Providence

COVID-19 Resource Desk

#65 | 7.18.21 to 7.24.21

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

Clinical Syndrome

1. **Ischemic and Hemorrhagic Stroke among Critically Ill Patients with Coronavirus Disease 2019: An International Multicenter Coronavirus Disease 2019 Critical Care Consortium Study.** Cho SM et al. *Crit Care Med*. 2021 Jul 19. doi: 10.1097/CCM.0000000000005209. https://journals.lww.com/ccmjournal/Abstract/9000/Ischemic_and_Hemorrhagic_Stroke_Among_Critically.95142.aspx
   In an international registry of ICU patients with coronavirus disease 2019, stroke was infrequent. Hemorrhagic stroke, but not ischemic stroke, was associated with increased mortality. Further, both hemorrhagic stroke and ischemic stroke were associated with traditional vascular risk factors. Extracorporeal membrane oxygenation use was strongly associated with both stroke and death.

Diagnostics & Screening

2. **Multidisciplinary assessment of the Abbott BinaxNOW SARS-CoV-2 point-of-care antigen test in the context of emerging viral variants and self-administration.** Frediani JK et al. *Sci Rep.* 2021 Jul 16;11(1):14604. doi: 10.1038/s41598-021-94055-1. https://www.nature.com/articles/s41598-021-94055-1
   BinaxNOW detected the highly infectious variants, B.1.1.7 (Alpha) first identified in the UK, B.1.351 (Beta) first identified in South Africa, P.1 (Gamma) first identified in Brazil, B.1.617.2 (Delta) first identified in India and B.1.2, a non-VOC, test sensitivity decreased with decreasing viral loads. Moreover, BinaxNOW sensitivity trended lower when devices were performed by patients/caregivers themselves compared to trained clinical staff, despite universally high usability assessments following self/caregiver-administration among different age groups. Overall, these data indicate that while BinaxNOW accurately detects the new viral variants, as rapid COVID-19 tests enter the home, their already lower sensitivities compared to RT-PCR may decrease even more due to user error.

3. **Detection of Severe Acute Respiratory Syndrome Coronavirus 2 on Self-Collected Saliva or Anterior Nasal Specimens Compared with Healthcare Personnel-Collected Nasopharyngeal**

Specimens. Marx GE et al. *Clin Infect Dis*. 2021 Jul 15;73(Suppl 1):S65-S73. doi: 10.1093/cid/ciab330. https://academic.oup.com/cid/article/73/Supplement_1/S65/6257585
SS were slightly more sensitive than ANS for SARS-CoV-2 detection with rRT-PCR. With both SS and ANS, SARS-CoV-2 was reliably detected among participants with symptoms. Self-collected SS and ANS offer practical advantages, are preferred by patients, and might be most useful for testing people with coronavirus disease 2019 symptoms.

Epidemiology & Public Health

4. **COVID-19 Vaccination Coverage Among Insured Persons Aged ≥16 Years, by Race/Ethnicity and Other Selected Characteristics - Eight Integrated Health Care Organizations, United States, December 14, 2020-May 15, 2021.** Pingali C et al. *MMWR Morb Mortal Wkly Rep*. 2021 Jul 16;70(28):985-990. doi: 10.15585/mmwr.mm7028a1.
https://www.cdc.gov/mmwr/volumes/70/wr/mm7028a1.htm
Among 9.6 million persons aged ≥16 years enrolled in VSD during December 14, 2020-May 15, 2021, ≥1-dose coverage was 48.3%, and 38.3% were fully vaccinated. As of May 15, 2021, coverage with ≥1 dose was lower among non-Hispanic Black (Black) and Hispanic persons (40.7% and 41.1%, respectively) than it was among non-Hispanic White (White) persons (54.6%). Coverage was highest among non-Hispanic Asian (Asian) persons (57.4%). Coverage with ≥1 dose was higher among persons with certain medical conditions that place them at higher risk for severe COVID-19 (high-risk conditions) (63.8%) than it was among persons without such conditions (41.5%) and was higher among persons who had not had COVID-19 (48.8%) than it was among those who had (42.4%). Persons aged 18-24 years had the lowest ≥1-dose coverage (28.7%) among all age groups. Continued monitoring of vaccination coverage and efforts to improve equity in coverage are critical, especially among populations disproportionately affected by COVID-19.

5. **Acceptability of Adolescent COVID-19 Vaccination among Adolescents and Parents of Adolescents - United States, April 15-23, 2021.** Scherer AM, et al. *MMWR Morb Mortal Wkly Rep*. 2021 Jul 16;70(28):997-1003. doi: 10.15585/mmwr.mm7028e1.
https://www.cdc.gov/mmwr/volumes/70/wr/mm7028e1.htm
Vaccination intent was assessed among independently recruited samples of 985 adolescents aged 13-17 years and 1,022 parents of adolescents aged 12-17 years during April 15-April 23, 2021, prior to vaccine authorization for this age group. Approximately one quarter (27.6%) of parents whose adolescents were already vaccine-eligible (i.e., aged 16-17 years) reported their adolescent had received ≥1 COVID-19 vaccine dose, similar to the proportion reported by vaccine-eligible adolescents aged 16-17 years (26.1%). However, vaccine receipt reported by parents of adolescents differed across demographic groups; parents identifying as female or Hispanic, or who had an education lower than a bachelor's degree reported the lowest adolescent COVID-19 vaccination receipt. Among parents of unvaccinated adolescents aged 12-17 years, 55.5% reported they would "definitely" or "probably" have their adolescent receive a COVID-19 vaccination. Among unvaccinated adolescents aged 13-17 years, 51.7% reported they would "definitely" or "probably" receive a COVID-19 vaccination. Obtaining more information about adolescent COVID-19 vaccine safety and efficacy, as well as school COVID-19 vaccination

requirements, were the most commonly reported factors that would increase vaccination intentions among both parents and adolescents.

6. **Exploring the Gap between Excess Mortality and COVID-19 Deaths in 67 Countries.** Sanmarchi F, et al. *JAMA Netw Open*. 2021 Jul 1;4(7):e2117359. doi: 10.1001/jamanetworkopen.2021.17359.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781968
This comparison of CCM and EM revealed the different national health systems' capacity to test and diagnose COVID-19 and their responsiveness to the health crisis. Underreporting of COVID-19 deaths because of strained health care systems' capacity might explain our findings for countries where EM exceeded CCM. In contrast, the effects of nonpharmaceutical interventions on populations' main causes of deaths, such as the decrease in work and road accidents, could be responsible for the reduction in overall mortality in countries where CCM exceeded EM. Notably, most of the countries that presented reduced overall mortality during 2020 had extremely high testing capacity and were praised for their effective response measures against the pandemic.

7. **Changes in Influenza and Other Respiratory Virus Activity during the COVID-19 Pandemic - United States, 2020-2021.** Olsen SJ et al. *MMWR Morb Mortal Wkly Rep*. 2021 Jul 23;70(29):1013-1019. doi: 10.15585/mmwr.mm7029a1.
https://www.cdc.gov/mmwr/volumes/70/wr/mm7029a1.htm
In the United States, influenza activity decreased in March 2020, was historically low through the summer of 2020, and remained low during October 2020-May 2021 (<0.4% of respiratory specimens with positive test results for each week of the season). Circulation of other respiratory pathogens, including respiratory syncytial virus (RSV), common human coronaviruses (HCoVs) types OC43, NL63, 229E, and HKU1, and parainfluenza viruses (PIVs) types 1-4 also decreased in early 2020 and did not increase until spring 2021. Human metapneumovirus (HMPV) circulation decreased in March 2020 and remained low through May 2021. Respiratory adenovirus (RAdV) circulated at lower levels throughout 2020 and as of early May 2021. Rhinovirus and enterovirus (RV/EV) circulation decreased in March 2020, remained low until May 2020, and then increased to near prepandemic seasonal levels. Circulation of respiratory viruses could resume at prepandemic levels after COVID-19 mitigation practices become less stringent. Clinicians should be aware of increases in some respiratory virus activity and remain vigilant for off-season increases. In addition to the use of everyday preventive actions, fall influenza vaccination campaigns are an important component of prevention as COVID-19 mitigation measures are relaxed and schools and workplaces resume in-person activities.

Healthcare Delivery & Healthcare Workers

8. **Intention to COVID-19 vaccination and associated factors among health care workers: A systematic review and meta-analysis of cross-sectional studies.** Luo C, et al. *Am J Infect Control.* 2021 Jul 14:S0196-6553(21)00460-0. doi: 10.1016/j.ajic.2021.06.020.
https://www.ajicjournal.org/article/S0196-6553(21)00460-0/fulltext

COVID-19 vaccination acceptance of HCWs was at moderate level. Strengthening awareness of COVID-19 vaccine among HCWs, particularly female HCWs under 30 years who have no history of prior influenza vaccination, is crucial to eliminate concerns about vaccination and promote the application of COVID-19 vaccine in this population.

9. **Excess Mortality Among Patients Hospitalized During the COVID-19 Pandemic.** Sabbatini AK, Robicsek A, Chiu S-T, Gluckman TJ. **[Providence authors]**. *J Hosp Med.* July 21, 2021. DOI: 10.12788/jhm.3633 | 10.12788/jhm.3633
https://www.journalofhospitalmedicine.com/jhospmed/article/242997/hospital-medicine/excess-mortality-among-patients-hospitalized-during-covid?channel=28090
Pandemic COVID-19 surges were associated with higher rates of in-hospital mortality among patients without COVID-19, suggesting disruptions in care patterns for patients with many common acute and chronic illnesses.

Prognosis

10. **Relation of prior statin and anti-hypertensive use to severity of disease among patients hospitalized with COVID-19: Findings from the American Heart Association's COVID-19 Cardiovascular Disease Registry.** Daniels LB, et al. *PLoS One*. 2021 Jul 15;16(7):e0254635. doi: 10.1371/journal.pone.0254635. eCollection 2021.
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0254635
Patients taking statins prior to hospitalization for COVID-19 had substantially lower odds of death, primarily among individuals with a history of CVD and/or hypertension. These observations support the continuation and aggressive initiation of statin and anti-hypertensive therapies among patients at risk for COVID-19, if these treatments are indicated based upon underlying medical conditions.

11. **Predicting critical illness on initial diagnosis of COVID-19 based on easily-obtained clinical variables: development and validation of the PRIORITY model.** Martinez-Lacalzada M et al. *Clin Microbiol Infect.* 2021 Jul 15:S1198-743X(21)00380-3. doi: 10.1016/j.cmi.2021.07.006.
https://www.sciencedirect.com/science/article/pii/S1198743X21003803
The PRIORITY model included: age, cardiovascular disease, chronic kidney disease, dyspnea, tachypnea, confusion, systolic blood pressure, and SpO2≤93% or oxygen requirement. The model showed high discrimination for critical illness. A freely available web-based calculator was developed based on this model (https://www.evidencio.com/models/show/2344). The PRIORITY model, based on easily-obtained clinical information, had good discrimination and generalizability for identifying COVID-19 patients at risk of critical outcomes.

Survivorship & Rehabilitation

12. **Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol UK: a prospective, multicentre cohort study.** Drake TM et al. *Lancet.* 2021 Jul 17;398(10296):223-237. doi: 10.1016/S0140-6736(21)00799-6.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00799-6/fulltext

Complications and worse functional outcomes in patients admitted to hospital with COVID-19 are high, even in young, previously healthy individuals. Acute complications are associated with reduced ability to self-care at discharge, with neurological complications being associated with the worst functional outcomes. COVID-19 complications are likely to cause a substantial strain on health and social care in the coming years. These data will help in the design and provision of services aimed at the post-hospitalisation care of patients with COVID-19.

13. **Late Conditions Diagnosed 1-4 Months Following an Initial Coronavirus Disease 2019 (COVID-19) Encounter: A Matched-Cohort Study Using Inpatient and Outpatient Administrative Data-United States, 1 March-30 June 2020.** Chevinsky JR et al. *Clin Infect Dis.* 2021 Jul 15;73(Suppl 1):S5-S16. doi: 10.1093/cid/ciab338.
https://academic.oup.com/cid/article/73/Supplement_1/S5/6257082
During 31-120 days after an initial COVID-19 inpatient hospitalization, 7.0% of adults experienced ≥1 of 5 post-COVID conditions. Among adult outpatients with COVID-19, 7.7% experienced ≥1 of 10 post-COVID conditions. During 31-60 days after an initial outpatient encounter, adults with COVID-19 were 2.8 times as likely to experience acute pulmonary embolism as outpatient control-patients and also more likely to experience a range of conditions affecting multiple body systems (eg, nonspecific chest pain, fatigue, headache, and respiratory, nervous, circulatory, and gastrointestinal symptoms) than outpatient control-patients. These findings add to the evidence of late health conditions possibly related to COVID-19 in adults following COVID-19 diagnosis and can inform healthcare practice and resource planning for follow-up COVID-19 care.

Therapeutics

14. **Association of Remdesivir Treatment with Survival and Length of Hospital Stay Among US Veterans Hospitalized With COVID-19.** Ohl ME, et al. *JAMA Netw Open.* 2021 Jul 1;4(7):e2114741. doi: 10.1001/jamanetworkopen.2021.14741.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781959
In this cohort study of US veterans hospitalized with COVID-19, remdesivir treatment was not associated with improved survival but was associated with longer hospital stays. Routine use of remdesivir may be associated with increased use of hospital beds while not being associated with improvements in survival.

15. **Effect of Oral Azithromycin vs Placebo on COVID-19 Symptoms in Outpatients with SARS-CoV-2 Infection: A Randomized Clinical Trial.** Oldenburg CE et al. *JAMA.* 2021 Jul 16. doi: 10.1001/jama.2021.11517. https://jamanetwork.com/journals/jama/fullarticle/2782166
Among outpatients with SARS-CoV-2 infection, treatment with a single dose of azithromycin compared with placebo did not result in greater likelihood of being symptom free at day 14. These findings do not support the routine use of azithromycin for outpatient SARS-CoV-2 infection.

16. **Emergence of the E484K mutation in SARS-COV-2-infected immunocompromised patients treated with bamlanivimab in Germany.** Jensen B et al. *Lancet Reg Health Eur.* 2021

Sep;8:100164. doi: 10.1016/j.lanepe.2021.100164. Epub 2021 Jul 14. https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00141-1/fulltext
Treatment of SARS-CoV-2 with bamlanivimab in immunocompromised patients results in the rapid development of immune escape variants in a significant proportion of cases. Given that the E484K mutation can hamper natural immunity, the effectiveness of vaccination as well as antibody-based therapies, these findings may have important implications not only for individual treatment decisions but may also pose a risk to general prevention and treatment strategies.

17. **Real-World Clinical Outcomes of Bamlanivimab and Casirivimab-Imdevimab among High-Risk Patients with Mild to Moderate Coronavirus Disease 2019.** Ganesh R et al. *J Infect Dis.* 2021 Jul 19:jiab377. doi: 10.1093/infdis/jiab377. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab377/6323936
This observational study on the use of bamlanivimab and casirivimab-imdevimab in high-risk patients showed similarly low rates of hospitalization. The number and type of medical comorbidities are associated with hospitalizations after monoclonal antibody treatment.

18. **Efficacy and safety of sofosbuvir/velpatasvir versus the standard of care in adults hospitalized with COVID-19: a single-centre, randomized controlled trial.** Sayad B et al. *J Antimicrob Chemother*. 2021 Jul 15;76(8):2158-2167. doi: 10.1093/jac/dkab152. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8194643/
Although treatment with SOF/VEL was safe, adding SOF/VEL to the standard of care did not improve the clinical status or reduce mortality in patients with moderate to severe COVID-19. However, larger randomized clinical trials including more parameters are needed for accurate estimation of the efficacy of SOF/VEL.

19. **Effect of Canakinumab vs Placebo on Survival without Invasive Mechanical Ventilation in Patients Hospitalized with Severe COVID-19: A Randomized Clinical Trial.** Caricchio R et al. *JAMA*. 2021 Jul 20;326(3):230-239. doi: 10.1001/jama.2021.9508. https://jamanetwork.com/journals/jama/fullarticle/2782185
Among patients hospitalized with severe COVID-19, treatment with canakinumab, compared with placebo, did not significantly increase the likelihood of survival without IMV at day 29.

Vaccines / Immunology

20. **Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination.** Barros-Martins J et al. *Nat Med.* 2021 Jul 14. doi: 10.1038/s41591-021-01449-9. https://www.nature.com/articles/s41591-021-01449-9.pdf
After reports of thromboembolic events, several European governments recommended using AstraZeneca's ChAdOx1-nCov-19 (ChAd) only in individuals older than 60 years, leaving millions of already ChAd-primed individuals with the decision to receive either a second shot of ChAd or a heterologous boost with mRNA-based vaccines. However, such combinations have not been tested so far. We used Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals to monitor ChAd-primed immune responses before and 3 weeks after booster

with ChAd (n = 32) or BioNTech/Pfizer's BNT162b2 (n = 55). Although both vaccines boosted prime-induced immunity, BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells and, in particular, high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern of severe acute respiratory syndrome coronavirus 2.

21. **Comparison of IgG and neutralizing antibody responses after one or two doses of COVID-19 mRNA vaccine in previously infected and uninfected individuals.** Demonbreun AR et al. *EClinicalMedicine*. 2021 Aug;38:101018. doi: 10.1016/j.eclinm.2021.101018. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00298-4/fulltext
After one dose of mRNA vaccine, individuals previously diagnosed with COVID-19 responded with high levels of anti-RBD IgG and surrogate neutralization of spike-ACE2 interaction. One dose of mRNA vaccine was not sufficient to generate comparably high responses among most persons previously infected with SARS-CoV-2 without a clinical COVID-19 diagnosis, nor among seronegative persons.

22. **Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial.** Borobia AM et al. *Lancet.* 2021 Jul 10;398(10295):121-130. doi: 10.1016/S0140-6736(21)01420-3. Epub 2021 Jun 25. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01420-3/fulltext
BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile.

23. **Prevention of COVID-19 by mRNA-based vaccines within the general population of California.** Case-Control Study Team. *Clin Infect Dis.* 2021 Jul 20:ciab640. doi: 10.1093/cid/ciab640. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab640/6324500
Fully vaccinated participants receiving either product experienced 91.3% and 68.3% VE against symptomatic and asymptomatic infection, respectively. Among unvaccinated participants, 42.4% (159/375) residing in rural regions and 23.8% (67/281) residing in urban regions reported hesitancy to receive COVID-19 vaccination. Authorized mRNA-based vaccines are effective at reducing documented SARS-CoV-2 infections within the general population of California. Vaccine hesitancy presents a barrier to reaching coverage levels needed for herd immunity.

24. **Kinetics of the SARS-CoV-2 antibody response and serological estimation of time since infection.** Pelleau S et al. *J Infect Dis.* 2021 Jul 19:jiab375. doi: 10.1093/infdis/jiab375. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab375/6324228
One year after symptoms, we estimate that 36% of anti-Spike IgG remains, 31% anti-RBD IgG remains, and 7% anti-Nucleocapsid IgG remains. The multiplex assay classified previous infections into time intervals of 0-3 months, 3-6 months, and 6-12 months. In addition to diagnosing previous SARS-CoV-2 infection, multiplex serological assays can estimate the time since infection which can be used to reconstruct past epidemics.

25. **Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant.** Lopez Bernal J et al. *N Engl J Med.* 2021 Jul 21. doi: 10.1056/NEJMoa2108891.
https://www.nejm.org/doi/full/10.1056/NEJMoa2108891
Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses. Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose. This finding would support efforts to maximize vaccine uptake with two doses among vulnerable populations.

26. **Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples.** Bates TA, et al. *JAMA*. 2021 Jul 21. doi: 10.1001/jama.2021.11656.
https://jamanetwork.com/journals/jama/fullarticle/2782428
In this study, initial vaccine-elicited neutralizing antibody titers were negatively associated with age, resulting in a diminished ability to neutralize SARS-CoV-2 in vitro. Neutralizing titers against P.1 were reduced across all ages, although the magnitude of the age-dependent difference was smaller. Interim clinical trial data did not identify age as a contributing factor to overall vaccine efficacy. However, recent studies in vaccinated populations have found a measurable increase in COVID-19 cases among vaccinated older adults. The data from the current study are consistent with neutralizing antibody levels playing an important role in this observation.

Women & Children

27. **Longitudinal Outcomes for Multisystem Inflammatory Syndrome in Children.** Farooqi KM et al. *Pediatrics*. 2021 Jul 15:e2021051155. doi: 10.1542/peds.2021-051155.
https://pediatrics.aappublications.org/content/early/2021/07/14/peds.2021-051155
Although the majority of children with MIS-C present critically ill, most inflammatory and cardiac manifestations in our cohort resolved rapidly.

28. **Neurological manifestations of SARS-CoV-2 infection in hospitalised children and adolescents in the UK: a prospective national cohort study.** Ray STJ et al. *Lancet Child Adolesc Health*. 2021 Jul 14:S2352-4642(21)00193-0. doi: 10.1016/S2352-4642(21)00193-0. Online ahead of print.
https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00193-0/fulltext
This study identified key differences between those with a primary neurological disorder versus those with PIMS-TS. Compared with patients with a primary neurological disorder, more patients with PIMS-TS needed intensive care, but outcomes were similar overall. Further studies should investigate underlying mechanisms for neurological involvement in COVID-19 and the longer-term outcomes.

29. **Long-term Symptoms after SARS-CoV-2 Infection in Children and Adolescents.** Radtke T, et al. *JAMA.* 2021 Jul 15. doi: 10.1001/jama.2021.11880.
https://jamanetwork.com/journals/jama/fullarticle/2782164
Although long COVID exists in children, estimates of the prevalence of persisting symptoms based on scarce literature range from 0%2 to 27%. Initial SARS-CoV-2 infection severity, different methodological approaches (clinical assessment vs self-report), definition of cases (diagnosed vs suspected), variable follow-up times, and prevalence of preexisting clinical

conditions likely contribute to the variability in prevalence estimates. This study found a low prevalence of symptoms compatible with long COVID in a randomly selected cohort of children assessed 6 months after serologic testing.

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