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Microbiological sentinel surveillance of sexually-transmitted infection syndromes in South Africa, 2021–2024

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Summary

Syndromic management remains the mainstay of sexually transmitted infection (STI) management in South Africa. Surveillance of pathogens or aetiologies associated with the main STI syndromes – male urethritis syndrome (MUS), vaginal discharge syndrome (VDS), and genital ulcer syndrome (GUS) – is recommended. We conducted surveillance at sentinel sites from 2021–2024 to monitor trends in the aetiological causes of the main STI syndromes, validate the recommended treatment algorithms and monitor *Neisseria gonorrhoeae* (NG) antimicrobial resistance. During the surveillance period, consecutive, symptomatic STI service attendees, aged 18 years or older and presenting at any one of three primary healthcare clinics located in South Africa's Gauteng, KwaZulu-Natal, or Western Cape provinces, were enrolled. Demographic, behavioural and clinical information was collected from eligible and consenting attendees using an electronic surveillance officer-administered questionnaire. Attendees provided genital specimens for laboratory testing. Most male attendees with MUS had one or more STIs (93.2%) detected. *Neisseria gonorrhoeae* was the most frequently detected STI pathogen (83.1%), followed by *Chlamydia trachomatis* (CT) (21.1%), *Mycoplasma genitalium* (MG) (4.1%), and *Trichomonas vaginalis* (TV) (2.5%). *Neisseria gonorrhoeae* isolates remained sensitive to ceftriaxone, cefixime and gentamicin. However, azithromycin-resistant isolates were detected but did not exceed 5% of those tested – the recommended threshold for guideline change. For females with VDS, 37.2% had an STI pathogen detected. *Chlamydia trachomatis* was the most frequently detected STI pathogen at 17.8%, followed by TV, NG and MG at 13.9%, 13.5% and 5.4%, respectively. Bacterial vaginosis (BV) was the most common non-STI aetiology associated with VDS, with 58.2% of females tested having BV alone or in combination with an STI or candida infection. Almost 20% of female attendees with VDS had no pathogens or aetiologies associated with their discharge. Most attendees with GUS had one or more pathogens detected (71.8%). The most common aetiology associated with genital ulcers was herpes simplex virus type 2 (HSV-2) at 43.6%, followed by *Treponema pallidum* (which causes syphilis) at 30.2%, lymphogranuloma venereum (LGV) at 0.3% and herpes simplex type 1 (HSV-1) at 0.5%. Across all syndromes, there was no change in the relative prevalences of the aetiologies/pathogens over the surveillance period. Strengthening STI prevention, diagnosis and treatment through better information, education and communication on STIs, partner management, and the implementation of point-of-care diagnostics and asymptomatic screening is recommended.

Introduction

Sexually transmitted infections (STIs) remain a significant public health challenge. More than 30 different bacterial, viral, and parasitic pathogens are known to be sexually transmitted.[1] Three bacterial pathogens and one parasitic pathogen – *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), *Treponema pallidum* (TP), and *Trichomonas vaginalis* (TV), all of which are curable – and five viral pathogens: herpes simplex virus types 1 and 2 (HSV-1/HSV-2), hepatitis B virus, human papillomavirus, and HIV – cause the largest burden of STIs globally.[1] In 2020, among people aged 15–49 years , there were an estimated 374 million new infections with one or more of the curable bacterial (three) and parasitic (one) pathogens.[1] In 2016 and 2022, 490 million and 254 million people lived with herpes and hepatitis B, respectively.[1]

Untreated STIs can cause complications such as pelvic inflammatory disease in women, genital tract scarring resulting in sub-fertility, pregnancy complications including vertical transmission, cancer, and an increased risk of

HIV acquisition and onward transmission. Recommended interventions for the prevention, care and treatment of STIs include risk reduction counselling, condom use, male circumcision, early detection and treatment, partner management (through notification and treatment) and, more recently, doxycycline post-exposure prophylaxis.[1]

In South Africa, syndromic management has been the mainstay of STI management since the 1990s.[2,3] Using this approach, individuals reporting symptoms and/or showing signs of STIs are treated for the most likely pathogens without attempting to identify the specific pathogen. This allows for the early treatment of individuals likely to have STIs in the face of limited laboratory capacity for aetiological diagnosis and an increased risk of initial loss to follow-up. However, syndromic management has been associated with both over- and under-treatment of individuals.[3] Over-treatment occurs when individuals with non-STI causes of genital symptoms and signs are treated for STIs and are unnecessarily exposed to antibiotics, potentially fuelling antimicrobial resistance. Under-treatment occurs when individuals with asymptomatic or extra-genital STIs go untreated, leading to continued transmission in communities and possible complications. Epidemiological studies have shown that 53–60% of STIs in sub-Saharan Africa may be asymptomatic, depending on the pathogen.[4]

To ensure that current syndromic management algorithms continue to cover the most common causes of STI syndromes and to estimate the extent of over-treatment associated with the algorithms, aetiological surveillance for STIs among people attending STI services is recommended. We determined the prevalence of STI-associated pathogens among symptomatic males and females attending STI services at sentinel sites from 1st January 2021 to 31st December 2024.

Methods

Setting

The STI Reference Laboratory at the Centre for HIV and STIs of the National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service, has conducted aetiological surveillance of STIs at sentinel sites since 2005. The main objectives of this surveillance are to i) monitor trends in aetiological causes of the main STI syndromes – male urethritis syndrome (MUS), vaginal discharge syndrome (VDS) and genital ulcer disease (GUS); ii) validate the recommended treatment algorithms and regimens to ensure they continue to cover the most common causative STI pathogens for each syndrome; and iii) monitor NG antimicrobial resistance. Table 1 shows the recommended syndromic management regimens used during the surveillance period.[5] During this period, surveillance was conducted at three primary healthcare clinics (PHCs) located in Gauteng, KwaZulu-Natal and Western Cape (one in each province). These three sites were selected because they received at least 25 MUS clients per month, had space available for the surveillance officers to work from and could readily ship samples to the NICD for NG culturing. Each site aimed to enrol 150 males with MUS, 100 females with VDS and 100 individuals with GUS per site in a calendar year.

Table 1. Syndromic management regimens of sexually transmitted infections, South Africa, 2021–2024.[5,6]

Syndrome	Categories	Drug treatment
Male urethritis syndrome (MUS)	All	Single dose ceftriaxone 250mg IM and Single dose of azithromycin 1g OR Single dose azithromycin 2g (for those with penicillin allergy)
	If the partner has VDS	Add single dose metronidazole 2g.
Vaginal discharge syndrome (VDS)	Not sexually active in the preceding 3 months	Single dose metronidazole 2g.
	<25 years-of-age or sexually active	Single dose ceftriaxone 250mg IM and Single dose of azithromycin 1g and Single dose metronidazole 2g
	If discharge is itchy or curd-like or vulva is inflamed (suggestive of candidiasis)	Single dose clotrimazole vaginal pessary 500mg inserted at night OR Single dose clotrimazole vaginal cream, inserted with applicator, 12 hourly for 7 days. If the skin of the vulva inflamed or itchy, also give clotrimazole topical cream, apply 12 hourly for 7 days.
Genital ulcer syndrome (GUS)	Not sexually active in the preceding 3 months	Acyclovir 400mg 8 hourly for 7 days if living with HIV or pregnant
	Sexually active – no bubo	Single dose benzathine benzylpenicillin (BPG) 2.4MU IM In case of allergy or if BPG is unavailable, give instead doxycycline 100 mg twice daily for 14 days OR amoxicillin 1g 8 hourly and probenecid 250mg 8 hourly for 14 days if pregnant/ breastfeeding Add acyclovir 400mg 8 hourly for 7 days if living with HIV or pregnant
	Sexually active – with bubo	As for sexually active with no bubo, add azithromycin 1g at the initial visit and repeat azithromycin 1g weekly for 2 weeks.

Design

This was a cross-sectional study in which consecutive cisgender male and cisgender female STI service attendees presenting with MUS, VDS or GUS and aged 18 years or older were enrolled at one of the three sites.

Data collection

During the surveillance period, primary-care nurses referred symptomatic STI service attendees to surveillance officers stationed at the sentinel sites during regular clinic operating hours for an eligibility assessment and informed consent procedures. Eligible and consenting cisgender male and cisgender female attendees were enrolled, and demographic, behavioural and clinical information was collected using an electronic, surveillance officer-administered questionnaire and captured directly into a study-specific REDCap® database. Demographic and behavioural variables included age, sex, sexual orientation, age at first sex, number of sexual partners in the preceding three months, exposure to vaginal, oral or receptive anal sex, condom use at last sexual encounter, having sexual intercourse with a non-regular sexual partner in the preceding three months, and having sexual partners living outside the attendees' province or country in the preceding three months. Clinical variables included the clinical syndrome(s) diagnosed on the day of enrolment, history of STI syndromes in the preceding 12 months, non-resolution of STI symptoms in the preceding three months, referral from another STI treatment provider, knowledge of HIV status, date of most recent HIV status and the attendees' self-reported HIV status. Male attendees were asked about circumcision and the circumcision method, if applicable. Circumcision status was confirmed on genital examination. Attendees were asked to provide genital specimens – urethral, cervical, vaginal, and ulcer swabs – for those with MUS, VDS and GUS, respectively. Attendees each provided one 10ml venous blood specimen for laboratory testing.

Laboratory procedures

DNA was extracted from the genital swabs and tested using a validated in-house real-time multiplex PCR assay on the RotorGene platform (Qiagen, Hilden, Germany) or QuantStudio™ 5 System (Applied Biosystems, Foster City, California, USA) to detect the presence of the following STI pathogens: NG, CT, TV, and *Mycoplasma genitalium* (MG) from urethral and endocervical swab specimens; and HSV-1 and HSV-2, TP, *Haemophilus ducreyi* (HD), CT, and L1, L2 and L3 serovars (LGV) from genital ulcer swab specimens. HSV-1 and HSV-2 subtyping was performed using a commercial PCR assay (Sacace Biotechnologies, Como, Italy). Microscopy was used to detect bacterial vaginosis (BV) and vaginal candidiasis from vaginal swab smears, and *Klebsiella granulomatas* [KG- the cause of granuloma inguinale (GI*)* from ulcer swabs]. *Treponema pallidum* antibodies (TPAb) were detected using ARCHITECT i1000SR immunoassay analyser (Abbott Laboratories, Chicago Illinois, USA). Specimens reactive to the Syphilis TP assay (indicating past, recent or active infection) were tested using the Immutrep® RPR assay (Omega Diagnostics Ltd, Alva, UK) or BD Macro-Vue™ RPR (Becton, Dickinson and Company, Franklin Lakes, New Jersey, USA) to determine RPR seropositivity. HSV-2 seropositivity was determined using the Focus HerpeSelect® 2 ELISA IgG assay (Focus Diagnostics, Cypress, CA, USA). HIV and hepatitis B surface antigen (HBsAg) samples were processed using the ARCHITECT i1000SR immunoassay analyser (Abbott Laboratories, Chicago Illinois, USA).

Data management and analysis

The data were exported to Stata® (Stata Corporation, College Station, Texas) version 18.5 for analysis. Descriptive statistics were used to describe enrolled attendees overall and by year of enrolment.

Frequencies and percentages were used to describe attendees with respect to categorical variables, while medians and interquartile ranges were used to describe attendees with respect to continuous variables. Frequencies and percentages were also used to describe the prevalence of different STI pathogens associated with MUS, VDS and GUS, overall and by year of enrolment. Appropriate tables and graphs were used to visualise the data. The X^2 test and K-test for equality of medians were used to test the hypothesis that attendee characteristics or STI prevalence differed by year over the surveillance period, while the X^2 test for trend was used to test for a linear trend when differences by year were observed. In the analyses of pathogens and aetiologies associated with GUS, a new HSV-2 ulcer was defined as one where the ulcer PCR result was positive for HSV-2 while the serology result was negative for HSV-2. A new syphilitic ulcer was one where the ulcer PCR result was positive for TP while the serology results were negative for TP antibodies. Both represent newly acquired infections. The expected sample size was 150 male attendees with MUS per site, 100 female attendees with VDS per site and 100 attendees with GUS per site. These sample sizes were calculated to measure NG prevalence of 70–80% among males with MUS and at least 100 viable isolates for antimicrobial resistance testing, NG prevalence of 12–22% among females with VDS, and ulcer-derived herpes simplex virus prevalence of 60–70% among attendees with GUS, assuming an a-level of 0.05 and a power of 80%.

Ethical considerations

Approvals to undertake surveillance activities were obtained from the relevant provincial and district-level health departments. The protocol was approved by the University of the Witwatersrand Human Subjects Research Ethics Committee (WITS HREC Protocol number M220854) with reciprocal approvals by the University of Cape Town and University of KwaZulu-Natal ethics Committees. Written informed consent was obtained from eligible and consenting attendees before administering the questionnaire and specimen collection. Participants were informed that participation was voluntary and that they could withdraw consent at any time without consequence. To protect the privacy of participants, the surveillance was anonymous and unlinked until 2022, becoming anonymous and linked from 2023 onwards. From 2021 to 2022, no identifying information or contact details were collected, and all materials, questionnaires and specimens were identified and linked through a unique study number. From 2023 to 2024, national ID or passport numbers and contact information were collected to allow follow-up if needed. Identifying information was stored separately from test data, with only surveillance officers having access to the data. Attendees who wanted to be tested for HIV and those who self-reported an unknown or negative HIV status were referred to clinic staff for routine HIV counselling and testing. As syndromic management of STIs is standard of care, laboratory results were not used for management and were not returned to participating attendees. To ensure participant safety and validity of data collected, surveillance officers received annual protocol and sample collection training.

Results

During 2021–2024, 3 265 attendees were enrolled in the surveillance. The majority of those enrolled were male (2 329; 71.3%). The median age of all attendees was 30 years (IQR 25–37 years), with 18.9% aged <25 years. Almost all attendees were Black African (3 224; 98.7%) and self-reported heterosexual orientation (3 251; 99.6%).

The majority of attendees were enrolled at the Gauteng site (1 386; 42.5%), followed by the KwaZulu-Natal site (1 296; 39.7%), with the lowest number from the Western Cape site. Significant proportions of attendees reported high-risk sexual behaviours, such as having sex with a casual/non-regular sexual partner in the preceding three months (1 111, 34.0%), having two or more sexual partners in the preceding three months (1 277; 39.1%), and having sex with someone living in a different province (372; 11.0%) or another country (322; 9.9%) in the preceding three months. Almost 20% (576) reported being treated for at least one STI syndrome in the preceding 12 months. The majority of attendees knew their HIV status (3 088/3 264, 94.6%), with 20.6% (634/3 088) reporting that they were living with HIV. Of those self-reporting as living with HIV, 88% (557/633) reported ever taking ARVs, with 98.4% (548/557) taking ARVs in the preceding three days. Most male attendees were circumcised (1 591/2 316; 68.7%) with almost two-thirds of those having been circumcised medically (1 015/1 588; 63.9%) (Table 2). The proportion of attendees aged <25 years declined over time (X^2 test for linear trend $p<0.001$), as did the proportion who had an age of first sex <15 years of age (X^2 test for linear trend $p<0.001$) and the proportion of attendees who reported sex with a non-regular sexual partner in the past three months (X^2 test for linear trend $p<0.001$). On the other hand, attendees who reported having oral sex in the past three months increased over time (test for linear trend $p<0.001$), as did the proportion of attendees who would refer a recent sexual partner for treatment (test for linear trend $p=0.002$) and for male attendees circumcised medically (test for linear trend $p=0.038$) (Table 2).

Table 2. Demographic, behavioural, and clinical characteristics of sexually transmitted infections (STI) service attendees enrolled in the sentinel surveillance, South Africa, 2021–2024, N=3 265.

Variable	2021 (N=1 056)	2022 (N=793)	2023 (N=793)	2024 (N=623)	All (N=3 265)	X^2 p-value
Males (n,%)	751 (71.1)	548 (69.1)	574 (72.4)	456 (73.2)	2 329 (71.3)	0.330
Current age, Median (IQR)	30 (25–36)	30 (26–37)	31 (26 – 37)	30 (26–37)	30 (25-37)	0.023β
Age ≤24 years, (n,%)	236 (22.4)	148 (18.7)	134 (16.9)	99 (15.9)	617 (18.9)	0.003
Black Africans, (n,%)	1 038 (98.3)	785 (99.0)	787 (99.2)	614 (98.6)	3 224 (98.7)	0.521
Provincial facility, (n, %) Gauteng KwaZulu-Natal Western Cape	 391 (37.0) 413 (39.1) 252 (23.9)	 332 (41.9) 336 (42.4) 125 (15.8)	 349 (44.0) 333 (42.0) 111 (14.0)	 314 (50.4) 214 (34.4) 95 (15.3)	 1 386 (42.5) 1 296 (39.7) 583 (17.9)	 <0.001
Heterosexual orientation (n,%)	1 052 (99.6)	790 (99.6)	788 (99.5)	621 (99.7)	3 251 (99.6)	0.452
Age at first sex, median (IQR)	17(15–18)	17 (16–19)	17 (16–18)	17 (16–18)	17 (16–18)	<0.001β
Age at first sex <15 years, (n,%)	130 (12.3)	61 (7.7)	38 (4.8)	15 (2.4)	244 (7.5)	<0.001
Had sex with a non-regular sexual partner in the past three months, (n,%)	424 (40.2)	270 (34.1)	232 (29.3)	185 (29.7)	1 111 (34.0)	<0.001
Reported two or more sexual partners in the past three months (n,%)	426 (40.4)	298 (37.6)	314 (39.7)	235 (37.7)	1 273 (39.0)	0.555
Had oral sex at the most recent sexual encounter (n,%)	355 (33.6)	314 (39.6)	354 (44.6)	265 (42.5)	1 288 (39.5)	<0.001
Had receptive anal sex at most recent sexual encounter (n,%)	8 (0.8)	7 (0.9)	6 (0.8)	6 (1.0)	27 (0.8)	0.964
Sex with someone living outside province in the past three months, (n,%)	123 (11.7)	87 (11.0)	93 (11.7)	69 (11.1)	372 (11.4)	0.948
Sex with someone living outside the country in the past three months (n,%)	113 (10.7)	103 (13.0)	54 (6.8)	52 (8.4)	322 (9.9)	<0.001
Condom use at most recent sexual encounter, (n,%)	33 (3.1)	22 (2.8)	33 (4.2)	24 (3.9)	112 (3.4)	0.399
STI syndrome diagnosed in the past 12 months, (n,%)	183 (17.3)	148 (18.7)	138 (17.4)	107 (17.2)	576 (17.6)	0.858
Treated for an STI syndrome with no success in the past three months, (n,%)	37 (3.5)	22 (2.8)	38 (4.8)	10 (1.6)	107 (3.3)	0.007
Used an antibiotic in the past two weeks (n,%)	μ	μ	15 (2.0)	7 (1.1)	22 (1.6)	0.805
Main syndrome diagnosed, (n, %) MUS only VDS only GUS only VDS & GUS / MUS & GUS	 670 (63.5) 271 (25.7) 78 (7.4) 37 (3.5)	 481 (60.7) 196 (24.7) 78 (9.8) 38 (4.8)	 517 (65.2) 171 (21.6) 59 (7.4) 46 (5.8)	 413 (66.3) 138 (22.2) 55 (8.8) 17 (2.7)	 2 081 (63.7) 776 (23.8) 270 (8.3) 138 (4.2)	 0.016
Would refer recent sexual partner for examination and treatment, n(%)	688 (65.3)	513 (64.8)	556 (70.3)	444 (71.3)	2 201 (67.5)	0.008
Knew their HIV status, (n,%)	999 (94.7)	743 (93.7)	750 (94.6)	596 (95.7)	3 088 (94.6)	0.444
Self-reported being HIV positive, (n,%)@	204 (20.5)	140 (18.8)	167 (22.3)	123 (20.7)	634 (20.6)	0.430
Ever taken ARVs, (n,%) #	178 (87.8)	125 (89.3)	149 (89.2)	105 (85.4)	557 (88.0)	0.733
Taken ARVs in the past three days, (n,%) ##	177 (99.4)	122 (97.6)	147 (98.7)	102 (97.1)	548 (98.4)	0.327
Males ever circumcised,(n,%)*	527 (70.7	364 (66.7)	386 (67.7)	314 (69.0)	1 591 (68.7)	0.429
Males medically circumcised, (n,%) **	309 (58.6)	242 (66.5)	263 (68.1)	201 (64.2)	1 015 (63.8)	0.016

IQR= interquartile range; β=p-value for K-test for equality of medians; STI=sexually transmitted infection; μ=variable not collected in 2021 and 2022; MUS=male urethritis syndrome; GUS=genital ulcer syndrome; VDS=vaginal discharge syndrome; HIV= human immunodeficiency virus; @among those who knew their HIV status; # among those who self-reported being HIV positive; ## among those who have ever taken ARVs; * among male attendees; ** among those ever circumcised.

Pathogens and aetiologies associated with male urethritis syndrome (MUS)

A total of 2 113 male attendees with MUS were enrolled and each had a genital swab specimen collected. All samples yielded valid PCR results and were included in the analysis. The number of male attendees included was 150% of the target sample size for the period. The majority of the males had one or more STIs (1 969/2 113; 93.2%) detected. *Neisseria gonorrhoeae* was the most frequent STI pathogen detected (1 755/2 113 [83.1%]), followed by CT (446/2 113; 21.1%), MG (87/2 113; 4.1%) and TV (53/2 113, 2.5%). Seventy-six per cent of those tested had a single infection (1 611/2 113), while 16.9% (358/2 113) had mixed infections. *Neisseria gonorrhoeae* and CT accounted for most mixed infections, with 16.1% (340/2 113) and 14.7% (311/2 113) of all who were tested having these infections in combination with each other or with TV or MG (Figure 1). Among STIs detected through serology, current or past HSV-2 infection, HIV infection, and past/recent syphilis were the commonest at 56.2% (1 118/2 101), 22.9% (477/2 086), and 13.7% (286/2 083), respectively. Among attendees with recent infection (i.e., those who were RPR positive – 146/1 983; 7.5% of those tested with an initial screening test), 63.7% had high titres (≥1: 8) indicating active and untreated infection. A small proportion (90/2 083; 4.3%) of attendees had active hepatitis B infection (as indicated by an HBsAg positive result). There was no difference in the prevalence of these pathogens by year of enrolment across the surveillance period (Figure 2).

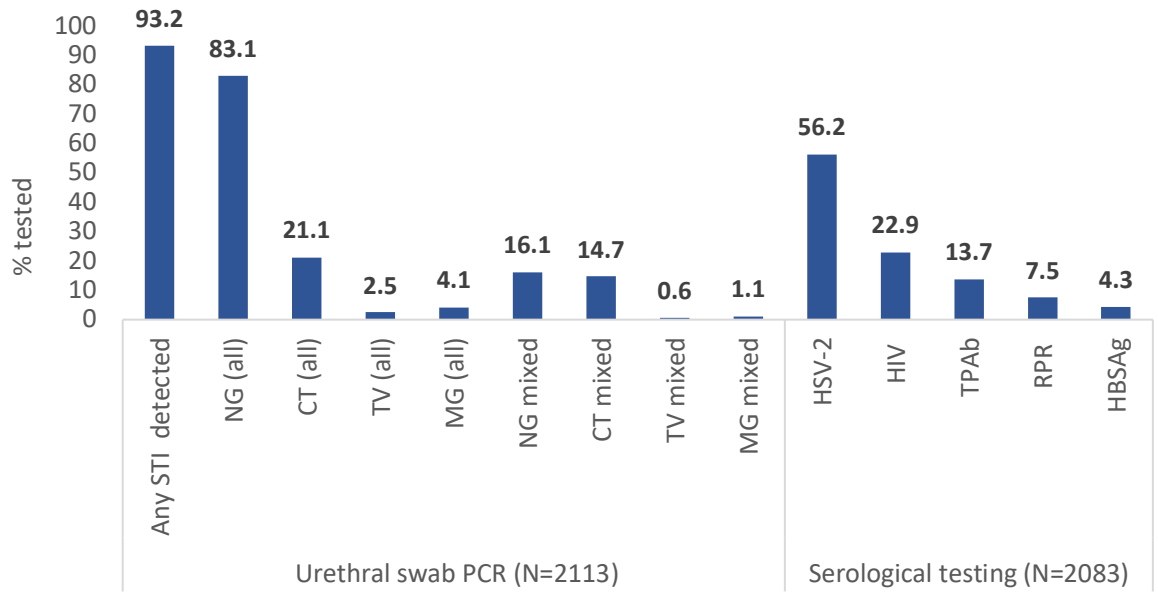

Figure 1. Prevalence of pathogens and aetiologies among attendees with male urethritis syndrome (MUS), South Africa, 2021–2024, N=2 113.

STI=sexually transmitted infection; NG=*Neisseria gonorrhoeae*; CT=*Chlamydia trachomatis*; TV=*Trichomonas vaginalis;* MG= *Mycoplasma vaginalis*; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

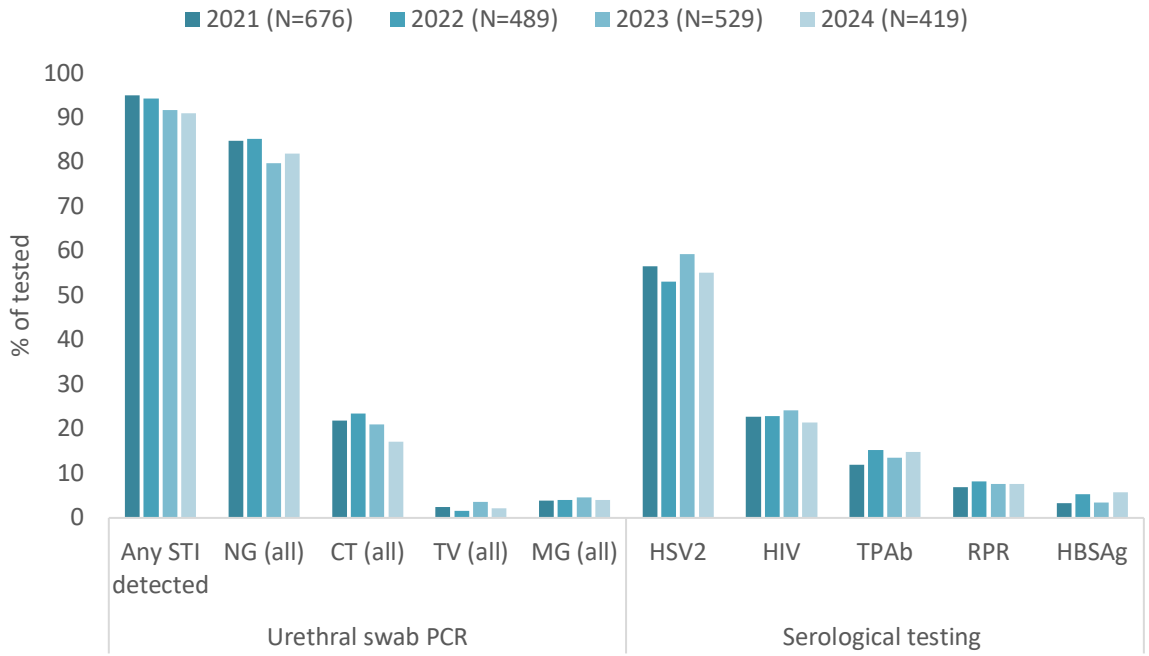

Figure 2. Prevalence of pathogens and aetiologies among attendees with male urethritis syndrome (MUS) by year, South Africa, 2021–2024, N=2 113.

STI=sexually transmitted infection; NG=*Neisseria gonorrhoeae*; CT=*Chlamydia trachomatis*; TV=*Trichomonas vaginalis;* MG=*Mycoplasma vaginalis*; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

Neisseria gonorrhoeae antimicrobial resistance among attendees with male urethritis syndrome (MUS)

A total of 1 442 (68.2%) NG isolates were obtained from the 2 113 urethral swabs that were cultured and had antimicrobial susceptibility testing done. Over the four-year surveillance period, all NG isolates tested exhibited sensitivity to all but one of the antibiotics (or their substitutes) included in the syndromic management guidelines at the time. In 2021, azithromycin-resistant strains were detected, with four isolates (0.8%) detected among isolates from the Gauteng sentinel site, increasing to 4.2% by 2024 among isolates from the Gauteng and KwaZulu-Natal sentinel sites (Table 3). Although there was a statistically significant increase in the proportion of azithromycin-resistant isolates during the surveillance period (X^2 p=0.016), the prevalence did not exceed the 5% threshold recommended for a treatment guideline change.

Table 3. *Neisseria gonorrhoeae* antimicrobial resistance among males with male urethritis syndrome (MUS), South Africa, 2021–2024, N=1 442.

Antibiotic	Parameter	2021	2022	2023	2024
Ceftriaxone	Tested	502	362	342	236
	MIC_{50}	0.002	0.004	0.004	0.002
	MIC_{90}	0.004	0.004	0.004	0.004
	Maximum MIC	0.016	0.016	0.016	0.008
	Resistant (>0.125 mg/L)* n(%)	0 (0)	0 (0)	0 (0)	0 (0)
Cefixime	Tested	502	362	342	236
	MIC_{50}	<0.016	<0.016	<0.016	<0.016
	MIC_{90}	<0.016	<0.016	<0.016	<0.016
	Maximum MIC	0.064	0.016	0.016	0.032
	Resistant (>0.125 mg/L)* n(%)	0 (0)	0 (0)	0 (0)	0 (0)
Gentamicin	Tested	502	362	342	236
	MIC_{50}	4	4	4	2
	MIC_{90}	8	4	8	4
	Maximum MIC	8	8	8	8
	Resistant (>16 mg/L) n(%)	0 (0)	0 (0)	0 (0)	0 (0)
Azithromycin	Tested	496	359	342	236
	MIC_{50}	0.064	0.064	0.064	0.064
	MIC_{90}	0.25	0.25	0.25	0.25
	Maximum MIC	256	256	256	256
	Resistant (>1mg/L)* n(%)	4 (0.8)	5 (1.4)	9 (2.6)	10 (4.2)

*according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints; MIC=minimum inhibitory concentration

Pathogens and aetiologies associated with vaginal discharge syndrome (VDS)

Of the 868 female attendees with VDS enrolled, 865 (99.7%), 863 (99.4%) and 849 (97.8%) had valid endocervical swab, vaginal swab and serological results available, respectively. The number enrolled represented 72% of the expected sample size for the surveillance period. Of the attendees with results, 37.2% (322/865) had an STI pathogen detected (Figure 3). *Chlamydia trachomatis* was the most frequent pathogen detected at 17.8% (154/865), followed by TV (120/865) and NG (117/865) at 13.9% and 13.5%, respectively, and lastly MG at 5.4% (47/865). Overall, 11.5% (99/865) of females tested had a mixed STI infection. The commonest mixed infections were with NG at 7.7% (67/865) and CT at 7.5% (65/865). Bacterial vaginosis was the most common aetiology associated with VDS, with 58% of women tested (502/863) having BV alone or in combination with an STI or candidiasis. Notably, almost 20% of female attendees tested (173/868) had no pathogens detected (among those tested for), which were associated with their discharge. Among STIs detected through serology, current or past HSV-2 infection, HIV infection and past/recent syphilis were the commonest at 69.2% (590/853), 31.3% (266/849), and 12.3% (104/849), respectively. Among attendees with recent infection – RPR positive, 46/849 (5.4%) of those tested with an initial syphilis screening test — 67.4% had high titres (≥1: 8) indicating active infection, and

2.2% (19/849) had active hepatitis B infection (HBsAg positive). The relative prevalence of STI pathogens and other VDS-associated aetiologies were similar from year to year across the four-year surveillance period (Figure 4).

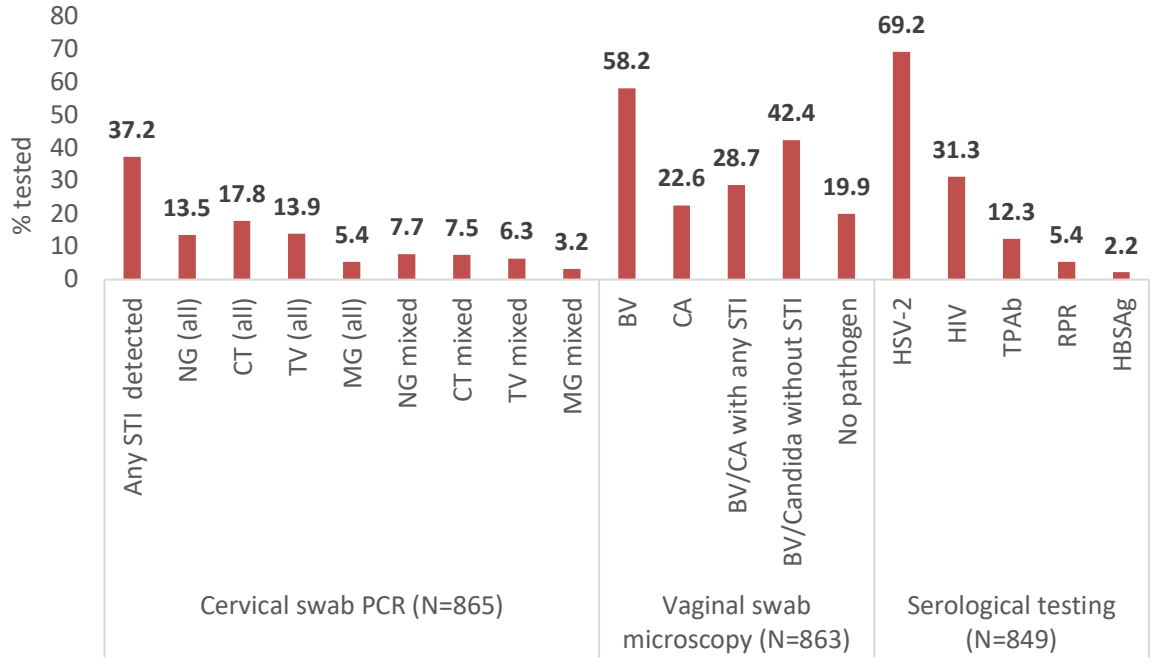

Figure 3. Prevalence of pathogens and aetiologies among attendees with vaginal discharge syndrome (VDS), South Africa, 2021–2024, N=865.

STI=sexually transmitted infection; NG=*Neisseria gonorrhoeae*; CT=*Chlamydia trachomatis*; TV=*Trichomonas vaginalis;* MG=*Mycoplasma vaginalis*; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

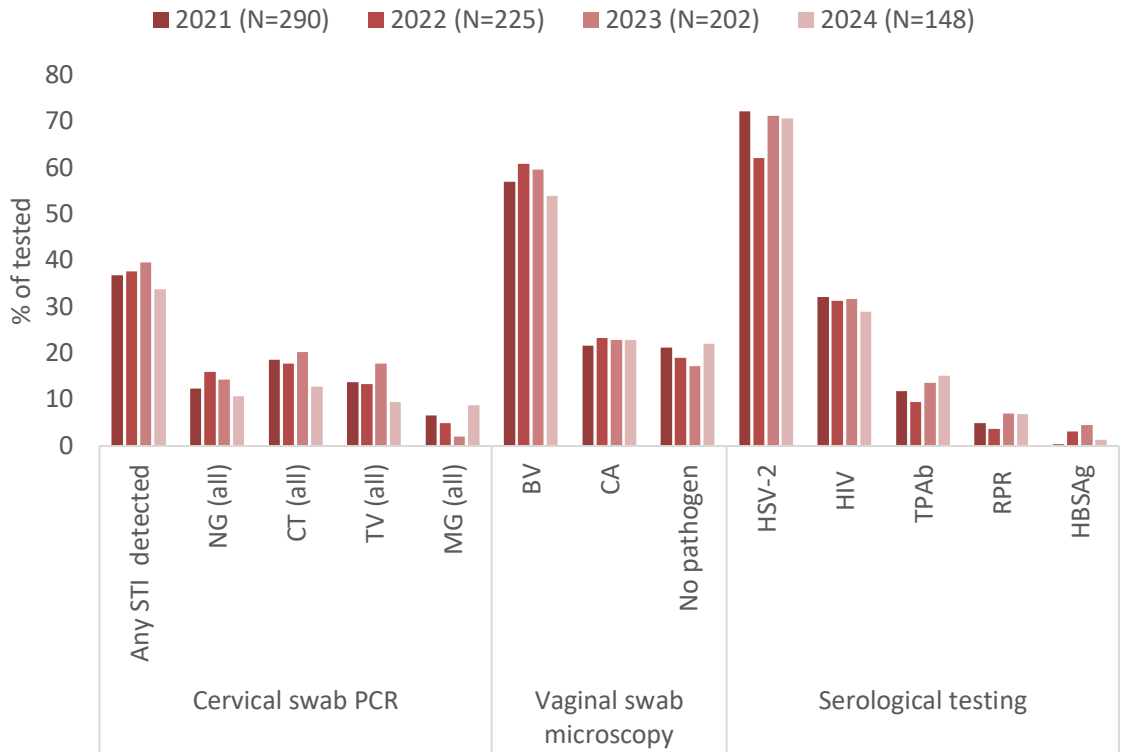

Figure 4. Prevalence of pathogens and aetiologies among attendees with vaginal discharge syndrome (VDS) by year, South Africa, 2021–2024, N=865.

STI=sexually transmitted infection; NG=*Neisseria gonorrhoeae*; CT=*Chlamydia trachomatis*; TV=*Trichomonas vaginalis*; MG=*Mycoplasma vaginalis*; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

Pathogens and aetiologies associated with genital ulcer syndrome (GUS)

Of 408 attendees (34% of the expected sample size) with valid genital ulcer swab results, 71.8% (293/408) had one or more ulcer-associated pathogens detected, while no pathogens were detected in 28.2% (115/408). The most common aetiology associated with genital ulcers was HSV-2 at 43.6% (178/408), followed by TP at 30.2% (123/408), HSV-1 at 0.5% (2/408) and LGV at 0.3% (1/408). Over the surveillance period, HD and GI were not detected at all. Of those tested, 11/408 2.7% of tested and 3.8% (11/293) of those with one or more pathogens detected had mixed HSV/TP infection (Figure 5). Among STIs detected through serology, current or past HSV-2 infection, HIV infection and past/recent syphilis infection (defined as TPAb positive) were the most frequent at 77% (311/408), 43.4% (173/408) and 42.7% (170/408), respectively. A total of 128/397 (32.2%) attendees had recent syphilis infection (RPR positive), of whom 99/128 (77.3%) had high titres (≥1: 8) indicating active and untreated infection. About 7% (28/398; 7.3%) had active hepatitis B infection (defined as HBsAg positive). The relative prevalence of ulcer-associated pathogens and aetiologies was similar from year to year across the four-year surveillance period (Figure 6).

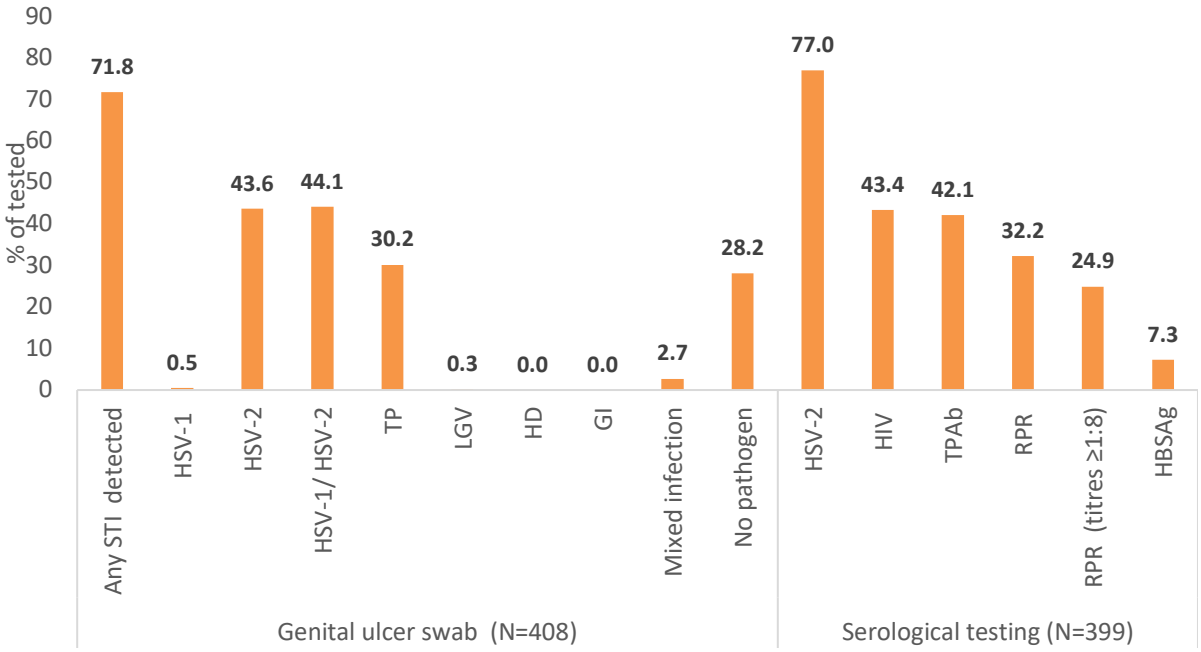

Figure 5. Prevalence of pathogens and aetiologies among attendees with genital ulcer syndrome (GUS), South Africa, 2021–2024, N=408.

STI=sexually transmitted infection; HSV-1=Herpes simplex virus type-1; HSV-2=Herpes simplex virus type-2; TP=*Treponema pallidum*; LGV=*Lymphogranuloma venereum*; HD=*Haemophilus ducreyi* infection; GI=granuloma inguinale; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

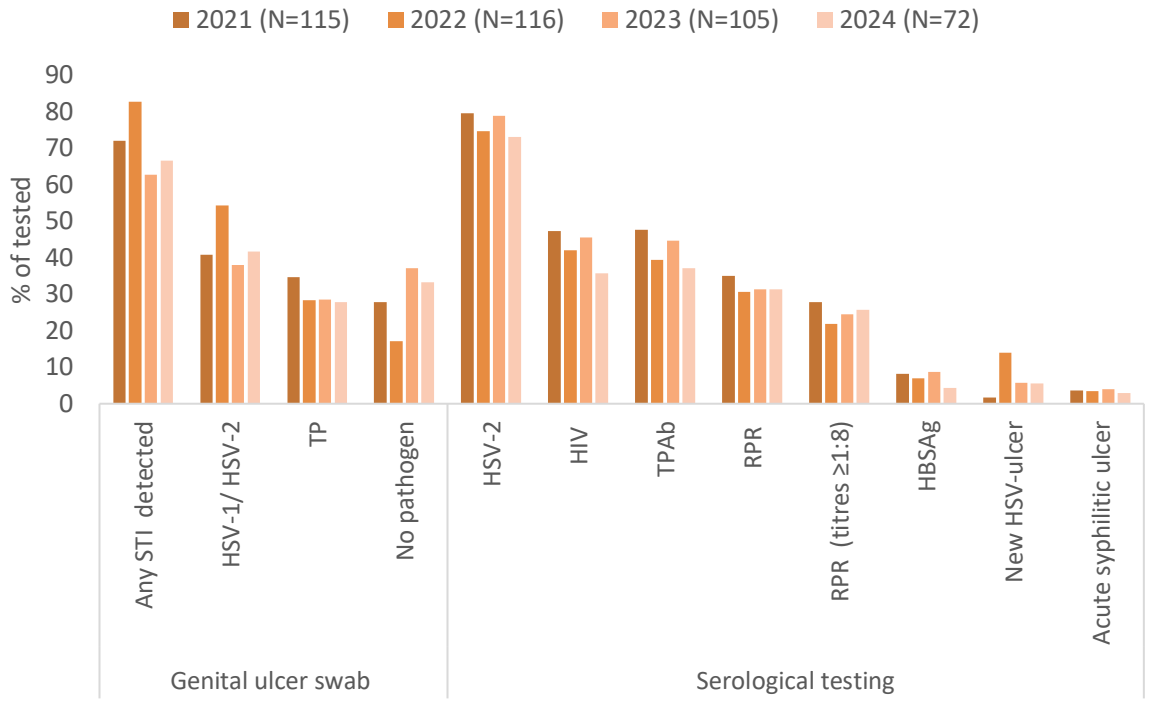

Figure 6. Prevalence of pathogens and aetiologies among attendees with genital ulcer syndrome (GUS) by year, South Africa, 2021–2024, N=408.

STI=sexually transmitted infection; HSV-1=Herpes simplex virus type-1; HSV-2=Herpes simplex virus type-2; TP=*Treponema pallidum*; LGV=*Lymphogranuloma venereum*; HD=*Haemophilus ducreyi* infection; GI=granuloma inguinale; HSV-2=herpes simplex virus type 2 antibodies; HIV=HIV antibodies; TPAb=*Treponema pallidum* antibodies; RPR=rapid plasma reagin antibodies; HBSAg=Hepatitis B surface antigen

Discussion

Here we describe the prevalence of different pathogens and aetiologies associated with MUS, VDS and GUS among cisgender males and cisgender females attending primary care-based STI services during the period 2021–2024. This report is an update of the surveillance reports from the period 2019–2020 which were published in 2022.[7-9] As in the past, we found a high prevalence of high-risk sexual behaviours among attendees, with encouraging trends towards self-reported intent to refer sexual partners, increased medical circumcision among male attendees and older age at first sex. We also found that among males with MUS, the majority had an STI pathogen detected, with NG remaining the most frequently detected STI pathogen, followed by CT. Additionally, we also observed a growing burden of azithromycin-resistant NG, although it did not exceed 5% of isolates tested. Among women with VDS, BV remained the most common aetiology identified, and just under 40% of female attendees had an STI pathogen detected, with CT being the commonest. Mixed infections/aetiologies were common; however, about 20% of females with VDS had no pathology/aetiology identified. Among male and female attendees with GUS, HSV-2 remained the most common aetiology associated with ulcers at 43.6%, with syphilis associated with almost 30% of ulcers. This was an increase from <10% during the period 2014–2016.[10,11] There were no significant changes in the prevalence of pathogens/aetiologies associated with the three main genital syndromes over the four-year surveillance period. HIV and syphilis remained the most frequent co-infections and were stable during the surveillance period.

The results from this surveillance are very similar to what has been reported in past sentinel surveillance activities, with a few exceptions. During the period 2014–2020,[7-11] NG was present in 72–88% of men with MUS, with CT present in 20–22%. For VDS, NG and CT were present in 10–19% and 14–20%, respectively.[6-10] During the same period, BV was the commonest aetiology at 50–60%.[7,10,11] With respect to serology results, RPR positivity was <5% for males with MUS and females with VDS during 2014–2020, increasing to 5–10% in the current surveillance period.[7-11] This mirrors the increase in the proportion of genital ulcers associated with TP observed in the current surveillance period. In 2014–2016, TP was present in <10% of genital ulcers. This increased to 26% in the period 2019–2020[7, 9], and 30% in the period 2021–2024. The increased contribution of syphilis as a cause of genital ulcers likely reflects increased transmission in communities and has been mirrored by increases in maternal seroprevalence[12] and reported cases of congenital syphilis.[13] The increased syphilis transmission seen from 2016 coincided with shortages of benzathine penicillin G (BPG), which were experienced from 2016–2023/24.[14] This period also saw the introduction and roll-out of pre-exposure prophylaxis for HIV, which may have resulted in the uncoupling of STI and HIV prevention. Benzathine penicillin supplies in the country should be normalising. A communication reinstating BPG as the treatment of choice for syphilis in all groups was sent out to healthcare providers during 2024.[15] The restoration of BPG as the drug of choice may improve cure rates compared to oral doxycycline, and thereby reduce transmission.

Because the relative prevalence of the STI syndrome aetiologies remains similar to that in the past, the syndromic management algorithms in use during the current surveillance period were assumed to be adequate and will continue to be used. However, the emergence of azithromycin-resistant NG requires closer monitoring and the possible rethinking of the VDS and MUS algorithms. Increasing azithromycin resistance will result in the current regimen being equivalent to giving ceftriaxone monotherapy for the treatment of NG. Alternative regimens could include increasing the dose of ceftriaxone to 500mg or 1g or dropping azithromycin from the MUS/VDS algorithm and replacing it with doxycycline to cover CT.[16] Another alternative would be to consider the new oral antibiotic zoliflodacin, which has been found to be as effective as ceftriaxone for curing gonorrhoea. The drug may be available in the future through an access programme via the Global Antibiotic Research and Development Partnership (GARDP).[17] *Chlamydia trachomatis*, TV, and MG antimicrobial resistance were not monitored during the surveillance period.

These latest surveillance data continue to highlight the limitations of syndromic management, particularly for females with VDS and for males and females with GUS. Almost 20% of females with VDS and 30% of males and females with GUS did not have any pathogens/aetiologies identified, representing the proportion of attendees who were over-treated. Female attendees with only Candida infection (10.2%) would also be over-treated with antibiotic treatment for STIs. The absence of detectable pathogens or aetiologies in the genital specimens could be due to the presence of non-STI causes of symptoms or limitations of the diagnostic assays used. Prior antibiotic use was an unlikely reason, as only 1.5% of the attendees enrolled in 2023 and 2024 reported taking antibiotics in the two weeks preceding enrolment. The introduction of point-of-care or near-point-of-care diagnosis should prioritise these groups in order to reduce over-treatment. The surveillance included a large number of attendees from the same sites over a four-year period, allowing for analyses of trends over time.

Our sentinel surveillance nevertheless had a number of limitations. The surveillance was limited to three sentinel sites (one in each province) and to males and females who had symptoms consistent with STIs and managed to seek and access care. The attendees enrolled, therefore, may not be representative of all individuals with symptomatic STIs in the country. Enrolment took place during regular clinic hours and therefore excludes people who sought care after hours or on weekends. Lastly, the surveillance was limited to males and females with symptomatic disease, thereby excluding the majority of people with STI who tend to have asymptomatic infections. Despite these limitations, this analysis provides valuable data needed for the management of STIs in South Africa.

Recommendations

Based on the findings of our surveillance, we recommend that:

- The government and other policymakers in South Africa create and facilitate an environment that enables improved STI prevention, diagnosis and treatment by developing and updating guidelines and protocols for prevention, diagnosis, and treatment of STIs. They should also make funding and budgets available for healthcare worker recruitment, training and retention, and improve data systems that enable accurate measuring, monitoring, and evaluation of the STI epidemic.
- The national and provincial departments of health and their partners implement a large-scale information, education and communication campaign on STIs. The campaign should provide information and educate the general public on STIs, including the different types of STIs, how to prevent them, symptoms and signs, treatment options, where to get treatment, the importance of partner treatment, and potential complications.
- The national and provincial Departments of Health, through the Essential Drugs programme and provincial pharmacies, ensure the adequate supply chain and stock management of STI-related commodities. These include condoms, speculums, bed lamps to facilitate appropriate genital examination, antibiotics for appropriate treatment and supplies for specimen collection in the case of persistent or complicated STI infections.
- The national and provincial Departments of Health prioritise training of healthcare workers in ongoing clinical support on STIs and STI management. The training should include sensitisation on stigma and discrimination against STIs, STI prevention, differentiated prevention and care for key and priority populations for STI care, aetiologic screening and diagnosis, pathogen-directed treatments, antimicrobial resistance and partner management. Healthcare providers need to improve sexual partner management, including notification and treatment, in order to limit onward transmission. Partner notification should include different approaches and platforms, such as electronic notification and expedited partner treatment, allowing STI service attendees to choose the appropriate approach and platform they prefer.
- The National Department of Health and its partners introduce and provide point-of-care multiplex diagnostics to screen for STIs among the asymptomatic at-risk populations. This will facilitate treatment and reduce the burden of transmission in communities. A key consideration should be the use of dual HIV/syphilis and single syphilis rapid tests to screen all STI service attendees for latent syphilis and to treat persons found to be positive.
- The National Department of Health and its partners introduce and provide point-of-care or near-point-of-care diagnostics to allow aetiological diagnoses of females with VDS who are more likely to have non-STI causes of vaginal discharge and, therefore, face the highest risk of over-treatment.

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Ethical considerations

The protocol for sentinel surveillance was approved by the University of the Witwatersrand Human Research Ethics Committee (protocol numbers M160667/M220854). The protocol also received secondary ethical clearance from the University of KwaZulu-Natal Human Research Ethics Committee and from the University of Cape Town Human Research Ethics Committee.

Conflict of interest

The authors declare no conflict of interest.

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