EVALUATION OF THE PATH GC-CHECK RAPID TEST FOR THE DETECTION OF GONOCOCCAL INFECTION AMONG FEMALE SEX WORKERS IN BENIN

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INTRODUCTION

- Syndromic approach is recommended for management of STIs in developing countries.
- In women, it may result in significant over-treatment, especially when prevalence is relatively low.
- Over-treatment of women may lead to social stigma related to a STI diagnosis and to domestic violence, especially in case of partner notification.
- It has been shown that a modified syndromic approach (clinical screening) targeting high risk women or the use of point-of-care test could have a better sensitivity than gold standard tests when taking into account the lack of attendance to return visits, both in developed [1] and developing [2] countries.
- There is clearly a need to develop and evaluate rapid point-of-care tests for cervical infections such as *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT).
- The involvement of our team in projects supporting female sex worker (FSW) clinics in Benin since 1993 and the fact that GC prevalence has repeatedly been > 15% in this population in the past provided an opportunity to evaluate a new GC rapid point-of-care test

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OBJECTIVE

- To assess the validity of the PATH (Seattle, WA) GC-Check rapid test, a point-of-care immunochromatographic strip test, in the detection of gonococcal infection (GC) among female sex workers (FSWs) in Benin.

METHODS

- Women consulting consecutively at 2 FSW-dedicated clinics in Cotonou, the largest city and economic capital of Benin [Dispensaire IST (DIST), a clinic with long-standing experience in clinical research)], and Porto Novo, the political capital of Benin [Clinique Solidarité-Sidaction (CSS), a clinic participating for the first time in a clinical study], were recruited over 3 one-month periods between October 2003 and July 2004.
- After written informed consent, participants were administered a short interview and underwent a speculum examination where two cervical swabs were collected (in a subset of women, a vaginal swab was also collected).
- One cervical swab and the vaginal swab were immediately tested with the rapid test and the results interpreted by two independent readers.
- Figure 1 shows the PATH GC-Check rapid test kit.
- Figure 2 shows the interpretation of results of the test.
- The other cervical swab was frozen at -20^{o}C for at most 4 weeks and then transported to Quebec (Canada), where it was tested using the Roche Amplicor CT/NG PCR assay.
- GC-positive samples were confirmed with a 16SrRNA PCR assay, using a real-time PCR technology (Light Cycler, Roche Diagnostics) at a laboratory designated by Roche Diagnostics in Montreal, Canada.
- The gold standard for GC positivity was defined as a positive GC Amplicor AND a positive 16SrRNA PCR assay.

METHODS (CONTINUED)

- The sensitivity (Se), specificity (Sp), positive and negative predictive values (PPV and NPV) were estimated for the PATH GC-Check rapid test used on both cervical and vaginal specimens.
- The Sp and PPV were also estimated for the Roche Amplicor CT/NG PCR assay used once (single Amplicor) or declared positive for GC when 2 tests out of 3 yield optical densities >2.0 (High OD criterion) [3].
- Comparisons of Se and Sp were carried out between types of samples, study sites and periods of recruitment using chi-square or Fisher's exact test (when appropriate).

RESULTS

- 1084 FSWs were recruited in the study (876 at DIST and 208 at CSS).
- Median age was 29 years.
- 50 (4.6%) women were GC-infected according to the gold standard (4.2% at DIST and 6.3% at CSS).
- 51 (4.7%) women were infected by CT (5.3% at DIST and 2.4% at CSS).
- Table 1 shows the comparison of the single Amplicor GC result with the gold standard.
- Table 2 shows the comparison of the High OD criterion GC result with the gold standard.
- Inter-reader agreement for the PATH GC-Check rapid test on cervical samples was 99.8%
- Table 3 shows the comparison of the PATH GC-Check rapid test result on cervical swabs with the gold standard (n=1084).
- Inter-reader agreement for the PATH GC-Check rapid test on vaginal samples was 99.9%.
- Table 4 shows the comparison of the PATH GC-Check rapid test result on vaginal swabs with the gold standard (n=759).

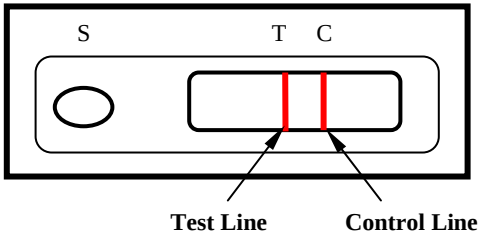
RESULTS (CONTINUED)

- Se of the rapid test was significantly lower on vaginal swabs compared to cervical swabs (p=0.008) whereas Sp was similar (p=0.13).
- Se of the rapid test on cervical swabs was significantly lower (p=0.011) at CSS (5/13=38.5%) than at DIST (30/37=81.1%) whereas Sp was comparable at 95.9% and 97.5%, respectively.
- Whereas Se was stable at DIST during the 3 rounds of data collection (between 80 and 82%), it varied significantly (p=0.021) between the first 2 rounds (0/6=0%) and the last round (5/7=71.4%) at CSS.

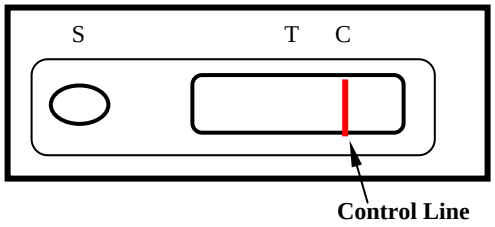
Figure 1. Photograph of the PATH GC-Check rapid test

Figure 2. Interpretation of results of the PATH GC-Check rapid test

1. **Two Visible Lines**—**Positive** for *N. gonorrhoeae* antigen. Both the procedural control and the test line of any intensity are observed. Interpretation: the test detected *N. gonorrhoeae* antigen in the specimen. Action: record the test as positive.



2. **Visible Control Line Only**—**Negative** for *N. gonorrhoeae* antigen. Only the procedural control line is observed. Interpretation: the test did not detect *N. gonorrhoeae* antigen in the specimen. Action: record the test as negative. Do not interpret results before the 20-minute end point**.**



3. **No Visible Control Line—Invalid test**. Control line is not observed. Interpretation: the test was improperly performed, or the test strip and/or reagents have deteriorated. Action: Repeat the test with a new test cassette. If the test is repeated, the remaining extracted solution in the reaction tube can be used, provided it has been extracted less than 1 hour previously.

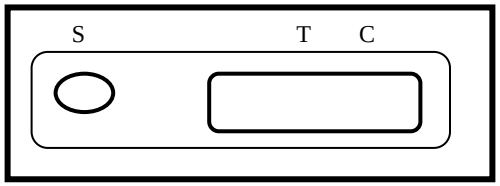


Table 1. Comparison of the single Amplicor GC result with the GC gold standard.

Single Amplicor GC results	Gold standard results	
	Positive	Negative
Positive	50	31
Negative	0	1003
Total	50	1034

Se: 100% (95%CI: 92.9-100)
Sp: 97.0% (95%CI: 95.8-98.0)
PPV: 61.7%
NPV: 100%

Table 2. Comparison of the High OD criterion GC result with the GC gold standard.

High OD criterion GC results	Gold standard results	
	Positive	Negative
Positive	50	22
Negative	0	1012
Total	50	1034

Se: 100% (95%CI: 92.9-100)
Sp: 97.9% (95%CI: 96.8-98.7)
PPV: 69.4%
NPV: 100%

Table 3. Comparison of the PATH GC-Check rapid test result on *cervical swabs* with the GC gold standard.

PATH GC-Check rapid test results	Gold standard results	
	Positive	Negative
Positive	35	29
Negative	15	1005
Total	50	1034

Se: 70.0% (95%CI: 55.4-82.1)
Sp: 97.2% (95%CI: 96.0-98.1)
PPV: 54.7%
NPV: 98.5%

Table 4. Comparison of the PATH GC-Check rapid test result on *vaginal swabs* with the GC gold standard.

PATH GC-Check rapid test results	Gold standard results	
	Positive	Negative
Positive	20	13
Negative	17	709
Total	37	722

Se: 54.1% (95%CI: 36.9-70.5)
Sp: 98.2% (95%CI: 96.9-99.0)
PPV: 60.6%
NPV: 97.7%

DISCUSSION

- The prevalence of GC was lower than previously estimated using the same gold standard, suggesting a significant impact of the FSW intervention in both cities.
- However, this lower prevalence reduced the scope of this evaluation, with only 50 GC-positive cases according to the gold standard, whereas 100 cases were initially expected.
- Not surprisingly, Se of the PATH GC-Check rapid test was lower on vaginal swabs than on cervical swabs.
- Se was also lower at CSS, a clinic with less research experience than DIST. However, with experience, Se of the test improved at CSS, suggesting that Se of the PATH GC-Check rapid test could in fact be higher than 70% when used by experienced users.
- Some previous data suggest that the confirmatory assay used in this study (16SrRNA PCR assay) could lack Se when the detection method is based on EIA [4], which would result in an overestimation of the Se of the PATH GC-Check rapid test.
- However, some recent data suggest that this confirmatory assay is in fact highly sensitive, especially when using a real time PCR methodology [5].

CONCLUSIONS

- The PATH GC-Check test using cervical samples may be at least as efficient as a gold standard test for treating GC when taking into account the proportion of women who do not return for their test results [6].
- In clinics serving populations with moderate GC prevalence and where speculum examination is possible, it could significantly reduce over-treatment compared to the syndromic approach.
- Cost-effectiveness studies are needed to compare the use of such tests with that of the syndromic approach in both high-risk and low-risk women.

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