AIDS and Behavior (2019) 23:1797–1802
https://doi.org/10.1007/s10461-018-2296-x

ORIGINAL PAPER

PrEP in the Real World: Predictors of 6-Month Retention in a Diverse Urban Cohort

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Published online: 19 October 2018

Abstract
The effectiveness of HIV pre-exposure prophylaxis (PrEP) depends on adherence, which requires retention in PrEP care. We sought to examine factors associated with six-month retention in PrEP care among individuals prescribed PrEP between 2011 and 2015 in a large, academic health system in the Bronx, New York. We used multivariable logistic regression to identify factors independently associated with six-month retention. Among 107 patients, retention at 6 months was 42%. In the multivariable analysis, heterosexual individuals were less likely to be retained in PrEP care at 6 months, but individuals who received prescriptions from attending physicians were more likely to be retained in care. Larger prospective studies are needed to better evaluate the individual and health system factors associated with long-term engagement in PrEP care.

Keywords HIV prevention · PrEP · Retention in care · Implementation

Resumen
La efectividad de la Profilaxis de Pre-Exposición para el VIH (PrEP) depende de la adherencia, la cual requiere retención en el cuidado de PrEP. Buscamos examinar los factores asociados con la retención durante seis meses en el cuidado de PrEP, entre las personas a las cuales se les recetó PrEP entre los años 2011 y 2015 en un amplio sistema académico de salud en el Bronx, Nueva York. Utilizamos análisis de regresión logística multivariada para identificar los factores independientemente asociados con seis meses de retención. Entre 107 pacientes, la retención a los seis meses fue del 42%. En el análisis multivariado, las personas que se identificaron como heterosexuales fueron menos propensas a estar recibiendo el cuidado de PrEP a los seis meses, pero las que recibieron su receta de parte de los médicos asistentes tuvieron más probabilidad de retención en el cuidado de PrEP. Se necesitan estudios prospectivos más amplios para evaluar mejor los factores individuales y del sistema de salud asociados con la participación a largo plazo en el cuidado de PrEP.

Palabras clave prevención del VIH · PrEP · retención en cuidado · implementación

Introduction

Pre-exposure prophylaxis (PrEP) with daily oral emtricitabine and tenofovir disoproxil fumarate (FTC/TDF) is effective in preventing HIV transmission among individuals at high risk of infection [1]. The effectiveness of PrEP is tightly linked to adherence [2], which requires retention in care. Regular follow-up visits allow health care providers to assess ongoing HIV risk and suitability of continuing PrEP, as well as to provide ongoing adherence and behavioral counseling to patients. Current Centers for Disease Control and Prevention (CDC) guidelines recommend

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follow-up visits within three months of PrEP initiation, and every three months thereafter [3].

Despite growing adoption of PrEP in clinical practice, there are limited data on retention in care among individuals taking PrEP. Several studies have now described initial PrEP outcomes in real-world settings [4, 5]; however, these still focus on specialized clinical programs and may not reflect a broad cross-section of individuals at risk of HIV acquisition. Emerging literature has demonstrated that PrEP can be adopted by a range of subspecialties and clinic environments [6, 7], but outcomes have not yet been examined.

Successful PrEP implementation requires an understanding of factors that influence retention in care across heterogeneous real-world settings, particularly among historically underserved populations. We examined PrEP care outcomes across a large integrated academic health system in the Bronx, New York City, where HIV incidence rates are among the highest in the United States [8]. The primary goal of this study is to characterize patient-, provider-, and clinic-level factors that may impact retention in PrEP care. We report initial PrEP retention outcomes in a cohort of individuals with diverse risk factors for HIV acquisition.

Methods

Study Design, Population, and Setting

We conducted a retrospective study of individuals prescribed PrEP within a large, urban, integrated academic health system with clinics located in the Bronx, New York. Using a large clinical database, we identified a cohort of patients initiating PrEP between 2011 and 2015. We included individuals age 18 and over who had a negative HIV test and received a prescription for FTC/TDF between January 1, 2011 and November 4, 2015. We excluded individuals prescribed FTC/TDF for Hepatitis B infection or exclusively for HIV post-exposure prophylaxis (PEP). Using a centralized electronic medical record database, we conducted a chart review to confirm PrEP prescriptions and extracted longitudinal prescription data and clinical data from office visits, phone encounters, and online communications through August 1, 2016. This date cut-off ensured that all patients included in the analysis had at least six months of follow-up time from when their PrEP prescription was initiated and, therefore, could be evaluated for the study outcome. During the period studied, there was no system-wide standard protocol or set of dedicated resources for PrEP management, although one clinic site was a dedicated sexual health center that employed health educators who provided PrEP-related counseling to patients during clinic visits.

Measures and Data Collection

All data were collected via manual chart review using a standardized data dictionary and chart abstraction tool. We extracted data on baseline characteristics as of the date of PrEP initiation. In addition to basic socio-demographic variables (age; assigned sex at birth; gender identity; race/ethnicity; sexual orientation; and insurance status), we also extracted data relating to HIV risk factors that were documented at the time of PrEP initiation, including partner HIV status, multiple concurrent sex partners, condomless sex, transactional sex, prior non-occupational PEP (nPEP), and intravenous drug use. Information relating to these behavioral risk factors were assessed and extracted only at the time of PrEP initiation. Finally, we collected provider- and clinic-level data, including the clinic setting where PrEP was initially prescribed (primary care, sexual health center, infectious diseases clinic, adolescent medicine clinic, or women's health center) and the level of training of the provider initially prescribing PrEP. Provider level of training was categorized as either attending-level physician, trainee-level physician (resident or fellow), or mid-level provider (nurse practitioner or physician assistant).

Our outcome of interest was retention in care six months after initial PrEP prescription. We defined 6-month retention as documentation of a renewed prescription for TDF/FTC and a repeat HIV test at 180 ± 60 days from the initial PrEP prescription. Among individuals who were known to have discontinued PrEP during the study period based on provider documentation in the medical record, we also extracted data on reasons for discontinuation.

Statistical Analysis

We used descriptive statistics to summarize the baseline characteristics (including socio-demographic information, HIV risk factors, provider-, and clinic-level data) and outcomes (including 6-month retention and reasons for PrEP discontinuation). To identify factors associated with our outcome of interest, we initially performed logistic regression analysis. Variables meeting a significance threshold of $p < 0.10$ in bivariate analysis were included in the multivariable logistic regression model. Data were analyzed using Stata version 11.2 (StataCorp, College Station, Texas).

Ethical Statement

This study was approved by the Albert Einstein College of Medicine Institutional Review Board.

Results

Baseline Characteristics

We identified a cohort of 107 individuals who initiated PrEP during the study period. The median age at PrEP initiation was 28 years (IQR 24–37). 69% were men, 28% were cisgender women, and 3% were transgender women. 36% were Hispanic and 26% were either Non-Hispanic Black or African-American. Just over half of the total cohort (52%) were men who have sex with men. Of the 36% who identified as heterosexual, most (72%) were female. At the time of PrEP initiation, 54% percent had at least one partner living with HIV, 49% reported condomless sex, 13% had previously received nPEP, and 4% had a documented history of injecting drugs.

Fifty-eight percent of all individuals had Medicaid or Medicare insurance, 37% had private insurance, and 8% received PrEP through a state prescription assistance program. The initial prescribing clinician was an attending physician for 71% of individuals, a resident or fellow trainee physician for 18%, and a mid-level provider for 11%. The majority (52%) were started on PrEP in a primary care setting; of the remainder, 21% were at a sexual health center, 16% at an infectious diseases clinic, 6% at an adolescent medicine clinic, and 5% at a women's health center.

6-Month Retention in Care and Reasons Cited for PrEP Discontinuation

Overall, 6-month retention in PrEP care was 42% (45/107). Among the 62 individuals not retained in care, 17 had one or more reasons for PrEP discontinuation documented. The most frequently documented reason was change in perceived risk of HIV acquisition (9/17), with seven of nine individuals having ended a relationship with a partner living with HIV. Side effects contributed to the decision to discontinue PrEP in four cases; of these, two had nausea/vomiting, one had dysgeusia (distorted sense of taste), and in one case the specific side effect was not documented. One individual died of unrelated causes. There was one seroconversion; however, review of provider documentation indicated that the individual had not started taking PrEP despite it being prescribed prior to the date of seroconversion. Several other reasons were cited in only one case each; these included concerns about stigma, trust issues in a relationship, and the burden of taking daily medication.

Predictors of 6-Month Retention in Care

In bivariate analysis, several factors were significantly associated with 6-month retention in care (Table 1). Compared to all other sexual orientations, heterosexuals were significantly less likely to be retained in care (OR 0.23, 95% CI 0.09–0.57), as were individuals who had a main partner living with HIV at the time of PrEP initiation (OR 0.43, 95% CI 0.19–0.98). Receiving PrEP from an attending physician (versus a resident/fellow trainee or mid-level provider; OR 5.20, 95% CI 1.81–15.0) was positively associated with retention. We did not observe significant association with clinic setting, alcohol use, insurance status, or demographic variables such as age, gender, and race/ethnicity.

Five variables were included in the multivariable model based on meeting the significance threshold of $p < 0.10$ in bivariate analysis: sexual orientation, main partner with HIV, any partner with HIV, multiple current partners, and provider level of training. Only sexual orientation and training level of the prescribing provider remained significant in this adjusted analysis. Heterosexual orientation was negatively associated with 6-month retention in care (aOR 0.25, 95% CI 0.08–0.77), while receipt of PrEP prescription from an attending-level provider (aOR 5.52, 95% CI 1.83–16.6) remained positively associated with our retention outcome. In addition, we conducted a sensitivity analysis in which the retention outcome was defined solely on the basis of a renewed prescription at 6 months (removing the HIV testing criterion). Our findings in this sensitivity analysis were similar to those of our primary analysis described above. As such, we present our primary analysis only.

Discussion

This study is among the first to describe factors associated with retention in PrEP care in a "real-world" clinical setting. In a diverse cohort representing the heterogeneous distribution of behavioral risk factors that contribute to ongoing HIV transmission in our community, we found that 42% of individuals who initiated PrEP were retained in care at six months. This work builds upon existing literature by assessing retention in PrEP care across a variety of HIV risk groups, clinical settings, and socio-demographic backgrounds. In addition to being racially and ethnically diverse, our cohort of PrEP users reflected the realities of the local HIV epidemic in our community, as we observed a relative distribution of HIV risk factors that closely mirrored that of recent incident HIV infections in the Bronx [8].

Although less than half of our cohort was retained in PrEP care at six months, it is worth noting that most previous studies have focused on specialized PrEP programs

Table 1 Predictors of 6-month retention in care (N = 107)

Variable	6-month retention		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	Yes (n = 43)	No (n = 64)		
Age > 25 years	30 (70%)	46 (72%)	0.90 (0.39–2.11)	
Female	9 (21%)	21 (33%)	0.54 (0.22–1.33)	
Race/ethnicity				
Hispanic	17 (59%)	17 (35%)	1.89 (0.74–4.79)[a]	
Non-hispanic black	7 (24%)	21 (43%)	0.42 (0.15–1.18)[a]	
Other	5 (17%)	7 (14%)	1.25 (0.36–4.37)[a]	
Heterosexual	8 (19%)	31 (51%)	**0.23 (0.09–0.57)**	**0.26 (0.08–0.84)**
Main partner HIV positive	13 (30%)	32 (50%)	**0.43 (0.19–0.98)**	0.61 (0.17–2.20)
Any partner HIV positive	20 (46%)	38 (59%)	0.59 (0.27–1.30)	
Multiple current partners	20 (47%)	18 (28%)	2.22 (0.99–5.00)	0.75 (0.22–2.58)
Condomless sex reported	21 (49%)	31 (48%)	1.02 (0.47–2.20)	
Prior nPEP	9 (21%)	5 (8%)	3.12 (0.97–10.1)	2.82 (0.67–11.8)
Active alcohol use	20 (47%)	26 (41%)	1.27 (0.58–2.77)	
Clinic setting				
Primary care	22 (51%)	34 (53%)	0.92 (0.43–2.00)[a]	
Sexual health center	9 (21%)	13 (20%)	1.26 (0.42–3.81)[a]	
Other	12 (28%)	17 (27%)	1.07 (0.45–2.55)[a]	
Provider prescribing PrEP				
Attending physician	38 (88%)	38 (59%)	**5.20 (1.81–15.0)**[a]	**7.64 (2.32–25.2)**[a]
Trainee physician	3 (7%)	16 (25%)	**0.23 (0.06–0.83)**[a]	
Mid-level provider	2 (5%)	10 (16%)	0.26 (0.05–1.27)[a]	
Insurance status				
Private	19 (44%)	21 (33%)	1.62 (0.73–3.60)[a]	
Medicare/medicaid	23 (53%)	39 (61%)	0.74 (0.34–1.61)[a]	
Uninsured	1 (2%)	4 (6%)	0.36 (0.04–3.31)[a]	

Bold denotes $p < 0.05$. Covariables with unadjusted $p < 0.10$ are included in the multivariable model. Percentages represent column percentages. Totals may not add up to 107 due to missing data

OR odds ratio, *nPEP* non-occupational post-exposure prophylaxis, *NP* nurse practitioner, *PA* physician assistant

[a]For variables presented as categorical rather than dichotomous, the referent group is all other sub-categories

and demonstration projects targeting specific risk groups such as MSM. In such settings, dedicated financial and administrative support for PrEP is typically available and PrEP knowledge among health care providers is likely to be higher [4, 9, 10]. One recent study reported a 57% rate of 6-month retention among 267 individuals prescribed PrEP in three US cities, although all clinic sites in that study had specialized PrEP programs with support from the pharmaceutical industry and received free ARVs [10]. In contrast, most individuals in our cohort were prescribed PrEP in a primary care setting with no dedicated resources for PrEP. Individuals who initiate PrEP with a primary care provider (PCP) may have different risk factors and needs compared to those who initiate PrEP at a sexual health center or in other specialized settings. Implementing PrEP across the broader population will require increased awareness and action among PCPs, who are uniquely positioned to identify and provide preventative care to at-risk individuals [7].

Retention in PrEP care was significantly lower among heterosexual individuals in this cohort. In contrast to most prior studies on retention with PrEP, which have focused primarily on MSM [4, 10, 11], we observed a relatively balanced distribution of MSM and heterosexuals, accounting for 52% and 36% of our study population, respectively. In one study of partners of HIV + individuals in New York City, heterosexuals were significantly less likely to be aware of PrEP compared with MSM [12]. Another study found that heterosexuals at risk of HIV acquisition may have lower HIV risk perceptions compared to MSM and be less willing to initiate and continue taking PrEP [13]. Individuals with a known HIV positive sexual partner may also decide to stop taking PrEP if the relationship ends. Similarly, individuals in a stable monogamous relationship with an HIV

positive partner may feel less compelled to continue PrEP over time if their partner has had a sustained undetectable viral load. Indeed, in bivariate analysis we observed that individuals documented as having a main partner living with HIV at the time of PrEP initiation had significantly lower 6-month retention. However, this association did not reach significance in the multivariable model, and it should be noted that partner HIV status was only assessed at baseline. Nonetheless, as public health messaging that an undetectable viral load effectively nullifies sexual transmission risk from an HIV positive individual on antiretroviral therapy (e.g. the "U = U" campaign) [14], such a situation may become increasingly common.

We also found that those started on PrEP by an attending-level provider were more likely to be retained in care at six months. This may be related to several factors that generally differentiate attending physicians from trainees or mid-level providers, including increased accessibility, greater ability to provide sustained longitudinal care, and greater knowledge about PrEP. In one study of PCPs in the United States, attending providers were more likely to provide PrEP compared to other provider types, although this association was not significant when adjusting for experience in providing HIV care [7]. Attending providers generally have more experience and are better positioned to provide long-term continuity of care than trainees, who typically rotate through multiple different clinical sites and may not be as easily accessible. Because of this, attending providers may be better suited to establish strong and durable relationships with patients, which could heighten patient engagement and retention in care. Clinics could consider implementing additional support structures (such as dedicated PrEP navigators, case managers, or other ancillary support) that specifically target patients seen by trainee providers in order to improve retention in care.

This study highlights several areas that should be addressed in expanding PrEP implementation. Our finding of low retention among heterosexual individuals underscores the notion that interventions may need to be individually tailored to target different risk groups. Changes in perceived risk may also affect willingness to continue taking PrEP, particularly among individuals with sexual partners living with HIV. Future research that explores why individuals discontinue PrEP will be important to improve retention and adherence, particularly among those who are at consistently high risk for HIV over time. One ongoing challenge is that, for many individuals, HIV risk fluctuates over time. Accordingly, a flexible model of care provision for PrEP is needed, in which the optimal level of retention within a population is similarly dynamic.

Operational research and programmatic work may also be needed to broaden clinical training around PrEP to all potential prescribers, including physician trainees and mid-level providers. In addition, novel interventions to promote adherence and engagement in care warrant further examination; these include mobile health applications [15], remote monitoring [16], and online peer counseling programs.

Our study has several limitations. We relied on chart review, introducing the possibility of reporting bias. For example, there was a relatively high frequency of individuals with either unknown or unspecified race/ethnicity, making it difficult to draw substantive conclusions with respect to this important factor. In addition, our inability to measure other key demographic characteristics such as socioeconomic status raises the possibility of confounding by this or other unmeasured factors. In particular, the observed association between having an attending-level provider and greater retention may be limited by the inability to adjust for certain factors. Although a majority of the > 30 individual clinic sites had a mix of attending, trainee, and mid-level providers, a small number of sites were exclusively staffed by attending physicians. It is unclear if there were any systematic differences between patients seen at these sites compared with those staffed by both attending and trainee physicians. Although we extracted data on reasons for PrEP discontinuation, most individuals who failed to be retained in care did not have a specific reason documented. It is conceivable that our definition of retention may underestimate the true number of individuals still taking PrEP, since it does not account for the possibility of moving between healthcare systems, nor for the possibility of intermittent use patterns that might require less frequent PrEP refills even if appropriate based on one's risk activities. We were also unable to assess for more complex social and behavioral factors (e.g. stigma, social support) that might impact retention. Finally, our study cohort represents early PrEP adopters, and patient and provider behavior may have since changed given recent increases in PrEP visibility.

In summary, this study highlights the realities involved in expanding PrEP from specialized programs into generalized medical practice. Our findings also lend support to a model of differentiated service delivery for PrEP care, in which interventions are tailored to address the specific barriers to care encountered by different sub-populations or risk groups across the broader population. Furthermore, it may be important for interventions to be targeted not only to specific patient sub-populations, but also on the basis of structural and provider-level factors that might be linked to retention in care, such as the training level of the of physician or mid-level provider prescribing PrEP. In addition, this study reinforces the importance of ensuring that health care providers across a spectrum of subspecialties and training levels have adequate support and education to enable them to care for patients taking PrEP. Finally, as PrEP uptake increases and becomes more generalized, interventions aimed at

improving retention in PrEP care should be a key focus of efforts to expand and optimize HIV prevention services.

Funding This work was supported in part by the Einstein-Rockefeller-CUNY Center for AIDS Research funded by the National Institutes of Health (P30-AI-051519). Viraj Patel is supported by K23-MH102118, Uriel Felsen is supported by K23-MH106386, and Oni Blackstock is supported by K23-MH102129.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments. For this type of study formal consent is not required.

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