Targeted point-of-care testing compared with syndromic management of urogenital infections in women (WISH): a cross-sectional screening and diagnostic accuracy study

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Summary

Background Sexually transmitted and urogenital infections are typically managed by WHO-recommended syndromic algorithms in resource-poor countries, and presumptively in Europe. However, algorithms for vaginal discharge and lower abdominal pain perform poorly in women. The women's improvement of sexual and reproductive health (WISH) study in Kigali, Rwanda, sought to improve case-finding and infection management in women by introducing point-of-care tests. The main aim was to compare the performance of the WISH algorithms and the WHO vaginal discharge and lower abdominal pain algorithms with gold standard testing.

Methods This cross-sectional screening and diagnostic accuracy study recruited women aged 18 years or older with or without urogenital symptoms at risk of acquiring sexually transmitted infections in Kigali, Rwanda. Recruitment activities were implemented by study staff with the help of community mobilisers at health centres, pharmacies, markets, women's organisations, and at "umuganda" community meetings. At the study visit, participants had a face-to-face interview that included questions about current urogenital symptoms. Participants were first asked without prompting (spontaneous reporting), followed by questions about 14 specific symptoms (structural reporting). Next, the WISH algorithms were implemented. All participants had point-of-care tests for bacterial vaginosis (vaginal pH of 5·0 or above) and *Trichomonas vaginalis* (immunoassay) regardless of symptom reporting. Women with a positive risk score had point-of-care tests for *Chlamydia trachomatis* and *Neisseria gonorrhoea* (nucleic acid amplification tests). Vulvovaginal candidiasis was treated presumptively. Nucleic acid amplification tests for *C trachomatis*, *N gonorrhoeae*, *T vaginalis*, bacterial vaginosis, and vulvovaginal candidiasis were the gold standard, and all patients provided swabs for these.

Findings Participants were recruited between July 5, 2016, and March 14, 2017. 705 participants were enrolled in the study and completed a study visit, and 51 attended 53 additional visits. Prevalence by gold standard testing was 8·5% for *C trachomatis*, 7·1% for *N gonorrhoeae*, 16·1% for *T vaginalis*, 18·1% for bacterial vaginosis, and 8·6% for vulvovaginal candidiasis. The WISH algorithms identified similar numbers of *C trachomatis*, *N gonorrhoeae*, and *T vaginalis* infections, but much higher numbers of bacterial vaginosis and vulvovaginal candidiasis infections. Compared with gold standard testing, the WISH algorithms had a good sensitivity and high specificity for *C trachomatis* (sensitivity 71·7%, specificity 100%), *N gonorrhoeae* (sensitivity 76·0%, specificity 100%), and *T vaginalis* (sensitivity 68·5%, specificity 97·4%), high sensitivity but low specificity for bacterial vaginosis (sensitivity 95·2%, specificity 41·2%), and moderate sensitivity and specificity for vulvovaginal candidiasis (sensitivity 64·4%, specificity 69·4%). The performance of vaginal pH testing for bacterial vaginosis improved by increasing the cutoff to 5·5, followed by confirmatory testing (sensitivity 73·6%, specificity 100%). The WHO algorithms had moderate sensitivity and poor specificity for all infections compared with gold standard testing: *C trachomatis* sensitivity 58·3%, specificity 44·7%; *N gonorrhoeae* sensitivity 66·0%, specificity 45·2%; *T vaginalis* sensitivity 60·4%, specificity 45·6%; bacterial vaginosis sensitivity 61·6%, specificity 46·0%; and vulvovaginal candidiasis sensitivity 74·6%, specificity 50·6%. Two participants attended additional visits because they had a mild allergic reaction to metronidazole. Staff and participants considered point-of-care testing feasible and acceptable.

Interpretation Point-of-care testing for urogenital infections might improve case-finding and infection management and is feasible in resource-poor settings. Point-of-care tests should be further developed, including those targeting multiple conditions. Additional studies in other populations, including populations with low prevalence of sexually transmitted and urogenital infections, are warranted.

Funding European and Developing Countries Clinical Trials Partnership.

Research in context

Evidence before this study

We did a scoping review of programmes and studies that had evaluated syndromic management of urogenital and sexually transmitted infections, on the basis of WHO recommendations, or point-of-care tests (POCTs). We searched PubMed and Embase for articles published between Jan 1, 2004 (the year in which WHO published a pivotal report on POCTs for sexually transmitted infections), and Oct 16, 2018. We searched without language restrictions, using the search terms ("sexually transmitted disease" OR "sexually transmitted infection" OR "HIV" OR "syphilis" OR "chlamydia" OR "gonorrhea" OR "trichomonas") AND ("rapid" OR "rapid test" OR "rapid diagnostic*" OR "point-of-care" OR "point of care" OR "on-site") AND ("low resource" OR "resource poor" OR "resource limited" OR "developing country" OR "low income" OR "Africa") AND ("implement" OR "introduc*" OR "feasib*" OR "accept*"). Additional information was identified by searching reference lists of published articles, and by searching WHO and other relevant reports. We found strong evidence that WHO algorithms for vaginal discharge and lower abdominal pain were inadequate, resulting in undertreatment, overtreatment, or inadequate treatment of symptomatic women. Furthermore, syndromic and presumptive approaches miss all asymptomatic infections by definition. POCTs for HIV, syphilis, and pregnancy have been successfully implemented on a large scale worldwide, but those for urogenital and sexually transmitted infections are rarely used, especially in resource-limited settings. POCTs for HIV, syphilis, and pregnancy comply with WHO ASSURED criteria (affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable to end-users). Fewer ASSURED-compliant POCTs are available for urogenital and sexually transmitted infections. Both symptomatic and asymptomatic infections fuel epidemics of HIV and sexually transmitted infections, and can cause infertility, pelvic inflammatory disease, pregnancy complications, and invasive neonatal infections.

Added value of this study

The WISH study in Kigali, Rwanda, improved case-finding and infection management in women at risk for HIV and sexually transmitted infections, with or without symptoms, by introducing POCTs for conditions that might cause vaginal discharge or lower abdominal pain (chlamydia, gonorrhoea, trichomoniasis, and bacterial vaginosis). Vulvovaginal candidiasis was treated presumptively. The CT/NG GeneXpert POCT did not comply with ASSURED criteria, but improved management of chlamydia and gonorrhoea compared with syndromic management. The OSOM test for trichomoniasis met ASSURED criteria and performed reasonably well. Treating all women with a vaginal pH of at least 5·0 for bacterial vaginosis resulted in overtreatment, but the algorithm could be improved by increasing the pH cutoff to 5·5 and adding a confirmatory test for results above the cutoff. We used a score comprising vaginal concentrations of lactobacillus and two bacterial vaginosis-associated bacteria by quantitative PCR (qPCR) as the confirmatory test, but lactobacillus concentration on its own had good performance, and Gram stain Nugent scoring could also be used. Similarly, treating all women reporting symptoms of vulvovaginal candidiasis resulted in overtreatment. The algorithm could be improved by only testing for vulvovaginal candidiasis in symptomatic women who tested negative for the other infections associated with vaginal discharge and lower abdominal pain, as well as pregnant women. Speculum and bimanual examinations by a physician had little additional value (except for cases of lower abdominal pain), and partner notification was suboptimal. Staff and participants considered the POCTs feasible and highly acceptable.

Implications of all the available evidence

The WHO syndromic algorithms for vaginal discharge and lower abdominal pain should be revised by incorporating POCTs. The WISH study showed that introducing available POCTs for vaginal discharge and lower abdominal pain is possible; however, programmes would benefit from more affordable combined POCTs for chlamydia and gonorrhoea, and ASSURED-compliant POCTs that combine diagnoses of bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis.

Introduction

Sexually transmitted infections and other urogenital infections cause a major burden of disease worldwide.[1] WHO estimated that 357 million new curable infections caused by *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, and *Treponema pallidum* occurred in 2012.[2] In women, bacterial vaginosis, vulvovaginal candidiasis, and urinary tract infections are also common.[3,4] Long-term sequelae include increased risk of HIV acquisition and transmission, pelvic inflammatory disease, pregnancy complications, and invasive neonatal infections.[4–6]

Most resource-poor countries diagnose genital infections syndromically, using local guidelines that are based on WHO guidelines for the management of sexually transmitted infections.[7,8] Each patient-reported symptom, potentially augmented by clinician-observed signs during a physical examination, is treated for all organisms that might cause that symptom.[7] In women, the four main syndromes on which the WHO algorithms are based are vaginal discharge without lower abdominal pain, lower abdominal pain with or without vaginal discharge, genital ulcers with or without inguinal buboes, and inguinal buboes without genital ulcers.[7]

The vaginal discharge syndrome is the most common.[8,9] WHO recommends that women with vaginal discharge should always be treated for bacterial vaginosis and trichomoniasis, and for chlamydia and gonorrhoea if local prevalence is high or if locally designed risk assessments are positive. WHO recommends additional treatment for vulvovaginal candidiasis if the discharge is curd-like or is accompanied by vulval oedema, erythema, or excoriations. In Europe, most sexually transmitted infections and urogenital infections in women are treated presumptively by primary care physicians.

By definition, syndromic and presumptive approaches miss all asymptomatic infections. Asymptomatic infections in women are common and are associated with the complications outlined above.[4,10] Furthermore, many studies in different countries have shown that the performance of algorithms for vaginal discharge and lower abdominal pain in symptomatic women are suboptimal, leading to undertreatment, overtreatment, or inadequate treatment of patients.[9,11–13]

The women's improvement of sexual and reproductive health (WISH) study in Kigali, Rwanda, sought to improve case-finding and infection management in women by introducing point-of-care tests (POCTs).[14] Our aim was to use POCTs that comply with WHO ASSURED criteria (affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable to end users) as much as possible.[15,16] Participants were first asked about urogenital symptoms as if we were to provide them with syndromic care, but were then offered the POCT-based WISH algorithms. Stored clinical samples from all women were also tested by gold standard nucleic acid amplification tests (NAATs). This study design allowed us to compare the performance of the WISH algorithms and the WHO vaginal discharge and lower abdominal pain algorithms with gold standard results, to evaluate the feasibility and acceptability of the WISH algorithms, recommend optimal algorithms given currently available POCTs, and identify POCT development gaps.

Methods

Study design and participants

This cross-sectional screening and diagnostic accuracy study was done at the Rinda Ubuzima research clinic and laboratory in Kigali, Rwanda. Study staff had extensive experience in sexual and reproductive health care. Our aim was to recruit women at risk of acquiring HIV and sexually transmitted infections, who were at varying degrees of risk and not exclusively sex workers.

Recruitment activities were implemented by study staff with the help of community mobilisers. Two mobilisers were women who had taken part in previous studies at Rinda Ubuzima, and one was a community organiser. Community mobilisers organised recruitment meetings and distributed flyers at health centres, pharmacies, markets, women's organisations, and at "umuganda" community meetings. Participants were encouraged to refer their friends. Women aged 18 years or older at risk of acquiring sexually transmitted infections (defined as having had more than one sex partner or having been treated for at least one sexually transmitted infection in the past year) with or without urogenital symptoms were enrolled. HIV-positive and pregnant women were not excluded. Women were told that they would be screened for urogenital infections free of charge, that they could only be screened once, and that they would not receive a monetary reimbursement for participation.

All participants provided written informed consent. The study was sponsored by the University of Liverpool and approved by the Rwanda National Ethics Committee and the University of Liverpool Research Ethics Subcommittee for Physical Interventions.

Procedures

At the study visit, participants had a face-to-face interview that included questions about current urogenital symptoms (including symptoms in the past 2 weeks). Participants were first asked if they had any symptoms without prompting (spontaneous reporting), followed by questions about 14 specific symptoms (structural reporting). All women were offered comprehensive counselling and could select topics themselves.

Next, the WISH algorithms were implemented (figure). All women were offered HIV, pregnancy, trichomoniasis, and bacterial vaginosis testing. We used ASSURED POCTs to diagnose HIV, pregnancy, and *T vaginalis* (OSOM; Sekisui Diagnostics, MA, USA), and a vaginal pH swab to diagnose bacterial vaginosis (EcoCare; Merete Medical, Luckenwalde, Germany). A vaginal pH of at least 5·0 was considered bacterial vaginosis. Since ASSURED POCTs for chlamydia and gonorrhoea with adequate performance are not yet available,[17,18] we used GeneXpert CT/NG (Cepheid, CA, USA). This point-of-care NAAT is more than 95% sensitive and specific for both organisms,[19] but it requires equipment, is expensive to run (we paid US$18·25 for consumables per test), and takes 90 min to return results. We therefore only offered GeneXpert CT/NG to women who had a positive risk score for chlamydia and gonorrhoea. To test for syphilis we used the Determine Syphilis test (Alere, MA, USA) with confirmation of active infection by the rapid plasma reagin test (SpinReact, Girona, Spain), but we only offered syphilis testing to women who had a positive syphilis risk score because syphilis prevalence was expected to be low.[20,21] Risk scores for chlamydia and gonorrhoea and for syphilis were positive if patients met one or more of the following criteria: currently pregnant, exchanged sex for money or goods in the past 12 months, new sexual partner in the past 3 months, or relevant clinical signs observed by a physician. The relevant physician-observed signs for

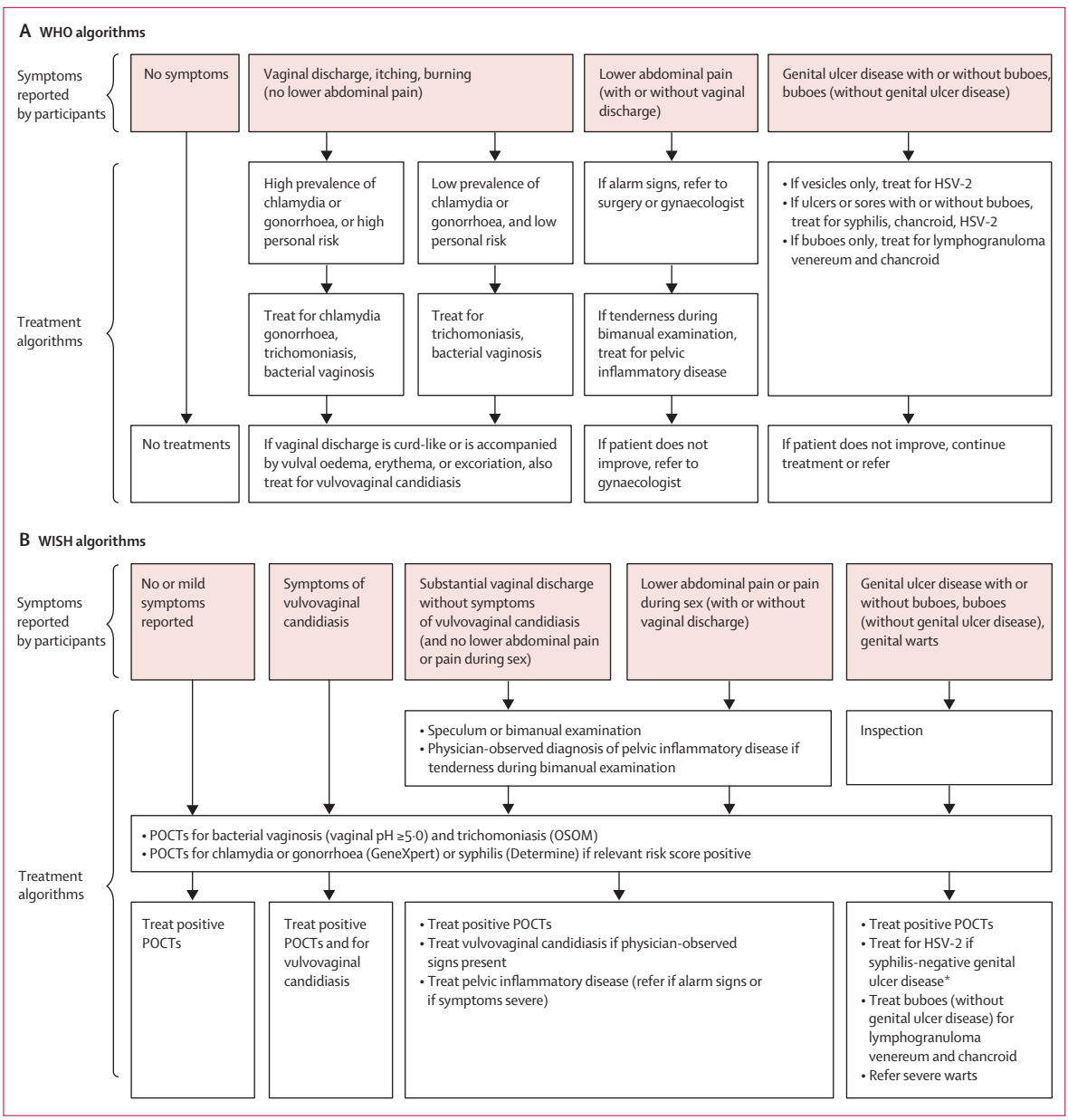

Figure: **WHO and WISH algorithms for management of sexually transmitted and urogenital infections**
Lower abdominal pain in the WHO algorithm and lower abdominal pain or pain during sex in the WISH algorithm require examination by a physician. Alarm signs include a missed or overdue period; recent delivery, abortion, or miscarriage; abdominal guarding, rebound tenderness, or both; abnormal vaginal bleeding; and abdominal mass. Both in the WHO and WISH algorithms, participants are treated for pelvic inflammatory disease if there are no alarm signs but cervical motion, uterine, or adnexal tenderness is observed during bimanual examination. Treatment for pelvic inflammatory disease covers treatment for chlamydia, gonorrhoea, trichomoniasis, and bacterial vaginosis. HSV-2=Herpes simplex virus type 2. POCT=point-of-care test. *Syphilis-negative genital ulcer disease to be treated for chancroid if no response to HSV-2 treatment.

the chlamydia and gonorrhoea risk score were vaginal discharge with an offensive smell or pelvic inflammatory disease. The relevant physician-observed clinical signs for the syphilis risk score were genital ulcer disease or inguinal buboes observed by a physician.

The WISH algorithms called for mild vaginal discharge to be ignored if none of the POCTs were positive, and for presumptive treatment for vulvovaginal candidiasis if the participant reported the discharge to be curdlike with or without genital itching or burning. Women reporting lower abdominal pain (including pain during sex) or substantial vaginal discharge not typical for vulvovaginal candidiasis were offered a speculum and bimanual examination by a physician. Substantial vaginal

	WHO algorithms	WISH algorithms	Gold standard testing
Chlamydia trachomatis	Vaginal discharge and high risk of acquiring STIs or high local prevalence; pelvic inflammatory disease (after bimanual examination for lower abdominal pain)	Positive for *C trachomatis* according to GeneXpert after positive risk score	Positive for *C trachomatis* by GeneXpert
Neisseria gonorrhoeae	Vaginal discharge and high risk of acquiring STIs or high local prevalence; pelvic inflammatory disease (after bimanual examination for lower abdominal pain)	Positive for *N gonorrhoeae* by GeneXpert after positive risk score	Positive for *N gonorrhoeae* by GeneXpert
Trichomonas vaginalis	Vaginal discharge; pelvic inflammatory disease (after bimanual examination for lower abdominal pain)	Positive for *T vaginalis* by OSOM	Positive *T vaginalis* PCR
Bacterial vaginosis	Vaginal discharge; pelvic inflammatory disease (after bimanual examination for lower abdominal pain)	Vaginal pH at least 5·0 on EcoCare pH swab	Bacterial vaginosis by vaginal qPCR score[23]
Vulvovaginal candidiasis	Vaginal discharge that is curd-like, or is accompanied by vulval oedema, erythema, or excoriation*	Participant-reported vaginal discharge that was curd-like or occurred with genital itching or burning, or clinician-observed curd-like vaginal discharge, vulval oedema, erythema, or excoriation	Positive for *C albicans* qPCR
Syphilis	Genital ulcer disease (after visualisation by provider)†	Positive for *T pallidum* by Determine Syphilis (confirmed by rapid plasma reagin test) after positive risk score	Not available

STI=sexually transmitted infection. qPCR=quantitative PCR. *The WHO-specified criteria of vulval oedema, erythema, and excoriations seemed inappropriate for the algorithm without examination by a physician. We therefore assumed that a woman would have been treated for vulvovaginal candidiasis if she reported vaginal discharge, and if the discharge was curd-like or occurred with genital itching or burning. †According to WHO recommendations, only women with a positive rapid plasma reagin test and no recent treatment should be treated for syphilis. However, in the absence of this information, we assumed that all women with genital ulcer disease would have been treated for syphilis.

Table 1: **Conditions under which organism-specific treatments were dispensed, or would have been dispensed, for each set of algorithms**

discharge or pelvic inflammatory disease observed by the physician resulted in a positive risk score for chlamydia and gonorrhoea and was followed by GeneXpert CT/NG testing, and patients were to be treated for pelvic inflammatory disease even if the test was negative.

Women with genital ulcers or buboes would be offered inspection by a physician. Any visible lesions resulted in a positive syphilis risk score, so the participants would qualify for syphilis testing. Diagnoses could be syphilis, syphilis-negative genital ulcer disease, inguinal buboes without genital ulcers, or genital warts (including multiple diagnoses). Urinalysis testing was only offered to women reporting urinary symptoms, and the presence of any nitrite or leucocytes in urine was considered a urinary tract infection.

Blood (4·5 mL EDTA), urine, and OSOM and EcoCare vaginal swabs were collected as required to implement the WISH algorithms. A GeneXpert swab and two polyester vaginal swabs were collected from all women for gold standard testing. The GeneXpert CT/NG assay was considered gold standard because of its excellent performance compared with other validated *C trachomatis* and *N gonorrhoeae* NAATs.[19] Although only women who had a positive risk score for chlamydia and gonorrhoea were tested the same day of their visit, GeneXpert swabs were also taken from all other women and tested in batches. All other gold standard NAATs were done at the HIV/STD Reference Laboratory of the Institute of Tropical Medicine in Antwerp, Belgium: *T vaginalis*, *Mycoplasma genitalium*, *Candida albicans*, *Lactobacillus* spp, *Gardnerella vaginalis*, and *Atopobium vaginae* on vaginal swabs, and *Escherichia coli* on urine (appendix).[22] *C albicans* qPCR is not a true gold standard test for vulvovaginal candidiasis, but we will refer to it as such in this paper, for convenience and because the majority of cases are caused by *C albicans* (appendix). A validated vaginal qPCR score ($\log_{10}$ geq/mL [*Lactobacillus* spp]−$\log_{10}$ geq/mL [*G vaginalis*+*A vaginae*]) lower than −2 identified true cases of bacterial vaginosis.[23] HIV, syphilis, pregnancy, and urinary tract infection POCTs were offered as a service to participants and the performance of these tests was not evaluated.[24,25]

See Online for appendix

Participants could opt out of each service offered and the reasons were recorded. Our aim was to deliver all services during the main visit within half a day. However, women could choose to leave before having received all results, and either return for a scheduled additional visit or receive instructions regarding the need for follow-up via letter or mobile phone. Treatment, partner notification, and referral procedures are described in table 1 and in the appendix. Care was taken to preserve participant confidentiality throughout the study.

A subset of participants were interviewed about their experiences with WISH procedures by an interviewer with no previous relationship with the interviewees, using a semi-structured client satisfaction survey (appendix). Another subset of participants was observed and timed throughout their clinic trajectory.

Outcomes

The main outcomes were performance of the WISH and WHO algorithms, each compared with gold standard diagnoses. Additionally, we optimised the bacterial vaginosis and vulvovaginal candidiasis algorithms post-hoc to improve performance (appendix).

Statistical analysis

The target sample size was 500–1000 participants, depending on resources. With a sample size of 500, we

	Participants (n=705)
Demographics	
Age, years	32·9 (28·2–38·0)
Sex	
Female	705 (100%)
Male	0
Marital status	
Never married	461 (65%)
Married	209 (30%)
Divorced	18 (3%)
Widowed	17 (2%)
Highest educational level attained	
No schooling	113 (16%)
Primary school not completed	159 (23%)
Primary school completed	176 (25%)
Secondary school not completed	135 (19%)
Secondary school completed	90 (13%)
Further than secondary school	32 (5%)
Sexual history	
Male sex partners in lifetime	4 (2–8)
Male sex partners in past 12 months	2 (1–3)
New sex partner in the past 3 months	227 (32%)
Currently has a main sex partner	618 (88%)
Number of vaginal sex acts in the past 2 weeks	4 (2–10)
Has had anal sex in the past 2 weeks	7 (1%)
Condom use during vaginal sex in past 2 weeks (n=704)	
Always	24 (3%)
Sometimes but not always	114 (16%)
Never	566 (80%)
Used condom during last vaginal sex act (n=704)	83 (12%)
Exchanged sex for money or goods in past 12 months	250 (35%)
Reproductive and contraceptive history	
Pregnancies in lifetime	3 (2–4)
Ever used a product to prevent pregnancy	527 (75%)
Currently using a product to prevent pregnancy	222 (31%)
Combined estrogen and progestin pills*	38 (17%)
Progestin injections†	61 (27%)
Progestin implant‡	77 (35%)
Copper intrauterine device	37 (17%)
Participant had a tubal ligation	9 (4%)
General medical history	
Currently taking antibiotics or antifungals§	134 (19%)
Tested for HIV in the past	698 (99%)
Number of times tested for HIV in lifetime	4 (3–6)
Known to be HIV-positive before main visit	135 (19%)
Treated for a sexually transmitted infection in the past	502 (71%)
Treated for bacterial vaginosis in the past	35 (5%)
Treated for vulvovaginal candidiasis in the past	129 (18%)
Treated for urinary tract infection in the past	100 (14%)

(Table 2 continues in next column)

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	Participants (n=705)
Participant-reported symptoms	
Any structural reported urogenital symptom	604 (86%)
Vaginal discharge curd-like	265 (38%)
Vaginal discharge offensive-smelling	119 (17%)
Lower abdominal pain	245 (35%)
Genital ulcers, blisters, or sores	41 (6%)
Inguinal buboes	1 (<1%)
Genital warts	0

Data are median (IQR) or n (%). All data are self-reported by participants. *All participants reported using pills containing ethinylestradiol and levonorgestrel. No participants reported using progestin-only pills. †48 (21·6%) of 222 participants who were using progestin injections reported using depot medroxyprogesterone acetate and 13 (5·9%) reported using norethisterone. ‡All patients with a progestin implant reported using a levonorgestrel-releasing implant. §Includes 124 (17·6%) HIV-positive participants who were taking trimethoprim and sulfamethoxazole as prophylaxis.

Table 2: **Characteristics of study participants**

expected to identify 50–175 true cases for each infection tested.[20,21] Statistical analyses were done with Stata 13 (StataCorp, TX, USA). We determined the proportions of women who were treated according to the WISH algorithms, or would have been treated according to the WHO algorithms, for bacterial vaginosis, trichomoniasis, chlamydia, gonorrhoea, and vulvovaginal candidiasis (table 1). WHO published two algorithms for vaginal discharge: one that incorporates a speculum examination and one that does not. We used the algorithm without a speculum examination, which is most widely used. We assumed that all women with vaginal discharge would have been treated for chlamydia and gonorrhoea, in addition to bacterial vaginosis and trichomoniasis, because of high prevalences in our study population (appendix). Women with vaginal discharge that was curd-like or accompanied by genital itching or burning would have been treated for those four infections as well as for vulvovaginal candidiasis. We also calculated sensitivities, specificities, positive predictive values, and negative predictive values (with 95% CIs) of the WISH and WHO algorithms, each compared with gold standard results. Finally, we optimised the algorithms for bacterial vaginosis and vulvovaginal candidiasis by post-hoc analysis of our data.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Participants were recruited between July 5, 2016, and March 14, 2017. All 705 enrolled participants completed a

	Gold standard testing (n=705)	WHO algorithms (n=705)	WISH algorithms (n=705)
Infections associated with vaginal discharge or lower abdominal pain			
At least one	306/690* (44%)	392 (56%)	608 (86%)
Chlamydia trachomatis	60 (9%)	392 (56%)	43 (6%)
Neisseria gonorrhoea	50 (7%)	392 (56%)	38 (5%)
Trichomonas vaginalis	111/690* (16%)	392 (56%)	92 (13%)
Bacterial vaginosis	125/690* (18%)	392 (56%)	466 (66%)†
Vulvovaginal candidiasis	59/690* (9%)	366 (52%)	235 (33%)
Other conditions			
Mycoplasma genitalium	26/690* (4%)	NA	NA
Syphilis	NA	16 (2%)	21 (3%)
Pelvic inflammatory disease	NA	29 (4%)	32 (5%)
HIV	NA	NA	55‡ (8%)
Urinary tract infection	NA	NA	161 (23%)
Pregnancy	NA	NA	33 (5%)

Data are n (%). The HIV status of participants for the WISH algorithm was measured at the Rinda Ubuzima research clinic. WHO published two algorithms for vaginal discharge: one that incorporates a speculum examination and one that does not. We used the algorithm without speculum examination, which is most widely used. We assumed that all women with vaginal discharge would have been treated for chlamydia and gonorrhoea, in addition to bacterial vaginosis and trichomoniasis, because of the high local prevalence in our study population (appendix). Women with vaginal discharge that was curd-like or accompanied by genital itching or burning would have also been treated for those four infections, as well as for vulvovaginal candidiasis. NA=not applicable. *15 PCR results were invalid during gold standard testing, so the results of only 690 participants were recorded for these infections. †The vaginal pH results of all 705 participants are in the appendix. ‡Includes 24 known HIV-positive women who wanted to be retested.

Table 3: **Infections that were treated with the WISH algorithms, infections that would have been treated with the WHO algorithms, and gold standard results**

study visit, and 51 attended 53 additional visits. 40 of 51 participants attended additional visits because they received results or additional treatment, 11 had persistent or new symptoms, two had a mild allergic reaction to metronidazole, one patient returned for a speculum examination, and one to obtain information. No other adverse events or social harms were reported apart from the mild allergic reactions to metronidazole. Participants had a median age of 32·9 years (IQR 28·2–38·0); 461 (65·4%) of 705 were never married, 227 (32·2%) reported a new sex partner in the past 3 months, and 250 (35·5%) had engaged in sex work in the past 12 months (table 2). Most women reported having been tested for HIV (698 [99·0%]) and having been treated for a sexually transmitted infection in the past (502 [71·2%]), and 135 (19·2%) reported to be HIV-positive. Most women reported at least one urogenital symptom (604 [85·7%]), and more symptoms were reported structurally than spontaneously (appendix). Of the 604 women structurally reporting symptoms, 43 (7·1%) had already sought medical care for these symptoms, and 103 (17·1%) had used traditional medications.

Almost half of the participants (306 [44·3%] of 690) had at least one of the five infections associated with vaginal discharge and lower abdominal pain by gold standard testing: 60 (8·5%) of 705 had chlamydia, 50 (7·1%) of 705 had gonorrhoea, 111 (16·1%) of 690 had trichomoniasis, 125 (18·1%) of 690 had bacterial vaginosis, and 59 (8·6%) of 690 had vulvovaginal candidiasis (table 3). The vaginal pH results of all 705 participants are in the appendix. 229 (33·2%) of 690 had one infection and 77 (11·2%) of 690 had two or more infections (appendix). An additional 26 (3·8%) of 690 tested positive for *M genitalium*, but this infection was not included in the WISH or WHO algorithms. Compared with gold standard testing, WISH algorithms identified similar numbers of *C trachomatis*, *N gonorrhoeae*, and *T vaginalis* infections, but much higher numbers of bacterial vaginosis and vulvovaginal candidiasis infections (table 3). If the WHO algorithms had been used, 392 (51·9%) of 705 women would have received treatment for all five infections and an additional 26 (3·7%) for all except vulvovaginal candidiasis. Compared with gold standard testing, the WISH algorithms had good sensitivity and high specificity for *C trachomatis* (sensitivity 71·7%, specificity 100%), *N gonorrhoeae* (sensitivity 76·0%, specificity 100%), and *T vaginalis* (sensitivity 68·5%, specificity 97·4%), high sensitivity but low specificity for bacterial vaginosis (sensitivity 95·2%, specificity 41·2%), and moderate sensitivity and specificity for vulvovaginal candidiasis (sensitivity 64·4%, specificity 69·4%). The WHO algorithms had moderate sensitivity and poor specificity for all infections compared with gold standard testing (table 4): *C trachomatis* sensitivity 58·3%, specificity 44·7%; *N gonorrhoeae* sensitivity 66·0%, specificity 45·2%; *T vaginalis* sensitivity 60·4%, specificity 45·6%; bacterial vaginosis sensitivity 61·6%, specificity 46·0%; and vulvovaginal candidiasis sensitivity 74·6%, specificity 50·6%.

We used the GeneXpert CT/NG assay in WISH and for gold standard testing, but in the WISH algorithms only women with a positive CT/NG risk score were tested. This resulted in 396 (56·2%) of 705 women being tested with this assay, but 25 (25·0%) of 100 true infections were missed (table 4). The *T vaginalis* POCT was offered to all women and had moderate sensitivity (68·5%). The main problem with the WISH algorithms was the high number of false positive diagnoses of bacterial vaginosis and vulvovaginal candidiasis. We therefore used WISH study data to design optimal bacterial vaginosis and vulvovaginal candidiasis algorithms post-hoc (appendix). We achieved the best balance between reducing bacterial vaginosis false positives and numbers of women requiring testing by measuring vaginal pH in all women (as had previously been done), but then adding a confirmatory test if the pH was at least 5·5, resulting in 275 confirmatory tests being required (223 if women who already tested positive for *T vaginalis* are deducted because the treatment they receive is the same as the treatment for bacterial vaginosis). Sensitivity, specificity, positive predictive values, and negative predictive values of diagnoses made with the optimal bacterial vaginosis algorithm (table 4) were 73·6%, 100%, 100%, and 94·5%, when using the vaginal qPCR score as the confirmatory test. They were only slightly reduced when the lactobacillus qPCR was used as a standalone confirmatory

	Chlamydia trachomatis	*Neisseria gonorrhoeae*	*C trachomatis* and *N gonorrhoeae*	*Trichomonas vaginalis*	Bacterial vaginosis	Bacterial vaginosis and *T vaginalis*	Vulvovaginal candidiasis
Gold standard testing							
Negative	645/705 (91·5%)	655/705 (92·9%)	605/705 (85·8%)	579/690 (83·9%)	565/690 (81·9%)	481/690 (69·7%)	631/690 (91·4%)
Positive	60/705 (8·5%)	50/705 (7·1%)	100/705 (14·2%)	111/690 (16·1%)	125/690 (18·1%)	209/690 (30·3%)	59/690 (8·6%)
WHO algorithm							
True positives	35/705 (5·0%)	33/705 (4·7%)	61/705 (8·7%)	67/690 (9·7%)	77/690 (11·2%)	124/690 (18·0%)	44/690 (6·4%)
False positives	357/705 (50·6%)	359/705 (50·9%)	331/705 (47·0%)	315/690 (45·7%)	305/690 (44·2%)	258/690 (37·4%)	312/690 (45·2%)
False negatives	25/705 (3·5%)	17/705 (2·4%)	39/705 (5·5%)	44/690 (6·4%)	260/690 (37·7%)	85/690 (12·3%)	15/690 (2·2%)
True negatives	288/705 (40·9%)	296/705 (42·0%)	274/705 (38·9%)	264/690 (38·3%)	48/690 (7·0%)	223/690 (32·3%)	319/690 (46·2%)
Sensitivity	58·3% (45·5–70·2)	66·0% (51·8–77·8)	61·0% (51·1–70·1)	60·4% (50·9–69·1)	61·6% (52·7–69·7)	59·3% (52·5–65·8)	74·6% (61·9–84·1)
Specificity	44·7% (40·8–48·5)	45·2% (41·4–49·0)	45·3% (41·4–49·3)	45·6% (41·6–49·7)	46·0% (41·9–50·2)	46·4% (41·3–50·8)	50·6% (46·6–54·5)
Positive predictive value	8·9% (6·5–12·2)	8·4% (6·0–11·6)	15·6% (12·3–19·5)	17·5% (14·0–21·7)	20·2% (16·4–24·5)	32·5% (27·9–72·1)	12·4% (9·3–16·2)
Negative predictive value	92·0% (88·4–94·6)	94·6% (91·4–96·6)	87·5% (83·4–90·8)	85·7% (81·3–89·2)	84·4% (79·9–88·1)	72·4% (67·1–77·1)	95·5% (92·7–97·3)
WISH algorithm							
True positives	43/705 (6·1%)	38/705 (5·4%)	75/705 (10·6%)	76/690 (11·0%)	119/690 (17·2%)	194/690 (28·1%)	38/690 (5·5%)
False positives	0	0	0	15/690 (2·2%)	332/690 (48·1%)	274/690 (39·7%)	193/690 (28·0%)
False negatives	17/705 (2·4%)	12/705 (1·7%)	25/705 (3·5%)	35/690 (5·1%)	6/690 (8·7%)	15/690 (2·2%)	21/690 (3·0%)
True negatives	645/705 (91·5%)	655 (92·9%)	605/705 (85·8%)	564/690 (81·7%)	233/690 (33·8%)	207/690 (30·0%)	438/690 (63·5%)
Sensitivity	71·7% (58·3–81·7)	76·0% (62·2–85·9)	75·0% (65·5–82·6)	68·5% (59·2–76·5)	95·2% (89·7–97·8)	92·8% (88·4–95·6)	64·4% (51·4–75·6)
Specificity	100% (100–100)	100% (100–100)	100% (100–100)	97·4% (95·7–98·4)	41·2% (37·2–45·4)	43·0% (38·7–47·5)	69·4% (65·7–72·9)
Positive predictive value	100% (100–100)	100% (100–100)	100% (100–100)	83·5% (74·4–89·8)	26·4% (22·5–30·7)	41·5% (37·1–46·0)	16·5% (12·2–21·8)
Negative predictive value	97·4% (95·9–98·4)	98·2% (96·9–99·0)	96·0% (94·2–97·3)	94·2% (92·0–95·8)	97·5% (94·5–98·9)	93·2% (89·1–95·9)	95·4% (93·1–97·0)
Optimal bacterial vaginosis and vulvovaginal candidiasis algorithm							
True positives	NA	NA	NA	NA	92/690 (13·3%)	152/690 (22·0%)	35/690 (5·1%)
False positives	NA	NA	NA	NA	0	10/690 (1·4%)	0
False negatives	NA	NA	NA	NA	33/690 (4·8%)	57/690 (8·3%)	24/690 (3·5%)
True negatives	NA	NA	NA	NA	565/690 (81·9%)	471/690 (68·3%)	631/690 (91·4%)
Sensitivity	NA	NA	NA	NA	73·6% (65·1–80·6)	72·7% (66·3–78·4)	59·3% (46·3–71·1)
Specificity	NA	NA	NA	NA	100% (100–100)	97·9% (96·2–98·9)	100% (100–100)
Positive predictive value	NA	NA	NA	NA	100% (100–100)	93·8% (88·9–96·7)	100% (100–100)
Negative predictive value	NA	NA	NA	NA	94·5% (92·3–96·1)	89·2% (86·2–91·6)	96·3% (94·6–97·5)

Data are n/N (%) or % (95% CI). The combined performance for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* was calculated because the same assay was used to test for both organisms (GeneXpert CT/NG). The combined performance for bacterial vaginosis and *Trichomonas vaginalis* was calculated because both conditions require the same treatment. 15 PCR results were invalid during gold standard testing, so only the results of 690 participants were recorded for *Trichomonas vaginalis*, bacterial vaginosis, and vulvovaginal candidiasis. NA=not applicable.

Table 4: **Performance of the WHO syndromic algorithms, WISH algorithms, and optimal bacterial vaginosis and vulvovaginal candidiasis algorithms compared with gold standard testing**

test (with $<1\times10^5$ geq/mL considered the threshold for bacterial vaginosis; appendix).

The optimal vulvovaginal candidiasis algorithm was based on the following observations (appendix): no vaginal pH cutoff could adequately predict vulvovaginal candidiasis (data not shown), and pregnant women were much more likely to have vulvovaginal candidiasis than bacterial vaginosis (12 [19·4%] of 62 had vulvovaginal candidiasis and 4 [6·5%] had bacterial vaginosis). In the optimal vulvovaginal candidiasis algorithm, women would only be tested for vulvovaginal candidiasis if they had symptoms of vulvovaginal candidiasis and had tested negative for *C trachomatis*, *N gonorrhoeae*, *T vaginalis*, and bacterial vaginosis (with the optimal algorithm) or were pregnant. This applied to 279 women. The sensitivity, specificity, positive predictive value, and negative predictive value of the optimal vulvovaginal candidiasis algorithm was 59·3%, 100%, 100%, and 96·3%.

Neither participant-reported symptoms nor clinician-observed signs correlated with the presence of any infection (table 5, table 6). Furthermore, performance of the WISH and optimal bacterial vaginosis and vulvovaginal candidiasis algorithms were similar or slightly worse when restricted to a subgroup of women who had been seeking care or were taking traditional medications for their current symptoms (appendix).

	Chlamydia trachomatis and *Neisseria gonorrhoeae* diagnoses (n=100)	*Trichomonas vaginalis* diagnoses (n=111)	Bacterial vaginosis diagnoses (n=125)	Vulvovaginal candidiasis diagnoses (n=59)	Syphilis diagnoses (n=21)	No infection (n=377)
No symptoms (n=136)	14 (10·3%)	17/134 (12·7%)	22/134 (16·4%)	3/134 (2·2%)	3/66 (4·6%)	84/134 (62·7%)
Any unusual vaginal discharge (n=386)	57 (14·8%)	65/376 (17·3%)	76/376 (20·2%)	44/376 (11·7%)	11/209 (5·3%)	193/376 (51·3%)
Curd-like vaginal discharge (n=265)	36 (13·6%)	41/261 (15·7%)	41/261 (15·7%)	31/261 (11·9%)	8/144 (5·6%)	142/261 (54·4%)
Any unusual vaginal discharge without other symptoms (n=25)	9 (36·0%)	6/24 (25·0%)	6/24 (25·0%)	0	0	9/24 (37·5%)
Genital itching or burning (n=470)	68 (14·5%)	80/458 (17·5%)	85/458 (18·6%)	51/458 (11·1%)	16/249 (6·4%)	239/458 (52·2%)
Genital itching or burning without other symptoms (n=80)	17 (21·3%)	18/79 (22·8%)	14/79 (17·7%)	6/79 (7·6%)	3/40 (7·5%)	35/79 (44·3%)
Lower abdominal pain or pain during sex (n=308)	42 (13·6%)	42/301 (14·0%)	48/301 (16·0%)	26/301 (8·6%)	8/160 (5·0%)	173/301 (57·5%)
Lower abdominal pain or pain during sex without other symptoms (n=31)	3 (9·7%)	0	4 (12·9%)	2 (6·5%)	1/21 (4·8%)	22 (71·0%)
Genital ulcer disease (n=41)	4 (9·8%)	3/39 (7·7%)	4/39 (10·3%)	4/39 (10·3%)	3/19 (10·3%)	25/39 (64·1%)
Genital ulcer disease without other symptoms (n=3)	0	0	0	0	0	3 (100%)

Data are n/N (%), where the denominator N is the total number of structurally-reported symptoms. The actual denominator per cell may vary slightly due to the 15 invalid gold standard results. No inguinal buboes were structurally reported or clinician-observed. Some women had multiple infections. No infection was defined as no *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, bacterial vaginosis, and vulvovaginal candidiasis by gold standard testing, and no syphilis by point-of-care test.

Table 5: **Associations between structurally-reported symptoms with infections diagnosed by gold standard testing**

	Chlamydia trachomatis and *Neisseria gonorrhoeae* diagnoses (n=59)	*Trichomonas vaginalis* diagnoses (n=61)	Bacterial vaginosis diagnoses (n=77)	Vulvovaginal candidiasis diagnoses (n=42)	Syphilis diagnoses (n=15)	No infection (n=203)
Any abnormal vaginal or cervical discharge, or pus (n=139)	44 (31·7%)	34/138 (24·6%)	31/138 (22·5%)	25/138 (18·1%)	5/83 (6·0%)	47/138 (34·1%)
Abnormal vaginal or cervical discharge or pus, curd-like (n=66)	5 (7·6%)	9 (13·6%)	7 (10·6%)	22 (33·3%)	1/36 (2·8%)	31 (47·0%)
Abnormal genital odour (n=34)	6 (17·7%)	3/33 (9·1%)	10/33 (30·3%)	3/33 (9·1%)	1/19 (5·3%)	16/33 (48·5%)
Cervicitis, vaginitis, or vulvitis (n=84)	18 (21·4%)	13/82 (15·9%)	21/82 (25·6%)	20/82 (24·4%)	1/42 (2·4%)	28/82 (34·2%)
Uterine, adnexal, or cervical motion tenderness (n=31)	16 (51·6%)	8/30 (26·7%)	7/30 (23·3%)	3/30 (10·0%)	0	6/30 (20·0%)
Genital ulcer disease with or without inguinal buboes, any location (n=40)	5 (12·5%)	5/37 (13·5%)	10/37 (27·0%)	6/37 (16·2%)	6 (15·0%)	14/37 (37·8%)

Data are n/N (%), where the denominator N is the total number of clinician-observed signs. The actual denominator per cell may vary slightly due to the 15 invalid gold standard results. No inguinal buboes were structurally reported or clinician-observed. Some women had multiple infections. No infection was defined as no *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, bacterial vaginosis, and vulvovaginal candidiasis by gold standard testing, and no syphilis by point-of-care test.

Table 6: **Associations between clinician-observed signs with infections diagnosed by gold standard testing**

161 (22·8%) of 705 participants were treated for a urinary tract infection because urinalysis detected nitrite or leucocytes in their urine, whereas only 41 (25·5%) of 161 patients had an *E coli* concentration greater than 1×10^5 geq/mL by qPCR when samples were analyses by gold standard tests (appendix).

The five infections associated with vaginal discharge or lower abdominal pain were by far the most common

diagnoses made, followed by urinalysis-based urinary tract infections. POCT-confirmed syphilis, and syndromic diagnoses of pelvic inflammatory disease, non-syphilis genital ulcers, inguinal buboes without genital ulcers, and genital warts were much less common (table 3). Study physicians did bimanual examinations on 399 (56·6%) of 705 participants, which was more than had been anticipated (appendix). Treatments and referrals were delivered as required with few treatment failures, but the uptake of partner notification was suboptimal: 782 identified partners of 201 women required partner notification but only 61 (7·8%) were treated at the study clinic (appendix).

Participants accepted all testing services offered to them except for HIV testing (rejected by 107 [15·3%] of 700, mostly because of their known HIV-positive status) and pregnancy testing (rejected by 199 [17·0%] of 702, mainly because of reliable contraceptive use or known pregnancy; appendix). Most women (344 [86·9%] of 396) who were offered a GeneXpert CT/NG POCT chose to wait for the results, 41 (10·4%) elected to be contacted by phone or letter, and only 5 (1·3%) elected to schedule a follow-up appointment. All women accepted counselling, and various topics were chosen, but only 44 (6·2%) of 705 were interested in a condom demonstration (appendix). Women who did not have to wait for a GeneXpert CT/NG result spent a median of 98 min (SD 31) at the clinic, whereas women who did have to wait spent a median of 212 min (SD 37; appendix).

All 107 participants who completed a client satisfaction survey liked all WISH procedures (appendix). The main point of criticism was the visit duration: 45 (42·1%) of the women thought the visit was long, but all women thought that the services received were worth it. Study staff reported that POCTs were easy to complete and interpret, and did not identify any major testing or clinic flow problems (data not shown).

Discussion

The WISH study showed that POCT integration in first-line urogenital care is feasible and improves case-finding and infection management in Rwandan women. Vaginal discharge (including genital itching and burning) and lower abdominal pain (including pain during sex) were by far the most common symptoms reported. Most women reporting these symptoms did not require immediate treatment because they either had no infection or had mild vaginal dysbiosis (defined as above-normal vaginal concentrations of inflammatory microorganisms that did not reach diagnostic thresholds), which might have resolved without treatment.[10,26] When a condition was present, participant-reported symptoms and clinician-observed signs did not accurately predict the condition, as has been shown in other studies.[9,11–13] We therefore believe that the WHO algorithms should be revised and that the revised algorithms should incorporate POCTs. The WISH study showed that POCTs are implementable and highly acceptable in resource-poor settings. An additional advantage of implementing POCTs might be that clinicians improve their diagnostic skills over time by comparing their diagnoses (based on patient-reported symptoms and observed signs) to POCT results. However, major barriers include the lack of ASSURED POCTs for some infections, time constraints, and costs. The goal for the coming years therefore should be to continue POCT development and design algorithms that maximise delivery of appropriate treatments; minimise complications, overtreatment, and drug resistance; and minimise the number of POCTs required to achieve this. Some of the time and human resources required to use POCTs might be recuperated by integrating sexual and reproductive health services for women, and minimising the number of speculum examinations. In the WISH study, these speculum examinations did not have much added value, other than identifying some cases of suspected pelvic inflammatory disease. The number of POCTs required could also be reduced by risk scoring based on local epidemiology as we did in WISH, but risk scores would have to be locally validated.

The WHO algorithms were designed for women seeking care for urogenital symptoms. The WISH study tested women at risk of urogenital infections regardless of symptoms, recognising the fact that asymptomatic infections are common, continue to fuel epidemics of HIV and sexually transmitted infections, and can cause complications.[4,10] Moving forward, we recommend that guidelines address both types of case-finding. Women who proactively seek care for vaginal discharge and lower abdominal pain because their quality of life is negatively affected would benefit from testing for *C trachomatis*, *N gonorrhoeae*, *T vaginalis*, bacterial vaginosis, and vulvovaginal candidiasis. Pregnant women are at risk of the most severe complications (such as preterm birth and neonatal sepsis),[4] and we therefore believe that they should be comprehensively screened for HIV, sexually transmitted infections, bacterial vaginosis, vulvovaginal candidiasis, and vaginal pathobiont carriage (eg, *Streptococcus agalactiae*), regardless of symptoms. Women at high risk of acquiring HIV and sexually transmitted infections (to be defined locally) should be tested regardless of symptoms, and possibly also for bacterial vaginosis and vulvovaginal candidiasis, in an effort to control epidemics and minimise infertility and pelvic inflammatory disease. We believe that these recommendations should not just apply to resource-poor countries but also to primary care settings in Europe and elsewhere.

ASSURED POCTs would improve feasibility, performance, and cost-effectiveness of case-finding, both for symptomatic infections and asymptomatic infections in at-risk women.[15,16] HIV, syphilis, and pregnancy POCTs have already been successfully integrated in many clinics and screening programmes.[24,25] We have obtained good results with GeneXpert CT/NG and *T vaginalis* OSOM POCTs,

and so have other studies,[19] but the GeneXpert CT/NG could be improved by reducing turnaround time and costs, and next-generation *T vaginalis* POCTs with improved performance would be welcomed. Better POCTs for bacterial vaginosis and vulvovaginal candidiasis should also be developed. The WISH study showed that vaginal pH can be used as an initial screening test for bacterial vaginosis, but would require confirmatory testing. We used three qPCR assays to identify true bacterial vaginosis cases (lactobacillus, *G vaginalis*, and *A vaginae*), but we also showed that a qPCR for *Lactobacillus* spp only would suffice. Gram stain Nugent scoring[27] could also be used as a confirmatory test. Unfortunately, POCTs based on detecting *G vaginalis* enzymes or metabolites, or *C albicans* antigens or antibodies, have shown inadequate sensitivity and specificity thus far.[28,29] A combined NAAT-based POCT for bacterial vaginosis (lactobacillus concentration), trichomoniasis (*T vaginalis* presence), and vulvovaginal candidiasis (*Candida* spp presence) might provide the best balance between optimising diagnostic accuracy and minimising required resources. Such a POCT could be used in combination with a chlamydia and gonorrhoea POCT (eg, in women seeking care for vaginal discharge or lower abdominal pain) and other POCTs used to screen pregnant women and women at high risk of acquiring HIV and sexually transmitted infections. The WISH data also suggest that better POCTs for urinary tract infections should be developed.[30]

The WISH study was implemented in a high-prevalence population by highly trained and experienced staff who had access to adequate clinic and laboratory resources. Additional studies are required in low-prevalence settings and in public primary-care clinics. Although we tried to recruit women with and without symptoms, our recruitment strategies mostly attracted women with symptoms, and it was not always clear which women would have sought care for their symptoms in real life. Furthermore, the 95% CIs of our sensitivity estimates were wide. Future studies should enrol women who are seeking care for urogenital symptoms, as well as women not seeking care, in sufficient numbers to achieve high-precision performance estimates in both groups. Despite our best efforts to minimise these sources of bias during data collection, selection and social desirability will have affected our results, as in most observational studies. Finally, the WISH study did not include a cost-effectiveness component. Cost-effectiveness studies of different POCT-based algorithms in different settings will be essential.

We conclude that POCTs should be integrated into algorithms for sexually transmitted and urogenital infections, directed at women seeking care for symptoms and women with high risk—regardless of symptoms. However, improved availability of ASSURED POCTs is required, and we particularly recommend the development of a NAAT-based POCTs combining bacterial vaginosis, trichomoniasis, and vulvovaginal candidiasis diagnoses.

Contributors

JHHMvdW obtained the research funding and wrote the study protocol and data collection documents, with input from VJ and TC. SKA, J-CS, MMU, LM, VM, MU, MCV, and JHHMvdW collected the primary data. LM and VM did the point-of-care tests and GeneXpert CT/NG assays. VC and TC did all other gold standard testing. MCV and JHHMvdW developed the analytical approach and completed the statistical analyses. JHHMvdW and MCV wrote the manuscript. All authors commented on and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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