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Point-of-Care Testing to Guide Treatment and Estimate Risk Factors for Sexually Transmitted Infections in Adolescents and Young People With Human Immunodeficiency Virus in Eswatini

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Background. The World Health Organization (WHO) estimates 127 million new cases of *Chlamydia trachomatis* (CT), 87 million new cases of *Neisseria gonorrhea* (NG), and 156 million new cases of *Trichomonas vaginalis* (TV) each year, which corresponds to 355 (219–606), 303 (216–468), and 243 (97.6–425) thousand disability-adjusted life-years. In low-resource settings, however, sexually transmitted infections (STIs) are treated syndromically and many individuals with asymptomatic infection may be missed, especially adolescents and young adults with human immunodeficiency virus (HIV).

Methods. We enrolled patients aged 15–24 with HIV (N = 300) attending a family-centered HIV clinic in Mbabane, Eswatini. Participants completed a sexual history questionnaire and provided urine as well as oropharyngeal and/or vaginal swabs, if sexually active, for testing with Xpert CT/NG and TV tests. Analysis included bivariate and multivariate odds ratios and test sensitivity and specificity.

Results. Sexually transmitted infection rates were highest (25.0%; 95% confidence interval [CI], 15.2–37.3) in females ages 20–24 who were ever sexually active. In patients with confirmed STIs, NG (15 of 32, 47%) was more common than CT (9 of 32, 28%) and TV (8 of 32, 25%). Syndromic screening alone had a sensitivity of 32.0% (95% CI, 14.9–53.3) and specificity of 86.0% (95% CI, 79.0–91.4) but varied by gender. The presence of an STI was associated with reporting new sexual partner(s) (OR = 2.6; 95% CI, 1.1–6.4), sometimes to never using condoms (OR = 4.2; 95% CI, 1.7–10.2), most recent sexual partner >25 years old (OR = 3.2; 95% CI, 1.3–7.9), and HIV diagnosis at age ≥15 years (OR = 3.4; 95% CI, 1.4–8.2).

Conclusions. Syndromic screening alone performed poorly. Routine diagnostic testing significantly increases STI detection and should be considered in high-risk populations, such as adolescents and young adults with HIV.

Keywords. adolescents; Eswatini; HIV/AIDS; sub-Saharan Africa; STIs.

Sexually transmitted infections (STIs) associated with cervicitis and urethritis such as *Chlamydia trachomatis* (CT), *Neisseria gonorrhea* (NG), and *Trichomonas vaginalis* (TV) are associated with pelvic inflammatory disease (PID), infertility, adverse birth outcomes for the mother and child, and facilitate the horizontal and vertical transmission of human immunodeficiency virus

(HIV) [1–7]. The scope of the problem is large with the World Health Organization (WHO) estimating 127 million new cases of CT, 87 million new cases of NG, and 156 million new cases of TV each year [8]. This corresponds to 355 (219–606), 303 (216–468), and 243 (97.6–425) thousand disability-adjusted life-years (DALYs) due to CT, NG, and TV, respectively [9]. Although surveillance data are limited, persons in low- and middle-income countries (LMICs) are disproportionately impacted by STIs, as are adolescents, women, and people with HIV [8].

The WHO currently recommends syndromic screening and management for STIs; however, this approach has poor sensitivity for CT, NG, and TV, low predictive accuracy and low agreement with laboratory diagnosis [10–13]. Furthermore, the presence of symptoms related to an STI does not correlate with adverse sequelae such as pelvic inflammation and infertility, HIV acquisition, and secondary transmission [14]. Nucleic acid amplification tests (NAATs) are highly sensitive (CT 97.2,

NG 99.9, TV 98.6) and specific (CT 98.0, NG 99.9, TV 99.8) but have not been considered accessible or cost effective in most LMICs [15, 16]. Self-contained NAAT testing through the GeneXpert platform performs comparably to other NAAT testing platforms and is a platform that is available throughout much of sub-Saharan Africa, increasing the feasibility of this method for diagnostic testing in these settings. This is especially true for patients already enrolled in comprehensive HIV care and treatment.

There are data clearly linking CT, NG, and TV with acquisition and transmission of HIV when the HIV viral load is detectable [1, 4]. Existing data suggests that adolescents living with HIV and with detectable viral loads (DVLs) have a higher prevalence of STIs [17]. The effect of STIs in increasing the risk of maternal-to-child transmission of HIV has also recently been elucidated [2, 18, 19]. There is both sentinel site surveillance data demonstrating high rates of CT, NG, and TV among the general population in LMICs with generalized HIV epidemics, such as South Africa [10] and Eswatini [20], as well as baseline data on prevalence in populations at risk for HIV acquisition from HIV prevention studies [21]. Adolescents and young people, aged 15 to 24 years, are a priority group for the detection of STIs as are people living with HIV, but there is very little data defining STI prevalence and risk factors in adolescents and young adults living with HIV who are engaged in care and treatment in LMICs. This is a population in whom targeted testing and treatment for STIs, regardless of symptoms, may be feasible and pathways for laboratory testing and interpretation are generally established [22].

Existing data suggest that the current paradigm for syndromic STI screening performs poorly and that there is a global epidemic of undiagnosed STIs resulting in PID, an increased risk of HIV transmission, and infertility. In this study, we seek to determine the prevalence of and risk factors for CT, NG, and TV among adolescents and young adults living with HIV enrolled at a family-centered HIV clinic in Mbabane, Eswatini. The aim of the study was to determine the need for and guide development of NAAT-based STI screening protocols for the highest risk adolescents and young people with HIV. In addition, we evaluate the performance of adjunctive diagnostics such as urinalysis, the concordance of urine versus vaginal self-swabs as testing specimens, and rates of oropharyngeal carriage in our population. We also provide evidence on the feasibility of disease-specific treatment and partner management.

METHODS

Study Population and Setting
This cross-sectional study was done at Baylor Clinic in Mbabane, Eswatini from October 2017 to June 2018. Baylor Clinic is a well established HIV and Tuberculosis Center of Excellence providing care and treatment to children and adolescents with HIV as well as their families at no charge in partnership with the Eswatini Ministry of Health. The study population of 300 adolescents and young adults captured 40% (300 of 767) of the total population of adolescents and young adults enrolled in care. As part of comprehensive HIV care, all adolescents and young adults at the clinic are actively screened for risk of STIs and for STI symptoms. For male urethritis or vaginal discharge syndromes, patients are treated with ceftriaxone, azithromycin, and metronidazole per national guidelines. Additional doses of azithromycin, and extended metronidazole in women, are recommended for scrotal swelling and lower abdominal pain syndromes, respectively. Erythromycin or doxycycline is substituted when azithromycin is unavailable. Integrated cervical cancer screening is offered to sexually active women via a screen and treat approach, and sexual and reproductive health counseling and screening is routinely offered to all patients beginning in adolescence. Condoms (male and female) as well as hormonal contraceptive options are available. Human immunodeficiency virus-positive patients, 15 to 24 years of age, were enrolled consecutively (4 per day). Participants completed a paper-based sexual health history survey (SHHS), discussed SHHS results and STI symptoms with a healthcare worker, and provided urine and/or swab specimens. If positive for an STI, participants were called to come back to the clinic for treatment. Symptomatic patients received syndromic management as per National Guidelines, inclusive of treatment for CT, NG, or TV if identified by testing. Asymptomatic patients received treatment specific to the pathogen identified by Xpert testing. All patients with an STI syndrome or a positive STI test were advised to inform sexual partners to go to the nearest clinic for treatment, following national STI treatment guidelines. Three months to 12 months posttreatment, patients were tested again to confirm the successful treatment without reinfection or treatment failure.

All participants provided written informed consent. Adolescents in Eswatini who are older than 12 years of age are able to provide consent independently for participation in studies related to sexual and reproductive health. The study was approved by the Baylor Children's Foundation Internal Review Board, Eswatini National Health Research Review Board and the Baylor College of Medicine Internal Review Board.

Data Collection
The SHHS was created using EpiInfo (Centers for Disease Control and Prevention, Atlanta, GA) software. All of the information from the SHHS was then entered into the EpiInfo database.

Laboratory Testing
All urinalysis and Xpert testing were conducted by existing staff from Baylor Clinic. Urinalysis was done using Mission

Urinalysis Reagent Strips (ACON Laboratories, San Diego, CA). All samples were tested with the Xpert CT/NG test as per the manufacturer's guidelines using the GeneXpert instrument (Cepheid, Sunnyvale, CA). Indeterminate results were retested using the same protocol. Approximately 2 mL of the urine from the transport tube was stored in a −80°C freezer for future Xpert TV testing. When Xpert TV testing was being done, samples were thawed, vortexed, and tested using the manufacturer's protocol.

Statistical Analysis

Sample size calculations were performed to detect a difference in sensitivity between NAAT testing and syndromic measurement assuming 95% and 20%, respectively, to achieve 80% power and 5% significance level. The study was also powered to estimate the prevalence of CT, NG, or TV in our population with a half-width of 5% of a 95% confidence interval (CI) [20]. Therefore, we enrolled 300 participants. Descriptive statistics are shown including frequencies and proportions for categorical variables and medians and interquartile ranges (IQRs) for continuous variables. Logistic regression models were used to estimate the unadjusted and adjusted association between STIs covariates reflecting demographic, behavioral, and clinical factors. Variables were included in the model if the *P* value was ≤ .05 in bivariate analysis. Results are presented as odds ratios and corresponding 95% CIs. Diagnostic performance of Xpert and syndromic measurement was described using sensitivity, specificity, negative predictive value, and positive predictive value, to compare between the current standard of care and the newly introduced reference standard. Statistical analysis was performed using STATA (StataCorp, College Station, TX).

RESULTS

A total of 300 HIV-positive adolescents and young adults were enrolled at Baylor Clinic in Mbabane, representing 40% of the clinic population in this age range, 299 of whom provided urine for testing (Figure 1). There were 141 (47.2%) males and 158 (52.8%) females with a median age of 19.6 years (IQR, 15.0–24.2) (Table 1). The majority of the cohort was vertically infected: 229 (76.6%) and 253 (84.6%) were diagnosed with HIV before the age of 15. Most participants, 180 (63.6%), reported being single. Of the 299 participants, 160 (53.5%) reported ever being sexually active. The median age of sexual debut was 18 years (IQR, 15–21) and did not differ between males and females. Most ever sexually active participants (ESAP) (61 of 160) reported having only 1 sexual partner in their lifetime (IQR, 1–5) with a range of 1–25 partners. Of the 160 ESAP, 101 (63.1%) said they had been sexually active in the past 6 months. The majority of ESAP reported "always" using condoms (57.6%). The median age at HIV diagnosis was 10 years of age (IQR, 4–16), with a range of 0–24 years. Most patients had undetectable viral loads, 165 (55.9%) within the prior year, and 80% had viral loads <1000 copies/mL. Two hundred thirty-eight (79.3%) participants had CD4 counts equal to or above 350 cells/mL.

There was a total of 26 (8.7%) participants that were positive for an STI, and the prevalence was highest among 20- to 24-year-old females ESAP at 25.0% (15 of 60) (Table 2). Only 1
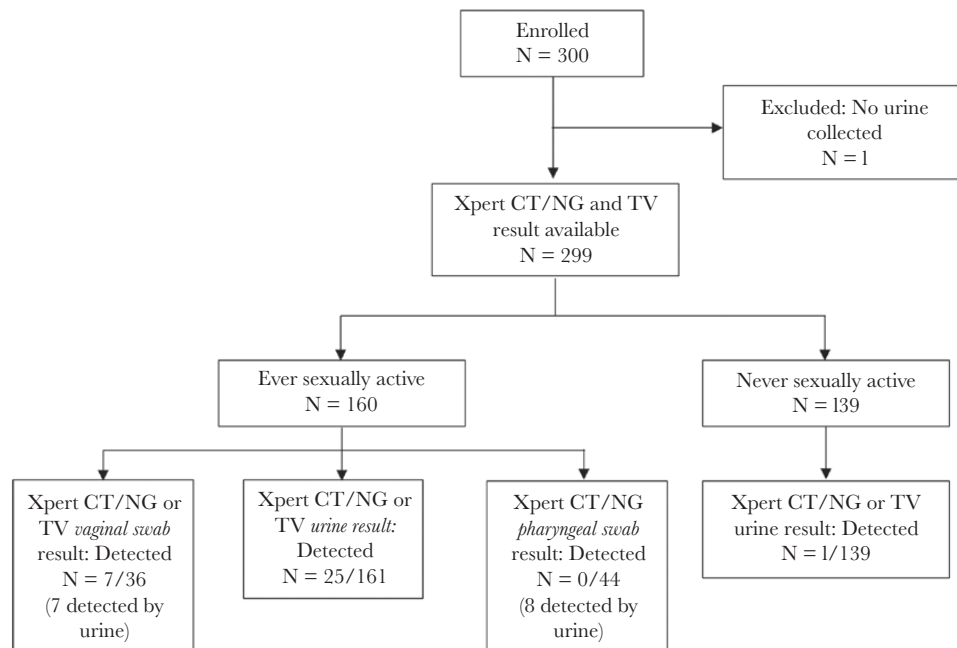

Figure 1. Participant flow chart. This chart indicates completion of urine specimen collection and stratifies patients by self-report of prior sexual activity. Performance of Xpert *Chlamydia trachomatis* (CT)/*Neisseria gonorrhea* (NG) and *Trichomonas vaginalis* (TV) on different specimen types are reported compared with urine.

Table 1. Demographic, Behavioral, and Clinical Cohort Characteristics

Demographics	n (%)
Age, N = 299	
Median (IQR)	19.6 (15.0–24.2)
15–19	173 (57.9)
20–24	126 (42.1)
Sex, N = 299	
Male	141 (47.2)
Female	158 (52.8)
Marital Status, N = 283	
Single	180 (63.6)
Relationship	99 (35.0)
Married	4 (1.4)
Current Highest Level of Education, N = 292	
No education	1 (0.3)
Primary	66 (22.6)
Secondary	35 (12.0)
High school	170 (56.9)
Tertiary	20 (6.7)
Attends Teen Club, N = 299	
Yes	120 (40.1)
Ever Sexually Active, N = 299	
Yes	160 (53.5)
Age at sexual debut: median age (IQR)	18 (15–21)
Sexually Active in the Past 6 Months, N = 160	
Yes	101 (63.1)
Number of Sexual Partners in Lifetime, N = 160	
1–2	101 (63.1)
3–4	30 (18.8)
>4	28 (17.5)
Number of Sexual Partners in Last 6 Months, N = 160	
0	35 (21.8)
1	96 (60.0)
2	16 (10.0)
3	9 (5.6)
4–7	4 (2.5)
Condom Use, N = 158	
Always	91 (57.6)
Most of the time	17 (10.8)
Sometimes/rarely	40 (25.3)
Never	10 (6.3)
Age of Most Recent Sexual Partner, N = 158	
15–24	121 (76.6)
25–34	33 (20.9)
≥35	4 (2.5)
Currently using contraceptives, N = 154	101 (65.6)
Age at HIV Diagnosis, N = 298	
Median (IQR)	10 (4–16)
0–4	14 (4.7)
5–9	114 (38.1)
10–14	124 (41.5)
15–19	35 (12.0)
20–25	11 (3.7)
Mode of HIV Acquisition, N = 299	
Vertical	229 (76.6)
Horizontal	16 (5.4)
Unknown	54 (18.1)
ARV Adherence at Current Visit, N = 271	
0–80	13 (4.8)

Demographics	n (%)
81–105	246 (90.8)
≥106	12 (4.4)
Current Viral Load, N = 294	
0	165 (56.1)
20–1000	72 (24.5)
≥1001	57 (19.4)
Current CD4 Count, N = 299	
0–200	21 (7.0)
201–350	40 (13.4)
≥351	238 (79.6)
WHO T-Stage, N = 295	
I	286 (95.3)
II–IV	4 (1.3)
III	3 (1.0)
IV	2 (0.7)

Abbreviations: ARV, antiretroviral; HIV, human immunodeficiency virus; IQR, interquartile range; WHO, World Health Organization.

STI was detected among 139 patients reporting no prior sexual activity; therefore, the reported results focus primarily on the 160 ESAP. A total of 38 vaginal swabs and 46 (38 female) oropharyngeal swabs were provided and tested for CT and NG only. The vaginal swabs were 100% (38 of 38) concordant with the urine results for CT and NG. All oropharyngeal swabs came back negative for CT and/or NG, regardless of urine and/or vaginal swab results, which included 8 with positive urine/vaginal results (Figure 1). Of the ESAP, 15.6% (25 of 160) were positive for an STI versus 0.7% (1 of 139) reporting no prior sexual activity. *Neisseria gonorrhea* was the most common pathogen identified representing 15 of 32 (47%) of the pathogens detected and was followed by CT (9 of 32; 28%) and TV (8 of 32; 25%). The majority of participants with an identified STI were positive for a single pathogen (21 of 26; 80%).

With Xpert CT/NG and Xpert TV as the reference standard, urine leukocyte esterase (LE) in ESAP had a sensitivity of 84.0% (male, 100.0%; female, 80.0%) and specificity of 65.9% (male, 83.6%; female, 53.8%) (Table 3). Syndromic screening alone, inferred from the sexual health survey and routine clinical interview, in ESAP had a sensitivity of 32.0% (male, 80.0%; female, 20.0%) and specificity of 86.0% (male, 94.6%; female, 80.3%) (Table 3). There were large differences in test performance attributable to sex, with LE testing and syndromic screening offering higher sensitivity, specificity, and negative predictive values in males (Table 3).

The risk factors associated with STI infection in ESAP were a new sexual partner in the last 6 months (OR = 2.6; 95% CI, 1.1–6.4), sometimes to never using condoms (OR = 4.2; 95% CI, 1.7–10.2), most recent sexual partner 25 years or older (OR = 3.4; 95% CI, 1.4–8.2), and HIV diagnosis at age 15 years or older (OR = 3.4; 95% CI, 1.4–8.2) (Table 4). In the logistic regression model that included variables with a *P* value of ≤ 0.05

Table 2. Prevalence of STIs by Age Category and Gender Among Participants Reporting Ever Being Sexually Active

Age	Sex	CT	NG	TV	Any STI
		Sexually Active Cohort (N = 160)			
(Years)		N, % (95% CI)	N, % (95% CI)	N, % (95% CI)	N, % (95% CI)
15–24	All	8, 5.0 (2.5–9.7)	15, 9.3 (5.7–15.0)	8, 5.0 (2.5–9.7)	25, 15.5 (10.7–22.1)
	N = 160				
15–24	Male	1, 1.7 (0.2–11.5)	4, 6.7 (2.5–16.9)	0, 0.0 (0–0)	5, 8.3 (3.4–18.9)
	N = 60				
	Female	7, 7.0 (3.3–14.0)	11, 11.0 (6.1–18.8)	8, 8.0 (4.0–15.2)	20, 20.0 (13.0–28.9)
	N = 100				
15–19	Male	0, 0.0 (0–0)	0, 0.0 (0–0)	0, 0.0 (0–0)	0, 0.0 (0–0)
	N = 20				
	Female	1, 2.5 (0.3–17.0)	3, 7.5 (0.2–21.7)	1, 2.5 (0.3–17.0)	5, 12.5 (5.1–27.6)
	N = 40				
20–24	Male	1, 2.5 (0.3–17.0)	4, 10.0 (3.6–24.6)	0, 0.0 (0–0)	5, 12.5 (5.1–27.6)
	N = 40				
	Female	6, 10.0 (4.4–20.6)	8, 13.3 (6.6–24.5)	7, 11.7 (5.5–22.6)	15, 25.0 (15.2–37.3)
	N = 60				

Abbreviations: CI, confidence interval; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoea*; STIs, sexually transmitted infections; TV, *Trichomonas vaginalis*.

on bivariate testing, only inconsistent condom use remained a risk factor for STI detection (OR = 3.4; 95% CI, 1.3–8.3; *P* = .011).

Of the 26 participants that were positive for an STI, 26 have been treated (100%) following WHO STI treatment guidelines or were treated based on the STI test result in the absence of symptoms. All patients treated for NG in this cohort received ceftriaxone, in accordance with current national guidelines, and all who were symptomatic at the time of diagnosis experienced symptomatic improvement. Of the 26 who have been treated, 21 retested and 17 retested negative (81.0.0%) at 3–12 months posttreatment, 4 retested positive (16%) at 3–12 months posttreatment, 5 are due for retesting (20.0%).

DISCUSSION

The high STI prevalence in this study highlights adolescents and young adults with HIV as a priority population for STI prevention, diagnosis, and treatment. Furthermore, these

Table 3. Performance of Screening Tests (Presence of Leukocyte Esterase in Urine or Active Screening for Genitourinary Symptoms) as Compared to Any Positive by Xpert CT/NG and TV Testing

Screening Test	n Positive, % (95% CI)		
Leukocyte Esterase: Total Population, N = 299	Total	Male	Female
Sensitivity	21/26, 80.8 (60.6–93.4)	5/6, 83.3 (35.9–99.6)	16/20, 80.0 (56.3–94.3)
Specificity	200/273, 73.3 (67.6–78.4)	112/135, 83.0 (75.5–88.9)	88/138, 63.8 (55.2–71.8)
PPV	21/94, 22.3 (14.4–32.1)	5/28, 17.9 (6.1–36.9)	16/66, 24.2 (14.5–36.4)
NPV	200/205, 97.6 (94.4–99.2)	112/113, 99.1 (95.2–100.0)	88/92, 95.7 (89.2–98.8)
Leukocyte Esterase: Ever Sexually Active, N = 160			
Sensitivity	21/25, 84.0 (63.9–95.5)	5/5, 100.0 (47.8–100)	16/20, 80.0 (56.3–94.3)
Specificity	89/135, 65.9 (57.3–73.9)	46/55, 83.6 (71.2–92.2)	43/80, 53.8 (42.2–65.0)
PPV	21/67, 31.3 (20.6–43.8)	5/14, 35.7 (12.8–64.9)	16/53, 30.2 (18.3–44.3)
NPV	89/93, 95.7 (89.4–98.8)	46/46, 100.0 (92.3–100)	43/47, 91.5 (79.6–97.6)
Symptom Screening: Total Population, N = 299			
Sensitivity	8/26, 30.8 (14.3–51.8)	4/6, 66.7 (22.3–95.7)	4/20, 20.0 (5.7–43.7)
Specificity	255/274, 93.1 (89.4–95.8)	132/135, 97.8 (93.6–99.5)	123/139, 88.5 (82.0–93.3)
PPV	8/27, 29.6 (13.8–50.2)	4/7, 57.1 (18.4–90.1)	4/20, 20.0 (5.7–43.7)
NPV	255/273, 93.4 (89.8–96.0)	132/134, 98.5 (94.7–99.8)	123/189, 88.5 (82.0–93.3)
Symptom Screening: Ever Sexually Active N = 160			
Sensitivity	8/25, 32.0 (14.9–53.3)	4/5, 80.0 (28.4–99.5)	4/20, 20.0 (5.7–43.7)
Specificity	117/136, 86.0 (79.0–91.4)	52/55, 94.5 (84.9–98.9)	65/81, 80.2 (69.9–88.3)
PPV	8/27, 29.6 (13.8–50.2)	4/7, 57.1 (18.4–90.1)	4/20, 20.0 (5.7–43.7)
NPV	117/134, 87.3 (80.5–92.4)	52/53, 98.1 (89.9–100.0)	65/81, 80.2 (69.9–88.3)

Abbreviations: CI, confidence interval; CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoea*; NPV, negative predictive value; PPV, positive predictive value; TV, *Trichomonas vaginalis*.

Table 4. Behavioral, Clinical, and Demographic Risk Factors Associated With STI Detection

Risk Factors	Unadjusted Bivariate			Adjusted Multivariate
	STI Pos. n (%)	STI Neg. n (%)	OR (95% CI; P Value)	OR (95% CI; P Value)
Age Range, N = 160				
15–19	5 (20.0)	55 (40.7)	Reference	
20–24	20 (80.0)	80 (59.3)	**2.8 (1.0–7.8; 0.056)**	1.9 (0.6–6.2; 0.294)
Sex, N = 160				
Male	5 (20.0)	55 (40.7)	Reference	
Female	20 (80.0)	80 (59.3)	**2.8 (1.0–7.8; 0.056)**	2.6 (0.7–9.4; 0.156)
Relationship Status, N = 160				
Single	20 (80.0)	106 (78.5)	0.9 (0.3–2.6; 0.868)	
In a relationship/married	5 (20.0)	29 (21.5)	Reference	
Currently in School, N = 159				
Yes	11 (44.0)	81 (60.5)	Reference	
No	14 (56.0)	53 (39.6)	1.9 (0.8–4.6; 0.130)	
Attends Teen Club, N = 160				
Yes	6 (24.0)	56 (41.5)	0.5 (0.2–1.2; 0.106)	
No	19 (76.0)	79 (58.5)	Reference	
Age of Sexual Debut, N = 156				
6–18	16 (66.7)	89 (67.4)	1.0 (0.4–2.4; 0.942)	
19–23	8 (33.3)	43 (32.6)	Reference	
Number of Sexual Partners in Lifetime, N = 159				
≤2	12 (48.0)	89 (66.4)	Reference	
≥3	13 (52.0)	45 (33.6)	2.1 (0.9–5.1; 0.083)	
Sexually Active in the Past 6 Months, N = 160				
Yes	20 (80.0)	81 (60.0)	2.7 (0.9–7.5; 0.064)	
No	5 (20.0)	54 (40.0)	Reference	
New Sexual Partner in the Past 6 Months, N = 160				
Yes	11 (44.0)	31 (23.0)	**2.6 (1.1–6.4; 0.032)**	2.2 (0.8–6.0; 0.116)
No	14 (56.0)	104 (77.0)	Reference	
Condom Use, N = 158				
Always/Most of the Time	10 (40.0)	98 (73.7)	Reference	
Sometimes/Rarely/Never	15 (60.0)	35 (26.3)	**4.2 (1.7–10.2; 0.002)**	**3.4 (1.3–8.3; 0.011)**
Age of Most Recent Sexual Partner, N = 158				
15–24	14 (56.0)	107 (80.5)	Reference	
≥25	11 (44.0)	26 (19.6)	**3.2 (1.3–7.9; 0.010)**	1.0 (0.31–3.24; 0.983)
Age at HIV Diagnosis, N = 160				
0–14	13 (52.0)	106 (78.5)	Reference	
15–25	12 (48.0)	29 (21.5)	**3.4 (1.4–8.2; 0.007)**	2.2 (0.82–5.97; 0.116)
ARV Adherence at Current Visit, N = 142				
0–80 and ≥106	2 (9.1)	10 (8.3)	1.1 (0.2–5.4)	
81–105	20 (90.9)	110 (91.7)	Reference	
Current Viral Load, N = 155				
Undetectable	15 (68.2)	72 (54.1)	Reference	
≥20	7 (31.8)	61 (45.9)	0.6 (0.2–1.4; 0.223)	
Current CD4 Count, N = 160				
0–350	5 (20.0)	22 (16.3)	Reference	
≥351	20 (80.0)	113 (83.7)	1.3 (0.4–3.8; 0.650)	

Risk factors associated with an STI (P value of .05 or less) are bolded.

Abbreviations: ARV, antiretroviral; CI, confidence interval; HIV, human immunodeficiency virus; Neg., negative; OR, odds ratio; Pos., positive; STI, sexually transmitted infection.

data suggest that STI risks and rates are not evenly distributed among adolescents and young adults with HIV with various demographic, behavioral, and clinical risk factors contributing to STI risk. Targeted testing and treatment of STIs in this population may represent another strategy to reduce HIV transmission.

There is very little data on the prevalence of STIs among adolescents and young adults with HIV and enrolled in chronic care in high-burden settings. Existing data on incidence in adolescents and young adults with HIV, primarily from US populations, estimate an incidence of any bacterial STI at approximately 1.56–2.6 per 100 patient-years, which was similar to

HIV-uninfected populations [17, 23]. These data are not directly comparable to our own because we collected cross-sectional data on prevalence rather than incidence, but our prevalence of 8.7% among all participants and 15.5% among ESAP suggest that adolescents (15–19 years) and young people (20–24 years) with HIV in high-burden settings are at significant risk for STIs. This high prevalence in a population routinely screened for STI symptoms is consistent with surveillance data demonstrating the lack of efficacy of syndromic screening and management on reducing STI prevalence [13]. Self-report of any prior sexual activity by questionnaire was a reliable predictor of STI risk in this cohort, indicating that if adolescents are approached in a way that allows them to answer truthfully, this can be an effective initial screening question to assess STI risk.

We did not find an association with STI detection and detectable viremia, although this has been reported previously from a cohort in the United States, which represents a significantly different population [17]. Rates of viral suppression are lower among adolescents and young people than in older adults [24, 25], and STIs can increase the risk of HIV transmission in patients with DVLs. This fact, coupled with the high rates of STIs in this population, suggest that testing and treatment of STIs may help reduce HIV transmission among this group of adolescents and young adults with HIV.

The gender disparity in STIs among people with HIV in sub-Saharan Africa holds true in Eswatini among adolescents and young adults with HIV. In addition to a disproportionate burden of STI prevalence, women are more likely to experience negative health outcomes secondary to STIs. Among female ESAP, 19.8% (20 of 101) had an STI, but of those with an STI, only 20.0% (4 of 20) were identified through syndromic screening. This high prevalence at baseline in a comprehensive HIV care setting, already incorporating robust syndromic screening, indicates the need to introduce Xpert CT/NG and TV screening for sexually active adolescents and young adults who are enrolled in comprehensive HIV care.

Although costly at approximately US $15 to $20 per Xpert CT/NG cartridge, the diagnostic accuracy, ease of sample collection (urine or vaginal self-swab), rapid integration into an existing testing platform, and the known consequences of untreated asymptomatic STIs, unidentified by syndromic management, further support the need for appropriate laboratory-based screening. Initial WHO evaluations of Xpert CT/NG and TV test performance support the previously reported high diagnostic accuracy of these assays, further indicating the need to move past syndromic STI screening and management [26]. Additional data are needed on how to incorporate longitudinal screening for sexually active participants and whether risk factors identified in this cohort—such as recent sexual activity, frequency of condom use, and age-disparate sexual partnerships—could be used to guide the need for repeat screening in females with HIV. Syndromic and LE screening performed

better in male versus female participants and may be a more appropriate strategy in this lower risk group. Cost-effectiveness analysis of screening people with HIV for CT, NG, and TV in HIV high-burden settings is urgently needed to support integration of point-of-care Xpert STI testing into the HIV comprehensive care package. Emerging data are identifying clinical and economic benefits to introducing multidisease testing into the GeneXpert platform, indicating that introducing Xpert-based STI testing may have economic benefits beyond the clear clinical need [27].

Infrequent condom use was associated with a higher risk of STI detection on bivariate and multivariate analysis, pointing to the effectiveness of this intervention when used. Although the majority of respondents reported always using condoms, 43% used them less frequently, indicating the need for prevention programs to discuss the multiple beneficial effects of condom use among adolescents and young people with HIV. Having an older sexual partner was associated with 3-fold increase in the risk of STI detection on bivariate analysis. Although not always indicative of a transactional sexual relationship, this association with STI infection and age-disparate relationships has been observed in South Africa [28, 29], and it may indicate that adolescents and young women with HIV in Eswatini also engage in transactional sexual relationships leading to an increased risk of STI acquisition. Prevention programs need to focus not just on empowering women with condom use, but also changing the dialogue around healthy sexual relationships.

The cohort who were diagnosed with HIV at an older age, generally indicating horizontal rather than vertical transmission, were another group at risk for the presence of an STI on bivariate but not multivariate analysis. This may speak to the different needs of adolescents and young adults who acquired HIV through sexual activity as opposed to perinatally. Attention to distinctions among these 2 patient populations is needed in settings where both populations are engaged in care in large numbers.

Treatment of STIs was successfully provided in 100% of patients through normal clinic processes and providers, and without additional resources provided to study participants, indicating that STI testing and treatment can be integrated into a comprehensive HIV care model. In this cohort, Xpert testing identified an additional 16 patients with STI infections compared with syndromic screening; furthermore, if Xpert testing had been used to exclude an STI as the cause of urethritis, cervicitis, or lower abdominal pain syndromes, antibiotics could have also been avoided in an additional 19 patients within this cohort. Using point-of-care testing in this way allows for antibiotics to target specific infections, such as azithromycin alone for CT, rather than providing syndromic treatment for all potential pathogens. Although the risk of repeat infection among patients diagnosed with CT, NG, and TV is known to be high [30], only 16% of this cohort was found to be positive upon repeat

testing. This suggests that when coupled with appropriate counseling surrounding partner treatment and prevention methods, treatment is effective and reinfection rates are low.

The relative increased prevalence of NG as opposed to CT and TV in this cohort was remarkable. Prior assessments of STI prevalence among young people in South Africa identified CT as the most common cervicitis- and urethritis-associated STI [10], whereas an assessment of STIs in women of all ages in Eswatini demonstrated a higher prevalence of TV, with relatively equal numbers of patients found to have CT and NG [20]. In this cohort, NG was present at approximately twice the rate of CT or TV. Additional data are needed to determine whether this is representative of larger populations of adolescents and young people living with HIV in high-burden settings; however, this is concerning given the increased risk of PID associated with NG infections [7]. It may also reflect the inadequacy of previously recommended oral treatment regimens and increasing antimicrobial resistance among strains of NG.

The cross-sectional design of this study does not provide data on how integration of STI Xpert testing as a screening diagnostic will impact incidence of STIs within a population or its potential to decrease HIV transmission rates. It is possible that repeat testing, even based on risk factors, may result in a lower yield. Operational research is needed to understand how effective screening impacts the prevalence of STIs overtime within a clinical cohort enrolled in comprehensive HIV care. Assessment of oropharyngeal carriage rates was limited by the small subgroup sample size and should be assessed in larger groups to draw definitive conclusions. Concordance testing with vaginal and urinary specimens was also limited, and we cannot exclude the possibility that additional cases might have been identified through greater use of vaginal self-testing swabs, which may be a slightly more sensitive approach. As with any cross-sectional study, our data may be subject to reporting bias and lack generalizability due to the single-entry point. The results will be confirmed through ongoing enrollment of larger cohorts from multiple-entry points.

CONCLUSIONS

These data highlight the inadequacy of syndromic management, the current standard of care, for CT, NG, and TV in this high-risk population of adolescents and young adults with HIV. Our evidence indicates that the majority of these infections are asymptomatic and supports the introduction of targeted molecular STI testing as a key element of comprehensive HIV care for adolescents and young adults in low-resource, high-burden settings. Prevention programs need to target correct and consistent condom use and empower women to seek alternatives to transactional and age discordant relationships. Differentiated service delivery may be needed for adolescents and young adults who have acquired HIV horizontally as opposed to adolescents and young adults who acquired HIV perinatally. Point-of-care Xpert

screening and testing services for adolescents and young adults living with HIV should be rapidly adopted, particularly for females, given the poor performance of syndromic screening and the potential for adverse health consequences due to untreated CT, NG, or TV. Adoption of such testing, if financial resources allow, is possible within the framework of comprehensive HIV care for adolescents and young adults with HIV living in high-burden settings and has the potential to decrease HIV transmission via improved identification and treatment of STIs.

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