8. VAGINAL DISCHARGE SYNDROME

Vulvovaginal symptoms are one of the commonest reasons for women attending a health facility. The symptoms include a vaginal discharge perceived by the woman to be abnormal, vulval irritation or itching. Other conditions may include vulvovaginal growths, such as warts and cancer, especially of the cervix – these are not discussed in these guidelines.

The three most common causes of vaginal discharge are bacterial vaginosis and infection with *T. vaginalis* and *C. albicans*. Among postpubertal women, *N. gonorrhoeae* and *C. trachomatis* infect the endocervix rather than the vagina, and they therefore may not present with vaginal discharge. These infections may be present without any clinically evident abnormality of the cervical os. If an abnormality is present at the cervical os because of infection with *C. trachomatis* or *N. gonorrhoeae*, it would be a mucus discharge or a purulent discharge (mucopus) or inflammation and friability of the cervical os. In the context of STIs, it should therefore be emphasized that vaginal discharge more reliably indicates vaginal infections but poorly predicts cervical infection caused by *N. gonorrhoeae* and/or *C. trachomatis*. The challenge for a health-care provider consulting a woman with vaginal discharge is to determine the cause of the discharge when a variety of infectious and non-infectious causes may be at play.

The summary of the systemic review and the recommendations given in this section offer guidance on how to manage people presenting with symptoms of abnormal vaginal discharge. The commonest causes of vaginal discharge are briefly discussed below.

8.1 *T. vaginalis*

T. vaginalis is a sexually transmitted protozoan that specifically infects women's vagina, urethra and paraurethral glands. Although many women are asymptomatic, more than 50% of women with *T. vaginalis* infection have vaginal discharge.

8.1.1 Clinical presentation – symptoms

Among symptomatic women, infection with *T. vaginalis* presents with an abnormal vaginal discharge as perceived by the woman. About 50% of symptomatic women report vulval itching. The discharge may be described as yellow and may appear purulent.

8.1.2 Examination findings – signs

On examination, vulval erythema and oedema may be noted.

On speculum examination, a discharge of variable colour can be seen in the vagina – classically described as yellow or greenish and may be frothy. The vaginal walls may be erythematous. The cervix may have punctate haemorrhages, giving rise to what has been referred to as "strawberry cervix". Although this finding is uncommon, it is highly indicative of trichomoniasis.

8.1.3 Molecular testing

NAAT has the highest sensitivity of all diagnostic methods to detect *T. vaginalis*. Vaginal swabs are the samples of choice, but endocervical samples and urine can be used for some assays. Additionally, residual genital samples used for diagnosing chlamydia and gonorrhoea using NAAT are also good enough for detecting *T. vaginalis* nucleic acids. NAAT is, however, not currently widely available as rapid point-of-care tests. However, when resources permit, such tests can be incorporated strategically to use as near-patient rapid point-of-care testing in managing people with STIs.

8.1.4 Microscopy

T. vaginalis has historically been diagnosed by performing wet mount microscopy. Although it is not the gold standard technique for diagnosing trichomoniasis, a wet mount is frequently used because it is quick, inexpensive and easy to perform. However, to have a good chance of successfully identifying the motile trichomonads, the slide should be read within 10 minutes of collection since trichomonads quickly lose their motility *(50)*. Non-motile cells cannot be diagnosed as trichomonads.

8.1.5 Culture methods

Culture of *T. vaginalis*, which has a higher sensitivity than the wet mount microscopic examination, was the cornerstone for detecting *T. vaginalis* before the advent of point-of-care antigen tests and NAAT. Although a culture medium is commercially available, cultures from women with trichomoniasis are usually positive in the first three days of inoculation, but they have to be incubated for up to seven days to rule out infection. Routine culture methods detecting *T. vaginalis* are no longer widely performed.

8.2 Candidiasis

Vulvovaginal candidiasis is caused by *C. albicans* in about 90% of cases. The non-albicans species cause the rest of vulvovaginal candidiasis – *C. glabrata* in about 8% of cases, and the other non-albicans species, such as *C. tropicalis*, *C. krusei* and *C. parapsilosis* cause most of the remainder *(51)*. Although men can be colonized with *Candida* species and the male sex partners of women with candidiasis are transiently colonized, candida balanitis and balanoposthitis among men are not recognized as STIs *(52)*. *Candida* yeasts may be detected in 20–30% of asymptomatic nonpregnant women of childbearing age *(53)*. The detection of candida yeasts among asymptomatic women therefore does not necessarily require treatment.

8.2.1 Clinical presentation – symptoms

Candidiasis presents with pruritus (itching) or a burning sensation of the vulva and vaginal soreness or irritation. Other clinical manifestations include pain during sexual intercourse (dyspareunia) and dysuria. If there is discharge, it characteristically is curdy, white or creamy and thick. The discharge is not always curd-like (sometimes described as cottage-cheese-like in character) but can vary from watery to homogeneously thick.

8.2.2 Examination findings – signs

On examination, the vulva may be erythematous and excoriated. The vulva and the labia may be swollen. Some pimples with pus (pustulopapular) lesions peripheral to the erythematous area of the vulva may be present.

Speculum examination shows the vaginal wall to be erythematous, and an adherent discharge may be seen, either curd-like or homogeneously white. The cervix looks normal.

8.2.3 Microscopy

Vaginal pH is normally between 4 and 4.5 among most women with candidiasis. A Gram stain of vaginal secretions from the walls of the vagina demonstrates gram-positive *Candida* species. A 10% potassium hydroxide preparation is also useful in identifying germinated yeasts.

8.2.4 Culture methods

Candida culture on solid media is the most sensitive diagnostic test for candidiasis but does not offer same-day treatment. The results may take up to three days to confirm the growth of fungal colonies.

8.3 Bacterial vaginosis

Bacterial vaginosis is the most common cause of vaginal discharge among women of childbearing age. It is a polymicrobial disorder of the vaginal microbiome. The condition is characterized by low concentrations or an absence of lactobacilli and a florid presence of anaerobic flora *(54)*.

Bacterial vaginosis is not a sexually transmitted condition, but it has been linked to several adverse outcomes, including adverse outcomes of pregnancy and an increased risk of STIs, including HIV, pelvic inflammatory disease and tubal factor infertility *(55,56)*.

8.3.1 Clinical presentation – symptoms

About 90% of symptomatic women have a white vaginal discharge, which can be seen on the vulva, and an abnormal vaginal odour *(52)*.

8.3.2 Examination findings – signs

On external visual examination and digital examination of the vagina, the thin, white, homogenous discharge may be observed externally on the posterior fourchette of the vulva or the labia. If speculum examination is feasible, the homogeneous discharge may be observed to be adherent to the vaginal wall, and the cervix is usually normal in appearance.

8.3.3 Laboratory diagnosis

The vaginal pH is greater than 4.5, and an amine odour can be sensed spontaneously or after addition of a drop of 10% potassium hydroxide to vaginal fluid on a slide (KOH test or Whiff test).

However, examining the woman during menses, within a day of sexual intercourse, after recent douching and when taking antimicrobial agents can affect the clinical and laboratory assessments of a woman with bacterial vaginosis. The pH paper may give a wrong reading if it samples the water used to lubricate the speculum or if it samples cervical secretions, which are relatively alkaline. The amine smell, described as smelling like "dead fish", can be subjective, since some people cannot discern the smell.

8.3.3.1 Microscopy

If the microscope is available at the point of care, a wet-mount microscopic test for clue cells can be done. Clue cells are vaginal epithelial squamous cells coated with coccobacilli with absence of rods of lactobacilli. When visualized, clue cells predict bacterial vaginosis. Identifying clue cells requires adequate training and good skills and good knowledge of the microscope.

Microscopic examination of a Gram-stained vaginal smear collected with a swab from the vagina reveals large numbers of gram-positive and gram-negative cocci with reduced or absent lactobacilli (gram-positive bacilli).

8.4 Cervical infection – gonococcal and/or chlamydial cervicitis

N. gonorrhoeae and *C. trachomatis* infections among postpubertal women infect the endocervix rather than the vagina and can thus cause a cervical discharge, which may manifest as vaginal discharge. However, these two pathogens are less commonly associated with vaginal discharge.

8.4.1 Risk factors for STI-related cervical infections

Several demographic and behavioural factors have also been frequently associated with cervical infections and have been established as risk factors for STIs. Some of those that have been found to predict cervical infection in the presence of abnormal vaginal discharge in some settings are: being younger than 21 years (25 years in some places); having more than one sex partner in the previous three months; having a new partner in the previous three months; and having a current partner with an STI *(57)*. Such risk factors are, however, usually specific to the population group for which they have been identified and validated and cannot be extrapolated to other populations or to other locations. Most researchers have suggested that obtaining more than one demographic risk factor from any particular person is important but that clinical signs such as cervical erosion can be valid as a single factor.

8.4.2 Clinical presentation – symptoms

At least 50% of women with gonococcal infection of the cervix are asymptomatic. Women with symptoms may have vaginal discharge, abnormal vaginal bleeding or dysuria. Most women with chlamydial cervical infection are asymptomatic. The ones who may be symptomatic have vaginal discharge, dyspareunia and dysuria. Several women may have lower abdominal pain because of ascending infection, causing pelvic inflammatory disease.

8.4.3 Examination findings – signs

Speculum examination may reveal a normal-looking cervix in the presence of endocervical infection. For those with abnormalities, the cervix may be erythematous or severely eroded and associated with a muco-purulent cervical discharge. The cervix may be friable and bleed easily on contact.

8.4.4 Microscopy

Gram-stained smears from the cervix are considered positive for the presumptive diagnosis of gonorrhoea in women if intracellular gram-negative diplococci are observed in polymorphonuclear leukocytes. Gram stain of urethral samples among women has low yield and may not be cost-effective *(58)*.

8.4.5 Molecular detection

Molecular testing has greatly improved the detection of *C. trachomatis* and *N. gonorrhoeae* among both symptomatic and asymptomatic women and has become the recommended gold standard technology to diagnose and screen populations for *C. trachomatis* and *N. gonorrhoeae*. Among women, a vulvovaginal specimen, which may be self-collected, can be used for testing for these infections. An endocervical swab can also be an alternative but requires a speculum. First-catch urine is another option, but the sensitivity and specificity tend to be lower in women.

8.4.6 Culture methods

Processing *C. trachomatis* for culture requires highly experienced laboratories and technicians and is complex, laborious and time-consuming to be of economic value. It is rarely performed in middle- or high-income countries nowadays except for special purposes *(59)*.

Culture for *N. gonorrhoeae* requires a special culture medium with nutrient supplementation for the organism to grow. Cervical and anorectal specimens can be used. The process is still necessary to undertake antimicrobial susceptibility testing to guide therapy, especially in cases of infection with N. gonorrhoeae isolates resistant to standard recommended therapies.

8.5 Recommendations for the management of vaginal discharge

For people with symptom of vaginal discharge, WHO recommends treatment for *N. gonorrhoeae* and/or *C. trachomatis* and/or *T. vaginalis* on the same visit. WHO suggests treatment based on the results of quality-assured molecular assays for N. gonorrhoeae and/or *C. trachomatis* and/or *T. vaginalis*. In settings in which treatment based on the results of molecular assay in the same visit is not feasible or that have limited or no molecular testing, WHO suggests treatment based on testing with quality-assured rapid point-of-care tests or on syndromic treatment.

(Strong recommendation; moderate-certainty evidence

For people with symptom of vaginal discharge, good practice includes:

Good practice statement

- taking a medical and sexual history and assessing the risk of STIs;
- performing a physical examination, including abdominal and pelvic examination, to assess for pelvic inflammatory disease, surgical conditions or pregnancy and external vulvovaginal examination to visualize any lesions, overt genital discharge or vulval erythema and excoriations;
- bimanual digital examination of the vagina (1) to assess for cervical motion tenderness or pain with palpation of the pelvic area to exclude pelvic inflammatory disease; and (2) to assess for the presence of vaginal discharge and the colour and consistency of the discharge on the glove; and
- offering HIV and syphilis testing and other preventive services as recommended in other guidelines.

Settings in which treatment is based on quality-assured molecular assays in a laboratory with a fully operational quality management system and results available on the same day of the visit

(Strong recommendation; moderate-certainty evidence)

1. WHO recommends treating *N. gonorrhoeae* and/or *C. trachomatis* and/or *T. vaginalis* based on the results of quality-assured molecular assays on a self-collected, or clinician-collected, vaginal swab or on a urine specimen (Algorithm ①).
2. WHO suggests treating for bacterial vaginosis if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available.
3. WHO suggests treating for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available.

Settings in which same-day treatment is not feasible with molecular testing or with limited or no molecular testing

(Conditional recommendation; low-certainty evidence)

1. WHO suggests treating based on a quality-assured rapid test with a minimum sensitivity of 80% and specificity of 90%, if available, to confirm or exclude infection with *N. gonorrhoeae* and *C. trachomatis* (Algorithm ②).
2. If the availability of a low-cost rapid test or molecular assay is limited, WHO suggests performing a speculum examination and treating for *N. gonorrhoeae* and *C. trachomatis* if there is evidence of cervicitis and performing a low-cost rapid test or molecular assay for people with a negative speculum examination who are at high risk of infection with *N. gonorrhoeae* and *C. trachomatis* and treating based on the test results (Algorithm ③[a]).
3. If a rapid test is not available, WHO suggests treating people who have signs of cervicitis on speculum examination for infection with *N. gonorrhoeae* and *C. trachomatis* (Algorithm ③).
4. If a rapid test is not available and a speculum examination is not feasible or acceptable, WHO suggests treating people for *N. gonorrhoeae* and *C. trachomatis*, all people at high risk of STIs and all people who have vaginal discharge on genital examination (Algorithm ④).
5. WHO suggests treating people for bacterial vaginosis and *T. vaginalis* if vaginal discharge is present or based on the results of microscopy, if available.
6. WHO suggests treating people for candidiasis, where indicated by type of discharge (such as curd-like with vaginal itching) or by the results of microscopy, if available.

Good practice includes the following.

Good practice statement

- For people with recurrent or persistent vaginal discharge, good practice includes referring to a centre with laboratory capacity to diagnose infection with *N. gonorrhoeae*, *C. trachomatis*, *M. genitalium* and *T. vaginalis* and bacterial vaginosis and to test for antimicrobial-resistant N. gonorrhoeae and *M. genitalium* (if there is a test) or for a specialist's assessment (STI expert and physician or a gynaecologist), when no such testing is available in primary health care centres.

Fig. 4 offers programme managers guidance on the most applicable approaches to manage people presenting with vaginal discharge. It can be used to select sites or health facilities that can implement an option that has the appropriate diagnostic capacity and expertise. For example, a rural health centre with only basic commodities could follow one option, whereas a referral centre could implement a different option.

Fig. 4. Flow chart for programme managers to determine which management options to implement for vaginal discharge

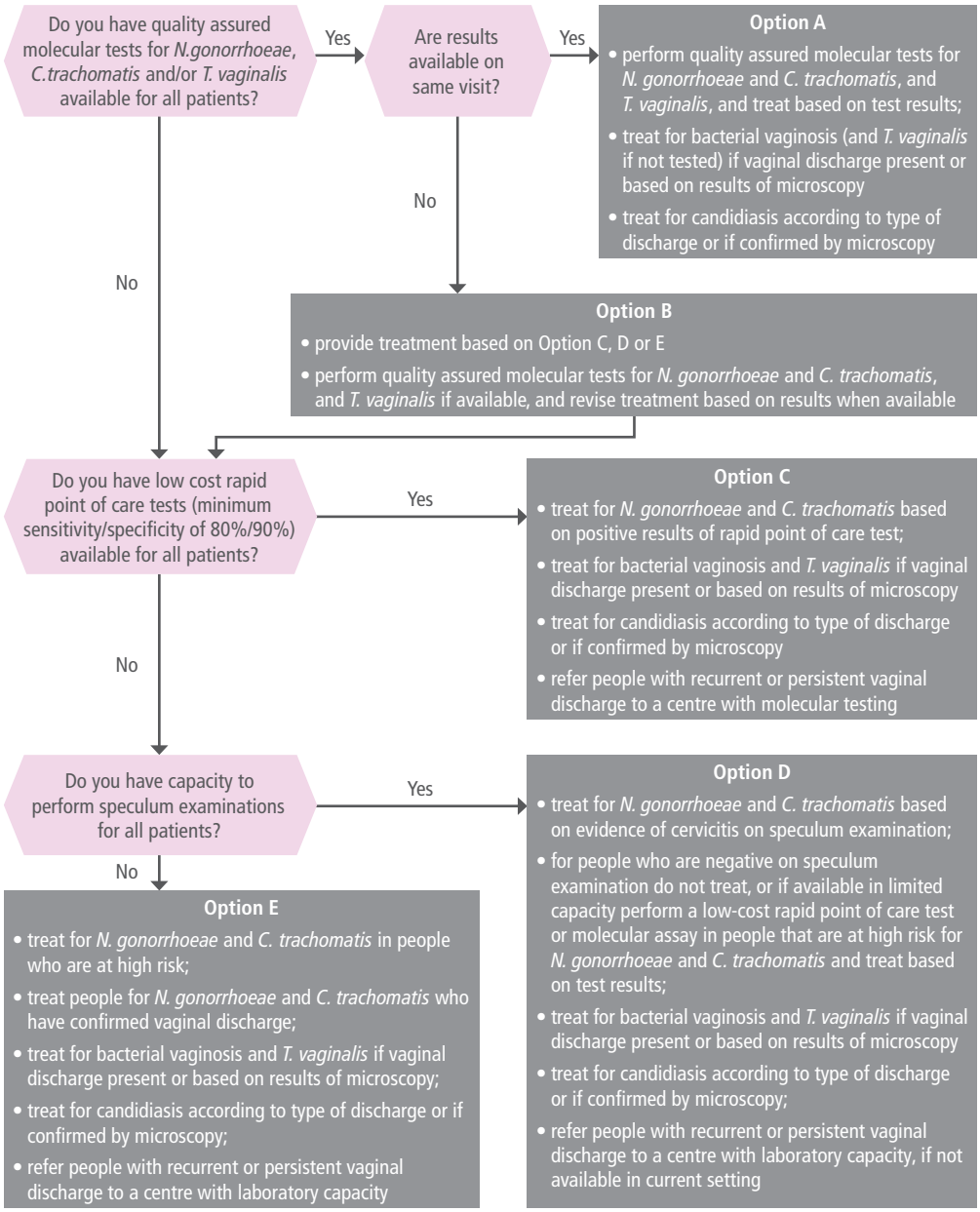
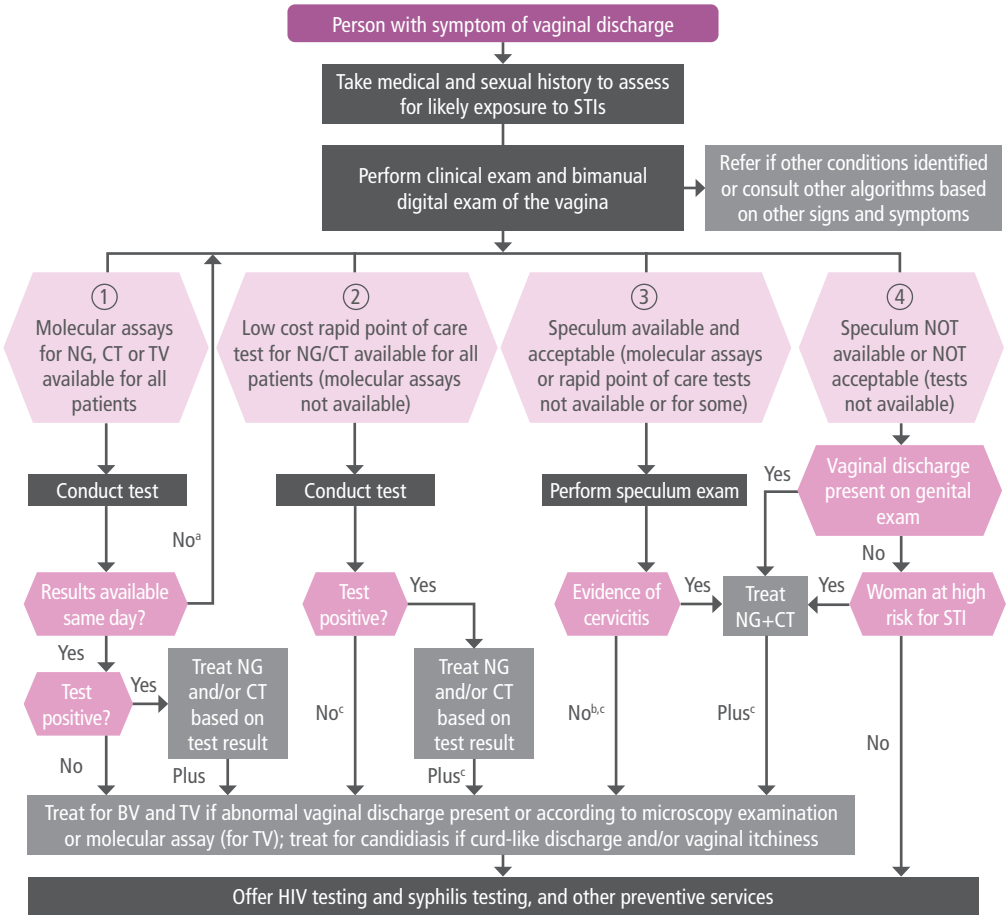


Fig. 5 is a proposed flow chart for health-care providers to follow in the process of managing people presenting with vaginal discharge. This flow chart can be adopted as it is or adapted to respond to the situation at the country level.

Fig. 5. Flow chart for health-care providers to manage vaginal discharge according to local availability of resources and preferences



NG, *N. gonorrhoeae*; CT, *Chlamydia trachomatis*; TV, *Trichomonas vaginalis*; BV, bacterial vaginosis.

[a] If molecular assay was performed and results were not available on same day, revise the syndromic treatment initially provided according to the test results when available

[b] perform rapid point of care test or molecular assay if available to confirm NG/CT and treat if positive; if negative do not treat and ask woman to return if symptoms recur

[c] if woman complains of recurrent or persistent discharge refer to a centre with laboratory capacity

8.6.1 Evidence summary (Annex 4)

Using a model, we compared the benefits, harm and costs of different combinations of using a risk assessment, speculum examination, microscopy, rapid point-of-care test and/or molecular assay test or treating none or all people who have vaginal discharge (supplementary materials – description of the modelling of vaginal discharge). We modelled two scenarios in which the prevalence of *N. gonorrhoeae* and/or *C. trachomatis* among people with vaginal discharge is low (5%) and high (20%) and applied different levels of antimicrobial resistance. We assumed same-day treatment for the different combinations of assessment and calculated the number of people with pelvic inflammatory disease as a critical harm and accounted for loss to follow-up and transmission. The evidence for the effects of the different strategies is moderate-certainty evidence because of the risk of bias of the included studies for calculating sensitivity and specificity.

In the model, we assumed that the costs of treatment for bacterial vaginosis or *T. vaginalis* is about US$ 0.10, and we assumed that everyone with confirmed vaginal discharge would be treated for bacterial vaginosis and *T. vaginalis*. These figures are based on a review of the accuracy of risk assessment, speculum examination and/or laboratory testing for bacterial vaginosis and *T. vaginalis* (supplemental materials – systematic review vaginal discharge).

Although microscopy was accurate, with no false-positive treatments and less than 1% of cases missed, the costs of implementing microscopy in settings that currently do not have facilities outweighs the costs of treating everyone with confirmed vaginal discharge for bacterial vaginosis and *T. vaginalis* and the harm to people unnecessarily treated (about 40% of the people). We considered the effects of screening for bacterial vaginosis and *T. vaginalis* using pH testing compared with confirmed vaginal discharge and found that the differences in people missed and people treated unnecessarily were negligible and the costs and harm of treatment or missing treatment are relatively low.

When available, performing molecular tests for *N. gonorrhoeae*, *C. trachomatis* or *T. vaginalis* and treating on the same day based on the results leads to the most people treated correctly. However, when the results of the tests are not available on the same day of the visit, delay in treatment may lead to complications, transmission of infections and loss to treatment. Therefore, treatment could be determined based on signs and/or symptoms or on rapid diagnostic tests.

- Using a low-cost rapid point-of-care test with 80% sensitivity and 90% specificity will lead to fewer missed and falsely treated people compared with other syndromic approaches or with no treatment. Since there is a reduction in missed cases, the number of people who progress to pelvic inflammatory disease (and consequently to poor fertility and other negative reproductive health outcomes for some people) may be reduced by 70%, resulting in 4 per 1000 people experiencing pelvic inflammatory disease in settings in which the prevalence of *N. gonorrhoeae* and *C. trachomatis* is low versus 15 people per 1000 in settings in which it is high compared with no treatment. Since the accuracy of the test increases towards 95% sensitivity and 98% specificity, there are even greater reductions in missed cases and unnecessary treatments, but costs will increase. Using diagnostic tests with higher sensitivity and specificity may also lead to greater understanding of the prevalence of STIs in the community, enhanced sex partner tracing and improved overall quality of care.

We also modelled strategies in which molecular assays or rapid point-of-care tests are not widely available. The following observations were made.

- Performing a speculum examination and treating people with cervicitis and then microscopy for people who were negative on speculum examination may also lead to fewer missed cases and falsely treated people than using a rapid point-of-care test (at a minimum of 80% sensitivity and 90% specificity) for everyone. Alternatively, if a rapid point-of-care test is used for the people with a negative speculum examination, there would be even fewer missed cases and falsely treated people.
- Treating based only on the results of a speculum examination will still result in pelvic inflammatory disease cases and costs similar to a rapid point-of-care test, although the number of people treated unnecessarily would be slightly higher when using the speculum.

However, performing a speculum examination on everyone with vaginal discharge may not be feasible in some settings.

- Thus, when speculum examination is not feasible, the costs of an approach in which everyone at high risk (including with risk factors in high-prevalence settings) and/or people with confirmed vaginal discharge are treated may be higher than strategies with rapid point-of-care tests or speculum examination, but there are large beneficial reductions in the number of pelvic inflammatory disease cases. Compared with treating everyone, fewer people are unnecessarily treated.

8.6 Treatment options for vaginal discharge

Table 4 lists the options for the respective medicines to cover vaginal infections. If a decision was reached to include treatment for *N. gonorrhoeae* and/or *C. trachomatis*, Table 5 lists the options for the recommended medicines.

Bacterial vaginosis and *T. vaginalis* may be treated simultaneously with the same medicine, metronidazole. Similarly, in the treatment of cervicitis, some medicines, such as doxycycline and azithromycin, can simultaneously treat *C. trachomatis* and *M. genitalium*.

Table 4. Treatment options for vaginal infections

- Therapy for bacterial vaginosis and trichomoniasis

Plus

- Therapy for yeast infection if curd-like white discharge, vulvovaginal redness and itching are present

Infections covered	First-line options	Effective substitutes	Note: In pregnancy, metronidazole should, ideally, be avoided in the first trimester
Bacterial vaginosis	**Metronidazole** **400 mg or 500 mg,** orally, twice daily for 7 days	**Clindamycin 300 mg,** orally, twice daily for 7 days *or* **Metronidazole 2 grams,** orally, single dose	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days *or* **Clindamycin 300 mg,** orally, twice daily for 7 days
T. vaginalis	**Metronidazole 2 grams,** orally, in a single dose *or* **Metronidazole** **400 mg or 500 mg,** orally, twice daily for 7 days	**Tinidazole 2 grams orally,** single dose *or* **Tinidazole 500 mg orally,** twice daily for 5 days	**Metronidazole 200 mg or 250 mg,** orally, 3 times a day for 7 days *or* **Metronidazole gel** 0.75%, one full applicator (5 grams) intravaginally, twice a day for 7 days
C. albicans (yeast infection)	**Miconazole vaginal pessaries, 200 mg** inserted at night for 3 nights *or* **Clotrimazole vaginal tablet, 100 mg,** inserted at night for 7 nights	**Fluconazole 150 mg (or 200mg),** orally, single dose *OR* **Nystatin, 200,000-unit vaginal tablet,** inserted at night for 7 nights	**Miconazole 200 mg vaginal pessaries** inserted once daily for 3 days *or* **Clotrimazole vaginal tablet 100 mg** inserted at night for 7 days *or* **Nystatin pessaries 200,000 units,** inserted at night for 7 nights

People taking metronidazole should be cautioned to avoid alcohol. Use of metronidazole in the first trimester of pregnancy is not recommended unless the benefits outweigh the potential hazards.

Table 5. Treatment options for cervical infection[a]

- Therapy for uncomplicated *N. gonorrhoeae (24)*

Plus

- Therapy for *C. trachomatis (25)*

Infections covered	First-line options	Effective substitutes	Options for pregnant women or during breastfeeding
In settings in which local antimicrobial resistance data are not available, the WHO STI guidelines suggest dual therapy for gonorrhoea.			
N. gonorrhoeae[a]	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose	Cefixime 400 mg, orally, single dose *plus* Azithromycin 1 gram, orally, single dose	**Ceftriaxone 250 mg,** intramuscularly, single dose *plus* **Azithromycin 1 gram,** orally, single dose *or* **Cefixime 400 mg,** orally, single dose *plus* **Azithromycin 1 gram,** orally, single dose
C. trachomatis	**Doxycycline 100 mg,** orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)	**Azithromycin 1 gram,** orally, single dose *or* **Erythromycin 500 mg,** orally, 4 times a day for 7 days *or* **Ofloxacin 200–400 mg,** orally, twice daily for 7 days (to be given only if gonorrhoea therapy did not include azithromycin)	**Erythromycin 500 mg,** orally, 4 times a day for 7 days *or* **Azithromycin 1 gram,** orally, single dose (to be given only if gonorrhoea therapy did not include azithromycin)
M. genitalium	**Azithromycin 500 gram,** orally day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)		**Azithromycin 500 gram,** orally, day 1, 250 mg daily, days 2–5 (absence of macrolide resistance)

[a]Because of increasing antimicrobial resistance to azithromycin in *N. gonorrhoeae* and *M. genitalium* and reduced susceptibility of *N. gonorrhoeae* to cephalosporins, WHO is in the process of revising current treatment recommendations and dosages.