Provision of Sexually Transmitted Infection Services in a Mobile Clinic Reveals High Unmet Need in Remote Areas of South Africa: A Cross-sectional Study

Charlotte M. Hoffman, BSc^{1,2}; Nontembeko Mbambazela¹; Phumzile Sithole¹; Servaas A. Morré, PhD³; Jan Henk Dubbink, PhD¹; Jean Railton, Fam Med¹; James A. McIntyre, FRCOG^{1,4}; Marleen M. Kock, PhD^{5,6}; Remco P.H. Peters, PhD^{1,2,6}

- 1. Anova Health Institute, Johannesburg, South Africa
- Department of Medical Microbiology, School of Public Health & Primary Care (CAPHRI), Maastricht University Medical Centre, Maastricht, The Netherlands
- VU University Medical Center, Department of Medical Microbiology, Laboratory of Immunogenetics, Amsterdam, The Netherlands
- 4. School of Public Health & Family Medicine, University of Cape Town, Cape Town, South Africa
- 5. Tshwane Academic Division, National Health Laboratory Service, Pretoria, South Africa
- 6. Department of Medical Microbiology, University of Pretoria, Pretoria, South Africa

Correspondence

Address for correspondence: Prof R.P.H. Peters, Anova Health Institute, 12 Sherborne Road, Parktown, PostNet Suite 242, Private Bag X30500, Houghton, South Africa. Email: rph.peters@gmail.com. Tel: +27 11 5815000.

Conflicts of Interest and Source of Funding

The authors declare that there is no conflict of interest. This work was supported by a grant (DHKF15/D27) from the Netherlands Enterprise Agency (Rijksdienst voor Ondernemend Nederland) to provide diagnostic tests. Anova Health Institute's Mobile Clinic is funded by Orange Babies (The Netherlands), Stichting Opstap (The Netherlands) and Sala Kuchi Kuchi (The Netherlands).

ABSTRACT (238/250)

Background: The burden of sexually transmitted infections (STIs) in areas of sub-Saharan Africa with poor access to healthcare services is not well documented. In remote areas of South Africa we investigated the prevalence of STIs and approaches to providing STI services through a mobile clinic.

Methods: We recruited 251 adult women visiting a mobile clinic that normally provides general health education and screening services, but not STI care. Clinical and sexual history was obtained and vaginal specimens were tested for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Mycoplasma genitalium* infection and for *C. albicans* and bacterial vaginosis.

Results: Laboratory test was positive for 133/251 (53%) of women for at least one STI: *C. trachomatis* was observed in 52 (21%) women, *N. gonorrhoeae* in 39 (16%) women, *T. vaginalis* in 81 (32%) women and *M. genitalium* in 21 (8%) women. Eighty-one women (32%) met the criteria for vaginal discharge syndrome, of which 58% (47/81) would have been treated accurately. Among asymptomatic women 84/170 (49%) were diagnosed with an STI but untreated under the syndromic approach. We could not identify factors associated with asymptomatic STI infection.

Conclusions: There is a high unmet need for STI care in rural South African settings with poor access to healthcare services. Provision of STI services in a mobile clinic using the syndromic management approach provides a useful approach, but would have to be enhanced by targeted diagnostics to successfully address the burden of infection.

KEY WORDS (5)

Sexually transmitted infections; vaginal discharge syndrome; syndromic management; mobile clinic; rural South Africa.

INTRODUCTION

The sexually transmitted infections (STIs) *Chlamydia trachomatis, Neisseria gonorrhoeae*, *Trichomonas vaginalis* and *Mycoplasma genitalium* are common worldwide. The African region is particularly affected by these curable diseases, with an estimated incidence of respectively 12.0 million, 11.4 million and 37.4 million new infections per year.^{1,2} There is currently no accurate estimate available of incidence of *M. genitalium* infection in Africa, but prevalence has been reported in the range of 6-11% among women.^{3,4} South Africa is known for one of the highest prevalence rates of HIV worldwide.⁵ Also, it is one of the countries most affected by STIs, with prevalence and incidence rates higher than in other African countries.⁶ Incidence rates of 14% for *C. trachomatis*, 4% for *N. gonorrhoeae* and 7% for *T. vaginalis* per person-years at risk have been reported in community settings⁷; prevalence of STIs among pregnant women is even higher.⁸ Despite counselling and condom provision to reduce risk, incidence rates remain high.⁷

South Africa has implemented syndromic guidelines for management of STIs, meaning that symptomatic individuals are treated with a combination of empirical antibiotics.⁹ Several studies have demonstrated that a large proportion of cases receives under- or overtreatment result of using a syndromic instead of aetiological approach.¹⁰⁻¹² In the long term, untreated STIs can lead to severe complications, such as pelvic inflammatory disease, infertility, a predisposition to ectopic pregnancy and an increased risk of transmitting and acquiring human immunodeficiency virus (HIV) when exposed.^{13,14}

Most studies addressing STIs in sub-Saharan Africa have been conducted among individuals visiting healthcare facilities or in specific key populations such as sex workers and men who have sex with men. However, there are limited data about the need for STI care and treatment in deep rural areas with high levels of poverty and poor access to healthcare facilities. Access to healthcare for people living in these remote areas can be challenging due to long distances

3

and often impassable roads to the nearest primary healthcare clinic (PHC) as well as lack of personal funds to afford transportation fees.¹⁵ In some of these areas, basic healthcare is provided through mobile clinics. The healthcare package provided in mobile clinics generally consists of testing for HIV and screening for tuberculosis (TB), diabetes mellitus, hypertension and cervical cancer. The effectiveness of delivering STI services through a mobile clinic has, to our best knowledge, never been investigated or reported on. In this study we explored the need for provision of STI services in a mobile clinic in the deep rural parts of Mopani district, South Africa. In particular, we investigated the effectiveness of offering STI services using a syndromic and an aetiological approach through this mobile clinic to inform the best strategy for providing STI care in remote rural African settings.

MATERIALS AND METHODS

Study design and population

This cross-sectional study was conducted in 2016 using a non-governmental organisation (NGO)-deployed mobile clinic that visits deep rural parts of Mopani district, Limpopo Province, South Africa. This mobile clinic is operated by an experienced nurse practitioner and counsellor, and has been operational in the region for more than four years. It provides health information and screening services for HIV, TB, non-communicable diseases and cervical cancer. The clinic is stationed in a particular rural area from one up to several days following agreement with the traditional leader of that area. In this evaluation, we only included areas that were at least 20 kilometres away from the nearest healthcare facility. All adult women (≥18 years) who attended the mobile clinic for any of the health services were eligible for this project, regardless of the presence of STI-associated symptoms. Women that were having menses at the time of recruitment were excluded. This study was approved by the Faculty of Health Sciences Research Ethics Committee of the University of Pretoria and by the Limpopo Provincial Health Research Committee of the Department of Health (Reference number: 498/2016).

Study procedures

After obtaining written informed consent, a short questionnaire was administered by the nurse including questions related to demographics, sexual behaviour, and symptoms. Physical examination was conducted. Clinician-collected vaginal smear was obtained for microscopy to detect *Candida* infection and bacterial vaginosis (BV) and a clinician-collected standard flocked vaginal swab (Copan diagnostics, Italy) was obtained for diagnostic testing.

Laboratory analysis

All specimens were transported to and processed at the Department of Medical Microbiology of the University of Pretoria. After Gram staining, microscopic assessment of smears was performed to detect bacterial vaginosis by Nugent Score and *C. albicans* infection based on typical morphological appearance. The High Pure PCR Template Preparation Kit (Roche Molecular Diagnostics, Mannheim, Germany) was used to extract DNA from the swabs followed by real-time polymerase chain reaction on the LightCycler 480 (Roche Molecular Diagnostics, Mannheim, Germany) using the Presto *C. trachomatis/N. gonorrhoeae* assay for detection of *C. trachomatis* and *N. gonorrhoeae*.¹⁶ The presence of *T. vaginalis* was assessed by using the Presto^{plus} assay and the presence of *M. genitalium* by using an in-house multiplex PCR assay as described elsewhere.¹⁷⁻¹⁹

Clinical definitions and management

Women were considered symptomatic if they met the criteria of the national guideline for management of the vaginal discharge syndrome (VDS)⁹: self-report of (altered) vaginal discharge, dysuria and/or vaginal itch which is then confirmed through clinical examination. Following the national guidelines for VDS, women that were <35 years old and had no lower abdominal pain or pain on moving the cervix were empirically treated for STIs with a

combination of azithromycin (oral, 1 mg), ceftriaxone (intramuscular, 250 mg) and metronidazole (oral, 2 mg). Women >35 years old were treated with a combination of clotrimazole (pessary, 500 mg) and metronidazole (oral, 2 mg). For this analysis, women with a positive molecular test for at least one of the four STIs were classified as having an STI; these could be symptomatic or asymptomatic. Symptomatic women with bacterial vaginosis or *C. albicans* infection on vaginal smear were classified as having a non-sexually transmitted reproductive tract infection (RTI). Symptomatic women with both STI and BV or *C. albicans* were classified as STI and analyzed separately when appropriate. HIV status was classified as positive based on self-reported positive status, negative based on result of rapid HIV test, and unknown in case HIV testing was declined. Symptomatic women were treated syndromically upon recruitment. All participants were contacted to discuss the results of STI testing; in case of asymptomatic STI or inadequate empirical treatment for the STI diagnosed, women were requested to visit the nearest healthcare facility and to meet with a member of the study team to receive appropriate treatment.

Data analysis

The results were analyzed using IBM SPSS Statistics Version 24 (SPSS Inc., Chicago, USA). Data are presented as numbers with proportion (%) and median with range. Comparative statistics were done using Chi-square test, with Fisher's Exact test if appropriate, for dichotomous and Mann-Whitney Test for continuous variables. A *p*-value of <0.05 was considered statistically significant. Odds ratios (ORs) with 95% confidence intervals (CIs) are provided. Univariate analysis was performed to examine factors associated with STIs. Age and other relevant variables with a *p*-value of <0.01 through univariate analysis, were analyzed with multivariate analysis through logistic regression.

RESULTS

Participant characteristics

We recruited 251 women, with a median age of 34 years (range: 18 – 75), who visited the mobile clinic for any of the offered services (Table 1). Three-quarters (75%) of the women were literate, sixty-one (25%) were employed. Three (1%) women were pregnant. Three-quarters (75%) of the participants were HIV-negative; 11% were HIV-infected and 8% had unknown HIV status and refused HIV testing. Almost all women (95%) reported practicing vaginal sex in the past six months; only 6% reported having oral sex and 2% anal intercourse. Only forty-four (18%) of the women reported condom use during their last sex act. Forty-seven (19%) participants reported an experience of sexual coercion in the past six months. Eighty-one (32%) of the women met the criteria for vaginal discharge syndrome. Abnormal or altered discharge was reported in thirty-six (14%) women, twenty (8%) reported dysuria and forty-eight (19%) genital itch. Other genital symptoms that were reported, but are not included as entry point in the VDS algorithm, include lower abdominal pain (29%), pain during sexual intercourse (9%) and blood loss related to sexual intercourse (5%).

More than half of the women (53%; n = 133) tested positive for at least one STI: *C. trachomatis* was observed in 52 (21%) women, *N. gonorrhoeae* in 39 (16%) women, *T. vaginalis* in 81 (32%) women and *M. genitalium* in 21 (8%) women (Table 2). Thirty-four women were infected with two STIs, of which the combination *C. trachomatis* and *T. vaginalis* was the most common (n = 15). Thirteen women were infected with three STIs, most commonly the combination of *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis* (n = 6). Eighty-one (37%) of all STI-infected women were symptomatic. Thirty-eight (15%) women were diagnosed with another non-sexually transmitted RTI: bacterial vaginosis in 34 (14%) women and *C. albicans* in six (2%). In twenty-five women with bacterial vaginosis and three with *C. albicans*-infection, concurrent STI was diagnosed.

	No. (%) or Median (Range)
Demographics	8
Age, y	34 (18-75)
< 35	124 (51)
35-49	71 (29)
50-75	46 (18)
Literacy level	
Illiterate	62 (25)
Literate	189 (75)
Main source of income	185 (75)
Employed or self-employed	61 (25)
Unsemployed of sen-employed	118 (49)
Unemployed or partner employed Grant	64 (26)
Relationship status	5555778778850
Single	128 (52)
Living together	21 (9)
Married	97 (39)
Sexual relationship	21 (52
No partner	19 (8)
Stable partner only	142 (58
Occasional partner only	68 (28
Stable and occasional partner	14 (6)
Currently pregnant	3 (1)
Clinical history	
HIV status	
Positive	28 (11)
Negative	189 (75)
Declined to disclose	16 (6)
Unknown	19 (8)
History of STI treatment	23 (9)
Sexual practice in past 6 mo	200-10/00/07
Traditional practice*	71 (29)
Use of contraceptives	210,820,8
Condom (male/female)	50 (20
Hormonal contraceptives*	80 (32)
Sterilization	6(2)
No contraceptives	113 (45)
Practiced vaginal sex	239 (95)
Practiced fellatio	16 (6)
Receptive anal intercourse	6(2)
Condom use (last sexual act)	44 (18)
>1 sex partner	12 (5)
Sexual partner >10 years older	47 (19)
Sex for money or material benefits	4 (2)
Behavioral factors in past 6 mo	102 M
Intravaginal cleansing	115 (47)
Alcohol use before sexual intercourse	31 (12)
Experienced sexual coercion	47 (19)

TABLE 1. Characteristics of Women Visiting the Mobile Clinic in	Mopani District	South Africa
---	-----------------	--------------

*Injectable contraceptive, oral contraceptive, implant. *Genital scarring and labia elongation.

TABLE 2. Microbiological Detection of S	I in Women Visiting the Mobile	Clinic in Mopani District. South
		,

Africa

	Total No. Women (%) (N = 251)	No. Symptomatic* Women (%) (n = 81)	No. Asymptomatic Women (%) (n = 170)
STI	133 (53)	49 (60)	84 (49)
Chlamydia trachomatis	52 (21)	19 (24)	33 (19)
Neisseria gonorrhoeae	39 (16)	12 (15)	27 (16)
Trichomonas vaginalis	81 (32)	31 (38)	50 (29)
Mycoplasma genitalium	21 (8)	11 (14)	10 (6)
Other reproductive tract infection	38 (15)	38 (47)	
Bacterial vaginosis	34 (14)	34 (42)	-
Candida albicans	6(2)	6(7)	—
No reproductive tract infection detected	106 (42)	20 (25)	86 (51)

*Vaginal discharge, dysuria, and genital itch, according to the VDS management guidelines of South Africa.

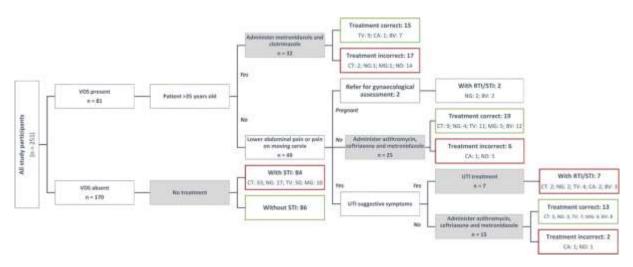


Figure 1. Evaluation of VDS management guidelines when applied to women visiting the Mobile Clinic in Mopani district, South Africa. UTI, urinary tract infection; CT, Chlamydia trachomatis;NG, Neisseria gonorrhoeae;TV,Trichomonas vaginalis;MG,Mycoplasma genitalium;CA, Candida albicans;ND,no diagnosis.

Effectiveness of the syndromic approach for STI screening and management

VDS was present in 81 (32%) women. Adequate empirical treatment (covering the microbiological aetiology) based on the VDS algorithm was provided to 47 (58%) of these symptomatic women (Figure 1): this was in 37 (79%) women with one or more STI and 29 (62%) women with one or more RTI. Of the 49 women with symptomatic STI, 37 (76%) would have been treated accurately; this is 29/38 (76%) in women infected with one or more RTI. Twenty (25%) women without diagnosed STI or RTI, were treated unnecessarily for either STI or RTI. In addition, 84/170 (49%) asymptomatic women were diagnosed with an STI but remained untreated under the syndromic approach. Fewer women with a positive VDS screening (11%) had a sexual partner >10 years older (p = 0.038) than women who did not meet the criteria for VDS (22%). Also, a trend for alcohol use and positive VDS screening was observed (p = 0.063), but no other demographic or behavioural factors were associated. Other symptoms related to reproductive tract infections, but not included in the VDS algorithm, such as blood loss during sexual intercourse (p = 0.031) and lower abdominal pain (p = 0.002) were positively associated with the presence of VDS. We did not observe an association between individual STIs and presence of symptoms, although a tendency was observed for *M. genitalium*

infection with presence of VDS symptoms (OR 2.5; 1.0-6.2 and p = 0.051). Three of eleven symptomatic women with *M. genitalium* infection had a concurrent *T. vaginalis* infection.

TABLE 3. Factors Associated With Adequate Treatment in Symptomatic Nonpregnant Women (N = 79) Visiting
the Mobile Clinic in Mopani District, South Africa

	Adequate Treatment (n = 47) n (%)	Inadequate Treatment (n = 32) n (%)	P	OR (95% CI)
Age, y				
Median (range)	29 (18-61)	43 (19-68)	0.073	
< 35	30 (67)	12 (41)		
≥ 35	15 (33)	17 (59)	0.034	2.8 (1.1-7.4)
Literacy level				10 M
Illiterate	8 (17)	10 (31)		
Literate	39 (83)	22 (69)	0.144	2.2 (0.8-6.4)
Main source of income	20.00			100000000000
Employed or self-employed	13 (30)	8 (26)		
Grant	8 (19)	12 (39)		
Unemployed	22 (51)	11 (36)	0.149	
HIV status				
Negative	8 (62)	4 (57)		
Positive	5 (39)	3 (43)	0.848	0.8 (0.1-5.4)
Relationship status	2 (37)	2 (12)	0.010	010 (011 - 011)
Married	15 (32)	13 (41)		
Living together	7 (15)	4(13)		
Single	25 (53)	15 (47)	0.728	
Type of relationship	20 (00)	15 (47)	0.720	
Stable partner	25 (63)	19 (83)		
Occasional partner	15 (38)	4 (17)	0.102	2.9 (0.8-10)
History of STI treatment			0.102	5.4 (0.6-46)
Clinical presentation	7 (15)	1 (3)	0.125	5.4 (0.0-40)
	26.1852	10 (21)	0.037	27/11 70
Vaginal discharge	26 (55)	10 (31)		2.7 (1.1-7.0)
Dysuria	5 (11)	15 (47)	< 0.001	
Genital itch	26 (55)	20 (63)	0.526	0.7 (0.3-1.9)
Lower abdominal pain	17 (36)	17 (53)	0.137	0.5 (0.2-1.2)
Pain during sexual intercourse	5 (11)	6 (19)	0.312	0.5 (0.1-1.9)
Blood loss during sexual intercourse	5 (11)	3 (9)	0.855	1.2 (0.3-5.2)
Vaginal discharge observed	1210/1222211	12/12/201		
Yes	26 (55)	7 (22)		11122
No	21 (45)	25 (78)	0.005	4.4 (1.6-12)
Sexual behavior and risk		12/010	10102020	an esta estad
Practiced anal sex past 6 mo.	2 (4)	0 (0)	0.512	0.6 (0.5-0.7)
Practiced fellatio past 6 mo.	9 (19)	1 (3)	0.065	7.3 (0.9-61)
Condom use last sex act	12 (27)	0(0)	0.001	0.5 (0.4-0.7)
>1 sex partner past 6 mo.	3 (7)	1 (3)	0.542	2.1 (0.2-21)
Intravaginal cleansing	24 (51)	10 (33)	0.129	2.1 (0.8-5.4)
Alcohol use past 6 mo.	9 (19)	6 (19)	0.965	1.0 (0.3-3.2)
Experienced sexual coercion	12 (26)	6 (19)	0.482	1.5 (0.5-4.5)
Number of infections	2012020202020	22220-000 V		- N-50 (DAUD-681)5
Mono-infection	21 (57)	7 (70)		
Multi-infection	16 (43)	3 (30)	0.452	1.8 (0.4-8.0)

Adequately treated symptomatic women had a median age of 29 years (range: 18 - 61), compared with a median age of 43 years (range: 19 - 68) of inadequately treated women (Table 3). Adequate treatment was significantly associated with clinical presentation with vaginal discharge (OR 2.7; 1.1-7.0 and p = 0.037) and inadequate treatment with dysuria (OR 7.4; 2.3-24 and p = <0.001). Vaginal discharge was more often healthcare worker observed in adequately treated women (OR 4.4; 1.6-12 and p = 0.005) compared to women that were

inadequately treated. Furthermore, we found a significant association for lack of condom use (OR 0.5; 0.4-0.7 and p = 0.001) in inadequately treated women.

Effectiveness of the aetiological approach for STI screening and management

STIs were detected in 133 (53%) women; only 49 (37%) of these women were symptomatic. Factors associated with STI were: age <35 years (OR 2.5; 1.5-4.2 and p = <0.001), literacy (OR 2.0; 1.1-3.5 and p = 0.022), occasional sexual partner (OR 1.9; 1.1-3.4 and p = 0.037), intravaginal cleansing (OR 1.7; 1.1-2.8 and p = 0.040) and the use of alcohol (OR 2.9; 1.2-6.7 and p = 0.016) (Table 4). *C. trachomatis* infection was more often seen in younger women (OR 4.3; 2.1-8.8), women that had an history of STI treatment (OR 2.8; 1.1-6.8) and those who reported the use of alcohol (OR 2.4; 1.1-5.4). Factors associated with infection with *N. gonorrhoea* were age <35 years (OR 2.6; 1.2-5.4), pregnancy (OR 11; 1.0-128), practicing anal sex (OR 0.8; 0.8-0.9) and intravaginal cleansing (OR 2.6; 1.3-5.3). Women infected with *M. genitalium* more often reported fellatio (OR 8.8; 2.8-27), the use of alcohol (OR 3.3; 1.2-9.2) and experienced sexual coercion (OR 3.8; 1.5-9.6). Vaginal discharge was significantly associated with *M. genitalium* (OR 3.5; 1.3-9.3) and *T. vaginalis* (OR 2.8; 1.3-5.7). Also, *T. vaginalis* infection was significantly associated with having an occasional sexual partner (OR 2.2; 1.2-4.0). TABLE 4. Factors Associated With Positive Etiological Screening in Women Visiting the Mobile Clinic in

Mopani District, South Africa

	STI + No. (%)	STI - No. (%)	P	OR STI (95% CI)	OR for CT (95% CI)	OR for NG (95% CI)	OR for MG (95% CI)	OR for TV (95% CI)
Age, y						100000		
Median (range)	30 (18-75)	39 (18-69)	0.001					
< 35	79 (62)	45 (40)						
≥ 35	48 (38)	69 (61)	<0.001	2.5 (1.5-4.2)	43 (2.1-8.8)	2.6 (1.2-5.4)	2.2 (0.8-5.9)	1.5 (0.9-2.6
Literacy level	1.1.1.1.1.1.1	1.002.000.00		0.7.77 A 5.70 C 1.77 A	1022/04202-0129	NUT STORE OF A 1990 - 1990 A	0.00 100 (MARCON 100 100 M	CARLON AND COLORS
Illiterate	25 (19)	37 (31)						
Literate	108 (81)	81 (69)	0.022	2.0 (1.1-3.5)	1.3 (0.6-2.7)	2.5 (0.9-6.7)	0.5 (0.2-1.3)	1.2 (0.7-2.3
Main source of income					in (one any	and four and		the form and
Employed or self-employed	30 (23)	31 (27)						
Grant	31 (24)	33 (29)						
Unemployed	67 (52)	51 (44)	0.459				$f : \mathbb{R} \to \mathbb{R}$	
HIV status	100.000		199460					
Negative	16 (62)	12 (57)						
Positive	10 (39)	9 (43)	0.760	0.8 (0.3-2.7)	0.4 (0.1-1.9)	1.6 (0.4-6.7)	0.9 (0.8-1.0)	1.1 (0.3-3.5
Relationship status					on (our may	and for the second	are fore tray	and four-pic
Married	45 (34)	52 (45)						
Living together	11 (8)	10 (9)						
Single	75 (57)	53 (46)	0.191					
Type of relationship	20.000	44.1144	0.000.000					
Stable partner	70 (62)	72 (75)						
Occasional partner	44 (39)	24 (25)	0.037	1.9 (1.1-3.4)	1.6 (0.8-3.3)	0.9 (0.4-2.0)	0.9 (0.3-2.8)	2.2 (1.2-4.0
Currently pregnant		and they		the first stud	the (old she)	tote for the most	Tota Carlo wish	and Crite. 110
No	129	110 (99)						
Yes	(98) 2 (2)	1(1)	0.665	1.7 (0.2-19)	1.0(1.0-1.0)	11 (1.1-128)	1.0(1.0-1.0)	1.0 (1.0-1.0
History of	14(11)	9 (8)		1.4 (0.6-3.4)				
STI treatment		050.8556	0.015 0.09				10.000	
Clinical presentation								
Symptoms								
Vaginal discharge	27 (20)	9 (8)	0.006	3.1 (1.4-6.9)	1.9 (0.9-4.1)	1.1 (0.4-2.9)	3.5 (1.3-9.3)	2.8 (1.3-5.7
Dysuria	10 (8)	10 (9)		0.9 (0.4-2.2)				
Genital itch	26 (20)	22 (19)		1.1 (0.6-2.0)				
Lower abdominal pain	40 (30)	32 (27)		1.2 (0.7-2.0)				
Pain during sexual intercourse	16(12)	7 (6)		2.2 (0.9-5.5)				
Blood loss during sexual intercourse	9 (7)	4 (3)		2.1(0.6-6.9)				
Vaginal discharge observed	10000			0.2319200-00055	000000000000000000000000000000000000000	1000200000000		0.0500.0500.0500
Yes	52 (39)	39 (33)						
No	81 (61)	79 (67)	0.320	1.3 (0.8-2.2)	0.8 (0.4-1.6)	0.6(0.3-1.4)	1.7 (0.7-4.1)	1.2 (0.7-2.1
Sexual behavior and risk	000.0000	1.555 1.5757	0.0000000	A THE ASSESSMENT		1. 10 M. N. 1990		(1999) A. (11), 1812.
Practiced anal sex past 6 mo.	3 (2)	3 (3)	0.882	0.9 (0.2-4.5)	0.8 (0.1-6.7)	0.8 (0.8-0.9)	2.3 (0.3-20)	1.1 (0.2-5.9
Practiced fellatio past 6 mo.	11 (8)	5 (4)		2.0 (0.7-6.0)				
Condom use (last sex act)	27 (21)	17 (15)		1.6 (0.8-3.0)				
>1 sex partner past 6 mo.	9 (8)	3 (3)	0.109				1.0 (0.1-8.2)	
Intravaginal cleansing	70 (53)	45 (40)		1.7 (1.1-2.8)				
Alcohol use past 6 mo	23 (17)	8 (7)		2.9 (1.2-6.7)				
Experienced sexual coercion	25 (19)	22 (19)		1.0 (0.5-1.9)				

All odds ratios with P value <0.05 are indicated in bold.

CT, Chlamydia trachomatis; NG, Neisseria gonorrhoeae; MG, Mycoplasma genitalium; TV, Trichomonas vaginalis.

DISCUSSION

In this study we show that there is a large burden of untreated symptomatic and asymptomatic STIs in a remote area of South Africa with poor access to healthcare services. We demonstrate that both syndromic and aetiological screening and management can contribute to STI control in this setting, but with variable efficiency. To our knowledge, this is one of the first studies showing the importance of out-of-facility STI services through a mobile clinic in a rural area in Africa.

The high proportion (53%) of women infected with at least one STI is of concern; the observed prevalence in our study is relatively high, even for South Africa. A recently published structured review showed a prevalence of 7-8% of *C. trachomatis* for studies conducted in community settings and 2-28% at PHC facilities; prevalence for *N. gonorrhoeae* was 1% and 8-23%, respectively.⁶ In addition, recent STI Spectrum model estimates of *C. trachomatis* and *N. gonorrhoeae* infection in women of reproductive age are 7% and 15%, respectively.²⁰ The prevalence of *C. trachomatis* (25%) and especially *T. vaginalis* (32%) was higher in this study than reported for a similar study of women visiting PHC facilities in the same district several years ago, whereas the prevalence of *N. gonorrhoeae* (16%) and *M. genitalium* (8%) was similar.^{3,21-23} Women in our study reported less often condom use during last sex act (18%) and previous STI treatment (9%) compared to women in the aforementioned facility-based study (36% respectively 22%).²¹ These findings suggest that lack of access to healthcare facilities may contribute considerably to the untreated burden of STIs in our region and that a concerning large number of symptomatic and asymptomatic women are left untreated in this area.

Our study confirms the limitations of the syndromic management approach for STI control due to high proportions of asymptomatic infections as reported by various others.¹⁰⁻¹² Only 37% of all STI-infected women would have been adequately treated by using the South African syndromic management guidelines for VDS; two-thirds of infected women would not have received adequate treatment. However, despite its limitations, the syndromic approach may be useful in a mobile setting with limited diagnostic resources, since 58% of symptomatic women would be treated adequately using this approach. However, as previously suggested, we would advocate for removing the age cut-off from the algorithm, since women \geq 35 years with STI would not receive adequate treatment; this is the case in 48/133 (36%) women with STI in our study.¹⁰ We did not identify clear and useful factors associated with inadequate treatment that could be included in a potentially revised algorithm. Therefore, it should be considered to refer women with persistent or recurrent symptoms for diagnostic testing in case there is no clinical response to syndromic management.

The main limitation of the syndromic approach is that it leaves asymptomatic women with STI untreated. Therefore, systematic screening and diagnostic testing of high-risk asymptomatic women should be considered. Such introduction of aetiological approach could be achieved by creating laboratory-based testing infrastructure or by inclusion of near-patient diagnostics in the mobile clinic. The latter has the advantage of same-day diagnosis and targeted treatment for the patient. The GeneXpert platform for near-patient testing for *C. trachomatis*, *N. gonorrhoeae* and *T. vaginalis* provides an opportunity to initiate aetiological testing in mobile clinics and has recently been evaluated in two studies.^{8,24} The development of rapid point-of-care testing for *M. genitalium* is in the pipeline.²⁵ This could be further augmented by building infrastructure for laboratory-based testing for other causes of VDS.

It is imperative to include remote areas in the public health response to the STI epidemic. Provision of STI services through a mobile clinic could address this unmet need. We did not include men in this study, but expect a similar unmet need for STI care. Mobile clinics are proven to be feasible and successful for providing healthcare in rural and hard-to-reach settings as shown by the implementation of a large infrastructure for mobile clinics in India.²⁶ The first step would be to enhance the implementation of syndromic STI management guidelines across the healthcare sector and to include the mobile clinics. There is much progress to be made in the quality of provision of STI services in general in South Africa: a recent study that evaluated the quality of STI service delivery through standardised patient actors showed that the syndromic management according to guidelines was provided in only 61% of cases.²⁷ Improvement of services would require deployment of specific resources (treatment) and training of the nurses on STI guidelines and identification of individuals at high risk for STIs. Moreover, a community awareness component would be essential to mobilise symptomatic

individuals for STI care. Syndromic management for STIs in South Africa seems to have reached its use-by date and should be replaced by an aetiological approach, which should be implemented in mobile clinics too.²⁸ Further research is required to evaluate the full impact on the STI epidemic of delivering STI services through mobile clinics in resource-constraint remote settings and the potential effectiveness of implementing a combined symptomatic and aetiological approach to STI control. A cost evaluation for delivering reproductive and primary health care services through a mobile clinic in South Africa, has shown that staffing costs are the largest component of providing mobile health services to rural communities; screening and treatment of STI had marginal cost.²⁹

This study has several limitations. First, although the women in our study were invited for any of the healthcare services provided by the mobile clinic, we cannot rule out that some degree of selection of high-risk women occurred, resulting in an overestimation of prevalence. Second, we only recruited women in this study and the results cannot necessarily be translated to providing STI services in mobile clinics for men in general, and those with male urethritis syndrome in particular. Furthermore, the study was only conducted in one mobile clinic and operational factors may impact on generalisability of the implementation results. Finally, collection of sexual behaviour data can be challenging and may have results in underreporting of sexual risk behaviour by participants.

In conclusion, this study emphasises the importance of providing STI services in remote areas with poor access to healthcare services to address the large STI epidemic in South Africa. In such areas, symptomatic STI screening and treatment through mobile clinics provides an important initial intervention that has to be enhanced by introduction of, preferably near-by patient, aetiological testing and STI management.

ACKNOWLEDGMENTS

We thank the patients for participating in this study as well as the staff at Anova Health Institute in Tzaneen and at the laboratory of Medical Microbiology at the University of Pretoria for their support.

REFERENCES

- Newman L, Rowley J, Vander Hoorn S, *et al.* Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. *PLoS One* 2015; 10: e0143304.
- Unemo M, Bradshaw CS, Hocking JS, *et al.* Sexually transmitted infections: challenges ahead. *Lancet Infect Dis* 2017; 17: e235-e279. doi:10.1016/S1473-3099(17)30310
- Hay B, Dubbink JH, Ouburg S, *et al.* Prevalence and macrolide resistance of Mycoplasma genitalium in South African women. *Sex Transm Dis* 2015; 42: 140–142. doi:10.1097/OLQ.00000000000246
- Le Roux MC, Mafunise M, de Villiers BE, *et al.* Antimicrobial susceptibility of Mycoplasma genitalium isolates from Pretoria, South Africa in 2012 and 2016. *S Afr J Infect Dis* 2017; 33(2): 46-49. doi:10.1080/23120053.2017.1391505
- UNAIDS, Joint United Nations Programme on HIV/AIDS (UNAIDS). The Gap Report. 2014;ISBN978-92-9253-062-4. UNAIDS/JC2656 (English original, July 2014, updated September 2014).
- Dubbink JH, Verweij SP, Struthers HE, *et al.* Genital Chlamydia trachomatis and Neisseria gonorrhoeae infections among women in sub-Saharan Africa: A structured review. *Int J STD AIDS* 2018; 29(8): 806-824. doi:10.1177/0956462418758224
- 7. Chirenje ZM, Gundacker HM, Richardson B, *et al.* Risk Factors for Incidence of Sexually Transmitted Infections Among Women in a Human Immunodeficiency Virus

Chemoprevention Trial: VOICE (MTN-003). Sex Transm Dis 2017; 44(3): 135–140. doi:10.1097/OLQ.00000000000568

- Mudau M, Peters RP, De Vos L, *et al.* High prevalence of asymptomatic sexually transmitted infections among human immunodeficiency virus-infected pregnant women in a low-income South African community. *Int J STD AIDS* 2018; 29(4): 324-333. doi:10.1177/0956462418758224
- Department of Health; Republic of South Africa. Sexually transmitted infections management guidelines, 2015. Available from: http://www.sahivsoc.org/upload/documents/STIguidelines-1-28-15(LC).pdf Accessed 24 November 2017.
- van der Eem L, Dubbink JH, Struthers HE, *et al.* Evaluation of syndromic management guidelines for treatment of sexually transmitted infections in South African women. *Trop Med Int Health* 2016; 21: 1138–1146. doi:10.1111/tmi.12742
- Mlisana K, Naicker N, Werner L, *et al.* Symptomatic vaginal discharge is a poor predictor of sexually transmitted infections and genital tract inflammation in high-risk women in South Africa. *J Infect Dis* 2012; 206: 6–14. doi:10.1093/infdis/jis298
- Pettifor A, Walsh J, Wilkins V, *et al.* How effective is syndromic management of STDs?: a review of current studies. *Sex Transm Dis* 2000; 27: 371–385.
- World Health Organization. WHO Sexually Transmitted Infections (STIs) Fact Sheet 2017. Available from: <u>http://who.int/mediacentre/factsheets/fs110/en/</u> Accessed 5 January 2018.
- Cohen MS. Classical sexually transmitted diseases drive the spread of HIV-1: back to the future. *J Infect Dis* 2012; 206(1): 1–2. doi:10.1093/infdis/jis303
- 15. Tanser F, Gijsbertsen B, Herbst K. Modelling and understanding primary health care accessibility and utilization in rural South Africa: An exploration using a geographical information system. *Soc Sci Med* 2006; *63*(3): 691–705.
- 16. de Waaij DJ, Dubbink JH, Peters RP, *et al.* Comparison of GMT presto assay and Roche cobas(R) 4800 CT/NG assay for detection of Chlamydia trachomatis and Neisseria

gonorrhoeae in dry swabs. *J Microbiol Methods* 2015; 118: 70–74. doi: 10.1016/j.mimet.2015.08.020

- Hayes RJ, Watson-Jones D, Celum C, *et al.* Treatment of sexually transmitted infections for HIV prevention: end of the road or new beginning. *AIDS* 2010; 24: S15–S26. doi: 10.1097/01.aids.0000390704.35642.47
- 18. de Waaij DJ, Ouburg S, Dubbink JH, *et al.* Evaluation of Presto(plus) assay and LightMix kit Trichomonas vaginalis assay for detection of Trichomonas vaginalis in dry vaginal swabs. *J Microbiol Methods* 2016; 127: 102–4. doi:10.1016/j.mimet.2016.06.002
- Edberg A, Jurstrand M, Johansson E, *et al.* A comparative study of three different PCR assays for detection of Mycoplasma genitalium in urogenital specimens from men and women. *J Med Microbiol* 2008; 57: 304–309. doi:10.1099/jmm.0.47498-0
- 20. Kularatne R, Niit R, Rowley J, *et al.* Adult gonorrhoea, chlamydia and syphilis prevalence, incidence, treatment and syndromic case reporting in South Africa: estimates using the Spectrum-STI model, 1990-2017. *PLoS One* 2018; *submitted for publication*
- Peters RP, Dubbink JH, van der Eem L, *et al.* Cross-Sectional Study of Genital, Rectal, and Pharyngeal Chlamydia and Gonorrhea in Women in Rural South Africa. *Sex Transm Dis* 2014; 41(9). doi: 10.1097/OLQ.00000000000175
- de Waaij DJ, Dubbink JH, Ouburg S, *et al.* Prevalence of Trichomonas vaginalis infection and protozoan load in South African women: a cross-sectional study. *BMJ Open* 2017; 7: e016959. doi:10.1136/bmjopen-2017-016959
- 23. Naidoo S, Wand H, Abbai NS, *et al.* High prevalence and incidence of sexually transmitted infections among women living in Kwazulu-Natal, South Africa. *AIDS Res Ther* 2014; 11: 31. doi:10.1186/1742-6405-11-31
- 24. Peters RP, de Vos L, Liteboho M, *et al.* Laboratory validation of Xpert[®] CT/NG and TV testing as performed by nurses at three primary healthcare facilities in South Africa. *J Clin Microbiol* 2017; 55(12): 3563-3565. doi:10.1128/JCM.01430-17
- 25. Sadiq ST, Mazzaferri F, Unemo M. Rapid accurate point-of-care tests combining diagnostics and antimicrobial resistance prediction for Neisseria gonorrhoeae and

Mycoplasma genitalium. *Sex Transm Infect* 2017; 93(S4): S65-S68. doi:10.1136/sextrans-2016-053072

- 26. Kojima N, Krupp K, Ravi K, *et al.* Implementing and sustaining a mobile medical clinic for prenatal care and sexually transmitted infection prevention in rural Mysore, India. *BMC Infect Dis* 2017; 17(1): 189. doi: 10.1186/s12879-017-2282-3
- 27. Kohler PK, Marumo E, Jed SL, *et al.* A national evaluation using standardised patient actors to assess STI services in public sector clinical sentinel surveillance facilities in South Africa. *Sex Transm Infect* 2017; 93: 247-252. doi: 10.1136/sextrans-2016-052930
- Garrett NJ, Osman F, Maharaj B, *et al.* Beyond syndromic management: Opportunities for diagnosis-based treatment of sexually transmitted infections in low- and middle-income countries. *PLoS One* 2018; 24;13(4): e0196209. doi:10.1371/journal.pone.0196209
- 29. Schnippel K, Lince-Deroche N, van den Handel T, *et al.* Cost Evaluation of Reproductive and Primary Health Care Mobile Service Delivery for Women in Two Rural Districts in South Africa. *PLoS One* 2015; 10(3): e0119236. doi:10.1371/journal.pone.0119236