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No New HIV Infections with Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting

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Abstract

Referrals for and initiation of preexposure prophylaxis (PrEP) for HIV infection increased dramatically in a large clinical practice setting since 2012. Despite high rates of sexually transmitted infections among PrEP users and reported decreases in condom use in a subset, there were no new HIV infections in this population.

Introduction

The effectiveness of once-daily oral preexposure prophylaxis (PrEP) using tenofovir/emtricitabine for prevention of sexually acquired HIV infection has been demonstrated in trials and open-label studies [1, 2]; however, data on PrEP use outside of the research context are limited. Interest in PrEP was high among men who have sex with men (MSM) in a demonstration project in the U.S. [3], yet initial pharmacy data indicated that many at-risk individuals were not accessing PrEP [4]. In addition, despite reassuring data suggesting that sexual risk behavior and the incidence of sexually transmitted infections (STIs) did not increase in PrEP trials [5, 6], few data on sexual behavior or STIs have been reported among PrEP users outside of research settings.

We aimed to characterize patterns of PrEP use among members of the Kaiser Permanente Medical Center in San Francisco (KPSF). We describe characteristics of individuals evaluated for and initiating PrEP, trends in PrEP referrals and initiation, incidence of HIV and other STIs among PrEP users, and self-reported changes in condom use and number of sexual partners after PrEP initiation.

Methods

Kaiser Permanente is a large integrated healthcare system that provides comprehensive medical services to over 170,000 adult residents in San Francisco. Our study population included all adult KPSF members evaluated for PrEP from July 2012 (the date of approval by the U.S. Food and Drug Administration) through February 2015. At KPSF, primary care or other providers refer patients to a specialized PrEP program after assessment of risk or patient-initiated request. This program, created to meet the growing demand for PrEP, provides adherence support and clinical monitoring by infectious disease physicians, pharmacists, nurses, and administrative staff.

As part of the PrEP program, patients were screened for medical contraindications to the use of tenofovir/emtricitabine and for HIV antibody and viral load. Demographic data and reasons for starting or not starting PrEP were assessed during an in-person intake visit. Similar to PrEP trials [1], safety assessments and HIV/STI screening were repeated every 1-3 months after PrEP initiation. Chlamydia and gonorrhea were tested using nucleic acid amplification tests of urine and self-collected swabs of the throat and rectum. Beginning in

July 2014, patients were surveyed by secure email after six months of PrEP use about changes in sexual behavior since starting PrEP.

We used descriptive statistics to compare PrEP initiators and non-initiators and those who did and did not report increases in risk behavior, with chi-square tests for categorical variables and t-tests for continuous variables. We used Kaplan-Meier analysis to compute the cumulative incidence of STIs and HIV after 6 and 12 months of PrEP use. Concurrent diagnosis of an STI at multiple anatomic sites (i.e., pharyngeal, urethral, and/or rectal) was considered one infection, while diagnoses of gonorrhea and chlamydia in one anatomic site were considered multiple infections. Analyses were conducted in SAS 9.1 (Cary, NC). Statistical tests were two-sided except where otherwise indicated, and statistical significance was defined as $P<0.05$.

The institutional review board at KPNC approved this analysis with a waiver of written informed consent.

Results

From July 2012 through February 2015, there were 1045 referrals for PrEP. Of those, 835 (80%) resulted in an in-person evaluation within the study period. Of 801 unique individuals with at least one intake visit, there were 657 PrEP initiators (82%), with 20 restarting PrEP after discontinuing it during the study period, and 144 individuals (18%) who did not initiate PrEP. We observed 388 person-years of PrEP use, and the mean duration of use during the study period was 7.2 months. There was an increase in PrEP referrals and initiation beginning in September 2013 (Figure 1).

Of the 657 individuals initiating PrEP, the mean age was 37 (range 20-68) and 653 (99%) were MSM, with three heterosexual women and one transgender man whose sexual partners were men. One PrEP user reported injection drug use, and 15 reported postexposure prophylaxis (PEP) use in the three months prior to PrEP initiation. There were no differences in age or gender between PrEP initiators and individuals who attended an intake visit but did not initiate PrEP. Compared with non-initiators, PrEP initiators were more likely to report multiple sex partners (84% vs. 69%, $P<0.001$) and prior PrEP use from an outside provider or as part of a PrEP study (7.8% vs. 0.7%, $P=0.002$), but were not more likely to report having an HIV-infected sex partner (30% vs. 25%, $P=0.18$). Non-initiators were more likely to have no disclosed indication for use (7.6% vs. 1.7%, $p<0.001$). Among 144 non-initiators, reasons for not starting PrEP included low risk for HIV (35%),

concern about cost (15%), not wanting to do the required follow-up (10%), preferring PEP as a prevention strategy (6.3%), concern about potential side effects (2.8%), or concern about potentially increasing their sexual risk behavior (1.4%). Few individuals were ineligible for medical reasons, including HIV infection at baseline (2.8%), estimated creatinine clearance ≤60 (1.4%), or osteoporosis (0.7%).

Of the 657 PrEP initiators, 187 were diagnosed with at least one STI during follow-up; 78 individuals were diagnosed with multiple STIs (range 2-10), for a total of 344 STI diagnoses. After six months of PrEP use, 30% of PrEP users were diagnosed with any STI (95% confidence interval [CI]: 26-35%), 18% with a rectal STI (95% CI: 14-22%), 17% with chlamydia (95% CI: 14-21%), 15% with gonorrhea (95% CI: 12-19%), and 3.3% with syphilis (95% CI: 1.9-5.6%). After 12 months of PrEP use, 50% of PrEP users were diagnosed with any STI (95% CI: 43-56%), 33% with a rectal STI (95% CI: 27-39%), 33% with chlamydia (95% CI: 27-39%), 28% with gonorrhea (95% CI: 23-34%), and 5.5% with syphilis (95% CI: 3.3-9.1%). There were no HIV diagnoses during the 388 person-years of follow-up (upper limit of one-sided 97.5% CI: 1.0%).

Of 188 PrEP users who were asked about behavior change after six months of PrEP use, 143 (76%) completed the survey. The number of sexual partners was unchanged in 74%, decreased in 15%, and increased in 11%. Condom use was unchanged in 56%, decreased in 41%, and increased in 3%. No factors were associated with an increase in number of partners or a decrease in condom use, including age, self-reported history of STI, condom use in the three months prior to PrEP initiation, having a known HIV-infected partner, recent methamphetamine or cocaine use, or self-reported number of missed tenofovir/emtricitabine doses in the last month.

Discussion

We observed a dramatic increase in PrEP use in a clinical practice setting, with no new HIV infections among PrEP users. This was despite high rates of STIs – rectal STIs in particular – and self-reported decreases in condom use in 41% of a subset of PrEP users. Interest in and use of PrEP was almost exclusively among MSM, reflecting the HIV epidemic in San Francisco and a rapid increase in awareness and acceptance of PrEP use in this community.

Based on data from the placebo arm of a recent PrEP trial with a similarly high rate of rectal STIs [7], we would have expected an HIV incidence as high as 8.9 per 100 person-

years in our study population in the absence of effective PrEP use. Our data suggest that fears about risk compensation resulting in increased HIV acquisition among PrEP users [8] may be unfounded. High rates of STIs are concerning, however, and reinforce that ongoing screening and treatment for STIs, including hepatitis C [9], remain an essential component of PrEP delivery. Given that STIs are independently associated with HIV acquisition [10, 11], the frequent STI screening in our PrEP program may have facilitated earlier diagnosis and treatment of these infections and thus contributed to the protective benefit of PrEP against HIV infection.

Our study has several limitations. First, the lack of a control group limits our ability to attribute behaviors or incident STIs to PrEP use. Moreover, comprehensive pre-PrEP STI data were not available for analysis. Second, although Kaiser Permanente patients are demographically comparable to the overall population in California [12], San Francisco has relatively high rates of HIV incidence, prevalence, treatment, and viral undetectability; thus, our results may not be generalizable to other settings. Third, behavioral data were collected for clinical and not research purposes, and thus lacked information on HIV treatment and viral load among partners, "PrEP-sorting" (selective non-use of condoms with partners on PrEP), or the magnitude of change in condom use. Additionally, individuals with low HIV risk may have been more likely to discontinue PrEP use before six months, and thus not been surveyed.

In summary, in this experience with increasing PrEP use in a clinical setting, there were no new HIV infections despite high rates of STIs and reported decreases in condom use. While demand for PrEP is growing among MSM, outreach is needed to others at risk for HIV, including transgender women, heterosexual men and women, and people using injection drugs. Finally, with increased use of PrEP in the community, a more refined understanding of "risk compensation" is needed to understand how changes in sexual behavior may impact risk for HIV and other STIs among PrEP users.

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Conflict of Interest Declaration

JLM has received research grant support from Merck. All other authors: no reported conflicts.

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Figure 1.

HIV preexposure prophylaxis (PrEP) referrals, intakes, and initiation by month at Kaiser Permanente San Francisco, July 2012 – February 2015. The graph includes a total of 1035 referrals, 835 intakes, and 677 initiations, including 20 individuals who restarted PrEP after discontinuing during the study period.