

## COVID-19 Resource Desk

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### New Research

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#### Basic Science / Virology / Pre-clinical

- 1. SARS-CoV-2 infection is effectively treated and prevented by EIDD-2801.** Wahl A, Gralinski LE, Johnson CE, et al. *Nature*. 2021 Feb 9. doi: 10.1038/s41586-021-03312-w. <https://www.nature.com/articles/s41586-021-03312-w>  
Findings: All known recently emerged human coronaviruses probably originated in bats<sup>1</sup>. Here we used a single experimental platform based on human lung-only mice (LoM) to demonstrate efficient in vivo replication of all recently emerged human coronaviruses (SARS-CoV, MERS-CoV and SARS-CoV-2) and two highly relevant endogenous pre-pandemic SARS-like bat coronaviruses. Virus replication in this model occurs in bona fide human lung tissue and does not require any type of adaptation of the virus or the host. Our results indicate that bats harbour endogenous coronaviruses capable of direct transmission into humans. Further detailed analysis of pandemic SARS-CoV-2 in vivo infection of LoM human lung tissue showed predominant infection of human lung epithelial cells, including type II pneumocytes present in alveoli and ciliated airway cells. Acute SARS-CoV-2 infection was highly cytopathic and induced a robust and sustained type I interferon and inflammatory cytokine/chemokine response. Finally, we evaluated a therapeutic and pre-exposure prophylaxis strategy for coronavirus infection. Our results show that therapeutic and prophylactic administration of EIDD-2801, an oral broad spectrum antiviral currently in phase II-III clinical trials, dramatically inhibited SARS-CoV-2 replication in vivo and thus has significant potential for the prevention and treatment of COVID-19.
- 2. AT-527, a double prodrug of a guanosine nucleotide analog, is a potent inhibitor of SARS-CoV-2 in vitro and a promising oral antiviral for treatment of COVID-19.** Good SS, Westover J, Jung KH, et al. *Antimicrob Agents Chemother*. 2021 Feb 8:AAC.02479-20. doi: 10.1128/AAC.02479-20. <https://aac.asm.org/content/aac/early/2021/02/02/AAC.02479-20.full.pdf>  
Findings: AT-527, an orally administered double prodrug of a guanosine nucleotide analog, was previously shown to be highly efficacious and well tolerated in HCV-infected subjects. Here, we report the potent in vitro activity of AT-511, the free base of AT-527, against several coronaviruses, including SARS-CoV-2. In normal human airway epithelial cells, the concentration of AT-511 required to inhibit replication of SARS-CoV-2 by 90% (EC90) was 0.47 μM, very similar to its EC90 against HCoV-229E, HCoV-OC43 and SARS-CoV in Huh-7 cells. Little to no cytotoxicity

was observed for AT-511 at concentrations up to 100  $\mu\text{M}$ . Substantial levels of the active triphosphate metabolite AT-9010 were formed in normal human bronchial and nasal epithelial cells incubated with 10  $\mu\text{M}$  AT-511 ( $698 \pm 15$  and  $236 \pm 14$   $\mu\text{M}$ , respectively), with a half-life of at least 38 h. Results from steady-state pharmacokinetic and tissue distribution studies of non-human primates administered oral doses of AT-527, as well as pharmacokinetic data from subjects given daily oral doses of AT-527, predict that twice daily oral doses of 550 mg AT-527 will produce AT-9010 trough concentrations in human lung that exceed the EC<sub>90</sub> observed for the prodrug against SARS-CoV-2 replication. This suggests that AT-527 may be an effective treatment option for COVID-19.

**3. The Spike D614G mutation increases SARS-CoV-2 infection of multiple human cell types.**

Daniloski Z, Jordan TX, Ilmain JK, et al. *Elife*. 2021 Feb 11;10:e65365. doi: 10.7554/eLife.65365. <https://elifesciences.org/articles/65365#content>

Findings: A novel variant of the SARS-CoV-2 virus carrying a point mutation in the Spike protein (D614G) has recently emerged and rapidly surpassed others in prevalence. This mutation is in linkage disequilibrium with an ORF1b protein variant (P314L), making it difficult to discern the functional significance of the Spike D614G mutation from population genetics alone. Here, we perform site-directed mutagenesis on wild-type human codon optimized Spike to introduce the D614G variant. Using multiple human cell lines, including human lung epithelial cells, we found that the lentiviral particles pseudotyped with Spike D614G are more effective at transducing cells than ones pseudotyped with wild-type Spike. The increased transduction with Spike D614G ranged from 1.3 to 2.4-fold in Caco-2 and Calu-3 cells expressing endogenous ACE2, and 1.5 to 7.7-fold in A549ACE2 and Huh7.5ACE2 overexpressing ACE2. Furthermore, trans-complementation of SARS-CoV-2 virus with Spike D614G showed an increased infectivity of human cells. Although there is minimal difference in ACE2 receptor binding between the D614 and G614 Spike variants, we show that the G614 variant is more resistant to proteolytic cleavage in human cells, suggesting a possible mechanism for the increased transduction.

**4. Maturation and persistence of the anti-SARS-CoV-2 memory B cell response.** Sokal A,

Chappert P, Barba-Spaeth G, et al. *Cell*. 2021 Feb 2:S0092-8674(21)00093-3. doi: 10.1016/j.cell.2021.01.050. [https://www.cell.com/cell/pdf/S0092-8674\(21\)00093-3.pdf](https://www.cell.com/cell/pdf/S0092-8674(21)00093-3.pdf)

Findings: Memory B cells play a fundamental role in host defenses against viruses, but to date, their role has been relatively unsettled in the context of SARS-CoV-2. We report here a longitudinal single-cell and repertoire profiling of the B cell response up to 6 months in mild and severe COVID-19 patients. Distinct SARS-CoV-2 spike-specific activated B cell clones fueled an early antibody-secreting cell burst as well as a durable synchronous germinal center response. While highly mutated memory B cells, including pre-existing cross-reactive seasonal Betacoronavirus-specific clones, were recruited early in the response, neutralizing SARS-CoV-2 RBD-specific clones accumulated with time and largely contributed to the late, remarkably stable, memory B cell pool. Highlighting germinal center maturation, these cells displayed clear accumulation of somatic mutations in their variable region genes over time. Overall, these findings demonstrate that an antigen-driven activation persisted and matured up to 6 months after SARS-CoV-2 infection and may provide long-term protection.

## Clinical Syndrome

5. **Clinical characteristics and risk factors for the isolation of multidrug-resistant Gram-negative bacteria from critically ill patients with Coronavirus Disease 2019.** Baiou A, Elbuzidi AA, Bakdach D, et al. *J Hosp Infect.* 2021 Feb 6:S0195-6701(21)00047-5. doi:

10.1016/j.jhin.2021.01.027. [https://www.journalofhospitalinfection.com/article/S0195-6701\(21\)00047-5/fulltext](https://www.journalofhospitalinfection.com/article/S0195-6701(21)00047-5/fulltext)

Findings: We retrospectively matched (1:2) critical COVID-19 patients with one or more MDR GNB from any clinical specimen (cases), with those with no MDR GNB isolates (controls). Seventy-eight cases were identified (4.5 per 1,000 ICU days). Out of 98 MDR GNB isolates, the most frequent species were *Stenotrophomonas maltophilia* (24, 24.5%), and *Klebsiella pneumoniae* (23, 23.5%). Two (8.7%) *K. pneumoniae*, and six (85.7%) *Pseudomonas aeruginosa* isolates were carbapenem resistant. A total of 24 (24.5%) isolates were not considered to be associated with active infection. Those with active infection received appropriate antimicrobial agent within a median of one day. The case group had significantly longer median central venous line days, mechanical ventilation days, and hospital length of stay. All-cause mortality at 28 days was not significantly different between the two groups. Mechanical ventilation days, but not receipt of corticosteroids or tocilizumab, was independently associated with the isolation of MDR GNB. There was no association between MDR GNB and 28-day all-cause mortality (aOR 2.426, 95% CI 0.833 to 7.069; P = 0.104). In critically ill COVID-19 patients, prevention of MDR GNB colonization and infections requires minimising the use of invasive devices, and to remove them as soon as their presence is no longer necessary.

6. **Static compliance of the respiratory system in COVID-19 related ARDS: an international multicenter study.** COVADIS study group. *Crit Care.* 2021 Feb 8;25(1):52. doi: 10.1186/s13054-020-03433-0. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7868865/>

Findings: In this observational multicenter cohort of patients with moderate to severe Covid-19 ARDS, Crs was measured at day-1 and day-14. The mean Crs in 372 patients was  $37.6 \pm 13$  mL/cmH<sub>2</sub>O, similar to as in ARDS of other causes. Multivariate linear regression identified chronic hypertension, low PaO<sub>2</sub>/FiO<sub>2</sub> ratio, low PEEP, and low tidal volume as associated with lower Crs/IBW. After adjustment on confounders, nor Crs [OR 1.0 (CI 95% 0.98-1.02)] neither Crs/IBW [OR 0.63 (CI 95% 0.13-3.1)] were associated with the chance of breathing without assistance at day-28 whereas plateau pressure was [OR 0.93 (CI 95% 0.88-0.99)]. In a subset of 108 patients, day-14 Crs decreased compared to day-1 Crs ( $31.2 \pm 14.4$  mL/cmH<sub>2</sub>O vs  $37.8 \pm 11.4$  mL/cmH<sub>2</sub>O, p < 0.001). The decrease in Crs was not associated with day-28 outcome. In a large multicenter cohort of moderate to severe COVID-19 ARDS, mean Crs was decreased below 40 mL/cmH<sub>2</sub>O and was not associated with day-28 outcome. Crs decreased between day-1 and day-14 but the decrease was not associated with day-28 outcome.

7. **Comparing Clinical Features and Outcomes in Mechanically Ventilated Patients with COVID-19 and the Acute Respiratory Distress Syndrome.** Sjoding MW, Admon AJ, Saha AK, et al. *Ann Am Thorac Soc.* 2021 Feb 12. doi: 10.1513/AnnalsATS.202008-1076OC. <https://www.atsjournals.org/doi/10.1513/AnnalsATS.202008-1076OC>

Findings: We performed a retrospective cohort study, comparing 130 consecutive mechanically ventilated patients with severe COVID-19 with 382 consecutive mechanically ventilated patients with non-COVID-19 ARDS. Comparison of patients with COVID-19 and non-COVID-19 ARDS suggested small differences in respiratory compliance, ventilatory efficiency, and oxygenation. 28-day mortality was 30% in COVID-19 patients and 38% in non-COVID ARDS. In this single center cohort, we found no evidence for large differences between COVID-19 and non-COVID ARDS. Many key clinical features of severe COVID-19 were similar to those of non-COVID-19 ARDS, including respiratory physiology and clinical outcomes, although our sample size precludes definitive conclusions. Further studies are needed to define COVID-19-specific pathophysiology before deviation from evidence-based treatment practices can be recommended.

8. **Thrombotic complications in 2928 patients with COVID-19 treated in intensive care: a systematic review.** Jenner WJ, Kanji R, Mirsadraee S, et al. *J Thromb Thrombolysis*. 2021 Feb 14. doi: 10.1007/s11239-021-02394-7. <https://link.springer.com/article/10.1007/s11239-021-02394-7>

Findings: In 28 studies including 2928 patients, thrombotic complications occurred in 34% of ICU-managed patients, with deep venous thrombosis reported in 16.1% and pulmonary embolism in 12.6% of patients, despite anticoagulant thromboprophylaxis, and were associated with high mortality. Studies adopting systematic screening for venous thrombosis with Duplex ultrasound reported a significantly higher incidence of venous thrombosis compared to those relying on clinical suspicion (56.3% vs. 11.0%,  $p < 0.001$ ). Despite thromboprophylaxis, there is a very high incidence of thrombotic complications in patients with COVID-19 on the ICU. Systematic screening identifies many thrombotic complications that would be missed by relying on clinical suspicion and should be employed, with consideration given to increased dose anticoagulant thromboprophylaxis, whilst awaiting results of prospective trials of anticoagulation in this cohort.

9. **Assessment of the SpO<sub>2</sub>/FiO<sub>2</sub> ratio as a tool for hypoxemia screening in the emergency department.** Catoire P, Tellier E, de la Rivière C, et al. *Am J Emerg Med*. 2021 Feb 6;44:116-120. doi: 10.1016/j.ajem.2021.01.092.

<https://www.sciencedirect.com/science/article/pii/S0735675721001030?via%3Dihub>

Findings: During the study period from February to April 2020, a total of 430 arterial samples were analyzed and collected from 395 patients. The SpO<sub>2</sub>/FiO<sub>2</sub> ratio may be a reliable tool for hypoxemia screening among patients admitted to the ED, particularly during the SARS-CoV-2 outbreak.

## Diagnosics & Screening

10. **Comparison of nasopharyngeal and saliva swabs for the detection of RNA SARS-CoV-2 during mass screening (SALICOV study).** Castelain S, François C, Demey B, et al. *New Microbiol*. 2021 Feb 14;44(1). [http://www.newmicrobiologica.org/PUB/allegati\\_pdf/AOP/496N202.pdf](http://www.newmicrobiologica.org/PUB/allegati_pdf/AOP/496N202.pdf)

Findings: In the context of a second wave of SARS-CoV-2 transmission, the use of saliva sampling has become an issue of real importance. SARS-CoV-2 RNA screening was performed on nasopharyngeal and saliva swabs collected from 501 individuals from residential homes for the elderly. The saliva samples were collected at the same time as the nasopharyngeal samples. Nasopharyngeal samples yielded positive results for 26 individuals, only two of whom also tested positive with saliva swabs. In this context, saliva collected by swabbing the fluid is not an ideal sample.

**11. Simpler and faster Covid-19 testing: Strategies to streamline SARS-CoV-2 molecular assays.**

Panpradist N, Wang Q, Ruth PS, et al. *EBioMedicine*. 2021 Feb 11;64:103236. doi: 10.1016/j.ebiom.2021.103236.

<https://www.sciencedirect.com/science/article/pii/S2352396421000293>

Findings: Detection of SARS-CoV-2 infections is important for treatment, isolation of infected and exposed individuals, and contact tracing. RT-qPCR is the "gold-standard" method to sensitively detect SARS-CoV-2 RNA, but most laboratory-developed RT-qPCR assays involve complex steps. Here, we aimed to simplify RT-qPCR assays by streamlining reaction setup, eliminating RNA extraction, and proposing reduced-cost detection workflows that avoid the need for expensive qPCR instruments. A low-cost RT-PCR based "kit" was developed for faster turnaround than the CDC developed protocol. We demonstrated three detection workflows: two that can be deployed in laboratories conducting assays of variable complexity, and one that could be simple enough for point-of-care. Analytical sensitivity was assessed using SARS-CoV-2 RNA spiked in simulated nasal matrix. Clinical performance was evaluated using contrived human nasal matrix (n = 41) and clinical nasal specimens collected from individuals with respiratory symptoms (n = 110). The analytical sensitivity of the lyophilised RT-PCR was 10 copies/reaction using purified SARS-CoV-2 RNA, and 20 copies/reaction when using direct lysate in simulated nasal matrix. Evaluation of assay performance on contrived human matrix showed 96.7-100% specificity and 100% sensitivity at  $\geq 20$  RNA copies. A head-to-head comparison with the standard CDC protocol on clinical specimens showed 83.8-94.6% sensitivity and 96.8-100% specificity. We found 3.6% indeterminate samples (undetected human control), lower than 8.1% with the standard protocol. This preliminary work should support laboratories or commercial entities to develop and expand access to Covid-19 testing. Software guidance development for this assay is ongoing to enable implementation in other settings.

**12. Prevalence and impact factors of recurrent positive SARS-CoV-2 detection in 599 hospitalized COVID-19 patients.** Gao C, Zhu L, Jin CC, et al. *Clin Microbiol Infect*. 2021 Feb 8:S1198-743X(21)00055-0. doi: 10.1016/j.cmi.2021.01.028.

doi: 10.1016/j.cmi.2021.01.028.

[https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(21\)00055-0/pdf](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00055-0/pdf)

Findings: Among 599 enrolled COVID-19 patients, the median time for viral RNA shedding was 24 days (IQR, 19-33 days). The positive rate of RT-PCR was 35.9% (215/599), 17.0% (65/383) and 12.4% (23/185) after one, two and three consecutive negative RT-PCR test results respectively. Medians of CT-values of initial positive test, rebound positive after two consecutive negative results, and rebound positive after three consecutive negative results were 28.8, 32.8 and 36.1 respectively. Compare with male patients, females had a significant

higher rate of recurrent positive RT-PCR after three consecutive negative results (18.2%, 18/99 vs. 5.8%, 5/86,  $p=0.013$ ). Older age ( $\geq 55$  yrs) had a significant higher rate of recurrent positive RT-PCR after one negative result (42.3%, 165/390, vs. 23.9%, 50/209,  $p<0.001$ ). Nasopharyngeal swab tests produced a higher positive rate than oropharyngeal swab tests (37.3%, 152/408 vs. 35.8%, 1111/3105). Our study revealed the prevalence and dynamic characteristics of recurrent positive RT-PCR to SARS-CoV-2. We showed that around 17.0% (65/383) patients were tested positive for SARS-CoV-2 after two consecutive negative results. Patients with rebound positive RT-PCR test had a low viral load. Older age and female were risk factors for recurrent positive results.

13. **Age- and Sex-Associated Variations in the Sensitivity of Serological Tests Among Individuals Infected With SARS-CoV-2.** Vashisht R, Patel A, Crews BO, et al. *JAMA Netw Open*. 2021 Feb 1;4(2):e210337. doi: 10.1001/jamanetworkopen.2021.0337.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776300>

Findings: The findings of this cohort study suggest that measuring serological levels too soon after SARS-CoV-2 infection might lead to an incorrect assessment of immune response. The sensitivity of antibody testing was higher in males and patients aged 40 to 59 years, but our subset cohort sizes are small. If these findings are validated, then accounting for differences in sex and age in interpreting serological levels may be warranted. Antibody test sensitivity was stable at 112 days and beyond after a known positive RT-PCR result, suggesting a detectable antibody response long after infection.

14. **Comparison of Severe Acute Respiratory Syndrome Coronavirus 2 Screening Using Reverse Transcriptase-Quantitative Polymerase Chain Reaction or CRISPR-Based Assays in Asymptomatic College Students.** Rauch JN, Valois E, Ponce-Rojas JC, et al. *JAMA Netw Open*. 2021 Feb 1;4(2):e2037129. doi: 10.1001/jamanetworkopen.2020.37129.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776173>

Findings: For this cohort study, a total of 1808 asymptomatic participants were screened for SARS-CoV-2 using a CRISPR-based assay and a point-of-reference reverse transcriptase-quantitative polymerase chain reaction (RT-qPCR) test. Among the 1808 participants (mean [SD] age, 27.3 [11.0] years; 955 [52.8%] female), 732 underwent testing from May to early June (mean [SD] age, 28.4 [11.7] years; 392 [53.6%] female). All test results in this cohort were negative. In contrast, 1076 participants underwent testing from late June to early July (mean [SD] age, 26.6 [10.5] years; 563 [52.3%] female), with 9 positive results by RT-qPCR. Eight of these positive samples were detected by the CRISPR-based assay and confirmed by Clinical Laboratory Improvement Amendments-certified diagnostic testing. These findings reveal a shift in SARS-CoV-2 prevalence in a young and asymptomatic population and uncover the leading edge of a local outbreak that coincided with rising case counts in the surrounding county and the state of California. The concordance between CRISPR-based and RT-qPCR testing suggests that CRISPR-based assays are reliable and offer alternative options for surveillance testing and detection of SARS-CoV-2 outbreaks, as is required to resume operations in higher-education institutions in the US and abroad.

15. **Quantifying asymptomatic infection and transmission of COVID-19 in New York City using observed cases, serology, and testing capacity.** Subramanian R, He Q, Pascual M. *Proc Natl Acad Sci U S A*. 2021 Mar 2;118(9):e2019716118. doi: 10.1073/pnas.2019716118. <https://www.pnas.org/content/118/9/e2019716118>

Findings: Using a model that incorporates daily testing information fit to the case and serology data from New York City, we show that the proportion of symptomatic cases is low, ranging from 13 to 18%, and that the reproductive number may be larger than often assumed. Asymptomatic infections contribute substantially to herd immunity, and to community transmission together with presymptomatic ones. If asymptomatic infections transmit at similar rates as symptomatic ones, the overall reproductive number across all classes is larger than often assumed, with estimates ranging from 3.2 to 4.4. If they transmit poorly, then symptomatic cases have a larger reproductive number ranging from 3.9 to 8.1. Even in this regime, presymptomatic and asymptomatic cases together comprise at least 50% of the force of infection at the outbreak peak. We find no regimes in which all infection subpopulations have reproductive numbers lower than three. These findings elucidate the uncertainty that current case and serology data cannot resolve, despite consideration of different model structures. They also emphasize how temporal data on testing can reduce and better define this uncertainty, as we move forward through longer surveillance and second epidemic waves. Regardless, current assumptions about the basic reproductive number of SARS-CoV-2 should be reconsidered.

16. **Increased hazard of death in community-tested cases of SARS-CoV-2 Variant of Concern 202012/01.** Davies NG, Jarvis CI, Edmunds WJ, Jewell NP, Diaz-Ordaz K, Keogh RH. *medRxiv PREPRINT*. 2021 Feb 3:2021.02.01.21250959. doi: 10.1101/2021.02.01.21250959. <https://www.medrxiv.org/content/10.1101/2021.02.01.21250959v1>

Findings: VOC 202012/01, a SARS-CoV-2 variant first detected in the United Kingdom in September 2020, has spread to multiple countries worldwide. Several studies have established that this novel variant is more transmissible than preexisting variants of SARS-CoV-2, but have not identified whether the new variant leads to any change in disease severity. We analyse a large database of SARS-CoV-2 community test results and COVID-19 deaths for England, representing approximately 47% of all SARS-CoV-2 community tests and 7% of COVID-19 deaths in England from 1 September 2020 to 22 January 2021. Fortunately, these SARS-CoV-2 tests can identify VOC 202012/01 because mutations in this lineage prevent PCR amplification of the spike gene target (S gene target failure, SGTF). We estimate that the hazard of death among SGTF cases is 30% (95% CI 9-56%) higher than among non-SGTF cases after adjustment for age, sex, ethnicity, deprivation level, care home residence, local authority of residence and date of test. In absolute terms, this increased hazard of death corresponds to the risk of death for a male aged 55-69 increasing from 0.56% to 0.73% (95% CI 0.60-0.86%) over the 28 days following a positive SARS-CoV-2 test in the community. Correcting for misclassification of SGTF, we estimate a 35% (12-64%) higher hazard of death associated with VOC 202012/01. Our analysis suggests that VOC 202012/01 is not only more transmissible than preexisting SARS-CoV-2 variants but may also cause more severe illness.

17. **Public policy and health in the Trump era.** Woolhandler S et al. *Lancet* 2021 Feb 10.

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This report by the Lancet Commission on Public Policy and Health in the Trump Era assesses the repercussions of President Donald Trump's health-related policies and examines the failures and social schisms that enabled his election. Trump exploited low and middle-income white people's anger over their deteriorating life prospects to mobilise racial animus and xenophobia and enlist their support for policies that benefit high-income people and corporations and threaten health. His signature legislative achievement, a trillion-dollar tax cut for corporations and high-income individuals, opened a budget hole that he used to justify cutting food subsidies and health care. His appeals to racism, nativism, and religious bigotry have emboldened white nationalists and vigilantes, and encouraged police violence and, at the end of his term in office, insurrection. He chose judges for US courts who are dismissive of affirmative action and reproductive, labour, civil, and voting rights; ordered the mass detention of immigrants in hazardous conditions; and promulgated regulations that reduce access to abortion and contraception in the USA and globally. Although his effort to repeal the Affordable Care Act failed, he weakened its coverage and increased the number of uninsured people by 2.3 million, even before the mass dislocation of the COVID-19 pandemic, and has accelerated the privatisation of government health programmes. Trump's hostility to environmental regulations has already worsened pollution—resulting in more than 22 000 extra deaths in 2019 alone—hastened global warming, and despoiled national monuments and lands sacred to Native people. Disdain for science and cuts to global health programmes and public health agencies have impeded the response to the COVID-19 pandemic, causing tens of thousands of unnecessary deaths, and imperil advances against HIV and other diseases. And Trump's bellicose trade, defence, and foreign policies have led to economic disruption and threaten an upswing in armed conflict.

18. **Emergence of a Novel SARS-CoV-2 Variant in Southern California.** Zhang W, Davis BD, Chen SS, et al. *JAMA*. 2021 Feb 11. doi: 10.1001/jama.2021.1612.

<https://jamanetwork.com/journals/jama/fullarticle/2776543>

Findings: A spike in coronavirus disease 2019 (COVID-19) has occurred in Southern California since October 2020. Analysis of the severe acute respiratory syndrome coronavirus (SARS-CoV-2) in Southern California prior to October indicated most isolates originated from clade 20C that likely emerged from New York via Europe early in the pandemic.<sup>1</sup> Since then, novel variants of SARS-CoV-2 including those seen in the UK (20I/501Y.V1/B.1.1.7), South Africa (20H/501Y.V2/B.1.351), and Brazil (P.1/20J/501Y.V3/B.1.1.248) have emerged with the concern of increased infectivity and virulence.<sup>2,3</sup> Thus, we analyzed variants of SARS-CoV-2 in Southern California to establish whether one of these known strains or a novel variant had emerged.

### Healthcare Delivery & Healthcare Workers

19. **Rapid decline of neutralizing antibodies against SARS-CoV-2 among infected healthcare workers.** Sorbonne Université SARS-CoV-2 Neutralizing Antibodies Study Group. *Nat Commun*.

2021 Feb 8;12(1):844. doi: 10.1038/s41467-021-21111-9.

<https://www.nature.com/articles/s41467-021-21111-9>

Findings: We followed 26 HCW with mild COVID-19 three weeks (D21), two months (M2) and three months (M3) after the onset of symptoms. All the HCW had anti-receptor binding domain (RBD) IgA at D21, decreasing to 38.5% at M3 ( $p < 0.0001$ ). Concomitantly a significant decrease in NAb titers was observed between D21 and M2 ( $p = 0.03$ ) and between D21 and M3 ( $p < 0.0001$ ). Here, we report that SARS-CoV-2 can elicit a NAb response correlated with anti-RBD antibody levels. However, this neutralizing activity declines, and may even be lost, in association with a decrease in systemic IgA antibody levels, from two months after disease onset. This short-lasting humoral protection supports strong recommendations to maintain infection prevention and control measures in HCW, and suggests that periodic boosts of SARS-CoV-2 vaccination may be required.

20. **Occupational Risk Factors for SARS-CoV-2 Infection among Healthcare Personnel: A Cross-Sectional Analysis of Subjects Enrolled in the COPE Study.** Howard-Anderson J, Adams C, Sherman AC, et al. *Infect Control Hosp Epidemiol.* 2021 Feb 9:1-20. doi: 10.1017/ice.2021.54. <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/occupational-risk-factors-for-sarscov2-infection-among-healthcare-personnel-a-crosssectional-analysis-of-subjects-enrolled-in-the-cope-study/CE69F4CE5EC7817E4AAFEC444009C27>

Findings: Among 353 healthcare personnel in a longitudinal cohort in four hospitals in Atlanta, GA (May-June 2020), 23 (6.5%) had SARS-CoV-2 antibodies. Spending  $>50\%$  of a typical shift at bedside (OR 3.4, 95% CI: 1.2-10.5) and Black race (OR 8.4, 95% CI: 2.7-27.4) were associated with SARS-CoV-2 seropositivity.

21. **Seroprevalence of antibodies to SARS-CoV-2 in healthcare workers: a cross-sectional study.**

Ebinger JE, Botwin GJ, Albert CM, et al. *BMJ Open.* 2021 Feb 12;11(2):e043584. doi: 10.1136/bmjopen-2020-043584. <https://bmjopen.bmj.com/content/11/2/e043584>

Findings: A diverse and unselected population of adults ( $n=6062$ ) employed in a multisite healthcare delivery system located in Los Angeles County, including individuals with direct patient contact and others with non-patient-oriented work functions. We estimated seroprevalence and factors associated with seropositivity and antibody levels, including pre-existing demographic and clinical characteristics; potential COVID-19 illness-related exposures; and symptoms consistent with COVID-19 infection. We observed a seroprevalence rate of 4.1%, with anosmia as the most prominently associated self-reported symptom (OR 11.04,  $p < 0.001$ ) in addition to fever (OR 2.02,  $p = 0.002$ ) and myalgias (OR 1.65,  $p = 0.035$ ). After adjusting for potential confounders, seroprevalence was also associated with Hispanic ethnicity (OR 1.98,  $p = 0.001$ ) and African-American race (OR 2.02,  $p = 0.027$ ) as well as contact with a COVID-19-diagnosed individual in the household (OR 5.73,  $p < 0.001$ ) or clinical work setting (OR 1.76,  $p = 0.002$ ). Importantly, African-American race and Hispanic ethnicity were associated with antibody positivity even after adjusting for personal COVID-19 diagnosis status, suggesting the contribution of unmeasured structural or societal factors. The demographic factors associated with SARS-CoV-2 seroprevalence among our healthcare workers underscore the importance of exposure sources beyond the workplace. The size and diversity of our study population,

combined with robust survey and modelling techniques, provide a vibrant picture of the demographic factors, exposures and symptoms that can identify individuals with susceptibility as well as potential to mount an immune response to COVID-19.

### Laboratory Results

22. **Emergence in late 2020 of multiple lineages of SARS-CoV-2 Spike protein variants affecting amino acid position 677.** Hodcroft EB, Domman DB, Oguntuyo K, et al. *medRxiv PREPRINT*. Feb 14, 2021. <https://doi.org/10.1101/2021.02.12.21251658>  
Findings: Seven variants of the COVID-19 virus have been detected in the U.S., and all or some of them may contain mutations similar to the qualities exhibited by a strain of extra-contagious COVID-19 spreading in the United Kingdom.
24. **Differences of blood cells, lymphocyte subsets and cytokines in COVID-19 patients with different clinical stages: a network meta-analysis.** Yan W, Chen D, Bigambo FM, et al. *BMC Infect Dis*. 2021 Feb 8;21(1):156. doi: 10.1186/s12879-021-05847-9. <https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-05847-9>  
Findings: Seventy-one studies were included involving 8647 COVID-19 patients, White blood cell (WBC), neutrophil (NEUT), IL-6, and IL-10 counts increased significantly with worsening of the COVID-19, while lymphocyte (LYM) counts decreased. The levels of platelet (PLT), CD3+, CD4+, CD8+, and CD19+ cells in severe and critical patients were significantly lower than those in mild patients. IL-1 $\beta$  count was significantly elevated in critical patients. Immune suppression and inflammatory injury play crucial roles in the progression of COVID-19, and the identification of susceptible cells and cytokines provide guidance for the early and accurate treatment of COVID-19 patients.

### Prognosis

25. **Association of  $\alpha$ 1-Blocker Receipt With 30-Day Mortality and Risk of Intensive Care Unit Admission among Adults Hospitalized with Influenza or Pneumonia in Denmark.** Thomsen RW, Christiansen CF, Heide-Jørgensen U, et al. *JAMA Netw Open*. 2021 Feb 1;4(2):e2037053. doi: 10.1001/jamanetworkopen.2020.37053. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776101>  
Findings: A total of 528 467 adult patients (median age, 75.0 years; interquartile range, 64.4-83.6 years; 273 005 men [51.7%]) were hospitalized with influenza or pneumonia in Denmark between 2005 and 2018. Of those, 21 772 patients (4.1%) were currently receiving  $\alpha$ 1-blockers compared with a population of 22 117 patients not receiving  $\alpha$ 1-blockers who were weighted to the propensity score distribution of those receiving  $\alpha$ 1-blockers. In the propensity score-weighted analyses, patients receiving  $\alpha$ 1-blockers had lower 30-day mortality (15.9%) compared with patients not receiving  $\alpha$ 1-blockers (18.5%), with a corresponding risk difference of -2.7% (95% CI, -3.2% to -2.2%) and a risk ratio (RR) of 0.85 (95% CI, 0.83-0.88). The risk of ICU admission was 7.3% among patients receiving  $\alpha$ 1-blockers and 7.7% among those not receiving  $\alpha$ 1-blockers (risk difference, -0.4% [95% CI, -0.8% to 0%]; RR, 0.95 [95% CI, 0.90-1.00]). A comparison between 18 280 male patients currently receiving  $\alpha$ 1-blockers and 18 228

propensity score-weighted male patients currently receiving 5 $\alpha$ -reductase inhibitors indicated that those receiving  $\alpha$ 1-blockers had lower 30-day mortality and a similar risk of ICU admission. This cohort study's findings suggest that the receipt of  $\alpha$ 1-blockers is associated with protective benefits among adult patients hospitalized with influenza or pneumonia.

26. **ABO blood group and COVID-19: a review on behalf of the ISBT COVID-19 working group.** ISBT COVID-19 Working Group. *Vox Sang.* 2021 Feb 12. doi: 10.1111/vox.13076.

<https://onlinelibrary.wiley.com/doi/10.1111/vox.13076>

Findings: The level of evidence supporting an association between ABO type and SARS-CoV-2/COVID-19 ranges from small observational studies, to genome-wide-association-analyses and country-level meta-regression analyses. ABO blood group antigens are oligosaccharides expressed on red cells and other tissues (notably endothelium). There are several hypotheses to explain the differences in SARS-CoV-2 infection by ABO type. For example, anti-A and/or anti-B antibodies (e.g. present in group O individuals) could bind to corresponding antigens on the viral envelope and contribute to viral neutralization, thereby preventing target cell infection. The SARS-CoV-2 virus and SARS-CoV spike (S) proteins may be bound by anti-A isoagglutinins (e.g. present in group O and group B individuals), which may block interactions between virus and angiotensin-converting-enzyme-2-receptor, thereby preventing entry into lung epithelial cells. ABO type-associated variations in angiotensin-converting enzyme-1 activity and levels of von Willebrand factor (VWF) and factor VIII could also influence adverse outcomes, notably in group A individuals who express high VWF levels. In conclusion, group O may be associated with a lower risk of SARS-CoV-2 infection and group A may be associated with a higher risk of SARS-CoV-2 infection along with severe disease. However, prospective and mechanistic studies are needed to verify several of the proposed associations. Based on the strength of available studies, there are insufficient data for guiding policy in this regard.

27. **Association of mortality and aspirin prescription for COVID-19 patients at the Veterans Health Administration.** Osborne TF, Veigulis ZP, Arreola DM, et al. *PLoS One.* 2021 Feb 11;16(2):e0246825. doi: 10.1371/journal.pone.0246825. eCollection 2021.

<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246825>

Findings: This retrospective assessment was designed to quantify the correlation between pre-diagnosis aspirin and mortality for COVID-19 positive patients in our care. Data from the Veterans Health Administration national electronic health record database was utilized for the evaluation. Veterans from across the country with a first positive COVID-19 polymerase chain reaction lab result were included in the evaluation which comprised 35,370 patients from March 2, 2020 to September 13, 2020 for the 14-day mortality cohort and 32,836 patients from March 2, 2020 to August 28, 2020 for the 30-day mortality cohort. Patients were matched via propensity scores and the odds of mortality were then compared. Among COVID-19 positive Veterans, preexisting aspirin prescription was associated with a statistically and clinically significant decrease in overall mortality at 14-days (OR 0.38, 95% CI 0.32-0.46) and at 30-days (OR 0.38, 95% CI 0.33-0.45), cutting the odds of mortality by more than half. Findings demonstrated that pre-diagnosis aspirin prescription was strongly associated with decreased mortality rates for Veterans diagnosed with COVID-19. Prospective evaluation is required to more completely assess this correlation and its implications for patient care.

## Survivorship & Rehabilitation

- 28. COVID-19: patient characteristics in the first phase of post-intensive care rehabilitation.** Wiertz CMH, Vints WAJ, Maas GJCM, et al. *Arch Rehabil Res Clin Transl.* 2021 Feb 4:100108. doi: 10.1016/j.arrct.2021.100108. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7859717/>  
Findings: Sixty patients participated with the mean age of 59.9 and the majority being men(75%). Most important findings for rehabilitation: in the first week after discharge to the rehabilitation centre 38.3% of all patients experienced exercise-induced oxygen desaturation, in 72.7% muscle weakness was present in all major muscle groups and 21.7% had a reduced mobility in one or both shoulders. Furthermore 40% suffered from dysphagia and 39.2% reported symptoms of anxiety. Post-ICU COVID-19 patients, display physical and anxiety symptoms as reported in other post-ICU patient groups. However this study showed some remarkable clinical characteristics of post-ICU COVID-19 patients. Rehabilitation programs need to anticipate on this. Long-term follow-up studies are necessary.
- 29. Establishing a Peer Support Program for Survivors of COVID-19: A Report From the Critical and Acute Illness Recovery Organization.** Hope AA, Johnson AA, McPeake J, et al. *Am J Crit Care.* 2021 Feb 15:e1-e5. doi: 10.4037/ajcc2021675. <https://aacnjournals.org/ajconline/article/doi/10.4037/ajcc2021675/31287/Establishing-a-Peer-Support-Program-for-Survivors>  
Findings: Peer support is a complex intervention that allows COVID-19 survivors to give and receive practical and emotional support in relationship with other survivors of acute illness. The growing expertise within CAIRO can be leveraged by stakeholders interested in starting and sustaining a peer support program for COVID-19 survivors.
- 30. Lasting antibody and T cell responses to SARS-CoV-2 in COVID-19 patients three months after infection.** Jiang XL, Wang GL, Zhao XN, et al. *Nat Commun.* 2021 Feb 9;12(1):897. doi: 10.1038/s41467-021-21155-x. <https://www.nature.com/articles/s41467-021-21155-x>  
Findings: Here, we longitudinally measured virus-neutralising antibody, specific antibodies against the spike (S) protein, receptor-binding domain (RBD), and the nucleoprotein (N) of SARS-CoV-2, as well as T cell responses, in 25 SARS-CoV-2-infected patients up to 121 days post-symptom onset (PSO). All patients seroconvert for IgG against N, S, or RBD, as well as IgM against RBD, and produce neutralising antibodies (NAb) by 14 days PSO, with the peak levels attained by 15-30 days PSO. Anti-SARS-CoV-2 IgG and NAb remain detectable and relatively stable 3-4 months PSO, whereas IgM antibody rapidly decay. Approximately 65% of patients have detectable SARS-CoV-2-specific CD4+ or CD8+ T cell responses 3-4 months PSO. Our results thus provide critical evidence that IgG, NAb, and T cell responses persist in the majority of patients for at least 3-4 months after infection.
- 31. Cardiovascular sequelae in uncomplicated COVID-19 survivors.** Zhou M, Wong CK, Un KC, et al. *PLoS One.* 2021 Feb 11;16(2):e0246732. doi: 10.1371/journal.pone.0246732. eCollection 2021. <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0246732>

Findings: We performed a systematic cardiac screening for 97 consecutive COVID-19 survivors including electrocardiogram (ECG), echocardiography, serum troponin and NT-proBNP assay 1-4 weeks after hospital discharge. The mean age was  $46.5 \pm 18.6$  years; 53.6% were men. Cardiac abnormality is common amongst COVID-survivors with mild disease, which is mostly self-limiting. Nonetheless, cardiac surveillance in form of ECG and/or serum biomarkers may be advisable to detect more severe cardiac involvement including atrial fibrillation and left ventricular dysfunction.

## Therapeutics

32. **Major Update: Remdesivir for Adults with COVID-19: A Living Systematic Review and Meta-analysis for the American College of Physicians Practice Points.** Kaka AS, MacDonald R, Greer N, et al. *Ann Intern Med.* 2021 Feb 9. doi: 10.7326/M20-8148.

<https://www.acpjournals.org/doi/10.7326/M20-8148>

Findings: The update includes 5 RCTs, incorporating data from a new large RCT and the final results of a previous RCT. Compared with control, a 10-day course of remdesivir probably results in little to no reduction in mortality (risk ratio [RR], 0.93 [95% CI, 0.82 to 1.06]; 4 RCTs) but may result in a small reduction in the proportion of patients receiving mechanical ventilation (RR, 0.71 [CI, 0.56 to 0.90]; 3 RCTs). In hospitalized adults with COVID-19, remdesivir probably results in little to no mortality difference but probably improves the percentage recovered and reduces serious harms and may result in a small reduction in the proportion receiving ventilation. For patients not receiving ventilation, a 5-day course may provide greater benefits and fewer harms with lower drug costs than a 10-day course.

33. **Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study.** Rentsch CT, Beckman JA, Tomlinson L, Gellad WF, et al. *BMJ.* 2021 Feb 11;372:n311. doi: 10.1136/bmj.n311.

<https://www.bmj.com/content/372/bmj.n311>

Findings: Of 4297 patients admitted to hospital with covid-19, 3627 (84.4%) received prophylactic anticoagulation within 24 hours of admission. More than 99% (n=3600) of treated patients received subcutaneous heparin or enoxaparin. 622 deaths occurred within 30 days of hospital admission, 513 among those who received prophylactic anticoagulation. Most deaths (510/622, 82%) occurred during hospital stay. Early initiation of prophylactic anticoagulation compared with no anticoagulation among patients admitted to hospital with covid-19 was associated with a decreased risk of 30 day mortality and no increased risk of serious bleeding events. These findings provide strong real world evidence to support guidelines recommending the use of prophylactic anticoagulation as initial treatment for patients with covid-19 on hospital admission.

34. **Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial.** Horby PW, Campbell M, Staplin N, et al. *medRxiv PREPRINT* 2021.02.11.21249258; doi:

<https://doi.org/10.1101/2021.02.11.21249258>

Findings: Between 23 April 2020 and 25 January 2021, 4116 adults were included in the assessment of tocilizumab, including 562 (14%) patients receiving invasive mechanical ventilation, 1686 (41%) receiving non-invasive respiratory support, and 1868 (45%) receiving no respiratory support other than oxygen. Median CRP was 143 [IQR 107-205] mg/L and 3385 (82%) patients were receiving systemic corticosteroids at randomisation. Overall, 596 (29%) of the 2022 patients allocated tocilizumab and 694 (33%) of the 2094 patients allocated to usual care died within 28 days (rate ratio 0.86; 95% confidence interval [CI] 0.77-0.96;  $p=0.007$ ). Consistent results were seen in all pre-specified subgroups of patients, including those receiving systemic corticosteroids. Patients allocated to tocilizumab were more likely to be discharged from hospital alive within 28 days (54% vs. 47%; rate ratio 1.23; 95% CI 1.12-1.34;  $p<0.0001$ ). Among those not receiving invasive mechanical ventilation at baseline, patients allocated tocilizumab were less likely to reach the composite endpoint of invasive mechanical ventilation or death (33% vs. 38%; risk ratio 0.85; 95% CI 0.78-0.93;  $p=0.0005$ ). Interpretation: In hospitalised COVID-19 patients with hypoxia and systemic inflammation, tocilizumab improved survival and other clinical outcomes regardless of the level of respiratory support received and in addition to the use of systemic corticosteroids.

35. **Systematic review and meta-analysis of anakinra, sarilumab, siltuximab and tocilizumab for COVID-19.** Khan FA, Stewart I, Fabbri L, et al. *Thorax*. 2021 Feb 12:thoraxjnl-2020-215266. doi: 10.1136/thoraxjnl-2020-215266. <https://thorax.bmj.com/content/early/2021/02/11/thoraxjnl-2020-215266>

Findings: 71 studies totalling 22 058 patients were included, 6 were randomised trials. Most studies explored outcomes in patients who received tocilizumab (60/71). In prospective studies, tocilizumab was associated with improved unadjusted survival (risk ratio 0.83, 95% CI 0.72 to 0.96,  $I^2=0.0\%$ ), but conclusive benefit was not demonstrated for other outcomes. In retrospective studies, tocilizumab was associated with less severe outcomes on an Ordinal Scale (generalised OR 1.34, 95% CI 1.10 to 1.64,  $I^2=98\%$ ) and adjusted mortality risk (HR 0.52, 95% CI 0.41 to 0.66,  $I^2=76.6\%$ ). The mean difference in duration of hospitalisation was 0.36 days (95% CI -0.07 to 0.80,  $I^2=93.8\%$ ). There was substantial heterogeneity in retrospective studies, and estimates should be interpreted cautiously. Other immunomodulatory agents showed similar effects to tocilizumab, but insufficient data precluded meta-analysis by agent. Tocilizumab was associated with a lower relative risk of mortality in prospective studies, but effects were inconclusive for other outcomes. Current evidence for the efficacy of anakinra, siltuximab or sarilumab in COVID-19 is insufficient, with further studies urgently needed for conclusive findings.

36. **Early Lopinavir/ritonavir does not reduce mortality in COVID-19 patients: results of a large multicenter study.** SEMI-COVID-19 Network. *J Infect*. 2021 Feb 11:S0163-4453(21)00077-3. doi: 10.1016/j.jinf.2021.02.011. [https://www.journalofinfection.com/article/S0163-4453\(21\)00077-3/fulltext](https://www.journalofinfection.com/article/S0163-4453(21)00077-3/fulltext)

Findings: This is the largest study assessing the efficacy of LPV/r against SARS-CoV-2. The overall use of LPV/r was not associated with lower mortality in COVID-19 patients. The early use of LPV/r (median 5 days) showed no benefit either.

- 37. Clinical and laboratory evaluation of patients with SARS-CoV-2 pneumonia treated with high-titer convalescent plasma.** Donato ML, Park S, Baker M, et al. *JCI Insight*. 2021 Feb 11:143196. doi: 10.1172/jci.insight.143196. <https://insight.jci.org/articles/view/143196/pdf>  
Findings: We are reporting on a phase IIa study which aimed to determine the intubation rate, survival, viral clearance, and the development of endogenous antibodies in patients with COVID-19 pneumonia treated with convalescent plasma (CCP) containing high levels of neutralizing anti-SARS-CoV-2 antibodies. All 51 treated patients had COVID-19 pneumonia by radiographic and laboratory evaluation. Fresh or frozen CCP from donors with high titers of neutralizing antibodies was administered. The non-mechanically ventilated patients (n=36) had an intubation rate of 13.9% and a day-30 survival of 88.9%. The overall survival for a comparative group based on network data was 72.5% (1625/2241). Patients had rates of negative nasopharyngeal swab on day +10 and +30 of 43.8% and 73% respectively. Patients mechanically ventilated had a day-30 mortality of 46.7%; the mortality for a comparative group based on network data was 71% (369/520). All evaluable patients were found to have neutralizing antibodies on day +3 (n=47), and all but 1 had antibodies on day +30 and +60. The only adverse event was a mild rash. We are concluding that in this study of patients with COVID-19 pneumonia, CCP was safe and conferred transfer of antibodies while preserving endogenous immune response.
- 38. Assessment of Outpatient Dispensing of Products Proposed for Treatment or Prevention of COVID-19 by US Retail Pharmacies During the Pandemic.** Geller AI, Lovegrove MC, Lind JN, Datta SD, Budnitz DS. *JAMA Intern Med*. 2021 Feb 11. doi: 10.1001/jamainternmed.2021.0299. <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2776456>  
Findings: Single peaks in hydroxychloroquine, chloroquine, and lopinavir-ritonavir dispensing in March to April, 2020, coincided with increases in cases, and did not recur as evidence of lack of efficacy in treating or preventing COVID-19 accumulated. Although the National Institutes of Health COVID-19 Treatment Guidelines Panel has not recommended outpatient use of ivermectin, zinc, or dexamethasone for treatment or prevention of COVID-19, increased dispensing of each of these products has coincided with a national increase in COVID-19 cases beginning in July 2020 and another national increase in the fall which continued into December 2020.
- 39. Oral corticoid, aspirin, anticoagulant, colchicine, and furosemide to improve the outcome of hospitalized COVID-19 patients - the COCAA-COLA cohort study.** Kevorkian JP, Lopes A, Sène D, et al. *J Infect*. 2021 Feb 9:S0163-4453(21)00058-X. doi: 10.1016/j.jinf.2021.02.008. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7871882/>  
Findings: Corticosteroids mitigate 28-day all-cause mortality in coronavirus disease-2019 (COVID-19) patients requiring oxygen or mechanical ventilation (meta-analysis summary odds ratio (OR), 0.66; 95%-confidence interval (95%CI), [0.53–0.82]; P < 0.001); however, mortality remains high (32.7%). In a previous observational cohort study, we established that an early 4-day treatment combining corticosteroid (prednisolone dose equivalent, 1.25 mg/kg/24 h) and furosemide (80 mg/day) was effective in reducing the need for mechanical ventilation and overall mortality (OR, 0.35 [0.11–1.01]; P = 0.04) in non-critically ill COVID-19 patients.

40. **Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction among Ambulatory Patients with SARS-CoV-2 Infection: The COVID A to Z Randomized Clinical Trial.** Thomas S, Patel D, Bittel B, et al. *JAMA Netw Open*. 2021 Feb 1;4(2):e210369. doi: 10.1001/jamanetworkopen.2021.0369.  
<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776305>  
Findings: A total of 214 patients were randomized, with a mean (SD) age of 45.2 (14.6) years and 132 (61.7%) women. The study was stopped for a low conditional power for benefit with no significant difference among the 4 groups for the primary end point. In this randomized clinical trial of ambulatory patients diagnosed with SARS-CoV-2 infection, treatment with high-dose zinc gluconate, ascorbic acid, or a combination of the 2 supplements did not significantly decrease the duration of symptoms compared with standard of care.
41. **A Phase II Safety and Efficacy Study on Prognosis of Moderate Pneumonia in COVID-19 patients with Regular Intravenous Immunoglobulin Therapy.** R S R, Barge VB, Darivenula AK, et al. *J Infect Dis*. 2021 Feb 15:jiab098. doi: 10.1093/infdis/jiab098.  
<https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab098/6135116>  
Findings: An open-label, multicenter, comparative, randomized study was conducted on COVID-19 patients with moderate pneumonia. 100 eligible patients were randomized in 1:1 ratio either to receive IVIG + standard of care (SOC) or SOC. Duration of hospital stay was significantly shorter in IVIG group to that of SOC alone (7.7 Vs. 17.5 days). Duration for normalization of body temperature, oxygen saturation and mechanical ventilation were significantly shorter in IVIG compared to SOC. Percentages of patients on mechanical ventilation in two groups were not significantly different (24% Vs. 38%). Median time to RT-PCR negativity was significantly shorter with IVIG than SOC (7 Vs.18 days). There were only mild to moderate adverse events in both groups except for one patient (2%), who died in SOC. IVIG was safe and efficacious as an adjuvant with other antiviral drugs in the treatment of COVID-19.
42. **Safety and efficacy of convalescent plasma in elderly COVID-19 patients: the RESCUE trial.** Franchini M, Glingani C, Morandi M, et al. *Mayo Clin Proc Innov Qual Outcomes*. 2021 Feb 8. doi: 10.1016/j.mayocpiqo.2021.01.010.  
<https://www.sciencedirect.com/science/article/pii/S2542454821000291?via%3Dihub>  
Findings: Twenty-two consecutive elderly COVID-19 patients living in a LTCF in Lombardy who were given CP during the period May 15-July 31, 2020 were enrolled in a prospective cohort study. Of the 22 patients enrolled, 68.2% (n=15) received one CP unit, 27.3% (n=6) received two units and 4.5% (n=1) received three units. Of the CP units transfused, 76.7% (23/30) had a neutralizing antibody titer  $\geq 1:160$ . No adverse reactions were recorded during or after CP administration. Improvements of clinical, functional, radiological and laboratory parameters during the 14 days following CP transfusion were observed in all 19 patients who survived. Viral clearance was achieved in all patients by the end of follow-up (median 66 days, IQR 48-80 days). The overall mortality rate was 13.6% (3/22), which compared favorably with that in the control group (38.3%, 281/733, P=0.02) and corresponded to a 65% reduction of mortality risk. Early administration of CP with an adequate anti-SARS-CoV-2 antibody-titer to elderly, symptomatic, COVID-19 patients in a LTCF was safe and effective in eliminating the virus,

restoring patients' immunity and blocking the progression of COVID-19, thereby improving patients' survival.

43. **Use of Helmet CPAP in COVID-19 - A practical review.** Amirfarzan H, Cereda M, Gaulton TG, et al. *Pulmonology*. 2021 Feb 1:S2531-0437(21)00040-4. doi: 10.1016/j.pulmoe.2021.01.008. <https://www.sciencedirect.com/science/article/pii/S2531043721000404?via%3Dihub>  
Helmet CPAP (H-CPAP) has been recommended in many guidelines as a noninvasive respiratory support during COVID-19 pandemic in many countries around the world. It has the least amount of particle dispersion and air contamination among all noninvasive devices and may mitigate the ICU bed shortage during a COVID surge as well as a decreased need for intubation/mechanical ventilation. It can be attached to many oxygen delivery sources. The MaxVenturi setup is preferred as it allows for natural humidification, low noise burden, and easy transition to HFNC during breaks and it is the recommended transport set-up. The patients can safely be prone with the helmet. It can also be used to wean the patients from invasive mechanical ventilation. Our article reviews in depth the pathophysiology of COVID-19 ARDS, provides rationale of using H-CPAP, suggests a respiratory failure algorithm, guides through its setup and discusses the issues and concerns around using it.

#### **Transmission / Infection Control**

44. **SARS-CoV-2 setting-specific transmission rates: a systematic review and meta-analysis.** Thompson HA, Mousa A, Dighe A, et al. *Clin Infect Dis*. 2021 Feb 9:ciab100. doi: 10.1093/cid/ciab100. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab100/6131730>  
Findings: Households showed the highest transmission rates, with a pooled SAR of 21.1%. SARs were significantly higher where the duration of household exposure exceeded 5 days compared with exposure of  $\leq 5$  days. SARs related to contacts at social events with family and friends were higher than those for low-risk casual contacts (5.9% vs. 1.2%). Estimates of SAR and Robs for asymptomatic index cases were approximately a seventh, and for pre-symptomatic two thirds of those for symptomatic index cases. We found some evidence for reduced transmission potential both from and to individuals under 20 years of age in the household context, which is more limited when examining all settings. Our results suggest that exposure in settings with familiar contacts increases SARS-CoV-2 transmission potential. Additionally, the differences observed in transmissibility by index case symptom status and duration of exposure have important implications for control strategies such as contact tracing, testing and rapid isolation of cases. There was limited data to explore transmission patterns in workplaces, schools, and care-homes, highlighting the need for further research in such settings.
45. **Hydrogen Peroxide Vapor Decontamination of N95 Respirators for Reuse.** Kenney PA, Chan BK, Kortright KE, et al. *Infect Control Hosp Epidemiol*. 2021 Feb 9:1-14. doi: 10.1017/ice.2021.48. <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/hydrogen-peroxide-vapor-decontamination-of-n95-respirators-for-reuse/7DC12335D07A9FD0407259B4ED2E007E>

Findings: Bioquell VHP demonstrated high viricidal activity for N95 respirators inoculated with aerosolized bacteriophages. Bioquell technology can be scaled for simultaneous decontamination of a large number of used but otherwise intact respirators. Reprocessing should be limited to 3 cycles due to concerns both about impact of clinical wear and tear on fit, and to decrement in filtration after 3 cycles.

**46. Surgical Mask Covering of N95 Filtering Facepiece Respirators: The Risk of Increased Leakage.**

Mueller JT, Karimi S, Poterack KA, Seville MTA, Tipton SM. *Infect Control Hosp Epidemiol*. 2021 Feb 9:1-6. doi: 10.1017/ice.2021.50. <https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/surgical-mask-covering-of-n95-filtering-facepiece-respirators-the-risk-of-increased-leakage/2B5591D489CEEE97A9AB734B652674C4>

Findings: This report demonstrates the potential risk of increased face-to-mask seal leakage when N95 filtering facepiece respirators (N95 FFR) are covered by surgical, cloth, or medical masks, (collectively referred to as surgical masks), through analytical modeling of the associated fluid mechanics and seal pressures. Previously published experimental studies of respirator pressures and leakage are applicable to this problem. Properly utilized N95 FFRs will remain an essential component of healthcare worker safety for the foreseeable future, especially for those engaged in aerosol-generating procedures (AGPs) such as endotracheal intubation. When considering leakage risk, it is important to understand the general challenges to ensuring an adequate mask-to-face seal. The fit and seal degrade with repeated donning and doffing, and some N95 FFR reprocessing or recycling techniques have been reported to accelerate this degradation. In short, the N95 mask-to-face seal is fragile and can be compromised by a number of factors.

**47. Maximizing Fit for Cloth and Medical Procedure Masks to Improve Performance and Reduce SARS-CoV-2 Transmission and Exposure, 2021.** Brooks JT, Beezhold DH, Noti JD, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 10 February 2021.

[https://www.cdc.gov/mmwr/volumes/70/wr/mm7007e1.htm?s\\_cid=mm7007e1\\_x](https://www.cdc.gov/mmwr/volumes/70/wr/mm7007e1.htm?s_cid=mm7007e1_x)

Findings: CDC conducted experiments to assess two ways of improving the fit of medical procedure masks: fitting a cloth mask over a medical procedure mask, and knotting the ear loops of a medical procedure mask and then tucking in and flattening the extra material close to the face. Each modification substantially improved source control and reduced wearer exposure. These experiments highlight the importance of good fit to maximize mask performance. There are multiple simple ways to achieve better fit of masks to more effectively slow the spread of COVID-19.

**48. Why coronavirus survives longer on impermeable than porous surfaces.** Chatterjee S, Murallidharan JS, Agrawala A, Bhardwaja R. *Physics of Fluids* 33, 021701 (2021);

<https://doi.org/10.1063/5.0037924> <https://aip.scitation.org/doi/10.1063/5.0037924>

Findings: Previous studies reported that the drying time of a respiratory droplet on an impermeable surface along with a residual film left on it is correlated with the coronavirus survival time. Notably, earlier virus titer measurements revealed that the survival time is surprisingly less on porous surfaces such as paper and cloth than that on impermeable surfaces. Previous studies could not capture this distinct aspect of the porous media. We demonstrate

how the mass loss of a respiratory droplet and the evaporation mechanism of a thin liquid film are modified for the porous media, which leads to a faster decay of the coronavirus on such media. While diffusion-limited evaporation governs the mass loss from the bulk droplet for the impermeable surface, a much faster capillary imbibition process dominates the mass loss for the porous material. After the bulk droplet vanishes, a thin liquid film remaining on the exposed solid area serves as a medium for the virus survival. However, the thin film evaporates much faster on porous surfaces than on impermeable surfaces. The aforesaid faster film evaporation is attributed to droplet spreading due to the capillary action between the contact line and fibers present on the porous surface and the modified effective wetted area due to the voids of porous materials, which leads to an enhanced disjoining pressure within the film, thereby accelerating the film evaporation. Therefore, the porous materials are less susceptible to virus survival. The findings have been compared with the previous virus titer measurements.

49. **Severe reinfection with South African SARS-CoV-2 variant 501Y.V2: A case report.** Zucman N, Uhel F, Descamps D, et al. *Clin Infect Dis.* 2021 Feb 10:ciab129. doi: 10.1093/cid/ciab129. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab129/6132402>  
We here report a case of severe SARS-CoV-2 reinfection with South African variant 501Y.V2, four months after recovering from a first episode of COVID-19. In September 2020, a 58-year old immunocompetent male with a history of asthma presented with mild fever and dyspnea. SARSCoV-2 infection was diagnosed by real-time RT-PCR on a nasopharyngeal swab. Symptoms resolved within a few days and the patient tested negative twice in December 2020. In January 2021, 129 days after onset of the first infection, he presented to hospital for recurrent dyspnea and fever. SARS-CoV-2 RT-PCR was positive again, and viral genome sequencing identified D80A, E484K and N501Y mutations in the spike region, characterizing the 501Y.V2 lineage B.1.351 variant. Seven days later, the patient developed a severe acute respiratory distress syndrome requiring intubation and mechanical ventilation. He was treated with dexamethasone and tocilizumab. Antibody testing was positive for IgG against SARS-CoV-2. The patient was negative for HIV, and showed no biological evidence for immunological disorder. He is still in critical condition at the time of submission. The strain responsible for the first episode of COVID-19 was not available for sequencing. However, the occurrence of the primary infection one month before emergence of the 501Y.V2 strain in South Africa and three months before its first description in France rules out the hypothesis of a persistent viral shedding from the first infection.
50. **Decontamination of skin from SARS-CoV-2 with disinfectants active during and after application.** Campos RK, Mirchandani D, Rafael G, et al. *J Hosp Infect.* 2021 Feb 9:S0195-6701(21)00050-5. doi: 10.1016/j.jhin.2021.02.004. <https://www.sciencedirect.com/science/article/pii/S0195670121000505>  
Findings: Two disinfectants, BIAKÖS™ Antimicrobial Skin & Wound Cleanser (AWC) and AWC2 (Sanara MedTech, Fort Worth, TX, USA) were tested to determine whether they can inactivate SARS-CoV-2 upon contact or as a coating applied before contact with the virus. AWC and AWC2 were effective in reducing SARS-CoV-2 infectious titers in both liquid form during the application, and in dried form, 4 h after the application. Virus on skin was reduced up to 2

log<sub>10</sub>-fold and 3.5 log<sub>10</sub>-fold after treatment with AWC or AWC2, respectively. Application of AWC and AWC2 to skin reduces SARS-CoV-2 levels and the risk of infection.

51. **Transmission of SARS-CoV-2 among healthcare workers and patients in a teaching hospital in the Netherlands confirmed by whole genome sequencing.** Paltansing S, Sikkema RS, Man SJ, et al. *J Hosp Infect.* 2021 Feb 8:S0195-6701(21)00051-7. doi: 10.1016/j.jhin.2021.02.005. [https://www.journalofhospitalinfection.com/article/S0195-6701\(21\)00051-7/pdf](https://www.journalofhospitalinfection.com/article/S0195-6701(21)00051-7/pdf)  
Findings: We investigated the sources of infection among healthcare workers (HCWs) and patients in a teaching hospital during the early stages of the COVID-19 pandemic with epidemiological and whole genome sequencing data. From 3rd April to 11th May 2020 88 HCWs and 215 patients were diagnosed with SARS-CoV-2 infection. Whole genome sequences were obtained for 30 HCWs and 20 patients. We found 7 sequence types in HCW and 11 in patients. Sequence Cluster A was the most predominant sequence type detected in 23 (77%) HCW, of whom 14 (74%) had direct patient contact and 9 (90%) with indirect patient contact. In addition, seven patients outside of the COVID-19 cohort isolation ward who became positive during their admission were infected with SARS-CoV-2 cluster A. Following universal masking of all HCWs and emphasis on physical distancing during meals and breaks, no further evidence was found for patient to HCW or HCW-to-HCW transmission or vice versa. The identification of genomic cluster A in patients and HCWs infected with SARS-CoV-2 by whole genome sequencing suggests transmission between HCWs, but also from HCWs to patients.

## Vaccine

52. **COVID-19 Vaccination Intent, Perceptions, and Reasons for Not Vaccinating Among Groups Prioritized for Early Vaccination — United States, September and December 2020.** Nguyen KH, Srivastav A, Razzaghi H, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 9 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7006e3>  
[https://www.cdc.gov/mmwr/volumes/70/wr/mm7006e3.htm?s\\_cid=mm7006e3\\_x](https://www.cdc.gov/mmwr/volumes/70/wr/mm7006e3.htm?s_cid=mm7006e3_x)  
Findings: From September to December 2020, intent to receive COVID-19 vaccination increased from 39.4% to 49.1% among adults and across all priority groups, and nonintent decreased from 38.1% to 32.1%. Despite decreases in nonintent from September to December, younger adults, women, non-Hispanic Black adults, adults living in nonmetropolitan areas, and adults with less education and income, and without health insurance continue to have the highest estimates of nonintent to receive COVID-19 vaccination. Ensuring high and equitable vaccination coverage among all populations, including by addressing reasons for not intending to receive vaccination, is critical to prevent the spread of COVID-19 and bring an end to the pandemic.
53. **Poor antigen-specific responses to the second BNT162b2 mRNA vaccine dose in SARS-CoV-2-experienced individuals.** Samanovic MI, Cornelius AR, Wilson JP, et al. *medRxiv PREPRINT.* Feb 9, 2021 doi: <https://doi.org/10.1101/2021.02.07.21251311>  
Findings: COVID-19 vaccine candidates have demonstrated robust humoral responses and have protected against infection. However, efficacy trials were focused on individuals with no prior exposure to SARS-CoV-2, and, as a result, little is known about immune responses induced by

these mRNA vaccines in individuals who recovered from COVID-19. Here, we evaluated immune responses in 32 subjects who received two-dose BNT162b2 mRNA vaccination. In individuals naive to SARS-CoV-2, we observed robust increases in humoral and antigen-specific antibody-secreting cell (ASC) responses following each dose of vaccine, whereas individuals with prior exposure to SARS-CoV-2 demonstrated strong humoral and antigen-specific ASC responses to the first dose but muted responses to the second dose of the vaccine for the time points studied. These data highlight an important gap in our knowledge and may have major implications for how these vaccines should be used to prevent COVID-19.

54. **mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants.** Wang Z, Schmidt F, Weisblum Y, et al. *Nature*. 2021 Feb 10. doi: 10.1038/s41586-021-03324-6.

<https://www.nature.com/articles/s41586-021-03324-6>

Findings: Here we report on the antibody and memory B cell responses in a cohort of 20 volunteers who received either the Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines<sup>1-4</sup>. Eight weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-SARS-CoV-2 spike protein (S) and receptor binding domain (RBD) binding titers. Moreover, the plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells were equivalent to individuals who recovered from natural infection<sup>5,6</sup>. However, activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin. Vaccine-elicited monoclonal antibodies (mAbs) potently neutralize SARS-CoV-2, targeting a number of different RBD epitopes in common with mAbs isolated from infected donors<sup>5-8</sup>. However, neutralization by 14 of the 17 most potent mAbs tested was reduced or abolished by either K417N, or E484K, or N501Y mutations. Notably, the same mutations were selected when recombinant vesicular stomatitis virus (rVSV)/SARS-CoV-2 S was cultured in the presence of the vaccine elicited mAbs. Taken together the results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated periodically to avoid potential loss of clinical efficacy.

55. **Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021.** Abu Jabal K, Ben-Amram H, Beiruti K, et al. *Euro Surveill*. 2021 Feb;26(6). doi: 10.2807/1560-7917.ES.2021.26.6.2100096.

<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.6.2100096>

Findings: The BNT162b2 mRNA COVID-19 vaccine showed high efficacy in clinical trials but observational data from populations not included in trials are needed. We describe immunogenicity 21 days post-dose 1 among 514 Israeli healthcare workers by age, ethnicity, sex and prior COVID-19 infection. Immunogenicity was similar by ethnicity and sex but decreased with age. Those with prior infection had antibody titres one magnitude order higher than naïve individuals regardless of the presence of detectable IgG antibodies pre-vaccination.

56. **Reports of Anaphylaxis after Receipt of mRNA COVID-19 Vaccines in the US-December 14, 2020-January 18, 2021.** Shimabukuro TT, Cole M, Su JR. *JAMA*. 2021 Feb 12. doi:

10.1001/jama.2021.1967. <https://jamanetwork.com/journals/jama/fullarticle/2776557>

Findings: The initial estimated reporting rates for anaphylaxis in the US were 11.1 cases per million doses administered of the Pfizer-BioNTech vaccine (December 14-23, 2020) and 2.5 cases per million doses administered of the Moderna vaccine (December 21, 2020-January 10, 2021). Since these early estimates were generated, millions more doses of both vaccines have been administered and safety monitoring has detected additional cases of anaphylaxis. This analysis updates the reporting rates of anaphylaxis in individuals following receipt of either the Pfizer-BioNTech or Moderna vaccine.

**57. COVID-19/SARS-CoV-2 virus spike protein-related delayed inflammatory reaction to hyaluronic acid dermal fillers: a challenging clinical conundrum in diagnosis and treatment.**

Munavalli GG, Guthridge R, Knutsen-Larson S, et al. Arch Dermatol Res. 2021 Feb 9:1-15. doi: 10.1007/s00403-021-02190-6. <https://link.springer.com/article/10.1007/s00403-021-02190-6>

We present the first reported cases of delayed inflammatory reactions (DIR) to hyaluronic acid (HA) dermal fillers after exposure to the COVID-19 spike protein. DIR to HA is reported to occur in the different scenarios including: secondary to poor injection technique, following dental cleaning procedures, following bacterial/viral illness, and after vaccination. In this report of 4 cases with distinct clinical histories and presentations: one case occurred following a community acquired COVID-19 infection, one case occurred in a study subject in the mRNA-1273 clinical phase III trial, one case occurred following the first dose of publically available mRNA-1273 vaccine (Moderna, Cambridge MA), and the last case occurred after the second dose of BNT162b2 vaccine (Pfizer, New York, NY). Injectable HA dermal fillers are prevalent in aesthetic medicine for facial rejuvenation. Structural modifications in the crosslinking of HA fillers have enhanced the products' resistance to enzymatic breakdown and thus increased injected product longevity, however, have also led to a rise in DIR. Previous, DIR to HA dermal fillers can present clinically as edema with symptomatic and inflammatory erythematous papules and nodules. The mechanism of action for the delayed reaction to HA fillers is unknown and is likely to be multifactorial in nature. A potential mechanism of DIR to HA fillers in COVID-19 related cases is binding and blockade of angiotensin 2 converting enzyme receptors (ACE2), which are targeted by the SARS-CoV-2 virus spike protein to gain entry into the cell. Spike protein interaction with dermal ACE2 receptors favors a pro-inflammatory, loco-regional TH1 cascade, promoting a CD8+T cell mediated reaction to incipient granulomas, which previously formed around residual HA particles. Management to suppress the inflammatory response in the native COVID-19 case required high-dose corticosteroids (CS) to suppress inflammatory pathways, with concurrent ACE2 upregulation, along with high-dose intralesional hyaluronidase to dissolve the inciting HA filler. With regards to the two vaccine related cases; in the mRNA-1273 case, a low dose angiotensin converting enzyme inhibitor (ACE-I) was utilized for treatment, to reduce pro-inflammatory Angiotensin II. Whereas, in the BNT162b2 case the filler reaction was suppressed with oral corticosteroids. Regarding final disposition of the cases; the vaccine-related cases returned to baseline appearance within 3 days, whereas the native COVID-19 case continued to have migratory, evanescent, periorbital edema for weeks which ultimately subsided.

**Women & Children**

**58. Disease Severity and Perinatal Outcomes of Pregnant Patients with Coronavirus Disease 2019 (COVID-19).** Metz TD, Clifton RG, Hughes BL, et al. *Obstet Gynecol.* 2021 Feb 8. doi: 10.1097/AOG.0000000000004339.

[https://journals.lww.com/greenjournal/Fulltext/9900/Disease\\_Severity\\_and\\_Perinatal\\_Outcomes\\_of.121.aspx?Ppt=Article%7Cgreenjournal:9900:00000:00121%7C10.1097/aog.0000000000004339%7C](https://journals.lww.com/greenjournal/Fulltext/9900/Disease_Severity_and_Perinatal_Outcomes_of.121.aspx?Ppt=Article%7Cgreenjournal:9900:00000:00121%7C10.1097/aog.0000000000004339%7C)

Findings: A total of 1,219 patients were included: 47% asymptomatic, 27% mild, 14% moderate, 8% severe, 4% critical. Overall, 53% were Hispanic; there was no trend in race-ethnicity distribution by disease severity. Those with more severe illness had older mean age, higher median body mass index, and pre-existing medical comorbidities. Four maternal deaths (0.3%) were attributed to COVID-19. Frequency of perinatal death or a positive neonatal SARS-CoV-2 test result did not differ by severity. Adverse perinatal outcomes were more frequent among patients with more severe illness, including 6% (95% CI 2-11%) incidence of venous thromboembolism among those with severe-critical illness compared with 0.2% in mild-moderate and 0% in asymptomatic ( $P < .001$  for trend across severity). In adjusted analyses, severe-critical COVID-19 was associated with increased risk of cesarean birth (59.6% vs 34.0%, adjusted relative risk [aRR] 1.57, 95% CI 1.30-1.90), hypertensive disorders of pregnancy (40.4% vs 18.8%, aRR 1.61, 95% CI 1.18-2.20), and preterm birth (41.8% vs 11.9%, aRR 3.53, 95% CI 2.42-5.14) compared with asymptomatic patients. Mild-moderate COVID-19 was not associated with adverse perinatal outcomes compared with asymptomatic patients. Compared with pregnant patients with SARS-CoV-2 infection without symptoms, those with severe-critical COVID-19, but not those with mild-moderate COVID-19, were at increased risk of perinatal complications.

**59. Maternal and perinatal outcomes related to COVID-19 and pregnancy: overview of systematic reviews.** Vergara-Merino L, Meza N, Couve-Pérez C, et al. *Acta Obstet Gynecol Scand.* 2021 Feb 9. doi: 10.1111/aogs.14118. <https://obgyn.onlinelibrary.wiley.com/doi/10.1111/aogs.14118>

Findings: 52 systematic reviews met inclusion criteria and were included in this overview. Only one review had a low risk of bias, three had an unclear risk of bias, and 48 had a high risk of bias. Most of the included reviews were highly overlapped among each other. In the included reviews, rates of maternal death varied from 0% to 11.1%, admission to intensive care from 2.1% to 28.5%, preterm deliveries before 37 weeks from 14.3% to 61.2%, and cesarean delivery from 48.3% to 100%. Regarding neonatal outcomes, neonatal death varied from 0% to 11.7% while the estimated infection status of the newborn varied between 0% and 11.5%. Only one of 52 systematic reviews had a low risk of bias. Results were heterogenous and the overlap of primary studies was frequently very high between pairs of systematic reviews. High quality evidence syntheses of comparative studies are needed to guide future clinical decisions.

**60. Pulmonary sequelae of pediatric patients after discharge for COVID-19: An observational study.** Zhang C, Huang L, Tang X, Zhang Y, Zhou X. *Pediatr Pulmonol.* 2021 Feb 9. doi: 10.1002/ppul.25239. <https://onlinelibrary.wiley.com/doi/10.1002/ppul.25239>

Findings: Radiological findings indicated that pulmonary sequelae occurred in a significant percentage (7/14, 50%) of patients, 30.1 (27.5–33.3) days post-discharge, although no statistically significant difference was observed in dyspnea grades between patients with and

without sequelae. The percentage was similar to that (47%) observed in adults with pulmonary sequelae, 21 days post-discharge. Fibrosis was reported in 9% (14/149) of patients at the 21-day follow-up and in 44% (14/32) of patients at the 9-day follow-up. In our study fibrosis occurred in four (4/14, 29%) patients. The disparities in patient characteristics (e.g., age and general health condition), as well as different follow-up periods across various studies, may have contributed to the differences in pulmonary sequelae observed between pediatric and adult patients. Notably, fibrosis was detected in pediatric patients, approximately 30 days post-discharge. Fibrous stripes were detected at sites other than the original lesion in some patients, which indicates the progressive nature of lesions, even after discharge. Therefore, pulmonary function monitoring is important in pediatric patients with pulmonary fibrosis.

**61. Remestemcel-L Therapy for COVID-19-Associated Multisystem Inflammatory Syndrome in**

**Children.** Ross Eckard A, Borow KM, Mack EH, Burke E, Atz AM. *Pediatrics*. 2021 Feb 12:e2020046573. doi: 10.1542/peds.2020-046573.

<https://pediatrics.aappublications.org/content/pediatrics/early/2021/02/11/peds.2020-046573.full.pdf>

Findings: Remestemcel-L, an investigational mesenchymal stromal cell therapy, is a promising candidate for treatment of MIS-C due to its beneficial anti-inflammatory, immunomodulatory, endothelial function, and vascular stabilizing effects which align well with the pathophysiology of MIS-C. Here, we present the first two patients with life-threatening MIS-C ever treated with remestemcel-L under an expanded access program. Both were previously healthy children without any indication of prior COVID-19 infection or exposure. They presented with severe clinical illness including myocardial dysfunction, hemodynamic instability, hypotension, acute kidney injury, and shock. At the time of hospital admission, both had negative PCR tests and positive serology for SARS-CoV-2. Both children received standard of care MIS-C treatment. Although they showed some clinical improvement, left ventricular ejection fraction remained reduced and inflammatory biomarkers significantly elevated. When treated with two intravenous doses of remestemcel-L separated by 48 hours, rapid normalization of left ventricular ejection fraction, notable reductions in biomarkers of systemic and cardiac inflammation, and improved clinical status occurred. Neither child experienced adverse effects associated with remestemcel-L administration. This treatment appears promising as a novel immunomodulatory cellular therapy for children with clinically-significant cardiovascular manifestations of MIS-C.

**62. Effect of the new SARS-CoV-2 variant B.1.1.7 on children and young people.** Brookman S, Cook

J, Zucherman M, et al. *Lancet Child Adolesc Health*. 2021 Feb 10:S2352-4642(21)00030-4. doi: 10.1016/S2352-4642(21)00030-4.

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(21\)00030-4/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00030-4/fulltext)

Findings: Between March 1, and May 31, 2020, 20 children and young people (aged 18 years or younger and positive for SARS-CoV-2) were admitted to King's College Hospital. Between Nov 1, 2020, and Jan 19, 2021, 60 children and young people positive for SARS-CoV-2 were admitted. No significant differences were found in age, proportion of patients with comorbidities, proportion of patients from Black, Asian, and minority ethnicity background, or deprivation score between groups. Disease severity necessitating oxygen therapy or ventilatory support

was infrequent in both waves and was lower as a proportion of total admission in the second wave than in the first.

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## GUIDELINES & CONSENSUS STATEMENTS

[ACC Health Policy Statement on Cardiovascular Disease Considerations for COVID-19 Vaccine Prioritization](#). Driggin E, Morris AA, Maddox TM, et al. *J Am Coll Cardiol*. 2021 Feb 9:S0735-1097(21)00386-7. doi: 10.1016/j.jacc.2021.02.017.

[Should Remdesivir Be Used for the Treatment of Patients With COVID-19? Rapid, Living Practice Points From the American College of Physicians \(Version 2\)](#). Qaseem A, Yost J, Etzeandia-Ikobaltzeta I, et al. *Ann Intern Med*. 2021 Feb 9. doi: 10.7326/M20-8101.

[American Society of Hematology 2021 guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19](#). Cuker A, Tseng EK, Nieuwlaat R, et al. *Blood Adv*. 2021 Feb 9;5(3):872-888. doi: 10.1182/bloodadvances.2020003763.

[EASL position paper on the use of COVID-19 vaccines in patients with chronic liver diseases, hepatobiliary cancer and liver transplant recipients](#). Cornberg M, Buti M, Eberhardt CS, Grossi PA, Shouval D. *J Hepatol*. 2021 Feb 6:S0168-8278(21)00081-7. doi: 10.1016/j.jhep.2021.01.032.

[AASLD Expert Panel Consensus Statement: Vaccines to Prevent COVID-19 Infection in Patients with Liver Disease](#). AASLD COVID-19 Vaccine Working Group. *Hepatology*. 2021 Feb 12. doi: 10.1002/hep.31751.

[European Task Force on Atopic Dermatitis \(ETFAD\): position on vaccination of adult patients with atopic dermatitis against COVID-19 \(SARS-CoV-2\) being treated with systemic medication and biologics](#). Thyssen JP, Vestergaard C, Barbarot S, et al. *J Eur Acad Dermatol Venereol*. 2021 Feb 15. doi: 10.1111/jdv.17167.

[COVID-19 convalescent plasma: interim recommendations from the AABB](#). Cohn CS, Estcourt L, Grossman BJ, et al. *Transfusion*. 2021 Feb 14. doi: 10.1111/trf.16328.

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## FDA / CDC / NIH / WHO Updates

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

CDC - [When to Quarantine: Stay home if you might have been exposed to COVID-19](#)

[CDC - Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2021.](#)

[FDA - Coronavirus \(COVID-19\) Update: FDA Authorizes Monoclonal Antibodies for Treatment of COVID-19](#)

[FDA - Using Ventilator Splitters During the COVID-19 Pandemic - Letter to Health Care Providers](#)

[WHO lists two additional COVID-19 vaccines for emergency use and COVAX roll-out AstraZeneca/Oxford-developed vaccines to reach countries in the coming weeks](#)

[WHO - Interim recommendations for use of the AZD1222 \(ChAdOx1-S \[recombinant\]\) vaccine against COVID-19 developed by Oxford University and AstraZeneca. 2-10-21](#)

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## **Commentary**

[Pfizer-BioNTech vaccine sharply reduces symptomatic Covid-19 in the real world, Israeli researchers say](#)

[KFF COVID-19 Vaccine Monitor: In Their Own Words](#)

[Health in the USA: under examination and under repair](#)

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