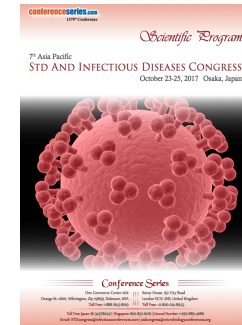


**SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA**
Azienda Unità Sanitaria Locale della Romagna



How to facilitate and improve screening of sexually-transmitted infections in women population

Vittorio Sambri

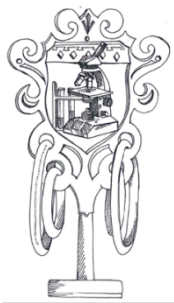
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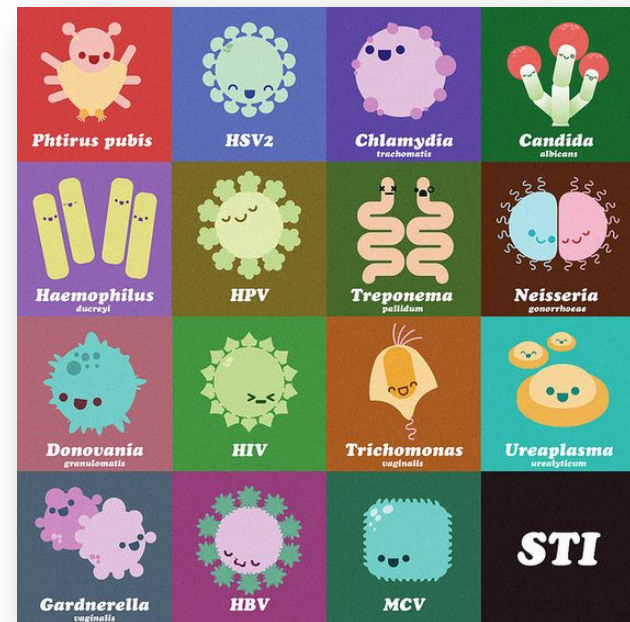
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Agenda

- Global prevalence of Curable Sexually Transmitted Infections in 2012
- Diagnostic Guidelines
- Home based Self Vaginal collection approach
- Objective of our evaluation study
- Material and Methods
- Results
- Conclusions
- Take home message



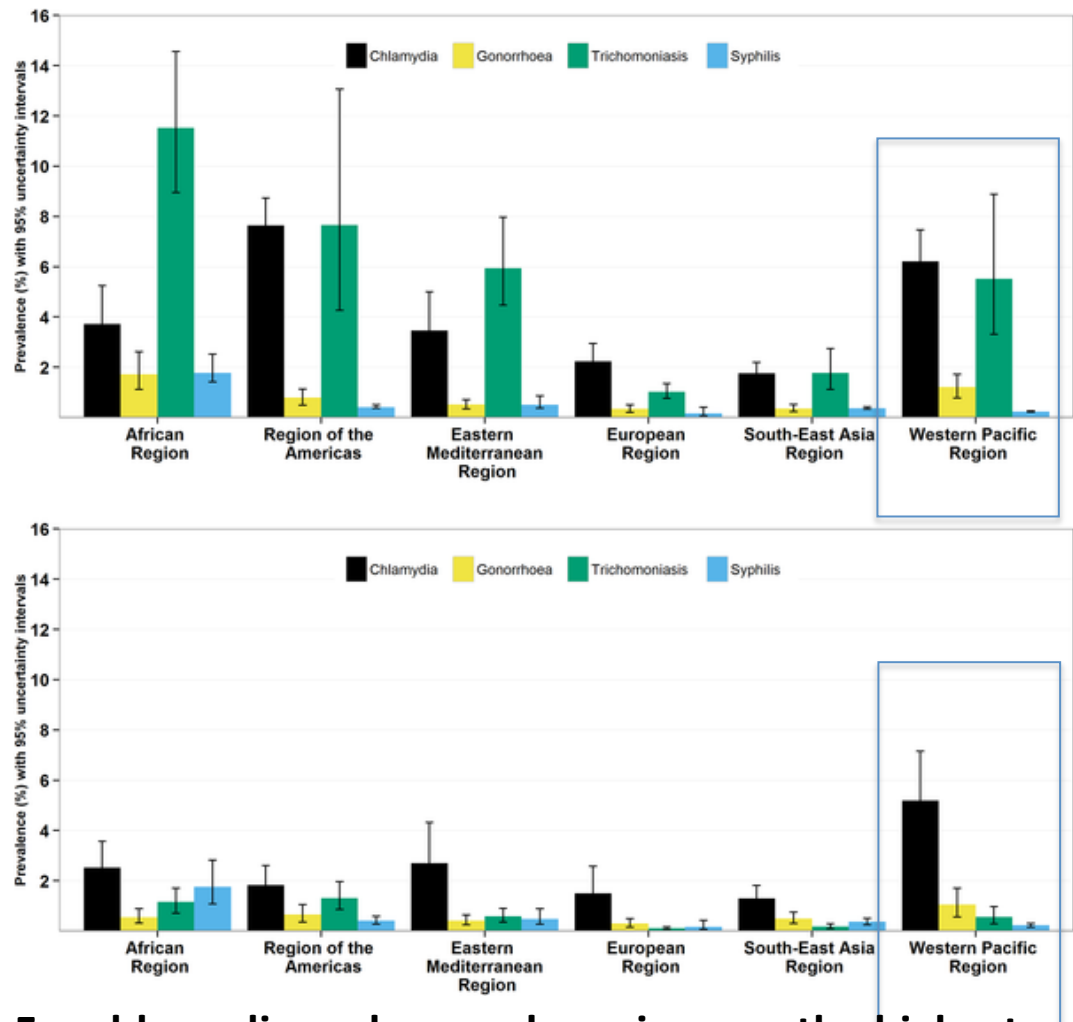
Global Estimates of Four Curable Sexually Transmitted Infections in 2012

- The **World Health Organization (WHO)** periodically estimates **global and regional prevalence and incidence of four curable STIs: chlamydia, gonorrhoea, trichomoniasis and syphilis.**
- These four infections cause **acute conditions:**
 - **cervicitis,**
 - **urethritis**
 - **genital ulceration.**
- Severe complications and long term sequelae (pelvic inflammatory disease, ectopic pregnancy, infertility, chronic pelvic pain and neurological and cardiovascular disease in adults).
- Increased risk of HIV acquisition and transmission [1,2].



World Health Organization

Estimated prevalence of chlamydia, gonorrhoea, trichomoniasis, and syphilis in women and men aged 15–49 years by WHO region, (based on 2005–2012 data).



For chlamydia and gonorrhoea in men, the highest estimated prevalence rates were in the Western Pacific Region

Estimated global prevalence of STIs in women and men

- Based on data for 2005 to 2012:
 - *Chlamydia trachomatis* 4.2%
 - Gonorrhoea 0.8%
 - Trichomoniasis 5.0%
 - Syphilis 0.5%

- *Chlamydia trachomatis* 2.7%
- Gonorrhoea 0.6%
- Trichomoniasis 0.6%
- Syphilis 0.5%



Global estimates of new cases of curable STIs in 2012

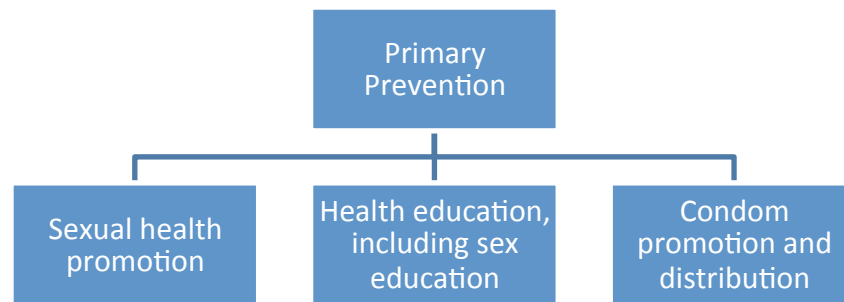
Sexually Transmitted Infection	n (million)
Chlamydia trachomatis	130.9
Neisseria gonorrhoeae	78.3
Syphilis	5.6
Trichomonas vaginalis	142.6
Total	357.4

Source: Newman et al. (2015)

Interventions for the control of Chlamydia

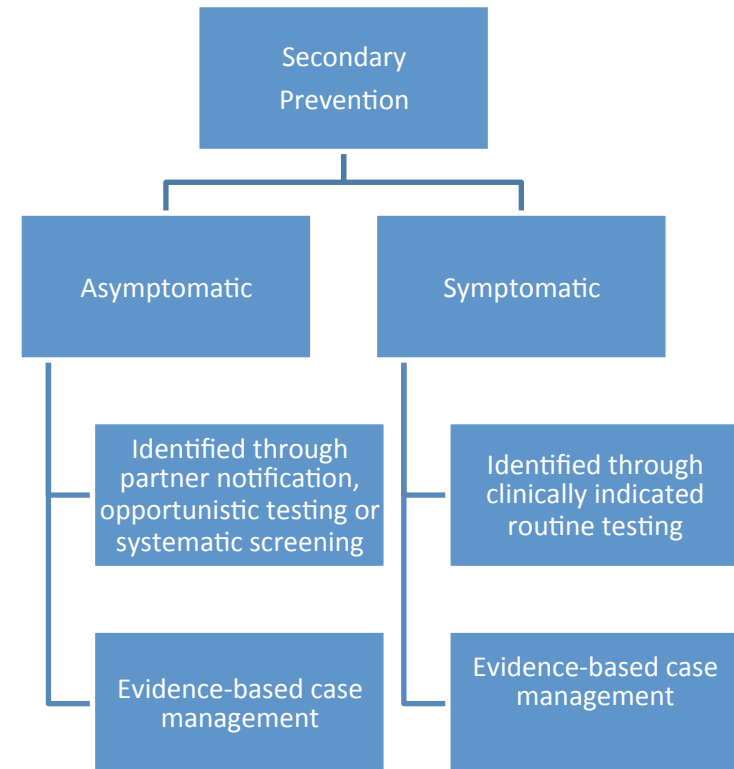
- The term “chlamydia control” describes a **broad range of activities that aim to reduce the incidence and prevalence** of chlamydia and the incidence of reproductive tract complications.
- **Primary prevention & Secondary prevention**

Interventions for the control of Chlamydia

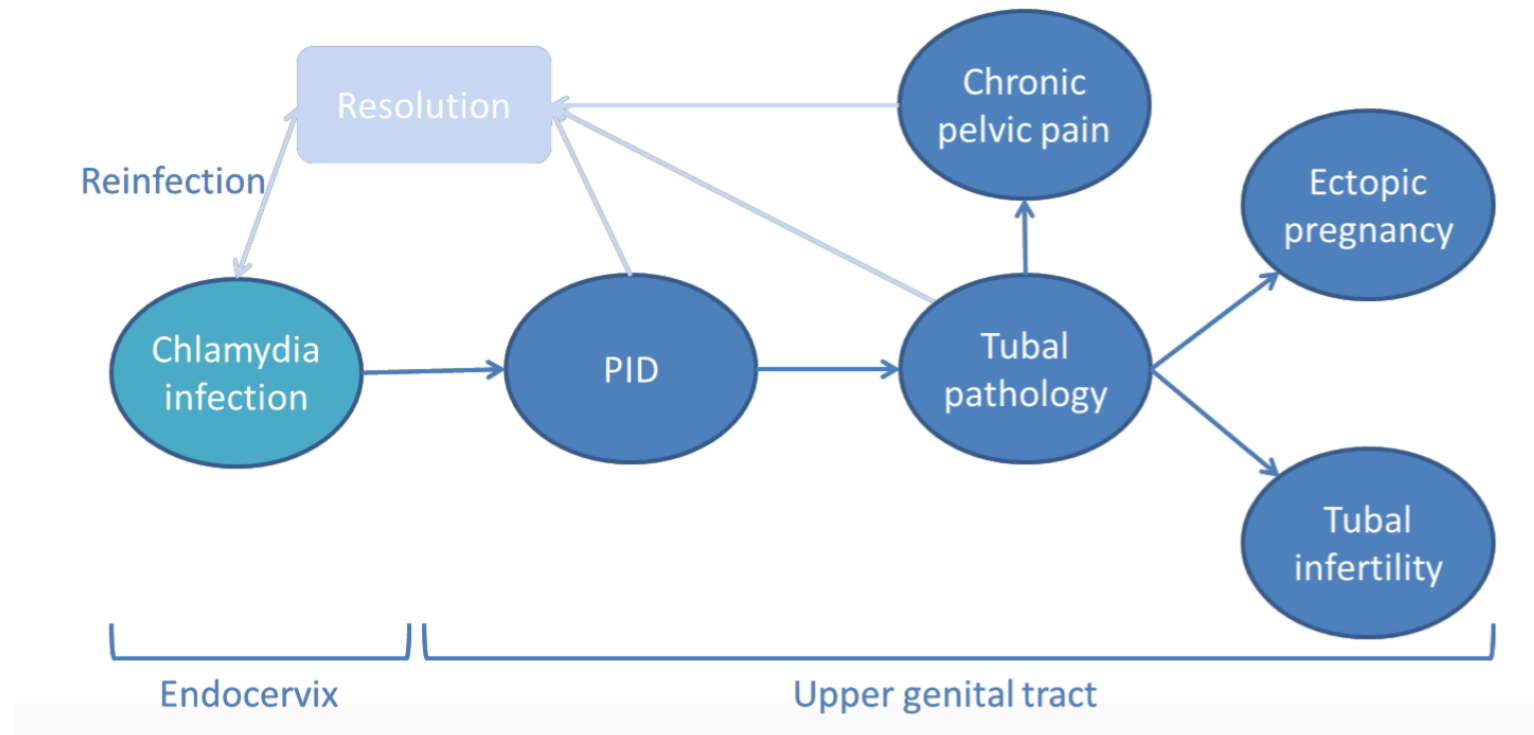


Screening refers to offering chlamydia tests to asymptomatic people in a defined population who are considered to be at increased risk of infection compared with the general population

Opportunistic chlamydia testing refers to chlamydia tests which are offered to people in predefined risk groups (e.g. based on age and sex) in healthcare settings, through outreach programs, or via internet-based services.



Natural history and sequelae of chlamydia infection in women



Several sequelae can result from *C. trachomatis* infection in women, the most serious of which include PID, ectopic pregnancy, and infertility. Some women who receive a diagnosis of uncomplicated cervical infection already have subclinical upper-reproductive-tract infection.



Chlamydial Infection

- Asymptomatic infection is common among both men and women.
- **Annual screening of all sexually active women aged <25 years is recommended,**
- **Chlamydia screening programs have been demonstrated to reduce the rates of PID in women.**
- Screening of sexually active young men in clinical settings with a high prevalence of chlamydia or in populations with high burden of infection (e.g., MSM).

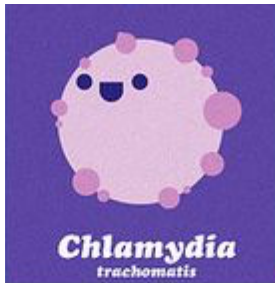


Diagnostic Considerations

- *C. trachomatis* urogenital infection can be diagnosed in women:
 - testing first-catch urine
 - collecting swab specimens from the endo-cervix or vagina.
- Diagnosis of *C. trachomatis* urethral infection in men can be made by testing:
 - a urethral swab or first-catch urine specimen.
- **NAATs are the most sensitive tests for these specimens and therefore are recommended for detecting *C. trachomatis* infection¹.**
- **Self-collected vaginal swab specimens are equivalent in sensitivity and specificity to those collected by a clinician using NAATs².**

1. Papp JR, Schachter J, Gaydos C, et al. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. MMWR Recomm Rep 2014;63(No. RR-02).

2. Masek BJ, Arora N, Quinn N, et al. Performance of three nucleic acid amplification tests for detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by use of self-collected vaginal swabs obtained via an Internet-based screening program. J Clin Microbiol 2009;47:1663–7



Diagnostic Considerations

- Rectal and oropharyngeal *C. trachomatis* infection in persons engaging in receptive anal or oral intercourse can be diagnosed by testing at the anatomic site of exposure.
- **NAATs are not FDA-cleared for use with rectal or oropharyngeal swab specimens.**
- However, **NAATs have been demonstrated to have improved sensitivity and specificity compared with culture for the detection of *C. trachomatis* at rectal sites and at oropharyngeal sites among men.**



Chlamydia Treatment

- Chlamydia treatment should be provided promptly for all persons testing positive for infection;
- treatment delays have been associated with complications (e.g., PID).



Recommended Regimens
Azithromycin 1 g orally in a single dose
OR
Doxycycline 100 mg orally twice a day for 7 days



Gonococcal Infections

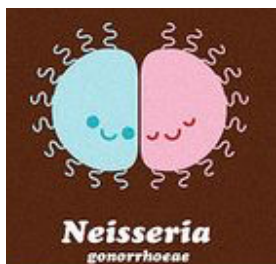
- **Gonorrhea is the second most commonly reported communicable disease.**
- Urethral infections caused by *N. gonorrhoeae*:
 - **among men can produce symptoms** that cause them to seek curative treatment soon enough to prevent sequelae.
 - **Among women, gonococcal infections are commonly asymptomatic** or might not produce recognizable symptoms until complications (e.g., PID) have occurred.
 - **Annual screening for *N. gonorrhoeae* infection is recommended for all sexually active women aged <25 years** and for older women at increased risk for infection



Diagnostic Considerations

- Culture and NAAT are available for the detection of genitourinary infection with *N. gonorrhoeae*¹:
 - **culture requires endo-cervical (women) or urethral (men) swab specimens.**
 - **NAAT allows for the widest variety of FDA-cleared specimen types, including endo-cervical swabs, vaginal swabs, urethral swabs (men), and urine (from both men and women).**
 - **The sensitivity of NAAT for the detection of *N. gonorrhoeae* in urogenital and non-genital anatomic sites is superior to culture but certain NAATs have been demonstrated to detect commensal *Neisseria* species (low specificity) when testing oropharyngeal specimens.**
 - **In cases of suspected or documented treatment failure, clinicians should perform both culture and antimicrobial susceptibility testing because nonculture tests cannot provide antimicrobial susceptibility result.**

1. Papp JR, Schachter J, Gaydos C, et al. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. MMWR Recomm Rep 2014;63(No. RR-02).



Gonorrhea Treatment: uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

- Gonorrhea treatment is complicated by the ability of *N. gonorrhoeae* to develop resistance to antimicrobials.
- **Dual treatment with ceftriaxone and azithromycin, is recommended** for treatment of gonorrhea in the United States.
- Criteria for resistance to cefixime and ceftriaxone have not been defined by the Clinical and Laboratory Standards Institute (CLSI).
 - isolates with cefixime or ceftriaxone MICs $\geq 0.5 \mu\text{g/mL}$ are considered to have decreased susceptibility.

Gonococcal infections of the pharynx are more difficult to eradicate than are infections at urogenital and anorectal sites.

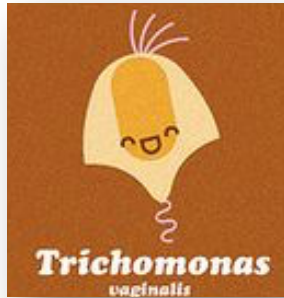


Recommended Regimen

Ceftriaxone 250 mg IM in a single dose

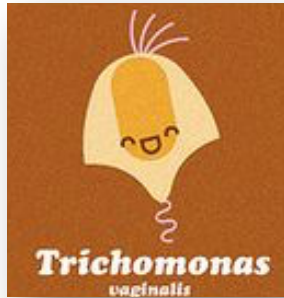
PLUS

Azithromycin 1g orally in a single dose



Trichomoniasis

- *T. vaginalis* infection affects >11% of women aged ≥ 40 years.
- particularly high prevalence has been detected among STD clinic patients (26% of symptomatic women and 6.5% asymptomatic women tested)
- High prevalence in incarcerated persons (9%–32% of incarcerated women and 2%–9% of incarcerated men).
- The prevalence of trichomoniasis in MSM is low.
- Most infected persons (70%–85%) have minimal or no symptoms, and untreated infections might last for months to years.



Trichomoniasis

- *T. vaginalis* infection is associated with two- to threefold increased risk for HIV acquisition.
- *T. vaginalis* infection is associated with preterm birth, and other adverse pregnancy outcomes among pregnant women.
- Among women with HIV infection, *T. vaginalis* infection is associated with increased risk for PID.
- Routine screening of asymptomatic women with HIV infection for *T. vaginalis* is recommended because of the adverse events associated with asymptomatic trichomoniasis and HIV infection.

Diagnostic Considerations

- The use of highly sensitive and specific tests is recommended for detecting *T. vaginalis*.
- Among women, NAAT is highly sensitive, often detecting three to five times more *T. vaginalis* infections than wet-mount microscopy, a method with poor sensitivity (51%–65%).
- Culture (sensitivity of 75%–96% and a specificity of up to 100%) was considered the gold standard method for diagnosing *T. vaginalis* infection before molecular detection methods became available.
- In women, vaginal secretions are the preferred specimen type for culture, as urine culture is less sensitive.
- In men, culture specimens require a urethral swab, urine sediment, and/or semen. To improve yield, multiple specimens from men can be used to inoculate a single culture.

Diagnostic Considerations

- The most common method for *T. vaginalis* diagnosis might be microscopic evaluation of wet preparations of genital secretions because of convenience and relatively low cost.
- Unfortunately, the sensitivity of wet mount is low in vaginal specimens and lower in specimens from men (e.g., urethral specimens, urine sediment, and semen).

Trichomonas's Treatment

- Treatment reduces symptoms and signs of *T. vaginalis* infection and might reduce transmission. Likelihood of adverse outcomes in women with HIV also is reduced with *T. vaginalis* therapy.

Recommended Regimen
Metronidazole 2 g orally in a single dose
OR
Tinidazole 2 g orally in a single dose

How to facilitate and improve screening of sexually-transmitted infections in women population

- **Sexually Transmitted Infections (STIs) are increasing worldwide.**
- **More innovative interventions are required to eliminate barriers to STI testing** (internet-based or mail-in home and community service testing for patients).
- **Home Based Self Vaginal sampling is a new collection approach** for detection of STI and is able to guarantee privacy and comfort during the collection.



Self-Collected versus Clinician-Collected Sampling: A Systemic Review

The sensitivity and specificity of vaginal self-collected swabs compared to swabs collected by clinicians supports the use of vaginal swab as the recommended specimen of choice in home-based screening for chlamydia and gonorrhoea¹.

PLOS ONE

RESEARCH ARTICLE

Self-Collected versus Clinician-Collected Sampling for Chlamydia and Gonorrhoea Screening: A Systemic Review and Meta-Analysis

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OPEN ACCESS

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Abstract

Background

The increases in STI rates since the late 1990s in Canada have occurred despite widespread primary care and targeted public health programs and in the setting of universal health care. More innovative interventions are required that would eliminate barriers to STI testing such as internet-based or mail-in home and community service testing for patients that are hard to reach, who refuse to go for clinician-based testing, or who decline an examination. Jurisdictions such as New Zealand and some American states currently use self-collected sampling, but without the required evidence to determine whether self-collected specimens are as accurate as clinician-collected specimens in terms of chlamydia and gonorrhoea diagnostic accuracy. The objective of the review is to compare self-collected vaginal, urine, pharyngeal and rectal samples to our reference standard - clinician-collected cervical, urethral, pharyngeal and rectal sampling techniques to identify a positive specimen using nucleic acid amplification test assays.

Methods

The hierarchical summary receiver operating characteristic and the fixed effect models were used to assess the accuracy of comparable specimens that were collected by patients compared to clinicians. Sensitivity and specificity estimates with 95% confidence intervals (CI) were reported as our main outcome measures.

Findings

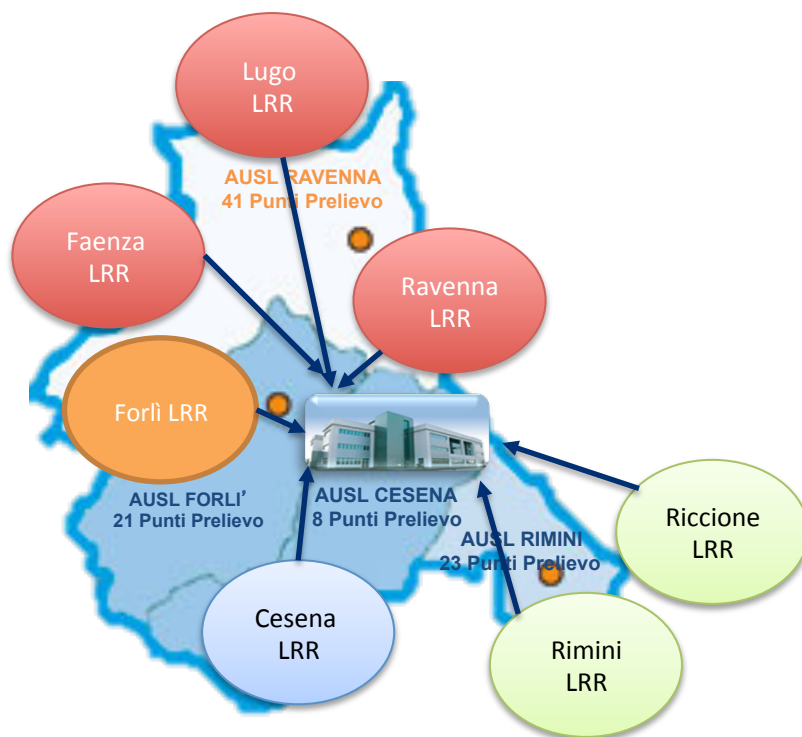
We included 21 studies based on over 6100 paired samples. Fourteen included studies examined chlamydia only, 6 compared both gonorrhoea and chlamydia separately in the same study, and one examined gonorrhoea. The six chlamydia studies comparing self-collection by



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1 / 23

The Greater Romagna Area: my reality. Organization of *Hub and spoke laboratory model*



ROMAGNA: organization of labs	
AUSL	4
Laboratories on site	7
Tests performed/year	18.000.000
Employees	312

Daily Routine in Area Vasta Romagna	
N° of Samples Collection Sites	93
Out patients	4500
Access Sites	400
In Patients	1500
Hospitals in Area Vasta	7

Objectives of the study

- To evaluate the performance of a **new Home-based Self Vaginal FLOQSwab™** (HBSVF, COPAN Italia, Brescia) in combination with a commercially available real-time PCR assay, (Anyplex™ II STI-7 Seegene, Seoul, Korea).
- To evaluate acceptability of the new Self Vaginal device in a population of asymptomatic women with different level of education.
- Define the samples workflow and protocol on NAATs for Self collected samples.





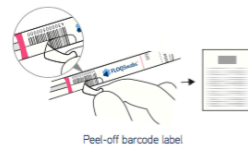
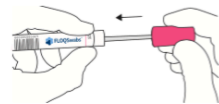
Material & Methods

- Pievesestina laboratory offered to **78 asymptomatic** employees of a private industry (aged **18 to 45 years**) a free STIs screening with a new Home based Self Vaginal device (COPAN Italia S.p.A).

The subjects answered to a standardized anonymous questionnaire regarding the ease of use of self collection.

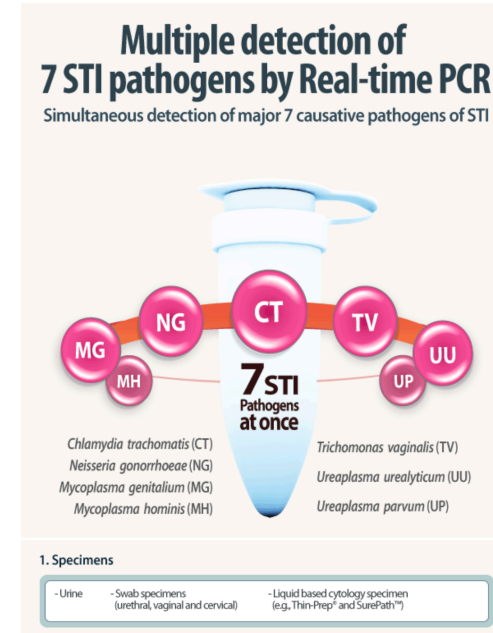
The swab was collected in a domestic context by following the detailed “how to use” instructions.

After collection, swabs were shipped with regular mail using a customized kit for shipment at room temperature to the laboratory in Pievesestina and processed within five weeks.

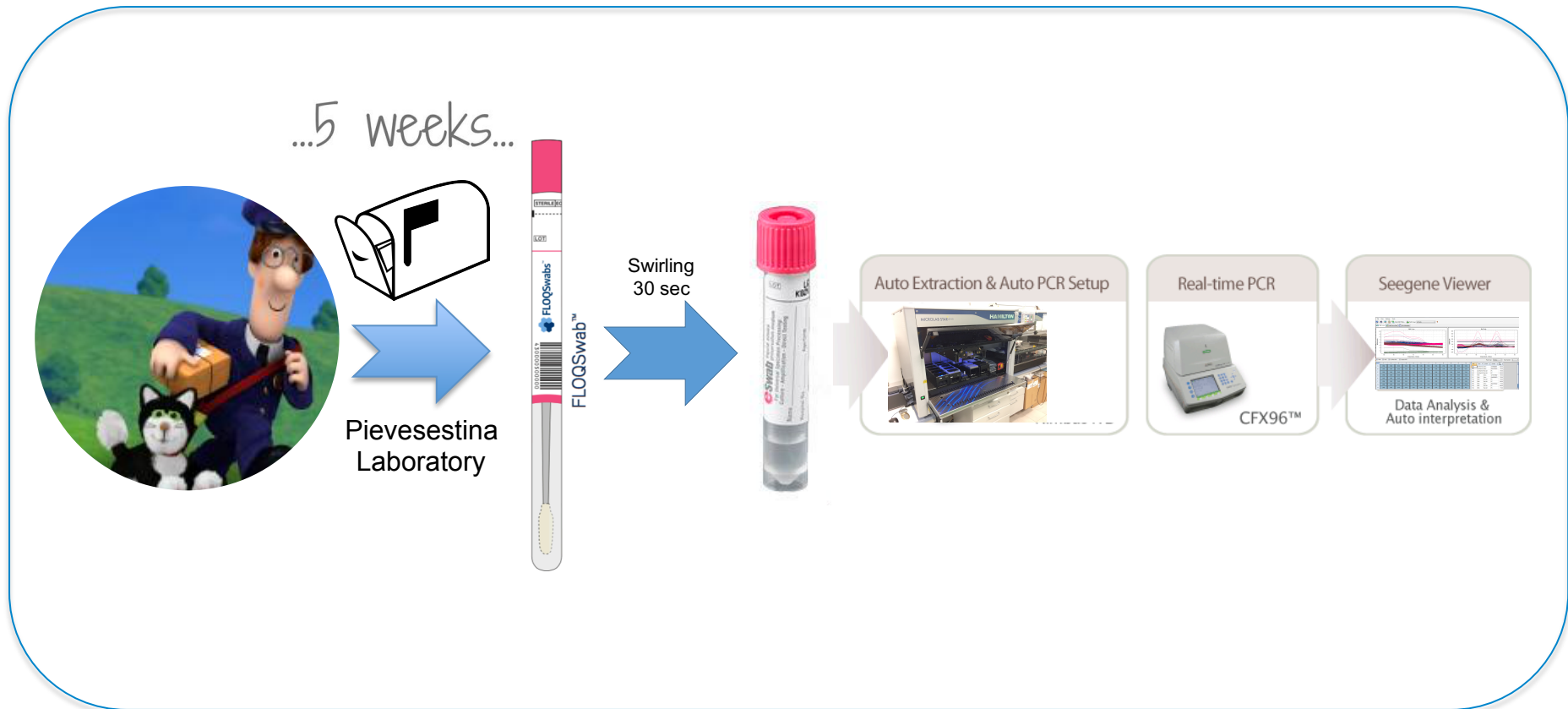


Material and Methods: NAATs System used

- Anyplex™ II STI-7 (Seegene, Seoul, Korea) which detects seven pathogens in a single reaction:
 - *Chlamydia trachomatis* CT,
 - *Neisseria gonorrhoeae* NG,
 - *Trichomonas vaginalis* TV,
 - *Mycoplasma hominis* MH,
 - *Mycoplasma genitalium* MG,
 - *Ureaplasma urealyticum* UU,
 - *Ureaplasma parvum* UP

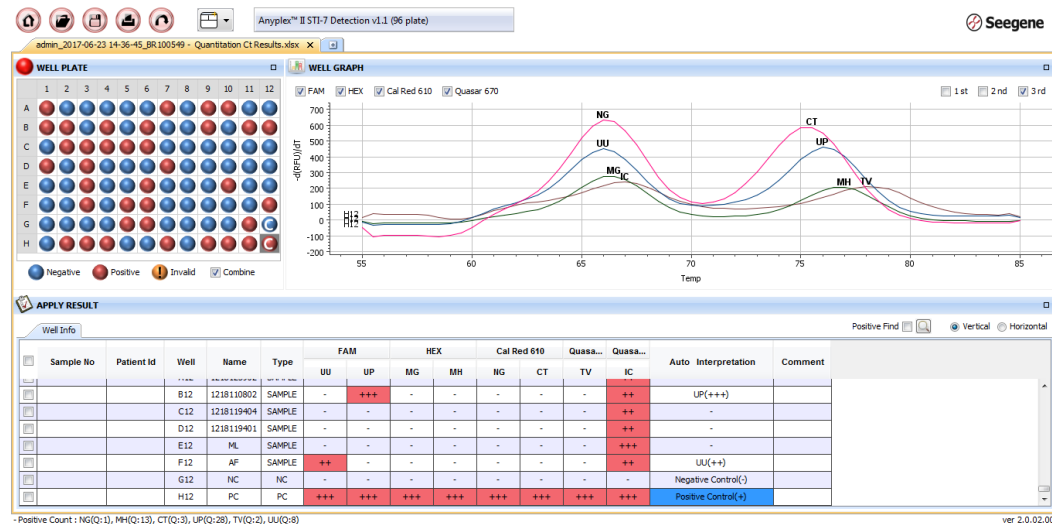


Samples workflow



Parameters Considered

- The threshold cycle value (Ct) of
 - a human genomic target (internal control, IC)
 - Ct of pathogens (CT, NG, TV, MH, MG, UU, UP)
- to assess respectively,
- **the efficiency of self-sampling**
- **presence of any inhibitor effects**
- **the stability of nucleic acids on dry swabs.**



Results

- No failure results were observed.
- The IC of all samples was amplified (n=78 average of Ct 30).
- The real time PCR assay was able to identify 2/78 CT, 4/78 UU, 40/78 UP, 6/78 MH, 1/78 TV positive patients.
- No MG and NG positive patients were detected.

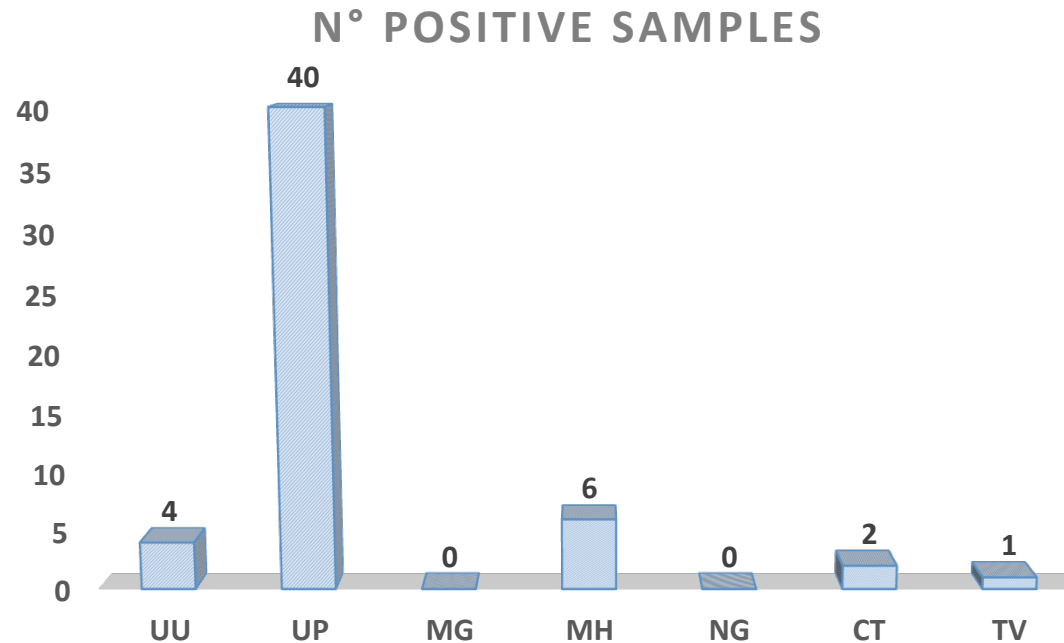
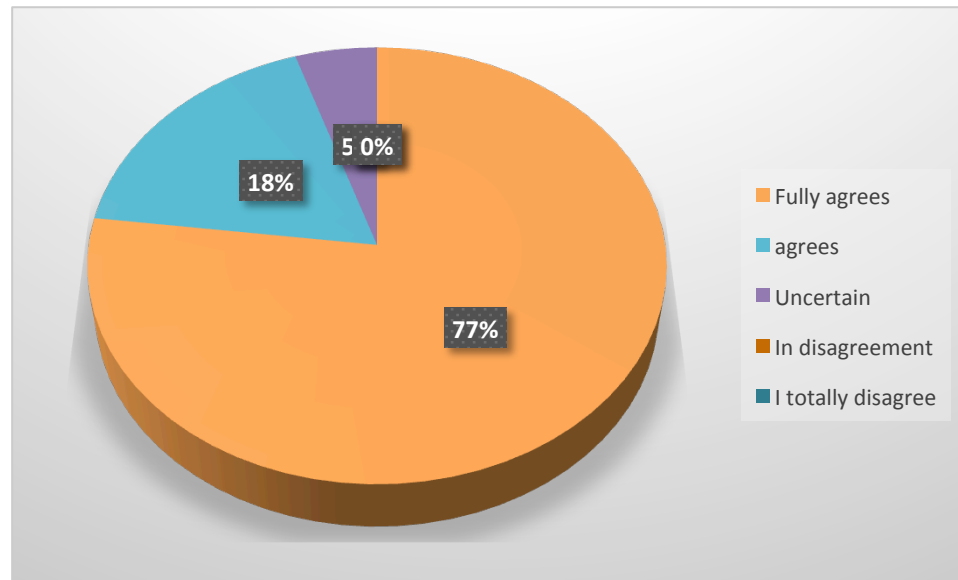


Figure. Number of positive samples distributed between pathogens (*Chlamydia trachomatis* CT, *Neisseria gonorrhoeae* NG, *Trichomonas vaginalis* TV, *Mycoplasma hominis* MH, *Mycoplasma genitalium* MG, *Ureaplasma urealyticum* UU, and *Ureaplasma parvum* UP) detected by Anyplex™ II STI-7 (Seegene assay).

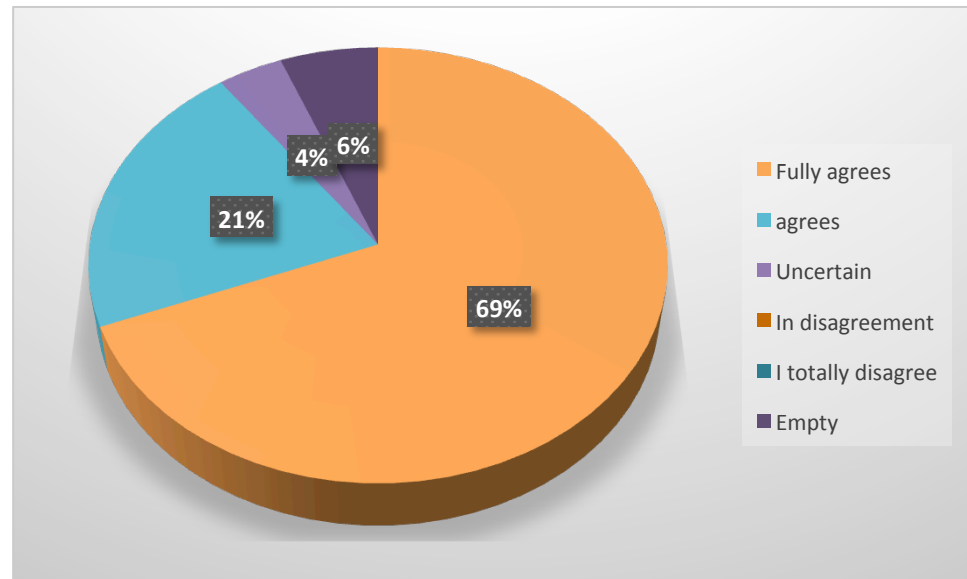
Results

- Regarding the answers to the questionnaire:
 - The Home based Self Vaginal Device is easy to use (consider the steps described in PATIENT USE INSTRUCTIONS).
 - 95% of positive feedback
 - 5% uncertain
 - 0% negative answers



Results

- Are the how to use clear and exhaustive?
 - Positive answers 90%
 - Negative answer 4%
 - No answers 6%

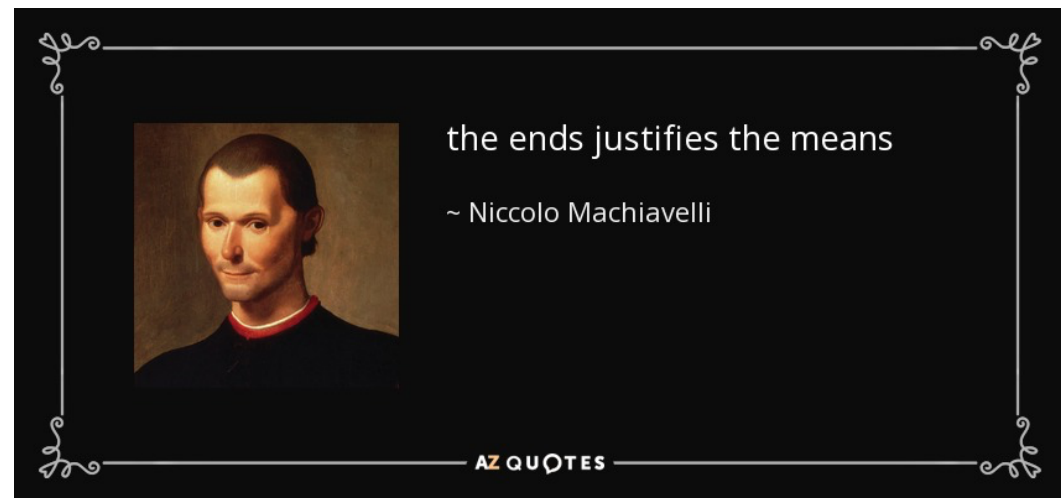


Conclusions

- Home Based Self Vaginal device showed excellent recovery and stability of nucleic acid of STI pathogens up to 4-5 weeks at room temperature.
- The Home Based Self Vaginal device is suitable for screening of STIs with real-time PCR methods.
- The Home Based Self Vaginal collection has shown a good acceptability by women.

Take home message

- The evidence provided in our study could help the introduction of home based self collected specimens as a new testing modality in STIs control programs for patients that are difficult to reach and who refuse to go for clinicians based testing.



Thank you for your attention