Providence

COVID-19 Resource Desk

#76 | 10.3.21 to 10.9.21

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. **Emergence and spread of SARS-CoV-2 lineage B.1.620 with variant of concern-like mutations and deletions.** Dudas G et al. *Nat Commun.* 2021 Oct 1;12(1):5769. doi: 10.1038/s41467-021-26055-8.
https://www.nature.com/articles/s41467-021-26055-8
We here describe a SARS-CoV-2 lineage - designated B.1.620 - discovered in Lithuania and carrying many mutations and deletions in the spike protein shared with widespread variants of concern, including E484K, S477N and deletions HV69Δ, Y144Δ, and LLA241/243Δ. As well as documenting the suite of mutations this lineage carries, we also describe its potential to be resistant to neutralising antibodies, accompanying travel histories for a subset of European cases, evidence of local B.1.620 transmission in Europe with a focus on Lithuania, and significance of its prevalence in Central Africa owing to recent genome sequencing efforts there. We make a case for its likely Central African origin using advanced phylogeographic inference methodologies incorporating recorded travel histories of infected travellers.

2. **Racial and Ethnic Disparities in Excess Deaths During the COVID-19 Pandemic, March to December 2020.** Shiels MS et al. *Ann Intern Med.* 2021 Oct 5. doi: 10.7326/M21-2134.
https://www.acpjournals.org/doi/10.7326/M21-2134
There were profound racial/ethnic disparities in excess deaths in the United States in 2020 during the COVID-19 pandemic, resulting in rapid increases in racial/ethnic disparities in all-cause mortality between 2019 and 2020.

3. **COVID-19 hospital prevalence as a risk factor for mortality: an observational study of a multistate cohort of 62 hospitals.** Fakih MG, et al. *BMJ Qual Saf.* 2021 Oct 5:bmjqs-2021-013721. doi: 10.1136/bmjqs-2021-013721.
https://qualitysafety.bmj.com/content/early/2021/10/04/bmjqs-2021-013721.long
Although inpatient mortality for patients with COVID-19 has sharply declined compared with earlier in the pandemic, higher COVID-19 hospital prevalence remained a common risk factor for COVID-19 mortality. Hospital leaders need to reconsider how we provide support to care for patients in times of increased volume and complexity, such as those experienced during COVID-19 surges.

4. **Distribution of SARS-CoV-2 Variants in a Large Integrated Health Care System - California, March-July 2021.** Malden DE et al. *MMWR Morb Mortal Wkly Rep*. 2021 Oct 8;70(40):1415-1419. doi: 10.15585/mmwr.mm7040a4.
https://www.cdc.gov/mmwr/volumes/70/wr/mm7040a4.htm?s_cid=mm7040a4_x
This study used whole genome sequencing (WGS) data on SARS-CoV-2-positive specimens collected across Kaiser Permanente Southern California (KPSC), a large integrated health care system, to describe the distribution and risk of hospitalization associated with SARS-CoV-2 variants during March 4-July 21, 2021, by patient vaccination status. Among 13,039 SARS-CoV-2-positive specimens identified from KPSC patients during this period, 6,798 (52%) were sequenced and included in this report. Of these, 5,994 (88%) were collected from unvaccinated persons, 648 (10%) from fully vaccinated persons, and 156 (2%) from partially vaccinated persons. Among all sequenced specimens, the weekly percentage of B.1.1.7 (Alpha) variant infections increased from 20% to 67% during March 4-May 19, 2021. During April 15-July 21, 2021, the weekly percentage of Delta variant infections increased from 0% to 95%. During March 4-July 21, 2021, the weekly percentage of variants was similar among fully vaccinated and unvaccinated persons, but the Delta variant was more commonly identified among vaccinated persons then unvaccinated persons overall, relative to other variants. The Delta variant was more prevalent among younger persons, with the highest percentage (55%) identified among persons aged 18-44 years. Infections attributed to the Delta variant were also more commonly identified among non-Hispanic Black persons, relative to other variants. These findings reinforce the importance of continued monitoring of SARS-CoV-2 variants and implementing multiple COVID-19 prevention strategies, particularly during the current period in which Delta is the predominant variant circulating in the United States.

Healthcare Delivery & Healthcare Workers

5. **Moral Injury and Burnout in Health Care Professionals During the COVID-19 Pandemic.** Mantri S, Song YK, Lawson JM, Berger EJ, Koenig HG. *J Nerv Ment Dis*. 2021 Oct 1;209(10):720-726. doi: 10.1097/NMD.0000000000001367.
https://journals.lww.com/jonmd/Fulltext/2021/10000/Moral_Injury_and_Burnout_in_Health_Care.5.aspx
The coronavirus pandemic (COVID-19) is predicted to increase burnout in health professionals (HPs), but little is known about moral injury (MI) in this context. We administered the Moral Injury Symptoms Scale for Health Professionals (MISS-HP) and the abbreviated Maslach Burnout Inventory via online survey to a global sample of 1831 HPs in April and October 2020. Mean MISS-HP increased from 27.4 (SD, 11.6) in April to 36.4 (SD, 13.8) in October ($p < 0.001$), with an accompanying increase in personal accomplishment (April: 4.7; SD, 3.1; October: 9.3; SD, 3.1; $p < 0.001$) and no change in other burnout subscales. In April, 26.7% of respondents reported at least moderate functional impairment from MI, increasing to 45.7% in October ($p < 0.001$). Predictors of MISS-HP included younger age and being a nurse. Odds of functional impairment were higher in respondents who were widowed, divorced, never married, or had direct experience caring for patients with COVID-19. COVID-19 has increased MI but not

burnout in HPs; younger or unmarried individuals, nurses, and frontline workers may benefit from targeted outreach to reduce downstream effects of MI, depression, and/or posttraumatic stress disorder.

Prognosis

6. **Comparison of Outcomes in Patients With COVID-19 and Thrombosis Versus Those Without Thrombosis.** Case BC et al. *Am J Cardiol*. 2021 Aug 28:S0002-9149(21)00822-5. doi: 10.1016/j.amjcard.2021.08.038.
https://www.ajconline.org/article/S0002-9149(21)00822-5/fulltext
The in-hospital mortality rate was significantly higher (16.0%) in patients with COVID-19 with concomitant non-cardiac thrombosis than in those without thrombosis (7.9%) but lower than in patients with COVID-19 with cardiac thrombosis (24.7%). In conclusion, patients with COVID-19 with thrombosis, especially cardiac thrombosis, are at higher risk for in-hospital mortality. However, this prognosis is not as grim as for patients with COVID-19 and cardiac thrombosis. Efforts should be focused on early recognition, evaluation, and intensifying antithrombotic management for these patients.

Therapeutics

7. **Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry.** Barbaro RP et al. *Lancet.* 2021 Oct 2;398(10307):1230-1238. doi: 10.1016/S0140-6736(21)01960-7. Epub 2021 Sep 29.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01960-7/fulltext
Mortality after ECMO for patients with COVID-19 worsened during 2020. These findings inform the role of ECMO in COVID-19 for patients, clinicians, and policy makers.

8. **Treatments Associated with Lower Mortality among Critically Ill COVID-19 Patients.** Zhao X, et al. *Anesthesiology.* 2021 Oct 1. doi: 10.1097/ALN.0000000000003999.
https://pubs.asahq.org/anesthesiology/article-abstract/doi/10.1097/ALN.0000000000003999/117698
Consistent with the known hypercoagulability in severe COVID-19, the use of apixaban, enoxaparin, or aspirin was independently associated with lower mortality in critically ill COVID-19 patients.

9. **Remdesivir treatment in hospitalized patients with COVID-19: a comparative analysis of in-hospital all-cause mortality in a large multi-center observational cohort.** Mozaffari E et al. *Clin Infect Dis*. 2021 Oct 1:ciab875. doi: 10.1093/cid/ciab875.
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab875/6378778
RDV initiated upon hospital admission was associated with improved survival among COVID-19 patients. Our findings complement ACTT-1 and support RDV as a foundational treatment for hospitalized COVID-19 patients.

10. **Antibody and cellular therapies for treatment of covid-19: a living systematic review and network meta-analysis.** Siemieniuk RA et al. *BMJ.* 2021 Sep 23;374:n2231. doi: 10.1136/bmj.n2231.
https://www.bmj.com/content/374/bmj.n2231
In patients with non-severe covid-19, casirivimab-imdevimab probably reduces hospitalisation; bamlanivimab-etesevimab, bamlanivimab, and sotrovimab may reduce hospitalisation. Convalescent plasma, IVIg, and other antibody and cellular interventions may not confer any meaningful benefit.
READERS' NOTE: This article is a living systematic review that will be updated to reflect emerging evidence. Interim updates and additional study data will be posted on our website (www.covid19lnma.com).

11. **Effect of Convalescent Plasma on Organ Support-Free Days in Critically Ill Patients With COVID-19: A Randomized Clinical Trial.** Writing Committee for the REMAP-CAP Investigators, Estcourt LJ et al. *JAMA*. 2021 Oct 4. doi: 10.1001/jama.2021.18178.
https://jamanetwork.com/journals/jama/fullarticle/2784914
Among critically ill adults with confirmed COVID-19, treatment with 2 units of high-titer, ABO-compatible convalescent plasma had a low likelihood of providing improvement in the number of organ support-free days.

12. **Update Alert 2: Remdesivir for Adults With COVID-19.** Kaka AS, et al. *Ann Intern Med*. 2021 Oct 5. doi: 10.7326/L21-0600. https://www.acpjournals.org/doi/10.7326/L21-0600
This is the fourth update for our living, rapid review on remdesivir for adults with COVID-19 (1). Our first update, which included studies published through 7 December 2020, led to a major update. Our second update found no new evidence (3). Our third update included 1 new, small randomized controlled study with high risk of bias that did not change our original conclusions. This fourth quarterly update, done using the same search strategies as the original review, identified 650 citations between 11 May and 9 August 2021. One newly published add-on substudy of the World Health Organization (WHO) Solidarity trial, the Norwegian (NOR) Solidarity trial, was eligible for inclusion.
    See also: Update Alert 2: Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid, Living Practice Points From the American College of Physicians (Version 2). Qaseem A et al. *Ann Intern Med.* 2021 Oct 5. doi: 10.7326/L21-0607.

13. **Tocilizumab and remdesivir in hospitalized patients with severe COVID-19 pneumonia: a randomized clinical trial.** Rosas IO et al. *Intensive Care Med.* 2021 Oct 5:1-13. doi: 10.1007/s00134-021-06507-x.
https://www.nejm.org/doi/full/10.1056/NEJMoa2028700
Tocilizumab plus remdesivir did not shorten time to hospital discharge or "ready for discharge" to day 28 compared with placebo plus remdesivir in patients with severe COVID-19 pneumonia.

14. **Antiplatelet therapy and outcome in COVID-19: the Health Outcome Predictive Evaluation Registry.** Santoro F et al. *Heart.* 2021 Oct 5:heartjnl-2021-319552. doi: 10.1136/heartjnl-2021-319552.

https://heart.bmj.com/content/early/2021/10/05/heartjnl-2021-319552.long
APT during hospitalisation for COVID-19 could be associated with lower mortality risk and shorter duration of mechanical ventilation, without increased risk of bleeding.
TRIAL REGISTRATION NUMBER: NCT04334291.

15. **Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With COVID-19: The HEP-COVID Randomized Clinical Trial.** Spyropoulos AC et al. *JAMA Intern Med*. 2021 Oct 7. doi: 10.1001/jamainternmed.2021.6203. Online ahead of print.
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2785004
CONCLUSIONS AND RELEVANCE: In this randomized clinical trial, therapeutic-dose LMWH reduced major thromboembolism and death compared with institutional standard heparin thromboprophylaxis among inpatients with COVID-19 with very elevated D-dimer levels. The treatment effect was not seen in ICU patients.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04401293.

Vaccines / Immunology

16. **COVID-19 hospital admissions and deaths after BNT162b2 and ChAdOx1 nCoV-19 vaccinations in 2·57 million people in Scotland (EAVE II): a prospective cohort study.** Agrawal U et al. *Lancet Respir Med.* 2021 Sep 29:S2213-2600(21)00380-5. doi: 10.1016/S2213-2600(21)00380-5.
https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00380-5/fulltext
COVID-19 hospitalisations and deaths were uncommon 14 days or more after the first vaccine dose in this national analysis in the context of a high background incidence of SARS-CoV-2 infection and with extensive social distancing measures in place. Sociodemographic and clinical features known to increase the risk of severe disease in unvaccinated populations were also associated with severe outcomes in people receiving their first dose of vaccine and could help inform case management and future vaccine policy formulation.

17. **Immune responses to two and three doses of the BNT162b2 mRNA vaccine in adults with solid tumors.** Shroff RT et al. *Nat Med.* 2021 Sep 30. doi: 10.1038/s41591-021-01542-z.
https://www.nature.com/articles/s41591-021-01542-z
We initiated a phase 1 trial for 20 cancer cohort participants of a third vaccine dose of BNT162b2; primary outcomes were immune responses, with a secondary outcome of safety. At 1 week after a third immunization, 16 participants demonstrated a median threefold increase in neutralizing antibody responses, but no improvement was observed in T cell responses. Adverse events were mild. These results suggest that a third dose of BNT162b2 is safe, improves humoral immunity against SARS-CoV-2 and could be immunologically beneficial for patients with cancer on active chemotherapy.

18. **Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older.** Simone A, et al. *JAMA Intern Med.* 2021 Oct 4. doi: 10.1001/jamainternmed.2021.5511.
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2784800

Vaccination is an essential component of the public health strategy to end the COVID-19 pandemic. Recently, there have been reports of acute myocarditis following COVID-19 mRNA vaccine administration. We evaluated acute myocarditis incidence and clinical outcomes among adults following mRNA vaccination in an integrated health care system in the US.

19. **Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study.** Tartof SY et al. *Lancet* 2021 Oct 4. doi: https://doi.org/10.1016/S0140-6736(21)02183-8
Our results provide support for high effectiveness of BNT162b2 against hospital admissions up until around 6 months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection.

20. **One-year sustained cellular and humoral immunities of COVID-19 convalescents.** Zhang J et al. *Clin Infect Dis.* 2021 Oct 5:ciab884. doi: 10.1093/cid/ciab884.
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab884/6381561
SARS-CoV-2-specific cellular and humoral immunities are durable at least until one year after disease onset.

21. **An observational study of breakthrough SARS-CoV-2 Delta variant infections among vaccinated healthcare workers in Vietnam.** Chau NVV et al. *EClinicalMedicine.* 2021 Nov;41:101143. doi: 10.1016/j.eclinm.2021.101143.
https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00423-5/fulltext
Breakthrough Delta variant infections following Oxford-AstraZeneca vaccination may cause asymptomatic or mild disease, but are associated with high viral loads, prolonged PCR positivity and low levels of vaccine-induced neutralizing antibodies. Epidemiological and sequence data suggested ongoing transmission had occurred between fully vaccinated individuals.

22. **Myocarditis after Covid-19 Vaccination in a Large Health Care Organization.** Witberg G, et al. *N Engl J Med.* 2021 Oct 6. doi: 10.1056/NEJMoa2110737.
https://www.nejm.org/doi/full/10.1056/NEJMoa2110737
Among patients in a large Israeli health care system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 100,000 persons; the highest incidence was among male patients between the ages of 16 and 29 years.

23. **Myocarditis after BNT162b2 mRNA Vaccine against Covid-19 in Israel.** Mevorach D et al. *N Engl J Med.* 2021 Oct 6. doi: 10.1056/NEJMoa2109730.
https://www.nejm.org/doi/full/10.1056/NEJMoa2109730
The incidence of myocarditis, although low, increased after the receipt of the BNT162b2 vaccine, particularly after the second dose among young male recipients. The clinical presentation of myocarditis after vaccination was usually mild.

24. **Waning of BNT162b2 Vaccine Protection against SARS-CoV-2 Infection in Qatar.** Chemaitelly H et al. *N Engl J Med.* 2021 Oct 6. doi: 10.1056/NEJMoa2114114.
https://www.nejm.org/doi/full/10.1056/NEJMoa2114114
BNT162b2-induced protection against SARS-COV-2 infection appeared to wane rapidly following its peak after the second dose, but protection against hospitalization and death persisted at a robust level for 6 months after the second dose.

25. **Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months.** Levin EG et al. *N Engl J Med*. 2021 Oct 6. doi: 10.1056/NEJMoa2114583.
https://www.nejm.org/doi/full/10.1056/NEJMoa2114583
Six months after receipt of the second dose of the BNT162b2 vaccine, humoral response was substantially decreased, especially among men, among persons 65 years of age or older, and among persons with immunosuppression.

26. **Immunological response against SARS-CoV-2 following full-dose administration of Comirnaty® COVID-19 vaccine in nursing home residents.** Albert E et al. *Clin Microbiol Infect*. 2021 Oct 4:S1198-743X(21)00560-7. doi: 10.1016/j.cmi.2021.09.031. Online ahead of print.
https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00560-7/fulltext
RESULTS: The SARS-CoV-2-S antibody detection rate in nursing home residents was 99.6% (283/289) and 98.3% (587/597) for SARS-CoV-2 recovered and naïve residents, respectively, within a median of 99 days (range, 17-125 days) after full vaccination. Three out of five residents lacking SARS-CoV-2-S antibodies had detectable S-reactive CD8+ and/or CD4+ T cells. 50/50 and 40/50 participants with detectable SARS-CoV-2 antibodies also had SARS-CoV-2-S-reactive IFN-γ-producing CD4+ and CD8+ T cells, respectively.
CONCLUSION: The Comirnaty® COVID-19 vaccine is highly immunogenic in nursing home residents.

27. **Association of Receipt of the Ad26.COV2.S COVID-19 Vaccine With Presumptive Guillain-Barré Syndrome, February-July 2021.** Woo EJ, Mba-Jonas A, Dimova RB, Alimchandani M, Zinderman CE, Nair N. *JAMA*. 2021 Oct 7. doi: 10.1001/jama.2021.16496. Online ahead of print.
https://jamanetwork.com/journals/jama/fullarticle/2785009
CONCLUSIONS AND RELEVANCE: These findings suggest a potential small but statistically significant safety concern for Guillain-Barré syndrome following receipt of the Ad26.COV2.S vaccine. However, the findings are subject to the limitations of passive reporting systems and presumptive case definition, and they must be considered preliminary pending analysis of medical records to establish a definitive diagnosis.

Women & Children

28. **Common seasonal respiratory viral infections in children before and during the coronavirus disease 2019 (COVID-19) pandemic.** Song X, et al. *Infect Control Hosp Epidemiol.* 2021 Oct 5:1-5. doi: 10.1017/ice.2021.430.
https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/common-seasonal-respiratory-viral-infections-in-children-before-and-

during-the-coronavirus-disease-2019-covid19-pandemic/8294198E62551F6AFB33334C198E49DE
Compared to COVID-19, s-RVI cases were associated with a higher proportion of inpatient admissions but were similar in ICU admission and death rates in hospitalized pediatric patients. Public health interventions for preventing COVID-19 were highly effective in preventing pediatrics s-RVIs.

29. **SARS-CoV-2 vaccine effectiveness in preventing confirmed infection in pregnant women.** Butt AA et al. *J Clin Invest*. 2021 Oct 6:e153662. doi: 10.1172/JCI153662. Online ahead of print.
https://www.jci.org/articles/view/153662
CONCLUSIONS: The mRNA vaccines provide high level of protection against documented SARS-CoV-2 infection, which supports including pregnant women in vaccination campaigns.

30. **Association of the COVID-19 Pandemic With Routine Childhood Vaccination Rates and Proportion Up to Date With Vaccinations Across 8 US Health Systems in the Vaccine Safety Datalink.** DeSilva MB et al. *JAMA Pediatr*. 2021 Oct 7. doi: 10.1001/jamapediatrics.2021.4251. Online ahead of print.
https://jamanetwork.com/journals/jamapediatrics
CONCLUSIONS AND RELEVANCE: As of September 2020, childhood vaccination rates and the proportion who were UTD remained lower than 2019 levels. Interventions are needed to promote catch-up vaccination, particularly in populations at risk for underimmunization.

GUIDELINES & CONSENSUS STATEMENTS

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021.
Evans L. et al. *Intensive Care Med* (2021)

FDA / CDC / NIH / WHO Updates

FDA - Potential for False Positive Results with Certain Lots of Ellume COVID-19 Home Tests Due to a Manufacturing Issue: FDA Safety Communication

FDA - FDA Authorizes Additional OTC Home Test to Increase Access to Rapid Testing for Consumers

WHO - A clinical case definition of post COVID-19 condition by a Delphi consensus, 6 October 2021

WHO - Interim statement on booster doses for COVID-19 vaccination

News/Commentary

News: **Pfizer, BioNTech seek U.S. COVID-19 vaccine clearance for children 5-11**

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