

COVID-19 Resource Desk

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New Research

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COVID-19 related publications by Providence caregivers – see [Digital Commons](#)

Clinical Syndrome

1. **Fulminant Myocarditis Following SARS-CoV-2 Infection: JACC Patient Care Pathways.**

Gluckman Ty J, et al. [Providence author]. *J Am Coll Cardiol*. 2022 Mar 29:S0735-1097(22)04559-4. doi: 10.1016/j.jacc.2022.03.346.

<https://www.jacc.org/doi/10.1016/j.jacc.2022.03.346>

See also: **Fulminant Myocarditis Following SARS-CoV-2 Infection: JACC Patient Care Pathways.** Gluckman Ty J, et al. [Providence author]. *JACC Case Rep*. 2022 Mar 29. doi: 10.1016/j.jaccas.2022.03.013.

This case of fulminant myocarditis following SARS-CoV-2 infection highlights many of the severe clinical manifestations that may occur with this condition. Early recognition and implementation of supportive care (e.g., ECLS) in cases such as this is critically important. Close monitoring of these patients after discharge is also paramount, as additional risks (e.g., arrhythmic) may persist.

2. **Cardiac Complications After SARS-CoV-2 Infection and mRNA COVID-19 Vaccination — PCORnet, United States, January 2021–January 2022.** Block JP, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 1 April 2022. DOI: <http://dx.doi.org/10.15585/mmwr.mm7114e1>

Studies have found an increased risk for cardiac complications after SARS-CoV-2 infection and mRNA COVID-19 vaccination, but few have compared these risks. Data from 40 health care systems participating in a large network found that the risk for cardiac complications was significantly higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination for both males and females in all age groups. These findings support continued use of recommended mRNA COVID-19 vaccines among all eligible persons aged ≥5 years.

Epidemiology & Public Health

3. **Association Between SARS-CoV-2 Viral Load in Wastewater and Reported Cases, Hospitalizations, and Vaccinations in Milan, March 2020 to November 2021.** Nattino G, et al. *JAMA*. 2022 Apr 1. doi: 10.1001/jama.2022.4908.

<https://jamanetwork.com/journals/jama/fullarticle/2790911>

Several studies have demonstrated that wastewater surveillance can be used to monitor SARS-CoV-2 incidence.¹⁻³ This surveillance intends to overcome the limitations of traditional surveillance

indicators,⁴ such as the number of positive tests, which depends on test availability and indications, or COVID-19–related hospitalizations, which occur weeks after the spread of SARS-CoV-2 and do not include mild or asymptomatic cases. This study evaluated the association between SARS-CoV-2 load in urban wastewater and surveillance indicators of infection prevalence and severity in Milan, Italy.

4. **SARS-CoV-2 Naturally Acquired Immunity vs. Vaccine-induced Immunity, Reinfections versus Breakthrough Infections: a Retrospective Cohort Study.** Gazit S, et al. *Clin Infect Dis.* 2022 Apr 5:ciac262. doi: 10.1093/cid/ciac262. <https://doi.org/10.1093/cid/ciac262>

SARS-CoV-2-naïve vaccinees had a 13.06-fold increased risk for breakthrough infection with the Delta variant compared to unvaccinated-previously-infected individuals, when the first event (infection or vaccination) occurred during January and February of 2021. The increased risk was significant for symptomatic disease as well. When allowing the infection to occur at any time between March 2020 to February 2021, evidence of waning naturally acquired immunity was demonstrated, though SARS-CoV-2 naïve vaccinees still had a 5.96-fold increased risk for breakthrough infection and a 7.13-fold increased risk for symptomatic disease. Naturally acquired immunity confers stronger protection against infection and symptomatic disease caused by the Delta variant of SARS-CoV-2, compared to the BNT162b2 two-dose vaccine-induced immunity.

5. **Notes from the Field: SARS-CoV-2 Omicron Variant Infection in 10 Persons Within 90 Days of Previous SARS-CoV-2 Delta Variant Infection — Four States, October 2021–January 2022.**

Roskosky M, et al. *MMWR Morb Mortal Wkly Rep* 2022;71:524–526. DOI: <http://dx.doi.org/10.15585/mmwr.mm7114a2>

This study highlights potential limits of infection-induced immunity against novel variants.

Healthcare Delivery & Healthcare Workers

6. **Estimated Health Outcomes and Costs Associated with Use of Monoclonal Antibodies for Prevention or Mitigation of SARS-CoV-2 Infections.** Park M, et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e225750. doi: 10.1001/jamanetworkopen.2022.5750.

<https://doi.org/10.1001/jamanetworkopen.2022.5750>

These findings suggest that in high-income settings, adults aged 60 years and older who are not fully vaccinated should be given priority to receive REGEN-COV for treating recently diagnosed COVID-19, particularly when supply is limited. It should be noted, however, that clinical trials on the use of REGEN-COV as PEP² or for treatment³ were conducted before widespread circulation of the SARS-CoV-2 Delta and Omicron variants; therefore, a limitation of this analysis is that the estimated cost-effectiveness may be influenced if the efficacy of REGEN-COV differs by variant. Care must be taken to prevent the availability of monoclonal antibodies from deterring vaccination, which should remain the preferred means of preventing severe COVID-19.

7. **Implementation of Clinical Practice Guidelines for Hospitalized Patients With COVID-19 in Academic Medical Centers.** HOMERuN COVID-19 Collaborative Group. *JAMA Netw Open.* 2022 Apr 1;5(4):e225657. doi: 10.1001/jamanetworkopen.2022.5657.

<https://doi.org/10.1001/jamanetworkopen.2022.5657>

Our findings demonstrate that AMCs were capable of responding nimbly to emerging data and shifting guidelines, although both overtreatment and experimentation were observed where significant uncertainty persisted. While factors unique to the early pandemic likely shaped this performance, we hope some strategies, such as use of focused multidisciplinary teams and novel information sharing tools, can be harnessed to accelerate the translation of evidence to bedside for COVID-19 and beyond.

8. Clinical Trial Participation and COVID-19: a Descriptive Analysis from the American Heart Association's Get with the Guidelines Registry. Ty J. Gluckman [Providence author]. *Journal of Racial and Ethnic Health Disparities* April, 2022. <https://doi.org/10.1007/s40615-022-01277-8>

As COVID-19 cases begin to decrease in the USA, learning from the pandemic experience will provide insights regarding disparities of care delivery. We sought to determine if specific populations hospitalized with COVID-19 are equally likely to be enrolled in clinical trials. We examined patients hospitalized with COVID-19 at centers participating in the American Heart Association's COVID-19 CVD Registry. The primary outcome was odds of enrollment in a clinical trial, according to sex, race, and ethnicity. Among 14,397 adults hospitalized with COVID-19, 9.5% (n = 1,377) were enrolled in a clinical trial. The proportion of enrolled patients was the lowest for Black patients (8%); in multivariable analysis, female and Black patients were less likely to be enrolled in a clinical trial related to COVID-19 compared to men and other racial groups, respectively. Determination of specific reasons for the disparities in trial participation related to COVID-19 in these populations should be further investigated.

9. Pulse Oximetry for Monitoring Patients with Covid-19 at Home - A Pragmatic, Randomized Trial. Lee KC, et al. *N Engl J Med.* 2022 Apr 6. doi: 10.1056/NEJMc2201541. <https://doi.org/10.1056/nejmc2201541>

Among patients with Covid-19, the addition of home pulse oximetry to remote monitoring did not result in a greater number of days alive and out of the hospital than subjective assessments of dyspnea alone.

Prognosis

10. Incidence, Mortality, and Imaging Outcomes of Atrial Arrhythmias in COVID-19. Jehangir Q, et al. *Am J Cardiol.* 2022 Apr 2:S0002-9149(22)00243-0. doi: 10.1016/j.amjcard.2022.02.051. <https://doi.org/10.1016/j.amjcard.2022.02.051>

In a subset of the patients with COVID-19 for which echocardiographic data were captured, abnormalities were common, including valvular abnormalities (40.9%), right ventricular dilation (29.6%), and elevated pulmonary artery systolic pressure (16.5%); although there was no evidence of a difference in incidence among the 3 groups. In conclusion, new-onset AAs are associated with poor clinical outcomes in patients with COVID-19.

11. Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study. Katsoularis I, et al. *BMJ.* 2022 Apr 6;377:e069590. doi: 10.1136/bmj-2021-069590. <https://doi.org/10.1136/bmj-2021-069590>

The findings of this study suggest that covid-19 is a risk factor for deep vein thrombosis, pulmonary embolism, and bleeding. The rate ratios were highest in patients with critical covid-19 and highest

during the first pandemic wave in Sweden compared with the second and third waves. In the same period, the absolute risk among patients with covid-19 was 0.039% (401 events) for deep vein thrombosis, 0.17% (1761 events) for pulmonary embolism, and 0.101% (1002 events) for bleeding.

Therapeutics

12. **Ruxolitinib in addition to standard of care for the treatment of patients admitted to hospital with COVID-19 (RUXCOVID): a randomised, double-blind, placebo-controlled, phase 3 trial.**

Han MK, et al. *Lancet Rheumatol*. 2022 Mar 29. doi: 10.1016/S2665-9913(22)00044-3.

[https://doi.org/10.1016/s2665-9913\(22\)00044-3](https://doi.org/10.1016/s2665-9913(22)00044-3)

Ruxolitinib 5 mg twice per day showed no benefit in the overall study population. A larger sample is required to determine the clinical importance of trends for increased efficacy in patient subgroups.

13. **Fluvoxamine for Outpatient Management of COVID-19 to Prevent Hospitalization: A Systematic Review and Meta-analysis.** Lee TC, et al. *JAMA Netw Open*. 2022 Apr

1;5(4):e226269. doi: 10.1001/jamanetworkopen.2022.6269.

<https://doi.org/10.1001/jamanetworkopen.2022.6269>

In this systematic review and meta-analysis of data from 3 trials, under a variety of assumptions, fluvoxamine showed a high probability of being associated with reduced hospitalization in outpatients with COVID-19. Ongoing randomized trials are important to evaluate alternative doses, explore the effectiveness in vaccinated patients, and provide further refinement to these estimates. Meanwhile, fluvoxamine could be recommended as a management option, particularly in resource-limited settings or for individuals without access to SARS-CoV-2 monoclonal antibody therapy or direct antivirals.

Vaccines / Immunology

14. **Protection with a Third Dose of mRNA Vaccine against SARS-CoV-2 Variants in Frontline Workers.** HEROES-RECOVER Network Investigators. *N Engl J Med*. 2022 Apr 6. doi:

10.1056/NEJMc2201821. <https://doi.org/10.1056/nejmc2201821>

In this prospective cohort of frontline workers, a third mRNA vaccine dose provided strong (91%) protection against delta infection, similar to the findings of a study showing an effectiveness of 89 to 94% for three doses of mRNA vaccine against medically attended Covid-19 during a period when the delta variant was predominant.⁴ In contrast, our estimate of vaccine effectiveness of 60% for three doses against omicron infection was lower than the corresponding effectiveness of three doses against medically attended Covid-19 (82 to 90%) in the same study. Although in our study a third dose improved protection against omicron infection (relative vaccine effectiveness, 60%), relative protection was much higher against delta infection (86%). Lower vaccine effectiveness against mild or asymptomatic omicron infection is consistent with recent data showing lower protection in the ambulatory care setting and among adults who were tested for SARS-CoV-2 during the periods of circulation of the delta and omicron variants.⁵ Despite indicating a decline in vaccine effectiveness, these results show continued effectiveness against clinically severe outcomes related to both variants.

15. **Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India.**

Khobragade A et al. *Lancet*. 2022 Apr 2;399(10332):1313-1321. doi: 10.1016/S0140-6736(22)00151-9. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(22\)00151-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00151-9/fulltext)

Between Jan 16, and June 23, 2021 (data cutoff), 33 194 individuals were screened, of whom 5241 did not meet screening criteria and 27 703 were enrolled and randomly assigned to receive ZyCoV-D (n=13 851) or placebo (n=13 852). Per-protocol, 81 cases were eligible and included in efficacy analysis (20 of 12 350 in the ZyCoV-D group and 61 of 12 320 in placebo group). The ZyCoV-D vaccine efficacy was found to be 66·6% (95% CI 47·6-80·7). The occurrence of solicited adverse events was similar between the treatment groups (623 [4·49%] in the ZyCoV-D group vs 620 [4·47%] in the placebo group). There were two deaths (one in each group) reported at the data cutoff, neither of which was considered related to the study treatments. In this interim analysis, ZyCoV-D vaccine was found to be efficacious, safe, and immunogenic in a phase 3 trial.

- 16. Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden.** Nordström P, et al. *Lancet Infect Dis*. 2022 Mar 31:S1473-3099(22)00143-8. doi:10.1016/S1473-3099(22)00143-8. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00143-8/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00143-8/fulltext)

The risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals who have survived and recovered from a previous infection remained low for up to 20 months. Vaccination seemed to further decrease the risk of both outcomes for up to 9 months, although the differences in absolute numbers, especially in hospitalisations, were small. These findings suggest that if passports are used for societal restrictions, they should acknowledge either a previous infection or vaccination as proof of immunity, as opposed to vaccination only.

- 17. Effectiveness of CoronaVac, ChAdOx1 nCoV-19, BNT162b2, and Ad26.COV2.S among individuals with previous SARS-CoV-2 infection in Brazil: a test-negative, case-control study.** Cerqueira-Silva T et al. *Lancet Infect Dis*. 2022 Mar 31:S1473-3099(22)00140-2. doi: 10.1016/S1473-3099(22)00140-2. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00140-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00140-2/fulltext)

All four vaccines conferred additional protection against symptomatic infections and severe outcomes among individuals with previous SARS-CoV-2 infection. The provision of a full vaccine series to individuals after recovery from COVID-19 might reduce morbidity and mortality.

- 18. Induction of SARS-CoV-2 neutralizing antibodies by CoronaVac and BNT162b2 vaccines in naïve and previously infected individuals.** Muena NA et al. *EBioMedicine*. 2022 Mar 30;78:103972. doi: 10.1016/j.ebiom.2022.103972. [https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(22\)00156-6/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00156-6/fulltext)

The decay of nAbs titres in previously infected individuals over time indicates that vaccination is needed to boost humoral memory responses. Immunization of naïve individuals with two doses of CoronaVac induced nAbs titres that were significantly lower to that of convalescent patients, and similar to vaccination with one dose of BNT162b2. The real life effectiveness for CoronaVac in Chile was higher than estimated; indicating that lower titres and additional cellular immune responses induced by CoronaVac might afford protection in a highly immunized population. Nevertheless, the lower nAb titre induced by two doses of CoronaVac as compared to the BNT162b2 vaccine in naïve

individuals, highlights the need of booster immunizations over time to maintain protective levels of antibody, particularly with the emergence of new SARS-CoV-2 variants.

19. High failure rate of ChAdOx1-nCoV19 immunization against asymptomatic infection in healthcare workers during a Delta variant surge. Ujjainiya R et al. *Nat Commun.* 2022 Apr 1;13(1):1726. doi: 10.1038/s41467-022-29404-3. <https://www.nature.com/articles/s41467-022-29404-3>

Immunization is expected to confer protection against infection and severe disease for vaccines while reducing risks to unimmunized populations by inhibiting transmission. Here, based on serial serological studies of an observational cohort of healthcare workers, we show that during a Severe Acute Respiratory Syndrome -Coronavirus 2 Delta-variant outbreak in Delhi, 25.3% (95% Confidence Interval 16.9-35.2) of previously uninfected, ChAdOx1-nCoV19 double vaccinated, healthcare workers were infected within less than two months, based on serology. Induction of anti-spike response was similar between groups with breakthrough infection (541 U/ml, Inter Quartile Range 374) and without (342 U/ml, Inter Quartile Range 497), as was the induction of neutralization activity to wildtype. This was not vaccine failure since vaccine effectiveness estimate based on infection rates in an unvaccinated cohort were about 70% and most infections were asymptomatic. We find that while ChAdOx1-nCoV19 vaccination remains effective in preventing severe infections, it is unlikely to be completely able to block transmission and provide herd immunity.

20. Defining the risk of SARS-CoV-2 variants on immune protection. DeGrace MM et al. *Nature.* 2022 Mar 31. doi: 10.1038/s41586-022-04690-5. <https://www.nature.com/articles/s41586-022-04690-5>

The global emergence of many severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants jeopardizes the protective antiviral immunity induced following infection or vaccination. To address the public health threat caused by the increasing SARS-CoV-2 genomic diversity, the National Institute of Allergy and Infectious Diseases (NIAID) within the National Institutes of Health (NIH) established the SARS-CoV-2 Assessment of Viral Evolution (SAVE) program. This effort was designed to provide a real-time risk assessment of SARS-CoV-2 variants potentially impacting transmission, virulence, and resistance to convalescent and vaccine-induced immunity. The SAVE program serves as a critical data-generating component of the United States Government SARS-CoV-2 Interagency Group to assess implications of SARS-CoV-2 variants on diagnostics, vaccines, and therapeutics and for communicating public health risk. Here we describe the coordinated approach used to identify and curate data about emerging variants, their impact on immunity, and effects on vaccine protection using animal models. We report the development of reagents, methodologies, models, and pivotal findings facilitated by this collaborative approach and identify future challenges. This program serves as a template for the response against rapidly evolving pandemic pathogens by monitoring viral evolution in the human population to identify variants that could erode the effectiveness of countermeasures.

21. Effectiveness of BNT162b2 Vaccine Booster against SARS-CoV-2 Infection and Breakthrough Complications, Israel. Glatman-Freedman A, et al. *Emerg Infect Dis.* 2022 Apr 1;28(5). doi: 10.3201/eid2805.220141. https://wwwnc.cdc.gov/eid/article/28/5/22-0141_article

We estimated vaccine effectiveness of the BNT162b2 (Pfizer-BioNTech) booster dose against SARS-CoV-2 infection and reduction of complications (hospitalization, severe disease, and death) among

breakthrough cases in persons in Israel >16 years of age for <20 weeks. VE estimates reached 96.8% (95% CI 96.0%-97.5%) for persons 16-59 years of age and 93.1% (95% CI 91.8%-94.2%) for persons >60 years of age on week 3. VE estimates remained at these levels for 8 weeks in the 16-59 age group and 11 weeks in those >60. A slow decline followed, becoming more pronounced in the last 2-3 weeks of evaluation. Estimates in the last week of evaluation were 77.6% (95% CI 68.4%-84.2%) and 61.3% (52.5%-68.4%) for persons 16-59 years and >60 years. The more pronounced VE decline coincided with rapid increase in Omicron variant activity. Rate reduction of breakthrough complications remained moderate to high throughout the evaluation.

22. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. Bar-On YM, et al. *N Engl J Med.* 2022 Apr 5. doi: 10.1056/NEJMoa2201570. <https://doi.org/10.1056/nejmoa2201570>

Rates of confirmed SARS-CoV-2 infection and severe Covid-19 were lower after a fourth dose of BNT162b2 vaccine than after only three doses. Protection against confirmed infection appeared short-lived, whereas protection against severe illness did not wane during the study period.

23. Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India.

ZyCoV-D phase 3 Study Investigator Group. *Lancet.* 2022 Apr 2;399(10332):1313-1321. doi: 10.1016/S0140-6736(22)00151-9. [https://doi.org/10.1016/s0140-6736\(22\)00151-9](https://doi.org/10.1016/s0140-6736(22)00151-9)

The ZyCoV-D vaccine efficacy was found to be 66.6%. The occurrence of solicited adverse events was similar between the treatment groups (623 [4.49%] in the ZyCoV-D group vs 620 [4.47%] in the placebo group). There were two deaths (one in each group) reported at the data cutoff, neither of which was considered related to the study treatments. In this interim analysis, ZyCoV-D vaccine was found to be efficacious, safe, and immunogenic in a phase 3 trial.

Women & Children

24. Long COVID (post-COVID-19 condition) in children: a modified Delphi process. Stephenson T et al. *Arch Dis Child.* 2022 Apr 1:archdischild-2021-323624. doi: 10.1136/archdischild-2021-323624. <https://adc.bmj.com/content/early/2022/03/31/archdischild-2021-323624>

The research definition, aligned to the clinical case definition of the WHO, is proposed as follows: Post-COVID-19 condition occurs in young people with a history of confirmed SARS-CoV-2 infection, with at least one persisting physical symptom for a minimum duration of 12 weeks after initial testing that cannot be explained by an alternative diagnosis. The symptoms have an impact on everyday functioning, may continue or develop after COVID infection, and may fluctuate or relapse over time. The positive COVID-19 test referred to in this definition can be a lateral flow antigen test, a PCR test or an antibody test.

25. Incidence Rates and Clinical Outcomes of SARS-CoV-2 Infection with the Omicron and Delta Variants in Children Younger Than 5 Years in the US. Wang L, et al. *JAMA Pediatr.* 2022 Apr 1. doi: 10.1001/jamapediatrics.2022.0945.

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2790793>

With the Omicron variant (B.1.1.529), SARS-CoV-2 infections and hospitalizations reached record levels.¹ Children younger than 5 years may be especially vulnerable because they are not eligible for

COVID-19 vaccination.² We examined incidence rates and clinical outcomes of Omicron infection before and after Omicron became the predominant variant in the US.

26. Association of COVID-19 Vaccination During Early Pregnancy with Risk of Congenital Fetal Anomalies. Ruderman RS, et al. *JAMA Pediatr.* 2022 Apr 4. doi:

10.1001/jamapediatrics.2022.0164. <https://doi.org/10.1001/jamapediatrics.2022.0164>

In 3% to 5% of births in the US, neonates are born with structural defects, which are associated with increased infant morbidity, mortality, and billions of dollars in cost. Our findings suggest that COVID-19 vaccination during early pregnancy is not associated with an increased risk of fetal structural anomalies identified with ultrasonography.

GUIDELINES & CONSENSUS STATEMENTS

[Definition, diagnosis, and management of COVID-19-associated pulmonary mucormycosis: Delphi consensus statement from the Fungal Infection Study Forum and Academy of Pulmonary Sciences, India.](#) *Lancet Infect Dis.* 2022 Apr 4:S1473-3099(22)00124-4. doi: 10.1016/S1473-3099(22)00124-4.

FDA / CDC / NIH / WHO Updates

NIH – COVID-19 Treatment Guidelines, [Therapeutic Management of Nonhospitalized Adults With COVID-19.](#) April 1, 2022

Commentary

A Look Back on Leadership Lessons from the Early Days of the COVID-19 Pandemic and What We Can Learn for the Future. Guenser-Onstot Jessica [Providence author]. *J Nurs Adm.* 2022 Apr 1;52(4):197-199. doi: 10.1097/NNA.0000000000001130. <https://doi.org/10.1097/nna.0000000000001130>

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