Four polyvalent screening assays in comparison to the TPPA

Juliane Fazio[1], Marie-Christin Höppner[1], Thomas Neiße[1], Kristin Meyer-Schlinkmann[1], Klaus Jansen[2], Hans-Jochen Hagedorn[1], Dieter Münstermann[1]

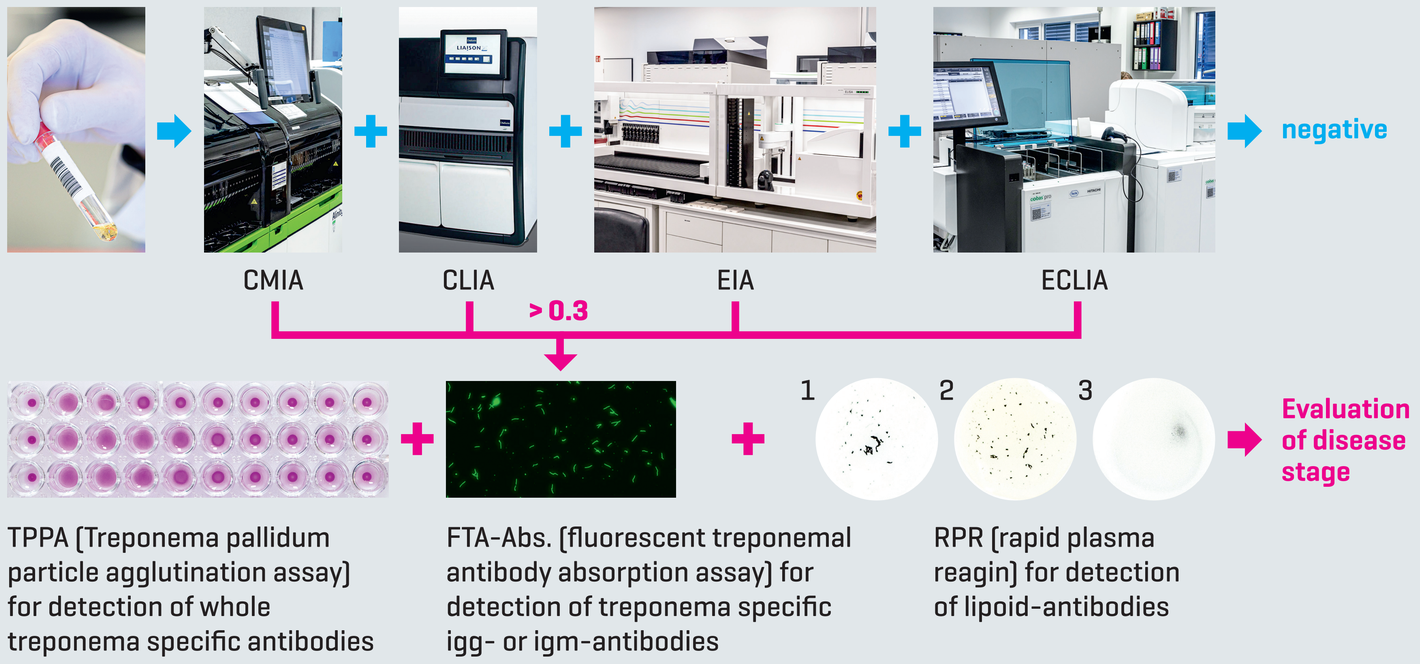
[1]MVZ Labor Krone GbR, Konsiliarlabor für Treponema, Siemensstraße 40, 32105 Bad Salzuflen [2]Robert Koch-Institut, Abteilung für Infektionsepidemiologie, Nordufer 20, 13353 Berlin

Introduction

Annually, more than 7 million novel infections with treponema pallidum spp. pallidum causing syphilis occur worldwide with an upward trend [1]. Especially in the early phase of syphilis patients are highly infectious and need to be identified to avoid clinical sequalae and further transmission. Without treatment those bacteria can cause severe symptoms such as neurosyphilis [2].

In 2021, Fujirebio company announced to stop the production of the treponema pallidum particle agglutination assay (TPPA), which is a backbone for syphilis diagnostics in Europe. To develop an alternative diagnostic strategy, we evaluated the diagnostic quality of polyvalent screening tests in terms of their sensitivity and specificity compared to the TPPA.

Material and Methods



A total of 1,813 samples were included: 392 submissions from a blood donor service (21.6%), 390 maternity screening examinations (21.5%), 366 submissions from AIDS services and counseling centers (20.2%), 436 requests from public health services (24.1%), and 229 samples not further defined (12.6%).

Samples were analyzed with Alinity Syphilis TP CMIA (Chemiluminescence microparticle immunoassay, Abbott), Elecsys Syphilis TP ECLIA (Electrochemiluminescence immunoassay, Roche), Liaison Treponema Screen CLIA (Chemiluminescence immunoassay, DiaSorin) and anti-Treponema-pallidum-Screen-ELISA EIA (Euroimmun AG), and compared with the results of routine diagnostic based on TPPA as the gold standard.

To increase the sensitivity, samples with Index/COI > 0.3 were further characterized according to the syphilis stepwise diagnostic using TPPA, IgG-FTA-ABS-Test, 19S-IgM-FTA-ABS-Test and RPR-Test.

Specificity and sensitivity for all four assays were 1) calculated according to the manufacturer's evaluation instructions and 2) using a reduced cut off if possible. Therefore, the lowest confirmed positive sample determined the limit for a reduced cut off for each test.

The correlation coefficient according to Spearman Rho was determined.

Results

Table 1: Overall sensitivity, specificity and correlation of the test systems CMIA, EIA, ECLIA and CLIA in comparison to the TPPA.

	CMIA (Abbott)	EIA (Euroimmun)	ECLIA (Roche)	CLIA (DiaSorin)
Sensitivity [%]	94.32	69.89	94.89	96.55
Specificity [%]	99.74	98.84	98.97	99.29
Correlation to TPPA [p < 0.001]	0.85	0.89	0.88	0.84

In terms of test performance, the diagnostic accuracy for sensitivity and specificity in comparison to the TPPA was partly distinct lower for all polyvalent tests (table 1).

Table 2: Sensitivity of the test systems CMIA, ECLIA and CLIA according to manufacturer's specification and with reduced cut off for different cohorts.

	CMIA		ECLIA		CLIA	
	< 1.0 (manufacturer's specification)	< 0.3 (reduced cut off)	< 1.0 (manufacturer's specification)	< 0.5 (reduced cut off)	< 0.9 – 1.1 (manufacturer's specification)	< 0.4 (reduced cut off)
0.30 < CMIA < 0.99* [n = 256]	Preselection with CMIA		76.0	88.9	42.3	96.3
Pregnant woman [n = 390]	No information possible, as there were no positive cases					
Healthy blood donors [n = 392]						
AIDS support and counseling centers [n = 366]	87.7	100.0	92.2	100.0	94.1	100.0
Public health services [n = 436]	90.7	100.0	95.3	95.3	95.0	97.5

Table 3: Specificity of the test systems CMIA, ECLIA and CLIA according to manufacturer's specification and with reduced cut off for different cohorts.

	CMIA		ECLIA		CLIA	
	< 1.0 (manufacturer's specification)	< 0.3 (reduced cut off)	< 1.0 (manufacturer's specification)	< 0.5 (reduced cut off)	< 0.9 – 1.1 (manufacturer's specification)	< 0.4 (reduced cut off)
0.30 < CMIA < 0.99* [n = 256]	Preselection with CMIA		100.0	90.2	96.7	90.2
Pregnant woman [n = 390]	100.0	98.7	100.0	100.0	99.7	99.2
Healthy blood donors [n = 392]	Preselection with CMIA		96.4	94.6	97.2	92.9
AIDS support and counseling centers [n = 366]	99.7	98.3	99.3	99.0	99.7	99.3
Public health services [n = 436]	100.0	99.2	100.0	100.0	100.0	99.7

* In a previous study, a reduced cutoff was introduced for the CMIA, resulting in a sensitivity comparable to the TPPA [3].

For CMIA, ECLIA and CLIA a reduced cut off could be determined to increase the sensitivity for the detection of reactive samples in different patient groups (table 2) without a significant decrease in specificity (table 3 and figure 1).

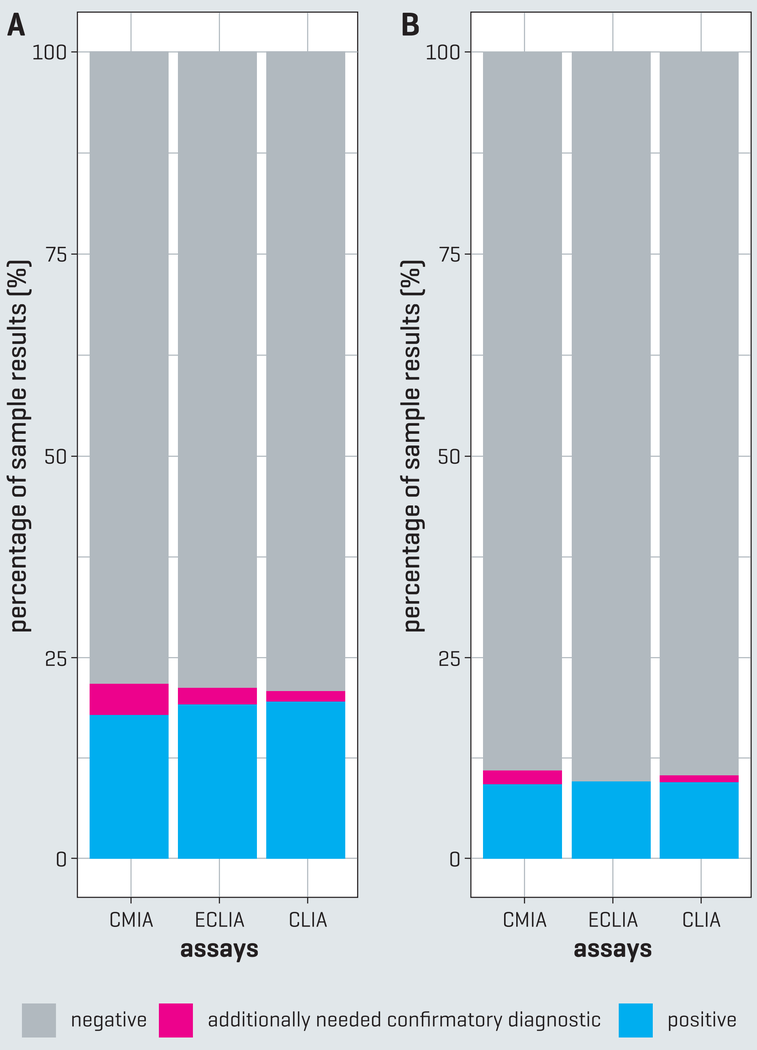


Figure 1: Results of the different test systems for samples from AIDS support and counseling centers (A) (n = 366) and samples from public health services (B) (n = 436).

Conclusion

The results of our study show that reducing the cut off for the CMIA, ECLIA and CLIA is useful to increase the proportion of true positive results. A reduction of cut offs would be feasible in terms of diagnostic accuracy, resulting in only a low proportion of additional, false-positive test results. This approach would increase the sensitivity of the respective assays especially to detect infections in the early phases of syphilis distinctly without a substantial negative impact on their specificity. Increasing the sensitivity of the EIA by using a reduced cut off was not possible without a decrease in specificity.

References [1] World Health Organization (WHO). (2023). Syphilis. Retrieved June 16, 2023, from Fact sheets website: https://www.who.int/news-room/fact-sheets/detail/syphilis. [2] Janier et al., 2020 European guideline on thea management of syphilis, JEADV 2021, 35, 574–588. [3] Hagedorn et al., Screening in the context of syphilis diagnostics: threshold ranges for automated syphilis immunoassays, 74. Jahrestagung DGHM 2022.