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RESEARCH ARTICLE

Prevalence, incidence and recurrence of sexually transmitted infections in HIV-negative adult women in a rural South African setting

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Abstract

Objective: Sexually transmitted infections (STIs), including syphilis, chlamydia, gonorrhoea and trichomoniasis, are of global public health concern. While STI incidence rates in sub-Saharan Africa are high, longitudinal data on incidence and recurrence of STIs are scarce, particularly in rural areas. We determined the incidence rates of curable STIs in HIV-negative women during 96 weeks in a rural South African setting.

Methods: We prospectively followed participants enrolled in a randomised controlled trial to evaluate the safety and efficacy of a dapivirine-containing vaginal ring for HIV prevention in Limpopo province, South Africa. Participants were included if they were female, aged 18–45, sexually active, not pregnant and HIV-negative. Twelve-weekly laboratory STI testing was performed during 96 weeks of follow-up. Treatment was provided based on vaginal discharge by physical examination or after a laboratory-confirmed STI.

Results: A total of 119 women were included in the study. Prevalence of one or more STIs at baseline was 35.3%. Over 182 person-years at risk (PYAR), a total of 149 incident STIs were diagnosed in 75 (65.2%) women with incidence rates of 45.6 events/PYAR for chlamydia, 27.4 events/100 PYAR for gonorrhoea and 8.2 events/100 PYAR for trichomoniasis. Forty-four women developed ≥2 incident STIs. Risk factors for incident STI were in a relationship ≤3 years (adjusted hazard ratio [aHR]: 1.86; 95% confidece interval [CI]: 1.04–2.65) and having an STI at baseline (aHR: 1.66; 95% CI: 1.17–2.96). Sensitivity and specificity of vaginal discharge for laboratory-confirmed STI were 23.6% and 87.7%, respectively.

Conclusion: This study demonstrates high STI incidence in HIV-negative women in rural South Africa. Sensitivity of vaginal discharge was poor and STI recurrence rates were high, highlighting the shortcomings of syndromic management in the face of asymptomatic STIs in this setting.

KEYWORDS
HIV prevention, STIs, syndromic management

INTRODUCTION

Curable sexually transmitted infections (STIs), such as syphilis, chlamydia, gonorrhoea, and trichomoniasis, cause

Mathapelo Maphanga and Chijioke N. Umunnakwe contributed equally to this study.

Sustainable Development Goal: Good Health and Wellbeing.

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significant morbidity and mortality worldwide and are of global public health concern [1, 2]. Low and middle-income countries (LMICs) remain disproportionately affected, with sub-Saharan Africa (SSA) accounting for 40% of the global STI prevalence [3, 4]. In SSA, South Africa has the highest prevalence of curable STIs and HIV and the two epidemics are closely intertwined as STIs increase the risk of HIV transmission and acquisition [5–8].

STI morbidity skews heavily towards women, who are not only more predisposed to infection due to a more susceptible genitourinary tract, but are also exclusively affected by majority of STI-related severe health outcomes, including obstetric complications, infertility, pelvic inflammatory disease and cervical neoplasia [1, 3, 9–12]. Furthermore, large numbers of women remain untreated for STIs due to lack of symptoms and misattribution of STI symptoms to other medical conditions [13–15].

South African STI treatment guidelines are based on syndromic management, wherein patients are treated for the most common aetiological causes associated with certain signs and symptoms [1, 16]. Although cost- and time-effective, syndromic management has key drawbacks: many asymptomatic STIs are missed, especially in women, and, symptoms which are not caused by an STI are treated as such, leading to overtreatment, and potentially contributing to development of antibiotic resistance [17–19]. Lack of epidemiological data also results in significant gaps in knowledge at the population level, and negatively impacts public health policy and guidelines.

The most recent WHO global strategy on HIV and STIs emphasises a data-driven approach with disaggregated data by sex, age and other key population characteristics with a shift from syndromic management to active surveillance and causative treatment [1]. Within this framework, active STI surveillance encompasses prevalence and incidence monitoring and aetiological diagnosis and management. While many cross-sectional studies have been performed to investigate the prevalence and incidence of STIs in SSA, little is known about long-term incidence and recurrence, especially in rural areas. In this study, we aimed to determine the prevalence and incidence of chlamydia, gonorrhoea and trichomoniasis in HIV-negative sexually active women in a rural South African setting.

MATERIALS AND METHODS

Participants and study design

Prospectively collected data were sourced from all participants in the IPM 027 Ring trial at Ndlovu Research Centre, Elandsdoorn, Limpopo, South Africa. IPM027 was a multicentre randomised, double-blind, placebo-controlled study evaluating the safety and efficacy of a dapivirine vaginal ring for the prevention of HIV-1 [20].

Elandsdoorn is in the Elias Motsoaledi Municipality of Limpopo's Sekhukhune District. Demographic data for Elandsdoorn are scarce but, at the time of the study closure, 2016, Elias Motsoaledi had a population of approximately 268,256 inhabitants, of whom 97.9% were black with the remaining 2.1% comprised of other population groups. Unemployment rate in the municipality was recorded at 42.9% in 2011 [21]. Although regional Limpopo HIV prevalence rates are not well documented, an HIV prevalence between 9% and 14% in Elandsdoorn was estimated in 2012, while provincial HIV prevalence was estimated at 11.18% for females aged 15–49 in 2016 [22, 23].

Ethical approval for the IPM027 trial was obtained from the University of Pretoria ethics committee. Women were identified during special events in the community where their partners could also attend, and flyers with information were handed out at different locations. Women who gave their information were phoned and invited to the clinic. At the clinic, the informed consent form was discussed with the women and the forms were provided in different languages to ensure the information was understood. HIV-negative, sexually active, non-pregnant women between the age of 18 and 45 years from Elandsdoorn were enrolled between March and November 2014. Enrolled women were followed up for 104 weeks with HIV testing at baseline and 4-weekly thereafter and STI testing at screening for enrolment and 12-weekly thereafter. Additional eligibility criteria included being stable on contraception during the trial period. If an STI was diagnosed at screening, treatment had to be taken at least 1 week before enrolment could occur. The last enrolment was in November 2014 and the last follow-up visit took place in October 2016.

Study procedures

All participants received risk reduction counselling on HIV, STIs and on contraceptive and condom adherence at every study visit. Condoms were provided at every study visit, and participants kept a diary of sexual activity and adherence to the vaginal ring. Participants underwent baseline and 12-weekly pelvic examination to examine abnormal findings and to collect cervicovaginal swabs for STI testing. Cervicovaginal samples were tested for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GN) using nucleic acid-amplification testing, and for *Trichomonas vaginalis* (TV) using the OSOM® Rapid Trichomonas (Sekisui Diagnostics). Bacterial vaginosis was scored using the Nugent score and the presence of *Candida* was observed using microscopy. Syphilis testing was performed at screening. Screening for syphilis was done on blood using a rapid plasma regain (RPR) test. When a blood sample was RPR-reactive, a treponemal-specific assay (TPHA/TPPA) was performed. HIV testing was performed following an algorithm as described in Nel et al. [20]. Women were treated according to South African STI syndromic management guidelines in case of vaginal discharge syndrome during follow-up and partner treatment was provided [16]. Asymptomatic women that tested positive for an STI were contacted and pathogen-driven treatment as well as a prescription for the partner was given. No follow-up of partner treatment was provided.

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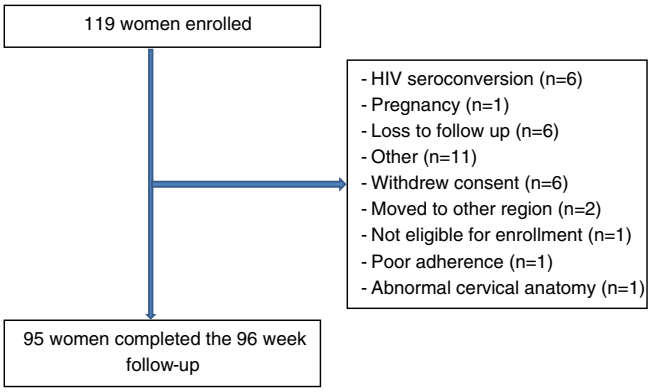

FIGURE 1 Study CONSORT diagram.

Statistics

StataSE 11 was used for statistical analysis. Since most women were enrolled in another IPM study after 96 weeks, data were analysed up to 96 weeks. Prevalence was reported as the percentage of participants with an STI at enrolment. Incidence was calculated as the number of incident STIs after enrolment divided by the total person-years at risk (PYAR) and reported as the number of events/100 PYAR. STI recurrence was defined as detection of the same pathogen twice in an individual with an episode of treatment and ≥1 negative test between the two detection time points. A consecutive positive STI test between enrolment and the first follow-up visit (Week 12) was also interpreted as recurrence because STI treatment with full resolution of symptoms was an inclusion criterion for enrolment. Time-to-event analysis of possible risk factors for STI acquisition was performed using Cox proportional hazard models. Proportional hazard assumptions were evaluated using the ph estat test for each variable before entry into the Cox regression model, and excluded from analysis if the proportional hazard assumption was not met. Continuous covariables were dichotomised along the median, and age was further categorised in quartiles. The presence of vaginal discharge was assessed during the physical examination. Diagnostic accuracy of vaginal discharge for the presence of a positive STI test was assessed and reported as sensitivity, specificity and positive and negative predictive values.

TABLE 1 Baseline characteristics.

Characteristics	*n* (%)
Age in years (median, IQR)	23 (22–28)
Age group in years	
<21	16 (13.4)
21–23	31 (26.0)
24–37	19 (16.0)
≥28	19 (16.0)
Education	
Primary school	8 (6.7)
Secondary school	110 (92.4)
Tertiary school	1 (0.8)
Marital status	
Single	110 (92.4)
Married	9 (7.6)
Duration of relationship	
≤3 years	43 (36.1)
>3 years	76 (63.9)
Reported sex acts per month	
≤4 acts	68 (57.1)
>4 acts	51 (42.9)
Reported condomless sex	
Yes	77 (64.7)
No	34 (28.6)
Mode of contraception	
Oral	6 (5.0)
Injection	66 (55.5)
Implant	41 (34.5)
Sterilisation	1 (0.8)
Vaginal discharge during pelvic examination	51 (42.9)
Any STI at screening	42 (35.3)
Chlamydia prevalence	31 (26.1)
Gonorrhoea prevalence	4 (3.4)
Trichomoniasis prevalence	9 (7.6)
Syphilis prevalence	2 (1.7)
2 STIs at screening	4 (13.4)
Bacterial vaginosis prevalence	22 (18.5)
Candidiasis prevalence	34 (28.6)

Abbreviations: IQR, interquartile range; STI, sexually transmitted infection.

RESULTS

Participant characteristics

A total of 119 women were enrolled in the trial. Of enrolled participants, 79.8% (95/119) completed the full 96 weeks of follow-up. Six women experienced HIV seroconversion during follow-up (Figure 1). The median age was 23 years (interquartile range, 22–28). The highest achieved level of education level was secondary school in 92.4% (110/119) cases. 92.4% (110/119) of women were unmarried and all reported to have one sexual partner. Most women were in relationships for ≥3 years (63.9%; 76/119), and 64.7% (77/119) of the women reported to have had sex without a condom in the last 3 months before enrolment (Table 1).

At baseline, 35.3% of women (42/119) had one or more STI. CT had the highest prevalence at 26.1% (31/119). The prevalence of GN, TV and syphilis was 3.4% (4/119), 7.6% (9/119) and 1.7% (2/119), respectively (Table 1).

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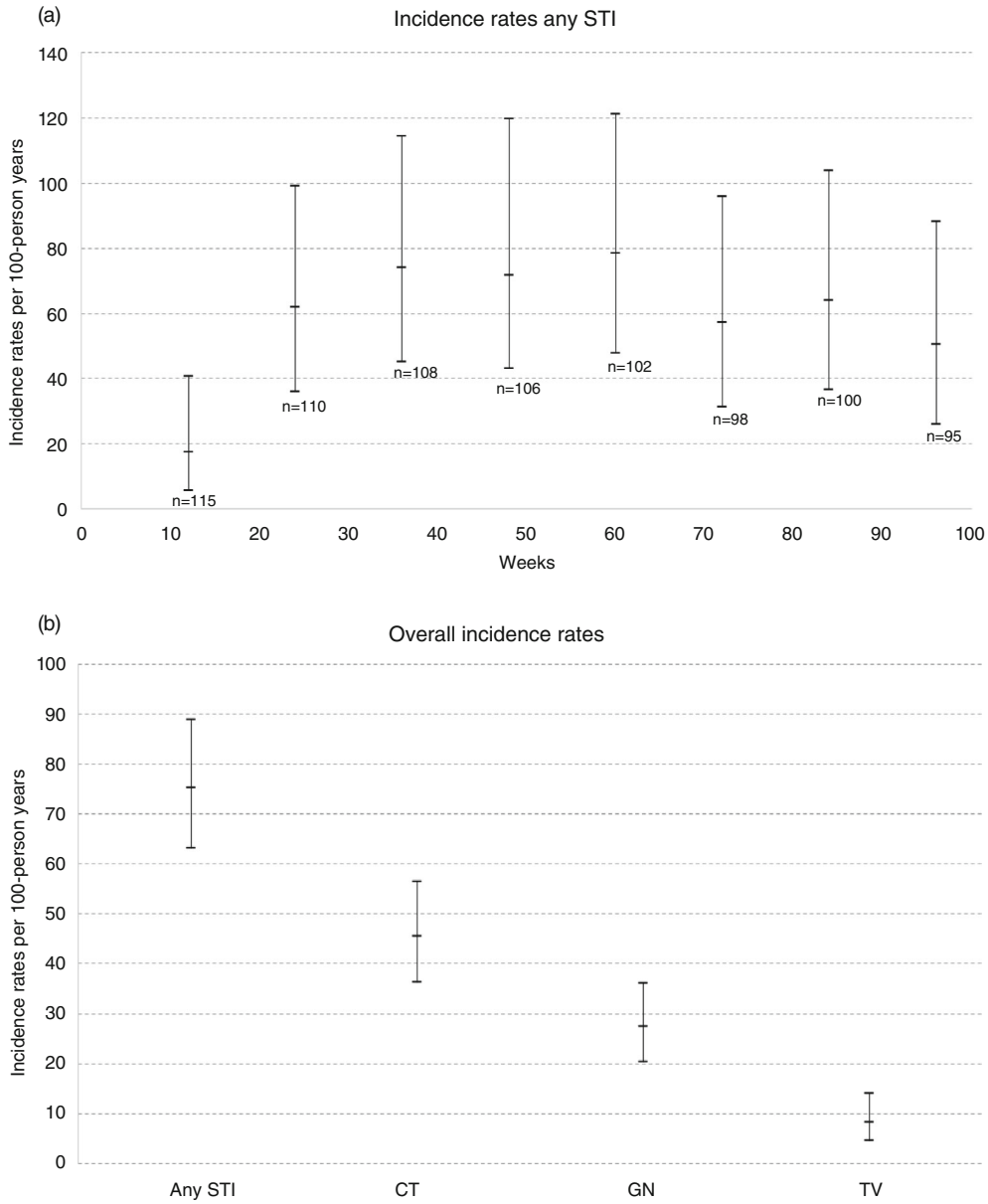

FIGURE 2 (a) Twelve-weekly incidence rates for any STI (*Chlamydia trachomatis*; CT, *Neisseria gonorrhoeae*; GN and *Trichomonas vaginalis*; TV) and the (b) overall incidence rates for all sexually transmitted infections (CT, GN or TV or combined) during 96 weeks of follow-up. STI, sexually transmitted infection.

STI incidence

A total of 149 STIs were diagnosed in 75 (65.2%) women during 182 PYAR. Thirteen women (10.9%) were infected with multiple STIs at a single time point. The overall 96-week incidence for any STI (CT, GN or TV) was 75.27 events/100 PYAR for any STI and 45.60 events/PYAR for CT, 27.43 events/100 PYAR for GN and 8.24 events/100 PYAR for TV (Figure 2). Twelve-weekly incidence rates were consistently highest for CT and lowest for TV (see Figure S1).

In 44 women, at least two STIs occurred during baseline and follow-up. Table 2 represents the incident STIs in these women. During follow-up, chlamydia recurred once, twice and thrice in 19, three and two women, respectively. For gonorrhoea, recurrence occurred once in four women and twice in two women. Four women had trichomonas recur once during follow-up, and one woman had recurrence twice (Table S1). All participants who acquired HIV during the study had an STI either during screening or follow-up or both, and four out of six participants had an incident STI at the time of HIV diagnosis.

Correlates of new STI diagnosis

In multivariable analysis, women with a relationship ≤3 years and women with any STI at baseline were at increased risk of being diagnosed with a new STI during follow-up (adjusted hazard ratio [aHR]: 1.86. 95%

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TABLE 2 Incident STIs in women with recurring STI cases. Chlamydia (blue), gonorrhoea (green) and trichomoniasis (yellow) infections during follow-up in different women with incident STIs.

Participant	Baseline	Week 12	Week 24	Week 36	Week 48	Week 60	Week 72	Week 84	Week 96
1	CT	CT							
2	CT					GN			
3	CT			CT					
4			CT					CT	
5	CT						TV		
6						CT	TV		
7			CT					CT	
8	CT	GN							
9	TV	TV				GN	moved away		
10	CT					GN			
11			CT GN			GN			
12	CT TV		TV		GN	HIV seroconversion			
13	CT		CT			CT			CT
14	CT	GN			GN	CT			
15	CT							CT	
16				CT		CT GN			
17	CT		CT	CT	CT				
18	TV	TV	GN	TV	CT				
19	CT			CT TV		CT	GN	GN	CT GN
20	CT						GN		
21	CT				CT				
22	CT	TV			GN	CT TV		CT	CT
23				CT			GN		CT
24		CT	GN	loss to follow up					
25	CT								CT
26			CT	CT		CT GN		CT	switched studies
27	CT	GN							
28	TV								GN
29	CT				TV				
30		CT	CT	CT GN		GN	GN	CT	
31	GN	GN			GN	GN			
32			GN				CT		
33				CT GN	CT		GN		GN
34	CT				CT				
35	CT TV					TV	CT	GN	CT
36	CT	GN							
37			CT		CT			TV	
38	CT				CT	CT	CT	CT	CT
38						CT		GN	
40			CT	CT			CT GN	GN	HIV seroconversion
41				GN		CT			GN
42				CT				CT GN	CT
43	TV	GN							
44	CT		CT						

Abbreviations: CT, Chlamydia; GN, gonorrhoea; TV, trichomoniasis.

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TABLE 3 Risk assessment for diagnosis of a new STI during follow-up.

		Cases (*n*)	HR	*p* Value	aHR	*p* Value
Age group	<25	43	1.37 [0.85–2.21]	0.19		
	≥25	29	Ref			
Marital status	Married	6	Ref			
	Single	66	1.14 [0.49–2.64]	0.76		
Duration partnership	≤3 years	**27**	**1.81 [1.14–2.88]**	**0.01**	**1.86 [1.04–2.65]**	**0.04**
	>3 years	45	Ref		Ref	
Sex acts per month	≤4 acts	43	Ref			
	>4 acts	27	0.67 [0.42–1.08]	0.67		
STI at baseline	No	43	Ref		Ref	
	Yes	**29**	**1.60 [1.00–2.56]**	**0.05**	**1.66 [1.17–2.96]**	**0.01**

Abbreviations: aHR, adjusted hazard ratio; HR, hazard ratio; STI, sexually transmitted infection.

TABLE 4 Vaginal discharge as a diagnostic test for STI.

	CT (95% CI)	GN (95% CI)	TV (95% CI)	Any STI (95% CI)	CT/GN (95% CI)
Sensitivity	**27.8** (19.9–37.0)	**14.8** (6.6–27.1)	**25** (9.8–46.7)	**23.6** (17.8–30.5)	**23.9** (17.5–31.3)
Specificity	87.5 (85.2–89.7)	85.7 (83.3–88.0)	85.9 (83.61–88.1)	87.7 (85.3–90.0)	87.5 (85.2–89.9)
PPV	23.5 (17.9–30.3)	5.9 (3.1–10.8)	4.4 (2.2–8.6)	30.9 (24.4–38.2)	27.9 (21.7–35.1)
NPV	89.7 (88.7–90.8)	94.4 (93.7–95.0)	97.8 (97.2–98.2)	83.3 (82.1–84.5)	85.2 (84.0–86.3)

Abbreviations: CI, confidence interval; CT, chlamydia; GN, gonorrhoea; NPV, negative predictive value; PPV, positive predictive value; STI, sexually transmitted infection; TV, trichomoniasis.

confidence interval [CI]: 1.04–2.65; and aHR: 1.66 95% CI: 1.17–2.96, respectively) (Table 3). Age group, condom use, marital status and sex acts per month showed no significant association in univariate analysis.

Diagnostic accuracy of vaginal discharge

The overall sensitivity and specificity of vaginal discharge for laboratory-confirmed STI were 23.6 and 87.7%, respectively (PPV: 30.9; NPV: 83.3%). The sensitivity and specificity were highest for CT (sensitivity: 27.8%; specificity: 87.5%; PPV: 23.5% and NPV: 89.7%) and lowest for GN (sensitivity: 14.8%; specificity: 85.7%; PPV: 5.9%; NPV: 94.4) (Table 4).

DISCUSSION

This longitudinal study of STIs in HIV-negative women in a rural South African setting showed high prevalence and incidence of STIs as well as low sensitivity of vaginal discharge-based syndromic management for laboratory-confirmed STIs. Despite adequate detection, targeted treatment and a comprehensive STI prevention intervention package, STI incidence remained high throughout follow-up with 60% of the women contracting at least one new STI during 96 weeks of follow-up. Risk factors for STI acquisition included a shorter relationship duration with the current sexual partner and an STI at baseline, suggesting that the main drivers of STI acquisition in this population are more linked to stability and number of sexual relationships than sex practices per se. HIV seroconversion was observed in six participants and all six had at least one STI during follow-up, while four had an incident STI at the time of HIV diagnosis. These results illustrate the extent and complexity of the STI epidemic in the studied population, and highlight the need for linkage between prevention, testing and treatment strategies for HIV and STIs.

The high prevalence of curable STIs in SSA, particularly in South African communities, has been extensively documented [4, 24–28]. However, STI incidence data especially in rural South Africa is limited. A sub-study of the VOICE trial, investigating oral HIV pre-exposure prophylaxis in South Africa, revealed incidence rates of 15.9, 3.8 and 6.6 events/100 PYARs for CT, GN and TV, respectively, while another HIV prevention vaginal ring study in South Africa also showed similar incidence rates [29, 30]. However, these two studies enrolled participants from marginalised communities in urban areas with high risk of HIV acquisition and metropolitan cities, respectively. In contrast, our data are exclusively derived from a rural South African setting with no preselection of participants from any particular high-risk group. Interestingly, we observed higher incidence rates for CT and GN compared to the previously cited studies. Although comparative STI data of urban versus rural South African settings remains scarce [31, 32], two South African studies found no or reverse associations between STI incidence and rural settings.

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In our study, it was shown that syndromic management is insufficient for the treatment and control of STIs, as is also described in literature [24, 33–38]. It has to be addressed that our data on the diagnostic accuracy of vaginal discharge originates from 2014 to 2016. Currently, the shift from syndromic management towards causative treatment is being recommended, which hopefully will minimalize syndromic management [1]. Routine laboratory testing and targeted treatment, although necessary, are not sufficient to eliminate STI transmission as evidenced by the high incidence rates observed in our study despite frequent STI testing and directed treatment. We hypothesize that the inability to sufficiently provide for and follow up on partner treatment is an important contributing factor to high recurrence rates in the context of regular testing and treatment. Several studies in the South African setting indicate that structural and socio-economic obstacles including power imbalances between men and women in relationships and social stigma (which could influence compliance), and gender-based violence, contribute to the lack of partner notification and hinder efforts of reducing STIs in women [39–41]. Partner treatment and people-centred services are incorporated in the WHO strategy of 2022, which hopefully leads to more awareness and reduction of transmission [1].

Several limitations of this study should be mentioned. While we collected data on sexual behaviour, we did not collect detailed data on specific sexual risk factors or sexual practices, nor did we document changes in sexual behaviour or sexual relationships during follow-up. As this was a single-centre study, our results may not be generalizable to other geographical areas. The selection of individuals enrolled in an HIV prevention clinical trial creates a potential selection bias towards individuals who perceive themselves to be at increased risk of STIs. We expect this bias to be limited, given that the observed incidence of HIV in control arm participants was comparable to that of the general population, corrected for age, sex and geographical area [42]. Twelve-weekly testing of STIs in our study allows for more rapid detection and treatment of a new incident STI, which may have inadvertently resulted in more rapid STI recurrence and higher incidence rates compared to settings in which less frequent testing is used. Finally, all our analysis was performed on data obtained between 2014 and 2016, which is somewhat dated. However, STI rates have remained high in South Africa and continue to pose a major health risk; therefore, it remains imperative to systematically document prevalence and incidence from past years to comprehensively assess the extent of progress being made currently and identify areas for improvement.

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DATA AVAILABILITY STATEMENT

Access to data is restricted as set out by the regulations of the Ethical Committees as well as privacy regulations from the South African Government. Individual access to the data for this study can be made available upon reasonable request from the corresponding author L.E.P.H.

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