Providence

COVID-19 Resource Desk

#60 | 6.13.21 to 6.19.21

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

Epidemiology & Public Health

1. **SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness.** Public Health Scotland and the EAVE II Collaborators. *Lancet.* 2021 Jun 14:S0140-6736(21)01358-1. doi: 10.1016/S0140-6736(21)01358-1.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01358-1/fulltext
In summary, we show that the Delta VOC in Scotland was found mainly in younger, more affluent groups. Risk of COVID-19 hospital admission was approximately doubled in those with the Delta VOC when compared to the Alpha VOC, with risk of admission particularly increased in those with five or more relevant comorbidities. Both the Oxford–AstraZeneca and Pfizer–BioNTech COVID-19 vaccines were effective in reducing the risk of SARS-CoV-2 infection and COVID-19 hospitalisation in people with the Delta VOC, but these effects on infection appeared to be diminished when compared to those with the Alpha VOC.

2. **Community-level evidence for SARS-CoV-2 vaccine protection of unvaccinated individuals.** Milman O, et al. *Nat Med.* 2021 Jun 10. doi: 10.1038/s41591-021-01407-5.
https://www.nature.com/articles/s41591-021-01407-5
By analyzing vaccination records and test results collected during the rapid vaccine rollout in a large population from 177 geographically defined communities, we find that the rates of vaccination in each community are associated with a substantial later decline in infections among a cohort of individuals aged under 16 years, who are unvaccinated. On average, for each 20 percentage points of individuals who are vaccinated in a given population, the positive test fraction for the unvaccinated population decreased approximately twofold. These results provide observational evidence that vaccination not only protects individuals who have been vaccinated but also provides cross-protection to unvaccinated individuals in the community.

Healthcare Delivery & Healthcare Workers

3. **The seroprevalence of SARS-CoV-2 antibodies among health care workers before the Era of vaccination: A systematic review and meta-analysis.** Kayı İ, et al. *Clin Microbiol Infect.* 2021 Jun 8:S1198-743X(21)00284-6. doi: 10.1016/j.cmi.2021.05.036.
https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00284-6/abstract

Our analysis indicate a SARS-CoV-2 seroprevalence rate of 8% among studies included >1,000 HCWs for the year 2020 before vaccinations started. The most common risk factors associated with higher seroprevalence rate were ethnicity, male gender, and having higher number of household contacts. Working as a frontline HCW was inconsistent in its association with higher seroprevalence.

4. **Validation of a Crisis Standards of Care Model for Prioritization of Limited Resources During the Coronavirus Disease 2019 Crisis in an Urban, Safety-Net, Academic Medical Center.** Nadjarian A, et al. *Crit Care Med.* 2021 Jun 9. doi: 10.1097/CCM.0000000000005155. https://journals.lww.com/ccmjournal/Abstract/9000/Validation_of_a_Crisis_Standards_of_Care_Model_for.95193.aspx
   Patients with major and severe chronic medical conditions overall had 46.55% and 50.00% mortality at 1 and 5 years, respectively. However, mortality varied between conditions. Our findings appear to support a crisis standards protocol which focuses on acute illness severity and only considers underlying conditions carrying a greater than 50% predicted likelihood of 1-year mortality.

Prognosis

5. **Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis.** Nyberg T, et al. *BMJ*. 2021 Jun 15;373:n1412. doi: 10.1136/bmj.n1412. https://www.bmj.com/content/373/bmj.n1412
   The results suggest that the risk of hospital admission is higher for people infected with the B.1.1.7 variant compared with wild-type SARS-CoV-2, likely reflecting a more severe disease. The higher severity may be specific to adults older than 30 years.

6. **Polypharmacy among COVID-19 patients: A systematic review.** Iloanusi S, et al. *J Am Pharm Assoc*. 2021 May 26:S1544-3191(21)00188-6. doi: 10.1016/j.japh.2021.05.006. https://www.sciencedirect.com/science/article/pii/S1544319121001886
   Polypharmacy and selected drug classes are associated with increased risk of adverse clinical outcomes among COVID-19 patients. Antipsychotic drugs were associated with severe COVID-19 morbidity and increased risk of death among COVID-19 infected men and women.

7. **Renin-Angiotensin-Aldosterone System Inhibitors and SARS-CoV-2 Infection: An Analysis from the Veteran's Affairs Healthcare System: Sandhu. ACEI, ARB, and Association with COVID.** Sandhu AT, et al. *Am Heart J.* 2021 Jun 11:S0002-8703(21)00151-4. doi: 10.1016/j.ahj.2021.06.004. https://www.sciencedirect.com/journal/american-heart-journal
   Results suggest the safety of continuing ACEI and ARB therapy. The association between ACEI therapy and lower odds of SARS-CoV-2 infection requires further investigation.

   *see also **Discontinuation versus continuation of renin-angiotensin-system inhibitors in COVID-19 (ACEI-COVID): a prospective, parallel group, randomised, controlled, open-label trial.** ACEI-COVID investigators. *Lancet Respir Med.* 2021 Jun 11:S2213-2600(21)00214-9. doi:10.1016/S2213-2600(21)00214-9. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00214-9/fulltext

Discontinuation of RAS-inhibition in COVID-19 had no significant effect on the maximum severity of COVID-19 but may lead to a faster and better recovery.

8. **Patient and Hospital Factors Associated with Differences in Mortality Rates Among Black and White US Medicare Beneficiaries Hospitalized with COVID-19 Infection.** Asch DA, et al. *JAMA Netw Open*. 2021 Jun 1;4(6):e2112842. doi: 10.1001/jamanetworkopen.2021.12842. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781182
This cohort study found that Black patients hospitalized with COVID-19 had higher rates of hospital mortality or discharge to hospice than White patients after adjustment for the personal characteristics of those patients. However, those differences were explained by differences in the hospitals to which Black and White patients were admitted.

Survivorship & Rehabilitation

9. **Persistence of SARS-CoV-2 RNA in lung tissue after mild COVID-19.** Ceulemans LJ, et al. *Lancet Respir Med.* 2021 Jun 9:S2213-2600(21)00240-X. doi: 10.1016/S2213-2600(21)00240-X. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00240-X/fulltext
A fourth of individuals admitted to hospital for COVID-19 still had three or more persistent symptoms at 6 months.

10. **Early Rehabilitation Feasibility in a COVID-19 Intensive Care Unit.** Stutz MR, et al. *Chest.* 2021 Jun 5:S0012-3692(21)01092-8. doi: 10.1016/j.chest.2021.05.059. https://www.sciencedirect.com/science/article/pii/S0012369221010928
This report demonstrates the feasibility of conducting physical and occupational therapy in COVID-19 specific ICUs. Providing therapy services appeared to be safe for patients and members of the therapy team, as adverse events were rare and no therapist was diagnosed with COVID-19. Patients tolerated therapy in spite of receiving advanced respiratory support. The discharge location of our patients was notably different than other COVID-19 cohorts with more patients discharged to acute rehabilitation and home, suggesting that shifting rehabilitation efforts earlier in acute illness can improve functional outcomes.

11. **Rehabilitation and COVID-19: update of the rapid living systematic review by Cochrane Rehabilitation Field as of April 30th, 2021.** International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action. *Eur J Phys Rehabil Med.* 2021 Jun 15. doi: 10.23736/S1973-9087.21.07125-2. https://europepmc.org/article/med/33118719
The most recently published COVID-19 research focuses more on describing the clinical presentations and the natural history of the pathology, rather than rehabilitation interventions or service delivery. Studies with high levels of evidence regarding the efficacy of interventions, long-term monitoring, or new organization models remain lacking.

Therapeutics

12. **Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia.** STOP-COVID Trial Investigators. *N Engl J Med.* 2021 Jun 16. doi: 10.1056/NEJMoa2101643. https://www.nejm.org/doi/full/10.1056/NEJMoa2101643
    Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo.

13. **Awake prone positioning in patients with hypoxemic respiratory failure due to COVID-19: the PROFLO multicenter randomized clinical trial.** PROFLO Study Group. *Crit Care.* 2021 Jun 14;25(1):209. doi: 10.1186/s13054-021-03602-9. https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03602-9
    This implemented protocol for awake prone positioning increased duration of prone positioning, but did not reduce the rate of intubation in patients with hypoxemic respiratory failure due to COVID-19 compared to standard care.

14. **Extracorporeal membrane oxygenation for COVID-19: a systematic review and meta-analysis.** Ramanathan K, et al. *Crit Care.* 2021 Jun 14;25(1):211. doi: 10.1186/s13054-021-03634-1. https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03634-1
    In-hospital mortality in patients receiving ECMO support for COVID-19 was 37.1% during the first year of the pandemic, similar to those with non-COVID-19-related ARDS. Increasing age was a risk factor for death. Venovenous ECMO appears to be an effective intervention in selected patients with COVID-19-related ARDS.

15. **Outcomes of Extracorporeal Membrane Oxygenation in Patients with Severe Acute Respiratory Distress Syndrome Caused by COVID-19 versus Influenza.** Shih E, et al. *Ann Thorac Surg*. 2021 Jun 14:S0003-4975(21)01033-X. doi: 10.1016/j.athoracsur.2021.05.060. https://www.annalsthoracicsurgery.org/article/S0003-4975(21)01033-X/fulltext
    In patients with refractory ARDS from COVID-19 or Influenza placed on ECMO, there was no significant difference in survival to hospital discharge. In patients surviving to decannulation, the duration of ECMO support and total length of stay were longer in COVID-19 patients.

16. **Low-dose hydrocortisone in patients with COVID-19 and severe hypoxia: the COVID STEROID randomised, placebo-controlled trial.** Munch MW, et al. *Acta Anaesthesiol Scand.* 2021 Jun 17. doi: 10.1111/aas.13941. https://onlinelibrary.wiley.com/doi/10.1111/aas.13941
    In this trial of adults with COVID-19 and severe hypoxia, we were unable to provide precise estimates of the benefits and harms of hydrocortisone as compared with placebo as only 3% of the planned sample size were enrolled. The trial was terminated early when 30 out of 1,000 participants had been enrolled because of external evidence indicating benefit from corticosteroids in severe COVID-19.

Transmission / Infection Control

17. **Rapidly emerging SARS-CoV-2 B.1.1.7 sub-lineage in the United States of America with spike protein D178H and membrane protein V70L mutations.** Shen L, et al. *Emerg Microbes Infect.* 2021 Jun 14:1-13. doi: 10.1080/22221751.2021.1943540. https://www.tandfonline.com/doi/full/10.1080/22221751.2021.1943540
The percentage of B.1.1.7 isolates in the U.S. that belong to this sub-lineage increased from 0.15% in February 2021 to 1.8% in April 2021. To date this sub-lineage appears to be U.S.-specific with reported cases in 31 states, including Hawaii. As of April 2021 it constituted 36.8% of all B.1.1.7 isolates in Washington. Phylogenetic analysis and transmission inference with Nextstrain suggests this sub-lineage likely originated in either California or Washington. Structural analysis revealed that the S:D178H mutation is in the NTD of the S protein and close to two other signature mutations of B.1.1.7, HV69-70del and Y144del. It is surface exposed and may alter NTD tertiary configuration or accessibility, and thus has the potential to affect neutralization by NTD directed antibodies.

18. **The incubation period distribution of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis.** Xin H, et al. *Clin Infect Dis.* 2021 Jun 12:ciab501. doi: 10.1093/cid/ciab501. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab501/6297425
We conducted a systematic review on published estimates of the incubation period distribution of COVID-19 and showed that the pooled median of the point estimates of the mean, median and 95th percentile for incubation period are 6.3 days, 5.4 days and 13.1 days respectively. Estimates of the mean and 95th percentile of the incubation period distribution were considerably shorter before the epidemic peak in China compared to after the peak, and variation was also noticed for different choices of methodological approach in estimation. Our findings implied that corrections may be needed before directly applying estimates of incubation period into control of or further studies on emerging infectious diseases.

Vaccines / Immunology

19. **Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2-mRNA-vaccinated individuals.** Kustin T, et al. *Nat Med.* 2021 Jun 14. doi: 10.1038/s41591-021-01413-7. https://www.nature.com/articles/s41591-021-01413-7
Analyzing 813 viral genome sequences from nasopharyngeal swabs, we showed that vaccinees who tested positive at least 7 days after the second dose were disproportionally infected with B.1.351, compared with controls. Those who tested positive between 2 weeks after the first dose and 6 days after the second dose were disproportionally infected by B.1.1.7. These findings suggest reduced vaccine effectiveness against both VOCs within particular time windows.

20. **Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection.** Wang Z, et al. *Nature.* 2021 Jun 14. doi: 10.1038/s41586-021-03696-9. https://www.nature.com/articles/s41586-021-03696-9

The data suggest that immunity in convalescent individuals will be very long lasting and that convalescent individuals who receive available mRNA vaccines will produce antibodies and memory B cells that should be protective against circulating SARS-CoV-2 variants.

21. **Severe Exacerbations of Systemic Capillary Leak Syndrome after COVID-19 Vaccination: A Case Series.** Matheny M, et al. *Ann Intern Med.* 2021 Jun 15. doi: 10.7326/L21-0250. https://www.acpjournals.org/doi/10.7326/L21-0250
We describe 3 patients with SCLS or a history suggestive of SCLS who developed life-threatening flares 1 to 2 days after COVID-19 vaccination. We believe these patients identify SCLS as a risk factor for the development of serious adverse reactions after COVID-19 vaccination. However, we recognize that these observations do not rule out other causes of these flares. For example, infection-related symptoms precede 44% to 64% of all acute flares, and flares have been reported with SARS-CoV-2 infection. However, we were unable to identify any of these other triggers.

22. **Safety and Immunogenicity of a Third Dose of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series.** Werbel WA, et al. *Ann Intern Med.* 2021 Jun 15. doi: 10.7326/L21-0282. https://www.acpjournals.org/doi/10.7326/L21-0282
To our knowledge, this is the first report of patients with solid organ transplants receiving a third dose of vaccine directed against SARS-CoV-2. It is encouraging that antibody titers increased after the third dose in one third of patients who had negative antibody titers and in all patients who had low-positive antibody titers. In addition, the vaccine reactions seem acceptable, given the benefits that these vaccines can confer. Antibody responses, however, appear to vary, and potential risks, such as organ rejection, should be evaluated on an individual basis.

23. **Myocarditis Temporally Associated with COVID-19 Vaccination.** Rosner CM, et al. *Circulation.* 2021 Jun 16. doi: 10.1161/CIRCULATIONAHA.121.055891. DOI: 10.1161/CIRCULATIONAHA.121.055891
https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.121.055891
Our series of 7 male COVID-19 vaccination recipients who presented with myocarditis-like illness supports a potential causal association with vaccination given the temporal relationship, clinical presentation and CMR findings. Additional study is needed to confirm if the rate of myocarditis-like illness is higher after vaccination than the background rate of myocarditis among similar aged individuals in the population. Globally, myocarditis is diagnosed in approximately 10-20 individuals per 100,000/year. The clinical course of vaccine-associated myocarditis-like illness appears favorable, with resolution of symptoms in all patients.

    *see also **Myocarditis after SARS-CoV-2 Vaccination: A Vaccine-induced Reaction?** D'Angelo T, et al. *Can J Cardiol.* 2021 Jun 9:S0828-282X(21)00286-5. doi: 10.1016/j.cjca.2021.05.010.
    https://www.sciencedirect.com/science/article/abs/pii/S0828282X21002865
    We report a case of a 30-year-old male who presented progressive dyspnea and constrictive retrosternal pain after receiving SARS-CoV-2 vaccine. Cardiac magnetic resonance and laboratory data revealed typical findings of acute myopericarditis.

24. **Seroconversion rates following COVID-19 vaccination among patients with cancer.** Thakkar A, et al. *Cancer Cell.* 2021 Jun 5:S1535-6108(21)00285-3. doi: 10.1016/j.ccell.2021.06.002. https://www.sciencedirect.com/science/article/pii/S1535610821002853
There is a generally high immunogenicity of COVID-19 vaccination in oncology patients except immunosuppressed cohorts that need novel vaccination or passive immunization strategies.

Whole Person Care

25. **Mental Health among Parents of Children Aged <18 Years and Unpaid Caregivers of Adults during the COVID-19 Pandemic — United States, December 2020 and February–March 2021.** Czeisler MÉ, et al. *MMWR Morb Mortal Wkly Rep* 2021;70:879–887. DOI: http://dx.doi.org/10.15585/mmwr.mm7024a3
Among 10,444 U.S. adults surveyed during December 6–27, 2020, and February 16–March 8, 2021, parents, unpaid caregivers of adults, and parents-caregivers (persons in both roles) had significantly worse mental health than adults not in these roles, including five times the odds of any adverse mental health symptoms (parents-caregivers). Persons who had someone to rely on for support had lower odds of experiencing any adverse mental health symptoms. Parents and unpaid caregivers of adults, and particularly those in both roles, might benefit from mental health support and services tailored to their roles.

Women & Children

26. **Adverse effects of COVID-19 mRNA vaccines among pregnant women: A cross-sectional study on healthcare workers with detailed self-reported symptoms.** Kalyan Kadali RA, et al. *Am J Obstet Gynecol.* 2021 Jun 9:S0002-9378(21)00638-4. doi: 10.1016/j.ajog.2021.06.007. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8189739/
The side-effect profile obtained from a detailed systematic review of organ systems among pregnant women who received either of the mRNA vaccines in the immediate or early postvaccination period were nonlife threatening and they appeared to be similar (with no significant statistical difference) when compared with nonpregnant women. The pregnancy-related adverse events were very rarely reported. There is high acceptance of the second vaccine dose, which is an encouraging aspect for future pregnant vaccine recipients.

27. **COVID-19 Vaccination Coverage Among Pregnant Women During Pregnancy - Eight Integrated Health Care Organizations, United States, December 14, 2020-May 8, 2021.** Razzaghi H, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Jun 18;70(24):895-899. doi: 10.15585/mmwr.mm7024e2. https://www.cdc.gov/mmwr/volumes/70/wr/mm7024e2.htm?s_cid=mm7024e2_x
Among 135,968 women, 7,154 (5.3%) had initiated and 15,043 (11.1%) had completed vaccination during pregnancy. Receipt of ≥1 dose of COVID-19 vaccine during pregnancy was highest among women aged 35-49 years (22.7%) and lowest among those aged 18-24 years (5.5%), and higher among non-Hispanic Asian (Asian) (24.7%) and non-Hispanic White (White) women (19.7%) than among Hispanic (11.9%) and non-Hispanic Black (Black) women (6.0%). Vaccination coverage increased among all racial and ethnic groups over the analytic period,

likely because of increased eligibility for vaccination† and increased availability of vaccine over time. These findings indicate the need for improved outreach to and engagement with pregnant women, especially those from racial and ethnic minority groups who might be at higher risk for severe health outcomes because of COVID-19.

28. **International Analysis of Electronic Health Records of Children and Youth Hospitalized With COVID-19 Infection in 6 Countries.** Consortium for Clinical Characterization of COVID-19 by EHR (4CE). *JAMA Netw Open.* 2021 Jun 1;4(6):e2112596. doi: 10.1001/jamanetworkopen.2021.12596.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2780925
This study of EHRs of children and youth hospitalized for COVID-19 in 6 countries demonstrated variability in hospitalization trends across countries and identified common complications and laboratory abnormalities in children and youth with COVID-19 infection. Trends in hospitalizations for 671 children and youth found discrete surges with variable timing across 6 countries. Common complications included cardiac arrhythmias, viral pneumonia, and respiratory failure. Few children were treated with COVID-19-directed medications.

29. **Comparison of Symptoms and RNA Levels in Children and Adults with SARS-CoV-2 Infection in the Community Setting.** Chung E, et al. *JAMA Pediatr.* 2021 Jun 11. doi:10.1001/jamapediatrics.2021.2025.
https://jamanetwork.com/journals/jamapediatrics/fullarticle/2780963
In this community-based cross-sectional study, SARS-CoV-2 RNA levels, as determined by Ct values, were significantly higher in symptomatic individuals than in asymptomatic individuals and no significant age-related differences were found. Further research is needed to understand the role of SARS-CoV-2 RNA levels and viral transmission.

30. **Multisystem Inflammatory Syndrome in Children - Initial Therapy and Outcomes.** Overcoming COVID-19 Investigators. *N Engl J Med.* 2021 Jun 16. doi: 10.1056/NEJMoa2102605.
https://www.nejm.org/doi/full/10.1056/NEJMoa2102605
Among children and adolescents with MIS-C, initial treatment with IVIG plus glucocorticoids was associated with a lower risk of new or persistent cardiovascular dysfunction than IVIG alone.

31. **Multisystem inflammatory syndrome in children occurred in one of four thousand children with severe acute respiratory syndrome coronavirus-2.** Holm M, et al. *Acta Paediatr.* 2021 Jun 15. doi: 10.1111/apa.15985. https://onlinelibrary.wiley.com/doi/10.1111/apa.15985
This study from the New York State has reported an incidence of MIS-C of 2 per 100,000 persons younger than 21 years of age between 1 March 1 and 10 May 2020.

GUIDELINES & CONSENSUS STATEMENTS

Update Alert: Remdesivir for Adults With COVID-19. Kaka AS, et al. *Ann Intern Med.* 2021 Jun 15. doi: 10.7326/L21-0375.

Treatment of Multisystem Inflammatory Syndrome in Children. BATS Consortium. *N Engl J Med.* 2021 Jun 16. doi: 10.1056/NEJMoa2102968.

FDA / CDC / NIH / WHO Updates

CDC – Delta variant now categorized as Variant of Concern, June 15, 2021

NIH - The COVID-19 Treatment Guidelines Panel's Statement on the Updated Emergency Use Authorization of the Anti-SARS-CoV-2 Monoclonal Antibody Combination Casirivimab Plus Imdevimab for the Treatment of COVID-19, updated 6-17-21

WHO - Evaluation of post-introduction COVID-19 vaccine effectiveness: Summary of interim guidance of the World Health Organization. *Vaccine.* 2021 Jun 1:S0264-410X(21)00707-6. doi: 10.1016/j.vaccine.2021.05.099.

Commentary / Press Releases

RECOVERY trial finds Regeneron's monoclonal antibody combination reduces deaths for hospitalised COVID-19 patients who have not mounted their own immune response. June 16, 2021.
*see research preprint here

Novavax COVID-19 Vaccine Demonstrates 90% Overall Efficacy and 100% Protection Against Moderate and Severe Disease in PREVENT-19 Phase 3 Trial. June 14, 2021

Should we vaccinate children against SARS-CoV-2? *Lancet Infect Dis.* 2021 Jun 10:S1473-3099(21)00339-X. doi: 10.1016/S1473-3099(21)00339-X.

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