

## COVID-19 Resource Desk

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### New Research

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

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

### Clinical Syndrome

1. **Antibiotic Resistant Infections among COVID-19 Inpatients in U.S. Hospitals.** Baggs J, et al. *Clin Infect Dis.* 2022 Jul 2:ciac517. doi: 10.1093/cid/ciac517.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac517/6627591>

We described bacterial/fungal co-infections and antibiotic resistant infections among inpatients diagnosed with COVID-19 and compared findings with inpatients diagnosed with influenza-like-illness. Less than 10% of COVID-19 inpatients had bacterial/fungal co-infection. Longer lengths of stay, critical care stay, and mechanical ventilation contribute to increased incidence of hospital-onset infections among COVID-19 inpatients.

2. **Clinical and survival differences during separate COVID-19 surges: Investigating the impact of the Sars-CoV-2 alpha variant in critical care patients.** Ritchie AI et al. *PLoS One.* 2022 Jul 1;17(7):e0269244. doi: 10.1371/journal.pone.0269244. eCollection 2022.

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0269244>

We compared ventilatory parameters, biochemical and physiological data and mortality between the first and second COVID-19 surges in the United Kingdom, where distinct variants of SARS-CoV-2 were the dominant stain. We performed a retrospective cohort study investigating critically unwell patients admitted with COVID-19 across three tertiary regional ICUs in London, UK. Of 1782 adult ICU patients screened, 330 intubated and ventilated patients diagnosed with COVID-19 were included. In the second wave where B.1.1.7 variant was the dominant strain, patients were had increased severity of ARDS whilst compliance was greater ( $p < 0.05$ ) and d-dimer lower. The 28-day mortality was not statistically significant (1st wave: 42.2% vs 2nd wave: 39.8%). However, when adjusted for key covariates, the hazard ratio for 28-day mortality in those patients with B.1.1.7 was 3.79 (CI 1.04-13.8;  $p = 0.043$ ) compared to the original strain. During the second surge in the UK, where the COVID-19 variant B.1.1.7 was most prevalent, significantly more patients presented to critical care with severe ARDS. Furthermore, mortality risk was significantly greater in our ICU population during the second wave of the pandemic in those patients with B.1.1.7. As ICUs are experiencing further waves (particularly by the delta (B.1.617.2) variant), we highlight the urgent need for prospective studies describing immunological and pathophysiological differences across novel emerging variants.

3. **Leading Causes of Death in the US During the COVID-19 Pandemic, March 2020 to October**

**2021.** Shiels MS, et al. *JAMA Intern Med.* Published online July 05, 2022.

doi:10.1001/jamainternmed.2022.2476

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2794043>

From March 2020 to October 2021, COVID-19 accounted for 1 in 8 deaths in the US and was a top 5 cause of death in every age group aged 15 years and older. Cancer and heart disease deaths exceeded COVID-19 deaths overall and in most age groups, whereas accidents were the leading cause of death among those aged 1 to 44 years. Compared with the 2020 time period, deaths from COVID-19 in the 2021 time period decreased in ranking among those aged 85 years or older but increased in ranking among those aged 15 to 54 years and became the leading cause of death among those aged 45 to 54 years. The increased ranking of COVID-19 as a leading cause of death in some age groups is consistent with a downward age shift in the distribution of COVID-19 deaths in the US in 2021 compared with 2020, perhaps driven by higher COVID-19 vaccination rates in 2021 in the oldest age groups. The pandemic also has had indirect effects on other causes of death in the US. From 2019 to 2020, death rates increased for heart disease, accidents, stroke, Alzheimer disease, and diabetes.<sup>2</sup> Potential explanations are fear of accessing health care or misattribution of COVID-19 deaths to other causes.<sup>4</sup> Accidental deaths (including drug overdoses and unintentional alcohol poisoning), assault, and suicide remain major causes of death in the US, particularly in younger age groups; the pandemic may have contributed to some of these deaths.

4. **Associations of BMI with COVID-19 vaccine uptake, vaccine effectiveness, and risk of severe COVID-19 outcomes after vaccination in England: a population-based cohort study.** Piernas C

et al. *Lancet Diabetes Endocrinol.* 2022 Jun 30. DOI:[https://doi.org/10.1016/S2213-](https://doi.org/10.1016/S2213-8587(22)00158-9)

[8587\(22\)00158-9](https://doi.org/10.1016/S2213-8587(22)00158-9) [https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(22\)00158-9/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00158-9/fulltext)

Using BMI categories, there is evidence of protection against severe COVID-19 in people with overweight or obesity who have been vaccinated, which was of a similar magnitude to that of people of healthy weight. Vaccine effectiveness was slightly lower in people with underweight, in whom vaccine uptake was also the lowest for all ages. In the vaccinated cohort, there were increased risks of severe COVID-19 outcomes for people with underweight or obesity compared with the vaccinated population with a healthy weight. These results suggest the need for targeted efforts to increase uptake in people with low BMI (<18.5 kg/m<sup>2</sup>), in whom uptake is lower and vaccine effectiveness seems to be reduced. Strategies to achieve and maintain a healthy weight should be prioritised at the population level, which could help reduce the burden of COVID-19 disease.

5. **Estimated Number of COVID-19 Infections, Hospitalizations, and Deaths Prevented Among Vaccinated Persons in the US, December 2020 to September 2021.** Steele MK, et al. *JAMA*

*Netw Open.* 2022 Jul 1;5(7):e2220385. doi: 10.1001/jamanetworkopen.2022.20385.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793913>

COVID-19 vaccination was estimated to prevent approximately 27 million infections, 1.6 million hospitalizations, and 235 000 deaths in the US from December 1, 2020, to September 30, 2021, among vaccinated adults 18 years or older. From September 1 to September 30, 2021, vaccination was

estimated to prevent 52% of expected infections, 56% of expected hospitalizations, and 58% of expected deaths in adults 18 years or older. These findings indicate that the US COVID-19 vaccination program prevented a substantial burden of morbidity and mortality through direct protection of vaccinated individuals.

- 6. Changes in the Relationship Between Income and Life Expectancy Before and During the COVID-19 Pandemic, California, 2015-2021.** Schwandt H, et al. *JAMA*. 2022 Jul 7. doi: 10.1001/jama.2022.10952. <https://jamanetwork.com/journals/jama/fullarticle/2794146>

This retrospective analysis of census tract-level income and mortality data in California from 2015 to 2021 demonstrated a decrease in life expectancy in both 2020 and 2021 and an increase in the life expectancy gap by income level relative to the prepandemic period that disproportionately affected some racial and ethnic minority populations. Inferences at the individual level are limited by the ecological nature of the study, and the generalizability of the findings outside of California are unknown.

### Healthcare Delivery & Healthcare Workers

- 7. Patient experience and healthcare utilization for a COVID-19 telemedicine home monitoring program offered in English and Spanish.** Vartanian KB, Holtorf M, Cox EJ, Diaz G, Khurana H, Schlegel S, Raganit C, Ong B, Czartoski T. **[Providence authors]**. *PLoS One*. 2022 Jun 30;17(6):e0270754. doi: 10.1371/journal.pone.0270754. eCollection 2022. <https://doi.org/10.1371/journal.pone.0270754>

Of the 4,358 HMP participants, 75.5% identified as English speakers and 18.2% identified as Spanish speakers. There was high level of responsiveness to three daily text-based surveys monitoring symptoms engagement (>80%) and a high level of comfort using the home monitoring devices (thermometers and pulse oximeters) for English- and Spanish-speaking participants (97.3% and 99.6%, respectively). The majority of English (95.7%) and Spanish-speaking (100%) patients felt safe monitoring their condition from home and had high satisfaction with the HMP (76.5% and 83.6%, respectively). English and Spanish-speaking COVID-19 positive HMP participants had more outpatient and emergency departments (ED) encounters than non-participants 7 and 30 days after their positive test. This widely implemented HMP provided participants with a sense of safety and satisfaction and its use was associated with more outpatient care and ED encounters. These outcomes were comparable across English and Spanish-speakers, highlighting the importance and potential impact of language-concordant telemedicine.

- 8. The role of routine SARS-CoV-2 screening of healthcare-workers in acute care hospitals in 2020: a systematic review and meta-analysis.** Jabs JM et al. *BMC Infect Dis*. 2022 Jul 2;22(1):587. doi: 10.1186/s12879-022-07554-5. <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-022-07554-5>

The heterogeneous proportions might be explained by different regional incidences, lock-downs, and pre-analytical pitfalls that reduce the sensitivity of the nasopharyngeal swab. The very high prevalence in some studies indicates that screening HCW for SARS-CoV-2 may be important particularly in geographical regions and pandemic periods with a high-incidence. With low numbers and an increasing rate of vaccinated HCW, a strict cost-benefit consideration must be made, especially in times of low

incidences. Since we found no studies that reported on HCW-screening related reductions in infected person-days, re-evaluation should be done when these are available.

## Prognosis

- 9. NEGATIVE PREDICTIVE VALUE OF PROCALCITONIN TO RULE OUT BACTERIAL RESPIRATORY CO-INFECTION IN CRITICAL COVID-19 PATIENTS.** Carbonell R et al. *J Infect.* 2022 Jun 30:S0163-4453(22)00380-2. doi: 10.1016/j.jinf.2022.06.024.

<https://www.sciencedirect.com/science/article/pii/S0163445322003802>

These biomarkers at ICU admission led to a poor ability to predict BC among patients with COVID-19 pneumonia. Baseline values of PCT<0.3ng/mL may be useful to rule out BC, providing clinicians a valuable tool to guide antibiotic stewardship and allowing the unjustified overuse of antibiotics observed during the pandemic, additionally PCT≥0.50ng/mL might predict worsening outcomes.

- 10. Factors Associated with Severe Outcomes Among Immunocompromised Adults Hospitalized for COVID-19 — COVID-NET, 10 States, March 2020–February 2022.** Singson JR, et al. *MMWR Morb Mortal Wkly Rep* 2022;71:878–884. DOI: <http://dx.doi.org/10.15585/mmwr.mm7127a3>

[https://www.cdc.gov/mmwr/volumes/71/wr/mm7127a3.htm?s\\_cid=mm7127a3\\_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm7127a3.htm?s_cid=mm7127a3_w)

Immunocompromised patients accounted for 12.2% of all adult COVID-19 hospitalizations among 10 states and had increased odds of ICU admission and in-hospital death compared with non-immunocompromised patients, irrespective of vaccination status. Known multilayered prevention measures, including nonpharmaceutical interventions, up-to-date COVID-19 vaccination, and therapeutics, can prevent hospitalization and subsequent severe COVID-19 outcomes among immunocompromised persons.

## Survivorship & Rehabilitation

- 11. Point Prevalence Estimates of Activity-Limiting Long-Term Symptoms among U.S. Adults ≥1 Month After Reported SARS-CoV-2 Infection, November 1, 2021.** Tenforde MW et al. *J Infect Dis.* 2022 Jul 1:jjac281. doi: 10.1093/infdis/jiac281. <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac281/6625825>

On November 1, 2021, at least 3.0-5.0 million US adults were estimated to have activity-limiting PCC of ≥1 month duration, or 1.2%-1.9% of US adults. Population prevalence was higher in females (1.4%-2.2%) than males. The estimated prevalence after adjusting for under-ascertainment of infections was 1.7%-3.8%. Millions of US adults were estimated to have activity-limiting PCC. These estimates can support future efforts to address the impact of PCC on the U.S. population.

- 12. Association Between BNT162b2 Vaccination and Long COVID After Infections Not Requiring Hospitalization in Health Care Workers.** Azzolini E, et al. *JAMA.* Published online July 01, 2022. doi:10.1001/jama.2022.11691 <https://jamanetwork.com/journals/jama/fullarticle/2794072>

Survivors of COVID-19 may present with long-lasting symptoms. Some factors have been associated with the development of post-COVID conditions (also referred to as “long COVID”), including hospitalization. A study of older US veterans showed 15% reduction of long COVID after vaccination; however, study limitations included the low number of women and suboptimal vaccination schedules.

## Therapeutics

13. **Sotrovimab lowers the risk of COVID-19 related hospitalization or death in a large population cohort in the United Arab Emirates.** Saheb Sharif-Askari F, et al. *Clin Pharmacol Ther.* 2022 Jul 2. doi: 10.1002/cpt.2700. <https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.2700>

We have conducted a retrospective analysis of all non-hospitalized patients with symptomatic COVID-19 who received a single infusion of sotrovimab and/or oral favipiravir at any Dubai COVID-19 related health care center between July 1, 2021 to Oct 31, 2021. The main outcome was to evaluate the risk of hospitalization for COVID-19 or all-cause death within 28 days of treatment initiation. In this analysis, which included 10882 patients (1135 in the sotrovimab group, 2653 in the sotrovimab/favipiravir group, and 7094 in the favipiravir group), sotrovimab or sotrovimab/favipiravir reduced the risk of hospitalization (13 patients [1.5 %] in the sotrovimab group and 71 patients [2.9%] in the sotrovimab/favipiravir group versus, 251 patients [4%] in the favipiravir group; Hazard ratio (HR) for sotrovimab, 0.16, 95% confidence interval [CI], 0.09 to 0.28, P<0.001; and for sotrovimab/favipiravir, 0.42, 95% CI, 0.32 to 0.56, P<0.001), or death by day 28 from the start of treatment (no death in sotrovimab group and 2 deaths in the sotrovimab/favipiravir group, versus 10 deaths in the favipiravir group; Odds ratio, 0.18, 95% confidence interval, 0.04 to 0.81, P=026). Safety was assessed in all the 3788 patients in sotrovimab and sotrovimab/favipiravir groups, and the reported adverse events were by 34 patients (<1%). In conclusion, sotrovimab was found to reduce the risk of progression of COVID-19 when administrated early to non-hospitalized patients with symptomatic COVID-19. No safety concern was detected.

14. **Resilience of S309 and AZD7442 monoclonal antibody treatments against infection by SARS-CoV-2 Omicron lineage strains.** Case JB et al. *Nat Commun.* 2022 Jul 2;13(1):3824. doi: 10.1038/s41467-022-31615-7. <https://www.nature.com/articles/s41467-022-31615-7>

Here, we report on the protective efficacy against three SARS-CoV-2 Omicron lineage strains (BA.1, BA.1.1, and BA.2) of two monoclonal antibody therapeutics (S309 [Vir Biotechnology] monotherapy and AZD7442 [AstraZeneca] combination), which correspond to ones used to treat or prevent SARS-CoV-2 infections in humans. Despite losses in neutralization potency in cell culture, S309 or AZD7442 treatments reduced BA.1, BA.1.1, and BA.2 lung infection in susceptible mice that express human ACE2 (K18-hACE2) in prophylactic and therapeutic settings. Correlation analyses between in vitro neutralizing activity and reductions in viral burden in K18-hACE2 or human FcγR transgenic mice suggest that S309 and AZD7442 have different mechanisms of protection against Omicron variants, with S309 utilizing Fc effector function interactions and AZD7442 acting principally by direct neutralization. Our data in mice demonstrate the resilience of S309 and AZD7442 mAbs against emerging SARS-CoV-2 variant strains and provide insight into the relationship between loss of antibody neutralization potency and retained protection in vivo.

15. **Thromboprophylactic low-molecular-weight heparin versus standard of care in unvaccinated, at-risk outpatients with COVID-19 (ETHIC): an open-label, multicentre, randomised, controlled, phase 3b trial.** Cools F et al. *Lancet Haematol.* 2022 Jun 29:S2352-3026(22)00173-9. doi: 10.1016/S2352-3026(22)00173-9. [https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(22\)00173-9/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00173-9/fulltext)

The ETHIC trial results suggest that prophylaxis with low-molecular-weight heparin had no benefit for at-risk outpatients with COVID-19. Although the trial was terminated early, our data, combined with data from similar studies, provide further insights to inform international guidelines and influence clinical practice.

FUNDING: The Thrombosis Research Institute and Sanofi UK.

16. **Enoxaparin for primary thromboprophylaxis in symptomatic outpatients with COVID-19 (OVID): a randomised, open-label, parallel-group, multicentre, phase 3 trial.** Barco S et al. *Lancet Haematol.* 2022 Jun 29:S2352-3026(22)00175-2. doi: 10.1016/S2352-3026(22)00175-2. [https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(22\)00175-2/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(22)00175-2/fulltext)

These findings suggest thromboprophylaxis with enoxaparin does not reduce early hospitalisations and deaths among outpatients with symptomatic COVID-19. Futility of the treatment under the initial study design assumptions could not be conclusively assessed owing to under-representation of older patients and consequent low event rates.

FUNDING: SNSF (National Research Programme COVID-19 NRP78: 198352), University Hospital Zurich, University of Zurich, Dr-Ing Georg Pollert (Berlin), Johanna Dürmüller-Bol Foundation.

17. **High-Dose Dexamethasone and Oxygen Support Strategies in Intensive Care Unit Patients With Severe COVID-19 Acute Hypoxemic Respiratory Failure: The COVIDICUS Randomized Clinical Trial.** Bouadma L et al. *JAMA Intern Med.* 2022 Jul 5. doi: 10.1001/jamainternmed.2022.2168. <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2794040>

In this randomized clinical trial among ICU patients with COVID-19-related AHRF, high-dose dexamethasone did not significantly improve 60-day survival. The oxygenation strategies in patients who were not initially receiving IMV did not significantly modify 28-day risk of IMV requirement.

TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT04344730; EudraCT: 2020-001457-43.

18. **Neutralizing COVID-19 Convalescent Plasma in Adults Hospitalized with COVID-19: A Blinded Randomized Placebo-Controlled Trial.** Self WH et al. *Chest.* 2022 Jun 30:S0012-3692(22)01201-6. doi: 10.1016/j.chest.2022.06.029. <https://www.sciencedirect.com/science/article/pii/S0012369222012016>

Among adults hospitalized with COVID-19, including those seronegative for anti-SARS-CoV-2 antibodies, treatment with convalescent plasma did not improve clinical outcomes.

19. **C reactive protein utilisation, a biomarker for early COVID-19 treatment, improves lenzilumab efficacy: results from the randomised phase 3 'LIVE-AIR' trial.** Temesgen Z et al. *Thorax.* 2022 Jul 6:thoraxjnl-2022-218744. doi: 10.1136/thoraxjnl-2022-218744. <https://thorax.bmj.com/content/early/2022/07/05/thoraxjnl-2022-218744>

Hospitalised hypoxemic patients with COVID-19 with baseline CRP <150 mg/L derived the greatest clinical benefit from treatment with lenzilumab.

TRIAL REGISTRATION NUMBER: NCT04351152; ClinicalTrials.gov.

20. **Virological and clinical rebounds of COVID-19 soon after nirmatrelvir/ritonavir discontinuation.** Antonelli G, et al. *Clin Microbiol Infect.* 2022 Jul 2:S1198-743X(22)00344-5. doi:

10.1016/j.cmi.2022.06.029.

<https://www.sciencedirect.com/science/article/pii/S1198743X22003445>

Oral small-chemical antivirals have been recently authorized around the world and come with the promise of simplifying the management and reducing hospitalization of COVID-19 outpatients at risk of disease progression. Nirmatrelvir tablets co-packaged with ritonavir tablets (Paxlovid®, Pfizer) (300/100 mg dose twice daily for 5 days) was granted a conditional marketing authorization by EMA on January 29, 2022 on the basis of a phase 2/3 randomized controlled trial (RCT) in 2246 unvaccinated outpatients (mostly during the wave driven by the Delta variant of concern (VOC) – July to December 2021) in which treatment at a median of 3 days since onset of symptoms led to a 88.9% reduction in the relative risk of hospitalization (-5.81%). Retained nirmatrelvir efficacy against VOC Omicron BA.1 and BA.2 sublineages has been confirmed in vitro but there are remaining issues to be explored in details, as demonstrated by the following 2 case reports.

21. **Efficacy and Safety of Saline Nasal Irrigation Plus Theophylline for Treatment of COVID-19-Related Olfactory Dysfunction: The SCENT2 Phase 2 Randomized Clinical Trial.** Gupta S, et al. *JAMA Otolaryngol Head Neck Surg.* 2022 Jul 7. doi: 10.1001/jamaoto.2022.1573.

<https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2793987>

This randomized clinical trial suggests that the clinical benefit of theophylline nasal irrigations on olfaction in participants with COVID-19-related OD is inconclusive, though suggested by subjective assessments. Larger studies are warranted to investigate the efficacy of this treatment more fully.

### Transmission / Infection Control

22. **Magnitude and determinants of SARS-CoV-2 household transmission: a longitudinal cohort study.** Daniel Kelly J et al. *Clin Infect Dis.* 2022 Jul 5:ciac545. doi: 10.1093/cid/ciac545.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac545/6631204>

Among households including individuals with symptomatic SARS-CoV-2 infection, both vaccinated-to-vaccinated and unvaccinated-to-unvaccinated transmission of SARS-CoV-2 to household contacts was common. Because vaccination alone did not notably reduce risk of infection, household contacts will need to employ additional interventions to avoid infection.

23. **Filtration efficiency of N95 filtering facepiece respirators during multi-cycles of "8-hour simulated donning + disinfection".** Zhu J, et al. *J Hosp Infect.* 2022 Jul 2:S0195-6701(22)00204-3. doi: 10.1016/j.jhin.2022.06.016.

<https://www.sciencedirect.com/science/article/pii/S0195670122002043>

Multi-cycles of dry heating and UV radiation treatments on the reused (i.e., multiple 8-hour donning) N95 respirators have a minimal effect (<0.5%) on the respirator filtration efficiency, and even at 85 L/min, all tested N95 respirators are able to maintain filtration efficiencies  $\geq 95\%$  for at least 30 hours or 4 reuse cycles of "8-hour donning + disinfection", while a lower breathing flow rate (15 L/min) plus the exhalation valve can further extend the N95 respirator usable duration up to 140 hours or 18 reuse cycles of "8-hour donning + disinfection". As the respirator wearing time extends, aerosol penetration slowly increases in a quadratic function with a negative second-order coefficient, and the penetration increment during each cycle of 8-hour donning is less than 0.9%. Multi-cycles N95 respirator reuse + dry heating or UV irradiation disinfection are feasible.

## Vaccines / Immunology

24. **Impact of vaccination on the symptoms of hospitalised patients with SARS-CoV-2 delta variant (B.1.617.1) infection.** Olivier E et al. *Clin Microbiol Infect.* 2022 Jun 29:S1198-743X(22)00332-9. doi:10.1016/j.cmi.2022.06.019.

[https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(22\)00332-9/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(22)00332-9/fulltext)

Among patients hospitalised with a delta variant SARS-CoV-2 infection, vaccination was associated with less severe forms, even in the presence of comorbidities.

25. **Antibody evasion by SARS-CoV-2 Omicron subvariants BA.2.12.1, BA.4, & BA.5.** Wang Q et al. *Nature.* 2022 Jul 5. doi: 10.1038/s41586-022-05053-w.

<https://www.nature.com/articles/s41586-022-05053-w>

SARS-CoV-2 Omicron subvariants BA.2.12.1 and BA.4/5 have surged dramatically to become dominant in the United States and South Africa, respectively<sup>1,2</sup>. These novel subvariants carrying additional mutations in their spike proteins raise concerns that they may further evade neutralizing antibodies, thereby further compromising the efficacy of COVID-19 vaccines and therapeutic monoclonals. We now report findings from a systematic antigenic analysis of these surging Omicron subvariants. BA.2.12.1 is only modestly (1.8-fold) more resistant to sera from vaccinated and boosted individuals than BA.2. However, BA.4/5 is substantially (4.2-fold) more resistant and thus more likely to lead to vaccine breakthrough infections. Mutation at spike residue L452 found in both BA.2.12.1 and BA.4/5 facilitates escape from some antibodies directed to the so-called class 2 and 3 regions of the receptor-binding domain<sup>3</sup>. The F486V mutation found in BA.4/5 facilitates escape from certain class 1 and 2 antibodies but compromises the spike affinity for the viral receptor. The R493Q reversion mutation, however, restores receptor affinity and consequently the fitness of BA.4/5. Among therapeutic antibodies authorized for clinical use, only bebtelovimab retains full potency against both BA.2.12.1 and BA.4/5. The Omicron lineage of SARS-CoV-2 continues to evolve, successively yielding subvariants that are not only more transmissible but also more evasive to antibodies.

26. **Neutralization capacity of antibodies elicited through homologous or heterologous infection or vaccination against SARS-CoV-2 VOCs.** Bekliz M et al. *Nat Commun.* 2022 Jul 4;13(1):3840. doi: 10.1038/s41467-022-31556-1. <https://www.nature.com/articles/s41467-022-31556-1>

Here, we have assessed neutralizing capacity of 120 blood specimens from convalescent individuals infected with ancestral SARS-CoV-2, Alpha, Beta, Gamma or Delta, double vaccinated individuals and patients after breakthrough infections with Delta or Omicron-BA.1. Neutralization against seven authentic SARS-CoV-2 isolates (B.1, Alpha, Beta, Gamma, Delta, Zeta and Omicron-BA.1) determined by plaque-reduction neutralization assay allowed us to map the antigenic relationship of SARS-CoV-2 variants. Highest neutralization titers were observed against the homologous variant. Antigenic cartography identified Zeta and Omicron-BA.1 as separate antigenic clusters. Substantial immune escape in vaccinated individuals was detected for Omicron-BA.1 but not Zeta. Combined infection/vaccination derived immunity results in less Omicron-BA.1 immune escape. Last, breakthrough infections with Omicron-BA.1 lead to broadly neutralizing sera.



**27. Antinucleocapsid Antibodies After SARS-CoV-2 Infection in the Blinded Phase of the Randomized, Placebo-Controlled mRNA-1273 COVID-19 Vaccine Efficacy Clinical Trial.**

Follmann D et al. *Ann Intern Med.* 2022 Jul 5. doi: 10.7326/M22-1300.

<https://www.acpjournals.org/doi/10.7326/M22-1300>

Vaccination status should be considered when interpreting seroprevalence and seropositivity data based solely on anti-N Ab testing. Primary Funding source: National Institute of Allergy and Infectious Diseases of the National Institutes of Health.

**28. Effectiveness of a fourth dose of covid-19 mRNA vaccine against the omicron variant among long term care residents in Ontario, Canada: test negative design study.** Grewal R, et al. *BMJ.*

2022 Jul 6;378:e071502. doi: 10.1136/bmj-2022-071502.

<https://www.bmj.com/content/378/bmj-2022-071502>

The findings suggest that compared with a third dose of mRNA covid-19 vaccine, a fourth dose improved protection against infection, symptomatic infection, and severe outcomes among long term care residents during an omicron dominant period. A fourth vaccine dose was associated with strong protection against severe outcomes in vaccinated residents compared with unvaccinated residents, although the duration of protection remains unknown.

**29. Omicron SARS-CoV-2 Neutralization from Inactivated and ZF2001 Vaccines.** Zhao X, et al. *N Engl J Med.* 2022 Jul 6. doi: 10.1056/NEJMc2206900.

<https://www.nejm.org/doi/10.1056/NEJMc2206900>

In the third year of the coronavirus disease 2019 (Covid-19) pandemic, the omicron variant of SARS-CoV-2 has swept the globe and yielded several subvariants. Currently, BA.2 is overtaking BA.1 in frequency. In addition, BA.2.12.1 infection is increasing quickly and already accounts for more than 50% of new infections in the United States. Therefore, the protection of current vaccines and the need to develop future vaccination strategies are of great concern.

**30. Neutralization of Omicron sublineages and Deltacron SARS-CoV-2 by 3 doses of BNT162b2 vaccine or BA.1 infection.** Kurhade C, et al. *Emerg Microbes Infect.* 2022 Jul 6:1-18.

doi:10.1080/22221751.2022.2099305.

<https://www.tandfonline.com/doi/full/10.1080/22221751.2022.2099305>

Here we report the neutralization activity of sera from BNT162b2 vaccinated individuals or unimmunized Omicron BA.1-infected individuals against Omicron sublineages and "Deltacron" variant (XD). BNT162b2 post-dose 3 immune sera neutralized USA-WA1/2020, Omicron BA.1-, BA.2-, BA.2.12.1-, BA.3-, BA.4/5-, and XD-spike SARS-CoV-2s with geometric mean titers (GMTs) of 1335, 393, 298, 315, 216, 103, and 301, respectively; thus, BA.4/5 SARS-CoV-2 spike variant showed the highest propensity to evade vaccine neutralization compared to the original Omicron variants BA.1. BA.1-convalescent sera neutralized USA-WA1/2020, BA.1-, BA.2-, BA.2.12.1-, BA.3-, BA.4/5-, and Deltacron-spike SARS-CoV-2s with GMTs of 15, 430, 110, 109, 102, 25, and 284, respectively. The unique mutation F486V in the BA.4/5 spike contributes to the increased evasion of antibody neutralization by sublineage BA.4/5. The low neutralization titers of vaccinated sera or convalescent sera from BA.1 infected individuals against the emerging and rapidly spreading Omicron BA.4/5 variants provide important results for consideration in the selection of an updated vaccine in the current Omicron wave.

31. **Association of BNT162b2 Vaccine Third Dose Receipt with Incidence of SARS-CoV-2 Infection, COVID-19-Related Hospitalization, and Death Among Residents of Long-term Care Facilities, August to October 2021.** Muhsen K, et al. *JAMA Netw Open*. 2022 Jul 1;5(7):e2219940. doi: 10.1001/jamanetworkopen.2022.19940.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793804>

This cohort study found significant inverse associations between vaccination with the third dose of the BNT162b2 vaccine with overall SARS-CoV-2 infection, COVID-19 hospitalizations, severe disease, and COVID-19-related deaths among LTCF residents during a massive surge caused by the Delta variant in Israel.

### Women & Children

32. **Giant coronary aneurysms in an infant: Dilemma of MIS-C.** Wold K, Healan S, Garg A. [Providence authors] *Echocardiography*. 2022 Jun 25. doi: 10.1111/echo.15408.

<https://doi.org/10.1111/echo.15408>

The majority of MIS-C associated coronary artery abnormalities are dilation or small aneurysms which are transient and resolve in a few weeks. We present here a case of a 3-month-old child who was noted to have giant aneurysms of her coronary arteries (LAD and RCA) 26 days after testing positive for COVID-19. She was treated with IVIG, infliximab, and glucocorticoids along with aspirin, clopidogrel, and enoxaparin. She did not show any signs of coronary ischemia or cardiac dysfunction but continued to have persistent giant coronary artery aneurysms involving the LAD (z-score ~35) and RCA (z-score ~30). This study emphasizes the importance of early detection and aggressive management of MIS-C to prevent potentially life-threatening consequences.

33. **Lower Risk of Multisystem Inflammatory Syndrome in Children (MIS-C) with the Delta and Omicron variants of SARS-CoV-2.** Evelina PIMS-TS Study Group. *Clin Infect Dis*. 2022 Jul 5:ciac553. doi: 10.1093/cid/ciac553. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac553/6631205>

Little is known about the MIS-C risk with different SARS-CoV-2 variants. In Southeast England, MIS-C rates per confirmed SARS-CoV-2 infections in 0-16 years-olds were 56% lower during pre-vaccine Delta, 66% lower during post-vaccine Delta and 95% lower during the Omicron period.

34. **Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection and severe COVID-19 in children aged 5-11 years in Italy: a retrospective analysis of January-April, 2022.** Sacco C et al. *Lancet*. 2022 Jun 30:S0140-6736(22)01185-0. doi: 10.1016/S0140-6736(22)01185-0.

<https://www.sciencedirect.com/science/article/pii/S0140673622011850>

Vaccination against COVID-19 in children aged 5-11 years in Italy showed a lower effectiveness in preventing SARS-CoV-2 infection and severe COVID-19 than in individuals aged 12 years and older. Effectiveness against infection appears to decrease after completion of the current primary vaccination cycle.

[FDA Authorizes Pharmacists to Prescribe Paxlovid with Certain Limitations.](#)

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