Providence

COVID-19 Resource Desk

#112 | 6.19.2022 to 6.24.2022

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

Epidemiology & Public Health

1. **Increased deaths from fungal infections during the COVID-19 pandemic-National Vital Statistics System, United States, January 2020-December 2021.** Gold JAW, et al. *Clin Infect Dis.* 2022 Jun 19:ciac489. doi: 10.1093/cid/ciac489. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac489/6611491

Fungal deaths increased during 2020-2021 compared with previous years, primarily driven by COVID-19-associated fungal deaths, particularly those involving Aspergillus and Candida. Our findings may inform efforts to prevent, identify, and treat severe fungal infections in COVID-19 patients, especially in certain racial/ethnic groups and geographic areas.

2. **Delayed Recognition of COVID-19 in New York City: A descriptive analysis of COVID-19 illness prior to February 29, 2020.** Keating P, et al. *Clin Infect Dis.* 2022 Jun 20:ciac490. doi: 10.1093/cid/ciac490. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac490/6611571

COVID-19 was in NYC before being classified as a PHEIC, and eluded surveillance for another month. The delay in recognition limited mitigation efforts; by the time city and state-wide mandates were enacted,16 and 22 days later, there was already widespread community transmission.

3. **Hospitalization and Emergency Department Encounters for COVID-19 After Paxlovid Treatment — California, December 2021–May 2022.** Malden DE, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 21 June 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7125e2

Recurrence of COVID-19 symptoms and positive SARS-CoV-2 test results have been reported after completion of Paxlovid oral antiviral treatment for COVID-19, but real-world evidence of severe illness following Paxlovid is lacking. COVID-19–related hospital admissions and emergency department (ED) encounters occurring 5–15 days after Paxlovid treatment were described using data from a large integrated health care system. Reports of such hospitalizations or ED encounters occurred infrequently, representing <1% of Paxlovid-treated patients over the study period. When administered as an early-stage treatment, Paxlovid might prevent COVID-19–related hospitalization among persons with mild-to-moderate COVID-19 who are at risk for progression to severe disease.

4. **Dispensing of Oral Antiviral Drugs for Treatment of COVID-19 by Zip Code–Level Social Vulnerability — United States, December 23, 2021–May 21, 2022.** Gold JA, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 21 June 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7125e1

Lagevrio and Paxlovid are oral antiviral drugs effective at preventing hospitalization and death in patients with mild to moderate COVID-19 who are at risk for progression to severe disease. During December 23, 2021–May 21, 2022, 1,076,762 oral antiviral prescriptions were dispensed in the United States. The overall number of antivirals dispensed increased; however, by the end of the study period, dispensing rates were lowest in high vulnerability zip codes, despite these zip codes having the largest number of dispensing sites. Additional public health, regulatory, and policy efforts might help decrease barriers to oral antiviral access, particularly in communities with high social vulnerability.

5. **Early SARS-CoV-2 Reinfections within 60 Days and Implications for Retesting Policies.** Nevejan L, et al. *Emerg Infect Dis*. 2022 Jun 23;28(8). doi: 10.3201/eid2808.220617. https://wwwnc.cdc.gov/eid/article/28/8/22-0617_article

Illustrated by a clinical case supplemented by epidemiologic data, early reinfections with SARS-CoV-2 Omicron BA.1 after infection with Delta variant, and reinfection with Omicron BA.2 after Omicron BA.1 infection, can occur within 60 days, especially in young, unvaccinated persons. The case definition of reinfection, which influences retesting policies, should be reconsidered.

Survivorship & Rehabilitation

6. **Long-COVID in children and adolescents: a systematic review and meta-analyses.** Lopez-Leon, S., Wegman-Ostrosky, T., Ayuzo del Valle, N.C. et al. *Sci Rep* 12, 9950 (2022). https://doi.org/10.1038/s41598-022-13495-5

The literature search yielded 8373 publications, of which 21 studies met the inclusion criteria, and a total of 80,071 children and adolescents were included. The prevalence of long-COVID was 25.24%, and the most prevalent clinical manifestations were mood symptoms (16.50%), fatigue (9.66%), and sleep disorders (8.42%). Children infected by SARS-CoV-2 had a higher risk of persistent dyspnea, anosmia/ageusia, and/or fever compared to controls. Limitations of the studies analyzed include lack of standardized definitions, recall, selection, misclassification, nonresponse and/or loss of follow-up, and a high level of heterogeneity.

7. **Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2.** Antonelli M, et al. *Lancet.* 2022 Jun 18;399(10343):2263-2264. doi: 10.1016/S0140-6736(22)00941-2. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00941-2/fulltext

Overall, we found a reduction in odds of long COVID with the omicron variant versus the delta variant of 0·24–0·50 depending on age and time since vaccination. However, the absolute number of people experiencing long COVID at a given time depends on the shape and amplitude of the pandemic curve. For example, given the high numbers of people infected with omicron in the UK from December, 2021, to February, 2022, our data are consistent with the UK Office for National Statistics, who estimated that the numbers of people experiencing long COVID actually increased from 1·3 million in January, 2022, to 1·7 million in March, 2022.4 Considering the UK omicron peak of more than 350 000 new symptomatic COVID-19 cases per day estimated on March 26, 2022, by the ZOE app model and 4% of cases being long COVID, future numbers with long COVID will inevitably rise.

Therapeutics

8. **Preadmission Statin Treatment and Outcome in Patients Hospitalized With COVID-19.** Saad M, et al. *Am J Cardiol.* 2022 Jun 14:S0002-9149(22)00521-5. doi: 10.1016/j.amjcard.2022.04.045. https://www.ajconline.org/article/S0002-9149(22)00521-5/fulltext

Among patients with established cardiovascular disease who were hospitalized with COVID-19, preadmission statin therapy was associated with improved in-hospital outcome, an association that was negated once inflammation and myocardial injury were considered.

9. **Janus kinase inhibitors for the treatment of COVID-19.** Kramer A et al. *Cochrane Database Syst Rev.* 2022 Jun 13;6(6):CD015209. doi: 10.1002/14651858.CD015209. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD015209/full

In hospitalised individuals with moderate to severe COVID-19, moderate-certainty evidence shows that systemic JAK inhibitors probably decrease all-cause mortality. Baricitinib was the most often evaluated JAK inhibitor. Moderate-certainty evidence suggests that they probably make little or no difference in improvement in clinical status. Moderate-certainty evidence indicates that systemic JAK inhibitors probably decrease the risk of worsening of clinical status and make little or no difference in the rate of adverse events of any grade, whilst they probably decrease the occurrence of serious adverse events. Based on low-certainty evidence, JAK inhibitors may make little or no difference in the rate of secondary infection. Subgroup analysis by severity of COVID-19 or type of agent failed to identify specific subgroups which benefit more or less from systemic JAK inhibitors. Currently, there is no evidence on the efficacy and safety of systemic JAK inhibitors for individuals with asymptomatic or mild disease (non-hospitalised individuals).

10. **Annals for Hospitalists Inpatient Notes - Venous Thromboembolism Prophylaxis in COVID-19: Making Sense of the Evidence.** Smith CA, Barnes GD. *Ann Intern Med*. 2022 Jun;175(6):HO2-HO3. doi: 10.7326/M22-1425. https://www.acpjournals.org/doi/10.7326/M22-1425

In patients hospitalized with COVID-19, venous thromboembolism (VTE) has been recognized as an important complication despite the use of prophylactic anticoagulation. The causes of this hypercoagulability in COVID-19 include a hyperinflammatory state, endothelial injury, platelet and complement activation, and coagulopathy.

11. **Virologic and Immunologic Characterization of COVID-19 Recrudescence after Nirmatrelvir/Ritonavir Treatment.** Carlin AF, et al. *Clin Infect Dis.* 2022 Jun 20:ciac496. doi: 10.1093/cid/ciac496. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac496/6611663

We isolated a SARS-CoV-2 BA.2 variant from a person with COVID-19 recrudescence after nirmatrelvir/ritonavir treatment. Antiviral sensitivity and neutralizing antibody testing were performed with both parental SARS-CoV-2 and multiple variants of concern. We found that neither NM resistance nor absence of neutralizing immunity were likely causes of the recrudescence.

12. **Regdanvimab improves disease mortality and morbidity in patients with COVID-19: a meta-analysis.** Yang M, et al. *J Infect*. 2022 Jun 18:S0163-4453(22)00369-3. doi:

10.1016/j.jinf.2022.05.044. https://www.journalofinfection.com/article/S0163-4453(22)00369-3/fulltext

There have been no prior meta-analyses describing the association between the usage of regdanvimab and patient prognosis following COVID-19 infection to the best of our knowledge. We perform in this study the first meta-analysis in the literature to evaluate the relationship between regdanvimab administration and patient outcomes following COVID-19 infection.

13. **Major candidate variables to guide personalised treatment with steroids in critically ill patients with COVID-19: CIBERESUCICOVID study.** Torres A et al. *Intensive Care Med*. 2022 Jun 21. doi: 10.1007/s00134-022-06726-w. https://link.springer.com/article/10.1007/s00134-022-06726-w

Corticosteroid in ICU-admitted patients with COVID-19 may be administered based on age, severity, baseline inflammation, and invasive mechanical ventilation. Early administration since symptom onset may prove harmful.

14. **Aspirin Therapy on Prophylactic Anticoagulation for Patients Hospitalized With COVID-19: A Propensity Score-Matched Cohort Analysis of the HOPE-COVID-19 Registry.** Santoro F et al. *J Am Heart Assoc.* 2022 Jun 22:e024530. doi: 10.1161/JAHA.121.024530. https://www.ahajournals.org/doi/10.1161/JAHA.121.024530

PAC and aspirin was associated with lower mortality risk among patients hospitalized with COVID-19 in a propensity score matched population compared to PAC alone.

15. **Characterization of virologic rebound following nirmatrelvir-ritonavir treatment for COVID-19.** Boucau J et al. *Clin Infect Dis*. 2022 Jun 23:ciac512. doi: 10.1093/cid/ciac512. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac512/6614635

We enrolled seven individuals with recurrent symptoms or antigen test conversion following nirmatrelvir-ritonavir treatment. High viral loads (median 6.1 log10 copies/mL) were detected after rebound for a median of 17 days after initial diagnosis. Three had culturable virus for up to 16 days after initial diagnosis. No known resistance-associated mutations were identified.

Vaccines / Immunology

16. **Safety and immunogenicity of the inactivated whole-virus adjuvanted vaccine VLA2001: a randomized, dose escalation, double-blind phase 1/2 clinical trial in healthy adults.** Lazarus R et al. *J Infect.* 2022 Jun 16:S0163-4453(22)00361-9. doi: 10.1016/j.jinf.2022.06.009. https://www.journalofinfection.com/article/S0163-4453(22)00361-9/fulltext

VLA2001 was well tolerated in all tested dose groups, and no safety signal of concern was identified. The highest dose group showed statistically significantly stronger immunogenicity with similar tolerability and safety, and was selected for phase 3 clinical development.

17. **Vaccine effectiveness of CanSino (Adv5-nCoV) COVID-19 vaccine among childcare workers - Mexico, March-December 2021.** Richardson VL et al. *Clin Infect Dis*. 2022 Jun 19:ciac488. doi: 10.1093/cid/ciac488. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac488/6611492

CanSino vaccine was effective at preventing COVID-19 illness and highly effective at preventing hospitalization and death. It will be useful to further evaluate duration of protection and assess the value of booster doses to prevent COVID-19 and severe outcomes.

18. **BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection.** Cao Y et al. *Nature.* 2022 Jun 17. doi: 10.1038/s41586-022-04980-y. https://www.nature.com/articles/s41586-022-04980-y

Here, coupled with Spike structural comparisons, we show that BA.2.12.1 and BA.4/BA.5 exhibit comparable ACE2-binding affinities to BA.2. Importantly, BA.2.12.1 and BA.4/BA.5 display stronger neutralization evasion than BA.2 against the plasma from 3-dose vaccination and, most strikingly, from post-vaccination BA.1 infections. To delineate the underlying antibody evasion mechanism, we determined the escaping mutation profiles2, epitope distribution3 and Omicron neutralization efficacy of 1640 RBD-directed neutralizing antibodies (NAbs), including 614 isolated from BA.1 convalescents. Interestingly, post-vaccination BA.1 infection mainly recalls wildtype-induced humoral memory. The resulting elicited antibodies could neutralize both wildtype and BA.1 and are enriched on non-ACE2-competing epitopes. However, most of these cross-reactive NAbs are heavily escaped by L452Q, L452R and F486V. BA.1 infection can also induce new clones of BA.1-specific antibodies that potently neutralize BA.1; nevertheless, these NAbs are largely escaped by BA.2/BA.4/BA.5 due to D405N and F486V, and react weakly to pre-Omicron variants, exhibiting poor neutralization breadths. As for therapeutic NAbs, Bebtelovimab4 and Cilgavimab5 can effectively neutralize BA.2.12.1 and BA.4/BA.5, while the S371F, D405N and R408S mutations would undermine most broad sarbecovirus NAbs. Together, our results indicate that Omicron may evolve mutations to evade the humoral immunity elicited by BA.1 infection, suggesting that BA.1-derived vaccine boosters may not achieve broad-spectrum protection against new Omicron variants.

19. **Hospitalized patients with severe COVID-19 during the Omicron wave in Israel - benefits of a fourth vaccine dose.** Brosh-Nissimov T et al. *Clin Infect Dis*. 2022 Jun 20:ciac501. doi: 10.1093/cid/ciac501. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac501/6611845

Among hospitalized patients with severe/critical breakthrough COVID-19, a recent fourth dose was associated with significant protection against mechanical ventilation or death, compared to three doses.

20. **Management of suspected and confirmed COVID-19 (SARS-CoV-2) vaccine hypersensitivity.** Worm M et al. *Allergy.* 2022 Jun 20. doi: 10.1111/all.15414. https://onlinelibrary.wiley.com/doi/10.1111/all.15414

Proven IgE-mediated hypersensitivity to SARS-CoV-2 vaccines is extremely rare and not increased in comparison with reported hypersensitivity to other vaccines. The value of skin tests is unclear and nonspecific reactions, in particular when intradermal testing is applied, should be considered.

21. **Neutralization Escape by SARS-CoV-2 Omicron Subvariants BA.2.12.1, BA.4, and BA.5.** Hachmann NP, et al. *N Engl J Med.* 2022 Jun 22. doi: 10.1056/NEJMc2206576. https://www.nejm.org/doi/10.1056/NEJMc2206576

In recent months, multiple lineages of the omicron (B.1.1.529) variant of SARS-CoV-2 have emerged, with subvariants BA.1 and BA.2 showing substantial escape from neutralizing antibodies. Subvariant BA.2.12.1 is now the dominant strain in the United States, and BA.4 and BA.5 are dominant in South Africa. Subvariants BA.4 and BA.5 have identical sequences of the spike protein.

22. **Association of Receipt of the Fourth BNT162b2 Dose with Omicron Infection and COVID-19 Hospitalizations Among Residents of Long-term Care Facilities.** Muhsen K, et al. *JAMA Intern Med.* 2022 Jun 23. doi: 10.1001/jamainternmed.2022.2658. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2793699

The results of this cohort study suggest that receipt of a fourth BNT162b2 dose conferred high protection against COVID-19 hospitalizations and deaths among LTCF residents during a substantial Omicron variant surge, but protection was modest against infection. These findings are relevant to the control of COVID-19 pandemic globally, especially among the population of LTCFs.

23. **Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study.** Li X et al. *BMJ.* 2021 Jun 14;373:n1435. doi: 10.1136/bmj.n1435. https://www.bmj.com/content/373/bmj.n1435

This study found large variations in the observed rates of AESIs by age group and sex, showing the need for stratification or standardisation before using background rates for safety surveillance. Considerable population level heterogeneity in AESI rates was found between databases.

Women & Children

24. **Immunogenicity and reactogenicity of an inactivated SARS-CoV-2 vaccine (BBV152) in children aged 2-18 years: interim data from an open-label, non-randomised, age de-escalation phase 2/3 study.** Vadrevu KM et al. *Lancet Infect Dis*. 2022 Jun 16:S1473-3099(22)00307-3. doi: 10.1016/S1473-3099(22)00307-3. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00307-3/fulltext

BBV152 was well tolerated in children aged 2-18 years, and induced higher neutralising antibody responses than those observed in adults, in whom the efficacy (ie, the prevention or decrease in the severity of COVID-19 infection) has been demonstrated.
FUNDING: Bharat Biotech International.

25. **COVID-19 Severity among Women of Reproductive Age with Symptomatic Laboratory-Confirmed SARS-CoV-2 by Pregnancy Status - United States, Jan 1, 2020 - Dec 25, 2021.** Strid P, et al. *Clin Infect Dis.* 2022 Jun 19:ciac479. doi: 10.1093/cid/ciac479. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac479/6611488

Compared with the pre-Delta period, pregnant and nonpregnant WRA were at increased risk for severe COVID-19 in the Delta period.

26. **Life-Threatening Complications of Influenza versus COVID-19 in U.S. Children.** Halasa NB et al. *Clin Infect Dis.* 2022 Jun 19:ciac477. doi: 10.1093/cid/ciac477. https://go.openathens.net/redirector/providence.org?url=https%3A%2F%2Facademic.oup.com%2Fcid%2Fadvance-article%2Fdoi%2F10.1093%2Fcid%2Fciac477%2F6611483%3Flogin%3Dtrue

Despite differences in demographics and clinical characteristics of children with influenza or COVID-19, the frequency of life-threatening complications was similar. Our findings highlight the importance of implementing prevention measures to reduce transmission and disease severity of influenza and COVID-19.

27. **COVID-19 Vaccines in Infants, Children, and Adolescents.** Infectious Diseases CO. *Pediatrics.* 2022 Jun 18. doi: 10.1542/peds.2022-058700. https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2022-058700/188297/COVID-19-Vaccines-in-Infants-Children-and

Vaccines are safe and effective in protecting individuals and populations against infectious diseases. New vaccines are evaluated by a long-standing, rigorous, and transparent process by the US Food and Drug Administration and the Centers for Disease Control and Prevention (CDC). All available safety and efficacy data are reviewed before authorization or approval of policy recommendations.

28. **Evaluation of Acute Adverse Events after Covid-19 Vaccination during Pregnancy.** DeSilva M et al. *N Engl J Med.* 2022 Jun 22. doi: 10.1056/NEJMc2205276. https://www.nejm.org/doi/10.1056/NEJMc2205276

We performed a retrospective, observational, matched-cohort study involving pregnant women between the ages of 16 and 49 years at eight Vaccine Safety Datalink sites from December 15, 2020, through July 1, 2021. We matched each dose of a Food and Drug Administration–authorized Covid-19 vaccine received by a pregnant woman to an unvaccinated pregnant woman, according to study site and pregnancy start date. Included in the pregnancy cohort were women who were subsequently found to be pregnant within 28 days after receiving the vaccine. Vaccinations were captured through electronic health records, claims data, and bidirectional linkages with state and local immunization registries.

29. **Maternal Vaccination and Risk of Hospitalization for Covid-19 among Infants.** Halasa NB et al. *N Engl J Med*. 2022 Jun 22. doi: 10.1056/NEJMoa2204399. https://www.nejm.org/doi/10.1056/NEJMoa2204399

Maternal vaccination with two doses of mRNA vaccine was associated with a reduced risk of hospitalization for Covid-19, including for critical illness, among infants younger than 6 months of age. (Funded by the Centers for Disease Control and Prevention.).

30. **Severity of SARS-CoV-2 Omicron BA.2 infection in unvaccinated hospitalized children: Comparison to influenza and parainfluenza infections.** Tso WWY et al. *Emerg Microbes Infect.* 2022 Jun 22:1-29. doi: 10.1080/22221751.2022.2093135. https://www.tandfonline.com/doi/full/10.1080/22221751.2022.2093135

Our findings showed that for hospitalized children who had no past COVID-19 or vaccination, Omicron BA.2 was not mild. Omicron BA.2 appeared to be more neuropathogenic than influenza and parainfluenza viruses. It targeted the upper airways more than influenza virus.

31. **SARS-CoV-2 co-detection with influenza A and other respiratory viruses among school-aged children and their household members- March 12, 2020, to February 22, 2022, Dane County,**

Wisconsin. Temte JL, et al. *Clin Infect Dis.* 2022 Jun 23:ciac487. doi: 10.1093/cid/ciac487. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac487/6614626

Of 2,109 participants (497 index children in 497 households with 1,612 additional household members), two (0.1%) were positive for both SARS-CoV-2 and influenza A; an additional 11 (0.5%) were positive for SARS-CoV-2 and another RPP-covered respiratory virus. Co-detections predominantly affected school-aged children (12 out of 13 total) and were noted in 11 of 497 households. SARS-CoV-2 co-detections with other respiratory viruses were uncommon and predominated in school-aged children.

GUIDELINES & CONSENSUS STATEMENTS

American Academy of Pediatrics Applauds CDC Approval of Safe, Effective COVID-19 Vaccines for Children Ages 6 Months and Older

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FDA / CDC / NIH / WHO Updates

CDC Recommends COVID-19 Vaccines for Young Children

CDC Recommends Moderna COVID-19 Vaccine for Children and Adolescents

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Commentary & Press Releases

MODERNA ANNOUNCES BIVALENT BOOSTER MRNA-1273.214 DEMONSTRATES POTENT NEUTRALIZING ANTIBODY RESPONSE AGAINST OMICRON SUBVARIANTS BA.4 AND BA.5

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