Determinants of pre-exposure prophylaxis (PrEP) persistence in a high-risk population in Central Florida

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ABSTRACT

Orlando has the second highest HIV incidence in the USA. Tenofovir disoproxil fumarate/emtricitabine is approved as pre-exposure prophylaxis (PrEP) to minimize HIV transmission. Our study describes the PrEP care continuum and factors impacting PrEP persistence during the first year of PrEP care at a sexual health clinic in Orlando. Patients initiating PrEP between 2014 and 2017 with at least 1 year of follow-up were eligible for inclusion. Demographic and clinical factors were extracted from medical records. At the end of the first year of PrEP care, patients seen within the last 6 months were defined as 'persistent' whereas patients lost to follow-up for ≥6 months were defined as 'not persistent'. We evaluated factors associated with PrEP persistence with Firth's multivariable logistic regression. Of 300 patients meeting inclusion criteria, 96% were male, 59% were ≥30 years old, 59% identified as men who have sex with men and 57% endorsed recent condomless anal intercourse. Of PrEP initiators, 133 (44.3%) were persistent in the first year, whereas 167 (55.7%) were not persistent. PrEP persistence was positively associated with age ≥30 years (OR 1.04, 95% CI 1.0 to 1.08) and negatively associated with non-white race (OR 0.33, 95% CI 0.12 to 0.83). There were no HIV seroconversions among persistent patients. In our study, younger and minority patients were less likely to persist in PrEP care and persistence was poor despite many being insured and 'high-risk'. Further research is needed to identify and address barriers that hinder PrEP persistence, specifically among younger, minority patients.

INTRODUCTION

Pre-exposure prophylaxis (PrEP) consisting of tenofovir disoproxil fumarate/emtricitabine taken daily can minimize HIV acquisition.[1] PrEP use in the South is suboptimal despite higher HIV incidence rates.[2] In 2016, while 52% of new HIV diagnoses occurred in the Southern USA, only 27% of PrEP users resided in this area.[3] Studies from the South have demonstrated that inadequate insurance frequently impedes PrEP uptake and persistence[4 5] due to high-deductibles and out-of-pocket costs.[6] This may especially impact young adults who are usually covered by their parents' insurance up to 26 years of age under the Affordable Care Act,[7] but may find themselves without a stable form of insurance afterwards. This problem is likely amplified by the fact that many Southern States chose not to participate in Medicaid expansion leaving large segments of the population uninsured.

In Mississippi, despite the implementation of an industry-sponsored PrEP assistance program to ameliorate structural barriers, researchers found that PrEP use remained suboptimal due to social barriers,[4] which included distrust of medical providers, misconceptions of who PrEP is intended for and fear of stigma from PrEP use.[4 8] These data imply that interventions to promote PrEP persistence in the South will likely need to address both social and structural barriers to ensure at-risk populations access and use this highly effective prevention tool.

According to the 2018 Centers for Disease Control and Prevention HIV Surveillance Report, Orlando had the second highest HIV incidence in the USA. In 2012, the Orlando Immunology Center (OIC) implemented one of the first PrEP clinics in Central Florida. Here, we describe the PrEP care continuum at the OIC and evaluate factors associated with PrEP persistence to understand how we can improve HIV prevention care outcomes in Central Florida.

METHODS

The OIC is a private infectious disease practice in Orlando, which provides primary care including sexual health services to approximately 1000 at-risk adults aged ≥18 years. Referral sources include self-referral, other physician offices and community-based organizations. Patients are PrEP eligible if they meet risk criteria outlined in the Centers for Disease Control and Prevention (CDC) summary of guidance for PrEP use,[9] have a negative fourth-generation HIV antigen/antibody test and a creatinine clearance of ≥60 mL/min. Most patients use private insurance to pay for provider visits, lab services and medication. There is an income-based sliding scale program

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for those without insurance seeking PrEP services. Manufacturer co-pays cards are provided to patients with health insurance to minimize associated prescription costs, and uninsured patients use the manufacturer assistance program to obtain the medication free of charge.

All PrEP eligible patients undergo testing for urethral, rectal and pharyngeal chlamydia and gonorrhea in addition to syphilis prior to starting PrEP. At the initial PrEP visit and all follow-up visits, patients are asked about sexual behaviors (number of sexual partners, number of HIV-infected partners, engagement in condomless anal intercourse (CAI)) and undergo intensive risk reduction and adherence counseling. A 30-day prescription is given at the first PrEP visit and patients follow-up after 1 month. All subsequent visits are scheduled quarterly, and a 90-day prescription is given at each follow-up visit. At these visits, patients are asked about PrEP side effects and adherence.

Patients initiating PrEP between January 2014 and August 2017 with at least 1 year of follow-up data were eligible for the study. Patients receiving postexposure prophylaxis were excluded. At the end of the first year of PrEP care, patients seen within the last 6 months were defined as 'persistent' whereas patients lost to follow-up for ≥6 months were defined as 'not persistent'. This definition was based on prior research studies, which examined PrEP persistence in various cities across the USA.[10–12]

We examined PrEP uptake and persistence to describe the PrEP care cascade at the OIC. Descriptive statistics were used to describe demographic and clinical characteristics of the study sample. Factors associated with PrEP persistence were analyzed with Firth's multivariable logistic regression. Sensitivity analyses to examine factors associated with complete PrEP follow-up (defined as attendance at all quarterly visits during the first year of PrEP care) compared with early PrEP drop-out (defined as PrEP initiation without attendance at any follow-up visit) was performed using multinomial logistic-linear regression. All analyses were carried out using SAS V.9.4.

RESULTS

As of August 2017, 300 patients met inclusion criteria; 178 (59%) were ≥30 years old, 287 (96%) were men, 57 (19%) were non-white and 178 (59%) identified as men who had sex with men (MSM) (table 1). Two hundred and eighty-three (94%) had private insurance. Regarding the CDC risk criteria for PrEP use, 85% fulfilled at least one risk behavior with 170 (57%) reporting CAI within 6 months prior to initiating PrEP, 67 (22%) were diagnosed with a baseline sexually transmitted infection (STI) at PrEP initiation, 95 (32%) reported having at least one HIV-infected partner and 115 (38%) endorsed having multiple sexual partners within 1 year prior to PrEP initiation. Of patients with

Table 1 Factors affecting PrEP persistence among a high-risk cohort at the Orlando Immunology Center (n=300)

Characteristic	PrEP persistent (n=133) n (%)	PrEP non-persistent (n=167) n (%)	Multivariable OR (95% CI)	P value
Age				
<30 years	46 (35)	76 (46)	Ref	**0.02**
≥30 years	87 (65)	91 (54)	**1.04 (1.0 to 1.08)**	
Sex				
Male	131 (98)	156 (93)	Ref	0.99
Female	2 (2)	11 (7)	12.74 (0.32 to 2616)	
Race/Ethnicity*				
White	80 (60)	65 (39)	Ref	**0.04**
Non-white	18 (7)	32 (10)	**0.33 (0.12 to 0.83)**	
Sexual orientation*				
MSM	89 (30)	89 (30)	Ref	
Bisexual	24 (8)	37 (12)	0.56 (0.19 to 1.57)	0.17
Heterosexual	2 (0.6)	12 (4)	0.12 (0 to 2.18)	0.99
Insurance status				
Private	126 (42)	157 (52)	Ref	
Public	4 (1)	4 (1)	0.56 (0.04 to 5.85)	0.27
Uninsured	1 (0.3)	3 (1)	0.34 (0 to 5.13)	0.99
Sexual partners*				
Single	49 (37)	67 (40)	Ref	0.14
Multiple	59 (44)	56 (34)	1.46 (0.64 to 3.39)	
Baseline STI*				
No	102 (77)	115 (69)	Ref	0.34
Yes	31 (23)	36 (22)	0.99 (0.4 to 2.44)	
Condomless anal intercourse*				
No	22 (17)	34 (20)	Ref	0.89
Yes	84 (63)	86 (51)	0.85 (0.32 to 2.24)	

P values <0.05 have been made bold for ease of interpretation.
*Missing data not shown and not included in analysis.
MSM, men who have sex with men; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection.

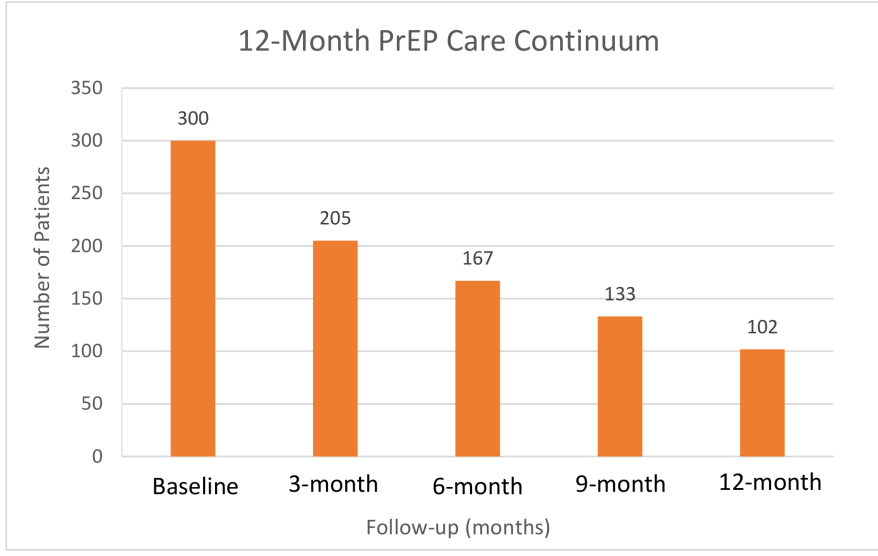

Figure 1 12-month pre-exposure prophylaxis (PrEP) care continuum at the Orlando Immunology Center, 2014–2017 (n=300).

baseline STI, 36 (12%) were infected with syphilis, 25 (8%) were infected with chlamydia and 11 (4%) were infected with gonorrhea, 5 (2%) were co-infected with >1 STI.

At the end of the first year of PrEP care, 133 (44%) patients remained persistent (95% CI 0.49 to 0.61) whereas 167 (56%) were not persistent. Of 300 patients, 102 (34%) completed every quarterly follow-up visit during the 12-month period (figure 1). Five patients discontinued PrEP due to side effects; one due to constipation, three due to gastrointestinal upset and one due to fatigue. There were no HIV seroconversions among persistent patients. Evaluated factors positively associated with PrEP persistence included age ≥30 years (OR 1.04, 95% CI 1.0 to 1.08) whereas non-white race was negatively associated with PrEP persistence (OR 0.33, 95% CI 0.12 to 0.83) (table 1). Sensitivity analyses confirmed that age ≥30 years was the only factor positively associated with complete PrEP follow-up (OR 1.08, 95% CI 1.02 to 1.16) whereas non-white race was the only factor negatively associated with complete PrEP follow-up (OR 0.24, 95% CI 0.07 to 0.83).

We also assessed adherence and risk factors for the 205 patients who attended at least one follow-up visit. One hundred and eighty-eight (63%) reported 100% adherence to their PrEP regimen at the most recent follow-up visit. Seventeen reported non-adherence and of those, four experienced refill delays, one misplaced the medication, one discontinued due to fatigue, one experienced clavicular fracture and the others had no reason documented. At the most recent follow-up visit, 62 (21%) endorsed multiple partners, 43 (14%) had at least one HIV-infected partner, 97 (32%) engaged in CAI with a partner of unknown HIV status and 29 (10%) were diagnosed with an STI. Fifty-nine (20%) reported more than one risk factor.

DISCUSSION

This is the first study evaluating PrEP persistence among a high-risk population from Central Florida and demonstrated that patients who were <30 years of age and non-white were less likely to persist in PrEP care. Prior data collected from STD clinics in San Francisco, Miami and Washington DC have demonstrated that black race is associated with early loss to follow-up in PrEP care, even despite intensive PrEP navigation and provision of low or no-cost medication.[13] Other studies have shown that high-deductibles and out-of-pocket costs could hinder PrEP persistence among black MSM, but patients with private insurance and government-subsidized plans experienced minimal PrEP discontinuation.[6] Social barriers such as fear of stigma and distrust of medical providers have also been shown to impact PrEP persistence among minority patients.[14] At the OIC, most patients had private insurance and used the manufacturer co-pay assistance program to obtain the medication. However, patients were responsible for co-pays and out-of-pocket costs related to provider visits and laboratory testing, and it is unknown whether this may have created significant financial barriers, particularly for non-white patients who may be more affected by the latter. We do acknowledge that reasons for PrEP non-persistence were not obtained in our study, however interventions to reduce out-of-pocket costs and efforts to incorporate provider training on cultural sensitivity may improve PrEP persistence among minority patients in our clinic.

Other studies evaluating PrEP persistence have also identified that younger patients are less likely to persist in PrEP care with commonly cited reasons being lack of insurance and transportation barriers.[15–17] At the OIC, we observed similar findings even though many of our younger patients had adequate insurance and were instructed to use the manufacturer co-pay assistance program to obtain the medication. However, high out-of-pocket costs associated with provider visits and labs may have been a significant barrier for this group who are often unfamiliar with navigating the healthcare system and accessing other assistance programs.[18 19] Our results suggest that intensive PrEP care navigation services and interventions should make PrEP care as convenient and easy as possible, that is, on-site pharmacy refills, utilization of telemedicine visits and remote or mobile clinics may improve PrEP persistence among younger patients at the OIC.

Our study did not reveal differences in PrEP persistence by gender, although prior studies have demonstrated lower PrEP persistence among women.[15] Women only accounted for 4% of our sample and this number was likely too small to make meaningful comparisons. However, this does highlight the low number of women seeking PrEP services at our clinic and the need to improve PrEP uptake among high-risk women. In 2018, females accounted for 19% of new HIV diagnoses in the USA with African-American and Hispanic women disproportionately affected.[20] Although traditional HIV risk factors defined by the CDC[21] are shared by both sexes, there are unique risk factors among women that may be poorly identified during a routine sexual risk assessment. For example, a history of trauma with engagement in violent relationships has been shown to significantly increase a woman's risk of HIV acquisition.[22 23] However, the CDC-guidance criteria for PrEP use in women does not acknowledge a history of trauma as an important PrEP indicator.[9] This suggests that risk-based identification tools for PrEP need to be revised to incorporate assessments of other less obvious factors known to affect HIV risk among women to improve PrEP uptake in this population.

A concerning finding is the suboptimal PrEP persistence in our sample with 85% fulfilling at least one CDC risk criteria for PrEP use. Less than half of our sample remained persistent and even less completed every quarterly follow-up visit during the first year of PrEP care (figure 1). Of those who discontinued, only five were due to side effects. Of those who persisted, none seroconverted. This reaffirms the efficacy and good tolerability of PrEP for those who take it as prescribed. Furthermore, 94% of our cohort was privately insured suggesting that barriers such as side effects, lack of efficacy and inadequate insurance were not responsible for the poor PrEP persistence observed. Previous studies have demonstrated that outside of cost, difficulty attending visits, inability to obtain PrEP through primary care services, unstable housing and low HIV risk perception are other important reasons for non-persistence.[13 24–26] This suggests that efforts to streamline PrEP care, including incorporation into primary care and other support services may be helpful to improve PrEP persistence. Other tools include the use of routine sexual risk assessments to help individuals accurately identify and stratify their HIV risk.

Our study has several limitations, which included the inability to contact patients lost to follow-up and address reasons for PrEP non-persistence. Also, as previously noted, our sample had a limited number of female patients and therefore data may not have been statistically powered to detect meaningful associations by gender.

In conclusion, our study revealed that PrEP persistence was suboptimal among a high-risk population in Central Florida despite that many had private insurance and adequate healthcare access. This suggests that further research to understand other factors, including social and cultural barriers which impact PrEP care, are urgently needed to develop interventions to promote PrEP efficacy, particularly among younger and minority populations.

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