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ORIGINAL PAPER

Temporal Trends and Sociodemographic Correlates of PrEP Uptake in Tennessee, 2017

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Abstract
Client-level data from two Tennessee-based PrEP navigation demonstration projects reported to the Tennessee Department of Health from January to December 2017 were evaluated to determine the proportion of clients who accepted, were linked to, and were prescribed PrEP. Disparities by age, race, transmission risk, and geographic region as well as trends over time were examined via bivariate and multivariable modified Poisson regression models accounting for potential confounders. Among 1385 PrEP-eligible individuals, 50.5% accepted, 33.4% were linked, and 27.3% were prescribed PrEP. PrEP uptake varied by age, race, and HIV transmission risk, and most disparities persisted across Tennessee throughout evaluation period. Multivariable regression models revealed significant independent associations between age, race/ethnicity, transmission risk, and region and PrEP acceptance and linkage. While differences in PrEP acceptance by race narrowed over time, success among black MSM was limited, underscoring a significant need to improve upstream PrEP continuum outcomes for this important population.

Keywords HIV prevention · Pre-exposure prophylaxis (PrEP) · PrEP navigation · PrEP uptake · Men who have sex with men (MSM)

Background

In 2016, nearly 40,000 individuals were newly diagnosed with HIV infection in the United States (U.S.), where the southern U.S. region, black communities, and men who have sex with men (MSM) experience the greatest burden of the epidemic [1]. The southern U.S. accounts for more than half (52%) of new HIV diagnoses, despite representing one-third of the total population [1]. Reasons for the disproportionate distribution of HIV in the southern U.S. are complex; contributing factors include HIV-related stigma, racial discrimination, poverty, increased sexually transmitted infections (STIs), HIV criminalization, and disproportionate incarceration of black men [2–4]. Racial disparities in HIV also exist in the US. Blacks represented 13% of the U.S. population in 2017 [5], but accounted for 41% of the new HIV diagnoses in the same year [1]. Moreover, HIV in the U.S. has a disproportionate impact on MSM, particularly individuals of color representing these communities [1, 6]. In Tennessee, these disparities are even more severe, with alarming rates of new diagnoses among MSM living in urban settings such as Memphis (43.7 per 100,000; ~67% attributed to MSM) and Nashville (39.9 per 100,000; ~76% attributed to MSM) [7].

Pre-Exposure Prophylaxis (PrEP), a once-daily antiretroviral regimen consisting of a combination of tenofovir (TDF) and emtricitabine (FTC), recently emerged as an HIV prevention tool for use by individuals at high-risk of infection. PrEP has been shown to be a safe and effective method of reducing HIV risk by 44–86%, with higher efficacy rates among persons with better adherence [8]. PrEP was approved by the U.S. Federal Drug Administration (FDA) for HIV acquisition risk reduction in combination with safer sex practices in July 2012 [9]. In 2014, the U.S. Centers for Disease Control and Prevention (CDC) released recommendations on the use of

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PrEP among sexually active adult MSM and heterosexual men and women, in addition to people who inject drugs (PWID) at substantial risk of HIV acquisition [10]. It is estimated that in 2015, 492,000 sexually active adult MSM, 624,000 sexually active heterosexual adults, and 115,000 PWID in the U.S. were eligible for PrEP [11].

Despite the known efficacy and safety of PrEP, uptake has been slow and particularly poor in the southern U.S. Moreover, racial disparities in the uptake of PrEP in this region are evident, with black patients less likely to access PrEP compared to white patients [12]. Potential barriers to PrEP uptake include lack of PrEP knowledge, structural and cultural factors (e.g., lack of insurance; poverty; stigma; racial, sexual, and gender identity discrimination), issues surrounding adherence, and perceived HIV risk. However, studies focused on barriers to PrEP uptake in the South are limited [12–16]. Data are even more limited for transgender women, and especially for those living in the southern U.S. The CDC's Division of HIV/AIDS 2017–2020 Strategic Plan prioritizes increasing the knowledge of, use of, support for, and adherence to PrEP among these populations with substantial HIV acquisition risk [17].

To increase the accessibility of PrEP, acquire a better understanding of PrEP acceptance and prescription rates, and gain insight into disparities in PrEP uptake in Tennessee, the Tennessee Department of Health (TDH) received funding for Project PrIDE, a CDC demonstration project (PS 15-1506) that was launched in the Memphis metropolitan statistical area (MSA) in June 2016 [18]. An additional PrEP demonstration project supported by CDC's HIV Prevention for Health Departments grant (PS 12-1201) [19] was implemented in Nashville, Knoxville, Chattanooga, and Johnson City in January 2017 to complement Project PrIDE activities. Both projects utilized PrEP navigators to inform, link, and monitor patient acceptance of this preventive service.

The objective of this study is to examine the extent to which clients identified as eligible by these two PrEP demonstration programs accepted, were linked to, and were prescribed PrEP. In addition, we sought to identify demographic, social, and geographic correlates of PrEP uptake while measuring trends in potential PrEP uptake disparities during the first year of the pilot. Findings will drive future PrEP navigation programming and ensure the public health response is tailored to meet PrEP needs that are unique to Tennessee.

Methods

Study Population

PrEP eligibility was determined based on CDC PrEP Guidelines [10] and grant objectives. These guidelines suggest a focus on engaging HIV discordant couples and persons reporting condomless anal sex in the past 6 months; injection drug use; and heterosexual contact with persons at substantial risk of infection. As part of Project PrIDE, TDH funded four Memphis-based community-based organizations (CBOs) to conduct PrEP navigation services, and two navigators were placed in the Shelby County Health Department (SCHD), for a total of six navigators in the Memphis MSA. In Memphis, each funded CBO's priority populations were black MSM and transgender persons who had identified risks for HIV. SCHD determined client eligibility based on an algorithm provided by the TDH HIV Prevention Program [20], which prioritized male and transgender clients with a positive syphilis result or positive rectal swab for chlamydia or gonorrhea, any male or transgender partner of a male or transgender STI case, client reported anal sex, or client reported injection drug use. For PS 12-1201 sites (Nashville, Knoxville, Chattanooga, and Johnson City), client eligibility was not specific to MSM of color and transgender women, and also included white MSM and other high-risk clients (PWID) who were seeking PrEP. Clients who tested positive for HIV were not eligible for PrEP, and were instead referred for HIV care and treatment. Each navigator (six navigators in Memphis and six navigators collectively in Nashville, Knoxville, Chattanooga, and Johnson City) was responsible for identifying ≥ 20 eligible clients per month. Upon identification the navigators were responsible for documenting client-level outcomes along a 'PrEP continuum,' including acceptance of PrEP, linkage to a PrEP provider, and prescription of PrEP [21]. Potentially eligible clients were identified at the time they sought HIV testing at a local health department or CBO, by PrEP navigator peer recruitment, via promotion of the website www.getpreptn.com on social media, and by a media campaign on MSM online dating sites.

Study Definitions

Outcomes

Following the initial client encounter and determination of PrEP eligibility, PrEP acceptance was ascertained (i.e., the client indicated interest in PrEP). Linkage to provider was defined as those who accepted the PrEP provider referral and attended their appointment. Lastly, navigators captured prescription of PrEP through electronic medical records, by following up with PrEP providers, or via self-report by clients. PrEP outcomes were documented if they occurred in the 6-month period during which the client was followed by the PrEP navigator.

Dates capturing each of the following events in the PrEP continuum were documented in a research electronic data capture (REDCap) database [21]: initial client encounter, determination of eligibility for PrEP, client acceptance of

PrEP, referral to PrEP provider, linkage to PrEP provider, and prescription of PrEP. The occurrence of each event was contingent on the preceding event (e.g., client acceptance was only reported among clients who were deemed eligible).

Three binary outcomes were included in our analyses: client acceptance, linkage to provider, and prescription of PrEP. To determine the timing of each outcome and properly define risk sets, dates reflecting when clients accepted PrEP, were linked to a provider, and received a prescription were extracted from the REDCap database. In order to describe trends in PrEP outcomes over the four quarters of the study period, we assigned dates for "non-acceptance of PrEP," "lack of PrEP linkage," and "lack of PrEP prescription." The date of each negative outcome for an individual client was assigned based on the mean number of days elapsed from the prior PrEP outcome among the overall population of clients with a negative outcome. For example, for clients who did not accept PrEP, their date of "non-acceptance" was assigned as the date they were identified as eligible plus the mean of the number of days between eligibility and acceptance among those who did accept PrEP. Dates were assigned similarly for PrEP linkage and prescription. Acceptance outcomes were compared among participants who were identified as eligible, linkage outcomes among participants who accepted, and prescription outcomes among participants who were linked.

Dates of respective PrEP outcomes were categorized into quarters for the analysis period of January–December 2017 (i.e., Q1: January–March, Q2: April–June, Q3: July–September, Q4: October–December). Initial encounters were documented once per unique client and clients contributed observations only once per outcome.

Demographic, Social, and Geographic Factors

Potential correlates of PrEP uptake examined for analysis included: age at first encounter (15–19, 20–24, 25–34, 35–44, ≥45 years), race/ethnicity (black non-Hispanic, white non-Hispanic, Hispanic, other), gender (male, female, transgender), transmission risk (male to male sexual contact [MSM], persons with a history of injection drug use [PWID], high risk heterosexual contact [HET], other/unknown), and geographic region of residence (Memphis/Shelby County: 'Memphis', Nashville/Davidson County: 'Nashville', Knoxville/Knox County: 'Knoxville', Chattanooga/Hamilton County: 'Chattanooga', and all other Tennessee counties: 'Other'; see Fig. 1). Information was entered into REDCap by the PrEP navigator upon intake, according to client self-report.

Statistical Analysis

Data from the Project PrIDE and 12-1201 project REDCap databases were combined to allow for examination of PrEP uptake throughout the state, and limited to initial client encounters that occurred during January–December 2017. Descriptive statistics of participants were generated to understand the distribution of clients by age, race, gender, transmission risk, region, and quarter. The three indicators of PrEP uptake were examined to determine the proportion of clients with each outcome, overall and by descriptive characteristics. In addition, the proportion of clients who accepted, were linked to, and prescribed PrEP were assessed overall and by quarter to identify any trends over time. Differences in proportions across categorical variables were detected using Chi square (X^2) tests.

Modified Poisson regression was used to derive unadjusted and adjusted prevalence ratios (PR) of each outcome, accounting for age, sex, race, transmission risk, and geographic region of residence [22]. Modified Poisson regression may be used when the outcome is binary yet we wish to directly estimate relative risks. In this instance, because the outcomes are not rare, estimated odds ratios will not approximate risk ratios, but rather will exaggerate them. For

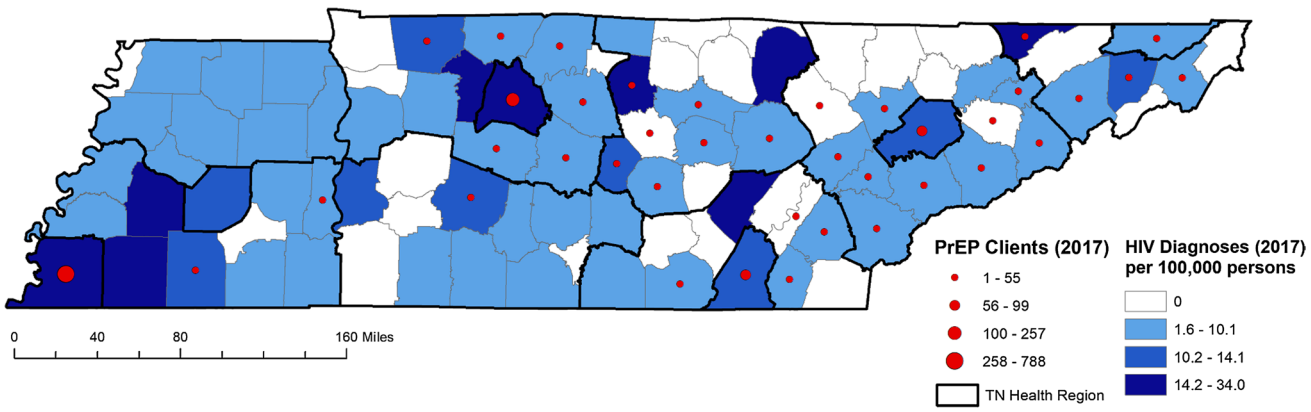

Fig. 1 Geographic distribution of PrEP program participants and new HIV diagnoses, by county, Tennessee, 2017

the purposes of communicating the risk, which we believe to be the more relevant quantity, we have opted for modified Poisson regression, which also avoids convergence issues that log-binomial regression may have [22].

Temporal trends were tested using orthogonal polynomial tests across quarters for each outcome [23]. Disparities by race, HIV/STI risk behavior, and geographic region were examined in both bivariate and multivariable (fully adjusted) models accounting for potential confounders and the quarter of observation. Age-by-time and race-by-time interactions were included in multivariable regression models in secondary analyses to examine changing outcome disparities over time. The joint effects were not included in the primary analysis; they were included in secondary analyses to assess changes in disparities over time. As such, they did not fall within the purview of the full model presented in the tables for the primary analysis. We also conducted a sensitivity analysis excluding individuals from sites in Nashville, which differed from other sites in client eligibility documentation in the first 3 months of the evaluation period. As we are limited in the number of tables/figures we are allowed to present, we felt that the focus should be maintained on the primary analysis and have described the results from our secondary and sensitivity analyses in the text only.

The evaluation of Project PrIDE and 12-1201 PrEP navigation outcomes was approved by the TDH Institutional Review Board (IRB).

Results

Among 1479 client encounters, 1385 individuals (93.6%) were identified as eligible for PrEP. A greater percentage of individuals who were ineligible for PrEP (versus eligible) were female (21.5% vs. 7%), transgender (10.8% vs. 4.0%), and black non-Hispanic (73.4% vs. 58.8%) ($p < 0.01$ each); a smaller percentage of individuals ineligible for PrEP (versus eligible) were MSM (54.3% vs. 77.0%, $p < 0.01$). The majority of eligible clients were young (15–34 years, n = 1062; 76.5%), black (n = 814; 58.7%), and MSM (n = 1067; 77.0%) (Table 1). Slightly more than half of clients (n = 724, 52.3%) resided in Memphis, and the remaining 47.7% of eligible clients were based in Nashville (n = 250, 18.1%), Knoxville (n = 84, 6.1%), Chattanooga (n = 52, 3.8%), or other counties across Tennessee (n = 275, 19.9%; Table 1).

Overall, approximately half of all eligible clients accepted PrEP (n = 700, 50.5%), but this varied by age (15–19 years: 45.2%, ≥ 45 years: 56.8%; $p = 0.03$), race/ethnicity (black non-Hispanic: 43.5%, white non-Hispanic: 61.6%, Hispanic: 66.0%; $p < 0.01$), transmission risk behavior (MSM: 52.0%, other: 38.9%; $p = 0.06$), and region (Memphis: 42.1%, Nashville: 71.6%, Knoxville: 53.6%, Chattanooga: 82.7%; $p < 0.01$). One-third (n = 463, 33.4%) of eligible clients were linked to PrEP, which increased with age (19.9% of 15–19 year olds vs. 47.3% of clients aged 45 years and older; $p < 0.01$). Twenty-seven percent (n = 26) of eligible females were linked to PrEP, compared to 30.9% (n = 17) of transgender clients and 34.1% (n = 418) of male clients ($p = 0.83$). A smaller proportion of black non-Hispanic clients were linked to PrEP (25.6%) compared to white non-Hispanic (47.1%) and Hispanic (48.9%) clients ($p < 0.01$); linkage rates also varied by region (Memphis: 22.2%, Nashville: 61.2%, Knoxville: 36.9%, Chattanooga: 59.6%; $p < 0.01$). Ultimately, 27.3% of all eligible clients were prescribed PrEP, and ranged from 12.3% of PWID and 13.0% of 15–19 year olds to 53.6% of Nashville-based clients and 43.6% of Hispanic clients.

Among MSM, black MSM were less likely to accept PrEP (44%) compared to their white (65%) and Hispanic (68%) counterparts ($p < 0.01$). Similarly, the percent of black MSM who were linked (26%) was lower than those who were white (49%) or Hispanic (49%, $p < 0.01$) and the percent of black MSM who were prescribed PrEP (22%) was lower than those who were white (38%) or Hispanic (43%, $p < 0.01$). Findings among young MSM (< 35 years) were largely similar, with significant racial differences across the three PrEP uptake outcomes (data not shown).

The percent differences between acceptance, linkage, and PrEP receipt varied by select subpopulations, including MSM, transgender clients, and black non-Hispanics (Fig. 2). Among MSM, acceptance to linkage accounted for an 18-point percentage decrease, and linkage to prescription was relatively stable (six-point decrease). Similarly, black non-Hispanics demonstrated a 17-point percentage decrease between acceptance to linkage and a five-point decrease from linkage to prescription. In contrast, acceptance to linkage differed by 20 percentage points among transgender clients and ten additional percentage points between linkage to prescription. Overall, when considering the number of non-Hispanic blacks that were eligible for PrEP (n = 814) and proceeded to fill a prescription (n = 171), the number was significantly lower when compared to white non-Hispanics, Hispanics, and other ($p < 0.05$).

Modified Poisson regression models revealed significant associations between demographic, social, and geographic characteristics (age, race/ethnicity, MSM, region) and acceptance and linkage to PrEP (Table 2). In both unadjusted and adjusted models, 20–24 year-olds were more likely to accept PrEP compared to 25–34 year-olds (aPR 1.2, 95% CI 1.0–1.3), and white non-Hispanics (aPR 1.3, 95% CI 1.1–1.5) and Hispanics (aPR 1.4, 95% CI 1.2–1.7) were more likely to accept PrEP compared to black non-Hispanics. Adjusting for all other factors, MSM were more likely to accept PrEP than non-MSM (aPR 1.2, 95% CI 1.0–1.3). In addition, clients residing in Nashville (aPR 1.6, 95% CI 1.5–1.8) and Chattanooga (aPR 1.7, 95% CI 1.4–2.0)

Table 1 Demographic, risk, and geographic characteristics of clients by stage of the PrEP continuum, Tennessee, 2017

	PrEP eligible		Accepted PrEP		Linked to PrEP		Prescribed PrEP	
	N	Col. %	n	% of eligible	n	% of eligible	n	% of eligible
Overall	1385	93.6	700	50.5	463	33.4	378	27.3
Age (years)								
15–19	146	10.5	66	45.2	29	19.9	19	13.0
20–24	379	27.4	203	53.6	128	33.8	104	27.4
25–34	535	38.6	248	46.4	163	30.5	141	26.4
35–44	177	12.8	98	55.4	73	41.2	60	33.9
≥45	146	10.5	83	56.8	69	47.3	53	36.3
Gender								
Male	1226	88.5	620	50.6	418	34.1	346	28.2
Female	97	7.0	49	50.5	26	26.8	19	19.6
Transgender	55	4.0	28	50.9	17	30.9	11	20.0
Race/ethnicity								
Black non-Hispanic	814	58.8	354	43.5	208	25.6	171	21.0
White non-Hispanic	401	29.0	247	61.6	189	47.1	149	37.2
Hispanic	94	6.8	62	66.0	46	48.9	41	43.6
HIV transmission risk								
MSM	1067	77.0	554	52.0	364	34.1	296	27.8
PWID	65	4.7	20	30.8	13	20.0	8	12.3
HET	140	10.1	82	58.6	61	43.6	52	37.1
Other/unknown	113	8.2	44	38.9	25	22.1	22	19.5
Region								
Memphis/Shelby Co.	724	52.3	305	42.1	161	22.2	126	17.4
Nashville/Davidson Co.	250	18.1	179	71.6	153	61.2	134	53.6
Knoxville/Knox Co.	84	6.1	45	53.6	31	36.9	16	19.0
Chattanooga/Hamilton Co.	52	3.8	43	82.7	31	59.6	26	50.0
Other counties	275	19.9	128	46.5	87	31.6	76	27.6

Col. column, *MSM* male sex with another male, *PWID* persons with history of injection drug use, *HET* high-risk heterosexual contact

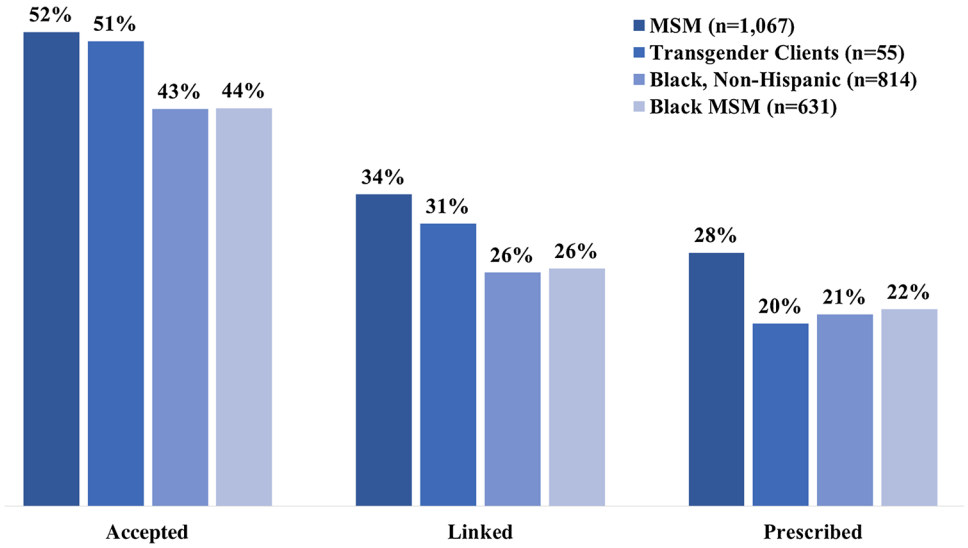

Fig. 2 Proportion of eligible clients who accepted, were linked to, and were prescribed PrEP, by select subpopulations, Tennessee, 2017

Table 2 Adjusted prevalence ratios (aPRs) and 95% confidence intervals (CI) for PrEP acceptance, linkage, and prescription by individual demographic, risk, and socioeconomic characteristics, Tennessee, 2017

	Accepted PrEP (N = 1385) aPR (95% CI)	Linked to PrEP (N = 621) aPR (95% CI)	Prescribed PrEP (N = 397) aPR (95% CI)
Age (years)			
15–19	1.05 (0.86, 1.28)	0.75* (0.58, 0.98)	0.89 (0.74, 1.07)
20–24	1.17* (1.03, 1.33)	0.99 (0.88, 1.12)	0.99 (0.95, 1.04)
25–34	Reference	Reference	Reference
35–44	1.14 (0.97, 1.34)	1.10 (0.98, 1.25)	1.00 (0.95, 1.05)
≥ 45	1.13 (0.96, 1.33)	1.18** (1.06, 1.30)	0.95 (0.88, 1.03)
Gender			
Male	Reference	Reference	Reference
Female	1.07 (0.87, 1.33)	1.01 (0.81, 1.25)	1.02 (0.93, 1.13)
Transgender female	1.21 (0.93, 1.57)	1.18 (0.91, 1.51)	0.83 (0.64, 1.09)
Race/ethnicity			
Black non-Hispanic	Reference	Reference	Reference
White non-Hispanic	1.39*** (1.23, 1.57)	1.31*** (1.18, 1.45)	1.03 (0.99, 1.08)
Hispanic	1.45*** (1.23, 1.72)	1.28** (1.10, 1.48)	1.03 (0.97, 1.10)
HIV transmission risk			
MSM	1.14 (1.00, 1.31)	1.06 (0.95, 1.18)	1.04 (0.97, 1.12)
Other	Reference	Reference	Reference
Quarter			
Q1 (Jan–Mar 2017)	Reference	Reference	Reference
Q2 (Apr–Jun 2017)	1.05 (0.92, 1.20)	0.97 (0.87, 1.09)	1.01 (0.95, 1.08)
Q3 (Jul–Sep 2017)	0.95 (0.83, 1.09)	0.92 (0.83, 1.03)	0.98 (0.92, 1.05)
Q4 (Oct–Dec 2017)	0.86 (0.69, 1.06)	0.89 (0.74, 1.08)	1.02 (0.93, 1.11)
Socioeconomic factors by 5-digit ZIP code			
Median household income (per $10,000)	1.06** (1.02, 1.11)	1.02 (0.99, 1.05)	1.02 (1.00, 1.03)
Proportion with < high school education	0.36 (0.09, 1.50)	0.47 (0.12, 1.76)	1.08 (0.72, 1.63)
Proportion with no health insurance	9.38** (1.71, 1.41)	1.81 (0.44, 7.42)	1.91 (0.94, 3.88)

aPR adjusted prevalence ratio, *CI* confidence interval, *MSM* male sex with another male, *other* persons with a history of injection drug use, high-risk heterosexual, or no identified risk

*Significant at $p < 0.05$; **Significant at $p < 0.01$; ***Significant at $p < 0.001$

were more likely to accept PrEP compared to clients from Memphis.

With respect to linkage, white non-Hispanics (aPR 1.2, 95% CI 1.0–1.3) and Hispanics (aPR 1.2, 95% CI 1.1–1.4) were more likely to be linked to PrEP compared to black non-Hispanics, MSM were more likely to be linked compared to non-MSM (aPR 1.1, 95% CI 1.0–1.3), and clients based in Nashville (aPR 1.5, 95% CI 1.4–1.7), Knoxville (aPR 1.3, 95% CI 1.1–1.6), and Chattanooga (aPR 1.3, 95% CI 1.1–1.6) were all more likely to be linked than those in Memphis. In addition, clients aged 45 years and older were more likely to be linked to PrEP compared to 25–34 year-olds (aPR 1.1, 95% CI 1.0–1.3).

Orthogonal polynomial tests across quarters for each outcome showed no statistically significant linear trend, suggesting minimal differences in the likelihood of clients reaching each of the three outcomes over time. Of note, however, the likelihood of clients accepting PrEP decreased over the four quarters with a near-significant linear trend ($p = 0.07$).

Models including interaction terms for age-by-time and race-by-time effects showed no significant trends in age disparities over the four quarters for any of the three outcomes. However, with respect to accepting PrEP, white non-Hispanic and Hispanic individuals both showed narrowing disparities versus black non-Hispanic individuals over time (ratio of aPRs ranging from 0.7 to 0.8 for white non-Hispanics in quarters 3 and 2 vs. 1; ratio of aPRs ranging from 0.6 to 0.7 for Hispanics in quarters 3 and 2 vs. 1; linear trend $p = 0.04$).

In sensitivity analyses excluding Nashville participants due to different eligibility documentation during the first 3 months, there were no substantive differences in point estimates (either magnitude or direction) for the individual

demographic and clinical risk characteristics compared to the primary analyses for each outcome.

Discussion

Findings provide new and important insights into PrEP continuum outcomes for Tennessee and contribute to the broader literature on southern U.S. communities at high risk for HIV infection. Notably, while outcomes varied by region, both Project PrIDE and 12-1201 PrEP navigation achieved project goals of identifying and engaging MSM and transgender individuals across the state, and particularly MSM and transgender individuals of color. However, significant drop-offs were observed, from the time of initial encounter to client acceptance, with approximately half of clients accepting PrEP offers.

Results suggest that younger individuals were more likely to initially accept PrEP, but older clients were more likely to be linked to a PrEP provider. In addition, Hispanic clients and MSM were more likely to accept and be linked to a provider compared to black clients and non-MSM. While differences in PrEP acceptance by race narrowed over time, for MSM, the proportion of black MSM who accepted PrEP was lower than the proportion of black MSM who did not, underscoring a significant need to improve upstream PrEP continuum outcomes for black MSM. Racial disparities were observed in the acceptance and linkage stages prior to seeking a prescription, and led to an overall difference in the number of black participants filling prescriptions when compared to other racial groups. As a result of these findings, future PrEP programs may focus on bridging the gaps identified prior to prescription seeking, as pharmacy patient assistance programs have helped to facilitate availability of PrEP prescriptions to all who seek one, regardless of access to insurance or income.

Previous studies of PrEP acceptance, linkage and prescription have yielded similar findings to our study with slightly higher rates of linkage and acceptance overall [24–26]. Studies examining rates of prescription among PrEP seekers have shown higher linkage and prescription rates [24] compared to participants not seeking PrEP approached through community based methods as occurred with some clients in our study [25]. Similar to the findings of our study, black participants have been shown to have lower rates of acceptance, linkage and prescriptions compared to white and Hispanic participants [26].

Our findings that indicate lower rates of PrEP acceptance, linkage and prescription among black participants may be reflective of previous qualitative studies where comparisons were made between patients in the deep South versus those in the Northeast, these racial disparities were particularly pronounced. Medical mistrust, stigma regarding homosexuality, and non-identification as gay despite engaging in sex with men are all factors noted in qualitative studies among black MSM in the South but not among the same population in the Northeast [14, 26]. More research is needed to determine whether these factors significantly impact black participants' utilization of PrEP all along the cascade.

Our study provides important data on acceptance, linkage, and prescription of PrEP among transgender individuals. Rates of acceptance and linkage to PrEP among transgender participants in our study were similar to those of cisgender participants, men and women, indicating a promising interest among this population for PrEP, and an effective approach to PrEP navigation with this population in our study. Prescription, however, was considerably lower among this population. The medical mistrust and stigma reported by black MSM in the South in other studies may also be a factor in transgender prescription rates, but more studies are needed to determine the impact of these factors on this population [26].

Future programming may benefit from understanding how to increase client interest in PrEP to retain clients between the stages of identification and acceptance, which is where significant drop off occurred in this study, particularly for black MSM. It is possible that by funding all navigators at once during the inception of the PrEP navigation program, the small pool of potential clients were saturated early on, especially those that were more likely to be interested and seeking out PrEP (versus those that would be harder to reach and keep engaged in PrEP). Year two of implementation will yield more data to determine whether a saturation point was reached. Conversely this fourth quarter drop may be transient when compared to data collected in year two. If saturation is identified, programs might consider beginning a PrEP navigation program with a full-time dedicated navigator, but switching to a lower-cost model where PrEP navigation is integrated into the responsibilities of other existing HIV prevention and HIV testing staff. Full time navigation programs might also consider shifting recruitment strategies once they see a drop off in acceptance, using social network strategy/snowball sampling, peer recruiters, and partnerships with STD clinics to provide access to hard to reach community members at risk [27–29].

Though our analyses represented a novel and important look at PrEP continuum outcomes in the American South, they were subject to limitations. First, though individuals participated in PrEP programs within different regions of the state, our analyses did not cluster outcomes at the level of geographic region. We instead chose to use direct adjustment in the regression models to address confounding by regional factors, leaving our inferences potentially subject to false precision of the estimates, if our assumption that outcomes among individuals within a region are roughly

independent was violated. Further, while geographic indicators were defined by the major metropolitan regions across the state, there may have been unaccounted variation within the broad "other counties" category. Second, the trends we describe may be reflective of program changes in ease of client recruitment over the life cycle of a grant as opposed to individual likelihoods of accessing points in the PrEP continuum. Moreover, not all funded agencies approached documentation of 'encounters' in the same way, due to time/cost saving measures. In particular, one agency in Nashville only recorded client-level information on clients that had accepted their PrEP offer, thus their encounter numbers were the same as the accepted numbers, making their PrEP acceptance percentages artificially high. That said, a sensitivity analysis excluding these clients did not substantively alter our inferences for each outcome. Third, we did not adjust for facility-level characteristics such as financial aid or billing practices, or additional individual factors such as socioeconomic status, which may have influenced individual acceptance, linkage to, and receipt of PrEP [14]. However, we did conduct analyses accounting for ZIP Code-level socioeconomic indicators. Finally, the implementation of the program took place over a single year, and so our analyses were limited in the sample size and power to detect temporal trends. Future analyses should take advantage of longer follow-up, more refined and complete measures of site-level and individual-level characteristics, and different analytic techniques to address potential clustering of individual outcomes within regions.

Public Health Implications

Despite these limitations, gaining an understanding of the extent to which key populations in Tennessee accepted PrEP offers and eventually received PrEP prescriptions is critical for determining how to most effectively implement future PrEP navigation activities in Tennessee. Such evaluations are also important for funding agencies (e.g., TDH) seeking to determine technical assistance needs for new navigation programs. Additionally, identifying populations with lower PrEP success rates, such as black MSM, despite existing resources to assist with PrEP navigation, will guide resource allocation for these populations during HIV prevention program planning. The findings of this evaluation call for diligence in placing resources in traditionally under-represented communities, continuing to normalize PrEP use, and identifying and eliminating barriers to PrEP uptake in Tennessee.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

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