Screening in the context of syphilis diagnostics: threshold ranges for automated syphilis immunoassays

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Introduction

Automated syphilis screening tests are used in laboratory routine. Positive samples are further tested according to the syphilis stepwise diagnostic. During evaluation studies prior to the introduction of screening tests into routine use, it was noticed that some positive sera were not detected. There is no defined threshold range from the manufacturer for those routinely used screening assays. Therefore, we have tested whether the definition of a threshold range can identify samples, which can then be further investigated with other tests and reduce the number of false negative results.

Material and Methods

Samples were first analyzed with Architect Syphilis TP CMIA (Abbott) and Elecsys Syphilis TP ECLIA (Roche) and then further characterized according to the syphilis stepwise diagnostic using

- TPPA,
- IgG-FTA-ABS-Test,
- 19S-IgM-FTA-ABS-Test,
- RPR-Test and
- immunoblot if required.

Specificity was calculated for both screening tests. Sensitivity for both screening tests was on the one hand calculated according to the manufacturer's evaluation instructions (S/Co-Value <1.0= negative, S/Co-Value ≥1= positive) and on the other hand including a threshold range of 0.3 - <1.0. Samples within the threshold range also followed the stepwise diagnostic.

Results

In total, 2091 samples were included in this study. The measured collective included all stages of Syphilis. The treponema antibody status was positive for 173 (8.3%) samples and negative for 1,914 (91.3%) samples; 4 (0.4%) samples were classified as indeterminate. Both tests (ECLIA and CMIA) gave false positive results twice each (1,912/1,914), resulting in a specificity of 99.9% each.

Figure 1: Correlation of CMIA and ECLIA, n=2,091, Pearson Correlation: 0.89 p<0.001

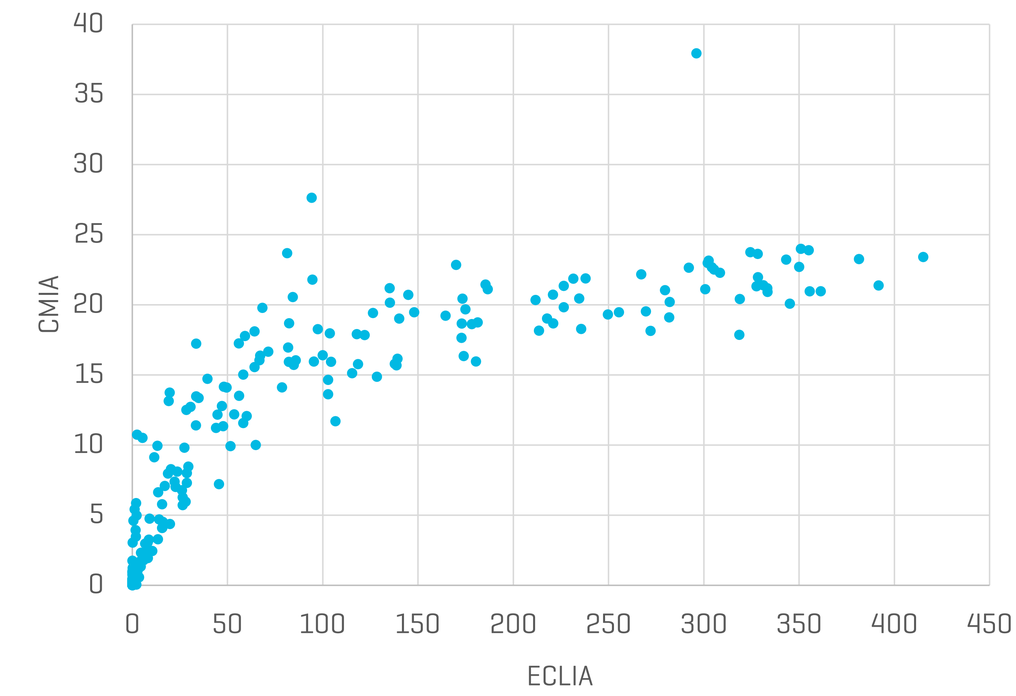

Figure 2: Example: Syphilis screening (CMIA) in a low prevalence population (pregnancy care testing), n=29,502

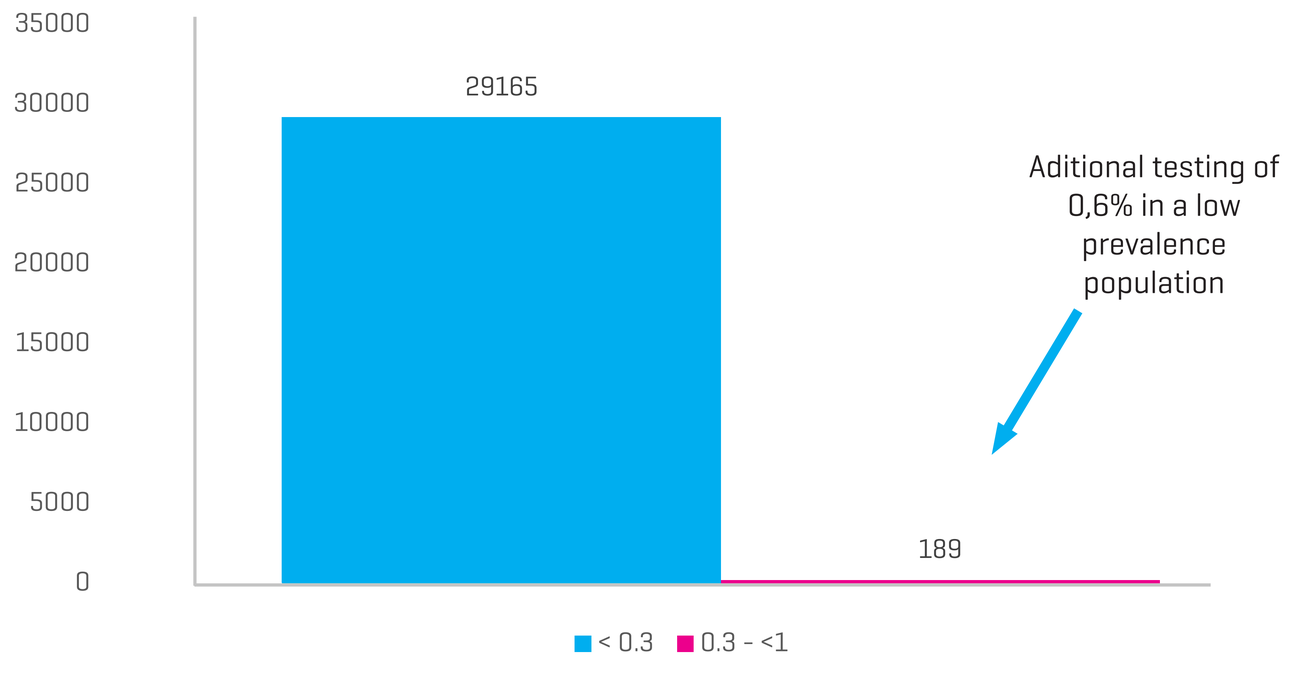

Table 1: Distribution of negative classified samples (findings in CMIA or ECLIA), n=1,922

		ECLIA					
		0 - < 0.3	0.3 - < 0.5	0.5 - < 0.8	0.8 - < 1	> 1	Total
CMIA	0 - < 0.3	1885	8	4	0	2	1899
	0.3 - < 0.5	7	0	2	2	0	11
	0.5 - < 0.8	3	0	0	0	4	7
	0.8 - < 1	1	0	0	0	1	2
	> 1	2	0	1	0	0	3
		1898	8	7	2	7	1922

Table 2: Sensitivity for CMIA and ECLIA, n=173

	manufacturer's evaluation instructions	including threshold range 0.3 - < 1	samples in threshold range	initally false negative samples
ECLIA	98.3% (n=170)	**100%**	17	3
CMIA	95.4% (n=165)	**100%**	20	7

Table 3: Example for initally false negative laboratory result

ECLIA	CMIA	TPPA	FTA-IgG	FTA-IgM	RPR
0.85	0.32	#1280	#++	#1280	#n

Discussion

The introduction of a threshold range of 0.3 - <1.0 led to a significant increase in diagnostic confidence. It is especially important to correctly diagnose samples in an early seroconversion phase, because those patients are highly infectious (e.g. for blood bank screenings). Besides, the effort of additional sample measurement is manageable with < 1% of all negative tested samples.