Prevalence of curable sexually transmitted infections in a population-representative sample of young adults in a high HIV incidence area in South Africa

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Summary

Prevalence of gonorrhea, chlamydia, and trichomoniasis is high among adolescents and young adults in rural South Africa, and higher among women and those residing in urban/peri-urban areas.

Abstract

Background

Recent population-representative estimates of STI prevalence in high HIV burden areas in southern Africa are limited. We estimated the prevalence and associated factors of three STIs among adolescents and young adults (AYA) in rural South Africa.

Methods

Between March 2020-May 2021, a population-representative sample of AYA aged 16-29 were randomly selected from a Health and Demographic Surveillance Site in rural KwaZulu-Natal, South Africa for a 2x2 factorial randomized controlled trial. Participants in two intervention arms were offered baseline testing for gonorrhea, chlamydia, and trichomoniasis using GeneXpert. Prevalence estimates were weighted for participation bias, and logistic regression models were used to assess factors associated with STIs.

Results

1743 (75%) of 2323 eligible AYA enrolled in the trial. Among 863 eligible for STI testing, 814 (94%) provided specimens; median age 21.8 years, 52% female, and 71% residing in rural areas. Population-weighted prevalence estimates were 5.0% (95%CI 4.2-5.8%) for gonorrhea, 17.9% (16.5-19.3%) for chlamydia, 5.4% (4.6-6.3%) for trichomoniasis, and 23.7% (22.2-25.3%) for any STI. In multivariable models, female sex (aOR 2.24, 95%CI 1.48-3.09) and urban/peri-urban (versus rural) residence (aOR 1.48, 95%CI 1.02-2.15) were associated with STIs; recent migration was associated with lower odds of STI (aOR 0.37, 95%CI 0.15-0.89). Among those with an STI, 53 (**31.0**%) were treated within 7 days; median time to treatment was 11 days (IQR 6-77 days).

Conclusions

We identified a high prevalence of curable STIs among AYA in rural South Africa. Improved access to STI testing to enable etiologic diagnosis and rapid treatment is needed.

Keywords: gonorrhea, chlamydia, trichomoniasis, sexually transmitted infections, South Africa

INTRODUCTION

Curable sexually transmitted infections (STIs) are common worldwide, with over one million new cases of gonorrhea, chlamydia, trichomoniasis, or syphilis estimated to occur globally every day.[1] When untreated, STIs can cause significant morbidity, particularly for women, leading to complications such as pelvic inflammatory disease, ectopic pregnancy, infertility, pregnancy complications, and newborn infection.[2,3] Furthermore, STI-induced genital inflammation and genital HIV shedding can increase risks of HIV acquisition and transmission, even when the STI is asymptomatic.[4–6] The majority of STIs occur in low- and middle-income countries (LMICs), with the highest age-standardized incidence rates and greatest number of disability-adjusted life years (DALYs) lost in sub-Saharan Africa.[7] In southern Africa, there is strong epidemiologic overlap between curable STIs and HIV, particularly among adolescents and young adults, who are at highest risk for STI acquisition and have the highest HIV incidence rates.[7,8] For these populations, improved diagnosis and treatment of curable STIs is key to reducing morbidity and is an important component of multimodal HIV prevention.

Due to a lack of accessible and affordable diagnostic testing, STIs in LMICs are predominantly managed using a syndromic approach.[9] This approach misses a substantial proportion of STIs because they frequently remain asymptomatic.[10] The World Health Organization (WHO) in the global health sector strategies for HIV, viral hepatitis, and sexually transmitted infections for 2022-2030 recommends a transition from syndromic to etiologic management of STIs and calls for increased screening of priority populations, including youth.[11] The WHO has additionally recommended integration of STI care with other health services, including HIV prevention and treatment.[11] However, screening and surveillance programs remain limited, and there are few recent population-representative data on STI prevalence to inform efforts at care integration.

In South Africa, which has among the highest HIV incidence and prevalence rates worldwide,[12] STI prevalence is predicted to be high, with model-based prevalence estimates of 6.6% for gonorrhea and 14.7% for chlamydia among women and 3.5% gonorrhea and 6.0% chlamydia among men.[13] Studies have found STI prevalence as high as 42% for chlamydia and 11% for gonorrhea among adolescent girls and young women in Cape Town.[14] However, few population-representative studies of STI prevalence exist from areas of high HIV incidence in South Africa, particularly among both women and men, and previous prevalence data have not been recently updated.[15] We aimed to use STI screening among a population-representative cohort of adolescents and young adults selected from a Health and Demographic Surveillance Site (HDSS) in rural KwaZulu-Natal, South Africa[16] to provide updated STI prevalence estimates among adolescents and young adults in this setting and assess for factors associated with having an STI.

MATERIALS AND METHODS

Study setting

This study was conducted within the HDSS in uMkhanyakude district in rural KwaZulu-Natal, South Africa. Since 2000, the Africa Health Research Institute (AHRI; formerly Africa Centre for Health and Population Studies) has been conducting annual household-based surveys to collect data on births, deaths, demographics, and migration patterns. The HDSS was expanded in 2017 to cover 845 km^2 with approximately 140,000 individuals in 20,000 households.[16] The area has a high rate of unemployment (62% of adults without formal employment) and HIV prevalence of 19% among men and 40% among women aged 15-54 years.[16]

Study design

This study reports baseline data from a 2x2 factorial randomized controlled trial evaluating the acceptability, feasibility, and preliminary population-level impact of integrated sexual and reproductive health services with or without peer support on the prevalence of transmissible HIV.[17] The AHRI HDSS was used as a sampling frame to randomly select 3000 men and women aged 16-29 years, stratified by sex and area, to be assessed for eligibility. All eligible were approached for enrollment with a goal of at least 1500 eligible and enrolled participants. Men and women aged 16-29 years, residing in the HDSS area, willing and able to provide informed consent, and willing to be contacted at 12 months for HIV testing, were eligible to enroll in the trial. At enrollment, participants were randomized to one of four study arms: a) enhanced standard of care (referral to adolescent and youth friendly services (AYFS) comprised of clinic-based, nurse-led HIV testing with linkage to antiretroviral therapy [ART] or HIV pre-exposure prophylaxis [PrEP]), b) sexual and reproductive health (SRH; home-based self-collection of STI specimens and referral to AYFS for integrated SRH and HIV testing), c) peer support (referral to peer navigator to assess health, social, and educational needs and provide risk-informed HIV prevention and referral to AYFS),[18] or d) SRH and peer support. Participants randomized to the two SRH intervention arms were offered STI testing at study enrollment. Sample size for this analysis was determined by the total number of participants randomized to the SRH arms and providing specimens for STI testing.

Study procedures

Following informed consent, participants randomized to either of the two SRH arms were offered home-based STI specimen collection. For female participants, research staff described the procedure to self-collect a vaginal swab. Menstruating females provided urine specimens. Male participants were

instructed to collect a first-catch urine specimen. All participants were provided an AYFS clinic referral to receive their STI test results in 7 days. Participants were informed that if any test results return positive and they do not present to the clinic, research staff will attempt to contact them to ensure they receive treatment. STI treatment was provided according to South African national clinical guidelines (single-dose ceftriaxone and azithromycin for gonorrhea; single-dose azithromycin or seven-day course of doxycycline for chlamydia; single-dose metronidazole for trichomoniasis).[19] Receipt of treatment was verified through AYFS clinic records and study documentation, participant self-report on follow-up contact, or documentation of failed contact attempts.

Data collection

STI specimens were transported to the AHRI central laboratory in Durban. Testing for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* was conducted by real-time polymerase chain reaction by GeneXpert (Cepheid, Sunnyvale, CA, USA). Valid STI test results were recorded as 'detected' or 'not detected'. Invalid test results were recorded as 'invalid' or 'error' based on test platform output. To minimize research procedures at enrollment to emulate real-world implementation of the interventions, study-specific questionnaires were not administered at the time of STI specimen collection. Socio-demographic data including education (years of completed education), employment (none, part-time, full-time), marital status (married, not married, informal union), household socioeconomic status (combined household asset index), and migration history (no migration, internal migration, in-migration, external migration) were derived from linking study participants to the annual HDSS household-level survey conducted in 2019.

Statistical analysis

We summarized participants' demographic data using medians and interquartile ranges (IQR) for continuous variables and frequency counts and percentages for categorical variables. Frequency counts and percentages with 95% confidence intervals (CIs) were calculated for the prevalence estimate of each individual STI and prevalence of any STI. To account for participation bias, we calculated weighted prevalence estimates to account for the stratified sample design, calculated as the inverse probability of study participation in strata defined by age group and sex. We used logistic regression to estimate the odds ratios and 95% confidence intervals for factors associated with the presence of any curable STI and factors associated with treatment in univariate and multivariable models. Age and sex were included a priori in the multivariable model; other factors with $p<0.2$ in univariate logistic regression were also included in the multivariable model; for treatment completion, age- and sex-adjusted models were used. Missing data were not imputed. All reported p-values were two-tailed; $p<0.05$ was considered statistically significant. Analyses were conducted using Stata version 16.1 (Stata Corp, College Station, TX, USA).

Ethical considerations

The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC/00000473/2019), the University College of London Research Ethics Committee (5672/003), and the Mass General Brigham Institutional Review Board (2021P002574). Written informed consent was obtained from all participants aged ≥18 years; verbal assent with written informed consent from a parent or guardian was obtained for all participants aged 16-17 years.

Patient and public involvement

The peer support and sexual health intervention was co-created with young people in uMkhanyakude district and delivered by peers. Young people and the AHRI community advisory board were involved from research inception through to analysis. Study findings were shared with the research participants and their communities, as well as health officials and program implementers.

RESULTS

Between 4 March 2020 and 24 May 2021, 3000 adolescents and young adults were assessed for eligibility; 2323 were found to be eligible and were invited to participate, of whom 1743 (75%) enrolled in the randomized controlled trial (**Figure 1**). Of these, 863 were randomized to the two study arms offering STI testing, and 814 (94%) accepted testing and provided specimens. There was no difference by sex between those who consented and did not consent to STI testing (p=0.270). Among 427 female participants who provided specimens, 116/427 (27.2%) provided urine specimens; the remainder (311/427, 72.8%) provided self-collected vaginal swab specimens. Among those tested for STIs, 52% were female, median age was 21.8 [IQR 18.8-25.6], and 29% resided in urban or peri-urban areas. Additional participant demographics are presented in **Table 1**.

Among the 814 specimens provided by participants, 14/814 (1.7%) had results of 'invalid' or 'error' for gonorrhea and chlamydia; of these, three (0.4%) also had invalid results for trichomoniasis. Of 800 participants with valid test results for all three STIs, 179 (22.4%) tested positive for at least one STI. Of these, 147 (82.1%) were mono-infections, while 32 (17.9%) participants were co-infected with more than one STI, including three participants (1.7%, all female) infected with three STIs concurrently (**Supplemental Digital Content Table S1**). Population-weighted prevalence estimates for any STI and each STI individually, by sex and age group, are shown in **Figure 2 and Supplemental Digital Content**

Table S2, demonstrating 30.2% prevalence of any STI among female participants and 17.3% prevalence among male participants.

In unadjusted analyses, STIs were more common among women, among those aged over 20 years than 15-19 years, and those with urban/peri-urban compared to rural residence. STIs were less common among those with unknown employment or marital status (who are also more likely to be <18 years old), and those with migration in the preceding two years. In adjusted analyses, STIs remained more than twice as likely among women than men (aOR 2.14, 95% CI 1.48-3.09, p=0.0001), more likely among those residing in urban/peri-urban areas (aOR 1.48, 95% CI 1.02-2.15, p=0.041; **Table 2**), and less likely among those with any recent migration (aOR 0.37, 95%CI 0.15-0.89, p=0.026).

Among participants with a positive STI result and complete follow-up data, 53/171 (31.0%) were treated within 7 days of specimen collection. Median time to treatment overall was 11 days (interquartile range, 6-77 days) and did not differ by sex or age group (data not shown). Among 73 participants not treated within 4 weeks of specimen collection, 51 (69.9%) could not be reached sooner and were treated later, 11 (15.1%) could not be contacted after multiple attempts, 6 (8.2%) had migrated outside of the area, and 5 (6.8%) refused treatment (reasons for refusal not provided). In analyses adjusted for age and sex, urban/peri-urban residence was associated with lower likelihood of treatment within 7 days compared to rural residence (aOR 0.42, 95% CI 0.20-0.87, p=0.019), while being in the highest socioeconomic tertile was associated with higher likelihood of treatment within 7 days (aOR 3.12, 95% CI 1.36-7.16, p=0.0032) **(Table 3).**

DISCUSSION

We found a very high prevalence of curable STIs among adolescents and young adults in a predominantly rural area of KwaZulu-Natal, South Africa. This study confirms the acceptability of home-based STI specimen collection among adolescents and young adults, as over 90% of study participants who were offered STI testing provided specimens. STI prevalence was significantly higher among female than male participants overall, even when adjusted for age and other demographic factors. The sex difference in prevalence was most pronounced for trichomoniasis and chlamydia; prevalence of gonorrhea was similar between males and females. Participants residing in urban/peri-urban areas were more likely to have an STI than those residing in rural areas. Despite multiple contact attempts by study staff, only one out of three participants who tested positive for an STI were treated within 7 days. Difficulties in follow-up contact compounded by a low (6.8%) treatment refusal indicates need for a robust tracking system and strategies to maximize treatment reach, and underscores the need for point-of-care STI tests to enable same-day treatment and decrease loss to follow-up.

In this cohort, women had a higher STI prevalence than men overall, particularly trichomoniasis and chlamydia. These results mirror both national-level estimates of STI prevalence in South Africa and previous studies among adolescents and young adults in rural KwaZulu-Natal; in both cases, chlamydia prevalence was over twice as high among women than men.[13,15] Young women in South Africa may face higher risk of STI acquisition than age-matched male counterparts due to earlier age of sexual debut,[15] higher rate of age-disparate relationships,[20] and lesser ability to navigate safe sex. Gender inequalities contribute to the higher rates of STIs among women than men in many parts of the world, and adolescent girls and young women have been identified as priority populations for STI programming by the WHO.[11] Furthermore, since STIs are more often asymptomatic in women than men, fewer women may receive treatment through syndromic management pathways, leading to longer

duration of infection and thus detection of a greater prevalence of active infections among women. However, we found that among those aged 20-24 years, men had a higher prevalence of gonorrhea and chlamydia than women. A previous study in this setting also found a higher prevalence of chlamydia among men than women in this age group (12.2% vs 10.6%, respectively).[15] Reasons for this finding are not clear, though may relate to later sexual debut among men in this setting.[15] Differences in sexual networks, transactional sex, or migration may also contribute to this finding, however, due to limited data on young men, it is difficult to know which factors account for it. This is, however, an important observation that requires further study.

We found a substantially higher prevalence of chlamydia and gonorrhea in this cohort than in a previous study conducted in the same geographic area in 2016-2017.[15] Weighted prevalence estimates for chlamydia were 8.1% in the previous study and 17.9% in the current study, and for gonorrhea 1.7% in the prior study and 4.6% in the current study. The previous study enrolled adolescents and young adults up to age 25 while the current study enrolled adults up to age 29, however, prevalence estimates were higher in the current study within each individual age group and overall, with the exception of trichomoniasis in men. The high STI prevalence estimates for women in the current study mirror emerging data on STI prevalence among women enrolled in PrEP trials and women living with HIV in Southern Africa.[21–23] The difference in prevalence estimates between this and the previous study may thus signal an increase in STIs over time in this area, supporting an urgent need for greater access to sexual health services for this population. Furthermore, non-pharmaceutical interventions adopted during the COVID-19 pandemic, such as national lockdowns, could have impacted transmission within sexual networks, contributing to the higher STI prevalence found in this study.

We additionally found that young men and women residing in urban or peri-urban areas were more likely to have an STI than those residing in rural areas, even after adjustment for other demographic factors, including age, employment status, and migration history. A recent study evaluating transmissible HIV among adolescent girls and young women exposed to the PEPFAR-supported DREAMS intervention, conducted at the same study site, similarly found that urban/peri-urban residence was associated with transmissible HIV.[24] HIV incidence over time was higher in urban and peri-urban areas of the study site in a separate study.[25] Despite the predominantly rural nature of the AHRI HDSS area, there are several informal peri-urban settlements and an urban township with high population density.[26] Potential differences between the urban/peri-urban and rural participants, such as differences in socioeconomic status, substance use, transactional sex, gender-based violence, patterns of sexual behavior, or migration history, may explain the difference in STI prevalence. Additionally, greater movement of people through the urban areas may contribute to higher turnover of partners and lead to more introduction of infections into the community, however, more study of potential drivers is needed. We additionally found that adolescents and young adults reporting recent migration had lower odds of having an STI than those who had not migrated in the same time period. While this finding could reflect higher STI transmission in local sexual networks, the small number of participants with recent migration events makes it difficult to draw conclusions from this finding. Additional data on sexual risk behavior obtained at the endpoint of the trial may help elucidate the reasons behind these observed differences.

Despite the robust infrastructure of the randomized trial and the long-standing experience of AHRI conducting research that is strongly linked with public sector health clinics in this area, less than half of the participants with STIs were able to be treated within 7 days, and less than two-thirds within 4 weeks.

Those living in urban areas were less likely to be treated within 7 days, possibly due to higher rate of employment or difficulty tracking participants. Those in the highest socioeconomic tertile were more likely to be treated within 7 days, which may either reflect greater access to technology such as mobile phones for contact by study staff, or easier access to clinic for treatment. Diagnostic testing for STIs remains inaccessible in most resource-limited settings, due to high costs and need for laboratory infrastructure; when STI testing is available in such settings, it is often restricted to centralized laboratories. For this study, STI specimens were transported from the rural study site to a centralized research laboratory in Durban (approximately 230 kilometers away), resulting in an extended time from specimen collection to test result. Loss to follow-up increases with extensions in test turn-around-time, and delays in treatment lead to the potential for ongoing transmission and increased risk for sequelae of untreated infection. A study assessing community-based STI testing for adolescents and young adults in Zimbabwe found that even with an expected 90-minute time to result, only 67% of those with positive test results were treated.[27] These findings highlight the urgency of development and implementation of affordable point-of-care STI diagnostics that meet WHO REASSURED criteria (Real-time connectivity, Ease of specimen collection, Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment free or simple and Environmentally friendly, Deliverable to end-users) [28] and enable immediate treatment and partner notification services.

Our assessment of factors associated with STIs was limited by the scope of demographic data available and lack of contemporaneous data on symptoms and sexual risk behavior. The trial did not include study-specific questionnaires at time of enrollment in order to measure the real-world effect of offering the combination of interventions. Demographics were thus linked from annual HDSS household surveys. These surveys include annually updated, individual- (e.g., education level, employment status)

and household-level (e.g., socioeconomic status, rural vs urban residence) data. Despite a lack of detail regarding sexual risk behavior, the HDSS data provide information on several important demographics that are standardized across prior studies and have previously been found to be associated with STIs and HIV in this area.[15,24,25,29] We were also unable to assess prevalence of STI symptoms, however a previous study in this area found 75% of females with an STI were asymptomatic.[15] Additionally, concurrent HIV testing was not conducted, as linkage to HIV testing was part of the primary outcome of the randomized controlled trial. Thus, STI prevalence in this cohort cannot be stratified by HIV status, however, other studies have found a higher prevalence of curable STIs among people living with HIV than those without HIV, particularly among women.[23] Furthermore, approximately one-quarter of female participants provided urine specimens, which have a slightly lower sensitivity than vaginal swab specimens,[30] and may have led to an underestimation of STI prevalence among female participants. Finally, several participants had invalid STI test results, however, this was a small percentage of the total cohort (<2%). The use of point-of-care tests in future surveillance or clinical settings could allow for the collection of a repeat specimen if a first is found to be inadequate or does not pass an internal control.

In conclusion, we found a very high prevalence of curable STIs among adolescent and young adult men and women, which is higher than in a previous study five years ago, in a predominantly rural area with high HIV incidence in KwaZulu-Natal, South Africa. STI prevalence was higher among women than men and among those residing in urban/peri-urban areas than those residing in rural areas. Despite multiple attempts by study staff, fewer than two-thirds of participants with positive test results were able to be treated within four weeks. These results highlight the need for implementation of STI testing and

376 treatment programs in settings with both STIs and HIV, as well as the need for point-of-care STI tests to
377 allow immediate treatment for those who test positive and decrease loss to follow-up.

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Trial registration: *ClinicalTrials.gov Identifier* - NCT04532307

Data availability statement: Data are available upon request. Data can be can access and downloaded through the AHRI data repository: https://data.africacentre.ac.za. https://data.ahri.org/index.php/home. To access the licensed datasets, the applicant must agree to the terms and conditions of use by completing an Application for Access to a Licensed Dataset. This request will be reviewed by the AHRI Data Release Committee, who may decide to approve the request, to deny access to the data, or to request additional information from the applicant.

Figure Legends

Figure 1. Flow diagram of study participants.

Figure 2. Population-weighted prevalence estimates for any STI and each individual STI, by sex and age group (with 95% CI).

Supplemental Digital Content

1. Jarolimova et al_Supplemental Digital Content 1_Table S1.docx

2. Jarolimova et al_Supplemental Digital Content 2_Table S2.docx

Prevalence of curable sexually transmitted infections in a population-representative sample of young adults in a high HIV incidence area in South Africa

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Summary

Prevalence of gonorrhea, chlamydia, and trichomoniasis is high among adolescents and young adults in rural South Africa, and higher among women and those residing in urban/peri-urban areas.

Abstract

Background

Recent population-representative estimates of STI prevalence in high HIV burden areas in southern Africa are limited. We estimated the prevalence and associated factors of three STIs among adolescents and young adults (AYA) in rural South Africa.

Methods

Between March 2020-May 2021, a population-representative sample of AYA aged 16-29 were randomly selected from a Health and Demographic Surveillance Site in rural KwaZulu-Natal, South Africa for a 2x2 factorial randomized controlled trial. Participants in two intervention arms were offered baseline testing for gonorrhea, chlamydia, and trichomoniasis using GeneXpert. Prevalence estimates were weighted for participation bias, and logistic regression models were used to assess factors associated with STIs.

Results

1743 (75%) of 2323 eligible AYA enrolled in the trial. Among 863 eligible for STI testing, 814 (94%) provided specimens; median age 21.8 years, 52% female, and 71% residing in rural areas. Population-weighted prevalence estimates were 5.0% (95%CI 4.2-5.8%) for gonorrhea, 17.9% (16.5-19.3%) for chlamydia, 5.4% (4.6-6.3%) for trichomoniasis, and 23.7% (22.2-25.3%) for any STI. In multivariable models, female sex (aOR 2.24, 95%CI 1.48-3.09) and urban/peri-urban (versus rural) residence (aOR 1.48, 95%CI 1.02-2.15) were associated with STIs; recent migration was associated with lower odds of STI (aOR 0.37, 95%CI 0.15-0.89). Among those with an STI, 53 (**31.0**%) were treated within 7 days; median time to treatment was 11 days (IQR 6-77 days).

Conclusions

We identified a high prevalence of curable STIs among AYA in rural South Africa. Improved access to STI testing to enable etiologic diagnosis and rapid treatment is needed.

Keywords: gonorrhea, chlamydia, trichomoniasis, sexually transmitted infections, South Africa

INTRODUCTION

Curable sexually transmitted infections (STIs) are common worldwide, with over one million new cases of gonorrhea, chlamydia, trichomoniasis, or syphilis estimated to occur globally every day.[1] When untreated, STIs can cause significant morbidity, particularly for women, leading to complications such as pelvic inflammatory disease, ectopic pregnancy, infertility, pregnancy complications, and newborn infection.[2,3] Furthermore, STI-induced genital inflammation and genital HIV shedding can increase risks of HIV acquisition and transmission, even when the STI is asymptomatic.[4–6] The majority of STIs occur in low- and middle-income countries (LMICs), with the highest age-standardized incidence rates and greatest number of disability-adjusted life years (DALYs) lost in sub-Saharan Africa.[7] In southern Africa, there is strong epidemiologic overlap between curable STIs and HIV, particularly among adolescents and young adults, who are at highest risk for STI acquisition and have the highest HIV incidence rates.[7,8] For these populations, improved diagnosis and treatment of curable STIs is key to reducing morbidity and is an important component of multimodal HIV prevention.

Due to a lack of accessible and affordable diagnostic testing, STIs in LMICs are predominantly managed using a syndromic approach.[9] This approach misses a substantial proportion of STIs because they frequently remain asymptomatic.[10] The World Health Organization (WHO) in the global health sector strategies for HIV, viral hepatitis, and sexually transmitted infections for 2022-2030 recommends a transition from syndromic to etiologic management of STIs and calls for increased screening of priority populations, including youth.[11] The WHO has additionally recommended integration of STI care with other health services, including HIV prevention and treatment.[11] However, screening and surveillance programs remain limited, and there are few recent population-representative data on STI prevalence to inform efforts at care integration.

In South Africa, which has among the highest HIV incidence and prevalence rates worldwide,[12] STI prevalence is predicted to be high, with model-based prevalence estimates of 6.6% for gonorrhea and 14.7% for chlamydia among women and 3.5% gonorrhea and 6.0% chlamydia among men.[13] Studies have found STI prevalence as high as 42% for chlamydia and 11% for gonorrhea among adolescent girls and young women in Cape Town.[14] However, few population-representative studies of STI prevalence exist from areas of high HIV incidence in South Africa, particularly among both women and men, and previous prevalence data have not been recently updated.[15] We aimed to use STI screening among a population-representative cohort of adolescents and young adults selected from a Health and Demographic Surveillance Site (HDSS) in rural KwaZulu-Natal, South Africa[16] to provide updated STI prevalence estimates among adolescents and young adults in this setting and assess for factors associated with having an STI.

MATERIALS AND METHODS

Study setting

This study was conducted within the HDSS in uMkhanyakude district in rural KwaZulu-Natal, South Africa. Since 2000, the Africa Health Research Institute (AHRI; formerly Africa Centre for Health and Population Studies) has been conducting annual household-based surveys to collect data on births, deaths, demographics, and migration patterns. The HDSS was expanded in 2017 to cover 845 km^2 with approximately 140,000 individuals in 20,000 households.[16] The area has a high rate of unemployment (62% of adults without formal employment) and HIV prevalence of 19% among men and 40% among women aged 15-54 years.[16]

Study design

This study reports baseline data from a 2x2 factorial randomized controlled trial evaluating the acceptability, feasibility, and preliminary population-level impact of integrated sexual and reproductive health services with or without peer support on the prevalence of transmissible HIV.[17] The AHRI HDSS was used as a sampling frame to randomly select 3000 men and women aged 16-29 years, stratified by sex and area, **to be assessed for eligibility. All eligible were** approached for enrollment with a goal of **at least** 1500 eligible **and enrolled** participants. Men and women aged 16-29 years, residing in the HDSS area, willing and able to provide informed consent, and willing to be contacted at 12 months for HIV testing, were eligible to enroll in the trial. At enrollment, participants were randomized to one of four study arms: a) enhanced standard of care (referral to adolescent and youth friendly services (AYFS) comprised of clinic-based, nurse-led HIV testing with linkage to antiretroviral therapy [ART] or HIV pre-exposure prophylaxis [PrEP]), b) sexual and reproductive health (SRH; home-based self-collection of STI specimens and referral to AYFS for integrated SRH and HIV testing), c) peer support (referral to peer navigator to assess health, social, and educational needs and provide risk-informed HIV prevention and referral to AYFS),[18] or d) SRH and peer support. Participants randomized to the two SRH intervention arms were offered STI testing at study enrollment. **Sample size for this analysis was determined by the total number of participants randomized to the SRH arms and providing specimens for STI testing.**

Study procedures

Following informed consent, participants randomized to either of the two SRH arms were offered home-based STI specimen collection. For female participants, research staff described the procedure to self-collect a vaginal swab. Menstruating females provided urine specimens. Male participants were

instructed to collect a first-catch urine specimen. All participants were provided an AYFS clinic referral to receive their STI test results in 7 days. Participants were informed that if any test results return positive and they do not present to the clinic, research staff will attempt to contact them to ensure they receive treatment. STI treatment was provided according to South African national clinical guidelines **(single-dose ceftriaxone and azithromycin for gonorrhea; single-dose azithromycin or seven-day course of doxycycline for chlamydia; single-dose metronidazole for trichomoniasis).**[19] **Receipt of treatment was verified through AYFS clinic records and study documentation, participant self-report on follow-up contact, or documentation of failed contact attempts.**

Data collection

STI specimens were transported to the AHRI central laboratory in Durban. Testing for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* was conducted by real-time polymerase chain reaction by GeneXpert (Cepheid, Sunnyvale, CA, USA). Valid STI test results were recorded as 'detected' or 'not detected'. Invalid test results were recorded as 'invalid' or 'error' based on test platform output. **To minimize research procedures at enrollment to emulate real-world implementation of the interventions, study-specific questionnaires were not administered at the time of STI specimen collection.** Socio-demographic data including education (years of completed education), employment (none, part-time, full-time), marital status (married, not married, informal union), household socioeconomic status (combined household asset index), and migration history (no migration, internal migration, in-migration, external migration) were derived from linking study participants to the annual HDSS household-level survey conducted in 2019.

Statistical analysis

We summarized participants' demographic data using medians and interquartile ranges (IQR) for continuous variables and frequency counts and percentages for categorical variables. Frequency counts and percentages with 95% confidence intervals (CIs) were calculated for the prevalence estimate of each individual STI and prevalence of any STI. To account for participation bias, we calculated weighted prevalence estimates to account for the stratified sample design, calculated as the inverse probability of study participation in strata defined by age group and sex. We used logistic regression to estimate the odds ratios and 95% confidence intervals for factors associated with the presence of any curable STI **and factors associated with treatment** in univariate and multivariable models. Age and sex were included a priori in the multivariable model; other factors with $p<0.2$ in univariate logistic regression were also included in the multivariable model; **for treatment completion, age- and sex-adjusted models were used.** Missing data were not imputed. All reported p-values were two-tailed; $p<0.05$ was considered statistically significant. Analyses were conducted using Stata version 16.1 (Stata Corp, College Station, TX, USA).

Ethical considerations

The study protocol was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC/00000473/2019), the University College of London Research Ethics Committee (5672/003), and the Mass General Brigham Institutional Review Board (2021P002574). Written informed consent was obtained from all participants aged ≥18 years; verbal assent with written informed consent from a parent or guardian was obtained for all participants aged 16-17 years.

Patient and public involvement

The peer support and sexual health intervention was co-created with young people in uMkhanyakude district and delivered by peers. Young people and the AHRI community advisory board were involved from research inception through to analysis. Study findings were shared with the research participants and their communities, as well as health officials and program implementers.

RESULTS

Between 4 March 2020 and 24 May 2021, **3000 adolescents and young adults were assessed for eligibility**; 2323 **were found to be** eligible **and** were invited to participate, of whom 1743 (75%) enrolled **in the randomized controlled trial** (**Figure 1**). Of these, 863 were randomized to the two study arms offering STI testing, and 814 (94%) accepted testing and provided specimens. **There was no difference by sex between those who consented and did not consent to STI testing (p=0.270). Among 427 female participants who provided specimens, 116/427 (27.2%) provided urine specimens; the remainder (311/427, 72.8%) provided self-collected vaginal swab specimens.** Among those tested for STIs, 52% were female, median age was 21.8 [IQR 18.8-25.6], and 29% resided in urban or peri-urban areas. Additional participant demographics are presented in **Table 1**.

Among the 814 specimens provided by participants, 14/814 (1.7%) had results of 'invalid' or 'error' for gonorrhea and chlamydia; of these, three (0.4%) also had invalid results for trichomoniasis. Of 800 participants with valid test results for all three STIs, 179 (22.4%) tested positive for at least one STI. Of these, 147 (82.1%) were mono-infections, while 32 (17.9%) participants were co-infected with more than one STI, including three participants (1.7%, all female) infected with three STIs concurrently (**Supplemental Digital Content Table S1**). Population-weighted prevalence estimates for any STI and each STI individually, by sex and age group, are shown in **Figure 2 and**

Supplemental Digital Content Table S2, demonstrating 30.2% prevalence of any STI among female participants and 17.3% prevalence among male participants.

In unadjusted analyses, STIs were more common among women, among those aged over 20 years than 15-19 years, and those with urban/peri-urban compared to rural residence. STIs were less common among those with unknown employment or marital status (who are also more likely to be <18 years old), and those with migration in the preceding two years. In adjusted analyses, STIs remained more than twice as likely among women than men (aOR 2.14, 95% CI 1.48-3.09, p=0.0001), more likely among those residing in urban/peri-urban areas (aOR 1.48, 95% CI 1.02-2.15, p=0.041; **Table 2**), and less likely among those with any recent migration (aOR 0.37, 95%CI 0.15-0.89, p=0.026).

Among participants with a positive STI result and complete follow-up data, 53/17**1** (**31.0**%) were treated within 7 days of specimen collection. Median time to treatment overall was 11 days (interquartile range, 6-77 days) and did not differ by sex or age group (data not shown). Among 73 participants not treated within 4 weeks of specimen collection, 51 (69.9%) could not be reached sooner and were treated later, 11 (15.1%) could not be contacted after multiple attempts, 6 (8.2%) had migrated outside of the area, and 5 (6.8%) refused treatment **(reasons for refusal not provided). In analyses adjusted for age and sex, urban/peri-urban residence was associated with lower likelihood of treatment within 7 days compared to rural residence (aOR 0.42, 95% CI 0.20-0.87, p=0.019), while being in the highest socioeconomic tertile was associated with higher likelihood of treatment within 7 days (aOR 3.12, 95% CI 1.36-7.16, p=0.0032) (Table 3).**

DISCUSSION

We found a very high prevalence of curable STIs among adolescents and young adults in a predominantly rural area of KwaZulu-Natal, South Africa. This study confirms the acceptability of home-based STI specimen collection among adolescents and young adults, as over 90% of study participants who were offered STI testing provided specimens. STI prevalence was significantly higher among female than male participants overall, even when adjusted for age and other demographic factors. The sex difference in prevalence was most pronounced for trichomoniasis and chlamydia; prevalence of gonorrhea was similar between males and females. Participants residing in urban/peri-urban areas were more likely to have an STI than those residing in rural areas. Despite multiple contact attempts by study staff, only one out of three participants who tested positive for an STI were treated within 7 days. Difficulties in follow-up contact compounded by a low (6.8%) treatment refusal indicates need for a robust tracking system and strategies to maximize treatment reach, **and underscores the need for point-of-care STI tests to enable same-day treatment and decrease loss to follow-up.**

In this cohort, women had a higher STI prevalence than men overall, particularly trichomoniasis and chlamydia. These results mirror both national-level estimates of STI prevalence in South Africa and previous studies among adolescents and young adults in rural KwaZulu-Natal; in both cases, chlamydia prevalence was over twice as high among women than men.[13,15] Young women in South Africa may face higher risk of STI acquisition than age-matched male counterparts due to earlier age of sexual debut,[15] higher rate of age-disparate relationships,[20] and lesser ability to navigate safe sex. Gender inequalities contribute to the higher rates of STIs among women than men in many parts of the world, and adolescent girls and young women have been identified as priority populations for STI programming by the WHO.[11] Furthermore, since STIs are more often asymptomatic in women than men, fewer women may receive treatment through syndromic management pathways, leading to **longer**

duration of infection **and thus detection of a greater prevalence of active infections among women. However, we found that among those aged 20-24 years, men had a higher prevalence of gonorrhea and chlamydia than women. A previous study in this setting also found a higher prevalence of chlamydia among men than women in this age group (12.2% vs 10.6%, respectively).**[15] **Reasons for this finding are not clear, though may relate to later sexual debut among men in this setting.**[15] **Differences in sexual networks, transactional sex, or migration may also contribute to this finding, however, due to limited data on young men, it is difficult to know which factors account for it. This is, however, an important observation that requires further study.**

We found a substantially higher prevalence of chlamydia and gonorrhea in this cohort than in a previous study conducted in the same geographic area in 2016-2017.[15] Weighted prevalence estimates for chlamydia were 8.1% in the previous study and 17.9% in the current study, and for gonorrhea 1.7% in the prior study and 4.6% in the current study. The previous study enrolled adolescents and young adults up to age 25 while the current study enrolled adults up to age 29, however, prevalence estimates were higher in the current study within each individual age group and overall, with the exception of trichomoniasis in men. The high STI prevalence estimates for women in the current study mirror emerging data on STI prevalence among women enrolled in PrEP trials and women living with HIV in Southern Africa.[21–23] The difference in prevalence estimates between this and the previous study may thus signal an increase in STIs over time in this area, supporting an urgent need for greater access to sexual health services for this population. Furthermore, non-pharmaceutical interventions adopted during the COVID-19 pandemic, such as national lockdowns, could have impacted transmission within sexual networks, contributing to the higher STI prevalence found in this study.

We additionally found that young men and women residing in urban or peri-urban areas were more likely to have an STI than those residing in rural areas, even after adjustment for other demographic factors, including age, employment status, and migration history. A recent study evaluating transmissible HIV among adolescent girls and young women exposed to the PEPFAR-supported DREAMS intervention, conducted at the same study site, similarly found that urban/peri-urban residence was associated with transmissible HIV.[24] HIV incidence over time was higher in urban and peri-urban areas of the study site in a separate study.[25] Despite the predominantly rural nature of the AHRI HDSS area, there are several informal peri-urban settlements and an urban township with high population density.[26] Potential differences between the urban/peri-urban and rural participants, such as differences in socioeconomic status, substance use, transactional sex, gender-based violence, patterns of sexual behavior, or migration history, may explain the difference in STI prevalence. Additionally, greater movement of people through the urban areas may contribute to higher turnover of partners and lead to more introduction of infections into the community, however, more study of potential drivers is needed. We additionally found that adolescents and young adults reporting recent migration had lower odds of having an STI than those who had not migrated in the same time period. While this finding could reflect higher STI transmission in local sexual networks, the small number of participants with recent migration events makes it difficult to draw conclusions from this finding. Additional data on sexual risk behavior obtained at the endpoint of the trial may help elucidate the reasons behind these observed differences.

Despite the robust infrastructure of the randomized trial and the long-standing experience of AHRI conducting research that is strongly linked with public sector health clinics in this area, less than half of the participants with STIs were able to be treated within 7 days, and less than two-thirds within 4 weeks.

Those living in urban areas were less likely to be treated within 7 days, possibly due to higher rate of employment or difficulty tracking participants. Those in the highest socioeconomic tertile were more likely to be treated within 7 days, which may either reflect greater access to technology such as mobile phones for contact by study staff, or easier access to clinic for treatment. Diagnostic testing for STIs remains inaccessible in most resource-limited settings, due to high costs and need for laboratory infrastructure; when STI testing is available in such settings, it is often restricted to centralized laboratories. For this study, STI specimens were transported from the rural study site to a centralized research laboratory in Durban (approximately 230 kilometers away), resulting in an extended time from specimen collection to test result. Loss to follow-up increases with extensions in test turn-around-time, and delays in treatment lead to the potential for ongoing transmission and increased risk for sequelae of untreated infection. A study assessing community-based STI testing for adolescents and young adults in Zimbabwe found that even with an expected 90-minute time to result, only 67% of those with positive test results were treated.[27] These findings highlight the urgency of development and implementation of affordable point-of-care STI diagnostics that meet WHO REASSURED criteria (Real-time connectivity, Ease of specimen collection, Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment free or simple and Environmentally friendly, Deliverable to end-users) [28] and enable immediate treatment and partner notification services.

Our assessment of factors associated with STIs was limited by the scope of demographic data available and lack of contemporaneous data on symptoms and sexual risk behavior. The trial did not include study-specific questionnaires at time of enrollment in order to measure the real-world effect of offering the combination of interventions. Demographics were thus linked from annual HDSS household surveys. These surveys include annually updated, individual- (e.g., education level, employment status)

and household-level (e.g., socioeconomic status, rural vs urban residence) data. Despite a lack of detail regarding sexual risk behavior, the HDSS data provide information on several important demographics that are standardized across prior studies and have previously been found to be associated with STIs and HIV in this area.[15,24,25,29] **We were also unable to assess prevalence of STI symptoms, however a previous study in this area found 75% of females with an STI were asymptomatic.[15] Additionally, concurrent HIV testing was not conducted, as linkage to HIV testing was part of the primary outcome of the randomized controlled trial. Thus, STI prevalence in this cohort cannot be stratified by HIV status, however, other studies have found a higher prevalence of curable STIs among people living with HIV than those without HIV, particularly among women.[23] Furthermore, approximately one-quarter of female participants provided urine specimens, which have a slightly lower sensitivity than vaginal swab specimens,[30] and may have led to an underestimation of STI prevalence among female participants.** Finally, several participants had invalid STI test results, however, this was a small percentage of the total cohort (<2%). The use of point-of-care tests in future surveillance or clinical settings could allow for the collection of a repeat specimen if a first is found to be inadequate or does not pass an internal control.

In conclusion, we found a very high prevalence of curable STIs among adolescent and young adult men and women, which is higher than in a previous study five years ago, in a predominantly rural area with high HIV incidence in KwaZulu-Natal, South Africa. STI prevalence was higher among women than men and among those residing in urban/peri-urban areas than those residing in rural areas. Despite multiple attempts by study staff, fewer than two-thirds of participants with positive test results were able to be treated within four weeks. These results highlight the need for implementation of STI testing and

376 treatment programs in settings with both STIs and HIV, as well as the need for point-of-care STI tests to
377 allow immediate treatment for those who test positive and decrease loss to follow-up.

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Trial registration: *ClinicalTrials.gov Identifier* - NCT04532307

Data availability statement: Data are available upon request. Data can be can access and downloaded through the AHRI data repository: https://data.africacentre.ac.za. https://data.ahri.org/index.php/home. To access the licensed datasets, the applicant must agree to the terms and conditions of use by completing an Application for Access to a Licensed Dataset. This request will be reviewed by the AHRI Data Release Committee, who may decide to approve the request, to deny access to the data, or to request additional information from the applicant.

Figure Legends

Figure 1. Flow diagram of study participants.

Figure 2. Population-weighted prevalence estimates for any STI and each individual STI, by sex and age group (with 95% CI).

Supplemental Digital Content

1. Jarolimova et al_Supplemental Digital Content 1_Table S1.docx

2. Jarolimova et al_Supplemental Digital Content 2_Table S2.docx

Figure 1

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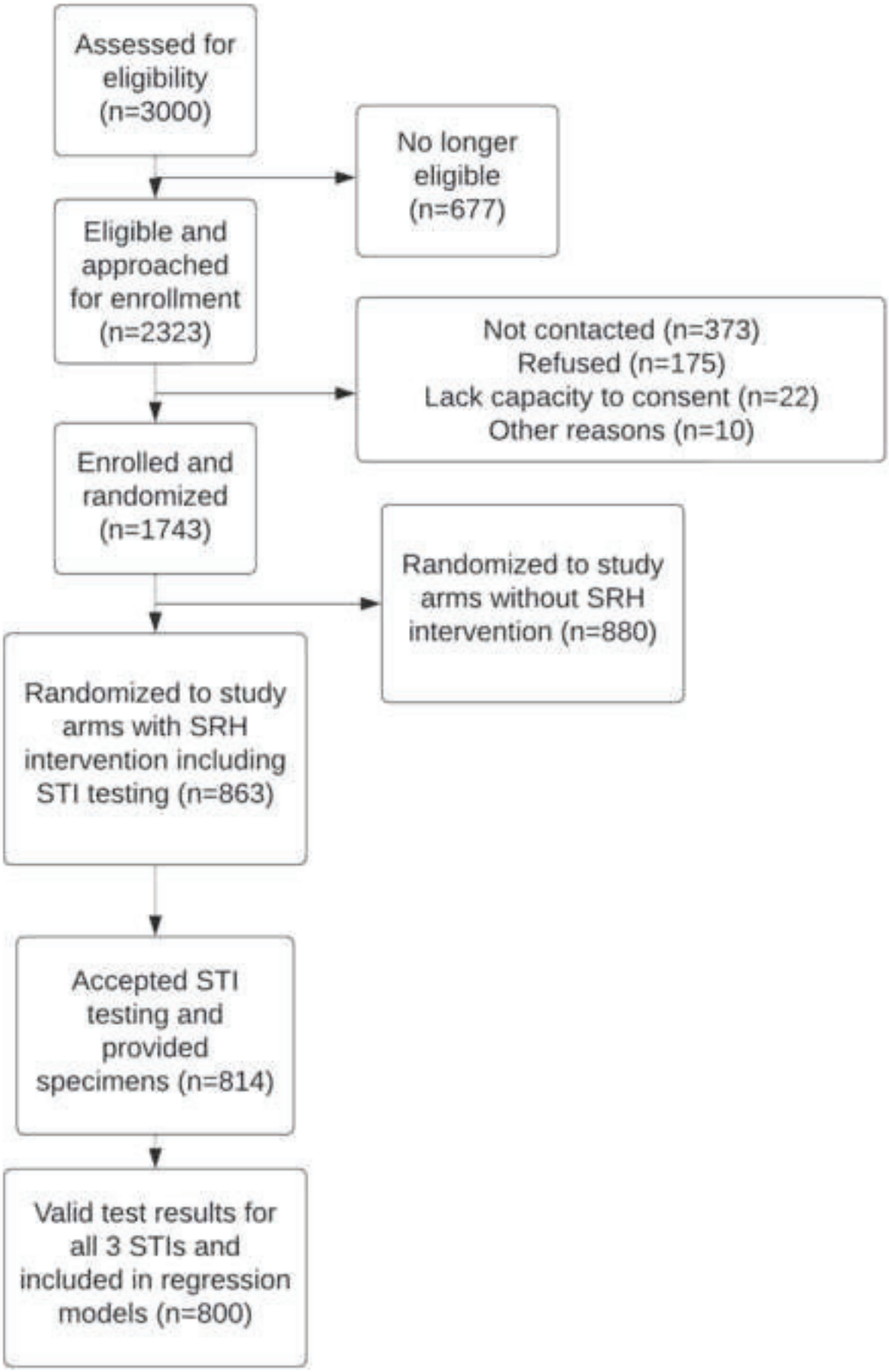

Figure 2

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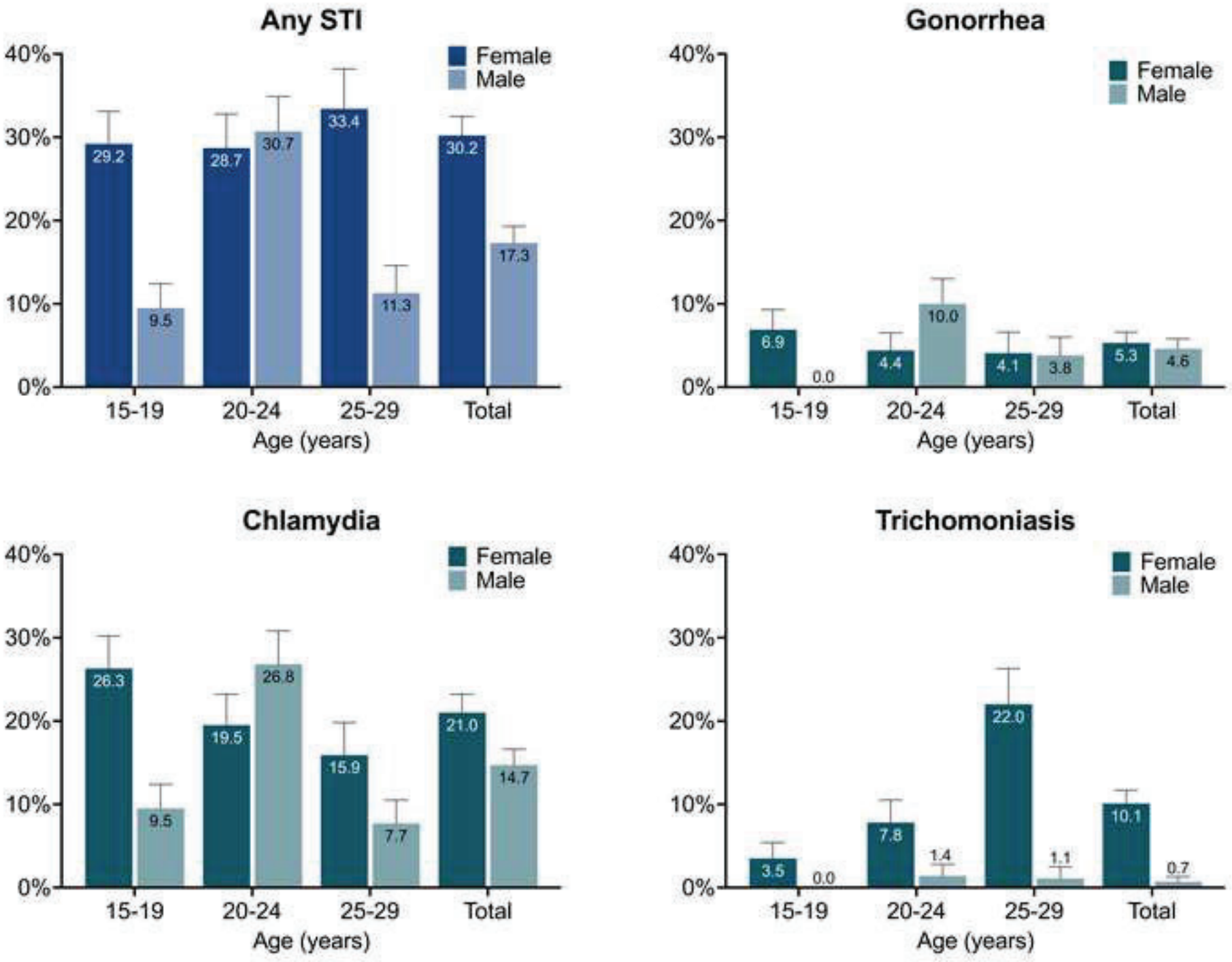

Table 1. Demographic characteristics of participants, by sex

	Female, n=427 n (%)	Male, n=387 n (%)	Total, n=814 n (%)
Age, median [IQR]	22.5 [18.9-25.8]	21.2 [18.8-25.3]	21.8 [18.8-25.6]
Age category			
16-19	142 (33)	151 (39)	293 (36)
20-24	148 (35)	133 (34)	281 (35)
25-29	137 (32)	103 (27)	240 (29)
Highest level of education			
Some primary	13 (3)	14 (4)	27 (3)
Some secondary	183 (43)	211 (55)	394 (48)
Matric or above	178 (42)	116 (30)	294 (36)
Missing	53 (12)	46 (12)	99 (12)
Employment[a]			
Employed	25 (6)	38 (10)	63 (8)
Not employed	256 (60)	200 (52)	456 (56)
Missing	146 (34)	149 (39)	295 (36)
Marital status[b]			
Not married	98 (23)	123 (32)	221 (27)
Married or informal union	216 (51)	131 (34)	347 (43)
Missing	113 (26)	133 (34)	246 (30)
Socioeconomic status- tertiles			
Low	145 (34)	114 (29)	259 (32)
Middle	140 (33)	121 (31)	261 (32)
High	123 (29)	133 (34)	256 (31)
Missing	19 (4)	19 (5)	38 (5)
Residence			
Rural	296 (69)	281 (73)	577 (71)
Urban or Peri-urban	130 (30)	105 (27)	235 (29)
Missing	1 (0.2)	1 (0.2)	2 (0.25)
Migration in preceding 2 years[c]			
Never	368 (86)	331 (86)	699 (86)
Internal Migration	2 (0.5)	3 (1)	5 (1)
External Migration	27 (6)	26 (7)	53 (7)
Missing	30 (7)	27 (7)	57 (7)

[a]'Employed' = full-time and part-time employed. Employment not reported for majority of participants ≤18yo.
[b]Only 5 participants reported as 'married'. Marital status not reported for majority of participants ≤18yo.
[c]In the 2 years preceding date of STI testing. Internal migration is migration within the HDSS area. External migration includes participants who migrated into or outside of the HDSS area .

Table 2. Factors associated with diagnosis of any STI (chlamydia, gonorrhea, or trichomoniasis)

Demographic factor	Number with any curable STI n/N (%)	Unadjusted OR (95% CI)	Age- and Sex-Adjusted OR (95% CI)	aOR, multivariable analysis, n=743
Age group, n=800		p=0.004	p=0.0062	p=0.08
16-19	48/291 (16.5)	1	1	1
20-24	76/272 (27.9)	1.96 (1.31-2.95)	1.96 (1.29-2.95)	1.72 (0.87-3.40)
25-29	55/237 (23.2)	1.53 (0.99- 2.36)	1.45 (0.94-2.25)	1.10 (0.53-2.30)
Sex, n=800		p<0.0001	p<0.0001	**p=0.0001**
Male	60/386 (15.5)	1	1	**1**
Female	119/414 (28.7)	2.19 (1.55-3.10)	2.18 (1.54-3.10)	**2.14 (1.48-3.09)**
Education completed, n=704		p=0.49	p=0.74	
Some primary	7/27 (25.9)	1	1	
Some secondary	80/390 (20.5)	0.74 (0.30-1.80)	0.71 (0.28-1.76)	
Matric or above	69/287 (24.0)	0.90 (0.37-2.23)	0.69 (0.26-1.81)	
Employment, n=800		p=0.024	p=0.12	
Unemployed	107/444 (24.1)	1	1	
Employed[a]	20/63 (31.8)	1.46 (0.83-2.60)	1.84 (1.01-3.37)	
Unknown	52/293 (17.8)	0.68 (0.47-0.98)	1.30 (0.61-2.80)	
Marital status, n=800		p=0.013	p=0.90	p=0.93
Not married	52/218 (23.9)	1	1	1
Married or informal union	88/339 (26.0)	1.12 (0.75-1.66)	1.01 (0.65-1.57)	1.07 (0.68-1.68)
Unknown	39/243 (16.1)	0.61 (0.38-0.97)	0.86 (0.43-1.70)	0.93 (0.46-1.88)
Migration in past 2yrs, n=745[b]		p=0.013	p=0.017	**p=0.026**
Never	164/688 (23.8)	1	1	**1**
Any migration	6/57 (10.5)	0.38 (0.16-0.89)	0.34 (0.14-0.82)	**0.37 (0.15-0.89)**
Residence, n=798		p=0.0022	p=0.0069	**p=0.041**
Rural	111/569 (19.5)	1	1	**1**
Urban or Peri-urban	68/229 (29.7)	1.74 (1.23-2.48)	1.64 (1.15-2.36)	**1.48 (1.02-2.15)**
SE status tertile, n=764		p=0.36	p=0.61	
Low	64/255 (25.1)	1	1	
Medium	51/254 (20.1)	0.75 (0.49-1.14)	0.81 (0.53-1.24)	
High	54/255 (21.2)	0.80 (0.53-1.21)	0.89 (0.58-1.36)	

[a]Includes full-time and part time employed. [b]Any migration includes internal and external migration. SE, socioeconomic.

Table 3. Factors associated with STI treatment (within 7 days), n=171

	Treated within 7 days, n/N (%)	Unadjusted OR (95% CI)	Age- and Sex-Adjusted OR (95% CI)
Age group		p=0.32	p=0.33
15-19	13/48 (27)	1	1
20-24	20/72 (28)	1.04 (0.46-2.35)	1.09 (0.47-2.53)
25-29	20/51 (39)	1.74 (0.74-4.06)	1.78 (0.76-4.17)
Sex		p=0.56	p=0.59
Male	16/57 (28)	1	1
Female	37/114 (32)	1.23 (0.61-2.48)	1.22 (0.59-2.51)
Education completed, n=149		p=0.057	p=0.18
Primary or less	1/7 (14)	1	1
Some secondary	19/77 (25)	1.97 (0.22-17.37)	2.15 (0.24-19.21)
Matric or above	27/65 (42)	4.26 (0.48-37.48)	4.69 (0.49-44.67)
Employment		p=0.46	p=0.44
Unemployed	35/101 (35)	1	1
Employed[a]	5/20 (25)	0.63 (0.21-1.87)	0.54 (0.17-1.69)
Unknown	13/50 (26)	0.66 (0.31-1.41)	0.57 (0.14-2.36)
Marital status		p=0.016	p=0.053
Not married	9/49 (18)	1	1
Married or informal union	34/83 (41)	3.08 (1.32-7.18)	3.06 (1.22-7.67)
Unknown	10/39 (26)	1.53 (0.55-4.25)	1.12 (0.27-4.73)
Migration in past 2yrs, n=167		p=0.93	p=0.83
Never	51/161 (32)	1	1
Any migration[b]	2/6 (33)	1.08 (0.19-6.08)	1.22 (0.21-7.18)
Residence		p=0.026	**p=0.019**
Rural	39/105 (37)	1	**1**
Urban or Peri-urban	14/66 (21)	0.46 (0.22-0.93)	**0.42 (0.20-0.87)**
SE status tertile, n=163		p=0.0086	**p=0.0032**
Low	17/61 (28)	1	**1**
Medium	10/48 (21)	0.68 (0.28-1.66)	**0.76 (0.30-1.89)**
High	26/54 (48)	2.40 (1.11-5.21)	**3.12 (1.36-7.16)**

[a]Includes full-time and part time employment. [b]Any migration includes internal and external migration. SE, socioeconomic.