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

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

Clinical Syndrome


   Our findings suggest that ICH is rare among patients hospitalized for COVID-19. While mortality in ICH is typically high, it may be higher than expected in ICH patients with COVID-19. Further studies are needed to determine the risk, predictors, and outcomes of ICH during COVID-19, particularly among patients who are treated with anticoagulation.

Epidemiology & Public Health


   This study found that, similar to the general population, increased age and preexisting health conditions were associated with COVID-19 outcomes for people with IDD receiving residential support services in New York City. As with older adults living in nursing homes, number of residents was also associated with more severe COVID-19 outcomes. Unique to people with IDD was an increased risk of COVID-19 diagnosis for people with Down syndrome.


   By May 1, 2021, 82%, 63%, and 42% of persons aged ≥65, 50-64, and 18-49 years, respectively, had received ≥1 COVID-19 vaccine dose. CDC calculated the rates of COVID-19 cases, emergency department (ED) visits, hospital admissions, and deaths by age group during November 29-December 12, 2020 (prevaccine) and April 18-May 1, 2021. The rate ratios
comparing the oldest age groups (≥70 years for hospital admissions; ≥65 years for other measures) with adults aged 18-49 years were 40%, 59%, 65%, and 66% lower, respectively, in the latter period. These differential declines are likely due, in part, to higher COVID-19 vaccination coverage among older adults, highlighting the potential benefits of rapidly increasing vaccination coverage.


For all regions, seroprevalence was <1.0% in March 2020. New York experienced the biggest increase with peak seroprevalence of 15.8% in May. All other regions experienced modest increases in seroprevalence (1-2% in May-June to 2-4% in July-August). In August, 1.3-5.6 estimated cumulative infections (based on seroprevalence data) per COVID-19 case reported to CDC. Increases in seroprevalence were found in all regions, with the largest increase in New York. Seroprevalence was higher in non-Hispanic Black and Hispanic blood donors than in non-Hispanic White blood donors. SARS-CoV-2 antibody testing of blood donor samples can be used to estimate the seroprevalence in the general population by region and demographic group. The methods derived from the RESPONSE seroprevalence study served as the basis for expanding SARS-CoV-2 seroprevalence surveillance to all 50 states and Puerto Rico.


During the 2-week period ending April 24, 2021, the B.1.1.7 and P.1 variants represented an estimated 66.0% and 5.0% of U.S. SARS-CoV-2 infections, respectively, demonstrating the rise to predominance of the B.1.1.7 variant of concern (VOC) and emergence of the P.1 VOC in the United States.

Healthcare Delivery & Healthcare Workers


HAIs occur in a small proportion of patients hospitalized with COVID-19 and are most often caused by gram-negative and fungal pathogens. Antibiotic resistance is more prevalent with prolonged hospital stays. Antimicrobial stewardship is imperative in this population to minimize unnecessary broad-spectrum antibiotic use.

We report 11 cases of SARS-CoV-2 infection in healthcare workers (HCW) naïve for COVID-19 and seropositive after the second dose of the BNT162b2 mRNA vaccine. Based on voluntary-based surveillance, they tested positive for different strains of SARS-CoV-2, as Spike gene sequencing showed. Five of them reported mild symptoms. Given the risk for SARS-CoV-2 introduction from asymptomatic vaccinees, this case series suggests the need to continue nasopharyngeal screening programs.

**Prognosis**


A total of 398,579 adult patients with cancer were identified from the N3C cohort; 15.9% were COVID-19-positive. COVID-19 positivity was significantly associated with increased risk of all-cause mortality. Among COVID-19-positive patients, age ≥ 65 years, male gender, Southern or Western US residence, an adjusted Charlson Comorbidity Index score ≥ 4, hematologic malignancy, multistumor sites, and recent cytotoxic therapy were associated with increased risk of all-cause mortality. Patients who received recent immunotherapies or targeted therapies did not have higher risk of overall mortality.


Cardio-metabolic disease was a common condition among hospitalized patients with COVID-19, and it was associated with higher risks of in-hospital mortality.


This large study demonstrates a significant association between AKI and all-cause mortality and, for the first time, major adverse cardiovascular events in patients hospitalized with COVID-19.

**Survivorship & Rehabilitation**


Patients recovering from severe COVID-19 requiring invasive mechanical ventilation surviving hospital discharge present with early mild to moderate functional impairment, mildly reduced quality of life from hospital discharge with an overall improvement of mobility, self-care and the ability of performing usual activities, while a worsening of pain and depression/anxiety
symptoms at 6 months and a large proportion of symptoms of post-traumatic distress soon after hospital discharge.


Cardiopulmonary symptoms (35.7% and 28%), especially dyspnoea (22.1% and 15.9%), were the most common reported symptoms at 3-month and 6-month encounters, respectively. Additionally, a large number of patients reported generalised (26.4%) or neuropsychiatric (24.2%) symptoms 6 months after hospitalisation. Patients with severe COVID-19 were more likely to have reduced mobility, reduced independence or a new dialysis requirement in the 6 months after hospitalisation. Patients hospitalised with SARS-CoV-2 infection reported persistent symptoms up to 6 months after diagnosis. These results highlight the long-term morbidity of COVID-19 and its burden on patients and healthcare resources.

**Therapeutics**


This large, multicenter cohort of patients hospitalized with COVID-19, found evidence of rapid dissemination and implementation of anticoagulation strategies, including use of treatment-dose anticoagulation. As only prophylactic-dose anticoagulation was associated with lower 60-day mortality, prophylactic dosing strategies may be optimal for patients hospitalized with COVID-19.


On the 5 day of therapy, PaO2/FiO2 improved significantly in the surfactant group compared to the control group. The inhaled surfactant significantly reduced the need for transfer of patients to intensive care units and invasive mechanical ventilation. Even more, the nebulized surfactant shortened the length of non-invasive ventilation and time spent in hospital in patients suffering from COVID-19-linked ARDS. Our preliminary data provided indications that inhaled surfactant therapy may represent a promising option for patients with COVID-19-associated ARDS. However, larger clinical trials are crucially needed.

In patients hospitalised with COVID-19 and elevated D-dimer concentration, in-hospital therapeutic anticoagulation with rivaroxaban or enoxaparin followed by rivaroxaban to day 30 did not improve clinical outcomes and increased bleeding compared with prophylactic anticoagulation. Therefore, use of therapeutic-dose rivaroxaban, and other direct oral anticoagulants, should be avoided in these patients in the absence of an evidence-based indication for oral anticoagulation.


The 30-d mortality rate of 1694 individuals treated with remdesivir and dexamethasone in addition to SOC was 12.6% compared to 19.7% for 1053 individuals receiving SOC alone. Similarly, progression to MV was reduced. Treatment of moderate to severe COVID-19 during June through December that included remdesivir and dexamethasone was associated with reduced 30-day mortality and need of MV compared to treatment in February through May.


Venous and arterial thromboembolic complications affect 16 and 31–49 per cent of patients hospitalized with COVID-19 and in intensive care units (ICUs) respectively. Of these, 90 per cent have venous thromboembolism. Pulmonary complications can occur in half of surgical patients with COVID-19. These are associated with a 30-day mortality rate of 23.8 per cent. Anticoagulants are used in the prevention and treatment of venous or arterial thromboembolic events. However, adverse events, such as bleeding, may occur, and can have a significant impact on patient care. A Cochrane systematic review was performed to assess the effects of prophylactic anticoagulants for people hospitalized with COVID-19.

Transmission / Infection Control


We compared secondary attack rates in households with B.1.1.7 variant of concern (VOC) versus non-VOC index cases in a matched cohort in Ontario, Canada. The secondary attack rate for VOC index cases was 1.31 times higher than non-VOC index cases. This increase was particularly accentuated for asymptomatic or presymptomatic index cases.

We describe an outbreak due to the same variant in a long term care home in Canada. In this home, 138 of 139 residents were fully vaccinated with BNT162b2, with doses received between January 9th and March 18th, 2021. Of 243 staff, 204 (84%) had received at least one dose of an mRNA vaccine (122 fully vaccinated, and 82 with second dose delayed as part of Canada’s vaccination strategy). In the second week of April, an unvaccinated staff member was diagnosed with COVID-19, due to SARS-CoV-2 variant B.1.351. Over the next 3 weeks, 4 staff members (2 fully vaccinated, 1 single dose, one unvaccinated) and 9 fully vaccinated residents developed COVID-19 due to variant B.1.351. Two unvaccinated staff members had infections due to other variants and 3 had positive tests with concentrations too low to identify lineage. Of the 9 residents infected with B.1.351, 1 was asymptomatic, 1 had symptoms without fever or other indicators of severity, 3 had a febrile cough illness which did not progress, and 4 developed hypoxemia. Of these latter 4, 2 required hospitalization, and 3 (including both hospitalized patients) died. Two of 4 staff were asymptomatic; 2 (1 unvaccinated, 1 single dose) had mild symptoms. Genomic analysis revealed that all B.1.351 genomes were highly related.


To determine vaccine-induced NAb escape by B.1.617.2 and compare activity to previous strains with existing estimates for population-based vaccine efficacy, we carried out an initial analysis of the Legacy study, established in January 2021. Single-dose recipients are likely to be less protected against these SARS-CoV-2 variants. In the longer term, we note that both increased age and time since the second dose of BNT162b2 significantly correlate with decreased NAb activity against B.1.617.2 and B.1.351. Consequently, further booster immunisations of JCVI Priority Groups in the UK and similar groups in other counties, as well as others with lower vaccine-induced NAbTs than the cohort of BNT162b2 recipients studied here (ideally with modified vaccines that induce NAbs that broadly neutralise emerging VOCs) are more likely to be required to maintain the highest levels of NAbs in regions where B.1.617.2 or other equally NAb-resistant strains become prevalent.


In this comparative effectiveness study of a single dose of the BNT162b2 vaccine, results were comparable to that of the phase III randomized clinical trial. Vaccine effectiveness against symptomatic COVID-19 was 54.4%.
We collected and tested a panel of human sera randomly selected from 37 volunteers obtained between 10 and 20 days after the administration of the second dose of BNT162b2. All the serum samples efficiently neutralized SARS-CoV-2 B.1 lineage and all the viral variants.

[https://www.nature.com/articles/s41586-021-03681-2](https://www.nature.com/articles/s41586-021-03681-2)
Our data show that neutralizing antibody responses induced by Ad26.COV2.S were reduced against the B.1.351 and P.1 variants, but functional non-neutralizing antibody responses and T cell responses were largely preserved against SARS-CoV-2 variants. These findings have implications for vaccine protection against SARS-CoV-2 variants of concern.

We describe the response to IVIG therapy in three of the first patients in whom VITT was identified in Canada after the receipt of the ChAdOx1 nCoV-19 vaccine. The patients were between the ages of 63 and 72 years; one was female. At the time of this report, Canada had restricted the use of the ChAdOx1 nCoV-19 vaccine to persons who were 55 years of age or older on the basis of reports that VITT had occurred primarily in younger persons. Two of the patients in our study presented with limb-artery thrombosis; the third had cerebral venous and arterial thrombosis. After the initiation of IVIG, reduced antibody-induced platelet activation in serum was seen in all three patients.

25. **First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland.** Simpson CR et al. *Nat Med.* 2021 Jun 9. doi: https://doi.org/10.1038/s41591-021-01408-4 
[https://www.nature.com/articles/s41591-021-01408-4](https://www.nature.com/articles/s41591-021-01408-4)
A first dose of ChAdOx1 was found to be associated with small increased risks of ITP, with suggestive evidence of an increased risk of arterial thromboembolic and hemorrhagic events. No positive associations were seen between BNT162b2 and thrombocytopenic, thromboembolic and hemorrhagic events.

In this study, vaccination with BNT162b2 reduced infection rates among individuals who underwent screening by frequent SARS-CoV-2 PCR testing. Using a cohort of frequently tested
individuals reduced the indication bias for the PCR testing, which enabled estimation of infection rates.

27. **Community-level evidence for SARS-CoV-2 vaccine protection of unvaccinated individuals.**

Mass vaccination has the potential to curb the current COVID-19 pandemic by protecting individuals who have been vaccinated against the disease and possibly lowering the likelihood of transmission to individuals who have not been vaccinated. Here, by analyzing vaccination records and test results collected during the rapid vaccine rollout in a large population from 177 geographically defined communities, we find that the rates of vaccination in each community are associated with a substantial later decline in infections among a cohort of individuals aged under 16 years, who are unvaccinated. On average, for each 20 percentage points of individuals who are vaccinated in a given population, the positive test fraction for the unvaccinated population decreased approximately twofold. These results provide observational evidence that vaccination not only protects individuals who have been vaccinated but also provides cross-protection to unvaccinated individuals in the community.

28. **BNT162b2-elicited neutralization of B.1.617 and other SARS-CoV-2 variants.**

Here we report that 20 human sera, drawn 2 or 4 weeks after two doses of BNT162b2, neutralize engineered SARS-CoV-2 with a USA-WA1/2020 genetic background (a virus strain isolated in January 2020) and spike glycoproteins from the newly emerged B.1.617.1, B.1.617.2, B.1.618 (all first identified in India) or B.1.525 (first identified in Nigeria) lineages. Geometric mean plaque reduction neutralization titers against the variant viruses, particularly the B.1.617.1 variant, appear lower than the titer against USA-WA1/2020 virus, but all sera tested neutralize the variant viruses at titers of at least 40. The susceptibility of these newly emerged variants to BNT162b2 vaccine-elicited neutralization supports mass immunization as a central strategy to end the COVID-19 pandemic across geographies.

29. **Quantitative SARS-CoV-2 anti-spike responses to Pfizer-BioNTech and Oxford-AstraZeneca vaccines by previous infection status.**

SARS-CoV-2 vaccination leads to detectable anti-spike antibodies in nearly all adult HCWs. Whether differences in response impact vaccine efficacy needs further study.

30. **Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom.**

Overall, COVID-19 vaccination reduced the number of new SARS-CoV-2 infections, with the largest benefit received after two vaccinations and against symptomatic and high viral burden infections, and with no evidence of a difference between the BNT162b2 and ChAdOx1 vaccines.

The reports of delayed large local reactions after the receipt of Covid-19 vaccines included 55 events in BIPOC patients. The reactions were reported in patients who were Asian 5%; of mixed race, which included American Indian–Alaska Native and Native Hawaiian–Pacific Islander 4%; and Black 1%. Six of these patients (11%) were Hispanic. A majority of these delayed large local reactions occurred after the receipt of the first vaccine dose (in 53 patients [96%]) and after the receipt of the mRNA-1273 vaccine (in 47 [85%]). The mean time from vaccination until the onset of the reaction was 8±2 days. Eleven patients (20%) had cutaneous reactions other than at the injection site, such as diffuse itching, hives or other rash, or angioedema.

**Women & Children**


Thirty-seven studies with low-to-moderate risk of bias, reporting on 1,677,858 pregnancies during the pandemic period and 21,028,650 pregnancies during the pre-pandemic period, were included. The COVID-19 pandemic time period may be associated with a reduction in preterm birth; however, referral bias cannot be excluded. There was no difference in stillbirth between pandemic and pre-pandemic period.


In this cohort study, MIS-C was a rare complication associated with SARS-CoV-2 infection. Estimates for population-based incidence and incidence among persons with infection were higher among Black, Hispanic or Latino, and Asian or Pacific Islander persons. Further study is needed to understand variability by race/ethnicity and age group.


This cross-sectional study found a higher risk of severe COVID-19 illness among children with medical complexity and certain underlying conditions, such as type 1 diabetes, cardiac and circulatory congenital anomalies, and obesity. Health care practitioners could consider the potential need for close observation and cautious clinical management of children with these conditions and COVID-19.
Among 204 adolescents who were likely hospitalized primarily for COVID-19 during January 1-March 31, 2021, 31.4% were admitted to an ICU, and 4.9% required invasive mechanical ventilation; there were no associated deaths. During March 1, 2020-April 24, 2021, weekly adolescent hospitalization rates peaked at 2.1 per 100,000 in early January 2021, declined to 0.6 in mid-March, and then rose to 1.3 in April. Cumulative COVID-19-associated hospitalization rates during October 1, 2020-April 24, 2021, were 2.5-3.0 times higher than were influenza-associated hospitalization rates from three recent influenza seasons obtained from the Influenza Hospitalization Surveillance Network. Recent increased COVID-19-associated hospitalization rates in March and April 2021 and the potential for severe disease in adolescents reinforce the importance of continued COVID-19 prevention measures, including vaccination and correct and consistent wearing of masks by persons not yet fully vaccinated or when required by laws, rules, or regulations.

GUIDELINES & CONSENSUS STATEMENTS

Society for Healthcare Epidemiology of America  
Ambulatory Management of Neonates Born to COVID-19-Positive Mothers

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Commentary


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