

Appraising a diagnostic test study using a critical appraisal checklist

Mahilum-Tapay L, et al. New point of care *Chlamydia* Rapid Test – bridging the gap between diagnosis and treatment: performance evaluation study. *BMJ* 2007;335:1190.

Why are we looking at the test?

- **The problem:**
- An 18-year-old woman comes to your surgery because she has pain when passing urine and has noticed a change in her vaginal discharge. You suspect that she might have *Chlamydia*, but the woman hates the idea of going to the hospital or being examined by a clinician and asks if there is a test she can do herself instead
- So, we research alternative test methods for *Chlamydia*

Results of our search

- We find this reference, which assesses a new *Chlamydia* Rapid Test:
Mahilum-Tapay L, et al. New point of care *Chlamydia* Rapid Test – bridging the gap between diagnosis and treatment: performance evaluation study. *BMJ* 2007;335:1190
- The objective of this study is to evaluate the performance of a new *Chlamydia* Rapid Test with vaginal swab specimens as a potential tool for *Chlamydia* diagnosis and screening compared with nucleic acid amplification tests with first void urine, and vulvo-vaginal swab specimens.
- Importantly for us, the study also assessed if there is any difference between results of the *Chlamydia* Rapid Test when the swabs are self collected compared with clinician collected

Critical appraisal

- Now we have found a study that may give a solution to our current problem, we need to assess the quality of the research we have found in terms of validity and the importance of the results to see if we can apply this test to the patient. To do this we can use the critical appraisal checklist to evaluate the study

Is the study valid? Screening

- ***Was there a clear question for the study to address?***
- Remember it should include information about the population, test, setting, and outcome
- In this case yes, the study asked:
 1. “What is the diagnostic accuracy of the *Chlamydia* Rapid Test compared with polymerase chain reaction and strand displacement amplification assays in the diagnosis of *Chlamydia* in women presenting to a sexual health centre (site 1) and genitourinary medicine clinics (site 2 and 3)?”
 2. “Is there a difference in the diagnostic accuracy of the *Chlamydia* Rapid Test between self-collected samples and clinician-collected samples?”
- This information can usually be found in the abstract or the introduction to the study

Is the study valid? Screening

- ***Is there comparison with an appropriate (gold) reference standard for diagnosing the disorder under assessment? The reference standard comparison should be the best available indicator of the target disorder***

- In this case yes, the study stated that:

“We assessed the performance of the Chlamydia Rapid Test in order to meet the requirements for Conformité Européenne licensure, which stipulate that the comparator test should be a “state of the art” assay and use specimens approved for the test. Participants from site 1 did not provide endocervical swabs, preventing the pooling of data from all three sites. Given this condition, we chose polymerase chain reaction testing, which is licensed for both urine and endocervical specimens, as the “gold standard” for the study. Studies of Chlamydia trachomatis polymerase chain reaction testing have shown equal performance with cervical and urine specimens, across all volumes of urine tested (<20-90 ml), and good reproducibility. For the genitourinary medicine clinics, endocervical specimens were additionally collected by the clinician and were tested by strand displacement amplification assay at the hospital laboratory.”

- As the answer is yes to both of our initial screening questions, we should continue with our analysis of the diagnostic test study

Is the study valid? Population

- ***Did the study include people with all the common presentations of the target disorder? For example, symptoms of early manifestations as well as people with more severe symptoms, and/or people with other disorders that are commonly confused with the target disorder when diagnosing?***
- Yes, the study states that:

“All women 16 years and over presenting to any of the three sites were invited to participate in the study . Most participants at site 1 were asymptomatic [663 women], in contrast with 441/662 [67%] of the participants from the genitourinary medicine clinics presented with symptoms that included vaginal discharge 305/662 [46%], and lower abdominal pain 149/657 [23%]. In addition 23/668 [3%] of women were diagnosed as having pelvic inflammatory disease.”

Is the study valid? Blinding

- ***Were the people assessing the results of the index diagnostic test blinded to the results of the reference standard?***
- Yes, while the study does not explicitly state blinding, it is very specific about where the samples were analysed for the three different tests. These were:
 - ***Chlamydia Rapid Test:*** “Clinic staff tested vaginal swabs on site; all staff had passed testers’ requirements in accordance with the National Committee on Clinical Laboratory Standards.”
 - **Polymerase chain reaction assay:** “We sent urine specimens to a laboratory accredited by the UK Accreditation Service for testing for *Chlamydia trachomatis* with the Amplicor *Chlamydia trachomatis* polymerase chain reaction assay.”
 - **Transcription mediated assay:** “Samples that yielded discordant results between the *Chlamydia* Rapid Test and the polymerase chain reaction assay were tested by transcription mediated assay at the Sexually Transmitted Bacteria Reference Laboratory.”

Is the study valid? Testing

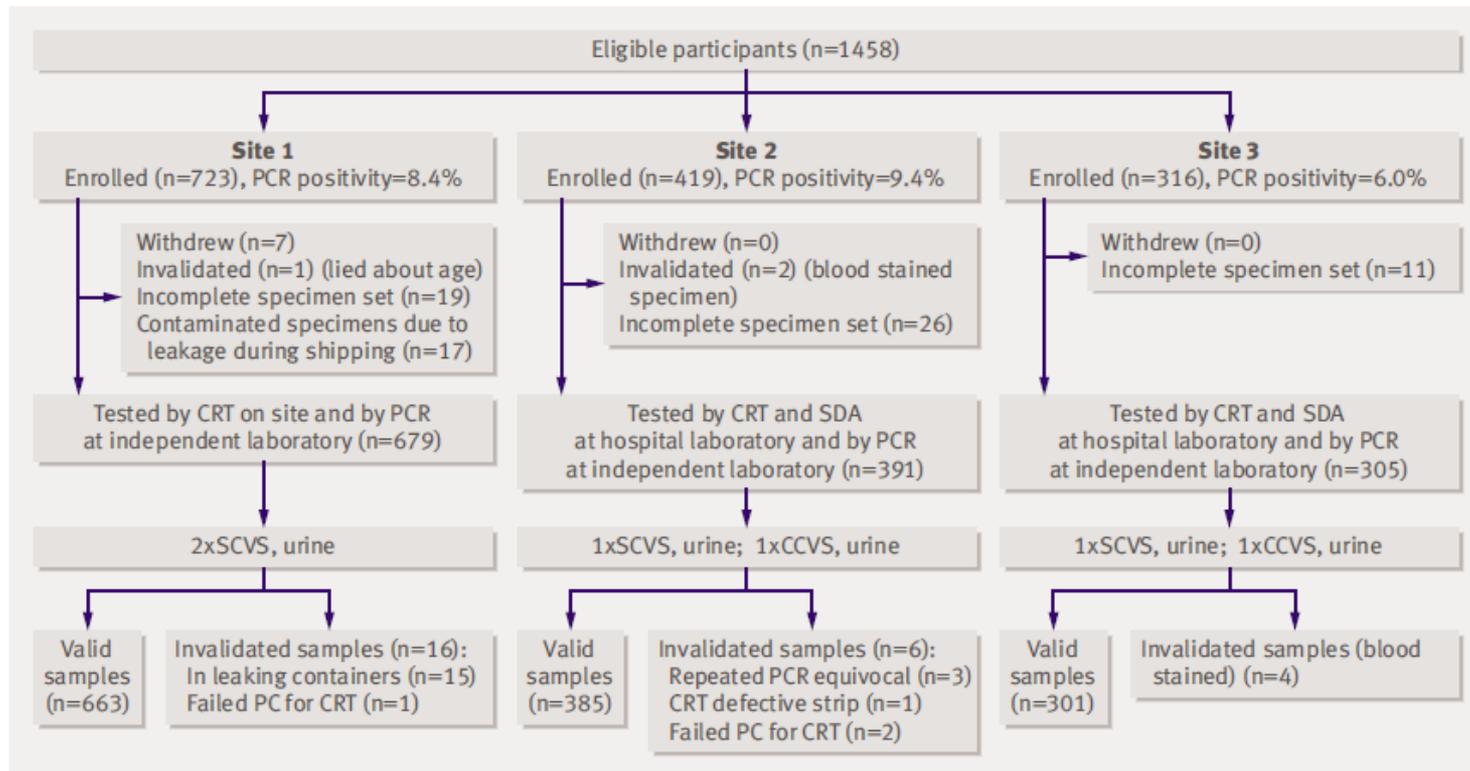
- ***Was the reference standard applied regardless of the index test result?***
- Yes, as already discussed, all samples were tested with both the *Chlamydia* Rapid test and polymerase chain reaction assay. With discordant samples further tested with transcription mediated assay
- ***Was the diagnostic test validated in a second independent group of patients?***
- Yes, as the test was given in three different sites, a total of three populations were tested

Is the study valid? Methods

- ***Were the methods of the diagnostic test described in sufficient detail? Consider if descriptions of the following are included:***
- ***Rationale for the ref standard.*** “We assessed the performance of the Chlamydia Rapid Test in order to meet the requirements for Conformité Européenne licensure, which stipulate that the comparator test should be a “state of the art” assay and use specimens approved for the test. Participants from site 1 did not provide endocervical swabs, preventing the pooling of data from all three sites. Given this condition, we chose polymerase chain reaction testing, which is licensed for both urine and endocervical specimens, as the “gold standard” for the study. Studies of Chlamydia trachomatis polymerase chain reaction testing have shown equal performance with cervical and urine specimens, across all volumes of urine tested (<20-90 ml),¹⁶ and good reproducibility. For the genitourinary medicine clinics, endocervical specimens were additionally collected by the clinician and were tested by strand displacement amplification assay at the hospital laboratory.”
- ***Technical specifications or references for running the index test and reference standard (e.g., including enough information that the tests could be replicated)*** Yes, the study outlined in detail how each different type of sample was analysed for each test. See pages 2 and 3 for descriptions of sample collection, storage, and testing.
- ***Methods for calculating or comparing measures of diagnostic accuracy and statistical uncertainty (95% CI).*** Yes, 95% confidence intervals were included for all comparisons discussed.
- ***Now that we have established that the study is valid, we should consider the results***

Results

- *Do the results include information about people who satisfied inclusion criteria for the study but did not receive the diagnostic index or reference standard test?*
- In this case yes, the study includes a flow chart for all three sites, which specifies how many women were enrolled and explicit reasons for any withdrawals. From this flow chart it appears that all withdrawals were excluded from the final analysis which only included valid specimens



Results

- ***Do the results include how indeterminate results, missing results, and outliers of the index test were handled?***
- The study states that samples that had discordant results were further tested by transcription mediated assay, in addition 100 of the total number of polymerase chain reaction negative specimens and 20 of the concordant positive samples were also randomly tested by the assay to minimise potential bias introduced by testing discordant samples only. The study only included valid samples in the analysis with explicit reasons for any samples not included (please see table on previous slide)

Results

- Do the results include criteria for defining the severity of the target disorder?
- In this case no — infection and sequelae may be asymptomatic in cases of *Chlamydia*

Results

- **Do the results include cross tabulation of the index test results by the reference standard results? Or enough information to generate this table?**
- Yes, the study includes sensitivity, specificity, and positive and negative predictive values for all of the comparisons made, and the calculations used. Using these results, you could if needed generate the cross tabulation table, for example below:
- Site 1, *Chlamydia* Rapid Test with self collected vaginal swab specimens versus polymerase chain reaction

	Reference Standard			
Index test		Positive	Negative	Total
	Positive	47	7	54
	Negative	9	600	609
	Total	56	607	663

From here we can generate any statistic that we need using the instructions in the previous document “Diagnostic test studies: assessment and critical appraisal”.

Results

- **Do the results include estimates of diagnostic test accuracy and statistical uncertainty (95% CI)?**
- Yes the study includes 95% CI for all comparisons made. For example:

Table 1 | Unresolved performance of *Chlamydia* Rapid Test with self collected vaginal swab specimens versus polymerase chain reaction. Values are percentages (numbers) (95% confidence intervals)

Site	Sensitivity	Specificity	Positive predictive value	Negative predictive value
1 (n=663)	83.9 (47/56) (74.3 to 93.5)	98.8 (600/607) (98.0 to 99.7)	87.0 (47/54) (78.1 to 96.0)	98.5 (600/609) (97.6 to 99.5)
2 (n=385)	80.6 (29/36) (67.6 to 93.5)	98.0 (342/349) (96.5 to 99.5)	80.6 (29/36) (67.6 to 93.5)	98.0 (342/349) (96.5 to 99.5)
3 (n=301)	83.3 (15/18) (66.1 to 100)	99.6 (282/283) (99.0 to 100)	93.8 (15/16) (81.9 to 100)	98.9 (282/285) (97.8 to 100)
Total (n=1349)	82.7 (91/110) (75.7 to 89.8)	98.8 (1224/1239) (98.2 to 99.4)	85.8 (91/106) (79.2 to 92.5)	98.5 (1224/1243) (97.8 to 99.2)

No significant difference in *Chlamydia* Rapid Test performance was apparent among three sites (P=0.278, κ statistics).

Does this diagnostic test apply to your specific patient?

- ***Is your patient similar to the people in the study in terms of clinical and demographic characteristics?***
- Yes, in this case our patient is a young woman, the study population is women 16 years and over

- ***Is the diagnostic test available, and if so, does it reflect current practice?***
- To answer this question you would need to check availability, and also how current the research is at the time of assessment

- ***Will the test result change the way the patient is managed?***
- Yes, with the Rapid *Chlamydia* test, diagnosis and treatment (if needed) is much quicker

In conclusion

- This study seems to be valid with no major methodological flaws
- The results of the study indicate that compared with the polymerase chain reaction testing, the *Chlamydia* Rapid Test has moderate sensitivity and good specificity for screening and diagnosis of *Chlamydia* whether the vaginal swab was collected by a participant of the study or a clinician
- The study population does in this case match our patient, so we can be reasonably comfortable in the knowledge that if the patient is allowed to collect her own vaginal swab, the test result will be accurate, and also as an added bonus if the test is positive for *Chlamydia*, treatment can be started immediately