ORIGINAL PAPER



PrEP Use and Adherence Among Transgender Patients

Jae Downing¹ · Kimberly Yee^{1,3} · Jae M. Sevelius²

Accepted: 21 September 2021

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

Abstract

This cross-sectional study used 2012 to 2019 Oregon Medicaid claims to estimate the prevalence of PrEP use and identify determinants of high adherence across transgender and cisgender men and women. Gender identity (cisgender woman/man; transgender, assigned female sex at birth [AFAB]; transgender, assigned male sex at birth [AMAB]) was based on medical history and enrollment records. Proportion of days covered ≥ 0.80 was considered high adherence to PrEP. The association between gender identity and PrEP uptake or high adherence was estimated using multivariable logistic regression. 1555 PrEP users, including 171 (11.0%) cis women, 1171 (75.3%) cis men, 67 (4.3%) AFAB, and 146 (9.4%) AMAB individuals, were included. The probability of PrEP use per 10,000 people was highest in transgender groups (AMAB 546.8, 95% CI 462.4–631.3; AFAB 226.5, 95% CI 173.4–279.6), followed by cisgender men (20.6, 95% CI 19.4, 21.8) and women (2.6, 95% CI 2.2, 3.0). High adherence was significantly lower in AMAB recipients (72.6%) than cisgender women (86.0%) and cisgender men (82.2%). Among the 279 PrEP users with female on their enrollment record, 76 (27.2%) were AMAB, while among the 1276 PrEP users with male on their enrollment record, 35 (2.7%) were AFAB. This demonstrates the importance of surveillance methods that take gender identity into account in addition to sex assigned at birth. There were significant differences in PrEP use and adherence by gender identity. PrEP surveillance, outreach, and prescribing practices must consider gender identity-unique risk factors.

 $\textbf{Keywords} \ \ Pre-exposure \ prophylaxis \ (PrEP) \cdot Transgender \cdot Medicaid \cdot Adherence \cdot Differential \ misclassification$

Introduction

Transgender and gender diverse (henceforth "trans") people are disproportionately affected by HIV [1]. An estimated 14 percent of trans women and 3 percent of trans men have a HIV diagnosis, compared to 0.4% of the US population [2, 3]. Pre-exposure prophylaxis (PrEP) can be an effective means to prevent new HIV infections. PrEP can decrease the probability of HIV acquisition by more than 90% among HIV-negative persons who adhere to the daily regimen [4].

Very little is known about the prevalence of PrEP use among trans populations. In a nationally representative study of 112 trans people in the US at risk for HIV, an estimated 3% (n=5) people were currently using PrEP [5]. Monitoring data on PrEP uptake at national and state levels among trans people is also limited. AIDSVu, a public resource for visualizing HIV surveillance data, presents data on PrEP use and new cases of HIV, yet it does not identify PrEP use or new cases of HIV by gender identity. Rather, AIDSVu reports sex-specific estimates; 6.3% of PrEP users in the U.S. were female, and 93.7% were male in 2018 [6]. Because both HIV risk and access to healthcare differs for cisgender (henceforth "cis") and trans people, the addition of a gender identity measure would improve PrEP surveillance [7].

There are several factors that could cause differences in uptake of PrEP and adherence by gender identity. While some risk factors for HIV are shared among individuals with the same types of organs used during sex (for example, trans men and cis women with vaginas), many more risk factors are gender-based. Compared to cis women, trans men have less contact with the healthcare system, less knowledge about sexual health, and more cis male sexual partners that identify as gay or bisexual. Furthermore, trans men are

Published online: 13 October 2021



Department of Health Policy and Management, OHSU-PSU School of Public Health, Portland, OR, USA

Department of Medicine, University of California, San Francisco, San Francisco, CA, USA

OHSU-PSU School of Public Health, 840 SW Gaines St, Gaines Hall, Room 230, Portland, OR 97239, USA

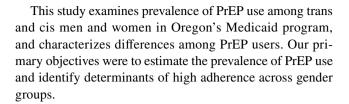
more likely to engage in survival sex and report substance use during sexual activity than cis women [8, 9]. These factors not only can explain risk for HIV, but also awareness, knowledge, and uptake of PrEP.

Trans individuals experience unique barriers in accessing PrEP and maintaining a daily pill regimen. PrEP and HIV testing are often part of preventive care, and trans people use less preventive care [10] because of fear of discrimination by providers [11], limited access to knowledgeable, culturally competent providers [12], and lack of insurance coverage for gender-affirming care. In 2015, Oregon became one of the first of 21 states' (and Guam) Medicaid programs to cover gender-affirming hormones and surgeries. This new coverage may increase use of preventive care among trans people who are seeking a primary care provider for a gender-affirming hormones prescription.

Another unique barrier trans people face in accessing PrEP is the failure of PrEP marketing campaigns to address trans-specific concerns. This can contribute to a lower level of awareness of PrEP among trans people compared to cis men who have sex with men [13]. PrEP uptake and adherence among trans women have been particularly challenging. Community concerns about potential drug—drug interactions between feminizing hormones and PrEP persist despite evidence that PrEP and hormones are safe and effective to use concurrently [14–17].

Cost—even among people with insurance—is a major barrier to PrEP uptake for many people [18], including trans individuals [19], who are more likely to be unemployed or underemployed than cis individuals. PrEP use is lower among people enrolled in Medicaid compared to private health insurance [20], even though Medicaid is the largest payer of people who have been diagnosed with HIV [21, 22]. This is in part because there has been high variability in coverage generosity and cost sharing for PrEP. In June of 2019, the US Preventive Services Task Force updated its recommendation for PrEP to a grade A, which effectively required Medicaid expansion states to provide PrEP without cost sharing [23]. At the time of this study, all state Medicaid programs provide some coverage for PrEP [24]. Despite this, very little is known about general PrEP uptake within state Medicaid programs [25, 26], and uptake specifically among trans Medicaid beneficiaries is unknown.

Furthermore, it is unknown whether trans individuals are less likely to be adherent to PrEP once they receive their first prescription. Trans populations have higher burdens of substance use and depression than cis populations [27], which could reduce adherence to PrEP. Prior studies have shown mixed associations: depression and substance use was linked with low adherence of PrEP in some populations [28, 29], but not others [29, 30]. No research we are aware of has studied the relationship of substance use and depression with PrEP adherence among trans men and women.



Methods

Study Population

We used administrative claims data from Oregon's Medicaid Program from 2012 to 2019. This data contained information on diagnostic codes, medical claims (for outpatient, inpatient, and emergency care), and pharmaceutical claims for every beneficiary who used Medicaid to pay for health care or medications during the study period. Unique identifiers allowed us to follow an individual across multiple years and enrollment discontinuities. The data also included information on providers' National Provider Identifier number and on beneficiaries' age, gender, race/ethnicity, and county of residence. We excluded beneficiaries who were dually-eligible for Medicare because claims were incomplete, and those who were under 18 because PrEP was not approved for youth until 2018, when approval was expanded to include adolescents who weigh at least 77 pounds [31].

Measures

Outcome Variables

The main outcomes of interest were whether beneficiaries had ever taken PrEP and the level of adherence to PrEP. We applied an algorithm used in prior work [20] to differentiate HIV-negative patients taking tenofovir/emtricitabine (TDF/FTC) for PrEP from HIV-positive patients taking FTC/TDF for HIV treatment, hepatitis B treatment, and for post-exposure prophylaxis (eFigure 1, eTable I in the Supplement). The proportion of days covered (PDC) was used to measure adherence. PDC was calculated by: (1) calculating the number of days with TDF/FTC between the first day of the first TDF/FTC fill and the last day of the last fill in the year and (2) dividing this number by the number of days in this interval [32]. We created a binary indicator variable for high adherence (PDC 0.8 or higher), consistent with prior work [33].

Exposure Variables

The main exposure of interest was gender identity. We identified trans beneficiaries as those who had at least one gender identity-related diagnosis code (ICD-9: 302.5x,



302.6, 302.85, ICD-10: F640, F642, F641, F648, F649, Z87.890) over the period. While not all individuals with a gender identity-related diagnosis code identify as trans, and not all trans people receive these diagnoses, previous studies have found very high sensitivity and specificity using this method [34, 35]. Sex assigned at birth for trans beneficiaries was based on sex-specific claims, use of gender-affirming medications (i.e. masculinizing or feminizing hormones), and gender patterns on the enrollment record (eFigure 2 in the Supplement). Trans beneficiaries were characterized as being assigned female (AFAB) or male sex at birth (AMAB). Cis men and women were beneficiaries who were not identified as trans and had male and female on their enrollment record, respectively.

Beneficiary Characteristics

Demographic variables included age, race and ethnicity, county of residence, and year(s) of enrollment. Age was calculated as age at the time of PrEP initiation among PrEP users, and age at the time of enrollment among nonusers. Age was categorized as 18-24 years, 25-34 years, 35-49 years, or 50 years and older. Beneficiaries with selfreported race and ethnicity on their enrollment records were categorized as Non-Hispanic White, Non-Hispanic Black, Hispanic, or Other, while those with missing race and ethnicity were categorized as Unknown. County of residence was obtained from enrollment records and a binary indicator was created to denote residence within the Portland Metro region or outside it. Binary indicators were created to specify whether beneficiaries were annually enrolled during the study period. Demographic variables were operationalized consistent with a previous claims-based study of PrEP use [36].

Characteristics of PrEP Users

For those who used PrEP, we also included history of substance use disorder or depression during the year PrEP was initiated, existence of a concurrent daily pill regimen when PrEP was initiated, and, among trans beneficiaries, whether PrEP and gender-affirming hormones were prescribed by the same provider. Diagnosis codes for substance use disorder and depression were obtained from 2018 Healthcare Effectiveness Data and Information Set value sets [37]. Concurrent daily pill regimens were identified from beneficiaries' pharmaceutical claims. Receipt of PrEP and gender-affirming hormones from the same provider was identified using the National Provider Identifier field on beneficiaries' pharmaceutical claims.

Statistical Analysis

Descriptive

We first descriptively analyzed all Oregon Medicaid beneficiaries who did and did not use TDF/FTC for PrEP during the analytic period. Second, among the beneficiaries who ever used PrEP, we compared demographic and health characteristics by gender identity. Chi-square and Fisher's Exact tests were used to compare the distributions of characteristics across the four gender identity groups (AFAB, AMAB, cis women, and cis men).

Differences in PrEP Use and Adherence

Next, to understand whether trans individuals who were AFAB or AMAB differed in their probability of using PrEP compared to cis women and men, we conducted a multivariable logistic regression analysis to evaluate the association between gender identity and ever taking PrEP, and included age, race and ethnicity, residence, and enrollment variables as covariates. To understand whether trans and cis men and women differed in their probability of having high adherence, we conducted a multivariate logistic regression analysis with high adherence to PrEP (PDC \geq 0.8) as the outcome measure. This model controlled for demographic and health covariates. Post-estimation predictive margins were reported to aid interpretation.

All data analyses were completed in November of 2020 in R version 4.0.3. The study protocol was approved by the Oregon Health & Sciences University Institutional Review Board.

Results

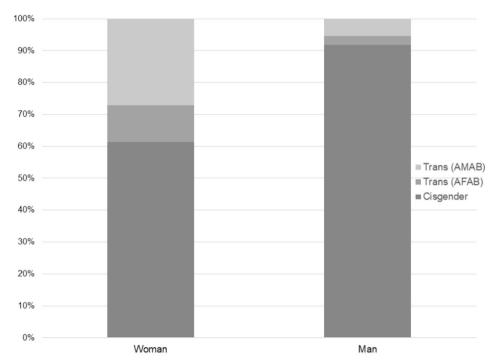
Population Description

A total of 1,225,243 adult beneficiaries were included, of whom 1555 (0.13%) received PrEP (Table 1, eFigure 1 in the Supplement). Among PrEP users, 213 (13.7%) were trans (9.4% AMAB and 4.3% AFAB), 171 (11.0%) were cis women, and 1171 (75.3%) were cis men (p < 0.001). PrEP use was concentrated among those aged 25–34 years (47.0% of all recipients) compared to other age groups (p < 0.001), and in those residing in the Portland Metro area (72.2% of all recipients, p < 0.001; Table 1).

Among the 279 PrEP users with female on their enrollment record at PrEP start, 171 (61.3%) were cis women, 32 (11.5%) were AFAB, and 76 (27.2%) were AMAB (Fig. 1). Among the 1276 PrEP users with male on their enrollment



Fig. 1 Gender on enrollment record of PrEP users. *AFAB* assigned female sex at birth, *AMAB* assigned male sex at birth; PrEP Pre-Exposure Prophylaxis



Abbreviations: AFAB assigned female sex at birth; AMAB assigned male sex at birth; PrEP Pre-Exposure Prophylaxis

record at PrEP start, 1171 (91.8%) were cis men, 35 (2.7%) were AFAB, and 70 (5.5%) were AMAB.

Description of PrEP Users

Of the 1555 PrEP users, the highest proportion of users were aged 25-34 years at PrEP initiation (Table 2). Thirty-nine percent of AFAB were aged 18-24 compared to 18.1-23.3% of the other gender groups (p < 0.001). A higher proportion of AFAB (61.2%) and cis women (60.2%) were non-Hispanic white, compared to other groups (p < 0.001). A higher proportion of AFAB recipients (86.6%) resided in the Portland metro area compared to 67.3–72.6% of other groups (p = 0.03). Forty-two percent of AMAB individuals and 42.7% of cis women had a substance use disorder, compared to 26.9% of AFAB and 25.1% of cis men (p < 0.001). The prevalence of diagnosed depression was 44.8% in AFAB and 45.9% in AMAB, compared to 36.8% in cis women and 24.8% in cis men (p < 0.001). High adherence to PrEP was lower among AMAB beneficiaries (72.6% compared to 80.6% or higher in all other groups; p = 0.02). An estimated 3 in 4 trans beneficiaries were prescribed PrEP and genderaffirming hormones from the same provider (Table 2).

Gender Identity-Based Differences in PrEP Use and Adherence

The predicted probability of PrEP use per 10,000 people was 226.5 in the AFAB group (95% CI 173.4, 279.6), 546.8 in the AMAB group (95% CI 462.4, 631.3), 20.6 in cis men (95% CI 19.4, 21.8), and 2.6 in cis women (95% CI 2.2, 3.0). The predicted probability of high adherence among PrEP users was 86.0% in cis women, 82.2% in cis men, 80.6% in AFAB, and 72.6% in AMAB recipients.

High adherence was significantly lower in AMAB recipients (72.6%, 95% CI: 65.4%, 79.8%) than among cisgender women (86.0%, 95% CI: 80.8%, 91.2%) and cisgender men (82.2%, 95% CI: 80.0%, 84.3%) (Table 3, eTables II and III in the Supplement).

Discussion

This study is, to our knowledge, the first to use Medicaid claims data to evaluate state-wide PrEP use. In Oregon's Medicaid program, trans people assigned female or male sex at birth used PrEP at far higher rates than cis women and men. If these rates were applied at the national level across the 27.6 million non-elderly adults enrolled in Medicaid, the estimated number of users would include 9300 trans individuals, 2750 cis women, and 26,460 cis men. These rates of use (5.8% of AMAB and 2.3% of AFAB) are consistent



Table 1 Characteristics of PrEP users and non-users in Oregon's Medicaid program, 2012–2019

Characteristic, n (%)	PrEP non-users $(n=1,223,688)$	PrEP users $(n=1555)$	P value (χ^2)
Gender group ^{a, b}			< 0.001
Cisgender woman	650,404 (53.2)	171 (11.0)	
Cisgender man	567,869 (46.4)	1,171 (75.3)	
Transgender, assigned female sex at birth	2891 (0.2)	67 (4.3)	
Transgender, assigned male sex at birth	2524 (0.2)	146 (9.4)	
Age group ^c			$< 0.001 (\chi 2357.1, df = 3)$
18–24	400,328 (32.7)	309 (19.9)	
25–34	343,589 (28.1)	731 (47.0)	
35–49	301,952 (24.7)	421 (27.1)	
50+	177,819 (14.5)	94 (6.0)	
Race/ethnicity			$< 0.001 (\chi 2 136.7, df=4)$
Non-Hispanic white	657,104 (53.7)	815 (52.4)	
Non-Hispanic Black	35,735 (2.9)	61 (3.9)	
Hispanic	196,154 (16.0)	117 (7.5)	
Other	235,084 (19.2)	356 (22.9)	
Unknown ^d	99,611 (8.1)	206 (13.2)	
Portland Metro ^e	480,956 (39.3)	1,123 (72.2)	$< 0.001 (\chi 2703.7, df = 1)$
Year ^f			
2012	261,528 (21.4)	174 (11.2)	$< 0.001 (\chi 2 95.3, df = 1)$
2013	260,077 (21.3)	178 (11.4)	$< 0.001 (\chi 2 88.7, df = 1)$
2014	589,146 (48.1)	631 (40.6)	$< 0.001 (\chi 2 35.3, df = 1)$
2015	719,624 (58.8)	845 (54.3)	$< 0.001 (\chi 2 12.6, df = 1)$
2016	747,776 (61.1)	988 (63.5)	$0.053 (\chi 2 3.8, df = 1)$
2017	703,137 (57.5)	1126 (72.4)	$< 0.001 (\chi 2 141.4, df = 1)$
2018	663,475 (54.2)	1214 (78.1)	$< 0.001 (\chi 2 355.0, df = 1)$
2019	678,528 (55.4)	1252 (80.5)	$< 0.001 (\chi 2 394.0, df = 1)$

Abbreviations: PrEP Pre-Exposure Prophylaxis

with prior work that found 2.5–9% of transgender people at risk for HIV used PrEP nationwide [5, 38]. To date, only one other study has used claims data to evaluate PrEP use by gender identity. In that study, which comprised commercially- and publicly-insured Rhode Island youth aged 18–25 years, 1.75% of trans and gender diverse beneficiaries received PrEP, compared to 0.17% of cis men and 0.02% of cis women [39]. Although that study did not assess specific gender identity within the trans and gender diverse population, the disproportionate ratios of PrEP use between trans and cis populations are similar to those seen in our study.

One surprising and important finding from this study is the misclassification of gender that can occur when using claims data for PrEP research. As trans people comprise a relatively high share of PrEP users compared to cis women, failure to identify trans people will inadvertently overestimate PrEP use among cis women. Our present study found that more than 1 in 3 PrEP users with female on their enrollment record had a transgender-specific diagnosis, and 70% of those with transgender-specific diagnoses were AMAB. Misclassification matters for monitoring trends in PrEP use. For example, AIDSVu reports the PrEP-to-Need Ratio each year for males and females based on sex assigned at birth in



^aCisgender woman and man are identified based on the absence of a transgender-specific diagnosis and the gender on the enrollment record. Transgender groups are identified based on the presence of a transgender-specific diagnosis, sex-specific claims, use of gender-affirming masculinizing or feminizing hormones, and gender patterns on the enrollment record

^bP value derived using Fisher's Exact test

^cAge is ascertained at time of first PrEP prescription for PrEP users and age at earliest enrollment for non-users

^dSince 2014, a design change in the Oregon Eligibility System online application allowed the race/ethnicity question to be skippable

ePortland Metro refers to residence in the Tri-county area

^fYear refers to enrollment at any time during the year

Table 2 Characteristics of PrEP users in Oregon's Medicaid Program

Characteristic, n (%)	Cisgender Women (n=171)	Cisgender Men (n=1171)	Transgender, assigned female sex at birth $(n=67)$	Transgender, assigned male sex at birth $(n = 146)$	P value ^a
Age group ^b					< 0.001
18–24	37 (21.6)	212 (18.1)	26 (38.8)	34 (23.3)	
25–34	66 (38.6)	560 (47.8)	32 (47.8)	73 (50.0)	
35–49	63 (36.8)	314 (26.8)	9 (13.4)	35 (24.0)	
50+	5 (2.9)	85 (7.3)	0 (0)	4 (2.7)	
Race/ethnicity					< 0.001
Non-Hispanic white	103 (60.2)	591 (50.5)	41 (61.2)	80 (54.8)	
Non-Hispanic Black	14 (8.2)	40 (3.4)	2 (3.0)	5 (3.4)	
Hispanic	15 (8.8)	95 (8.1)	2 (3.0)	5 (3.4)	
Other	28 (16.4)	277 (23.7)	17 (25.4)	34 (23.3)	
Unknown ^c	11 (6.4)	168 (14.3)	5 (7.5)	22 (15.1)	
Portland Metro ^d	115 (67.3)	844 (72.1)	58 (86.6)	106 (72.6)	0.025
Substance use disorder ^e	73 (42.7)	294 (25.1)	18 (26.9)	61 (41.8)	< 0.001
Depression ^e	63 (36.8)	290 (24.8)	30 (44.8)	67 (45.9)	< 0.001
Daily pill regimen f	90 (52.6)	433 (37.0)	36 (53.7)	105 (71.9)	< 0.001
High adherence $(PDC \ge 0.8)^g$	147 (86.0)	962 (82.2)	54 (80.6)	106 (72.6)	0.020
PrEP from gender-affirming hormone prescriber h	-	_	52 (77.6)	109 (74.7)	< 0.001

Abbreviations: proportion of days covered; PrEP pre-exposure prophylaxis

Table 3 Predicted probability of PrEP use and high adherence by gender group

	Use of PrEP per 10 k ^{a, b} (n=1,225,243)	High adherence among all PrEP users, $\%$ c $(n = 1555)$
Gender group ^d		
Cisgender woman	2.6 (2.2, 3.0)	86.0 (80.8, 91.2)
Cisgender man	20.6 (19.4, 21.8)	82.2 (80.0, 84.3)
Transgender, assigned female sex at birth	226.5 (173.4, 279.6)	80.6 (71.1, 90.1)
Transgender, assigned male sex at birth	546.8 (462.4, 631.3)	72.6 (65.4, 79.8)

PrEP pre-exposure prophylaxis



^aAll P values derived using Fisher's Exact test

^bAge is ascertained at time of first PrEP prescription for PrEP users and age at earliest enrollment for non-users

^cSince 2014, a design change in the Oregon Eligibility System online application allowed the race/ethnicity question to be skippable

^dPortland Metro refers to residence in the Tri-county area

^eDiagnosed in the year starting PrEP

^fConcurrent daily pill regimen at the date of PrEP initiation

^gProportion of days covered is calculated by: (1) calculating the number of days with PrEP between the first day of the first PrEP fill and the last day of the last fill in the year and (2) dividing this number by the number of days in this interval

^hGender-affirming hormones are provided to transgender beneficiaries only

^aA logistic regression model followed by post-estimation predictive margins for gender was used for interpretation. This model was adjusted for age, race/ethnicity, Portland Metro residence, and enrollment during the year

^bProbabilities were multiplied by 10,000 to improve interpretation

^cA logistic regression model followed by post-estimation predictive margins for gender was used for interpretation. This model was adjusted for age, race/ethnicity, Portland Metro residence, substance use disorder, depression, and having a daily pill regimen

^dCisgender woman and man are identified based on the absence of a transgender-specific diagnosis and the gender on the enrollment record. Transgender groups are identified based on the presence of a transgender-specific diagnosis, sex-specific claims, use of gender-affirming masculinizing or feminizing hormones, and gender patterns on the enrollment record

each state but does not report trans identity. Furthermore, trans populations experience unique barriers to care, such as concerns about drug interactions among those taking feminizing hormones, failure of PrEP campaigns to reach trans people, and experiencing discrimination in healthcare [14–17, 40], which further differentiates trends in uptake. A study of 843 HIV-negative trans and gender diverse individuals suggests the cisnormative approach to identifying PrEP candidates is inappropriate: AFAB who identified as transmasculine had borderline higher odds of PrEP uptake than those who identified as nonbinary, while not experiencing any cisgender male partner stigma was significantly associated with higher odds of PrEP adherence [40]. Inclusion of trans identities in data collection and reporting efforts will increase the accuracy of surveillance efforts as well as help monitor outreach and improve targeted spending for at-risk populations.

While AFAB are often presumed to have cis female sex partners and thereby to be low risk for HIV [8], our study identified 4.3% of PrEP users as AFAB. Prior research found 1 in 5 AFAB had a positive or unknown HIV/STI status partner in their lifetime [41]. Our study found AFAB differed from AMAB PrEP users in several ways. A higher proportion of AFAB PrEP users were younger and located within the Portland metro area. This may reflect the changing sexual behaviors of younger AFAB people [8].

Our study found important demographic and health differences among PrEP users based on gender identity. A higher proportion of trans PrEP users in our study were younger than 35 years compared to cis people. This age distribution was similar to that observed in a prior national study of commercially insured PrEP users [42]. Our study also found AMAB had lower adherence compared to the other gender identity groups, even after adjusting for other factors that can impact risk. This may be due to fears that hormones may interact with PrEP, discriminatory experiences with providers, and health systems inaccessibility [43].

Cis women and AMAB PrEP users had similarly high rates of a diagnosed substance use disorder (40%), which differed from gender identity-based prevalence observed in Behavioral Risk Factor Surveillance data [44]. Future studies should explore whether populations of women at risk of HIV transmission may experience similar levels of vulnerability. Trans PrEP users in our study had higher prevalence of diagnosed depression than cis PrEP users, which was consistent with prior literature in the general US population [44].

This study has several limitations. First, claims data lack qualitative or narrative data regarding a patient's risk of contracting HIV. Consequently, we could not estimate whether PrEP was adequately prescribed among the at-risk population. Second, while we were able to use a published algorithm to differentiate PrEP users from HIV-positive

patients taking TDF/FTC or for HIV-negative patients using TDF/FTC for post-exposure prophylaxis, we were not able to confirm whether TDF/FTC was being used for PrEP. However, given the limited indications for TDF/FTC prescription, we believe the algorithm captures PrEP use with high sensitivity. Third, our method for ascertaining trans identity and sex assigned at birth has high specificity, but moderate sensitivity [34]. We likely misclassified some of the trans population as cisgender, which may have biased our results toward the null. Fourth, we grouped our population into four gender identity categories, which may reinforce the rigid categorization of gender expansive people by failing to capture the diversity of trans communities, including nonbinary-identified people.

Despite these limitations, this study suggests sex assigned at birth and gender identity are fundamental risk modifiers for PrEP uptake and adherence. Among Oregon Medicaid beneficiaries, AFAB and AMAB had significantly elevated rates of PrEP use compared to cis women and men. These results suggest the necessity of accurate surveillance using both sex and gender, targeted outreach, and culturally-competent HIV preventive care that takes into account the specific needs and risk factors of trans people.

Supplementary Information The online version of this article contains supplementary material available https://doi.org/10.1007/s10461-021-03482-8.

Acknowledgements JD and KY contributed substantially to the design, analysis, interpretation, and composition of this study. JS contributed critical revisions to this study. All authors agree to be accountable for the accuracy and integrity of this study. Research reported in this publication was supported by National Institute on Minority Health and Health Disparities (3R01MD011212-0S31 [Administrative Supplement to 1R01MD011212], PI McConnell), the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health (K12HD043488, PI Downing), and the National Institute on Drug Abuse (K24 DA051328, PI Sevelius). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Author Contributions JD and KY contributed substantially to the design, analysis, interpretation, and composition of this study. JS contributed critical revisions to this study. All authors agree to be accountable for the accuracy and integrity of this study.

Funding Research reported in this publication was supported by National Institute on Minority Health and Health Disparities (3R01MD011212-0S31 [Administrative Supplement to 1R01MD011212], PI McConnell), the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health (K12HD043488, PI Downing), and the National Institute on Drug Abuse (K24 DA051328, PI Sevelius).

Availability of Data and Material A de-identified limited data set was obtained from the Oregon Health Authority for this study. Data rights cannot be transferred.



Code Availability All code used for the data management, analysis, and replication of this study is available upon request.

Declarations

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

Ethical Approval This research study was conducted retrospectively from data obtained for health insurance purposes. The study protocol was approved by the Oregon Health & Science University Institutional Review Board and a waiver of ethical approval was granted.

Consent to Participate This research study used secondary data from a de-identified data set. As such, the Oregon Health & Science University Institutional Review Board deemed obtaining informed consent was unnecessary.

References

- Clark H, Babu AS, Wiewel EW, Opoku J, Crepaz N. Diagnosed HIV infection in transgender adults and adolescents: results from the National HIV Surveillance System, 2009–2014. AIDS Behav. 2017;21(9):2774–83.
- Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N, et al. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. AIDS Behav. 2008;12(1):1–17.
- Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2010–2015. HIV Surveillance Supplemental Report 2018; 23(No. 1).
- Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363(27):2587–99.
- Sevelius JM, Poteat T, Luhur WE, Reisner SL, Meyer IH. HIV testing and PrEP use in a national probability sample of sexually active transgender people in the United States. JAIDS J Acquir Immune Defic Syndr. 2020;84(5):437.
- AIDSVu. Local Data: PrEP (Pre-Exposure Prophylaxis) [Internet]. Atlanta, GA: Center for AIDS Research at Emory University; 2018 [updated 2021; cited 2021 September]. Available from: https://aidsvu.org/local-data/united-states/#prep.
- Lake JE, Clark JL. Optimizing HIV prevention and care for transgender adults. AIDS (London, England). 2019;33(3):363.
- 8. Golub SA, Fikslin RA, Starbuck L, Klein A. High rates of PrEP eligibility but low rates of PrEP access among a national sample of transmasculine individuals. JAIDS J Acquir Immune Defic Syndr. 2019;82(1):e1–7.
- Reisner SL, Moore CS, Asquith A, Pardee DJ, Sarvet A, Mayer G, et al. High risk and low uptake of pre-exposure prophylaxis to prevent HIV acquisition in a national online sample of transgender men who have sex with men in the United States. J Int AIDS Soc. 2019;22(9):5391.
- Edmiston EK, Donald CA, Sattler AR, Peebles JK, Ehrenfeld JM, Eckstrand KL. Opportunities and gaps in primary care preventative health services for transgender patients: a systematic review. Transgender Health. 2016;1(1):216–30.
- Keith K. HHS proposes to strip gender identity, language access protections from ACA anti-discrimination rule [Internet]. Health Affairs Blog; 2019 [updated 2019 May 25; cited 2021 September]. Available from: https://www.healthaffairs.org/do/https://doi.org/ 10.1377/hblog20190525.831858/full/.

- Rael CT, Martinez M, Giguere R, Bockting W, MacCrate C, Mellman W, et al. Barriers and facilitators to oral PrEP use among transgender women in New York City. AIDS Behav. 2018;22(11):3627–36.
- Schueler K, Ferreira M, Nikolopoulos G, Skaathun B, Paraskevis D, Hatzakis A, et al. Pre-exposure prophylaxis (PrEP) awareness and use within high HIV transmission networks. AIDS Behav. 2019;23(7):1893–903.
- 14. Mehrotra ML, Westreich D, McMahan VM, Glymour MM, Geng E, Grant RM, et al. Baseline characteristics explain differences in effectiveness of randomization to daily oral TDF/FTC PrEP between transgender women and cisgender men who have sex with men in the iPrEx trial. JAIDS J Acquir Immune Defic Syndr. 2019;81(3):e94–8.
- Klein A, Golub SA. Increasing access to pre-exposure prophylaxis among transgender women and transfeminine nonbinary individuals. AIDS Patient Care STDS. 2019;33(6):262-9.
- Grant RM, Pellegrini M, Defechereux PA, Anderson PL, Yu M, Glidden DV, et al. Sex Hormone Therapy and Tenofovir Diphosphate Concentration in Dried Blood Spots: Primary Results of the iBrEATHe Study. Clinical Infectious Diseases. 2020.
- 17. Yager JL, Anderson PL. Pharmacology and drug interactions with HIV PrEP in transgender persons receiving gender affirming hormone therapy. Expert Opin Drug Metab Toxicol. 2020;16(6):463–74.
- 18. Kay ES, Pinto RM. Is insurance a barrier to HIV preexposure prophylaxis? Clarifying the issue. Am J Public Health. 2020;110(1):61-4.
- Wood SM, Lee S, Barg FK, Castillo M, Dowshen N. Young transgender women's attitudes toward HIV pre-exposure prophylaxis. J Adolesc Health. 2017;60(5):549–55.
- Raifman J, Nocka K, Galárraga O, Wilson IB, Crowley C, Tao J, et al. Evaluating statewide HIV pre-exposure prophylaxis implementation using All Payer Claims Data. Ann Epidemiol. 2020;44:1-7.
- Kates J. Medicaid and HIV: a national analysis [Internet]. San Francisco, CA: Kaiser Family Foundation; 2011 [updated 2011 October; cited 2021 September]. Available from: https://www. kff.org/hivaids/report/medicaid-and-hiv-a-national-analysis/.
- Macinski SE, Gunn JK, Goyal M, Neighbors C, Yerneni R, Anderson BJ. Validation of an optimized algorithm for identifying persons living with diagnosed HIV from New York State Medicaid Data, 2006–2014. Am J Epidemiol. 2020;189(5):470–80.
- Walensky RP, Paltiel AD. New USPSTF guidelines for HIV screening and preexposure prophylaxis (PrEP): straight A's. JAMA Netw Open. 2019;2(6):e195042.
- Dawson L, Dolan R.. State Medicaid Management of Prescription Drugs for HIV Treatment and Prevention [Internet]. San Francisco, CA: Kaiser Family Foundation; 2020 [updated 2020 June 4; cited 2021 September]. Available from: https://www.kff.org/hivaids/issue-brief/state-medicaid-management-of-prescription-drugs-for-hiv-treatment-and-prevention/.
- Chan PA, Seiler N, Chu CT. Leveraging medicaid to enhance preexposure prophylaxis implementation efforts and ending the HIV epidemic. Am J Public Health. 2020;110(1):65–6.
- Laufer FN, O'Connell DA, Feldman I, Zucker HA. Vital signs: increased medicaid prescriptions for preexposure prophylaxis against HIV infection—New York, 2012–2015. Morb Mortal Wkly Rep. 2015;64(46):1296–301.
- Connolly D, Gilchrist G. Prevalence and correlates of substance use among transgender adults: a systematic review. Addict Behav. 2020. https://doi.org/10.1016/j.addbeh.2020.106544.
- Velloza J, Baeten JM, Haberer J, Ngure K, Irungu E, Mugo NR, et al. Effect of depression on adherence to oral PrEP among men



- and women in East Africa. JAIDS J Acquir Immune Defic Syndr. 2018;79(3):330–8.
- Shuper PA, Joharchi N, Bogoch II, Loutfy M, Crouzat F, El-Helou P, et al. Alcohol consumption, substance use, and depression in relation to HIV Pre-Exposure Prophylaxis (PrEP) nonadherence among gay, bisexual, and other men-who-have-sex-with-men. BMC Public Health. 2020;20(1):1–12.
- Okafor CN, Hucks-Ortiz C, Hightow-Weidman LB, Magnus M, Emel L, Beauchamp G, et al. Brief report: associations between self-reported substance use behaviors and PrEP acceptance and adherence among black MSM in the HPTN 073 study. JAIDS J Acquir Immune Defic Syndr. 2020;85(1):23–9.
- 31. Hosek SG, Landovitz RJ, Kapogiannis B, Siberry GK, Rudy B, Rutledge B, et al. Safety and feasibility of antiretroviral pre-exposure prophylaxis for adolescent men who have sex with men aged 15 to 17 years in the United States. JAMA Pediatr. 2017;171(11):1063–71.
- 32. Raebel MA, Schmittdiel J, Karter AJ, Konieczny JL, Steiner JF. Standardizing terminology and definitions of medication adherence and persistence in research employing electronic databases. Med Care. 2013;51(8 0 3):S11–21.
- 33. van Epps P, Maier M, Lund B, Howren MB, Beck B, Beste L, et al. Medication adherence in a nationwide cohort of veterans initiating pre-exposure prophylaxis (PrEP) to prevent HIV infection. JAIDS J Acquir Immune Defic Syndr. 2018;77(3):272–8.
- Proctor K, Haffer SC, Ewald E, Hodge C, James CV. Identifying the transgender population in the Medicare program. Transgender Health. 2016;1(1):250–65.
- Blosnich JR, Cashy J, Gordon AJ, Shipherd JC, Kauth MR, Brown GR, et al. Using clinician text notes in electronic medical record data to validate transgender-related diagnosis codes. J Am Med Inform Assoc. 2018;25(7):905–8.
- Raifman J, Nocka K, Galárraga O, Wilson IB, Crowley C, Tao J, et al. Evaluating statewide HIV preexposure prophylaxis implementation using All-Payer Claims Data. Ann Epidemiol. 2020;44:1–7.

- National Committee for Quality Assurance. Healthcare Effectiveness Data and Information Set (HEDIS) 2019 Technical Specifications for Health Plans, Volume 2 [Internet]. Washington, DC: NCQA; 2018. Available from: https://www.ncqa.org/hedis/measures/.
- 38. Baldwin A, Light B, Allison WE. Pre-Exposure Prophylaxis (PrEP) for HIV Infection in Cisgender and Transgender Women in the US: A Narrative Review of the Literature. Arch Sex Behav. 2021;50(4):1713–28.
- Nocka K, Montgomery MC, Progovac A, Guss CE, Chan PA, Raifman J. Primary care for transgender adolescents and young adults in Rhode Island: an analysis of the All Payers Claims Database. J Adolesc Health. 2021;68(3):472–9.
- 40. Reisner SL, Moore CS, Asquith A, Pardee DJ, Mayer KH. The pre-exposure prophylaxis cascade in at-risk transgender men who have sex with men in the United States. LGBT Health. 2021;8(2):116–24.
- 41. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis, 2006–2017. Am J Public Health. 2019;109(1):e1–8.
- Song HJ, Squires P, Wilson D, Lo-Ciganic W-H, Cook RL, Park H. Trends in HIV preexposure prophylaxis prescribing in the United States, 2012–2018. JAMA. 2020;324(4):395–7.
- Wood S, Gross R, Shea JA, Bauermeister JA, Franklin J, Petsis D, et al. Barriers and facilitators of PrEP adherence for young men and transgender women of color. AIDS Behav. 2019;23(10):2719–29.
- 44. Downing JM, Przedworski JM. Health of Transgender Adults in the US, 2014–2016. Am J Prev Med. 2018;55(3):336–44.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

