any STI in past 12 months, n (%)	32 (34.8)	223 (53.6)	94 (26.9)

PrEP = HIV pre-exposure prophylaxis, doxy PEP = doxycycline post-exposure prophylaxis, IQR=Interquartile range

Sex Transm Dis. Author manuscript; available in PMC 2025 July 31.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Estimates of doxy PEP effectiveness against incident sexually transmitted infections among men who have sex with men on HIV PrEP using a cohort design, Philadelphia, 2019–2023

	PrEP only (N=92)					PrEP and doxy PEP (N=416)					
	n*	Person Days	Person Years	Incidence Rate**	(95% CI)	n*	Person Days	Person Years	Incidence Rate**	(95% CI)	Hazard Ratio (95% CI)
Primary analysis											
Any STI	27	9,289	25.43	1.06	(0.70, 1.55)	238	114,829	314.38	0.76	(0.66, 0.87)	**0.61 (0.40, 0.93)**
Secondary analysis											
Any gonorrhea	18	9,945	27.23	0.66	(0.39, 1.04)	204	134,868	369.25	0.55	(0.48, 0.64)	0.75 (0.45, 1.24)
Any chlamydia	11	11,604	31.77	0.35	(0.17, 0.62)	87	180,786	494.97	0.18	(0.14, 0.22)	**0.40 (0.21, 0.78)**
Any syphilis	4	12,238	33.51	0.12	(0.03, 0.31)	41	203,712	557.73	0.07	(0.05, 0.10)	0.51 (0.17, 1.54)

PrEP = HIV pre-exposure prophylaxis, doxy PEP = doxycycline post-exposure prophylaxis, CI=confidence interval, STI=sexually transmitted infections

*STI diagnoses documented in STI clinic records and reported through case-based surveillance were included

**Incidence rate per person-year

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Estimates of doxy PEP effectiveness against incident sexually transmitted infections among men who have sex with men on HIV pre-exposure prophylaxis using a crossover study design, Philadelphia, 2019–2023

	Up to 365 Days BEFORE doxy PEP (N=350)					Up to 365 Days AFTER doxy PEP (N=350)					
	n*	Person Days	Person Years	Incidence Rate**	(95% CI)	n*	Person Days	Person Years	Incidence Rate**	(95% CI)	Incidence Rate Ratio (95% CI)
Primary analysis											
Any STI	300	63,520	173.91	1.19	(1.02, 1.39)	188	92,019	251.93	0.46	(0.36, 0.58)	**0.38 (0.29, 0.50)**
Secondary analysis											
Any gonorrhea	198	63,477	173.79	0.82	(0.69, 0.99)	144	92,011	251.91	0.40	(0.32, 0.51)	**0.49 (0.37, 0.65)**
Any chlamydia	120	63,132	172.85	0.67	(0.55, 0.81)	50	91,689	251.03	0.19	(0.14, 0.25)	**0.28 (0.20, 0.39)**
Any syphilis	2	--	--	--	--	2	--	--	--	--	--

doxy PEP = doxycycline post-exposure prophylaxis, CI=confidence interval, STI=sexually transmitted infections

*STI diagnoses documented in STI clinic records and reported through case-based surveillance were included

**Incidence rate per person-year

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 4.

Doxy PEP usage patterns among men who have sex with men on HIV pre-exposure prophylaxis, Philadelphia, 2019–2023

	Total n (%)	2019 n (%)	2020 n (%)	2021 n (%)	2022 n (%)	2023 n (%)
doxy PEP usage, n (%)						
Low (≤25% of visits with doxy PEP dispensed)	88 (21.2%)	3 (2.5)	89 (37.2)	49 (31.8)	70 (40.7)	64 (44.4)
Medium (25–74% of visits with doxy PEP dispensed)	226 (54.3%)	8 (6.6)	79 (33.1)	68 (44.2)	63 (36.6)	44 (30.6)
High (≥75% of visits with doxy PEP dispensed)	102 (24.5%)	111 (91.0)	71 (29.7)	37 (24.0)	39 (22.7)	36 (25.0)

doxy PEP = doxycycline post-exposure prophylaxis