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

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

Clinical Syndrome

SARS-CoV-2 infection is associated with a high prevalence of distal airspace mucus accumulation and increased MUC5B expression in COVID-19 autopsy lungs. HBE culture studies identified roles for EGFR and IL-1R signaling in mucin gene regulation post SARS-CoV-2 infection. These data suggest that time-sensitive mucolytic agents, specific pathway inhibitors, or corticosteroid administration may be therapeutic for COVID-19 lung disease.

In a nationwide cohort of COVID-19 patients supported by ECMO, bleeding incidence was high and associated with mortality. Intracranial hemorrhage incidence was higher than reported for non-COVID patients and carried the highest risk of death. Thrombotic events were less frequent and not associated with mortality. Length of ECMO support was associated with a higher risk of both bleeding and thrombosis, supporting the development of strategies to minimize ECMO duration.

Healthcare Delivery & Healthcare Workers

   [https://www.acpjournals.org/doi/10.7326/L22-0235](https://www.acpjournals.org/doi/10.7326/L22-0235)
This is the 11th and final update alert for a living rapid review on the epidemiology of and risk factors for coronavirus infection in health care workers. Updates were monthly through update alert 7, bimonthly for updates 8 and 9, and then biannual. Searches for this update were done from 25 October 2021 to 24 May 2022 using the same search strategies as the original review.
Survivorship & Rehabilitation


People who have COVID-19 can experience symptoms for months. Studies on long COVID in the population lack representative samples and longitudinal data focusing on new-onset symptoms occurring with COVID while accounting for pre-infection symptoms. We use a sample representing the U.S. community population from the Understanding America Study COVID-19 Survey, which surveyed around 8000 respondents bi-weekly from March 2020 to March 2021. Our final sample includes 308 infected individuals who were interviewed one month before, around the time of, and 12 weeks after infection. About 23% of the sample experienced new-onset symptoms during infection which lasted for more than 12 weeks, and thus can be considered as having long COVID. The most common new-onset persistent symptoms among those included in the study were headache (22%), runny or stuffy nose (19%), abdominal discomfort (18%), fatigue (17%), and diarrhea (13%). Long COVID was more likely among obese individuals (OR = 5.44, 95% CI 2.12-13.96) and those who experienced hair loss (OR = 6.94, 95% CI 1.03-46.92), headache (OR = 3.37, 95% CI 1.18-9.60), and sore throat (OR = 3.56, 95% CI 1.21-10.46) during infection. There was a lack of evidence relating risk to age, gender, race/ethnicity, education, current smoking status, or comorbid chronic conditions. This work provides national estimates of long COVID in a representative sample after accounting for pre-infection symptoms.

Therapeutics


Among patients admitted with mild to moderate COVID-19 infection, additional treatment with aspirin, atorvastatin, or a combination of the two does not prevent clinical deterioration. Trial Registry Number CTRI/2020/07/026791 (http://ctri.nic.in; registered on 25/07/2020).


We recently showed that early administration of Sotrovimab in Omicron-infected patients with very high-risk for progression was associated with a low rate of COVID-19-related hospitalization within one month after treatment administration (3%), and with no death. However, the dominance of the Omicron sublineage BA.2 led health agencies to suspend Sotrovimab emergency use authorizations because of its lower neutralizing ability in vitro compared to BA.1 sublineage. Clinical efficiency of Sotrovimab to prevent COVID-19 related complications in high-risk patients with mild-to-moderate COVID-19 Omicron BA.2 remains unknown. Our aim was to compare the clinical and virological
outcomes of Omicron BA.1 and BA.2-infected patients with mild-to-moderate COVID-19 who received 500 mg of Sotrovimab IV to prevent COVID-19-related complications.

7. **Efficacy and safety of a single dose of casirivimab and imdevimab for the prevention of COVID-19 over an 8-month period: a randomised, double-blind, placebo-controlled trial.**

CAS + IMD is not authorised in any US region as of Jan 24, 2022, because data show that CAS + IMD is not active against omicron-lineage variants. In this study, done before the emergence of omicron-lineage variants, a single subcutaneous 1200 mg dose of CAS + IMD protected against COVID-19 for up to 5 months of community exposure to susceptible strains of SARS-CoV-2 in the pre-exposure prophylaxis setting, in addition to the post-exposure prophylaxis setting that was previously shown.

**FUNDING:** Regeneron Pharmaceuticals, F Hoffmann-La Roche, US National Institute of Allergy and Infectious Diseases, US National Institutes of Health.


Among patients hospitalised with COVID-19 receiving remdesivir and other standard care, tixagevimab-cilgavimab did not improve the primary outcome of time to sustained recovery but was safe and mortality was lower.

**FUNDING:** US National Institutes of Health (NIH) and Operation Warp Speed.

9. **Update to living systematic review on drug treatments for covid-19.** *BMJ.* 2022 Jul 13;378:o1717. doi: 10.1136/bmj.o1717. [https://www.bmj.com/content/378/bmj.o1717](https://www.bmj.com/content/378/bmj.o1717)

In this update, 463 trials enrolling 166,581 patients were included; 267 (57.7%) trials and 89,814 (53.9%) patients are new from the previous iteration. Compared with standard care, three drugs reduced mortality in patients with mostly severe disease with at least moderate certainty: systemic corticosteroids, interleukin-6 receptor antagonists when given with corticosteroids, and Janus kinase inhibitors. Compared with standard care, two drugs probably reduce hospital admission in patients with non-severe disease: nirmatrelvir/ritonavir and molnupiravir. Remdesivir may reduce hospital admission. Only molnupiravir had at least moderate quality evidence of a reduction in time to symptom resolution; several others showed a possible benefit. Several drugs may increase the risk of adverse effects leading to drug discontinuation; hydroxychloroquine probably increases the risk of mechanical ventilation (moderate certainty).

Administration of either tocilizumab or sarilumab was associated with lower 28-day all-cause mortality compared with usual care or placebo. The association is not dependent on the choice of interleukin-6 receptor antagonist.


Corticosteroid in ICU-admitted patients with COVID-19 may be administered based on age, severity, baseline inflammation, and invasive mechanical ventilation. Early administration since symptom onset may prove harmful.


In patients having developed severe COVID-19 pneumonia requiring invasive mechanical ventilation, transdermal nicotine did not significantly reduce day-28 mortality. There is no indication to use nicotine in this situation.

**Transmission / Infection Control**


We report 242 cases of rapid reinfection of <60 days with different or same Omicron sub-variants and have evidence for a second symptomatic course.

**Vaccines / Immunology**


We analysed breakthrough infection patterns, COVID-19-related hospitalisations (ie, hospitalisations of participants who tested positive for COVID-19), and COVID-19-related deaths overall between Feb 17, 2021, and Jan 31, 2022—inclusive of when participants received their first and second doses of Ad26.COV2.S. We also evaluated the frequency and severity of breakthrough infections during the first 78 days during which participants were predominantly exposed to the delta and omicron variants after a single dose of the Ad26.COV2.S vaccine.

Many high-income countries have rapidly pivoted from hard decisions about who may receive COVID-19 vaccines, due to shortages, to equally hard decisions about who must receive them. As lasting containment of COVID-19 remains elusive, many nations—from Costa Rica, to Austria, to Turkmenistan—are turning to vaccination mandates of various kinds. Mandates, however, are controversial in many countries. Austria's proposed mandate for adults, for example, provoked mass protests. Some objectors argue mandates represent undue encroachment on individual liberty. Some other objectors maintain that mandates will not be an effective policy for COVID-19 because many individuals will seek to evade them, and mandates might erode support for other public health measures such as mask wearing.


Findings indicate that adolescent and young adult men are at the highest risk of myocarditis after mRNA vaccination. Use of a Pfizer vaccine over a Moderna vaccine and waiting for more than 30 days between doses might be preferred for this population. Incidence of myocarditis in children aged 5-11 years is very rare but certainty was low. Data for clinical risk factors were very limited. A clinical course of mRNA related myocarditis appeared to be benign, although longer term follow-up data were limited. Prospective studies with appropriate testing (eg, biopsy and tissue morphology) will enhance understanding of mechanism.


In this cohort study of Italian children and adults following SARS-CoV-2 infection different kinetics of SARS-CoV-2 antibodies were found across several age classes of individuals with asymptomatic or mild COVID-19, which could help in optimizing COVID-19 vaccination strategies and prevention policies. This work provides further evidence of sustained immune response in children up to 1 year after primary SARS-CoV-2 infection.

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**GUIDELINES & CONSENSUS STATEMENTS**


**Update to living WHO guideline on drugs for covid-19.** *BMJ.* 2022 Jul 13;378:o1713. doi: 10.1136/bmj.o1713.

FDA / CDC / NIH / WHO Updates

CDC: 2022 SPECIAL REPORT COVID-19 U.S. IMPACT ON ANTIMICROBIAL RESISTANCE

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