Providence

COVID-19 Resource Desk

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Prepared by System Library Services Retraction Watch

New Research

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

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

Clinical Syndrome

1. **The associations between COVID-19 diagnosis, type 1 diabetes, and the risk of diabetic ketoacidosis: A nationwide cohort from the US using the Cerner Real-World Data.** Qeadan F, et al. *PLoS One*. 2022 Apr 19;17(4):e0266809. doi: 10.1371/journal.pone.0266809. eCollection 2022. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0266809

COVID-19 diagnosis is associated with significantly increased risk of new-onset T1D, and American Indian/Alaskan Native, Asian/Pacific Islander, and Black populations are disproportionately at risk. In patients with pre-existing T1D, the risk of developing DKA is significantly increased following COVID-19 diagnosis.

2. **SARS-CoV-2 co-infection with influenza viruses, respiratory syncytial virus, or adenoviruses.** Swets MC et al. *Lancet.* 2022 Apr 16;399(10334):1463-1464. doi: 10.1016/S0140-6736(22)00383-X. Epub 2022 Mar 25. https://www.sciencedirect.com/science/article/pii/S014067362200383X

Measures to reduce transmission of SARS-CoV-2 have also been effective in reducing the transmission of other endemic respiratory viruses. As many countries decrease the use of such measures, we expect that SARS-CoV-2 will circulate with other respiratory viruses, increasing the probability of co-infections. The clinical outcome of respiratory viral co-infections with SARS-CoV-2 is unknown.

3. **Multisystem inflammatory syndrome in adults (MIS-A): case finding through systematic review of electronic medical records.** Melgar M et al. *Clin Infect Dis.* 2022 Apr 20:ciac303. doi: 10.1093/cid/ciac303. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac303/6571412

We identified 11 MIS-A cases, none of which were diagnosed by the treatment team, and 5,755 COVID-19 hospitalizations (ratio 1: 523). Compared with patients with COVID-19, patients with MIS-A were more likely to be younger than 50 years and to be non-Hispanic Black persons. Ten patients with MIS-A (90.9%) had at least one underlying medical condition. Two MIS-A patients (18.2%) had a previous episode of laboratory-confirmed COVID-19, occurring 37 and 55 days prior to admission. MIS-A is severe but likely underrecognized complication of SARS-CoV-2 infection. Improved recognition of MIS-A is needed to quantify its burden and identify populations at highest risk.

Epidemiology & Public Health

4. **Rates of COVID-19 Among Unvaccinated Adults with Prior COVID-19.** Samuel Tideman, Bill Wright, Ari Robicsek, et al **[Providence authors].** *JAMA Netw Open.* 2022 Apr 1;5(4):e227650. doi: 10.1001/jamanetworkopen.2022.7650. https://doi.org/10.1001/jamanetworkopen.2022.7650

Among 121 615 patients with more than 10 million days of follow-up, unvaccinated individuals with prior symptomatic COVID-19 had 85% lower risk of acquiring COVID-19 than unvaccinated individuals without prior COVID-19. Prior studies investigating protection against SARS-CoV-2 reinfection found similar results, with protection associated with natural immunity ranging from 80.5% to 100%. This level of protection is similar to that reported for mRNA vaccines. The findings that patients with prior COVID-19 had 88% protection against hospitalization for COVID-19 and 83% protection against COVID-19 not requiring hospitalization suggest that natural immunity was associated with similar protection against mild and severe disease. mRNA vaccines are associated with similar prolonged protection from severe COVID-19 as found in our study, although vaccine-associated protection from mild COVID-19 has been shown to wane at 6 months.

5. **Associations between SARS-CoV-2 variants and risk of COVID-19 hospitalization among confirmed cases in Washington State: a retrospective cohort study.** Hartman Matthew E, et al. **[Providence author]**. *Clin Infect Dis.* 2022 Apr 12:ciac279. doi: 10.1093/cid/ciac279. https://doi.org/10.1093/cid/ciac279

Infection with Alpha, Gamma, or Delta results in a higher hospitalization risk, with vaccination attenuating that risk. Our findings support hospital preparedness, vaccination, and genomic surveillance.

6. **Provisional COVID-19 Age-Adjusted Death Rates, by Race and Ethnicity — United States, 2020–2021.** Truman BI, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 22 April 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7117e2

In 2020, racial and ethnic disparities in COVID-19 age-adjusted death rates (AADR) were reported among U.S. residents. From 2020 to 2021, disparities in AADR ratios from COVID-19 decreased significantly by 14.0%–40.2% for most racial and ethnic groups, including non-Hispanic White persons, who accounted for 59.6%–65.2% of all decedents; and increased nonsignificantly (7.2%) for non-Hispanic Native Hawaiian and other Pacific Islander persons (0.2%–0.3% of all decedents) compared with non-Hispanic multiracial persons. Providing effective preventive interventions, including vaccination and clinical care, to all communities in proportion to their need for these interventions is necessary to reduce racial and ethnic disparities in COVID-19 deaths.

7. **Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21.** COVID-19 Excess Mortality Collaborators. *Lancet.* 2022 Apr 16;399(10334):1513-1536. doi: 10.1016/S0140-6736(21)02796-3. Epub 2022 Mar 10. https://www.sciencedirect.com/science/article/pii/S0140673621027963

The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone. Strengthening death registration systems around the world, long understood to be crucial to global public health strategy, is necessary for improved monitoring of

this pandemic and future pandemics. In addition, further research is warranted to help distinguish the proportion of excess mortality that was directly caused by SARS-CoV-2 infection and the changes in causes of death as an indirect consequence of the pandemic.

8. **Pandemic preparedness and COVID-19: an exploratory analysis of infection and fatality rates, and contextual factors associated with preparedness in 177 countries, from Jan 1, 2020, to Sept 30, 2021.** COVID-19 National Preparedness Collaborators. *Lancet.* 2022 Apr 16;399(10334):1489-1512. doi: 10.1016/S0140-6736(22)00172-6. Epub 2022 Feb 1. https://www.sciencedirect.com/science/article/pii/S0140673622001726

Efforts to improve pandemic preparedness and response for the next pandemic might benefit from greater investment in risk communication and community engagement strategies to boost the confidence that individuals have in public health guidance. Our results suggest that increasing health promotion for key modifiable risks is associated with a reduction of fatalities in such a scenario.

Prognosis

9. **Effect of common maintenance drugs on the risk and severity of COVID-19 in elderly patients.** Fung KW, et al. *PLoS One.* 2022 Apr 18;17(4):e0266922. doi: 10.1371/journal.pone.0266922. eCollection 2022. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0266922

Up to December 2020, our sample contained 374,229 Medicare patients over 65 who were diagnosed with COVID-19. Among the COVID-19 patients, 278,912 (74.6%) were on at least one study drug. The three most common study drugs among COVID-19 patients were statins 187,374 (50.1%), ACEI 97,843 (26.2%) and ARB 83,290 (22.3%). Maintenance use of ACEI, ARB, warfarin, statins, direct factor Xa inhibitors and P2Y12 inhibitors was associated with reduction in risk of acquiring COVID-19 and dying from it.

10. **Comparison of hospitalized COVID-19 and influenza patients requiring supplemental oxygen in a cohort study: clinical impact and resource consumption.** López Montesinos I et al. *Clin Infect Dis.* 2022 Apr 20:ciac314. doi: 10.1093/cid/ciac314. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac314/6571459

Although influenza patients were older and had more comorbidities, COVID-19 cases requiring supplemental oxygen on admission had worse clinical and economic outcomes.

Survivorship & Rehabilitation

11. **Global Prevalence of Post COVID-19 Condition or Long COVID: A Meta-Analysis and Systematic Review.** Chen C, et al. *J Infect Dis.* 2022 Apr 16:jiac136. doi: 10.1093/infdis/jiac136. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac136/6569364

50 studies were included, and 41 were meta-analyzed. Global estimated pooled prevalence of post COVID-19 condition was 0.43. Hospitalized and non-hospitalized patients have estimates of 0.54 and 0.34, respectively. This study finds post COVID-19 condition prevalence is substantial; the health effects of COVID-19 appear to be prolonged and can exert stress on the healthcare system.

12. **Persistent symptoms after the first wave of COVID-19 in relation to SARS-CoV-2 serology and experience of acute symptoms: A nested survey in a population-based cohort.** Robineau O et al. *Lancet Reg Health Eur*. 2022 Jun;17:100363. doi: 10.1016/j.lanepe.2022.100363. Epub 2022 Apr 12. https://www.sciencedirect.com/science/article/pii/S2666776222000564

A greater risk of persistent dysgeusia/anosmia, dyspnea and asthenia was observed in SARS-CoV-2 infected people. The initial clinical presentation substantially drives the association of positive serological test results with persistent symptoms.

Therapeutics

13. **Add-on Prostaglandin E1 in Venovenous Extracorporeal Membrane Oxygenation: A Randomized, Double-blind, Placebo-controlled Pilot Trial.** Buchtele N et al. *Am J Respir Crit Care Med.* 2022 Apr 15. doi: 10.1164/rccm.202110-2359OC. https://www.atsjournals.org/doi/10.1164/rccm.202110-2359OC

Add-on treatment with PGE1 was safe but did not meet the primary endpoint of reducing the rate of red blood cell transfusions in patients on venovenous ECMO. Larger studies need to evaluate the safety and efficacy of additional PGE1 in ECMO. Clinical trial registration available at www.

14. **Pre-exposure anti-SARS-CoV-2 monoclonal antibodies in severely immunocompromised patients with immune-mediated inflammatory diseases.** Goulenok T, et al. *Lancet Rheumatol.* 2022 Apr 11. doi: 10.1016/S2665-9913(22)00099-6. https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(22)00099-6/fulltext

Our objective was to determine whether pre-exposure prophylaxis with tixagevimab and cilgavimab—a monoclonal antibody combination with neutralising activity against alpha (B.1.1.7), beta (B.1.351), gamma (P.1), delta (B.1.617.2), and omicron (B.1.1.529) SARS-CoV-2 variants—might be of benefit to patients with immune-mediated inflammatory diseases who did not generate a humoral response to mRNA vaccination.

15. **Identification of Drug Interaction Adverse Events in Patients With COVID-19: A Systematic Review.** Conti V et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e227970. doi: 10.1001/jamanetworkopen.2022.7970. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791291

The main finding of this systematic review is that the use of drug interaction checkers could have identified several DDI-associated adverse drug reactions, including severe and life-threatening events. Both the interactions between the drugs used to treat COVID-19 and between the COVID-19 drugs and those already used by the patients should be evaluated.

16. **Clinical efficacy and safety of interleukin-6 receptor antagonists (tocilizumab and sarilumab) in patients with COVID-19: a systematic review and meta-analysis.** Yu SY, et al. *Emerg Microbes Infect.* 2022 Dec;11(1):1154-1165. doi: 10.1080/22221751.2022.2059405. https://www.tandfonline.com/doi/full/10.1080/22221751.2022.2059405

Our meta-analysis demonstrated that tocilizumab treatment showed promising results in reducing 28-day mortality and progression to mechanical ventilation in patients with moderate-to-severe COVID-19, without the burden of serious adverse events.

17. **Intramuscular AZD7442 (Tixagevimab-Cilgavimab) for Prevention of Covid-19.** Levin MJ et al. *N Engl J Med.* 2022 Apr 20. doi: 10.1056/NEJMoa2116620. https://www.nejm.org/doi/10.1056/NEJMoa2116620

A total of 5197 participants underwent randomization and received one dose of AZD7442 or placebo (3460 in the AZD7442 group and 1737 in the placebo group). The primary analysis was conducted after 30% of the participants had become aware of their randomized assignment. In total, 1221 of 3461 participants (35.3%) in the AZD7442 group and 593 of 1736 participants (34.2%) in the placebo group reported having at least one adverse event, most of which were mild or moderate in severity. Symptomatic Covid-19 occurred in 8 of 3441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group. A single dose of AZD7442 had efficacy for the prevention of Covid-19, without evident safety concerns.

18. **An open label randomized clinical trial of Indomethacin for mild and moderate hospitalised Covid-19 patients.** Ravichandran R, et al. *Sci Rep*. 2022 Apr 19;12(1):6413. doi: 10.1038/s41598-022-10370-1. https://www.nature.com/articles/s41598-022-10370-1

Patients who received indomethacin also experienced more rapid symptomatic relief than those in the paracetamol arm, with most symptoms disappearing in half the time. In addition, 56 out of 107 in the paracetamol arm had fever on the seventh day, while no patient in the indomethacin group had fever. Neither arm reported any adverse event. The fourteenth-day follow-up revealed that the paracetamol arm patients had faced several discomforts; indomethacin arm patients mostly complained only of tiredness. Indomethacin is a safe and effective drug for treating patients with mild and moderate covid-19.

19. **Favipiravir for treatment of outpatients with asymptomatic or uncomplicated COVID-19: a double-blind randomized, placebo-controlled, phase 2 trial.** Holubar M et al. *Clin Infect Dis.* 2022 Apr 21:ciac312. doi: 10.1093/cid/ciac312. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac312/6572081

Our data do not support favipiravir use at commonly used doses in outpatients with uncomplicated COVID-19. Further research is needed to ascertain if higher doses of favipiravir are effective and safe for patients with COVID-19.

20. **Impact of Vaccination and Early Monoclonal Antibody Therapy on COVID-19 Outcomes in Organ Transplant Recipients During the Omicron Wave.** Solera JT, et al. *Clin Infect Dis.* 2022 Apr 21:ciac324. doi: 10.1093/cid/ciac324. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac324/6571785

In a cohort of SOT recipients with Omicron variant COVID-19 infection, prior receipt of ≥3 mRNA vaccine doses and early monoclonal antibody therapy were independently associated with significantly reduced disease severity.

21. **Effect of Androgen Suppression on Clinical Outcomes in Hospitalized Men With COVID-19: The HITCH Randomized Clinical Trial.** Nickols NG et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e227852. doi: 10.1001/jamanetworkopen.2022.7852. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791293

In this randomized clinical trial of androgen suppression vs placebo and usual care for men hospitalized with COVID-19, degarelix did not result in amelioration of COVID-19 severity.

Vaccines / Immunology

22. **Comparable neutralisation evasion of SARS-CoV-2 omicron subvariants BA.1, BA.2, and BA.3.** Arora P et al. *Lancet Infect Dis*. 2022 Apr 12:S1473-3099(22)00224-9. doi: 10.1016/S1473-3099(22)00224-9. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00224-9/fulltext

The SARS-CoV-2 omicron (B.1.1.529) variant has rapidly become globally dominant, displacing the previously dominant delta (B1.617.2) variant. The viral spike (S) protein is the key target of the neutralising antibody response, and the omicron variant harbours more than 35 mutations in the S protein, which allow highly efficient evasion from neutralising antibodies. In keeping with these findings, the omicron variant efficiently spreads in populations with a high percentage of convalescent or vaccinated individuals.

23. **Safety and immunogenicity of SpikoGen®, an advax-cpg55.2-adjuvanted sars-cov-2 spike protein vaccine: a phase 2 randomized placebo-controlled trial in both seropositive and seronegative populations.** Tabarsi P et al. *Clin Microbiol Infect.* 2022 Apr 15:S1198-743X(22)00207-5. doi: 10.1016/j.cmi.2022.04.004. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(22)00207-5/fulltext

SpikoGen® had an acceptable safety profile and induced promising humoral and cellular immune responses against SARS-CoV-2.

24. **Safety, tolerability, and immunogenicity of a SARS-CoV-2 recombinant spike RBD protein vaccine: A randomised, double-blind, placebo-controlled, phase 1-2 clinical trial (ABDALA Study).** Hernández-Bernal F et al. *EClinicalMedicine.* 2022 Apr 9:101383. doi: 10.1016/j.eclinm.2022.101383. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(22)00113-4/fulltext

The Abdala vaccine was safe, well tolerated, and induced humoral immune responses against SARS-CoV-2. These results, in the context of the emergency COVID-19 pandemic, support the 50 µg dose, applied in a 0-14-28 days schedule, for further clinical trials to confirm vaccine efficacy.

25. **Short-term Adverse Events After the Third Dose of the BNT162b2 mRNA COVID-19 Vaccine in Adults 60 Years or Older.** Auster O, et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e227657. doi: 10.1001/jamanetworkopen.2022.7657. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791203

On July 29, 2021, concerns of waning immunity after Pfizer-BioNTech BNT162B2 mRNA vaccination led the Israeli Ministry of Health to start a campaign to administer booster (third) doses to individuals who received their second dose at least 5 months prior. The booster was initially approved for individuals 60 years or older. This survey study assessed the occurrence of adverse effects (AEs) in adults 60 years or older who received a booster dose.

26. **Assessment of Sudden Sensorineural Hearing Loss After COVID-19 Vaccination.** Formeister EJ et al. *JAMA Otolaryngol Head Neck Surg*. 2022 Apr 1;148(4):307-315. doi: 10.1001/jamaoto.2021.4414. https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2789496

In this cross-sectional study, findings from an updated analysis of VAERS data and a case series of patients who experienced SSNHL after COVID-19 vaccination did not suggest an association between COVID-19 vaccination and an increased incidence of hearing loss compared with the expected incidence in the general population.

See also: Association Between the BNT162b2 Messenger RNA COVID-19 Vaccine and the Risk of Sudden Sensorineural Hearing Loss. Yanir Y, et al. *JAMA Otolaryngol Head Neck Surg.* 2022 Apr 1;148(4):299-306. doi: 10.1001/jamaoto.2021.4278.

27. **Impact of previous exposure to SARS-CoV-2 and of S-Trimer (SCB-2019) COVID-19 vaccination on the risk of reinfection: a randomised, double-blinded, placebo-controlled, phase 2 and 3 trial.** Smolenov I et al. *Lancet Infect Dis.* 2022 Apr 18:S1473-3099(22)00144-X. doi: 10.1016/S1473-3099(22)00144-X. https://www.sciencedirect.com/science/article/pii/S147330992200144X

Previous exposure to SARS-CoV-2 decreased the risk and severity of subsequent COVID-19 infection, even against newly emerging variants. Protection is further enhanced by one or two doses of SCB-2019.

Women & Children

28. **Boosting maternal and neonatal humoral immunity following SARS-CoV-2 infection using a single mRNA vaccine dose.** Nevo L et al. *Am J Obstet Gynecol.* 2022 Apr 14:S0002-9378(22)00282-4. doi: 10.1016/j.ajog.2022.04.010. https://www.ajog.org/article/S0002-9378(22)00282-4/pdf

Post-infection maternal humoral immunity wanes during pregnancy, resulting in low or absent protective titers for a significant proportion of patients. A single boosting dose of BNT162b2 mRNA vaccine induced a robust increase in protective titers for both mother and newborn with modest reported side effects.

29. **Acute Upper Airway Disease in Children with the Omicron (B.1.1.529) Variant of SARS-CoV-2-A Report From the US National COVID Cohort Collaborative.** Martin B, et al. *JAMA Pediatr*. 2022 Apr 15. doi: 10.1001/jamapediatrics.2022.1110. https://jamanetwork.com/journals/jamapediatrics/fullarticle/2791278

SARS-CoV-2 can cause severe pediatric disease, including acute COVID-19 and multisystem inflammatory syndrome. Published reports associating SARS-CoV-2 with upper airway infection (UAI), such as laryngotracheobronchitis (croup), have been limited to small case series. Although noncoronaviruses, including parainfluenza and respiratory syncytial virus, most frequently cause UAI, coronaviruses (eg, type NL63) are also commonly implicated. Young children are especially vulnerable to UAI given their small and relatively collapsible airways.

GUIDELINES & CONSENSUS STATEMENTS

Which actionable statements qualify as good practice statements In Covid-19 guidelines? A systematic appraisal. Dewidar O et al. *BMJ Evid Based Med*. 2022 Apr 15:bmjebm-2021-111866. doi: 10.1136/bmjebm-2021-111866.

Risk for Reinfection After SARS-CoV-2: A Living, Rapid Review for American College of Physicians Practice Points on the Role of the Antibody Response in Conferring Immunity Following SARS-CoV-2 Infection. Helfand M, et al. *Ann Intern Med*. 2022 Apr;175(4):547-555. doi: 10.7326/M21-4245. Epub 2022 Jan 25.

FDA / CDC / NIH / WHO Updates

A living WHO guideline on drugs for covid-19. *BMJ* 2020;370:m3379

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