Identifying Missed Opportunities for Human Immunodeficiency Virus Pre-exposure Prophylaxis During Preventive Care and Reproductive Visits in Adolescents in the Deep South

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Background: Pre-exposure prophylaxis (PrEP) for individuals at significant risk for Human Immunodeficiency Virus acquisition is approved for individuals weighing at least 35 kg by the Food and Drug Administration. This cross-sectional study analyzed indications for PrEP in a clinical setting.

Methods: There were 429 charts reviewed from adolescents between 15 and 21 years old seen for preventive care visits at an adolescent primary care center in the Deep South during a 1-year timeframe. Univariate and multivariable regression analyses were completed to identify factors associated with indications for PrEP.

Results: Forty-four percent of 429 adolescents (between 15 and 21 years) had a PrEP indication; 77% were women and 95% heterosexual. Significant factors associated with an indication for PrEP included living with a nonparent or nonrelative and polysubstance use. No adolescents with an indication for PrEP were prescribed PrEP. A sensitivity analysis comparing indications for PrEP between the 2014 and 2017 The Centers for Disease Control and Prevention Guidelines revealed no significant differences in percent with an indication (44.5% vs. 42.8%) or factors associated with indications.

Conclusions: Pre-exposure prophylaxis as a biomedical tool for adolescents and young adults (AYAs) may remain underutilized. A key factor in improving utilization involves providers being able to recognize AYAs who may have an indication for PrEP with a specific focus on those AYAs who do not live in households with parents or a surrogate family member and those who are polysubstance users.

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Many tools including highly effective anti-retroviral therapy and expanded human immunodeficiency virus (HIV) testing have aided in the declining incidence of HIV in the United States since 2005; yet health disparities have persisted.[1] In 2015, adolescents and young adults (AYA) aged 13 to 24 years accounted for 20% of new HIV diagnoses in the United States with 81% self-identifying as gay or bisexual.[2] Racial inequities were also apparent, as black men accounted for the majority of new HIV diagnoses (38.5%), with even higher rates seen among young, black men who have sex with men.[2] Black women were also disproportionately affected as they were 13 times more likely to become infected with HIV compared with white women (26% vs. 2%).[3] These health disparities are amplified in the Southern United States.[4] Notably, in Alabama, AYA black men have the highest incidence of new HIV diagnoses.[5] Black AYA women accounted for only 14.4% of new diagnoses, and their infection rate was almost 10 times higher than their white counterparts.[5]

Adoption of biomedical prevention tools like HIV pre-exposure prophylaxis (PrEP) in populations at highest risk for HIV has the potential to substantially change these existing inequities.[6] Pre-exposure prophylaxis can greatly reduce the risk of acquiring HIV by up to 92%.[7] Given its high efficacy, the United States Preventive Services Task Force has issued a grade A recommendation for PrEP.[8] Expansion of PrEP services to adolescents has been strengthened with the Food and Drug Administration's (FDA) approval for individuals weighing at least 35 kg.[9] However, there is still decreased uptake of PrEP among AYAs with several studies documenting potential provider concerns, such as possible effects on bone density and bone accrual, ability to adhere to a daily medication, confidentiality, parental concerns, general lack of knowledge about the medication, and prior lack of FDA approval for this age group.[6,9–13] Another unevaluated barrier is lack of awareness among adolescent providers of how many clinic patients may have a PrEP indication based on The Centers for Disease Control and Prevention (CDC) guidelines. One study shows that although pediatricians (75%) are more likely than other primary care providers (38–68%) to ask about sexual activity during routine care, only 20% to 53% of providers who routinely ask about sexual history ask about number of partners, types of sexual practices, or sexually transmitted infections (STIs).[13] In line with national strategic plans to end the HIV epidemic by adoption of prevention tools like PrEP, there is an urgent need to understand missed opportunities for PrEP utilization to inform effective PrEP implementation strategies.[14] We conducted a retrospective, cross-sectional study at an adolescent primary care clinic located in the Southern United States to assess how many adolescents may have an indication for PrEP to inform future systematic PrEP implementation strategies.

MATERIALS AND METHODS

As part of a quality improvement initiative, we reviewed electronic medical records of 15 to 21 year olds presenting for

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preventive care and family planning visits at an adolescent health center in Alabama between January 1, 2016, and December 31, 2016. Exclusion criteria included known HIV-positive status and weight less than 35 kg. Our primary outcome was PrEP indications. Patients with multiple visits (N = 135) during the 1-year study period who met CDC recommendations at any visit were determined to have an indication for PrEP. This allowed for a more accurate assessment of how many adolescents may have an indication for PrEP during the 1-year timeframe, acknowledging that risk behaviors are not static nor is having an indication for PrEP. The PrEP indications were defined based on the 2014 CDC PrEP guidelines because this correlated with PrEP indications during the time of the visits and included the following: being in a serodiscordant relationship; history of a recent bacterial STI, such as gonorrhea, syphilis, or chlamydia; infrequent condom use; multiple sexual partners in high prevalence areas; participation in commercial sex work; injection drug use; or having a partner who uses injection drugs[15] (we rephrased the CDC recommendations pertaining to injection drug use to reflect the low prevalence of injection drug use and low prevalence of having knowledge of partner's HIV status among this population.[16]). Independent variables were self-reported (except where otherwise mentioned) and included: demographics (sex assigned at birth, age, race, and insurance type), visit type (preventive care, annual/initial family planning visits, or periodic family planning visits), reported sexual behaviors (men who have sex with men [MSM], men who have sex with women [MSW], women who have sex with men [WSM], and women who have sex with women [WSW]), depression, anxiety, recent bacterial STI, living arrangement, substance use, contraceptive practices (intrauterine device [IUD]/implant, hormonal injection, pills/patch/ring, condoms only, none), patient HIV status, and partner HIV status. Gender identity was not collected. Living arrangement was a categorical variable including 1 parent, 2 parents, Child Protective Services (CPS) custody, foster care, living with surrogate family (aunt, uncle, brother, grandparent), living with a significant other (boy/girlfriend, fiancé, husband, wife), living at college or with a roommate, or other (inpatient psychiatry facility or other). Depression and anxiety (both dichotomous variables) were categorized based on documented International Classification of Diseases 10 codes. History of bacterial STI was determined by documented positive nucleic acid amplification testing or empiric treatment for an STI within 6 months of the visit. Substance use was further categorized based on the number of substances an AYA used regularly: single substance, polysubstance, or no substance. Given the small numbers of individuals using only one substance, alcohol, marijuana, tobacco, and other substances were grouped into one category to better compare the risk associated with using one substance as compared with polysubstances. Inconsistent condom use was a dichotomous variable defined as less than 100% condom use. Contraception use was determined based on provider medication reconciliation documentation in the chart at the end of the visit. Patient HIV status was determined by laboratory results.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables were summarized using counts and percentages while continuous measures were summarized using medians and interquartile ranges. Findings were dichotomized by PrEP indication status (qualify vs. do not qualify). Unadjusted and multivariable logistic regression models were fit to identify factors associated with having a PrEP indication. Amount of missing data was a consideration when deciding which variables to include in multivariable models. The Firth penalized likelihood method was used for models that resulted in complete or quasicomplete separation due to a small number of events at specific levels of independent variables. Variables for the multivariable model were chosen from literature review and significance and effect size in the univariate models. The variables for sex and sexually active (dichotomous variable) were not used in the multivariable model as they were already accounted for in the analysis of contraception and sexual behavior. Odds ratios (OR) and associated 95% confidence intervals are reported. Analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC). This study was reviewed and classified as exempt by the institution's institutional review board.

RESULTS

Demographics

Five hundred seventy-three visits were reviewed from January 1 through December 31, 2016, representing 429 unique patients (Table 1). Median age was 17 years. Study demographics were consistent with clinic demographics. The majority of patients were women (72%), black (84%), and receiving Medicaid (73%). Fifty percent of patients lived in a single parent household, 23% lived in 2-parent households, 10% lived with a surrogate family, and approximately 5% reported living in either CPS custody or foster care. Sixteen percent of patients were diagnosed with depression and 6% with anxiety. Twenty-one percent of patients reported any substance use with most (11%) using only one substance (most commonly tobacco) followed by polysubstance users (10%). Ninety percent reported being sexually active. Eighty-two percent were WSM or MSW, 1% was MSM, and 4% were WSW. Thirteen percent reported never being sexually active, whereas 22% did not have sexual behavior documented. Among female patients, 27% reported use of pills/patch/ring, 16% an IUD/implant, and 25% did not use any hormonal contraception. The most common method of contraception was the hormonal injection (31%). Forty-three percent had a documented negative HIV test within the past 12 months with the remainder having no documented test.

PrEP Indications

Having met at least one of the criteria set forth by the 2014 CDC guidelines, 44% of patients (191 of 429) had an indication for PrEP. There were no PrEP prescriptions documented among any AYA who had a PrEP indication either for AYAs 18 years or older for whom PrEP had been FDA approved (51%) or AYAs younger than 18 years for whom it would have been an off-label use. Among all AYAs with an indication for PrEP, 76% had inconsistent condom use, 45% had multiple sex partners, and 31% had a bacterial STI within the past 3 months (76% had chlamydia). Figure 1 shows the percentage of patients with an indication for PrEP per indication. No patients reported being in a known serodiscordant relationship, participating in commercial sex work, using injection drugs, or having a partner who used injection drugs. Of those who were queried about partner HIV status, 99% were unaware of their partner's status.

Factors Associated With Having an Indication for PrEP

Univariate models revealed several factors associated with PrEP indications (Table 2). Individuals with older age had 20% higher odds of having an indication for PrEP than younger patients (OR, 1.2). Annual/initial (OR, 2.8) and periodic family planning visits (OR, 4.0) had higher odds of having an indication compared

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TABLE 1. Patient Characteristics

	Total, N = 429, N (%)	Indications for PrEP, n = 191, n (%)	No Indications for PrEP, n = 238, n (%)
Sex			
Male	122 (28.4)	43 (22.5)	79 (33.2)
Female	307 (71.6)	148 (77.5)	159 (66.8)
Type of visit			
Annual/initial family planning	68 (15.8)	39 (20.4)	29 (12.2)
Periodic family planning	105 (24.5)	69 (36.1)	36 (15.1)
Preventive care	256 (59.7)	83 (43.5)	173 (72.7)
Age			
Median age (Q_1-Q_3), y	17 (16, 18)	18 (16, 18)	17 (16, 18)
15	68 (15.9)	22 (11.5)	46 (19.3)
16	87 (20.3)	32 (16.8)	55 (23.1)
17	93 (21.7)	39 (20.4)	54 (22.7)
18	96 (22.4)	54 (28.3)	42 (17.7)
19	42 (9.8)	20 (10.5)	22 (9.2)
20	33 (7.7)	19 (10.0)	14 (5.9)
21	10 (2.3)	5 (2.6)	5 (2.1)
Race			
Black	360 (84.5)	164 (86.8)	196 (82.7)
White	66 (15.5)	25 (13.2)	41 (17.3)
Insurance type			
Blue cross	80 (18.6)	36 (18.8)	44 (18.5)
Medicaid	311 (72.7)	137 (71.7)	174 (73.1)
Other plans	38 (8.9)	18 (9.4)	20 (8.4)
Living arrangement			
2 Parents	74 (22.7)	23 (18.4)	51 (25.4)
1 Parent	162 (49.8)	50 (40.0)	112 (55.6)
Surrogate family	34 (10.4)	14 (11.2)	20 (10.0)
Foster care	16 (4.9)	10 (8.0)	6 (3.0)
CPS	16 (4.9)	10 (8.0)	6 (3.0)
College	11 (3.4)	9 (7.2)	2 (1.0)
Significant other	7 (2.1)	6 (4.8)	1 (0.5)
Other	6 (1.8)	3 (2.4)	3 (1.5)
Depression			
Yes	68 (16.0)	33 (17.3)	35 (14.9)
No	358 (84.0)	158 (82.7)	200 (85.1)
Anxiety			
Yes	25 (5.9)	9 (4.8)	16 (6.8)
No	399 (94.1)	180 (95.2)	219 (93.2)
Substance use			
Yes	87 (21.0)	60 (32.4)	27 (11.7
No	328 (79.0)	125 (67.6)	203 (88.3)
Special substance use categories			
Single substance*	47 (11.3)	30 (16.1)	17 (7.4)
Polysubstance	40 (9.6)	30 (16.1)	10 (4.3)
None	329 (79.1)	126 (67.7)	203 (88.3)
Sexually active			
Yes	385 (89.7)	191 (100.0)	194 (81.5)
No	44 (10.3)	0 (0.0)	44 (18.5)
Sexual behavior			
Male, sex with men	5 (1.5)	3 (1.8)	2 (1.2)
Male, sex with female	75 (22.5)	36 (21.0)	39 (24.1)
Female, sex with men	197 (59.2)	126 (73.7)	71 (43.8)
Female, sex with female	12 (3.6)	6 (3.5)	6 (3.7)
Never been sexually active	44 (13.2)	0 (0.0)	44 (27.2)
Contraception			
IUD/implant	41 (10.6)	28 (14.9)	13 (6.6)
Hormonal injection	83 (21.6)	49 (26.1)	34 (17.3)
Pills/patch/ring	72 (18.7)	33 (17.6)	39 (19.8)
None	67 (17.4)	35 (18.6)	32 (16.2)
Not applicable (male)	122 (31.7)	43 (22.8)	79 (40.1)
History of pregnancy			
Yes	8 (3.1)	7 (5.4)	1 (0.8)
No	125 (49.1)	79 (61.2)	46 (36.5)
Not applicable (male)	122 (47/8)	43 (33.4)	79 (62.7)
Interpersonal violence			
Yes	7 (2.8)	4 (2.9)	3 (26.5)

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TABLE 1. *(Continued)*

	Total, N = 429, N (%)	Indications for PrEP, n = 191, n (%)	No Indications for PrEP, n = 238, n (%)
No	240 (97.2)	133 (97.1)	107 (97.3)
Patient documented HIV test			
Negative	186 (43.4)	123 (64.4)	63 (26.5)
Unknown	243 (56.6)	68 (35.6)	175 (73.5)

* Single substance including tobacco, alcohol, marijuana or other. Other—gasoline, triple c pills, cough syrup, prescription pills/ polysubstance—alcohol, tobacco, marijuana, vaping, IV drugs, pills.

† Nontraditional living situations included: at college, with a roommate, in an inpatient psychiatric facility, living alone, living with aunt, uncle, boyfriend, brother, fiancé, husband, other, or "complicated."

Number missing: race 3; family type 103; Depression 3; Anxiety 5; Substance Use 14; Special Substance Use Categories 13; Sexual behavior 96; Contraception 44; History of pregnancy 174; Interpersonal violence 182.

with preventive care. Patients living with CPS (OR, 3.7), in foster care (OR, 3.7), in college (OR, 10.0), or with a significant other (OR, 13.3) had higher odds of having an indication for PrEP compared with individuals in a 2-parent household. Women who have sex with men compared with MSW (OR, 1.9), substance use compared with no substance use (OR, 3.6), single substance use (OR, 2.8) compared with no substance use, and polysubstance use compared with no substance use (OR, 4.8) were all associated with PrEP indications. Finally, long acting reversible contraception compared with short-acting methods (OR, 0.4) had a higher odds of having an indication for PrEP.

Factors associated with PrEP indications in the multivariable model included: polysubstance use compared with no substance use (OR, 4.3), LARC compared with no contraception use (OR, 0.3) and undocumented contraception use (OR, 0.2), and MSW compared with those with missing information pertaining to sexual preference (OR, 0.2) (Table 2).

Sensitivity Analysis

In 2017, the CDC updated its guidelines regarding PrEP indications and chlamydia infections. Although chlamydia infection should be considered as evidence that a sexually active individual may be at risk for HIV exposure and taken into consideration when discussing PrEP as an HIV prevention tool, chlamydia alone is no longer a PrEP indication for heterosexually active men and women.[17] A sensitivity analysis of PrEP indications and factors associated with PrEP indications based on the 2014 CDC guidelines compared with the recently updated 2017 CDC guidelines showed no major differences in total percent of individuals who may have

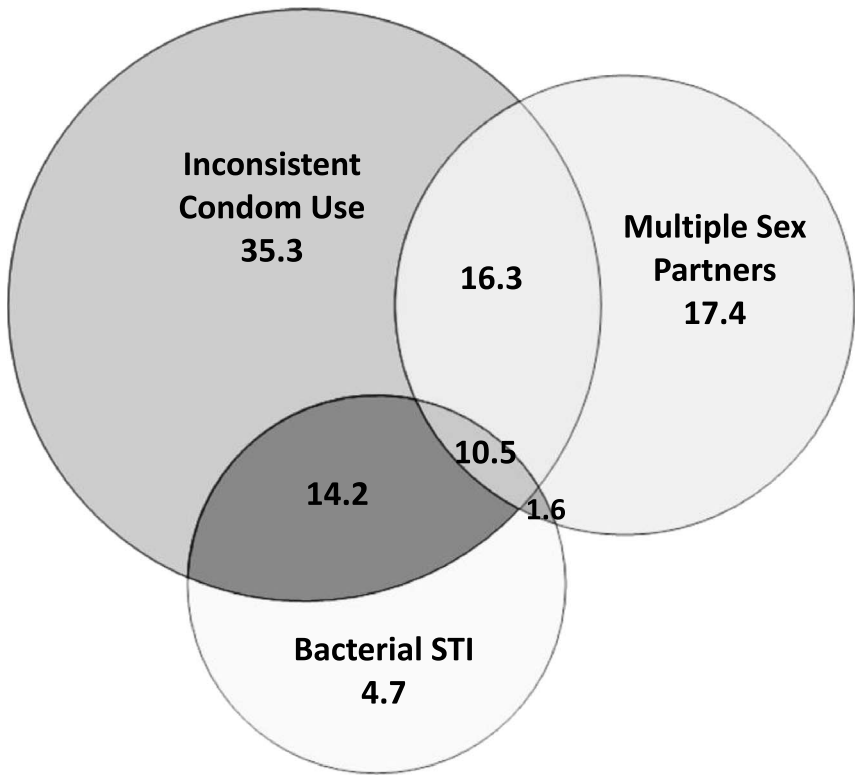

Figure 1. Indications for PrEP (N = 191): This figure represents the percent of patients with PrEP indications (inconsistent condom use, multiple sex partners, bacterial STI, commercial sex work, injection drug use, and HIV positive partner). Each circle represents 1 criterion. Areas of overlap represent the percent of patients who had more than 1 criterion. There were no individuals with history of commercial sex work, injection drug use, and HIV-positive partners, and therefore, there are no circles for these indications.

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TABLE 2. Predictors for PrEP Indications Among Adolescents Presenting for Primary Care Visits at an Urban Adolescent Clinic in the Deep South

	Univariate OR (95% CI)	*Multivariable OR (95% CI)
Age	**1.2 (1.1–1.4)**	1.1 (0.9–1.2)
Visit type		
Annual/initial family planning	**2.8 (1.6–4.8)**	2.0 (0.9–4.6)
Periodic family planning	**4.0 (2.5–6.5)**	2.0 (0.8–4.6)
Preventive care (reference)	–	–
Race		
Black	1.4 (0.8–2.4)	
Unknown	3.3 (0.3–38.1)	
White (reference)	–	
Insurance		
Medicaid	1.0 (0.6–1.6)	
Other plans	1.1 (0.5–2.4)	
Blue cross (reference)	–	
Living arrangement		
1 Parent	1.0 (0.6–1.8)	1.0 (0.4–2.1)
CPS	**3.7 (1.2–11.4)**	2.4 (0.6–9.8)
Foster care	**3.7 (1.2–11.2)**	2.74 (0.7–10.8)
Surrogate family	1.6 (0.7–3.6)	1.5 (0.5–4.3)
College	**10.0 (2.0–49.9)**	3.5 (0.6–19.8)
Significant other	**13.3 (1.5–116.8)**	4.0 (0.5–33.6)
Other	2.2 (0.4–11.8)	3.66 (0.4–30.6)
Not documented	**4.0 (2.1–7.5)**	1.9 (0.8–4.6)
2 Parents (reference)	–	–
Sexual preference		
Men, sex with men	1.5 (0.2–9.5)	1.6 (0.2–12.1)
Women, sex with men	**1.9 (1.1–3.3)**	0.9 (0.2–4.0)
Women, sex with women	1.1 (0.3–3.7)	0.5 (0.1–3.8)
Never sexually active	**0.0 (0.0–0.2)**	**0.0 (<0.001–0.3)**
Not documented	**0.3 (0.2–0.6)**	**0.2 (0.1–0.8)**
Men, sex with women (reference)	–	–
History of pregnancy		
Yes	4.1 (0.5–34.1)	
Not applicable (male)	0.3 (0.2–0.5)	
Not documented	0.3 (0.2–0.5)	
Never (reference)	–	
Depression		
Yes	3.6 (2.2–6.0)	
Not documented	0.2 (0.0–5.6)	
No (reference)	–	
Anxiety		
Yes	0.7 (0.3–1.6)	
Not documented	0.8 (0.1–4.9)	
No (reference)	–	
Substance use		
Yes	**3.6 (2.2–6.0)**	
Not documented	1.2 (0.4–3.6)	
No (reference)	–	
Special substance use categories		
Single substance†	**2.8 (1.5–5.4)**	2.1 (0.9–4.8)
Polysubstance	**4.8 (2.3–10.2)**	**4.3 (1.8–10.3)**
Not documented	1.0 (0.3–3.2)	0.5 (0.1–2.3)
None (reference)	–	–
Interpersonal violence		
Yes	1.1 (0.2–4.9)	
Not documented	0.3 (0.2–0.5)	
No (reference)	–	
Contraception		
Hormonal injection	0.7 (0.3–1.5)	1.0 (0.4–2.6)
Pills/patch/ring	**0.4 (0.2–0.9)**	0.4 (0.2–1.0)
None	0.5 (0.2–1.2)	**0.3 (0.1–0.9)**
Not applicable (male)	0.3 (0.1–0.5)	0.5 (0.1–2.3)
Not documented	**0.0 (0.0–0.1)**	**0.2 (0.1–0.8)**
IUD/implant (reference)	–	–

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TABLE 2. *(Continued)*

	Univariate OR (95% CI)	*Multivariable OR (95% CI)
Patient documented HIV test		
Unknown	**0.2 (0.1–0.3)**	**0.4 (0.3–0.8)**
Negative (reference)	–	–

* Single substance including tobacco, alcohol, marijuana or other. Other—gasoline, triple c pills, cough syrup, prescription pills/polysubstance—alcohol, tobacco, marijuana, vaping, IV drugs, pills.

Significant results ($P < 0.05$) in bold.

† MV model included all variables with results shown.

95% CI, 95% confidence interval.

an indication for PrEP (44% vs. 43%) or factors associated with PrEP indication as seen in Table 3.

DISCUSSION

Recently, there has been an increased number of studies focusing on the feasibility of initiating PrEP among patients in middle and late adolescence (15–17 years and 18–21 years).[6,14] Yet, there have been few studies to date that have looked at the need of PrEP specifically among predominately non-MSM AYA populations in real-world settings in the United States; and the few that exist typically assess young adult MSW and women 18 years and older.[18] Although data are very clear that black and Latino adolescent MSM are at greatest risk for HIV, data also allude to the likelihood of HIV rates increasing among black and Latina heterosexual women, specifically given the fluidity of sexual behavior, especially during adolescence.[5,6,19] This study is, therefore, highly relevant given the current U.S. HIV epidemiology in that it characterizes PrEP indications among an AYA population located in the Southern United States and illustrates the lack of provider recommendations for this highly effective biomedical HIV prevention tool for populations at risk. Although this study is germane to the HIV epidemic due to it being conducted in a clinic located in the Southern United States, this also limits its generalizability to other clinical settings located in different geographic regions. Furthermore, given this study's retrospective nature, it cannot infer causal links in the results that have been found.

Overall, we found that 44% of patients presenting for routine care may have an indication for PrEP based on CDC recommendations. Factors predictive of PrEP indication in multivariable models included heterosexual women, polysubstance use, and LARC for contraception. The data suggest that while all sexually

TABLE 3. Sensitivity Analysis

		PrEP Indication Includes Chlamydia	PrEP Indication Excludes Chlamydia
Eligible for PrEP	n (%)	191 (44.5%)	184 (42.8%)
		Multivariable OR (95% CI)	Multivariable OR (95% CI)
Age		1.1 (0.9–1.2)	1.1 (0.9–1.2)
Visit type	Annual/initial family planning	2.0 (0.9–4.6)	**2.1 (1.0–4.9)**
	Periodic family planning	2.0 (0.8–4.6)	**2.3 (1.0–5.4)**
	Preventive care (reference)	–	
Living Arrangement	1 Parent	1.0 (0.4–2.1)	1.2 (0.5–2.5)
	CPS	2.4 (0.6–9.8)	3.1 (0.7–12.8)
	Foster care	2.74 (0.7–10.8)	3.6 (0.9–14.2)
	Surrogate family	1.5 (0.5–4.3)	1.9 (0.6–5.6)
	College	3.5 (0.6–19.8)	4.2 (0.7–23.6)
	Significant other	4.0 (0.5–33.6)	1.6 (0.6–38.4)
	Other	3.66 (0.4–30.6)	4.4 (0.5–36.2)
	Not documented	1.9 (0.8–4.6)	1.8 (0.8–4.3)
	2 Parents (reference)	–	
Sexual preference	Men, sex with men	1.6 (0.2–12.1)	1.4 (0.2–10.7)
	Women, sex with men	0.9 (0.2–4.0)	0.9 (0.2–3.6)
	Women, sex with women	0.5 (0.1–3.8)	0.6 (0.1–4.1)
	Not documented	**0.2 (0.1–0.8)**	**0.2 (0.1–0.8)**
	Men, sex with women (reference)	–	
	No (reference)		
Special substance use categories	Single substance[a]	2.1 (0.9–4.8)	**2.2 (1.0–5.0)**
	Polysubstance	**4.3 (1.8–10.3)**	**3.5 (1.5–7.9)**
	Not documented	0.5 (0.1–2.3)	0.6 (0.1–2.8)
	None (reference)	–	
Contraception	Hormonal injection	1.0 (0.4–2.6)	1.3 (0.5–3.3)
	Pills/patch/ring	0.4 (0.2–1.0)	0.6 (0.2–1.4)
	None	**0.3 (0.1–0.9)**	0.4 (0.2–1.1)
	Not applicable (male)	0.5 (0.1–2.3)	0.7 (0.2–3.1)
	Not documented	**0.2 (0.1–0.8)**	0.3 (0.1–1.1)
	IUD/implant (reference)	–	
Patient HIV status	Unknown	**0.4 (0.3–0.8)**	**0.5 (0.3–0.9)**
	Negative (reference)	–	

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active adolescents should be assessed, there are 3 main missed opportunities to screen for PrEP indications: 1) individuals presenting for contraceptive services, 2) individuals identified as having a substance use disorder, and 3) individuals not living with parents or related surrogate guardians.

Based on the demographic data, the majority of patients in this study were 16- to 18-year-old women, which is not surprising given women are more likely to access health care than their male counterparts.[20] This is likely primarily related to the utilization of contraceptive care by female AYAs. Previous studies have found that individuals who are using hormonal contraception, specifically LARC may be more likely to engage in higher risk behaviors such as condomless sex due to an increased feeling of security knowing that they are not at risk for pregnancy.[21–23] Similar to those studies, this study also found individuals using LARC had increased odds of having an indication for PrEP. These findings coupled with findings from previous studies suggest reproductive health visits may be a prime opportunity to engage female adolescents; optimally, in conjunction with discussions surrounding safe sexual practices. Future research may focus on how to effectively integrate PrEP education for female AYAs into larger discussions around reproductive health. Prime settings for such interventions would include pediatric, family medicine as well as gynecology visits.

A nonclinical setting that should also be considered for PrEP implementation among adolescents is substance abuse treatment centers, given the potential link between polysubstance abuse and PrEP indication. Prior research has found that among AYA and young MSM of color who are high or under the influence of alcohol, higher rates of risky sexual behavior may occur.[24–26] Specifically, these studies point to the influence substances have on overall judgment regarding where and when AYAs will participate in sexual encounters.[25] Our findings also support the need for bundled, comprehensive services for AYAs accessing PrEP care. For those individuals who report daily use and or behavior indicative of a substance use disorder, combining substance use screening and treatment with PrEP services would be ideal and has the potential to improve adolescents' uptake of PrEP.

Living with someone other than a parent or surrogate family member was also predictive of PrEP indications. Studies illustrate adolescents living in foster care have been shown to have higher rates of unprotected sex causing them to be at greater risk for HIV infection; unfortunately, more data are needed to understand the relationship between nontraditional households and HIV risk.[27,28] Unstable housing may also result in frequent interruptions in general routine care screenings, contraceptive care, and STI/HIV prevention counseling. This may not only affect an AYA's ability to comply with the frequent visit requirements for PrEP, but could potentially exacerbate barriers to PrEP care, like parental consent. Creative strategies to implement PrEP and monitor adherence among patients with less adult supervision and among those with more transient housing are needed within this at-risk population.

Findings from this study draw attention to 2 important nuances when applying the guidelines to AYA populations. First, the most recent guidelines no longer recommend using chlamydia as a stand-alone indication for PrEP for heterosexual individuals due to its high prevalence and lifetime risks. A sensitivity analysis revealed that the percent of individuals who had an indication for PrEP and the factors predictive of having a PrEP indication were similar regardless of whether chlamydia infection were included as a PrEP indicator. This suggests that data from this study are in alignment with the CDC's recommendation to use bacterial STIs, such as chlamydia, as evidence of possible HIV exposure and that among AYAs, the specific bacterial STI may not be as important as the behaviors that have led to the STI. Second, 99% of AYAs in this high-prevalence area did not know their partner's HIV status. It is unclear if this reflects poor AYA self-efficacy related to safe sex negotiation. This highlights not only the need to provide further education about the importance of HIV testing among AYAs but also the importance of empowering AYAs to ask about their partners' HIV statuses before engaging in sexual activities. Both of these findings suggest there may be nuances in how to apply the CDC guidelines to high-risk AYA populations and that more research is needed.

Interestingly, we found that among our patient population very few AYAs disclosed MSM behavior. Fluidity of sexual behavior during adolescence and the fear and stigma related to disclosing sexual identity are important factors that must be considered in this age group and region of the country.[19] In fact, Bosse and Chiodo suggest that not only is sexual identity nonlinear and capable of shifting over time, but it is also influenced by race, class, systems of power, and geography.[29] Providers who work with AYAs in southern communities where certain sexual identities and/or practices may be more stigmatized may need to find creative approaches to discuss sex, sexual health, and HIV prevention with adolescents. Ideally, education regarding HIV prevention tools would happen prior to sexual debut; outreach workers as well as researchers may need to adjust targeted messaging when taking these findings into consideration. Educational materials and awareness campaigns may need to better represent the fluidity many AYAs experience with sexual behaviors and identities.

Perhaps, the most remarkable finding from this study is that among AYAs 18 years and older who had an indication for PrEP at the time of study analysis, there was no documentation regarding discussion or recommendations for PrEP services. This is alarming considering this clinic is located in an epicenter for HIV and is serviced by trained adolescent medicine providers. This may have been due to lack of provider recognition of patients at substantial risk for HIV, lack of awareness of PrEP or comfort regarding PrEP management.[13] Furthermore, providers, who were potentially aware of PrEP, may have been concerned about long-term management of adolescents on PrEP, side effects, or reimbursement from third party insurers.[11,12,29] Studies even suggest providers may only consider PrEP for certain groups such as adult MSM.[11,12] In addition, there likely are systematic factors in health care systems that make identification of those who have a PrEP indication and in need of subsequent recommendation more difficult. For instance, at the time this review was conducted, there were no standardized reproductive health templates that screened for sexual risk factors to aid in identifying patients with indications for PrEP. As a result of this baseline quality improvement cycle, the clinic has now implemented preventive health visit templates that include standardized sexual history questions allowing providers to more adequately screen for PrEP indications. It is also important to recognize that half of the AYAs did not meet FDA approved prescribing guidelines for PrEP because of age. However, with the FDA expanded approval for adolescents and adults weighing at least 35 kg as of May 2018, these youth now meet standard prescribing guidelines. The AYA providers, particularly those in high HIV-prevalence areas, need more awareness and training on PrEP to identify younger AYAs who might benefit from its use.

These findings highlight the need for more implementation of systematic approaches that enhance identifying and prescribing PrEP in AYA populations. Furthermore, for those individuals who live in foster care or are in state custody, more research is needed on how to incorporate PrEP discussions into visits and explore barriers to accessing PrEP where parental consent may be required but is not readily accessible. Also sexual fluidity needs to be taken

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into consideration when targeting at-risk groups for awareness campaigns regarding HIV prevention, including PrEP. Given that female AYAs are more likely to access health care than their male counterparts, designing creative approaches to reach this demographic may help eliminate the disparity of HIV infection among black and Latina AYAs and their racial and ethnic counterparts. The findings of this study highlight the urgent need for more implementation research to develop strategies that aid AYA providers in identifying patients with an indication for PrEP and prescribing it in clinical settings, particularly for heterosexual AYAs and women.

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