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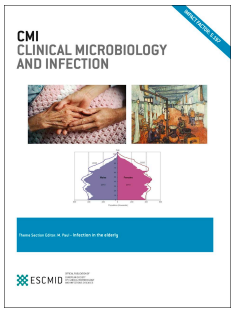

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Identifying a consensus sample type to test for *Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium, Trichomonas vaginalis* and human papillomavirus

RUNNING TITLE

The optimal sample type to diagnose STIs

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ABSTRACT

Objectives: Sexually transmitted infections (STIs) are a global cause of acute illness. Early detection plays a crucial role in interrupting transmission and preventing complications. However, the accessibility of STI testing is curbed by the lack of an overall preferred sample type. By means of a prospective study in female sex workers (FSW), we compared the sensitivity of samples from different anatomical sites in detecting *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, *Mycoplasma genitalium* and human papillomavirus. Besides, we documented the prevalence of each STI in this high-risk population.

Methods: We selected 303 FSW and tested them for each STI by nucleic acid amplification testing on two vaginal and cervical swabs from different manufacturers, cervical smearand first-void urine. The sensitivity of each sample type was compared for each infectious agent in order to identify a consensus sample type.

Results: Vaginal swabs were superior to all other sample types, with an overall sensitivity of 86%. The sensitivity was the lowest for first-void urine, detecting only 63% of positive cases. The prevalence was 3.3% (10/299) for *Neisseria gonorrhoeae*; 9.0% (27/299) for *Chlamydia trachomatis*; 7.4% (22/298) for *Trichomonas vaginalis*; 10.8% (32/296) for *Mycoplasma genitalium* and 55.6% (158/284) for human papillomavirus.

Conclusions: When testing for STIs, vaginal swabs are the sample of choice and first-void urine should be avoided. Designating (self-sampled) vaginal swabs as a consensus sample type enables harmonization of STI testing and extension of testing to large numbers of unscreened females.

KEYWORDS

Sexually transmitted infections

Laboratory diagnosis

Genital samples

Chlamydia trachomatis

Neisseria gonorrhoeae

Human papillomavirus

Mycoplasma genitalium

Trichomonas vaginalis

INTRODUCTION

Sexually transmitted infections (STIs) are a main global cause of acute illness, leading to serious complications, e.g. infertility. Early detection of (a)symptomatic infections has a crucial role in lowering the prevalence and hence preventing complications. Multiple molecular diagnostic tools have been developed to detect a variety of STIs but consensus on an overall preferred sample type lacks. Harmonization of testing is needed in order to improve the accessibility, in particular for hard-to-reach populations. This will result in diagnosis and treatment available more quickly in a patient-friendly way, thereby curbing the clinical impact of STIs.

To encourage this harmonization, we searched for a consensus sample type to test for the five most prevalent STIs for which nucleic acid amplification testing (NAAT) is the preferred diagnostic tool: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, *Mycoplasma genitalium* and human papillomavirus (HPV). We compared the sensitivities of six sample types (two vaginal and cervical swabs from different manufacturers, a cervical smear and a first-void urine) in detecting each STI. By documenting the prevalence of (co-)infections, data were collected on the local epidemiology and insight was gained in the clinical relevance and need for simultaneous detection.

MATERIALS AND METHODS

Between June 2015 and June 2016, a prospective study was conducted, including 303 female sex workers (FSW) with a mean age of 33 years (range 18-58 years), embedded in a health program for sex workers in Flanders (PASOP). PASOP provides specific outreach occupational health services, focused on prevention e.g. STI screening, vaccination against hepatitis B, contraceptive injections, sex education and psychological assistance. Women

eligible for STI screening (i.e. at first contact between PASOP and the sex worker or after perceived risk (e.g. condom failure)) were informed on our study and invited to participate, after documenting the informed consent. We intended to include 300 FSW, as preliminary research in the same population on *C. trachomatis* showed that this sample size should result in a representative number of positives (n>20) (4). Post hoc, we calculated the power sample size of our results, using the SAS Power and Sample Size software (SAS Institute Inc., Cary, NC, USA).

Six specimens were sampled consecutively: vaginal Abbott swab (Abbott, Illinois, USA), vaginal Copan FLOQswab (Copan, Brescia, Italy), ThinPrep cervical smear (Hologic Inc., Massachusetts, USA), cervical Abbott swab, cervical Copan FLOQswab and first-void urine collected on Abbott multi-Collect Sample medium. We defined this order based on other scientific literature and after own preliminary research (1-4). Cervical samples were taken using a speculum with gel lubricant, which has proven not to influence the quality of the samples. The cervical smear was taken before the cervical swabs, in the light of the correct assessment of cervical cytology. Vaginal swabs were taken prior to the cervical samples, in order to avoid potential dilution by the lubricant. Abbott swabs were sampled before Copan swabs, as the latter showed to have an advantage in detecting more positive samples. Urine samples were accepted at any time of the collection, as long as the FSW respected a one hour time-interval after the last pee.

Samples were sent to the Department of Laboratory Medicine of the Ghent University Hospital at room temperature within 24h. Immediately after arrival, the swabs were cultured for *N. gonorrhoeae* on BBL GC-Lect Agar (BD, New Jersey, USA) and read after 48h incubation at 37 °C with 5% CO_2. All cervical smears were sent to the Department of Pathology of the Ghent University Hospital for cervical cytology investigation,using the

Bethesda system: high-grade squamous intraepithelial lesion (HSIL), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells, cannot exclude HSIL (ASC-H), atypical cells of undetermined significance (ASC-US) or negative for intraepithelial lesion or malignancy (NILM). Subsequently, all samples were analyzed by NAAT for *C. trachomatis*, *N. gonorrhoeae*, *M. genitalium*, *T. vaginalis* and HPV using the Abbott m2000sp/rt systems and the Abbott RealTime CT/NG kit, the Diagenode S-DiaMGTV qPCR kit (Diagenode, New Jersey, USA) and the Abbott RealTime High Risk HPV kit. As the Abbott HPV kit is intended to detect 14 high risk HPV (hrHPV) genotypes (16/18/31/33/35/39/45/51/52/56/58/ 59/66/68), the results will be discussed as negative or positive for hrHPV. All Abbott analyses were performed according to the manufacturers' instructions. For Diagenode, the manufacturer's protocol was slightly modified by adding 5,0 µL Diagenode Optima DU Master Mix 2x DNA; 2,5 µL MGTV double-dye probe and primers; 2,5 µL Double-dye probe and primers Universal Inhibition Control (UIC); 2,5 µL UIC and 2,5 µL water to 10 µL DNA extract of each sample. In case of invalid results due to (pre-)analytical errors, the analyses were repeated after 1:2 dilution. In between analyses, all samples were stored at -20 °C. The stability of each infectious agent was verified under different storage conditions (data not published).

Given the high positive predictive value of NAAT – the reference technique – confirmatory testing of positive results is not recommended. Therefore, a FSW was considered infected whenever she tested positive on at least one sample type (consensus result). Because this approach cannot generate false positive results, we calculated the sensitivity and not the specificity of each sample type for a given infectious agent. All results were analyzed by SPSS Statistics software v24 using Generalized Estimation Equations and Linear Mixed Models

tests with the Holm–Bonferroni method. The study was approved by the Ethical Committee of the Ghent University Hospital with Belgian registration number B670201524867.

RESULTS

Figure 1 shows the procedure of inclusion and the results. Overall, we executed 1208 bacterial cultures and 8940 NAAT analyses. Internal control failures occurred in 23/8940 (0.3%) of NAAT analyses, mainly vaginal Copan swab (n=12) and urine (n=9), necessitating repeat testing which was successful in all cases. Fifteen participants were included twice. In case of repeat positive testing, the possible link was investigated in order to avoid overestimating the prevalence. Overall, 65.6% (196/299) of FSW tested positive for at least one STI on at least one sample type. The individual prevalence rates were 3.3% (10/299) for *N. gonorrhoeae*; 9.0% (27/299) for *C. trachomatis*; 7.4% (22/298) for *T. vaginalis;* 10.8% (32/296) for *M. genitalium* and 55.6% (158/284) for HPV (Figure 1). The mean age [+/-95% confidence interval] of the infected females was 30 years [24- 36] for *N. gonorrhoeae*; 30 years [27- 33] for *C. trachomatis*, 30 years [27- 33] for *T. vaginalis*; 31 years [28-34] for M. *genitalium* and 32 years [31-33] for HPV. Using the consensus result, we calculated the sensitivities of each sample type for each infectious agent. Figures 1 and 2 show that for *N. gonorrhoeae* culture, cervical Copan swabs showed a significant superiority compared to all other sample types. For all NAAT parameters combined, vaginal swabs detected significantly more cases compared to all other sample types, whilst first-void urine and cervical Abbott swabs detected significantly less cases compared to all other sample types. The power of these comparisons is 98.7%.

Taking each infectious agent into account, 19% (56/303) of FSW were co-infected with at least two STIs. However, when disregarding the HPV results – the most prevalent STI – only 4% (12/303) of FSW were co-infected. Of those, FSW with *N. gonorrhoeae*-infection were most likely co-infected (6/10), followed by *T. vaginalis* (7/22), *C. trachomatis* (7/27) and *M. genitalium* (5/32).

Remarkably for HPV, both vaginal swabs detected far more cases than all other sample types. In order to clarify this finding, we explored the results of cervical cytology. Overall, cervical cytology revealed 56% (168/302) NILM, 24% (72/302) ASC-US, 12% (35/302) LSIL, 7% (21/302) HSIL and 2% (6/302) ASC-H. Matching the HPV results on cervical smear with cervical cytology shows that normal cytology resulted significantly less often in HPV positivity compared to abnormal cytology (Figure 3). In case of normal cytology, vaginal swabs showed a significantly higher positivity rate than all other sample types, whilst in case of abnormal cytology, all sample types showed rather comparable rates of HPV positivity (Figure 3).

DISCUSSION

We aimed to optimize STI testing by conducting a prospective study in FSW who were tested for *C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, *M. genitalium* and HPV on six samples from different anatomical sites. We documented the prevalence of (co-)infections and explored the existence of a consensus sample type.

The *C. trachomatis* prevalence in this study (9.0%) is slightly higher compared to previous studies in the PASOP population (7.4% and 7.6%), though clearly lower than the worldwide

prevalence rates in FSW (12.5% (range 0.6- 46.2%)) (4-12). The same applies to *N. gonorrhoeae* and *T. vaginalis*, for which our prevalence rates (3.3% and 7.4% respectively) are clearly lower than the median prevalence rate reported worldwide amongst FSW (10.7% (range 0- 41.3%) and 13.5% (range 0.1-51.0%) respectively) (4-14). In contrast, the 11.1% prevalence of *M. genitalium* is in line with reports on FSW (13.1% (range 9.2 -26.3%)) (7, 15, 16). As for HPV, the 55.6% prevalence rate is comparable to previous PASOP reports (55.9%) but higher compared to multiple other studies in FSW worldwide (41.1% (range 2.3-100%)) (7, 8, 17, 18). Our prevalence could be overestimated due to the high yield of HPV in vaginal swabs compared to cervical smears, the reference sample type. Indeed, when considering the results on cervical smear as the consensus result, the prevalence falls back to 41.6%. One could presume that a positive STI test following recent sexual activity could be derived from the partner. Although a small study found no effect on HPV detection when vaginal intercourse occurred within 48 hours of self-sampling, further studies are needed to evaluate the effect of vaginal intercourse on STI screening and cervical cytology(19).

STI guidelines recommend the use of various specimens for STI detection: cervical swabs for *N. gonorrhoeae* culture, vaginal and cervical swabs for *N. gonorrhoeae* and *T. vaginalis*, vaginal swabs for *C. trachomatis* and vaginal swabs or urine for *M. genitalium* (20-25). Our data show that for *N. gonorrhoeae* culture, cervical Copan swabs were the only acceptable sample type. The inferiority of Abbott swabs for culture was expected, as Abbott transport medium contains guanidine thiocyanate, which lyses bacteria and denatures proteins, compromising bacterial growth. Given the inferiority of *N. gonorrhoeae* culture in comparison to NAAT in detecting *N. gonorrhoeae*, culture should be reserved for patients with persistent infection after treatment to exclude antimicrobial resistance. As for NAAT

testing, testing on vaginal swabs consistently resulted in the highest sensitivities, which offers an opportunity to improve STI screening coverage, as the vast majority of women favors self-sampling over physician-sampling (26). In contrast, first-void urine and cervical Abbott swabs had the lowest sensitivities. It should be noted that urine samples were accepted at any time of the collection with the only restriction being a one hour time-interval after the last urination. A more stringent approach, using at least 30 mL of first-voided morning urine and centrifugationcould render more valuable results.

Current cervical cancer screening programs are often cytology-based, with HPV testing only as triage of ASC-US positive smears or on follow-up samples. The evidence on the protection against development of cervical (pre-)cancerous lesions collected so far, however, suggests the introduction of HPV testing as a primary screening test. Non-participation is a major challenge concerning the effectiveness of screening programs and self-sampling, surely by easy to take vaginal swabs, might be a preferential approach to these non-attendees. Although a cervical smear is considered as the gold standard, vaginal or cervical self-sampling methods seem equivalent (27). In fact, HPV may be detected in vaginal sites even before it is detected in the cervix (28). This could explain the high number of positives on vaginal swabs in our study. However, one should take into account that the carcinogenic effects of HPV are not limited to the cervix, but also 43% of vulvar and 70% of vaginal cancers are attributable to HPV (29). Remarkably, our study showed that FSW with HPV detected exclusively in the vaginal region were more likely to have normal cervical cytology results. Hence, HPV detected in vaginal swabs could represent freshly infected vaginal cells – whether or not as a prelude of later cervical infection – rather than exfoliation from infected cervical cells. Alternatively, HPV detected in vaginal swabs could be derived from

the male sexual partner, whereas the cervical smear reflects the FSW's own HPV condition. In addition, it should be noted that about 90% of HPV infections are asymptomatic and resolve spontaneously within two years (30). As for vaginal swabs, the use of first-void urine for HPV testing assumes contamination with infected exfoliated cervical cells though it may detect urethral or vaginal infections, rather than cervical infections. Indeed, paired cervical and urine samples have showed to detect different types of HPV (31). Our data show that first-void urine is inferior in detecting HPV compared to all other sample types, reflected by both the lower number of positives, which is confirmed by others (31). The lack of standardized methods of urine sampling could be met by using collection devices, though even then cervical smear seems superior for HPV detection (32).

Some potential limitations need to be mentioned. As close consideration was given to the order in which samples were taken, the order was not altered during the study, whereby potential influences on the results cannot be fully excluded. Analyses were conducted following manufacturers' instructions, though not all sample types are cleared for each analysis. This is particularly true for HPV, where clinical cutoffs are applied when interpreting the results. Given the often asymptomatic nature of the selected STIs and excellent test performance of NAAT, we considered a FSW infected whenever she tested positive at least on one sample type, irrespective of signs and symptoms. Finally, as we studied a population of FSW, which are at higher risk for STI than the overall population, caution is to be made when generalizing our results to lower prevalence populations.

To our knowledge, this is the first study to explore a consensus sample type for STI testing. The strengths of our study include the simultaneous detection of five STIs and sampling of

different anatomical sites, including swabs of two manufacturers. Apart from HPV, we found relatively low prevalence rates in comparison with other studies conducted in FSW worldwide. This could be explained by geographical differences and/or the influence of a well-organized outreach health program, as FSW are often involved in clandestine practices. Vaginal swabs are the preferred sample for STI testing whilst first-void urine should be avoided. In addition to its promising ability to detect STIs, vaginal (self-)sampling should enhance participation in targeted screening programs and in women who refuse or not need a cervical examination, who may be discouraged from testing by the prospect of a speculum examination. The designation of a consensus sample type enables harmonization of STI testing, as it allows for simultaneous analysis of different STIs. This could result in diagnosis and treatment being available more quickly and in a more patient-friendly way, thereby curbing the clinical impact of STIs. The clinical accuracy of HPV on self-collected samples needs further investigation. Meanwhile, cervical smears are likely to remain the sample of choice, especially in a cytology based screening program where cervical smears are suitable both for cytology and HPV testing.

KEY MESSAGES

- When testing for STIs, vaginal swabs are the sample of choice.
- The designation of a non-invasive consensus sample type enables harmonization of STI diagnosis, by means of (self-)sampling and simultaneous testing for different STIs.
- Prevalence rates were the highest for HPV, followed by *M. genitalium*, *C. trachomatis*, *T. vaginalis* and *N. gonorrhoeae*.

REFERENCES

1. Schwebke JR, Hobbs MM, Taylor SN, Sena AC, Catania MG, Weinbaum BS, et al. Molecular testing for Trichomonas vaginalis in women: results from a prospective U.S. clinical trial. J Clin Microbiol. 2011;49(12):4106-11.
2. Fang J, Husman C, DeSilva L, Chang R, Peralta L. Evaluation of self-collected vaginal swab, first void urine, and endocervical swab specimens for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae in adolescent females. J Pediatr Adolesc Gynecol. 2008;21(6):355-60.
3. Griffith WF, Stuart GS, Gluck KL, Heartwell SF. Vaginal speculum lubrication and its effects on cervical cytology and microbiology. Contraception. 2005;72(1):60-4.
4. Coorevits L, Vanscheeuwijck C, Traen A, Bingé L, Ryckaert I, Padalko E. Evaluation of Copan FLOQSwab for the molecular detection of Chlamydia trachomatis by Abbott RealTime CT PCR. Acta Clin Belg. 2015;70(6):398-402.
5. Mak RP, Van Renterghem L, Traen A. Chlamydia trachomatis in female sex workers in Belgium: 1998-2003. Sex Transm Infect. 2005;81(1):89-90.
6. Verscheijden MM, Woestenberg PJ, Götz HM, van Veen MG, Koedijk FD, van Benthem BH. Sexually transmitted infections among female sex workers tested at STI clinics in the Netherlands, 2006-2013. Emerg Themes Epidemiol. 2015;12:12.
7. Vielot N, Hudgens MG, Mugo N, Chitwa M, Kimani J, Smith J. The Role of Chlamydia trachomatis in High-Risk Human Papillomavirus Persistence Among Female Sex Workers in Nairobi, Kenya. Sex Transm Dis. 2015;42(6):305-11.
8. Cwikel JG, Lazer T, Press F, Lazer S. Sexually transmissible infections among female sex workers: an international review with an emphasis on hard-to-access populations. Sex Health. 2008;5(1):9-16.
9. Poon AN, Li Z, Wang N, Hong Y. Review of HIV and other sexually transmitted infections among female sex workers in China. AIDS Care. 2011;23 Suppl 1:5-25.
10. Cárcamo CP, Campos PE, García PJ, Hughes JP, Garnett GP, Holmes KK, et al. Prevalences of sexually transmitted infections in young adults and female sex workers in Peru: a national population-based survey. Lancet Infect Dis. 2012;12(10):765-73.
11. Klingenberg RE, Mannherz S, Brockmeyer NH, Wach J, Winter R, Tiemann C, et al. [Local health study : Outreach medical services for female sex workers in Bochum]. Hautarzt. 2016;67(12):989-95.
12. Bremer V, Haar K, Gassowski M, Hamouda O, Nielsen S. STI tests and proportion of positive tests in female sex workers attending local public health departments in Germany in 2010/11. BMC Public Health. 2016;16(1):1175.
13. Luo L, Reilly KH, Xu JJ, Wang GX, Ding GW, Wang N, et al. Prevalence and correlates of Trichomonas vaginalis infection among female sex workers in a city in Yunnan Province, China. Int J STD AIDS. 2016;27(6):469-75.
14. Crucitti T, Jespers V, Mulenga C, Khondowe S, Vandepitte J, Buvé A. Trichomonas vaginalis is highly prevalent in adolescent girls, pregnant women, and commercial sex workers in Ndola, Zambia. Sex Transm Dis. 2010;37(4):223-7.
15. Gomih-Alakija A, Ting J, Mugo N, Kwatampora J, Getman D, Chitwa M, et al. Clinical characteristics associated with Mycoplasma genitalium among female sex workers in Nairobi, Kenya. J Clin Microbiol. 2014;52(10):3660-6.
16. Pépin J, Labbé AC, Khonde N, Deslandes S, Alary M, Dzokoto A, et al. Mycoplasma genitalium: an organism commonly associated with cervicitis among west African sex workers. Sex Transm Infect. 2005;81(1):67-72.
17. Soohoo M, Blas M, Byraiah G, Carcamo C, Brown B. Cervical HPV Infection in Female Sex Workers: A Global Perspective. Open AIDS J. 2013;7:58-66.
18. Mak R, Van Renterghem L, Cuvelier C. Cervical smears and human papillomavirus typing in sex workers. Sex Transm Infect. 2004;80(2):118-20.

19. Harper DM, Longacre MR, Noll WW, Belloni DR, Cole BF. Factors affecting the detection rate of human papillomavirus. Ann Fam Med. 2003;1(4):221-7.
20. Bignell C, Unemo M, Board ESGE. 2012 European guideline on the diagnosis and treatment of gonorrhoea in adults. Int J STD AIDS. 2013;24(2):85-92.
21. Prevention CfDCa. Recommendations for the laboratory-based detection of Chlamydia trachomatis and Neisseria gonorrhoeae--2014. MMWR Recomm Rep. 2014;63(RR-02):1-19.
22. Nwokolo NC, Dragovic B, Patel S, Tong CY, Barker G, Radcliffe K. 2015 UK national guideline for the management of infection with Chlamydia trachomatis. Int J STD AIDS. 2016;27(4):251-67.
23. Lanjouw E, Ouburg S, de Vries HJ, Stary A, Radcliffe K, Unemo M. 2015 European guideline on the management of Chlamydia trachomatis infections. Int J STD AIDS. 2016;27(5):333-48.
24. Sherrard J, Ison C, Moody J, Wainwright E, Wilson J, Sullivan A. United Kingdom National Guideline on the Management of Trichomonas vaginalis 2014. Int J STD AIDS. 2014;25(8):541-9.
25. S. JJ, M. C, M. G. 2016 European guideline on Mycoplasma genitalium infections. Norway: Prof Harald Moi, Osla University Hospital and Faculty of Medecing, University of Oslo, Norway; 2016.
26. Schachter J, Chernesky MA, Willis DE, Fine PM, Martin DH, Fuller D, et al. Vaginal swabs are the specimens of choice when screening for Chlamydia trachomatis and Neisseria gonorrhoeae: results from a multicenter evaluation of the APTIMA assays for both infections. Sex Transm Dis. 2005;32(12):725-8.
27. Petignat P, Faltin DL, Bruchim I, Tramèr MR, Franco EL, Coutlée F. Are self-collected samples comparable to physician-collected cervical specimens for human papillomavirus DNA testing? A systematic review and meta-analysis. Gynecol Oncol. 2007;105(2):530-5.
28. Winer RL, Lee SK, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. Am J Epidemiol. 2003;157(3):218-26.
29. Taylor S, Bunge E, Bakker M, Castellsagué X. The incidence, clearance and persistence of non-cervical human papillomavirus infections: a systematic review of the literature. BMC Infect Dis. 2016;16:293.
30. Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. N Engl J Med. 1998;338(7):423-8.
31. Sehgal A, Gupta S, Parashari A, Sodhani P, Singh V. Urine HPV-DNA detection for cervical cancer screening: prospects and prejudices. J Obstet Gynaecol. 2009;29(7):583-9.
32. Vorsters A, Van Keer S, Biesmans S, Hens A, De Coster I, Goossens H, et al. Long-Term Follow-up of HPV Infection Using Urine and Cervical Quantitative HPV DNA Testing. Int J Mol Sci. 2016;17(5).

FIGURE LEGENDS

Figure 1 – Flowchart of inclusion of FSW and number of positive results for each parameter on the different sample types. (NGc = *Neisseria gonorrhoeae* culture; NG= *Neisseria gonorrhoeae*; CT= *Chlamydia trachomatis*; TV = *Trichomonas vaginalis*; MG = *Mycoplasma genitalium*; HPV = human papilloma virus; FVU= first void urine; VA = vaginal Abbott swab; VC = vaginal Copan swab; CA = cervical Abbott swab; CC cervical Copan swab; CS = cervical smear; [a] significantly higher than CA ($p<0.05$); [b] significantly higher than FVU ($p<0.05$); [c] significantly higher than CC ($p<0.05$); [d] significantly higher than CS ($p<0.05$); [e] significantly higher than VA ($p<0.05$); [f] significantly higher than VC ($p<0.05$); grey background indicates sample type with highest sensitivity)

Figure 2 – Percentage of infections detected (■) or missed (■) for each parameter on the different sample types. (FVU= first void urine; VA = vaginal Abbott swab; VC = vaginal Copan swab; CA = cervical Abbott swab; CC = cervical Copan swab; CS = cervical smear)

Figure 3 – Analysis of high-risk HPV results in case of normal versus abnormal cytology. [a] significantly higher than FVU ($p<0.05$); [b] significantly higher than CA ($p<0.05$); [c] significantly higher than CC ($p<0.05$); [d] significantly higher than CS ($p<0.05$)

TRANSPARENCY DECLARATION

- Conflict of interest

The authors have nothing to disclose

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