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

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

Clinical Syndrome


   Thrombosis has emerged as a potentially important feature of COVID-19. Abnormal markers of hypercoagulability have been reported including elevated D-dimer, elevated fibrinogen levels, elevated factor VIII levels, elevated sepsis induced coagulopathy scores, and thrombocytopenia. Early in the pandemic multiple inpatient and autopsy studies suggested the possibility of an increased prevalence of venous thromboembolism (VTE) in COVID-19 patients. A meta-analysis of VTE among COVID-19 inpatients suggested an overall incidence of 17% although comparative data is lacking.


   In hospitalized patients with COVID-19, pericardial effusion is prevalent, but rarely attributable to acute pericarditis. It is associated with myocardial dysfunction and mortality. A limited echocardiographic examination, including left ventricular ejection fraction, tricuspid annular plane systolic excursion, and assessment for pericardial effusion, can contribute to outcome prediction.

Diagnostics & Screening


   A rapid increase in U.S. at-home test use occurred between the SARS-CoV-2 Delta- and Omicron-predominant periods; at-home test use was lower among persons who self-identified as Black, were aged ≥75 years, had lower incomes, and had a high school level education or less. Commonly reported reasons for using at-home tests included exposure concerns and symptoms. COVID-19 testing, including at-home tests, along with prevention measures such as quarantine and isolation when
warranted, wearing a well-fitted mask when recommended after a positive test or known exposure, and staying up to date with vaccination can help reduce the spread of COVID-19. Providing reliable and low-cost or free at-home test kits to underserved populations with otherwise limited access to COVID-19 testing could assist with continued prevention efforts.

**Epidemiology & Public Health**


   By November 2021, after the third wave of severe acute respiratory syndrome coronavirus 2 infections in South Africa, seroprevalence was 60% in a rural community and 70% in an urban community. High seroprevalence before the Omicron variant emerged may have contributed to reduced illness severity observed in the fourth wave.


   Data from the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET) were analyzed to compare COVID-19-associated hospitalization rates among adults aged ≥18 years during B.1.617.2 (Delta; July 1-December 18, 2021) and Omicron (December 19, 2021-January 31, 2022) variant predominance, overall and by race/ethnicity and vaccination status. Hospitalization rates during peak Omicron circulation (January 2022) among unvaccinated adults remained 12 times the rates among vaccinated adults who received booster or additional doses and four times the rates among adults who received a primary series, but no booster or additional dose. The rate among adults who received a primary series, but no booster or additional dose, was three times the rate among adults who received a booster or additional dose. During the Omicron-predominant period, peak hospitalization rates among non-Hispanic Black (Black) adults were nearly four times the rate of non-Hispanic White (White) adults and was the highest rate observed among any racial and ethnic group during the pandemic. Compared with the Delta-predominant period, the proportion of unvaccinated hospitalized Black adults increased during the Omicron-predominant period. All adults should stay up to date with COVID-19 vaccination to reduce their risk for COVID-19-associated hospitalization. Implementing strategies that result in the equitable receipt of COVID-19 vaccinations, through building vaccine confidence, raising awareness of the benefits of vaccination, and removing barriers to vaccination access among persons with disproportionately higher hospitalizations rates from COVID-19, including Black adults, is an urgent public health priority.

**Healthcare Delivery & Healthcare Workers**


   [https://journals.sagepub.com/doi/10.1177/21501319221085374](https://journals.sagepub.com/doi/10.1177/21501319221085374)
To safely manage patients with COVID-19 symptoms all clinics modified operations; 81.3% diverted patients with respiratory symptoms to a telemedicine evaluation, 68.8% diverted these patients to be seen in-person at another location, and 75% made in-clinic changes to maintain safety. The set of operational changes employed by clinics was diverse. To continue to provide routine patient care, all clinics employed telemedicine. Over 80% of clinics had never used telemedicine prior to March 2020. A diverse group of primary care clinics all rapidly implemented a variety of operational adaptations to address patient needs and maintain patient and staff safety at the onset of the COVID-19 pandemic. Telemedicine, together with other measures, provided critical pathways for maintaining delivery of care.


The purpose of this narrative review is to summarize and synthesize evidence comparing measured resting energy expenditure via IC with predicted resting energy expenditure determined via commonly used predictive equations in adult critically ill patients with COVID-19. Five articles met the inclusion criteria for this review. Their results suggest that many critically ill patients with COVID-19 are in a hypermetabolic state, which is underestimated by commonly used predictive equations in the ICU setting. In nonobese patients, energy expenditure appears to progressively increase over the course of ICU admission, peaking at week 3. The metabolic response pattern in patients with obesity is unclear because of conflicting findings. Based on limited evidence published thus far, the most accurate predictive equations appear to be the Penn State equations; however, they still had poor individual accuracy overall, which increases the risk of underfeeding or overfeeding and, as such, renders the equations an unsuitable alternative to IC.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00462-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00462-7/fulltext)

The risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

**FUNDING:** Medical Research Council, UK Research and Innovation, Department of Health and Social Care, National Institute for Health Research, Community Jameel, and Engineering and Physical Sciences Research Council.

Associations of statin use with lower adverse 30-day outcomes are weaker among individuals who tested positive for SARS-CoV-2 compared with individuals without a positive test, indicating that statins do not exert SARS-CoV-2 specific effects.

**Survivorship & Rehabilitation**

10. **Trajectories of Neurologic Recovery 12 Months After Hospitalization for COVID-19: A Prospective Longitudinal Study.** Frontera JA et al. *Neurology*. 2022 Mar 21:10.1212/WNL.0000000000200356. doi: 10.1212/WNL.0000000000200356. [https://n.neurology.org/content/early/2022/03/21/WNL.0000000000200356](https://n.neurology.org/content/early/2022/03/21/WNL.0000000000200356)

At 12-months post-hospitalization for severe COVID, 87% of patients had ongoing abnormalities in functional, cognitive or Neuro-QoL metrics and abnormal cognition persisted in 50% of patients without a prior history of dementia/cognitive abnormality. Only fatigue severity differed significantly between patients with or without neurological complications during index hospitalization. However, significant improvements in cognitive (t-MoCA) and anxiety (Neuro-QoL) scores occurred in 56% and 45% of patients, respectively, between 6- to 12-months. These results may not be generalizable to those with mild/moderate COVID.


In this prospective case-control study, cognitive status at 6 months was worse among survivors of COVID-19, but the overall burden of neuropsychiatric and neurologic signs and symptoms among survivors of COVID-19 requiring hospitalization was comparable with the burden observed among matched survivors hospitalized for non-COVID-19 causes.

**Therapeutics**


In patients with COVID-19-related acute hypoxaemic respiratory failure, awake prone positioning reduced the need for intubation, particularly among those requiring advanced respiratory support and those in ICU settings. Awake prone positioning should be used in patients who have acute hypoxaemic respiratory failure due to COVID-19 and require advanced respiratory support or are treated in the ICU.
Our findings are consistent with the European Medicines Agency's COVID-19 taskforce statement that there is currently insufficient evidence that inhaled corticosteroids are beneficial for people with COVID-19.

In this meta-analysis of 12 trials including 3901 patients, strongyloidiasis prevalence was found to interact with the RR of mortality for ivermectin as a treatment for COVID-19. No evidence was found to suggest ivermectin has any role in preventing mortality among patients with COVID-19 in regions where strongyloidiasis was not endemic.

Among critically ill patients with COVID-19, treatment with an antiplatelet agent, compared with no antiplatelet agent, had a low likelihood of providing improvement in the number of organ support-free days within 21 days.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02735707.

In this cohort study of US adults hospitalized with moderate COVID-19, early aspirin use was associated with lower odds of 28-day in-hospital mortality. A randomized clinical trial that includes diverse patients with moderate COVID-19 is warranted to adequately evaluate aspirin’s efficacy in patients with high-risk conditions.

The SARS-CoV-2 Omicron BA.1 sublineage has been supplanted in many countries by the BA.2 sublineage. BA.2 differs from BA.1 by about 21 mutations in its spike. Here, we first compared the sensitivity of BA.1 and BA.2 to neutralization by 9 therapeutic monoclonal antibodies (mAbs). In contrast to BA.1, BA.2 was sensitive to Cilgavimab, partly inhibited by Imdevimab and resistant to Adintrevimab and Sotrovimab. We then analyzed sera from 29 immunocompromised individuals up to one month after administration of the Ronapreve (Casirivimab and Imdevimab) and/or Evusheld
(Cilgavimab and Tixagevimab) antibody cocktails. All treated individuals displayed elevated antibody levels in their sera, which efficiently neutralized the Delta variant. Sera from Ronapreve recipients did not neutralize BA.1 and weakly inhibited BA.2. Neutralization of BA.1 and BA.2 was detected in 19 and 29 out of 29 Evusheld recipients, respectively. As compared to the Delta variant, neutralizing titers were more markedly decreased against BA.1 (344-fold) than BA.2 (9-fold). We further report 4 breakthrough Omicron infections among the 29 individuals, indicating that antibody treatment did not fully prevent infection. Collectively, BA.1 and BA.2 exhibit noticeable differences in their sensitivity to therapeutic mAbs. Anti-Omicron neutralizing activity of Ronapreve, and to a lesser extent that of Evusheld, is reduced in patients’ sera.


Among non-critically ill patients with hypoxaemia who were admitted to hospital with covid-19, a multifaceted intervention to increase prone positioning did not improve outcomes. However, wide confidence intervals preclude definitively ruling out benefit or harm. Adherence to prone positioning was poor, despite multiple efforts to increase it. Subsequent trials of prone positioning should aim to develop strategies to improve adherence to awake prone positioning.

STUDY REGISTRATION: ClinicalTrials.gov NCT04383613.


To determine optimal quarantine duration, we evaluated time from exposure to diagnosis for 107 close contacts of severe acute respiratory syndrome coronavirus 2 Omicron variant case-patients. Average time from exposure to diagnosis was 3.7 days; 70% of diagnoses were made on day 5 and 99.1% by day 10, suggesting 10-day quarantine.

Vaccines / Immunology


INTERPRETATION: These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that boosting with licensed vaccines might be sufficient to raise neutralising antibody titres to protective levels.


We conclude that the increase in the proportion of BA.2 has not led to a faster spread of the virus; which seems to indicate that the immunity induced by BA.1 infection is effective against BA.2. Further studies are needed to determine the contributions of the vaccine booster and a BA.1 infection to protection against BA.2.


A third Comirnaty® vaccine dose increased SARS-CoV-2-receptor binding domain antibody levels (median of 93-fold) and neutralizing antibody titers against Wuhan-Hu-1 (median, 57-fold), Beta (median, 22-fold), Delta, (median, 43-fold) and Omicron (median, 8-fold) variants, particularly in SARS-CoV-2-naïve individuals, but had a negligible impact on S-reactive T-cell immunity in nursing home residents.


Serum samples obtained from unvaccinated persons after infection with the B.1.1.7 (alpha), B.1.351 (beta), or B.1.617.2 (delta) variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been shown to neutralize the B.1.1.529 (omicron) variant only occasionally.1 Similarly, levels of neutralizing antibodies against the omicron variant are low and only short-lived after one or two doses of a coronavirus disease 2019 (Covid-19) vaccine but are enhanced in persons who have been vaccinated and have also been infected (i.e., those with hybrid immunity) or in vaccinated persons who have received a booster dose.


A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months. ( Funded by BioNTech and Pfizer; C4591031 ClinicalTrials.gov number, NCT04955626. )

Using a case-control design, mRNA vaccine effectiveness (VE) against COVID-19-associated IMV and in-hospital death was evaluated among adults aged ≥18 years hospitalized at 21 U.S. medical centers during March 11, 2021-January 24, 2022. During this period, the most commonly circulating variants of SARS-CoV-2, the virus that causes COVID-19, were B.1.1.7 (Alpha), B.1.617.2 (Delta), and B.1.1.529 (Omicron). Among 1,440 COVID-19 case-patients who received IMV or died, 307 (21%) had received 2 or 3 vaccine doses before illness onset. Among 6,104 control-patients, 4,020 (66%) had received 2 or 3 vaccine doses. Among the 1,440 case-patients who received IMV or died, those who were vaccinated were older (median age = 69 years), more likely to be immunocompromised (40%), and had more chronic medical conditions compared with unvaccinated case-patients (median age = 55 years; immunocompromised = 10%; p<0.001 for both). VE against IMV or in-hospital death was 90% (95% CI = 88%-91%) overall, including 88% (95% CI = 86%-90%) for 2 doses and 94% (95% CI = 91%-96%) for 3 doses, and 94% (95% CI = 88%-97%) for 3 doses during the Omicron-predominant period. COVID-19 mRNA vaccines are highly effective in preventing COVID-19-associated death and respiratory failure treated with IMV. CDC recommends that all persons eligible for vaccination get vaccinated and stay up to date with COVID-19 vaccination.

Women & Children

As of January 27, 2022 over 11.4 million children in the United States (US) have tested positive for COVID-19.1 COVID-19 cases among US children have seen an exponential increase in December 2021 and January 2022. These recent data suggest the omicron (B.1.1.529) variant is more transmissible compared to the delta (B.1.617.2) and alpha (B.1.1.7) variants. These data are particularly troubling as they coincide with school re-openings after the 2021-22 holiday break across the country. Information about the durability of SARS-CoV-2-specific natural immune responses in children is important to inform community-based transmission mitigation and pediatric vaccination strategies, for both current and potential future variants. However, the true incidence and longitudinal presence of natural (not-vaccine induced) antibody response to SARS-CoV-2 infection is not known in the pediatric population due to the high proportion of asymptomatic infection and prioritization of testing for adults and those with severe illness early in the pandemic. This is important information for the field as not all parents can or will choose to vaccinate their child.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2790318
In this cohort study, SARS-CoV-2 infection was associated with increased risk of severe maternal morbidity, preterm birth, and VTE. The study findings inform clinicians and patients about the risk of
perinatal complications associated with SARS-CoV-2 infection in pregnancy and support vaccination of pregnant individuals and those planning conception.


The Omicron (B.1.1.529) variant of SARS-CoV-2 has spread rapidly but appears to cause less severe disease than the Delta (B.1.617.2) variant. During pregnancy, Delta was associated with increased COVID-19 severity, but infections and severity have not been examined during Omicron. We examined infections, illness severity, vaccinations, and early neonatal infections among obstetric patients during the pre-Delta, Delta, and Omicron epochs.


In this population-based study conducted in Sweden and Norway, vaccination against SARS-CoV-2 during pregnancy, compared with no SARS-CoV-2 vaccination during pregnancy, was not significantly associated with an increased risk of adverse pregnancy outcomes. The majority of the vaccinations were with mRNA vaccines during the second and third trimesters of pregnancy, which should be considered in interpreting the findings.


In this population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.


Although 1 in 16 children infected with the SARS-CoV-2 virus experienced moderate or severe illness, the risk of severe disease did not change with the emergence of the Delta variant, despite its high transmissibility.

FDA / CDC / NIH / WHO Updates


News

Moderna - Moderna Announces its COVID-19 Vaccine Phase 2/3 Study in Children 6 Months to Under 6 Years Has Successfully Met Its Primary Endpoint (modernatx.com)

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