# How Good are COVID-19 Diagnostic PCR Tests?

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**Julie McDowell:**

With a dramatic rise in demand for COVID-19 testing, laboratories have implemented a variety of testing methods. Among them polymerase chain reaction or PCR tests. Regularly published research findings seem to question the validity or efficacy of many of the testing methods, and PCR is no different, as Dr. Sophia Yohe explains in this CAPcast interview.

Dr. Yohe, director of the University of Minnesota Medical School's Molecular Diagnostics Laboratory, addressed many questions about diagnostic PCR testing for SARS-CoV-2, the virus that causes COVID-19, and an article recently posted on the Precision Medicine Resource Center on cap.org.

Dr. Yohe, in your article, you address the difference between analytical and clinical performance for PCR testing. The analytical performance is near a hundred percent, but this is like the analytical performance of PCR testing on other viruses, correct?

**Dr. Sophia Yohe:**

Yes, that is true. And the issues regarding both analytic performance as well as clinical performance are seen in other infectious disease settings, including other respiratory viruses like influenza for example.

**Julie McDowell:**

When will we have a gold standard available for clinical testing performance?

**Dr. Sophia Yohe:**

I think the best clinic gold standard is going to be a combination of things such as clinical imaging, X radiography, repeated COVID testing, pre and post serology and negative testing for all of the respiratory viruses.

I think we actually have all of these pieces in place and they exist, but to run all of these for every comparison would be very costly and time consuming, and it's therefore unlikely to be used much, and we're more likely to use established assays as a gold standard, especially as we accumulate better data on all the new assays that have come out about their performance.

**Julie McDowell:**

What has been the experience of your laboratory and clinical performance for PCR testing for SARS-CoV-2?

**Dr. Sophia Yohe:**

Unfortunately, we don't get a lot of feedback on the clinical status, so it's a little hard to tell, and all I have are a few anecdotes. So again, analytical and clinical performance are different. Analytical performance is how well your test measures whatever you're measuring in the sample that you have. The clinical performance is how well the test predicts the disease, and that may be affected by how good the sample is as well.

We've had instances, for example, where we've been called with a concern about someone who has a positive test, but they don't have symptoms. Sometimes these are people who are barely positive. It's kind of at the limit of detection. We've confirmed some of these cases on more than one platform, and they reproducibly are positive, but they don't have symptoms.

The test is probably analytically performing well. The virus is probably there at a low level. But it doesn't necessarily mean that a person has disease. It's also unclear at this time if it means that person is infectious or could be infectious in the future.

**Julie McDowell:**

In your CAP article, you mentioned that pre-analytical factors and biologics play an important role in the performance of laboratory testing. What has your laboratory done to address the impact of these factors on PCR testing?

**Dr. Sophia Yohe:**

The pre-analytic factors like collection is really so important, but for respiratory samples, the laboratory really doesn't have much say in the collection. Unlike blood collections, which typically are done by phlebotomy, which has often oversight from the laboratory standpoint, or at least some interaction with the laboratory, respiratory specimens and especially for COVID are often being collected in a wide variety of settings with variable personnel and variably trained personnel.

There's also a difference in the type of collection, whether it's a nasal pharyngeal swab or an oral pharyngeal swab or nasal or a tracheal aspirate for someone who's intubated. And there's differences between if you collect from those different sites, where we've done some comparisons between nasopharynx, kind of the middle of the nose collection called mid turbinate and saliva, and other places have done the same and they differ from patient to patient.

I think it would be of interest to determine if these sites of collection are performed differently at different phases of the disease. Are you more reliably positive in one site or another if you're early on in the disease versus late, or if patients have different symptoms. If you have a cough, are you more likely to be oral pharyngeal positive? Or if you have a runny nose, are you more likely to have positivity in your nasal cavity? We don't really know the answer to those questions. And to answer those questions, you have to collect multiple samples in patients at many different time points or possibly review retrospective data. And all of that is considered research, so it requires some sort of institutional review board approval, which really increases the time and effort required to answer some of these basic questions that are so important for testing.

**Julie McDowell:**

Since sample collection may affect the test result, has your institution set up a collection protocol for SARS-CoV-2 PCR testing?

**Dr. Sophia Yohe:**

So our laboratory is doing collection for our health system, as well as from testing from around the state as part of the Minnesota State Initiative. So again, our lab does not have direct control over the collection sites. I know that our health system has designed some collection protocols and the state has developed their own collection protocols, but the samples we get are from various different health systems or community collections or various things, so it's really not been something we've had a direct role in doing.

**Julie McDowell:**

Finally, Dr. Yohe, many people, whether medical or non-medical, have questions about diagnostic PCR tests. What can pathologists and other laboratory professionals do to address this question accurately?

**Dr. Sophia Yohe:**

Well, I think first of all, be patient. Remember that we're the experts on laboratory testing, or if you as a pathologist are not a particular expert in COVID or this sort of testing, refer them to someone else who is. And remember that topics like sensitivity, specificity, positive and negative predictive value, and how they actually affect testing and test results, they're not easy topics to grasp.

I think it's also important to be honest and not oversell or undersell the test performance but try to put it in context. If possible, serve as an expert at your institution, your local organization, or even your state level to help guide a thoughtful approach to testing and using the results of the testing.

For example, here in Minnesota, we have a state of experts who include some pathologists as well as some individuals from the public health and others who meet every other week currently to provide guidance to the state of Minnesota on issues about COVID testing.

**Julie McDowell:**

Well, thank you, Dr. Yohe. To access Dr Yohe's article, visit cap.org and search for Precision Medicine. Click on Precision Medicine, where Dr. Yohe's article entitled 'How Good Are COVID-19 SARS-CoV-2 Diagnostic PCR Tests?' is posted.

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