Highly variable use of diagnostic methods for sexually transmitted infections- results of a nationwide survey, Germany 2005

1. Field Epidemiology Training Program (FETP), Berlin, Germany
2. Department for Infectious Disease Epidemiology, Robert Koch-Institute, Berlin, Germany

*Corresponding author

Email addresses:

AG: GilsdorfA@rki.de
AH: HofmannA@rki.de
OH: HamoudaO@rki.de
VB: BremerV@rki.de
Abstract

Background
Sexual transmitted infections (STIs) have increased in Germany and other countries in Europe since the mid-nineties. To obtain a better picture of diagnostic methods used in STI testing institutions in Germany, we performed a nationwide survey amongst STI specialists in order to evaluate the quality of STI reports and provide recommendations to harmonize and possibly improve STI diagnostics in Germany.

Methods
We asked sentinel physicians and randomly chosen gynaecologists, urologists and dermato-venerologists, about the diagnostic methods used in 2005 to diagnose HIV, chlamydia (CT), gonorrhoea (GO) and syphilis (SY) in a national cross-sectional survey in order to recognize potential problems and provide recommendations.

Results
A total of 739/2287 (32%) physicians participated. Of all participants, 80% offered tests for HIV, 84% for CT, 83% for GO and 83% for SY. Of all participants who performed HIV testing, 90% requested an antibody test, 3% a rapid test and 1% a nucleic acid amplification test (NAAT). For CT testing, NAAT was used in 33% and rapid tests in 34% of participants. GO resistance testing was performed by 31% of the participants. SY testing was performed in 98% by serology.

Conclusions
Diagnostic methods for STI vary highly among the participants. Diagnostic guidelines should be reviewed and harmonised to ensure consistent use of the optimal STI diagnostic methods.
**Background**

Sexual transmitted infections (STIs) have increased in Germany and other countries in Europe since the mid-nineties (1,2), raising fears of subsequent increased HIV transmission. Early detection and treatment are the most efficient methods to control the transmission of STIs (3). Since 2001, syphilis and HIV are the only notifiable STIs in Germany. Further data for STIs are collected through a sentinel surveillance system put in place in 2002 (4). Thus, data for STIs such as HIV, syphilis, chlamydia, gonorrhoea and trichomoniasis is being collected from approximately 250 selected institutions nationwide. However, sentinel sites seemed to employ a variety of laboratory methods.

To obtain a better picture of diagnostic methods used in STI testing institutions in Germany, we performed a nationwide survey amongst the sentinel participants and other practicing STI specialists. This information will be used to evaluate the quality of STI reports and provide recommendations to harmonize and possibly improve STI diagnostics in Germany.

**Methods**

We performed a national cross-sectional study. The study population included all sentinel sites (local health offices, hospital based STI clinics and private practitioners) participating in the STI sentinel surveillance plus randomly chosen private practitioners specialising in gynaecology, urology, or dermato-venerology. Lists of practitioners available from the state chambers of physicians were used for the random selection. We calculated the required sample size with StatCalc, EpiInfo6, with focus on the diagnosis on chlamydia. Assuming that 30% of the participants would employ NAAT for chlamydia testing this led to a calculated sample size
requiring 620 participants. We expected a response of approximately one third of the contacted practitioners.

We developed a self-administered standardized questionnaire, with mainly closed questions, which was pretested before use. The questionnaire covered the different laboratory methods used for the detection of HIV, syphilis, chlamydia, gonorrhoea and trichomoniasis. We also asked information on the kind of samples taken (vaginal swab, urine, blood) and if asymptomatic patients were also tested for chlamydia, gonorrhoea or syphilis. In addition, the participants needed to provide the number and demographic characteristics of patients they see, as well as specify their type of catchment area (small or middle-sized cities, metropolitan etc).

In the first months of 2006 we asked sentinel sites and private practitioners to complete the questionnaire on laboratory methods used in the year 2005. This included both tests being performed in their own lab or sent away to external labs.

<table>
<thead>
<tr>
<th>Laboratory methods</th>
<th>The laboratory methods for the following STIs were included in the questionnaire (multiple answers possible)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Antibody test, rapid-test</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Rapid test, DNA probe, nucleic acid amplification test (NAAT), antibody test; testing of asymptomatic patients</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>Microscopy, NAAT, DNA probe, culture; resistance patterns, testing of asymptomatic patients</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Microscopy, culture</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Direct testing, dark field microscopy, serology; testing of asymptomatic patients</td>
</tr>
</tbody>
</table>

No further details on the specific tests were collected.
The completed questionnaires were entered into an MS Access database and analysed with EpiInfo 3.2.2. The results were stratified by medical speciality.

**Results**

Of 2287 contacted institutions and practitioners, 739 (32%) returned a questionnaire. Within the sentinel surveillance institutions, the response rate was 56%, while 30% of the randomly selected private practitioners responded.

A comparison between the sentinel and non-sentinel institutions participating did not show any major differences regarding the used diagnostic methods. Therefore, results are presented here not stratified by sentinel system participation.

In total, 219 dermato-venerologists, 355 gynaecologists, 85 urologists and 48 public health offices replied, 32 participants did not specify their specialisation. Fifty-two percent of the participants were situated in a metropolitan catchment area, 38% working in small or middle-sized cities. Participants replied from all federal states of Germany.

Chlamydia testing was offered by 621 participants (84%), followed by testing for syphilis (83%) and gonorrhoea (83%). Tests for HIV and trichimoniasis were offered by 592 (80%) participants and 575 (77%) respectively.

The proportions of participants testing for the different STIs, stratified by medical speciality, can be seen in Table 1.

**HIV**

Of all participants who reported testing for HIV, 89% used antibody tests, 3% a rapid test and 1% NAAT. The remaining participants did not disclose the detection methods used. There were no differences between different medical specialisations.
**Chlamydia**
The proportions of the different detection methods for chlamydia, stratified by medical speciality, are shown in Table 2.

Cervical swabs were the most frequently used samples for testing chlamydia (this varied depending on the method, median 77%). While gynaecologists relied almost exclusively on cervical samples (95%), urethral swabs were preferred by dermatovenerologists and urologists (89% resp. 81%).

**Gonorrhoea**
For the detection of gonorrhoea, microscopy (64%) and culture (60%) were the most frequently used diagnostic tools.

Dermato-venerologists used microscopy 91% of the time, culture 56%.
Gynaecologists performed cultures on 65% of samples and microscopy on 41%.

Samples for gonorrhoea examination were mainly urethral swabs (76%) followed by cervical swabs. Gynaecologists preferred cervical swabs (93%). Dermato-venerologists also performed regularly anal swabs (49%).

Testing for antimicrobial resistance was requested by 30% of the participants.
Urologists most frequently requested resistance testing (47%), followed by gynaecologists (33%).

**Trichomoniasis**
Trichomoniasis were examined in 94% of the participants by microscopy and in 22% with culture. There were no differences between the specialisations.

**Syphilis**
Serology was used by 98% of the responding participants to look for syphilis.

Serology was also used for confirmatory tests, to determine whether treatment is needed and for follow up. However, when asked for the different types of serological tests, participants’ responses varied a lot. Eighteen point three percent of participants
used dark field microscopy to identify syphilis, among dermatologic-venerologists this technique was frequent (42%). There were no further differences between the medical specialisations.

**Asymptomatic patients**
Asymptomatic patients were tested for Chlamydia and syphilis by 65% and 65% of the participants, respectively. Antenatal screening was the main reason for these tests. Also, 33% of the participants reported testing of asymptomatic patients for gonorrhoea, giving “infection in the patient’s partner” or “sexual risk behaviour” (unprotected sex or frequent changing of sex partners) as the main reasons for testing (Table 3).

**Discussion**
The results show that STI diagnostic methods varied a lot among the participants all over Germany. In addition, STI detection methods varied substantially between the different medical specialists. Sample materials, antimicrobial resistance testing and testing of asymptomatic patients also differed considerably between participants.

It is possible that practitioners who responded to the survey are generally more aware of STIs and therefore more likely to offer comprehensive STI testing and adhere to testing guidelines. In reality, it is possible that fewer practitioners might offer STI testing and the test methods used may be even more diverse than shown by this survey.

Nearly all participants used the same test method for HIV, the antibody test: the recommended standard for detecting HIV infection (5). This could be a sign that clear
recommendations on testing methods lead to consistent nationwide use of comparable diagnostic tests.

The best diagnostic method for chlamydia is NAAT (6) because of the high sensitivity (90-95%) and specificity (up to 100%). Our survey showed that only public health offices widely used NAAT.

Most participants followed the current recommendations (6) regarding sampling for chlamydia testing and took cervical or urethral swabs. Recent studies (7, 8) showed that the first morning urine from men or self-collected vaginal swabs from women also provide good test results. In addition, these collection methods are less invasive, require less equipment and are well accepted by patients. However, the participants seldom requested these samples of the patients. Clinical practitioners need to be more widely informed on the advantages of using them.

The DNA probe test requires less complex transport, and is cheaper than NAAT, but is also less sensitive (60-80%) and specific (99.5%). (6, 8). In settings with few resources or those unable to access transport facilities, the DNA probe could be preferred.

Rapid tests for chlamydia, which show results within 30 minutes and require little technical effort, were used frequently. However, some studies show a considerably lower sensitivity and specificity compared to traditional detecting methods (6, 9). So the use of rapid tests cannot currently be recommended for routine diagnosis of chlamydia (9).

Serological testing for specific antibodies is not recommended for detection of acute uro-genital chlamydia infections, as many infections do not lead to a serological response (10). However, it might be a useful tool to diagnose chlamydia-associated
secondary complications in the absence of chlamydia symptoms, such as tubar sterility, reactive arthritis or Reiter-syndrome.

Since 2008, chlamydia screening has been introduced in Germany for a certain age group: all women under 25 years of age are offered a chlamydia test when visiting a gynaecologist (11). Pooled urine samples are tested using NAAT. Though the use of pooled samples in the context of screening is perhaps controversial, this programme allows for the detection and treatment of asymptomatic infections in a higher proportion of young women than previously.

But women over the age of 25 years also need access to reliable methods for diagnosing chlamydia infections, as up to 80% of infections in these women are asymptomatic (12) and can lead to severe complications if untreated. Therefore, chlamydia testing using NAAT should be covered by all health insurances, regardless of the age of the patient.

Microscopy and culture are still considered the gold standard for the detection of gonorrhoea (13, 14), even though NAAT is more sensitive (8,13), especially for cervical or urethral swabs in women and men, respectively (8). As antimicrobial resistance has increased recently (15, 16, 17), we recommend resistance testing on gonorrhoea isolates (18). The number of participants performing antimicrobial resistance testing in our study was clearly inadequate, which raises concerns as infections with antibiotic-resistant strains will remain undetected, allowing spread of infections caused by antimicrobial-resistant gonorrhoea.

The most common and recommended method for detection of trichomoniasis is microscopy. This is reflected in our results. Microscopy shows immediate but slightly
unreliable results with sensitivity varying between 36 and 80% (8). Culture before microscopy can increase the sensitivity (14).

A vast majority of the participants used serological tests for the different levels of syphilis diagnosis. However, test methods were not used consistently. The availability of various diagnostic methods using different serological markers led to high variety in testing. Clearer guidelines indicating the tests which should be used for different purposes are necessary to harmonize the diagnostics of syphilis in Germany.

A high percentage of participants also offered syphilis and chlamydia testing for asymptomatic patients. Most of these tests were performed during mandatory antenatal screening. The guidelines regarding medical care during pregnancy (19), formulated by the German Federal Joint Committee require a pooled urine test for chlamydia and a serology test for syphilis during the first visits to a gynaecologist during pregnancy. Outside of antenatal care asymptomatic tests should be offered especially to persons reporting frequent changing of sexual partners or unprotected sexual contact.

**Conclusions**

Our results showed dramatically inconsistent use of STI diagnostic methods across Germany. These methods should be harmonised to ensure comparable, high quality STI testing. Physicians require evidence-based information on the strengths and weaknesses of different diagnostic methods which will allow them to make an informed choice of the most appropriate tests, to correctly evaluate the results and therefore optimise treatment.
To achieve this, education on current standard diagnostic tools should be part of
continuous professional education. Additionally, the physicians should be provided
with harmonized, regularly updated guidelines from STI associations to ensure
reliable, coordinated and high quality diagnosis and treatment of sexual transmitted
diseases in Germany.

**Competing interests**
The authors declare that they have no competing interests.

**Authors' contributions**
AG und VB designed the study and the protocol. They were responsible for
implementation of the survey. AH was strongly involved in data collection and
analysis. AG produced the first draft of the paper, which was revised by VB. OH
contributed to the protocol and survey, and revised the final paper.

**Acknowledgements**
We want to thank all participants to the study, who took the time to respond to our
questionnaire. We further want to thank Dr. Naomi Boxall for her help in editing the
article.

**References**
1. Nicoll A and Hamers FF. Are trends in HIV, gonorrhea, and syphilis worsening
in Western Europe? *Bmj* 2002; 324 (7349): 1324–1327
2. Marcus U, et al.. Understanding recent increases in the incidence of sexually
transmitted infections in men having sex with men: changes in risk behavior
from risk avoidance to risk reduction. *Sex Transm Dis* 2006; 33 (1): 11–17


7. Schachter J, 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): 725–728


19. Richtlinien des Bundesausschusses der Ärzte und Krankenkassen über die ärztliche Betreuung während der Schwangerschaft und nach der Entbindung („Mutterschafts-Richtlinien“). *Bundesanzeiger* Nr. 239, 21 December 2007: 8326 (only in German)
**Tables**

**Table 1 - Proportions of participants testing for the different STIs in Germany in 2005, stratified by medical speciality**

<table>
<thead>
<tr>
<th></th>
<th>Dermato-Venerology</th>
<th>Urology</th>
<th>Gynaecology</th>
<th>Public health offices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=219</td>
<td>n=85</td>
<td>n=335</td>
<td>n=48</td>
</tr>
<tr>
<td>HIV</td>
<td>76</td>
<td>65</td>
<td>85</td>
<td>94</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>72</td>
<td>84</td>
<td>95</td>
<td>67</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>94</td>
<td>87</td>
<td>77</td>
<td>75</td>
</tr>
<tr>
<td>Trichonomas</td>
<td>63</td>
<td>79</td>
<td>95</td>
<td>44</td>
</tr>
<tr>
<td>Syphilis</td>
<td>90</td>
<td>68</td>
<td>82</td>
<td>92</td>
</tr>
</tbody>
</table>

**Table 2 - Proportions of the different detection methods for chlamydia used in Germany in 2005, stratified by medical speciality**

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Dermato-Venerology</th>
<th>Urology</th>
<th>Gynaecology</th>
<th>Public health offices</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=621*</td>
<td>n=159</td>
<td>n=71</td>
<td>n=337</td>
<td>n=32</td>
</tr>
<tr>
<td>Rapid test</td>
<td>34%</td>
<td>44%</td>
<td>17%</td>
<td>48%</td>
<td>6%</td>
</tr>
<tr>
<td>DNA probe</td>
<td>25%</td>
<td>22%</td>
<td>34%</td>
<td>26%</td>
<td>16%</td>
</tr>
<tr>
<td>NAAT (e.g. PCR)</td>
<td>33%</td>
<td>34%</td>
<td>38%</td>
<td>29%</td>
<td>56%</td>
</tr>
<tr>
<td>Antigen test</td>
<td>26%</td>
<td>26%</td>
<td>25%</td>
<td>28%</td>
<td>13%</td>
</tr>
<tr>
<td>Serology</td>
<td>26%</td>
<td>38%</td>
<td>31%</td>
<td>19%</td>
<td>16%</td>
</tr>
<tr>
<td>Others</td>
<td>1%</td>
<td>1%</td>
<td>3%</td>
<td>1%</td>
<td>3%</td>
</tr>
</tbody>
</table>

*Difference in overall sum due to lacking information of speciality of 22 participants testing on Chlamydia

**Table 3 - Reasons for testing asymptomatic patients for chlamydia, gonorrhoea and syphilis, Germany 2005**

<table>
<thead>
<tr>
<th></th>
<th>Chlamydia (n=387)</th>
<th>Gonorrhoea (n=188)</th>
<th>Syphilis (n=376)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Partner infection</td>
<td>68</td>
<td>18</td>
<td>71</td>
</tr>
<tr>
<td>Antenatal care</td>
<td>205</td>
<td>53</td>
<td>18</td>
</tr>
<tr>
<td>Unspecific fluor</td>
<td>10</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Skin diseases</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Risk behaviour</td>
<td>31</td>
<td>8</td>
<td>44</td>
</tr>
<tr>
<td>Others</td>
<td>73</td>
<td>19</td>
<td>48</td>
</tr>
</tbody>
</table>
Additional files provided with this submission:

Additional file 1: STI-Diagnostics-Qx.pdf, 86K