Evidence-Based Medicine InfoSheet: COVID-19 Diagnostics and Testing
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<u>**WHO TO TEST:**</u>
The CDC recommends PCR or antigen testing priority for (updated 8/2/21)[1]:
- Individuals who present with symptoms of COVID-19.
- Individuals who have had exposure to someone with suspected or confirmed COVID-19.
    - Fully vaccinated individuals should be tested 3-5 days following exposure and should wear a mask when in public indoor settings for 14 days or until they receive a negative test result.
    - Individuals who are not fully vaccinated should quarantine and be tested as soon as possible, and, if negative, should take another test 3-5 days after exposure or immediately if any symptoms appear.
- Individuals who are not fully vaccinated and are prioritized for expanded community screening.
- Individuals who are not fully vaccinated and have referred to testing by their school, workplace, healthcare provider, or health department.

<u>**UPDATED CDC GUIDELINES (02/02/2021):**</u>[2]
Role of PCR testing to discontinue isolation/precautions: For all people except those severely immunocompromised, CDC no longer recommends test-based strategy *except* to discontinue isolation/precautions earlier than the 10-day period. Test based strategies are not to be used to discontinue quarantine (for people who are close contacts of someone with COVID-19 and exposed but not symptomatic).

Role of PCR after discontinuation of isolation/precautions: For persons previously diagnosed with COVID-19 who remain asymptomatic, retesting is not recommended within 3 months after symptom onset of COVID-19 infection. Quarantine is not recommended either for those with previously diagnosed COVID-19. If the person develops new symptoms consistent with COVID-19 during 3 months after the date of initial symptom onset and alternative etiology cannot be identified, then the person may undergo retesting. Quarantine may be recommended. For those who never developed symptoms, the date of the first RT-PCR test should be used in place.

Role of serologic testing: Serologic testing should **not** be used to establish presence or absence of COVID-19 infection or reinfection, with the exception of delayed viral testing.

<u>**THE TESTS:**</u>
RT-PCR AND OTHER NUCLEIC ACID AMPLIFICATION ASSAYS: Can be performed in 4 hours, though most providers obtain results in 2-4 days. Diagnostic testing involves using a real-time reverse transcription-PCR (RT-PCR) assay that targets SARS-CoV-2 nucleocapsid gene.[3]

CDC recommends healthcare workers obtain a nasopharyngeal specimen, but if not possible an oropharyngeal, nasal mid-turbinate, anterior nares swab, nasopharyngeal/nasal wash/aspirate, or a saliva specimen collected by supervised self-collection is acceptable. An at home nasal mid-turbinate swab specimen collected following kit collection instructions is also acceptable.[4] A specimen study suggests lower respiratory samples have higher detection rates than upper respiratory samples, and PCR via saliva samples have been shown to detect SARS-CoV 2 in 87-92% of positive patients (n=35).[4,5] If available and if upper respiratory specimen is negative despite high clinical suspicion, a lower respiratory specimen is recommended including testing of sputum if cough is productive (induction of sputum is not recommended), a lower respiratory tract aspirate, or bronchoalveolar lavage sample.[6] In a study of specimen type detection rates, bronchoalveolar lavage showed the highest positive rates (93%), followed by sputum (72%), nasal swab (63%), fibrobronchoscope brush biopsy (46%), pharyngeal swabs (32%), feces (29%), and blood (1%).[5] This suggests nasal swabs may be superior to oral swabs, however, only 8 nasal swabs were taken in the study versus 398 pharyngeal swabs. Another non-peer reviewed, retrospective study of 866 samples also found sputum to have the highest positive rate (74%-89%) among upper respiratory specimens,

followed by nasal swabs (54%-73%) within the first 14 days since onset of symptoms.[7] A direct study comparing mid-turbinate and nasal swab specimen's sensitivity to nasopharyngeal specimen's sensitivity found a positive percentage agreement of 94% and 96% respectively.[8]

Collecting saliva specimens for diagnosis has the advantages of ease of collection and reduced risk to healthcare workers compared to nasopharyngeal or oropharyngeal swabs.[9] A study from Brazil consisting of 155 patients, compared both nasopharyngeal and saliva samples collected from each patient. Saliva samples had a 94.4% sensitivity and there was 96.1% agreement between the tests of the two different sample types.[10] Another study of 224 patients directly comparing nasopharyngeal and saliva samples using the CDC RT-PCR test found a 100% positive percent agreement and a 99.4% negative percent agreement.[11]

POC RT-PCR TESTS[12]**:** Three POC diagnostics, Cepheid Xpert Xpress, Abbott ID NOW, and GenMark ePlex have been granted EUA and their clinical performances were determined by detection of nasopharyngeal specimens from 108 positive patients. Xpert Xpress had the lowest limit of detection (LOD) (100 viral copies/ml) and the highest positive percent agreement (98.3%) compared to reference RT-PCR test with results being returned after 46 minutes on average. ID NOW had the fastest result time (17 min average) but had a higher LOD (20,000 copies/ml) and lower positive percent agreement (87.7%). Currently, Xpert Xpress and Abbott ID NOW are used in 29% and 26% of public health laboratories, respectively.[13]

A meta-analysis found the Xpert Xpress assay to have a 99.4% sensitivity and 96.8% specificity and the ID NOW assay to have a 76.8% sensitivity and 99.6% specificity.[14]

The cycle threshold (Ct) in reverse transcription polymerase chain reaction (RT-PCR) SARS-CoV-2 test is suspected to be a potential marker for disease severity and infectivity. A review published in July in Infectious Diseases and Therapy found an association between lower Ct values and worse outcomes. [15] Additionally, the results of one retrospective cohort study found that high genomic load estimated by Ct value was an independent risk factor for adverse outcomes. [16] The study evaluated 314 patients admitted to the hospital with a positive SARS-CoV-2 test and viral pneumonia. This study grouped patients into three genomic load cohorts: low (Ct ≥35), intermediate (25<Ct<35), and high (Ct≤ 25) and followed them for a median of 25 days. Using a multivariate model, controlling for patient age, sex, BMI, CCI, smoking and transplant history, duration of symptoms, and PSI they found that high genomic load remained an independent risk factor for the adverse outcomes (OR, 1.59; P = 0.02). These results suggest that Ct values can potentially be used to make inferences for disease outcomes. Lastly, a study conducted by Bullard *et al* assessed the correlation between RT-PCR cycle threshold (Ct) value and the time from the onset of symptoms to testing with SARSCoV-2 infectivity in cell culture. The study utilized 90 samples that were positive for SARS-CoV-2 in a RT-PCR assay targeting the sarbecovirus envelope gene. Of these samples inoculated into a Vero cell culture line a cytopathic effect consistent with SARS-CoV-2 was observed in 26 (28.9%) cases. Notably, SARS-CoV-2 Vero cell infectivity was only observed for RT-PCR Ct < 24 and STT < 8 days. These results suggest that infectivity of patients with Ct > 24 and duration of symptoms > 8 days may be low and that Ct values obtained from RT-PCR could potentially help with assessing SARS-CoV-2 infectivity in patients. However, further studies of larger sample sizes are needed. [17]

ANTIGEN DETECTION: Studies show that antigens are generally only detected when the virus is actively replicating, therefore these tests are recommended mainly for acute or early infection. Performance of the test is heavily dependent on time from onset of illness and concentration of virus. Due to the low sensitivity of antigen tests, RT-PCR should be used to confirm negative antigen test results in high risk individuals.[18] WHO recommends that if access to RT-PCR assay is limited or turnaround times for test results are excessive to the point of limited utility, then antigen tests with a minimum sensitivity and specificity of 80% and 97% respectively can be used if the test is used within the first 5-7 days of symptom onset.[19]

Guidelines from the Infectious Diseases Society of America (IDSA) provide five diagnostic recommendations for the utilization of antigen testing compared with NAAT in symptomatic and asymptomatic individuals, as well as the use of single versus repeat testing. The five recommendations are as follows:

1) Symptomatic individuals suspected to have SARS-CoV-2 should be tested with NAAT (either a rapid RT-PCR or lab-based NAAT) over antigen tests.[20] This recommendation is based on 12 studies comparing the accuracy of NAAT with Ag testing.[21,22,31,23–30] The analysis focused on the sensitivity of each test in order to determine their accuracy.[20] With standard NAAT being used as the reference standard, AG testing was found to have a pooled sensitivity of 81%. When Ag testing was performed within the first seven days of onset of symptoms, the sensitivity increased to 84%. This indicated the likelihood of Ag testing increasing the risk of providing a false negative. Based on this analysis, the use of NAAT over Ag has a higher sensitivity, making NAAT testing more accurate and the test of choice. However, due to the ease of use or availability of Ag testing, it will continue to be used in some settings. When Ag testing is utilized for a symptomatic individual and the result is negative, this should be followed with NAAT for confirmation, but if the result is positive then no further testing is necessary.

2) Asymptomatic individuals at risk for exposure to SARS-CoV-2 should be tested using a single NAAT over a single rapid antigen test.[20] This recommendation is based on the analysis of 6 studies that compared the accuracy of NAAT with Ag testing for asymptomatic individuals.[22,25,27–29,32] The analysis stratified into two groups: 1) those who were asymptomatic who had not been known to have been at risk of exposure to SARS-CoV-2 and 2) those who were also asymptomatic but had been exposed to SARS-CoV-2.[20] For asymptomatic individuals without known exposure to SARs-CoV-2, the pre-test probability range assigned was 1%, 5%, and 10%. A low pre-test probability of 1% had approximately the same number of true positives as false negatives, with 1,000 individuals being tested and 5 true positives and 5 false negatives. In comparison, NAAT for the same pre-test probability of 1% had 990 true negatives and 0 false positives. For asymptomatic individuals with known exposure to SARs-CoV-2, the pre-test probabilities assigned were 20% and 30%. With a pre-test probability of 30%, the number of true positives and false negatives was also approximately the same, with 147 true positives and 153 false negatives out of 1,000 tested individuals. When NAAT was used at a pre-test probability of 30% there was 700 true negatives and 0 false positives. This indicates the advantage of utilizing NAAT over Ag testing to ensure accuracy of results.

3) Asymptomatic individuals at risk for SARS-CoV-2 exposure should be tested using a single standard NAAT, rather than two consecutive rapid antigen tests.[20] This recommendation is based on a single study comparing the accuracy of using 1 NAAT with 2 Ag tests performed within 30 minutes of each other.[33] The intention of performing 2 consecutive tests is to determine whether consecutive Ag tests can increase test sensitivity. The NAAT had a 15.8% test positivity versus a positivity rate of 12.5% and 12.7% for two consecutive Ag tests. Since the recommendation was based on a single study, the IDSA considers the certainty of this recommendation to be very low and indicates the need for future studies that look at the ideal timing between performing multiple Ag tests.[20]

4) The IDSA does not advise for or against single rapid antigen testing versus no testing for asymptomatic individuals at risk for SARS-CoV-2.[20] No studies comparing the outcome of performing a single Ag test versus no test were available for this recommendation, so instead the diagnostic test accuracy of Ag testing for asymptomatic patients was utilized.[34] The IDSA indicates that the decision to test with Ag testing or to not test at all will vary between individuals and will typically depend on the circumstances.[20] Since Ag testing has been shown to have low sensitivity, the risk of reporting a false positive or false negative should be taken into consideration.

5) The IDSA does not advise for or against repeat rapid antigen testing versus no testing for asymptomatic individuals at risk for SARS-CoV-2.[20] No studies directly comparing the outcome of performing repeat Ag test versus no test were available for this recommendation. However, 2 studies looking at repeat testing with EUA Ag testing were available. The first study looked at the accuracy of utilizing rapid Ag testing among staff and residents of a nursing home where there was a SARS-CoV-2 outbreak.[35] The positive percent agreement for Ag and NAAT was 80% for both symptomatic and asymptomatic groups, but the study did not indicate whether asymptomatic individuals eventually developed symptoms. The second study was an observational study that assessed the potential benefits of weekly screening of students, teachers, and staff at a primary school and found that doing so reduced infections rates by 50% in high schools and by 35% at primary schools.[36] Taking the information from these two studies into consideration, the IDSA indicates that there may be benefit in the utilization of a repeat

testing strategy in order to prevent outbreaks in congregate settings, but that more studies on repeat testing would need to be performed to further validate this.[20]

A study conducted by Stanford tested 3,302 samples collected in the community setting using the BinaxNOW test found the assay's sensitivity to be 100%, 98.5%, and 89% using Ct threshold values of 30, 35, and no threshold, respectively. The assay's sensitivity in asymptomatic individuals or individuals who symptom onset was greater than 7 days ago was 100%, 97.5%, and 81.4% using Ct threshold values of 30, 35, and no threshold, respectively. Overall specificity was 99.9% with an estimated false positive rate of 2% if prevalence is higher than 5% and 5% if the prevalence is lower than 2%.[37] Another study evaluating the BinaxNOW using RT-PCR as a standard, tested 3419 specimens collected from individuals from two community testing sites in Arizona (nasal swab samples were used for the BinaxNOW and nasopharyngeal samples for RT-PCR). Testing in asymptomatic individuals resulted in a sensitivity of 35.8%, specificity of 99.8%, positive predictive value (PPV) of 91.7%, and negative predictive value (NPV) of 96.9%. Sensitivity when compared to only nasopharyngeal samples from asymptomatic individuals that had a positive viral culture in addition to a positive RT-PCR was 78.6%. Another study compared the Abbott BinaxNOW COVID-19 Antigen card to a standard RT-PCR assay (ThermoFisher TaqPath COVID-19 Combo Kit) for the detection of SARS-CoV-2 in 2,645 asymptomatic students presenting for screening at the University of Utah. SARS-CoV-2 RNA was detected in 1.7% by RT-PCR. BinaxNOW identified 24 infections but missed 21 infections that were detected by RT-PCR. The sensitivity for BinaxNOW was 53.3% and the specificity was 100% when compared against the RT-PCR assay. The median cycle threshold (Ct) value in the specimens that had concordant positive BinaxNOW antigen results were significantly lower compared to those that were discordant (Ct 17.6 vs. 29.6; p < 0.001). In individuals with presumably high viral loads (Ct <23.0), a 95.8% positive agreement was observed between the RT-PCR assay and BinaxNOW. [32]

POOLED TESTING: Many countries around the world have implemented pooled testing, which allows multiple samples to be initially tested together in pools followed by testing individual samples from positive pools. This has the potential to save significant amounts of time, resources, and money, as well as aiding institutions such as schools, offices, religious organizations, and factories in reopening safely. A study of pooled testing from India tested 4620 samples in 462 pools of 10 and 14940 samples in 2990 pools of 5. 61 10 sample pools returned positive and then the individual samples from these pools were tested resulting in 72 positives. The same two-step approach was done for the pools of 5 and overall this method used 76%-93% less tests compared to individual testing.[38] Another study in Israel tested 133,816 samples over a 5 month period in either 8-sample or 5-sample pools depending on the changes in prevalence rate. 76% of PCR tests were spared compared to an individual testing method with minimal losses in sensitivity (average Ct increase of 2.9 compared to positive sample Ct value).[39]

Optimal pool size based on prevalence of virus has been studied and using a test that has 95-100% sensitivity, a pool size of 5 for a prevalence rate of 5% reduced expected number of tests by 57% and increased testing efficiency by 133%. With a prevalence of 10%, a pool size of 4 would be optimal with a 41% reduction in tests needed with a 69% increase in efficiency.[40] Once prevalence is above 10%, pooled testing starts to have diminishing returns. Pooling does dilute individual samples so if a positive sample with low viral load is present in a pool, there is potential for false negatives. A study showed Ct values of pools containing up to 30 samples were under 30 with the average Ct values of the pool being 5 cycles higher than the Ct values of the individual positive specimens (Ct values in the 21-29 range).[41] Detection of a single positive sample in pools of up to 32 and even 64 with additional cycles has been reported.[42] Pooling seems to not affect test sensitivity if Ct values are under 35, but in pools that had specimens with values greater than 35 a false negative rate of 13.3% was found in one study.[43] A two-fold dilution results in a 1.24 increase in the Ct value[42] so if a specimen with a Ct value > 38 is in a pool of 5 then the pool's Ct value will be over 40 resulting in a negative result.

A recent study investigating optimal COVID-19 testing strategies for schools and businesses found that increasing testing frequency was associated with a non-linear positive effect on cases averted over 100 days. The study used a simulated data set that incorporated actual community prevalence and test performance characteristics to a susceptible, infectious, removed (SIR) compartmental model. The researchers found that testing every 3 days versus every 14, even with a test that had lower sensitivity reduced the burden of disease by a significant amount. [44] One strategy the study proposed to increase testing frequency and efficacy while saving cost was pooled testing. The

researchers found that through pooled testing the cost per person of testing every 3 days could be reduced to as low as $1.32.

SEROLOGY / ANTIBODY TESTING: The utility of serology lies primarily in surveillance and epidemiology as well as confirmation of COVID-19. Guidelines from the Infectious Diseases Society of America (IDSA) recommend that serology be used for the three following reasons: 1) evaluation of patients with a high clinical suspicion for COVID-19 when molecular diagnostic testing is negative and at least two weeks have passed since symptom onset; 2) assessment of multisystem inflammatory syndrome in children; and 3) for serosurveillance studies. Data suggests that serology lacks the sensitivity to exclude the diagnosis of COVID in its acute phase.[45]

The CDC uses a serologic test to detect SARS-CoV-2 antibodies in serum using purified SARS-CoV-2 protein as an antigen in the ELISA. It has a specificity greater than 99% and a sensitivity of 96%, and can be used to identify prior SARS-CoV-2 infections without molecular diagnostic confirmation.[46] A serology study of patients in China with COVID-19 showed that IgG and IgM antibodies were observed as early as the 4th day after symptom onset and did comparisons between IgG and IgM sensitivity, specificity, PPV, NPV, and consistency rate.[47] IgG was more sensitive, but IgM was more specific and had a greater positive predictive value.

Many studies have investigated the persistence of antibodies post infection. A study of 5,882 people in Arizona showed individuals with severe disease exhibited elevated virus-neutralizing titers and antibodies against the nucleocapsid (N) and the receptor binding domain (RBD) of the spike protein. Spike RBD and S2 and neutralizing antibodies remained detectable through 5–7 months after onset, whereas α-N titers diminished.[48] A study in New York with 30,082 individuals also showed similar evidence with the vast majority of infected individuals with mild-to-moderate COVID-19 experiencing robust IgG antibody responses against the viral spike protein. Titers are relatively stable for at least a period approximating 5 months and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2.[49] A third study showed a slightly reduced period of antibody persistence; longitudinal analysis revealed that anti-SARS-CoV-2 IgA and IgM antibodies rapidly decayed, while IgG antibodies remained relatively stable up to 105 days post symptom onset in both serum and saliva. This study was done in Ontario Canada with n=439 (serum) and n=128 (saliva) patients with COVID-19.[50] In contrast, a study of 156 frontline health care personnel who had positive SARS-CoV-2 antibody test results in spring 2020 showed that 94% experienced a decline at repeat testing approximately 60 days later, and 28% seroreverted to below the threshold of positivity. This indicates a negative serology test does not reliably exclude previous infection.[51]

A study examined at whether infected individuals would produce persistent immune memory by looking at peripheral blood mononuclear cells (PBMCs) and plasma from 15 individuals who had recovered from mild disease with symptoms lasting a median of 13 days. One month after symptom onset, the blood samples from the individuals demonstrated retained plasma anti-RBD IgG above the threshold of healthy control individuals. Anti-RBD IgM and anti-RBD IgA were present as well. Approximately 2 months after onset of symptoms, anti-RBD IgG levels decreased slightly. Individuals who maintained anti-RBD IgM and IgA levels were fewer. The slight decrease in anti-RBD IgG after 60 days suggests that the IgG levels were being stabilized by plasma cells, unlike IgA and IgM, which demonstrated drastic decreases in levels. The study further tested for neutralization of SARS-CoV-2 by measuring antibodies targeting the RBD. It was determined that the plasma of infected individuals inhibited RBD binding to host cell angiotensin converting enzyme 2 significantly more than uninfected individuals, both 30 and 90 days after symptom onset. [52]

A recent longitudinal study was conducted over 11 months to determine changes in circulating antibodies after natural infection with COVID-19 [53]. 228 participants were enrolled in the study from April 2020 to February 2021, where plasma or study samples were drawn at each visit. VITROS Anti-SARS-CoV-2 Total and IgG assays and in-house fluorescence reduction neutralization assay were used to detect antibodies. The study demonstrated that 97% of individuals had Anti-SARS-CoV-2 antibodies at the first visit. 91.4% of the participants had IgG antibodies up to 11 months after infection. 63% of the participants had neutralizing titers; however, 25% of the participants had neutralizing titer levels that became undetectable over time.

A rapid and reliable saliva-based test for COVID-19 antibodies, known as the CovAb has been developed by Diabetomics and was granted Emergency Use Authorization by the FDA. [54] CovAb successfully detects three different antibodies present throughout the stages of infection. The test is less invasive than the standard blood test used for detecting antibodies for prior COVID-19 infection. Additionally, it can be performed quickly, allowing results to be delivered in about 15 minutes. When utilized at least 15 days after the onset of symptoms, the test had a high sensitivity and specificity, with a false-negative rate under 3% and a false-positive rate of about 1%.

A recent study followed immunity and long-term symptoms one year after COVID-19 infection. In 78% and 66% of participants, IgA and IgG antibodies respectively were detected 12 months post-infection. [55] The IgA/IgG antibody levels decreased from 92% and 95% at a 6-week follow up, and 78% and 70% at a 6 month follow up. T-helper cells and memory T-cells were detected in 80% of participants at a one year follow up. Longer acute phase of COVID-19 and older age were associated with higher T-cell and humoral responses. Finally, 28% of the participants complained of long-lasting symptoms one year after infection, with the most frequent symptoms being loss of smell or taste, headache, and difficulty concentrating.

COMBINATION TESTING: Detection of other respiratory pathogens does not exclude SARS-CoV-2 infection as concomitant infection has been reported from below 6% to as high as 37%.[56–58] Combined testing modalities are available such as Cepheid's point of care (POC) Xpert Xpress SARS-Cov-2/Flu/RSV test which received emergency use authorization (EUA) in October 2020 and showed 97.9% positive predictive agreement with the benchmark SARS-CoV-2 RT-PCR test.[59] Other tests such as the CDC Influenza SARS-CoV-2 Multiplex Assay are available as well.[60]

VIRAL CULTURE: It is important to note that detection of viral RNA does not confirm the presence of infectious virus. For patients with moderate symptoms infectious virus has not been retrievable after 10 days since the onset of symptoms.[17,61] However, infectious virus from a few severe cases has been found to be recoverable up to 32 days since onset of symptoms and with high cycle threshold (Ct) values.[62,63] Cycle threshold is the number of PCR cycles required for fluorescent signal to be detected from a given nucleic acid sample. A Ct value of 40 is typically the cut off for a positive test to be returned.[64] There has been limited research into the relationship between viral load detection by RT-PCR and transmission potential. A study from Taiwan evaluating infective potential of 60 upper respiratory clinical specimens found that samples containing higher viral loads and showing greater genome integrity tended to have a higher culture success rate. 5-6 $\log_{10}$ genome copies/ml appeared to be a reasonable viral load requirement for culture, but there were non-culturable samples that had greater than 7 $\log_{10}$ copies. Another study using multivariate analysis found viral loads above 7 $\log_{10}$ copies/ml to be associated with isolation of infectious virus from respiratory specimens.[62] Viral genome integrity also appears to be a significant factor as there was a higher correlation of expression of structural (envelope, nucleocapsid) and non-structural (RNA-dependent polymerase) genes in culturable specimens compared to non-culturable specimens.[65] Another study from England assessing culturability of 324 positive samples based on Ct values found that the estimated odds ratio of recovering infectious virus decreased by 0.67 for every 1 increase in Ct value. 38/44 samples with Ct values between 20-25 were culturable compared to 5/60 samples with Ct values over 35. The temporality of infectious potential was also assessed, and it was estimated that 40.1% of samples collected 7 days after symptom onset would be culturable compared to 6% of samples collected 10 days after symptom onset.[66]

A study assessing the shedding of viable virus in immunosuppressed cancer patients found 10 out of 14 nasopharyngeal samples contained viable virus on the first day of testing and 5 follow-up samples had culturable virus for 8,17,25,25, and 61 days after onset of symptoms. This indicates that immunosuppressed patients can still harbor transmissible virus for up to 2 months.[67]

OLFACTORY DYSFUNCTION TESTING[68]**:** Loss of smell has been reported in 76-83% of SARS-CoV-2 infections[69] and is typically one of the first symptoms to present before other overt symptoms.[70] A study examined the efficacy of olfactory dysfunction (OD) screening by comparing the olfactory function of 864 participants to their COVID-19 status using reverse transcriptase-polymerase chain reaction and found 20 of the 58 participants who tested positive for SARS-CoV-2 reported symptoms of olfactory dysfunction. [71] Findings suggest olfactory dysfunction to be suggestive

of COVID-19. However, olfaction function was found to be intact in more patients who tested positive for SARS-CoV-2 indicating that olfactory dysfunction testing is complementary and specific when testing for SAR-CoV-2.

REPEATED TESTING: For populations that are at significantly higher risk such as male and older populations, repeated testing should be considered especially if the initial test displays negative results. An increase in the amount of testing as well as repeated testing is seen to improve diagnosis rates, excluding patients that currently present with pneumonia. Performing three total tests per patient displayed a 1.43-fold improvement (27.9% to 39.9%) and it was seen that performing more than 3 testing administrations was not helpful for further improvement.

CRISPR: These test results are available within 40 minutes on a point of care lateral flow strip, using a nasopharyngeal swab specimen. Thus far, CRISPR has been shown to have a 95% positive predictive value and 100% negative predictive value but is not available to the public yet.[72] One study describes a method of virus detection that combines a simplified extraction of viral RNA with the benefits of CRISPR-mediated detection. This study shows a sensitivity for this test of 93.1% and a specificity of 98.5%. The test can be performed in less than an hour and can detect a smaller viral load than more traditional PCR. More data will be necessary to determine this test's efficacy and its ability to be implemented on a wider scale.[73]

CURRENT STATUS OF TESTING IN SAN ANTONIO? TEXAS? US?
There are currently over 90 testing sites in Bexar county with many offering drive-thru testing (PCR), 21 of them being drive-thru testing or walk up (PCR).[74] This drive through method was successful in South Korea, allowing for higher testing capacity and less likely to lead to cross infection between patients.[75] When discussing the cost of tests, many large health insurers are waiving fees and coinsurance for medically necessary SARS-CoV 2 testing.[76] If a patient does not have insurance, resources are available for access to testing at no charge.[77]
As of September 9th, 2021, in Bexar county, percent positivity is declining from 10.6% during 8/21-8/27 down to 7.6% during 8/28-9/3. The tests performed are both molecular (PCR/NAAT) and antigen (FIA) tests.[77] These indicators, alongside a significant rise in people hospitalized for COVID-19, demonstrate the continuation of our summer 2021 surge.

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