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

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

Clinical Syndrome

1. **Antimicrobial resistance in patients with COVID-19: a systematic review and meta-analysis.**
   Although infrequently assessed, antimicrobial resistance is highly prevalent in patients with COVID-19 and bacterial infections. Future research and surveillance assessing the effect of COVID-19 on antimicrobial resistance at the patient and population level are urgently needed.
   FUNDING: WHO.

2. **Acute Cardiac Events During COVID-19-Associated Hospitalizations.**
   Acute cardiac events were common during COVID-19-associated hospitalizations, particularly among patients with underlying cardiac disease, and are associated with severe disease outcomes. Persons at greater risk for experiencing acute cardiac events during COVID-19-associated hospitalizations might benefit from more intensive clinical evaluation and monitoring during hospitalization.

Diagnostics & Screening

   Although the EUA requirement was not consistently met, more investigation is needed to understand how serology and molecular tests are used, including indication and protocol fidelity. Improved data interoperability of test and clinical/demographic data are needed to enable rapid assessment of the real-world performance of in vitro diagnostic tests.

Epidemiology & Public Health

We assessed COVID-19 booster vaccination coverage and reasons for non-receipt using a large, nationally representative survey (June - August, 2022). Booster vaccination coverage was 71.7% among adults, 36.8% among children, and 51.6% among adolescents. Reasons for non-receipt included the belief that it was not necessary and lack of time for vaccination. All eligible individuals should receive the updated booster vaccines as soon as possible to protect against new variants of COVID-19.


As of January 20, 2023, >90% of circulating SARS-CoV-2 variants in the United States, specifically Omicron BQ.1, BQ.1.1, XBB, and XBB.1.5 sublineages, are unlikely to be susceptible to the combined monoclonal antibodies, tixagevimab and cilgavimab (Evusheld) used for preexposure prophylaxis against SARS-CoV-2 infection. The Food and Drug Administration announced on January 26, 2023, that Evusheld is not currently authorized for preexposure prophylaxis against SARS-CoV-2 infection in the United States. It is important that persons who are moderately to severely immunocompromised, those who might have an inadequate immune response to COVID-19 vaccination, and those with contraindications to receipt of COVID-19 vaccines, exercise caution and recognize the need for additional preventive measures (Box). In addition, persons should have a care plan that includes prompt testing at the onset of COVID-19 symptoms and rapid access to antivirals if SARS-CoV-2 infection is detected.


In both analyses, when compared with unvaccinated persons, persons who had received bivalent boosters were provided additional protection against death over monovalent doses or monovalent boosters. Restored protection was highest in older adults. All persons should stay up to date with COVID-19 vaccination, including receipt of a bivalent booster by eligible persons, to reduce the risk for severe COVID-19.

**Healthcare Delivery & Healthcare Workers**


Plain Language Summary: This cross-sectional study examines the death rates among active and nonactive physicians aged 45 to 84 years.
**Prognosis**

   https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-023-08010-8

Critically ill patients with COVID-19 who were concomitantly infected with other respiratory viruses had comparable 30-day mortality to those not concomitantly infected. Further proactive testing and care may be required in the case of co-infection with respiratory viruses and COVID-19. The results of our study need to be confirmed by larger studies.

**Survivorship & Rehabilitation**

   https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2800885

In this prospective cohort study, pre-infection healthy lifestyle was associated with a substantially lower risk of PCC. Future research should investigate whether lifestyle interventions may reduce risk of developing PCC or mitigate symptoms among individuals with PCC or possibly other postinfection syndromes.

    Comment in *Radiology*. 2023 Feb 7;230113.
    https://pubs.rsna.org/doi/10.1148/radiol.222557

Pulmonary function, gas-exchange, exercise capacity, quality-of-life, and 129Xe MRI ventilation defect percent (VDP) improved in participants with post-acute COVID-19 syndrome evaluated at 15-months as compared to 3-months post-infection. VDP measured at 3-months post-infection correlated with improved exercise capacity, whilst treatment with respiratory medication was associated with improved quality-of-life score at 15-months post-infection. Clinical Trial Registration: www.clinicaltrials.gov NCT05014516

   https://journals.lww.com/ajpmr/Abstract/9900/Regular_Exercise_is_Associated_with_Low_Fatigue_176.aspx

Low levels of exercise are an independent risk factor for post-COVID sequelae. Patients who report less exercise have low grip strength, higher levels of fatigue, memory loss, SOB, depression and poorer quality of life.

Lung transplantation offers a safe and effective option for carefully selected patients with end-stage lung disease from prior COVID-19, with short-term and long-term outcomes similar to lung transplant recipients of non-COVID etiology.

**Therapeutics**


COVID-19 convalescent plasma (CCP) is a safe and effective treatment for COVID-19 in immune compromised (IC) patients. IC patients have a higher risk of persistent infection, severe disease and death from COVID-19. Despite the continued clinical use of CCP to treat IC patients, the optimal dose, frequency/schedule, and duration of CCP treatment has yet to be determined, and related best practices guidelines are lacking. A group of individuals with expertise spanning infectious diseases, virology and transfusion medicine was assembled to render an expert opinion statement pertaining to the use of CCP for IC patients. For optimal effect, CCP should be recently and locally collected to match circulating variant. CCP should be considered for the treatment of IC patients with acute and protracted COVID-19; dosage depends on clinical setting (acute vs protracted COVID-19). CCP containing high-titer SARS-CoV-2 antibodies, retains activity against circulating SARS-CoV-2 variants, which have otherwise rendered monoclonal antibodies ineffective.


Awake prone positioning compared with usual care reduces the risk of endotracheal intubation in adults with hypoxemic respiratory failure due to covid-19 but probably has little to no effect on mortality or other outcomes.

**Transmission / Infection Control**


Regulations for measures to protect against SARS-CoV-2 transmission vary widely around the world, with very strict regulations in Germany where respirators (FFP2 or comparable) are often mandatory. The efficiency of respirators, however, depends essentially on the tight facial fit avoiding the bypass of contaminated air via gaps between mask and wearer's face. The facial fit can be verified in a fit test. The aim of this review was to describe the quantitative fit test results depending on the respirator designs. A literature search revealed 29 suitable studies. Of all respirators with circumferential head
straps, three-panel folded dome shaped respirators showed the best fit (80.8% of 4625 fit tests passed), followed by rigid dome shaped respirators (72.4% of 8234 fit tests passed), duckbill shaped respirators (31.6% of 2120 fit tests passed), and coffee filter shaped respirators (30.9% of 3392 fit tests passed). Respirators with ear loops showed very poor tight fit (3.6% of 222 fit tests passed). In four randomized controlled trials, single use respirators were not shown to be superior to surgical masks for the prevention of laboratory-confirmed viral respiratory infections, even when adjusted with a fit test. Therefore, we consider the mandatory use of respirators to be disproportionate and not supported by evidence. Further evidence should be generated, in which scenarios respirators might provide an effective benefit as part of occupational health and safety. For situations with confirmed benefits only high quality disposable respirators with head straps or respiratory protective equipment of higher protective levels should be used.


We found the available evidence base identified through our search processes to be of variable quality. Reporting of sequence generation and allocation concealment were poor in 30% to 50% of studies across the categories of intervention comparisons. Given the nature of the intervention comparison, blinding of treatment allocation after randomisation was rarely achieved. Although blinding of outcome assessment is highly feasible and desirable, most outcomes were assessed by self-reports. Outcomes in some studies were poorly defined, with a lack of clarity as to the possible aetiological agents (bacterial versus viral). Some studies used laboratory-confirmed outcomes, both adding precision and avoiding indirectness by having an accurate outcome measure and lowering the risk of bias (see Table 9 for heterogeneity of trial outcome definitions). We found no evidence of selective reporting of outcomes within the included studies. We believe publication bias is unlikely, as the included studies demonstrated a range of effects, both positive and negative, over all study sizes. The variable quality of the studies hampers drawing any firm conclusions.

**Vaccines / Immunology**


COVID-19 vaccine antigen dose might affect protection against SARS-CoV-2 infection,1, 2 but direct evidence to quantify this effect is absent. We conducted a matched, retrospective, cohort study using a regression discontinuity design3 to emulate a randomised controlled trial in Qatar between Feb 3, 2022, and Nov 8, 2022, to provide a head-to-head, controlled comparison of protection induced by two different antigen doses of the BNT162b2 (Pfizer–BioNTech) vaccine (appendix pp 4–10).

In 2022, we elucidated the characteristics of a variety of newly emerging SARS-CoV-2 omicron subvariants. At the end of 2022, the XBB.1.5 variant, a descendant of XBB.1 that acquired the S:S486P substitution, emerged and is rapidly spreading in the USA, and is the latest variant of concern. Although the features of XBB.1.5 were reported by Yue and colleagues, a comprehensive understanding of the virological characteristics of newly emerging variants is needed for sustained global health. Our epidemic dynamics analysis revealed that the relative effective reproduction number (Re) of XBB.1.5 is 1.2 times greater than that of the parental XBB.1, and XBB.1.5 is outcompeting BQ.1.1, the predominant lineage in the USA as of December, 2022. Our data suggest that XBB.1.5 will rapidly spread worldwide in the near future.


Using spike (S)-gene target presence as a proxy for BA.2 sublineages, including XBB and XBB.1.5, during December 2022–January 2023, the results showed that a bivalent mRNA booster dose provided additional protection against symptomatic XBB/XBB.1.5 infection for at least the first 3 months after vaccination in persons who had previously received 2–4 monovalent vaccine doses.


Small sample sizes have limited prior studies' ability to capture severe COVID-19 outcomes, especially among Ad26.COV2.S vaccine recipients. This study of 18.9 million adults aged ≥18 years assessed relative vaccine effectiveness (rVE) in three recipient cohorts: primary Ad26.COV2.S vaccine and Ad26.COV2.S booster (two Ad26.COV2.S), primary Ad26.COV2.S vaccine and mRNA booster (Ad26.COV2.S+mRNA), two doses of primary mRNA vaccine and mRNA booster (three mRNA). The study analyzed two de-identified datasets linked using privacy-preserving record linkage (PPRL): medical and pharmacy insurance claims and COVID-19 vaccination data from retail pharmacies. It assessed the presence of COVID-19 during January 1-March 31, 2022 in: (1) any claim, (2) outpatient claim, (3) emergency department (ED) claim, inpatient claim, and inpatient claim with intensive care unit (ICU) admission. rVE for each outcome comparing three recipient cohorts (reference: two Ad26.COV2.S doses) was estimated from adjusted Cox proportional hazards models. Compared with two Ad26.COV2.S doses, Ad26.COV2.S+mRNA and three mRNA doses were more effective against all COVID-19 outcomes, including 57% (95% CI: 52-62) and 62% (95% CI: 58-65) rVE against an ED visit; 44% (95% CI: 34-52) and 54% (95% CI: 48-59) rVE against hospitalization; and 48% (95% CI: 22-66) and 66% (95% CI: 53-75) rVE against ICU admission, respectively. This study demonstrated that Ad26.COV2.S + mRNA doses were as good as three doses of mRNA, and better than two doses of Ad26.COV2.S. Vaccination continues to be an important preventive measure for reducing the public health impact of COVID-19.
https://journals.lww.com/greenjournal/Fulltext/9900/Pregnancy_Outcomes_in_Patients_After_Completion_of.683.aspx

In a large retrospective cohort study, receipt of the primary mRNA COVID-19 vaccination series was associated with a lower rate of several adverse pregnancy outcomes, including perinatal death, preterm delivery, neonates with very low birth weight, and NICU admission. Although the decreased rates of perinatal death did not remain significant after propensity score matching, there was evidence of directional benefit for vaccinated patients.

https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(23)00020-2/fulltext

In this RCT, treatment with methylprednisolone in children with PIMS-TS did not significantly affect the length of hospital stay compared with intravenous immunoglobulins. Intravenous methylprednisolone could be an acceptable first-line treatment in children with PIMS-TS.

**FUNDING:** NOMIS Foundation, Vontobel Foundation, and Gaydoul Foundation.

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00491-X/fulltext

In patients who underwent delivery during their ICU stay, maternal outcome deteriorated following delivery among those defined as critical compared with non-critical patients, who improved following delivery. Interventional delivery should be considered for maternal indications before patients deteriorate and require mechanical ventilation.

**FUNDING:** None.

https://www.bmj.com/content/380/bmj-2022-074035

Maternal covid-19 vaccination with a second dose during pregnancy was highly effective against delta and moderately effective against omicron infection and hospital admission in infants during the first six months of life. A third vaccine dose bolstered protection against omicron. Effectiveness for two doses was highest with maternal vaccination in the third trimester, and effectiveness decreased in infants beyond eight weeks of age.
FDA / CDC / NIH / WHO Updates

CDC and FDA Identify Preliminary COVID-19 Vaccine Safety Signal for Persons Aged 65 Years and Older

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