How to choose a COVID19 test ?

There are now multiple options for COVID19 testing from quick at home kits, to test that can only be performed by a healthcare worker.

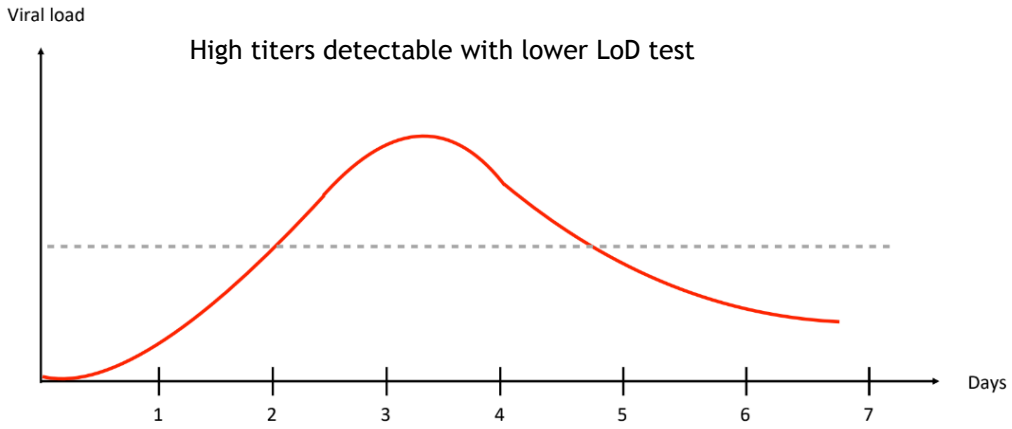
What are the key parameters that are important when selecting a test ?

There are 3 key parameters that all tests are measured on which are:

1) Limit of Detection (LoD) which is how many viral particles can be detected in the sample.
2) Sensitivity and Specificity which measures the % of true positives and true negatives concluded from the tests.
3) How many samples can be tested in a given timeframe.

If you use a test with a high LoD (high bad, low good), it can still be performing well on sensitivity and specificity. However, the test will not be able to detect low amount of virus in pre-symptomatic or asymptomatic individuals. Despite the lower performance of the LoD, some of these Point of Care Tests have been approved by the FDA through the issuance of an EUA[1]. Most test based on PCR have high sensitivity and specificity and low LoD and these type of test have therefore remained the gold standard and are typically performed in a central lab.

Limit of Detection Matters



1. LoD matters by scientist at Harvard concluding that current point of care tests misses up to 70% of positive cases https://www.ncbi.nlm.
2. Rapid Testing Is Less Accurate Than the Government Wants to Admit https://www.medscape.com/viewarticle/941054

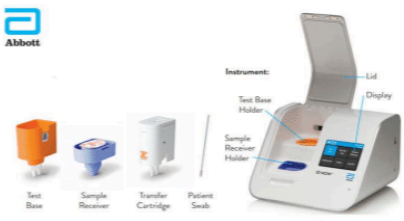
Point of care tests can miss up to 70% of positive cases due to high LoD

LoD matters[2] as some tests have only been approved for symptomatic individuals with high viral counts, such as the Abbott ID Now test. These test are EUA approved for symptomatic patients. Using these test for asymptomatic individuals will miss a significant number of positive cases. A primary example of this situation is the issue the White House experienced in early September. The White House was using Abbott's rapid testing methods as their primary testing method, which resulted in many false negatives. These people who came back as a false negative unknowingly spread the virus to others within the White House[3]. Abbott's Binax detected just 36% of infections in asymptomatic people and only 64% of the positive with symptoms[4]. That is also why the FDA have only approved these tests for Symptomatic people.

COVID-19 can only be detected using a rapid test when the viral load, i.e. the virus's presence in the body, is at its peak. This leaves a time period before and after the peak where the patient is infected, and contagious, but cannot be detected with the virus in a rapid test. Because of this, some point of care tests on the market can miss up to 70% of positive cases[2].

The other issue with point of care is that it's great for screening a small number of people, but it doesn't work well for analyzing a large group of people. For example, the Abbott ID Now test can produce one result every 30 minutes, which means it will take 20 days to analyze 1,000 samples.

It takes 20 days to analyze 1,000 tests using point-of-care



POC PCR: Low Throughput - Low Complexity
30 min AbbbottNow

500 hours = 20 days

PCR: High complexity - high throughput
1-3 hrs turnaround
Enabling Pooling
100 - 10,000 samples/day

24 hours = 1 day

PCR test performed in high complexity labs

The main disadvantage with testing in a high complexity lab is the wait time. It can take days to schedule the collection of the sample, and even longer to get the test results back. During the pandemic, that time can fluctuate between 2-4 days to 2 weeks depending on demand. This makes it impossible to contain the epidemic because all tracking and isolation of cases are seriously delayed.

Genomic Expression operates a private high complexity lab north of Boston and has a ***turn around time of 24 hrs after we receive the sample.*** *For very urgent samples we can produce same day results.*

Different sample types: Nasopharyngeal (NP) is the gold standard

The gold standard for COVID-19 testing is the nasopharyngeal (NP) method[4] which collects a substantial viral load, however it is invasive and very uncomfortable for the patient. It also needs to be administered by a trained healthcare professional, and there can be a variation in how much viral RNA is actually obtained, depending on how properly the sample was collected.

The alternative to the nasopharyngeal swab is the nasal swab, which only collects the sample from the nostril. It is a method of collection that is less comfortable than the nasopharyngeal swab. Nasal swabs have a high margin of error, and they typically lose 20% of the positive cases because it doesn't collect enough viral material[5].

How is saliva collection different than other collection methods?

Saliva as a sample specimen has many advantages. This method is done through self-collection, which means the individual collects it by themselves and there is less risk to healthcare workers. It is also less invasive for the patient than a nasopharyngeal test which goes way back into the nasal cavity. Finally, as long as the saliva is analyzed using PCR in a high complexity lab, it performs just as well as the nasopharyngeal swab test which is the gold standard.

Facts about the saliva test

With the saliva collection method there is no discomfort. The individual is able to collect their sample on their own, by simply spitting into a tube. There is enough viral RNA in saliva to detect the virus even when it is not at its peak. It is also safer for healthcare workers because the patients administer the test on their own, which cuts down on interactions between healthcare workers and COVID-19 positive patients.

Because it's possible to collect this test at home or in the office, it's possible to send the sample to a high complexity lab and get results back via an email. There is also less risk of getting exposed to others by not having to drive and stand in a line with other potentially infected people.

The saliva tests are a PCR test, which is currently the most accurate testing method. When compared to the commonly used nasopharyngeal collection method, the saliva collection method has showed the same results as the invasive NP swabs also in asymptomatic individuals[6].

More recently published data support that hight saliva viral load correlate with COVID-19 severity and mortality which enable physicians to stratify patients, whereas such correlation could not be found in nasal swabs[8].

Pro and Cons of different type of samples

	Pro	Con
Nasopharyngeal	• Effective sample collection • Can detect virus in asymptomatic	• Highly invasive and uncomfortable for the patient • Needs to be administered by a trained healthcare professional
Nasal Swab	• Not very invasive, comfortable • Self-administered • Fast	• Doesn't always collect enough viral material • Potential for human error
Saliva	• Non-invasive, comfortable • Can detect virus in asymptomatic • As affective a sample as NP swabs • Self-administered • High titers indicate serious case	• Individuals need to avoid eating and drinking before testing

Genomic Expression has entered into an agreement with Yale to offer their Saliva Direct saliva based PCR test in our lab.

To purchase a test, simply register at www.covid19.genomicexpression.com and place an order. Test kits can be bought individually or in bulk. Read the descriptions to make sure you are making the purchase that works best for you.

This test is licensed from Yale and based on Dr. Anne Wyllie and her team groundbreaking work proving that saliva is just as good a sample type as the Nasopharyngeal Swab which is have published in New England Journal of Medicine:

"Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs" https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1
"Saliva or Nasopharyngeal Swab Specimens For Detection of SARS-COV-2": https://www.nejm.org/doi/full/10.1056/NEJMc2016359

Saliva viral load is a dynamic unifying correlate of COVID-19 severity and mortality. https://www.sciencemag.org/news/2021/01/saliva-could-hold-clues-how-sick-you-will-get-covid-19
And the scientific paper https://www.medrxiv.org/content/10.1101/2021.01.04.21249236v1.full.pdf

This is important because this is the test from Yale that we licensed and because we started conversations with pharma to stratify patients for clinical studies for antivirals

Literature

[1] Rapid Testing Is Less Accurate Than the Government Wants to Admit https://www.medscape.com/viewarticle/941054
[2] LoD matters by scientist at Harvard concluding that current point of care tests misses up to 70% of positive cases https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7302192/pdf/nihpp-2020.06.02.131144.pdf
[3] Rapid covid tests can work – if you avoid making the White House's mistakes https://www.technologyreview.com/2020/10/07/1009636/rapid-covid-tests-can-work-white-houses-mistakes-trump-abbott/
[4] Abbott Test May Curb Virus Even Missing Some Cases, CDC Says https://www.bloomberg.com/news/articles/2021-01-19/abbott-s-binax-misses-some-covid-cases-making-repeat-tests-key
[5] Comparing Nasopharyngeal and Midturbinate Nasal Swab Testing for the Identification of Severe Acute Respiratory Syndrome Coronavirus 2 https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa882/5864592
[6] Saliva or Nasopharyngeal Swab Specimens For Detection of SARS-COV-2: https://www.nejm.org/doi/full/10.1056/NEJMc2016359
[7] "Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs" https://www.medrxiv.org/content/10.1101/2020.04.16.20067835v1
[8] "Saliva viral load is a dynamic unifying correlate of COVID-19 severity and mortality." https://www.medrxiv.org/content/10.1101/2021.01.04.21249236v1.full.pdf
9 Are we testing for Omicron Wrong ? - — South African study suggests nasal swabs aren't the best way https://www.medpagetoday.com/infectiousdisease/covid19/96385
10 Discordant SARS-CoV-2 PCR and Rapid Antigen Test Results When Infectious: A December 2021 Occupational Case Series https://www.medrxiv.org/content/10.1101/2022.01.04.22268770v1