

## COVID-19 Resource Desk

#80 | 10.31.2021 to 11.6.2021

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### New Research

\*note, **PREPRINTS** have not undergone formal peer review

**COVID-19 related publications by Providence caregivers – see [Digital Commons](#)**

#### Epidemiology & Public Health

1. **Effects of covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries.** Islam N, et al. *BMJ*. 2021 Nov 3;375:e066768. doi: 10.1136/bmj-2021-066768. <https://www.bmj.com/content/375/bmj-2021-066768>  
More than 28 million excess years of life were lost in 2020 in 31 countries, with a higher rate in men than women. Excess years of life lost associated with the covid-19 pandemic in 2020 were more than five times higher than those associated with the seasonal influenza epidemic in 2015.

#### Therapeutics

2. **A randomized, placebo-controlled clinical trial of bamlanivimab and etesevimab together in high-risk ambulatory patients with COVID-19 and validation of the prognostic value of persistently high viral load.** Dougan M et al. *Clin Infect Dis*. 2021 Oct 28:ciab912. doi: 10.1093/cid/ciab912. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab912/6413724>  
769 patients were infused. By day 29, 4/511 patients (0.8%) in the antibody treatment group had a COVID-19-related hospitalization or any-cause death, as compared with 15/258 patients (5.8%) in the placebo group. No deaths occurred in the bamlanivimab and etesevimab group compared with 4 deaths (all COVID-19-related) in the placebo group. Patients receiving antibody treatment had a greater mean reduction in viral load from baseline to Day 7 compared with those receiving placebo. Persistently high viral load at Day 7 correlated with COVID-19-related hospitalization or any-cause death by Day 29 in all BLAZE-1 cohorts investigated. These data support the use of bamlanivimab and etesevimab (700mg/1400mg) for ambulatory patients at high risk for severe COVID-19. Evolution of SARS-CoV-2 variants will require continued monitoring to determine the applicability of this treatment.
3. **Update on and Future Directions for Use of Anti-SARS-CoV-2 Antibodies: National Institutes of Health Summit on Treatment and Prevention of COVID-19.** Boggiano C, et al. *Ann Intern Med*. 2021 Nov 2. doi: 10.7326/M21-3669. <https://www.acpjournals.org/doi/10.7326/M21-3669>

As the fourth wave of the SARS-CoV-2 pandemic encircles the globe, there remains an urgent challenge to identify safe and effective treatment and prevention strategies that can be implemented in a range of health care and clinical settings. Substantial advances have been made in the use of anti-SARS-CoV-2 antibodies to mitigate the morbidity and mortality associated with COVID-19. On 15 June 2021, the National Institutes of Health, in collaboration with the U.S. Food and Drug Administration, convened a virtual summit to summarize existing knowledge on anti-SARS-CoV-2 antibodies and to identify key unanswered scientific questions to further catalyze the clinical development and implementation of antibodies.

4. **Nafamostat in hospitalized patients with moderate to severe COVID-19 pneumonia: a randomised Phase II clinical trial.** Zhuravel SV, et al. *EClinicalMedicine*. 2021 Nov;41:101169. doi: 10.1016/j.eclinm.2021.101169. Epub 2021 Oct 27. [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00449-1/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00449-1/fulltext)  
INTERPRETATION: Our study found no significant difference in time to clinical improvement between the nafamostat and SOC groups, but a shorter median time to clinical improvement in a small group of high-risk COVID-19 patients requiring oxygen treatment. To assess the efficacy further, a larger Phase 3 clinical trial is warranted.
5. **Decreased mortality and increased side effects in COVID-19 patients treated with IL-6 receptor antagonists: systematic review and meta-analysis.** Malgie J, et al. *Sci Rep*. 2021 Nov 2;11(1):21522. doi: 10.1038/s41598-021-00726-4. <https://www.nature.com/articles/s41598-021-00726-4>  
There is controversy whether IL-6 (receptor) antagonists are beneficial in treating COVID-19 patients. We therefore update our systematic review to answer the following research questions: (1) Do patients hospitalized for COVID-19 treated with IL-6 (receptor) antagonists have lower mortality compared to standard of care? The search strategy retrieved 2975 unique titles of which 71 studies (9 RCTs and 62 observational) studies comprising 29,495 patients were included. Mortality (RR 0.75) and mechanical ventilation (RR 0.78) were lower and the risk of neutropenia (RR 7.3), impaired liver function (RR 1.67) and secondary infections (RR 1.26) were higher for patients treated with IL-6 (receptor) antagonists compared to patients not treated with treated with IL-6 (receptor) antagonists. Our results showed that IL-6 (receptor) antagonists are effective in reducing mortality in COVID-19 patients, while the risk of side effects was higher. The baseline risk of mortality was an important effect modifier: IL-6 (receptor) antagonists were effective when the baseline mortality risk was high (e.g. ICU setting), while they could be harmful when the baseline mortality risk was low.
6. **Inhaled and intranasal ciclesonide for the treatment of covid-19 in adult outpatients: CONTAIN phase II randomised controlled trial.** Ezer N et al. *BMJ*. 2021 Nov 2;375:e068060. doi: 10.1136/bmj-2021-068060. <https://www.bmj.com/content/375/bmj-2021-068060>  
Compared with placebo, the combination of inhaled and intranasal ciclesonide did not show a statistically significant increase in resolution of symptoms among healthier young adults with covid-19 presenting with prominent respiratory symptoms. As evidence is insufficient to determine the benefit of inhaled and intranasal corticosteroids in the treatment of covid-19, further research is needed.

7. **Immunomodulatory therapies for the treatment of SARS-CoV-2 infection: an update of the systematic literature review to inform EULAR points to consider.** Alunno A, et al. *RMD Open*. 2021 Oct;7(3):e001899. doi: 10.1136/rmdopen-2021-001899.

<https://rmdopen.bmj.com/content/7/3/e001899.long>

This new SLR confirms that some immunomodulators (tocilizumab and JAK inhibitors) have a role for treating severe and critical COVID-19. Although better evidence is available compared with the previous SLR, the need of RCT with combination therapy (glucocorticoids+anti-cytokines) versus monotherapy with glucocorticoids still remains alongside the need for standardisation of inclusion criteria and outcomes to ultimately improve the care and prognosis of affected people. This SLR informed the 2021 update of the EULAR points to consider on the use of immunomodulatory therapies in COVID-19.

### Vaccines / Immunology

8. **Laboratory-Confirmed COVID-19 Among Adults Hospitalized with COVID-19–Like Illness with Infection-Induced or mRNA Vaccine-Induced SARS-CoV-2 Immunity — Nine States, January–September 2021.** Bozio CH, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 29 October 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7044e1>

Among COVID-19–like illness hospitalizations among adults aged  $\geq 18$  years whose previous infection or vaccination occurred 90–179 days earlier, the adjusted odds of laboratory-confirmed COVID-19 among unvaccinated adults with previous SARS-CoV-2 infection were 5.49-fold higher than the odds among fully vaccinated recipients of an mRNA COVID-19 vaccine who had no previous documented infection (95% confidence interval = 2.75–10.99).

9. **Durability of Antibody Levels after Vaccination with mRNA SARS-CoV-2 Vaccine in Individuals with or Without Prior Infection.** Zhong D, et al. *JAMA*. 2021 Nov 1. doi: 10.1001/jama.2021.19996. <https://jamanetwork.com/journals/jama/fullarticle/2785919>

Waning serum antibodies against SARS-CoV-2 have raised questions about long-term immunity. Lower antibody levels to SARS-CoV-2 spike protein are associated with breakthrough infections after vaccination, prompting consideration of booster doses.<sup>1,2</sup> Prior infection may enhance protection from vaccination, stimulating inquiry about hybrid immunity.<sup>3</sup> Our objective was to examine SARS-CoV-2 spike IgG antibodies in a longitudinal cohort, comparing antibody durability in individuals who received an mRNA SARS-CoV-2 vaccine with or without prior SARS-CoV-2 infection.

10. **Association of Prior SARS-CoV-2 Infection with Risk of Breakthrough Infection Following mRNA Vaccination in Qatar.** Abu-Raddad LJ et al. *JAMA*. 2021 Nov 1. doi: 10.1001/jama.2021.19623. <https://jamanetwork.com/journals/jama/fullarticle/2785918>

Prior SARS-CoV-2 infection was associated with a statistically significantly lower risk for breakthrough infection among individuals receiving the BNT162b2 or mRNA-1273 vaccines in Qatar between December 21, 2020, and September 19, 2021. The observational study design precludes direct comparisons of infection risk between the 2 vaccines.

- 11. Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant.** Elliott P et al. *Science*. 2021 Nov 2:eabl9551. doi: 10.1126/science.abl9551. <https://www.science.org/doi/10.1126/science.abl9551>  
SARS-CoV-2 infections were rising during early summer 2021 in many countries associated with the Delta variant. We assessed RT-PCR swab-positivity in the REal-time Assessment of Community Transmission-1 (REACT-1) study in England. We observed sustained exponential growth with average doubling time (June-July 2021) of 25 days driven by complete replacement of Alpha variant by Delta, and by high prevalence at younger less-vaccinated ages. Unvaccinated people were three times more likely than double-vaccinated people to test positive. However, after adjusting for age and other variables, vaccine effectiveness for double-vaccinated people was estimated at between ~50% and ~60% during this period in England. Increased social mixing in the presence of Delta had the potential to generate sustained growth in infections, even at high levels of vaccination.
- 12. Analysis of the Effectiveness of the Ad26.COVID-19 Adenoviral Vector Vaccine for Preventing COVID-19.** Corchado-Garcia J et al. *JAMA Netw Open*. 2021 Nov 1;4(11):e2132540. doi: 10.1001/jamanetworkopen.2021.32540. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2785664>  
The study was composed of 8889 vaccinated patients and 88 898 unvaccinated patients. The incidence rate ratio of SARS-CoV-2 infection in the vaccinated vs unvaccinated control cohorts was 0.26 (60 of 8889 vaccinated patients vs 2236 of 88 898 unvaccinated individuals), which corresponds to an effectiveness of 73.6% and a 3.73-fold reduction in SARS-CoV-2 infections. This study's findings are consistent with the clinical trial-reported efficacy of Ad26.COVID-19 and the first retrospective analysis, suggesting that the vaccine is effective at reducing SARS-CoV-2 infection, even with the spread of variants such as Alpha or Delta that were not present in the original studies, and reaffirm the urgent need to continue mass vaccination efforts globally.
- 13. BNT162b2 and mRNA-1273 COVID-19 vaccine effectiveness against the SARS-CoV-2 Delta variant in Qatar.** Tang P et al. *Nat Med*. 2021 Nov 2. doi: 10.1038/s41591-021-01583-4. <https://www.nature.com/articles/s41591-021-01583-4>  
With the global expansion of the highly transmissible SARS-CoV-2 Delta (B.1.617.2) variant, we conducted a matched test-negative case-control study to assess the real-world effectiveness of COVID-19 messenger RNA vaccines against infection with Delta in Qatar's population. BNT162b2 effectiveness against any, symptomatic or asymptomatic, Delta infection was 45.3%  $\geq 14$  d after the first vaccine dose, but only 51.9%  $\geq 14$  d after the second dose, with 50% of fully vaccinated individuals receiving their second dose before 11 May 2021. Corresponding mRNA-1273 effectiveness  $\geq 14$  d after the first or second dose was 73.7% and 73.1%, respectively. Notably, effectiveness against Delta-induced severe, critical or fatal disease was 93.4% (95% CI, 85.4-97.0%) for BNT162b2 and 96.1% for mRNA-1273  $\geq 14$  d after the second dose. Our findings show robust effectiveness for both BNT162b2 and mRNA-1273 in preventing Delta hospitalization and death in Qatar's population, despite lower effectiveness in preventing infection, particularly for the BNT162b2 vaccine.

14. **Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study.** Tartof SY et al. *Lancet*. 2021 Oct 16;398(10309):1407-1416. doi: 10.1016/S0140-6736(21)02183-8. Epub 2021 Oct 4. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02183-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02183-8/fulltext)  
Our results provide support for high effectiveness of BNT162b2 against hospital admissions up until around 6 months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection. FUNDING: Pfizer.
  
15. **Effectiveness of 2-Dose Vaccination with mRNA COVID-19 Vaccines against COVID-19–Associated Hospitalizations among Immunocompromised Adults — Nine States, January–September 2021.** Embi PJ, et al. *MMWR Morb Mortal Wkly Rep* 2021;70:1553–1559. DOI: <http://dx.doi.org/10.15585/mmwr.mm7044e3>  
Effectiveness of mRNA vaccination against laboratory-confirmed COVID-19–associated hospitalization was lower (77%) among immunocompromised adults than among immunocompetent adults (90%). Vaccine effectiveness varied considerably among immunocompromised patient subgroups. Immunocompromised persons benefit from COVID-19 mRNA vaccination but are less protected from severe COVID-19 outcomes than are immunocompetent persons. Immunocompromised persons receiving mRNA COVID-19 vaccines should receive 3 doses and a booster, consistent with CDC recommendations, practice nonpharmaceutical interventions, and, if infected, be monitored closely and considered early for proven therapies that can prevent severe outcomes.
  
16. **Association between mRNA Vaccination and COVID-19 Hospitalization and Disease Severity.** Tenforde MW et al. *JAMA*. 2021 Nov 4. doi: 10.1001/jama.2021.19499. <https://jamanetwork.com/journals/jama/fullarticle/2786039>  
Vaccination with an mRNA COVID-19 vaccine was significantly less likely among patients with COVID-19 hospitalization and disease progression to death or mechanical ventilation. These findings are consistent with risk reduction among vaccine breakthrough infections compared with absence of vaccination.
  
17. **Myocarditis Following COVID-19 mRNA Vaccine: A Case Series and Incidence Rate Determination.** Perez Y, et al. *Clin Infect Dis*. 2021 Nov 3:ciab926. doi: 10.1093/cid/ciab926. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab926/6420408>  
Myocarditis is a rare adverse event associated with COVID-19 mRNA vaccines, and in adult males it occurs with significantly higher incidence than the background population rate. Recurrence of myocarditis after a subsequent mRNA vaccine dose is not known at this time.

[CDC - The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Children Aged 5–11 Years — United States, November 2021](#)

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**Commentary & Press Releases**

[\*\*PFIZER'S NOVEL COVID-19 ORAL ANTIVIRAL TREATMENT CANDIDATE REDUCED RISK OF HOSPITALIZATION OR DEATH BY 89% IN INTERIM ANALYSIS OF PHASE 2/3 EPIC-HR STUDY\*\*](#)

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