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ORIGINAL PAPER

Health Care Facility Characteristics are Associated with Variation in Human Immunodeficiency Virus Pre-exposure Prophylaxis Initiation in Veteran's Health Administration

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Abstract

To quantify health care facility-level variation in pre-exposure prophylaxis (PrEP) use in the Veteran's Health Administration (VHA); to identify facility characteristics associated with PrEP use. Retrospective analysis of the health care facility-level rate of PrEP initiation in VHA through June 30, 2017. Standardized PrEP initiation rates were used to rank facilities. Characteristics of facilities, prescribers, and PrEP recipients were examined within quartiles. Multiple linear regression was used to identify associations between facility characteristics and PrEP use. We identified 1600 PrEP recipients. Mean PrEP initiation rate was 20.0/100,000 (SD 22.8), ranging from 3.0/100,000 (SD 2.0) in the lowest quartile to 48.1/100,000 (SD 29.1) in the highest. PrEP prescribing was positively associated with proportions of urban dwellers and individuals < 45, tertiary care status, and location. Variability in PrEP uptake across a national health care system highlights opportunities to expand access in non-tertiary care facilities and underserved areas.

Keywords Pre-exposure prophylaxis · HIV · Health care · Initiation

Resumen

Para cuantificar la variación a nivel de las instalaciones de atención médica en el uso de la profilaxis previa a la exposición (PrEP) en la Administración de Salud para Veteranos (VHA); para identificar las características de las instalaciones asociadas con el uso de PrEP. Análisis retrospectivo de la tasa de nivel de establecimiento de atención médica de inicio de PrEP en VHA hasta el 30 de junio de 2017. Se utilizaron índices de inicio de PrEP estandarizados para clasificar los establecimientos. Las características de las instalaciones, los prescriptores y los receptores de PrEP se examinaron dentro de los cuartiles. Se utilizó regresión lineal múltiple para identificar asociaciones entre las características de la instalación y el uso de PrEP. Identificamos 1600 beneficiarios de PrEP. La tasa media de iniciación de PrEP fue de 20.0/100.000 (SD 22.8), variando desde 3.0/100.000 (SD 2.0) en el cuartil más bajo hasta 48.1/100.000 (SD 29.1) en el más alto. La prescripción de PrEP se asoció positivamente con proporciones de habitantes urbanos e individuos < 45, estado terciario y ubicación. La variabilidad de la captación de PrEP a través de un sistema nacional de atención de salud resalta las oportunidades para ampliar el acceso en instalaciones no terciarias y áreas subatendidas o comunidades con bajos recursos.

Introduction

An estimated 39,782 new human immunodeficiency virus (HIV) diagnoses occurred in the United States (US) in 2016 despite prevention efforts [1]. Pre-exposure prophylaxis (PrEP) for HIV is an essential tool to reduce HIV acquisition among persons with ongoing risk behaviors, with greater than 90% efficacy depending on adherence and the demographic risk group. The single pill combination of tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) was

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FDA-approved for PrEP in July 2012. Multiple randomized controlled trials have demonstrated efficacy in preventing HIV infection among persons who inject drugs (PWID) [2], men who have sex with men (MSM) [3, 4], and heterosexual individuals [5].

Despite its efficacy, PrEP uptake has been uneven. Evidence suggests demographic and geographic disparities in PrEP uptake exist in the United States, with the result that PrEP is underutilized in many groups at highest risk for HIV infection. For example, PrEP usage and awareness has been found to be lower among African-American MSM compared to white MSM [6–9], despite African-American and Latino MSM experiencing a 4% and 14% increase in the rate of new HIV infections between 2011 and 2015, while white MSM experienced a 10% decrease [1]. Additionally, although five of the eight states with the highest rates of new HIV diagnoses (19/100,000 individuals or higher) were in the southeastern US in 2015 [10], individuals starting PrEP in the US almost exclusively live in urban areas and almost half live in the West [11].

While the demographic characteristics of individuals using PrEP have been well described, individual patient factors are not the sole or even primary determinant of PrEP access. Critical determinants of access to PrEP include provider attitude and willingness to prescribe, availability of PrEP on formularies, and the systems within which PrEP is prescribed. For example, researchers have identified a "purview paradox," where Infectious Diseases (ID) and Primary Care clinicians each identify the other as being the most qualified for PrEP care, resulting in neither specialty claiming responsibility for PrEP provision [12]. Health care facility characteristics (such as facility size or complexity) may modulate the purview paradox. Identifying health care facility characteristics associated with higher rates of PrEP use may identity targets for implementation strategies.

The Veterans Health Administration (VHA) presents a unique opportunity to evaluate the association between health care facility characteristics and PrEP uptake. VHA is the single largest health care provider in the US, with six million individuals in care across 140 facilities in 2016 [13]. The national extent of its infrastructure and breadth across prescribing environments (spanning rural to urban locations, small to large health care facilities, and primary to tertiary care settings) makes the VHA an ideal health system for examining health care infrastructure associated with PrEP uptake. Additionally, PrEP is on VHA formulary for $11 per month (email communication with Pamela Belperio, PharmD, National Public Health Clinical Pharmacy Specialist, VHA, October 2018), with the low cost facilitating access to PrEP within the system. We hypothesized that PrEP uptake would be higher in health care facilities that provide tertiary care, as well as those with ID specialists available. We also hypothesized that PrEP uptake would be higher in geographic areas with higher HIV incidence, and among facilities with higher proportions of African-Americans and Latinos (racial and ethnic groups with an HIV incidence disproportionate to their representation in the population). Our primary objective was to quantify facility-level variation in PrEP initiation in VHA and identify facility characteristics associated with greater PrEP use.

Methods

Data Sources and Study Population

We performed a retrospective analysis using data from the Computerized Data Warehouse (CDW), a comprehensive, national VHA database that extracts patient demographics, diagnoses, prescription data, laboratory results, and other elements from VHA's universal electronic medical record (EMR). We used these data to create a cohort of individuals initiating PrEP in VHA between July 1, 2012 and June 30, 2017.

We identified all PrEP recipients using an algorithm that first included all individuals in VHA care who received at least one $\geq$31-day course of TDF-FTC. We excluded individuals who received separate prescriptions for non-co-formulated TDF and FTC. We excluded recipients of one-time TDF-FTC prescriptions of $<$31 days, as these could be HIV post-exposure prophylaxis. We next excluded persons with a diagnosis of HIV, as determined by (1) receipt of any non-TDF or non-FTC antiretroviral prescriptions any time before or within 30 days after the release of the index TDF-FTC prescription or (2) $\geq$1 outpatient or inpatient encounters associated with International Classification of Diseases (ICD)-9 or ICD-10 codes for HIV any time before or within 30 days after the index TDF-FTC prescription (Supplementary Appendix). We excluded persons with chronic hepatitis B virus (HBV) infection, based on receipt of medications used for HBV treatment (monotherapy with lamivudine, entecavir, TDF, tenofovir alafenamide, or telbivudine) or laboratory evidence of chronic HBV (positive HBV surface antigen or positive HBV viral load) any time before or within 30 days after the index TDF-FTC prescription. We have previously verified a comparable algorithm via chart review where the positive predictive value was estimated to be 0.94 [14].

After identifying PrEP recipients, we identified the health care facility that initiated the individual's first PrEP prescription. The VHA health care network includes 140 medical centers [15]. We grouped the 140 primary VHA health care facilities into quartiles based on the facility's rate of PrEP initiation, defined as the number of unique individuals initiating PrEP in that facility between July 1, 2012 and June 30, 2017, standardized per 100,000 persons in care

at that facility in 2012 (quartile 1 = lowest PrEP initiation rate, quartile 2 = medium–low PrEP initiation rate, quartile 3 = medium–high PrEP initiation rate, quartile 4 = high PrEP initiation rate).

PrEP Recipient Demographic Characteristics within Each Facility PrEP Initiation Quartile

We assessed the demographic characteristics of PrEP recipients within quartiles based on facility PrEP initiation rate. We examined age, sex, self-reported race and ethnicity, and rurality of the recipient's most recent home address as defined by the Rural–Urban Commuting Areas (RUCA) system [16]. Assessed comorbidities included prior history of mental health diagnoses (anxiety disorders, bipolar disorder, depression, post-traumatic stress disorder (PTSD), schizophrenia, and "other" mental health illnesses), prior history of an alcohol use or substance use disorder, all defined by ICD-9 and ICD-10 codes (Supplementary Appendix).

Prescribing Provider Characteristics Within Each Facility PrEP Initiation Quartile

We assessed the characteristics of PrEP prescribers within each quartile. We determined both the provider type (MD/DO trainee, MD/DO staff, nurse practitioner, physician assistant, pharmacist, and other) and specialty (Internal Medicine—Infectious Diseases, Internal Medicine—other, Family Medicine, Emergency Medicine, and Other/Unknown) of the provider issuing the index PrEP prescription.

Facility Characteristics Within Each Facility PrEP Initiation Quartile

We assessed the characteristics of facilities within each quartile. We compared quartiles according to VHA-designated facility "complexity", a surrogate for tertiary care status [17]. We assessed the availability of ID specialty care and considered a facility to have "ID access" if at least one outpatient ID encounter was associated with that facility annually between 2012 and 2017; geographic region based on the US Census Bureau's nine geographic divisions [18]; demographic characteristics of the population within each facility based on 2012 in care data and publicly-available background HIV prevalence rate of each state [10].

Statistical Analysis

We presented descriptive statistics as proportions (%) or means (SD). We used multiple linear regression to examine the relationship between facility characteristics and PrEP initiation rates. The independent variables consisted of facility demographics characteristics from 2012 (sex, age, race, ethnicity, and mental health and substance use diagnoses); facility characteristics (tertiary care status, geographic region, and ID staffing); and the background HIV prevalence rate of the state in which the facility was located. We used SAS Version 9.4 for all analyses.

Results

Study Population

Of the 13,855 unique individuals in VHA care between July 1, 2012 and June 30, 2017 who received at least one ≥ 31-day prescription for TDF-FTC, we excluded 12,255 individuals with evidence of HIV infection or chronic hepatitis B infection, yielding a cohort of 1600 unique PrEP recipients.

The mean PrEP initiation rate nationally was 20.0 recipients/100,000 (SD 22.8), with significant variation across the 140 facilities (range 0–146.4/100,000). Quartile 4 (the quartile with the highest PrEP initiation rate) had a mean PrEP initiation rate of 48.1 recipients/100,000 patients in care (SD 29.1), compared to 3.0/100,000 (SD 2.0) in quartile 1 (the lowest quartile). Quartile 3 (the medium–high quartile) had a mean PrEP initiation rate of 18.0/100,000 (SD 2.9); quartile 2 (the medium–low quartile) had a mean PrEP initiation rate of 9.6/100,000 (SD 2.1). The highest quartile accounted for 1110 of the 1600 PrEP initiations, quartile 3 accounted for 319, quartile 2 accounted for 133, and the lowest quartile (quartile one) accounted for 38.

PrEP Recipient Demographic Characteristics Within Each Facility PrEP Initiation Quartile

Almost all (97%) of the 1600 PrEP recipients were men (Table 1). Almost two-thirds were < 45 years of age, and nearly one-third were 45–60 years of age. Over two-thirds were white, 21% were African-American, 88% lived in an urban area, and 77% had a history of ever having a mental health diagnosis.

The age distribution of PrEP recipients was relatively constant across all quartiles. African-American and Hispanic individuals were represented at modestly higher proportions in the highest quartile compared to the lowest quartiles (23% vs. 18% for African Americans; 15% vs. 8% for Hispanic individuals). There were fewer rural recipients in the two highest quartiles (13% and 9%) compared to the two lowest (37% and 28%). Mental health diagnoses were represented with slightly increased proportions in the lowest two quartiles (82% and 80%) compared to the highest two quartiles (75% and 76%). The proportion with a history of alcohol or substance use disorders was higher in the lowest quartile

Table 1 Demographic characteristics of PrEP recipients, by facility PrEP initiation quartile

	Facility PrEP initiation quartiles				
	Quartile 1 (lowest)	Quartile 2	Quartile 3	Quartile 4 (highest)	Total
PrEP recipients within quartile (n)	38	133	319	1110	1600
Male, n (%)	38 (100)	128 (96)	305 (96)	1080 (97)	1551 (97)
Age, mn (SD)	43.6 (11.0)	43.5 (13.1)	43.3 (12.9)	40.7 (12.4)	41.6 (12.6)
< 45, n (%)	23 (61)	74 (56)	180 (56)	728 (66)	1005 (63)
45–64, n (%)	13 (34)	48 (36)	114 (36)	325 (29)	500 (31)
65+, n (%)	2 (5)	11 (8)	25 (8)	57 (5)	95 (6)
Race					
White, n (%)	27 (71)	106 (80)	241 (76)	723 (65)	1097 (69)
African-American, n (%)	7 (18)	16 (12)	52 (16)	257 (23)	332 (21)
Asian-American, n (%)	2 (5)	3 (2)	3 (1)	48 (4)	56 (4)
Native-American, n (%)	1 (3)	0 (0)	6 (2)	18 (2)	25 (2)
Hawaiian/Pacific Islander, n (%)	2 (5)	2 (2)	4 (1)	21 (2)	29 (2)
Missing/other, n (%)	1 (3)	7 (5)	20 (6)	74 (7)	102 (6)
More than one race reported, n (%)	5 (13)	9 (7)	24 (8)	156 (14)	194 (12)
Hispanic ethnicity, n (%)	3 (8)	11 (8)	25 (8)	166 (15)	205 (13)
Rural status					
Urban, n (%)	24 (63)	96 (72)	276 (87)	1005 (91)	1401 (88)
Rural/highly rural, n (%)	14 (37)	37 (28)	43 (13)	105 (9)	199 (12)
Mental health diagnosis[a], n (%)	31 (82)	107 (80)	238 (75)	848 (76)	1224 (77)
Alcohol use diagnosis, n (%)	13 (34)	29 (22)	82 (26)	280 (25)	404 (25)
Substance use diagnosis (excluding cannabis), n (%)	8 (21)	17 (13)	44 (14)	176 (16)	245 (15)
Substance use diagnosis (including cannabis), n (%)	10 (26)	25 (19)	60 (19)	230 (21)	325 (20)

PrEP initiation rate per facility = [# PrEP initiations 2012–2017/(# patients in care 2012/100,000)]. Comparison groups determined by ranking facilities by PrEP initiation rates and dividing into quartiles. Quartile 1 comprises the facilities with the lowest PrEP initiation; quartile 2 comprises the facilities with the 2nd lowest PrEP initiation; quartile 3 comprises the facilities with the 2nd highest PrEP initiation; quartile 4 comprises the facilities with the highest PrEP initiation

[a]Mental health diagnosis: anxiety disorder, bipolar disorder, depression, post-traumatic stress disorder, schizophrenia, other

(34% and 26%, respectively), compared to the highest quartile (25% and 21%, respectively).

Prescribing Provider Characteristics Within Each Facility PrEP Initiation Quartile

Staff physicians prescribed 56% of index PrEP prescriptions; physician trainees (interns, residents, and fellows) prescribed 21%; advanced practice clinicians (nurse practitioners and physician assistants) prescribed 16%; and pharmacists prescribed 6% (Table 2). Staff physicians accounted for 50% of prescriptions in the highest quartile compared to 71% in the lowest quartile. In the highest quartile, physician-trainees and advanced practice clinicians handled a greater percentage of prescriptions than in the other quartiles.

Among physician prescribers, ID specialists accounted for 67% of all index PrEP prescriptions and Internal Medicine physicians for 23%. Prescriptions by ID specialists were more prevalent in the two highest quartiles, accounting for 68–73% of prescriptions, compared to 44–56% of prescriptions in the two lowest quartiles. In the lowest quartile, prescriptions were more evenly split among ID, Internal Medicine, and Family Medicine. Family Medicine clinicians played a particularly important role in this quartile, accounting for 22% of prescriptions.

Facility Characteristics Within Each Facility PrEP Initiation Quartile

Fifty percent of facilities in the highest quartile were tertiary care facilities, compared to 12% in the lowest quartile (Table 3). Half of the highest quartile facilities were in Census Bureau geographic divisions 5 (Southeast) and 9 (West Coast, Hawaii, Alaska), while the lowest quartile facilities were more geographically diverse, with divisions 2, 3, 5, and 7 each accounting for at least 15% of facilities (Fig. 1).

The two highest quartiles each had near universal ID access at 91–97% of facilities, while the two lowest quartiles (quartiles one and two) had ID access at only 71–77% of facilities (Table 3). Facilities in the highest quartile

Table 2 Prescriber characteristics, by PrEP initiation quartile

	Facility PrEP initiation quartiles				
	Quartile 1 (lowest)	Quartile 2	Quartile 3	Quartile 4 (highest)	Total
PrEP recipients within quartile (n)	38	133	319	1110	1600
Prescriber training					
Physician—staff (attending, staff), n (%)	27 (71)	102 (77)	215 (67)	553 (50)	897 (56)
Physician—trainee (resident, fellow, intern), n (%)	4 (11)	10 (8)	46 (14)	270 (24)	330 (21)
Nurse practitioner/physician assistant, n (%)	6 (16)	16 (12)	31 (10)	205 (18)	258 (16)
Pharmacist, n (%)	0 (0)	3 (2)	23 (7)	70 (6)	96 (6)
Other/unknown, n (%)	1 (3)	2 (2)	4 (1)	12 (1)	19 (1)
Physician specialty (staff physicians only)					
Internal medicine—infectious disease, n (%)	12 (44)	57 (56)	158 (73)	377 (68)	604 (67)
Internal medicine—other, n (%)	8 (30)	26 (25)	38 (18)	131 (24)	203 (23)
Family medicine, n (%)	6 (22)	12 (12)	5 (2)	24 (4)	47 (5)
Emergency medicine, n (%)	1 (4)	1 (1)	0 (0)	3 (1)	5 (1)
Other/unknown, n (%)	0 (0)	6 (6)	14 (7)	18 (3)	38 (4)

PrEP initiation rate per facility = [# PrEP initiations 2012–2017/(# patients in care 2012/100,000)]. Comparison groups determined by ranking facilities by PrEP initiation rates and dividing into quartiles. Quartile 1 comprises the facilities with the lowest PrEP initiation; quartile 2 comprises the facilities with the 2nd lowest PrEP initiation; quartile 3 comprises the facilities with the 2nd highest PrEP initiation; quartile 4 comprises the facilities with the highest PrEP initiation

Table 3 Facility characteristics, by PrEP initiation quartile

	Facility PrEP initiation quartiles				
	Quartile 1 (lowest) (n = 34 facilities)	Quartile 2 (n = 35 facilities)	Quartile 3 (n = 35 facilities)	Quartile 4 (highest) (n = 36 facilities)	Total (n = 140 facilities)
Facility characteristics, n (%)					
Tertiary care status	4 (12)	6 (17)	11 (31)	18 (50)	39 (28)
ID access each year from 2012 to 2017	24 (71)	27 (77)	32 (91)	35 (97)	118 (84)
Population characteristics of prescribing facility, mean percentage (SD)					
Male	92% (2%)	92% (2%)	91% (3%)	90% (2%)	91% (3%)
Age < 45	15% (3%)	15% (4%)	16% (7%)	18% (4%)	16% (5%)
African-American	11% (13%)	12% (11%)	10% (9%)	20% (15%)	13% (13%)
Hispanic	5% (16%)	3% (5%)	3% (3%)	7% (7%)	5% (9%)
Urban residence	42% (20%)	56% (19%)	61% (20%)	78% (12%)	59% (22%)
Mental health diagnosis	70% (15%)	72% (15%)	68% (9%)	72% (11%)	70% (13%)
Substance use diagnosis	14% (7%)	18% (11%)	15% (5%)	19% (7%)	16% (8%)
State HIV prevalence rate, mean (SD)[a]	288 (197)	310 (212)	255 (146)	436 (440)	323 (281)

Comparison groups determined by ranking facilities by PrEP initiation rate and dividing into quartiles. Quartile 1 comprises the facilities with the lowest PrEP initiation; quartile 2 comprises the facilities with the 2nd lowest PrEP initiation; quartile 3 comprises the facilities with the 2nd highest PrEP initiation; quartile 4 comprises the facilities with the highest PrEP initiation

[a]*Source* AIDSVu, Emory University, https://aidsvu.org/resources/downloadable-maps-and-resources/

were in states with the highest background state HIV prevalence rate (436 persons/100,000 state population) [10]. Facilities in the second highest quartile were in states with the lowest background state HIV prevalence rate (255 persons with/100,000 state population) [10].

Multiple Linear Regression Analysis Evaluating Facility Characteristics Associated with PrEP Initiation Rate

In a multiple linear regression model, PrEP initiation rates

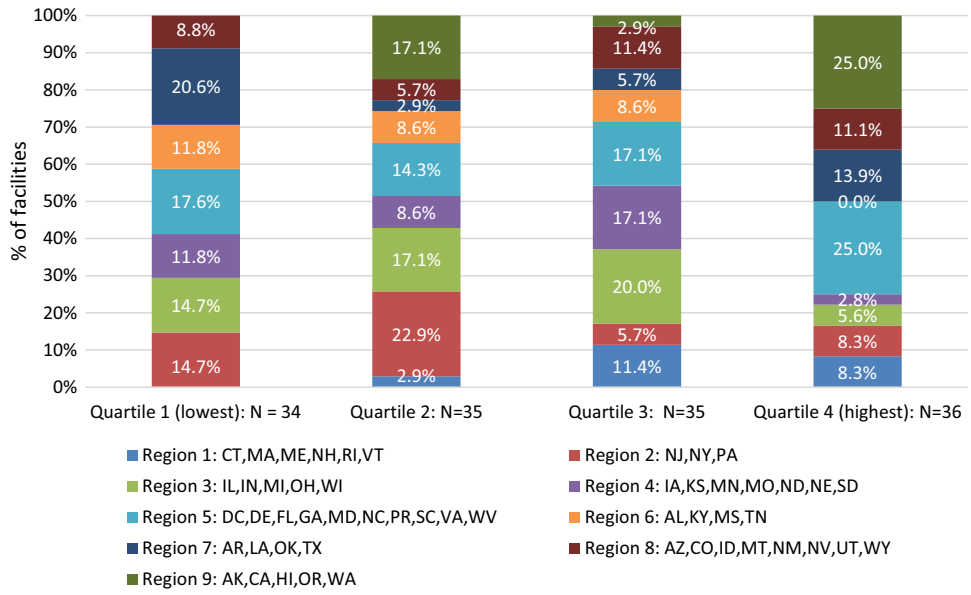

Fig. 1 Geographic distribution within PrEP initiation quartiles

were positively associated with the facility-wide proportions of individuals younger than age 45 (β = 142.7, two-tailed *p* value 0.018), urban dwellers (β = 18.3, two-tailed p-value 0.038), tertiary care status (β = 12.2, two-tailed p-value 0.001), and geographic location on the West Coast/Alaska/Hawaii (US Census Bureau geographic division 9) (β = 22.1, two-tailed p-value < .0001). Background state HIV prevalence rate was positively associated with PrEP initiation, but this association was weak (β = 0.023, two-tailed p-value < .0001). The proportion of African-Americans in care within a facility was not associated with PrEP initiation (β = 8.3, two-tailed p-value 0.599) (Table 4).

Discussion

We observed dramatic facility level variation in PrEP use between the 140 VHA facilities. The standardized facility-wide rate of PrEP initiation varied by a factor of sixteen between the lowest and highest-prescribing quartiles, and

Table 4 Adjusted linear regression coefficients for association between facility characteristics and PrEP initiation rate

Parameters	Beta	95% CI	p-value
Facility in-care rates 2012			
% males in facility	207.0	−33.6 to 447.7	0.094
% age < 45 in facility	142.7	25.9 to 259.5	0.018*
% African-American in facility	8.3	−22.6 to 39.2	0.599
% urban residence in facility	18.3	1.2 to 35.5	0.038*
% with mental health diagnosis in facility	20.5	−14.8 to 55.8	0.256
% with substance use diagnosis in facility	−26.2	−84.0 to 31.7	0.377
Facility characteristics			
Tertiary care facility	12.2	5.1 to 19.3	0.001*
West Coast, Alaska, or Hawaii	22.1	12.2 to 32.0	< 0.0001*
Infectious diseases access 2012–2017	4.3	−4.7 to 13.2	0.349
HIV prevalence rate[a]			
HIV rate in state	0.023	0.011 to 0.035	< 0.0001*

PrEP initiation rate per facility = [# PrEP initiations 2012–2017/(# people in care 2012/100,000)]. Comparison groups determined by ranking facilities by rates and dividing into quartiles. Rates were based on persons living with diagnosed HIV infection in 2012 per 100,000 population

[a]*Source* AIDSVu, Emory University, https://aidsvu.org/resources/downloadable-maps-and-resources/

*p < .0.05

eight facilities had zero PrEP initiations. In multiple regression analysis, the highest-prescribing facilities were more likely to be classified as tertiary care facilities; located in the West Coast, Hawaii, or Alaska; and to have a greater proportion of younger, urban-dwelling individuals. This is consistent with other research that identified higher PrEP uptake in metropolitan areas and the West [11]. The facility-wide proportion of African-Americans in care was not associated with PrEP initiation rates. In addition, high-prescribing facilities tended to have a higher proportion of PrEP initiations by physician trainees (e.g., interns, residents, fellows). As a group, the lowest-prescribing facilities tended to be non-tertiary care facilities, to serve a greater percentage of rural individuals, and to have lower access to ID specialists.

Although HIV acquisition risk varies at both the population level (e.g. community HIV prevalence or virologic suppression) and individual level (e.g. HIV prevalence or virologic suppression within one's immediate sexual networks), a 16-fold variation in PrEP initiation between the lowest and highest quartiles was greater than would be expected based on socio-demographic factors alone. Variation across VHA is disproportionate to the background HIV prevalence or incidence rate in many geographic areas. For example, only 38 of VHA's total PrEP initiations were initiated by facilities in the lowest quartile, yet some facilities in the lowest quartile are located in areas with high HIV prevalence or incidence [10]. (While in aggregate there was a weak positive association between state HIV prevalence and PrEP initiation, there were outliers.) In addition, the variation seems too great to be explained by background population risk among individuals with indications for PrEP (such as people who inject drugs or sexual risk behaviors).

Our observation that tertiary care facilities (especially those with physician trainees) prescribed PrEP at a higher rate suggests that provider expertise was a strong determinant of PrEP initiation. Facilities without academic affiliations relied more heavily on non-physician clinicians, such as clinical pharmacists, to initiate PrEP. Tools are needed to build provider awareness and confidence in prescribing PrEP.

Another key predictor of PrEP initiation was rurality of the patient populations. Research in access to care for HIV has shown that rural status is a potent barrier to optimal care [19, 20]. Although rural MSM have a lower HIV prevalence than urban MSM, they are also less likely to access HIV prevention care [20, 21]. Future consideration should be given to supporting primary care providers and increasing capacity of clinical pharmacists and nurse practitioners in prescribing PrEP, especially in rural areas, as has successfully been done for hepatitis C treatment in VHA [22, 23].

Our analysis benefitted from a complete national sample of all VHA facilities spanning the first 5 years after FDA approval of PrEP. However, our results should be interpreted within the context of several limitations. The population of individuals in VHA care, including PrEP recipients, is predominantly male and therefore our results cannot be generalized to female PrEP recipients; nor can they be generalized to those without health insurance. However, of new HIV diagnoses in the US in 2016, the majority (81%) were among men, and African-Americans and Latinos accounted for 69% of new diagnoses [24]. The VHA population is therefore enriched for the groups that account for most new infections. Access to health insurance and to PrEP at the low copay of $11 per month also permitted an analysis focused on health care facility characteristics that was not compromised by barriers to insurance access or medication access. Another limitation is the small number of unique PrEP recipients in the lowest quartile, making interpretation of patterns in this quartile less reliable. Since many patients receive testing for sexually transmitted infections (STIs) and care for opioid use disorders from county or city-funded clinics, we were also limited in that VHA administrative datasets provide incomplete information about the population of individuals with indications for PrEP. Chart review can overcome this limitation, but is not feasible for a cohort of this size. Therefore, we were not able to ascertain patient-level risk behaviors (e.g., unprotected sex and on-going injection drug use) from administrative data resources, and could not determine the indication for PrEP, or identify individuals with HIV risk factors who did not receive PrEP. Since we could not evaluate individuals who did not receive PrEP, we could not evaluate whether factors such as race and ethnicity were associated with PrEP receipt at the individual patient level. Future work should investigate whether PrEP use is lower among African American MSM compared to other at-risk groups, as seen in the general US population. Future research is also needed to validate surrogates for HIV risk factors (e.g. diagnosis of sexually transmitted infections, active opioid use disorder) from administrative data sets; this would permit more precise estimates of variability in PrEP indication, access, and uptake.

Our results have important implications for expanding the use of PrEP within a large health care system. Our findings demonstrate the importance of examining facility and clinician characteristics when promoting PrEP uptake as a fundamental component of HIV prevention, and not relying solely patient demographic factors. Implementation strategies targeted at augmenting uptake should be sensitive to the PrEP prescribing environment, especially at smaller facilities with fewer subspecialty providers. Implementation strategies will need to support non-ID physicians in prescribing PrEP, as well as expanding the role for clinical pharmacists and advanced practice clinicians. For healthcare systems, such as VHA, with national and regional networks, consideration should also be given to using telehealth to leverage PrEP expertise across state lines. Efforts such as these can

help ensure equitable access to PrEP across all regions and prescribing environments across health systems.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with animals performed by any of the authors. Under guidance from the VHA Office of Research Oversight (ORO), the HIV, Hepatitis, and Related Conditions Office in Specialty Care Services has the authority to perform the analyses presented here as part of their healthcare operations work which does not require Institutional Review Board approval.

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