Providence

COVID-19 Resource Desk

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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. **Neurological manifestations of COVID-19 in adults and children.** Cho SM et al. *Brain.* 2022 Sep 10:awac332. doi: 10.1093/brain/awac332. https://academic.oup.com/brain/advance-article/doi/10.1093/brain/awac332/6695387

In adults and children, the most frequent neurological manifestations at admission were fatigue (adults: 37.4%; children: 20.4%), altered consciousness (20.9%; 6.8%), myalgia (16.9%; 7.6%), dysgeusia (7.4%; 1.9%), anosmia (6.0%; 2.2%), and seizure (1.1%; 5.2%). In adults, the most frequent in-hospital neurological complications were stroke (1.5%), seizure (1%), and central nervous system (CNS) infection (0.2%). Each occurred more frequently in ICU than in non-ICU patients. In children, seizure was the only neurological complication to occur more frequently in ICU vs. non-ICU (7.1% vs. 2.3%, $P < .001$). Stroke prevalence increased with increasing age, while CNS infection and seizure steadily decreased with age. There was a dramatic decrease in stroke over time during the pandemic. Hypertension, chronic neurological disease, and the use of extracorporeal membrane oxygenation were associated with increased risk of stroke. Altered consciousness was associated with CNS infection, seizure, and stroke. All in-hospital neurological complications were associated with increased odds of death. The likelihood of death rose with increasing age, especially after 25 years of age. In conclusion, adults and children have different neurological manifestations and in-hospital complications associated with COVID-19. Stroke risk increased with increasing age, while CNS infection and seizure risk decreased with age.

Epidemiology & Public Health

2. **Cognitive Decline in Long-term Care Residents Before and During the COVID-19 Pandemic in Ontario, Canada.** Webber C, et al. *JAMA*. 2022 Sep 12. doi: 10.1001/jama.2022.17214. https://jamanetwork.com/journals/jama/fullarticle/2796449

In this matched population-based study, the incidence of cognitive decline was lower among LTC residents during the COVID-19 pandemic than before the pandemic. This finding may be due to the indirect effects of the higher incidence of death in the COVID-19 group. Importantly, cognitive decline was similar between residents in LTC homes with and without COVID-19 outbreaks, suggesting that greater exposure to public health restrictions (eg, in-room isolation) was not associated with increased

decline. These results do not support anecdotal concerns that the pandemic has resulted in greater cognitive decline in LTC residents.

Prognosis

3. **Procalcitonin as a predictive marker in COVID-19: A systematic review and meta-analysis.** Kumar A, et al. *PLoS One.* 2022 Sep 9;17(9):e0272840. doi: 10.1371/journal.pone.0272840. eCollection 2022. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0272840

Procalcitonin has good discriminatory power for predicting mortality and disease severity in COVID-19 patients. Therefore, procalcitonin measurement may help identify potentially severe cases and thus decrease mortality by offering early aggressive treatment.

4. **Mortality Risk Among Patients Hospitalized Primarily for COVID-19 During the Omicron and Delta Variant Pandemic Periods - United States, April 2020-June 2022.** Adjei S, et al. *MMWR Morb Mortal Wkly Rep*. 2022 Sep 16;71(37):1182-1189. doi: 10.15585/mmwr.mm7137a4. https://www.cdc.gov/mmwr/volumes/71/wr/mm7137a4.htm?s_cid=mm7137a4_w#suggestedcitation

Risk for severe COVID-19 increases with age, disability, and underlying medical conditions. The SARS-CoV-2 Omicron variant is more infectious but has been associated with less severe disease. In-hospital mortality among patients hospitalized primarily for COVID-19 decreased from 15.1% (Delta period) to 4.9% (later Omicron period; April–June 2022), despite high-risk patient groups representing a larger proportion of hospitalizations. During the later Omicron period, the majority of in-hospital deaths occurred among adults aged ≥65 years (81.9%) and persons with three or more underlying medical conditions (73.4%). Vaccination, early treatment, and appropriate nonpharmaceutical interventions remain important public health priorities to prevent COVID-19 deaths, especially among persons most at risk.

Survivorship & Rehabilitation

5. **Two-Year Health Outcomes in Hospitalized COVID-19 Survivors in China.** Yang X, et al. *JAMA Netw Open*. 2022 Sep 1;5(9):e2231790. doi: 10.1001/jamanetworkopen.2022.31790. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796276

In this longitudinal cohort study that included 1864 patients, the most common symptoms at 2 years after SARS-CoV-2 infection were fatigue, chest tightness, anxiety, dyspnea, and myalgia, and most symptoms resolved from 1-year to 2-year follow-up, although the incidence of dyspnea showed no significant change. Patients with severe disease during hospitalization, especially those who required intensive care unit admission, had higher risks of persistent symptoms and higher chronic obstructive pulmonary disease assessment test scores.

6. **Lung function and radiological findings 1 year after COVID-19: a prospective follow-up.** Tarraso, J, et al. *Respir Res* 23, 242 (2022). https://doi.org/10.1186/s12931-022-02166-8

Our data suggest that a significant percentage of individuals would develop pulmonary sequelae after COVID 19 pneumonia, regardless of severity of the acute process.

7. **Association of COVID-19 with New-Onset Alzheimer's Disease.** Wang, L, et al. *Journal of Alzheimer's Disease*, vol. 89, no. 2, pp. 411-414, 2022 DOI: 10.3233/JAD-220717 https://content.iospress.com/articles/journal-of-alzheimers-disease/jad220717

An infectious etiology of Alzheimer's disease has been postulated for decades. It remains unknown whether SARS-CoV-2 viral infection is associated with increased risk for Alzheimer's disease. In this retrospective cohort study of 6,245,282 older adults (age ≥65 years) who had medical encounters between 2/2020–5/2021, we show that people with COVID-19 were at significantly increased risk for new diagnosis of Alzheimer's disease within 360 days after the initial COVID-19 diagnosis (hazard ratio or HR:1.69, 95% CI: 1.53–1.72), especially in people age ≥85 years and in women. Our findings call for research to understand the underlying mechanisms and for continuous surveillance of long-term impacts of COVID-19 on Alzheimer's disease.

Therapeutics

8. **Anti-C5a antibody (vilobelimab) therapy for critically ill, invasively mechanically ventilated patients with COVID-19 (PANAMO): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial.** Vlaar APJ et al. *Lancet Respir Med.* 2022 Sep 7:S2213-2600(22)00297-1. doi: 10.1016/S2213-2600(22)00297-1. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00297-1/fulltext

In addition to standard of care, vilobelimab improves survival of invasive mechanically ventilated patients with COVID-19 and leads to a significant decrease in mortality. Vilobelimab could be considered as an additional therapy for patients in this setting and further research is needed on the role of vilobelimab and C5a in other acute respiratory distress syndrome-causing viral infections.

9. **Coronavirus disease 2019 subphenotypes and differential treatment response to convalescent plasma in critically ill adults: secondary analyses of a randomized clinical trial.** Fish M et al. *Intensive Care Med.* 2022 Sep 14. doi: 10.1007/s00134-022-06869-w. https://link.springer.com/article/10.1007/s00134-022-06869-w

We reported three COVID-19 subphenotypes, among critically ill adults, with differential treatment effects to ABO-compatible convalescent plasma therapy. Differences in subphenotype prevalence between RCT populations probably explain inconsistent results with COVID-19 immunotherapies.

10. **Dupilumab use is associated with protection from COVID-19 mortality: A retrospective analysis.** Donlan AN, et al. *Clin Infect Dis.* 2022 Sep 15:ciac745. doi: 10.1093/cid/ciac745. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac745/6698736?login=true

Through utilization of two databases, we have found that prior dupilumab usage in COVID-19 patients was associated with improved survival compared to matched controls. Previous work supported this finding, where, in atopic dermatitis patients dupilumab use was also associated with a reduction in severe outcomes from COVID-19. We report these findings building off of in vivo work supporting a causal role for IL-13 in COVID-19 pathogenesis and a small randomized clinical trial demonstrating a decreased mortality in subjects randomized to dupilumab. Due to the mechanism of action of dupilumab, we hypothesize this protection, then, is mediated by blocking pathogenic IL-13 signaling

Vaccines / Immunology

11. **Management of patients with immediate reactions to COVID vaccines.** Picard M, Stone CA Jr, Greenhawt M. *J Allergy Clin Immunol.* 2022 Sep 8:S0091-6749(22)01183-6. doi: 10.1016/j.jaci.2022.09.003. https://www.jacionline.org/article/S0091-6749(22)01183-6/pdf

Immediate reactions suggestive of an allergic reaction to either a 1st 48 or subsequent mRNA COVID-19 vaccine dose are very rare. Few such reactions meet level 1 Brighton Collaboration Criteria (BCC), and of those meeting level 1-3 BCC, many would not meet stringent anaphylaxis criteria established by either the National Institutes of Allergy and Infectious Diseases (NIAID) or the World Allergy Organization (WAO). In adjudication of these reports, it has become clear that multiple post vaccination symptom patterns can mimic and be interpreted as anaphylaxis. Such reported symptoms which can mimic anaphylaxis include flushing, erythema, dizziness, nausea, throat tightness, urticaria, wheezing and dyspnea. Although there is considerable overlap, several phenotypes of immediate reactions can be recognized and used to guide management. Our field's increasing awareness of the phenotypes of "immediate adverse vaccine responses", the majority of which are non-allergic, has provided allergists with a new perspective on management of such responses.

12. **Protection against SARS-CoV-2 transmission by a parenteral prime-Intranasal boost vaccine strategy.** Christensen D et al. *EBioMedicine.* 2022 Sep 5:104248. doi: 10.1016/j.ebiom.2022.104248. https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00430-3/fulltext

This study suggests that parenteral-prime mucosal boost is an effective strategy for protecting against SARS-CoV-2 infection and highlights that protection against virus transmission may be obtained despite incomplete clearance of virus from the upper respiratory tract. It should be noted that protection against onward transmission was not compared to standard parenteral prime-boost, which should be a focus for future studies.

13. **Neutralization of SARS-CoV-2 Omicron BA.2.75 after mRNA-1273 Vaccination.** Shen X, et al. *N Engl J Med*. 2022 Sep 9. doi: 10.1056/NEJMc2210648. https://www.nejm.org/doi/10.1056/NEJMc2210648

A booster dose of mRNA-1273 after the initial two-dose vaccination resulted in neutralization titers against the BA.2.75 variant that were similar to those against BA.1 and BA.2 and higher than those against BA.5.

14. **Heterologous vector versus homologous mRNA COVID-19 booster vaccination in non-seroconverted immunosuppressed patients: a randomized controlled trial.** Mrak D et al. *Nat Commun.* 2022 Sep 12;13(1):5362. doi: 10.1038/s41467-022-33036-y. https://www.nature.com/articles/s41467-022-33036-y

Impaired response to COVID-19 vaccination is of particular concern in immunosuppressed patients. To determine the best vaccination strategy for this vulnerable group we performed a single center, 1:1 randomized blinded clinical trial. Patients who failed to seroconvert upon two mRNA vaccinations (BNT162b2 or mRNA-1273) are randomized to receive either a third dose of the same mRNA or the vector vaccine ChAdOx1 nCoV-19. Primary endpoint is the difference in SARS-CoV-2 spike antibody seroconversion rate between vector and mRNA vaccinated patients four weeks after the third dose. Secondary outcomes include cellular immune responses. Seroconversion rates at week four are

significantly higher in the mRNA (homologous vaccination, 15/24, 63%) as compared to the vector vaccine group (heterologous vaccination, 4/22, 18%). SARS-CoV-2-specific T-cell responses are reduced but could be increased after a third dose of either vector or mRNA vaccine. In a multivariable logistic regression analysis, patient age and vaccine type are associated with seroconversion. No serious adverse event is attributed to COVID-19 booster vaccination. Efficacy and safety data underline the importance of a booster vaccination and support the use of a homologous mRNA booster vaccination in immunosuppressed patients.

15. **Effectiveness of a Fourth Dose of COVID-19 mRNA Vaccine Against Omicron Variant Among Elderly People in Singapore.** Tan CY, et al. *Ann Intern Med.* 2022 Sep 13. doi: 10.7326/M22-2042. https://www.acpjournals.org/doi/10.7326/M22-2042

A total of 40 030 persons 80 years of age or older who received their fourth mRNA vaccine dose were identified and matched to 39 936 control participants who were eligible but had not received their fourth dose (0.2% unmatched). Persons who received 4 doses had lower risk for symptomatic SARS-CoV-2 infection, COVID-19–related hospitalization, and severe disease, with VE estimates at 22.2%, 55.0%, and 63.0%, respectively. Analysis stratified by time since vaccination showed that VE-H and VE-S remained high despite a fall in VE-I.

16. **Response to SARS-CoV-2 vaccines in patients receiving B-cell modulating antibodies for renal autoimmune disease.** Arnold F, et al. *BMC Infect Dis.* 2022 Sep 14;22(1):734. doi: 10.1186/s12879-022-07722-7. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-022-07722-7

Adequate timing of SARS-CoV-2-vaccinations after anti-CD20 antibody treatment and CD19 measurements are crucial to generate immunity. Awaiting partial B-cell recovery by postponing regularly scheduled anti-CD20 treatment should be considered in patients with stable immune disease.

17. **Anti-Spike Mucosal IgA Protection against SARS-CoV-2 Omicron Infection.** Havervall S et al. N Engl J Med. 2022 Sep 14. doi: 10.1056/NEJMc2209651. https://www.nejm.org/doi/10.1056/NEJMc2209651

Mucosal IgA can provide immunity against respiratory viruses. Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) boosts mucosal IgA responses, and neutralizing IgA, including neutralizing IgA against the B.1.1.529 (omicron) variant of SARS-CoV-2, has been detected after infection with wild-type SARS-CoV-2.3 However, the potential role of mucosal IgA in protection against SARS-CoV-2 infection is still largely unknown.

18. **Durability of Immune Response After COVID-19 Booster Vaccination and Association With COVID-19 Omicron Infection.** Gilboa M, et al. *JAMA Netw Open.* 2022 Sep 1;5(9):e2231778. doi: 10.1001/jamanetworkopen.2022.31778. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796277

This study found that the third vaccine dose was associated with greater durability than the second dose; however, Omicron was associated with greater resistance to neutralization than wild type and Delta variants of concern. Humoral response dynamics were associated with susceptibility to Omicron infection.

Women & Children

19. **Initial protection against SARS-CoV-2 omicron lineage infection in children and adolescents by BNT162b2 in Israel: an observational study.** Amir O, et al. *Lancet Infect Dis.* 2022 Sep 9:S1473-3099(22)00527-8. doi: 10.1016/S1473-3099(22)00527-8. https://www.sciencedirect.com/science/article/pii/S1473309922005278

A recent two-dose vaccination regimen with BNT162b2 and a recent booster dose in adolescents substantially reduced the rate of confirmed infection compared with the internal control groups. Future studies are needed to assess the duration of this protection and protection against other outcomes such as paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 and long-COVID.

20. **Effectiveness of REGEN-COV combination monoclonal antibody infusion to reduce risk of COVID-19 hospitalization in pregnancy: A retrospective cohort study.** Williams FB, et al. *Am J Obstet Gynecol.* 2022 Sep 12:S0002-9378(22)00741-4. doi: 10.1016/j.ajog.2022.09.017. https://www.sciencedirect.com/science/article/pii/S0002937822007414?via%3Dihub

In a retrospective cohort of unvaccinated pregnant patients with symptomatic COVID-19, administration of REGEN-COV combination monoclonal antibody infusion did not reduce subsequent COVID-related admission. Findings were primarily related to infrequent admission in the untreated group (1.2%), well below the 3-5% reported in non pregnant efficacy trials. As novel therapies are developed for both new and existing diseases that affect pregnant women, ensuring inclusion in clinical trials is essential

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FDA / CDC / NIH / WHO Updates

Update to living WHO guideline on drugs for covid-19. *BMJ*. 2022 Sep 15;378:o2224. doi: 10.1136/bmj.o2224.

Commentary

Current Clinical Challenges in the Prevention and Management of COVID-19. Laine C, Cotton D. *Ann Intern Med.* 2022 Sep 9. doi: 10.7326/M22-2684. Online ahead of print.

Audio Interview: Developing Mucosal Immunity to Covid-19. Rubin EJ, et al. *N Engl J Med*. 2022 Sep 15;387(11):e29. doi: 10.1056/NEJMe2212241.

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