RT-PCR and NAAT for COVID-19

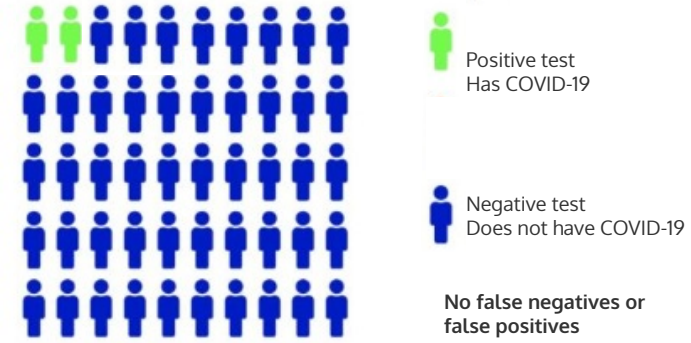
The Basics

For Current Infection

Specimen types: Nasopharyngeal preferred. Acceptable alternatives: oropharyngeal, nasal mid-turbinate, anterior nares, nasopharyngeal wash/aspirate, nasal aspirate, nasal washings and sputum. Mid-turbinate and anterior nares swabs can be self-collected [1]
Validation study performance: Limit of detection 316 copies/mL for CDC version. No cross-reactivity with other respiratory pathogens [2]
Real-world performance: Still unknown. A similar test in China had low sensitivity in a non-peer-reviewed article [3]
FDA Emergency Use Authorization: Yes
Advantages: Gold standard to date
Disadvantages: Uncomfortable. Requires PPE and special collection kits

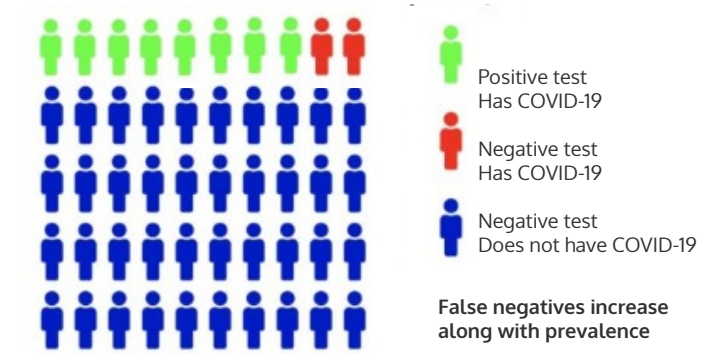
False negatives?

If COVID-19 prevalence is 4%...



No false negatives or false positives

If COVID-19 prevalence is 20%...



False negatives increase along with prevalence

Test performance is tied to disease prevalence. Because of concerns about possible low sensitivity of NAAT and RT-PCR for COVID-19, this graphic shows what happens in 50 people with a test that has only 80% sensitivity. Specificity is assumed to be 99%, and fractions were rounded to the nearest whole number.

Footnotes

[1] CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19)
[2] CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel Instructions for Use, 3/30/20
[3] Yang Y, Yang M, Shen C et al. (2020.) Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. https://doi.org/10.1101/2020.02.11.20021493

IgG and IgM for COVID-19

The Basics

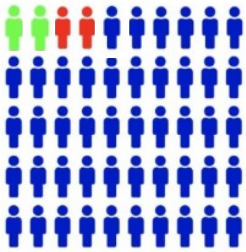
For prior infection

Specimen types: Venipuncture or fingerstick
Validation study performance: Not always stated. For Cellex, 94% positive agreement when compared to samples from people with known illness, 96% negative agreement when compared to samples from before Sept. 2019 [3] In an unpublished, non-peer-reviewed California article comparing 12 tests, 81% to 100% positive agreement at 3 weeks after symptom onset, 84% to 100% negative agreement with 2018 samples [4]
Real-world performance: Still unknown.
FDA Emergency Use Authorization: 8 tests as of 4/27/2020 (Cellex, Chembio, Ortho IgG, Ortho IgG/IgM, Mt. Sinai, Abbott, DiaSorin, Autobio)
Advantages: Speed.
Disadvantages: 1) A negative result does not rule out active infection or prior infection. It may take 3 to 7 days before an infected individual produces detectable IgM antibodies. This window corresponds to when individuals are also highly infectious. A negative result also may be due to an insensitive test device (false negative).
2) A positive result does not mean an individual has or had COVID-19. A swab is still required--the antibody test result is not accepted by the Centers for Disease Control & Prevention (CDC) and is not counted for case reports. Positive results may be due to either past or present infection with SARS-CoV-2, or with similar non-SARS-CoV-2 strains (false positive).
3) The antibody test does not provide any useful information about a person's immune status to COVID-19 at this time. Although people who test positive for antibodies and negative for active infection probably have some level of immunity, the strength and duration of immunity are not known.

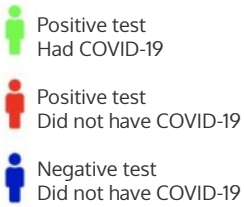
False positives?

Test performance is tied to disease prevalence. This graphic shows what happens in 50 people with a test that has 99% sensitivity and 95% specificity, with fractions rounded to the nearest whole number.

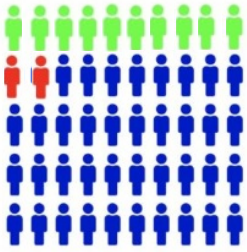
If prevalence is 4%...



A positive result is just as likely to be false as true



If prevalence is 20%...



A positive result is more likely to be a true positive

Footnotes

[3] Cellex FDA Summary https://www.fda.gov/media/136625/download
[4] Whitman JD, Hiatt BA, Mowery CT el al. (2020.) Test performance evaluation of SARS-CoV-2 serological assays. https://www.dropbox.com/s/cd1628cau09288a/SARS-CoV-2_Serology_Manuscript.pdf?dl=0&referringSource=articleShare