

## COVID-19 Resource Desk

#73 | 9.12.2021 to 9.18.21

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### New Research

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

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

### Clinical Syndrome

1. **Integrated analysis of plasma and single immune cells uncovers metabolic changes in individuals with COVID-19.** Jihoon W Lee, Yapeng Su, Priyanka Baloni, Daniel Chen, Ana Jimena Pavlovitch-Bedzyk, Dan Yuan, Venkata R Duvvuri, Rachel H Ng, Jongchan Choi, Jingyi Xie, Rongyu Zhang, Kim Murray, Sergey Kornilov, Brett Smith, Andrew T Magis, Dave S B Hoon, Jennifer J Hadlock, Jason D Goldman, Nathan D Price, Raphael Gottardo, Mark M Davis, Leroy Hood, Philip D Greenberg, James R Heath [**Providence authors**]. *Nat Biotechnol.* 2021 Sep 6. doi: 10.1038/s41587-021-01020-4.

<https://www.nature.com/articles/s41587-021-01020-4>

Here, we report the metabolic changes associated with the peripheral immune response of 198 individuals with COVID-19 through an integrated analysis of plasma metabolite and protein levels as well as single-cell multiomics analyses from serial blood draws collected during the first week after clinical diagnosis. We document the emergence of rare but metabolically dominant T cell subpopulations and find that increasing disease severity correlates with a bifurcation of monocytes into two metabolically distinct subsets. This integrated analysis reveals a robust interplay between plasma metabolites and cell-type-specific metabolic reprogramming networks that is associated with disease severity and could predict survival.

2. **Multinational Observational Cohort Study of COVID-19-Associated Pulmonary Aspergillosis.** Janssen NAF et al. *Emerg Infect Dis.* 2021 Sep 14;27(11). doi: 10.3201/eid2711.211174.

[https://wwwnc.cdc.gov/eid/article/27/11/21-1174\\_article](https://wwwnc.cdc.gov/eid/article/27/11/21-1174_article)

We performed an observational study to investigate intensive care unit incidence, risk factors, and outcomes of coronavirus disease-associated pulmonary aspergillosis (CAPA). We found 10%-15% CAPA incidence among 823 patients in 2 cohorts. Several factors were independently associated with CAPA in 1 cohort and mortality rates were 43%-52%.

### Epidemiology & Public Health

3. **Population Immunity against COVID-19 in the United States.** Moghadas SM, et al. *Ann Intern Med.* 2021 Sep 14. doi: 10.7326/M21-2721. <https://www.acpjournals.org/doi/10.7326/M21-2721>

Using age-specific estimates from the CDC, it was estimated that as of 15 July 2021, 114.9 million persons had been infected with SARS-CoV-2 in the United States. The mean overall population immunity was 62.0%. Adults aged 65 years or older were estimated to have the highest immunity level (77.2%), and children younger than 12 years had the lowest immunity level (17.9%). U.S. population immunity against COVID-19 may still have been insufficient to contain the outbreaks and safely revert to prepandemic social behavior.

4. **Association of Health Care Factors with Excess Deaths Not Assigned to COVID-19 in the US.**

Stokes AC, et al. *JAMA Netw Open*. 2021 Sep 1;4(9):e2125287. doi: 10.1001/jamanetworkopen.2021.25287.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783986>

Approximately 20% of excess deaths in the US in 2020 were not reflected in COVID-19 death counts. These excess deaths included deaths caused by COVID-19 but not assigned to it as well as indirect deaths from other causes associated with delays in health care and the social and economic consequences of the pandemic. Prior research has documented differences in the percentage of excess deaths not assigned to COVID-19 at the state and county levels. In this study, we examined health care factors associated with excess deaths not assigned to COVID-19 at the county level.

### Healthcare Delivery & Healthcare Workers

5. **Nurses' Intent to Leave their Position and the Profession during the COVID-19 Pandemic.** Raso

R, et al. *J Nurs Adm*. 2021 Sep 13. doi: 10.1097/NNA.0000000000001052.

[https://journals.lww.com/jonajournal/Abstract/9000/Nurses\\_Intent\\_to\\_Leave\\_their\\_Position\\_and\\_the.99780.aspx](https://journals.lww.com/jonajournal/Abstract/9000/Nurses_Intent_to_Leave_their_Position_and_the.99780.aspx)

This is the 1st quantitative report of perceived level of pandemic impact on direct care nurses and nurse managers/directors at the time of this writing. The combination of those who intend to leave and those who are uncertain about leaving their positions could cause instability in the workforce if not reversed. Organizational attention to nurse well-being, work environment and staffing is imperative.

### Prognosis

6. **The evolution of the ventilatory ratio is a prognostic factor in mechanically ventilated COVID-19 ARDS patients.** Torres A et al. *Crit Care*. 2021 Sep 13;25(1):331. doi: 10.1186/s13054-021-03727-x.

<https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03727-x>

Higher ventilatory ratio and its increase at day 3 is associated with mortality in patients with COVID-19 receiving mechanical ventilation at ICU admission. No association was found in the PaO<sub>2</sub>/FiO<sub>2</sub> variation.

## Therapeutics

7. **Convalescent plasma for hospitalized patients with COVID-19: an open-label, randomized controlled trial.** Bégin P et al. *Nat Med*. 2021 Sep 9. doi: 10.1038/s41591-021-01488-2. <https://www.nature.com/articles/s41591-021-01488-2>

In total, 940 patients were randomized, and 921 patients were included in the intention-to-treat analysis. Intubation or death occurred in 199/614 (32.4%) patients in the convalescent plasma arm and 86/307 (28.0%) patients in the standard of care. Patients in the convalescent plasma arm had more serious adverse events (33.4% versus 26.4%). Convalescent plasma did not reduce the risk of intubation or death at 30 d in hospitalized patients with COVID-19. Transfusion of convalescent plasma with unfavorable antibody profiles could be associated with worse clinical outcomes compared to standard care.

8. **Conventional oxygen therapy versus CPAP as a ceiling of care in ward-based patients with COVID-19: a multi-centre cohort evaluation.** Bradley P et al. *EClinicalMedicine*. 2021 Sep 8:101122. doi: 10.1016/j.eclinm.2021.101122. [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00402-8/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00402-8/fulltext)

No survival difference was found between using oxygen alone or CPAP to treat patients with severe COVID-19 who were nIMV. A high patient-initiated discontinuation rate for CPAP suggests a significant treatment burden. Further reflection is warranted on the current treatment guidance and widespread application of CPAP in this setting.

9. **Metoprolol in Critically Ill Patients with COVID-19.** Clemente-Moragón A et al. *J Am Coll Cardiol*. 2021 Sep 7;78(10):1001-1011. doi: 10.1016/j.jacc.2021.07.003. <https://www.jacc.org/doi/10.1016/j.jacc.2021.07.003>

In this pilot trial, intravenous metoprolol administration to patients with COVID-19-associated ARDS was safe, reduced exacerbated lung inflammation, and improved oxygenation. Repurposing metoprolol for COVID-19-associated ARDS appears to be a safe and inexpensive strategy that can alleviate the burden of the COVID-19 pandemic.

10. **Randomized study of rivaroxaban vs. placebo on disease progression and symptoms resolution in high-risk adults with mild COVID-19.** Ananworanich J, et al. *Clin Infect Dis*. 2021 Sep 15:ciab813. doi: 10.1093/cid/ciab813. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab813/6370549>

Our study did not demonstrate an impact of rivaroxaban on disease progression in high-risk adults with mild COVID-19. There remains a critical public health gap in identifying scalable effective therapies for high-risk people in the outpatient setting to prevent COVID-19 progression.

## Transmission / Infection Control

11. **Infectious SARS-CoV-2 in Exhaled Aerosols and Efficacy of Masks During Early Mild Infection.** Adenaiye OO et al. *Clin Infect Dis*. 2021 Sep 14:ciab797. doi: 10.1093/cid/ciab797. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab797/6370149>

SARS-CoV-2 is evolving toward more efficient aerosol generation and loose-fitting masks provide significant but only modest source control. Therefore, until vaccination rates are very high, continued layered controls and tight-fitting masks and respirators will be necessary.

## Vaccines / Immunology

12. **Comparative Effectiveness of Moderna, Pfizer-BioNTech, and Janssen (Johnson & Johnson) Vaccines in Preventing COVID-19 Hospitalizations among Adults without Immunocompromising Conditions — United States, March–August 2021.** Self WH, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 17 September 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7038e1>  
Among U.S. adults without immunocompromising conditions, vaccine effectiveness against COVID-19 hospitalization during March 11–August 15, 2021, was higher for the Moderna vaccine (93%) than the Pfizer-BioNTech vaccine (88%) and the Janssen vaccine (71%). Although these real-world data suggest some variation in levels of protection by vaccine, all FDA-approved or authorized COVID-19 vaccines provide substantial protection against COVID-19 hospitalization.
13. **A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use in healthcare workers- first results from India.** Kaur U, et al. *EClinicalMedicine.* 2021 Jul 23;38:101038. doi: 10.1016/j.eclinm.2021.101038. eCollection 2021 Aug. [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00318-7/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00318-7/fulltext)  
COVISHIELD carries an overall favourable safety profile with AEFI rates much less than reported for other adenoviral vaccines. Females, those with hypertension, individuals with history of allergy and hypothyroidism may need watchful vaccine administration. This being an interim analysis and based on healthcare workers who may not reflect the general population demographics, larger inclusive studies are warranted for confirming the findings.
14. **ROCCA observational study: Early results on safety of Sputnik V vaccine (Gam-COVID-Vac) in the Republic of San Marino using active surveillance.** Montalti M et al. *EClinicalMedicine.* 2021 Jul 8;38:101027. doi: 10.1016/j.eclinm.2021.101027. eCollection 2021 Aug. [https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(21\)00307-2/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00307-2/fulltext)  
Our results, albeit preliminary, suggest that Sputnik V has a high tolerability profile in the population aged ≥60 years in terms of short-term AEFIs.
15. **Hospitalisation among vaccine breakthrough COVID-19 infections.** Juthani PJ, et al. *Lancet Infectious Diseases.* September 07, 2021 DOI:[https://doi.org/10.1016/S1473-3099\(21\)00558-2](https://doi.org/10.1016/S1473-3099(21)00558-2)  
[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00558-2/fulltext#sec1](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00558-2/fulltext#sec1)  
54 patients who were fully vaccinated were evaluated for illness severity. Among this cohort, we found that 25 (46%) patients were asymptomatic (admitted to hospital for a non-COVID-19-related diagnosis but with an incidental positive PCR test for SARS-CoV-2), four (7%) had mild disease, 11 (20%) had moderate disease, and 14 (26%) had severe or critical illness. Among those with severe or critical illness, the median age was 80.5 years. Pre-existing comorbidities in the 14 patients with severe or critical illness included overweight (n=9), cardiovascular

disease (n=12), lung disease (n=7), malignancy (n=4), type 2 diabetes (n=7), and use of an immunosuppressive agent (n=4). 13 of 14 patients had received BNT162b2.

**16. Vaccination reduces need for emergency care in breakthrough COVID-19 infections: A multicenter cohort study.** Bahl A, et al. *Lancet Regional Health*. September 09,

2021DOI:<https://doi.org/10.1016/j.lana.2021.100065>

[https://www.thelancet.com/journals/lanam/article/PIIS2667-193X\(21\)00061-2/fulltext#seccesectitle0001](https://www.thelancet.com/journals/lanam/article/PIIS2667-193X(21)00061-2/fulltext#seccesectitle0001)

The need for emergency care/hospitalization due to breakthrough COVID-19 is an exceedingly rare event in fully vaccinated patients. As vaccination has increased regionally, EC visits amongst fully vaccinated individuals have remained low and occur much less frequently than unvaccinated individuals. Accounting for the SARS-CoV-2 vaccination population groups in Michigan, the ED encounters/hospitalizations rate relevant to COVID-19 was 96% lower in FV versus UV. If hospital-based treatment is required, elderly patients with significant comorbidities are at high-risk for severe outcomes regardless of vaccination status.

**17. Dynamics of antibody response to BNT162b2 vaccine after six months: a longitudinal prospective study.** Naaber P et al. *Lancet Reg Health Eur*. 2021 Sep 6:100208. doi:

10.1016/j.lanep.2021.100208. [https://www.thelancet.com/journals/lanep/article/PIIS2666-7762\(21\)00185-X/fulltext](https://www.thelancet.com/journals/lanep/article/PIIS2666-7762(21)00185-X/fulltext)

The mRNA vaccine induces a strong antibody response to SARS-CoV-2 and five VOCs at 1 week post-vaccination that decreases thereafter. T cell responses, although detectable in the majority, were lower in individuals with higher T cell immunosenescence. The deterioration of vaccine response suggests the need to monitor for the potential booster vaccination.

**18. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months.** Thomas SJ et al. *N Engl J Med*. 2021 Sep 15. doi: 10.1056/NEJMoa2110345.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2110345>

Through 6 months of follow-up and despite a gradual decline in vaccine efficacy, BNT162b2 had a favorable safety profile and was highly efficacious in preventing Covid-19. (Funded by BioNTech and Pfizer; ClinicalTrials.gov number, NCT04368728.).

**19. SARS-CoV-2 Neutralization with BNT162b2 Vaccine Dose 3.** Falsey AR et al. *N Engl J Med*. 2021 Sep 15. doi: 10.1056/NEJMc2113468. <https://www.nejm.org/doi/full/10.1056/NEJMc2113468>

We conducted a global, randomized, placebo-controlled, phase 1–2–3 pivotal trial in which two 30- $\mu$ g doses of BNT162b2 (Pfizer–BioNTech) were administered 21 days apart. These doses of vaccine had mainly low-grade side effects and provided 95% efficacy against Covid-19 from 7 days to approximately 2 months after dose 2. Efficacy waned to 84% between 4 and approximately 6 months after dose 2. Since vaccine authorization, viral variants have replaced the original strain, with the highly transmissible B.1.617.2 (delta) variant currently dominant. Although the effectiveness of the vaccine against severe disease, hospitalization, and death remains high, waning immunity and viral diversification create a possible need for a third vaccine dose.

20. **Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel.** Bar-On YM, et al. *N Engl J Med.* 2021 Sep 15. doi: 10.1056/NEJMoa2114255.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2114255>

In this study involving participants who were 60 years of age or older and had received two doses of the BNT162b2 vaccine at least 5 months earlier, we found that the rates of confirmed Covid-19 and severe illness were substantially lower among those who received a booster (third) dose of the BNT162b2 vaccine.

21. **New-onset IgG autoantibodies in hospitalized patients with COVID-19.** Chang SE et al. *Nat Commun.* 2021 Sep 14;12(1):5417. doi: 10.1038/s41467-021-25509-3.

<https://www.nature.com/articles/s41467-021-25509-3>

COVID-19 is associated with a wide range of clinical manifestations, including autoimmune features and autoantibody production. Here we develop three protein arrays to measure IgG autoantibodies associated with connective tissue diseases, anti-cytokine antibodies, and anti-viral antibody responses in serum from 147 hospitalized COVID-19 patients. Autoantibodies are identified in approximately 50% of patients but in less than 15% of healthy controls. When present, autoantibodies largely target autoantigens associated with rare disorders such as myositis, systemic sclerosis and overlap syndromes. A subset of autoantibodies targeting traditional autoantigens or cytokines develop de novo following SARS-CoV-2 infection. Autoantibodies track with longitudinal development of IgG antibodies recognizing SARS-CoV-2 structural proteins and a subset of non-structural proteins, but not proteins from influenza, seasonal coronaviruses or other pathogenic viruses. We conclude that SARS-CoV-2 causes development of new-onset IgG autoantibodies in a significant proportion of hospitalized COVID-19 patients and are positively correlated with immune responses to SARS-CoV-2 proteins.

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## FDA / CDC / NIH / WHO Updates

FDA - [FDA authorizes bamlanivimab and etesevimab monoclonal antibody therapy for post-exposure prophylaxis \(prevention\) for COVID-19.](#)

NIH - [The COVID-19 Treatment Guidelines Panel's Statement on Bamlanivimab Plus Etesevimab for the Treatment of Mild to Moderate COVID-19 in Nonhospitalized Patients](#), updated 9-15-21

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## Commentary

[Considerations in boosting COVID-19 vaccine immune responses.](#) *Lancet* September 13, 2021

DOI:[https://doi.org/10.1016/S0140-6736\(21\)02046-8](https://doi.org/10.1016/S0140-6736(21)02046-8)

[F.D.A. Panel Recommends Authorizing Pfizer Booster for Elderly or at High Risk of Severe Covid](#), NYT September 17, 2021

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