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MAJOR ARTICLE

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

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Background. Rates of bacterial sexually transmitted infections (STIs) have risen dramatically over the past decades. Doxycycline postexposure prophylaxis (DP) is a novel intervention to prevent bacterial STIs. Recent randomized controlled clinical trials reported high DP efficacy at preventing syphilis and chlamydia in cisgender men who have sex with men and transgender women.

Methods. We abstracted data from the electronic health records of 2083 patients at the Los Angeles LGBT Center (the Center) who were prescribed DP between 2019 and June 2024. Patient information included race, income, gender, sex, DP prescriptions, and STI tests dating back to 1998.

Results. More than half of the patients prescribed DP at the Center were White, and 48.1% were between 31 and 40 years old. Most of these patients were not diagnosed with an STI in the previous year but ever having an STI correlated with early DP initiation. We demonstrate high real-world DP effectiveness in preventing infections with syphilis (86.4%) and chlamydia (89.7%), and moderate effectiveness for gonorrhea (54.7%), all remarkably similar to published clinical trials. DP use was highly variable, and DP failure for syphilis or chlamydia occurred only in patients with low DP use. There was similar effectiveness for chlamydia and gonorrhea regardless of anatomical site (rectal or throat swabs or urine sample).

Conclusions. We show that DP is highly effective at STI prevention in a real-world setting and describe patterns of DP prescribing and use, in addition to STI testing, that can directly inform best clinical practice.

Keywords. bacterial STIs; doxycycline postexposure prophylaxis; doxyPEP; prevention; sexually transmitted infections.

Over the past quarter century, there has been a dramatic increase in US cases of syphilis, gonorrhea, and chlamydia [1]. HIV preexposure prophylaxis (PrEP) and antiretroviral regimens that render HIV untransmissible among people with HIV (PWH) have been associated with decreased condom use, but these trends have not been directly associated with sexually transmitted infection (STI) rates [2]. Although decreased condom use probably contributes to STI incidence, STI rates also may be elevated because of more frequent STI testing and diagnosis of asymptomatic infections among people who use PrEP [3].

STI prevention methods include reducing the number of sexual partners, using a barrier (e.g., condom), vaccination, and chemoprophylaxis. No vaccines currently prevent syphilis, gonorrhea, or chlamydia.

A pilot study using open-label doxycycline as PrEP was associated with a decreased incidence of syphilis, *Chlamydia trachomatis*, or *Neisseria gonorrhoeae* incident infections among a core group of men having sex with men (MSM) living with HIV [4]. Subsequently, several randomized controlled trials have studied doxycycline as postexposure prophylaxis (DP) among MSM, transgender women, and cisgender women [5–9]. The study of DP among cisgender women in Kenya found no benefit, but hair sample analysis showed doxycycline use was low.

The DoxyPEP trial, conducted in the United States (San Francisco and Seattle), found that MSM and transgender women participants randomized to doxycycline had decreases

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in STIs of 66% among the HIV PrEP cohort and of 62% among the PWH cohort [8]. The French DOXYVAC study found the incidence of a first episode of chlamydia and/or syphilis while using doxycycline PEP was 83% lower than in the no PEP group [6]. However, there was not a significant difference for gonorrhea infections, presumably because of preexisting high prevalence of tetracycline resistant *N gonorrhoeae* in France. By contrast, the DoxyPEP trial in the United States did demonstrate an approximate 55% reduction in gonorrhea infections.

Since publication of these studies, uptake of DP has been remarkable, and public health jurisdictions in the United States and elsewhere have released statements and/or guidelines on its use [10, 11].

Here, we describe the introduction and promotion of DP at a Los Angeles community-based clinic primarily serving LGBT individuals. We review the patient demographics, STI testing history, use patterns, and short-term effectiveness of DP in this cohort of patients, and address some of the challenges to its management and monitoring.

METHODS

The Los Angeles LGBT Center (the Center) is a Federally Qualified Health Center (FQHC). Between April 2019 and July 2024, there were 63 666 registered patients; 5259 were PWH, most receiving primary care and HIV management at the Center; most of the 22 881 who sought only sexual health care in the Sexual Health and Education Program were HIV negative, and the remaining PWH were receiving their HIV healthcare elsewhere. Since October 2022, the Center's recommendation has been to offer DP to patients who have had ≥1 bacterial STI in the prior 12 months, while allowing providers to exercise shared decision-making with patients who have not had a bacterial STI but who are, or believe themselves to be, at risk for them.

Measures

In the electronic health record (EHR), DP prescriptions contain both a unique code and distinct dosing instructions to differentiate them from other uses of doxycycline. The Allscripts Veradigm Electronic Health Record (Clinical Module 22.2.3) was searched for all patient charts containing at least 1 DP prescription. Selected charts were then queried using Microsoft SQL Server to extract the following data: birth sex; gender; age; race; ethnicity; sexual orientation; HIV status (Supplementary Table 1). We also obtained dates of all DP visits and prescriptions, including number of refills authorized, and all STI test results (available since 1998). DP visits are defined as those in-person or virtual patient encounters where DP was prescribed or refilled, whether or not STI testing occurred.

A Sexual Risk Assessment, completed by patients visiting the Sexual Health and Education Program (but not primary care), is stored as a searchable document in the EHR. This questionnaire includes self-reported number of sexual partners in the previous 3 months.

The Center's QS/1 Pharmacy Software was queried to obtain DP prescription fill/refill dates for patients who used the Center pharmacy. All data were saved to an Excel spreadsheet with a unique identifier for each patient; chart numbers were deleted.

Data Analysis

Data were sorted and verified with Excel. Data analysis used Python v 3.10.13, pandas version 2.2.2 and NumPy version 1.26.4. Data were visualized in Prism, and Prism was used to perform statistical comparisons. To determine whether patient and clinician decisions about DP were stable over time, patients were sorted into quartiles based on DP start date. Confidence intervals were calculated in Python using the scipy.stats module norm. Demographic data were analyzed in Python and Excel. Demographic data occasionally used specific identifiers (e.g., Korean) that were manually sorted into the more common bin (e.g., Asian).

Sti Test Analysis

Gonorrhea and Chlamydia infections were diagnosed with nucleic acid amplification tests. Blood testing for syphilis used the nontreponemal Rapid Plasma Reagin (RPR) and quantitative titer determination was performed on reactive samples. A treponemal test, the Microhemagglutination Assay for Treponema pallidum, was performed on reactive RPR sera, with a positive result confirming current or past syphilis. Treponemal tests usually remain positive for life following an infection and, although RPR titers usually decline at least 4-fold within 6 months after successful treatment, there is considerable variability, and for many patients this takes longer. Subsequent reinfection leads to 4-fold or greater rise in RPR titer compared to the most recent titer. To identify new syphilis infections, we used clinician diagnoses. When necessary, we used the RPR testing date and the clinician diagnosis to determine the date of a positive syphilis infection.

To see if shared decision making, patient experience or demographics were stable over time, we separated the patient sample into quartiles to compare the first and most recent individuals who were prescribed DP. Quartile 1 (early cohort) includes 521 individuals who initiated DP on or before 12 October 2023 and quartile 4 (late cohort) includes 521 individuals who initiated DP on or after 11 March 2024 (Supplementary Table 2).

RESULTS

DP Demographics

Between February 2019 and 27 June 2024, 2083 patients were prescribed DP. The Center issued formal clinician guidance

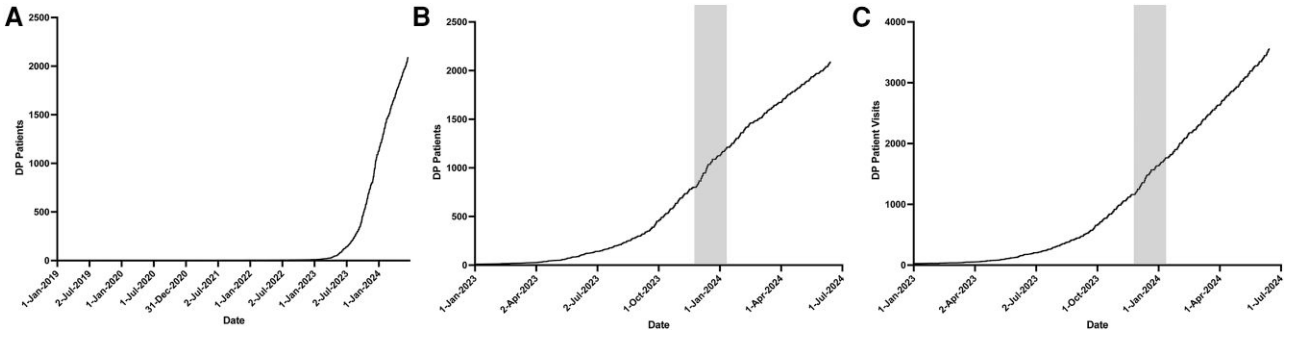

Figure 1. Trends in DP patients and prescriptions at the LA LGBT Center. *A*, Number of total patients with 1 or more prescriptions for DP. *B*, Data presented as in *A* but highlighting 1 January 2023, through the end of the study, 28 June 2024. *C*, Total number of DP prescriptions. Doses per prescription and refill number vary. The gray bar in Figures 1*B* and 1*C* highlights an online marketing campaign from 27 November 2023 through 8 January 2024.

on DP use in October 2022. Nearly half of the DP patients were between 31 and 40 years of age (48.1%); more than half were White (55.9%); and the majority were cisgender gay or bisexual men (85.2%) (Supplementary Table 1).

Both the number of DP patients (Figures 1*A* and *B*) and the number of visits (Figure 1*C*), increased sharply from late 2023 through 2024. Between 1 January 2024 and 15 April 2024, 510 patients received their first DP prescriptions, representing 24.5% of the total DP patients. The gray bar in Figures 1*B* and 1*C* represents the timing of a patient-focused multimedia marketing campaign for DP awareness by the Center from 27 November 2023 through 8 January 2024.

Prior STI Diagnosis Correlates With Early DP Initiation

Of the 2083 individuals in the total DP cohort, 862 (41.4%) had a history of 2 or more STI diagnoses in the year before DP initiation (Supplementary Figure 1), the main Centers for Disease Control and Prevention indication for DP use [11]. However, it was not possible to systematically search EHR visit notes for details about the influence of patient requests, provider recommendations, and shared decision making on other justifications for using DP. To see if prescribing was stable over time, we separated the patient sample into quartiles to compare the first and most recent individuals prescribed DP. Quartile 1 (early cohort) includes 521 individuals who initiated DP on or before 12 October 2023 and quartile 4 (late cohort) includes 521 individuals who initiated DP on or after 11 March 2024. The overall demographics of the cohorts are similar (Supplementary Table 1 and Supplementary Table 2).

Among the early DP cohort, 401 (77.0%) had a previous STI diagnosis before DP initiation, whereas the late DP cohort had 359 individuals (68.9%) with any previous STI diagnosis (Supplementary Figure 1, $chi^2 = 8.5764$, $P = .00341$). We evaluated STI diagnoses in the 12 months before DP initiation and found similar trends in early and late cohorts (Supplementary Figure 1). Significantly more individuals in the early DP cohort were HIV negative (445/521) than in the late DP cohort (411/521, $chi^2 = 7.5655$, $P = .00595$, Supplementary Table 2).

DP Use Varies Among Patients

To evaluate DP use over time and to assure a reasonable follow-up period, we examined the charts of 1115 patients (53.5% of the full cohort) where first DP prescriptions recorded were 6 months before our analysis. Individual DP prescriptions varied extensively between clinicians (from 1 dose per prescription to 45 doses per prescription) (Supplementary Table 3).

Although the EHR records each DP prescription, including the number of tablets and refills authorized, it cannot track when and how frequently a prescription is filled. Patients can use any pharmacy they wish, but prescription fill data (dates and number of tablets dispensed) was only available from the Center's pharmacy. Thus, we searched the Center's QS/1 Pharmacy Software for patients who consistently used this pharmacy. Of the 1115 DP patients with 6 or more months since their first prescription, 366 filled at least 1 DP prescription from the Center's pharmacy (Supplementary Table 1). Among this sample, DP use varied from 2 doses total since DP initiation to 24.6 DP doses per month (Figure 2*A*). Mean use was 5.24 DP doses per month (standard deviation = 3.80 doses per month). DP use was significantly higher among patients with an STI diagnosis prior to DP initiation (Figure 2*B*, Welch's *t*-test, $P = .0195$).

Of the 366 patients with consistent DP use data, 300 had completed 1 or more Risk Assessment (Supplementary Table 1). We plotted the self-reported partner number per month against DP use (Figure 2*C*) and found no association. We superimposed a colored plot of DP failures within 6 months of DP initiation. DP failure for syphilis and chlamydia was only observed in patients with fewer than 5 uses per month, whereas gonorrhea failure occurred over a wide range of use, from less than 1 dose a month to more than 20.

Estimation of DP Effectiveness

We evaluated all STI testing in the 6 months before and following initial DP prescriptions for patients with 6 months or more

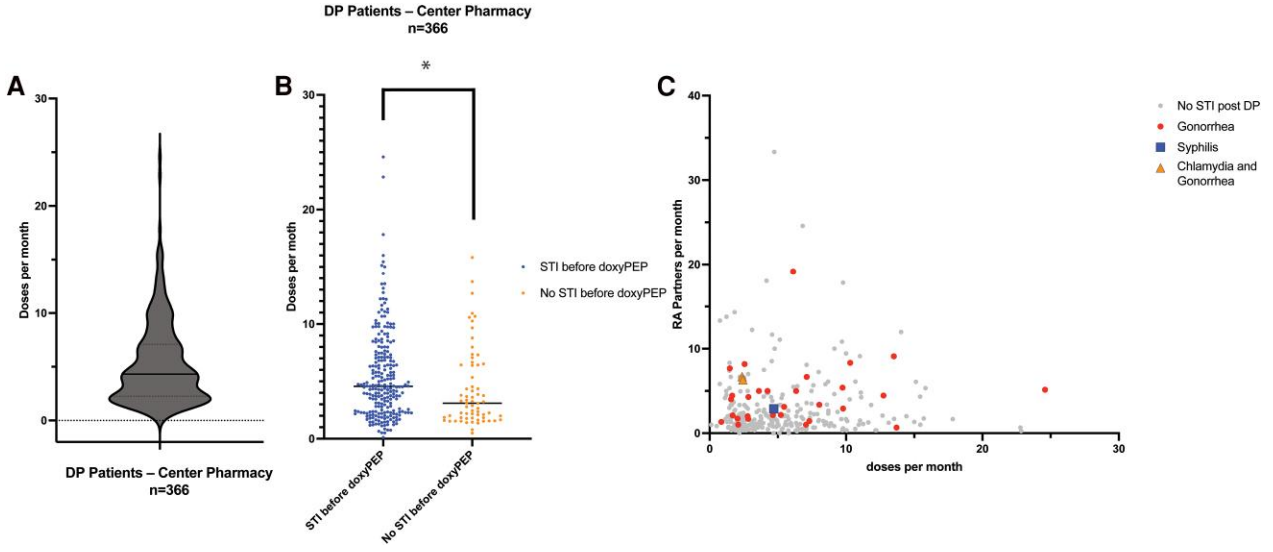

Figure 2. DP use among patients who use the Center pharmacy. *B*, DP use per month calculated by the number of doses prescribed and dispensed by the LA LGBT Center pharmacy among 366 DP patients with consistent pharmacy use. *B, A* previous positive STI result correlated with higher DP use as indicated by doses prescribed and dispensed per month. *C*, Self-reported number of sex partners and DP use. Patients with pharmacy information and one or more Risk Assessment (RA) with self-reported number of partners in the last three months were analyzed. The number of sex partners was averaged across all available risk assessments per patient and divided by 3 to approximate the number of partners per month.

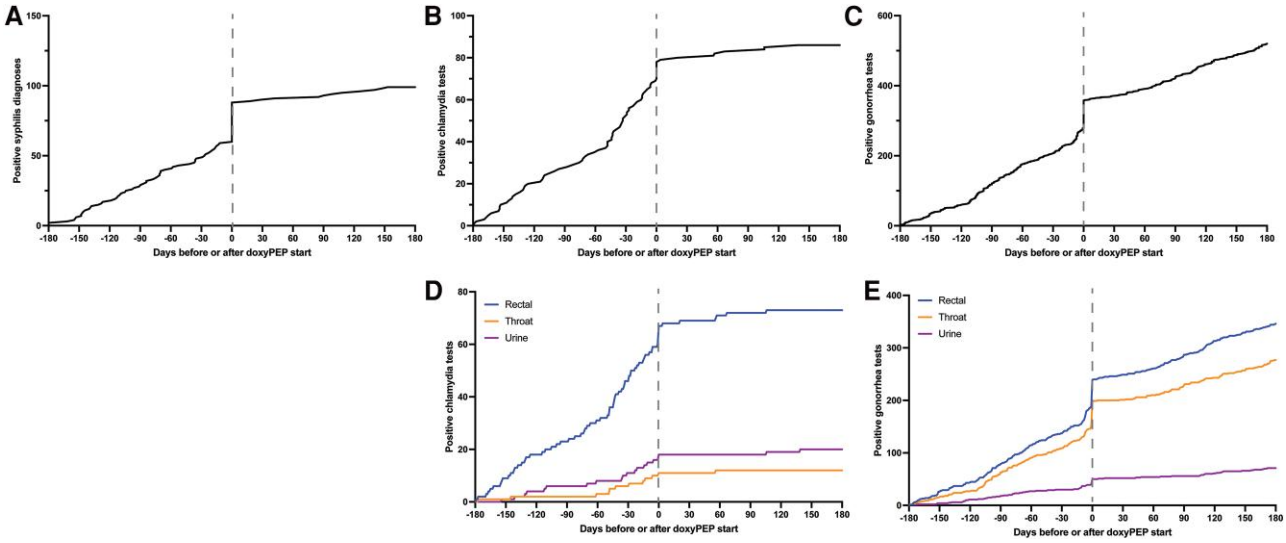

Figure 3. STI test results for six months before and six months after a patient's first DP prescription. New diagnoses for syphilis (*A*), and positive tests for chlamydia (*B*), and gonorrhea (*C*) were plotted against the relative date of DP initiation (e.g., days before or after DP initiation, n = 1115). DP initiation (0 on the *x*-axis) is indicated with a dashed gray line and positive STI results from the same date as DP initiation are counted as prior to the intervention. *D* and *E* are plotted as above but disaggregate chlamydia (*D*) and gonorrhea (*E*) positive tests by tested site.

of DP use. These 1115 individuals had 78 positive chlamydia and 358 positive gonorrhea tests, and 88 new syphilis diagnoses in the 6 months before DP initiation (Figure 3). A positive test occurred on the date of DP initiation in 8.6% of the patient (infections co-incident with the dashed gray line in Figure 3). During the 6 months after DP initiation, the reduction in positive results was 86.4% for syphilis (12 cases, relative risk 0.136; confidence interval [CI], .0746–.249), 89.7% for chlamydia (9 cases, relative risk 0.135; CI, .0738–.246), and 54.7% for gonorrhea (162 cases, relative risk 0.452; CI, .376–.545).

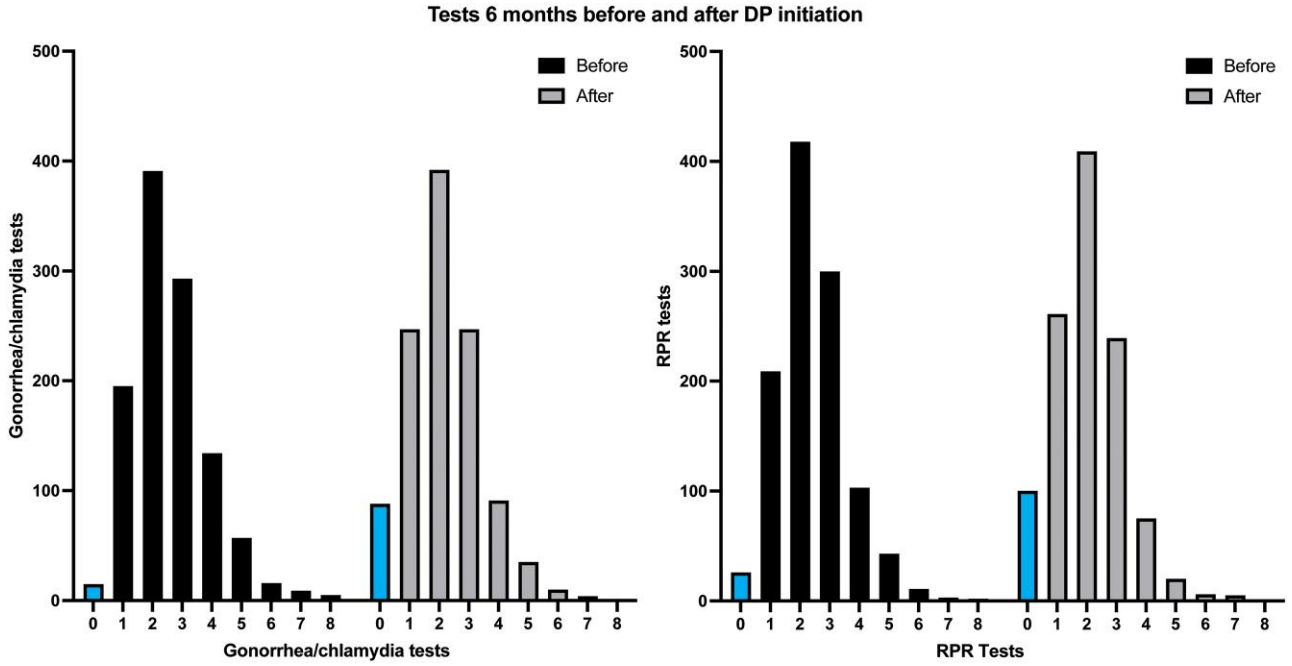

Figure 4. STI testing patterns before and after DP initiation. *A*, The number of combined gonorrhea/chlamydia tests and RPR tests for syphilis in the 6 months prior to and after DP initiation in patients >6 months on DP at the LALGBT Center. The number of patients with zero STI tests in a 6-month period are noted below.

Because our data include STI results for gonorrhea and chlamydia by anatomical site, we evaluated site-specific positive gonorrhea and chlamydia tests from the same patients. Figure 3*D* shows that most positive chlamydia tests were in the rectum (relative risk 0.0896; CI, .0388–.206), but similar effectiveness was found in urine (relative risk 0.111; CI, .0258–.479) and throat (0.0909; CI, .0117–.704), albeit with wider CIs.

Figure 3*E* shows that positive gonorrhea tests were most common in rectal and throat swabs, and DP effectiveness was similar in both samples (gonorrhea infection in throat relative risk 0.400 [CI, .307–0. 518]) and gonorrhea infection in rectum relative risk 0.365 (CI, .293–.455)) with a similar relative risk in urine tests (0.420; CI, .252–.699).

In the early DP cohort, we determined a large number of positive STI tests occurred on the date of DP initiation (in Figure 3 such cases are co-incident with the dashed gray line indicating DP initiation). We compared this trend in the early DP cohort and the late DP cohort to see if it remained stable over time. The number of STI diagnoses on the DP start date in the early cohort of 521 patients was 69 compared to the late cohort of 38 (Supplementary Table 4); because some patients had more than 1 STI, we evaluated diagnoses by chi^2 independently. Gonorrhea infection upon DP initiation was significantly different in the early (45 diagnoses; 8.6%) compared to the late (24 diagnoses; 4.6%) cohort (chi^2 = 6.84, P = .00891, Supplementary Table 4).

STI Testing Before and After DP initiation

To determine whether the DP effectiveness data might be affected by altered testing patterns, we calculated the number of gonorrhea/chlamydia and RPR tests in the 6 months before and after DP initiation. We noted an increase in the number of individuals without STI testing in the 6 months after DP initiation (Figure 4*A*).

In this cohort of 1115 DP patients, 73 (6.54%) and 82 (7.35%) had had no gonorrhea/chlamydia or RPR testing after DP initiation, respectively. We found that 59 of 73 (80.8%) patients with zero gonorrhea/chlamydia tests after DP initiation and 65 of 82 (79.3%) patients with zero RPR testing after DP initiation had zero additional DP visits after initiation. To verify that the results of DP effectiveness were not dependent on a decrease in STI testing after initiation, we performed the analysis only in patients with STI tests after DP initiation (Supplementary Figure 2).

DISCUSSION

The rapid uptake and use of DP by 2083 patients of an LGBT-focused FQHC in a large metropolitan health jurisdiction provides an opportunity to review the prescribing and management of this novel STI prevention tool in a nonresearch setting.

Although most demographic trends in our study group were similar to the overall patient population at the Center (Supplementary Table 5), nearly half of our DP patients were between ages 31 and 40 years, more than half were White, and 85% were cisgender gay or bisexual men.

Real-world DP Effectiveness Matches Findings From Randomized Controlled Clinical Trials

The reduction in new bacterial STIs among DP users was similar to the ANRS 174 DOXYVAC and DoxyPEP studies. Furthermore, our results for gonorrhea reduction are comparable to those in the San Francisco/Seattle DoxyPEP study, where the prevalence of tetracycline resistant *N gonorrhoeae* is similar to that in Los Angeles.

Uptake of DP

Although the Center's provider guidelines for DP use was introduced in October 2022, very few prescriptions were written for DP before April 2023. However, by early October 2023, there were nearly 500 first DP prescriptions written. One factor that influenced this rapid upsurge of DP prescribing among Center providers was a nationwide shortage of benzathine penicillin (BPG), the treatment of choice for syphilis in patients not allergic to penicillin. Pfizer, the sole manufacturer of BPG, submitted a letter to the Food and Drug Administration dated 14 June 2023 announcing this shortage, which was not expected to recover until quarter 2 of 2024 [12]. Because efficacy of DP in decreasing syphilis had recently been demonstrated in randomized controlled trials, and because of the high incidence of syphilis among the Center's patient population, this impending BPG shortage presented another compelling reason for providers to consider DP for eligible patients.

Between 27 November 2023 and 8 January 2024, the Center conducted a multimedia DP information campaign which included links on the Center's website landing page; videos by local influencers that were posted on their Instagram and/or Twitter/X pages; and sex-positive photos with DP messaging that were posted prominently in all Center locations. The shaded bars in Figures 1*B* and 1*C* suggest a modest acceleration of DP patients and prescriptions at the Center during this time but without long-term effects.

Incident STIs, DP Initiation, and Subsequent Use Patterns

The occurrence of an STI was the sentinel event preceding 8.6% of the initial DP prescriptions for the entire DP study population. The difference in prior STI prevalence between the early and late cohorts (Supplementary Figure 1) suggests that the personal experience of a previous STI may have been relatively more important for early adopters. It is also possible that during the 5 months between 12 October 2023 and 11 March 2024, awareness of the effectiveness of DP increased among both providers and patients, resulting in more prescriptions, including among those without prior bacterial STIs. Shared decision-making between patient and provider seems like a reasonable way to characterize these changes.

Monitoring actual use of any medication is complex and may require not only pharmacy data, but both self-reported survey data and biological analyses (eg, mass spectrometry of collected hair samples) to achieve the best approximation. Retrospectively monitoring the use of a nondaily, event-driven medication, such as DP, is even more challenging. As the most practical estimate, we chose pharmacy dispensing records, which we obtained for 366 DP patients. The mean use was 5.24 doses per month, midway between the 6 and 4 mean doses per month reported by the French DOXYVAC and US DoxyPEP studies, respectively [6, 8].

Regarding the number of doses prescribed and number of refills authorized, there appears to be room for provider education and for a better discussion with the patient about the number of doses anticipated. Although most patients are prescribed a total of 2, 3, or 4 initial prescriptions and refills per clinic visit where DP was reviewed, 15 patients received 15-dose prescriptions with 5 refills in between visits. Providers may be accustomed to managing patients with profiles containing several medications for chronic diseases (eg, for HIV, hypertension, diabetes, hyperlipidemia) and view DP as a maintenance medication, authorizing refills so that requests come less frequently. However, DP is not a maintenance medication. The patient should be checked for STIs on at least a quarterly basis, especially if their DP use is high.

Our finding of no association between a patient's reported number of sex partners and their DP use does make determining the appropriate number of doses and refills per appointment challenging. However, more detailed discussions may be helpful. For instance, those patients who had high use of DP but reported few partners (see Figure 2*C*) could be using DP after repeated sexual contacts with partners who may have multiple other concurrent partners. Frank and nonjudgmental discussions between patient and provider are essential.

A recent study on the pharmacokinetics of a single 200-mg dose of doxycycline shows that it rapidly reaches levels in rectal, vaginal, and urethral secretions that are between 3 and 20 times reported minimum inhibitory concentration 90 (MIC_{90}) values for bacterial STIs [13]. Thus DP, if taken correctly, should be effective among all individuals. However, it is critically important that a clinical study be undertaken among individuals assigned female at birth that includes measures to assist with appropriate use. If shown to be efficacious, such evidence could be incorporated into stronger DP use guidelines that could reduce cases of congenital syphilis and PID.

Limitations

The data presented here are from patients at a single LGBT-serving FQHC and may not be representative of all clinical settings. The patient population we describe contains few cis women and trans men, and therefore we cannot evaluate use and effectiveness among these populations, where additional clinical trials are necessary. Full prescription refill data were only available for the 32% of DP users who used the Center's pharmacy and initiated DP more than 6 months before our analysis.

Although there may be some unidentified patient variables driving patients' pharmacy choices that may affect other outcomes, we believe that the subset is sufficiently representative of all DP users that our reported findings and interpretations remain valid.

CONCLUSIONS

DP has become an important and ever more widely used tool for preventing transmission of bacterial STIs. There are still important questions about possible tradeoffs or consequences to its consistent use. Researchers should closely examine use patterns and establish quality improvement programs in all settings where DP use is recommended to minimize adverse outcomes while trying to achieve population impact on the STI and HIV syndemics.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Acknowledgments. J. O.: Conceptualization, study design, data analysis, writing (original draft). I. W. H.: Conceptualization, study design, writing (review and edit). R. M. G.: Conceptualization, study design, writing (review and edit). J. T. J.: Data analysis, writing (review and edit). C. H.: Conceptualization, study design, writing (review and edit). R. K. B.: Conceptualization, study design, data analysis, writing (original draft).

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Potential conflicts of interest. All authors declare no conflict.

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