New Research
*note, PREPRINTS have not undergone formal peer review

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

Clinical Syndrome

There were 8 patients diagnosed with CVST and COVID-19 during the study period at 7 out of 31 participating centers. The superior sagittal and transverse sinuses were the most common sites for acute CVST formation (6/8, 75%). Median time to onset of focal neurologic deficit from initial COVID-19 diagnosis was 3 days. Median time from onset of COVID-19 symptoms to CVST radiologic diagnosis was 11 days. Mortality was low in this cohort (1/8 or 12.5%). Clinicians should consider the risk of acute CVST in patients positive for COVID-19, especially if neurological symptoms develop.

We found that the severe COVID-19 patients significantly had abdominal pain compared to the non-severe COVID-19 patients by analyzed 609 patients of 4 studies who reported both abdominal pain and COVID-19 severity. However, there was no significant difference in the incidence of diarrhea, nausea, or vomiting between the two groups. Thus, this systematic review and meta-analysis demonstrated that abdominal pain could be characteristic of severe COVID-19 infections.

Diagnostics & Screening

We analyzed feasibility of pooling saliva samples for severe acute respiratory syndrome coronavirus 2 testing and found that sensitivity decreased according to pool size: 5 samples/pool, 7.4% reduction; 10 samples/pool, 11.1%; and 20 samples/pool, 14.8%. When
virus prevalence is >2.6%, pools of 5 require fewer tests; when <0.6%, pools of 20 support screening strategies.


NS samples are more reliable than SS samples and can be an alternative to NPS samples. They can be a useful diagnostic method in the future.


AUTHORS’ CONCLUSIONS: Antigen tests vary in sensitivity. In people with signs and symptoms of COVID-19, sensitivities are highest in the first week of illness when viral loads are higher. The assays shown to meet appropriate criteria, such as WHO’s priority target product profiles for COVID-19 diagnostics, can be considered as a replacement for laboratory-based RT-PCR when immediate decisions about patient care must be made, or where RT-PCR cannot be delivered in a timely manner. Positive predictive values suggest that confirmatory testing of those with positive results may be considered in low prevalence settings. Due to the variable sensitivity of antigen tests, people who test negative may still be infected. Evidence for testing in asymptomatic cohorts was limited. Test accuracy studies cannot adequately assess the ability of antigen tests to differentiate those who are infectious and require isolation from those who pose no risk, as there is no reference standard for infectiousness. A small number of molecular tests showed high accuracy and may be suitable alternatives to RT-PCR. However, further evaluations of the tests in settings as they are intended to be used are required to fully establish performance in practice. Several important studies in asymptomatic individuals have been reported since the close of our search and will be incorporated at the next update of this review. Comparative studies of antigen tests in their intended use settings and according to test operator (including self-testing) are required.

Epidemiology & Public Health


6-92% of a cross-sectional sample of the population of Wuhan developed antibodies against SARS-CoV-2, with 39·8% of this population seroconverting to have neutralising antibodies. Our durability data on humoral responses indicate that mass vaccination is needed to effect herd protection to prevent the resurgence of the epidemic.

In late 2020, several "variants of concern" emerged globally, including the UK variant (B.1.1.7), South Africa variant (B.1.351), Brazil variants (P.1 and P.2), and two related California "variants of interest" (B.1.429 and B.1.427). These variants are believed to have enhanced transmissibility. For the South Africa and Brazil variants, there is evidence that mutations in spike protein permit it to escape from some vaccines and therapeutic monoclonal antibodies. Based on our extensive genome sequencing program involving 20,453 COVID-19 patient samples collected from March 2020 to February 2021, we report identification of all six of these SARS-CoV-2 variants among Houston Methodist Hospital patients residing in the greater metropolitan area.


The SARS-CoV-2 B.1.1.7 variant of concern (VOC) is increasing in prevalence across Europe. Accurate estimation of disease severity associated with this VOC is critical for pandemic planning. We found increased risk of death for VOC compared with non-VOC cases in England (hazard ratio: 1.67; 95% confidence interval: 1.34-2.09; p < 0.0001). Absolute risk of death by 28 days increased with age and comorbidities. This VOC has potential to spread faster with higher mortality than the pandemic to date.


In contrast to wave 1, evidence existed of increased risk of reported SARS-CoV-2 infection and covid-19 outcomes among adults living with children during wave 2. However, this did not translate into a materially increased risk of covid-19 mortality, and absolute increases in risk were small.

10. **Sharing a household with children and risk of COVID-19: a study of over 300 000 adults living in healthcare worker households in Scotland.** Wood R, et al. *Arch Dis Child.* 2021 Mar 18:archdischild-2021-321604. doi: 10.1136/archdischild-2021-321604. [https://adc.bmj.com/content/early/2021/03/17/archdischild-2021-321604](https://adc.bmj.com/content/early/2021/03/17/archdischild-2021-321604)

Between March and October 2020, living with young children was associated with an attenuated risk of any COVID-19 and COVID-19 requiring hospitalisation among adults living in healthcare worker households. There was no evidence that living with young children increased adults' risk of COVID-19, including during the period after schools reopened.
[https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777682](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777682)

In this cohort study of 4638 individuals with a measured vitamin D level in the year before undergoing COVID-19 testing, the risk of having positive results in Black individuals was 2.64-fold greater with a vitamin D level of 30 to 39.9 ng/mL than a level of 40 ng/mL or greater and decreased by 5% per 1-ng/mL increase in level among individuals with a level of 30 ng/mL or greater. There were no statistically significant associations of vitamin D levels with COVID-19 positivity rates in White individuals. These findings suggest that randomized clinical trials to determine whether increasing vitamin D levels to greater than 30 to 40 ng/mL affect COVID-19 risk are warranted, especially in Black individuals.

12. **Minimal SARS-CoV-2 Transmission after Implementation of a Comprehensive Mitigation Strategy at a School — New Jersey, August 20–November 27, 2020.** Volpp KG, et al. *MMWR Morb Mortal Wkly Rep* 2021;70:377–381. DOI: [http://dx.doi.org/10.15585/mmwr.mm7011a2](http://dx.doi.org/10.15585/mmwr.mm7011a2)

Frequent facility-wide SARS-CoV-2 testing in a high school with both residential and commuter students was part of a comprehensive strategy, including universal masking, that reduced in-school SARS-CoV-2 transmission while allowing significant daily on- and off-campus movement. Of 19 cases among faculty and staff members and eight among students, two (7%) were considered to represent on-campus transmission.

[https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243042](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243042)

An increased sustained proportion of COVID-19 incidence is present among children (age 0-19) and young adults (age 20-39) indicating an elevated role in disease spread during the epidemic creating a possible reservoir of disease with spillover risk to more vulnerable older persons and those with comorbid conditions. Media savvy age-appropriate messaging to enhance mitigation compliance among less vulnerable, more mobile and lower priority vaccination age groups will be a continued necessity and priority to reduce overall population incidence.


AUTHORS' CONCLUSIONS: With much of the evidence derived from modelling studies, notably for travel restrictions reducing or stopping cross-border travel and quarantine of travellers, there is a lack of 'real-world' evidence. The certainty of the evidence for most travel-related control measures and outcomes is very low and the true effects are likely to be substantially different from those reported here. Broadly, travel restrictions may limit the spread of disease across national borders. Symptom/exposure-based screening measures at borders on their own are likely not effective; PCR testing at borders as a screening measure likely detects more cases.
than symptom/exposure-based screening at borders, although if performed only upon arrival this will likely also miss a meaningful proportion of cases. Quarantine, based on a sufficiently long quarantine period and high compliance is likely to largely avoid further transmission from travellers. Combining quarantine with PCR testing at borders will likely improve effectiveness. Many studies suggest that effects depend on factors, such as levels of community transmission, travel volumes and duration, other public health measures in place, and the exact specification and timing of the measure. Future research should be better reported, employ a range of designs beyond modelling and assess potential benefits and harms of the travel-related control measures from a societal perspective.


During August 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%. Increases were largest among adults aged 18–29 years and those with less than a high school education.

Healthcare Delivery & Healthcare Workers


The serial interval and the incubation period of COVID-19 in HCWs were shorter than in the general population. Rigorous contact tracing and isolation of infected HCWs could have resulted in shorter serial intervals. Implementation of more stringent in-hospital control measures focussed on transmission between HCWs should be considered.


In our cohort, the absolute risk of testing positive for SARS-CoV-2 after vaccination was 1.19% among health care workers at UCSD and 0.97% among those at UCLA; these rates are higher than the risks reported in the trials of mRNA-1273 vaccine and BNT162b2 vaccine. Possible explanations for this elevated risk include the availability of regular testing for asymptomatic and symptomatic persons at our institutions, a regional surge in infections in Southern California during our vaccination campaigns, and differences in demographic characteristics between the trial participants and the health care workers in our cohort. The health care workers were younger and had an overall higher risk of exposure to SARS-CoV-2 than the participants in the clinical trials.
Prognosis


Our study indicates that frailty is an independent predictor of mortality among patients with COVID-19. Thus, frailty could be a prognostic factor for clinicians to stratify high-risk groups and remind doctors and nurses to perform early screening and corresponding interventions urgently needed to reduce mortality rates in patients infected by SARS-CoV-2.

Survivorship & Rehabilitation


The multi-organ sequelae of COVID-19 beyond the acute phase of infection are increasingly being appreciated as data and clinical experience in this timeframe accrue. It is clear that care for patients with COVID-19 does not conclude at the time of hospital discharge, and interdisciplinary cooperation is needed for comprehensive care of these patients in the outpatient setting. As such, it is crucial for healthcare systems and hospitals to recognize the need to establish dedicated COVID-19 clinics, where specialists from multiple disciplines are able to provide integrated care.


This systematic review suggested that about half of the patients with COVID-19 still had residual abnormalities on chest CT and PFT at about 3 months. Further studies with longer follow-up term are warranted.

Therapeutics


Available data show that, in mechanically ventilated patients with COVID-19, respiratory mechanics and MV settings within 24 h from ICU admission are heterogeneous but similar to those reported for "classical" ARDS. However, to date, complete data regarding mechanical properties of respiratory system, optimal setting of MV and the role of rescue treatments for refractory hypoxemia are still lacking in the medical literature.

Optimal thromboprophylactic regimens remain unknown across the spectrum of illness severity of COVID-19. A variety of antithrombotic agents, doses, and durations of therapy are being assessed in ongoing randomized controlled trials (RCTs) that focus on outpatients, hospitalized patients in medical wards, and patients critically ill with COVID-19. This paper provides a perspective of the ongoing or completed RCTs related to antithrombotic strategies used in COVID-19, the opportunities and challenges for the clinical trial enterprise, and areas of existing knowledge, as well as data gaps that may motivate the design of future RCTs.

Rescue therapies exert specific pathophysiological mechanisms, resulting in different effects on systemic and cerebral oxygenation in critically ill COVID-19 patients with ARDS. Cerebral and systemic oxygenation are correlated. The choice of rescue strategy to be adopted should take into account both lung and brain needs.

380 patients were randomly allocated into Favipiravir (193) and Lopinavir/Ritonavir (187) groups in 13 centers. Adding Favipiravir to the treatment protocol did not reduce the number of ICU admissions or intubations or In-hospital mortality compared to Lopinavir/Ritonavir regimen. It also did not shorten time to clinical recovery and length of hospital stay.

Among patients admitted to the ICU with COVID-19, intermediate-dose prophylactic anticoagulation, compared with standard-dose prophylactic anticoagulation, did not result in a significant difference in the primary outcome of a composite of adjudicated venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or mortality within 30 days. These results do not support the routine empirical use of intermediate-dose prophylactic anticoagulation in unselected patients admitted to the ICU with COVID-19.

In this retrospective cohort study colchicine was associated with reduced mortality and accelerated recovery in COVID-19 patients. This support the rationale for current larger randomized controlled trials testing the safety/efficacy profile of colchicine in COVID-19 patients.


In this comparative effectiveness research study of adults hospitalized with COVID-19, receipt of remdesivir was associated with faster clinical improvement in a cohort of predominantly non-White patients. Remdesivir plus corticosteroid administration did not reduce the time to death compared with remdesivir administered alone.


Remdesivir can help improve the clinical outcome of hospitalized patients with COVID-19 and a 5 day regimen, instead of a 10 day regimen, may be sufficient for treatment. Moreover, remdesivir appears as tolerable as other comparators or placebo.


Among patients with COVID-19 and moderate to severe hypoxemia, treatment with helmet noninvasive ventilation, compared with high-flow nasal oxygen, resulted in no significant difference in the number of days free of respiratory support within 28 days. Further research is warranted to determine effects on other outcomes, including the need for endotracheal intubation.

**Transmission / Infection Control**


There is limited to no published data regarding aerosol generation and risk of transmission with nasopharyngeal and oropharyngeal swabs for the detection of SARS-CoV-2. Field experiments to quantify this risk are warranted. Vigilance in adhering to current standards for infection control is suggested.
There was no significant difference in the proportion of patients alive and off oxygen therapy at day 14, although benefit or harm of mavrilimumab therapy in this patient population remains possible given the wide confidence intervals, and larger trials should be completed.

Severe acute respiratory syndrome coronavirus 2 can persist on surfaces, suggesting possible surface-mediated transmission of this pathogen. We found that fomites might be a substantial source of transmission risk, particularly in schools and child daycares. Combining surface cleaning and decontamination with mask wearing can help mitigate this risk.

_Vaccines / Immunology_

The safety of the SARS-CoV-2 mRNA vaccines in patients with rheumatic and musculoskeletal diseases (RMD) on immunomodulatory therapy is unknown because these individuals were largely excluded from the vaccine trials. In this sample of patients with RMD vaccinated against SARS-CoV-2, we observed expected transient local and systemic reactions that were typically mild. There were no allergic reactions requiring epinephrine. The most common adverse events were injection site pain and fatigue. These early, reassuring results may ameliorate concern among patients and provide guidance for rheumatology providers in critical discussions regarding vaccine hesitancy or refusal.

This study found neutralizing activity of infection- and vaccine-elicited antibodies against 4 SARS-CoV-2 variants, including B.1, B.1.1.7, and N501Y. Because neutralization studies measure the ability of antibodies to block virus infection, these results suggest that infection- and vaccine-induced immunity may be retained against the B.1.1.7 variant. As additional variants emerge, neutralizing-antibody responses after infection and vaccination should be monitored.

The results of this study suggest that SARS-CoV-2 viral specific antibody response profiles are distinct in different age groups. Patients aged 19 to 30 years exhibited the lowest IgG levels. Age-targeted strategies for disease screening and management as well as vaccine development may be warranted.


A vigorous, healthy, full-term female was born to a COVID-19 naïve mother who had received a single dose of messenger RNA (mRNA) vaccine for SARS-CoV-2 3 weeks prior to delivery. IgG cord blood antibodies were detected to SARS-CoV-2 at the time of birth. Here, we report the first known case of an infant with SARS-CoV-2 IgG antibodies detectable in cord blood after maternal vaccination.


Variant B.1.1.7, now dominant in the UK, with increased transmission, harbors 9 amino acid changes in the spike, including N501Y in the ACE2 interacting surface. We examine the ability of B.1.1.7 to evade antibody responses elicited by natural SARS-CoV-2 infection or vaccination. We map the impact of N501Y by structure/function analysis of a large panel of well-characterized monoclonal antibodies. B.1.1.7 is harder to neutralize than parental virus, compromising neutralization by some members of a major class of public antibodies through light-chain contacts with residue 501. However, widespread escape from monoclonal antibodies or antibody responses generated by natural infection or vaccination was not observed.

38. **Risk of reinfection after seroconversion to SARS-CoV-2: A population-based propensity-score matched cohort study.** SEROCov-POP study group. *medRxiv PREPRINT.* 2021.03.19.21253889; doi: [https://doi.org/10.1101/2021.03.19.21253889](https://doi.org/10.1101/2021.03.19.21253889)

Seroconversion after SARS-CoV-2 infection confers protection to successive viral contamination lasting at least 8 months. These findings could help global health authorities establishing priority for vaccine allocation.


We examined antibody levels after BNT162b2 mRNA vaccine to spike, receptor binding domain (RBD) and for virus neutralization in 149 NH residents and 111 health care worker controls. SARS-CoV-2-naive NH residents mount antibody responses with nearly 4-fold lower median neutralization titers and half the anti-spike level compared to SARS-CoV-2-naive healthcare workers. By contrast, SARS-CoV-2-recovered vaccinated NH residents had neutralization, anti-spike and anti-RBD titers similar to SARS-CoV-2-recovered vaccinated healthcare workers. NH residents’ blunted antibody responses have important implications regarding the quality and durability of protection afforded by neoantigen vaccines. We urgently need better longitudinal
evidence on vaccine effectiveness specific to NH resident populations to inform best practices for NH infection control measures, outbreak prevention and potential indication for a vaccine boost.

**Women & Children**


We included 42 studies involving 438 548 people who were pregnant. COVID-19 may be associated with increased risks of preeclampsia, preterm birth and other adverse pregnancy outcomes.

**GUIDELINES & CONSENSUS STATEMENTS**


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

CDC - [Information about COVID-19 Vaccines for People with Allergies](https://www.cdc.gov/coronavirus/2019-ncov/vaccines/allergies.html)


**Press Release / Commentary**

*AZD1222 US Phase III trial met primary efficacy endpoint in preventing COVID-19 at interim analysis*

March 22, 2021

*See also: NIAID Statement on AstraZeneca Vaccine*

*AZD1222 US Phase III primary analysis confirms safety and efficacy*

March 25, 2021

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