

COVID-19 Resource Desk

#46 | 3.3.2021 to 3.9.2021

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New Research

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

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

Basic Science / Virology / Pre-clinical (see vaccine related under Vaccines / Immunology)

1. **The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A.** Wu SC, Arthur CM, Wang J, et al. *Blood Adv.* 2021 Mar 9;5(5):1305-1309. doi: 10.1182/bloodadvances.2020003259. <https://ashpublications.org/bloodadvances/article/5/5/1305/475250/The-SARS-CoV-2-receptor-binding-domain>
Findings: The RBD of SARS-CoV-2 shares sequence similarity with an ancient lectin family known to bind blood group antigens. SARS-CoV-2 RBD binds the blood group A expressed on respiratory epithelial cells, directly linking blood group A and SARS-CoV-2.

Diagnostics & Screening

2. **A multiplexed, next generation sequencing platform for high-throughput detection of SARS-CoV-2.** Aynaud MM, Hernandez JJ, Barutcu S, et al. *Nat Commun.* 2021 Mar 3;12(1):1405. doi: 10.1038/s41467-021-21653-y. <https://www.nature.com/articles/s41467-021-21653-y>
Findings: Here, we describe "Systematic Parallel Analysis of RNA coupled to Sequencing for Covid-19 screening" (C19-SPAR-Seq), a multiplexed, scalable, readily automated platform for SARS-CoV-2 detection that is capable of analyzing tens of thousands of patient samples in a single run. To address strict requirements for control of assay parameters and output demanded by clinical diagnostics, we employ a control-based Precision-Recall and Receiver Operator Characteristics (coPR) analysis to assign run-specific quality control metrics. C19-SPAR-Seq coupled to coPR on a trial cohort of several hundred patients performs with a specificity of 100% and sensitivity of 91% on samples with low viral loads, and a sensitivity of >95% on high viral loads associated with disease onset and peak transmissibility. This study establishes the feasibility of employing C19-SPAR-Seq for the large-scale monitoring of SARS-CoV-2 and other pathogens.
3. **SARS-CoV-2 lateral flow assays for possible use in national covid-19 seroprevalence surveys (React 2): diagnostic accuracy study.** React study team. *BMJ.* 2021 Mar 2;372:n423. doi: 10.1136/bmj.n423. <https://www.bmj.com/content/372/bmj.n423>

Findings: We determine the accuracy of LFIA in detecting IgG antibodies to SARS-CoV-2 compared with two reference standards. The sensitivity and specificity of seven new LFIA that were analysed using sera varied from 69% to 100%, and from 98.6% to 100%, respectively (compared with the two reference standards). Sensitivity on finger prick testing was 77% for Panbio, 86% for Surescreen, and 69% for AbC-19 compared with the reference standards. Sensitivity for sera from matched clinical samples performed on AbC-19 was significantly higher with serum than finger prick at 92%. Antibody titres varied considerably among cohorts. The numbers of positive samples identified by finger prick in the lowest antibody titre quarter varied among LFIA. CONCLUSIONS: One new LFIA was identified with clinical performance suitable for potential inclusion in seroprevalence studies. However, none of the LFIA tested had clearly superior performance to the LFIA currently used in React 2 seroprevalence surveys, and none showed sufficient sensitivity and specificity to be considered for routine clinical use.

4. **Infection sustained by lineage B.1.1.7 of SARS-CoV-2 is characterised by longer persistence and higher viral RNA loads in nasopharyngeal swabs.** Calistri P, Amato L, Puglia I, et al. *Int J Infect Dis.* 2021 Mar 5:S1201-9712(21)00210-1. doi:10.1016/j.ijid.2021.03.005.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7934691/>

Findings: Following the announcement on December 2020 about the emergence of a new variant in the United Kingdom a targeted surveillance was put in place in Abruzzo region (Italy), which allowed to detect 313 persons affected by lineage B.1.1.7, up to the 20th of February 2021. We investigated the results of RT-PCR on nasopharyngeal swabs tested from December 2020 to February 2021, to verify any difference on the viral load and persistence between people infected by lineage B.1.1.7 and others. Statistically significant lower values of CT associated with the detection of the N protein encoding gene (CT N) were observed in persons with lineage B.1.1.7 infection (median CT N = 15.8) in comparison to those infected by other lineages (median CT N = 16.9). A significant longer duration of the persistence of SARS-CoV-2 RNA in nasopharyngeal swabs was observed in persons with lineage B.1.1.7 infection (16 days) in comparison to those infected by other lineages (14 days).

5. **Clinical and Economic Effects of Widespread Rapid Testing to Decrease SARS-CoV-2 Transmission.** Paltiel AD, Zheng A, Sax PE. *Ann Intern Med.* 2021 Mar 9. doi: 10.7326/M21-0510. <https://www.acpjournals.org/doi/10.7326/M21-0510>

Findings: Without a testing intervention, the model anticipates 11.6 million infections, 119 000 deaths, and \$10.1 billion in costs (\$6.5 billion in inpatient care and \$3.5 billion in lost productivity) over a 60-day horizon. Weekly availability of testing would avert 2.8 million infections and 15 700 deaths, increasing costs by \$22.3 billion. Lower inpatient outlays (\$5.9 billion) would partially offset additional testing expenditures (\$12.5 billion) and workdays lost (\$14.0 billion), yielding incremental cost-effectiveness ratios of \$7890 per infection averted and \$1 430 000 per death averted. High-frequency home testing for SARS-CoV-2 with an inexpensive, imperfect test could contribute to pandemic control at justifiable cost and warrants consideration as part of a national containment strategy.

6. **SARS-CoV-2 transmission in intercollegiate athletics not fully mitigated with daily antigen testing.** Moreno GK, Braun KM, Pray IW, et al. *medRxiv* 2021.03.03.21252838; doi: <https://doi.org/10.1101/2021.03.03.21252838> **Preprint**

Findings: During the fall 2020 semester, athletes and staff in both programs were tested daily, with positive antigen results requiring confirmatory testing with real-time RT-PCR. We used genomic sequencing to investigate transmission dynamics in these two outbreaks. In Outbreak 1, 32 confirmed cases occurred within a university athletics program after the index patient attended a meeting while infectious despite a negative antigen test on the day of the meeting. Among isolates sequenced from Outbreak 1, 24 (92%) of 26 were closely related, suggesting sustained transmission following an initial introduction event. In Outbreak 2, 12 confirmed cases occurred among athletes from two university programs that faced each other in an athletic competition despite receiving negative antigen test results on the day of the competition. Sequences from both teams were closely related and unique from strains circulating in the community, suggesting transmission during intercollegiate competition. These findings suggest that antigen testing alone, even when mandated and directly observed, may not be sufficient as an intervention to prevent SARS-CoV-2 outbreaks in congregate settings, and highlights the importance of supplementing serial antigen testing with appropriate mitigation strategies to prevent SARS-CoV-2 outbreak in congregate settings.

Epidemiology & Public Health

7. **Household COVID-19 risk and in-person schooling.** Lessler J, Grabowski MK, Grantz KH, et al. *medRxiv* 2021.02.27.21252597; doi: <https://doi.org/10.1101/2021.02.27.21252597> **Preprint**
- Findings: In-person schooling has proved contentious and difficult to study throughout the SARS-CoV-2 pandemic. Data from a massive online survey in the United States indicates an increased risk of COVID-19-related outcomes among respondents living with a child attending school in-person. School-based mitigation measures are associated with significant reductions in risk, particularly daily symptoms screens, teacher masking, and closure of extra-curricular activities. With seven or more mitigation measures, the association between in-person schooling and COVID-19-related outcomes all but disappears. Teachers working outside the home were more likely to report COVID-19-related outcomes, but this association is similar to other occupations. In-person schooling is associated with household COVID-19 risk, but this risk can likely be controlled with properly implemented school-based mitigation measures.
8. **Estimated SARS-CoV-2 Seroprevalence among Persons Aged <18 Years - Mississippi, May-September 2020.** CDC COVID-19 Response Team. *MMWR Morb Mortal Wkly Rep.* 2021 Mar 5;70(9):312-315. doi: 10.15585/mmwr.mm7009a4. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7009a4.htm>
- Findings: Serosurveys estimating prior SARS-CoV-2 infections in the United States have focused on adults; little is known about seroprevalence among young persons. Serologic testing of residual blood specimens collected during May–September 2020, from 1,603 persons aged <18 years suggested that approximately 113,842 (16.3%) of 698,420 young persons in Mississippi might have been infected with SARS-CoV-2 by mid-September 2020, and only 8,993 confirmed and probable COVID-19 cases among young persons had been reported to the Mississippi State

Department of Health by August 31. Serosurveys including pediatric age groups help estimate cumulative disease incidence and frequency of undiagnosed cases of COVID-19 among young persons to guide prevention efforts.

9. **Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England.** Davies NG, Abbott S, Barnard RC, et al. *Science*. 2021 Mar 3:eabg3055. doi: 10.1126/science.abg3055. <https://science.sciencemag.org/content/early/2021/03/03/science.abg3055>
Findings: A novel SARS-CoV-2 variant, VOC 202012/01 (lineage B.1.1.7), emerged in southeast England in November 2020 and is rapidly spreading toward fixation. Using a variety of statistical and dynamic modelling approaches, we estimate that this variant has a 43-90% higher reproduction number than preexisting variants. A fitted two-strain dynamic transmission model shows that VOC 202012/01 will lead to large resurgences of COVID-19 cases. Without stringent control measures, including limited closure of educational institutions and a greatly accelerated vaccine roll-out, COVID-19 hospitalisations and deaths across England in 2021 will exceed those in 2020. Concerningly, VOC 202012/01 has spread globally and exhibits a similar transmission increase (59-74%) in Denmark, Switzerland, and the United States.
10. **Estimation of secondary household attack rates for emergent SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco.** Peng J, Mann SA, Mitchell AM, et al. *medRxiv* 2021.03.01.21252705; **Preprint**. doi: <https://doi.org/10.1101/2021.03.01.21252705>
Findings: SARS-CoV-2 genomic sequences were generated from positive samples collected, along with epidemiological metadata, at a walk-up, rapid testing site in the Mission District of San Francisco, California during November 22-December 2, 2020 and January 10-29, 2021. Secondary household attack rates and mean sample viral load were estimated and compared across observed variants. A total of 12,124 tests were performed yielding 1,099 positives. From these, 811 high quality genomes were generated. Certain viral lineages bearing spike mutations, defined in part by L452R, S13I, and W152C, comprised 54.9% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to "West Coast" variants were at higher risk of infection compared to household contacts exposed to lineages lacking these variants. The reproductive number was estimated to be modestly higher than other lineages spreading in California during the second half of 2020. Viral loads were similar among persons infected with West Coast versus non-West Coast strains, as was the proportion of individuals with symptoms (60.9% vs 64.1%). The increase in prevalence, relative household attack rates, and reproductive number are consistent with a modest transmissibility increase of the "West Coast" variants; however, additional laboratory and epidemiological studies are required to better understand differences between these variants.
11. **Association of State-Issued Mask Mandates and Allowing On-Premises Restaurant Dining with County-Level COVID-19 Case and Death Growth Rates — United States, March 1–December 31, 2020.** Guy GP Jr., Lee FC, Sunshine G, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 5 March 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7010e3>
Findings: Universal masking and avoiding nonessential indoor spaces are recommended to mitigate the spread of COVID-19. Mandating masks was associated with a decrease in daily

COVID-19 case and death growth rates within 20 days of implementation. Allowing on-premises restaurant dining was associated with an increase in daily COVID-19 case growth rates 41–100 days after implementation and an increase in daily death growth rates 61–100 days after implementation. Mask mandates and restricting any on-premises dining at restaurants can help limit community transmission of COVID-19 and reduce case and death growth rates. These findings can inform public policies to reduce community spread of COVID-19.

Healthcare Delivery & Healthcare Workers

12. **Antibody response to SARS-CoV-2 infection is not associated with Post-COVID-19 Syndrome in healthcare workers.** Pereira C, Harris BHL, Di Giovannantonio M, et al. *J Infect Dis.* 2021 Mar 2;jiab120. doi: 10.1093/infdis/jiab120. <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab120/6155862>

Findings: It is currently unknown how Post-COVID-19 Syndrome (PCS) may affect those infected with SARS-CoV-2. This longitudinal study reports on healthcare staff who tested positive for SARS-CoV-2 between March-April 2020 and follows their antibody titres and symptomatology. Over half (n=21/38) had PCS at 7-8 months. There was no statistically significant difference between initial RT-PCR viral titres or serial antibody levels between those who did and did not develop PCS. This study highlights the relative commonality of PCS in healthcare workers and this should be considered in vaccination scheduling and workforce planning to allow adequate frontline staffing numbers.

Prognosis

13. **Outcomes and Mortality Among Adults Hospitalized With COVID-19 at US Medical Centers.**

Nguyen NT, Chinn J, Nahmias J, et al. *JAMA Netw Open.* 2021 Mar 1;4(3):e210417. doi: 10.1001/jamanetworkopen.2021.0417.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777028>

Findings: This cohort study of patients with COVID-19 who were admitted to US medical centers revealed high in-hospital mortality of 13.6%. However, over the course of the pandemic, there was a reduction in mortality of more than 15 percentage points between March (22.1%) and August (6.5%). The in-hospital mortality in the current study was similar to that reported in other published US studies (15.3%-24.5%). Mortality increased in association with increasing age. Patients 80 years or older represented the age group with the highest mortality. This study provides data on characteristics and outcomes in, to our knowledge, the largest US cohort of hospitalized COVID-19 adults to date; identified subgroups of patients with higher mortality; and determined mortality over time (from March 1 to August 31, 2020) at 555 US medical centers.

14. **Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK.** ISARIC investigators. *Lancet Respir Med.* 2021 Mar 4:S2213-2600(21)00013-8. doi:10.1016/S2213-2600(21)00013-8.

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00013-8/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00013-8/fulltext)

Findings: Underlying respiratory conditions are common in patients admitted to hospital with COVID-19. Regardless of the severity of symptoms at admission and comorbidities, patients with asthma were more likely, and those with chronic pulmonary disease less likely, to receive critical care than patients without an underlying respiratory condition. In patients aged 16 years and older, severe asthma was associated with increased mortality compared to non-severe asthma. In patients aged 50 years and older, inhaled corticosteroid use in those with asthma was associated with lower mortality than in patients without an underlying respiratory condition; patients with chronic pulmonary disease had significantly increased mortality compared to those with no underlying respiratory condition, regardless of inhaled corticosteroid use. Our results suggest that the use of inhaled corticosteroids, within 2 weeks of admission, improves survival for patients aged 50 years and older with asthma, but not for those with chronic pulmonary disease.

15. **Predictors of failure with high-flow nasal oxygen therapy in COVID-19 patients with acute respiratory failure: a multicenter observational study.** COVID-19 Spanish ICU Network. *J Intensive Care*. 2021 Mar 5;9(1):23. doi: 10.1186/s40560-021-00538-8.

<https://jintensivecare.biomedcentral.com/articles/10.1186/s40560-021-00538-8>

Findings: From a total of 259 patients initially treated with HFNO, 140 patients (54%) required invasive mechanical ventilation. Baseline non-respiratory SOFA score, and the ROX index calculated as the ratio of partial pressure of arterial oxygen to inspired oxygen fraction divided by respiratory rate, and pH were associated with intubation. Hospital site explained 1% of the variability in the likelihood of intubation after initial treatment with HFNO. A predictive model including non-respiratory SOFA score and the ROX index showed excellent performance. Among adult critically ill patients with COVID-19 initially treated with HFNO, the SOFA score and the ROX index may help to identify patients with higher likelihood of intubation.

16. **Body Mass Index and Risk for COVID-19–Related Hospitalization, Intensive Care Unit Admission, Invasive Mechanical Ventilation, and Death — United States, March–December 2020.** Kompaniyets L, Goodman AB, Belay B, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 8 March 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7010e4>

Findings: Among 148,494 U.S. adults with COVID-19, a nonlinear relationship was found between BMI and COVID-19 severity, with lowest risks at BMIs near the threshold between healthy weight and overweight in most instances, then increasing with higher BMI. Overweight and obesity were risk factors for invasive mechanical ventilation. Obesity was a risk factor for hospitalization and death, particularly among adults aged <65 years. What are the implications for public health practice? These findings highlight clinical and public health implications of higher BMIs, including the need for intensive management of COVID-19–associated illness, continued vaccine prioritization and masking, and policies to support healthy behaviors.

Survivorship & Rehabilitation

17. **Prevalence of Inflammatory Heart Disease Among Professional Athletes with Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening.** Martinez MW, Tucker

AM, Bloom OJ, et al. *JAMA Cardiol.* 2021 Mar 4. doi: 10.1001/jamacardio.2021.0565.

<https://jamanetwork.com/journals/jamacardiology/fullarticle/2777308>

Findings: The study included 789 professional athletes (mean age, 25 [3] years; 777 men [98.5%]). A total of 460 athletes (58.3%) had prior symptomatic COVID-19 illness, and 329 (41.7%) were asymptomatic or minimally symptomatic. Abnormal screening results were identified in 30 athletes (3.8%; troponin, 6 athletes [0.8%]; ECG, 10 athletes [1.3%]; echocardiography, 20 athletes [2.5%]), necessitating additional testing; 5 athletes (0.6%) ultimately had cardiac magnetic resonance imaging findings suggesting inflammatory heart disease that resulted in restriction from play. No adverse cardiac events occurred in athletes who underwent cardiac screening and resumed professional sport participation. This study provides large-scale data assessing the prevalence of relevant COVID-19-associated cardiac pathology with implementation of current RTP screening recommendations. While long-term follow-up is ongoing, few cases of inflammatory heart disease have been detected, and a safe return to professional sports activity has thus far been achieved.

18. **Muscle weakness, functional capacities and recovery for COVID-19 ICU survivors.** Medrinal C, Prieur G, Bonnevie T, et al. *BMC Anesthesiol.* 2021 Mar 2;21(1):64. doi: 10.1186/s12871-021-01274-0. <https://bmcanesthesiol.biomedcentral.com/articles/10.1186/s12871-021-01274-0>

Findings: We performed a cross sectional study in two ICU tertiary Hospital Settings. COVID-19 ICU survivors were screened and respiratory and limb muscle strength were measured at the time of extubation. An ICU mobility scale was performed at ICU discharge and walking capacity was self-evaluated by patients 30 days after weaning from mechanical ventilation. Twenty-three patients were included. Sixteen (69%) had limb muscle weakness and 6 (26%) had overlap limb and respiratory muscle weakness. Amount of physiotherapy was not associated with muscle strength. 44% of patients with limb weakness were unable to walk 100 m 30 days after weaning. The large majority of COVID-19 ICU survivors developed ICU acquired limb muscle weakness. 44% of patients with limb weakness still had severely limited function one-month post weaning.

19. **PULMONARY FUNCTION AND RADIOLOGICAL FEATURES IN SURVIVORS OF CRITICAL COVID-19: A 3-MONTH PROSPECTIVE COHORT.** CIBERESUCICOVID Project (COV20/00110, ISCIII).

Chest. 2021 Mar 4:S0012-3692(21)00464-5. doi: 10.1016/j.chest.2021.02.062.

[https://journal.chestnet.org/article/S0012-3692\(21\)00464-5/pdf](https://journal.chestnet.org/article/S0012-3692(21)00464-5/pdf)

Findings: 125 ICU patients with ARDS secondary to COVID-19 were recruited between March and June 2020. At the 3-month follow-up, 62 patients were available for pulmonary evaluation. The most frequent symptoms were dyspnea (46.7%), and cough (34.4%). Eighty-two percent of patients showed a lung diffusing capacity of less than 80%. The median distance in the 6MWT was 400 meters. CT scans were abnormal in 70.2% of patients, showing reticular lesions in 49.1% and fibrotic patterns in 21.1%. Patients with more severe alterations on chest CT had worse pulmonary function and presented more degrees of desaturation in the 6MWT. Factors associated with the severity of lung damage on chest CT were age and length of invasive mechanical ventilation during the ICU stay. Pulmonary structural abnormalities and functional impairment are highly prevalent in surviving ICU patients with ARDS secondary to COVID-19 3

months after hospital discharge. Pulmonary evaluation should be considered for all critical COVID-19 survivors 3 months post discharge.

20. **Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection.** Zuo J, Dowell AC, Pearce H, et al. *Nat Immunol*. 2021 Mar 5. doi: 10.1038/s41590-021-00902-8. <https://www.nature.com/articles/s41590-021-00902-8>

Findings: The immune response to SARS-CoV-2 is critical in controlling disease, but there is concern that waning immunity may predispose to reinfection. We analyzed the magnitude and phenotype of the SARS-CoV-2-specific T cell response in 100 donors at 6 months following infection. T cell responses were present by ELISPOT and/or intracellular cytokine staining analysis in all donors and characterized by predominant CD4⁺ T cell responses with strong interleukin (IL)-2 cytokine expression. Median T cell responses were 50% higher in donors who had experienced a symptomatic infection, indicating that the severity of primary infection establishes a 'set point' for cellular immunity. T cell responses to spike and nucleoprotein/membrane proteins were correlated with peak antibody levels. Furthermore, higher levels of nucleoprotein-specific T cells were associated with preservation of nucleoprotein-specific antibody level although no such correlation was observed in relation to spike-specific responses. In conclusion, our data are reassuring that functional SARS-CoV-2-specific T cell responses are retained at 6 months following infection.

21. **Nutritional evaluation and management of critically ill patients with COVID-19 during post-intensive care rehabilitation.** Hoyois A, Ballarin A, Thomas J, et al. *JPEN J Parenter Enteral Nutr*. 2021 Mar 5. doi: 10.1002/jpen.2101.

<https://aspenjournals.onlinelibrary.wiley.com/doi/10.1002/jpen.2101>

Findings: All patients with COVID-19 requiring a minimum of 14 days stay in the ICU with mechanical ventilation were included. Nutritional status was assessed at inclusion (ICU discharge) and follow-up (after 15, 30 and 60 days). All patients had standardized medical nutrition therapy with defined targets regarding energy and protein intake. Fifteen patients were included (67% Males); median age was 60 years old. Body Mass index at ICU admission was 25,7 kg/m². After a median ICU stays of 33 days, malnutrition was present in all patients. Because of post-intubation dysphagia in 60% of patients, enteral nutrition was administered (57% naso-gastric tube; 43% percutaneous endoscopic gastrostomy). After 2-month, a significant improvement in muscle strength was observed of the predicted values for age vs 19% at ICU discharge, as well as weight gain of 4,3 kg. Critically ill patients with COVID-19 requiring ICU admission and mechanical ventilation have malnutrition and low muscle mass at ICU discharge. Nutritional parameters improve during rehabilitation with standardized medical nutrition therapy. This article is protected by copyright. All rights reserved.

Therapeutics

22. **Clinical outcome with different doses of low-molecular-weight heparin in patients hospitalized for COVID-19.** COVID-UPO Clinical Team. *J Thromb Thrombolysis*. 2021 Mar 1. doi: 10.1007/s11239-021-02401-x <https://link.springer.com/article/10.1007/s11239-021-02401-x>

Findings: A pro-thrombotic milieu and a higher risk of thrombotic events were observed in patients with COVID-19. We evaluated the association between prophylactic vs. intermediate-to-fully anticoagulant doses of enoxaparin and in-hospital adverse events in patients with COVID-19. We retrospectively included 436 consecutive patients admitted in three Italian hospitals. A total of 287 patients (65.8%) were treated with the prophylactic enoxaparin regimen and 149 (34.2%) with a higher dosing regimen. The use of prophylactic enoxaparin dose was associated with a similar incidence of all-cause mortality (25.4% vs. 26.9% with the higher dose). In the prophylactic dose group, a significantly lower incidence of cardiovascular death, venous thromboembolism, new-onset ARDS and mechanical intubation was observed. In patients hospitalized for COVID-19, the use of a prophylactic dosage of enoxaparin appears to be associated with similar in-hospital overall mortality compared to higher doses. These findings require confirmation in a randomized, controlled study.

23. **Human Safety, Tolerability, and Pharmacokinetics of Molnupiravir, a Novel Broad-Spectrum Oral Antiviral Agent with Activity Against SARS-CoV-2.** Painter WP, Holman W, Bush JA, et al. *Antimicrob Agents Chemother.* 2021 Mar 1:AAC.02428-20. doi: 10.1128/AAC.02428-20. <https://aac.asm.org/content/early/2021/02/24/AAC.02428-20>

Findings: Molnupiravir, EIDD-2801/MK-4482, the prodrug of the active antiviral ribonucleoside analog β -d-N4-hydroxycytidine (NHC; EIDD-1931), has activity against a number of RNA viruses. Single and multiple doses of molnupiravir were evaluated in this first-in-human, phase 1, randomized, double-blind, placebo-controlled study in healthy volunteers, which included evaluation of the effect of food on pharmacokinetics. EIDD-1931 appeared rapidly in plasma, with a median time of maximum observed concentration of 1.00 to 1.75 hours, and declined with a geometric half-life of approximately 1 hour, with a slower elimination phase apparent following multiple doses or higher single doses. Mean maximum observed concentration and area under the concentration versus time curve increased in a dose-proportional manner, and there was no accumulation following multiple doses. When administered in a fed state, there was a decrease in the rate of absorption, but no decrease in overall exposure. Molnupiravir was well tolerated. Fewer than half of subjects reported an adverse event, the incidence of adverse events was higher following administration of placebo, and 93.3% of adverse events were mild. One discontinued early due to rash. There were no serious adverse events and there were no clinically significant findings in clinical laboratory, vital signs, or electrocardiography. Plasma exposures exceeded expected efficacious doses based on scaling from animal models; therefore, dose escalations were discontinued before a maximum tolerated dose was reached.

24. **Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial.** PRINCIPLE Trial Collaborative Group. *Lancet* 2021 Mar 4. doi: [https://doi.org/10.1016/S0140-6736\(21\)00461-X](https://doi.org/10.1016/S0140-6736(21)00461-X)

Findings: We found little evidence of a meaningful benefit in the azithromycin plus usual care group in time to first reported recovery versus usual care alone, equating to an estimated benefit in median time to first recovery of 0.94 days. The probability that there was a clinically meaningful benefit of at least 1.5 days in time to recovery was 0.23. 16 (3%) of 500 participants in the azithromycin plus usual care group and 28 (3%) of 823 participants in the usual care

alone group were hospitalised. There were no deaths in either study group. Safety outcomes were similar in both groups. Two of 455 participants in the azithromycin plus usual care group and four of 668 participants in the usual care alone group reported admission to hospital during the trial, not related to COVID-19. Our findings do not justify the routine use of azithromycin for reducing time to recovery or risk of hospitalisation for people with suspected COVID-19 in the community. These findings have important antibiotic stewardship implications during this pandemic, as inappropriate use of antibiotics leads to increased antimicrobial resistance, and there is evidence that azithromycin use increased during the pandemic in the UK.

25. Effect of Ivermectin on Time to Resolution of Symptoms among Adults with Mild COVID-19: A Randomized Clinical Trial. López-Medina E, López P, et al. *JAMA*. 2021 Mar 4. doi:

10.1001/jama.2021.3071. <https://jamanetwork.com/journals/jama/fullarticle/2777389>

Findings: Among 400 patients who were randomized in the primary analysis population (median age, 37 years; 231 women [58%]), 398 (99.5%) completed the trial. The median time to resolution of symptoms was 10 days in the ivermectin group compared with 12 days in the placebo group. By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. The most common solicited adverse event was headache, reported by 104 patients (52%) given ivermectin and 111 (56%) who received placebo. The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group). Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms. The findings do not support the use of ivermectin for treatment of mild COVID-19, although larger trials may be needed to understand the effects of ivermectin on other clinically relevant outcomes.

26. High-flow nasal cannulae for respiratory support in adult intensive care patients. Lewis SR, Baker PE, Parker R, Smith AF. *Cochrane Database Syst Rev*. 2021 Mar 4;3:CD010172. doi: 10.1002/14651858.CD010172.pub3.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010172.pub3/full>

AUTHORS' CONCLUSIONS: HFNC may lead to less treatment failure when compared to standard oxygen therapy, but probably makes little or no difference to treatment failure when compared to NIV or NIPPV. For most other review outcomes, we found no evidence of a difference in effect. However, the evidence was often of low or very low certainty. We found a large number of ongoing studies; including these in future updates could increase the certainty or may alter the direction of these effects.

27. Mechanisms and Potential Roles of Glucose-Lowering Agents in COVID-19: A Review. Berlie HD, Kale-Pradhan PB, Orzechowski T, Jaber LA. *Ann Pharmacother*. 2021 Mar 4:1060028021999473. doi: 10.1177/1060028021999473.

<https://journals.sagepub.com/doi/full/10.1177/1060028021999473>

This review summarizes the current knowledge of glucose-lowering agents and their potential roles in COVID-19 outcomes. Considering beneficial mechanisms on COVID-19 outcomes that extend beyond glycemic control as well as safety profiles, current data suggest that dipeptidyl peptidase-IV (DPP-IV) inhibitors and metformin may have the most promise and warrant further investigation. Certain glucose-lowering agents may offer additional benefits beyond

glucose control—namely, by modulating the mechanisms contributing to adverse outcomes related to COVID-19 in patients with diabetes. DPP-IV inhibitors and metformin appear to have the most promise. However, current published literature on diabetes medications and COVID-19 should be interpreted with caution. Most published studies are retrospective and consist of convenience samples, and some lack adequate analytical approaches with confounding biases. Ongoing trials aim to evaluate the effects of glucose-lowering agents in reducing the severity of COVID-19 outcomes.

28. **Early versus deferred anti-SARS-CoV-2 convalescent plasma in patients admitted for COVID-19: A randomized phase II clinical trial.** Balcells ME, Rojas L, Le Corre N, et al. *PLoS Med.* 2021 Mar 3;18(3):e1003415. doi: 10.1371/journal.pmed.1003415. eCollection 2021 Mar. <https://journals.plos.org/plosmedicine/article/figure?id=10.1371/journal.pmed.1003415.t001>
Findings: In the present study, we failed to find evidence of benefit in mortality, length of hospitalization, or mechanical ventilation requirement by immediate addition of CP therapy in the early stages of COVID-19 compared to its use only in case of patient deterioration.
29. **Interleukin-1 and interleukin-6 inhibition compared with standard management in patients with COVID-19 and hyperinflammation: a cohort study.** Cavalli G, Larcher A, Tomelleri A, et al. *Lancet Rheumatol.* 2021 Feb 3. doi: 10.1016/S2665-9913(21)00012-6. [https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913\(21\)00012-6/fulltext](https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00012-6/fulltext)
FINDINGS: Of 392 patients included between Feb 25 and May 20, 2020, 275 did not receive interleukin inhibitors, 62 received the IL-1 inhibitor anakinra, and 55 received an IL-6 inhibitor. IL-1 inhibition, but not IL-6 inhibition, was associated with a significant reduction of mortality in patients admitted to hospital with COVID-19, respiratory insufficiency, and hyperinflammation. IL-6 inhibition was effective in a subgroup of patients with markedly high C-reactive protein concentrations, whereas both IL-1 and IL-6 inhibition were effective in patients with low lactate dehydrogenase concentrations.
30. **High Failure Rate of Noninvasive Oxygenation Strategies in Critically Ill Subjects with Acute Hypoxemic Respiratory Failure Due to COVID-19.** Menga LS, Cese LD, Bongiovanni F, et al. *Respir Care.* 2021 Mar 2:respcare.08622. doi: 10.4187/respcare.08622. <http://rc.rcjournal.com/content/early/2021/03/02/respcare.08622>
Findings: We conducted a prospective observational study to assess the rate of NIOS failure in subjects treated in the ICU for hypoxemic respiratory failure due to COVID-19. A total of 85 subjects received first-line treatment with NIOS. The most frequently used methods were helmet noninvasive ventilation and high-flow nasal cannula; of these, 52 subjects (61%) required endotracheal intubation. In the propensity-matched cohorts (54 pairs), subjects with COVID-19 showed higher risk of NIOS failure than those with other causes of hypoxemic respiratory failure (59% vs 35%). As compared to hypoxemic respiratory failure due to other etiologies, subjects with COVID-19 who were treated with NIOS in the ICU were burdened by a 2-fold higher risk of failure. Subjects with a SAPS II score ≥ 33 and serum lactate dehydrogenase ≥ 405 units/L represent the population with the greatest risk.

31. **Sulodexide in the treatment of patients with early stages of COVID-19: a randomized controlled trial.** Gonzalez Ochoa AJ, Raffetto J, Hernandez Ibarra AG, et al. *Thromb Haemost.* 2021 Mar 7. doi: 10.1055/a-1414-5216. <https://www.thieme-connect.com/products/ejournals/abstract/10.1055/a-1414-5216>
Findings: We aimed to evaluate the effect of sulodexide when used in the early clinical stages of COVID-19. Methods In an outpatient setting, we conducted a randomized controlled trial with a parallel-group design. Including patients within three days of clinical onset, who were at a high risk of severe clinical progression due to chronic comorbidities. Participants were randomly assigned to receive an oral dose of sulodexide or placebo for 21 days. At 21 days follow-up, 17.7% patients required hospitalization in the sulodexide group compared to 29.4% in the placebo group, p=0.03. 29.8% required oxygen support in the sulodexide group vs 42% in the placebo group, p=0.05 and for fewer days. There was no between-group difference concerning the length of hospital stay. Early intervention in COVID-19 patients with sulodexide reduced hospital admissions and oxygen support requirements. This has beneficial implications in the patient's well-being, making sulodexide a favorable medication until an effective vaccine or an antiviral becomes available.
32. **Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial.** Sarilumab COVID-19 Global Study Group. *Lancet Respir Med.* 2021 Mar 4:S2213-2600(21)00099-0. doi: 10.1016/S2213-2600(21)00099-0. [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00099-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00099-0/fulltext)
FINDINGS: Between March 28 and July 3, 2020, of 431 patients who were screened, 420 patients were randomly assigned and 416 received placebo (n=84 [20%]), sarilumab 200 mg (n=159 [38%]), or sarilumab 400 mg (n=173 [42%]). This trial did not show efficacy of sarilumab in patients admitted to hospital with COVID-19 and receiving supplemental oxygen. Adequately powered trials of targeted immunomodulatory therapies assessing survival as a primary endpoint are suggested in patients with critical COVID-19.
33. **Impact of remdesivir on 28 day mortality in hospitalized patients with COVID-19: February 2021 Meta-analysis.** Robinson R, Prakash V, Tamimi RA, Albast N, Wieland E, Garcia C. *medRxiv* 2021.03.04.21252903; **Preprint.** doi: <https://doi.org/10.1101/2021.03.04.21252903>
Findings: Four English language RCTs were identified, including data from 7,333 hospitalized patients worldwide using remdesivir in COVID-19 positive patients. Meta-analysis of all identified RCTs showed no difference in survival in patients who received remdesivir therapy compared to usual care or placebo. The random effects meta-analysis has a summary odd ratio is 0.89. Considerable variability in the severity of illness is noted with the rates of IMV at the time of randomization ranging from 0% to 27%. This meta-analysis of randomized controlled trials published in peer-reviewed literature by February 1, 2021 did not show reduced mortality in hospitalized patients with COVID-19 who received remdesivir.

Transmission / Infection Control

34. Persistent SARS-CoV-2 RNA Shedding without Evidence of Infectiousness: A Cohort Study of

Individuals with COVID-19. Household Transmission Study Team. *J Infect Dis.* 2021 Feb

27:jiab107. doi: 10.1093/infdis/jiab107. <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab107/6154064>

Findings: We collected serial nasopharyngeal specimens at various time points from 109 individuals with rRT-PCR-confirmed COVID-19 in Utah and Wisconsin. The likelihood of viral RNA shedding resolution at 10 days after symptom onset was approximately 3%. Time to shedding resolution was shorter among participants aged <18 years and longer among those aged ≥50 years compared to participants aged 18-49 years. No replication-competent viruses were recovered. Although most patients were positive for SARS-CoV-2 for ≥10 days after symptom onset, our findings suggest that individuals with mild to moderate COVID-19 are unlikely to be infectious ≥10 days after symptom onset.

35. Filtering Facepiece Respirator (N95 Respirator) Reprocessing: A Systematic Review. Schumm

MA, Hadaya JE, Mody N, Myers BA, Maggard-Gibbons M. *JAMA.* 2021 Mar 3. doi:

10.1001/jama.2021.2531. <https://jamanetwork.com/journals/jama/fullarticle/2777342>

FINDINGS: Forty-two studies were included that examined 65 total types of masks. All were laboratory studies (no clinical trials), and 2 evaluated respirator performance and fit with actual clinical use of N95 respirators. Twenty-seven evaluated UV germicidal irradiation, 19 vaporized hydrogen peroxide, 9 moist-heat incubation, 10 microwave-generated steam, and 7 ethylene oxide. Conclusion: Ultraviolet germicidal irradiation, vaporized hydrogen peroxide, moist heat, and microwave-generated steam processing effectively sterilized N95 respirators and retained filtration performance. Ultraviolet irradiation and vaporized hydrogen peroxide damaged respirators the least. More research is needed on decontamination effectiveness for SARS-CoV-2 because few studies specifically examined this pathogen.

Vaccines / Immunology

36. SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma.

Wibmer CK, Ayres F, Hermanus T, et al. *Nat Med.* 2021 Mar 2. doi: 10.1038/s41591-021-01285-x. <https://www.nature.com/articles/s41591-021-01285-x>

Findings: SARS-CoV-2 501Y.V2 (B.1.351), a novel lineage of coronavirus causing COVID-19, contains substitutions in two immunodominant domains of the spike protein. Here, we show that pseudovirus expressing 501Y.V2 spike protein completely escapes three classes of therapeutically relevant antibodies. This pseudovirus also exhibits substantial to complete escape from neutralization, but not binding, by convalescent plasma. These data highlight the prospect of reinfection with antigenically distinct variants and foreshadows reduced efficacy of spike-based vaccines.

37. Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7. Wang P, Nair MS, Liu L, et al.

Nature. 2021 Mar 8. doi: 10.1038/s41586-021-03398-2.

<https://www.nature.com/articles/s41586-021-03398-2>

Findings: The recent emergence of new SARS-CoV-2 variants B.1.1.7 in the UK11 and B.1.351 in South Africa¹² is of concern because of their purported ease of transmission and extensive mutations in the spike protein. We now report that B.1.1.7 is refractory to neutralization by most mAbs to the N-terminal domain (NTD) of the spike and relatively resistant to a few mAbs to the receptor-binding domain (RBD). It is not more resistant to convalescent plasma or vaccinee sera. Findings on B.1.351 are more worrisome in that this variant is not only refractory to neutralization by most NTD mAbs but also by multiple individual mAbs to the receptor-binding motif on RBD, largely owing to an E484K mutation. Moreover, B.1.351 is markedly more resistant to neutralization by convalescent plasma (9.4 fold) and vaccinee sera (10.3-12.4 fold). B.1.351 and emergent variants with similar spike mutations present new challenges for mAb therapy and threaten the protective efficacy of current vaccines.

38. **Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies.** Chen RE et al. *Nat Med.* 2021 Mar 4. doi: 10.1038/s41591-021-01294-w. <https://www.nature.com/articles/s41591-021-01294-w>

Findings: Here, using monoclonal antibodies (mAbs), animal immune sera, human convalescent sera and human sera from recipients of the BNT162b2 mRNA vaccine, we report the impact on antibody neutralization of a panel of authentic SARS-CoV-2 variants including a B.1.1.7 isolate, chimeric strains with South African or Brazilian spike genes and isogenic recombinant viral variants. Many highly neutralizing mAbs engaging the receptor-binding domain or N-terminal domain and most convalescent sera and mRNA vaccine-induced immune sera showed reduced inhibitory activity against viruses containing an E484K spike mutation. As antibodies binding to spike receptor-binding domain and N-terminal domain demonstrate diminished neutralization potency in vitro against some emerging variants, updated mAb cocktails targeting highly conserved regions, enhancement of mAb potency or adjustments to the spike sequences of vaccines may be needed to prevent loss of protection in vivo.

39. **Reduction in COVID-19 Patients Requiring Mechanical Ventilation Following Implementation of a National COVID-19 Vaccination Program - Israel, December 2020-February 2021.** Rinott E, Youngster I, Lewis YE. *MMWR Morb Mortal Wkly Rep.* 2021 Mar 5;70(9):326-328. doi:10.15585/mmwr.mm7009e3. https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e3.htm?s_cid=mm7009e3_x

Findings: Clinical trials have demonstrated the efficacy of COVID-19 vaccines in a controlled setting. Israel initiated a national vaccination campaign in December 2020, prioritizing persons aged >60 years and other high-risk populations. By February 2021, 2-dose vaccination coverage was 84% among persons aged ≥70 years and 10% among those aged <50 years. The ratio of COVID-19 patients aged ≥70 years requiring mechanical ventilation to those aged <50 years declined 67% from October–December 2020 to February 2021. These findings provide preliminary evidence of the effectiveness of vaccines in preventing severe cases of COVID-19 at the national level in Israel.

40. **Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older**

adults in England. Lopez Bernal J, Andrews N, Gower C, et al. *medRxiv* 2021.03.01.21252652; doi: <https://doi.org/10.1101/2021.03.01.21252652> **Preprint**

Findings: Vaccination with either a single dose of BNT162b2 or ChAdOx1 COVID-19 vaccination was associated with a significant reduction in symptomatic SARS-CoV2 positive cases in older adults with even greater protection against severe disease. Both vaccines show similar effects. Protection was maintained for the duration of follow-up (>6 weeks). A second dose of BNT162b2 provides further protection against symptomatic disease but second doses of ChAdOx1 have not yet been rolled out in England. There is a clear effect of the vaccines against the UK variant of concern.

41. **Evaluation of a SARS-CoV-2 Vaccine NVX-CoV2373 in Younger and Older Adults.** the 2019nCoV-101 Study Group. *medRxiv* 2021.02.26.21252482; doi:

<https://doi.org/10.1101/2021.02.26.21252482> **Preprint**

Findings: The study confirmed that the two-dose regimen of 5- μ g NVX-CoV2373 is highly immunogenic and well tolerated in both younger and older participants.

42. **Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees.** Tarke A, Sidney J, Methot N, et al. *bioRxiv* 2021.02.27.433180; doi: <https://doi.org/10.1101/2021.02.27.433180> **Preprint**

Findings: Here we performed a comprehensive analysis of SARS-CoV-2-specific CD4+ and CD8+ T cell responses from COVID-19 convalescent subjects recognizing the ancestral strain, compared to variant lineages B.1.1.7, B.1.351, P.1, and CAL.20C as well as recipients of the Moderna (mRNA-1273) or Pfizer/BioNTech (BNT162b2) COVID-19 vaccines. Similarly, we demonstrate that the sequences of the vast majority of SARS-CoV-2 T cell epitopes are not affected by the mutations found in the variants analyzed. Overall, the results demonstrate that CD4+ and CD8+ T cell responses in convalescent COVID-19 subjects or COVID-19 mRNA vaccinees are not substantially affected by mutations found in the SARS-CoV-2 variants.

43. **Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2.** Blumenthal KG, Freeman EE, Saff RR, et al. *N Engl J Med.* 2021 Mar 3. doi: 10.1056/NEJMc2102131.

<https://www.nejm.org/doi/10.1056/NEJMc2102131>

Here, we report on a series of 12 patients with these reactions, all of which appeared near the injection site after complete resolution of the initial local and systemic symptoms associated with vaccination. Five of the reactions were grade 3 plaques (≥ 10 cm in diameter). Some patients had concurrent systemic adverse effects, and among these patients, 2 had additional skin findings. Most patients received treatment for their symptoms (e.g., with ice and antihistamines). Some patients received glucocorticoids (topical, oral, or both), and 1 patient received antibiotic therapy for presumptive cellulitis. The symptoms resolved a median of 6 days after onset (range, 2 to 11).

44. **Reduced binding and neutralization of infection- and vaccine-induced antibodies to the B.1.351 (South African) SARS-CoV-2 variant.** Edara VV, Norwood C, Floyd K, et al. *bioRxiv.* 2021 Feb 22:2021.02.20.432046. doi: 10.1101/2021.02.20.432046. **Preprint.**

<https://www.biorxiv.org/content/10.1101/2021.02.20.432046v1.full>

Findings: We compared antibody binding and live virus neutralization of sera from naturally infected and spike mRNA vaccinated individuals against a circulating SARS-CoV-2 B.1 variant and the emerging B.1.351 variant. In acutely-infected (5-19 days post-symptom onset), convalescent COVID-19 individuals (through 8 months post-symptom onset) and mRNA-1273 vaccinated individuals (day 14 post-second dose), we observed an average 4.3-fold reduction in antibody titers to the B.1.351-derived receptor binding domain of the spike protein and an average 3.5-fold reduction in neutralizing antibody titers to the SARS-CoV-2 B.1.351 variant as compared to the B.1 variant (spike D614G). However, most acute and convalescent sera from infected and all vaccinated individuals neutralize the SARS-CoV-2 B.1.351 variant, suggesting that protective immunity is retained against COVID-19.

45. **Preliminary Efficacy of the NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant.** Shinde V et al, for the 2019nCoV-501 Study Group *medRxiv* 2021.02.25.21252477; **Preprint.** doi: <https://doi.org/10.1101/2021.02.25.21252477>

Findings: In this phase 2a/b, multicenter, randomized, observer-blinded, placebo-controlled trial in South Africa, healthy HIV-negative adults or medically stable people living with HIV were randomized in a 1:1 ratio to receive two doses, administered 21 days apart, of either NVX-CoV2373 nanoparticle vaccine or placebo. A total of 4387 participants were randomized and dosed at least once, 2199 with NVX-CoV2373 and 2188 with placebo. Approximately 30% of participants were seropositive at baseline. Among 2684 baseline seronegative participants, there were 15 and 29 predominantly mild to moderate Covid-19 cases in NVX-CoV2373 and placebo recipients, respectively; vaccine efficacy was 49.4%. Efficacy in HIV-negative participants was 60.1% and did not differ by baseline serostatus. Of the primary endpoint cases with available whole genome sequencing, 38 (92.7%) of 41 were the B.1.351 variant. Post-hoc vaccine efficacy against B.1.351 was 51.0% in HIV-negative participants. Among placebo recipients, the incidence of symptomatic Covid-19 was similar in baseline seronegative vs baseline seropositive participants during the first 2 months of follow-up (5.3% vs 5.2%). Preliminary local and systemic reactogenicity were primarily mild to moderate and transient, and higher with NVX-CoV2373; serious adverse events were rare in both groups. Conclusions The NVX-CoV2373 vaccine was efficacious in preventing Covid-19, which was predominantly mild to moderate and due to the B.1.351 variant, while evidence of prior infection with the presumptive original SARS-CoV-2 did not confer protection against probable B.1.351 disease.

46. **Acute Allergic Reactions to mRNA COVID-19 Vaccines.** Blumenthal KG, Robinson LB, Camargo CA Jr, et al. *JAMA*. 2021 Mar 8. doi: 10.1001/jama.2021.3976. <https://jamanetwork.com/journals/jama/fullarticle/2777417>

Findings: Anaphylaxis to the mRNA COVID-19 vaccines is currently estimated to occur in 2.5 to 11.1 cases per million doses, largely in individuals with a history of allergy. Allergic concerns contribute to vaccine hesitancy; we investigated acute allergic reaction incidence after more than 60 000 mRNA COVID-19 vaccine administrations.

47. **An increase in willingness to vaccinate against COVID-19 in the US between October 2020 and February 2021: longitudinal evidence from the Understanding America Study.** Daly M, Jones

A, Robinson E. *medRxiv* 2021.03.04.21252918; **Preprint**. doi:

<https://doi.org/10.1101/2021.03.04.21252918>

Findings: Observational study using a nationally representative longitudinal sample (N =7,840) from the Understanding America Study (UAS). Changes in the percentage of respondents willing to vaccinate, undecided, or intending to refuse a COVID-19 vaccine were examined over 20 survey waves from April 1 2020 to February 15 2021. After a sharp decline in willingness to vaccinate against COVID-19 between April and October 2020 (from 74.0% to 52.7%), willingness to vaccinate increased by 8.1% (p <.001) to 60.8% between October 2020 and February 2021. A significant increase in willingness to vaccinate was observed across all demographic groups examined and Black (15.6% increase) and Hispanic participants (12.1% increase) showed particularly large changes. Willingness to vaccinate against COVID-19 increased in the US from October 2020 to February 2021.

Women & Children

48. **Assessment of Respiratory Function in Infants and Young Children Wearing Face Masks during the COVID-19 Pandemic.** Lubrano R, Bloise S, Testa A, et al. *JAMA Netw Open*. 2021 Mar 1;4(3):e210414. doi: 10.1001/jamanetworkopen.2021.0414.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776928>

Findings: This cohort study was conducted from May through June 2020 in a secondary-level hospital pediatric unit in Italy. Included participants were 47 healthy children divided by age. All participants were monitored every 15 minutes for changes in respiratory parameters for the first 30 minutes while not wearing a surgical face mask and for the next 30 minutes while wearing a face mask. Children aged 24 months and older then participated in a walking test for 12 minutes. This cohort study among infants and young children in Italy found that the use of facial masks was not associated with significant changes in Sao2 or Petco2, including among children aged 24 months and younger.

49. **SARS-CoV-2 antibodies detected in human breast milk post-vaccination.** Baird JK, Jensen SM, Urba WJ, Fox BA, Baird JR. **[Providence authors]**. *medRxiv* 2021.02.23.21252328; **Preprint**. doi: <https://doi.org/10.1101/2021.02.23.21252328>

Findings: Six lactating women who planned to receive both doses of the Pfizer-BioNTech or Moderna vaccine between December 2020 and January 2021. Breast milk samples were collected pre-vaccination and at 11 additional timepoints, with last sample at 14 days post 2nd dose of vaccine. We observed significantly elevated levels of SARS-CoV-2 specific IgG and IgA antibodies in breast milk beginning at Day 7 after the initial vaccine dose, with an IgG-dominant response. We are the first to show that maternal vaccination results in SARS-CoV-2 specific immunoglobulins in breast milk that may be protective for infants.

50. **COVID-19 Infection and Hypertensive Disorders of Pregnancy.** Rosenbloom JI, Raghuraman N, Carter EB, Kelly JC. *Am J Obstet Gynecol*. 2021 Mar 3:S0002-9378(21)00150-2. doi: 10.1016/j.ajog.2021.03.001. [https://www.ajog.org/article/S0002-9378\(21\)00150-2/fulltext](https://www.ajog.org/article/S0002-9378(21)00150-2/fulltext)

Findings: Of 1856 births, there were 83 women (4.5%) with COVID-19 infection. There was no significant difference in baseline characteristics between COVID-19 infected women and

controls. Patients with COVID-19 infection had almost a two-fold risk of HDP. However, COVID-19 infection was not associated with severity of HDP, and severity of COVID-19 was not associated with HDP development. Early COVID-19 infections are associated with HDP, even when accounting for differential exposure and delivery times, suggesting that COVID-19 infection may alter pregnancy physiology and increase the risk of HDP development over time. Infection closer to term is not associated with HDP, which likely reflects our high proportion of asymptomatic infections found at the time of delivery from a universal testing policy and insufficient time to develop HDP in these cases. Furthermore, emerging evidence suggests that COVID-19 modulates placental ACE2 expression, which may be related to HDP development. Our study is limited by sampling in a single institution with a high HDP incidence. However, our results suggest that monitoring of patients with antepartum COVID-19 infection should encompass precautions for HDP development.

51. **Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome.** LaRovere KL et al. *JAMA Neurol.* 2021 Mar 5. doi: 10.1001/jamaneurol.2021.0504.

<https://jamanetwork.com/journals/jamaneurology/fullarticle/2777392>

Findings: Of 1695 patients (909 [54%] male; median age, 9.1 years), 365 (22%) from 52 sites had documented neurologic involvement. Patients with neurologic involvement were more likely to have underlying neurologic disorders compared with those without, but a similar number were previously healthy and met criteria for multisystem inflammatory syndrome in children. Among those with neurologic involvement, 322 (88%) had transient symptoms and survived, and 43 (12%) developed life-threatening conditions clinically adjudicated to be associated with COVID-19, including severe encephalopathy, stroke, central nervous system infection/demyelination, Guillain-Barré syndrome/variants, and acute fulminant cerebral edema. Of 43 patients who developed COVID-19-related life-threatening neurologic involvement, 17 survivors (40%) had new neurologic deficits at hospital discharge, and 11 patients (26%) died. In this study, many children and adolescents hospitalized for COVID-19 or multisystem inflammatory syndrome in children had neurologic involvement, mostly transient symptoms. A range of life-threatening and fatal neurologic conditions associated with COVID-19 infrequently occurred. Effects on long-term neurodevelopmental outcomes are unknown.

52. **Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy.** Gill L, Jones CW. *Obstet Gynecol.* 2021 Mar 8. doi: 10.1097/AOG.0000000000004367.

https://journals.lww.com/greenjournal/Fulltext/9900/Severe_Acute_Respiratory_Syndrome_Coronavirus_2.122.aspx

CASE: A 34-year-old multigravid patient working in health care received the Pfizer-BioNTech mRNA vaccine for SARS-CoV-2 in the third trimester of pregnancy. Uncomplicated spontaneous vaginal delivery of a female neonate with Apgar scores of 9 and 9 occurred at term. The patient's blood as well as neonatal cord blood were evaluated for SARS-CoV-2-specific antibodies. Both the patient and the neonate were positive for antibodies at a titer of 1:25,600. In this case, passage of transplacental antibodies for SARS-CoV-2 was shown after vaccination in the third trimester of pregnancy.

GUIDELINES & CONSENSUS STATEMENTS

[The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Janssen COVID-19 Vaccine — United States, February 2021.](#) Oliver SE, Gargano JW, Scobie H, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 2 March 2021.

[A living WHO guideline on drugs to prevent covid-19.](#) Lamontagne F, Agoritsas T, Siemieniuk R, et al. *BMJ.* 2021 Mar 1;372:n526. doi: 10.1136/bmj.n526.

[ECMO for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization \(ELSO\).](#) Badulak J, Antonini MV, Stead CM, et al. *ASAIO J.* 2021 Feb 26. doi: 10.1097/MAT.0000000000001422.

[Update Alert 5: Masks for Prevention of Respiratory Virus Infections, Including SARS-CoV-2, in Health Care and Community Settings.](#) Chou R, Dana T, Jungbauer R, Weeks C. *Ann Intern Med.* 2021 Mar 9. doi: 10.7326/L21-0116.

FDA / CDC / NIH / WHO Updates

CDC - [Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Authorized in the United States](#)

CDC - [When You've Been Fully Vaccinated: How to Protect Yourself and Others](#)

CDC - [Interim Public Health Recommendations for Fully Vaccinated People](#)

CDC - [Health Department-Reported Cases of Multisystem Inflammatory Syndrome in Children \(MIS-C\) in the United States](#)

[Coronavirus \(COVID-19\) Update: FDA Issues Authorization for First Molecular Non-Prescription, At-Home Test](#)

NIH - [The COVID-19 Treatment Guidelines Panel's Statement on the Use of Tocilizumab for the Treatment of COVID-19](#)

Commentary & News

[Health care groups urge more race, ethnicity data for COVID vaccinations](#)

[WHO: New virus cases rising globally for first time in weeks](#)

[Choices in a Crisis - Individual Preferences among SARS-CoV-2 Vaccines.](#) Kramer DB, Opel DJ, Parasidis E, Mello MM. *N Engl J Med.* 2021 Mar 3. doi: 10.1056/NEJMp2102146.

[Single-dose Oxford-AstraZeneca COVID-19 vaccine followed by a 12-week booster.](#) Hung IFN, Poland GA. *Lancet*. 2021 Mar 6;397(10277):854-855. doi: 10.1016/S0140-6736(21)00528-6.

[Ridgeback Biotherapeutics and Merck Announce Preliminary Findings from a Phase 2a Trial of Investigational COVID-19 Therapeutic Molnupiravir](#)

[In Oregon, Scientists Find a Virus Variant With a Worrying Mutation](#)

[The Devastating Impact of Covid-19 on Individuals with Intellectual Disabilities in the United States](#)

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