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# Missed Opportunities to Prescribe HIV Pre-Exposure Prophylaxis by Primary Care Providers in Saint Louis, Missouri

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## Abstract

**Purpose:** Optimal HIV pre-exposure prophylaxis (PrEP) scale-up in the United States requires prescribing by primary care providers (PCPs). We assessed barriers to patients obtaining PrEP from their PCPs.

**Methods:** Patients seeking PrEP at an Infectious Diseases (ID) Clinic in St. Louis, Missouri from 2014 to 2016 were asked about demographics, sexual behaviors, whether PrEP was initially sought from their PCP, and barriers to obtaining PrEP from their PCP. Multivariable logistic regression was performed to identify predictors for having asked a PCP for PrEP.

**Results:** Among 102 patients, the median age was 29 years, 58% were white, and 88% were men who have sex with men. Most (65%) had a PCP and, of these, 48% had asked their PCP for PrEP, but were not prescribed it. About half (52%) reported that their PCPs perceived prescribing PrEP as specialty care. Many (39%) indicated that they felt uncomfortable discussing their sexual behaviors with their PCP. Patients with an HIV-positive sex partner in the last 3 months were less likely to ask for PrEP from their PCPs than others (Adjusted Odds Ratio: 0.07; 95% CI: 0.01–0.53). Eighty-three percent of patients were referred to a new PCP with whom they could feel more comfortable discussing PrEP.

**Conclusions:** During initial PrEP implementation, ID specialists can play an important role in providing education and linking PrEP patients to PCPs. However, PCPs may need additional training about PrEP and how to provide culturally sensitive sexual healthcare, if widespread scale-up is to be effective in decreasing HIV incidence.

**Keywords:** healthcare providers, HIV prevention, implementation, pre-exposure prophylaxis (PrEP), primary care

## Introduction

IN 2014, OVER 40,000 HUMAN immunodeficiency virus (HIV) infections were diagnosed in the United States.<sup>1</sup> Antiretroviral pre-exposure prophylaxis (PrEP) is an HIV prevention approach that has the potential to reduce the number of new HIV infections significantly. Currently available, FDA-approved PrEP is a fixed dose combination of emtricitabine and tenofovir disoproxil fumarate (FTC/TDF), which is taken once daily by at-risk HIV-negative individuals to prevent HIV acquisition. Major studies have demonstrated the efficacy of PrEP in preventing HIV among men who

have sex with men (MSM), heterosexuals, and injection drug users.<sup>2-6</sup> The Centers for Disease Control and Prevention (CDC) estimates that national PrEP implementation could potentially reduce HIV incidence by 70% by 2020.<sup>7</sup> Expanding PrEP use alone among key populations has the potential to prevent an estimated 50,000 new infections.<sup>8</sup> The CDC and the International Antiviral Society-USA Panel recommend integrating PrEP into routine HIV prevention services offered by primary care providers (PCPs).<sup>9,10</sup>

As PrEP is implemented in nonresearch settings, non-infectious diseases (ID) specialists will play a critical role in scale-up. The number of ID specialists is declining.<sup>11-13</sup>

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Moreover, encouraging PCPs to prescribe PrEP will integrate sexual health services with primary care, which is more holistic for otherwise healthy patients.<sup>14</sup> However, few (7%) PCPs have prescribed PrEP despite moderate levels of awareness of (66%) and high willingness to prescribe PrEP (91%).<sup>15</sup> Reasons for a lack of provider prescribing include a lack of awareness, comfort with prescribing antiretrovirals, and organization administrative support, as well as concerns regarding risk compensation.<sup>16–28</sup> The goals of this study were to explore whether patients seeking PrEP at an ID specialty clinic were engaged in primary care, if they had asked their PCPs about PrEP before seeking specialty care, and to identify the reasons why patients did not ask their PCPs for PrEP and why PCPs had declined to prescribe PrEP.

## Methods

We conducted a cross-sectional survey among new patients who presented for PrEP care at the Washington University in St. Louis (WUSTL) ID specialty clinic between June 2014 and February 2016. Referrals to the clinic were from friends, word of mouth, community providers, community-based organizations, and self-referral. The self-administered survey, performed during the first appointment at the WUSTL ID specialty clinic, included questions about demographics, sexual behaviors, and whether patients had a PCP for PrEP. Survey answers were verified by the ID physician. A PCP was defined as a “primary care provider” whom they visited within the 12 months before visiting the WUSTL ID clinic. Patients with a PCP were asked why they did not seek or obtain PrEP services from their PCP. We reviewed medical records to see if patients, who were referred to a PCP, had obtained a PCP within 12 months of the patient’s initial clinic visit date. We obtained the reasons for not obtaining a new PCP after referral from clinic charts and patient verification. Study inclusion criteria were 18 years or older, presented at the WUSTL ID specialty clinic for care, and were able to provide written informed consent. The study was approved by the WUSTL Institutional Review Board.

We also reviewed available results of sexually transmitted infections (STI) testing, which was performed during routine PrEP care in accordance with the CDC PrEP Clinical Practice Guidelines.<sup>10</sup> STIs tested for were syphilis with rapid plasma reagin (RPR) and *Neisseria gonorrhoea* (NG) and *Chlamydia trachomatis* (CT) with nucleic acid amplification testing at any one site, including pharyngeal, urine, or rectal (Gen-Probe TIGRIS APTIMA Combo 2<sup>®</sup> Assay, Hologic, Inc., San Diego, CA for NG/CT and Alere Inc., Waltham, MA for RPR). RPR tests were confirmed with fluorescent treponemal antibody absorption testing (ZEUS Scientific, Branchburg, NJ).

Data were analyzed by multivariable logistic regression to determine the association of demographic and behavioral variables with patients who: (1) Had a PCP; and (2) Asked their PCP for PrEP; and (3) Felt uncomfortable discussing sexual behaviors with their PCP. Demographic variables were age, gender, race, education, annual income, and insurance. Behavioral variables were total sexual partners and had anal or vaginal sex with a known HIV-positive partner in the last 3 months, MSM, laboratory-confirmed STI test on initial visit, MSM who had condomless anal sex in the past 3 months, having ever used intravenous drugs, and self-reported history

of mental illness (e.g., anxiety, depression, schizophrenia, attention-deficit/hyperactivity disorder, or bipolar disorder). MSM was defined as a male patient who reported a history of having sex with men on the self-administered survey. The association between independent variables and the outcomes was initially assessed using chi-square and Fisher’s exact tests. Statistical tests were two-sided and the significance level was set at 0.05. Multivariable logistic regression was performed for all outcomes. Variables included in the regression analysis included those that were significant in

TABLE 1. PATIENT CHARACTERISTICS (N=102)

	n	%
Demographics		
Median age (years) (IQR)	29 (25–34)	
Age (years)		
18–24	23	22.5
25–34	55	53.9
>34	24	23.5
Gender		
Male	93	91.1
Female	8	7.8
Other	1	1.0
Race		
White	59	57.8
Black	32	31.4
Latino/Hispanic	3	2.9
Asian	3	2.9
Multiracial	5	4.9
Highest level of education		
Less than college	35	34.7
College graduate	36	35.6
Postgraduate	30	29.7
Annual income (\$)		
≤12,000	24	24.2
12,001–24,000	20	20.2
24,001–36,000	22	22.2
>36,000	33	33.3
Has insurance coverage		
None	5	4.9
Public <sup>a</sup>	8	7.8
Private	88	86.3
Other	1	1.0
Sexual risk		
Median sexual partners in the last 3 months (IQR)	2 (1–5)	
Men who have sex with men (MSM)	90	88.2
Having an HIV-positive sex partner in the last 3 months	43	42.2
Laboratory-confirmed STI on initial visit <sup>b</sup>	14	14.0
MSM who had condomless anal sex in the past 3 months (n=90)	63	70.0
Has ever used intravenous drugs	2	2.0
Self-reported history of mental illness	33	32.4

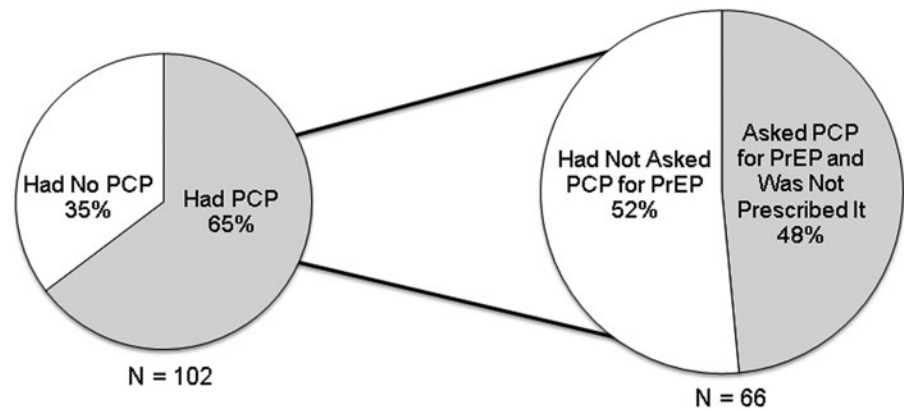
Certain numbers may not sum to the total sample due to missing data.

<sup>a</sup>Public insurance includes Medicaid, Medicare, and a city insurance program called Gateway to Better Health.

<sup>b</sup>Laboratory-confirmed STI includes any one positive test result for syphilis, *Neisseria gonorrhoea* (pharyngeal, urine, or rectal), or *Chlamydia trachomatis* (pharyngeal, urine, or rectal).

IQR, interquartile range; STI, sexually transmitted infection.

**FIG. 1** Forty-eight percent (32/66) of PrEP seekers with a PCP were not prescribed PrEP and potentially missed the opportunity to obtain PrEP within a primary care setting before presenting to an academic infectious diseases clinic. PCP, primary care provider; PrEP, pre-exposure prophylaxis.



bivariate analysis and also the demographic variables of age, race, education, and annual income. In addition, we adjusted for gender for the outcome of having had a PCP. For each independent variable, an odds ratio (OR), 95% confidence interval (95% CI), and *P* value were calculated. Analysis was performed in SPSS Statistics for Windows Version 23 (IBM Corporation, Armonk, NY).

Reasons for not being prescribed or not asking for PrEP were obtained by using open-ended survey questions. These answers were categorized by two independent study team members and the frequencies for each category were reported. Reasons for not obtaining a new PCP after referral were categorized and the frequencies reported. Each patient could have multiple reasons for each question.

## Results

A total of 108 new patients presented at the WUSTL ID specialty clinic for PrEP care during the study period; 102 were enrolled in the study and six declined to participate in the study. Among the 102 patients, the median age was 29 years (Interquartile Range [IQR] 25–34); 91% were male, 58% white, 31% Black, 3% Latino/Hispanic, 65% graduated college, median annual income was \$27,000 (IQR \$13,350–\$46,000), and 95% had any insurance coverage. Most (88%) patients were MSM, 42% had an HIV-positive sex partner in the last 3 months, 14% had a laboratory-confirmed STI, and 2% had ever used intravenous drugs. Among MSM, 70% reported condomless anal sex in the past 3 months. Notably, 32% of the patients self-reported a history of mental illness (Table 1).

Thirty-five percent (36/102) of patients did not have a PCP when they sought PrEP at the clinic (Fig. 1). Compared with those with a PCP, those without a PCP were more often non-white: 69% (25/36) versus 27% (18/66,  $P < 0.001$ ). Of those who had a PCP, 48% reported asking their PCP for PrEP, but were not prescribed it (Fig. 1). Age, race, education, and self-reported history of mental illness were significantly associated with having had a PCP in bivariate analysis. Multivariable regression analysis for having a PCP is demonstrated in Table 2. When adjusting for age, gender, education, annual income, and self-reported history of mental illness, race remained a significant predictor for having a PCP; non-whites were less likely to have a PCP than whites (OR: 0.32; 95% CI: 0.10–0.96,  $P = 0.04$ ).

Compared with those who asked for PrEP from their PCP, those who did not more often had an HIV-positive sex partner (65%, 22/34 vs. 21%, 6/28;  $P < 0.001$ ) and felt un-

comfortable discussing their sexual behaviors with their PCP (55%, 18/33 vs. 23%, 7/31;  $P = 0.01$ ). Age, race, annual income, self-reported history of mental illness, and having had an HIV-positive sex partner were significantly associated with having asked a PCP for PrEP in bivariate analysis. Table 3 displays the multivariable regression analysis results for patients having asked their PCP for PrEP when adjusting for age, race, education, annual income, self-reported history of mental illness, and having an HIV-positive sex partner. Self-reported history of mental illness (OR: 18.19; 95% CI:

**TABLE 2. MULTIVARIABLE REGRESSION ANALYSIS FOR HAVING A PRIMARY CARE PROVIDER AMONG 102 PATIENTS WHO SOUGHT HIV PRE-EXPOSURE PROPHYLAXIS CARE AT AN ACADEMIC INFECTIOUS DISEASES CLINIC, JUNE 2014–FEBRUARY 2016**

Variable	OR	95% CI	aOR <sup>a</sup>	95% CI
Age (years)				
18–24	1.0		1.0	
25–34	2.07	0.77–5.56	1.05	0.27–4.05
>34	4.15*	1.15–14.92	1.42	0.25–8.02
Gender				
Male	1.0		1.0	
Female	1.73	0.33–9.05	6.99	0.95–51.16
Race				
White	1.0		1.0	
Non-white	0.17***	0.07–0.43	0.32*	0.10–0.96
Education				
Less than college	1.0		1.0	
College graduate	4.00**	1.46–10.97	3.12	0.88–11.15
Postgraduate	4.38**	1.49–12.89	2.44	0.59–10.07
Annual income (\$)				
≤12,000	1.0		1.0	
12,001–24,000	0.69	0.21–2.28	0.77	0.18–3.24
24,001–36,000	2.26	0.66–7.76	1.90	0.40–8.99
>36,000	3.14	0.99–10.01	1.72	0.36–8.30
Self-reported history of mental illness				
No	1.0		1.0	
Yes	3.46*	1.27–9.45	2.78	0.78–9.93

<sup>a</sup>Adjusted for age, gender, race, education, annual income, and self-reported history of mental illness.

\* $P \leq 0.05$ .

\*\* $P \leq 0.01$ .

\*\*\* $P \leq 0.001$ .

OR, odds ratio; aOR, adjusted odds ratio; 95% CI, 95% confidence interval.

TABLE 3. MULTIVARIABLE REGRESSION ANALYSIS FOR PATIENTS HAVING ASKED A PRIMARY CARE PROVIDER FOR HIV PRE-EXPOSURE PROPHYLAXIS BEFORE SEEKING CARE AT AN ACADEMIC INFECTIOUS DISEASES CLINIC, JUNE 2014–FEBRUARY 2016 (N=66)

Variable	OR	95% CI	aOR <sup>a</sup>	95% CI
Age (years)				
18–24	1.0		1.0	
25–34	0.47	0.11–2.06	2.30	0.21–25.75
>34	0.10**	0.02–0.56	0.46	0.03–6.70
Race				
White	1.0		1.0	
Non-white	0.30*	0.09–0.97	0.25	0.04–1.55
Education				
Less than college	1.0		1.0	
College graduate	1.88	0.52–6.76	1.46	0.18–11.92
Postgraduate	1.38	0.37–5.14	1.18	0.11–13.02
Annual income (\$)				
≤12,000	1.0		1.0	
12,001–24,000	0.56	0.10–3.25	1.03	0.03–31.96
24,001–36,000	0.74	0.16–3.50	1.00	0.08–13.53
>36,000	0.20*	0.05–0.84	0.05	0.002–1.10
Self-reported history of mental illness				
No	1.0		1.0	
Yes	8.91***	2.84–27.98	18.19**	2.73–121.39
Having an HIV-positive sex partner in the last 3 months				
No	1.0		1.0	
Yes	0.13***	0.04–0.39	0.07**	0.01–0.53

<sup>a</sup>Adjusted for age, race, education, annual income, self-reported history of mental illness, and having an HIV-positive sex partner.  
 \*P ≤ 0.05.  
 \*\*P ≤ 0.01.  
 \*\*\*P ≤ 0.001.

2.73–121.39, P=0.003) was a significant positive predictor of having asked their PCP for PrEP; however, having an HIV-positive sex partner in the last 3 months (OR: 0.07; 95% CI: 0.01–0.53, P=0.01) was a significant negative predictor for having asked for PrEP.

Overall, 39% of those who reported having a PCP indicated that they had felt uncomfortable speaking to their PCP about their sexual behavior. However, of those who felt comfortable, 62% asked their PCP for PrEP, but were not provided with a prescription (Fig. 2). Having had an HIV-positive sex partner was significantly associated with patients having felt uncomfortable discussing their sexual behavior with their PCP in bivariate analysis. Table 4 displays the multivariable regression analysis results for patients who felt uncomfortable discussing their sexual behaviors with their PCP. When adjusting for age, race, education, and annual income, patients who had an HIV-positive sex partner in the last 3 months were more likely to have felt uncomfortable discussing their sexual behavior with their PCP (OR: 5.46; 95% CI: 1.37–21.77, P=0.02).

Of the 32 patients who asked their PCP for PrEP and were not prescribed it, 29 reported reasons; some reasons were (1) the PCP’s perception that prescribing PrEP is not a primary care activity (52%), (2) the PCP was unaware of PrEP (21%), and (3) the PCP did not feel comfortable prescribing PrEP (10%). Furthermore, of the 34 patients who did not ask their PCP for PrEP, 32 patients shared their reasons, which included: (1) PrEP was initiated by an ID specialist (i.e., at an inpatient or outpatient visit) for patients who were not seeking PrEP, but rather were offered PrEP, and they followed up at the WUSTL ID specialty clinic (i.e., without engaging the PCP) (31%), (2) they were uncomfortable discussing their sexual behaviors with their PCP (22%), (3) they were uncomfortable revealing that they had an HIV-positive sex partner to their PCP (19%), and (4) the perception that PrEP should be obtained from an ID or HIV specialist (16%).

As a part of PrEP services at the ID clinic, those who had indications for PrEP but did not have a PCP (n=36), were uncomfortable with their PCP (n=25), or who were comfortable with but not prescribed PrEP by their PCP (n=24) were referred to a new PCP. Overall, ID doctors referred 83% (85/102) of PrEP seekers who sought care at the clinic to another

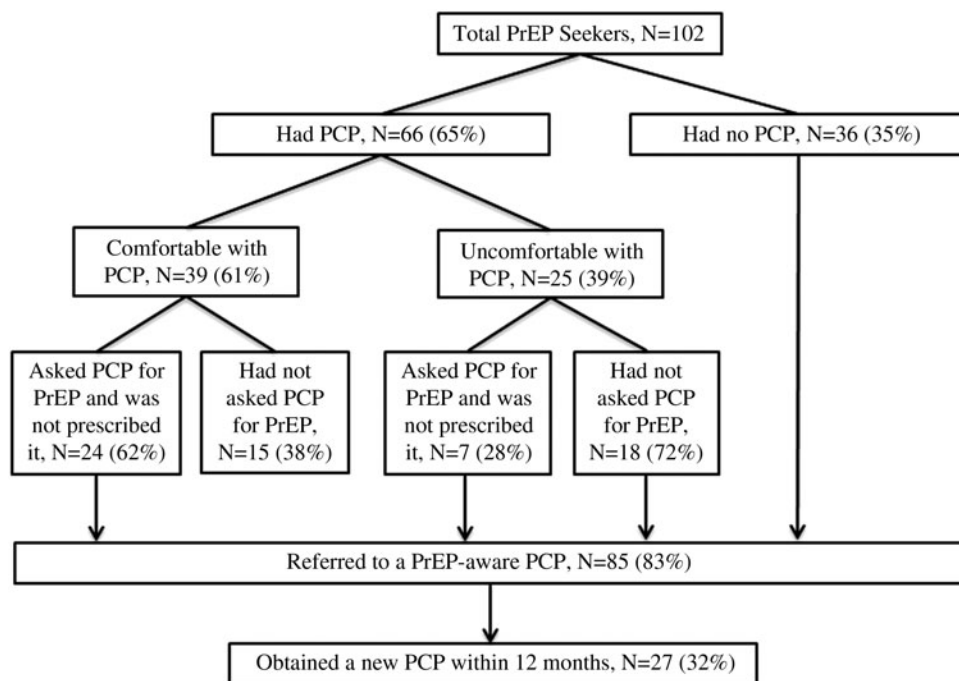


FIG. 2. Number of primary care referrals made as part of routine PrEP care at an academic infectious diseases clinic.

TABLE 4. MULTIVARIABLE REGRESSION ANALYSIS FOR PATIENTS WHO FELT UNCOMFORTABLE DISCUSSING THEIR SEXUAL BEHAVIORS WITH THEIR PRIMARY CARE PROVIDER BEFORE SEEKING HIV PRE-EXPOSURE PROPHYLAXIS CARE AT AN ACADEMIC INFECTIOUS DISEASES CLINIC, JUNE 2014–FEBRUARY 2016 (N=64)

Variable	OR	95% CI	aOR <sup>a</sup>	95% CI
Age (years)				
18–24	1.0		1.0	
25–34	0.73	0.17–3.06	1.10	0.15–8.02
>34	2.41	0.52–11.10	6.25	0.59–65.98
Race				
White	1.0		1.0	
Non-white	0.99	0.32–3.03	0.59	0.13–2.62
Education				
Less than college	1.0		1.0	
College graduate	0.58	0.15–2.26	0.77	0.14–4.18
Postgraduate	1.64	0.44–6.11	6.12	0.79–47.11
Annual income (\$)				
≤12,000	1.0		1.0	
12,001–24,000	0.51	0.09–3.11	0.16	0.01–2.01
24,001–36,000	0.57	0.13–2.57	0.47	0.07–3.30
>36,000	0.45	0.12–1.76	0.05*	0.01–0.55
Having an HIV-positive sex partner in the last 3 months				
No	1.0		1.0	
Yes	2.86*	1.01–8.12	5.46*	1.37–21.77

<sup>a</sup>Adjusted for age, race, education, annual income, and having an HIV-positive sex partner.

\*P≤0.05.

PCP (Fig. 2). Patients were referred to a PCP who was able to assess sexual risk in a culturally sensitive manner and who was PrEP aware; this referral network had been developed by the clinic. Thirty-two percent of the total referred patients obtained a PCP within 12 months of their initial clinic date (Fig. 2); of those without a PCP on intake, 36% (13/36) obtained a PCP. There were 19 total PCPs located at 14 different healthcare centers: three providers at three federally qualified health centers (FQHC), one provider at a university student health clinic, nine providers at seven private practices, and six providers at three health systems-based clinics.

Of the 27 patients who obtained a PCP, 15% (4/27) selected a FQHC provider, 7% (2/27) a student health clinic provider, and 78% (21/27) a private or health systems-based PCP. Patients (n=58) who did not obtain a PCP reported the following reasons: (1) they did not follow-up with the referral because they forgot, did not have time, or wanted to get a PCP “later” (36%), (2) moved out of state or discontinued PrEP before the 12-month time period of analysis (28%), (3) felt comfortable with their established PCP, did not want a new one, and wanted to receive PrEP from a specialist (24%), (4) did not have options to obtain a new PCP due to their insurance coverage (10%), and (5) became infected with HIV (2%).

## Discussion

We documented that individuals seeking PrEP faced numerous barriers to obtaining PrEP from PCPs in metropolitan Saint Louis, Missouri. Major barriers included not having a PCP, having a PCP who was unaware of and/or perceived

PrEP to be a specialist’s responsibility, not knowing a PCP could prescribe PrEP, and having a PCP but not feeling comfortable discussing sexual behaviors. Forty-eight percent of these at-risk patients asked for PrEP from their PCPs, but were not prescribed it, creating a large missed PrEP-prescribing opportunity by PCPs. In the United States, widespread implementation of PrEP requires PCPs to be aware of and willing to prescribe PrEP.

The study findings are consistent with previous studies and suggest several potential approaches to improve PrEP delivery by PCPs.<sup>14,16,18–28</sup> These include improved education and training about sexual behaviors and PrEP, as well as interventions to address bias and stigma related to sexual behaviors.<sup>29</sup> This study supports findings by Oldenburg et al., which revealed that structural stigma at the state level leads to decreased use of PrEP for HIV prevention.<sup>30</sup> Oldenburg et al. demonstrated that Missouri had a less supportive social environment based on state-level structural stigma.<sup>30</sup> We corroborate this study with our finding that 39% of individuals did not feel comfortable discussing their sexual behaviors with their PCPs, highlighting the importance of combating this stigma on an individual provider–patient level. The importance of eliciting sexual histories in culturally competent ways is increasingly recognized, and tools are available to enhance primary provider cultural competence. Knowledge on how to initiate sexual behavior discussions will allow for adequate risk assessments and provide an avenue to prescribe PrEP if indicated.<sup>31</sup> Resources exist to assist providers in developing comfortable settings for patients who identify as sexual or gender minorities or who have HIV-positive sex partners.

As noted in other PrEP studies, we observed the “purview paradox,” a term referring to the contradictory belief among HIV specialists and PCPs about whose domain it is to be the main PrEP prescriber.<sup>18</sup> Many PCPs report perceiving that PrEP was not a part of their expertise, and preferred to refer PrEP patients to ID specialists.<sup>18</sup> We observed that patients reported this reason when they asked for PrEP from their PCPs, but also reported believing that PrEP was not under the PCP’s prescribing jurisdiction. These challenges might be best addressed by local provider training programs and community awareness events about PrEP provision.

Our study also highlights the importance of access to care and having a PCP. A third of patients who sought PrEP care at our clinic had not engaged with a PCP in the last 12 months. This study’s findings are consistent with national data showing that 47% of Americans of all ages reported not visiting a PCP in 2012.<sup>8</sup> Referrals for PCPs within this study resulted in 32% of patients obtaining a PCP with whom they could feel more comfortable.

This study reports on the potential of a PrEP referral to be the *gateway* for comprehensive primary and preventive care. In this capacity, PrEP is an opportunity to link otherwise healthy people to other services, including vaccinations and mental health. In this study, ID and HIV specialists became *the gateway to PrEP* while also being *the gateway to primary care homes* for a proportion of PrEP seekers. ID physicians and specialty clinics have the ability to play an important role in providing PrEP services, while also training PCPs and garnering support from healthcare organization administrative leaders to establish a network of PrEP-prescribing PCPs during initial local implementation as we had. We saw

an increase in several new PrEP-providing locations (three FQHCs, a student health center, and several private sector clinic locations) that were not previously providing PrEP, as a result of our efforts to create a PCP referral network for our patients.

Further studies are needed to evaluate how to successfully link individuals prescribed PrEP to primary care services, and to assess if these individuals are comfortable receiving PrEP from their PCPs. Over 60% of patients who were referred to a PCP did not follow through within 12 months. Understanding the gaps in the specialist-to-PCP PrEP care transition or the desire not to have a PCP will help better incorporate PrEP into broader preventive care on a population level.

### Limitations

Limitations to this study include a small sample size, patient self-reported reasons for not being prescribed PrEP, and study conduction at a single academic institution, which lessens generalizability. Although we did not categorize denial of prescription by the provider based on individual risk, we reported many characteristics regarding this patient sample that demonstrated substantial risk for HIV acquisition.

### Conclusion

PrEP has the potential to curb HIV incidence in the United States and PrEP implementation will need to be adapted for each geographic and cultural context. PrEP holds the power to engage individuals in comprehensive preventive healthcare who were not in routine care previously. However, these early adopting PrEP users will need to have a comfortable environment in which to disclose their sexual behaviors and to have supportive interactions with the healthcare system. Addressing these factors will help to establish the foundation for successful PrEP care retention in the region. Until primary care organizations develop a large cadre of clinically competent and culturally sensitive PrEP providers, ID specialists will need to assist in initial PrEP care provision and to develop networks where PrEP seekers can transition their care to the hands of PCPs, thereby fostering a sustainable PrEP implementation platform.

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### Disclaimer

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