Urban Sexual Health Clinic Patients With "Undetermined Risk" for HIV Are Less Likely to Receive Preexposure Prophylaxis

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Background: New diagnoses of HIV increasingly occur among people who fall outside traditional transmission risk categories. This group remains poorly defined, and HIV prevention efforts for this group lag behind efforts for patients in other risk groups.

Methods: We conducted a retrospective review of patient visits at sexual health clinics in Boston, MA, over a 14-month period. Patients were classified into Centers for Disease Control and Prevention–defined HIV transmission risk categories. We compared frequencies of sexually transmitted infections (STIs), HIV, preexposure prophylaxis (PrEP) indications, and PrEP prescriptions. Predictors of HIV or STI among patients in the undetermined risk category were assessed with logistic regression.

Results: There were 4723 clinic visits during the study period. Patients in the undetermined risk group constituted the largest proportion (55.8%), followed by men who have sex with men (MSM; 42.7%). The proportion of visits by patients in the undetermined risk group with an indication for PrEP was low (28.0%) compared with MSM (91.3%) and MSM who also inject drugs (93.8%); however, the absolute number was high (737). Among patients with an indication for PrEP, those in the undetermined risk group were least likely to receive a prescription. Behavioral risk factors were poorly predictive of STI or HIV among patients in the undetermined risk group.

Conclusions: Patients with undetermined risk for HIV constituted a large proportion of clinic visits and had a large volume of sexual health needs but rarely received PrEP when indicated. To end the HIV epidemic in the United States, prevention efforts must include people who fall outside traditional risk categories.

At both state and national levels, standardized classifications of HIV transmission risk among new cases of HIV are used to better understand the epidemic and inform prevention efforts such as the provision of preexposure prophylaxis (PrEP). The primary HIV transmission risk categories currently used by the Centers for Disease Control and Prevention (CDC) are as follows: men who have sex with men (MSM), injection drug use (IDU), MSM who also inject drugs (MSM/IDU), and heterosexual contact.[1,2] "Heterosexual contact" includes heterosexually active adults whose partners are known to be at high risk for transmitting HIV (i.e., partners who inject drugs, are HIV positive, or are MSM). Patients with missing information about transmission category are assigned to the most likely category using multiple imputation. In the state of Massachusetts, however, patients who do not fall into traditional risk categories are classified as "undetermined risk" rather than reassigned to another group. The undetermined risk category includes heterosexually active adults whose partners are not known to be at high risk for transmitting HIV as well as transgender individuals and those whose partners are transgender.[1] In Massachusetts, the proportion of new HIV diagnoses assigned undetermined risk is increasing.[3] Among the 608 new diagnoses of HIV in 2017, more than a quarter were classified as undetermined risk. This is now the second most common mode of transmission after MSM in Massachusetts despite expanded public health evaluation for all new HIV diagnoses.[3]

A significant pillar in HIV transmission prevention is PrEP, which is highly effective in MSM, people who inject drugs (PWID), and heterosexually active adults.[4–6] Heterosexually active adults with an indication for PrEP include those who would fall into both the high-risk heterosexual and undetermined risk transmission categories. The CDC recommends it as an HIV prevention option for all adults at high risk for HIV acquisition.[7] Nevertheless, PrEP uptake lags behind need.[8–11] Unique barriers contributing to low uptake have been identified for people in each transmission risk group.[12] We examined data from 2 urban sexual health clinics and outreach programs in Boston, MA, that routinely conduct risk assessments of all patients. We assessed how indications for PrEP and use of PrEP varied by HIV transmission risk category. We sought to further characterize patients in the undetermined risk category by identifying factors predictive of HIV or bacterial sexually transmitted infection (STI) diagnoses most suggestive of heightened HIV risk (gonorrhea and infectious syphilis), as this group is less well understood than others and is not traditionally prioritized in HIV prevention efforts despite their increasing representation among new HIV diagnoses in our state. These results can be used to better define gaps in HIV prevention strategies and inform future prevention efforts.

MATERIALS AND METHODS

Setting and Population

We conducted a retrospective review of adult patients (18 years or older) who received care at 2 sexual health clinics and

community outreach sites in Boston, MA, from January 2, 2019, to March 27, 2020. The sexual health clinics are located in Suffolk County, 1 of 48 counties in the United States identified as having a high burden of HIV.[13] Both clinics offer comprehensive sexual health services including STI screening, treatment, and longitudinal PrEP provision. One clinic is located on an academic hospital campus, and the other is located at a community health center. A smaller number of patients were seen at community outreach settings such as mobile vans or community testing centers. These sites offer HIV and STI testing along with PrEP initiations. Together, these clinics and community venues have an average of 338 total monthly visits.

Routinely collected data at each visit include demographic information (age, patient-reported gender identity, race/ethnicity, country of birth, and zip code), personal risk-associated behaviors (IDU, sexual practices), and characteristics of sexual partners that increase the risk of transmitting HIV and STIs (known HIV, IDU, MSM). Based on reported personal and partner behaviors, we classified patients into 1 of 5 transmission risk categories: MSM, IDU, MSM/IDU, high-risk heterosexual, or undetermined risk. Patients were classified as MSM if they self-identify as male and report at least one male sex partner ever or reported their sexual orientation as MSM. Patients were classified in the IDU risk category if they reported ever injecting drugs. Patients who met the criteria for both MSM and IDU categories were classified as MSM/IDU. Patients were classified as high-risk heterosexual if they report having sex with someone of the opposite sex who injects drugs, is MSM, or is HIV positive. Open-ended time frames were chosen to align with state and CDC HIV transmission categories. An individual patient may be assigned to different risk categories at different visits if their reported behaviors changed.

Routinely recorded clinical information includes STI symptoms and exposures, laboratory testing results, and prescriptions such as antibiotics and PrEP. Gonorrhea and chlamydia were diagnosed by NAAT from exposed sites (urine/urethral, vaginal, rectal, or pharyngeal). Patients presenting with symptoms of urethritis or cervicitis were evaluated with Gram stain, and those with intracellular, gram-negative diplococci were presumed to have a gonococcal infection. Syphilis was diagnosed by 2-tiered serologic testing and clinical examination. Patient symptoms and treatment history were used to stage syphilis as infectious (primary, secondary, or early latent syphilis) or noninfectious (late or serofast). HIV was diagnosed by screening enzyme immunoassay followed by confirmatory differentiation assay. This study was approved by the Partner's Human Subjects Research Committee (Protocol 2001P001195, Boston, MA).

Statistical Analysis

Demographic characteristics, reported risk-associated behaviors, and STI testing results from patient visits were summarized using frequencies and medians as appropriate. We compared baseline characteristics, behaviors, and STI frequencies across different risk categories using simple generalized linear multinomial logistic regression to obtain a likelihood ratio χ^2 test with Rao-Scott adjustment *P* values. Primary outcomes of interest included having a documented indication for PrEP and current use of PrEP. Indications for PrEP were aligned as best as possible with CDC and US Preventive Services Task Force (USPSTF) recommendations and included being HIV negative, not in a monogamous relationship with an HIV-negative partner, having multiple sex partners without consistent condom use, and having one of the following: diagnosis or treatment of gonorrhea or syphilis for any patient in the previous year, diagnosis or treatment of chlamydia for patients in MSM and MSM/IDU categories in the previous year, IDU in the previous year, and transactional sex during the previous year.[7,14] Anyone with

a current PrEP prescription was considered to have an indication even if the reason was not documented. Use of PrEP was defined as reporting currently taking PrEP or having a new prescription for PrEP started during a given clinic visit, including when contacted with positive STI testing results. Clinic visits for patients with known HIV were excluded from analyses regarding PrEP indications and use.

We further analyzed patients in the undetermined risk group using a series of simple generalized linear logistic regressions and multivariable generalized linear logistic regression to determine factors independently associated with a composite outcome of HIV or bacterial STI suggestive of high HIV risk (gonorrhea or infectious syphilis). Because some individuals contribute data to more than one visit, all analyses were adjusted for intracluster correlations within subjects. Covariates of interest included patient age, gender identity, race/ethnicity, place of birth, insurance status, number of sexual partners in the prior year, transactional sex in the prior year, noninjection stimulant or opioid drug use in the prior year, and sex with a transgender person in the prior year. We also used patient zip code to calculate a neighborhood deprivation index (NDI), described hereinafter, which was used as a summary indicator of socioeconomic status.[15] Starting with an a priori list of models that includes different combinations of variables, we used Akaike information criteria to select variables to include in the final regression models. Models with the fewest parameters and the lowest Akaike information criteria were selected.

The NDI was generated using zip codes that were matched with data from the American Community Survey from the US Census Bureau 2014–2018 5-year data (https://www.census.gov/data/developers/data-sets/acs-5year.html). We conducted a principal components analysis using 20 variables measuring education, employment, housing, occupation, poverty, racial composition, and residential stability. Variables were included in the component if the variable load was >0.25 and if the lower 95% confidence interval (CI) of the variable loading was not less than the lower 95% CI of the median factor loading. We retained 6 of the 20 variables (percent males in management, percent households on public assistance, percent females in management, percent female-headed households with dependent children, percent females in professional occupations, and percent of the population with less than a high school education). Next, principal components analysis was rerun using those 6 variables to obtain the final item loadings and NDI. Higher scores represent lower socioeconomic status (i.e., neighborhoods with higher "deprivation"). Statistical analyses were conducted using SAS software (version 9.4; SAS Institute, Carey, NC).

RESULTS

During the study period, 2787 unique patients had 4723 clinic visits that contributed data to this analysis. The demographic characteristics, reported risk-associated behaviors, and STI frequencies of this cohort are outlined by visit in Table 1. Patients in the undetermined risk group constituted the largest proportion of clinic visits (55.6%), followed by MSM (42.9%). Patients in IDU, MSM/IDU, and high-risk heterosexual risk groups constituted a small proportion of visits (0.7%, 0.5%, and 0.3%, respectively). The median patient age was 30 years. Those in the undetermined risk category were the youngest with a median age of 30 years, whereas those in the MSM/IDU category were the oldest with a median age of 36 years. Approximately half (54.4%) of the visits were for patients identifying as non-Hispanic White, with smaller proportions identifying as Hispanic/Latinx (17.3%) and non-Hispanic Black (12.9%). About one-third (36%) of visits were for foreign-born adults. Among the risk categories, those in IDU and MSU/IDU

TABLE 1. Demographics, Risk-Associated Behaviors, and STI Frequencies for Each Transmission Risk Category by Visit

	Total (n = 4723)	MSM (n = 2017)	IDU (n = 31)	MSM/IDU (n = 24)	High-Risk Heterosexual (n = 16)	Undetermined Risk (n = 2635)	*P*
No. visits for each unique patient, median (IQR)	1.0 (1.0–2.0)	1.0 (1.0–3.0)	1.0 (1.0–2.0)	1.0 (1.0–3.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	<0.001
Age, y							<0.001
Median (IQR)	30 (25–39)	31 (26–40)	36 (33–62)	32 (29–56)	35 (28–39)	30 (25–37)	
Gender identity, n (%)							<0.001
Male	3645 (77.2)	2017 (100)	25 (80.7)	24 (100.0)	6 (37.5)	1573 (59.7)	
Female	1023 (21.7)	0 (0.0)	4 (12.9)	0 (0.0)	10 (62.5)	1009 (38.3)	
Trans female	9 (0.2)	0 (0.0)	2 (6.5)	0 (0.0)	0 (0.0)	7 (0.3)	
Trans male	7 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.3)	
Other	26 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	26 (1.0)	
Unknown	13 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (0.5)	
Race/ethnicity, n (%)							<0.001
Non-Hispanic White	2568 (54.4)	1048 (52.0)	19 (61.3)	23 (95.8)	5 (31.3)	1473 (55.9)	
Non-Hispanic Black	607 (12.9)	179 (8.9)	2 (6.5)	1 (4.2)	2 (12.5)	423 (16.1)	
Hispanic/Latinx	818 (17.3)	415 (20.6)	10 (32.3)	0 (0.0)	4 (25.0)	389 (14.8)	
Other	700 (14.8)	364 (18.1)	0 (0.0)	0 (0.0)	5 (31.3)	331 (12.6)	
Unknown	30 (0.6)	11 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	19 (0.7)	
Place of birth, n (%)							<0.001
US-born	3019 (63.9)	1158 (57.4)	24 (77.4)	24 (100.0)	9 (56.3)	1804 (68.5)	
Foreign-born	1704 (36.1)	859 (42.6)	7 (22.6)	0 (0.0)	7 (43.8)	831 (31.5)	
Clinic visit site, n (%)							<0.001
Academic clinic	3843 (81.4)	1632 (80.9)	24 (77.4)	19 (79.2)	13 (81.3)	2155 (81.8)	
Community clinic	777 (16.5)	299 (14.8)	7 (22.0)	1 (4.2)	3 (18.8)	467 (17.7)	
Nonclinical site	102 (2.2)	85 (4.2)	0 (0.0)	4 (16.7)	0 (0.0)	13 (0.5)	
Unknown	1 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Health insurance status, n (%)							0.301
Insured	3700 (78.3)	1589 (78.8)	24 (77.4)	14 (58.3)	11 (68.8)	2062 (78.3)	
Uninsured	914 (19.4)	371 (18.4)	4 (12.9)	8 (33.3)	5 (31.3)	526 (20.0)	
Unknown	109 (2.3)	57 (2.8)	3 (9.7)	2 (8.3)	0 (0.0)	47 (1.8)	
NDI, median (IQR)	−0.3 (−0.7–0.8)	−0.2 (−0.7–0.8)	0.4 (−0.2–1.4)	−0.4 (−0.7–1.3)	0.4 (−0.4–1.5)	−0.4 (−0.8–0.8)	<0.001
No. sexual partners in prior year, n (%)							<0.001
0	49 (1.0)	3 (0.2)	4 (12.9)	0 (0.0)	0 (0.0)	42 (1.6)	
1–5	2723 (57.7)	789 (39.1)	19 (61.3)	4 (16.7)	10 (62.5)	1901 (72.1)	
6–10	804 (17.0)	408 (20.2)	3 (9.7)	5 (20.8)	2 (12.5)	386 (14.7)	
>10	994 (21.1)	786 (39.0)	3 (9.7)	15 (62.5)	3 (18.8)	187 (7.1)	
Unknown	153 (3.2)	31 (1.5)	2 (6.5)	0 (0.0)	1 (6.3)	119 (4.5)	
Transactional sex in prior year, n (%)							0.011
Yes	139 (2.9)	46 (2.3)	3 (9.7)	3 (12.5)	1 (6.3)	86 (3.3)	
No	4584 (97.1)	1971 (97.7)	28 (90.3)	21 (87.5)	15 (93.8)	2549 (96.7)	
Sex with transgender person in prior year, n (%)							<0.001
Yes	121 (2.6)	59 (2.9)	0 (0.0)	6 (25.0)	0 (0.0)	56 (2.1)	
No	4602 (97.4)	1958 (97.1)	31 (100.0)	18 (75.0)	16 (100.0)	2579 (97.9)	
Noninjection drug use in prior year, n (%)							<0.001
Yes	292 (6.2)	141 (7.0)	7 (22.6)	12 (50.0)	0 (0.0)	132 (5.0)	
No	4431 (93.8)	1876 (93.0)	20 (77.4)	12 (50.0)	16 (100.0)	2503 (95.0)	
HIV positive, n (%)	153 (3.2)	138 (6.8)	0 (0.0)	8 (33.3)	0 (0.0)	7 (0.2)	<0.001
New diagnosis of HIV, n (%)	3 (0.01)	3 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Exposure to STI prompting empiric treatment, n (%)							
Chlamydia	287 (6.1)	160 (7.9)	3 (9.7)	4 (16.7)	0 (0.0)	120 (4.6)	<0.001
Gonorrhea	128 (2.7)	103 (5.1)	2 (6.5)	4 (16.7)	0 (0.0)	19 (0.7)	<0.001
Infectious syphilis	53 (1.1)	44 (2.2)	2 (6.5)	1 (4.2)	0 (0.0)	6 (0.2)	<0.001
Symptoms of STI prompting empiric treatment, n (%)							
Chlamydia	406 (8.6)	157 (7.8)	5 (16.1)	1 (4.2)	0 (0.0)	243 (9.2)	<0.001
Gonorrhea	256 (5.4)	197 (9.8)	3 (9.7)	6 (25.0)	0 (0.0)	50 (1.9)	<0.001
Infectious syphilis	181 (3.8)	152 (7.5)	2 (6.5)	3 (12.5)	0 (0.0)	24 (0.9)	<0.001
Laboratory diagnosis of new bacterial STI, n (%)							
Chlamydia	260 (5.5)	128 (6.4)	1 (3.2)	1 (4.2)	1 (6.3)	129 (4.9)	0.341

TABLE 1. *(Continued)*

	Total (n = 4723)	MSM (n = 2017)	IDU (n = 31)	MSM/IDU (n = 24)	High-Risk Heterosexual (n = 16)	Undetermined Risk (n = 2635)	P
Gonorrhea	152 (3.2)	123 (6.1)	2 (6.5)	1 (4.2)	0 (0.0)	26 (1.0)	<0.001
Infectious syphilis	70 (1.5)	54 (2.7)	0 (0.0)	2 (8.3)	0 (0.0)	14 (0.5)	<0.001
HIV/STI composite outcome, n (%)	882 (18.7)	755 (37.4)	5 (16.1)	15 (62.5)	0 (0.0)	107 (4.1)	<0.001

risk categories were most likely to be born in the United States (77.4% and 100%, respectively). Those in the high-risk heterosexual category were least likely to be born in the United States (56.7%). Those in the IDU and high-risk heterosexual transmission risk groups came from neighborhoods with the highest deprivation (each with a median NDI of 0.4). Those in the MSM/IDU and undetermined risk groups came from neighborhoods with the lowest deprivation (each with a median NDI of −0.4). The composite outcome of HIV or STI was identified in 882 (18.7%) of clinic visits and was most common among visits for patients in the MSM/IDU category (62.5%) and least common among patients in the undetermined risk category (18.7%).

Frequencies of PrEP indications and use among patients without known HIV in each risk category are presented in Table 2. Indications for PrEP were identified in 2473 patient visits. Visits for patients in the MSM/IDU risk group were the most likely to identify an indication for PrEP (93.8%), followed by MSM (90.7%), and high-risk heterosexuals (50.0%). Those in the undetermined risk group were the least likely to have an indication for PrEP (28.0%). However, those in the undetermined risk group constituted the second-largest group by absolute numbers (n = 737), exceeded only by MSM (n = 1704). Among the 2473 clinic visits for patients with an indication for PrEP, approximately one-third (915; 37.0%) were on PrEP. Those in the MSM risk group were the most likely to be on PrEP (873/1704; 51.2%), followed by MSM/IDU (6/15; 40.0%), high-risk heterosexual (2/8; 25.0%), and IDU (2/9; 22.2%). Those in the undetermined risk category with an indication for PrEP were the least likely to be on PrEP (32/770; 4.3%).

Among patients in the undetermined risk category, several features were significantly associated with the composite outcome of HIV or STI (Table 3). Using simple logistic regression, age, gender identity, race/ethnicity, health insurance status, and NDI were each independently associated with the composite outcome. Behavioral factors such as the number of sexual partners, transactional sex, non-IDU, and sex with a transgender partner were not significant predictors of HIV or STI. When evaluated in a multivariable logistic regression, all variables found predictive on simple logistic regression remained predictive. In our final model, we observed a 3% increase in the odds of being diagnosed with HIV or STI for every 1-year increase in age (odds ratio [OR], 1.03; adjusted OR [aOR], 1.03; 95% CI, 1.01–1.05). In evaluating associations with gender identity, those identifying as "other" had significantly higher odds of being diagnosed with STI or HIV than did patients identifying as male (OR, 8.55; aOR, 7.04; 95% CI,

1.87–26.5). A racial/ethnic disparity was observed with those who reported being anything other than non-Hispanic White having over twice the odds of HIV or STI compared with patients who identified as non-Hispanic White (OR, 2.43; aOR, 1.97; 95% CI, 1.17–3.31). Those coming from neighborhoods with lower socioeconomic status had higher odds of HIV or STI (OR, 1.56; aOR, 1.32; 95% CI, 1.03–1.68). Among the behavioral factors considered, none was predictive of STI or HIV in adjusted and unadjusted analyses.

DISCUSSION

At 2 large urban sexual health clinics and community sites, we found that patients with undetermined risk for HIV composed the largest proportion of clinic visits. Although among these, there was a relatively low proportion of visits in which a CDC indication for PrEP was identified (28.0%), the total number was high (737), second only to MSM. The large number of clinic visits for patients in the undetermined risk category in which an indication for PrEP is identified aligns with data suggesting that heterosexual sex has contributed to an increasing proportion of new HIV transmissions compared with earlier in the epidemic.[16] The frequency of PrEP use in our clinic was high, although it varied by transmission group. In our cohort, half of MSM with an indication were on PrEP. Over one-third of patients in the MSM/IDU category and over one-fifth in the IDU category with an indication for PrEP were receiving it. This is noteworthy given well-documented struggles in PrEP uptake among individuals who inject drugs.[17,18] Higher proportions of PrEP prescriptions among PWID in our cohort may be related to heightened awareness among patients and providers because of an outbreak of HIV among PWID in the Boston area during the time of this study.[19]

Among visits in which there were CDC indications for PrEP, patients in the undetermined risk group were the least likely to be on PrEP, at less than 5%. Lower fractions of PrEP prescriptions among those with undetermined risk are likely multifactorial including decreased awareness and other patient-level and provider-level factors. From the patient perspective, a survey conducted among heterosexual adults in Philadelphia found that PrEP awareness was low (4.9%), and high-risk behavior was not associated with higher PrEP awareness.[20] From the provider perspective, a survey of 363 HIV providers assessing attitudes about PrEP found that providers were least likely to consider prescribing PrEP to heterosexuals.[21]

TABLE 2. PrEP Indications and Use for Each Transmission Risk Category by Visit

	Total (n = 4571)	MSM (n = 1879)	IDU (n = 31)	MSM/IDU (n = 16)	High-Risk Heterosexual (n = 16)	Undetermined Risk (n = 2629)	P
CDC indication for PrEP, n (%)	2473 (54.1)	1704 (90.7)	9 (29.0)	15 (93.8)	8 (50.0)	737 (28.4)	<0.001
Current PrEP use, n (%)	915 (20.0)	873 (46.5)	2 (6.5)	6 (37.5)	2 (12.5)	32 (1.2)	<0.001

TABLE 3. Predictors of HIV or STI Among Patients in the Undetermined Risk Category

	Unadjusted Odds Ratio* (95% CI)	P	Adjusted Odds Ratio† (95% CI)	P
Age	1.03 (1.00–1.04)	0.043	1.03 (1.01–1.05)	0.011
Gender identity		0.008		0.012
Male	Ref		Ref	
Female	0.81 (0.47–1.39)		0.83 (0.47–1.45)	
Transgender	1.79 (0.21–15.2)		2.25 (0.38–16.8)	
Other	8.55 (2.29–31.88)		7.04 (1.87–26.5)	
Race/Ethnicity		<0.001		0.011
Non-Hispanic White	Ref		Ref	
Other	2.43 (1.49–3.94)		1.97 (1.17–3.31)	
Place of birth		0.348	N/A	
US-born	Ref			
Foreign-born	1.26 (0.78–2.03)			
Health insurance status		0.001		0.006
Insured	Ref		Ref	
Uninsured	2.09 (1.33–3.29)		1.89 (1.20–2.99)	
Neighborhood deprivation index	1.56 (1.25–1.95)	<0.001	1.32 (1.03–1.68)	0.027
No. sexual partners in prior year		0.071	N/A	
0	3.70 (0.93–14.69)			
1–5	Ref			
6–10	1.34 (0.72–2.49)			
>10	2.22 (1.08–4.56)			
Unknown	0.71 (0.22–2.26)			
Transactional sex in prior year		0.094	N/A	
Yes	2.17 (0.88–5.38)			
No	Ref			
Noninjection drug use in prior year		0.322	N/A	
Yes	1.58 (0.64–3.81)			
No	Ref			
Sex with a transgender partner in prior year		0.850	N/A	
Yes	0.87 (0.21–3.60)			
No	Ref			

*Unadjusted OR determined through a series of simple logistic regressions.

†Adjusted OR determined through a multivariable model. The final model included the following variables: age, gender identity, race/ethnicity, health insurance status, and neighborhood deprivation index.

A major challenge in identifying patients at the highest risk for HIV transmission is reliance on knowing the risk status of one's partners. In our large study sample, there were only 16 visits in which heterosexual adults reported high-risk partners. Despite these challenges, we note that this study was conducted in sexual health clinics where providers have a strong understanding of HIV risk factors and are highly experienced in prescribing PrEP. In other settings where PrEP prescribing is less routine, patients who fall outside of classic HIV transmission risk categories may be even less likely to have full-risk assessments and to receive PrEP.

Public health efforts and funding have primarily focused on groups with easily identifiable risk factors. It is more challenging to target efforts toward patients in heterogeneous groups with poorly defined risk factors, such as those who fall into the undetermined risk category. When evaluating the characteristics associated with HIV or STI in those with undetermined risk, behavioral characteristics were not predictive. On the other hand, several demographic factors were predictive of HIV or STI. We found that age, gender identity, race/ethnicity, health insurance status, and neighborhood socioeconomic status were all associated with HIV or STI among patients in the undetermined risk group. Although our findings of the increased likelihood of HIV or STI among those in racial/ethnic minority groups, those identifying as gender minorities, and those from neighborhoods with lower socioeconomic status are consistent with prior studies,[22–24] our finding of increased risk among older adults is surprising and different from general trends described in the literature.[25,26] It is possible that older adults in this group felt more stigma and were thus less comfortable endorsing behaviors such as IDU or being a male who has sex with men.

The relative importance of demographic and structural factors (age, race/ethnicity, health insurance status, and neighborhood socioeconomic status) in association with STIs and HIV suggests a need to expand our exploration of the syndemic of STIs and HIV beyond behavioral factors. Maulsby and others[27] have outlined the importance of social context and sexual networks in contributing to racial disparities in HIV. Similarly, when exploring drivers of racial disparities in STIs, the impact of social context and sexual networks has been well described.[22] In addition to emphasizing the importance of identifying individuals at high risk of acquiring HIV by factors other than individual behaviors, these trends also suggest a role for interventions that occur above an individual level to more completely address disparities associated with race, ethnicity, gender identity, health care access, and socioeconomic status.

Apart from HIV treatment and prevention, a noteworthy finding was that patients in the undetermined risk group have significant sexual health needs, including the treatment of bacterial STIs. These infections were frequently found among those in the undetermined risk category, and bacterial STIs have arguably the greatest consequences in this cohort, including pelvic inflammatory disease, infertility, and adverse and birth outcomes. However, funding mechanisms often have not prioritized the undetermined risk group.

Limitations of this study include its use of clinical data obtained in one urban area. These trends may not be generalizable to other cities or rural settings. Because of the demands of our high-volume clinics, incomplete patient histories or incomplete documentation may limit the accuracy of data recorded. Reliance on patient report may also limit data quality with potential underdisclosure of risk behaviors due to concerns surrounding

stigma and privacy. Studies have found that for new cases of HIV for which there was initially no identifiable risk, risk factors can often be identified upon further investigation.[28,29] It is likely that some of the participants categorized in the undetermined risk group in this study would be better classified in MSM, IDU, or high-risk heterosexual categories if more complete histories were obtained. However, the extent to which such misclassifications occur may be systematically overestimated.[30] It is also possible that some patients have other sources of risk for HIV transmission (transfusion, hemophilia, perinatal). However, these modes of transmission are currently rare in the United States and may be less frequently encountered in a sexual health clinic than in other settings. Finally, the information routinely collected by our clinic does not perfectly align with that used by the CDC and USPSTF in their recommendations regarding PrEP. We collect information about behaviors and STI diagnoses over a 12-month period rather than the 6-month period suggested by the CDC and USPSTF. This may result in an overestimate for the frequency of PrEP indications. We frequently see patients who are referred for treatment based on outside testing. As a result, we have used diagnosis or treatment of an STI as our indications for PrEP rather than the CDC recommendation of diagnosis or patient-reported STI. This again may overestimate the frequency PrEP indications in our clinic population.

Our study found that most patients seeking care at 2 urban sexual health clinics do not fall into traditional HIV transmission risk categories, although many have strong indications for PrEP use and other sexual health needs. Although PrEP was widely used in the clinics, including among PWID, its use lagged among people in the undetermined risk category. In addition to targeted HIV prevention efforts for MSM, PWID, and heterosexuals in HIV serodiscordant relationships, our study demonstrates the need to include other heterosexually active adults in HIV prevention efforts. Targeting individuals within this heterogeneous group is impeded by difficulty identifying those who are at the highest risk. We found that many demographic and structural factors were more predictive than behavioral risk factors. Additional research is needed to identify characteristics associated with STIs and HIV beyond the classic risk factors and to expand efforts to assess neighborhood- and network-level in addition to individual-level risks and interventions.

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