OPTUM Care®

Forum for Evidence-Based Medicine

Special COVID Edition 2
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COVID–19
+ stay informed

What is the value of social distancing?[1]

Using simulation models, researchers in Singapore estimated the number of SARS-CoV-2 infections that would occur at 80 days after the first 100 cases of community spread were confirmed, assuming that 7.5% of infections were asymptomatic. We are uncertain of how infectious the virus is but if we used an accepted estimate of one infected person infecting on average an additional 2.5 patients, this would result in 1.2 million patients being infected by day 80. If all recommended social distancing measures were enacted to include isolation of infected individuals plus family quarantine, workplace distancing, and school closures, this number would be reduced to 258,000. This would mean that social distancing would reduce by 78.5% the number of new cases.

Asymptomatic patients — what is their role in the propagation of the pandemic? [2, 3]

This is an area of intense research. When studied in Wuhan, it was estimated that 7.5% of patients were asymptomatic and these were more commonly younger adults and children who are reported to experience fewer symptoms when infected. A recent study from Italy challenges that estimate. When the outbreak began in northern Italy, a small town of 3,000 individuals was completely closed off in mid-February, after which the entire village was tested. Of individuals that tested positive, 50-75% were either asymptomatic or minimally symptomatic. With controlled quarantine of every infected person, new cases diminished by 90% within ten days. Because of the increased exposure in health care providers (HCP) who are seeing patients during the pandemic, if these numbers prove to be accurate, asymptomatic HCP could be significant vectors of disease transmission. This would suggest that routine screening of HCP involved in direct patient care could be important. However even here, the available literature is not clear. Over 40,000 HCP have been deployed from other areas of China to support the response in Wuhan. Notwithstanding discrete and limited instances of nosocomial outbreaks (e.g., a nosocomial outbreak involving 15 HCP in Wuhan), transmission within health care settings and amongst health care workers does not appear to be a major transmission feature of COVID-19 in China. Additionally, investigations among HCP suggest that many may have been infected within the household rather than in a health care setting. Since we have no effective treatments and no vaccine, it will only be through understanding and responding to the epidemiology of the pandemic that will allow us to bring it under control. We are in dire need of clear data informing us of the asymptomatic infection rate of the COVID-19 infection.

Nasal swabs compared to deep nasopharyngeal swabs for the diagnosis of COVID-19 infection

In a study to be published in the NEJM by our colleagues at the Everett Clinic and UHG R&D, alternatives to deep nasopharyngeal swab for the diagnosis of COVID-19 were explored. Nasal passage (NP) sampling requires the use of personal protective equipment that is in limited supply and is uncomfortable for the patient. This study explored the equivalency of patient-collected tongue, anterior nares (nasal), and mid-turbinate (MT) samples to health care worker-collected NP samples for detecting SARS-CoV-2. The study looked at a cohort more than 420 patients with respiratory symptoms. The sensitivity for detecting SARS-CoV-2 in patient-collected tongue, nasal, and mid-turbinate samples was 90.7%, 90.9% and 92.9% respectively. Using patient (or clinician) collected nasal swabs has several advantages. First, patients are likely to better tolerate this collection method. NP sampling can cause coughing and sneezing which may be uncomfortable to the patient and increase the risk of aerosol transmission to health care providers. Next, this collection method may reduce personal protective equipment use, which is currently in short supply. Lastly, when testing availability becomes more widespread, patient-acquired samples can be used for epidemiologic purposes and to confirm disease resolution when appropriate. There are other limited data that tongue sampling has reduced sensitivity, therefore until more data become available, nasal and mid-turbinate collections are recommended.

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EDUCATIONAL FORUM

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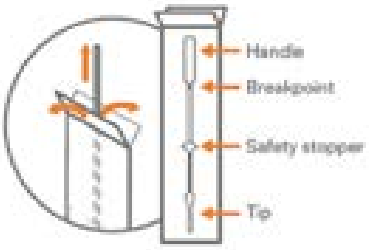
Self-swab nasal specimen collection

Please follow the step-by-step instructions to self-administer your test. Tube the swab and properly place it in the provided bag.

1 Open nasal swab

Remove the nasal swab from the wrapper by pulling the two ends of the wrapper apart like pulling a band aid apart.

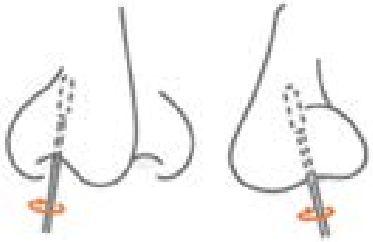
Note: Be careful to only touch the handle not the tip.



2 Swab nose

Gently insert the entire soft tip of the swab into one nostril until you feel a bit of resistance and rub it in a circle around your nostril **4 times.**

Next, gently insert **the same swab** into the other nostril and rub it around the same way.

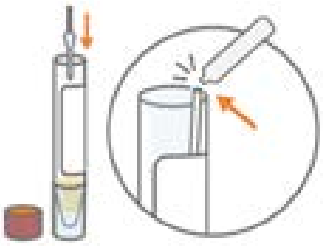


3 Put swab in tube

Lower the swab, tip first, into the provided tube.

Once the tip is at the bottom, break the swab handle at the top of the tube by bending back and forth.

Screw the red cap on tightly and hand it to the clinician in the sealed bag.



See video, **Self-swab Instructions:**

https://uhg.video.uhc.com/media/Self+Swab+instructions/1_e7rq51fx

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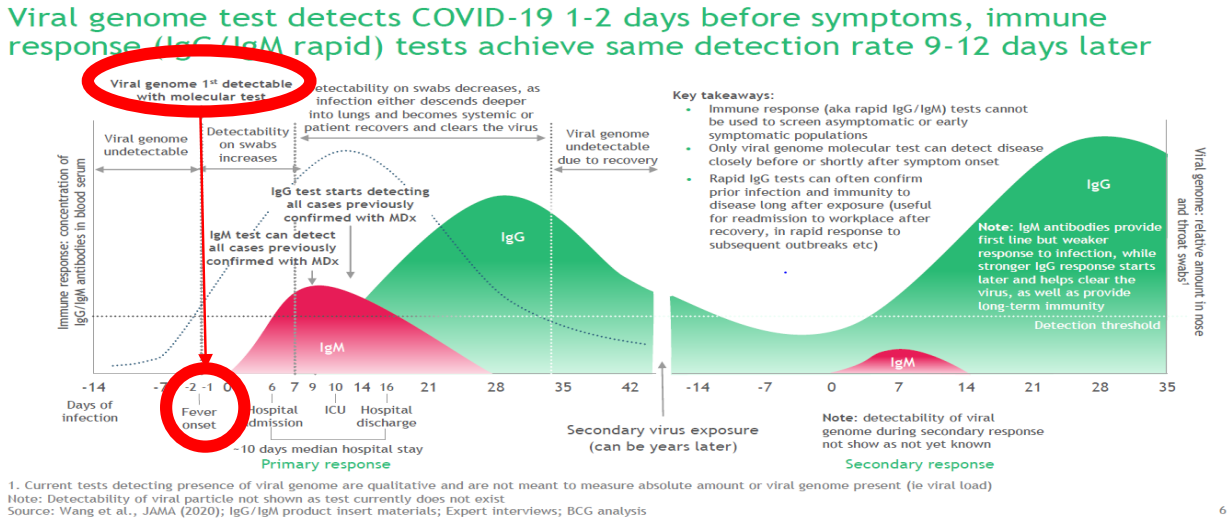
OptumCare COVID-19 testing strategy and IgM/IgG response curves

Understanding the timeline from disease onset to positivity of various tests helps define our testing strategy. Our primary test continues to be the viral PCR. Antibody testing is beginning to get a lot of attention. This is important as there are now office-based point-of-care (POC) tests which, although not yet FDA approved, are being marketed as diagnostic tools. As noted on the below graph, because of the lag time from disease onset to positivity, the IgM level will not become detectable until day 6–8 of the illness and therefore has no role in the acute diagnosis of COVID infection. IgG antibodies may have a role in confirming immunity which may have implications on the timing of the return to work of the health care workforce after an infection. If the pandemic becomes prolonged, confirming immunity may have implications for discontinuing social isolation in these individuals. Also below are the Infectious Disease Society of America (IDSA) recommendations for testing which are in alignment with the OptumCare strategy. In our current environment of limited testing supplies, only Tier 1 and 2 patients should be tested using the PCR methodology. Given unlimited testing supplies, testing could be liberalized to Tier 3 when clinically appropriate and Tier 4 when part of an ongoing epidemiologic study.



IDSA definitions

Tier 1
Critically ill patients receiving ICU level care
Individuals with fever or signs/symptoms of a lower respiratory tract illness who are also immunosuppressed
Individuals with fever or signs/symptoms of a lower respiratory tract illness who are critical to pandemic response, including health care workers, public health officials and other essential leaders
Any person, including health care workers, with fever or signs/symptoms of a lower respiratory tract illness and close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset or history of travel
Tier 2
Hospitalized (non-ICU) patients and long-term care residents with unexplained fever and signs/symptoms of a lower respiratory tract illness
Tier 3
Symptomatic patients in outpatient settings with co-morbid conditions including diabetes, COPD, congestive heart failure, age >50, immunocompromised hosts among others. Given limited available data, testing of pregnant women and symptomatic children with similar risk factors for complications is encouraged
Tier 4
Community surveillance as directed by public health and/or infectious diseases authorities

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Pharmacotherapy update including chloroquine and hydroxychloroquine[5]

Randomized clinical trials have been initiated with 8 different drugs ranging from antivirals including neuraminidase inhibitors used for influenza, anti-malarials, protease inhibitors used for HIV infection, and macrolides. To date, one small randomized trial of 30 patients looking at hydroxychloroquine published in a Chinese journal, did not show any evidence of benefit. This is in contrast to two small observational studies which showed potential benefit. The FDA guidance is as follows:

The U.S. Food and Drug Administration has authorized clinicians to prescribe chloroquine and hydroxychloroquine for patients admitted to hospital with COVID-19, despite warnings from scientific advisers that no randomized controlled trial has been conducted to support the drugs' safety and efficacy in this population. In the emergency use authorization issued on March 28, the agency acknowledged that the approval was based on "limited in-vitro and anecdotal clinical data."

Additionally, an article in the BMJ published on April 2, 2020 commented on the small observational French study which apparently showed some promise. However, on closer scrutiny of the data, they noted the following: "The French study was led by Didier Raoult and evaluated 26 patients treated with hydroxychloroquine and 16 control patients, all of whom had tested positive for the virus at baseline. Although Raoult reported the results as positive, he excluded from the analysis six patients in the hydroxychloroquine arm because they had not remained in the study for six days. The reasons for non-completion were that one patient died, three were transferred to the intensive care unit (ICU), and two withdrew. None of the 16 patients in the control group died, withdrew, or needed care in an ICU. Raoult announced that the study was of "great importance," since it showed that "hydroxychloroquine is efficient in clearing viral nasopharyngeal carriage of SARS-CoV-2."

As you can see, to date there are no compelling data suggesting a clinical benefit of the anti-malarials. These are not benign drugs and for those practicing in the outpatient setting, this underscores that they should not be prescribed until there are clear data showing that the potential benefit outweighs the risks of treatment. On the inpatient side, in critically ill patients, there are various protocols nationwide that have been implemented while awaiting the results of controlled clinical trials. The British Medical Journal published an excellent short update of the ongoing drug trials for COVID-19 infections.[6] https://www.bmj.com/content/368/bmj.m1252?=&utm_source=adestra&utm_medium=email&utm_campaign=usage&utm_content=daily&utm_term=text

Myocarditis and cardiomyopathy associated with severe COVID-19 infection[7,8]

In a single center observational cohort study from a hospital in Wuhan province, 416 consecutive patients admitted for COVID-19 infection were followed through hospital discharge. The median age was 64. Twenty percent of the cohort had myocardial injury as defined by elevated troponin levels. These patients were on average 74 years of age, had a higher comorbidity status, and had a significantly higher need for mechanical ventilation (22% vs. 4%). In terms of cardiac markers, the median peak high-sensitivity troponin I was 0.19 compared to <.001, and the median peak N-terminal pro-B-type natriuretic peptide was 1689 compared to 139 in those without cardiac injury. ARDS developed in 58% of patients with myocardial injury compared to 15% in those without. Patients with myocardial injury had higher mortality than those without cardiac injury (51% vs 4.5%). In a second study of 187 hospitalized patients, also from Wuhan, 28% of patients had myocardial injury as measured by troponin and BNP levels. The mortality rate for these individuals was 37% if there was no prior history of CV disease and a striking 69% in those with both myocardial injury and a history of CV disease. In observational studies, it is always difficult to know whether the severity of the underlying COVID-19 infection and subsequent respiratory failure contributed to a secondary myocardial injury or whether there is a direct myocarditis caused by the virus. Very limited autopsy data have shown evidence of an acute myocarditis. Although it will take some time to sort this out, acute cardiomyopathy may contribute to the progressive respiratory failure and increased mortality in the critical care setting and should be recognized and treated when present.

ACE/ARB therapy in patients with COVID-19 infection

This topic has raised questions for many providers. The ACE2 receptor functions as a receptor for SARS viruses. The interaction between the receptor and the SARS viruses could relate to the infectivity of the virus. There are thus concerns about the use of RAAS inhibitors that may alter ACE2 and whether this may be in part responsible for disease virulence in the ongoing COVID-19 pandemic. Unfortunately, data showing the effects of ACE/ARB therapy on lung-specific expression of ACE2 are lacking, but there are not data suggesting a deleterious effect. Looking at this clinically, part of this concern relates to the fact that coexisting conditions treated with ACE/ARB therapy including hypertension, have consistently been reported to be more common among patients with COVID-19 who have had severe illness, been admitted to the intensive care unit, received mechanical ventilation, or died than among patients who have had mild illness. This raises concerns as to whether the medical management of these coexisting conditions, including the use of RAAS inhibitors, may have contributed to the adverse

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health outcomes observed. However, these conditions appear to track closely with advancing age which is emerging as the strongest predictor of COVID-19-related death. Unfortunately, reports to date have not rigorously accounted for age or other key factors that contribute to health as potential confounders in risk prediction.

At the same time, there are data suggesting a possible benefit to ACE/ARB therapy. The infection downregulates ACE2 levels and interferes with its activity, and this may be a factor in increasing tissue destruction in both the lungs and the heart. ACE/ARB therapy therefore could be protective against viral mediated cardiopulmonary tissue damage. There are in fact trials of losartan in infected patients to see whether this might be protective. Additionally, in these more severely infected patients, as noted above, an acute cardiomyopathy may be present, which would benefit from ACE/ARB therapy. When looked at in its totality, the data does not support withdrawal of ACE/ARB therapy in the general population in an attempt to reduce the risk of infection. In the more severely affected elderly patients who may already be on ACE/ARB therapy, the clinical benefits seem to outweigh any potential adverse effects such that withdrawal of therapy would not be indicated.

Anosmia and ageusia in COVID-19 infections[9]

The typical human coronaviruses that cause seasonal URIs have always been associated with taste and smell disturbance in some affected patients, as they can directly affect the nasal smell receptors. It is therefore consistent that COVID-19 would do the same. There are however, a few small reports suggesting that the frequency may be as high as 30% and in some cases may be the first presenting symptom, particularly in milder cases. Since it is the mildly affected patients who may be the largest group causing transmission of the infection, it would make sense to use the same self-isolation recommendations that we are using for mildly infected patients and apply them to those individuals who have sudden loss of taste or smell during the pandemic.

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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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