Providence

COVID-19 Resource Desk

#102 | 4.10.2022 to 4.16.2022

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. **Prevalence, Characteristics, and Outcomes of COVID-19-Associated Acute Myocarditis.** Ammirati E, et al. *Circulation.* 2022 Apr 12;145(15):1123-1139. doi: 10.1161/CIRCULATIONAHA.121.056817. https://doi.org/10.1161/circulationaha.121.056817

AM occurrence is estimated between 2.4 and 4.1 out of 1000 patients hospitalized for COVID-19. The majority of AM occurs in the absence of pneumonia and is often complicated by hemodynamic instability. AM is a rare complication in patients hospitalized for COVID-19, with an outcome that differs on the basis of the presence of concomitant pneumonia.

2. **Early Th2 inflammation in the upper respiratory mucosa as a predictor of severe COVID-19 and modulation by early treatment with inhaled corticosteroids: a mechanistic analysis.** Baker JR, et al. *Lancet Respir Med.* 2022 Apr 7:S2213-2600(22)00002-9. doi: 10.1016/S2213-2600(22)00002-9. https://doi.org/10.1016/s2213-2600(22)00002-9

An initial blunted interferon response and heightened T-helper 2 inflammatory response in the respiratory tract following SARS-CoV-2 infection could be a biomarker for predicting the development of severe COVID-19 disease. The clinical benefit of inhaled budesonide in early COVID-19 is likely to be as a consequence of its inflammatory modulatory effect, suggesting efficacy by reducing epithelial damage and an improved T-cell response.

Epidemiology & Public Health

3. **Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study.** Menni C, et al. *Lancet.* 2022 Apr 7:S0140-6736(22)00327-0. doi: 10.1016/S0140-6736(22)00327-0. https://doi.org/10.1016/s0140-6736(22)00327-0

The prevalence of symptoms that characterise an omicron infection differs from those of the delta SARS-CoV-2 variant, apparently with less involvement of the lower respiratory tract and reduced probability of hospital admission. Our data indicate a shorter period of illness and potentially of infectiousness which should impact work-health policies and public health advice.

4. **Breakthrough SARS-CoV-2 Infections, Hospitalizations, and Mortality in Vaccinated Patients with Cancer in the US Between December 2020 and November 2021.** Wang W, et al. *JAMA Oncol.* 2022 Apr 8. doi: 10.1001/jamaoncol.2022.1096. https://doi.org/10.1001/jamaoncol.2022.1096

The cumulative risk of breakthrough infections in patients with all cancer was 13.6%, with highest risk for pancreatic (24.7%), liver (22.8%), lung (20.4%), and colorectal (17.5%) cancers, and lowest risk for thyroid (10.3%), endometrial (11.9%), and breast (11.9%) cancers, vs 4.9% in the noncancer population. This cohort study showed significantly increased risks for breakthrough infection in vaccinated patients with cancer, especially those undergoing active cancer care, with marked heterogeneity among specific cancer types. Breakthrough infections in patients with cancer were associated with significant and substantial risks for hospitalizations and mortality.

5. **Estimating global, regional, and national daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis.** COVID-19 Cumulative Infection Collaborators. *Lancet*. 2022 Apr 8:S0140-6736(22)00484-6. doi: 10.1016/S0140-6736(22)00484-6. https://doi.org/10.1016/s0140-6736(22)00484-6

Global daily SARS-CoV-2 infections fluctuated between 3 million and 17 million new infections per day between April, 2020, and October, 2021, peaking in mid-April, 2021, primarily as a result of surges in India. Between the start of the pandemic and Nov 14, 2021, there were an estimated 3·80 billion total SARS-CoV-2 infections and reinfections combined, and an estimated 3·39 billion individuals, or 43·9% of the global population, had been infected one or more times. 1·34 billion of these infections occurred in south Asia, the highest among the seven super-regions, although the sub-Saharan Africa super-region had the highest infection rate. The high-income super-region had the fewest infections, and southeast Asia, east Asia, and Oceania had the lowest infection rate. COVID-19 has already had a staggering impact on the world up to the beginning of the omicron (B.1.1.529) wave, with over 40% of the global population infected at least once by Nov 14, 2021.

6. **Changes in Life Expectancy Between 2019 and 2020 in the US and 21 Peer Countries.** Woolf SH, Masters RK, Aron LY. *JAMA Netw Open.* 2022 Apr 1;5(4):e227067. doi: 10.1001/jamanetworkopen.2022.7067. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791004

Official death counts confirm that US life expectancy decreased between 2019 and 2020 on a scale not seen in 21 peer countries, substantially widening the preexisting gap in life expectancy between the US and peer countries. The decrease in US life expectancy was experienced disproportionately by Hispanic and non-Hispanic Black populations, consistent with a larger history of racial and ethnic health inequities resulting from policies of exclusion and systemic racism. Policies to address the systemic causes of the US health disadvantage relative to peer countries and persistent racial and ethnic inequities are essential.

7. **COVID-19 Mortality and Vaccine Coverage - Hong Kong Special Administrative Region, China, January 6, 2022-March 21, 2022.** Smith DJ, et al. *MMWR Morb Mortal Wkly Rep*. 2022 Apr 15;71(15):545-548. doi:10.15585/mmwr.mm7115e1. https://www.cdc.gov/mmwr/volumes/71/wr/mm7115e1.htm?s_cid=mm7115e1_w

The overall rates of COVID-19-associated mortality among persons aged ≥60 years who were unvaccinated, who had received 1 COVID-19 vaccine dose, and who had received ≥2 vaccine doses were 10,076, 1,099, and 473 per million population, respectively; the risk for COVID-19-associated death among unvaccinated persons was 21.3 times that among recipients of 2-3 doses in this age group. The high overall mortality rate during the ongoing 2022 Hong Kong Omicron COVID-19 outbreak is being driven by deaths among unvaccinated persons aged ≥60 years. Efforts to identify and address gaps in age-specific vaccination coverage can help prevent high mortality from COVID-19, especially among persons aged ≥60 years.

Healthcare Delivery & Healthcare Workers

8. **Antibiotic Prescriptions Associated With COVID-19 Outpatient Visits Among Medicare Beneficiaries, April 2020 to April 2021.** Tsay SV, et al. *JAMA*. 2022 Apr 8. doi: 10.1001/jama.2022.5471. https://doi.org/10.1001/jama.2022.5471

During the first year of the COVID-19 pandemic, 30% of outpatient visits for COVID-19 among Medicare beneficiaries were linked to an antibiotic prescription, 50.7% of which were for azithromycin. Randomized clinical trials demonstrated no benefit of azithromycin in treating COVID-19 and its use for the disease has been linked to antimicrobial resistance. The largest number of visits and highest rates of antibiotic prescribing were observed in the ED, perhaps reflecting acuity of care, and urgent care centers had the highest rate of azithromycin prescribing.

9. **Systemic Corticosteroid Use for COVID-19 in US Outpatient Settings from April 2020 to August 2021.** Bradley MC, et al. *JAMA.* 2022 Apr 8. doi: 10.1001/jama.2022.4877. https://doi.org/10.1001/jama.2022.4877

Despite NIH recommendations, increasing numbers of nonhospitalized patients with COVID-19 were prescribed systemic corticosteroids, often on the day of diagnosis. Use appeared to be more prominent in the South and was not restricted to older patients.

10. **Discontinuing vs. Continuing ACEIs and ARBs in Hospitalized Patients with COVID-19 According to Disease Severity: Insights from the BRACE CORONA Trial.** Macedo AVS, et al. *Am Heart J.* 2022 Apr 8:S0002-8703(22)00067-9. doi: 10.1016/j.ahj.2022.04.001. https://doi.org/10.1016/j.ahj.2022.04.001

Unlike patients with mild disease, patients with moderate disease who continued ACEIs/ARBs had more days alive and out of hospital through 30 days than those who discontinued ACEIs/ARBs. This suggests that ACEIs/ARBs should be continued for patients with moderate COVID-19 disease severity.

Prognosis

11. **Prognostic value of maximum NEWS-2 scores in addition to ISARIC 4C scores for patients admitted to hospital with COVID-19.** Akbar S, et al. *J Infect.* 2022 Apr 7:S0163-4453(22)00195-5. doi: 10.1016/j.jinf.2022.04.013. https://doi.org/10.1016/j.jinf.2022.04.013

This study has found that a combination of an admission ISARIC score, followed by NEWS-2 score monitoring most accurately predicts in-hospital mortality in hospitalised patients with COVID-19.

Previous studies have only made head-to-head comparisons of different scoring systems without considering them synergistically.

Survivorship & Rehabilitation

12. **No venous thromboembolic (VTE) recurrence after one-year follow-up of hospitalized COVID-19 patients diagnosed with VTE event: a prospective study.** Delrue M, et al. *Chest.* 2022 Apr 7:S0012-3692(22)00588-8. doi: 10.1016/j.chest.2022.03.043. https://doi.org/10.1016/j.chest.2022.03.043

This is one of the first prospective real-life studies evaluating outcomes over 12-months following COVID-19-related VTE diagnosis in hospitalized patients. We report the absence of VTE recurrence during the follow-up on anticoagulant therapy and after discontinuation. Only few studies reported shorter follow-up (from 10 to 159 days) in cohorts of 24 to 737 COVID-19-related VTE patients, showing a very low rate of VTE recurrence (0.0 to 2.4%) during anticoagulant therapy, consistently with our data. Moreover, we provided new data confirming the low VTE recurrence risk up to 6 months after anticoagulant discontinuation.

13. **Persistent COVID-19 symptoms in a community study of 606,434 people in England.** Whitaker M, et al. *Nat Commun*. 2022 Apr 12;13(1):1957. doi: 10.1038/s41467-022-29521-z. https://www.nature.com/articles/s41467-022-29521-z

Long COVID remains a broadly defined syndrome, with estimates of prevalence and duration varying widely. We use data from rounds 3-5 of the REACT-2 study, a representative community survey of adults in England, and replication data from round 6 to estimate the prevalence and identify predictors of persistent symptoms lasting 12 weeks or more; and unsupervised learning to cluster individuals by reported symptoms. At 12 weeks in rounds 3-5, 37.7% experienced at least one symptom, falling to 21.6% in round 6. Female sex, increasing age, obesity, smoking, vaping, hospitalisation with COVID-19, deprivation, and being a healthcare worker are associated with higher probability of persistent symptoms in rounds 3-5, and Asian ethnicity with lower probability. Clustering analysis identifies a subset of participants with predominantly respiratory symptoms. Managing the long-term sequelae of COVID-19 will remain a major challenge for affected individuals and their families and for health services.

Therapeutics

14. **Outcome of very high-risk patients treated by Sotrovimab for mild-to-moderate COVID-19 Omicron, a prospective cohort study (the ANRS 0003S CoCoPrev study).** COCOPREV Study Group. *J Infect.* 2022 Apr 7:S0163-4453(22)00196-7. doi: 10.1016/j.jinf.2022.04.010. https://doi.org/10.1016/j.jinf.2022.04.010

Sotrovimab was found to effectively protect from progression very high-risk Omicron-infected patients with mild-to-moderate COVID-19. However, emergence of Omicron BA.2 that contains compared to BA.1 eight unique mutations in the spike protein, and which was shown to escape Sotrovimab 9, may abrogate this protection, highlighting the urgent need for availability of therapeutic strategies that could adequately treat all sublineages of the Omicron variant, and future emerging variants.

15. **Defibrotide therapy for SARS-CoV2 Acute Respiratory Distress Syndrome (ARDS).** Frame D, et al. *Chest.* 2022 Apr 9:S0012-3692(22)00593-1. doi: 10.1016/j.chest.2022.03.046. https://doi.org/10.1016/j.chest.2022.03.046

The use of DF for management of SARS-CoV-2-related ARDS proved safe and tolerable. No hemorrhagic or thrombotic complications were reported during therapy, with promising outcomes in a patient population with a historically high mortality rate.

16. **Association of Subcutaneous or Intravenous Administration of Casirivimab and Imdevimab Monoclonal Antibodies with Clinical Outcomes in Adults With COVID-19.** McCreary EK, et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e226920. doi: 10.1001/jamanetworkopen.2022.6920. https://doi.org/10.1001/jamanetworkopen.2022.6920

In this cohort study of high-risk outpatients with mild to moderate COVID-19 symptoms, subcutaneously administered casirivimab and imdevimab was associated with reduced hospitalization and death when compared with no treatment. These results provide preliminary evidence of potential expanded use of subcutaneous mAb treatment, particularly in areas that are facing treatment capacity and/or staffing shortages.

Vaccines / Immunology

17. **Effectiveness of COVID-19 mRNA Vaccination in Preventing COVID-19–Associated Hospitalization Among Adults with Previous SARS-CoV-2 Infection — United States, June 2021–February 2022.** Plumb ID, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 12 April 2022. DOI: http://dx.doi.org/10.15585/mmwr.mm7115e2

Among persons with previous infection, COVID-19 mRNA vaccination provided protection against subsequent COVID-19–associated hospitalization. Estimated vaccine effectiveness against reinfection leading to hospitalization during the Omicron-predominant period was approximately 35% after dose 2, and 68% after a booster dose. To prevent COVID-19–associated hospitalization, all eligible persons should stay up to date with vaccination, including those with previous SARS-CoV-2 infection.

18. **Safety and immunogenicity of an inactivated virus particle vaccine for SARS-CoV-2, BIV1-CovIran: findings from double-blind, randomised, placebo-controlled, phase I and II clinical trials among healthy adults.** Mohraz M, et al. *BMJ Open.* 2022 Apr 8;12(4):e056872. doi: 10.1136/bmjopen-2021-056872. https://doi.org/10.1136/bmjopen-2021-056872

All adverse events were mild or moderate and transient in both phase I and phase II, and no AEs of special interest were reported. The seroconversion-rate of neutralising, antireceptor binding-domain (RBD) and anti-spike-glycoprotein (anti-S) antibodies 14-days after second dose of 5 µg vaccine in stage I was 70.8%, 87.5%, 91.7%. The antibody titres increased more among 5 µg than 3 µg. The corresponding rates for 3 µg vaccine were 45.8%, 54.2% and 70.8%, respectively. In stage II, 100%, 86.4% and 86.4% of participants seroconverted for neutralising, anti-RBD and anti-S antibodies. In phase II, the seroconversion rate of neutralising-antibody was 82.8%, anti-RBD 77.0% and anti-S 79.9% on day 42. In the cVNT, the sera at 1/64 times dilution would neutralise SARS-CoV-2 among 91.7%, 77.3% and 82.5% of vaccinated participants in phase I-stage I, phase I-stage II and phase II clinical trials, respectively. These results support further evaluation of this inactivated whole virus particle vaccine.

19. **Persistence of immunogenicity after seven COVID-19 vaccines given as third dose boosters following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK: three month analyses of the COV-BOOST trial.** COV-BOOST study group. *J Infect*. 2022 Apr 8:S0163-4453(22)00200-6. doi: 10.1016/j.jinf.2022.04.018. https://doi.org/10.1016/j.jinf.2022.04.018

84 days after a third dose of COVID-19 vaccine the decay rates of humoral response were different between vaccines. Adenoviral vector vaccine anti-spike IgG concentration at D84 following BNT/BNT initial doses were higher than for a three dose (BNT/BNT/BNT) schedule. Half dose BNT immune responses were similar to full dose responses. While high antibody tires are desirable in situations of high transmission of new variants of concern, the maintenance of immune responses that confer long-lasting protection against severe disease or death is also of critical importance. Policymakers may also consider adenoviral vector, fractional dose of mRNA, or other non-mRNA vaccines as third doses.

20. **Immunogenicity and early clinical outcome after two or three doses of SARS-CoV-2 mRNA-BNT162b2 vaccine in actively treated cancer patients: results from the prospective observational Vax-On-Third study.** Nelli F, et al. *Ann Oncol.* 2022 Apr 9:S0923-7534(22)00674-3. doi: 10.1016/j.annonc.2022.04.002. https://doi.org/10.1016/j.annonc.2022.04.002

This cohort study confirms a favorable safety profile of the third dose of tozinameran in a broad sample of cancer patients receiving active treatments. While residual confounding may still be present, comparative evaluation within the PSM population suggests improved immunogenicity of booster dosing, independent of types and timing of systemic therapies and consistent with similar studies that employed the same serologic testing methodology. Although longer follow-up is required, the effects of booster vaccine dosing appear to translate into a reduced risk of infection during intense SARS-CoV-2 VOC outbreaks.

21. **Comparative Effectiveness of mRNA and Inactivated Whole Virus Vaccines against COVID-19 Infection and Severe Disease in Singapore.** Premikha M, et al. *Clin Infect Dis.* 2022 Apr 12:ciac288. doi: 10.1093/cid/ciac288. https://doi.org/10.1093/cid/ciac288

Compared to individuals vaccinated with Pfizer-BioNTech/Comirnaty, recipients of Sinovac-CoronaVac and Sinopharm were 2.37 and 1.62 times more likely to be infected with COVID-19 respectively, while individuals vaccinated with Moderna were 0.42 (95% CI 0.25-0.70) times less likely to develop severe disease.

22. **Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting.** Magen O, et al. *N Engl J Med.* 2022 Apr 13. doi: 10.1056/NEJMoa2201688. https://www.nejm.org/doi/10.1056/NEJMoa2201688

A fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of Covid-19-related outcomes among persons who had received a third dose at least 4 months earlier. (Funded by the Ivan and Francesca Berkowitz Family Living Laboratory Collaboration at Harvard Medical School and Clalit Research Institute.).

23. **Myopericarditis following COVID-19 vaccination and non-COVID-19 vaccination: a systematic review and meta-analysis.** Ling RR, et al. *Lancet Respir Med.* 2022 Apr 11:S2213-2600(22)00059-5. doi: 10.1016/S2213-2600(22)00059-5. https://www.sciencedirect.com/science/article/pii/S2213260022000595

INTERPRETATION: The overall risk of myopericarditis after receiving a COVID-19 vaccine is low. However, younger males have an increased incidence of myopericarditis, particularly after receiving mRNA vaccines. Nevertheless, the risks of such rare adverse events should be balanced against the risks of COVID-19 infection (including myopericarditis).

24. **Effectiveness of COVID-19 mRNA Vaccination in Preventing COVID-19-Associated Hospitalization Among Adults with Previous SARS-CoV-2 Infection - United States, June 2021-February 2022.** Plumb ID, et al. *MMWR Morb Mortal Wkly Rep.* 2022 Apr 15;71(15):549-555. doi: 10.15585/mmwr.mm7115e2. https://www.cdc.gov/mmwr/volumes/71/wr/mm7115e2.htm?s_cid=mm7115e2_w

Previous infection with SARS-CoV-2, the virus that causes COVID-19, has been estimated to confer up to 90% protection against reinfection, although this protection was lower against the Omicron variant compared with that against other SARS-CoV-2 variants. After previous SARS-CoV-2 infection, estimated vaccine effectiveness (VE) against COVID-19-associated hospitalization was 47.5% after 2 vaccine doses and 57.8% after a booster dose during the Delta-predominant period (June 20-December 18, 2021), and 34.6% after 2 doses and 67.6% after a booster dose during the Omicron-predominant period (December 19, 2021-February 24, 2022). Vaccination provides protection against COVID-19-associated hospitalization among adults with previous SARS-CoV-2 infection, with the highest level of protection conferred by a booster dose. All eligible persons, including those with previous SARS-CoV-2 infection, should stay up to date with vaccination to prevent COVID-19-associated hospitalization.

25. **Surveillance of Safety of 3 Doses of COVID-19 mRNA Vaccination Using Electronic Health Records.** Niesen MJM et al. *JAMA Netw Open.* 2022 Apr 1;5(4):e227038. doi:10.1001/jamanetworkopen.2022.7038. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2791034

This study found that although third-dose vaccination against SARS-CoV-2 infection was associated with increased reporting of low-severity adverse events, risk of severe adverse events remained comparable with risk associated with the standard 2-dose regime. These findings suggest the safety of third vaccination doses in individuals who were eligible for booster vaccination at the time of this study.

26. **BNT162b2 mRNA COVID-19 vaccine and booster in patients with autoimmune rheumatic diseases: a national cohort study.** Bieber A, et al. *Ann Rheum Dis.* 2022 Apr 13:annrheumdis-2021-221824. doi: 10.1136/annrheumdis-2021-221824. https://ard.bmj.com/content/early/2022/04/12/annrheumdis-2021-221824

We included 127 928 patients with ARD, of whom, by the end of the study follow-up, there were 27 350 (21.3%) unvaccinated patients, 31 407 (24.5%) vaccinated patients and 69 171 (54.1%) patients who also received a third booster-dose. We identified 8470 (6.6%) patients with a positive SARS-CoV-2 PCR test during the study period. Our results indicate that both the BNT162b2 mRNA COVID-19 vaccine and the booster are associated with better COVID-19 outcomes in patients with ARD.

Women & Children

27. **COVID-19 Disease Severity in Children Infected with the Omicron Variant.** Butt AA, et al. *Clin Infect Dis*. 2022 Apr 11:ciac275. doi: 10.1093/cid/ciac275. https://doi.org/10.1093/cid/ciac275

Omicron variant infection in children/adolescents is associated with less severe disease than Delta variant infection as measured by hospitalization rates and need for ICU care or mechanical ventilation. Those 6 to <18 years also have less severe disease than those <6 years old.

28. **Predictors of severe illness in children with multisystem inflammatory syndrome after SARS-CoV-2 infection: a multicentre cohort study.** Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC). *CMAJ.* 2022 Apr 11;194(14):E513-E523. doi: 10.1503/cmaj.210873. https://doi.org/10.1503/cmaj.210873

We observed that age and higher ferritin levels were associated with more severe MIS-C. We observed greater severity of MIS-C later in the study period. Whether emerging SARS-CoV-2 variants pose different risks of severe MIS-C needs to be determined.

29. **Risk of adverse events after covid-19 in Danish children and adolescents and effectiveness of BNT162b2 in adolescents: cohort study.** Kildegaard H, et al. *BMJ.* 2022 Apr 11;377:e068898. doi: 10.1136/bmj-2021-068898. https://www.bmj.com/content/377/bmj-2021-068898

The absolute risks of adverse events after SARS-CoV-2 infection were generally low in Danish children and adolescents, although MIS-C occurred in 0.05% (32/70 666) of participants with RT-PCR confirmed SARS-CoV-2 infection. In adjusted analyses, rates of general practitioner visits were slightly increased in SARS-CoV-2 positive children and adolescents, which could indicate persisting symptoms. BNT162b2 appeared to be effective in reducing the risk of SARS-CoV-2 infection with the delta variant in adolescents.

GUIDELINES & CONSENSUS STATEMENTS

SARS-CoV-2 Infection and Associated Cardiovascular Manifestations and Complications in Children and Young Adults: A Scientific Statement From the American Heart Association. American Heart Association Leadership Committee and Congenital Cardiac Defects Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Hypertension, and Council on Peripheral Vascular Disease. *Circulation.* 2022 Apr 11:101161CIR0000000000001064. doi: 10.1161/CIR.0000000000001064.

FDA / CDC / NIH / WHO Updates

Coronavirus (COVID-19) Update: FDA Authorizes First COVID-19 Diagnostic Test Using Breath Samples | FDA

Statement on the eleventh meeting of the International Health Regulations (2005) Emergency Committee regarding the coronavirus disease (COVID-19) pandemic (who.int)

Commentary

Estimating disease severity of Omicron and Delta SARS-CoV-2 infections. Sigal A, et al. *Nat Rev Immunol.* 2022 Apr 12. doi: 10.1038/s41577-022-00720-5.

If you would like to receive a **customized COVID-19 Topic Alert** related to your specialty or area of interest, would like a **literature search** conducted, or have difficulty **accessing** any of the above articles please contact us at **librarian@providence.org**

Find previous weeks **here.**