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

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

Clinical Syndrome


Compared to ARDS patients without COVID-19, patients with COVID-19 had similar lung mechanics, but higher EVLWi and PVPI values from the beginning of the disease. This was associated with worse oxygenation and with more requirement of prone positioning and ECMO. This is compatible with the specific lung inflammation and severe diffuse alveolar damage related to COVID-19. By contrast, patients with COVID-19 had fewer hemodynamic derangement. Eventually, mortality was similar between groups.


147 studies were included in the meta-analysis. The symptoms with the highest prevalence were anosmia, weakness, fatigue, dysgeusia, myalgia, depression, headache, anxiety and altered mental status. Heterogeneity for most clinical manifestations was high. Neurological and neuropsychiatric symptoms of COVID-19 in the pandemic's early phase are varied and common. The neurological and psychiatric academic communities should develop systems to facilitate high-quality methodologies, including more rapid examination of the longitudinal course of neuropsychiatric complications of newly emerging diseases and their relationship to neuroimaging and inflammatory biomarkers.

Epidemiology & Public Health

The study results suggest that reinfections are rare events and patients who have recovered from COVID-19 have a lower risk of reinfection. Natural immunity to SARS-CoV-2 appears to confer a protective effect for at least a year, which is similar to the protection reported in recent vaccine studies. However, the observation ended before SARS-CoV-2 variants began to spread, and it is unknown how well natural immunity to the wild-type virus will protect against variants.


During December 14, 2020-May 1, 2021, disparities in vaccination coverage by SVI increased, especially in large fringe metropolitan (e.g., suburban) and nonmetropolitan counties. By May 1, 2021, vaccination coverage was lower among adults living in counties with the highest overall SVI; differences were most pronounced in large fringe metropolitan and nonmetropolitan counties. Vaccination coverage disparities were largest for two SVI themes: socioeconomic status and household composition and disability. Outreach efforts, including expanding public health messaging tailored to local populations and increasing vaccination access, could help increase vaccination coverage in high-SVI counties.


In this randomized clinical trial, an opt-out framed recruitment strategy increased enrollment into a COVID-19 screening program and increased the overall rate of test completion. This study is limited to a single academic health system. If applied more broadly, the increase of 5.1 percentage points may have substantial implications for uptake. This study is one of the first to examine the effect of default options on enrollment in a COVID-19-related program. These findings could inform other health promotion efforts needed to address the COVID-19 pandemic.


In this cross-sectional study of US local COVID-19 surveillance data, testing named contacts was a high-yield activity for case finding. However, this assessment suggests that contact tracing had suboptimal impact on SARS-CoV-2 transmission, largely because 2 of 3 cases were either not reached for interview or named no contacts when interviewed. These findings are relevant to decisions regarding the allocation of public health resources among the various prevention strategies and for the prioritization of case investigations and contact tracing efforts.

7. **Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre,
https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00090-2/fulltext
In patients admitted to hospital with COVID-19, microbiologically confirmed bacterial infections are rare, and more likely to be secondary infections. Gram-negative organisms and S aureus are the predominant pathogens. The frequency and nature of antimicrobial use are concerning, but tractable targets for stewardship interventions exist.

Patients with end-stage renal disease (ESRD) are at increased risk for COVID-19–associated morbidity and mortality. Based on the national trend in ESRD deaths during the first 7 months of the U.S. COVID-19 pandemic (February 1–August 31, 2020), an estimated 8.7–12.9 excess deaths per 1,000 patients or 6,953–10,316 excess deaths in a population of 798,611 U.S. ESRD patients occurred.

Healthcare Delivery & Healthcare Workers

Medicare FFS costs for COVID-19-related medical care were $6.3 billion; 92.6% of costs were for hospitalizations. The mean hospitalization cost was $21 752, and the mean length of stay was 9.2 days; hospitalization cost and length of stay were higher if the patient needed a ventilator ($49 441 and 17.1 days) or died ($32 015 and 11.3 days). The mean cost per outpatient visit was $164. Patients aged 75 years or older were more likely to be hospitalized, but their hospitalizations were associated with lower costs than for younger patients. Male sex and non-White race/ethnicity were associated with higher probability of being hospitalized and higher medical costs.

Using data from the National Healthcare Safety Network (NHSN), we assessed changes to intensive care unit (ICU) bed capacity during the early months of the COVID-19 pandemic. Changes in capacity varied by hospital type and size. ICU beds increased by 36%, highlighting the pressure placed on hospitals during the pandemic.
Prognosis


The QCovid population-based risk algorithm performed well, showing high levels of discrimination for COVID-19 deaths in men and women for both time periods. QCovid has the potential to be dynamically updated as the pandemic evolves and, therefore, has potential use in guiding national policy.


Data regarding the use of echocardiography on hospitalized, predominantly ICU, COVID-19 patients were retrieved from studies with heterogeneous designs, variable sample sizes, and severity scores. Normal echocardiographic findings were reported in about 50% of subjects, with LVEF usually not affected. Overall, RV dysfunction seems more likely associated with increased mortality.


Inhaled Corticosteroids (ICS) are commonly prescribed to patients with severe COPD and recurrent exacerbations. ICS therapy did not increase COVID-19 related healthcare utilization or mortality outcome in patients with COPD followed at the Cleveland Clinic health system. These findings should encourage clinicians to continue ICS therapy for COPD patients during the COVID-19 pandemic.

Survivorship & Rehabilitation


In this study of 119 survivors, 39% had impaired diffusing capacity during the 1-year follow-up. 42% survivors had abnormal total vital capacity during the 1-year follow-up.

Therapeutics

Tocilizumab therapy improves outcomes of mortality and need for mechanical ventilation, in hospitalized patients with COVID-19 infection compared with standard therapy or placebo. Our findings suggest the efficacy of tocilizumab therapy in hospitalized COVID-19 patients and strengthen the concept that tocilizumab is a promising therapeutic intervention to improve mortality and morbidity in COVID-19 patients.

In adults hospitalized for COVID-19, lopinavir/ritonavir, lopinavir/ritonavir-IFN-β-1a and hydroxychloroquine did not improve the clinical status at day 15, nor SARS-CoV-2 clearance in respiratory tract specimens.

The Seraph® 100 Microbind® Affinity adsorber is an extracorporeal treatment currently being explored as an approach to improve the clinical course and outcome of critically ill patients with COVID-19. On April 17, 2020, the FDA granted emergency use authorization for the Seraph® 100 for use in the context of severe and critical disease, for which effective treatment options are limited. Bacteria and viruses bind to the immobilized heparin on the ultra-high molecular weight polyethylene beads of the Seraph® device in a manner similar to the interaction with heparan sulfate on the cell surface and are thereby removed from the bloodstream. The spike protein of SARS-CoV-2 has been shown to bind to cellular heparan sulfate (and heparin) through its receptor-binding domain, and recent studies suggest the heparin binding of the spike protein is much more pronounced in SARS-CoV-2 than in other coronaviruses. In addition to an anecdotal report a recent multicenter study showed that mortality of COVID-19 patients was much lower (37.7%) in the Seraph 100 treated group compared to a control group.

Among residents and staff in skilled nursing and assisted living facilities, treatment during August-November 2020 with bamlanivimab monotherapy reduced the incidence of COVID-19 infection. Further research is needed to assess preventive efficacy with current patterns of viral strains with combination monoclonal antibody therapy.
Transmission / Infection Control


We provide a resource for healthcare institutions looking at making informed decisions about respirator decontamination. This informed decision making will help to improve infection prevention and control measures, and protect healthcare workers during this crucial time. The overall take home message is that institutions should not reuse respirators unless they have to. In the case of an emergency situation, there are some safe ways to decontaminate them.

Vaccines / Immunology


Our observation suggests that antiS1/S2 antibodies are fairly stable over one year. The few clinical events seem to occur almost only in those patients who had never responded and loss of protection in those who showed poor initial antibody response.


Using serum samples from recipients of either mRNA vaccines or inactivated virus vaccines, we identified that several VOCs, such as B.1.1.7 and B.1.429, were effectively neutralised despite the presence of RBD mutations, whereas other circulating VOCs bearing the E484K mutation exhibited substantially reduced neutralisation by sera from vaccinated individuals. Our findings underscore the need for enhanced viral surveillance and assessment of currently authorised vaccine effectiveness against emerging variants, especially in the presence of E484K.


There are concerns about neutralizing antibodies potency against SARS-CoV-2 variants. Despite decreased NAb titers elicited by BNT162b2-vaccine against VOC202012/01 and 501Y.V2 strains, 28/29 healthcare workers had a NAb titer ≥1:10. In contrast, six months after COVID-19 mild-forms, only 9/15 (60%) of HCW displayed detectable NAbs against 501Y.V2 strain.

This case of vaccine-induced immune thrombotic thrombocytopenia shows that a good outcome can be obtained even with multiple and life-threatening venous thrombotic lesions. Argatroban and high-dose IV immunoglobulin along with management of severe cerebral venous thrombosis played a major role in this epilogue.

In this cohort study of patients with cancer who were receiving active systemic therapy, 90% of patients exhibited adequate antibody response to the BNT162b2 vaccine, although their antibody titers were significantly lower than those of healthy controls. Further research into the clinical relevance of lower titers and their durability is required. Nonetheless, the data support vaccinating patients with cancer as a high priority, even during therapy.

Neutralizing antibodies in the subjects of an inactivated SARS-CoV-2 vaccine clinical trial showed a decreasing trend over months. An investigation studying the third immunization suggested that the waning of neutralizing antibodies in individuals administered two doses of inactivated vaccine does not mean the disappearance of immunity.

This study of healthcare workers demonstrated that prior COVID-19, but not Long-COVID, was associated with increased risk of AEs following BNT162b2/Pfizer vaccination, although there was no relationship with duration since COVID-19 illness. Women and younger individuals were also more likely to report AEs.

This case series describes a time association between coronavirus disease 2019 vaccine and perimyocarditis in adolescents. All patients were males 16-18 years old, of Jewish descent, who presented with chest pain that began 1-3 days following vaccination. In 6 of the 7 patients, symptoms began following the 2nd dose and in 1 patient following the 1st dose. All cases were
mild and none required cardiovascular or respiratory support. The incidence of perimyocarditis during the vaccination period was elevated in comparison to previous years.

   [https://pediatrics.aappublications.org/content/pediatrics/early/2021/06/02/peds.2021-052478.full.pdf](https://pediatrics.aappublications.org/content/pediatrics/early/2021/06/02/peds.2021-052478.full.pdf)
Myocarditis and myopericarditis after COVID-19 vaccination appear rare. As of May 23, 2021, the CDC reports that 1,560,652 people <18 years of age have completed a two-dose series of COVID-19 vaccine17. Of these, 652, 758 adolescents received their second dose more than fourteen days ago17. Currently, the PfizerBioNTech COVID-19 vaccine is the only COVID-19 vaccine authorized for children <18 years of age in the US. We urge physicians and healthcare providers to consider myocarditis in the evaluation of adolescents and young adults who develop chest pain after COVID-19 vaccination. All cases of myocarditis in patients with recent COVID-19 vaccination should be reported promptly to VAERS.

Resistance represents a major challenge for antibody-based therapy for coronavirus disease 2019 (COVID-19)1-4. Here we engineered an immunoglobulin M (IgM) neutralizing antibody (IgM-14) to overcome the resistance encountered by IgG-based therapeutics. One single intranasal (IN) dose of 0.044 and 0.4 mg/kg IgM-14 confers prophylactic and therapeutic efficacy against SARS-CoV-2 in mice, respectively. IgM-14, but not IgG-14, also confers potent therapeutic protection against the P.1 and B.1.351 variants. IgM-14 exhibits desirable IN pharmacokinetics and safety in rodents. Our results demonstrate that IN administration of an engineered IgM can improve efficacy, reduce resistance, and simplify the prophylactic and therapeutic treatment of COVID-19.

Here, we report interim safety data from the first 288,368 participants who were vaccinated with Ad26.COV2.S in the Sisonke study — an open label, single-group, phase 3b implementation study to monitor the effectiveness of the single-dose Ad26.COV2.S vaccine among 500,000 health care workers in South Africa. Enrollment in the study began on February 17, 2021, and as of April 12, 2021, a total of 288,368 health care workers had received the Ad26.COV2.S vaccine, among whom 5898 (2%) reported adverse events.

COVID-19 adolescent hospitalization rates from COVID-NET peaked at 2.1 per 100,000 in early January 2021, declined to 0.6 in mid-March, and rose to 1.3 in April. Among hospitalized adolescents, nearly one third required intensive care unit admission, and 5% required invasive mechanical ventilation; no associated deaths occurred. Recent increased hospitalization rates in spring 2021 and potential for severe disease reinforce the importance of continued COVID-19 prevention measures, including vaccination and correct and consistent mask wearing among persons not fully vaccinated or when required.


In this retrospective review of children who tested positive by RT-PCR for SARS-CoV-2, the mean Ct was significantly lower in symptomatic children and was lowest in children <5 years of age, indicating that symptomatic children and younger children infected with SARS-CoV-2 may have a higher viral load in the nasopharynx compared to asymptomatic children. Further studies are needed to assess the transmission potential from asymptomatic children.


Antenatal BNT162b2 mRNA vaccination induces a robust maternal humoral response that effectively transfers to the fetus, supporting the role of vaccination during pregnancy.


A vertical transmission in utero cannot be totally excluded. Since in newborns, the disease is often ambiguous with mild or absent symptoms, it is important to define the most efficient joint management for infants born to COVID-19 positive mothers, being aware that the risk of horizontal transmission from a positive mother, when protective measures are applied, does not seem to increase the risk of infection or to affect the development of newborns from birth to first four weeks of life, and encourages the benefits of breastfeeding and skin-to-skin practice.

The key cardiac marker that showed differences between patients with MIS-C/non-severe COVID-19 and between patients with severe/non-severe MIS-C was BNP. Other markers, such as troponin and AST, did not exhibit notable differences in indicating cardiac injury between patients with MIS-C and COVID-19.

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**Commentary**


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