

COVID-19 Resource Desk

#50 | 4.3.2021 to 4.9.2021

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New Research

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

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

Clinical Syndrome

- COVID-19 in Adults with Congenital Heart Disease.** Nicolarsen, Jeremy et al [**Providence author**]. *J Am Coll Cardiol*. 2021 Apr 6;77(13):1644-1655. doi: 10.1016/j.jacc.2021.02.023. <https://www.jacc.org/doi/10.1016/j.jacc.2021.02.023>
COVID-19 mortality in adults with CHD is commensurate with the general population. The most vulnerable patients are those with worse physiological stage, such as cyanosis and pulmonary hypertension, whereas anatomic complexity does not appear to predict infection severity.
- Pathophysiology of SARS-CoV-2: The Mount Sinai COVID-19 autopsy experience.** Bryce C, et al. *Mod Pathol*. 2021 Apr 1. doi: 10.1038/s41379-021-00793-y. <https://www.nature.com/articles/s41379-021-00793-y>
Our autopsy series of COVID-19-positive patients reveals that this disease, often conceptualized as a primarily respiratory viral illness, has widespread effects in the body including hypercoagulability, a hyperinflammatory state, and endothelial dysfunction. Targeting of these multisystemic pathways could lead to new treatment avenues as well as combination therapies against SARS-CoV-2 infection.
- The incidence of pleural effusion in COVID-19 pneumonia: State-of-the-art review.** Chong WH, et al. *Heart Lung*. 2021 Feb 27;50(4):481-490. doi: 10.1016/j.hrtlng.2021.02.015. <https://www.sciencedirect.com/science/article/pii/S0147956321000522>
The incidence of pleural effusions was low at 7.3% among the 47 observational studies. Pleural effusions were commonly observed in critically ill patients and had Multisystem Inflammatory Syndrome (MIS). COVID-19-related pleural effusions were identified 5-7 days and 11 days, after hospital admission and onset of COVID-19 symptoms. The characteristic findings of pleural fluid were exudative, lymphocytic or neutrophilic-predominant pleural fluid with markedly elevated lactate dehydrogenase (LDH) levels and pleural fluid to serum LDH ratio.

Diagnostics & Screening

4. **T cell assays differentiate clinical and subclinical SARS-CoV-2 infections from cross-reactive antiviral responses.** Ogbe A et al. *Nat Commun.* 2021 Apr 6;12(1):2055. doi: 10.1038/s41467-021-21856-3. <https://www.nature.com/articles/s41467-021-21856-3>
We show a range of T cell assays that differentially capture immune function to characterise SARS-CoV-2 responses. Strong ex vivo ELISpot and proliferation responses to multiple antigens (including M, NP and ORF3) are found in 168 PCR-confirmed SARS-CoV-2 infected volunteers, but are rare in 119 uninfected volunteers. Highly exposed seronegative healthcare workers with recent COVID-19-compatible illness show T cell response patterns characteristic of infection. By contrast, >90% of convalescent or unexposed people show proliferation and cellular lactate responses to spike subunits S1/S2, indicating pre-existing cross-reactive T cell populations. The detection of T cell responses to SARS-CoV-2 is therefore critically dependent on assay and antigen selection. Memory responses to specific non-spike proteins provide a method to distinguish recent infection from pre-existing immunity in exposed populations.

Epidemiology & Public Health

5. **Excess Deaths from COVID-19 and Other Causes in the US, March 1, 2020, to January 2, 2021.** Woolf SH, et al. *JAMA.* 2021 Apr 2. doi: 10.1001/jama.2021.5199. <https://jamanetwork.com/journals/jama/fullarticle/2778361>
A study analyzing US mortality in March-July 2020 reported a 20% increase in excess deaths, only partly explained by COVID-19. Surges in excess deaths varied in timing and duration across states and were accompanied by increased mortality from non-COVID-19 causes.¹ This study updates the analysis for the remainder of 2020.
6. **Racial and Ethnic Differences in COVID-19 Outcomes, Stressors, Fear, and Prevention Behaviors among U.S. Women: Web-based Cross-sectional Study.** Stockman JK, et al. *J Med Internet Res.* 2021 Apr 2. doi: 10.2196/26296. <https://preprints.jmir.org/preprint/26296/accepted>
Between May and June 2020, 491 women were recruited into The COPE Study. Among our sample of women, 16% reported COVID-19 symptoms, 22% were concerned about possible exposure from the people they knew who tested positive for COVID-19, and 51.4% knew where to get tested; yet only 5.8% had been tested. Racial/ethnic minority women reported less likely to know where to get tested. Significant differences in race/ethnicity were observed for select stressors (food insecurity, not enough money, homeschooling children, unable to have a doctor/telemedicine appointment) and prevention behaviors (handwashing with soap, self-isolation if sick, public glove use, not leaving home for any activities). Although no racial/ethnic differences emerged for the fear of COVID-19 scale.
7. **Association of Sociodemographic Factors and Blood Group Type with Risk of COVID-19 in a US Population.** Anderson JL, et al. *JAMA Netw Open.* 2021 Apr 1;4(4):e217429. doi: 10.1001/jamanetworkopen.2021.7429. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778155>

With contrasting reports from China, Europe, Boston, New York, and elsewhere, we embarked on a large, prospective case-control study that included more than 11 000 individuals who were newly infected with SARS-CoV-2, and we found no ABO associations with either disease susceptibility or severity. The smaller sample sizes and retrospective, observational nature of many prior studies, in addition to their striking heterogeneity of ABO associations with disease susceptibility and severity, could be due to chance variations, publication bias, differences in genetic background, geography and environment, and viral strains.

8. **Racial and Ethnic Differences and Clinical Outcomes of COVID-19 Patients Presenting to the Emergency Department.** Wiley Z, et al. *Clin Infect Dis*. 2021 Apr 2:ciab290. doi:

10.1093/cid/ciab290 <https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciab290/6209403>

Minority patients were overrepresented among COVID-19 ED patients, and while they had similar risks of hospitalization as Whites, in-hospital mortality risk was higher.

9. **Differences in COVID-19 Testing and Test Positivity among Veterans, United States, 2020.**

Ferguson JM, Abdel Magid HS, Purnell AL, Kiang MV, Osborne TF. *Public Health Rep*. 2021 Apr 7:333549211009498. doi: 10.1177/00333549211009498.

<https://link.springer.com/article/10.1007/s40615-021-00982-0>

Veterans who were female, Black/African American, Hispanic/Latino, urban, and low income and had a disability had an increased likelihood of obtaining a COVID-19 test, and veterans who were Asian had a decreased likelihood of obtaining a COVID-19 test. Compared with veterans who were White, veterans who were Black/African American and Native Hawaiian/Other Pacific Islander had an increased likelihood of receiving a positive test result. Hispanic/Latino veterans had a 43% higher likelihood of receiving a positive test result than non-Hispanic/Latino veterans did. Although veterans have access to subsidized health care at the VHA, the increased risk of receiving a positive test result for COVID-19 among Black and Hispanic/Latino veterans, despite receiving more tests than White and non-Hispanic/Latino veterans, suggests that other factors (eg, social inequities) are driving disparities in COVID-19 prevalence.

10. **Community Transmission of SARS-CoV-2 Associated with a Local Bar Opening Event — Illinois, February 2021.** Sami S, et al. *MMWR Morb Mortal Wkly Rep* 2021;70:528–532. DOI:

<http://dx.doi.org/10.15585/mmwr.mm7014e3>

Forty-six cases of COVID-19 were linked to an indoor bar opening event that occurred during February 2021 in a rural Illinois county. Event patrons were linked to secondary cases among household, long-term care facility, and school contacts, resulting in one hospitalization and one school closure affecting 650 students. Opening up settings such as bars, where mask wearing and physical distancing are challenging, can affect the community. As community businesses reopen, prevention measures should be emphasized, including limiting building occupancy, improving ventilation, prioritizing outdoor seating, enforcing correct mask wearing and physical distancing, staying home when ill, and encouraging COVID-19 vaccination to reduce transmission on site and within the community.

11. **The Impact of Changes in Diagnostic Testing Practices on Estimates of COVID-19 Transmission in the United States.** Pitzer VE, et al. *Am J Epidemiol.* 2021 Apr 8:kwab089. doi: 10.1093/aje/kwab089. <https://academic.oup.com/aje/advance-article/doi/10.1093/aje/kwab089/6217341?>

We explore the impact of secular changes in diagnostic testing and reporting on estimates of R_0 and R_t using simulated data. We then compare these patterns to data on reported cases of coronavirus disease and testing practices from different states in the United States from March 4 to August 30, 2020. We find that changes in testing practices and delays in reporting can result in biased estimates of R_0 and R_t . Examination of changes in the daily number of tests conducted and the percent of patients testing positive may be helpful for identifying the potential direction of bias. Changes in diagnostic testing and reporting processes should be monitored and taken into consideration when interpreting estimates of the reproductive number of coronavirus disease.

12. **Death Certificate-Based ICD-10 Diagnosis Codes for COVID-19 Mortality Surveillance - United States, January-December 2020.** Gundlapalli AV, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Apr 9;70(14):523-527. doi:10.15585/mmwr.mm7014e2. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7014e2.htm>

Approximately 375,000 deaths during 2020 were attributed to COVID-19 on death certificates reported to CDC. Concerns have been raised that some deaths are being improperly attributed to COVID-19. Overall, 97.3% of 357,133 death certificates with at least one other diagnosis (91.9% of all 378,048 death certificates) were noted to have a co-occurring diagnosis that was a plausible chain-of-event condition (e.g., pneumonia or respiratory failure), a significant contributing condition (e.g., hypertension or diabetes), or both. Overall, 70%-80% of death certificates had both a chain-of-event condition and a significant contributing condition or a chain-of-event condition only; this was noted for adults aged 18-84 years, both males and females, persons of all races and ethnicities, those who died in inpatient and outpatient or emergency department settings, and those whose manner of death was listed as natural. These findings support the accuracy of COVID-19 mortality surveillance in the United States using official death certificates. High-quality documentation of co-occurring diagnoses on the death certificate is essential for a comprehensive and authoritative public record. Continued messaging and training for professionals who complete death certificates remains important as the pandemic progresses. Accurate mortality surveillance is critical for understanding the impact of variants of SARS-CoV-2, the virus that causes COVID-19, and of COVID-19 vaccination and for guiding public health action.

Healthcare Delivery & Healthcare Workers

13. **Reactogenicity, safety and antibody response, after one and two doses of mRNA-1273 in seronegative and seropositive healthcare workers.** Tré-Hardy M, et al. *J Infect.* 2021 Mar 31:S0163-4453(21)00158-4. doi: 10.1016/j.jinf.2021.03.025. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8012163/>

We report our observations in a cohort of healthcare workers (HCWs) who were administered mRNA1273 at the inception of the national vaccination campaign. Our results plead, in a

supply-limited environment, for reserving the second dose scheme to seronegative individuals prior to vaccination, especially when the serological status is easily accessible, as the additional protective effect of the second dose has yet to be demonstrated in these individuals. The determination of the antibody titers after the initial dose could be used in order to catch-up the very few vaccinees with a weaker response.

- 14. Experiences of a Health System's Faculty, Staff, and Trainees' Career Development, Work Culture, and Childcare Needs during the COVID-19 Pandemic.** Delaney RK, et al. *JAMA Netw Open*. 2021 Apr 1;4(4):e213997. doi: 10.1001/jamanetworkopen.2021.3997.
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778144>
In this survey of 5030 faculty, staff, and trainees of a US health system, many participants with caregiving responsibilities, particularly women, faculty, trainees, and (in a subset of cases) those from racial/ethnic groups that underrepresented in medicine, considered leaving the workforce or reducing hours and were worried about their career development related to the pandemic. It is imperative that medical centers support their employees and trainees during this challenging time.
- 15. Variation in Initial U.S. Hospital Responses to the Coronavirus Disease 2019 Pandemic.** Mathews KS et al. *Crit Care Med*. 2021 Apr 8. doi: 10.1097/CCM.0000000000005013.
https://journals.lww.com/ccmjournal/Abstract/9000/Variation_in_Initial_U_S_Hospital_Responses_to.95272.aspx
The coronavirus disease 2019 pandemic prompted widespread system-level changes, but front-line clinical care varied widely according to specific hospital needs and infrastructure. Linking operational changes to care delivery processes is a necessary step to understand the impact of the coronavirus disease 2019 pandemic on patient outcomes.
- 16. Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers.** Havervall S, et al. *JAMA*. 2021 Apr 7. doi: 10.1001/jama.2021.5612.
<https://jamanetwork.com/journals/jama/fullarticle/2778528>
Approximately 80% of hospitalized patients with COVID-19 report persistent symptoms several months after infection onset. However, knowledge of long-term outcomes among individuals with mild COVID-19 is scarce, and prevalence data are hampered by selection bias and suboptimal control groups. This cohort study investigated COVID-19–related long-term symptoms in health care professionals.
- 17. Persistent post-covid symptoms in healthcare workers.** Gaber TAK, et al. *Occup Med (Lond)*. 2021 Apr 8;kqab043. doi: 10.1093/occmed/kqab043.
<https://academic.oup.com/occmed/advance-article/doi/10.1093/occmed/kqab043/6217385?>
Our data suggest that about a third of HCW who responded to the survey were still struggling to cope with the symptoms of what is now known as long covid several months after the acute COVID-19 infections. The overwhelming majority of this group seem to be reluctant to neither seek medical advice nor take sick leave.

Prognosis

- 18. Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study.** Aveyard P, et al. *Lancet Respir Med.* 2021 Apr 1:S2213-2600(21)00095-3. doi: 10.1016/S2213-2600(21)00095-3.
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00095-3/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00095-3/fulltext)
The risk of severe COVID-19 in people with asthma is relatively small. People with COPD and interstitial lung disease appear to have a modestly increased risk of severe disease, but their risk of death from COVID-19 at the height of the epidemic was mostly far lower than the ordinary risk of death from any cause. Use of inhaled steroids might be associated with a modestly increased risk of severe COVID-19.
- 19. Elevated liver enzymes, ferritin, CRP, D-dimer, and age are predictive markers of outcomes among Covid-19 African Americans and Hispanic patients.** Ashktorab H, et al. *Gastroenterology.* 2021 Mar 31:S0016-5085(21)00570-9. doi: 10.1053/j.gastro.2021.03.043.
<https://www.sciencedirect.com/science/article/pii/S0016508521005709>
In the overall cohort analysis, age was a major effector of outcome. This was further confirmed in subgroup analyses. Indeed, the youngest group had the lowest death rate while the oldest had the highest death rate. Respiratory issues such as shortness of breath, and pneumonia requiring ICU care and mechanical ventilation were strongly associated with poor outcome in our patients, re-gardless of race. Elevated Procalcitonin was also a common risk factor. Procalcitonin is primarily in-creased in response to bacterial-triggered inflammation pointing to potential opportunistic pathogens' activity in the course of COVID-19. Vasopressors' use in critically ill patients was also associated with poor outcome, attesting to unstable hemodynamics independently of race.
- 20. Prescription of glucose-lowering therapies and risk of COVID-19 mortality in people with type 2 diabetes: a nationwide observational study in England.** Khunti K, et al. *Lancet Diabetes Endocrinol.* 2021 Mar 30:S2213-8587(21)00050-4. doi: 10.1016/S2213-8587(21)00050-4.
[https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(21\)00050-4/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00050-4/fulltext)
Our results provide evidence of associations between prescription of some glucose-lowering drugs and COVID-19-related mortality, although the differences in risk are small and these findings are likely to be due to confounding by indication, in view of the use of different drug classes at different stages of type 2 diabetes disease progression. In the context of the COVID-19 pandemic, there is no clear indication to change prescribing of glucose-lowering drugs in people with type 2 diabetes.
- 21. Sex Disparities in COVID-19 Mortality Vary Across US Racial Groups.** Rushovich T, et al. *J Gen Intern Med.* 2021 Apr 5. doi: 10.1007/s11606-021-06699-4.
<https://link.springer.com/article/10.1007/s11606-021-06699-4>
Within race groups, men have a higher COVID-19 mortality rate than women. Black men have the highest rate of all race-sex groups. In Michigan, the COVID-19 mortality rate for Black women is higher than the rate for white men, white women, and Asian/Pacific Islander men and women. COVID-19 mortality rates in Georgia followed the same pattern. In MI, the

male:female mortality rate ratio among Black individuals is 1.7 while the rate ratio among White individuals is only 1.3. While overall, men have higher COVID-19 mortality rates than women, our findings show that this sex disparity does not hold across racial groups.

22. **Incidence of 30-Day Venous Thromboembolism in Adults Tested for SARS-CoV-2 Infection in an Integrated Health Care System in Northern California.** Roubinian NH, et al. *JAMA Intern Med.* 2021 Apr 5. doi: 10.1001/jamainternmed.2021.0488.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2778371?resultClick=1>

The incidence of outpatient VTE among symptomatic patients with positive SARS-CoV-2 test results was similar to that of patients with negative results. In parallel to recent reports, posthospital VTE incidence did not differ by SARS-CoV-2 status and was comparable with that seen in clinical trials of thromboprophylaxis. A VTE is a potentially preventable complication of SARS-CoV-2 infection, especially in outpatients with risk factors for thrombosis or severe COVID-19. Ongoing randomized clinical trials will determine whether the risks and benefits of prophylactic anticoagulation in outpatients with COVID-19 will improve clinical outcomes.

23. **Prognostic model to identify and quantify risk factors for mortality among hospitalised patients with COVID-19 in the USA.** Incerti D, et al. *BMJ Open.* 2021 Apr 7;11(4):e047121. doi: 10.1136/bmjopen-2020-047121. <https://bmjopen.bmj.com/content/11/4/e047121>

Age was the most important predictor of all-cause mortality, although vital signs and laboratory results added considerable prognostic information, with oxygen saturation, temperature, respiratory rate, lactate dehydrogenase and white cell count being among the most important predictors. Demographic and comorbidity factors did not improve model performance appreciably. The full model had good discrimination and was reasonably well calibrated, suggesting that it may be useful for assessment of prognosis.

Survivorship & Rehabilitation

24. **Recovery after critical illness in COVID-19 ICU survivors.** Parker AJ, et al. *Br J Anaesth.* 2021 Mar 19:S0007-0912(21)00162-8. doi: 10.1016/j.bja.2021.03.005.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7972647/>

Our dedicated ICU COVID-19 follow-up clinic has assessed all patients cared for during the first wave of the UK COVID-19 pandemic. We report our findings for invasively ventilated patients from this multidisciplinary assessment of patient recovery and rehabilitation. Our institution's research and innovation department determined that this project did not require ethical approval. Information governance safeguards were approved by our institution's Caldicott guardian.

25. **"How I Do It: Rapid Design & Implementation of Post-COVID Clinics".** Santhosh L, et al. *Chest.* 2021 Mar 31:S0012-3692(21)00655-3. doi: 10.1016/j.chest.2021.03.044.

[https://journal.chestnet.org/article/S0012-3692\(21\)00655-3/fulltext](https://journal.chestnet.org/article/S0012-3692(21)00655-3/fulltext)

We describe the design and implementation of multidisciplinary post-COVID-19 clinics at two academic health systems, Johns Hopkins and the University of California-San Francisco. We highlight components of the model which should be replicated across sites, while

acknowledging opportunities to tailor offerings to the local institutional context. Our goal is to provide a replicable framework for others to create these much-needed care delivery models for survivors of COVID-19.

- 26. Alterations in T and B cell function persist in convalescent COVID-19 patients.** Shuwa HA, et al. *Med (N Y)*. 2021 Mar 31. doi: 10.1016/j.medj.2021.03.013.
<https://www.sciencedirect.com/science/article/pii/S266663402100115X>
Lymphocyte alterations exist in previously hospitalized COVID-19 patients up to 6 months following hospital discharge and identify 3 subgroups of convalescent patients based on distinct lymphocyte phenotypes, with one subgroup associated with poorer clinical outcome. We propose that alterations in B and T cell function following hospitalisation with COVID-19 could impact longer term immunity and contribute to some persistent symptoms observed in convalescent COVID-19 patients.
- 27. Incidence and Severity of Depression among Recovered African Americans with COVID-19-Associated Respiratory Failure.** Olanipekun T, et al. *J Racial Ethn Health Disparities*. 2021 Apr 6. doi: 10.1007/s40615-021-01034-3. <https://link.springer.com/article/10.1007/s40615-021-01034-3>
The incidence of depression in a cohort of African American patients without prior psychiatric conditions who recovered from severe COVID-19 infection was 44%. More than 70% of these patients were not receiving treatment for depression.
- 28. Post-Discharge Thromboembolic Outcomes and Mortality of Hospitalized COVID-19 Patients: The CORE-19 Registry.** Giannis D et al. *Blood*. 2021 Apr 6: blood.2020010529. doi: 10.1182/blood.2020010529.
<https://ashpublications.org/blood/article/doi/10.1182/blood.2020010529/475684/Post-Discharge-Thromboembolic-Outcomes-and>
Post-discharge VTE, ATE, and ACM occur frequently following COVID-19 hospitalization. Advanced age, cardiovascular risk factors, CKD, IMPROVE-DD VTE score ≥ 4 , and ICU stay increase risk. Post-discharge anticoagulation reduced risk by 46%.
- 29. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records.** Taquet M, et al. *Lancet Psychiatry* 2021 Apr 6. doi: [https://doi.org/10.1016/S2215-0366\(21\)00084-5](https://doi.org/10.1016/S2215-0366(21)00084-5)
Our study provides evidence for substantial neurological and psychiatric morbidity in the 6 months after COVID-19 infection. Risks were greatest in, but not limited to, patients who had severe COVID-19. This information could help in service planning and identification of research priorities. Complementary study designs, including prospective cohorts, are needed to corroborate and explain these findings.

Therapeutics

- 30. Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries.** Bharat A, et al. *Lancet Respir Med*. 2021 Mar 31:S2213-2600(21)00077-1. doi: 10.1016/S2213-2600(21)00077-1.
[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00077-1/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00077-1/fulltext)
The findings from our report show that lung transplantation is the only option for survival in some patients with severe, unresolving COVID-19-associated ARDS, and that the procedure can be done successfully, with good early post-transplantation outcomes, in carefully selected patients.
- 31. Vitamin D supplementation to prevent acute respiratory infections: a systematic review and meta-analysis of aggregate data from randomised controlled trials.** Jolliffe DA et al. *Lancet Diabetes Endocrinol*. 2021 Mar 30:S2213-8587(21)00051-6. doi: 10.1016/S2213-8587(21)00051-6. [https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(21\)00051-6/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00051-6/fulltext)
Despite evidence of significant heterogeneity across trials, vitamin D supplementation was safe and overall reduced the risk of ARI compared with placebo, although the risk reduction was small. Protection was associated with administration of daily doses of 400-1000 IU for up to 12 months, and age at enrolment of 1·00-15·99 years. The relevance of these findings to COVID-19 is not known and requires further investigation.
- 32. 14-Day survival among older adults with severe SARS-Cov2 infection treated with corticosteroid: a cohort study.** COCO-OLD Study group. *Clin Microbiol Infect*. 2021 Apr 2:S1198-743X(21)00156-7. doi: 10.1016/j.cmi.2021.03.021.
<https://www.sciencedirect.com/science/article/abs/pii/S1198743X21001567>
Corticosteroids were associated with a significant increase in the overall survival at day 14 of patients aged 80 years and older hospitalised for severe COVID-19.
- 33. Outcomes of Hospitalized COVID-19 Patients Receiving Renin Angiotensin System Blockers and Calcium Channel Blockers.** Choksi TT, et al. *Am J Nephrol*. 2021 Apr 7:1-11. doi: 10.1159/000515232. <https://www.karger.com/Article/FullText/515232>
Among all hospitalized patients with COVID-19 infection, exposure to ACEI/ARB, as well as combined exposure to ACEI/ARB and CCB, were associated with reduced incidence of ICU admissions. In those admitted patients who had a personal history of hypertension, there was a trend towards reduced in-hospital mortality in those exposed to ACEI.
- 34. Convalescent Plasma for the Prevention and Treatment of COVID-19: A Systematic Review and Quantitative Analysis.** Peng HT, et al. *JMIR Public Health Surveill*. 2021 Apr 7;7(4):e25500. doi: 10.2196/25500. <https://publichealth.jmir.org/2021/4/e25500>
There is developing support for CP therapy, particularly for patients who are critically ill or mechanically ventilated and resistant to antivirals and supportive care. These studies provide important lessons that should inform the planning of well-designed RCTs to generate more robust knowledge for the efficacy of CP in patients with COVID-19. Future research is necessary

to fill the knowledge gap regarding prevention and treatment for patients with COVID-19 with CP while other therapeutics are being developed.

35. **Efficacy and safety of Tocilizumab in severe and critical COVID-19: A Systematic Review and Meta-Analysis.** Rezaei S, et al. *Expert Rev Clin Immunol.* 2021 Apr 7:1-13. doi: 10.1080/1744666X.2021.1908128.

<https://www.tandfonline.com/doi/full/10.1080/1744666X.2021.1908128>

Forty-five comparative studies involving 13,189 patients and 28 single-arm studies involving 1,770 patients were analyzed. Tocilizumab can improve clinical outcomes and reduce mortality rates in severe to critical COVID-19 patients. Large-scale randomized controlled trials are still required to improve the statistical power of meta-analysis.

Transmission / Infection Control

36. **Development of a new aerosol barrier mask for mitigation of spread of SARS-CoV-2 and other infectious pathogens.** Abi Karam K, et al. *Respir Med.* 2021 Mar 29;181:106381. doi: 10.1016/j.rmed.2021.106381.

<https://www.sciencedirect.com/science/article/abs/pii/S095461121000871>

This Aerosol Barrier Mask is designed for preventing SARS-CoV-2 transmission while transporting patients within hospital facilities. This mask can constrain aerosol and droplet particles and trap them in a biofilter, while the patient is normally breathing and administered with medical oxygen. The system can be characterized as an oxygen delivery and mitigation mask which has no unfiltered exhaled air dispersion. The mask helps to prevent the spread of SARS-CoV-2, and potentially other infectious respiratory pathogens and protects everyone in general, especially healthcare professionals.

37. **Providing safe care for patients in the coronavirus disease 2019 (COVID-19) era: A case series evaluating risk for hospital-associated COVID-19.** Habermann EB, et al. *Infect Control Hosp Epidemiol.* 2021 Apr 5:1-7. doi: 10.1017/ice.2021.38.

<https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/providing-safe-care-for-patients-in-the-coronavirus-disease-2019-covid19-era-a-case-series-evaluating-risk-for-hospital-associated-covid19/B63A84705AB2A8E7D690A10C9E06C5DF>

A case series of adult patients hospitalized for 2 or more nights from May 15 to June 15, 2020 at large tertiary-care hospital in the midwestern United States was reviewed. No healthcare-associated COVID-19 cases were detected during the study period. We found low likelihood of hospital-associated COVID-19 with strict adherence to universal masking, physical distancing, and hand hygiene along with limited visitors and screening of admissions with PCR.

38. **Barriers to Physical Distancing among Healthcare Workers on an Academic Hospital Unit during the COVID-19 Pandemic.** Keller SC et al. *Infect Control Hosp Epidemiol.* 2021 Apr 7:1-26. doi: 10.1017/ice.2021.154. <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/barriers-to-physical-distancing-among-healthcare-workers-on>

[an-academic-hospital-unit-during-the-covid19-pandemic/E59ADBA46A56125445ED4BCB55FC01AF](https://doi.org/10.1016/S0140-6736(21)00762-5)

Physical distancing can be improved in hospitals by restructuring computer workstations, work rooms, and breakrooms; applying visible cognitive aids; adapting shift times; and supporting rounds and meetings with virtual conferencing. Additional strategies to promote staff adherence to physical distancing include rewarding positive behaviors, having peer leaders model physical distancing, and encouraging additional safe avenues for social connection at a safe distance.

Vaccines / Immunology

39. **Thromboembolism and the Oxford-AstraZeneca COVID-19 vaccine: side-effect or coincidence?** Østergaard SD, et al. *Lancet*. 2021 Mar 30;S0140-6736(21)00762-5. doi: 10.1016/S0140-6736(21)00762-5. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00762-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00762-5/fulltext)

Based on pre-pandemic incidence rates from the entire Danish population, we report that the number of venous thromboembolisms reported in relation to the Oxford–AstraZeneca COVID-19 vaccine does not seem to be increased beyond the expected incidence rate. Nevertheless, recent reports of thrombocytopenia-associated cerebral venous sinus thrombosis, multiple thrombosis, and bleeding within a short timeframe after receipt of the vaccine are concerning and are receiving due attention from health authorities. On March 18, 2021, with reference to the Oxford–AstraZeneca COVID-19 vaccine, the EMA concluded that “benefits still outweigh the risks despite possible link to rare blood clots with low blood platelets”.

40. **Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination.** Schultz NH, et al. *NEJM* April 9, 2021 DOI: 10.1056/NEJMoa2104882 https://www.nejm.org/doi/full/10.1056/NEJMoa2104882?query=featured_home

We present five cases of severe venous thromboembolism in unusual sites and concomitant thrombocytopenia that occurred 7 to 10 days after vaccination for Covid-19. A common denominator in all five patients was a high level of antibodies to PF4–polyanion complexes. We propose that these cases represent a vaccine-related variant of spontaneous heparin-induced thrombocytopenia that we refer to as vaccine-induced immune thrombotic thrombocytopenia (VITT).

*see also [Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination](https://doi.org/10.1056/NEJMoa2104840). *NEJM* April 9, 2021 DOI: 10.1056/NEJMoa2104840

41. **Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2.** Ebinger JE, et al. *Nat Med*. 2021 Apr 1. doi: 10.1038/s41591-021-01325-6. <https://www.nature.com/articles/s41591-021-01325-6>

In a cohort of BNT162b2 (Pfizer-BioNTech) mRNA vaccine recipients, we observed that spike-specific IgG antibody levels and ACE2 antibody binding inhibition responses elicited by a single vaccine dose in individuals with prior SARS-CoV-2 infection were similar to those seen after two doses of vaccine in individuals without prior infection. Post-vaccine symptoms were more

prominent for those with prior infection after the first dose, but symptomology was similar between groups after the second dose.

42. **Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19.** mRNA-1273 Study Group. *N Engl J Med.* 2021 Apr 6. doi: 10.1056/NEJMc2103916. <https://www.nejm.org/doi/full/10.1056/NEJMc2103916>
Interim results from a phase 3 trial of the Moderna mRNA-1273 SARS-CoV-2 vaccine indicated 94% efficacy in preventing Covid-19. We describe mRNA1273-elicited binding and neutralizing antibodies in 33 healthy adult participants in an ongoing phase 1 trial, stratified according to age, at 180 days after the second dose. Antibody activity remained high in all age groups at day 209. Ongoing studies are monitoring immune responses beyond 6 months as well as determining the effect of a booster dose to extend the duration and breadth of activity against emerging viral variants.
43. **Susceptibility of Circulating SARS-CoV-2 Variants to Neutralization.** Wang GL, et al. *N Engl J Med.* 2021 Apr 6. doi: 10.1056/NEJMc2103022. <https://www.nejm.org/doi/full/10.1056/NEJMc2103022>
Most of the Sinovac vaccinee serum samples that were tested lost neutralizing activity, a finding that was consistent with the results of other recent studies of neutralization by convalescent serum or serum obtained from recipients of messenger RNA or BBIBP-CorV vaccines. Our findings also highlight the importance of sustained viral monitoring and evaluation of the protective efficacy of vaccines in areas where variants are circulating.
44. **Adverse effects of COVID-19 mRNA-1273 vaccine: A randomized, cross-sectional study on healthcare workers with detailed self-reported symptoms.** Kadali RAK, et al. *J Med Virol.* 2021 Apr 6. doi: 10.1002/jmv.26996. <https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26996>
Among all the symptoms reported by HCWs in the US, localized pain, generalized weakness, headache, myalgia, chills, fever, nausea, joint pains, sweating, localized swelling at the injection site, dizziness, itching, rash, decreased appetite, muscle spasm, decreased sleep quality, and brain fogging/confusion were the most reported symptoms (in descending order of occurrence). 98.34% of vaccine recipients reported at least one or more symptoms. 58.8% were able to continue their daily routine activities. 25% were temporarily unable to perform daily activities, 27.78% required transient time off from work, 3.94% required help from an outpatient provider, 0.23% required help from emergency department, and none of them were hospitalized. Despite the wide array of self-reported symptoms, 97.02% of the HCWs did not intend to skip the second dose of vaccine.
45. **Cross-Reactive Neutralizing Antibody Responses Elicited by SARS-CoV-2 501Y.V2 (B.1.351).** Moyo-Gwete T et al. *N Engl J Med.* 2021 Apr 7. doi: 10.1056/NEJMc2104192. <https://www.nejm.org/doi/full/10.1056/NEJMc2104192>
SARS-CoV-2 501Y.V2 lineage (also known as B.1.351), first identified in South Africa in October 2020, has mutations that confer increased resistance to plasma from convalescent patients and vaccine recipients, as well as to some monoclonal antibodies. However, the immune response to 501Y.V2 is unknown. Similarly, the ability of antibodies elicited by 501Y.V2

infection to cross-react with other variants is unknown, but such cross-reactivity would have implications for the ability of second-generation vaccines based on the 501Y.V2 spike protein to protect against infection with the original and emerging SARS-CoV-2 lineages.

46. Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2. Lustig Y, et al. *N Engl J Med*. 2021 Apr 7. doi: 10.1056/NEJMc2104036.

<https://www.nejm.org/doi/full/10.1056/NEJMc2104036>

One vaccine dose substantially increased neutralizing activity against all variants tested, with similar titers detected across patients for each variant. This highlights the importance of vaccination even in previously infected patients, given the added benefit of an increased antibody response to the variants tested.

47. Humoral and cellular immunogenicity of the BNT162b2 mRNA Covid-19 Vaccine in nursing home residents. Van Praet JT, et al. *Clin Infect Dis*. 2021 Apr 7:ciab300. doi:

10.1093/cid/ciab300. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab300/6213866>

Four weeks after the first vaccine dose, the humoral and cellular immunogenicity of the BNT162b2 mRNA vaccine was suboptimal in COVID-19-naïve nursing home residents in comparison to COVID-19-naïve healthcare workers. Longitudinal studies are required to determine whether these differences are the result of a delayed or a quantitatively lower immune response and will be informative to tailor the optimal vaccination strategy in this vulnerable population.

48. SARS-CoV-2 outbreak in a long-term care facility after vaccination with BNT162b2. Westhölter D, Taube C. *Clin Infect Dis*. 2021 Apr 7:ciab299. doi: 10.1093/cid/ciab299.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab299/6213878>

Here we report that a single dose of BNT162b2 did not prevent symptomatic and fatal outcomes of SARS-CoV-2 infections in this high-risk population up to 23 days after the initial vaccination indicating an incomplete protection against severe Covid-19 for that period.

49. Polyethylene glycol (PEG) is a cause of anaphylaxis to the Pfizer/BioNTech mRNA COVID-19 vaccine. Sellaturay P, et al. *Clin Exp Allergy*. 2021 Apr 6. doi: 10.1111/cea.13874.

<https://onlinelibrary.wiley.com/doi/10.1111/cea.13874>

Here we demonstrate for the first time that allergy to PEG can cause anaphylaxis to the Pfizer/BioNTech vaccine.

50. Administration of a Second Dose of the Moderna COVID-19 Vaccine After an Immediate Hypersensitivity Reaction with the First Dose: Two Case Reports. Mustafa SS, et al. *Ann Intern Med*. 2021 Apr 6. doi: 10.7326/L21-0104. <https://www.acpjournals.org/doi/10.7326/L21-0104>

Persons who have an immediate hypersensitivity reaction to dose 1 of the Pfizer-BioNTech or Moderna vaccine should not automatically defer dose 2. Instead, referral to an allergy and immunology physician for further evaluation and management should be considered. Although the mechanism of hypersensitivity reaction to messenger RNA vaccines is uncertain, skin testing may guide further vaccine administration. Third, we have shown that dose 2 of the Moderna

vaccine can be safely administered through a graded dosing protocol to persons who have symptoms consistent with an immediate hypersensitivity reaction to dose 1, resulting in protective antibodies against COVID-19.

51. **Single-dose BNT162b2 vaccine protects against asymptomatic SARS-CoV-2 infection.** Jones NK et al. *Elife*. 2021 Apr 8;10:e68808. doi: 10.7554/eLife.68808.

<https://elifesciences.org/articles/68808>

Here, we evaluate the effect of first-dose BNT162b2 vaccination on test positivity rates, and find a four-fold reduction in asymptomatic infection amongst HCWs ≥ 12 days post-vaccination. These data provide real-world evidence of short-term protection against asymptomatic SARS-CoV-2 infection following a single dose of BNT162b2 vaccine, suggesting that mass first-dose vaccination will reduce SARS-CoV-2 transmission, as well as the burden of COVID-19 disease.

52. **Postvaccination COVID-19 among Healthcare Workers, Israel.** Yousaf Z, Mushtaq K. *Emerg Infect Dis*. 2021 Apr 8;27(6). doi: 10.3201/eid2706.210410.

https://wwwnc.cdc.gov/eid/article/27/4/21-0016_article

Coronavirus disease (COVID-19) symptoms can be mistaken for vaccine-related side effects during initial days after immunization. Among 4,081 vaccinated healthcare workers in Israel, 22 (0.54%) developed COVID-19 from 1–10 days (median 3.5 days) after immunization. Clinicians should not dismiss postvaccination symptoms as vaccine-related and should promptly test for COVID-19.

Women & Children

53. **Cord Blood Antibodies following Maternal COVID-19 Vaccination During Pregnancy.** Mithal LB, et al. *Am J Obstet Gynecol*. 2021 Apr 1:S0002-9378(21)00215-5. doi:

10.1016/j.ajog.2021.03.035. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8012273/>

Most pregnant women who received the COVID-19 mRNA vaccine in the 3rd trimester had transplacental transfer of IgG to the infant. The observed mean IgG transfer ratio demonstrates about equal infant antibody level to maternal level. A novel finding is that the transfer ratio appears to increase with latency from vaccination. These data suggest, at least among women in their third trimester, that earlier vaccination may produce greater infant immunity, the immunobiology of which requires further study.

54. **Anti-SARS-CoV-2 antibodies induced in breast milk after Pfizer-BioNTech/BNT162b2 vaccination: SARS-CoV-2 antibodies in breast milk after vaccination.** Kelly JC, et al. *Am J Obstet Gynecol*. 2021 Mar 30:S0002-9378(21)00211-8. doi: 10.1016/j.ajog.2021.03.031.

[https://www.ajog.org/article/S0002-9378\(21\)00211-8/pdf](https://www.ajog.org/article/S0002-9378(21)00211-8/pdf)

Our study is limited by a small number of participants, but we report data that suggest potential immune benefit to infants of lactating people up to 80 days following COVID-19 vaccination. Further studies are needed to characterize the length of antibody production in breast milk, and the effect on infant infection rates after maternal COVID-19 vaccination.

55. **Initial clinical characteristics of gravid SARS-CoV-2 positive patients and the risk of progression to severe COVID-19 disease.** Yao R, et al. *Am J Obstet Gynecol MFM*. 2021 Apr 2;100365. doi: 10.1016/j.ajogmf.2021.100365.
<https://www.sciencedirect.com/science/article/pii/S2589933321000604>
Risk factors associated with advanced respiratory support (ARS) requirement were used to create the Obstetric Warning Score (OWS) which presents a validated method for providers to identify pregnant patients who are at risk of respiratory failure.
56. **Evaluation of the Abbott BinaxNOW rapid antigen test for SARS-CoV-2 infection in children: Implications for screening in a school setting.** Sood N, et al. *PLoS One*. 2021 Apr 5;16(4):e0249710. doi: 10.1371/journal.pone.0249710
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0249710>
Rapid antigen testing can successfully identify most COVID infections in children with viral load levels likely to be infectious. Serial rapid testing may help compensate for limited sensitivity in early infection.
57. **The association between SARS-CoV-2 infection and preterm delivery: a prospective study with a multivariable analysis.** Spanish Obstetric Emergency Group. *BMC Pregnancy Childbirth*. 2021 Apr 1;21(1):273. doi: 10.1186/s12884-021-03742-4.
<https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-021-03742-4>
Among 1009 screened pregnancies, 246 were SARS-CoV-2 positive. Compared to negative mothers, SARS-CoV-2 infection increased the odds of preterm birth; iatrogenic preterm delivery was more frequent in infected women, while the occurrence of spontaneous preterm deliveries was statistically similar (6.1% vs 4.7%). An increased risk of premature rupture of membranes at term and neonatal intensive care unit admissions was also observed in positive mothers. This prospective multicentre study demonstrated that pregnant women infected with SARS-CoV-2 have more infection-related obstetric morbidity. This hypothesis merits evaluation of a causal association in further research.
58. **Atypical Manifestations of Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Children: A Review.** Benou S, et al. *Curr Pediatr Rev*. 2021 Apr 6. doi: 10.2174/1573396317666210406153302.
Although fever and symptoms of upper respiratory infection are the most frequently presented, a variety of other atypical presentations has also been reported. The clinical spectrum includes dermatological, ophthalmological, neurological, cardiovascular, renal, reproductive, and gastrointestinal presentations. Clinicians need to be aware of the wider range of extrapulmonary atypical manifestations of SARS-CoV-2 infection in children, so that appropriate testing, treatment, and public health measures can be implemented rapidly.
59. **Trends in Geographic and Temporal Distribution of US Children with Multisystem Inflammatory Syndrome during the COVID-19 Pandemic.** Belay ED et al. *JAMA Pediatr*. 2021 Apr 6. doi: 10.1001/jamapediatrics.2021.0630.
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2778429>

In this cross-sectional study of a large cohort of patients with MIS-C, 2 peaks that followed COVID-19 peaks by 2 to 5 weeks were identified. The geographic and temporal association of MIS-C with the COVID-19 pandemic suggested that MIS-C resulted from delayed immunologic responses to SARS-CoV-2 infection. The clinical manifestations varied by age and by presence or absence of preceding COVID-19.

60. **The Society for Obstetric Anesthesia and Perinatology (SOAP) COVID-19 Registry: An analysis of outcomes among pregnant women delivering during the initial SARS-CoV-2 outbreak in the United States.** Katz D et al. *Anesth Analg*. 2021 Apr 8. doi: 10.1213/ANE.0000000000005592. In this large, multicenter U.S. cohort study of women with and without peripartum SARS-CoV-2 infection, differences in obstetric and neonatal outcomes seem to be mostly driven by symptomatic patients. Lower utilization of neuraxial analgesia in laboring patients with asymptomatic or symptomatic infection compared to patients without infection requires further investigation.

GUIDELINES & CONSENSUS STATEMENTS

[Diagnosis and Management of Vaccine-Related Thrombosis following AstraZeneca COVID-19 Vaccination: Guidance Statement from the GTH.](#) *Hamostaseologie*. 2021 Apr 1. doi: 10.1055/a-1469-7481.

[Management of anaphylaxis due to COVID-19 vaccines in the elderly.](#) Bousquet J et al. *Allergy*. 2021 Apr 2. doi: 10.1111/all.14838.

FDA / CDC / NIH / WHO Updates

CDC - [Strategies for Optimizing Supply of N95 Respirators](#) 4-8-21

WHO - [Interim statement of the COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety on AstraZeneca COVID-19 vaccine](#)

Commentary & News Releases

[Guidance produced from the Expert Haematology Panel \(EHP\) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus Vaccination](#)

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