

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

 Angiotensin II receptor I auto-antibodies following SARS-CoV-2 infection. Hadlock Jennifer, Chour William, Duvvuri Venkata R, Wallick Julie A, Murray Kim M, Kaplan Henry, Heath James R, Goldman Jason D, et al. [Providence authors]. *PLoS One.* 2021 Nov 17;16(11):e0259902. doi: 10.1371/journal.pone.0259902. eCollection 2021. <u>https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0259902</u> Findings support an association between COVID-19 and AT1R-Ab, emphasizing that vascular pathology may be present in individuals with mild COVID-19 as well as those with severe

disease.

Epidemiology & Public Health

2. Reduced sensitivity of the SARS-CoV-2 Lambda variant to monoclonal antibodies and neutralizing antibodies induced by infection and vaccination. Wang, M., et al. (2021)... *Emerging microbes & infections*, 1–30.

https://www.tandfonline.com/doi/full/10.1080/22221751.2021.2008775

In total, 12 monoclonal antibodies, 14 convalescent sera, and 23 immunized sera induced by mRNA vaccines, inactivated vaccine, and adenovirus type 5 vector vaccine were used to study the antigenicity of the Lambda variant. We found that compared with the D614G reference strain, Lambda demonstrated enhanced infectivity of Calu-3 and LLC-MK2 cells by 3.3-fold and 1.6-fold, respectively. Notably, the sensitivity of the Lambda variant to 5 of 12 neutralizing monoclonal antibodies, 9G11, AM180, R126, X593, and AbG3, was substantially diminished. Furthermore, convalescent- and vaccine-immunized sera showed on average 1.3-2.5-fold lower neutralizing titres against the Lambda variant. Single mutation analysis revealed that this reduction in neutralization was caused by L452Q and F490S mutations. Collectively, the reduced neutralization ability of the Lambda variant suggests that the efficacy of monoclonal antibodies and vaccines may be compromised during the current pandemic.

3. Major disparities in COVID-19 test positivity for patients with non-English preferred language even after accounting for race and social factors in the United States in 2020. Cohen-Cline H, Li HF, Gill M, Wolberg H, Lippa J, Vartanian K, et al. [Providence authors]. *BMC Public Health*.

2021 Nov 18;21(1):2121. doi: 10.1186/s12889-021-12171-z. https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-021-12171-z

People whose preferred language is not English are at greater risk of testing positive for COVID-19 regardless of age, race/ethnicity, geography, or social factors - demonstrating a significant inequity. Research demonstrates that our public health and healthcare systems are centered on English speakers, creating structural and systemic barriers to health. Addressing these barriers are long overdue and urgent for COVID-19 prevention.

4. Leading Causes of Death Among Adults Aged 25 to 44 Years by Race and Ethnicity in Texas During the COVID-19 Pandemic, March to December 2020. Faust JS et al. *JAMA Intern Med.* 2021 Nov 22. doi: 10.1001/jamainternmed.2021.6734.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2786015 In the United States, adults aged 25 to 44 years had the largest relative increase in all-cause mortality during the COVID-19 pandemic in 2020, with disproportionate increases among Black, Hispanic, and Latino adults.1,2 In the first 6 months of the pandemic, the number of COVID-19– attributed deaths among people aged 25 to 44 years in regions with major outbreaks was similar to or exceeded the number to deaths from drug overdoses, which has been the usual leading cause of death in this age group in prior years.3 To better understand excess mortality among adults aged 25 to 44 years during the early months of the COVID-19 pandemic, we examined mortality data from Texas, a racially and ethnically diverse state.

Healthcare Delivery & Healthcare Workers

 COVID-19 vaccination coverage among hospital-based healthcare personnel reported through the Department of Health and Human Services Unified Hospital Data Surveillance System, United States, January 20, 2021-September 15, 2021. Reses HE, et al. Am J Infect Control. 2021 Dec;49(12):1554-1557. doi: 10.1016/j.ajic.2021.10.008. Epub 2021 Nov 18. https://www.ajicjournal.org/article/S0196-6553(21)00673-8/fulltext

To protect both patients and staff, healthcare personnel (HCP) were among the first groups in the United States recommended to receive the COVID-19 vaccine. We analyzed data reported to the U.S. Department of Health and Human Services (HHS) Unified Hospital Data Surveillance System on COVID-19 vaccination coverage among hospital-based HCP. After vaccine introduction in December 2020, COVID-19 vaccine coverage rose steadily through April 2021, but the rate of uptake has since slowed; as of September 15, 2021, among 3,357,348 HCP in 2,086 hospitals included in this analysis, 70.0% were fully vaccinated. Additional efforts are needed to improve COVID-19 vaccine coverage among HCP.

Prognosis

 Prospective validation of the 4C prognostic models for adults hospitalised with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. Knight SR et al. *Thorax.* 2021 Nov 22:thoraxjnl-2021-217629. doi: 10.1136/thoraxjnl-2021-217629. https://thorax.bmj.com/content/early/2021/11/21/thoraxjnl-2021-217629.responses RESULTS: 76 588 participants were included, of whom 27 352 (37.4%) deteriorated and 12 581 (17.4%) died. Both the 4C Mortality (0.78 (0.77 to 0.78)) and 4C Deterioration scores (pooled C-statistic 0.76 (95% CI 0.75 to 0.77)) demonstrated consistent discrimination across all nine National Health Service regions, with similar performance metrics to the original validation cohorts. Calibration remained stable (4C Mortality: pooled slope 1.09, pooled calibration-in-the-large 0.12; 4C Deterioration: 1.00, -0.04), with no need for temporal recalibration during the second UK pandemic wave of hospital admissions. Both 4C risk stratification models demonstrate consistent performance to predict clinical deterioration and mortality in a large prospective second wave validation cohort of UK patients. Despite recent advances in the treatment and management of adults hospitalised with COVID-19, both scores can continue to inform clinical decision making.

Survivorship & Rehabilitation

7. Persistent symptoms following SARS-CoV-2 infection among children and young people: a meta-analysis of controlled and uncontrolled studies. Behnood SA et al. *J Infect.* 2021 Nov 20:S0163-4453(21)00555-7. doi: 10.1016/j.jinf.2021.11.011.

https://www.journalofinfection.com/article/S0163-4453(21)00555-7/fulltext

FINDINGS: Twenty two of 3357 unique studies were eligible, including 23,141 CYP. Median duration of follow-up was 125 days (IQR 99-231). Pooled risk difference in post-COVID cases compared to controls (5 studies) were significantly higher for cognitive difficulties (3% (95% CI 1, 4)), headache (5% (1, 8)), loss of smell (8%, (2, 15)), sore throat (2% (1, 2)) and sore eyes (2% (1, 3)) but not abdominal pain, cough, fatigue, myalgia, insomnia, diarrhoea, fever, dizziness or dyspnoea. Pooled prevalence of symptoms in post-COVID participants in 17 studies ranged from 15% (diarrhoea) to 47% (fatigue). Age was associated with higher prevalence of all symptoms except cough. Higher study quality was associated with lower prevalence of all symptoms, except loss of smell and cognitive symptoms. The frequency of the majority of reported persistent symptoms was similar in SARS-CoV-2 positive cases and controls. This systematic review and meta-analysis highlights the critical importance of a control group in studies on CYP post SARS-CoV-2 infection.

8. Factors Associated with Risk of Postdischarge Thrombosis in Patients With COVID-19. Li P, et al. JAMA Netw Open. 2021;4(11):e2135397. doi:10.1001/jamanetworkopen.2021.35397 <u>https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2786413</u> Although extended thromboprophylaxis in unselected patients with COVID-19 is not supported, these findings suggest that postdischarge anticoagulation may be considered for high-risk patients who have a history of venous thromboembolism, peak D-dimer level greater than 3 μg/mL, and predischarge C-reactive protein level greater than 10 mg/dL, if their bleeding risk is low.

Therapeutics

9. Phase III, Randomized, Double-blind, Placebo controlled trial of Efficacy, Safety and Tolerability of Antiviral drug Umifenovir vs Standard care of therapy in non-severe COVID-19 patients. Ramachandran R et al. Int J Infect Dis. 2021 Nov 18:S1201-9712(21)00872-9. doi: 10.1016/j.ijid.2021.11.025. <u>https://www.sciencedirect.com/science/article/pii/S1201971221008729</u> Umifenovir meets the primary and secondary endpoint criteria and exhibits statistically significant efficacy for Mild-asymptomatic patients. It is efficacious, safe and well-tolerated at

the tested dosage of 800mg BID, maximum 14 days.

- 10. Association between convalescent plasma treatment and mortality in COVID-19: a collaborative systematic review and meta-analysis of randomized clinical trials. Axfors C et al. *BMC Infect Dis.* 2021 Nov 20;21(1):1170. doi: 10.1186/s12879-021-06829-7. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06829-7. Convalescent plasma treatment of patients with COVID-19 did not reduce all-cause mortality. These results provide strong evidence that convalescent plasma treatment for patients with COVID-19 should not be used outside of randomized trials. Evidence synthesis from collaborations among trial investigators can inform both evidence generation and evidence application in patient care.
- 11. Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. RECOVERY Collaborative Group. Lancet. 2021 Nov 17:S0140-6736(21)01825-0. doi: 10.1016/S0140-6736(21)01825-0. Online ahead of print. In patients hospitalised with COVID-19, aspirin was not associated with reductions in 28 day mortality or in the risk of progressing to invasive mechanical ventilation or death, but was associated with a small increase in the rate of being discharged alive within 28 days.
- 12. Efficacy of Inhaled Ciclesonide for Outpatient Treatment of Adolescents and Adults with Symptomatic COVID-19: A Randomized Clinical Trial. Clemency BM et al. *JAMA Intern Med.* 2021 Nov 22. doi: 10.1001/jamainternmed.2021.6759.

https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2786012

RESULTS: A total of 413 participants were screened and 400 (96.9%) were enrolled and randomized (197 [49.3%] in the ciclesonide arm and 203 [50.7%] in the placebo arm; mean [SD] age, 43.3 [16.9] years; 221 [55.3%] female; 2 [0.5%] Asian, 47 [11.8%] Black or African American, 3 [0.8%] Native Hawaiian or other Pacific Islander, 345 [86.3%] White, and 1 multiracial individuals [0.3%]; 172 Hispanic or Latino individuals [43.0%]). The median time to alleviation of all COVID-19-related symptoms was 19.0 days (95% CI, 14.0-21.0) in the ciclesonide arm and 19.0 days (95% CI, 16.0-23.0) in the placebo arm. There was no difference in resolution of all symptoms by day 30 (odds ratio, 1.28; 95% CI, 0.84-1.97). Participants who were treated with ciclesonide had fewer subsequent emergency department visits or hospital admissions for reasons related to COVID-19 (odds ratio, 0.18; 95% CI, 0.04-0.85). No participants died during the study. CONCLUSIONS AND RELEVANCE: The results of this

randomized clinical trial demonstrated that ciclesonide did not achieve the primary efficacy end point of reduced time to alleviation of all COVID-19-related symptoms.

13. Prostacyclin in Mechanically Ventilated Patients with COVID-19 and Severe Endotheliopathy: A Multicenter, Randomized, Clinical Trial. Johansson PI et al. *Am J Respir Crit Care Med.* 2021 Nov 23. doi: 10.1164/rccm.202108-1855OC.

https://www.atsjournals.org/doi/pdf/10.1164/rccm.202108-1855OC

Main Results Eighty patients were randomized (41 prostacyclin, 39 placebo). The number of days alive without mechanical ventilation at 28-days was 16.0 days (SD 12) versus 5.0 days (SD 10), [95% CI -21.0 to 5.0], P=0.07) in the prostacyclin and the placebo groups, respectively. The 28-day mortality was 21.9% versus 43.6% in the prostacyclin and the placebo groups, respectively (risk ratio 0.50 [95% CI 0.24 to 0.96] P=0.056). The incidence of serious adverse events within 7 days were 2.4% vs. 12,8% (risk ratio 0.19 [95% CI 0.001 to 1.11], P=0.10) in the prostacyclin and the placebo groups, respectively. Prostacyclin were not associated with a significant reduction in the number of days alive and without mechanical ventilation within 28-days. The point estimates, however, favored the prostacyclin group in all analyses, including 28-day mortality, warranting further investigation in larger trials.

14. Sarilumab in adults hospitalised with moderate-to-severe COVID-19 pneumonia (CORIMUNO-SARI-1): An open-label randomised controlled trial. CORIMUNO-19 Collaborative group. *Lancet* Rheumatol. 2021 Nov 17. doi: 10.1016/S2665-9913(21)00315-5. <u>https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00315-5/fulltext</u> Sarilumab treatment did not improve early outcomes in patients with moderate-to-severe COVID-19 pneumonia. Further studies are warranted to evaluate the effect of sarilumab on long-term survival.

Vaccines / Immunology

15. Effectiveness of an inactivated virus-based SARS-CoV-2 vaccine, BBV152, in India: a testnegative, case-control study. Desai, D et al. (2021). *The Lancet. Infectious diseases*, S1473-3099(21)00674-5. <u>https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00674-5/fulltext</u>

This study shows the effectiveness of two doses of BBV152 against symptomatic COVID-19 in the context of a huge surge in cases, presumably dominated by the potentially immune-evasive delta (B.1.617.2) variant of SARS-CoV-2. Our findings support the ongoing roll-out of this vaccine to help control the spread of SARS-CoV-2, while continuing the emphasis on adherence to non-pharmacological measures.ES

16. Elapsed time since BNT162b2 vaccine and risk of SARS-CoV-2 infection: test negative design study. Israel, A., et al. (2021). *BMJ* (Clinical research ed.), 375, e067873. https://www.bmj.com/content/375/bmj-2021-067873

In this large population of adults tested for SARS-CoV-2 by RT-PCR after two doses of mRNA BNT162b2 vaccine, a gradual increase in the risk of infection was seen for individuals who received their second vaccine dose after at least 90 days.

17. Protective mucosal immunity against SARS-CoV-2 after heterologous systemic prime-mucosal boost immunization. Lapuente, D., et al. (2021). *Nature communications*, 12(1), 6871. https://www.nature.com/articles/s41467-021-27063-4

The mRNA prime provokes a comprehensive T cell response consisting of circulating and lung TRM after the boost, while the plasmid DNA prime induces mostly mucosal T cells. Concomitantly, the intranasal boost strategies lead to complete protection against a SARS-CoV-2 infection in mice. Our data thus suggest that mucosal booster immunizations after mRNA priming is a promising approach to establish mucosal immunity in addition to systemic responses.

18. Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: an exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial. Toback S et al. Lancet Respir Med. 2021 Nov 17:S2213-2600(21)00409-4. doi:10.1016/S2213-2600(21)00409-4. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00409-4/fulltext To our knowledge, this substudy is the first to show the safety, immunogenicity, and efficacy profile of a COVID-19 vaccine when co-administered with seasonal influenza vaccines. Our results suggest concomitant vaccination might be a viable immunisation strategy. See also: Vaccine efficacy and immune interference: co-administering COVID-19 and

influenza vaccines. Altmann DM, Boyton RJ. Lancet Respir Med. 2021 Nov 17:S2213-2600(21)00438-0. doi: 10.1016/S2213-2600(21)00438-0.

 Neutralization of SARS-CoV-2 Variants in Transplant Recipients after Two and Three Doses of mRNA-1273 Vaccine: Secondary Analysis of a Randomized Trial. Kumar D et al. Ann Intern Med. 2021 Nov 23. doi: 10.7326/M21-3480. <u>https://www.acpjournals.org/doi/10.7326/M21-3480</u>

In organ transplant recipients, a third dose of mRNA vaccine increases neutralizing antibody response against SARS-CoV-2 variants compared with placebo.

- 20. Myocardial Infarction, Stroke, and Pulmonary Embolism after BNT162b2 mRNA COVID-19 Vaccine in People Aged 75 Years or Older. Jabagi MJ, et al. JAMA. 2021 Nov 22. doi: 10.1001/jama.2021.21699. <u>https://jamanetwork.com/journals/jama/fullarticle/2786667</u> The BNT162b2 mRNA vaccine (Pfizer-BioNTech) was the first SARS-CoV-2 vaccine authorized and most widely used in older persons in France. Although no increases in cardiovascular events were reported in the phase 3 trials, questions emerged once the vaccine was used on a large scale because older people were underrepresented in the trials. We evaluated the shortterm risk of severe cardiovascular events among French people aged 75 years or older after the administration of the BNT162b2 mRNA vaccine.
- 21. Experience with polyethylene glycol allergy-guided risk management for COVID-19 vaccine anaphylaxis. Brockow K, et al. *Allergy*. 2021 Nov 22. doi: 10.1111/all.15183. https://onlinelibrary.wiley.com/doi/10.1111/all.15183

Taking a detailed history excluded PEG allergy in most referred patients and enabled direct safe vaccination. Immediate urticaria/anaphylaxis to typical elicitors identified patients requiring PEG allergy workup. Skin tests ± BAT identified PEG allergy and helped to select the vaccine and the vaccination approach. Even PEG-allergic patients can tolerate COVID-19 vaccines.

22. Neutralising antibody titres as predictors of protection against SARS-CoV-2 variants and the impact of boosting: a meta-analysis. Cromer D et al. *Lancet Microbe.* 2021 Nov 15. doi: 10.1016/S2666-5247(21)00267-6.

https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00267-6/fulltext In-vitro neutralisation titres remain a correlate of protection from SARS-CoV-2 variants and modelling of the effects of waning immunity predicts a loss of protection to the variants after vaccination. However, booster vaccination with current vaccines should enable higher neutralisation to SARS-CoV-2 variants than is achieved with primary vaccination, which is predicted to provide robust protection from severe infection outcomes with the current SARS-CoV-2 variants of concern, at least in the medium term.

23. Assessment of Response to a Third Dose of the SARS-CoV-2 BNT162b2 mRNA Vaccine in Patients with Solid Tumors Undergoing Active Treatment. Rottenberg Y, et al. *JAMA Oncol.* 2021 Nov 23. doi: 10.1001/jamaoncol.2021.6764.

https://jamanetwork.com/journals/jamaoncology/fullarticle/2786532

Following massive global initiatives, the US Food and Drug Administration approved several SARS-CoV-2 vaccines, including the BNT162b2 (Pfizer-BioNTech) mRNA vaccine. While manifestations of COVID-19 are heterogeneous, patients with solid tumors undergoing active therapy are at considerable risk for worse outcomes. Among these patients, humoral response to SARS-CoV-2 vaccines has been reported in approximately 90%. Although high, this proportion is considerably lower than the 99% to 100% found in control groups. Among patients who are treated with chemotherapy, further reduced humoral responses have been described.

24. Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy clinical trial. Gilbert PE et al. *Science* 23 Nov 2021. DOI: 10.1126/science.abm3425 https://www.science.org/doi/10.1126/science.abm3425

In the coronavirus efficacy (COVE) phase 3 clinical trial, vaccine recipients were assessed for neutralizing and binding antibodies as correlates of risk for COVID-19 disease and as correlates of protection. These immune markers were measured at second vaccination and 4 weeks later, with values reported in standardized WHO International Units. All markers were inversely associated with COVID-19 risk and directly associated with vaccine efficacy. Vaccine recipients with post-vaccination 50% neutralization titers 10, 100, and 1000 had estimated vaccine efficacy of 78% (95% confidence interval 54, 89%), 91% (87, 94%), and 96% (94, 98%), respectively. These results help define immune marker correlates of protection and may guide approval decisions for mRNA COVID-19 vaccines and other COVID-19 vaccines.

Women & Children

25. COVID-19-Associated Orphanhood and Caregiver Death in the United States. Hillis SD et al. *Pediatrics.* 2021 Oct 7:e2021053760. doi: 10.1542/peds.2021-053760.

https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2021-053760/183446/COVID-19-Associated-Orphanhood-and-Caregiver-Death

We found that from April 1, 2020 through June 30, 2021, over 140,000 children in the US experienced the death of a parent or grandparent caregiver. The risk of such loss was 1.1 to 4.5 times higher among children of racial and ethnic minorities, compared to Non-Hispanic White children. The highest burden of COVID-19-associated death of parents and caregivers occurred in Southern border states for Hispanic children, Southeastern states for Black children, and in states with tribal areas for American Indian/Alaska Native populations. We found substantial disparities in distributions of COVID-19-associated death of parents and caregivers across racial and ethnic groups. Children losing caregivers to COVID-19 need care and safe, stable, and nurturing families with economic support, quality childcare and evidence-based parenting support programs. There is an urgent need to mount an evidence-based comprehensive response focused on those children at greatest risk, in the states most affected.

- 26. Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization -United States, March 2020-September 2021. DeSisto, C. L., et al. (2021). MMWR. Morbidity and mortality weekly report, 70(47), 1640–1645. <u>https://doi.org/10.15585/mmwr.mm7047e1</u> COVID-19 documented at delivery was associated with increased risk for stillbirth, with a stronger association during the period of Delta variant predominance. Implementing evidencebased COVID-19 prevention strategies, including vaccination before or during pregnancy, is critical to reducing the impact of COVID-19 on stillbirths.
- 27. COVID-19-Associated Deaths After SARS-CoV-2 Infection During Pregnancy Mississippi, March 1, 2020-October 6, 2021. Kasehagen, L., et al. (2021). MMWR. Morbidity and mortality weekly report, 70(47), 1646–1648. <u>https://doi.org/10.15585/mmwr.mm7047e2</u> Pregnant and recently pregnant women are at increased risk for severe illness and death from COVID-19 compared with women who are not pregnant or were not recently pregnant. CDC recommends COVID-19 vaccination for women who are pregnant, recently pregnant, trying to become pregnant, or might become pregnant in the future. This report describes 15 COVID-19associated deaths after infection with SARS-CoV-2 during pregnancy in Mississippi during March 1, 2020-October 6, 2021.

GUIDELINES & CONSENSUS STATEMENTS

2021 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations: Summary From the Basic Life Support; Advanced Life Support; Neonatal Life Support; Education, Implementation, and Teams; First Aid Task Forces; and the COVID-19 Working Group. Wyckoff MH et al. *Circulation*. 2021 Nov 11:CIR000000000001017. doi: 10.1161/CIR.000000000001017. ESCMID COVID-19 Living guidelines: drug treatment and clinical management. Clinical Microbiol Infect. Bartoletti, M., et al. (2021). <u>https://doi.org/10.1016/j.cmi.2021.11.007</u>

FDA / CDC / NIH / WHO Updates

CDC: CDC Statement on B.1.1.529 (Omicron variant)

WHO: Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern (who.int)

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