Providence

COVID-19 Resource Desk

#119 | 8.7.2022 to 8.13.2022

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. **Performance of existing definitions and tests for the diagnosis of invasive aspergillosis in critically ill, nonneutropenic, adult patients: an update including COVID-19 data.** FUNDICU investigators. *J Infect.* 2022 Aug 4:S0163-4453(22)00465-0. doi: 10.1016/j.jinf.2022.08.003. https://www.journalofinfection.com/article/S0163-4453(22)00465-0/fulltext

Three major considerations stem from the present literature search update: (i) the updated evidence is in line with the conclusions of the original study on the better performance of BALF GM than serum GM and the suboptimal specificity of serum BDG for the diagnosis of IPA; (ii) four studies assessing the diagnostic performance for IPA of GM-LFA met our inclusion criteria, providing a structured baseline evidence for guiding panel discussion on this test in the next phases of the FUNDICU project; (iii) six of the included studies (55%) assessed the diagnostic performance of laboratory markers for the diagnosis of COVID-19-associated pulmonary aspergillosis (CAPA), an entity which was obviously unknown three years ago.

2. **Infection with the Omicron variant of SARS-CoV-2 is associated with less severe disease in hospitalized patients with COVID-19.** Aiello TF et al. *J Infect*. 2022 Aug 5:S0163-4453(22)00461-3. doi: 10.1016/j.jinf.2022.07.029. https://www.journalofinfection.com/article/S0163-4453(22)00461-3/fulltext

Here, we present a detailed description of the clinical characteristics, viral load, frequency of inflammatory phenotype, and outcomes in hospitalized patients with SARS-CoV-2 infection caused by the Omicron variant, comparing these data with previous admissions.

3. **Morphological, cellular, and molecular basis of brain infection in COVID-19 patients.** Crunfli F et al. *Proc Natl Acad Sci U S A.* 2022 Aug 30;119(35):e2200960119. doi: 10.1073/pnas.2200960119. https://www.pnas.org/doi/full/10.1073/pnas.2200960119

Although increasing evidence confirms neuropsychiatric manifestations associated mainly with severe COVID-19 infection, long-term neuropsychiatric dysfunction (recently characterized as part of "long COVID-19" syndrome) has been frequently observed after mild infection. We show the spectrum of cerebral impact of SARS-CoV-2 infection, ranging from long-term alterations in mildly infected individuals (orbitofrontal cortical atrophy, neurocognitive impairment, excessive fatigue and anxiety symptoms) to severe acute damage confirmed in brain tissue samples extracted from the orbitofrontal

region from individuals who died of COVID-19. In an independent cohort of 26 individuals who died of COVID-19, we used histopathological signs of brain damage as a guide for possible SARS-CoV-2 brain infection and found that among the 5 individuals who exhibited those signs, all of them had genetic material of the virus in the brain. Brain tissue samples from these five patients also exhibited foci of SARS-CoV-2 infection and replication, particularly in astrocytes. Supporting the hypothesis of astrocyte infection, neural stem cell-derived human astrocytes in vitro are susceptible to SARS-CoV-2 infection through a noncanonical mechanism that involves spike-NRP1 interaction. SARS-CoV-2-infected astrocytes manifested changes in energy metabolism and in key proteins and metabolites used to fuel neurons, as well as in the biogenesis of neurotransmitters. Moreover, human astrocyte infection elicits a secretory phenotype that reduces neuronal viability. Our data support the model in which SARS-CoV-2 reaches the brain, infects astrocytes, and consequently, leads to neuronal death or dysfunction. These deregulated processes could contribute to the structural and functional alterations seen in the brains of COVID-19 patients.

Diagnostics & Screening

4. **COVID-19 Self-Test Data: Challenges and Opportunities — United States, October 31, 2021–June 11, 2022.** Ritchey MD, et al. *MMWR Morb Mortal Wkly Rep* 2022;71:1005–1010. DOI: http://dx.doi.org/10.15585/mmwr.mm7132a1

Self-tests are a valuable risk-reduction tool that can guide individual actions, but they currently offer limited utility in enhancing public health surveillance. Laboratory-based and point-of-care test result data, in combination with other COVID-19 surveillance information, continue to provide strong situational awareness.

5. **Notes from the Field: School-Based and Laboratory-Based Reporting of Positive COVID-19 Test Results Among School-Aged Children - New York, September 11, 2021-April 29, 2022.** Shircliff EJ, et al. *MMWR Morb Mortal Wkly Rep.* 2022 Aug 12;71(32):1029-1031. doi: 10.15585/mmwr.mm7132a2. https://www.cdc.gov/mmwr/volumes/71/wr/mm7132a2.htm?s_cid=mm7132a2_w

By April 29, 2022, a total of 702,686 COVID-19 cases were reported among children and adolescents aged 5–17 years in the state of New York. Pediatric COVID-19 cases and hospitalizations increased during the 2021–22 school year, driven by transmission of the Omicron variant. In late 2021, during the surge in Omicron BA.1 variant cases, state and federal authorities expanded access to self-administered, at-home rapid antigen tests, which can increase a person's knowledge of their COVID-19 status and guide risk-reduction behaviors. New York government agencies sent millions of these tests to schools for distribution to teachers, students, and staff members. Because results of self-administered, at-home tests are not captured by electronic laboratory reporting (in contrast to health care provider–administered tests at a physician's office or laboratory that are reported through electronic health records or other means), expanded use of these tests might affect interpretation of trends in reported COVID-19 cases; however, this has yet to be assessed. Furthermore, understanding changes in testing behavior before and after the Omicron variant surge might help public health officials better use available COVID-19 data to guide future policy.

Epidemiology & Public Health

6. **Impact of the COVID-19 Pandemic on Cardiovascular Health in 2020: JACC State-of-the-Art Review.** Roth GA, et al. *J Am Coll Cardiol*. 2022 Aug 9;80(6):631-640. doi: 10.1016/j.jacc.2022.06.008. https://www.sciencedirect.com/science/article/pii/S0735109722053116

The impact of COVID-19 on the burden of cardiovascular diseases (CVD) during the early pandemic remains unclear. COVID-19 has become one of the leading causes of global mortality, with a disproportionate impact on persons with CVD. Studies of health facility admissions for CVD found significant decreases during the pandemic. Studies of hospital mortality for CVD were more variable. Studies of population-level CVD mortality differed across countries, with most showing decreases, although some revealed increases in deaths. In some countries where large increases in CVD deaths were reported in vital registration systems, misclassification of COVID-19 as CVD may have occurred. Taken together, studies suggest heterogeneous effects of the COVID-19 pandemic on CVD without large increases in CVD mortality in 2020 for a number of countries. Clinical and population science research is needed to examine the ways in which the pandemic has affected CVD burden.

Healthcare Delivery & Healthcare Workers

7. **Burnout Among Respiratory Therapists Amid the COVID-19 Pandemic.** Hinkson Carl, et al. **[Providence author]**. *Respir Care.* 2022 Aug 3:respcare.10144. doi: 10.4187/respcare.10144. https://rc.rcjournal.com/content/early/2022/08/02/respcare.10144

Themes associated with burnout in RTs included staffing, workload, physical and emotional exhaustion, lack of effective leadership, and lack of respect. These results provide potential targets for interventions to combat burnout among RTs.

Survivorship & Rehabilitation

8. **Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study.** Lifelines Corona Research Initiative. *Lancet.* 2022 Aug 6;400(10350):452-461. doi: 10.1016/S0140-6736(22)01214-4. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01214-4/fulltext

To our knowledge, this is the first study to report the nature and prevalence of post-COVID-19 condition, while correcting for individual symptoms present before COVID-19 and the symptom dynamics in the population without SARS-CoV-2 infection during the pandemic. Further research that distinguishes potential mechanisms driving post-COVID-19-related symptomatology is required.

9. **Readmissions, post-discharge mortality and sustained recovery among patients admitted to hospital with COVID-19.** Moestrup KS et al. *Clin Infect Dis.* 2022 Aug 8:ciac639. doi: 10.1093/cid/ciac639. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac639/6658187

Among 3,386 patients included in the study 2,796 (82.6%) reached recovery and 2,600 (77.0%) achieved sustained recovery. Of those discharged from hospital, 556 (19.9%) were readmitted, and 289

(10.3%) died. Overall, the median time to recovery was 6 days (Interquartile range (IQR), 3-10), and 19 days (IQR, 11-33) among patients in intensive care in the first two days of admission.
CONCLUSIONS: Post-discharge readmission and mortality rates were substantial. Therefore, sustained recovery should be favored to recovery outcomes in clinical COVID-19 trials. A 28-day follow-up period may be too short the critically ill.

Therapeutics

10. **Efficacy and Safety of Ensovibep for Adults Hospitalized With COVID-19 : A Randomized Controlled Trial.** ACTIV-3/TICO Study Group*. *Ann Intern Med.* 2022 Aug 9. doi: 10.7326/M22-1503. https://www.acpjournals.org/doi/10.7326/M22-1503

Compared with placebo, ensovibep did not improve clinical outcomes for hospitalized participants with COVID-19 receiving standard care, including remdesivir; no safety concerns were identified.

11. **Randomized clinical trial of nitazoxanide or sofosbuvir/daclatasvir for the prevention of SARS-CoV-2 infection.** Sokhela S, et al. *J Antimicrob Chemother.* 2022 Aug 12:dkac266. doi: 10.1093/jac/dkac266. https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkac266/6661458

In this randomized trial, nitazoxanide and sofosbuvir/daclatasvir had no significant preventative effect on infection with SARS-CoV-2 among healthcare workers and others at high risk of infection.

Transmission / Infection Control

12. **Evaluating the efficacy and safety of a novel prophylactic nasal spray in the prevention of SARS-CoV-2 infection: A multi-centre, double blind, placebo-controlled, randomised trial.** Balmforth D et al. *J Clin Virol.* 2022 Jul 25;155:105248. doi: 10.1016/j.jcv.2022.105248. https://www.sciencedirect.com/science/article/pii/S1386653222001809

Results Between 16th April 2021 and 26th July 2021, 556 participants were analysed for the primary endpoint (275 Test; 281 Placebo). The test agent significantly reduced SARS-CoV-2 infection compared to placebo [36 cases (13.1%) Vs 97 cases (34.5%). Fewer clinical symptoms were also seen in the test group [57 cases (17.6%) vs 112 cases (34.6%). No harmful effects were associated with taking the test agent. Conclusion The test agent significantly reduced SARS-CoV-2 infection in healthcare workers, with 62% fewer infections when compared to placebo. It was found to be safe and well tolerated and offers a novel treatment option for prophylaxis against SARS-CoV-2 infection.

Vaccines / Immunology

13. **Protection of Omicron sub-lineage infection against reinfection with another Omicron sub-lineage.** Chemaitelly H et al. *Nat Commun.* 2022 Aug 9;13(1):4675. doi: 10.1038/s41467-022-32363-4. https://www.nature.com/articles/s41467-022-32363-4

There is significant genetic distance between SARS-CoV-2 Omicron (B.1.1.529) variant BA.1 and BA.2 sub-lineages. This study investigates immune protection of infection with one sub-lineage against reinfection with the other sub-lineage in Qatar during a large BA.1 and BA.2 Omicron wave, from December 19, 2021 to March 21, 2022. Two national matched, retrospective cohort studies are

conducted to estimate effectiveness of BA.1 infection against reinfection with BA.2 (N = 20,994; BA.1-against-BA.2 study), and effectiveness of BA.2 infection against reinfection with BA.1 (N = 110,315; BA.2-against-BA.1 study). Associations are estimated using Cox proportional-hazards regression models after multiple imputation to assign a sub-lineage status for cases with no sub-lineage status (using probabilities based on the test date). Effectiveness of BA.1 infection against reinfection with BA.2 is estimated at 94.2% (95% CI: 89.2-96.9%). Effectiveness of BA.2 infection against reinfection with BA.1 is estimated at 80.9% (95% CI: 73.1-86.4%). Infection with the BA.1 sub-lineage appears to induce strong, but not full immune protection against reinfection with the BA.2 sub-lineage, and vice versa, for at least several weeks after the initial infection.

14. **Omicron BA.4/BA.5 escape neutralizing immunity elicited by BA.1 infection.** Khan K et al. *Nat Commun*. 2022 Aug 10;13(1):4686. doi: 10.1038/s41467-022-32396-9. https://www.nature.com/articles/s41467-022-32396-9

SARS-CoV-2 Omicron (B.1.1.529) BA.4 and BA.5 sub-lineages, first detected in South Africa, have changes relative to Omicron BA.1 including substitutions in the spike receptor binding domain. Here we isolated live BA.4 and BA.5 viruses and measured BA.4/BA.5 neutralization elicited by BA.1 infection either in the absence or presence of previous vaccination as well as from vaccination without BA.1 infection. In BA.1-infected unvaccinated individuals, neutralization relative to BA.1 declines 7.6-fold for BA.4 and 7.5-fold for BA.5. In vaccinated individuals with subsequent BA.1 infection, neutralization relative to BA.1 decreases 3.2-fold for BA.4 and 2.6-fold for BA.5. The fold-drop versus ancestral virus neutralization in this group is 4.0-fold for BA.1, 12.9-fold for BA.4, and 10.3-fold for BA.5. In contrast, BA.4/BA.5 escape is similar to BA.1 in the absence of BA.1 elicited immunity: fold-drop relative to ancestral virus neutralization is 19.8-fold for BA.1, 19.6-fold for BA.4, and 20.9-fold for BA.5. These results show considerable escape of BA.4/BA.5 from BA.1 elicited immunity which is moderated with vaccination and may indicate that BA.4/BA.5 may have the strongest selective advantage in evading neutralization relative to BA.1 in unvaccinated, BA.1 infected individuals.

15. **Durability of Heterologous and Homologous COVID-19 Vaccine Boosts.** Tan CS et al. *JAMA Netw Open.* 2022 Aug 1;5(8):e2226335. doi: 10.1001/jamanetworkopen.2022.26335. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2794985

Heterologous Ad26.COV2.S boosting was associated with durable humoral and cellular immune responses in individuals who originally received the BNT162b2 vaccine. These data suggest potential benefits of heterologous prime-boost vaccine regimens for SARS-CoV-2.

16. **Comparative immunogenicity and reactogenicity of heterologous ChAdOx1-nCoV-19-priming and BNT162b2 or mRNA-1273-boosting with homologous COVID-19 vaccine regimens.** Klemis V et al. *Nat Commun.* 2022 Aug 11;13(1):4710. doi: 10.1038/s41467-022-32321-0. https://www.nature.com/articles/s41467-022-32321-0

Comparative analyses of the immunogenicity and reactogenicity of homologous and heterologous SARS-CoV-2 vaccine-regimens will inform optimized vaccine strategies. Here we analyze the humoral and cellular immune response following heterologous and homologous vaccination strategies in a convenience cohort of 331 healthy individuals. All regimens induce immunity to the vaccine antigen. Immunity after vaccination with ChAdOx1-nCoV-19 followed by either BNT162b2 (n = 66) or mRNA-1273 (n = 101) is equivalent to or more pronounced than homologous mRNA-regimens (n = 43

BNT162b2, n = 59 mRNA-1273) or homologous ChAdOx1-nCoV-19 vaccination (n = 62). We note highest levels of spike-specific CD8 T-cells following both heterologous regimens. Among mRNA-containing combinations, spike-specific CD4 T-cell levels in regimens including mRNA-1273 are higher than respective combinations with BNT162b2. Polyfunctional T-cell levels are highest in regimens based on ChAdOx1-nCoV-19-priming. All five regimens are well tolerated with most pronounced reactogenicity upon ChAdOx1-nCoV-19-priming, and ChAdOx1-nCoV-19/mRNA-1273-boosting. In conclusion, we present comparative analyses of immunogenicity and reactogenicity for heterologous vector/mRNA-boosting and homologous mRNA-regimens.

17. **Vaccine effectiveness of two-dose BNT162b2 against symptomatic and severe COVID-19 among adolescents in Brazil and Scotland over time: a test-negative case-control study.** Florentino PTV et al. *Lancet Infect Dis.* 2022 Aug 8:S1473-3099(22)00451-0. doi: 10.1016/S1473-3099(22)00451-0. https://www.sciencedirect.com/science/article/pii/S1473309922004510

We found waning vaccine protection of BNT162b2 against symptomatic COVID-19 infection among adolescents in Brazil and Scotland from 27 days after the second dose. However, protection against severe COVID-19 outcomes remained high at 98 days or more after the second dose in the omicron-dominant period. Booster doses for adolescents need to be considered.

18. **Antibody Response in Immunocompromised Patients with Hematologic Cancers Who Received a 3-Dose mRNA-1273 Vaccination Schedule for COVID-19.** Haggenburg S et al. *JAMA Oncol.* 2022 Aug 11. doi: 10.1001/jamaoncol.2022.3227. https://jamanetwork.com/journals/jamaoncology/fullarticle/2795176

Results of this cohort study support that the primary schedule for immunocompromised patients with hematologic cancers should be supplemented with a delayed third vaccination. Patients with B-cell lymphoma and allogeneic HCT recipients need to be revaccinated after treatment or transplantation.

Women & Children

19. **SARS-CoV-2 Infections and Presymptomatic Type 1 Diabetes Autoimmunity in Children and Adolescents from Colorado, USA, and Bavaria, Germany.** ASK Study Group and Fr1da Study Group. *JAMA.* 2022 Aug 5. doi: 10.1001/jama.2022.14092. https://jamanetwork.com/journals/jama/fullarticle/2795226

An increased incidence of clinical diabetes has been reported in children with previous COVID-19.1,2 It is plausible that the virus may trigger autoimmune response to the islets or hasten metabolic decompensation in persons with already established islet autoimmunity. We tested the hypothesis that previous SARS-CoV-2 infection was associated with autoimmunity, which predicts future type 1 diabetes.

20. **Post-COVID-19 Symptoms and Conditions Among Children and Adolescents - United States, March 1, 2020-January 31, 2022.** Kompaniyets L, et al. *MMWR Morb Mortal Wkly Rep.* 2022 Aug 5;71(31):993-999. doi: 10.15585/mmwr.mm7131a3. https://www.cdc.gov/mmwr/volumes/71/wr/mm7131a3.htm?s_cid=mm7131a3_w

Using a large medical claims database, CDC assessed nine potential post-COVID signs and symptoms (symptoms) and 15 potential post-COVID conditions among 781,419 U.S. children and adolescents

aged 0-17 years with laboratory-confirmed COVID-19 (patients with COVID-19) compared with 2,344,257 U.S. children and adolescents without recognized COVID-19 (patients without COVID-19) during March 1, 2020-January 31, 2022. Patients with COVID-19 were less likely than were patients without to experience respiratory signs and symptoms, symptoms of mental conditions, muscle disorders, neurological conditions, anxiety and fear-related disorders, mood disorders, and sleeping disorders. COVID-19 prevention strategies, including vaccination for all eligible children and adolescents, are critical to prevent SARS-CoV-2 infection and subsequent illness, including post-COVID symptoms and conditions.

21. **COVID-19 and Acute Neurologic Complications in Children.** Antoon JW, et al. *Pediatrics.* 2022 Aug 11. doi: 10.1542/peds.2022-058167. https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-058167/188743/COVID-19-and-Acute-Neurologic-Complications-in

Neurologic complications are common in children hospitalized with COVID-19 and are associated with worse hospital outcomes. Our findings emphasize the importance of COVID-19 immunization in children, especially in high-risk populations, such as those with neurologic co-morbidity.

GUIDELINES & CONSENSUS STATEMENTS

Interim Recommendation of the Advisory Committee on Immunization Practices for Use of the Novavax COVID-19 Vaccine in Persons Aged ≥18 years - United States, July 2022. Twentyman E et al. *MMWR Morb Mortal Wkly Rep.* 2022 Aug 5;71(31):988-992. doi: 10.15585/mmwr.mm7131a2.

Summary of Guidance for Minimizing the Impact of COVID-19 on Individual Persons, Communities, and Health Care Systems — United States, August 2022. Massetti GM, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 11 August 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7133e1

FDA / CDC / NIH / WHO Updates

CDC streamlines COVID-19 guidance to help the public better protect themselves and understand their risk

FDA - At-Home COVID-19 Antigen Tests-Take Steps to Reduce Your Risk of False Negative

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