

Specificity of an automated Anti-SARS-CoV-2 immunoassay in COVID-19 pre-pandemic cohorts

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INTRODUCTION

- The COVID-19 pandemic has prompted the launch of several different serological assays. Reliable information regarding the relative performance of these assays in a wide range of settings is urgently needed.
- Research into antibody responses against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – the infectious agent responsible for COVID-19 – has revealed information about the timing of seroconversion, a critical consideration in serological testing.
 - Evidence suggests that immunoglobulin M (IgM) antibodies are detectable within 5 days of symptom onset, immunoglobulin G (IgG) antibodies within 5–14 days,^{1–3} and immunoglobulin A (IgA) antibodies after approximately 3–6 days.^{2,4} The chronological order in which IgM and IgG antibodies develop appears to be highly variable, as are antibody levels.^{3,5–7}
 - This supports the need for accurate serological tests for the detection of high-affinity (i.e. late-onset/mature) antibodies to SARS-CoV-2.
- The Elecsys[®] Anti-SARS-CoV-2 immunoassay (Roche Diagnostics International Ltd) was developed to provide an accurate and reliable method for detecting antibodies to SARS-CoV-2.
- This in vitro qualitative electrochemiluminescence assay detects various antibodies (including IgG) to SARS-CoV-2 in human serum and plasma and is intended for use on cobas e immunoassay analysers.^{8,9}
- The immunoassay uses an in-solution double-antigen sandwich test principle, with a recombinant protein representing the nucleocapsid antigen of SARS-CoV-2.^{8,9}

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OBJECTIVE

- To evaluate the specificity of the Elecsys Anti-SARS-CoV-2 immunoassay using pre-pandemic samples collected from five sites across Germany, Austria and Switzerland.



METHODS

- This retrospective, non-interventional study was conducted at five sites: one site (Innsbruck [Austria]) provided serum samples and four sites (Augsburg, Hagen, Heidelberg [Germany] and Bern [Switzerland]) provided serum and/or plasma samples and performed testing using the cobas e 801 analyser (Roche Diagnostics International Ltd).
- Samples were anonymised, frozen, residual serum and/or plasma specimens from blood donors or routine diagnostic testing obtained prior to September 2019, and were therefore assumed negative for SARS-CoV-2-specific antibodies. Specimens included pregnancy screening and paediatric samples.
- Specificity of the Elecsys Anti-SARS-CoV-2 immunoassay was assessed using the cobas e 801 analyser, which compared the electrochemiluminescence signal obtained from the reaction product of the sample with the signal of the cut-off value, previously obtained by calibration.
- Point estimates and 95% confidence intervals were calculated.

RESULTS

- A total of 9575 samples presumed negative for SARS-CoV-2 antibodies were analysed.
- Specificity of the Elecsys Anti-SARS-CoV-2 immunoassay for the overall sample cohort and by analysis group are shown in **Table 1**.
- Using an assay cut-off index of 1.0 resulted in an overall specificity of 99.85% in samples obtained across all five sites.
- Among 6714 serum and/or plasma samples from blood donors and 2861 serum and/or plasma samples from routine diagnostic samples, specificity was 99.82% and 99.93%, respectively.
- Among 2256 samples from pregnant women, specificity was 99.91% and among 205 paediatric samples, specificity was 100%.
- Across Groups A (blood donors) and B (routine diagnostic specimens), a total of 14 reactive samples were detected (Group A, n=12; Group B, n=2).

Table 1. Summary of specificity results for the Elecsys Anti-SARS-CoV-2 immunoassay in blood donor samples and routine diagnostic specimens

Group	Sample cohort	No. samples tested	No. samples reactive	No. samples non-reactive	Specificity, % (95% CI)
Groups A and B	All	9575	14	9561	99.85 (99.75–99.92)
Group A Blood donors	Austria (Innsbruck), flu season*	1048	5	1043	99.52 (98.89–99.84)
	Germany (Hagen)	2625	2	2623	99.92 (99.73–99.99)
	Switzerland (Bern)	3041	5	3036	99.84 (99.62–99.95)
	<i>Switzerland (Bern), no flu season</i>	<i>2003</i>	<i>2</i>	<i>2001</i>	<i>99.90 (99.64–99.99)</i>
	<i>Switzerland (Bern), flu season</i>	<i>1038</i>	<i>3</i>	<i>1035</i>	<i>99.71 (99.16–99.94)</i>
	All	6714	12	6702	99.82 (99.69–99.91)
Group B Routine diagnostic testing	Germany (Augsburg), diagnostic routine	400	0	400	100 (99.08–100)
	Germany (Augsburg and Heidelberg), pregnancy	2256	2	2254	99.91 (99.68–99.99)
	<i>Germany (Augsburg), pregnancy</i>	<i>1498</i>	<i>2</i>	<i>1496</i>	<i>99.87 (99.52–99.98)</i>
	<i>Germany (Heidelberg), pregnancy</i>	<i>758</i>	<i>0</i>	<i>758</i>	<i>100 (99.51–100)</i>
	Germany (Heidelberg), paediatrics	205	0	205	100 (98.22–100)
	All	2861	2	2859	99.93 (99.75–99.99)

*Samples from Innsbruck were analysed at Augsburg.
CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

RESULTS (cont)

- The COI distribution across samples is shown in **Figure 1**. Only 14 samples had a COI ≥ 1 (pre-specified cut-off for reactivity).

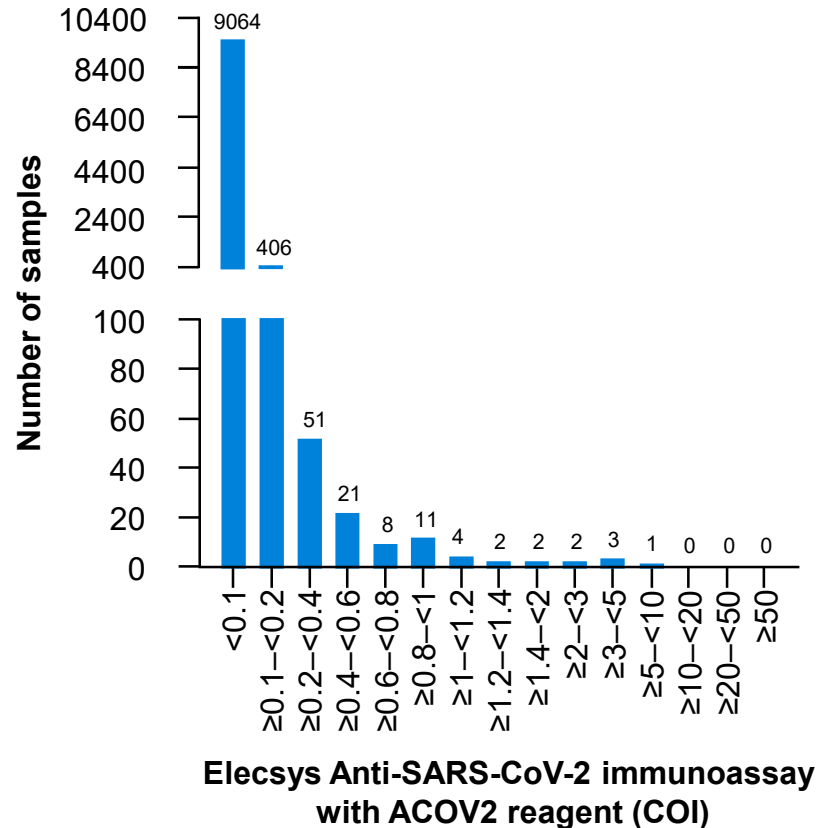


Figure 1. Cut-off index (COI) distribution of patient samples (n=9575)

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CONCLUSIONS

1

The performance of SARS-CoV-2 antibody assays in general is of high importance for public health and may affect political decision-making in pandemic management.

2

This study generated additional data on the performance of the Elecsys Anti-SARS-CoV-2 immunoassay and provided broader evidence on the very high specificity of the assay across various pre-pandemic cohort samples, including blood donors, pregnant women and paediatric populations.

3

Our findings support the use of the Elecsys Anti-SARS-CoV-2 immunoassay as a potential tool for determination of immune response following previous exposure to SARS-CoV-2 in the general population.