



Specificity vs. Sensitivity in COVID-19 Serological Testing

Specificity (very few or no false positives) is of greater importance than sensitivity in COVID-19 serological testing for the following reasons:

Prevalence of the disease (either active or convalescent): It is estimated that around 5% of the population worldwide has had COVID-19. If we assume for ease of calculation that 5% of 1000 people has COVID-19, that would be:

$$1000 * 0.05 = 50 \text{ people}$$

So that would be 50 positives we would expect to be 'true positives.' And 950 negatives that would be 'true negatives,' if the test were 100% accurate for both.

However, if the test is less than 100% specific, the rate of *false* positives climbs quickly, as shown in the table below (again, based on 5% prevalence, equal to 50 true positives and 950 true negatives):

Percent Specificity	Percent false positives	Total false positives per 950 true negative patients	PPV (TP / (TP+FP))
99%	1%	9.5	84%
98%	2%	19	72%
97%	3%	28.5	64%
96%	4%	38	57%
95%	5%	47.5	51%
94%	6%	57	47%
93%	7%	66.5	43%
92%	8%	76	40%
91%	9%	85.5	37%

At <95% specificity, the number of true positives is **equal to or LESS THAN** the number of false positives. That means that the positive predictive value of the test for positives is ~50% or less. So, it makes the positives that come from the test less trustworthy.

Also, false positives can give an incorrect sense to a person that they have 1) had COVID-19 already, and 2) have immunity. This will change their behavior, making them assume lower risk for the disease, therefore they may travel and engage in other activities that put them at risk.

On the other hand, the percent sensitivity at 95% gives a very different picture at 5% prevalence, or 50 true positives per 1000 patients, as shown in the table below:



Percent Sensitivity	Percent false negatives	Total false negatives per 50 true positive patients	NPV (TN / (TN+FN))
99%	1%	0.5	99%
98%	2%	1	98%
97%	3%	1.5	97%
96%	4%	2	96%
95%	5%	2.5	95%
94%	6%	3	94%
93%	7%	3.5	93%
92%	8%	4	93%
91%	9%	4.5	92%

Even at sensitivity of 91%, only **4.5 false negatives in 50 total true positive patients** will be seen! This also means that the number of false negatives will be a very small fraction of the number of true negatives (950 total true negatives). So, the test will still be very trustworthy for negative results.

Also, false negatives have less impact to healthcare because a person who tests as false negative will continue to assume that they do not have antibodies. Therefore, they will still take precautions to avoid exposure to the disease.

Data from recent external evaluations of the test true clinical settings is listed below and supports the performance of the test as having been optimized for specificity while still having acceptable sensitivity:

Ghaffari, A.; Meurant, R.; Ardakani, A. COVID-19 Serological Tests: How Well Do They Actually Perform? *Diagnostics* 2020, *10*, 453.

IgG Sensitivity (8-14 days)

31 samples 100%

IgG Specificity

49 samples 100%

Results from National Health Laboratories in Edinburgh, Scotland (Jun 17, 2020) using the BIOMERICA COVID-19 IgG/IgM Rapid Test

IgG/IgM Sensitivity (≥20 days)

Serum samples from hospitalized patients with a positive SARS-CoV2 PCR test and patients with a positive PCR test who did not require hospital admission.

83 samples 95.2%

**IgG/IgM Specificity**

A panel of confounder samples was also included to look for cross reactivity. These were from patients who had received a positive PCR for respiratory pathogens including human coronaviruses (hCoV) strains.

Patients with elevated Rheumatoid Factor, Cyclic Citrullinated Peptide, anti-nuclear antigen or positive for CMV IgG, IgM or EBV IgM were also included.

327 samples 99.1%

Results from Imperial College, London, England (Jun 25, 2020) using the BIOMERICA COVID-19 IgG/IgM Rapid Test**IgG/IgM Sensitivity (≥21 days)**

Serum samples from patients with a positive SARS-CoV-2 PCR Test.

320 samples 94.7%

IgG/IgM Specificity

Serum samples through the Airwave Health Monitoring Study.

500 samples 97.8%

Conclusion: The BIOMERICA COVID-19 IgG/IgM Rapid Test reported **excellent Specificity while still showing acceptable Sensitivity** in various external evaluations in highly reputable institutions with a large total amount of samples tested.