

COVID-19 Resource Desk

#148 |3.19.2023 to 3.25.2023

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 <u>Digital Commons</u>

Diagnostics & Screening

 Symptom and Viral Rebound in Untreated SARS-CoV-2 Infection. Deo R et al. Ann Intern Med. 2023 Mar;176(3):348-354. doi: 10.7326/M22-2381. https://www.acpjournals.org/doi/10.7326/M22-2381

RESULTS: Symptom rebound was identified in 26% of participants at a median of 11 days after initial symptom onset. Viral rebound was detected in 31% and high-level viral rebound in 13% of participants. Most symptom and viral rebound events were transient, because 89% of symptom rebound and 95% of viral rebound events occurred at only a single time point before improving. The combination of symptom and high-level viral rebound was observed in 3% of participants.

LIMITATION: A largely unvaccinated population infected with pre-Omicron variants was evaluated. CONCLUSION: Symptom or viral relapse in the absence of antiviral treatment is common, but the combination of symptom and viral rebound is rare.

PRIMARY FUNDING SOURCE: National Institute of Allergy and Infectious Diseases.

Epidemiology & Public Health

 School-Based Interventions to Increase Student COVID-19 Vaccination Coverage in Public School Populations with Low Coverage - Seattle, Washington, December 2021-June 2022. Fairlie T, et al. MMWR Morb Mortal Wkly Rep. 2023 Mar 17;72(11):283-287. doi: 10.15585/mmwr.mm7211a3.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7211a3.htm?s cid=mm7211a3 w

As of March 8, 2023, COVID-19 vaccination coverage among school-aged children remained low nationwide, with 61.7% of children aged 12-17 years and approximately one third (32.7%) of those aged 5-11 years having completed the primary series. Seattle Public Schools (SPS) implemented a program to increase COVID-19 vaccination coverage during the 2021-22 school year, focusing on children aged 5-11 years during November 2021-June 2022, with an added focus on populations with low vaccine coverage during January 2022-June 2022. The program included strategic messaging, school-located vaccination clinics, and school-led community engagement. Vaccination data from the Washington State Immunization Information System (WAIIS) were analyzed to examine disparities in COVID-19 vaccination by demographic and school characteristics and trends over time. In December

2021, 56.5% of all SPS students, 33.7% of children aged 5-11 years, and 81.3% of children aged 12-18 years had completed a COVID-19 primary vaccination series. By June 2022, overall series completion had increased to 80.3% and was 74.0% and 86.6% among children aged 5-11 years and 12-18 years, respectively. School-led vaccination programs can leverage community partnerships and relationships with families to improve COVID-19 vaccine access and coverage.

3. Covid-19 Surveillance Testing and Resident Outcomes in Nursing Homes. McGarry BE, Gandhi AD, Barnett ML. N Engl J Med. 2023 Mar 23;388(12):1101-1110. doi: 10.1056/NEJMoa2210063. https://www.nejm.org/doi/10.1056/NEJMoa2210063

Greater surveillance testing of staff members at skilled nursing facilities was associated with clinically meaningful reductions in Covid-19 cases and deaths among residents, particularly before vaccine availability.

4. **Isolation and quarantine for COVID-19 in the United States, 2020-2022.** Oeltmann JE et al. *Clin Infect Dis.* 2023 Mar 22:ciad163. doi: 10.1093/cid/ciad163.

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciad163/7083735

Engagement in contact tracing positively correlated with isolation and quarantine. However, most adults with COVID-19 isolated and self-notified contacts regardless of whether the public health workforce was able to reach them. Identifying and reaching contacts was challenging, and limited the ability to promote quarantining, and testing.

5. Postoperative mortality and complications in patients with and without pre-operative SARS-CoV-2 infection: a service evaluation of 24 million linked records using OpenSAFELY. McInerney CD et al. Anaesthesia. 2023 Mar 23. doi: 10.1111/anae.16001. https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.16001

Surgical decision-making after SARS-CoV-2 infection is influenced by the presence of comorbidity, infection severity and whether the surgical problem is time-sensitive. Contemporary surgical policy to delay surgery is informed by highly heterogeneous country-specific guidance. We evaluated surgical provision in England during the COVID-19 pandemic to assess real-world practice and whether deferral remains necessary. Using the OpenSAFELY platform, we adapted the COVIDSurg protocol for a service evaluation of surgical procedures that took place within the English NHS from 17 March 2018 to 17 March 2022. We assessed whether hospitals adhered to guidance not to operate on patients within 7 weeks of an indication of SARS-CoV-2 infection. Additional outcomes were postoperative all-cause mortality (30 days, 6 months) and complications (pulmonary, cardiac, cerebrovascular). The exposure was the interval between the most recent indication of SARS-CoV-2 infection and subsequent surgery. In any 6-month window, < 3% of surgical procedures were conducted within 7 weeks of an indication of SARS-CoV-2 infection. Mortality for surgery conducted within 2 weeks of a positive test in the era since widespread SARS-CoV-2 vaccine availability was 1.1%, declining to 0.3% by 4 weeks. Compared with the COVIDSurg study cohort, outcomes for patients in the English NHS cohort were better during the COVIDSurg data collection period and the pandemic era before vaccines became available. Clinicians within the English NHS followed national guidance by operating on very few patients within 7 weeks of a positive indication of SARS-CoV-2 infection. In England, surgical patients' overall risk following an indication of SARS-CoV-2 infection is lower than previously thought.

Survivorship & Rehabilitation

 Prevalence of physical frailty, including risk factors, up to 1 year after hospitalisation for COVID-19 in the UK: a multicentre, longitudinal cohort study. McAuley HJC et al. EClinicalMedicine. 2023 Mar 11;57:101896. doi: 10.1016/j.eclinm.2023.101896. eCollection 2023 Mar. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(23)00073-1/fulltext

Physical frailty and pre-frailty are common following hospitalisation with COVID-19. Improvement in frailty was seen between 5 and 12 months although two-thirds of the population remained pre-frail or frail. This suggests comprehensive assessment and interventions targeting pre-frailty and frailty beyond the initial illness are required.

FUNDING: UK Research and Innovation and National Institute for Health Research.

7. Myocardial Tissue Characterization in Cardiac Magnetic Resonance Studies of Patients Recovering From COVID-19: A Meta-Analysis. Jerosch-Herold M, et al. *J Am Heart Assoc.* 2023 Mar 21;12(6):e027801. doi: 10.1161/JAHA.122.027801. https://www.ahajournals.org/doi/10.1161/JAHA.122.027801

T1 and T2 are dynamic markers of cardiac involvement in COVID-19 that reflect the regression of cardiomyocyte injury and myocardial inflammation during recovery. Late gadolinium enhancement and to a lesser extent extracellular volume, are more static biomarkers moderated by preexisting risk factors linked to adverse myocardial tissue remodeling.

 Risk Factors Associated With Post-COVID-19 Condition: A Systematic Review and Metaanalysis. Tsampasian V., et al. *JAMA Intern Med.* 2023 Mar 23. doi: 10.1001/jamainternmed.2023.0750. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2802877

This systematic review and meta-analysis demonstrated that certain demographic characteristics (eg, age and sex), comorbidities, and severe COVID-19 were associated with an increased risk of PCC, whereas vaccination had a protective role against developing PCC sequelae. These findings may enable a better understanding of who may develop PCC and provide additional evidence for the benefits of vaccination.

TRIAL REGISTRATION: PROSPERO Identifier: CRD42022381002.

9. Association of Treatment With Nirmatrelvir and the Risk of Post-COVID-19 Condition. Xie Y, et al. JAMA Intern Med. 2023 Mar 23. doi: 10.1001/jamainternmed.2023.0743. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2802878

This cohort study found that in people with SARS-CoV-2 infection who had at least 1 risk factor for progression to severe disease, treatment with nirmatrelvir within 5 days of a positive SARS-CoV-2 test result was associated with reduced risk of PCC across the risk spectrum in this cohort and regardless of vaccination status and history of prior infection; the totality of findings suggests that treatment with nirmatrelvir during the acute phase of COVID-19 may reduce the risk of post-acute adverse health outcomes.

Therapeutics

10. Effectiveness of nirmatrelvir-ritonavir in preventing hospital admissions and deaths in people with COVID-19: a cohort study in a large US health-care system. Lewnard JA, et al. Lancet Infect Dis. 2023 Mar 15:S1473-3099(23)00118-4. doi: 10.1016/S1473-3099(23)00118-4. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(23)00118-4/fulltext

In a setting with high levels of COVID-19 vaccine uptake, nirmatrelvir-ritonavir effectively reduced the risk of hospital admission or death within 30 days of a positive outpatient SARS-CoV-2 test. FUNDING: US Centers for Disease Control and Prevention and US National Institutes of Health.

11. Outcomes of Extremely Prolonged (> 50 d) Venovenous Extracorporeal Membrane
Oxygenation Support. Malas J, et al. Crit Care Med. 2023 Mar 16. doi:
10.1097/CCM.0000000000005860.

https://journals.lww.com/ccmjournal/Abstract/9900/Outcomes of Extremely Prolonged 50 d .109.aspx

Our experience suggests that extremely prolonged venovenous ECMO support to allow native lung recovery or optimization for lung transplantation may be a feasible strategy in select critically ill patients, further supporting the expanded utilization of venovenous ECMO for refractory respiratory failure.

12. Effect of Thromboprophylaxis on Clinical Outcomes After COVID-19 Hospitalization. Wang TY et al. *Ann Intern Med*. 2023 Mar 21. doi: 10.7326/M22-3350. https://www.acpjournals.org/doi/10.7326/M22-3350

The incidence of death or thromboembolism was low in this cohort of patients discharged after hospitalization with COVID-19. Because of early enrollment termination, the results were imprecise and the study was inconclusive.

PRIMARY FUNDING SOURCE: National Institutes of Health.

13. Update Alert 10: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults. Mackey K, Kansagara D, Vela K. Ann Intern Med. 2023 Mar 21. doi: 10.7326/L23-0049. https://www.acpjournals.org/doi/10.7326/L23-0049

This living systematic review has addressed 3 key questions about COVID-19 and the use of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs): whether these medications increase susceptibility to SARS-CoV-2, increase the likelihood of worse outcomes, and paradoxically, whether they have protective effects and could be used as COVID-19 treatment (1). In previous update alerts, we summarized high-strength evidence that antecedent use of ACEIs and ARBs is not associated with increased risk for SARS-CoV-2 infection or severe disease and retired these key questions. In this final update alert, we summarize current evidence about our third key question: the benefits and harms of initiating ACEIs or ARBs in adults with COVID-19 who were not previously receiving these medications.

14. Sarilumab plus standard of care vs standard of care for the treatment of severe COVID-19: a phase 3, randomized, open-labeled, multi-center study (ESCAPE study). Mastrorosa I et al.

EClinicalMedicine. 2023 Mar 10;57:101895. doi: 10.1016/j.eclinm.2023.101895. eCollection 2023 Mar. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(23)00072-X/fulltext

The efficacy of sarilumab in severe COVID-19 was not demonstrated both in the overall and in the stratified for severity analysis population. Exploratory analyses suggested that subsets of patients with lower CRP values or lower lymphocyte counts might have had benefit with sarilumab treatment, but this finding would require replication in other studies. The relatively low rate of concomitant corticosteroid use, could partially explain our results.

FUNDING: This study was supported by INMI "Lazzaro Spallanzani" Ricerca Corrente Linea 1 on emerging and reemerging infections, funded by Italian Ministry of Health.

15. Heterogeneous Treatment Effects of Therapeutic-Dose Heparin in Patients Hospitalized for COVID-19. Goligher EC et al. *JAMA*. 2023 Mar 21. doi: 10.1001/jama.2023.3651. https://jamanetwork.com/journals/jama/fullarticle/2802856

Among patients hospitalized for COVID-19, the effect of therapeutic-dose heparin was heterogeneous. In all 3 approaches to assessing HTE, heparin was more likely to be beneficial in those who were less severely ill at presentation or had lower BMI and more likely to be harmful in sicker patients and those with higher BMI. The findings illustrate the importance of considering HTE in the design and analysis of RCTs.

TRIAL REGISTRATION: ClinicalTrials.gov Identifiers: NCT02735707, NCT04505774, NCT04359277, NCT04372589.

16. Effects of Standard-Dose Prophylactic, High-Dose Prophylactic, and Therapeutic Anticoagulation in Patients With Hypoxemic COVID-19 Pneumonia: The ANTICOVID Randomized Clinical Trial. Labbé V et al. *JAMA Intern Med.* 2023 Mar 22. doi: 10.1001/jamainternmed.2023.0456.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2802821

This randomized clinical trial found that compared with SD-PA, neither HD-PA nor TA use improved the primary hierarchical outcome of all-cause mortality or time to clinical improvement in patients with hypoxemic COVID-19 pneumonia; however, HD-PA resulted in significantly better net clinical outcome by decreasing the risk of de novo thrombosis.

TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04808882.

17. Intravenous ravulizumab in mechanically ventilated patients hospitalised with severe COVID-19: a phase 3, multicentre, open-label, randomised controlled trial. Annane D et al. *Lancet Respir Med.* 2023 Mar 20:S2213-2600(23)00082-6. doi: 10.1016/S2213-2600(23)00082-6. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(23)00082-6/fulltext

Addition of ravulizumab to BSC did not improve survival or other secondary outcomes. Safety findings were consistent with the known safety profile of ravulizumab in its approved indications. Despite the lack of efficacy, the study adds value for future research into complement therapeutics in critical illnesses by showing that C5 inhibition can be accomplished in severely ill patients. FUNDING: Alexion, AstraZeneca Rare Disease.

18. Effect of Higher-Dose Ivermectin for 6 Days vs Placebo on Time to Sustained Recovery in Outpatients With COVID-19: A Randomized Clinical Trial. Naggie S et al. JAMA. 2023 Mar

21;329(11):888-897. doi: 10.1001/jama.2023.1650.

Comment in

JAMA. 2023 Mar 21;329(11):897-898. JAMA. 2023 Mar 21;329(11):884-885.

https://jamanetwork.com/journals/jama/fullarticle/2801827

Among outpatients with mild to moderate COVID-19, treatment with ivermectin, with a maximum targeted dose of 600 µg/kg daily for 6 days, compared with placebo did not improve time to sustained recovery. These findings do not support the use of ivermectin in patients with mild to moderate COVID-19.

TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04885530.

Transmission / Infection Control

19. Update to living systematic review on prophylaxis against covid-19. BMJ. 2023 Mar 23;380:p688. doi: 10.1136/bmj.p688. https://www.bmj.com/content/380/bmj.p688 In this update, 32 randomised trials enrolled 25 147 participants and addressed 21 different prophylactic drugs; adding 21 trials (66%), 18 162 participants (75%), and 16 (76%) prophylactic drugs to the previous iteration. Of the 16 prophylactic drugs analysed, none provided convincing evidence of a reduction in the risk of laboratory confirmed SARS-CoV-2 infection. For admission to hospital and mortality outcomes, no prophylactic drug proved different than standard care or placebo. Hydroxychloroguine and vitamin C combined with zinc probably increase the risk of adverse effects leading to drug discontinuation (moderate certainty evidence).

Vaccines / Immunology

20. Correction and Republication: Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19-Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults - VISION Network, Nine States, September-November 2022. MMWR Morb Mortal Wkly Rep. 2023 Mar 17;72(11):292. doi: 10.15585/mmwr.mm7211a6.

https://www.cdc.gov/mmwr/volumes/72/wr/mm7211a6.htm?s_cid=mm7211a6_w

On January 25, 2023, one of the sites contributing data to the analysis notified CDC co-authors about an error in reporting history of receipt of bivalent doses. MMWR was notified about these concerns on February 10, 2023. The site corrected its vaccination history reporting, and the authors have corrected the report and confirmed that the reporting issue did not change the interpretation or the conclusions of the original report. In accordance with December 2017 guidance from the International Committee of Medical Journal Editors (2), MMWR is republishing the report (3). The republished report includes the original report with clearly marked corrections as supplementary materials.

21. Heterologous SARS-CoV-2 spike protein booster elicits durable and broad antibody responses against the receptor-binding domain. Takano T et al. Nat Commun. 2023 Mar 15;14(1):1451. doi: 10.1038/s41467-023-37128-1. https://www.nature.com/articles/s41467-023-37128-1

The immunogenicity of mRNA vaccines has not been well studied when compared to different vaccine modalities in the context of additional boosters. Here we show that longitudinal analysis reveals more sustained SARS-CoV-2 spike receptor-binding domain (RBD)-binding IgG titers with the breadth to antigenically distinct variants by the S-268019-b spike protein booster compared to the BNT162b2 mRNA homologous booster. The durability and breadth of RBD-angiotensin-converting enzyme 2 (ACE2) binding inhibitory antibodies are pronounced in the group without systemic adverse events (AEs) after the S-268019-b booster, leading to the elevated neutralizing activities against Omicron BA.1 and BA.5 variants in the stratified group. In contrast, BNT162b2 homologous booster elicited antibodies to spike N-terminal domain in proportion to the AE scores. High-dimensional immune profiling identifies early CD16+ natural killer cell dynamics with CCR3 upregulation, as one of the correlates for the distinct anti-RBD antibody responses by the S-268019-b booster. Our results illustrate the combinational effects of heterologous booster on the immune dynamics and the durability and breadth of recalled anti-RBD antibody responses against emerging virus variants.

- 22. Correlates of protection and viral load trajectories in omicron breakthrough infections in triple vaccinated healthcare workers. Marking U et al. Nat Commun. 2023 Mar 22;14(1):1577. doi: 10.1038/s41467-023-36984-1. https://www.nature.com/articles/s41467-023-36984-1 Vaccination offers protection against severe COVID-19 caused by SARS-CoV-2 omicron but is less effective against infection. Characteristics such as serum antibody titer correlation to protection, viral abundance and clearance of omicron infection in vaccinated individuals are scarce. We present a 4week twice-weekly SARS-CoV-2 qPCR screening in 368 triple vaccinated healthcare workers. Spikespecific IgG levels, neutralization titers and mucosal spike-specific IgA-levels were determined at study start and qPCR-positive participants were sampled repeatedly for two weeks. 81 (cumulative incidence 22%) BA.1, BA.1.1 and BA.2 infections were detected. High serum antibody titers are shown to be protective against infection (p < 0.01), linked to reduced viral load (p < 0.01) and time to viral clearance (p < 0.05). Pre-omicron SARS-CoV-2 infection is independently associated to increased protection against omicron, largely mediated by mucosal spike specific IgA responses (nested models Ir test p = 0.02 and 0.008). Only 10% of infected participants remain asymptomatic through the course of their infection. We demonstrate that high levels of vaccine-induced spike-specific WT antibodies are linked to increased protection against infection and to reduced viral load if infected, and suggest that the additional protection offered by pre-omicron SARS-CoV-2 infection largely is mediated by mucosal spike-specific IgA.
- 23. Adverse Events Following Immunization With mRNA and Viral Vector Vaccines in Individuals With Previous Severe Acute Respiratory Syndrome Coronavirus 2 Infection From the Canadian National Vaccine Safety Network. Bettinger JA et al. Clin Infect Dis. 2023 Mar 21;76(6):1088-1102. doi: 10.1093/cid/ciac852. https://academic.oup.com/cid/article/76/6/1088/6780916
 Adults with moderate or severe previous SARS-CoV-2 infection were more likely to have a health event sufficient to impact routine activities or require medical assessment in the week following each vaccine dose.

24. Developmental screening of full-term infants at 16 to 18 months of age after in-utero exposure to maternal SARS-CoV-2 infection. Shah AV, Howell HB, Kazmi SH, Zaccario M, Sklamberg FE, Groth T, Martindale P, Dreyer B, Verma S. *J Perinatol*. 2023 Mar 17:1-5. doi: 10.1038/s41372-023-01642-3. https://www.nature.com/articles/s41372-023-01642-3

We observed increased risk of neurodevelopmental delays during screening of infants born at full-term to mothers with SARS-CoV-2 at 16 to 18 months age. These results highlight the urgent need for follow-up studies of infants born to mothers with SARS-CoV-2.

25. Addressing the Long-term Effects of the COVID-19 Pandemic on Children and Families: A Report From the National Academies of Sciences, Engineering, and Medicine. Coker TR, Cheng TL, Ybarra M. JAMA. 2023 Mar 16. doi: 10.1001/jama.2023.4371. https://jamanetwork.com/journals/jama/fullarticle/2802732

This Viewpoint discusses a consensus report from the National Academies of Sciences, Engineering, and Medicine (NASEM) that reviews the impact of COVID-19 on the health and well-being of children and families and what needs to be done to attenuate longer-term negative effects.

26. Nirmatrelvir-Ritonavir (Paxlovid) for Mild Coronavirus Disease 2019 (COVID-19) in Pregnancy and Lactation. Lin CY, et al. Obstet Gynecol. 2023 Mar 16. doi:10.1097/AOG.000000000005152. https://journals.lww.com/greenjournal/Fulltext/9900/Nirmatrelvir Ritonavir Paxlovid for Mild.719.aspx

Nirmatrelvir-ritonavir (Paxlovid) is recommended to reduce the risk of hospitalization from coronavirus disease 2019 (COVID-19) in pregnancy. Data on use in pregnancy, including prescribing patterns and patient experience (adverse effects, incidence of rebound), are limited. We performed a cross-sectional study in which we surveyed a cohort of vaccinated pregnant or lactating individuals with breakthrough COVID-19. Of 35 pregnant respondents, 51.4% were prescribed and 34.3% took nirmatrelvir-ritonavir; of these, 91.7% experienced dysgeusia and 50.0% had rebound (50.0% positive test result, 33.3% return of symptoms). Three of five lactating respondents were prescribed and two took nirmatrelvir-ritonavir. There were no significant adverse outcomes. Unknown risk was the most common reason for declining nirmatrelvir-ritonavir. More research is needed to establish the safety of nirmatrelvir-ritonavir in pregnancy and lactation, to improve public health messaging, and to increase uptake of this treatment.

27. **SARS-CoV-2 Variants and Multisystem Inflammatory Syndrome in Children.** McCrindle BW et al. *N Engl J Med*. 2023 Mar 22. doi: 10.1056/NEJMc2215074. https://www.nejm.org/doi/10.1056/NEJMc2215074

Multisystem inflammatory syndrome in children (MIS-C), a delayed hyperinflammatory response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is an important cause of illness in children. Changes in the prevalent variant throughout the coronavirus disease 2019 pandemic have influenced the transmissibility and incidence of disease, but their association with clinical presentation and outcomes of MIS-C is incompletely known.

Ethical Guidance on Family Caregiving, Support, and Visitation in Hospitals and Residential Health Care Facilities, Including During Public Health Emergencies: an American College of Physicians Position

Paper. ACP Ethics, Professionalism and Human Rights Committee*. *J Gen Intern Med.* 2023 Mar 20. doi: 10.1007/s11606-023-08070-1.

<u>Update to living WHO guideline on drugs to prevent covid-19.</u> *BMJ.* 2023 Mar 23;380:p692. doi: 10.1136/bmj.p692.

FDA / CDC / NIH / WHO Updates

CDC and FDA Identify Preliminary COVID-19 Vaccine Safety Signal for Persons Aged 65 Years and Older

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