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COVID–19
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The effects of school closure on population-based COVID-19 transmission and mortality

The debate surrounding schools reopening or staying closed and teaching virtually during the COVID-19 pandemic has become politically charged. Reasonable public policy would balance the known benefits of in-person classroom education with the potential dangers of increased virus spread, but it is not known how — or to what degree — opening schools affects COVID-19 transmission. A recent population-based, observational study[1] assessed the association between school closures and subsequent COVID-19 incidence and mortality. All 50 U.S. states closed schools between March 13 and March 23, 2020. The analyses spanned the period from March 9 to May 7, 2020 and included all states. The following lag times were assumed: 5 days from exposure to symptom onset, with an additional 4 days included for a child to affect an adult, and 7 days from symptom onset to death.

School closures were associated with a significant decline in the adjusted incidence (-62%) and the adjusted mortality (-58%). The states that closed early, when the incidence of COVID-19 was lowest, had the greatest relative changes. Modeling for absolute effects of school closure yielded an estimated 638.7 cases per 100,000 that would have occurred had schools remained open. Additionally, closing school when the incidence of COVID-19 was low in a given state versus high was associated with 128.7 fewer cases per 100,000 over 26 days and 1.5 fewer deaths per 100,000 over 16 days. Extrapolating this mortality reduction to the U.S. population would result in an estimate of almost 10,000 fewer deaths during the study period in the setting where all schools remained closed. Unfortunately, these analyses cannot account for the effects of other policy interventions enacted at the state level such as stay at home and shelter in place orders, restaurant and bar closures, prohibitions of large gatherings, or the general changes in public behavior, all of which likely reduced virus transmission and mortality during the study period. Additionally, poor overall testing rates and changes in testing rates may have had some effect on the incidence data.

Antibody decay after COVID-19 illness

Researchers evaluated IgG antibody levels over time in 34 patients.[2] Thirty-one of the patients (91%) had PCR confirmation of COVID-19 illness. Three patients had clinical illness consistent with COVID-19 and a significant household contact. All patients had mild disease with only two patients requiring low flow oxygen. IgG was detected using an ELISA test. Samples for antibody detection were obtained at a mean time after symptom onset of 37 days (range, 18–65) for the first antibody measurement and a mean time after symptom onset of 86 days (range, 44–119) for the second time point. All patients had detectable IgG antibodies with an average level of 3.48 Log10 ng per milliliter. The half-life of the IgG antibody was 36 days. This rapid decay of IgG is not unexpected following acute infection. Other researchers have also shown low and apparently transient levels of IgG in asymptomatic infection with SARS-CoV-2.[3]

These findings emphasize what we do and don't understand about the immune response to infection with SARS-CoV-2. We know that the majority of persons develop IgG antibody after acute COVID-19 infection.

(continued on page 2)

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However, the CDC is finding 10% of those with PCR positivity for SARS-CoV-2 RNA do not develop detectable IgG antibody (personal communication). We do not know if those with IgG are protected against reinfection through a viral neutralizing effect of the antibody. We do know that convalescent serum neutralizes the infection in cell culture. We also know that with the appearance of antibody viral levels decrease precipitously. We do not fully understand the role of cell-mediated immunity in this infection, however there are case reports of persons infected with the original SARS-CoV having T-cell memory years after infection.

With over 18 million cases worldwide, there are no documented case series of second infections from SARS-CoV-2 infection, so it appears that transient immunity is almost a certainty. How long this immunity will last remains a critically important question. Further studies need to be done to fully characterize and understand the immune response to SARS-CoV-2 infection. This information will be vital in managing the pandemic, designing and administering vaccines and correctly setting public health policy.

Prevalence of SARS-CoV-2 infection among asymptomatic health care workers

Transmission of COVID-19 can occur from infected individuals who are asymptomatic. Accordingly, health care workers who are at high risk of infection could become inadvertent vehicles for transmission. A recent study evaluated the rates of COVID-19 infection among asymptomatic health care workers in Houston, Texas.[4] Nasopharyngeal swabs were collected from 2,872 health care workers in multiple job categories including nursing, technicians, clinicians, therapists, pharmacists, social workers, housekeeping staff, security staff, administrators and research staff from March 11 to April 19, 2020. In all, 3.9% tested positive. Among health care workers with direct patient contact, 5.4% of those who worked in COVID-19 units and 0.6% of those who work in non-COVID-19 units tested positive. This would suggest that regular surveillance testing of asymptomatic hospital staff should be considered among safety measures during the pandemic.

A similar trial is currently being conducted by UnitedHealth Group R&D. The Distance Trial is looking at daily nasal PCR monitoring for 30 days in high risk health care providers working in the inpatient setting or in one of the COVID-19 clinics. Several of our groups are participating and results are anticipated in the fall.

Cardiac MRI findings in patients recovered from COVID-19

Although there are a myriad of clinical consequences as a result of SARS-CoV-2 infection, cardiopulmonary disease is clinically the most important. As our evidence has accumulated, the pulmonary consequences of infection are now better understood. These include a newly recognized form of endotheliopathy with endothelial inflammation and in-situ small vessel thrombosis, as well as a severe alveolitis. The underlying cardiac pathophysiology however, is less well understood. A prospective cohort study was published last week looking at the cardiac MRI findings in 100 patients from Germany who had recently recovered from COVID-19, compared with a group of matched controls.[5] Two thirds of the patient group had been outpatients and one third had been hospitalized, with only two requiring mechanical ventilation. The median time from diagnosis to MRI was 71 days. Seventy percent of the patients still had detectable troponin levels, and in 5% they were significantly elevated. Compared with the healthy controls and risk factor-matched controls, patients recently recovered from COVID-19 had lower left ventricular ejection fraction (EF) and higher left ventricle volumes. Overall, 78% had abnormal MRI findings consistent with ongoing myocardial inflammation, including persistent gadolinium enhancement. Interestingly there was only a small difference between those who were admitted to the hospital and those who were not. Compared with pre-COVID-19 status, 36% of patients reported ongoing shortness of breath and general exhaustion, of whom 25% noted symptoms during less-than-ordinary daily activities, such as household chores. Twelve patients who had an ischemic pattern on MRI and an EF<50% were referred for endomyocardial biopsy, revealing active lymphocytic inflammation with no evidence of persistent viral genome. There were no significant differences in NT-proBNP levels between the patients and the controls. Overall, the findings demonstrate that patients with a relative paucity of preexisting cardiovascular conditions and with mostly home-based recovery had frequent cardiac inflammatory involvement, which was similar to the hospitalized subgroup with regards to severity and extent.

(continued on page 3)

Of concern was the frequency of significant cardiac involvement in outpatients, and the fact that these findings were present at a median of over two months from diagnosis. This suggests that there could be a residual long-term burden of post COVID-19 cardiomyopathy which needs to be studied in greater depth.

NEWS2 shows promise as a quick point of care risk model for predicting COVID-19 hospital outcomes

The ability to more reliably predict in-hospital outcomes for COVID-19 patients could help providers make better data-driven decisions about the need for early hospital admission. The National Early Warning Score 2 (NEWS2) has been widely used as a general, easily calculated risk tool to predict poor in-hospital outcome. The NEWS2 score includes temperature, respiratory rate, systolic blood pressure, pulse, SpO2, oxygen dependence, and consciousness on a multi-point scale. A small prospective study in 66 patients demonstrates its superiority to several other well-known risk scoring methods in predicting ICU admission (n = 7) or mortality (n = 13) in patients hospitalized with COVID-19.[6] In particular, a NEWS2 score of >6 achieved a sensitivity and specificity for ICU admission or death of 80% and 84.3% respectively. Other risk scores evaluated included the quick Sequential Organ Failure Assessment or qSOFA, typically used for early identification of sepsis, the Systemic Inflammatory Response Syndrome (SIRS) criteria, and the CRB-65 score, typically used to stratify risk in individuals with pneumonia. None of these inventories achieved an Area Under the Curve (AUC) better than 0.82 in patients with COVID-19.

NEWS2 probably outperforms qSOFA, SIRS and CRB-65 because it incorporates more nuanced measures of respiratory function (SpO2 and oxygen requirement). Importantly, scoring can be used to help identify patients at home who should be transitioned to hospital care and to add more sensitivity to assessments of symptom deterioration. Several of our groups have started using outpatient pulse oximetry monitoring in order to calculate the full score. Further validation is needed, but based on this early evidence, clinicians using a score for this purpose should select NEWS2 over these other options if feasible.

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(continued on page 4)

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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