

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](#)

Basic Science / Virology / Pre-clinical

1. **Association of upper respiratory *Streptococcus pneumoniae* colonization with SARS-CoV-2 infection among adults.** Parker AM et al. *Clin Infect Dis*. 2022 Nov 19:ciac907. doi: 10.1093/cid/ciac907. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac907/6833300>

Associations of pneumococcal carriage detection and density with SARS-CoV-2 suggest a synergistic relationship in the upper airway. Longitudinal studies are needed to determine interaction mechanisms between pneumococci and SARS-CoV-2.

Epidemiology & Public Health

2. **COVID-19 and Excess All-Cause Mortality in the US and 20 Comparison Countries, June 2021-March 2022.** Bilinski A, Thompson K, Emanuel E. *JAMA*. 2022 Nov 18. doi: 10.1001/jama.2022.21795. <https://jamanetwork.com/journals/jama/fullarticle/2798990>

Plain Language Summary: This study compares the COVID-19 per capita overall and excess mortality rates in the US vs rates for 20 Organization for Economic Co-operation and Development countries and the timing of any increases in excess mortality between June 2021 and December 2021 (Delta) and December 2021 to March 2022 (Omicron).

3. **Evaluation of the United States definitions for COVID-19 community risk levels.** Mokhtar S, Parpia AS, Lo NC, Ndeffo-Mbah ML. *Clin Infect Dis*. 2022 Nov 26:ciac922. doi: 10.1093/cid/ciac922. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac922/6847510>

The United States CDC defines a county metric of COVID-19 Community Levels to inform public health measures. We find that the COVID-19 Community Levels vary frequently over time, which may not be optimal for decision making. Alternative metric formulations that do not compromise predictive ability are shown to reduce variability.

4. **SARS-CoV-2 Serology and Self-Reported Infection Among Adults - National Health and Nutrition Examination Survey, United States, August 2021-May 2022.** Akinbami LJ, et al. *MMWR Morb Mortal Wkly Rep*. 2022 Dec 2;71(48):1522-1525. doi:

10.15585/mmwr.mm7148a4.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7148a4.htm?s_cid=mm7148a4_w

CDC COVID-19 surveillance systems monitor SARS-CoV-2 antibody prevalence to collect information about asymptomatic, undiagnosed, and unreported disease using national convenience samples of blood donor data from commercial laboratories. However, nonrandom sampling of data from these systems could affect prevalence estimates. The National Health and Nutrition Examination Survey (NHANES) collects SARS-CoV-2 serology data among a sample of the general U.S. civilian population (4). In addition, NHANES collects self-reported COVID-19 vaccination and disease history, and its statistical sampling design is not based on health care access or blood donation. Therefore, NHANES data can be used to better quantify asymptomatic SARS-CoV-2 infection prevalence and seropositivity attained through infection without vaccination. Preliminary NHANES 2021-2022 results indicated that 41.6% of adults aged ≥ 18 years had serology indicative of past infection and that 43.7% of these adults, including 57.1% of non-Hispanic Black or African American (Black) adults, reported never having had COVID-19, possibly representing asymptomatic infection. In addition, 25.5% of adults whose serology indicated past infection reported never having received COVID-19 vaccination. Prevalences of seropositivity in the absence of vaccination were higher among younger adults and Black adults, reflecting the lower observed vaccination rates among these groups. These findings raise health equity concerns given the disparities observed in SARS-CoV-2 infection and COVID-19 vaccination. Results from NHANES 2021-2022 can guide ongoing efforts to achieve vaccine equity in COVID-19 primary vaccination series and booster dose coverage.

Healthcare Delivery & Healthcare Workers

5. Analysis of Failure Rates for COVID-19 Entrance Screening at a US Academic Medical Center.

Roberts SC, et al. *JAMA Intern Med.* 2022 Nov 28. doi: 10.1001/jamainternmed.2022.5426.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2798551>

Plain Language Summary: This quality improvement study analyzes the rate of failures in entrance screening for COVID-19 among individuals entering a large academic medical center.

Prognosis

6. Electrocardiographic findings and prognostic values in patients hospitalised with COVID-19 in the World Heart Federation Global Study.

Pinto-Filho MM et al. *Heart.* 2022 Nov 25;heartjnl-2022-321754. doi: 10.1136/heartjnl-2022-321754.

<https://heart.bmj.com/content/early/2022/11/25/heartjnl-2022-321754>

RESULTS: Among 5313 participants, 2451 had at least one ECG and were included in this analysis. The mean age (SD) was 58.0 (16.1) years, 60.7% were male and 61.1% from lower-income to middle-income countries. The prevalence of major ECG abnormalities was 21.3% (n=521), 447 (18.2%) patients died, 196 (8.0%) had MACE and 1115 (45.5%) were admitted to an ICU. After adjustment, the presence of any major ECG abnormality was associated with a higher risk of death (OR 1.39; 95% CI 1.09 to 1.78) and cardiovascular events (OR 1.81; 95% CI 1.30 to 2.51). Sinus tachycardia (>120 bpm) with an increased risk of death (OR 3.86; 95% CI 1.97 to 7.48), MACE (OR 2.68; 95% CI 1.10 to 5.85) and ICU admission OR 1.99; 95% CI 1.03 to 4.00). Atrial fibrillation, bundle branch block, ischaemic abnormalities and prolonged QT interval did not relate to the outcomes.

CONCLUSION: Major ECG abnormalities and a heart rate >120 bpm were prognostic markers in adults hospitalised with COVID-19.

Survivorship & Rehabilitation

- 7. Post-covid medical complaints following infection with SARS-CoV-2 Omicron vs Delta variants.** Magnusson K, et al. *Nat Commun.* 2022 Nov 30;13(1):7363. doi: 10.1038/s41467-022-35240-2. <https://www.nature.com/articles/s41467-022-35240-2>

The SARS-CoV-2 Omicron (B.1.1.529) variant has been associated with less severe acute disease, however, concerns remain as to whether long-term complaints persist to a similar extent as for earlier variants. Studying 1 323 145 persons aged 18-70 years living in Norway with and without SARS-CoV-2 infection in a prospective cohort study, we found that individuals infected with Omicron had a similar risk of post-covid complaints (fatigue, cough, heart palpitations, shortness of breath and anxiety/depression) as individuals infected with Delta (B.1.617.2), from 14 to up to 126 days after testing positive, both in the acute (14 to 29 days), sub-acute (30 to 89 days) and chronic post-covid (≥ 90 days) phases. However, at ≥ 90 days after testing positive, individuals infected with Omicron had a lower risk of having any complaint (43 (95%CI = 14 to 72) fewer per 10,000), as well as a lower risk of musculoskeletal pain (23 (95%CI = 2-43) fewer per 10,000) than individuals infected with Delta. Our findings suggest that the acute and sub-acute burden of post-covid complaints on health services is similar for Omicron and Delta. The chronic burden may be lower for Omicron vs Delta when considering musculoskeletal pain, but not when considering other typical post-covid complaints.

- 8. Impact of pre-existing chronic viral infection and reactivation on the development of long COVID.** Peluso MJ et al. *J Clin Invest.* 2022 Dec 1:e163669. doi: 10.1172/JCI163669. <https://www.jci.org/articles/view/163669>

Overall, these findings suggest differential effects of chronic viral co-infections on the likelihood of developing LC and predicted distinct syndromic patterns. Further assessment during the acute phase of COVID-19 is warranted.

- 9. Association of Initial SARS-CoV-2 Test Positivity With Patient-Reported Well-being 3 Months After a Symptomatic Illness.** Wisk LE et al. *JAMA Netw Open.* 2022 Dec 1;5(12):e2244486. doi: 10.1001/jamanetworkopen.2022.44486. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799116>

In this study, participants in both the COVID-19-positive and COVID-19-negative groups reported persistently poor physical, mental, or social well-being at 3-month follow-up. Although some individuals had clinically meaningful improvements over time, many reported moderate to severe impairments in well-being 3 months later. These results highlight the importance of including a control group of participants with negative COVID-19 results for comparison when examining the sequelae of COVID-19.

Therapeutics

- 10. In-hospital and 6-month outcomes in patients with COVID-19 supported with extracorporeal membrane oxygenation (EuroECMO-COVID): a multicentre, prospective observational study.**

Lorusso R et al. *Lancet Respir Med*. 2022 Nov 16:S2213-2600(22)00403-9. doi: 10.1016/S2213-2600(22)00403-9. [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(22\)00403-9/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00403-9/fulltext)

Patient's age, timing of cannulation (<4 days vs ≥4 days from intubation), and use of inotropes and vasopressors are essential factors to consider when analysing the outcomes of patients receiving ECMO for COVID-19. Despite post-discharge survival being favourable, persisting long-term symptoms suggest that dedicated post-ECMO follow-up programmes are required.

FUNDING: None.

11. Rare, convergent antibodies targeting the stem helix broadly neutralize diverse

betacoronaviruses. Dacon C et al. *Cell Host Microbe*. 2022 Nov 4:S1931-3128(22)00523-6. doi: 10.1016/j.chom.2022.10.010.

<https://www.sciencedirect.com/science/article/pii/S1931312822005236>

Humanity has faced three recent outbreaks of novel betacoronaviruses, emphasizing the need to develop approaches that broadly target coronaviruses. Here, we identify 55 monoclonal antibodies from COVID-19 convalescent donors that bind diverse betacoronavirus spike proteins. Most antibodies targeted an S2 epitope that included the K814 residue and were non-neutralizing. However, 11 antibodies targeting the stem helix neutralized betacoronaviruses from different lineages. Eight antibodies in this group, including the six broadest and most potent neutralizers, were encoded by IGHV1-46 and IGKV3-20. Crystal structures of three antibodies of this class at 1.5-1.75-Å resolution revealed a conserved mode of binding. COV89-22 neutralized SARS-CoV-2 variants of concern including Omicron BA.4/5 and limited disease in Syrian hamsters. Collectively, these findings identify a class of IGHV1-46/IGKV3-20 antibodies that broadly neutralize betacoronaviruses by targeting the stem helix but indicate these antibodies constitute a small fraction of the broadly reactive antibody response to betacoronaviruses after SARS-CoV-2 infection.

12. AZD7442 (Tixagevimab/Cilgavimab) for Post-exposure Prophylaxis of Symptomatic COVID-19.

Levin MJ et al. *Clin Infect Dis*. 2022 Nov 22:ciac899. doi: 10.1093/cid/ciac899.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac899/6835900>

This study did not meet the primary efficacy endpoint of post-exposure prevention of symptomatic COVID-19 with AZD7442 versus placebo. However, predefined analysis of participants who were SARS-CoV-2 RT-PCR-negative or missing an RT-PCR result at baseline support a role for AZD7442 in preventing symptomatic COVID-19.

13. Monoclonal Antibodies as Long-Acting Products: What Are We Learning From Human Immunodeficiency Virus (HIV) and Coronavirus Disease 2019 (COVID-19)?

Caskey M, Kuritzkes DR. *Clin Infect Dis*. 2022 Nov 21;75(Supplement_4):S530-S540. doi: 10.1093/cid/ciac751.

https://academic.oup.com/cid/article/75/Supplement_4/S530/6835723

Broadly neutralizing antibodies directed against human immunodeficiency virus (HIV) offer promise as long-acting agents for prevention and treatment of HIV. Progress and challenges are discussed. Lessons may be learned from the development of monoclonal antibodies to treat and prevent COVID-19.

- 14. Omicron sublineage BQ.1.1 resistance to monoclonal antibodies.** Arora P, et al. *Lancet Infect Dis.* 2022 Nov 18:S1473-3099(22)00733-2. doi: 10.1016/S1473-3099(22)00733-2. <https://www.sciencedirect.com/science/article/pii/S1473309922007332>

We compared neutralisation of omicron sublineages BA.1, BA.4–5 (in which the amino acid sequence of the S protein is identical), BA.4.6, BA.2.75.2, BJ.1 and BQ.1.1 by single mAbs or mAb cocktails that are currently in clinical use, mAbs for which clinical use has been restricted or discontinued, and mAbs currently being evaluated in clinical trials.

- 15. Characterisation of SARS-CoV-2 genomic variation in response to molnupiravir treatment in the AGILE Phase IIa clinical trial.** Donovan-Banfield I et al. *Nat Commun.* 2022 Nov 26;13(1):7284. doi: 10.1038/s41467-022-34839-9. <https://www.nature.com/articles/s41467-022-34839-9>

Molnupiravir is an antiviral, currently approved by the UK Medicines and Healthcare products Regulatory Agency (MHRA) for treating at-risk COVID-19 patients, that induces lethal error catastrophe in SARS-CoV-2. How this drug-induced mechanism of action might impact the emergence of resistance mutations is unclear. To investigate this, we used samples from the AGILE Candidate Specific Trial (CST)-2 (clinical trial number NCT04746183). The primary outcomes of AGILE CST-2 were to measure the drug safety and antiviral efficacy of molnupiravir in humans (180 participants randomised 1:1 with placebo). Here, we describe the pre-specified exploratory virological endpoint of CST-2, which was to determine the possible genomic changes in SARS-CoV-2 induced by molnupiravir treatment. We use high-throughput amplicon sequencing and minor variant analysis to characterise viral genomics in each participant whose longitudinal samples (days 1, 3 and 5 post-randomisation) pass the viral genomic quality criteria (n = 59 for molnupiravir and n = 65 for placebo). Over the course of treatment, no specific mutations were associated with molnupiravir treatment. We find that molnupiravir significantly increased the transition:transversion mutation ratio in SARS-CoV-2, consistent with the model of lethal error catastrophe. This study highlights the utility of examining intra-host virus populations to strengthen the prediction, and surveillance, of potential treatment-emergent adaptations.

- 16. Convalescent or standard plasma versus standard of care in the treatment of COVID-19 patients with respiratory impairment: short and long-term effects. A three-arm randomized controlled clinical trial.** Manzini PM et al. *BMC Infect Dis.* 2022 Nov 22;22(1):879. doi: 10.1186/s12879-022-07716-5. <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-022-07716-5>

Neither high-titer Convalescent nor Standard plasma improve outcomes of COVID-19 patients with acute respiratory failure. Trial Registration Clinicaltrials.gov Identifier: NCT04428021. First posted: 11/06/2020.

- 17. Temporal Improvements in COVID-19 Outcomes for Hospitalized Adults: A Post Hoc Observational Study of Remdesivir Group Participants in the Adaptive COVID-19 Treatment Trial.** Potter GE et al. *Ann Intern Med.* 2022 Nov 29. doi: 10.7326/M22-2116. <https://www.acpjournals.org/doi/10.7326/M22-2116>

Changes in patient composition explained improved outcomes from ACTT-1 to ACTT-2 but not from ACTT-2 to ACTT-3, suggesting improved [standard of care]. These results support excluding nonconcurrent controls from analysis of platform trials in rapidly changing therapeutic areas. PRIMARY FUNDING SOURCE: National Institute of Allergy and Infectious Diseases.

18. Outpatient Treatment of Confirmed COVID-19 : A Living, Rapid Review for the American College of Physicians. Sommer I, et al. *Ann Intern Med.* 2022 Nov 29. doi: 10.7326/M22-2202. <https://www.acpjournals.org/doi/10.7326/M22-2202>

Some antiviral medications and monoclonal antibodies may improve outcomes for outpatients with mild to moderate COVID-19. However, the generalizability of the findings to the currently dominant Omicron variant is limited.

19. Outpatient Treatment of Confirmed COVID-19: Living, Rapid Practice Points From the American College of Physicians (Version 1). Scientific Medical Policy Committee of the American College of Physicians. *Ann Intern Med.* 2022 Nov 29. doi: 10.7326/M22-2249. <https://www.acpjournals.org/doi/10.7326/M22-2249>

Practice Point 1: Consider molnupiravir to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting who are within 5 to 7 days of the onset of symptoms and at high risk for progressing to severe disease. Practice Point 2: Consider nirmatrelvir-ritonavir combination therapy to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting who are within 5 days of the onset of symptoms and at high risk for progressing to severe disease. Practice Point 3: Consider remdesivir to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting who are within 7 days of the onset of symptoms and at high risk for progressing to severe disease. Practice Point 4: Do not use azithromycin to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 5: Do not use chloroquine or hydroxychloroquine to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 6: Do not use ivermectin to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 7: Do not use nitazoxanide to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 8: Do not use lopinavir-ritonavir combination therapy to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 9: Do not use casirivimab-imdevimab combination therapy to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting unless it is considered effective against a SARS-CoV-2 variant or subvariant locally in circulation. Practice Point 10: Do not use regdanvimab to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting unless it is considered effective against a SARS-CoV-2 variant or subvariant locally in circulation. Practice Point 11: Do not use sotrovimab to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting unless it is considered effective against a SARS-CoV-2 variant or subvariant locally in circulation. Practice Point 12: Do not use convalescent plasma to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 13: Do not use ciclesonide to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting. Practice Point 14: Do not use flvoxamine to treat patients with confirmed mild to moderate COVID-19 in the outpatient setting.

20. Higher versus Lower Dose Corticosteroids for Severe to Critical COVID-19: A Systematic Review and Dose-Response Meta-analysis. Pitre T, et al. *Ann Am Thorac Soc.* 2022 Nov 30. doi:

10.1513/AnnalsATS.202208-7200C.

<https://www.atsjournals.org/doi/10.1513/AnnalsATS.202208-7200C>

Relatively higher doses of corticosteroids may be beneficial in patients with severe-to-critical COVID-19 and may not increase the risk of nosocomial infections.

21. Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 - United States, April-September 2022. Shah MM, et al. *MMWR Morb Mortal Wkly Rep.* 2022 Dec 2;71(48):1531-1537. doi: 10.15585/mmwr.mm7148e2.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7148e2.htm?s_cid=mm7148e2_w

Nirmatrelvir-ritonavir (Paxlovid), an oral antiviral treatment, is authorized for adults with mild-to-moderate COVID-19 who are at increased risk for progression to severe illness. However, real-world evidence on the benefit of Paxlovid, according to vaccination status, age group, and underlying health conditions, is limited. To examine the benefit of Paxlovid in adults aged ≥ 18 years in the United States, a large electronic health record (EHR) data set (Cosmos⁺) was analyzed to assess the association between receiving a prescription for Paxlovid and hospitalization with a COVID-19 diagnosis in the ensuing 30 days. A Cox proportional hazards model was used to estimate this association, adjusted for demographic characteristics, geographic location, vaccination, previous infection, and number of underlying health conditions. Among 699,848 adults aged ≥ 18 years eligible for Paxlovid during April-August 2022, 28.4% received a Paxlovid prescription within 5 days of COVID-19 diagnosis. Being prescribed Paxlovid was associated with a lower hospitalization rate among the overall study population (adjusted hazard ratio [aHR] = 0.49), among those who had received ≥ 3 mRNA COVID-19 vaccines (aHR = 0.50), and across age groups (18-49 years: aHR = 0.59; 50-64 years: aHR = 0.40; and ≥ 65 years: aHR = 0.53). Paxlovid should be prescribed to eligible adults to reduce the risk of COVID-19-associated hospitalization.

22. Association of Remdesivir Treatment With Mortality Among Hospitalized Adults With COVID-19 in the United States. Chokkalingam AP, et al. *JAMA Netw Open.* 2022 Dec 1;5(12):e2244505. DOI: 10.1001/jamanetworkopen.2022.44505

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799114>

In this retrospective cohort study using health insurance claims and hospital chargemaster data, remdesivir treatment was associated with a significantly reduced inpatient mortality over all among patients hospitalized with COVID-19. Results of this analysis using data collected during routine clinical practice and state-of-the-art methods complement results from randomized clinical trials. Future areas of research include assessing the association of remdesivir treatment with inpatient mortality during the circulation of different variants and relative to time from symptom onset.

23. Trends in Cases, Hospitalization and Mortality Related to the Omicron BA.4/BA.5 Sub-Variants in South Africa. Jassat W et al. *Clin Infect Dis.* 2022 Dec 1:ciac921. doi: 10.1093/cid/ciac921.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799114>

Overall, admission incidence risk and in-hospital mortality, which had increased progressively in South Africa's first three waves, decreased in the fourth Omicron BA.1/BA.2 wave and declined even further in the fifth Omicron BA.4/BA.5 wave. Mortality risk was lower in those with natural infection and vaccination, declining further as the number of vaccine doses increased.

Transmission / Infection Control

- 24. Contamination of personal protective equipment and environmental surfaces in Fangcang shelter hospitals.** Yao Y, Cui Y, Gao X, Qian Y, Hu B. *Am J Infect Control*. 2022 Nov 23:S0196-6553(22)00816-1. doi: 10.1016/j.ajic.2022.11.016. [https://www.ajicjournal.org/article/S0196-6553\(22\)00816-1/fulltext](https://www.ajicjournal.org/article/S0196-6553(22)00816-1/fulltext)

SARS-CoV-2 RNA contamination is prevalent in Fangcang hospitals and healthcare workers are under risk of infection. Potentially contaminated areas and surfaces after cleaning and disinfection are negative, underlying the importance of infection control policy.

- 25. Medical Masks Versus N95 Respirators for Preventing COVID-19 Among Health Care Workers : A Randomized Trial.** Loeb M et al. *Ann Intern Med*. 2022 Nov 29. doi: 10.7326/M22-1966. <https://www.acpjournals.org/doi/10.7326/M22-1966>

Among health care workers who provided routine care to patients with COVID-19, the overall estimates rule out a doubling in hazard of RT-PCR-confirmed COVID-19 for medical masks when compared with HRs of RT-PCR-confirmed COVID-19 for N95 respirators. The subgroup results varied by country, and the overall estimates may not be applicable to individual countries because of treatment effect heterogeneity.

PRIMARY FUNDING SOURCE: Canadian Institutes of Health Research, World Health Organization, and Juravinski Research Institute.

- 26. Effect of Wearing Glasses on Risk of Infection With SARS-CoV-2 in the Community: A Randomized Clinical Trial.** Fretheim A, et al. *JAMA Netw Open*. 2022 Dec 1;5(12):e2244495. doi: 10.1001/jamanetworkopen.2022.44495.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799115>

In this randomized clinical trial, wearing glasses in the community was not protective regarding the primary outcome of a reported positive COVID-19 test. However, results were limited by a small sample size and other issues. Glasses may be worth considering as one component in infection control, pending further studies.

TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT05217797.

Vaccines / Immunology

- 27. Safety and Immunogenicity of a Bivalent SARS-CoV-2 Recombinant Protein Vaccine, SCTV01C in Unvaccinated Adults: A Randomized, Double-blinded, Placebo-controlled, Phase I Clinical Trial.** Wang G, et al. *J Infect*. 2022 Nov 17:S0163-4453(22)00649-1. doi: 10.1016/j.jinf.2022.11.008. [https://www.journalofinfection.com/article/S0163-4453\(22\)00649-1/fulltext](https://www.journalofinfection.com/article/S0163-4453(22)00649-1/fulltext)

We have performed a dose-escalation phase 1 trial to assess the reactogenicity and immunogenicity of SCTV01C in health adults (NCT05148091). Our results showed that SCTV01C vaccination with a two-dose regimen was safe with low AE rates (no SAE) and induced promising cross-neutralizing antibody titers against multiple SARS-CoV-2 VOC variants, including Delta, Omicron and its sublineages, with a near 100% seroconversion rates.

28. Antigenic sin of wild-type SARS-CoV-2 vaccine shapes poor cross-neutralization of BA.4/5/2.75 subvariants in BA.2 breakthrough infections. Ju B, et al. *Nat Commun.* 2022 Nov 19;13(1):7120. doi: 10.1038/s41467-022-34400-8. <https://www.nature.com/articles/s41467-022-34400-8>

With declining SARS-CoV-2-specific antibody titers and increasing numbers of spike mutations, the ongoing emergence of Omicron subvariants causes serious challenges to current vaccination strategies. BA.2 breakthrough infections have occurred in people who have received the wild-type vaccines, including mRNA, inactivated, or recombinant protein vaccines. Here, we evaluate the antibody evasion of recently emerged subvariants BA.4/5 and BA.2.75 in two inactivated vaccine-immunized cohorts with BA.2 breakthrough infections. Compared with the neutralizing antibody titers against BA.2, marked reductions are observed against BA.2.75 in both 2-dose and 3-dose vaccine groups. In addition, although BA.2 breakthrough infections induce a certain cross-neutralization capacity against later Omicron subvariants, the original antigenic sin phenomenon largely limits the improvement of variant-specific antibody response. These findings suggest that BA.2 breakthrough infections seem unable to provide sufficient antibody protection against later subvariants such as BA.2.75 in the current immunization background with wild-type vaccines.

29. Safety of the fourth COVID-19 BNT162b2 mRNA (second booster) vaccine: a prospective and retrospective cohort study. Yechezkel M, et al. *Lancet Respir Med.* 2022 Nov 18:S2213-2600(22)00407-6. doi: 10.1016/S2213-2600(22)00407-6. <https://www.sciencedirect.com/science/article/pii/S2213260022004076>

Both our retrospective and prospective analyses support the safety of the second booster, with our findings reflecting physicians' diagnoses, patients' objective physiological measures, and patients' subjective reactions. We believe this study provides safety assurances to the global population who are eligible to receive an additional COVID-19 booster inoculation. These assurances can help increase the number of high-risk individuals who opt to receive this booster vaccine and thereby prevent severe outcomes associated with COVID-19.

FUNDING: European Research Council (ERC).

30. High-dose corticosteroids in patients hospitalized for COVID-19 pneumonia: an observational study of comparative effectiveness. Langer-Gould A, et al. *Int J Infect Dis.* 2022 Oct 29;125:184-191. doi: 10.1016/j.ijid.2022.10.023. <https://www.sciencedirect.com/science/article/pii/S1201971222005628>

Initiating high-dose compared with low-dose corticosteroids among newly hospitalized patients with COVID-19 pneumonia did not improve survival. However, benefit of high-dose corticosteroids in specific subgroups cannot be excluded.

31. Effectiveness of Bivalent mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection — Increasing Community Access to Testing Program, United States, September–November 2022. Link-Gelles R, Ciesla AA, Fleming-Dutra KE, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 22 November 2022. DOI: <http://dx.doi.org/10.15585/mmwr.mm7148e1>

In this study of vaccine effectiveness of the U.S.-authorized bivalent mRNA booster formulations, bivalent boosters provided significant additional protection against symptomatic SARS-CoV-2 infection

in persons who had previously received 2, 3, or 4 monovalent vaccine doses. Due to waning immunity of monovalent doses, the benefit of the bivalent booster increased with time since receipt of the most recent monovalent vaccine dose.

32. Protection against symptomatic infection with delta (B.1.617.2) and omicron (B.1.1.529) BA.1 and BA.2 SARS-CoV-2 variants after previous infection and vaccination in adolescents in England, August, 2021-March, 2022: a national, observational, test-negative, case-control study. Powell AA, et al. *Lancet Infect Dis.* 2022 Nov 24:S1473-3099(22)00729-0. doi: 10.1016/S1473-3099(22)00729-0. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(22\)00729-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00729-0/fulltext)

Previous infection with any SARS-CoV-2 variant provided some protection against symptomatic reinfection, and vaccination added to this protection. Vaccination provides low-to-moderate protection against symptomatic omicron infection, with waning protection after each dose, while hybrid immunity provided the most robust protection. Although more data are needed to investigate longer-term protection and protection against infection with new variants, these data question the need for additional booster vaccine doses for adolescents in populations with already high protection against SARS-CoV-2 infection.

FUNDING: None.

*See also: [Considerations of hybrid immunity and the future of adolescent COVID-19 vaccination.](#) Irving SA, Buchan SA. *Lancet Infect Dis.* 2022 Nov 24:S1473-3099(22)00759-9. doi: 10.1016/S1473-3099(22)00759-9.

33. Protection of 2 and 3 mRNA Vaccine Doses Against Severe Outcomes Among Adults Hospitalized with COVID-19 - VISION Network, August 2021 - March 2022. DeSilva MB et al. *J Infect Dis.* 2022 Nov 23:jiac458. doi: 10.1093/infdis/jiac458. <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac458/6841302>

COVID-19 vaccination was associated with lower rates of ICU admission and in-hospital death in both Delta and Omicron periods compared with being unvaccinated.

34. Major Update 2: Antibody Response and Risk for Reinfection After SARS-CoV-2 Infection-Final Update of a Living, Rapid Review. Holmer HK, et al. *Ann Intern Med.* 2022 Nov 29. doi: 10.7326/M22-1745. <https://www.acpjournals.org/doi/10.7326/M22-1745>

Evidence for a sustained antibody response to SARS-CoV-2 infection is considerable for both Delta and Omicron variants. Prior infection protected against reinfection with both variants, but, for Omicron, protection was weaker and waned rapidly. This information may have limited clinical applicability as new variants emerge.

PRIMARY FUNDING SOURCE: Agency for Healthcare Research and Quality. (PROSPERO: CRD42020207098).

35. Effectiveness of mRNA-1273, BNT162b2, and BBIBP-CorV vaccines against infection and mortality in children in Argentina, during predominance of delta and omicron covid-19 variants: test negative, case-control study. Castelli JM et al. *BMJ.* 2022 Nov 30;379:e073070. doi: 10.1136/bmj-2022-073070.

<https://www.bmj.com/content/379/bmj-2022-073070>

Vaccine effectiveness in preventing mortality remained high in children and adolescents regardless of the circulating variant. Vaccine effectiveness in preventing SARS-CoV-2 infection in the short term after vaccination was lower during omicron predominance and decreasing sharply over time.

TRIAL REGISTRATION: National Registry of Health Research IS003720.

Women & Children

36. High antibody levels and reduced cellular response in children up to one year after SARS-CoV-2 infection. Jacobsen EM et al. *Nat Commun.* 2022 Nov 28;13(1):7315. doi: 10.1038/s41467-022-35055-1. <https://www.nature.com/articles/s41467-022-35055-1>

The COVID-19 course and immunity differ in children and adults. We analyzed immune response dynamics in 28 families up to 12 months after mild or asymptomatic infection. Unlike adults, the initial response is plasmablast-driven in children. Four months after infection, children show an enhanced specific antibody response and lower but detectable spike 1 protein (S1)-specific B and T cell responses than their parents. While specific antibodies decline, neutralizing antibody activity and breadth increase in both groups. The frequencies of S1-specific B and T cell responses remain stable. However, in children, one year after infection, an increase in the S1-specific IgA class switch and the expression of CD27 on S1-specific B cells and T cell maturation are observed. These results, together with the enhanced neutralizing potential and breadth of the specific antibodies, suggest a progressive maturation of the S1-specific immune response. Hence, the immune response in children persists over 12 months but dynamically changes in quality, with progressive neutralizing, breadth, and memory maturation. This implies a benefit for booster vaccination in children to consolidate memory formation.

37. A population-based serological study of post-COVID syndrome prevalence and risk factors in children and adolescents. Dumont R et al. *Nat Commun.* 2022 Nov 29;13(1):7086. doi: 10.1038/s41467-022-34616-8. <https://www.nature.com/articles/s41467-022-34616-8>

Post-COVID syndrome remains poorly studied in children and adolescents. Here, we aimed to investigate the prevalence and risk factors of pediatric post-COVID in a population-based sample, stratifying by serological status. Children from the SEROCOVID-KIDS cohort study (State of Geneva, Switzerland), aged 6 months to 17 years, were tested for anti-SARS-CoV-2 N antibodies (December 2021-February 2022) and parents filled in a questionnaire on persistent symptoms in their children (lasting over 12 weeks) compatible with post-COVID. Of 1034 children tested, 570 (55.1%) were seropositive. The sex- and age-adjusted prevalence of persistent symptoms among seropositive children was 9.1% (95%CI: 6.7;11.8) and 5.0% (95%CI: 3.0;7.1) among seronegatives, with an adjusted prevalence difference (Δ aPrev) of 4.1% (95%CI: 1.1;7.3). Stratifying per age group, only adolescents displayed a substantial risk of having post-COVID symptoms (Δ aPrev = 8.3%, 95%CI: 3.5;13.5). Identified risk factors for post-COVID syndrome were older age, having a lower socioeconomic status and suffering from chronic health conditions, especially asthma. Our findings show that a significant proportion of seropositive children, particularly adolescents, experienced persistent COVID symptoms. While there is a need for further investigations, growing evidence of pediatric post-COVID urges early screening and primary care management.

38. Effectiveness and safety of COVID-19 vaccine in pregnant women: a systematic review with meta-analysis. Tormen M, et al. *BJOG*. 2022 Nov 28. doi: 10.1111/1471-0528.17354.

<https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.17354>

COVID-19 vaccination administered during pregnancy seems to reduce SARS-CoV-2 infection and COVID-19-related hospitalisation, with no significant effects on maternal-fetal complications.

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