New Research

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome


The true incidence of CAPA likely remains unknown as the diagnosis is limited by the lack of standardized diagnostic criteria that rely solely on microbiological data with direct or indirect detection of Aspergillus in respiratory specimens, particularly in clinical conditions with a low pretest probability. A well-designed, multi-center study to determine the optimal diagnostic approach for CAPA is required.


In this cohort study, COVID-19 infection was independently associated with significant mean QTc prolongation at days 5 and 2 of hospitalization compared with day 0. More patients with COVID-19 had QTc of 500 milliseconds or greater compared with patients without COVID-19.

Diagnostics & Screening


Despite lower positive agreement compared with RT-PCR, antigen test positivity had higher agreement with shedding of replication-competent virus. These results suggest that antigen testing could be a useful tool to rapidly identify contagious people at risk for transmitting SARS-CoV-2 during nascent outbreaks and help reduce COVID-19 burden in nursing homes.

4. SARS-CoV-2 detection on self-collected saliva or anterior nasal specimens compared with healthcare personnel-collected nasopharyngeal specimens. CDC COVID-19 Laboratory
Saliva was slightly more sensitive than ANS for SARS-CoV-2 detection by rRT-PCR. Both saliva and ANS reliably detected SARS-CoV-2 among participants with symptoms. Self-collected saliva and ANS offer practical advantages, are preferred by patients, and might be most useful for testing people with COVID-19 symptoms.

Epidemiology & Public Health

5. **Linked Clusters of SARS-CoV-2 Variant B.1.351 — Maryland, January–February 2021.** Feder KA, et al. *MMWR Morb Mortal Wkly Rep* 2021;70:627–631. DOI: [http://dx.doi.org/10.15585/mmwr.mm7017a5](http://dx.doi.org/10.15585/mmwr.mm7017a5)

In January 2021, a SARS-CoV-2 specimen from a Maryland resident was determined to be the B.1.351 variant, first identified in South Africa. Investigation identified two linked clusters of SARS-CoV-2 infection, comprising 17 total patients (two were hospitalized and one died) who did not report recent travel. Four patients’ specimens were sequenced; all were the B.1.351 variant. These were the first identified clusters of B.1.351 in the United States with no link to travel. Completed contact investigations, expanded genetic sequencing, and universal prevention strategies, including vaccination, masking, and distance, might prevent the spread of SARS-CoV-2 variants of concern, including B.1.351.


We identified a low rate of re-infection confirmed by laboratory tests in a large cohort of patients with SARS-CoV-2 infection. Re-infection was identified in 0.7% during follow up of 9,119 patients with SARS-CoV-2 infection. The mean period between two positive tests was 116 ± 21 days. Although re-infection appeared to be milder than primary infection, there was associated mortality.


Our findings showed that flu-vaccination was associated with a significantly reduced likelihood of an ICU admission especially among aged <65 and non-obese patients. Public health promotion of flu-vaccination may help mitigate the overwhelming demand for critical COVID-19 care pending the large-scale availability of COVID-19 vaccines.

Broad reductions in respiratory test positivity and respiratory emergency department visits (excluding COVID-19) occurred during 2020. Interventions for mitigating spread of SARS-CoV-2 likely also reduced transmission of other pathogens.


As of December 6, 2020, 1,185 patients were included in the NACMI registry (230 COVID+ patients, 495 PUIs, and 460 control patients). COVID+ patients were more likely to have minority ethnicity and had a higher prevalence of diabetes mellitus. COVID+ patients were more likely to present with cardiogenic shock but were less likely to receive invasive angiography. Among COVID+ patients who received angiography, 71% received PPCI and 20% received medical therapy. COVID+ patients with STEMI represent a high-risk group of patients with unique demographic and clinical characteristics. PPCI is feasible and remains the predominant reperfusion strategy, supporting current recommendations.


Patients in the Texas cohort (n = 296) were younger, they had a higher BMI, and they had higher rates of diabetes mellitus. In contrast, patients in the New York state cohort (n = 218) had higher rates of coronary artery disease and atrial fibrillation. Pharmacologic circulatory support, mechanical ventilation, and hemodialysis were more frequent in the Texas cohort. In-hospital mortality was similar between the 2 cohorts. Geographical differences, including practice pattern variations and the impact of disease burden on provision of health care, are important for the evaluation of COVID-19 outcomes.


Our findings suggest that contact tracing among PEH should include a location-based approach, along with a person-based approach when resources allow, due to challenges in identifying, locating, and reaching cases among PEH and their contacts through person-based contact tracing efforts alone.


Using data from the CDC, we calculated both crude and age-adjusted COVID-19 mortality rates for the non-Hispanic White and non-Hispanic Black populations in each state. We explored the relationship between a state-level structural racism index and the observed differences in the racial disparities in COVID-19 mortality across states. We explored the potential mediating
effects of disparities in exposure based on occupation, underlying medical conditions, and health care access. The structural racism index was a robust predictor of the observed racial disparities. Structural racism should be considered a root cause of the Black-White disparity in COVID-19 mortality.

http://www.clinicalmicrobiologyandinfection.com/article/S1198743X21001932/pdf
Among 43,103 patients, mean age was 42.9 years; 93.0% of patients were < 65 years old and 61.9% were women. A small proportion of all patients 4.1% experienced clinical worsening. The rate of hospitalisation was 4.0% and 0.1% died. Factors associated with clinical worsening were male sex, older age, obesity and comorbidities such as chronic renal disease or cancer under treatment. Probability of worsening was reduced with anosmia/ageusia.

Among 3,171 nonhospitalized adults who had COVID-19, 69% had one or more outpatient visits during the follow-up period of 28-180-days. Compared with patients without an outpatient visit, a higher percentage of those who did have an outpatient visit were aged ≥50 years, were women, were non-Hispanic Black, and had underlying health conditions. Among adults with outpatient visits, 68% had a visit for a new primary diagnosis, and 38% had a new specialist visit. The presence of diagnoses of COVID-19 and related symptoms in the 28-180 days following acute illness suggests that some nonhospitalized adults, including those with asymptomatic or mild acute illness, likely have continued health care needs months after diagnosis.

Healthcare Delivery & Healthcare Workers

A total of 266 nurses throughout Italy completed the survey. Personal protective equipment was worn for a median duration of 5 hours (range 2-12 hours). While wearing PPE, 92.8% of nurses experienced pain and 77.1% developed device-related pressure injuries, mainly on the nose and forehead. Pain was more frequent among nurses with such injuries. Transparent dressings, emollient cream, and no dressing were associated with development of device-related pressure injury.

SARS-CoV-2 IgG antibodies and prior COVID-19 infection do not appear to offer meaningful protection against COVID-19 recurrence in healthcare workers. Recurrence would impact decisions regarding ongoing healthcare resource utilization. This study can inform considerations for vaccine administration to vulnerable groups.

**Prognosis**


Despite preoperative COVID-19 screening, there remains a risk of COVID infection within 30 days after elective surgery. This risk is increased for patients with a high comorbidity burden and those undergoing neurosurgical procedures. Higher intensity preoperative screening and closer postoperative monitoring is warranted in such patients because they have a significantly elevated risk of postoperative complications.


Among hospitalized COVID-19 patients with abnormal neuroimaging findings, those with ICH had the highest all-cause mortality; however, high mortality rates were also seen among COVID-19 patients with ischemic stroke in the acute/subacute period and leukoencephalopathy in the chronic period.


There is considerable interhospital variation in mortality for critically ill patients with COVID-19, which is mostly explained by hospital-level socioeconomic status, strain, and acute physiologic differences. Individual mortality is driven mostly by patient-level factors.

**Survivorship & Rehabilitation**


A significant proportion of COVID-19 with severe illness experience ongoing symptoms of breathlessness, fatigue, pain, reduced mobility, depression and reduced quality of life at 4-7
months from disease-onset. Symptomatic patients tend to have more residual CXR and LFT abnormalities.

During 31-120 days after an initial COVID-19 inpatient hospitalization, 7.0% of adults experienced at least one of five post-COVID conditions. Among adult outpatients with COVID-19, 7.7% experienced at least one of ten post-COVID conditions. During 31-60 days after an initial outpatient encounter, adults with COVID-19 were 2.8 times as likely to experience acute pulmonary embolism as outpatient control-patients and were also more likely to experience a range of conditions affecting multiple body systems (e.g. nonspecific chest pain, fatigue, headache, and respiratory, nervous, circulatory, and gastrointestinal system symptoms). These findings add to the evidence of late health conditions possibly related to COVID-19 in adults following COVID-19 diagnosis and can inform health care practice and resource planning for follow-up COVID-19 care.

55.4% of patients had some kind of sequelae. The most common symptoms were fatigue (25.3%), sleep disorder (23.2%) and shortness of breath (20.4%). Critical cases were more likely to have cough and hypomnesia than severe cases. Furthermore, women are more likely to have multiple symptoms, fatigue and sleep disorder, whereas critical illness was found as independent risk factor for hypomnesia.

We have included 117 studies with 2669 RP participants after discharge. To date, the causes and risk factors of RP result in discharged patients are not fully understood. High-quality etiological and clinical studies are needed to investigate these issues to further help us to make strategies to control and prevent its occurrence.

The long covid symptom and impact tools, constructed from patients' lived experiences, provide the first validated and reliable instruments for monitoring the symptoms and impact of long covid.

In a cohort of critically ill patients with a high prevalence of thromboembolic events, ET was associated with reduced ICU mortality without an increased burden of haemorrhagic complications. This study suggests ET strategies are safe and associated with favourable outcomes. Whilst full anticoagulation has been questioned for prophylaxis in these patients, our results suggest that there may nevertheless be a role for enhanced / intermediate levels of prophylaxis.


All 100 patients were separated from ECMO: 50 patients survived and 50 patients died. The rate of survival with veno-venous ECMO was 49 of 96 patients (51%), whereas that with veno-arterial ECMO was 1 of 4 patients (25%). Of 50 survivors, 49 have been discharged from the hospital and 1 remains hospitalized at the ECMO-providing hospital. Survivors were generally younger. In the 50 surviving patients, adjunctive therapies while on ECMO included intravenous steroids (26), anti-interleukin-6 receptor blockers (26), convalescent plasma (22), remdesivir (21), hydroxychloroquine (20), and prostaglandin (15). Extracorporeal membrane oxygenation may facilitate salvage and survival of selected critically ill patients with COVID-19. Substantial variation exists in the drug treatment of COVID-19, but ECMO offers a reasonable rescue strategy.


137 patients were assigned to receive camostat mesilate and 68 to placebo. Median time to clinical improvement was 5 days in the camostat group and 5 days in the placebo group. The frequency of adverse events was similar in the two groups. Under this protocol, camostat mesilate treatment was not associated with increased adverse events during hospitalization for Covid-19 and did not affect time to clinical improvement, progression to ICU admission or mortality.

Cumulative high certainty evidence shows that tocilizumab reduces the risk of mechanical ventilation in hospitalized patients with severe COVID-19. Moderate certainty evidence shows that tocilizumab reduces the risk of poor outcome and the risk of secondary infections in hospitalized COVID-19 patients. This review will continuously evaluate the role of tocilizumab in COVID-19 treatment.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00676-0/fulltext

In hospitalised COVID-19 patients with hypoxia and systemic inflammation, tocilizumab improved survival and other clinical outcomes. These benefits were seen regardless of the amount of respiratory support and were additional to the benefits of systemic corticosteroids.

**Transmission / Infection Control**

https://www.bmj.com/content/373/bmj.n949

Hydroxychloroquine prophylaxis has trivial to no effect on hospital admission and mortality, probably increases adverse effects, and probably does not reduce the risk of SARS-CoV-2 infection. Because of serious risk of bias and very serious imprecision, it is highly uncertain whether ivermectin combined with iota-carrageenan and ivermectin alone reduce the risk of SARS-CoV-2 infection. READERS' NOTE: This article is a living systematic review that will be updated to reflect emerging evidence.

**Vaccines / Immunology**


In this case series of 12 patients, all were women, younger than 60 years, and had symptom onset ranging from 6 to 15 days after vaccination requiring hospitalization. Of 11 patients with heparin-platelet factor 4 ELISA heparin-induced thrombocytopenia (HIT) antibody test results, all were positive. At last follow-up, outcomes were death (n = 3), intensive care unit (ICU) care (n = 3), non-ICU hospitalization (n = 2), and discharge to home (n = 4). This case series may inform clinical guidance and investigations into the potential relationship between the Ad26.COV2.S vaccine and CVST with thrombocytopenia.

Five mass vaccination sites reported 64 anxiety-related events, including 17 events of syncope (fainting) after receipt of Janssen COVID-19 vaccine. The reporting rates of syncope to VAERS after Janssen COVID-19 and influenza vaccines (2019–20) were 8.2 and 0.05 per 100,000 doses, respectively. Vaccine providers should be aware of anxiety-related events after vaccination and observe all COVID-19 vaccine recipients for any adverse reactions for at least 15 minutes after vaccine administration.


Over the first 2 months of 2021 vaccination coverage of staff at Hull Teaching Hospitals with BNT162b2 increased from 8.3% to 82.5% and was associated with a significant reduction in symptomatic and asymptomatic SARS-CoV-2 cases. The proportion of positive lateral flow tests from asymptomatic screening was maintained over this period.


These participants are randomized 1:1:1 to receive prime and boost vaccinations of 10 µg or 30 µg BNT162b1 or placebo, given 21 d apart, with equal allocation of younger (aged 18-55 years) and older adults (aged 65-85 years) to each treatment group. Local reactions and systemic events were generally dose dependent, transient and mild to moderate. Fever was the only grade 3 adverse event. In summary, BNT162b1 has an acceptable safety profile and produces high levels of humoral and T cell responses in an Asian population.


Our findings show that the BNT162b2 vaccine can prevent both symptomatic and asymptomatic infection in working-age adults. This cohort was vaccinated when the dominant variant in circulation was B1.1.7 and shows effectiveness against this variant.


Mass roll-out of the first doses of the BNT162b2 mRNA and ChAdOx1 vaccines was associated with substantial reductions in the risk of hospital admission due to COVID-19 in Scotland.
37. **Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination.**

Our data showed differences between the antibody responses raised after the first and second BNT162b2 vaccination, in particular lower frequencies of neutralizing antibodies in the elderly group. This suggests that this population needs to be closely monitored and may require earlier revaccination or an increased vaccine dose to ensure stronger long-lasting immunity and protection against infection.

[https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2779389](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2779389)

During the pivotal phase 3 clinical trials of mRNA COVID-19 vaccines, several cases of facial paralysis were observed in the vaccine groups (7 of 35,654) compared with 1 case among people who received placebo (1 of 35,611). Although a causal relationship could not be established from clinical trials, the US Food and Drug Administration recommended monitoring vaccine recipients for facial paralysis.

[https://pubs.rsna.org/doi/10.1148/radiol.2021210886](https://pubs.rsna.org/doi/10.1148/radiol.2021210886)

Ipsilateral avid axillary lymph node uptake at FDG PET/CT persists in 29% (49 of 169) of patients between 7 to 10 weeks after the second dose of the mRNA-based BNT162b2 COVID-19 vaccination.

40. **Infliximab is associated with attenuated immunogenicity to BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines in patients with IBD.** Kennedy NA et al. *Gut.* 2021 Apr 26:gutjnl-2021-324789. doi: 10.1136/gutjnl-2021-324789.
[https://gut.bmj.com/content/early/2021/04/25/gutjnl-2021-324789](https://gut.bmj.com/content/early/2021/04/25/gutjnl-2021-324789)

Infliximab is associated with attenuated immunogenicity to a single dose of the BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines. Vaccination after SARS-CoV-2 infection, or a second dose of vaccine, led to seroconversion in most patients. Delayed second dosing should be avoided in patients treated with infliximab.

[http://dx.doi.org/10.15585/mmwr.mm7018e1](http://dx.doi.org/10.15585/mmwr.mm7018e1)

Adjusted vaccine effectiveness against COVID-19–associated hospitalization among adults aged ≥65 years was estimated to be 94% for full vaccination and 64% for partial vaccination. These findings are consistent with efficacy determined from clinical trials in the subgroup of adults aged ≥65 years. This multisite U.S. evaluation under real-world conditions suggests that
vaccination provided protection against COVID-19–associated hospitalization among adults aged ≥65 years.

   In a large cohort of US healthcare personnel without prior COVID-19 infection, 94,382 doses of mRNA COVID-19 vaccine were administered to 49,220 individuals. The adjusted vaccine effectiveness following two doses of each of the two available brands of mRNA vaccine exceeded 96%.

   In patients with cancer, one dose of the BNT162b2 vaccine yields poor efficacy. Immunogenicity increased significantly in patients with solid cancer within 2 weeks of a vaccine boost at day 21 after the first dose. These data support prioritisation of patients with cancer for an early (day 21) second dose of the BNT162b2 vaccine.

   Systemic side-effects were reported by 13·5% of individuals after the first dose of BNT162b2, by 22·0% after the second dose of BNT162b2, and by 33·7% after the first dose of ChAdOx1 nCoV-19. Local side-effects were reported by 71·9% of individuals after the first dose of BNT162b2, by 68·5% after the second dose of BNT162b2, and by 58·7% after the first dose of ChAdOx1 nCoV-19. Significant reductions in infection risk were seen starting at 12 days after the first dose, reaching 60% for ChAdOx1 nCoV-19 and 69% for BNT162b2 at 21–44 days and 72% for BNT162b2 after 45–59 days. Systemic and local side-effects after BNT162b2 and ChAdOx1 nCoV-19 vaccination occur at frequencies lower than reported in phase 3 trials. Both vaccines decrease the risk of SARS-CoV-2 infection after 12 days.

**Women & Children**

   Among a total of 853 admissions (426 COVID-19, 138 MIS-C, and 289 asymptomatic SARS-CoV-2) in 814 patients, there were 20 patients with thrombotic events (including 1 stroke). Patients with MIS-C had the highest incidence versus COVID-19 or asymptomatic SARS-CoV-2. In patients with COVID-19 or MIS-C, the majority of thrombotic events (89%) occurred in patients ≥12 years. Patients > 12 years with MIS-C had the highest rate of thrombosis at 19% (9/48).
Notably, 71% of TE that were not present on admission occurred despite thromboprophylaxis. In patients with COVID-19 or MIS-C, hospital mortality was 2.3% (13/564), but was 28% (5/18) in patients with thrombotic events.


In a nationwide cohort of infants in Sweden, maternal SARS-CoV-2 infection in pregnancy was significantly associated with small increases in some neonatal morbidities. Of 88,159 infants 1.6% were delivered by mothers who tested positive for SARS-CoV-2. The proportions of preterm infants were 8.8% among infants of SARS-CoV-2-positive mothers and 5.5% among comparator infants. Maternal SARS-CoV-2 test positivity was significantly associated with admission for neonatal care and with neonatal morbidities such as respiratory distress syndrome. Twenty-one infants (0.90%) of SARS-CoV-2-positive mothers tested positive for SARS-CoV-2 in the neonatal period.


The cohort included 255 neonates with 250 mothers. Of the 255 neonates who were born to mothers with SARS-CoV-2 infection, 225 (88.2%) were tested for SARS-CoV-2 and 5 (2.2%) had positive results during the birth hospitalization. Of the 151 newborns with follow-up data, 28 had nonroutine clinical visits, 7 underwent SARS-CoV-2 testing, and 1 had a positive result. The findings emphasize the importance of both biological and social factors in perinatal SARS-CoV-2 infection outcomes. Newborns exposed to SARS-CoV-2 were at risk for both direct and indirect adverse health outcomes, supporting efforts of ongoing surveillance of the virus and long-term follow-up.


In England, the easing of national lockdown in response to the coronavirus disease 2019 pandemic included the reopening of some primary school years on June 1, 2020. National surveillance did not identify any increase in the year groups attending school. Most children had a severe acute respiratory syndrome coronavirus 2 positive household contact. Hospitalizations for coronavirus disease 2019 were rare, but 2.7% had persistent symptoms 1 month later.

Our study’s findings suggest that children aged 0 to 9 years did not have substantial rates of SARS-CoV-2 infection during school attendance periods, and it may be assumed that they did not have a substantial role in COVID-19 spread either during this period. Therefore, resuming school for this age group when lockdown was released appears to have been safe for them. It is probably safer to resume school attendance for youths aged 10 to 19 years only when the epidemic is under control and after implementation of steps to decrease spread in schools.


In this simulation modeling study of a synthetic US population, in the absence of vaccine availability for children, a targeted approach to rapidly identify silent COVID-19 infections in this age group was estimated to significantly mitigate disease burden. These findings suggest that without measures to interrupt transmission chains from silent infections, vaccination of adults is unlikely to contain the outbreaks in the near term.

**GUIDELINES & CONSENSUS STATEMENTS**

*A guideline to limit indoor airborne transmission of COVID-19.* Bazant MZ, Bush JWM. *Proc Natl Acad Sci* 2021 Apr 27. doi: https://doi.org/10.1073/pnas.2018995118


**FDA / CDC / NIH / WHO Updates**

*CDC - CDC Recommends Use of Johnson & Johnson’s Janssen COVID-19 Vaccine Resume,* updated April 30, 2021

*CDC - Guidance for Operating Youth and Summer Camps During COVID-19*

*CDC - Interim Public Health Recommendations for Fully Vaccinated People* updated April 27, 2021
Commentary


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